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ORIGINAL INVESTIGATIONS

Ideal Cardiovascular Health, Mortality, and Vascular Events in Elderly Subjects

The Three-City Study

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ABSTRACT

BACKGROUND The benefit of ideal cardiovascular health (CVH) on health-related outcomes in middle-aged patients is firmly established. In the growing elderly population, the high prevalence of comorbidities and medications for chronic diseases may offset such benefit.

OBJECTIVES This study analyzed the association of ideal CVH with mortality, incident coronary heart disease, and stroke events in elderly individuals from the community.

METHODS Between 1999 and 2001, 9,294 men and women, noninstitutionalized and aged 65 years and over were examined, and thereafter followed up for the occurrence of vascular events and mortality within the Three-City Study. Hazard ratios (HRs) were estimated by Cox proportional hazard model and compared subjects with 3 to 4 and subjects with 5 to 7 ideal metrics with those with 0 to 2 ideal metrics, respectively.

RESULTS The mean age was 73.8 ± 5.3 years, and 36.7% were men. Only 5% of the participants had ≥5 metrics at the ideal level. After a median follow-up of 10.9 years and 8.6 years, respectively 1,987 deaths and 680 adjudicated coronary heart disease or stroke events had occurred. In multivariate analysis, the risk of mortality and of vascular events decreased across the categories of ideal metrics. In particular, in subjects with ≥5 metrics at the ideal level (compared with those with ≤2), there was a 29% (hazard ratio [HR]: 0.71; 95% confidence interval [CI]: 0.55 to 0.90) decreased risk of all-cause mortality and 67% (HR: 0.33; 95% CI: 0.19 to 0.57) for coronary heart disease and stroke combined (p for trend <0.001).

CONCLUSIONS Even in the elderly, higher CVH status is highly beneficial regarding mortality and vascular event risks.

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ABBREVIATIONS AND ACRONYMS

AHA = American Heart Association

BMI = body mass index

CHD = coronary heart disease

CI = confidence Interval

CVD = cardiovascular disease

CVH = cardiovascular health

HR = hazard ratio

The concept of primordial prevention (i.e., preventing the development of cardiovascular risk factors) emerged as a complementary approach to primary prevention of cardiovascular disease (CVD) in the late 1970s (1). It has been recently re-emphasized by the American Heart Association (AHA), which has developed a simplified 7-item tool (body mass index [BMI], smoking status, diet, physical activity, blood pressure, blood cholesterol, and glycemia) to help promote ideal cardiovascular health (CVH) in the population (2). This is of primary importance, as several population-based cohort studies have reported substantial and progressive risk reduction in mortality and CVD with higher status (3–6). However, such evidence is derived from a middle-aged population.

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Although the promotion of ideal CVH should occur across the population, including those of older age (2), to the best of our knowledge, the possible benefit of ideal CVH regarding mortality and vascular events in elderly populations is yet to be evaluated. This issue is of particular importance and may have significant clinical implications, given the aging of the population worldwide, the exponential relationship of age with mortality and CVD risks, and the health-related costs attributable to CVD in the elderly population (7,8). Primordial prevention in the elderly may also contribute to extended life expectancy without disabilities (9). More specifically, elderly individuals are frequently taking several medications for chronic disease management, including hypertension, dyslipidemia, or type 2 diabetes, which may influence the prevalence of ideal CVH. Furthermore, comorbidities such as functional disability or depressive symptoms are highly prevalent in the elderly, and have been related to CVH, mortality, and vascular events (10–13). Hence, they may compromise the benefit of an ideal CVH on health in the elderly population.

Our main objective was to evaluate whether or not higher CVH status is associated with lower mortality and lower vascular event risks in an aging population. We addressed these issues in the 3C study (Three-City Study).

METHODS

The 3C study is a French, multisite, observational prospective study investigating the determinants of dementia, coronary heart disease (CHD) and stroke in initially noninstitutionalized elderly subjects (14). Between March 1999 and March 2001, 9,294 subjects aged ≥65 years were recruited from electoral rolls of 3 large French cities (Bordeaux, Dijon, and Montpellier). The study protocol was approved by the Ethics Committee of the University Hospital of Kremlin-Bicêtre and Sud-Mediterranée III. All participants gave their informed consent.

BASELINE AND FOLLOW-UP DATA COLLECTION. At baseline, trained interviewers conducted face-to-face interviews using a standardized questionnaire that included information on demographic characteristics, education, behaviors (including diet, exercise, smoking status, and alcohol consumption), and personal history of CHD (angina pectoris, myocardial infarction, or revascularization procedures) or stroke. The questionnaire also included an inventory of all medications taken over the preceding month based on medical prescriptions, medication packages, and any other relevant information to reduce under-reporting. Medication names were coded using the World Health Organization Anatomic Therapeutic Chemical classification. Brachial blood pressure was measured twice after at least 5 min of rest in a seated position, with an appropriately sized cuff placed on the right arm, using a validated digital electronic tensiometer (OMRON M4, OMRON Corp., Kyoto, Japan). Height and weight were measured in all subjects while lightly dressed. A venous blood sample was collected at baseline following an overnight fasting, and standard measures of blood lipids and glucose levels were performed.

Follow-up visits took place at 2, 4, 7, and 9 years after the baseline assessment, and permitted us to assess change in depressive symptoms and functional disability status over time. The presence of a high level of depressive symptoms was defined according to the 20-item Center for Epidemiologic Studies Depression Scale (15), using the widely employed cutoff value ≥16. Functional disability was defined as the self-reported difficulty or inability to perform at least 1 of the 8-item Instrumental Activities of Daily Living Scale without assistance (16).

