Association of Dietary Protein Consumption With Incident Silent Cerebral Infarcts and Stroke

The Atherosclerosis Risk in Communities (ARIC) Study

Bernhard Haring, MD, MPH; Jeffrey R. Misialek, MPH, PhD; Casey M. Rebholz, PhD; Natalia Petruski-Ivleva, MS; Rebecca F. Gottesman, MD, PhD; Thomas H. Mosley, PhD; Alvaro Alonso, MD, PhD

Background and Purpose—The effect of dietary protein on the risk of stroke has shown inconsistent results. We aimed to evaluate the relationship of dietary protein sources with the risk of stroke and silent cerebral infarcts in a large community-based cohort.

Methods—We studied 11,601 adults (age, 45–64 years at baseline in 1987–1989) enrolled in the Atherosclerosis Risk in Communities (ARIC) Study, free of diabetes mellitus and cardiovascular disease. Dietary protein intake was assessed with validated food frequency questionnaires at baseline and after 6 years of follow-up. Incident stroke events were identified through hospital discharge codes and stroke deaths and physician-adjudicated through December 31, 2011. A subset of participants (n=653) underwent brain magnetic resonance imaging in 1993 to 1995 and in 2004 to 2006. Cox proportional hazard models and logistic regression were used for statistical analyses.

Results—During a median follow-up of 22.7 years, there were 699 stroke events. In multivariable analyses, total, animal, and vegetable protein consumption was not associated with risk of stroke. Red meat consumption was associated with increased stroke risk, particularly ischemic events. The hazard ratios (95% confidence interval) for risk of ischemic stroke across ascending quintiles of red meat consumption were 1 (ref), 1.13 (0.85–1.49), 1.44 (1.09–1.90), 1.33 (0.99–1.79), and 1.47 (1.06–2.05); P_trend=0.01. No association of major dietary protein sources with silent cerebral infarcts was detected.

Conclusions—This study supports the notion that consumption of red meat may increase the risk of ischemic stroke. No association between dietary protein intake and silent cerebral infarcts was found. (Stroke. 2015;46:3443-3450. DOI: 10.1161/STROKEAHA.115.010693.)

Key Words: animal proteins dietary proteins silent cerebral infarcts stroke vegetable proteins

The relationship of dietary protein consumption with risk of stroke has shown inconsistent results. Moderate dietary protein intake of animal origin has been associated with a lower risk of stroke, whereas major animal sources of dietary protein, such as red meat, have been related to an increased risk.1–3 These inconsistencies may be explained by a previous focus on nutrients (dietary protein type) instead of food groups, which provide a more adequate assessment of the complexities of diet–disease associations. Dietary protein sources vary in their nonprotein constituents (eg, fat and sodium content), which may in part explain differential health effects. However, evidence derived from comprehensive food group analyses in community-based studies is sparse. Most current data originate from well-educated, ethnically homogenous study populations, such as health professionals or selected Swedish populations.3–5 Thus, generalizability of the existing data to more diverse populations is limited. Conclusions about the relation of dietary protein sources with stroke risk in the general population are difficult to draw.

Prior to clinically recognized stroke events, dietary protein intake may already have subclinical effects identified via incidence of silent cerebral infarcts (SCIs), an independent risk factor for developing symptomatic stroke events.6–8 Whether dietary protein consumption affects the risk of SCIs is largely unknown.9

The objective of this study was to evaluate the relationship between total, animal, and plant-derived dietary protein, as well as more specific protein-rich food groups, such as red and processed meat consumption, with the risk of stroke (hemorrhagic and ischemic) and SCIs in a large, community-based cohort of middle-aged adults.

Continuing medical education (CME) credit is available for this article. Go to http://cme.ahajournals.org to take the quiz.

Received July 8, 2015; final revision received September 3, 2015; accepted October 1, 2015.

From the Department of Internal Medicine I, Comprehensive Heart Failure Center, University of Würzburg, Würzburg, Bavaria, Germany (B.H.); Division of Epidemiology & Community Health, School of Public Health, University of Minnesota, Minneapolis, Minnesota (J.R.M., A.A.); Department of Epidemiology and the Welch Center for Prevention, Epidemiology and Clinical Research, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD (C.M.R.); Department of Epidemiology, University of North Carolina Gillings School of Global Public Health, Chapel Hill (N.P.-I.); Department of Neurology, Johns Hopkins School of Medicine, Baltimore, MD (R.F.G.); and Department of Neurology, University of Mississippi Medical Center, Jackson (T.H.M.).

The online-only Data Supplement is available with this article at http://stroke.ahajournals.orglookup/suppl/doi:10.1161/STROKEAHA.115.010693/-/DC1.

Correspondence to Bernhard Haring, MD, MPH, Department of Internal Medicine I, Comprehensive Heart Failure Center, University of Würzburg, Oberdärracherstrasse 6, Würzburg 97080, Germany. E-mail Haring_B@ukw.de

© 2015 American Heart Association, Inc.

Stroke is available at http://stroke.ahajournals.org

DOI: 10.1161/STROKEAHA.115.010693
Methods

Study Population
The Atherosclerosis Risk in Communities Study (ARIC) is a community-based prospective cohort study of 15,792 middle-aged adults (age, 45–64 years at baseline) from 4 US communities (Washington County, MD; Forsyth County, NC; Jackson, MS; and suburbs of Minneapolis, MN).10–12 For this analysis, only white and black adults were included; blacks from the Minneapolis and Washington County field centers were excluded because of small numbers. Participants with self-reported diabetes mellitus, fasting blood glucose ≥126 mg/dL, nonfasting blood glucose ≥200 mg/dL, or use of diabetes mellitus medication; a history of myocardial infarction, stroke, heart failure, coronary bypass surgery, or angioplasty; or with missing data on covariates of interest were not included. Individuals with diabetes mellitus and cardiovascular disease were not included as these conditions may lead to changes in diet. Finally, participants with incomplete dietary information or with extreme caloric intake (<600 or >4200 kcal per day for men, <500 or >3600 kcal per day for women) were excluded from further analysis.13 Our final study population included 11,601 persons.

