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# A priori– defined dietary patterns and markers of cardiovascular disease risk in the Multi-Ethnic Study of Atherosclerosis (MESA)<sup>2</sup>

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# Abstract

**Background**—The level of detail regarding the dietary intake necessary to characterize associations between diet and cardiovascular disease (CVD) risk is uncertain.

**Objective**—We evaluated a unique a priori– defined dietary pattern in relation to several traditional and novel CVD risk factors.

**Design**—At the baseline examination, diet (by food-frequency questionnaire), markers of inflammation, subclinical atherosclerosis, renal disease, vascular compliance, and other traditional risk factors were measured in 5089 men and women aged 45–84 y without clinical CVD or diabetes from the Multi-Ethnic Study of Atherosclerosis (MESA). We defined a Comprehensive Healthy Dietary Pattern by summing weighted categorical ranks of 36 narrowly defined food groups (21 rated favorably with categorical ranks × +1.0 and 15 rated unfavorably with categorical ranks × -1.0). We also defined a Simplified Healthy Dietary Pattern composed of 3 favorable (whole grains, fruit, and seeds and nuts) and 3 unfavorable (added fats and oils, processed meats, and fried potatoes) food groups using similar scoring techniques and determined the difference between the comprehensive and simplified scores.

**Results**—The Comprehensive Healthy Dietary Pattern was associated with lower urinary albumin:creatinine ratios, common carotid intima-media thickness, measures of adiposity, and inflammatory marker, triacylglycerol, and insulin concentrations. The magnitudes of most of the associations were similar between the 2 dietary patterns, but some differences were observed between scores. Dietary patterns were not associated with blood pressure, coronary artery calcification, internal carotid intima-media thickness, or the ankle brachial index.

**Conclusions**—Many food groups contribute to the characterization of relations with a variety of CVD risk markers, although only 6 food groups contribute much of the information in MESA.

# INTRODUCTION

In the past decade, nutritional epidemiology has experienced a shift in focus from investigations at the level of individual nutrients to investigations at the level of foods and dietary patterns

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(1). This shift is driven by several practical considerations. First, the effects of individual nutrients may not be equivalent when foods containing many nutrients are consumed or when foods are consumed as part of a larger dietary pattern containing many foods (2,3). Second, the magnitude of the effect of individual nutrients is often too small to overcome the noise of confounding and imprecise measurement, whereas the sum effect of many foods may be sufficiently large (1). Third, correlations among nutrients and among foods are often too high to allow their individual effects to be accurately determined with traditional statistical approaches. Regardless, reductive approaches potentially misrepresent the reality of the human diet.

Two main approaches to characterizing dietary patterns are commonly used: those that are determined a priori (eg, Healthy Eating Index, Recommended Food Score, and Diet Quality Index) and those that are derived a posteriori (eg, principal components or cluster analyses) (4). One key advantage of the latter approach is that it takes into account many aspects of the diet rather than focusing on a few hypothesized key food groups. Furthermore, food groups used in most a priori scores are usually broadly defined and do not take into account subtle differences in the nutrients and phytochemicals in individual food items (eg, all vegetables, or potatoes). A focus on broad groupings may result in important distinctions being missed. On the other hand, a posteriori dietary patterns do not build on previous research and thus do not appraise current diet-disease paradigms.

Our aim was to evaluate a unique approach to characterizing dietary patterns previously described by Lockheart et al (5), which takes into account prior research findings and includes narrowly defined food groups distinguished by nutrient and phytochemical characteristics. We tested the predictive validity of this approach in the Multi-Ethnic Study of Atherosclerosis (MESA) by cross-sectionally assessing associations between the a priori– defined dietary pattern and cardiovascular disease (CVD) risk factors and markers of subclinical disease. We additionally evaluated whether a similar, but simplified, dietary pattern that uses fewer narrowly defined food groups would comparably capture relations with CVD risk markers.

# SUBJECTS AND METHODS

#### Subjects

The Multi-Ethnic Study of Atherosclerosis (MESA) is a population-based study of 6814 white, African American, Hispanic, and Asian men and women aged 45–84 y, who were free of clinical CVD at baseline. Data were collected between 2000 and 2002 at 6 field centers: Baltimore City and County, MD; Chicago, IL; Forsyth County, NC; New York, NY; Los Angeles County, CA; and St Paul, MN (6). Each field center's Institutional Review Board approved the protocol, and all participants gave informed consent. Our cross-sectional investigation included 5042 men and women, excluding individuals with diabetes mellitus (n = 922) (7), with macroalbuminuria (n = 121), who were currently taking oral steroid or antiinflammatory asthma medications (n = 134), and who provided insufficient or implausible dietary information (n = 618) (8).

# **Dietary assessment**

Each participant completed a self-administered, 120-item, modified-Block style food frequency questionnaire (8–10). Daily frequency responses were weighted according to reported serving sizes (small: frequency  $\times$  0.5; medium: frequency  $\times$  1.0; large: frequency  $\times$  1.5) and consequent servings/d were then categorized into 47 food groups (Appendix A).

# A priori comprehensive healthy dietary pattern

The Comprehensive Healthy Dietary Pattern was defined a priori by consensus of the participating authors. Each of the 47 food groups defined by Nettleton et al (8) (Appendix A) were rated (considering CVD-nutrition research literature) as positive (anticipated to have favorably affect CVD outcomes), negative (anticipated to adversely affect CVD outcomes), or neutral (anticipated to neither favorably nor adversely affect CVD outcomes). Food groups were divided into range-dependent intake categories (details in Appendix A) and weighted according to their author-defined ratings (+1 for "positive" food groups and -1 for "negative "food groups). Food groups rated as "neutral" did not contribute to the overall Comprehensive Healthy Dietary Pattern score. Twenty-one of the 47 food groups were rated as positive, 15 as negative, and 11 as neutral. Individuals were assigned a total score based on their category rank for each food groups. Scores were examined continuously and by quintile categories.

# Simplified Healthy Dietary Pattern

To assess whether reducing the number of food groups included in the score would capture similar relations with outcomes, we created a Simplified Dietary Pattern based on intake of 6 food groups (divided into sample-dependent quartiles as above, *see* Appendix A). Three of the 6 food groups selected for inclusion in the Simplified Healthy Dietary Pattern were previously identified as positive-loading food groups in a healthy dietary pattern derived by principal components analysis (8): whole grains, fruit, and nuts/seeds (categorical ranks multiplied by + 1). The other 3 food groups selected were previously identified as positive-loading food groups in a Western-like dietary pattern derived by principal components analysis (8): added fats and oils, processed meats, and fried potatoes (categorical ranks multiplied by -1). The resulting Simplified Healthy Pattern scores were examined continuously and by quintile categories.

To characterize the portion of the Comprehensive Healthy Dietary Pattern not included in the Simplified Healthy Dietary Pattern, we calculated the difference between scores: Comprehensive Healthy Dietary Pattern score – Simplified Healthy Dietary Pattern score.

#### **Baseline CVD biomarkers**

C-reactive protein (CRP), fibrinogen antigen, interleukin-6 (IL-6), and homocysteine were measured as previously described (8,11). Analytic CVs were 3.6%, 2.6%, 6.3%, and 4.5% for CRP, fibrinogen antigen, IL-6, and homocysteine, respectively. Urinary albumin and creatinine concentrations were assayed from one untimed urine sample at the Fletcher Allen Health Care Clinical Chemistry Laboratory (Burlington, VT). Ratios of urinary albumin ( $\mu$ g/mL) to creatinine (mg/mL) (ACR) were calculated, correcting for known sex differences in creati-nine excretion (creatinine  $\times$  0.68 formen and creatinine  $\times$  1.00 for women) (12,13). Microalbuminuria was defined as an ACR of 25–249 mg/g and macroalbuminuria (exclusionary criterion) as an ACR  $\geq$  250 mg/g. Total and HDL-cholesterol, triacylglycerol, insulin, and glucose concentrations were measured directly with reagents from Roche Diagnostics, Indianapolis, IN (analyzed at the Collaborative Studies Clinical Laboratory, Fairview-University Medical Center, Minneapolis, MN), and LDL cholesterol was calculated with the Friedewald equation for specimens with a triacylglycerol value <400 mg/dL (14).

# Carotid artery plaque, coronary artery calcification, and intima-media thickness of the common and internal carotid arteries

Intima-media thickness (IMT) of the common carotid artery (CC-IMT) and of the internal carotid artery (IC-IMT) was determined by high-resolution B-mode ultrasonography (Logiq 700 ultrasound machine; GE Medical Systems, Waukesha WI). IMT was calculated at the

Coronary artery calcification (CAC) was measured by computed tomography (CT) with cardiac-gated (at 80% of the R-R interval) electron beam scanners at 3 centers (Imatron C-150; Imatron Inc, San Francisco, CA) (15) and with a prospective electrocardiogram-triggered scan acquisition at 50% of the R-R interval with multidetector scanners (16) at the remaining 3 centers. These scanners are comparable in their ability to measure calcium (17). Scans were read centrally (Harbor–University of California Medical Center, Los Angeles, CA). CAC scores (Agatston scores) were determined by blinded CT analysts. CAC presence was defined as an Agatston score > 0.

# Ankle brachial index

The ankle brachial index (ABI) was determined by measuring blood pressure with a Doppler probe in the bilateral brachial, dorsalis pedis, and posterior tibial arteries (18). Ratios were calculated separately for the left and right side, and the minimum ratio was used for analyses. An ABI < 0.9 indicated the presence of subclinical disease.

# Large and small artery elasticity

Arterial wave forms were recorded using the HDI/PulseWave CR2000 (Hypertension Diagnostics Inc, Minneapolis, MN) (19). Pulse contour of the radial artery of the dominant arm was measured with a tonometer. Once a stable measurement was achieved, a 30-s analog tracing of the radial waveform, excluding the dicrotic notch, was digitized at 200 samples per second. Before, during, and after the waveform assessment, oscillatory systolic and diastolic blood pressure measurements were also taken on the contralateral arm (oscillatory device built in HDI/PulseWave CR2000). Large artery elasticity (LAE) and small artery elasticity (SAE) were calculated from the measured pulse contour, oscillatory systolic and diastolic blood pressures, participants' age, sex, height, and weight using software from the manufacturer of the device.

# Other CVD risk factors

Resting seated blood pressure was measured 3 times with a Dinamap model Pro 100 automated oscillometer (Critikon, GE Healthcare, Little Chalfont, United Kingdom). The average of the last 2 measures was used in the analyses. Body mass index (BMI; in kg/m<sup>2</sup>) was calculated from measured weight and height, and waist circumference was measured at the umbilicus and rounded to the nearest centimeter. Baseline demographics, education history, medication use, smoking history, and physical activity were ascertained by self-report. Medication use was additionally assessed by medication bottle inventory.

# Statistical analyses

We calculated unadjusted means and frequencies of demographics and lifestyle characteristics and energy-adjusted nutrient intakes according to quintiles of the Healthy Dietary Pattern (SAS PROC GLM; SAS Institute, Cary, NC). We assessed associations between the Healthy Dietary Pattern and the following outcomes: markers of inflammation (CRP, IL-6, homocysteine, and fibrinogen), markers of subclinical atherosclerosis (IC-IMT, CC-IMT, carotid plaque, CAC score, and ABI), markers of vascular integrity (ACR, LAE, and SAE), lipids (HDL cholesterol, LDL cholesterol, and triacylglycerols), systolic and diastolic blood pressure, fasting glucose, insulin, BMI, and waist circumference. The analyses were repeated for the Simplified Healthy Dietary Pattern, and the difference between scores on the 2 dietary patterns (comprehensive – simplified scores). Because of skewed distributions, we transformed markers of inflammation, markers of vascular integrity, IMT, and triacylglycerols to the natural log scale for analyses and present geometric means with 95% CIs. We similarly accounted for skewness in CAC; however, to accommodate zeros and other small values, we added 1.00 before transformation.