CARDIOVASCULAR HEALTH. The 7 metrics of CVH were all measured at baseline examination, but not during follow-up visits. Hence, only baseline CVH status could be investigated here. Each metric was defined according to the AHA criteria except the diet and physical activity metrics, which needed adaptations (2). The definition of intermediate and poor levels of each metric, together with the diet and physical activity questionnaires, are provided in the Online Appendix and Online Table 1.

IDEAL METRICS OF CVH. Ideal BMI was defined as lower than 25 kg/m^2, and ideal smoking as those who

never smoked or who stopped smoking for at least 12 months. Physical activity was assessed through questions on the frequency of daily walking, sports activities, and recreational activities (Online Appendix). Based on the AHA definition of ≥75 min a week of vigorous activity or at least 150 min a week of moderate physical activity, ideal physical activity was defined as: 1) recreational walking for more than 2 h a day or practicing sports activities at least twice a week (in 2 study sites, Dijon and Montpellier); or 2) recreational walking for 8 h or more a week or practicing physical activity and sports activities for more than 4 h a week (in 1 study site, Bordeaux) (17). A brief food frequency questionnaire (Online Appendix) was administered at baseline to assess the dietary habits of the participants (18). Fiber and sodium intake could not be evaluated accurately in the whole 3C cohort, so the diet metric was defined on 3 instead of 5 items. Sugar-sweetened beverages were not measured. Sugar contained in alcohol was evaluated instead because it represents a main source of sugar consumed as a beverage in France, and was retrieved from detailed questions on alcohol consumption. Therefore, a subject was categorized as having an ideal diet if consuming: 1) vegetables and fresh fruits daily; *and* 2) fish twice or more a week; *and* 3) <450 kcal/week of sugar.

Ideal blood pressure was defined as untreated blood pressure of <120/80 mm Hg. Ideal total cholesterol and ideal fasting plasma glucose were defined as untreated values of <5.56 mmol/l and 5.20 mmol/l, respectively (equivalent to thresholds of <200 mg/dl and 100 mg/dl, respectively).

GLOBAL, BEHAVIORAL, AND BIOLOGICAL CVH. According to the AHA, an ideal CVH is defined by the presence of the 7 metrics at the ideal level and the absence of any previous CVD (2). Because only 1 participant met these requirements in the present study (see Results section), and consistent with previous studies, subjects having 0 to 2, 3 to 4, and 5 to 7 metrics at the ideal level were referred to as being in poor, intermediate, and ideal global CVH, respectively (3,11). Behavioral CVH comprises 4 health behaviors including BMI, smoking status, physical activity, and dietary habits; biological CVH comprises 4 health factors including blood pressure, total cholesterol, fasting plasma glucose, and smoking status (which is already considered in the behavioral CVH) (2). Participants who had 0 to 1, 2, or 3 to 4 metrics at the ideal level were defined as having poor, intermediate, and ideal behavioral or biological CVH, respectively (2).

MORTALITY STATUS AND CAUSES OF DEATH. The procedures to determine the vital status and causes of death have been previously published (19). Briefly, vital status was tracked at each follow-up, and the date of death was systematically confirmed up to the end of 2013 by the native city council or the participant's general practitioner. A 3C mortality classification committee reviewed medical records to determine the cause of death and the main associated conditions, according to the International Classification of Diseases-10th revision (ICD-10). All deaths of suspected vascular origin were reviewed by the CHD and a stroke validation committee to assign a final classification. In the present study, we classified death as death from cardiovascular, cancer, nonvascular noncancer origins, or death from unknown causes.

ASCERTAINMENT OF CHD AND STROKE. The protocol used to survey and adjudicate the occurrence of CHD and stroke events during follow-up has been described previously (20,21). At each follow-up visit, subjects were asked to report any new severe medical event or hospitalization since the last contact. For all subjects reporting possible CHD or stroke event(s), all available clinical information was collected including emergency and hospitalization reports and neuroimaging reports (for stroke), and an interview with the patient's physician or family was conducted. In deceased participants, information was obtained from general practitioner or hospital records. Finally, all possible CHD and stroke events were adjudicated by 2 independent expert committees. CHD was defined as a diagnosis of angina requiring hospitalization, hospitalized myocardial infarction, CHD death (ICD-10 codes I210–I219, I251–259, I461, and R960), or any revascularization procedure. Stroke was defined according to the criteria of the World Health Organization, as a new focal neurological deficit of sudden or rapid onset, of presumed vascular origin, lasting for 24 h or more, or causing death.

STUDY POPULATIONS. Subjects with prevalent CVD at baseline were excluded both for the analysis of mortality (Population 1) and for the analysis of incident CHD and stroke (Population 2). The study flowcharts of Population 1 and Population 2 are detailed in Online Figures 1 and 2, respectively. Participants in whom a global CVH status could not be assigned had worse baseline characteristics compared to those in whom a CVH status could be defined (Online Table 2).

STATISTICAL ANALYSIS. The characteristics by baseline CVH status were compared using age- and sex-adjusted linear or logistic regression analysis where appropriate. Unadjusted mortality rates and unadjusted incidence rates of combined CHD and stroke across baseline CVH status and by number of

