ORIGINAL RESEARCH

Ideal Cardiovascular Health and Cognitive Aging in the Northern Manhattan Study

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***Background*—**The American Heart Association defined target levels for 7 cardiovascular health (CVH) factors: smoking, body mass index, physical activity, diet, blood pressure, cholesterol, and glucose. We hypothesized that a greater number of American Heart Association ideal CVH metrics would be associated with less decline in cognitive performance in our multiethnic population.

***Methods and Results*—**A subsample from the population-based Northern Manhattan Study underwent repeated neuropsychological testing (mean interval 6±2 years). Domain-specific *Z* scores were derived by using factor analysis for the domains of Episodic Memory, Semantic Memory, Executive Function, and Processing Speed, based on initial performance and decline over time. Linear regression models were constructed to examine the relationship between the number of ideal CVH metrics at enrollment with later cognitive performance and decline, adjusting for sociodemographics and magnetic resonance imaging brain markers. Among 1033 participants (mean age at initial cognitive assessment 72±8 years, 39% male, 19% black, 16% white, 65% Hispanic; n=722 with repeat testing), 3% had 0 ideal factors, 15% had 1 factor, 33% had 2 factors, 30% had 3 factors, 14% had 4 factors, 4% had 5 factors, 1% had 6 factors, and 0% had 7 factors. An increasing number of ideal CVH factors was associated with better processing speed at initial assessment and less decline. The association was driven by nonsmoking and glucose. Among those with better cognitive performance at initial assessment, positive associations were observed between the number of ideal CVH factors and less decline in the domains of Executive Function and Episodic Memory.

***Conclusions*—**The number of ideal CVH metrics was associated with less decline in the domains of Processing Speed and, to a lesser extent, of Executive Function and Episodic Memory. Ideal CVH promotion benefits brain health and cognitive aging. **(*J Am Heart Assoc*. 2016;5:e002731 doi: 10.1161/JAHA.115.002731)**

Key Words: blood pressure • epidemiology • glucose • risk factors • smoking

The 2020 Strategic Impact Goal introduced by the American Heart Association (AHA) in 2010 includes the improvement of the cardiovascular health (CVH) of all Americans by 20%. To measure progress, the AHA defined ideal CVH across 7 established modifiable risk factors for cardiovascular diseases and created targets by defining ideal levels for each risk factor. These 7 health factors, responsible for a substantial portion of cardiovascular disease morbidity and mortality, were smoking, body mass index (BMI), physical activity, diet, blood pressure, total cholesterol, and fasting glucose. By moving more Americans into ideal CVH categories for these 7 risk factors, the AHA hopes to achieve its goal of reducing deaths from cardiovascular disease and stroke by 20% by 2020.[1]

Previous publications highlight the strong relationship between the number of ideal CVH factors and incidence of stroke, myocardial infarction, and vascular death.[2,3] Moreover, advancing the ideal CVH of all Americans will likely have measurable health benefits beyond heart disease and stroke. In particular, these vascular risk factors may also alter cognitive aging, as vascular and metabolic mechanisms are believed to underlie the etiology of cognitive impairment and decline in a large percentage of those with neurocognitive disorders. Previous studies have shown associations of smoking, obesity, physical inactivity, poor diet, elevated blood pressure, lipid levels, and blood glucose, individually and in various combinations, with cognitive deficits,[4–12] but less is

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known about how these ideal CVH metrics, individually and measured together as a composite score, relate to the various domains of cognitive performance and decline.

The Institute of Medicine recently published a report covering their assessment of the current literature on cognitive aging, in particular the epidemiological literature on preventive strategies.[13] The authors outlined steps for reducing the risk of cognitive decline, including engagement in physical activity and the management of cardiovascular disease risk factors (eg, hypertension, diabetes, and smoking). The report highlighted the need to better understand how to prevent cognitive impairment, and this need is heightened as our population ages and the US demographic profile shifts. Therefore, the current study examines the relationship between the number of ideal CVD health metrics, as defined by the AHA, and cognitive performance and decline in the domains of Semantic Memory, Episodic Memory, Executive Function, and Processing Speed, in the Northern Manhattan Study (NOMAS). An important strength of this study is the use of our complete battery of neuropsychological tests, which allows for a comprehensive assessment of cognitive capabilities necessary to elucidate the differential impact on cognitive processes of established vascular health metrics. The majority of participants in our study are of Caribbean Hispanic descent, which is a notable strength as well. Hispanics represent a growing minority of the aging US population that has been underrepresented in studies of cognitive health, allowing us to provide novel data on a large sample of mostly Caribbean Hispanics. Detecting vascular risk factors for cognitive impairment before individuals become demented may provide an opportunity to intervene and prevent disability.

Methods

Study Population

NOMAS is a prospective population-based cohort study designed to determine risk factors for stroke and other outcomes among a race/ethnicity–diverse urban population. Northern Manhattan is a well-defined area of New York City made up of 63% Hispanic, 20% non-Hispanic black, and 15% non-Hispanic white residents. Study details were published previously.[14] Eligible participants (1) had never been diagnosed with a stroke; (2) were >40 years old; and (3) had resided in Northern Manhattan for ≥3 months, in a household with a telephone. Subjects were identified by random-digit dialing and recruited from the telephone sample to have an in-person baseline interview and assessment from 1993 to 2001. The enrollment response rate was 75% and the overall participation rate was 69%, with a final cohort of 3298 participants. A substudy of 1091 participants with neuropsychological assessments was composed of participants remaining clinically stroke free who were recruited during annual follow-up and were age >50 with no contraindications to brain magnetic resonance imaging (MRI). Participants who were of "other" race (ie, not classified as white, black, or Hispanic) were excluded from the current analysis, as well as those with missing baseline data for cardiovascular disease health metrics. The study was approved by the institutional review boards of Columbia University and the University of Miami, and all subjects provided written informed consent.