We used a general linear model regression to assess cross-sectional associations between the dietary patterns and continuous outcome variables and logistic regression to assess associations between dietary patterns and dichotomous outcome variables. Our first multivariable model (model 1) included energy intake (kcal/d), study center, age (y), sex, and race-ethnicity (white, black, Hispanic, and Chinese). To model 2 we added education (less than high school, high school, and more than high school), physical activity (active and inactive leisure, in metabolic equivalents per min/wk), smoking (current or not current and pack years), and supplement use (weekly or more). Models for LAE and SAE were additionally corrected for height (m), weight (kg), and systolic blood pressure (mm Hg). Finally, we explored the effect of adjusting for waist circumference, because it may be informative to know how much of a given association can be mediated through this well-known diet-disease pathway. All analyses were performed with SAS version 9.1 (SAS Institute Inc).

# RESULTS

#### Participant characteristics and nutrient intakes

Characteristics generally considered to be "lower risk" or "heart healthy" behaviors were associated with higher scores on the Healthy Dietary Pattern (Table 1). For example, participants in the highest quintile of the Healthy Dietary Pattern were more likely to be female, active in their leisure time, and regularly take multivitamins and to be less likely to smoke and to have a lower BMI and waist circumference. In contrast, age increased across quintiles. Representation by the Chinese increased across quintiles, whereas representation by blacks decreased across quintiles. Intakes of saturated fat and *trans* fat were lower across quintiles of the Healthy Dietary Pattern, and intakes of fiber, calcium, folate, vitamin C, and  $\beta$ -carotene were higher across quintiles.

# Markers of inflammation

After adjustment for demographics and lifestyle characteristics (model 2), the Healthy Dietary Pattern was inversely associated with concentrations of CRP, IL-6, homocysteine, and fibrinogen (P < 0.001-0.05; Table 2). With the exception of fibrinogen, these associations remained statistically significant after adjustment for waist circumference (P = 0.002-0.04).

# Markers of subclinical atherosclerosis

Of the 5 markers of subclinical atherosclerosis studied, only CC-IMT measures differed significantly across quintiles of the Healthy Dietary Pattern after multivariable adjustment (P = 0.007;  $\approx 1.5\%$  lower CC-IMT in participants in quintile 5 than in participants in quintile 1; Table 2). This association did not withstand adjustment for waist circumference (P = 0.09) but maintained significance with adjustment for systolic and diastolic blood pressure (P = 0.003; data not shown).

# Markers of vascular integrity

Urinary ACR was inversely associated with Healthy Dietary Pattern scores before (P = 0.005) and after adjustment for waist circumference (P = 0.02) or blood pressure (P = 0.003). However, neither LAE nor SAE was associated with the Healthy Dietary Pattern in the multivariable-adjusted model (P > 0.10; Table 2).

#### Lipids

Concentrations of HDL cholesterol were positively associated, and triacylglycerols inversely associated, with the Healthy Dietary Pattern after multivariable adjustment (P = 0.002 and 0.01, respectively, Table 2). Associations were no longer significant after accounting for differences in waist circumference (P = 0.20 and 0.33 for HDL cholesterol and triacylglycerols, respectively). Concentrations of LDL cholesterol did not differ across quintiles of the Healthy Dietary Pattern.

# Other CVD risk factors

Fasting insulin, BMI, and waist circumference were each inversely associated with the Healthy Dietary Pattern after adjustment for demographics and lifestyle confounders (P < 0.001; Table 2). The inverse association with insulin remained statistically significant even after adjustment for differences in waist circumference (P < 0.001). Fasting glucose and systolic and diastolic blood pressure were not associated with the Healthy Dietary Pattern.

# **Simplified Healthy Dietary Pattern**

The Simplified Healthy Dietary Pattern composed of 6 food groups and the comprehensive Healthy Dietary Pattern were highly correlated (r = 0.72, P < 0.001). Agreement of quintile classification between the comprehensive and simplified dietary patterns was 41%, and only 5 participants were reclassified in extreme quintiles by the alternate method. Food groups included in the Comprehensive Healthy Dietary Pattern were significantly correlated with those in the Simplified Dietary Pattern (P < 0.0001-0.04), except for tomatoes (P = 0.59) and cottage/ricotta cheese (P = 0.31). However, the correlation coefficients for 4 foods that were rated as "healthy" in the Comprehensive Healthy Dietary Pattern (beer, other alcohol, coffee, and poultry) were negative. Similar to the distribution of demographics and lifestyle characteristics across quintiles of the comprehensive Healthy Dietary Pattern, older age, female sex, greater physical activity, lower BMI, and nonsmoking status were each associated with higher scores on the Simplified Healthy Dietary Pattern (data not shown).

Consistent with the high degree of correlation between the 2 dietary patterns, multivariableadjusted associations between the Simplified Healthy Dietary Pattern and the markers of CVD risk studied were in a direction and magnitude similar to those observed for the Comprehensive Healthy Dietary Pattern (data not shown). Exceptions included weaker associations between the Simplified Healthy Dietary Pattern and HDL cholesterol ( $\beta \pm$  SE per score SD (3.52): 0.08  $\pm$  0.2, P = 0.72) but stronger associations with SAE ( $\beta \pm$  SE per 1 SD = 0.03  $\pm$  0.01, P < 0.001), carotid plaque (odds ratio per 1 SD: 0.90; 95% CI: 0.84, 0.96; P = 0.003), and LDL cholesterol ( $\beta \pm$  SE per 1 SD =  $-1.0 \pm 0.4$ , P = 0.016).

To evaluate whether the Comprehensive Healthy Dietary Pattern contributed information beyond that of the Simplified Healthy Dietary Pattern, we calculated regression coefficients (or odds ratios) for the portion of the Comprehensive Healthy Dietary Pattern score contributed by food groups not included in the Simplified Dietary Pattern score (Comprehensive Healthy Dietary Pattern score – Simplified Healthy Dietary Pattern score) with multivariable adjustment including the Simplified Healthy Dietary Pattern score (Table 3). These data showed that the Comprehensive Healthy Dietary Pattern contributed significantly beyond the Simplified Healthy Dietary Pattern score, and insulin (P < 0.003). When adjusted for the difference between scores, the Simplified Dietary Pattern was no longer independently associated with IL-6 (P = 0.06), CC-IMT (P = 0.06), or triacylglycerol (P = 0.17).

# DISCUSSION

Considering current knowledge of diet-CVD associations, we created a dietary pattern reflecting a cardioprotective balance among 36 food groups: 21 food groups rated as positive and 15 food groups rated as negative. We evaluated associations between this dietary pattern and CVD risk markers. By incorporating many narrowly defined food groups, this Comprehensive Healthy Dietary Pattern included a greater number of narrowly defined food groups than traditional a priori dietary patterns and was strongly associated with several markers of CVD risk in MESA. A simplified version of this score that included only 6 food groups captured some, but not all, of the information in the Comprehensive Dietary Pattern with respect to CVD risk markers.

Previous studies showed that composite dietary pattern variables characterized by a high intake of fiber-rich plant foods and a low intake of processed and saturated-fat-rich foods are favorably associated with biomarkers of inflammation (8,20–25), plasma lipids (23,26,27), measures of glycemia (21,23,28–30), and IMT (31,32). On the basis of these studies and on studies that evaluated individual foods or nutrients (11,33–45), we created a comprehensive dietary pattern favoring the consumption of whole grains, low-fat dairy foods, fruit and vegetables, fish, and nuts to the consumption of red meat, high-fat dairy foods, and processed foods. In a recent Norwegian case-control study of myocardial infarction, Lockheart et al (5) used a similar approach to define a healthy, plant-centered dietary pattern based on the intake of 28 food groups that is associated with a lower risk of MI.

We also created a reduced version of the Comprehensive Healthy Dietary Pattern (Simplified Healthy Dietary Pattern) composed of 6 food groups derived by a previous principal components analysis in this cohort (8). Although the Comprehensive Healthy Dietary Pattern included more food groups (36), associations with CVD risk markers were generally similar between the Comprehensive and Simplified Healthy Dietary Patterns. The success of the Simplified Healthy Dietary Pattern in terms of predictive validity was likely due, in part, to high correlations among like foods. Although the combination of the 6 food groups composing the Simplified Healthy Dietary Pattern were, in their own right, strongly related to more than half of the CVD risk markers studied, food groups not included in the simplified pattern contributed further information in the case of some risk markers. Furthermore, differences between the comprehensive and simplified patterns in their associations with certain outcomes, such as HDL cholesterol, may be due to qualitative differences in the way particular food groups were characterized in each. Alcohol intake was rated favorably in the comprehensive pattern but was inversely correlated with the simplified pattern. Alcohol intake is generally positively associated with HDL cholesterol and was also the case here (every one serving per day of total alcohol intake alone was associated with a significant 3.1-mg/d increase in HDL cholesterol), which provides a possible explanation for the discrepancy between patterns in terms of HDL cholesterol.

The theoretical advantage of studying a dietary pattern characterized by fewer food groups is that it more readily lends itself to application across populations (46). Our results also suggest that a more rigorous assessment of fewer food groups may be a reasonable approach for studies seeking to lessen participant burden or for which time and resources are limited. However, the utility of this approach needs to be assessed across several populations before this can be established. We characterized our Simplified Healthy Dietary Pattern on the basis of a principal components analysis. Thus, by design, the component foods were known to be markers of variation in dietary intake in MESA. These same foods may not have similar predictive values in another data set, because food usage patterns of a population (correlation among foods) may differ greatly as a function of geographical location, participant sex, age, or disease status.

In the process of investigating our methodologic questions related to dietary pattern design, we also noted generally weak, to nonexistent, associations between dietary pattern and measures of coronary and carotid atherosclerosis, arterial elasticity, and ABI. Although it may be that acute diet-disease marker associations are adequately captured with a cross-sectional design, chronic, long-developing conditions, such as atherosclerosis, are more likely influenced by exposures of years past (47,48). Although diet generally tracks well over several years in a stable population (49), secular trends in the food supply, changes in population-level dietary recommendations, and individual-level changes in response to life course events may cause dietary intake reported at baseline to inadequately represent lifetime dietary exposures (50,51). In general, previous prospective studies have had better success in predicting atherosclerotic development from dietary intake (31). Although MESA participants underwent a second assessments of CAC and IMT 2 or 4 y after baseline ( $\approx$ 50% of the cohort at each time point), there were no associations between dietary patterns and these follow-up measures (data not shown), which may have been attributable to an inadequate duration of follow-up compared with the 12-y follow-up in a previous study (31). As more studies begin to include repeated measures of atherosclerosis, our understanding of the role of diet in this process will mature.

Our study is not without limitations. First, some degree of subjectivity was involved when rating food groups as positive or negative, although we attempted to balance this by surveying multiple authors and reaching a consensus. Nevertheless, it is possible that food groups not included in the Simplified Healthy Dietary Pattern may have been rated incorrectly in the Comprehensive Healthy Dietary Pattern. Furthermore, inclusion of food groups with only weak associations with outcomes may lessen the predictive validity of a comprehensive dietary pattern score such as ours. Second, as with most observational studies relying on FFQ data, measurement error and misclassification are likely. However, in most cases (especially here with respect to markers of subclinical diseases), this type of error would be nondifferential, biasing estimates to the null. Third, with respect to associations with CVD risk markers, we cannot define causality, given our cross-sectional design. Similarly, risk factor level awareness of routinely assessed clinical variables, such as blood pressure, may have attenuated associations with dietary intake. Last, we conducted multiple statistical comparisons without correction, although we observed a larger number of significant associations than would be expected by chance alone. Likewise, some of the noted differences in outcome associations between comprehensive and simplified healthy dietary patterns may have been simply due to the play of chance rather than to important underlying differences in the biological effects of the foods composing each dietary pattern.