TABLE 1 Baseline Characteristics by Global CVH Status

		Global Cardiovascular Health Status*			
	Overall (N = 7,371)	Poor (n = 2,870)	Intermediate (n = 4,132)	Ideal (n = 369)	p Value†
Age, yrs	73.82 ± 5.34	73.93 ± 5.18	73.86 ± 5.45	72.58 ± 5.13	<0.0001
Men	2,704 (36.68)	1,267 (44.15)	1,331 (32.21)	106 (28.73)	<0.0001
Marital status, single	2,619 (35.53)	961 (33.48)	1,523 (36.86)	135 (36.59)	0.80
Education level, ≥ Bachelor's degree	2,720 (36.90)	962 (33.52)	1,568 (37.95)	190 (51.49)	<0.0001
Depressive symptoms, CESD ≥16	1,714 (23.51)	689 (24.25)	961 (23.54)	64 (17.53)	0.0004
Body mass index, kg/m^2	25.60 ± 4.07	28.16 ± 3.64	24.11 ± 3.48	22.40 ± 2.38	<0.0001
Current smoker	420 (5.70)	308 (10.74)	111 (2.69)	1 (0.27)	<0.0001
Impaired fasting glycemia or diabetes	927 (12.60)	738 (25.80)	186 (4.50)	3 (0.81)	<0.0001
Systolic blood pressure, mm Hg	146.67 ± 21.58	151.14 ± 20.51	144.96 ± 21.25	131.04 ± 23.32	<0.0001
High density lipoprotein, mmol/l	1.63 ± 0.40	1.53 ± 0.37	1.69 ± 0.41	1.74 ± 0.41	<0.0001
Total cholesterol, mmol/l	5.85 ± 0.97	5.92 ± 0.95	5.84 ± 0.98	5.46 ± 0.92	<0.0001
Blood pressure-lowering drugs	3,440 (46.67)	1,656 (57.70)	1,704 (41.24)	80 (21.68)	<0.0001
Lipid-lowering drugs	2,155 (29.24)	1,029 (35.85)	1,059 (25.63)	67 (18.16)	<0.0001
Functional disability	566 (7.73)	253 (8.90)	301 (7.32)	12 (3.25)	0.0001

Values are mean ± SD or n (%). *Defined according to the number of ideal metrics: 0 to 2 (poor), 3 to 4 (intermediate), and 5 to 7 (ideal). †Linear and logistic regression adjusted for age and sex.

CESD = Center for Epidemiologic Studies Depression Scale; CVH = cardiovascular health.

metrics at the ideal level were plotted and compared using the log-rank test. Cause-specific hazard ratios (HRs) and 95% confidence intervals (CIs) of baseline intermediate and ideal CVH (main exposure) for all-cause and for vascular events (CHD and stroke) were estimated in separate Cox proportional hazard models, using baseline poor CVH as the reference exposure category. The same analysis was conducted for each metric. Associations with cause-specific mortality were assessed using competing risk analysis by calculating subdistribution HRs with the Fine and Gray method (22). Follow-up was censored either at the date of death, CHD or stroke event (time was censored at the first event), at the last visit, or at the end of follow-up, whichever came first. Models were adjusted for center, age, sex, education, and living alone. Analysis by metric was additionally adjusted for the other metrics. Models were then stratified by sex, age (tertiles), and study site; multiplicative terms were included in each model, and p values for interaction of <0.10 were considered significant. HRs per 1 additional metric at the ideal level were also provided. Finally, models were adjusted for time-dependent functional disability and depressive symptoms to evaluate their potential mediating effect. Analyses for the behavioral and the biological CVH were also conducted. The proportionality assumption of Cox regression analysis was verified graphically.

The following sensitivity analyses were performed to investigate the robustness of the association between CVH and combined CHD or stroke. First, missing global CVH status was imputed: 1) as being poor (worst-case scenario); and 2) using multiple imputations by fully conditional specification with SAS Proc MI and MIAnalyze (SAS Institute, Cary, North Carolina) (23). Second, to investigate reverse causality, the analysis was repeated after excluding deaths that occurred in the first 2 years of follow-up. Third, the competing effect of death on the association between CVH and vascular events was investigated using the Fine and Gray method as mentioned earlier in the text (22). Fourth, definite hospitalized angina cases were excluded from adjudicated CHD events. Last, using the total CVH score (range 0 to 14), we quantified the association of average (9 to 11) and optimal CVH (12 to 14) versus inadequate CVH (0 to 8) with all-cause mortality, CHD, and stroke.

All analyses were 2-sided and a p value <0.05 was considered as statistically significant except for the study of interaction. SAS software version 9.4 (SAS Institute) was employed.

RESULTS

BASELINE CHARACTERISTICS BY CVH STATUS. Among the 7,371 participants without prevalent CVD and with available CVH status, the mean age was 73.8 ± 5.3 years, and 37% were men. Only 1 participant had all 7 metrics at the ideal level, 48 had 6 metrics at the ideal level, and 320 had 5 metrics at the ideal level. Altogether, 5.01% of the participants had at least 5 metrics at the ideal level. As presented in Table 1, and after adjustment for age and sex, the

burden of risk factors decreased significantly with the number of metrics at the ideal level. The distribution of the metrics and of CVH overall, by sex and age, is reported in Online Table 3. Ideal blood pressure was the least frequent metric (6.16%), whereas ideal smoking was the most prevalent (93.21%). In women compared with men, all metrics except physical activity and total cholesterol were more often at ideal level. Accordingly, women more frequently than men had at least 5 metrics at the ideal level (5.64% vs. 3.92%; $p < 0.0001$). Furthermore, ideal physical activity and ideal blood pressure decreased markedly with age, whereas the opposite trend was found for ideal smoking, ideal BMI, and ideal total cholesterol. As a result, the proportion of participants with at least 5 metrics at the ideal level decreased with age, from 6.75% to 3.89% across tertiles of age (p for trend <0.001).