Baseline Data Collection

Data were collected through interviews with trained bilingual research assistants in English or Spanish. Physical and neurological examinations were conducted by study physicians. Race/ethnicity was based on self-identification through a series of questions modeled after the US Census and conforming to standard definitions outlined by Directive 15.[15] Standardized questions were adapted from the Behavioral Risk Factor Surveillance System by the Centers for Disease Control and Prevention regarding smoking and other cardiovascular risk factors.[16,17] Smoking was based on self-reported age of starting smoking and age of quitting smoking. Leisure-time physical activity was measured with a questionnaire based on the National Health Interview Survey regarding participation in ≥1 selected rigorous physical activity in a typical 14-day period.[18] Blood pressure was obtained from the right brachial artery after a 10-minute rest in a seated position (Dinamap Pro100; Critikon Inc). Blood pressure was measured twice, before and after the physical examination, and averaged for this analysis. Fasting blood specimens were analyzed to determine glucose and lipid profiles, as described previously.[19] Plasma levels of total cholesterol after fasting were measured by using standardized enzymatic procedures with a Hitachi 705 automated spectrophotometer (Boehringer Mannheim). Dietary behavior was measured with a comprehensive in-person assessment by using a modified Block National Cancer Institute food frequency questionnaire. In addition, a Mini-Mental State Examination (MMSE) was performed at study baseline.[20]

As previously defined by the AHA, the 7 CVH factors were classified into ideal, versus not ideal: (1) smoking ideal: never or quit >1 year; (2) BMI ideal: <25 kg/m^2; (3) physical activity ideal: ≥150 min/wk moderate intensity, ≥75 min/wk vigorous intensity, or equivalent combination; (4) diet ideal: 4 or 5 healthy components based on 5 health dietary metrics (≥4.5 cups of fruits and vegetables/d, 2 or more 3.5-oz servings of fish/wk, 3 or more 1-oz equivalent servings fiber-rich whole grains/d, <1500 mg sodium/d, and ≤450 kcal sugar-sweetened beverages/wk); (5) total cholesterol ideal: untreated and <200 mg/dL; (6) blood pressure ideal: untreated and

<120/<80 mm Hg; and (7) fasting plasma glucose ideal: untreated and <100 mg/dL.[1] These variables were all based on assessments done at baseline enrollment into the study.

DNA samples were extracted from peripheral blood white cells using *Hha*I digestion and amplified by polymerase chain reaction. Apolipoprotein ε4 (*ApoE4*) carriers were identified as individuals with a genotype of *ApoE4/2*, *ApoE4/4*, and *ApoE4/3*.

Neuropsychological Testing

The neuropsychological battery was administered in English or Spanish by trained research assistants in a quiet room. The mean time from baseline enrollment to the first neuropsychological assessment was 7.2±2.4 years. Domain-specific *Z* scores were calculated for the cognitive domains: Episodic Memory, Processing Speed, Semantic Memory, and Executive Function. The domain scores were calculated by averaging construct-relevant *Z*-transformed neuropsychological test scores. The tests included in each domain were determined based on the relationships among the tests in an exploratory factor analysis and the results of previous studies.[21,22] Episodic memory was assessed with 3 subscores on a 12-word 5 trial list-learning task: list learning total score, delayed recall score, and delayed recognition score. Executive function was assessed with 2 subscores: the difference in time to complete the Color Trails test Form 1 and Form 2 and the sum of the Odd-Man-Out subtests 2 and 4. Processing speed was assessed with the Grooved Pegboard task in the nondominant hand, the Color Trails test Form 1, and the Visual-Motor Integration test.[23] Semantic memory was defined by 3 tests: picture naming (modified Boston Naming) test, category fluency (Animal Naming) test, and phonemic fluency (C, F, and L in English speakers and P, S, and V in Spanish speakers). Consistent with previous NOMAS analyses, the domain *Z* scores for the initial neuropsychological tests were unadjusted.

Participants were invited to return for a second neuropsychological assessment, with a mean time between the first and second neuropsychological assessments of 6±2 years. For the changes in scores over time, composite scores for the changes in 4 domains were calculated by using regression-based reliable change indices of the corresponding individual test, adjusting for age, education years, and the time interval between the 2 tests.[24]

At the time of the first neuropsychological testing, a Center for Epidemiologic Studies–Depression Scale was administered, and a score of ≥16 was considered positive for depressive symptoms. In addition, imaging was performed on a 1.5-T MRI system (Philips Medical Systems) at the Hatch Research Center at the time of initial neuropsychological evaluation. Processing of magnetic resonance images to calculate white matter hyperintensity volumes and cerebral, lateral ventricular, and intracranial volumes and to identify MRI-defined infarcts has been described previously.[25] Silent brain infarcts were rated as (1) cavitations of ≥3 mm in size on the fluid-attenuated inversion recovery sequence (or similar characteristics on proton density and T2- and T1-weighted sequences), distinct from a vessel (because of the lack of signal void on T2 sequence), and of equal intensity to cerebrospinal fluid in the case of lacunar infarction or (2) as superficial encephalomalacia affecting the cerebral cortex or cerebellum suggestive of thromboembolism.