As a whole, the data we present show that present knowledge of the associations between nutrition and CVD risk can appropriately identify a "heart healthy" dietary pattern. However, the challenge to put these principles into practice on a population level remains. We concede the ambiguity in defining a food as "positive" or "negative," which is a dilemma shared by consumers when they sit down to a meal or enter a grocery store. This underscores the need for simple, yet evidenced-based, guidelines that are tangible to a broad population. Although it is enticing to think that targeting only a few key food groups will alleviate some consumer confusion, this may not be the best reflection of the true complexity of the diet. Our results showed that the Simplified Healthy Dietary Pattern as informative as was the Comprehensive Healthy Dietary Pattern in relation to CVD risk markers, but some differences between pattern scores were observed. Whereas we are reluctant to conclude that other aspects of intake are irrelevant if a person eats whole grains, fruit, and nuts while minimizing his or her intake of added fats and oils, processed meat, and fried potatoes, the encouragement of such practices is a practical starting point.

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The authors' responsibilities were as follows—JAN: responsible for the analytic design, data analysis, and manuscript preparation; DRJ: involved in data acquisition, analytic design, data analysis, and manuscript preparation; MBS, RJ, and NSJ: critically reviewed the manuscript; and GLB: involved in data acquisition and manuscript review. None of the authors had any conflicts of interest to report.

# APPENDIX A

Food groups used to calculate the Comprehensive Healthy Dietary Pattern  $score^{I}$ 

|  | Median intake                                    |   |  |   |  |
|--|--|---|--|---|--|
| Positive food groups                                     | 0 points   | 1 point   | 2 points   | 3 points                                    |  |
| 2  |  | servings/d  |  |   |  |
| Fruit <sup>2</sup><br>Dark-yellow vegetables             | 0.41 (0.0-0.79) [1260]<br>0.09 (0.0-0.15) [1262] | 1.2 (0.80–1.5) [1259]<br>0.23 (0.15                   | 1.9 (1.5–2.5) [1261]<br>0.46 (0.33               | 3.4 (2.5–14) [1262]<br>0.94 (0.64           |  |
| Green leafy vegetables                                   | 0.0 (0.0-0.0) [2362]                             | -0.33) [1256]<br>0.04 (0.02<br>-0.08) [1126]          | -0.64) [1261]<br>0.3 (0.08-3.0) [1544]           | -4.7) [1263]                                |  |
| Cruciferous vegetables                                   | 0.04 (0.0-0.09) [1256]                           | -0.08 [1130]<br>0.15 (0.09)<br>-0.25 [1242]           | 0.34 (0.25                                       | 0.79(0.51)                                  |  |
| Other vegetables   | 0.23 (0.0-0.36) [1261]                           | 0.51 (0.37<br>-0.66) [1260]                           | 0.84 (0.66–1.1) [1255]                           | 1.5 (1.1–9.0) [1266]                        |  |
| Avocados   | 0.0 (0.0-0.0) [3256]                             | 0.02 (0.02–0.03) [666]                                | 0.08 (0.04–0.21) [867]                           | 0.29 (0.25 - 1.5) [253]                     |  |
| Beans  | 0.0 (0.0-0.03) [1273]                            | 0.08 (0.04<br>-0.12) [1238]                           | 0.19 (0.13<br>-0.31) [1270]                      | 0.58 (0.31<br>-5.3) [1261]                  |  |
| Tomatoes   | 0.08 (0.0-0.17) [1237]                           | 0.29 (0.18<br>-0.41) [1280]                           | 0.56 (0.41<br>-0.76) [1260]                      | 1.1 (0.76<br>-5.1) [1265]                   |  |
| Low-fat milk   | 0.0 (0.0-0.02) [1260]                            | 0.14 (0.02<br>-0.32) [1257]                           | 0.54 (0.32<br>-0.93) [1262]                      | 1.5 (0.93–12) [1263]                        |  |
| Yogurt   | 0.0 (0.0-0.0) [3899]                             | 0.04 (0.02–0.24) [957]                                | 0.32 (0.25–1.3) [186]                            | —   |  |
| Fish   | 0.05 (0.0–0.10) [1258]                           | 0.03(0.02-0.03)[903]<br>0.15(0.10<br>-0.21)[1262]     | 0.14 (0.05 - 1.5) [728] 0.29 (0.21 -0.41) [1262] | 0.59 (0.41<br>-5 1) [1260]                  |  |
| Poultry  | 0.09 (0.0-0.15) [1255]                           | 0.22 (0.16<br>-0.30) [1266]                           | 0.39 (0.30<br>-0.52) [1261]                      | 0.72 (0.52<br>-4.2) [1260]                  |  |
| Soy foods or beverages                                   | 0.0 (0.0-0.0) [3503]                             | 0.03 (0.01-0.04) [291]                                | 0.11 (0.04–0.25) [573]                           | 0.59 (0.20<br>-7.8) [675]                   |  |
| Seeds and nuts <sup>2</sup>                              | 0.0 (0.0-0.03) [1264]                            | 0.07 (0.04<br>-0.14) [1217]                           | 0.22 (0.14<br>-0.39) [1296]                      | 0.65 (0.39<br>-6.8) [1265]                  |  |
| Whole-grain bread, rice, cereal, or pasta <sup>2</sup>   | 0.03 (0.0-0.12) [1264]                           | 0.27 (0.13<br>-0.44) [1258]                           | 0.61 (0.44<br>-0.89) [1258]                      | 1.2 (0.89<br>-6.1) [1262]                   |  |
| Noncream soups   | 0.02 (0.0-0.04) [1278]                           | 0.08 (0.04–1.0) [1250]                                | 0.15 (0.10<br>-0.25) [1245]                      | 0.44 (0.25<br>-3.4) [1269]                  |  |
| Coffee   | 0.0 (0.0–0.0) [1248]                             | 0.40 (0.04<br>-0.50) [1284]                           | 1.0 (0.65–2.3) [1224]                            | 2.5 (2.5–9.0) [1286]                        |  |
| Green or black tea<br>Beer                               | 0.0 (0.0–0.0) [2870]<br>0.0 (0.0–0.0) [3468]     | 0.07 (0.04–0.21) [849]<br>0.04 (0.04–0.04) [272]      | 0.43 (0.22–0.79) [795]<br>0.07 (0.07–0.22) [777] | 1.5 (1.0–9.0) [528]<br>0.50 (0.40           |  |
| Other alcohol  | 0.0 (0.0-0.0) [2563]                             | 0.07 (0.04–0.21) [823]                                | 0.29 (0.22–0.47) [687]                           | -9.0 [525]<br>0.93 (0.50<br>-9.1) [969]     |  |
| Negative food groups                                     | $0 \text{ points}^{I}$                           | -1 point  | -2 points  | -3 points                                   |  |
| Fried potatoes <sup>2</sup>                              | 0.0 (0.0-0.00) [1424]                            | 0.02 (0.02–0.03) [966]                                | 0.07 (0.04                                       | 0.25(0.12)                                  |  |
| High-fat cheese or cream sauce                           | 0.0 (0.0-0.05) [1256]                            | 0.11 (0.06<br>-0 18) [1264]                           | (0.12) [1391]<br>(0.29) (0.19<br>-0.44) [1261]   | 0.71 (0.44                                  |  |
| Ice cream  | 0.0 (0.0-0.0) [1835]                             | 0.03 (0.02)<br>-0.05) [1259]                          | 0.14 (0.05–3.0) [1948]                           |   |  |
| Whole milk   | 0.0 (0.0-0.0) [2627]                             | 0.03 (0.002 - 0.08) [1202]                            | 0.27 (0.08–1.0) [867]                            | 1.3 (1.0–9.0) [346]                         |  |
| Coffee or tea cream,<br>Added fats and oils <sup>2</sup> | 0.0 (0.0–0.0) [3473]<br>0.06 (0.0–0.19) [1266]   | 0.07 (0.04–0.07) [345]<br>0.37 (0.19<br>–0.57) [1255] | 0.40 (0.11–0.79) [692]<br>0.79 (0.57–1.1) [1260] | 1.3 (1.0–9.0) [532]<br>1.6 (1.1–9.1) [1261] |  |
| Red meat   | 0.07 (0.0-0.14) [1260]                           | 0.21 (0.14)   | 0.37 (0.28 - 0.50) [1252]                        | 0.74 (0.50)<br>-3.8) [1258]                 |  |
| Processed meat <sup>2</sup>                              | 0.0 (0.0–0.0) [1219]                             | 0.04 (0.02<br>-0.07) [1330]                           | 0.13 (0.08<br>-0.20) [1235]                      | 0.42 (0.21<br>-2.8) [1258]                  |  |

|   | Median intake  |   |                                  |                               |  |  |
|---|--|---|----------------------------------|-------------------------------|--|--|
| Positive food groups                                  | 0 points   | 1 point   | 2 points                         | 3 points                      |  |  |
| Pasta or potato salad                                 | 0.0 (0.0-0.0) [1654]   | 0.03 (0.02)<br>-0.08) [1871]  | 0.08 (0.08–1.0) [1517]           | _                             |  |  |
| Pizza   | 0.0 (0.0-0.0) [1723]   | 0.03 (0.02)<br>-0.08) [1876]  | 0.12 (0.08–1.2) [1443]           | —                             |  |  |
| Salty snack foods                                     | 0.0 (0.0-0.0) [1391]   | 0.05 (0.02<br>-0.08) [1213]   | 0.16 (0.09<br>-0.29) [1223]      | 0.55 (0.29<br>-4.5) [1215]    |  |  |
| Sweet breads  | 0.0 (0.0-0.0) [1253]   | 0.03 (0.02<br>-0.07) [1348]   | 0.11 (0.08<br>-0.16) [1119]      | 0.29 (0.16<br>-3.3) [1322]    |  |  |
| Desserts  | 0.0 (0.0-0.04) [1287]  | 0.08 (0.05<br>-0.14) [1273]   | 0.24 (0.14<br>-0.41) [1221]      | 0.74 (0.41<br>-6.1) [1261]    |  |  |
| Added sweets  | 0.02 (0.0-0.08) [1230]   | 0.18 (0.08<br>-0.38) [1290]   | 0.54 (0.39<br>-0.97) [1262]      | 1.5 (0.98–12) [1260]          |  |  |
| Soda  | 0.0 (0.0-0.0) [2248]   | 0.07 (0.04<br>-0.40) [1359]   | 0.8 (0.40–9.0) [1435]            | —                             |  |  |
| Neutral food groups <sup>3</sup>                      | 0 points   | 0 points  | 0 points                         | 0 points                      |  |  |
| Fruit juice   | 0.0 (0.0-0.0) [1370]   | 0.07 (0.0–0.15) [1151]  | 0.32 (0.15                       | 0.89 (0.52                    |  |  |
| Potatoes  | 0.0 (0.0-0.01) [1379]  | 0.03 (0.01 - 0.04) [1179]   | 0.08 (0.04) -0.14 [1244]         | 0.94 (0.14)<br>-2.1) [1240]   |  |  |
| Cream-based soup                                      | 0.0 (0.0-0.0) [2806]   | 0.03 (0.02–0.03) [915]  | 0.08(0.04)<br>-0.21)[1118]       | 0.29(0.25)<br>-1.5)[203]      |  |  |
| Low-fat dairy desserts                                | 0.0 (0.0-0.0) [2695]   | 0.03 (0.02  | 0.11 (0.08–0.25) [718]           | 0.46(0.25)<br>-6.0)[514]      |  |  |
| Eggs  | 0.02 (0.0-0.04) [1270]   | 0.08 (0.05)<br>-0.14) [1470]  | 0.29 (0.15 - 0.29) [1280]        | 0.50 (0.40<br>-3.0) [1022]    |  |  |
| Chow mein, fried rice, or<br>Chinese dumplings        | 0.0 (0.0-0.0) [1877]   | 0.02 (0.02-0.02) [331]  | 0.05 (0.03<br>-0.08) [1578]      | 0.16 (0.09<br>-2.1) [1256]    |  |  |
| Chicken, tuna, or egg salad                           | 0.0 (0.0-0.0) [1615]   | 0.03 (0.02<br>-0.03) [1263]   | 0.08 (0.04<br>-0.08) [1291]      | 0.15 (0.12<br>-2.0) [873]     |  |  |
| Refined-grain bread, rice, cereal, or pasta           | 0.37 (0.0-0.60) [1253]   | 0.83 (0.61–1.1) [1267]  | 1.4 (1.1–1.7) [1261]             | 2.4 (1.7–7.8) [1261]          |  |  |
| Diet soda<br>Hot chocolate<br>Meal-replacement drinks | 0.0 (0.0–0.0) [3035]<br>0.0 (0.0–0.0) [3654]<br>0.0 (0.0–0.0) [4642] | 0.07 (0.04–0.40) [750]<br>0.07 (0.04–4.5) [1388]<br>0.14 (0.04–6.0) [400] | 0.43 (0.43–0.79) [578]<br>—<br>— | 2.5 (1.0–9.0) [679]<br>—<br>— |  |  |

Range in parentheses; n in brackets. Points were assigned to each category of intake when the dietary pattern scores were calculated.