BASELINE CVH AND MORTALITY (POPULATION 1). After a median follow-up of 10.9 years (IQR: 8.9 to 11.7 years), among the 7,573 participants without prevalent CVD, 1,987 had died; 412 deaths were of cardiovascular origin, 559 due to cancer, 698 of noncardiovascular disease and noncancer origin, and 318 of unknown causes. The Kaplan-Meier curves indicate a graded decreased risk of all-cause mortality associated with better baseline CVH status (**Figure 1A**) and with an increasing number of ideal metrics (**Figure 1B**). In a Cox proportional hazard model adjusted for age, sex, study site, education, and living alone, intermediate (3 to 4 ideal metrics) and ideal (5 to 7 ideal metrics) CVH status were associated with a 16% (HR: 0.84; 95% CI: 0.76 to 0.92) and 29% (HR: 0.71; 95% CI: 0.55 to 0.90) decreased risk of all-cause mortality compared with poor (0 to 2 ideal metrics) CVH, respectively (p for trend <0.0001) (**Table 2**). This gradient was observed for death from cardiovascular, cancer, noncancer noncardiovascular origins and mortality of unknown causes (Online Table 4). Patterns for behavioral and biological CVH were consistent with those observed with global CVH (**Table 2,** Online Table 4). All 4 behavioral metrics were related to all-cause mortality, whereas fasting plasma glucose was the sole biological metric showing a significant association (**Table 3**). Finally, the HR for all-cause mortality decreased by 10% (HR: 0.90; 95% CI: 0.86 to 0.94) per additional metric at the ideal level (Online Table 5).

BASELINE CVH AND INCIDENT VASCULAR EVENTS (POPULATION 2). During a median follow-up of 8.6 years (IQR: 8.6 to 9.2 years), among the 7,371 participants without prevalent CVD and with available follow-up for vascular events, 680 developed a first CHD or stroke event: 257 stroke and 423 CHD events, respectively. The incidence of CHD and stroke combined decreased progressively and significantly with better baseline global CVH status (**Figure 2A**) and with an increasing number of ideal metrics (**Figure 2B**). In a Cox proportional hazard model adjusted for age, sex, study site, education, and living alone, intermediate and ideal CVH status were associated with a 31% (HR: 0.69; 95% CI: 0.59 to 0.81) and a 67% (HR: 0.33; 95% CI: 0.19 to 0.57) decreased risk of CHD and stroke combined, respectively, compared with baseline poor CVH (p for trend <0.0001) (**Table 2**). Analysis by event types showed consistent patterns for CHD and to a lesser extent for stroke.

Analysis by CVH components shows that behavioral CVH was associated significantly with CHD and stroke combined, as well as with stroke alone. Biological CVH was related to all types of vascular events (**Table 2**). Stratified analysis (**Central Illustration**) indicates that the association of intermediate and ideal global CVH with CHD and stroke combined was consistent by sex, age group, or study site, and no statistically significant interactions were noted. All metrics except physical activity and diet were significantly related to lower risk of CHD and stroke combined (**Table 3**). The 1.53-fold increase risk in CHD and stroke combined associated with intermediate smoking might include subjects who recently (<12 months) quit smoking due to an underlying medical condition. Also, the HR for CHD and stroke combined decreased by 22% (HR: 0.78; 95% CI: 0.72 to 0.84) per each additional metric at the ideal level (Online Table 5).

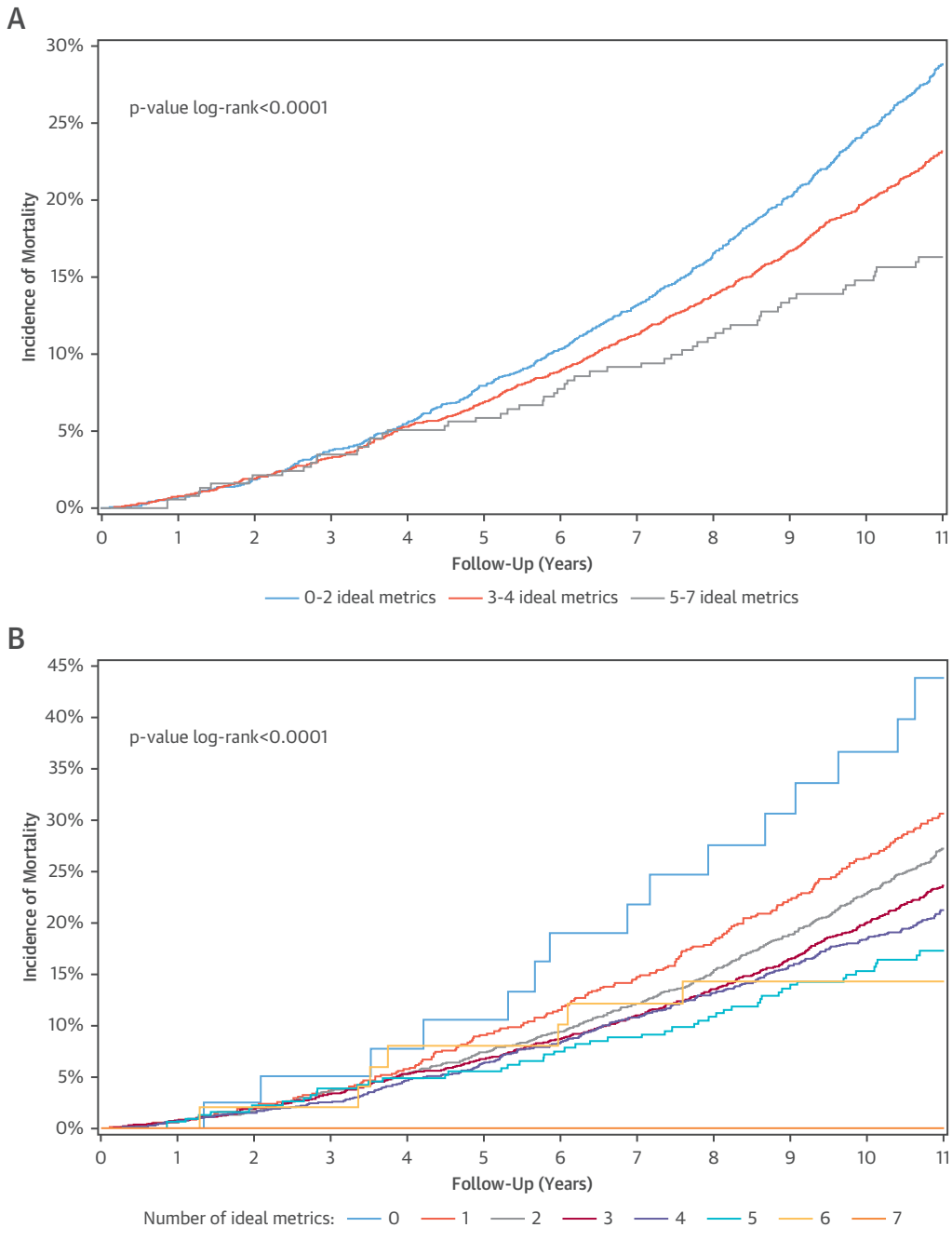
Time-dependent functional disability and a high level of depressive symptoms were each associated with CHD and stroke combined. Despite this, further adjusting the multivariable model for each variable did not influence the HRs of intermediate and ideal CVH (Online Table 6). This suggests that functional disability or depressive symptoms are unlikely to mediate the association under investigation.