The ARIC study was approved by the Institutional Review Boards (IRB) of all participating institutions, including the IRBs of the University of Minnesota, Johns Hopkins University, University of North Carolina, University of Mississippi Medical Center, and Wake Forest University. The written documentation of informed consent was obtained from all participants at each clinical site.

Assessment of Dietary Protein Intake
The ARIC study assessed protein intake using an interviewer-administered, 66-item food frequency questionnaire (FFQ) adapted from the 61-item FFQ developed by Willett et al.11 The FFQ was administered to all participants at visit 1 (baseline, 1987–1989) and at visit 3 (1993–1995). The residual method was applied to adjust for total energy intake.14–16 For determining dietary intake, we divided participants into quintiles of cumulative average intake of various protein sources. Cumulative updating of the FFQ (ie, visit 1 FFQ for follow-up between visit 1 and visit 3 and the average of visits 1 and 3 FFQ afterward for those who attended both examinations, or visit 1 FFQ for those who did not attend visit 3) was used to reduce within-person variation and best represent long-term dietary behavior.13

Assessment of Stroke Events
The primary end point for this study was stroke (definite or probable ischemic or hemorrhagic) after the completion of the first FFQ (between 1987 and 1989). The ARIC study identified incident stroke cases through hospital discharge codes and stroke deaths.14–16 Physician reviewers adjudicated all possible strokes and classified them as definite or probable ischemic or hemorrhagic events based on information abstracted from the medical record.14–16 Follow-up for stroke events was available until December 31, 2011.

Brain Magnetic Resonance Imaging and Subclinical Cerebral Infarcts
A subset of ARIC study participants (ARIC Brain MRI study), who were 55 years or older, were invited for a brain magnetic resonance imaging (MRI) during visit 3 (1993–1995) and a second brain MRI examination which took place in 2004 to 2006.13,14 Brain MRIs were performed using 1.5T scanners, and contiguous axial images of 5 mm thick were obtained.17,18 Interpretation was done at the ARIC MRI Reading Center. SCIs were defined as foci, nonmass lesions ≥2 mm that were bright on T2 and proton density and dark on T1 images. Further details of the MRI scanning protocol have been described previously.13,14

A total of 1945 participants successfully underwent brain MRI at visit 3, 1812 of whom had scans of sufficient quality. A total of 906 participants (60.6% women and 48.3% blacks) received MRI both at visit 3 and from 2004 to 2006. For this analysis, we examined incident SCIs in participants without evidence of SCIs or stroke history at visit 3. Our final study population consisted of 653 individuals.

Measurement of Participant Characteristics
Height, weight, and waist circumference were measured following a standardized protocol.19–21 Data on smoking, ethanol intake, education, intake of antihypertensive, or lipid-lowering medication were derived from standardized questionnaires.10 ARIC participants underwent fasting venipuncture at each examination.18 Sports-related physical activity and leisure-related physical activity were assessed with the use of Baehke’s questionnaire and scoring systems.22 Depressive symptoms were assessed using a 21-item questionnaire on vital exhaustion developed by Appels et al.23 Diabetes mellitus was defined as current use of glucose-lowering medications, fasting blood glucose ≥126 mg/dL, nonfasting blood glucose ≥200 mg/dL, or self-reported history of diabetes mellitus. Hypertension was defined based on the average of the last 2 of 3 blood pressure readings, as systolic blood pressure ≥140 mm Hg or diastolic blood pressure ≥90 mm Hg.

Statistical Analysis
To assess the association of total, animal, and vegetable protein intake with incidence of stroke and SCIs, we calculated incidence rates of stroke events per 1000 person-years as the number of diagnosed cases occurring during the entire follow-up period divided by person-years of follow-up. Follow-up time was defined as time from the baseline examination to the earliest of the first event, death, lost to follow-up, or December 31, 2011. Multivariable Cox proportional hazards regression models were used to calculate the hazard ratios (HR) and 95% confidence interval (CI) of total, ischemic, and hemorrhagic stroke by quintiles of the dietary exposure, using the lowest quintile as the reference. Similarly, logistic regression was used to calculate odds ratio and 95% CI of incident SCI by quintiles of protein intake. An initial model adjusted for age, race, sex, ARIC study center, and total energy intake (minimally adjusted model, model 1). A second model additionally adjusted for smoking (current, former, and never), pack-years of smoking, education (less than high school, high school, and more than high school), systolic blood pressure (mm Hg), use of antihypertensive medication, high-density lipoprotein cholesterol (mmol/L), total cholesterol (mmol/L), use of lipid-lowering medication, body mass index (kg/m²), waist/hip ratio, alcohol intake (g/wk), Baehke’s physical activity score, leisure-related physical activity, carbohydrate intake (quintiles), fiber intake (quintiles), dietary fat (quintiles), and magnesium intake (quintiles) (fully adjusted model, model 2). Median protein intake of each quintile (g/d) was modeled as a continuous variable to test for linear trend. Tests of the proportional hazards assumption were evaluated through the examination of an interaction term between each protein variable and follow-up time along with the inspection of log-negative log survival curves; no violations from the assumption were observed. All statistical tests were 2-tailed. Data were analyzed with SAS 9.3 (SAS Corp, Cary, NC).

Results
Baseline characteristics of the study participants according to quintiles of total protein intake are shown in Table 1. Compared with participants with high protein consumption, individuals with low protein consumption were more likely to be black, to be a current smoker, and less likely to have graduated from high school or to be less physically active. Participants with low protein intake were more likely to have a lower BMI and a higher systolic blood pressure; they were less likely to be using lipid-lowering medication, consumed more carbohydrates and alcohol but less fiber. Across dietary protein quintiles, we found no differences in age, sex, energy intake, blood lipids, or prevalence of hypertension.
During a median follow-up of 22.7 years, there were 699 total stroke events among 11,601 participants. When analyzing the association of dietary protein type with stroke incidence, neither total protein intake nor animal protein consumption was significantly related to total stroke events (Table 2) or hemorrhagic or ischemic stroke incidents (Table I in the online-only Data Supplement). In the minimally adjusted model, higher intake of vegetable sources of protein was significantly associated with a 21% reduced risk of incident stroke (HR_Q5 versus Q1, 0.79; 95% CI, 0.61–1.00; P_trend=0.03; Table 2). However, this association was no longer significant in the fully adjusted model (Table 2) and according to stroke subtypes (Table I in the online-only Data Supplement). Results were essentially the same once we accounted for depressive symptoms (Table II in the online-only Data Supplement) and once we included animal and vegetable protein simultaneously in the model (data not shown).