<sup>2</sup>Denotes food groups included in the Simplified Healthy Dietary Pattern.

<sup>3</sup>Denotes food groups not included in either the Comprehensive or the Simplified Healthy Dietary Pattern.

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| TABLE |
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Participant characteristics and nutrient intakes across quintiles (Q) of an a priori-defined Healthy Dietary Pattern in the Multi-Ethnic Study of Atherosclerosis<sup>1</sup>

|  |                   | Comprehe       | nsive Healthy Dietary Pat | tern Score        |                |                                 |
|--|-------------------|----------------|---------------------------|-------------------|----------------|---------------------------------|
|  | Q1 ( $n = 1073$ ) | Q2 $(n = 901)$ | Q3 $(n = 1037)$           | Q4 ( $n = 1079$ ) | Q5 $(n = 952)$ | <i>P</i> for trend <sup>2</sup> |
| Score                                      | -28 to -5         | -4 to 1        | 2 to 7                    | 8 to 14           | 15 to 40       | I                               |
| Sex (% male)                               | 55.3              | 50.0           | 47.2                      | 42.7              | 40.4           | <0.001                          |
| Age (y)                                    | $59.6\pm0.3$      | $60.8 \pm 0.3$ | $62.2 \pm 0.3$            | $62.2\pm0.3$      | $63.9 \pm 0.3$ | <0.001                          |
| Race-ethnicity                             |                   |                |                           |                   |                | $<0.001^{3}$                    |
| White (%)                                  | 43.8              | 44.1           | 43.3                      | 42.8              | 41.9           | 0.64                            |
| Black (%)                                  | 37.0              | 28.7           | 23.2                      | 18.2              | 12.8           | <0.001                          |
| Hispanic (%)                               | 18.4              | 23.2           | 23.1                      | 20.1              | 16.9           | 0.18                            |
| Chinese (%)                                | 1.0               | 4.0            | 10.4                      | 18.9              | 28.5           | <0.001                          |
| Education $\geq$ high school degree (%)    | 85.2              | 83.9           | 83.3                      | 84.1              | 84.2           | 0.69                            |
| Inactive leisure (MET-min/wk) <sup>4</sup> | $1798 \pm 34$     | $1659 \pm 36$  | $1711 \pm 37$             | $1633 \pm 33$     | $1558 \pm 36$  | <0.001                          |
| Active leisure (MET-min/wk) <sup>4</sup>   | $2323 \pm 93$     | $1382 \pm 97$  | $2471 \pm 101$            | $2443 \pm 90$     | $2959 \pm 99$  | <0.001                          |
| Multivitamin use ≥ weekly (%)              | 44.1              | 53.6           | 59.8                      | 65.3              | 72.1           | <0.001                          |
| Smoking status (% current)                 | 23.8              | 18.0           | 12.1                      | 10.7              | 8.2            | <0.001                          |
| Smoking (pack-years)                       | $17.0 \pm 0.7$    | $11.1 \pm 0.7$ | $10.0\pm0.7$              | $9.0\pm0.6$       | $8.1\pm0.7$    | <0.001                          |
| BMI $(kg/m^2)$                             | $29.1 \pm 0.2$    | $28.6 \pm 0.2$ | $28.0 \pm 0.2$            | $27.2 \pm 0.1$    | $26.1 \pm 0.2$ | <0.001                          |
| Waist circumference (cm)                   | $100 \pm 0.4$     | $98.8\pm0.4$   | $97.2\pm0.5$              | $94.8\pm0.4$      | $92.1 \pm 0.4$ | <0.001                          |
| Nutrients                                  |                   |                |                           |                   |                |                                 |
| Energy intake (kcal/d)                     | $1853 \pm 24$     | $1768 \pm 26$  | $1631 \pm 24$             | $1598 \pm 23$     | $1584 \pm 25$  | <0.001                          |
| Protein (% of energy)                      | $14.1 \pm 0.1$    | $15.2 \pm 0.1$ | $16.0 \pm 0.1$            | $16.7 \pm 0.1$    | $18.0 \pm 0.1$ | <0.001                          |
| Carbohydrate (% of energy)                 | $48.4 \pm 0.3$    | $49.2 \pm 0.3$ | $50.3 \pm 0.3$            | $51.1 \pm 0.3$    | $52.3 \pm 0.3$ | <0.001                          |
| Total fat (% of energy)                    | $37.5\pm0.2$      | $35.4\pm0.2$   | $33.7\pm0.2$              | $32.6\pm0.2$      | $30.7 \pm 0.2$ | <0.001                          |
| Saturated fat (% of energy)                | $12.6 \pm 0.1$    | $11.6 \pm 0.1$ | $10.6 \pm 0.1$            | $9.8\pm0.1$       | $8.3 \pm 0.1$  | <0.001                          |
| trans fat (g/d)                            | $4.5\pm0.04$      | $3.9\pm0.04$   | $3.3 \pm 0.04$            | $2.9 \pm 0.03$    | $2.1 \pm 0.04$ | <0.001                          |
| Fiber (g/d)                                | $12.1 \pm 0.2$    | $15.5\pm0.2$   | $17.8 \pm 0.2$            | $20.1 \pm 0.2$    | $24.0 \pm 0.2$ | <0.001                          |
| Calcium (mg/d)                             | $639 \pm 12$      | $744 \pm 13$   | $772 \pm 13$              | $824 \pm 12$      | $8661 \pm 13$  | <0.001                          |
| Folate (µg/d)                              | $269 \pm 2.4$     | $317 \pm 2.5$  | $339 \pm 2.6$             | $365 \pm 2.3$     | $400 \pm 2.6$  | <0.001                          |
| Vitamin C (mg/d)                           | $79.2 \pm 1.7$    | $104 \pm 1.8$  | $116 \pm 1.9$             | $129 \pm 1.6$     | $146 \pm 1.8$  | <0.001                          |
| $\beta$ -Carotene ( $\mu g/d$ )            | $1223 \pm 40$     | $1795 \pm 42$  | $2308 \pm 43$             | $2854 \pm 38$     | $3770 \pm 43$  | <0.001                          |
|  |                   |                |                           |                   |                |                                 |

I values are unadjusted  $x \pm SE$  or percentages, except for macro- and micronutrients, which are adjusted for total energy intake (kcal/d).

<sup>2</sup> P for trend across quintiles calculated from linear regression with the a priori Healthy Dietary Pattern modeled continuously (score).

 $^{3}$ Chi-square test for difference among race-ethnic groups.

<sup>4</sup>MET, metabolic equivalents.

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Geometric mean or odds ratios for select cardiovascular disease risk markers across quintiles (Q) of an a priori-defined Healthy Dietary **TABLE 2** 