SENSITIVITY ANALYSIS. The robustness of the association between baseline global CVH status and CHD and stroke combined is supported by the results of 6 sensitivity analyses (Online Tables 7 and 8).

DISCUSSION

In this French cohort of noninstitutionalized participants with an average age of 73.8 years, only 1 participant had all 7 metrics at the ideal level, and only 5.01% had at least 5 metrics at the ideal level

FIGURE 1 Unadjusted Incidence Rates of All-Cause Mortality



(A) Unadjusted incidence rates of all-cause mortality by baseline global cardiovascular health status. The presence of 0 to 2, 3 to 4, and 5 to 7 ideal metrics represents poor, intermediate, and ideal cardiovascular health, respectively. **(B)** Unadjusted incidence rates of all-cause mortality by number of metrics at the ideal level. Ideal metrics were defined according to the American Heart Association criteria (2). Kaplan-Meier curves were compared by the log-rank test, and time was censored at a point where <25% of the population had follow-up.

(**Central Illustration**). These latter subjects had a 29% decreased risk of all-cause mortality and a 67% decreased risk of CHD and stroke combined compared with those with up to 2 metrics at the ideal level.

We observed that the distribution of some CVH metrics differs in elderly subjects compared with that which is classically observed in younger people. Specifically, ideal blood pressure and ideal total

TABLE 2 HRs of Intermediate and Ideal CVH for All-Cause Mortality, CHD, and Stroke

	All-Cause Mortality		CHD or Stroke		Stroke		CHD	
	n/N	HR (95% CI)	n/N	HR (95% CI)	n/N	HR (95% CI)	n/N	HR (95% CI)
Global cardiovascular health*								
Poor	874/2,943	1.00	340/2,870	1.00	115/2,863	1.00	225/2,865	1.00
Intermediate	1,045/4,252	0.84 (0.76–0.92)	327/4,132	0.69 (0.59–0.81)	136/4,122	0.82 (0.64–1.06)	191/4,127	0.63 (0.52–0.77)
Ideal	68/378	0.71 (0.55–0.90)	13/369	0.33 (0.19–0.57)	6/368	0.45 (0.20–1.03)	7/368	0.27 (0.13–0.57)
p value for trend		<0.0001		<0.0001		0.03		<0.0001
Behavioral cardiovascular health†								
Poor	874/2,959	1.00	316/2,864	1.00	122/2,859	1.00	194/2,858	1.00
Intermediate	828/3,252	0.86 (0.79–0.95)	279/3,152	0.83 (0.70–0.97)	110/3,144	0.80 (0.62–1.04)	169/3,149	0.84 (0.69–1.04)
Ideal	288/1,372	0.75 (0.66–0.86)	96/1,345	0.72 (0.57–0.90)	29/1,340	0.53 (0.35–0.80)	67/1,342	0.85 (0.64–1.13)
p value for trend		<0.0001		0.002		0.002		0.15
Biological cardiovascular health‡								
Poor	515/1,562	1.00	211/1,518	1.00	62/1,511	1.00	149/1,516	1.00
Intermediate	1,279/5,059	0.78 (0.70–0.86)	434/4,932	0.65 (0.55–0.77)	171/4,920	0.84 (0.63–1.13)	263/4,925	0.58 (0.47–0.71)
Ideal	316/1,215	0.75 (0.66–0.87)	61/1,166	0.35 (0.27–0.47)	28/1,164	0.55 (0.35–0.85)	33/1,164	0.28 (0.19–0.41)
p value for trend		<0.001		<0.001		0.009		<0.001

n/N = number of health-related outcomes/number of subjects by level of cardiovascular health. Hazard ratios (HRs) and 95% confidence intervals (CIs) for intermediate and ideal cardiovascular health at baseline were estimated by Cox proportional hazard regression using poor cardiovascular health as the reference exposure category. Models were adjusted for age, sex, study site, education level, and living alone at baseline. *Defined according to the number of ideal metrics: 0 to 2 (poor), 3 to 4 (intermediate) and 5 to 7 (ideal). †Defined according to the number behavioral metrics at the ideal level: 0 to 1 (poor), 2 (intermediate) and 3 to 4 (ideal). ‡Defined according to the number of biological metrics (including smoking) at the ideal level: 0 to 1 (poor), 2 (intermediate) and 3 to 4 (ideal).

CHD = coronary heart disease; CVH = cardiovascular health.

cholesterol were particularly infrequent in our study. This is partly explained by the high proportion of participants using antihypertensive (almost 50%) and lipid-lowering medications (30%) at baseline. Indeed, according to the AHA definition, subjects who reach the target levels of blood pressure or total cholesterol while under medications are categorized at the intermediate level for these 2 metrics. Accordingly, the reported proportion of 5% of elderly subjects with at least 5 metrics at the ideal level is 2 to 3 times lower than what has been reported in the younger populations (3-6). Similarly, whereas women more frequently had at least 5 metrics at the ideal level compared with men in the present study, the sex differences were less marked than in the younger populations (1.5 times higher in elderly vs. 2 to 4 times higher in younger populations) (24).