In detailed food group analyses of major dietary protein sources (Table 3), higher intake of processed meat and red meat was significantly associated with an increased risk of total stroke (HR_Q5 versus Q1, 1.24; 95% CI, 0.94–1.63; P_trend=0.04 for processed meat; HR_Q5 versus Q1, 1.41; 95% CI, 1.04–1.92; P_trend=0.01 for red meat). Low-fat dairy and egg consumption were associated with a decreased risk of stroke in the minimally adjusted model, but these associations were attenuated and became insignificant after full adjustment for potential confounders. In stroke subtype analyses (Table III in the online-only Data Supplement), among dietary protein sources higher egg consumption was found to be associated with risk of hemorrhagic stroke (HR_Q5 versus Q1, 1.41; 95% CI, 0.77–2.57; P_trend=0.02), whereas only red meat consumption was related to ischemic stroke events (HR_Q5 versus Q1, 1.47; 95% CI, 1.06–2.05; P_trend=0.01). When we investigated the association of major dietary protein sources with stroke incidence by sex (Table IV in the online-only Data Supplement), we found

### Table 1. Baseline Characteristics According to Quintiles of Total Protein Intake, ARIC 1987 to 1989

<table>
<thead>
<tr>
<th>Quintile</th>
<th>Q1 (Low)</th>
<th>Q2</th>
<th>Q3</th>
<th>Q4</th>
<th>Q5 (High)</th>
<th>P_total *</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>2320</td>
<td>2320</td>
<td>2321</td>
<td>2320</td>
<td>2320</td>
<td></td>
</tr>
<tr>
<td>Total protein intake, g/d (SD)</td>
<td>49.3 (10.2)</td>
<td>62.9 (3.9)</td>
<td>70.1 (3.9)</td>
<td>77.7 (4.0)</td>
<td>93.3 (12.6)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Total protein intake, % of total energy</td>
<td>12.4 (1.7)</td>
<td>15.7 (1.0)</td>
<td>17.8 (1.5)</td>
<td>19.8 (2.0)</td>
<td>22.7 (3.3)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Animal protein intake, g/d (SD)</td>
<td>32.4 (10.0)</td>
<td>45.2 (5.5)</td>
<td>51.9 (5.7)</td>
<td>59.7 (5.8)</td>
<td>75.8 (14.3)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Vegetable protein intake, g/d (SD)</td>
<td>17.0 (5.8)</td>
<td>17.7 (4.7)</td>
<td>18.2 (5.0)</td>
<td>18.0 (5.1)</td>
<td>17.6 (5.7)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Age, y (SD)</td>
<td>53.4 (5.7)</td>
<td>53.9 (5.7)</td>
<td>54.0 (5.8)</td>
<td>53.7 (5.7)</td>
<td>53.8 (5.7)</td>
<td>0.10</td>
</tr>
<tr>
<td>Women, %</td>
<td>55.9</td>
<td>55.9</td>
<td>55.9</td>
<td>55.9</td>
<td>55.9</td>
<td>0.99</td>
</tr>
<tr>
<td>Black, %</td>
<td>25.2</td>
<td>24.7</td>
<td>21.8</td>
<td>21.7</td>
<td>22.6</td>
<td>0.004</td>
</tr>
<tr>
<td>High school graduate or higher, %</td>
<td>72.8</td>
<td>77.8</td>
<td>81.1</td>
<td>82.8</td>
<td>84.5</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Current smoker, %</td>
<td>32.1</td>
<td>28.5</td>
<td>24.3</td>
<td>22.7</td>
<td>21.1</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Vital exhaustion score (SD)</td>
<td>11.2 (8.9)</td>
<td>10.1 (8.5)</td>
<td>9.1 (8.0)</td>
<td>9.1 (7.8)</td>
<td>9.3 (8.2)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Hypertension, %</td>
<td>29.4</td>
<td>27.8</td>
<td>28.7</td>
<td>28.2</td>
<td>28.3</td>
<td>0.54</td>
</tr>
<tr>
<td>Body mass index, kg/m² (SD)</td>
<td>26.6 (5.1)</td>
<td>26.8 (4.9)</td>
<td>27.0 (4.9)</td>
<td>27.3 (5.0)</td>
<td>27.7 (5.0)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Waist/hip ratio (SD)</td>
<td>0.9 (0.1)</td>
<td>0.9 (0.1)</td>
<td>0.9 (0.1)</td>
<td>0.9 (0.1)</td>
<td>0.9 (0.1)</td>
<td>0.16</td>
</tr>
<tr>
<td>Baecke Sport Activity Score (SD)</td>
<td>2.4 (0.8)</td>
<td>2.4 (0.8)</td>
<td>2.5 (0.8)</td>
<td>2.5 (0.8)</td>
<td>2.6 (0.8)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Baecke Leisure Index (SD)</td>
<td>2.3 (0.6)</td>
<td>2.3 (0.6)</td>
<td>2.4 (0.6)</td>
<td>2.4 (0.6)</td>
<td>2.5 (0.6)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Systolic blood pressure, mm Hg (SD)</td>
<td>120.8 (18.7)</td>
<td>120.0 (17.7)</td>
<td>119.8 (17.4)</td>
<td>119.3 (17.7)</td>
<td>119.3 (18.0)</td>
<td>0.002</td>
</tr>
<tr>
<td>Serum HDL, mmol/L (SD)</td>
<td>1.4 (0.4)</td>
<td>1.4 (0.4)</td>
<td>1.4 (0.4)</td>
<td>1.4 (0.4)</td>
<td>1.4 (0.4)</td>
<td>0.31</td>
</tr>
<tr>
<td>Total cholesterol, mmol/L (SD)</td>
<td>5.5 (1.0)</td>
<td>5.5 (1.1)</td>
<td>5.5 (1.1)</td>
<td>5.5 (1.1)</td>
<td>5.5 (1.1)</td>
<td>0.30</td>
</tr>
<tr>
<td>Use of antihypertensive medication, %</td>
<td>21.6</td>
<td>22.0</td>
<td>24.3</td>
<td>22.4</td>
<td>22.8</td>
<td>0.33</td>
</tr>
<tr>
<td>Use of lipid lowering medication, %</td>
<td>1.3</td>
<td>1.7</td>
<td>2.3</td>
<td>3.2</td>
<td>2.7</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Carbohydrate intake, g/d (SD)</td>
<td>230.8 (47.4)</td>
<td>207.8 (31.4)</td>
<td>197.6 (31.4)</td>
<td>188.4 (22.2)</td>
<td>172.5 (37.9)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Carbohydrate intake, % of total energy (SD)</td>
<td>56.1 (9.5)</td>
<td>51.3 (7.9)</td>
<td>48.3 (7.7)</td>
<td>45.8 (7.5)</td>
<td>42.9 (7.7)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Fiber intake, g/d (SD)</td>
<td>15.5 (7.3)</td>
<td>16.7 (5.7)</td>
<td>17.3 (5.6)</td>
<td>17.6 (5.9)</td>
<td>18.3 (7.0)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Magnesium intake, mg/d (SD)</td>
<td>216.9 (65.6)</td>
<td>240.8 (52.7)</td>
<td>253.3 (54.1)</td>
<td>267.1 (57.7)</td>
<td>288.3 (65.5)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Alcohol intake, g/wk (SD)</td>
<td>67.9 (149.2)</td>
<td>44.9 (90.6)</td>
<td>40.7 (78.7)</td>
<td>37.0 (70.5)</td>
<td>32.4 (65.0)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Fish intake, servings/d (SD)</td>
<td>0.2 (0.1)</td>
<td>0.2 (0.2)</td>
<td>0.2 (0.2)</td>
<td>0.3 (0.2)</td>
<td>0.5 (0.5)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Total energy intake, kcal/d (SD)</td>
<td>1814.2 (694.2)</td>
<td>1487.8 (555.9)</td>
<td>1488.7 (537.5)</td>
<td>1566.3 (535.9)</td>
<td>1799.9 (603.7)</td>
<td>0.21</td>
</tr>
<tr>
<td>Total fat intake, g/d (SD)</td>
<td>53.9 (16.1)</td>
<td>59.7 (11.6)</td>
<td>61.3 (12.0)</td>
<td>62.4 (12.8)</td>
<td>63.2 (15.3)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Total fat intake, % of total energy (SD)</td>
<td>30.0 (7.2)</td>
<td>32.4 (6.2)</td>
<td>33.4 (6.3)</td>
<td>34.1 (6.2)</td>
<td>34.5 (6.5)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Values are % for categorical variables and mean (SD) for continuous variables. ARIC indicates Atherosclerosis Risk in Communities Study; and HDL, high-density lipoprotein.