Pattern in the Multi-Ethnic Study of Atherosclerosis<sup>1</sup>

| $ \begin{array}{c} \mbox{Inflammatory} \mbox{Intermatory} \mbox{Inflammatory} \mbox{Intermatory} \mbox{Inflammatory} $  | ç  |                       |                          |                       |                      |
|---|--|-----------------------|--------------------------|-----------------------|----------------------|
| $ \begin{array}{ccccc} \mbox{wodel} \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \$  | Inflammatory markers <sup>3</sup><br>CRP (mg/dL) |                       |                          |                       |                      |
| $ \begin{array}{cccccccccccccccccccccccccccccccccccc$   | Model 1 <sup>4</sup>                             | 2.03 (1.90, 2.18)     | 1.87 (1.75, 2.00)        | 1.87 (1.74, 2.01)     | 1.77 (1.66, 1.88     |
| $ \begin{array}{cccc} \mbox{wodel} \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \$   | Model 2 <sup>5</sup>                             | 1.92 (1.79, 2.05)     | 1.85 (1.72, 1.98)        | 1.87 (1.75, 2.01)     | 1.81 (1.69, 1.93     |
| $ \begin{array}{c ccccccccccccccccccccccccccccccccccc$  | Model 36   | 1.85 (1.73, 1.98)     | 1.80(1.68, 1.92)         | 1.86(1.74, 1.99)      | 1.84 (1.73, 1.96     |
| $ \begin{array}{cccccccccccccccccccccccccccccccccccc$   | IL-6 (mg/dL)                                     |                       |                          |                       |                      |
| $ \begin{array}{llllllllllllllllllllllllllllllllllll$   | Model 1 <sup>4</sup>                             | 1.28(1.23, 1.33)      | 1.21(1.16, 1.26)         | 1.17 (1.13, 1.22)     | 1.13 (1.08, 1.17     |
| $ \begin{array}{cccc} {\rm Model} 3^6 & 1.21 (1.16, 1.25) & 1.18 (1.14, 1.23) & 1.17 (1.13, 1.22) \\ {\rm Mondel} 2^6 & 90 (8.9, 9.2) & 8.9 (8.7, 9.0) & 8.6 (8.5, 8.8) \\ {\rm Mondel} 2^6 & 90 (8.9, 9.2) & 8.9 (8.7, 9.0) & 8.6 (8.5, 8.8) \\ {\rm Mondel} 2^6 & 90 (8.9, 9.2) & 8.9 (8.7, 9.0) & 8.6 (8.5, 8.8) \\ {\rm Mondel} 2^6 & 90 (8.9, 9.2) & 8.9 (8.7, 9.0) & 8.6 (8.5, 8.8) \\ {\rm Mondel} 2^6 & 90 (8.9, 9.2) & 8.9 (8.7, 9.0) & 8.6 (8.5, 8.8) \\ {\rm Mondel} 2^6 & 90 (8.9, 9.2) & 8.9 (8.7, 9.0) & 8.6 (8.5, 8.8) \\ {\rm Mondel} 2^6 & 90 (8.9, 9.2) & 8.3 (3.1, 339) & 335 (3.1, 339) \\ {\rm Mondel} 2^6 & 335 (3.1, 339) & 335 (3.1, 339) & 335 (3.1, 339) \\ {\rm Mondel} 2^6 & 335 (3.1, 339) & 335 (3.1, 339) & 335 (3.1, 339) \\ {\rm Mondel} 2^6 & 335 (3.1, 339) & 335 (3.1, 339) & 335 (3.1, 339) \\ {\rm Mondel} 2^6 & 0.84 (0.86) & 0.84 (0.83, 0.85) & 0.84 (0.83, 0.85) \\ {\rm Mondel} 2^6 & 0.84 (0.83, 0.85) & 0.84 (0.83, 0.85) & 0.84 (0.83, 0.85) \\ {\rm Mondel} 2^6 & 0.84 (0.83, 0.85) & 0.84 (0.83, 0.85) & 0.84 (0.83, 0.85) \\ {\rm Mondel} 2^6 & 0.84 (0.83, 0.94) & 0.94 (0.91, 0.96) \\ {\rm Mondel} 2^6 & 0.91 (0.96) & 0.92 (0.89, 0.94) & 0.94 (0.91, 0.97) \\ {\rm Mondel} 2^6 & 0.91 (0.96) & 0.91 (0.89, 0.94) & 0.94 (0.91, 0.97) \\ {\rm Mondel} 2^6 & 0.91 (0.96) & 0.92 (0.89, 0.94) & 0.94 (0.91, 0.96) \\ {\rm Mondel} 2^6 & 0.91 (0.99) & 0.91 (0.89, 0.94) & 0.94 (0.91, 0.96) \\ {\rm Mondel} 2^6 & 0.91 (0.99) & 0.91 (0.89, 0.94) & 0.94 (0.91, 0.96) \\ {\rm Mondel} 2^6 & 0.91 (0.99) & 0.91 (0.89, 0.94) & 0.94 (0.91, 0.96) \\ {\rm Mondel} 2^6 & 0.90 & 0.90 (0.72, 1.13) & 0.94 (0.91, 0.96) \\ {\rm Mondel} 2^6 & 0.91 (0.0) & 0.86 (0.70, 1.16) & 0.94 (0.91, 0.96) \\ {\rm Mondel} 2^6 & 0.91 (0.0) & 0.86 (0.70, 1.10) & 0.94 (0.91, 0.92) \\ {\rm Mondel} 2^6 & 0.91 & 0.90 & 0.96 (0.70, 1.10) & 0.94 (0.91, 1.27) \\ {\rm Mondel} 2^6 & 0.91 & 0.91 (0.96, 0.99) & 0.91 (0.06, 0.99) & 0.91 (0.06, 0.91) & 0.94 (0.91, 0.92) \\ {\rm Mondel} 2^6 & 0.91 & 0.91 (0.96, 0.99) & 0.91 (0.06, 0.91) & 0.94 (0.91, 0.96) & 0.94 (0.91, 0.92) \\ {\rm Mondel} 2^6 & 0.91 & 0.91 (0.95, 0.92) & 0.91 (0.55, 0.52) & 0.94 (0.92, 0.92) & 0.94 (0.92,$   | Model 2 <sup>5</sup>                             | 1.23 (1.18, 1.28)     | 1.20(1.16, 1.25)         | 1.18 (1.13, 1.22)     | 1.14 (1.10, 1.19     |
| $ \begin{array}{cccccccccccccccccccccccccccccccccccc$   | Model $3^6$                                      | 1.21 (1.16, 1.25)     | 1.18 (1.14, 1.23)        | 1.17 (1.13, 1.22)     | 1.16 (1.12, 1.20     |
| $ \begin{array}{ccccc} {\rm Model} 1^4 & & 9.1(9.0,9.5) & 8.9(8.7,9.0) & 8.6(8.5,8.8) \\ {\rm Model} 1^4 & & 9.1(9.0,9.2) & 8.9(8.7,9.0) & 8.6(8.5,8.8) \\ {\rm Model} 1^4 & & 9.0(8.9,9.2) & 8.9(8.7,9.0) & 8.6(8.5,8.8) \\ {\rm Model} 1^6 & & 9.0(8.9,9.2) & 8.9(8.7,9.0) & 8.6(8.5,8.8) \\ {\rm Model} 1^6 & & 337(331,339) & 335(331,339) & 335(331,339) \\ {\rm Model} 1^6 & & 337(332,331) & 335(331,339) & 335(331,339) \\ {\rm Model} 1^6 & & 337(332,331) & 335(331,339) & 335(331,339) \\ {\rm Model} 1^6 & & 0.84(0.83,0.86) & 0.84(0.83,0.85) & 0.84(0.83,0.85) \\ {\rm Model} 1^6 & & 0.84(0.83,0.86) & 0.84(0.83,0.85) & 0.84(0.83,0.85) \\ {\rm Model} 1^6 & & 0.84(0.83,0.86) & 0.94(0.94(0.94,0.96) \\ {\rm Model} 1^6 & & 0.91(0.96) & 0.92(0.94) & 0.94(0.91,0.96) \\ {\rm Model} 1^6 & & 0.91(0.96) & 0.91(0.89,0.94) & 0.94(0.91,0.96) \\ {\rm Model} 1^6 & & 0.91(0.96) & 0.91(0.89,0.94) & 0.94(0.91,0.96) \\ {\rm Model} 1^6 & & 0.91(0.96) & 0.91(0.89,0.94) & 0.94(0.91,0.96) \\ {\rm Model} 1^6 & & 0.91(0.96) & 0.91(0.89,0.94) & 0.94(0.91,0.96) \\ {\rm Model} 1^6 & & 0.91(0.96)(0.91(0.96)(0.91(0.96)(0.91(0.97(0.96)(0.94(0.91(0.96(0.94(0.92,0.91(0.96(0.94(0.92,0.91(0.96(0.94(0.92,0.91(0.96(0.94(0.92,0.91(0.96(0.94(0.92,0.91(0.96(0.94(0.92,0.91(0.96(0.94(0.92(0.91(0.96(0.94(0.92,0.91(0.96(0.94(0.92(0.91(0.96(0.94(0.92(0.91(0.96(0.94(0.92(0.91(0.96(0.94(0.93(0.94(0.93(0.94(0.93(0.94(0.93(0.94(0.93(0.94(0.94(0.93(0.94(0.93(0.94(0.94(0.93(0.94(0.94(0.93(0.94(0.94(0.93(0.94(0.94(0.94(0.85(0.94(0.94(0.94(0.85(0.94(0.94(0.94(0.85(0.94(0.94(0.94(0.85(0.94(0.94(0.95(0.94(0.94(0.95(0.94(0.94(0.94(0.94(0.95(0.94(0.94(0.94(0.95(0.94(0.94(0.94(0.85(0.94(0.94(0.94(0.85(0.94(0.94(0.94(0.85(0.94(0.94(0.94(0.85(0.94(0.94(0.94(0.95(0.94(0.94(0.94(0.94(0.94(0.95(0.94(0$   | Homocysteine (µmol/L)                            |                       |                          |                       |                      |
| $ \begin{array}{cccccccccccccccccccccccccccccccccccc$   | Model 1 <sup>4</sup>                             | 9.1(9.0, 9.3)         | 8.9 (8.7, 9.0)           | $8.6\ (8.5,\ 8.8)$    | 8.6 (8.5, 8.8)       |
| $ \begin{array}{cccccccccccccccccccccccccccccccccccc$   | Model 2 <sup>5</sup>                             | 9.0 (8.9, 9.2)        | 8.9(8.7, 9.0)            | 8.6 (8.5, 8.8)        | 8.7 (8.6, 8.8)       |
| $ \begin{array}{ccccc} Fibringen (mg/dL) \\ \mbox{Model 1}^{2} & 337 (332, 343) & 335 (331, 339) & 335 (331, 339) \\ \mbox{Model 2}^{5} & 337 (332, 341) & 335 (331, 339) & 335 (331, 339) \\ \mbox{Model 2}^{5} & 337 (332, 341) & 335 (331, 339) & 335 (331, 339) \\ \mbox{Markers of subclinical} & 335 (331, 339) & 333 (329, 337) & 335 (331, 339) \\ \mbox{Markers of subclinical} & 335 (331, 339) & 333 (329, 337) & 335 (331, 339) \\ \mbox{Markers of subclinical} & 335 (331, 339) & 333 (329, 337) & 335 (331, 339) \\ \mbox{Markers of subclinical} & 085 (084, 0.86) & 0.84 (0.83, 0.85) & 0.84 (0.83, 0.85) \\ \mbox{Model 1}^{2} & 085 (0.84, 0.86) & 0.84 (0.83, 0.85) & 0.84 (0.83, 0.85) \\ \mbox{Model 1}^{2} & 085 (0.84, 0.86) & 0.94 (0.83, 0.85) & 0.84 (0.83, 0.85) \\ \mbox{Model 1}^{2} & 093 (0.91, 0.96) & 0.94 (0.91, 0.96) \\ \mbox{Model 1}^{2} & 091 (0.89, 0.94) & 0.94 (0.91, 0.96) & 0.94 (0.91, 0.97) \\ \mbox{Model 1}^{2} & 0.91 (0.89, 0.94) & 0.91 (0.89, 0.94) & 0.94 (0.91, 0.97) $  | Model $3^6$                                      | 9.0 (8.9, 9.2)        | 8.8 (8.7, 9.0)           | 8.6 (8.5, 8.8)        | 8.7 (8.6, 8.8)       |
| $ \begin{array}{ccccc} {\rm Model} 1^4 & {\rm (335,343)} & {\rm (331,339)} & {\rm (331,339)} & {\rm (335,331)} & {\rm (332,337)} & {\rm (335,339)} & {\rm (336,339)} & {\rm (336,330)} & {\rm (339,339)} & {\rm (336,330)} & {\rm (337,330)} & {\rm (336,330)} & {\rm (337,310)} & {\rm (337,310)} & {\rm (336,31,390)} & {\rm (337,310)} &$  | Fibrinogen (mg/dL)                               |                       |                          |                       |                      |
| $ \begin{array}{cccccccccccccccccccccccccccccccccccc$   | Model 1 <sup>4</sup>                             | 339 (335, 343)        | 335 (331, 339)           | 335 (331, 339)        | 333 (329, 336)       |
|   | Model 2 <sup>5</sup>                             | 337 (332, 341)        | 335 (330, 339)           | 335 (331, 339)        | 333 (330, 337)       |
| $ \begin{array}{llllllllllllllllllllllllllllllllllll$   | Model 36   | 335 (331, 339)        | 333 (329, 337)           | 335 (331, 339)        | 334 (330, 338)       |
| atherosclerosis<br>$CC-IMT (mm)^{3} (mm)^{3} (0.84, 0.86) (0.84, 0.83, 0.85) (0.94, 0.91, 0.96) (0.94, 0.91, 0.97) (0.94, 0.93) (0.94, 0.93) (0.94, 0.91, 0.97) (0.94, 0.93) (0.94, 0.94, 0.93) (0.94, 0.93) (0.94, 0.93) (0.94, 0.9$  | Markers of subclinical                           |                       |                          |                       |                      |
| $ \begin{array}{cccc} C-IMT (mm)^{7} & 0.85 (0.84, 0.86) & 0.84 (0.83, 0.85) & 0.94 (0.91, 0.97) & 0.91 (0.89, 0.94) & 0.94 (0.91, 0.97) & 0.91 (0.89, 0.94) & 0.94 (0.91, 0.97) & 0.91 (0.82, 0.94) & 0.94 (0.91, 0.97) & 0.91 (0.82, 0.94) & 0.94 (0.91, 0.97) & 0.91 (0.82, 0.94) & 0.94 (0.91, 0.97) & 0.91 (0.82, 0.22) & 0.90 (0.74, 1.10) & 0.94 (0.91, 0.97) & 0.91 (0.82, 0.29) & 0.90 (0.74, 1.10) & 0.94 (0.91, 0.97) & 0.90 (0.72, 1.13) & 1.00 (0.82, 1.22) & 0.00 (0.72, 1.13) & 1.00 (0.82, 1.22) & 0.00 (0.72, 1.13) & 1.00 (0.82, 1.22) & 0.00 (0.72, 1.13) & 1.00 (0.82, 1.22) & 0.00 (0.72, 1.13) & 1.00 (0.82, 1.22) & 0.00 (0.72, 1.13) & 1.00 (0.82, 1.22) & 0.00 (0.72, 1.13) & 1.00 (0.82, 1.22) & 0.00 (0.72, 1.13) & 1.00 (0.82, 1.22) & 0.00 (0.72, 1.13) & 1.00 (0.82, 1.22) & 0.00 (0.72, 1.13) & 1.00 (0.82, 1.22) & 0.00 (0.72, 1.13) & 1.00 (0.82, 1.22) & 0.00 (0.72, 1.13) & 1.00 (0.82, 1.22) & 0.00 (0.72, 1.13) & 1.00 (0.82, 1.22) & 0.00 (0.72, 1.13) & 0.00 (0.82, 1.22) & 0.00 (0.72, 1.13) & 0.00 (0.82, 1.22) & 0.00 & 0.86 (0.70, 1.06) & 1.23 (0.94, 1.52) & 0.94 (0.94, 0.53) & 7.41 (64, 0.85, 8) & 7.41 (64, 0.85, 8) & 7.41 (64, 0.85, 8) & 7.41 (64, 0.85, 8) & 7.41 (64, 0.85, 8) & 7.41 (64, 0.83, 5) & 7.41 (64, 0.83, 5) & 7.41 (64, 0.83, 5) & 7.41 (64, 0.83, 5) & 7.41 (64, 0.83, 5) & 7.41 (64, 0.83, 5) & 7.41 (64, 0.83, 5) & 7.41 (64, 0.83, 5) & 7.41 (64, 0.83, 5) & 7.41 (64, 0.83, 5) & 7.41 (64, 0.83, 5) & 7.41 (64, 0.83, 5) & 7.41 (64, 0.83, 5) & 7.41 (64, 0.8$  | atherosclerosis $\frac{1}{2}$                    |                       |                          |                       |                      |