So far, only 2 large community studies have reported the distributions of the metrics of CVH in the elderly population (25,26). When comparing metrics with the same definitions, we noted that ideal total cholesterol was 2 times more prevalent in the Spanish study, whereas ideal smoking or ideal fasting plasma glucose and ideal BMI were 1.5 and 2.5 times, respectively, more prevalent in the 3C study (25). The absence of sex stratification in the Spanish study may partly explain this heterogeneity. In NHANES (National Health And Nutritional Evaluation Survey), the distributions of ideal metrics were tabulated by sex, permitting a more direct comparison with the 3C study (26). In women, ideal BMI and ideal fasting glycemia were 1.5 and 2 times, respectively, more frequent in the 3C study, whereas the opposite trends were observed for ideal blood pressure and ideal total cholesterol. In men, similar trends were observed between the 2 studies.

To the best of our knowledge, our study is the first to specifically investigate the association of CVH with mortality and vascular events in elderly people. Recent studies in the elderly have shown that even at 65 and 75 years of age, with the number of risk factors at optimal levels, the remaining lifetime risks of death from CVD decrease whereas the remaining lifetime risks of CVD disease free and of survival after CVD markedly increase (27,28). However, only 4 risk factors—smoking, diabetes, blood pressure, and blood cholesterol—were considered. Two other studies in the elderly have focused on lifestyle risk factors and have shown a linear relationship between the number of lifestyle risk factors at optimal levels and the risk of all-cause and cause-specific mortality or incident type 2 diabetes (29,30). By combining lifestyle and health factors using the AHA 7-item tool, we investigated an extended risk factors profile. Furthermore, by showing a graded and substantial decreased risk of mortality and of vascular events as a function of the number of metrics at the ideal level, our study results are consistent with those reported in younger persons (3-6). Interestingly, in our study, this risk reduction in mortality and vascular events was consistent

TABLE 3 HRs of Intermediate and Ideal CVH for All-Cause Mortality and for CHD and Stroke Combined: Analysis by Metric

	All-Cause Mortality			CHD or Stroke		
	n/N	HR* (95% CI)	HR† (95% CI)	n/N	HR* (95% CI)	HR† (95% CI)
Smoking status	2,320/8,368			765/8,075		
Poor	177/474	1.00	1.00	55/452	1.00	1.00
Intermediate	35/99	0.92 (0.64–1.32)	0.76 (0.51–1.15)	18/96	1.53 (0.90–2.60)	1.45 (0.81–2.60)
Ideal	2,108/7,795	0.65 (0.56–0.76)	0.63 (0.53–0.74)	692/7,527	0.74 (0.56–0.98)	0.76 (0.56–1.03)
p value for trend		<0.0001	<0.0001		0.008	0.03
Body mass index	2,268/8,281			755/7,999		
Poor	327/1,088	1.00	1.00	101/1,052	1.00	1.00
Intermediate	870/3,180	0.83 (0.73–0.94)	0.86 (0.74–0.99)	340/3,071	1.05 (0.84–1.31)	1.23 (0.96–1.58)
Ideal	1,071/4,013	0.83 (0.74–0.95)	0.91 (0.79–1.06)	314/3,876	0.82 (0.65–1.03)	1.08 (0.83–1.40)
p value for trend		0.03	0.62		0.01	0.92
Physical activity	1,989/7,558			685/7,339		
Poor	669/1,900	1.00	1.00	186/1,823	1.00	1.00
Intermediate	932/3,797	0.81 (0.73–0.90)	0.81 (0.73–0.91)	345/3,692	0.91 (0.76–1.10)	0.93 (0.77–1.12)
Ideal	388/1,861	0.70 (0.61–0.79)	0.71 (0.62–0.81)	154/1,824	0.84 (0.67–1.04)	0.84 (0.67–1.06)
p value for trend		<0.0001	<0.0001		0.11	0.14
Healthy diet score	2,313/8,359			764/8,070		
Poor	1,389/4,725	1.00	1.00	463/4,552	1.00	1.00
Intermediate	706/2,673	0.90 (0.82–0.99)	0.99 (0.89–1.10)	227/2,581	0.91 (0.78–1.07)	0.99 (0.83–1.17)
Ideal	218/961	0.84 (0.72–0.97)	0.94 (0.81–1.11)	74/937	0.91 (0.71–1.16)	0.92 (0.70–1.22)
p value for trend		0.003	0.52		0.25	0.61
Total cholesterol	2,126/7,875			712/7,649		
Poor	680/2,684	1.00	1.00	252/2,608	1.00	1.00
Intermediate	1032/3,986	0.93 (0.84–1.02)	0.94 (0.84–1.04)	356/3,894	0.82 (0.70–0.96)	0.82 (0.69–0.98)
Ideal	414/1,205	1.09 (0.96–1.23)	1.07 (0.93–1.22)	104/1,147	0.71 (0.56–0.90)	0.70 (0.54–0.89)
p value for trend		0.42	0.55		0.002	0.002
Blood pressure	2,306/8,352			764/8,068		
Poor	1,528/5,196	1.00	1.00	532/5,027	1.00	1.00
Intermediate	686/2,639	1.03 (0.94–1.13)	1.03 (0.93–1.15)	214/2,544	0.90 (0.77–1.06)	0.90 (0.75–1.07)
Ideal	92/517	0.86 (0.69–1.06)	0.94 (0.74–1.19)	18/497	0.41 (0.26–0.66)	0.46 (0.27–0.77)
p value for trend		0.65	0.89		0.0009	0.007
Fasting blood glucose	2,117/7,851			707/7,627		
Poor	162/385	1.00	1.00	76/367	1.00	1.00
Intermediate	361/1,152	0.76 (0.63–0.92)	0.80 (0.65–0.99)	137/1,118	0.58 (0.44–0.77)	0.52 (0.39–0.70)
Ideal	1,594/6,314	0.63 (0.53–0.74)	0.69 (0.58–0.84)	494/6,142	0.39 (0.31–0.50)	0.37 (0.29–0.48)
p value for trend		<0.0001	<0.0001		<0.0001	<0.0001