*P values from general linear models for continuous variables and Mantel–Haenszel 1-degree of freedom χ² statistic for categorical variables.
red and processed meat consumption to be associated with an increased risk for male participants (HR Q5 versus Q1, 1.62; 95% CI, 1.03–2.57; *P* trend=0.03).

During a median follow-up of 10.4 years, there were 127 SCIs among 653 participants. We did not observe any association between dietary protein type and risk of SCIs (Table 4).

In food group analyses (Table V in the online-only Data Supplement), nuts and low-fat dairy consumption were significantly associated with decreased risk of SCIs after minimal adjustment, but none of these associations remained significant after fully accounting for confounding factors. Poultry intake was not associated with incident SCIs after minimally adjusting, but became significant after fully adjusting for confounding factors (odds ratio Q4, 1.93; 95% CI, 1.02–3.67; *P* trend=0.05).

**Discussion**

In a large community-based study population, we did not find dietary protein type but more specific protein sources, such as red meat and processed meat, to be associated with an increased risk of total stroke events. This elevation of risk was mainly driven by an association of red meat intake with ischemic stroke cases. Neither dietary protein type nor protein sources were associated with SCIs.

Most recently, a large meta-analysis suggested that moderate dietary protein intake in particular of animal origin was associated with a lower risk of stroke events, but this risk may differ by the specific protein source consumed. To this point, the largest and most comprehensive investigation to examine an association between protein intake and stroke was undertaken using data from the Nurses’ Health Study and Health Professionals Follow-up Study. Higher intake of red meat was associated with an elevated risk for stroke, whereas higher intake of poultry was associated with a lower risk. Similarly, in Swedish men and women, higher intake of red and processed meat products was found to be associated with ischemic infarcts. Our data support the notion that high consumption of red and processed meat products does significantly affect stroke risk in a general Western community setting. Other major dietary protein sources, such as fish, low-fat dairy, and nut consumption, have been inversely associated with stroke risk in previous reports, whereas dietary legumes or egg...
<table>
<thead>
<tr>
<th>Protein Source</th>
<th>Q1</th>
<th>Q2</th>
<th>Q3</th>
<th>Q4</th>
<th>Q5</th>
<th>(P_{\text{trend}})</th>
</tr>
</thead>
<tbody>
<tr>
<td>Processed meat</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>2333</td>
<td>2731</td>
<td>1838</td>
<td>2427</td>
<td>2272</td>
<td></td>
</tr>
<tr>
<td>Events, (n)</td>
<td>122</td>
<td>156</td>
<td>116</td>
<td>119</td>
<td>186</td>
<td></td>
</tr>
<tr>
<td>Median, (\text{mg/d})</td>
<td>0</td>
<td>0.14</td>
<td>0.35</td>
<td>0.50</td>
<td>1.07</td>
<td></td>
</tr>
<tr>
<td>HR (95% CI)*</td>
<td>1 (ref)</td>
<td>1.18 (0.92–1.51)</td>
<td>1.12 (0.86–1.45)</td>
<td>1.02 (0.79–1.32)</td>
<td>1.54 (1.20–1.98)</td>
<td>0.0002</td>
</tr>
<tr>
<td>HR (95% CI)†</td>
<td>1 (ref)</td>
<td>1.06 (0.83–1.36)</td>
<td>1.02 (0.78–1.34)</td>
<td>0.86 (0.66–1.13)</td>
<td>1.24 (0.94–1.63)</td>
<td>0.04</td>
</tr>
<tr>
<td>Red meat</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>2510</td>
<td>2115</td>
<td>2506</td>
<td>2212</td>
<td>2258</td>
<td></td>
</tr>
<tr>
<td>Events, (n)</td>
<td>130</td>
<td>107</td>
<td>161</td>
<td>154</td>
<td>147</td>
<td></td>
</tr>
<tr>
<td>Median, (\text{mg/d})</td>
<td>0.14</td>
<td>0.28</td>
<td>0.50</td>
<td>0.65</td>
<td>1.08</td>
<td></td>
</tr>
<tr>
<td>HR (95% CI)*</td>
<td>1 (ref)</td>
<td>1.15 (0.89–1.48)</td>
<td>1.43 (1.12–1.82)</td>
<td>1.51 (1.18–1.94)</td>
<td>1.65 (1.26–2.15)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>HR (95% CI)†</td>
<td>1 (ref)</td>
<td>1.13 (0.87–1.47)</td>
<td>1.37 (1.06–1.77)</td>
<td>1.38 (1.05–1.81)</td>
<td>1.41 (1.04–1.92)</td>
<td>0.01</td>
</tr>
<tr>
<td>Red meat and processed</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>2379</td>
<td>2290</td>
<td>2314</td>
<td>2289</td>
<td>2329</td>
<td></td>
</tr>
<tr>
<td>Events, (n)</td>
<td>106</td>
<td>126</td>
<td>157</td>
<td>139</td>
<td>171</td>
<td></td>
</tr>
<tr>
<td>Median, (\text{mg/d})</td>
<td>0.25</td>
<td>0.54</td>
<td>0.85</td>
<td>1.21</td>
<td>1.90</td>
<td></td>
</tr>
<tr>
<td>HR (95% CI)*</td>