| $ \begin{array}{llllllllllllllllllllllllllllllllllll$   | CC-IMT (mm) <sup>2</sup>                         |                       |                          |                       |                      |
|   | Model 1 <sup>4</sup>                             | $0.85\ (0.84,0.86)$   | $0.84\ (0.83,\ 0.85)$    | $0.84 \ (0.83, .85)$  | 0.83 (0.82, 0.8)     |
| $ \begin{array}{llllllllllllllllllllllllllllllllllll$   | Model 2 <sup>5</sup>                             | 0.85(0.84, 0.86)      | $0.84\ (0.83,\ 0.85)$    | $0.84\ (0.83,\ 0.85)$ | 0.83 (0.83, 0.8)     |
| $ \begin{array}{c ccccccccccccccccccccccccccccccccccc$  | Model $3^6$                                      | $0.84\ (0.83,\ 0.85)$ | $0.84 \ (0.83, 0.85)$    | $0.84\ (0.83,\ 0.85)$ | $0.84 \ (0.83, 0.8)$ |
| $ \begin{array}{cccccccccccccccccccccccccccccccccccc$   | IC-IMT (mm) <sup>3</sup>                         |                       |                          |                       |                      |
| $ \begin{array}{ccccc} Model 2^{5} & 0.91 \left( 0.89, 0.94 \right) & 0.91 \left( 0.89, 0.94 \right) & 0.94 \left( 0.92, 0.97 \right) \\ Model 3^{6} & 0.91 \left( 0.89, 0.93 \right) & 0.91 \left( 0.89, 0.94 \right) & 0.94 \left( 0.91, 0.97 \right) \\ Carotid plaque & & & & & & & & & & & & & & & & & & &$  | Model 1 <sup>4</sup>                             | $0.93\ (0.91,\ 0.96)$ | $0.92\ (0.89,\ 0.94)$    | 0.94 (0.91, 0.96)     | 0.92 (0.90, 0.95     |
| $ \begin{array}{cccc} Model 3^6 & 0.91  (0.89, 0.93) & 0.91  (0.89, 0.94) & 0.94  (0.91, 0.97) \\ \mbox{Carctid} \ \mbox{plague}^7 & 1.00 & 0.98  (0.74, 1.10) & 0.90  (0.74, 1.10) & 0.90  (0.74, 1.10) & 0.90  (0.74, 1.10) & 0.90  (0.72, 1.13) & 1.00  (0.82, 1.22) & 0.90  (0.72, 1.13) & 1.00  (0.82, 1.22) & 0.90  (0.72, 1.13) & 1.00  (0.82, 1.22) & 0.90  (0.72, 1.13) & 1.00  (0.82, 1.22) & 0.90  (0.72, 1.13) & 1.00  (0.82, 1.22) & 0.90  (0.72, 1.13) & 1.00  (0.82, 1.22) & 0.90  (0.72, 1.13) & 1.00  (0.82, 1.22) & 0.90  (0.72, 1.13) & 1.00  (0.82, 1.22) & 0.90  (0.72, 1.13) & 1.00  (0.82, 1.22) & 0.90  (0.72, 1.13) & 1.00  (0.82, 1.22) & 0.90  (0.72, 1.13) & 1.00  (0.82, 1.22) & 0.90  (0.72, 1.13) & 1.00  (0.82, 1.22) & 0.90  (0.22, 1.13) & 1.00  (0.82, 1.22) & 0.90  (0.72, 1.13) & 1.00  (0.82, 1.22) & 0.91  (0.55, 1.50) & 0.91  (0.55, 1.50) & 0.91  (0.55, 1.50) & 0.91  (0.55, 1.50) & 0.91  (0.55, 1.50) & 0.91  (0.55, 1.50) & 0.91  (0.55, 1.50) & 0.91  (0.55, 1.50) & 0.91  (0.55, 1.50) & 0.91  (0.56, 1.29) & 0.91  (0.55, 1.50) & 0.91  (0.56, 1.29) & 0.91  (0.55, 1.20) & 0.91  (0.56, 1.29) & 0.91  (0.55, 1.20) & 0.91  (0.55, 1.20) & 0.91  (0.55, 1.20) & 0.91  (0.56, 1.20) & 0.91  (0.56, 1.20) & 0.91  (0.56, 1.20) & 0.91  (0.56, 1.20) & 0.91  (0.56, 1.20) & 0.91  (0.56, 1.20) & 0.91  (0.56, 1.20) & 0.91  (0.56, 1.20) & 0.91  (0.56, 1.20) & 0.91  (0.56, 1.20) & 0.91  (0.56, 1.20) & 0.91  (0.56, 1.20) & 0.91  (0.56, 1.20) & 0.91  (0.56, 1.20) & 0.91  (0.56, 1.20) & 0.91  (0.56, 1.20) & 0.91  (0.56, 1.20) & 0.91  (0.70, 1.90) & 0$   | Model 2 <sup>5</sup>                             | $0.91\ (0.89,\ 0.94)$ | 0.91 ( $0.89$ , $0.94$ ) | 0.94 (0.92, 0.97)     | $0.93 \ (0.91, 0.9)$ |
| $ \begin{array}{cccc} \mbox{Carotid plague} & \mbox{Link} & Lin$  | Model $3^6$                                      | $0.91\ (0.89,\ 0.93)$ | 0.91 (0.89, 0.94)        | 0.94 (0.91, 0.97)     | 0.93 (0.91, 0.9)     |
| $ \begin{array}{cccccccccccccccccccccccccccccccccccc$   | Carotid plaque <sup>7</sup>                      |                       |                          |                       |                      |
| $ \begin{array}{cccccccccccccccccccccccccccccccccccc$   | Model 1 <sup>4</sup>                             | 1.00                  | $0.89\ (0.74,1.08)$      | 0.90 (0.74, 1.10)     | 0.87 (0.72, 1.0)     |
| $ \begin{array}{cccccccccccccccccccccccccccccccccccc$   | Model 2 <sup>5</sup>                             | 1.00                  | 0.96(0.79, 1.17)         | 1.01 (0.82, 1.24)     | 0.99 (0.81, 1.2      |
| $ \begin{array}{cccc} {\rm CAC} \left( {\rm Agatston} > 0 \right)^7 \\ {\rm Model} 1^4 \\ {\rm Model} 1^2 \\ {\rm Model} 2^5 \\ {\rm Model} 2^5 \\ {\rm Model} 3^6 \\ {\rm Model} 3^6 \\ {\rm Model} 1^2 \\ {\rm Model} 1^2 \\ {\rm Model} 1^2 \\ {\rm Model} 1^2 \\ {\rm Model} 1^4 \\ {\rm Model} 2^5 \\ {\rm Model} 2^5 \\ {\rm Model} 2^5 \\ {\rm Model} 1^4 \\ {\rm Model} 2^5 \\ $ | Model $3^6$                                      | 1.00                  | 0.90 (0.72, 1.13)        | 1.00 (0.82, 1.22)     | 1.01 (0.83, 1.2)     |
| $ \begin{array}{cccccccccccccccccccccccccccccccccccc$   | $CAC (Agatston > 0)^7$                           |                       |                          |                       |                      |
| $ \begin{array}{cccccccccccccccccccccccccccccccccccc$   | Model 1 <sup>4</sup>                             | 1.00                  | 0.81 ( $0.66$ , $0.99$ ) | 1.11 (0.90, 1.37)     | 0.94 (0.77, 1.15)    |
| $ \begin{array}{cccc} Model 3^{6} & 1.00 & 0.86  (0.70, 1.06) & 1.23  (0.99, 1.52) \\ {\rm CAC} ({\rm Agatston score}), {}^{38} & 76.7  (66.1, 89.1) & 72.7  (63.1, 84.9) & 74.1  (64.0, 85.8) \\ {\rm Model 1}^{4} & 74.5  (63.2, 86.9) & 72.1  (61.6, 84.3) & 73.1  (65.0, 87.1) \\ {\rm Model 3}^{5} & 74.5  (63.4, 86.2) & 74.1  (61.0, 83.5) & 73.1  (65.0, 87.1) \\ {\rm ABI} (<0.9)^{7} & 1.00 & 0.81  (0.49, 1.33) & 0.91  (0.55, 1.50) \\ {\rm Model 2}^{5} & 1.00 & 1.01  (0.60, 1.70) & 1.18  (0.70, 1.99) \\ {\rm Model 2}^{5} & 1.00 & 1.02  (0.61, 1.71) & 1.19  (0.70, 2.00) \\ {\rm Model 2}^{5} & 1.00 & 1.02  (0.61, 1.71) & 1.19  (0.70, 2.00) \\ {\rm Model 2}^{5} & 1.00 & 1.02  (0.61, 1.71) & 1.19  (0.70, 2.00) \\ {\rm Model 2}^{5} & 1.00 & 1.02  (0.61, 1.71) & 1.19  (0.70, 2.00) \\ {\rm Model 2}^{5} & 1.00 & 1.02  (0.61, 1.71) & 1.19  (0.70, 2.00) \\ {\rm Model 2}^{5} & 1.00 & 1.00 & 1.02  (0.61, 1.71) & 1.19  (0.70, 2.00) \\ {\rm Model 2}^{5} & 1.00 & 1.02  (0.61, 1.71) & 1.19  (0.70, 2.00) \\ {\rm Model 2}^{5} & 1.00 & 1.00 & 1.02  (0.61, 1.71) & 1.19  (0.70, 2.00) \\ {\rm Model 2}^{5} & 1.00 & 1.00 & 1.02  (0.61, 1.71) & 1.19  (0.70, 2.00) \\ {\rm Model 2}^{5} & 1.00 & 1.00 & 1.02  (0.61, 1.71) & 1.19  (0.70, 2.00) \\ {\rm Model 2}^{5} & 1.00 & 1.00 & 1.02  (0.61, 1.71) & 1.19  (0.70, 2.00) \\ {\rm Model 2}^{5} & 1.00 & 1.00 & 1.02  (0.61, 1.71) & 1.19  (0.70, 2.00) \\ {\rm Model 2}^{5} & 1.00 & 1.00 & 1.02  (0.61, 1.71) & 1.19  (0.70, 2.00) \\ {\rm Model 2}^{5} & 1.00 & 1.00 & 1.02  (0.70, 1.70) & 1.10  (0.70, 1.90) \\ {\rm Model 2}^{5} & 1.00 & 1.00 & 1.02  (0.70, 1.70) & 1.10  (0.70, 1.90) \\ {\rm Model 2}^{5} & 1.00 & 1.00 & 1.02  (0.70, 1.70) & 1.10  (0.70, 1.90) \\ {\rm Model 2}^{5} & 1.00 & 1.00 & 1.00  (0.70, 1.70) & 1.10  (0.70, 1.90) \\ {\rm Model 2}^{5} & 1.00 & 1.00  (0.70, 1.70) & 1.10  (0.70, 1.90) \\ {\rm Model 2}^{5} & 1.00 & 1.00  (0.70, 1.70) & 1.10  (0.70, 1.90) \\ {\rm Model 2}^{5} & 1.00  (0.70, 1.70) & 1.10  (0.70, 1.90) \\ {\rm Model 2}^{5} & 1.00  (0.70, 1.70) & 1.00  (0.70, 1.70) & 1.00  (0.70, 1.90) \\ {\rm Model 2}^{5} & 1.0$   | Model 2 <sup>5</sup>                             | 1.00                  | 0.86(0.70, 1.06)         | 1.32(0.98, 1.50)      | 1.00(0.81, 1.23)     |
| $ \begin{array}{ccc} CAC (\operatorname{Agatston score})^{38} & 76.7 (66.1, 89.1) & 72.7 (63.1, 84.9) & 74.1 (64.0, 85.8) \\ \mathrm{Model} 1^4 & 76.7 (66.1, 89.1) & 72.7 (63.1, 84.9) & 74.1 (64.0, 85.8) \\ \mathrm{Model} 2^5 & 74.5 (63.3, 86.9) & 72.1 (61.6, 84.3) & 75.8 (63.4, 87.7) \\ \mathrm{Model} 3^6 & 74.0 (63.4, 86.2) & 74.1 (61.0, 83.5) & 73.1 (65.0, 87.1) \\ \mathrm{ABI} (<0.9)^7 & 1.00 & 0.81 (0.49, 1.33) & 0.91 (0.55, 1.50) \\ \mathrm{Model} 1^4 & 1.00 & 1.01 (0.60, 1.70) & 1.18 (0.70, 1.99) \\ \mathrm{Model} 2^5 & 1.00 & 1.02 (0.61, 1.71) & 1.19 (0.70, 1.99) \\ \mathrm{Model} 2^5 & 1.00 & 1.02 (0.61, 1.71) & 1.19 (0.70, 1.99) \\ \end{array} $   | Model 3 <sup>6</sup>                             | 1.00                  | 0.86 (0.70, 1.06)        | 1.23 (0.99, 1.52)     | 1.03 (0.84, 1.27)    |
| $ \begin{array}{cccccccccccccccccccccccccccccccccccc$   | CAC (Agatșton score), $3\delta$                  |                       |                          |                       |                      |
| Model $2^{5}$ 74.5 (63.9, 86.9)     72.1 (61.6, 84.3)     75.8 (63.4, 87.7)       Model $3^{6}$ 74.0 (63.4, 86.2)     74.1 (61.0, 83.5)     73.1 (65.0, 87.1)       ABI ( $<0.9)^{7}$ 1.00     0.81 (0.49, 1.33)     0.91 (0.55, 1.50)       Model $2^{5}$ 1.00     1.01 (0.60, 1.70)     1.18 (0.70, 1.99)       Model $2^{5}$ 1.00     1.01 (0.60, 1.71)     1.19 (0.70, 1.99)  | Model 1 <sup>4</sup>                             | 76.7~(66.1, 89.1)     | 72.7 (63.1, 84.9)        | 74.1 (64.0, 85.8)     | 71.9 (62.7, 82.4     |
| Model $3^{6}$ 74.0 (63.4, 86.2)     74.1 (61.0, 83.5)     73.1 (65.0, 87.1)       ABI (<0.9) <sup>7</sup> Model $1^{4}$ 1.00     0.81 (0.49, 1.33)     0.91 (0.55, 1.50)       Model $1^{4}$ 1.00     0.81 (0.49, 1.33)     0.91 (0.55, 1.50) $1.01 (0.60, 1.70)$ Model $2^{5}$ 1.00     1.01 (0.60, 1.70)     1.18 (0.70, 1.99)       Model $2^{5}$ 1.00     1.02 (0.61, 1.71)     1.19 (0.70, 2.00)   | Model 2  | 74.5 (63.9, 86.9)     | 72.1 (61.6, 84.3)        | 75.8 (63.4, 87.7)     | 72.7 (63.3, 83.4     |
| ABI (<0.9) <sup>7</sup> ABI (<0.9) <sup>7</sup> Model 1 <sup>4</sup> 1.00 0.81 (0.49, 1.33) 0.91 (0.55, 1.50)   Model 2 <sup>5</sup> 1.00 1.01 (0.60, 1.70) 1.18 (0.70, 1.99)   Model 2 <sup>5</sup> 1.00 1.01 (0.61, 1.71) 1.19 (0.70, 2.00)   | Model $3^6$                                      | 74.0 (63.4, 86.2)     | 74.1 (61.0, 83.5)        | 73.1 (65.0, 87.1)     | 71.6 (63.5, 83.7     |
| Model 1 <sup>4</sup> 1.00     0.81 (0.49, 1.33)     0.91 (0.55, 1.50)       Model 2 <sup>5</sup> 1.00     1.01 (0.60, 1.70)     1.18 (0.70, 1.99) $Model 2^5$ 1.00     1.01 (0.60, 1.70)     1.19 (0.70, 2.00)  | $\operatorname{ABI}(<0.9)^7$                     |                       |                          |                       |                      |
| Model $2^{\circ}$ Model $2^{\circ}$ 1.00 1.01 (0.60, 1.70) 1.18 (0.70, 1.99) 1.02 (0.61, 1.71) 1.19 (0.70, 2.00) 1.02 (0.61, 1.71) 1.19 (0.70, 2.00)  | Model 1 <sup>4</sup>                             | 1.00                  | 0.81 (0.49, 1.33)        | $0.91\ (0.55,1.50)$   | 0.76 (0.46, 1.28     |
| $M_{0,del}$ 20 1.00 1.02 (0.61, 1.71) 1.19 (0.70, 2.00)   | Model 2  | 1.00                  | 1.01(0.60, 1.70)         | 1.18(0.70, 1.99)      | 1.15(0.67, 1.98)     |
|   | Model 36   | 1.00                  | 1.02(0.61, 1.71)         | 1.19 (0.70, 2.00)     | 1.13 (0.66, 1.9      |