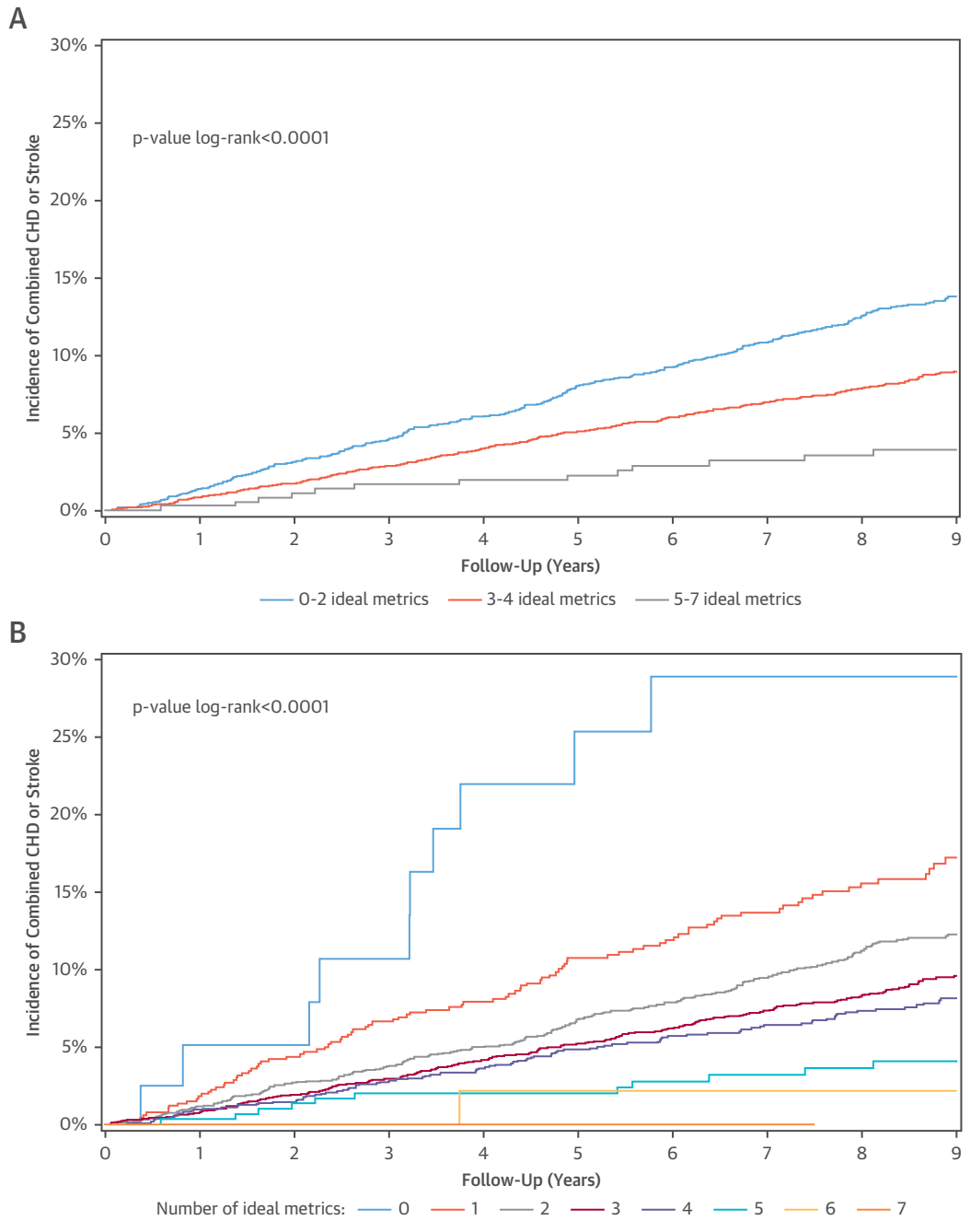
n/N = number of death or CHD and stroke combined/number of subjects by level of each metric. The HRs and 95% CIs of each metric were estimated in separate Cox proportional hazard regression model. *HRs were adjusted for age, sex, study site, education level and living alone status at baseline, using the poor level as the reference exposure category. †HRs were further adjusted for the other metrics.

Abbreviations as in Table 2.

across age groups, emphasizing the benefit of primordial prevention even in the elderly.