<td>1 (ref)</td>
<td>1.27 (0.98–1.64)</td>
<td>1.58 (1.23–2.04)</td>
<td>1.38 (1.06–1.81)</td>
<td>1.78 (1.35–2.35)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>HR (95% CI)†</td>
<td>1 (ref)</td>
<td>1.15 (0.88–1.51)</td>
<td>1.39 (1.06–1.81)</td>
<td>1.13 (0.84–1.52)</td>
<td>1.38 (1.00–1.91)</td>
<td>0.06</td>
</tr>
<tr>
<td>Poultry</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>1663</td>
<td>3163</td>
<td>1344</td>
<td>3176</td>
<td>2255</td>
<td></td>
</tr>
<tr>
<td>Events, (n)</td>
<td>111</td>
<td>185</td>
<td>76</td>
<td>208</td>
<td>119</td>
<td></td>
</tr>
<tr>
<td>Median, (\text{mg/d})</td>
<td>0.07</td>
<td>0.14</td>
<td>0.28</td>
<td>0.43</td>
<td>0.80</td>
<td></td>
</tr>
<tr>
<td>HR (95% CI)*</td>
<td>1 (ref)</td>
<td>0.92 (0.73–1.17)</td>
<td>0.73 (0.55–0.97)</td>
<td>0.87 (0.68–1.11)</td>
<td>0.78 (0.60–1.01)</td>
<td>0.12</td>
</tr>
<tr>
<td>HR (95% CI)†</td>
<td>1 (ref)</td>
<td>0.90 (0.71–1.15)</td>
<td>0.87 (0.65–1.15)</td>
<td>0.90 (0.70–1.16)</td>
<td>0.86 (0.65–1.14)</td>
<td>0.55</td>
</tr>
<tr>
<td>Dairy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>2367</td>
<td>2299</td>
<td>2326</td>
<td>2259</td>
<td>2350</td>
<td></td>
</tr>
<tr>
<td>Events, (n)</td>
<td>162</td>
<td>154</td>
<td>122</td>
<td>135</td>
<td>126</td>
<td></td>
</tr>
<tr>
<td>Median, (\text{mg/d})</td>
<td>0.07</td>
<td>0.57</td>
<td>1.07</td>
<td>1.50</td>
<td>2.86</td>
<td></td>
</tr>
<tr>
<td>HR (95% CI)*</td>
<td>1 (ref)</td>
<td>1.02 (0.82–1.28)</td>
<td>0.73 (0.57–0.93)</td>
<td>0.85 (0.67–1.08)</td>
<td>0.79 (0.61–1.03)</td>
<td>0.04</td>
</tr>
<tr>
<td>HR (95% CI)†</td>
<td>1 (ref)</td>
<td>1.12 (0.89–1.40)</td>
<td>0.78 (0.61–1.00)</td>
<td>0.93 (0.73–1.20)</td>
<td>0.86 (0.65–1.15)</td>
<td>0.15</td>
</tr>
<tr>
<td>High-fat dairy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>2298</td>
<td>2335</td>
<td>2547</td>
<td>2173</td>
<td>2248</td>
<td></td>
</tr>
<tr>
<td>Events, (n)</td>
<td>136</td>
<td>129</td>
<td>165</td>
<td>137</td>
<td>132</td>
<td></td>
</tr>
<tr>
<td>Median, (\text{mg/d})</td>
<td>0.07</td>
<td>0.14</td>
<td>0.43</td>
<td>0.80</td>
<td>1.23</td>
<td></td>
</tr>
<tr>
<td>HR (95% CI)*</td>
<td>1 (ref)</td>
<td>1.02 (0.80–1.29)</td>
<td>1.17 (0.93–1.49)</td>
<td>1.02 (0.80–1.31)</td>
<td>0.99 (0.77–1.28)</td>
<td>0.85</td>
</tr>
<tr>
<td>HR (95% CI)†</td>
<td>1 (ref)</td>
<td>1.05 (0.82–1.33)</td>
<td>1.17 (0.92–1.49)</td>
<td>1.06 (0.82–1.36)</td>
<td>0.92 (0.71–1.20)</td>
<td>0.37</td>
</tr>
<tr>
<td>Low-fat dairy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>3130</td>
<td>1649</td>
<td>2181</td>
<td>2439</td>
<td>2202</td>
<td></td>
</tr>
<tr>
<td>Events, (n)</td>
<td>213</td>
<td>117</td>
<td>126</td>
<td>131</td>
<td>112</td>
<td></td>
</tr>
<tr>
<td>Median, (\text{mg/d})</td>
<td>0</td>
<td>0.07</td>
<td>0.43</td>
<td>1.00</td>
<td>2.50</td>
<td></td>
</tr>
<tr>
<td>HR (95% CI)*</td>
<td>1 (ref)</td>
<td>1.11 (0.89–1.39)</td>
<td>0.81 (0.64–1.03)</td>
<td>0.86 (0.68–1.09)</td>
<td>0.74 (0.57–0.96)</td>
<td>0.005</td>
</tr>
<tr>
<td>HR (95% CI)†</td>
<td>1 (ref)</td>
<td>1.26 (1.00–1.58)</td>
<td>1.01 (0.79–1.28)</td>
<td>1.04 (0.81–1.33)</td>
<td>0.91 (0.68–1.21)</td>
<td>0.13</td>
</tr>
<tr>
<td>Fish and seafood</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>2076</td>
<td>3227</td>
<td>1795</td>
<td>2092</td>
<td>2411</td>
<td></td>
</tr>
<tr>
<td>Events, (n)</td>
<td>112</td>
<td>203</td>
<td>108</td>
<td>131</td>
<td>145</td>
<td></td>
</tr>
<tr>
<td>Median, (\text{mg/d})</td>
<td>0</td>
<td>0.14</td>
<td>0.21</td>
<td>0.28</td>
<td>0.57</td>
<td></td>
</tr>
<tr>
<td>HR (95% CI)*</td>
<td>1 (ref)</td>
<td>1.06 (0.84–1.33)</td>
<td>0.90 (0.70–1.16)</td>
<td>0.92 (0.72–1.17)</td>
<td>0.91 (0.71–1.15)</td>
<td>0.27</td>
</tr>
<tr>
<td>HR (95% CI)†</td>
<td>1 (ref)</td>
<td>1.08 (0.86–1.36)</td>
<td>0.97 (0.75–1.26)</td>
<td>0.98 (0.76–1.26)</td>
<td>0.95 (0.73–1.24)</td>
<td>0.46</td>
</tr>
</tbody>
</table>
intake were not found to be related to stroke risk.\textsuperscript{22,23,26,27} In our cohort, we did observe a decreased stroke risk with low-fat dairy consumption, whereas egg consumption seemed to increase stroke risk, but none of these findings remained significant after full adjustment for confounding variables. The increased risk of hemorrhagic stroke associated with higher egg consumption in subgroup analyses contradicts previous analysis and warrants further studies because this subgroup finding was based on a rather small number of events.\textsuperscript{27}