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<0.001 <0.001

1.47 (1.36, 1.58) 1.54 (1.43, 1.66) 1.63 (1.52, 1.75)

0.04

<0.001<br/><0.001

1.05 (1.01, 1.09) 1.09 (1.04, 1.13) 1.12 (1.07, 1.17)

0.01

<0.001 <0.001 0.002

8.6 (8.4, 8.7) 8.6 (8.4, 8.7) 8.5 (8.3, 8.6)

<0.001 0.05 0.54

328 (324, 332) 330 (326, 335) 332 (328, 337)

<0.001 0.007 0.09

0.83 (0.82, 0.84) 0.84 (0.83, 0.85)

0.83 (.82, 0.84)

0.05 0.83 0.86

 $\begin{array}{c} 0.91 \ (0.89, \ 0.94) \\ 0.92 \ (0.90, \ 0.95) \\ 0.93 \ (0.90, \ 0.95) \end{array}$ 

0.01 0.33 0.43

0.78 (0.63, 0.96) 0.90 (0.71, 1.11) 0.96 (0.79, 1.17)

0.93 0.46 0.20

0.96 (0.77, 1.20) 1.03 (0.82, 1.30) 1.09 (0.86, 1.37)

0.82 0.66 0.49

80.2 (68.9, 93.3) 79.1 (67.9, 92.2) 80.8 (68.9, 93.7)

P for trend<sup>2</sup>

Q5 (n = 941)

Q4 (n = 1151)

Q3 (n = 907)

Q2 (*n* = 978)

Q1 (n = 1065)

0.01 0.65 0.60

0.48 (0.25, 0.92) 0.78 (0.29, 1.53) 0.76 (0.38, 1.49)

Markers of vascular integrity ^3 LAE (mL/mm Hg  $\times$  10)

| $ \begin{array}{c} Model 1^{4} & 12 \\ Model 2^{5} & Model 2^{5} & 12 \\ Model 3^{6} & 12 \\ SAE (mL/mm Hg \times 100) & 3.7 \\ Model 1^{4} & 3.7 \\ Model 2^{5} & 3.7 \end{array} $ | (2001 - 1) 12  | Q2 (n = 978)  | Q3 $(n = 907)$   | Q4 ( <i>n</i> = 1151)  | Q5 $(n = 941)$  | <i>P</i> for trend <sup>2</sup>   |
|--|--|---|--|--|---|---|
| SAE (mL/mm Hg $\times$ 100)<br>Model 1 <sup>4</sup> 3.7<br>Model 2 <sup>5</sup> 3.7  | .4 (12.1, 12.6)<br>.4 (12.2, 12.6)<br>.4 (12.2, 12.6)                          | 12.5 (12.2, 12.7)<br>12.6 (12.4, 12.8)<br>12.6 (12.4, 12.8)                 | 12.4 (12.1, 12.7)<br>12.6 (12.3, 12.8)<br>12.6 (12.3, 12.8)                    | 12.7 (12.4, 12.9)<br>12.7 (12.4, 12.9)<br>12.7 (12.4, 12.9)          | 12.8 (12.5, 13.1)<br>12.6 (12.3, 12.8)<br>12.6 (12.4, 12.9)         | 0.006<br>0.14<br>0.11   |
| Model 3 <sup>6</sup> 3.7   | 75 (3.63, 3.87)<br>78 (3.67, 3.90)<br>79 (3.67, 3.91)                          | 3.81 (3.69, 3.93)<br>3.80 (3.68, 3.91)<br>3.80 (3.69, 3.92)                 | 3.87 (3.75, 4.00)<br>3.89 (3.77, 4.01)<br>3.89 (3.77, 4.01)                    | 3.82 (3.71, 3.94)<br>3.81 (3.70, 3.91)<br>3.80 (3.70, 3.91)          | 4.00 (3.86, 4.14)<br>3.96 (3.84, 4.09)<br>3.96 (3.83, 4.09)         | 0.01<br>0.10<br>0.13  |
| ACR<br>Model 1 <sup>4</sup><br>Model 2 <sup>5</sup><br>Model 3 <sup>6</sup><br>Libids <sup>3</sup>   | 7.3 (6.9, 7.7)<br>7.1 (6.7, 7.5)<br>7.1 (6.7, 7.5)                             | 7.1 (6.7, 7.5)<br>7.1 (6.7, 7.5)<br>7.0 (6.7, 7.4)                          | 6.9 (6.5, 7.3)<br>6.9 (6.5, 7.3)<br>6.9 (6.5, 7.3)                             | 6.7 (6.4, 7.1)<br>6.8 (6.5, 7.1)<br>6.8 (6.5, 7.2)                   | 6.4 (6.1, 6.8)<br>6.6 (6.2, 6.9)<br>6.6 (6.3, 7.0)                  | <0.001<br>0.005<br>0.02   |
| HDL cholesterol (mg/dL)<br>Model 1 <sup>4</sup><br>Model 2 <sup>5</sup><br>Model 3 <sup>6</sup>  | $50.1 \pm 0.4$<br>$50.6 \pm 0.4$<br>$51.0 \pm 0.4$                             | $51.3 \pm 0.4$<br>$51.5 \pm 0.4$<br>$51.8 \pm 0.4$                          | $51.8 \pm 0.5$<br>$51.8 \pm 0.5$<br>$51.9 \pm 0.4$                             | $52.3 \pm 0.4$<br>$52.1 \pm 0.4$<br>$51.9 \pm 0.4$                   | $53.5 \pm 0.5$<br>$53.0 \pm 0.5$<br>$52.4 \pm 0.5$                  | $< 0.001 \\ 0.002 \\ 0.20$  |
| LDL cholesterol (mg/dL)<br>Model 1 <sup>4</sup><br>Model 3 <sup>6</sup>  | $\begin{array}{c} 119.2 \pm 1.0 \\ 119.0 \pm 1.0 \\ 118.8 \pm 1.0 \end{array}$ | $117.5 \pm 1.0$<br>117.4 \pm 1.0<br>117.3 \pm 1.0                           | $\begin{array}{c} 118.0 \pm 1.0 \\ 118.0 \pm 1.0 \\ 117.9 \pm 1.0 \end{array}$ | $118.2 \pm 0.9$<br>118.3 ± 0.9<br>118.3 ± 0.9                        | $116.8 \pm 1.1$ $117.1 \pm 1.1$ $117.3 \pm 1.1$                     | 0.13<br>0.34<br>0.51  |
| Triglycerides (mg/dL) $16.7$<br>Model 1 <sup>4</sup> $116.7$<br>Model 2 <sup>5</sup> 113.5<br>Model 3 <sup>6</sup> 112.0<br>Other CVD risk factors <sup>9</sup>                      | 2 (112.6, 119.8)<br>5 (110.0, 117.1)<br>0 (108.6, 115.4)                       | 111.6 (108.2, 115.1)<br>111.2 (107.8, 114.7)<br>110.0 (106.8, 113.4)        | 111.2 (107.7, 114.7)<br>111.3 (107.8, 114.9)<br>111.0 (107.6, 114.5)           | 108.1 (105.1, 111.3)<br>108.9 (105.8, 112.0)<br>109.7 (106.7, 112.8) | 102.6 (99.3, 106.0)<br>104.5 (101.1, 108.0)<br>106.6 (103.2, 110.0) | <0.001<br>0.01<br>0.33  |
| Systolic blood pressure (mmHg)<br>Model 1 <sup>4</sup><br>Model 2 <sup>5</sup><br>Model 3 <sup>6</sup>   | $125.0 \pm 0.6$<br>$124.5 \pm 0.6$<br>$124.2 \pm 0.6$                          | $124.6 \pm 0.6$ $124.5 \pm 0.6$ $124.3 \pm 0.6$                             | $\begin{array}{c} 125.9\pm0.6\\ 125.9\pm0.6\\ 125.8\pm0.6\end{array}$          | 125.1 ± 0.6<br>125.3 ± 0.6<br>125.5 ± 0.6                            | $124.3 \pm 0.6$ $124.8 \pm 0.7$ $125.3 \pm 0.7$                     | 0.49<br>0.61<br>0.15  |
| Diastolic blood pressure (mmHg)<br>Model 1 <sup>4</sup><br>Model 2 <sup>5</sup>  | $71.9 \pm 0.3$<br>$71.7 \pm 0.3$<br>$71.6 \pm 0.3$                             | $71.8 \pm 0.3$<br>$72.0 \pm 0.3$<br>$71.7 \pm 0.3$                          | $72.0 \pm 0.3$<br>$72.1 \pm 0.3$<br>$72.0 \pm 0.3$                             | $71.8 \pm 0.3$ $71.8 \pm 0.3$ $71.9 \pm 0.3$                         | $71.3 \pm 0.3$ $71.4 \pm 0.3$ $71.5 \pm 0.3$                        | 0.57<br>0.44<br>0.99  |
| Fasting glucose (mg/dL)<br>Model 1 <sup>4</sup><br>Model 2 <sup>5</sup><br>Model 3 <sup>6</sup>  | $96.5 \pm 0.3$<br>$96.1 \pm 0.3$<br>$95.8 \pm 0.3$                             | $96.1 \pm 0.3$<br>$96.1 \pm 0.3$<br>$95.8 \pm 0.3$                          | $95.3 \pm 0.3$<br>$95.2 \pm 0.3$<br>$95.2 \pm 0.3$                             | $95.3 \pm 0.3$<br>$95.5 \pm 0.3$<br>$95.7 \pm 0.3$                   | $95.0 \pm 0.3$<br>$95.3 \pm 0.3$<br>$95.7 \pm 0.3$                  | <0.001<br>0.11<br>0.91  |
| Fasting institut (pmo/L)<br>Model 1 <sup>4</sup><br>Model 2 <sup>5</sup><br>Model 3 <sup>6</sup>   | $49.0 \pm 0.9 \\ 48.0 \pm 0.9 \\ 46.6 \pm 0.8$                                 | $\begin{array}{c} 45.9 \pm 0.9 \\ 45.7 \pm 0.9 \\ 44.7 \pm 0.8 \end{array}$ | $43.8 \pm 0.9$<br>$43.7 \pm 0.9$<br>$43.4 \pm 0.8$                             | $41.3 \pm 0.8 \\41.6 \pm 0.8 \\42.3 \pm 0.8$                         | $36.6 \pm 1.0$<br>$37.9 \pm 1.0$<br>$39.9 \pm 0.9$                  | <0.001<br><0.001<br><0.001<br>  |
| Wats currinterance (cm)<br>Model 1 <sup>4</sup><br>Model 2 <sup>5</sup><br>BMI (kg/m <sup>2</sup> )<br>Model 1 <sup>4</sup><br>Model 2 <sup>5</sup>                                  | $98.5 \pm 0.4$<br>$98.0 \pm 0.4$<br>$28.3 \pm 0.2$<br>$28.2 \pm 0.2$           | $98.0 \pm 0.4$ $97.7 \pm 0.4$ $28.2 \pm 0.2$ $28.1 \pm 0.2$                 | $97.0 \pm 0.4$<br>$96.9 \pm 0.4$<br>$27.9 \pm 0.2$<br>$27.9 \pm 0.2$           | $95.7 \pm 0.4$ $95.9 \pm 0.4$ $27.6 \pm 0.1$ $27.6 \pm 0.1$          | $93.9 \pm 0.4$ $94.5 \pm 0.4$ $27.0 \pm 0.2$ $27.2 \pm 0.2$         | <pre>&lt;0.001</pre> <pre>&lt;0.001</pre> <pre>&lt;0.001</pre> <pre>&lt;0.001</pre> |