Statistical Analysis

The primary independent variable of interest was the number of ideal CVH factors for each individual, represented as the ideal CVH score, with a range of 0 to 7. This score was examined continuously and divided into 4 categories: 0 to 1 (reference), 2, 3, and 4 to 7. As secondary exploratory analyses, we also examined each of the 7 ideal CVH components individually, categorized as ideal versus not ideal. First, we examined the distribution of the covariates of interest by category of the ideal CVH score in the study population. Next, multivariable-adjusted linear regression models were constructed to examine associations between ideal CVH scores and *Z* scores for the 4 cognitive domains (Executive Function, Episodic Memory, Semantic Memory, and Processing Speed) at the first neuropsychological assessment and then with the change in *Z* scores for the domains from the first to follow-up assessments. Because domain *Z* scores were not strongly correlated, we examined each domain as a separate outcome.

Model 1 included age at neuropsychological testing, sex, race/ethnicity, years of education, medical insurance status (Medicaid or no insurance versus Medicare without Medicaid or private insurance), and the time span from baseline data collection to the time of neuropsychological assessment. Model 2 added MRI variables that are predictors of cognitive impairment, including white matter hyperintensity volumes, brain atrophy (total cerebral volume/total intracranial volume), and MRI-defined infarction. For the analyses of the *Z* scores representing the change in performance in each cognitive domain from first assessment to follow-up, we ran both models again, but age and education were not added because they were included in the regression analyses used to create the *Z* scores. A sensitivity analysis was conducted including depression as a covariate in model 1. Effect modification by *ApoE4* carrier status and race/ethnicity was explored by including interaction terms for the ideal CVH score with *ApoE4* carrier status and race/ethnicity separately, adjusting for the variables included in model 1. The primary analyses (ideal CVH score examined in model 1) were

examined in sensitivity analyses restricted to Hispanic participants, as they represented the largest ethnic subgroup in the study population. Last, a sensitivity analysis was conducted restricted to those without cognitive impairment at baseline enrollment, which was defined as an MMSE score of ≥17 for those with <8 years of education and an MMSE score of ≥24 among those with ≥8 years of education (n=84 excluded).[26]

Results

In total, 1033 participants had data on the ideal CVH factors and neuropsychological testing, of whom 722 had repeated testing at follow-up. Ideal CVH score was not predictive of whether participants had follow-up neuropsychological assessments. Table 1 shows the characteristics of the study population. Table 2 shows the breakdown of the study population in relation to demographics and MRI variables by categories of the ideal CVH score.

An increasing number of ideal CVH factors was positively associated with processing speed at initial assessment, as shown in Table 3. This association persisted after controlling for MRI markers of subclinical vascular damage. The association was strongest for 3 of the CVH factors in particular—ideal BMI, lack of smoking, and ideal fasting glucose, which were all associated with greater processing speed performance at the initial assessment compared with those with less-than-ideal health for these factors after mutual adjustment (Table 3). The results remained unchanged in sensitivity analyses controlling for depression (not shown).

Figure shows the mean *Z* scores for the change in each cognitive domain from initial assessment to follow-up, by category of ideal CVH score, in the full study population, as well as among those without cognitive impairment at baseline enrollment. Having an increasing number of ideal CVH factors was associated with less decline over time in processing speed (Table 4). This association persisted after controlling for MRI markers of subclinical vascular damage. The association was driven by the ideal factors of not smoking and fasting glucose, as they were associated with less decline in processing speed, mutually adjusting for the other CVH factors.

An association between ideal CVH and episodic memory performance over time was also suggested (Table 4), and this association was statistically significant among those without cognitive impairment at baseline enrollment (Table 5). A categorical examination of the number of ideal CVH factors in relation to change in episodic memory performance over time suggested that those with 2 to 7 ideal CVH factors had less decline in episodic memory over time compared with those with 0 or 1 ideal CVH factors (Tables 4 and 5). The latter association also persisted after adjusting for MRI variables and appeared to be driven by positive effects of ideal fasting glucose, as this factor was significantly associated after adjusting for the other CVH factors. A positive association between number of ideal CVH factors and change in executive function over time also reached statistical significance among those not impaired at baseline enrollment (Table 5). Change in semantic memory performance was not significantly associated with ideal CVH factors. The results remained unchanged in sensitivity analyses controlling for depression.

Because of the small proportion of participants who met the criteria for ideal blood pressure, we decided to run

Table 1. Description of the Study Population With Initial Cognitive Assessment (N=1033)

Variables	n (%)
Male sex	407 (39)
Race/ethnicity	
Black	200 (19)
White	162 (16)
Hispanic	671 (65)
Medicare/privately insured	537 (52)
Silent infarct by MRI	102 (10)
Blood pressure ideal	72 (7)
BMI ideal	278 (27)
Total cholesterol ideal	416 (40)
Smoking ideal	827 (80)
Physical activity ideal	317 (31)
Fasting glucose ideal	692 (67)
Diet ideal	3 (<1)
No. of ideal factors	
0	32 (3)
1	155 (15)
2	340 (33)
3	311 (30)
4	144 (14)
5	45 (4)
6	6 (1)
7	0 (0)
	Mean (SD)
Age at first neuropsychological assessment, y	71.7 (8.4)
Education, y	9.6 (5.1)
White matter hyperintensity volume/total cranial volume, %	0.7 (0.8)
Total brain volume/total cranial volume, %	72.0 (4.2)
MMSE	26.8 (3.2)

MRI indicates magnetic resonance imaging; BMI, body mass index; MMSE, Mini-Mental State Examination.