SCIs do not cause acute symptoms and are clinically unrecognized. Nonetheless, these abnormalities are not benign, seem more common with advancing age, and are associated with a future risk of stroke.\textsuperscript{5,28} In our middle-aged population \textapprox 20\% of participants developed SCIs over a 10-year period. We did not observe any association between dietary protein type and SCIs. Among protein sources, dietary fish with higher dietary eicosapentaenoic and docosahexaenoic acid content has been reported to be associated with lower incidence of SCIs.\textsuperscript{9} Our results indeed suggest that higher fish, nuts, or low-fat dairy consumption tends to be associated with lower risk of SCIs. However, these findings have to be interpreted with caution as the number of SCIs was small, and individual results may be spurious.

Mechanisms that explain varying associations of dietary protein sources with stroke risk are numerous. Most importantly, processed meat is known to contain a high sodium amount, which is strongly correlated with incident hypertension.\textsuperscript{29,30} Heme iron intake and serum ferritin concentrations were found to be associated with an increased risk of stroke.\textsuperscript{31,32} The potential adverse effect of heme iron may be attributed to its pro-oxidative properties, whereas serum ferritin levels may further indicate a proinflammatory environment.

The strengths of our analysis include the study of a large biracial, community-based prospective cohort and the long follow-up with structured assessment of dietary intake, covariates, and adjudicated outcome events.\textsuperscript{13,33} Nonetheless, there are several limitations. Our dietary data assessment may misclassify diet as protein intake was only assessed at 2 time points and changing dietary habits over time may not have been covered adequately by our FFQs. Conversely, significant behavioral dietary changes are unlikely to occur in the overall population.\textsuperscript{34,35} Residual and unmeasured confounding could be partly responsible for the results, although we adjusted our analyses for a wide range of confounding factors. Finally, intake of certain food groups, such as fish, and the number of hemorrhagic stroke events were low, which may limit our analyses.