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CRP, C-reactive protein; IL-6, interleukin-6; CAC, coronary artery calcification; ABI, ankle brachial index; LAE, large artery elasticity; SAE, small artery elasticity; ACR, albumin to creatinine ratio; IMT, intima-media thickness; CC, common carotid artery; IC, internal carotid artery.

 $^2P$  for trend across quintiles calculated with the Healthy Dietary Pattern modeled continuously (score).

<sup>3</sup> All values are geometric  $\vec{x}$ , 95% CI in parentheses.

<sup>4</sup> Adjusted for energy intake (kcal/d), age (y), race-ethnicity (white, black, Hispanic, Chinese), and study center.

5 Adjusted as for model 1 plus education (<high school, high school, >high school), physical activity (active and inactive leisure in metabolic equivalents per min/wk), smoking (current or not current and pack-years), and supplement use (2 weekly). Data for LAE and SAE also adjusted for height, weight, systolic blood pressure, and pulse rate.

 $^{6}$  Adjusted as for model 2 plus waist circumference (cm).

 $^7$ All values are odds ratios; 95% CI in parentheses.

 $^8$ Values calculated in 2380 participants with an Agatston score > 0.

gAll values are  $\bar{x} \pm SD$ .

#### **TABLE 3**

Regression coefficients (or odds ratios) for the relation between select cardiovascular disease (CVD) risk markers and a priori Comprehensive and Simplified Healthy Diet Patterns in the Multi-Ethnic Study of Atherosclerosis<sup>1</sup>

|  | Comprehensive<br>Healthy Dietary<br>Pattern Score <sup>2</sup> | Simplified Healthy<br>Dietary Pattern<br>Score <sup>3</sup> | Difference between scores <sup>3</sup> |
|--|--|---|--|
| Inflammatory markers <sup>4</sup>                            |  |   |  |
| CRP (mg/dL)  | $-0.07 \pm 0.02,^{56}$   | $-0.12 \pm 0.02^{6}$  | $-0.02\pm0.02$                         |
| IL-6 $(mg/dL)$   | $-0.05 \pm 0.01^6$   | $-0.02 \pm 0.01$  | $-0.03 \pm 0.01^{6}$                   |
| Homocysteine (µmol/L)  | $-0.02 \pm 0.004^{6}$  | $-0.02 \pm 0.01^{6}$  | $-0.003 \pm 0.01$                      |
| Fibrinogen (mg/dL)   | $-0.01 \pm 0.003^{6}$  | $-0.004 \pm 0.003$  | $-0.003 \pm 0.003$                     |
| Markers of subclinical atherosclerosis                       |  |   |  |
| Common carotid IMT $(mm)^4$                                  | $-0.008 \pm 0.003^{6}$   | $-0.006 \pm 0.003$  | $-0.004 \pm 0.003$                     |
| Internal carotid IMT $(mm)^4$                                | $-0.001 \pm 0.007$   | $-0.015 \pm 0.007$  | $-0.009 \pm 0.007$                     |
| Carotid plaque   | $0.96(0.78, 1.16)^7$   | $0.88(0.82, 0.95)^6$  | 1.06 (0.98, 1.14)                      |
| CAC (Agatston $> 0$ )  | 1.03 (0.96, 1.11)  | 0.99 (0.92, 1.07)   | 1.04 (0.96, 1.12)                      |
| CAC (Agatston score) $^{\delta}$                             | $-0.03 \pm 0.04$   | $-0.04 \pm 0.04$  | $0.05 \pm 0.04$                        |
| ABI (<0.9)   | 0.96 (0.78, 1.16)  | 0.81 (0.66, 1.01)   | 1.11 (0.90, 1.36)                      |
| Markers of vascular integrity                                | 0.007 0.007  | 0.004 0.005   | 0.005 0.01                             |
| LAE (mL/mm Hg $\times$ 10) <sup>4,9</sup>                    | $0.007 \pm 0.005$  | $0.004 \pm 0.005$   | $0.005 \pm 0.01$                       |
| SAE $(mL/mm Hg \times 100)^{4,9}$                            | $0.01 \pm 0.01$  | $0.029 \pm 0.008$   | $0.007 \pm 0.01$                       |
| ACR  | $-0.04 \pm 0.01^{0}$   | $-0.05 \pm 0.02^{0}$  | $-0.005 \pm 0.02$                      |
| Lipids   | 6  | 0.00  | 6                                      |
| HDL cholesterol (mg/dL)                                      | $0.67 \pm 0.2^{\circ}$   | $-0.28 \pm 0.24$  | $0.90 \pm 0.2^{\circ}$                 |
| LDL cholesterol (mg/dL)                                      | $-0.48 \pm 0.5$  | $-1.1 \pm 0.5^{\circ}$                                      | $0.31 \pm 0.5$                         |
| Triglycerides (mg/dL) <sup>4</sup><br>Other CVD risk factors | $-0.02 \pm 0.01^{0}$   | $-0.01 \pm 0.01$  | $-0.01 \pm 0.01$                       |
| Systolic blood pressure (mm Hg)                              | $0.16 \pm 0.3$   | $-0.53 \pm 0.3$   | $0.54 \pm 0.3$                         |
| Diastolic blood pressure (mm Hg)                             | $-0.09 \pm 0.2$  | $-0.33 \pm 0.2$   | $0.14 \pm 0.2$                         |
| Fasting glucose (mg/dL)                                      | $-0.24 \pm 0.1$  | $-0.68 \pm 0.2^{6}$   | $0.24 \pm 0.2$                         |
| Fasting insulin (pmol/L)                                     | $-0.51 \pm 0.07^{6}$   | $0.26 \pm 0.07^6$   | $-0.34 \pm 0.07^{6}$                   |
| Waist circumference (cm)                                     | $-1.3 \pm 0.2^{6}$   | $-1.5 \pm 0.2^{6}$  | $-0.27 \pm 0.2$                        |
| BMI (kg/m <sup>2</sup> )                                     | $-0.38 \pm 0.08^{6}$   | $0.57\pm0.08^{6}$   | $-0.02\pm0.08$                         |
|  |  |   |  |

<sup>1</sup>CRP, C-reactive protein; IL-6, interleukin-6; IMT, intima-media thickness; CAC, coronary artery calsification; ABI, ankle brachial index; LAE, large artery elasticity; SAE, small artery elasticity; ACR, albumin to creatinine ratio.

 $^{2}$ Adjusted for energy intake (kcal/d), age (y), race-ethnicity (white, black, Hispanic, Chinese), study center, education (<high school, high school, >high school), physical activity (active and inactive leisure in metabolic equivalents per min/wk), smoking (current or not current and pack-years), and supplement use ( $\geq$ weekly).

<sup>3</sup>Model includes the covariates in footnote 2 and both the difference between scores (Healthy Dietary Pattern score — Simplified Healthy Dietary Pattern score) and the Simplified Healthy Dietary Pattern score.

<sup>4</sup>Data were analyzed on the natural log scale.

 $^{5}\beta$ -coefficient ± SE per 1 SD (10.2) for the Comprehensive Healthy Dietary Pattern score and per 1 SD (3.52) for the Simplified Healthy Dietary Pattern score.

 $^{6}P < 0.05.$ 

<sup>7</sup>Odds ratio; 95% CI in parentheses (all such values).

<sup>8</sup> Estimated from 2380 participants with an Agatston score >0.

<sup>9</sup>Data for LAE and SAE also adjusted for height, weight, systolic blood pressure, and pulse rate. Greater elasticity values are favorable.