Table 2. Demographics Stratified by Number of Ideal Cardiovascular Health Factors

Variables	0 to 1 Ideal Factors (n=187)	2 Ideal Factors (n=340)	3 Ideal Factors (n=311)	4 to 7 Ideal Factors (n=195)	*P* Value*
Male sex, n (%)	55 (29)	119 (35)	133 (43)	100 (51)	<0.0001
Race/ethnicity, n (%)					
Black	44 (24)	57 (17)	51 (16)	48 (25)	<0.0001
White	26 (14)	39 (11)	49 (16)	48 (25)	
Hispanic	117 (63)	244 (72)	211 (68)	99 (51)	
Insured, n (%)	104 (56)	171 (50)	150 (48)	71 (36)	0.001
Age at first neuropsychological assessment, y, mean (SD)	71.0 (7.7)	71.5 (8.1)	72.0 (8.4)	72.2 (9.5)	0.67
Education, y, mean (SD)	9.2 (4.7)	9.1 (5.0)	9.2 (5.1)	11.4 (5.2)	<0.0001
Silent infarct by MRI, n (%)	22 (12)	38 (11)	28 (9)	14 (7)	0.36
White matter hyperintensity volume/total cranial volume, %, mean (SD)	0.71 (0.65)	0.73 (0.91)	0.68 (0.79)	0.76 (0.95)	0.28†
Total brain volume/total cranial volume, %, mean (SD)	71.6 (4.1)	72.1 (3.9)	72.3 (4.1)	71.8 (4.9)	0.20†
MMSE, mean (SD)	26.5 (3.6)	26.3 (3.5)	26.6 (3.3)	27.4 (2.8)	0.01

MRI indicates magnetic resonance imaging; MMSE, Mini-Mental State Examination.
**P*-value obtained from χ^2 tests for categorical variables and ANOVA for continuous variables.
†*P*-values based on log-transformed values to achieve normality.

sensitivity analyses examining systolic and diastolic blood pressures as continuous measurements from baseline enrollment in relation to the cognitive domains, adjusting for the demographic variables in model 1. In these models, no significant associations were observed for diastolic blood pressure with the cognitive domain variables (data not shown). In relation to initial cognitive performance, systolic blood pressure was inversely associated with *Z* scores for the domains of Processing Speed (β=−0.003, *P*=0.03) and Executive Function (β=−0.003, *P*=0.04). In relation to *Z* scores for change in cognitive performance, systolic blood pressure was inversely associated with processing speed only (full study population: β=−0.005, *P*=0.03, among those without cognitive impairment at baseline enrollment: β=−0.005, *P*=0.05).

There were no significant interactions between the number of ideal CVH factors with *ApoE4* carrier status in relation to cognitive performance and decline (data not shown). Similarly, effect modification by race/ethnicity was not suggested for the associations between the number of ideal CVH factors and performance on the cognitive domains at the initial assessment and change in performance over time (data not shown). However, analyses restricted to Hispanics were conducted. Overall, conclusions regarding the relationship between number of ideal CVH factors and initial performance on cognitive domains and change over time remained consistent in the data set restricted to Hispanics, and the associations with processing speed persisted (Tables 3 and 4). When the data set was restricted to Hispanics without cognitive impairment at baseline enrollment (Table 5), the number of ideal CVH factors was significantly associated only with change in processing speed over time.

Discussion

In this prospective multiethnic population-based study, we found a positive association between the number of AHA-defined ideal CVH factors at baseline enrollment and processing speed performance years later at initial neuropsychological assessment as well as less decline in performance over time. These relationships with the domain of Processing Speed remained when the analysis was restricted to Hispanics and appeared to be driven in particular by a lack of smoking and ideal fasting glucose levels, as these variables were significantly associated after mutual adjustment for the other ideal CVH factors. Most important, we found that participants who were not impaired at baseline enrollment based on the MMSE and possessed a greater number of ideal CVH factors had less decline in performance over time in several domains, suggesting that such decline may be preventable with ideal CVH. Our data suggest that promoting ideal CVH on even a few of these factors may be required to see cognitive health benefits, as participants with only 2 or 3 ideal CVH factors had less decline over time across multiple domains, particularly Processing Speed and Episodic Memory.

We have previously shown a strong graded relationship between the number of ideal CVH metrics and cardiovascular risk overall and for stroke and myocardial infarction

Table 3. Ideal CVH in Relation to Cognitive Performance at Initial Assessment (N=1033)