In conclusion, using a large community-based cohort study, we found neither total nor animal or vegetable protein to be associated with stroke incidence. In detailed food group analyses of major protein sources, red meat consumption was related to an increased risk of ischemic stroke events. No association between dietary protein intake and SCIs was found.

\begin{table}
\centering
\caption{Continued}
\begin{tabular}{lcccccc}
\hline
\multicolumn{2}{c}{Eggs} & Q1 & Q2 & Q3 & Q4 & Q5 \\
\hline
n & 2077 & 2127 & 2885 & 3189 & 1322 & \ldots \\
Events, n & 121 & 92 & 169 & 218 & 99 & \ldots \\
Median, svg/d & 0 & 0.07 & 0.14 & 0.43 & 1.00 & \ldots \\
HR (95\% CI)* & 1 (ref) & 0.81 (0.62–1.07) & 1.09 (0.86–1.37) & 1.15 (0.90–1.47) & 1.23 (0.97–1.56) & 0.01 \\
HR (95\% CI)† & 1 (ref) & 0.79 (0.60–1.04) & 1.05 (0.83–1.33) & 1.03 (0.80–1.32) & 1.08 (0.84–1.39) & 0.19 \\
\hline
\multicolumn{2}{c}{Nuts and peanut butter} & & & & & \\
\hline
n & 1951 & 2842 & 2363 & 2183 & 2262 & \ldots \\
Events, n & 130 & 155 & 138 & 141 & 135 & \ldots \\
Median, svg/d & 0 & 0.07 & 0.21 & 0.43 & 1.00 & \ldots \\
HR (95\% CI)* & 1 (ref) & 0.79 (0.63–1.01) & 0.93 (0.73–1.19) & 0.92 (0.72–1.17) & 0.86 (0.67–1.11) & 0.74 \\
HR (95\% CI)† & 1 (ref) & 0.83 (0.65–1.05) & 1.03 (0.81–1.32) & 1.04 (0.81–1.33) & 1.00 (0.77–1.31) & 0.42 \\
\hline
\multicolumn{2}{c}{Legumes} & & & & & \\
\hline
n & 2767 & 2771 & 828 & 2853 & 2382 & \ldots \\
Events, n & 131 & 164 & 47 & 189 & 168 & \ldots \\
Median, svg/d & 0.07 & 0.14 & 0.21 & 0.28 & 0.57 & \ldots \\
HR (95\% CI)* & 1 (ref) & 1.05 (0.82–1.34) & 1.14 (0.88–1.47) & 1.08 (0.84–1.39) & 1.15 (0.90–1.49) & 0.42 \\
HR (95\% CI)† & 1 (ref) & 1.07 (0.84–1.37) & 1.16 (0.89–1.51) & 1.18 (0.91–1.53) & 1.29 (0.98–1.70) & 0.10 \\
\hline
\end{tabular}
\label{table:3}
\end{table}
Table 4.  Association of Total, Animal, and Vegetable Protein Intake (in Quartiles) With Incidence of Silent Cerebral Infarcts, ARIC 1993 to 2006

<table>
<thead>
<tr>
<th></th>
<th>Q1</th>
<th>Q2</th>
<th>Q3</th>
<th>Q4</th>
<th>(P_{\text{trend}})</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>162</td>
<td>164</td>
<td>164</td>
<td>163</td>
<td></td>
</tr>
<tr>
<td>Total protein intake</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female range, g/d</td>
<td>&lt;60.46</td>
<td>60.46–68.99</td>
<td>69.00–77.19</td>
<td>&gt;77.20</td>
<td></td>
</tr>
<tr>
<td>Male range, g/d</td>
<td>&lt;67.87</td>
<td>67.87–76.23</td>
<td>76.24–85.46</td>
<td>&gt;85.47</td>
<td></td>
</tr>
<tr>
<td>Events, n</td>
<td>32</td>
<td>39</td>
<td>28</td>
<td>28</td>
<td></td>
</tr>
<tr>
<td>OR (95% CI)*</td>
<td>1 (ref)</td>
<td>1.13 (0.66–1.94)</td>
<td>0.76 (0.42–1.34)</td>
<td>0.83 (0.47–1.47)</td>
<td>0.35</td>
</tr>
<tr>
<td>OR (95% CI)†</td>
<td>1 (ref)</td>
<td>1.17 (0.62–2.20)</td>
<td>0.73 (0.35–1.50)</td>
<td>0.89 (0.39–2.04)</td>
<td>0.65</td>
</tr>
<tr>
<td>Animal protein intake</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female range, g/d</td>
<td>&lt;47.92</td>
<td>47.92–55.28</td>
<td>55.29–66.23</td>
<td>&gt;66.24</td>
<td></td>
</tr>
<tr>
<td>Male range, g/d</td>
<td>&lt;17.07</td>
<td>17.07–19.19</td>
<td>19.20–22.22</td>
<td>&gt;22.23</td>
<td></td>
</tr>
<tr>
<td>Events, n</td>
<td>34</td>
<td>33</td>
<td>34</td>
<td>26</td>
<td></td>
</tr>
<tr>
<td>OR (95% CI)*</td>
<td>1 (ref)</td>
<td>0.88 (0.51–1.52)</td>
<td>0.91 (0.53–1.57)</td>
<td>0.72 (0.41–1.28)</td>
<td>0.29</td>
</tr>
<tr>
<td>OR (95% CI)†</td>
<td>1 (ref)</td>
<td>1.00 (0.54–1.85)</td>
<td>0.97 (0.49–1.89)</td>
<td>0.80 (0.36–1.79)</td>
<td>0.60</td>
</tr>
<tr>
<td>Vegetable protein intake</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female range, g/d</td>
<td>&lt;14.73</td>
<td>14.73–16.79</td>
<td>16.80–20.00</td>
<td>&gt;20.01</td>
<td></td>
</tr>
<tr>
<td>Male range, g/d</td>
<td>&lt;17.07</td>
<td>17.07–19.19</td>
<td>19.20–22.22</td>
<td>&gt;22.23</td>
<td></td>
</tr>
<tr>
<td>Events, n</td>
<td>33</td>
<td>32</td>
<td>33</td>
<td>29</td>
<td></td>
</tr>
<tr>
<td>OR (95% CI)*</td>
<td>1 (ref)</td>
<td>0.95 (0.54–1.67)</td>
<td>0.97 (0.56–1.69)</td>
<td>0.81 (0.45–1.45)</td>
<td>0.46</td>
</tr>
<tr>
<td>OR (95% CI)†</td>
<td>1 (ref)</td>
<td>1.15 (0.62–2.15)</td>
<td>1.27 (0.64–2.54)</td>
<td>0.97 (0.42–2.23)</td>
<td>0.90</td>
</tr>
</tbody>
</table>

ARIC indicates Atherosclerosis Risk in Communities Study; CI, confidence interval; HR, hazard ratio; and OR, odds ratio. *Adjusted for age, sex, race, study center, and total energy intake. **Adjusted for age, sex, race, study center, total energy intake, smoking, cigarette years, education, systolic blood pressure, use of antihypertensive medication, high-density lipoprotein cholesterol, total cholesterol, use of lipid lowering medication, body mass index, waist/hip ratio, alcohol intake, sports-related physical activity, leisure-related physical activity, carbohydrate intake, fiber intake, fat intake, and magnesium intake.