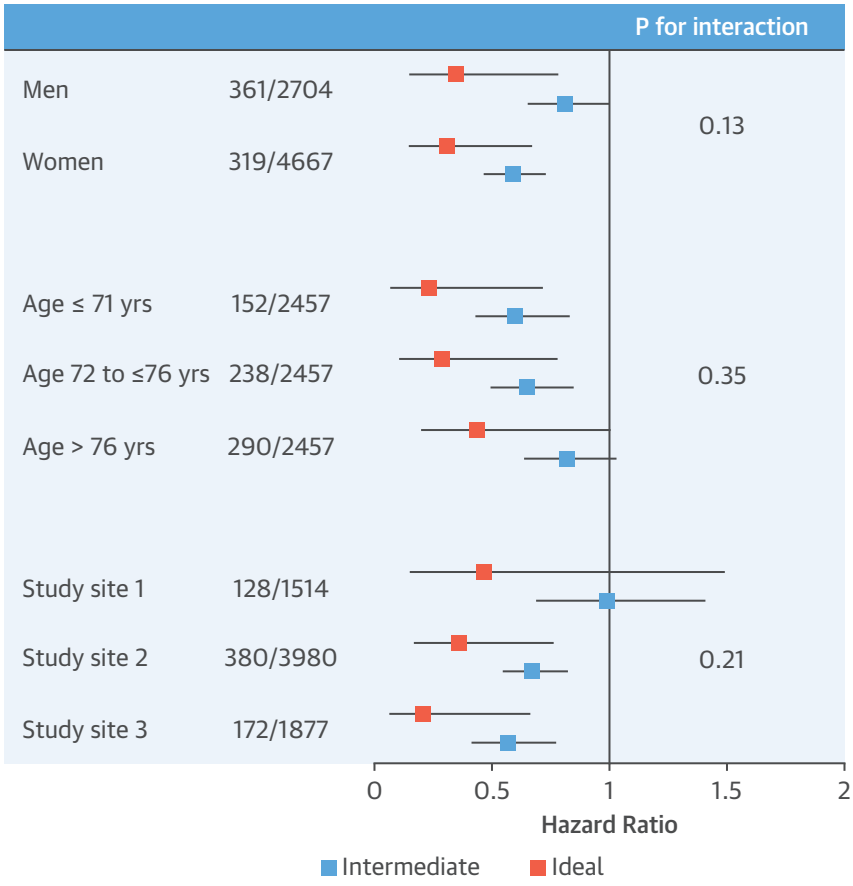
CLINICAL IMPLICATIONS. It should be stressed that the association between CVH and outcomes was linear, so that even intermediate CVH or the gain of 1 additional ideal metric was systematically associated with favorable outcomes. Hence, whereas promoting ideal CVH is the ultimate goal, a more conservative and perhaps realistic goal in the short term could be to promote intermediate CVH and/or to encourage the progressive attainment of ideal metrics 1 at a time. The most efficient ways to promote intermediate and/or ideal CVH in the elderly population remain to be defined. However, there is evidence supporting that moderate physical activity, smoking cessation, and optimal diet are beneficial for optimal cardiovascular function and for the prevention of CVD morbidity and mortality in older adults (31-34). The attainment of 90% of ideal smoking in our study and in the NHANES participants over 65 years on the one hand, and the low prevalence of ideal physical activity and optimal diet on the other, suggest that particular efforts should be made on these 2 latter metrics. This may

FIGURE 2 **Unadjusted Incidence Rates of CHD and Stroke Combined**



(A) Unadjusted incidence rates of coronary heart disease and stroke combined by baseline global cardiovascular health status. The presence of 0 to 2, 3 to 4, and 5 to 7 ideal metrics represents poor, intermediate, and ideal cardiovascular health, respectively. **(B)** Unadjusted incidence rates of coronary heart disease and stroke combined by number of metrics at the ideal level. Ideal metrics were defined according to the American Heart Association criteria (2). Kaplan-Meier curves were compared by the log-rank test, and time was censored at a point where <25% of the population had follow-up.

CENTRAL ILLUSTRATION **Stratified Analysis of Baseline Global CVH Status for CHD and Stroke Combined**



Gaye, B. et al. J Am Coll Cardiol. 2017;69(25):3015–26.

Global cardiovascular health (CVH) status was defined according to the numbers of ideal metrics: 0 to 2 (poor), 3 to 4 (intermediate), and 5 to 7 (ideal). In each stratum, the ratios represent the number of clinical events over the number of subjects present in the stratum. Hazard ratios and 95% confidence intervals (CIs) for intermediate and ideal cardiovascular health at baseline were estimated by Cox proportional hazard regression using poor cardiovascular health as the reference exposure category. Models were adjusted for age (where appropriate), sex (where appropriate), study site (where appropriate), education level, and living alone at baseline. The p value for interaction was obtained by including a multiplicative term in the model. CHD = coronary heart disease.

also impact the level of blood pressure, which was the least prevalent ideal metric in the current study.

STUDY LIMITATIONS. By design, only those who survived until at least 65 years of age could be recruited. The 3C study participants are also healthier and in higher socioeconomic status than their counterparts of similar age (14). Taken together, it is likely that the prevalence of subjects with at least 5 ideal metrics is overestimated, but this should not affect the associations between CVH and health-related outcomes observed. In the absence of repeated assessment of all of the 7 metrics during follow-up interviews, the extent to which change in CVH also affected mortality and vascular events risks could not be evaluated in the current study. As in many large prospective studies, the physical activity and diet metrics were exposed to misclassification bias. However, it is unlikely to be differential with respect to the outcomes, thus biasing associations towards the null. Finally, heart failure has not been adjudicated in the 3C study, but ideal CVH has been recently related to a lower risk of incident heart failure (35). We therefore may have underestimated the benefit of

ideal CVH on a more general CVD risk in elderly subjects.

CONCLUSIONS

This study shows for the first time the benefit of higher CVH on mortality and vascular event risk in the elderly population. Our results support the AHA statement that primordial prevention should be proposed to all segments of the population, including the elderly.

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PERSPECTIVES

COMPETENCY IN SYSTEMS-BASED PRACTICE: Although the influence of cardiovascular health on health-related outcomes is established for middle-aged people, the high prevalence of comorbidities and prescription of medication in older individuals might attenuate the reduction in mortality and vascular events. In noninstitutionalized participants at an average age of 73.8 years, those with at least 5 metrics at an ideal level had a 29% lower risk of all-cause mortality and a 67% lower risk of coronary events and stroke combined compared with those with 2 or fewer metrics at the ideal level.

TRANSLATIONAL OUTLOOK: Future studies should investigate how changes in cardiovascular health affect a wider spectrum of outcomes prevalent in the elderly, including heart failure and dementia.

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KEY WORDS cardiovascular health, elderly, primordial prevention, vascular events

APPENDIX For an expanded Methods section as well as supplemental tables and figures, please see the online version of this article.