	Executive Function		Semantic Memory		Episodic Memory		Processing Speed	
Ideal CVH*	β (SE)	*P* Value	β (SE)	*P* Value	β (SE)	*P* Value	β (SE)	*P* Value
No. of ideal factors, continuous								
Model 1†	0.011 (0.022)	0.620	0.012 (0.021)	0.570	0.038 (0.022)	0.090	0.115 (0.021)	<0.001
Model 2‡	0.015 (0.023)	0.500	0.010 (0.021)	0.650	0.035 (0.023)	0.120	0.108 (0.021)	<0.001
Model 1 among Hispanics	0.033 (0.030)	0.282	0.038 (0.026)	0.155	0.031 (0.029)	0.284	0.128 (0.029)	<0.001
No. of ideal factors								
Model 1								
2 vs 0–1	0.008 (0.074)	0.911	−0.108 (0.070)	0.123	0.136 (0.074)	0.068	0.133 (0.071)	0.060
3 vs 0–1	0.108 (0.076)	0.154	−0.056 (0.071)	0.434	0.165 (0.076)	0.031	0.345 (0.072)	<0.001
4–7 vs 0–1	−0.031 (0.085)	0.720	−0.010 (0.080)	0.904	0.120 (0.085)	0.162	0.357 (0.081)	<0.001
Model 2								
2 vs 0	0.022 (0.074)	0.762	−0.111 (0.070)	0.116	0.134 (0.075)	0.074	0.125 (0.070)	0.077
3 vs 0	0.124 (0.076)	0.104	−0.063 (0.072)	0.381	0.152 (0.077)	0.048	0.322 (0.072)	<0.001
4–7 vs 0–1	−0.016 (0.086)	0.850	−0.017 (0.081)	0.834	0.112 (0.086)	0.192	0.336 (0.081)	<0.001
Blood pressure ideal								
Model 1	0.122 (0.103)	0.238	0.049 (0.098)	0.614	−0.057 (0.104)	0.586	−0.025 (0.98)	0.801
Model 2	0.118 (0.103)	0.254	0.050 (0.098)	0.608	−0.053 (0.103)	0.609	−0.023 (0.98)	0.811
BMI ideal								
Model 1	0.037 (0.059)	0.533	0.042 (0.056)	0.453	0.014 (0.060)	0.821	0.171 (0.057)	0.003
Model 2	0.036 (0.060)	0.544	0.038 (0.057)	0.499	0.007 (0.060)	0.913	0.163 (0.057)	0.004
Total cholesterol ideal								
Model 1	−0.078 (0.053)	0.145	−0.018 (0.051)	0.729	0.091 (0.054)	0.093	0.042 (0.051)	0.413
Model 2	−0.073 (0.053)	0.174	−0.017 (0.051)	0.741	0.092 (0.054)	0.089	0.042 (0.051)	0.414
Smoking ideal								
Model 1	−0.019 (0.065)	0.776	−0.033 (0.061)	0.597	0.080 (0.065)	0.224	0.162 (0.062)	0.009
Model 2	−0.006 (0.066)	0.924	−0.037 (0.062)	0.548	0.068 (0.066)	0.308	0.138 (0.062)	0.027
Physical activity ideal								
Model 1	−0.003 (0.057)	0.956	0.049 (0.054)	0.364	0.086 (0.058)	0.139	0.092 (0.054)	0.092
Model 2	−0.002 (0.057)	0.976	0.049 (0.054)	0.372	0.090 (0.058)	0.123	0.094 (0.054)	0.086
Fasting glucose ideal								
Model 1	0.060 (0.055)	0.271	−0.010 (0.052)	0.851	−0.019 (0.055)	0.726	0.172 (0.052)	0.001
Model 2	0.071 (0.055)	0.198	−0.015 (0.052)	0.772	−0.025 (0.055)	0.649	0.162 (0.052)	0.002
Diet ideal								
Model 1	−0.305 (0.472)	0.518	−0.045 (0.453)	0.921	−0.210 (0.478)	0.661	0.559 (0.453)	0.218
Model 2	−0.307 (0.471)	0.515	−0.047 (0.453)	0.917	−0.225 (0.478)	0.639	0.530 (0.451)	0.241

CVH indicates cardiovascular health; BMI, body mass index.

*The analyses of the individual ideal CVH score components were mutually adjusted for the other components.

†Model 1: time from baseline cardiovascular disease risk factor assessment to initial neuropsychological assessment, age, sex, race/ethnicity, education, and insurance. Ideal CVH components are mutually adjusted for each other.

‡Model 2: variables in model 1+white matter hyperintensity volumes, brain atrophy, and Silent brain infarct.

separately in the NOMAS cohort, and this association was similar for whites, blacks, and Hispanics.[3] Although there is now evidence supporting the importance of these CVH metrics identified by the AHA for the promotion and assessment of cardiovascular health, data elucidating the relationship with cognitive aging are limited. However, a few

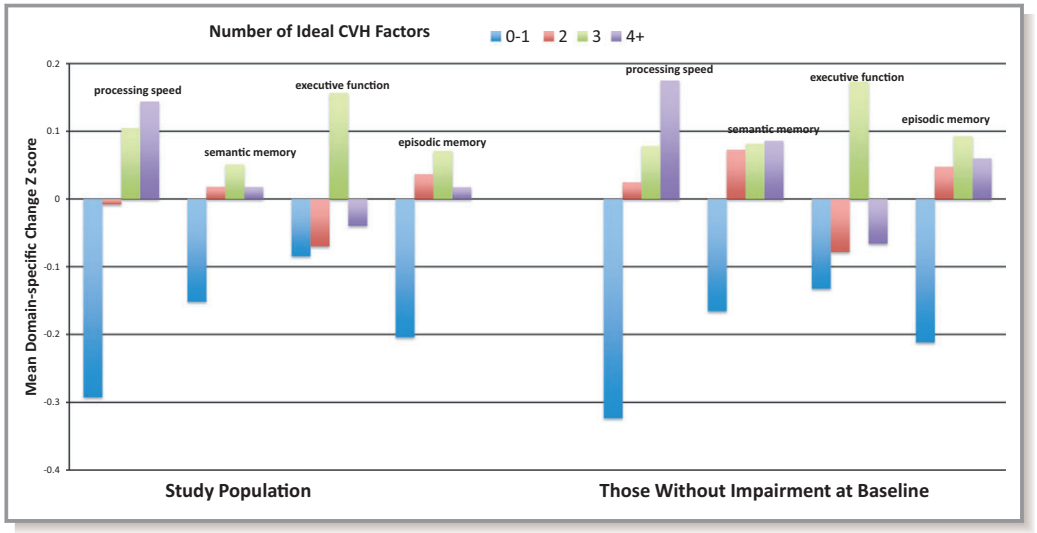

Figure. Mean *Z* scores for change in cognitive domain performance by the number of ideal cardiovascular health factors (CVH).

recent studies have demonstrated associations between the number of ideal CVH metrics and cognition. First, the Coronary Artery and Risk Development in Young Adults study (CARDIA) is a multicenter community-based prospective cohort study with 2932 participants followed for 25 years.[27] This cohort is substantially younger than ours (age 18–30 at baseline). In CARDIA, the number of ideal CVH factors in young adulthood and middle age was associated with better psychomotor speed, executive function, and verbal memory in midlife. Blood pressure and smoking were individually associated with all 3 domains, and BMI, glucose, and physical activity were predictive of both tests of executive function and psychomotor speed. Another cross-sectional study examined the number of ideal CVH metrics in relation to cognition in the smaller (N=972) Maine-Syracuse Longitudinal Study.[28] Similar to our study, these investigators used an extensive neuropsychological test battery that included 20 individual tests, grouped into 5 domains, and a global score, and they also found the number of ideal CVH factors associated with better performance across several domains. In the latter study, similar to ours, less than 1% achieved ideal status on all health metrics. They also examined the individual CVH metrics in relation to global cognitive performance and noted significant positive associations for ideal status in smoking, physical activity, BMI, blood glucose, and blood pressure. A recent analysis from the Reasons for Geographic and Racial Differences in Stroke (REGARDS) study examined adherence to the 7 AHA-defined CVH metrics (Life's Simple 7 score) in relation to incident cognitive impairment as measured using 3 tests of verbal learning, memory, and fluency.[29] Among 17 761 REGARDS participants without stroke or global cognitive impairment at baseline, both intermediate and high CVH scores were associated with reduced incidence of cognitive impairment among both black and white participants, and a dose-response relationship was not observed. Similar to our study, REGARDS investigators concluded that even moderate adherence to the AHA's CVH guidelines may be associated with cognitive benefits.

The vast majority of participants in the Maine-Syracuse Longitudinal Study were white, while the CARDIA study and the REGARDS study included a large number of both white and black participants. Unlike these studies, the NOMAS population is largely Hispanic. Our study extends their findings with prospective data and by showing that ideal CVH metrics relate to change in cognitive performance on specific domains over about half a decade, in a large racially/ethnically diverse sample with a large proportion of minorities, particularly Caribbean Hispanics.

Supporting evidence also exists for the relationship between the individual ideal CVH components and cognition. Elevated blood pressure, glucose, cholesterol, BMI, poor diet, physical inactivity, and smoking during adulthood have all been associated with impaired performance on neurocognitive assessments, as well as with decline in performance over time, in previous studies.[4–12] The results of our study add to a growing body of literature suggesting the effects of smoking and blood glucose levels on cognitive health in particular. Although we did not observe significant associations for physical activity and diet in relation to cognitive domains in this study, these negative results should be interpreted with caution as the scope of the current study prevented a thorough investigation of each of these individual factors, and they have been previously shown to relate to cognitive health in other studies. Previous studies have also examined the burden of CVH factors in relation to cognitive impairment and decline using other metrics to quantify vascular disease risk

Table 4. Ideal CVH in Relation to Change in Cognitive Performance (N=722)

Ideal CVH*	Change in Executive Function *Z* Score		Change in Semantic Memory *Z* Score		Change in Episodic Memory *Z* Score		Change in Processing Speed *Z* Score	
	β (SE)	*P* Value	β (SE)	*P* Value	β (SE)	*P* Value	β (SE)	*P* Value
No. of ideal factors, continuous								
Model 1†	0.055 (0.033)	0.098	0.037 (0.033)	0.250	0.064 (0.033)	0.060	0.122 (0.033)	<0.001
Model 2‡	0.060 (0.033)	0.080	0.031 (0.033)	0.350	0.061 (0.033)	0.060	0.120 (0.033)	<0.001
Model 1 among Hispanics	0.019 (0.043)	0656	0.007 (0.041)	0.872	0.063 (0.044)	0.147	0.126 (0.041)	0.002
No. of ideal factors								
Model 1								
2 vs 0–1	0.049 (0.108)	0.653	0.153 (0.107)	0.153	0.240 (0.108)	0.027	0.282 (0.106)	0.008
3 vs 0–1	0.270 (0.109)	0.014	0.182 (0.108)	0.091	0.285 (0.109)	0.009	0.386 (0.128)	0.004
4–7 vs 0–1	0.082 (0.124)	0.511	0.143 (0.123)	0.242	0.258 (0.124)	0.037	0.410 (0.122)	0.001
Model 2								
2 vs 0–1	0.061 (0.109)	0.575	0.153 (0.107)	0.151	0.240 (0.107)	0.026	0.286 (0.107)	0.008
3 vs 0–1	0.284 (0.110)	0.010	0.175 (0.108)	0.105	0.274 (0.109)	0.012	0.388 (0.108)	<0.001
4–7 vs 0–1	0.093 (0.125)	0.456	0.119 (0.123)	0.332	0.245 (0.123)	0.047	0.402 (0.123)	0.001
Blood pressure ideal								
Model 1	0.000 (0.151)	0.999	0.080 (0.150)	0.592	0.149 (0.152)	0.327	0.217 (0.149)	0.145
Model 2	0.003 (0.153)	0.986	0.030 (0.150)	0.841	0.136 (0.152)	0.370	0.189 (0.150)	0.208
BMI ideal								
Model 1	0.079 (0.088)	0.372	−0.086 (0.088)	0.330	−0.085 (0.089)	0.341	0.095 (0.087)	0.279
Model 2	0.080 (0.089)	0.371	−0.075 (0.087)	0.395	−0.072 (0.089)	0.417	0.103 (0.088)	0.240
Total cholesterol ideal								
Model 1	0.062 (0.078)	0.430	0.128 (0.077)	0.099	0.101 (0.078)	0.197	−0.002 (0.077)	0.974
Model 2	0.067 (0.079)	0.394	0.111 (0.077)	0.151	0.084 (0.078)	0.284	−0.010 (0.077)	0.893
Smoking ideal								
Model 1	−0.019 (0.094)	0.842	0.117 (0.092)	0.207	0.132 (0.093)	0.160	0.187 (0.092)	0.042
Model 2	−0.011 (0.094)	0.911	0.113 (0.092)	0.220	0.132 (0.093)	0.156	0.189 (0.092)	0.041
Physical activity ideal								
Model 1	0.081 (0.085)	0.337	0.028 (0.084)	0.740	−0.040 (0.086)	0.637	0.141 (0.084)	0.093
Model 2	0.083 (0.085)	0.332	0.023 (0.084)	0.781	−0.048 (0.085)	0.572	0.140 (0.084)	0.096
Fasting glucose ideal								
Model 1	0.060 (0.082)	0.466	−0.005 (0.081)	0.952	0.176 (0.082)	0.032	0.168 (0.080)	0.038
Model 2	0.067 (0.082)	0.418	−0.002 (0.081)	0.981	0.188 (0.081)	0.021	0.170 (0.081)	0.036
Diet ideal								
Model 1	1.243 (0.715)	0.083	0.274 (0.715)	0.702	−0.735 (0.719)	0.307	−0.420 (0.710)	0.554
Model 2	1.248 (0.717)	0.082	0.201 (0.712)	0.778	−0.811 (0.713)	0.255	−0.453 (0.711)	0.524

CVH indicates cardiovascular health; BMI, body mass index.

*The analyses of the individual ideal CVH score components were mutually adjusted for the other components.

†Model 1: time from baseline cardiovascular disease risk factor assessment to initial neuropsychological assessment, sex, race/ethnicity, and insurance. Ideal CVH components are mutually adjusted for each other.

‡Model 2: variables in model 1+white matter hyperintensity volumes, brain atrophy, and SBI.

factor burden. For example, the Framingham Risk Score, a well-established CVD risk assessment tool that is widely used in clinical practice, was associated with the domain of Executive Function in 1755 Framingham Offspring participants, and in that study, similar to ours, diabetes mellitus was a driving factor.[30] The Framingham Risk Score Profile was also

Table 5. Ideal CVH in Relation to Change in Cognitive Performance Among Those Without Impairment at Baseline (N=638)

	Change in Executive Function *Z* Score		Change in Semantic Memory *Z* Score		Change in Episodic Memory *Z* Score		Change in Processing Speed *Z* Score	
Ideal CVH	β (SE)*	*P* Value	β (SE)*	*P* Value	β (SE)*	*P* Value	β (SE)*	*P* Value
No. of ideal factors, continuous	0.069 (0.036)	0.050	0.059 (0.034)	0.090	0.073 (0.035)	0.040	0.139 (0.036)	0.000
Among Hispanics	0.031 (0.044)	0.491	−0.001 (0.042)	0.975	0.060 (0.046)	0.190	0.118 (0.043)	0.007
No. of ideal factors								
2 vs 0–1	0.076 (0.116)	0.513	0.220 (0.111)	0.047	0.268 (0.115)	0.020	0.343 (0.115)	0.003
3 vs 0–1	0.325 (0.118)	0.006	0.224 (0.112)	0.047	0.321 (0.117)	0.006	0.392 (0.117)	0.001
4–7 vs 0–1	0.091 (0.133)	0.497	0.222 (0.128)	0.082	0.314 (0.132)	0.018	0.489 (0.133)	<0.001
Blood pressure ideal	0.019 (0.163)	0.905	0.030 (0.157)	0.848	0.149 (0.164)	0.364	0.257 (0.164)	0.117
BMI ideal	0.120 (0.095)	0.206	−0.103 (0.091)	0.262	−0.106 (0.096)	0.269	0.119 (0.095)	0.212
Total cholesterol ideal	0.124 (0.083)	0.140	0.170 (0.080)	0.034	0.132 (0.083)	0.114	−0.011 (0.083)	0.895
Smoking ideal	−0.070 (0.101)	0.492	0.165 (0.096)	0.089	0.116 (0.101)	0.253	0.241 (0.101)	0.017
Physical activity ideal	0.112 (0.091)	0.224	0.070 (0.088)	0.429	0.010 (0.092)	0.915	0.148 (0.092)	0.107
Fasting Glucose ideal	0.042 (0.087)	0.632	0.024 (0.084)	0.777	0.164 (0.087)	0.061	0.181 (0.087)	0.039
Diet ideal	2.099 (1.013)	0.039	−0.742 (0.979)	0.449	−1.413 (1.014)	0.164	−1.243 (1.020)	0.224

CVH indicates cardiovascular health; BMI, body mass index.
*Controlling for time from baseline cardiovascular disease risk factor assessment to initial neuropsychological assessment, sex, race/ethnicity, and insurance. Ideal CVH components are mutually adjusted for each other. The analyses of the individual ideal CVH score components were mutually adjusted for the other components.

associated with incident cognitive impairment defined using longitudinal performance on a 6-item screener in REGARDS study.[31] Worse cardiovascular risk profile using the Framingham Risk Score has been cross-sectionally associated with poorer cognitive function in both older and younger (age 35–44) adults.[32] In the latter study, age, diabetes mellitus, and smoking were the most influential components, again consistent with the results of our study. Last, in an analysis in the British Whitehall II Cohort study (mean age 56 at baseline), both the Framingham General Cardiovascular Disease Risk Score and the Framingham Stroke Risk Score predicted decline in the cognitive domains of Reasoning, Verbal Fluency, Vocabulary, and Global Cognition, though not in Memory, and were more strongly associated with 10-year cognitive decline than a dementia risk score.[33]

The relationship between ideal CVH factors and cognitive domains in our study, as well as in others, supports the role of vascular damage and metabolic processes in the etiology of cognitive aging and dementia. In our study, ideal CVH was most strongly associated with the Processing Speed domain. This finding suggests the possibility of mediation, at least in part, by subclinical cerebrovascular disease processes involving intrahemispheric and interhemispheric connections. Although the associations observed in our study remained consistent in models adjusting for subclinical markers of cerebrovascular damage including white matter volume, brain atrophy, and MRI-defined infarcts, this does not negate the possibility of partial mediation by these important risk factors for cognitive impairment.[34,35]

Strengths of this study include the multiethnic, population-based cohort with a large percentage of Caribbean Hispanics, the prospective design, and the comprehensive neuropsychological test battery with 2 cognitive assessments, allowing for an analysis of cognitive change. In addition, we were able to control for MRI measures of subclinical vascular damage including white matter lesion load and MRI-defined infarcts. One limitation is the fact that this study was conducted within a subcohort of the overall NOMAS study population. As expected, NOMAS participants who were included in the MRI subcohort were slightly healthier than those who were not. Specifically, they were younger at baseline and more likely to be Hispanic, to be insured, to have hypercholesterolemia, and to have completed high school and were less likely to be obese, smoke, and have diabetes. Therefore, our findings may not be generalizable to the full study population. A related limitation is the lack of follow-up cognitive assessment for a portion of the cohort. Among those with initial neuropsychological assessment, participants with a follow-up assessment were slightly younger, but the other demographic variables were not related, and most notably, there was no difference in the ideal CVH score. We evaluated the hypothesis that those participants with follow-up neuropsychological assessment were more cognitively healthy than those who did not return. At the second neuropsychological assessment, the Informant Questionnaire for Cognitive Decline in the Elderly (IQCODE)[36] was completed with both informants for

participants who had follow-up neuropsychological assessment and informants for participants without follow-up assessments. As expected, the participants without a follow-up neuropsychological assessment were rated more poorly on the IQCODE (not shown). However, selection bias is unlikely as availability of follow-up neuropsychological data was unrelated to ideal CVH score. As in any observational epidemiologic study, residual confounding by unmeasured risk factors for cognitive impairment is a potential source of bias. Similar studies in race/ethnically diverse populations with different profiles of educational attainment, literacy, and employment status are needed. In addition, further study is needed to elucidate the sensitivity periods over the lifecourse during which CVH metrics may be most influential in determining late-life cognitive impairment across the range of domains and how behavioral and health modifications that target these CVH metrics may influence cognitive performance and mitigate decline over time. Because diet was only assessed at study baseline, that was the only time point available at which to calculate the complete ideal CVH score. Positive results should be interpreted with caution as a result of the large number of analyses conducted because, as always, associations observed may be the result of chance. Last, use of the MMSE cutpoint scores is not an ideal metric to identify individuals with cognitive impairment at baseline in the absence of dementia diagnosis.

In conclusion, the findings of our multiethnic study of whites, blacks, and Hispanics suggest that the number of ideal CVH metrics is associated with less decline in performance in the domain of Processing Speed and, to a lesser extent, the domains of Executive Function and Episodic Memory. Longitudinal effects of the ideal CVH metrics on cognitive aging were stronger than the cross-sectional ones on cognitive performance at initial assessment, particularly among those who were cognitively healthy at baseline. Therefore, the results of this study suggest that achievement of the AHA's ideal CVH metrics may have benefits for brain health in addition to preventing strokes and myocardial infarctions, even among elderly individuals, underscoring the importance of public health initiatives aimed to better control these 7 factors. The current study provides support for future studies assessing the value of routine assessment and treatment of these health factors by clinicians with the goal of reducing vascular cognitive impairment. As the US population ages and the number of people at risk for cognitive impairment grows, the public health implications of targeting these modifiable risk factors will be substantial.

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