Acknowledgments

We thank the staff and participants of the ARIC study for their important contributions.

Sources of Funding

The Atherosclerosis Risk in Communities Study is carried out as a collaborative study supported by National Heart, Lung, and Blood Institute contracts (HHSN268201100005C, HHSN268201100006C, HHSN268201100007C, HHSN268201100008C, HHSN268201100009C, HHSN268201100010C, HHSN268201100011C, and HHSN268201100012C). There are no relationships with industry to declare. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the article.

Disclosures

None.

References


Association of Dietary Protein Consumption With Incident Silent Cerebral Infarcts and Stroke: The Atherosclerosis Risk in Communities (ARIC) Study
Bernhard Haring, Jeffrey R. Misialek, Casey M. Rebholz, Natalia Petruski-Ivleva, Rebecca F. Gottesman, Thomas H. Mosley and Alvaro Alonso

*Stroke*. 2015;46:3443-3450; originally published online October 29, 2015;
doi: 10.1161/STROKEAHA.115.010693

*Stroke* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2015 American Heart Association, Inc. All rights reserved.
Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/46/12/3443

Data Supplement (unedited) at:
http://stroke.ahajournals.org/content/suppl/2015/11/03/STROKEAHA.115.010693.DC1

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in *Stroke* can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to *Stroke* is online at:
http://stroke.ahajournals.org//subscriptions/
### Supplemental Table I. Association of quintiles of protein intake with incidence of stroke subtypes (HR and 95%CI)*, ARIC 1987-2011

<table>
<thead>
<tr>
<th></th>
<th>Q 1</th>
<th>Q 2</th>
<th>Q 3</th>
<th>Q 4</th>
<th>Q 5</th>
<th>p_trend</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>n</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total Protein Intake</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemorrhagic Stroke</td>
<td>2320</td>
<td>2320</td>
<td>2321</td>
<td>2320</td>
<td>2320</td>
<td></td>
</tr>
<tr>
<td>HR (95%CI)^†</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ischemic Stroke</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Animal Protein Intake</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemorrhagic Stroke</td>
<td>2320</td>
<td>2320</td>
<td>2321</td>
<td>2320</td>
<td>2320</td>
<td></td>
</tr>
<tr>
<td>HR (95%CI)^†</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ischemic Stroke</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vegetable Protein Intake</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemorrhagic Stroke</td>
<td>2320</td>
<td>2320</td>
<td>2321</td>
<td>2320</td>
<td>2320</td>
<td></td>
</tr>
<tr>
<td>HR (95%CI)^†</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Model 2 adjusted for age, sex, race, study center, total energy intake, smoking, cigarette years, education, systolic blood pressure, use of antihypertensive medication, HDLc, total cholesterol, use of lipid lowering medication, body mass index, waist-to-hip ratio, alcohol intake, sports-related physical activity, leisure-related physical activity, carbohydrate intake, fiber intake, fat intake and magnesium intake.
**Supplemental Table II. Association of total protein, animal protein, vegetable protein and red meat intake (in quintiles) with stroke incidence after accounting for vital exhaustion score, ARIC 1987-2011**

<table>
<thead>
<tr>
<th></th>
<th>Q 1</th>
<th>Q 2</th>
<th>Q 3</th>
<th>Q 4</th>
<th>Q 5</th>
<th>p-trend</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total Protein Intake</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>2091</td>
<td>2115</td>
<td>2156</td>
<td>2170</td>
<td>2158</td>
<td></td>
</tr>
<tr>
<td>Events, n</td>
<td>121</td>
<td>113</td>
<td>136</td>
<td>130</td>
<td>133</td>
<td></td>
</tr>
<tr>
<td>HR (95%CI)*</td>
<td>1 (ref)</td>
<td>1.21 (0.92, 1.59)</td>
<td>1.36 (1.02, 1.82)</td>
<td>1.20 (0.88, 1.65)</td>
<td>1.28 (0.90, 1.83)</td>
<td>0.24</td>
</tr>
<tr>
<td><strong>Animal Protein Intake</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>2100</td>
<td>2131</td>
<td>2154</td>
<td>2163</td>
<td>2142</td>
<td></td>
</tr>
<tr>
<td>Events, n</td>
<td>111</td>
<td>116</td>
<td>130</td>
<td>143</td>
<td>133</td>
<td></td>
</tr>
<tr>
<td>HR (95%CI)*</td>
<td>1 (ref)</td>
<td>1.33 (1.02, 1.74)</td>
<td>1.22 (0.91, 1.62)</td>
<td>1.31 (0.97, 1.78)</td>
<td>1.25 (0.89, 1.75)</td>
<td>0.29</td>
</tr>
<tr>
<td><strong>Vegetable Protein Intake</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>2093</td>
<td>2130</td>
<td>2134</td>
<td>2156</td>
<td>2177</td>
<td></td>
</tr>
<tr>
<td>Events, n</td>
<td>133</td>
<td>129</td>
<td>130</td>
<td>129</td>
<td>112</td>
<td></td>
</tr>
<tr>
<td>HR (95%CI)*</td>
<td>1 (ref)</td>
<td>1.08 (0.83, 1.40)</td>
<td>1.14 (0.87, 1.49)</td>
<td>1.08 (0.81, 1.44)</td>
<td>1.00 (0.72, 1.38)</td>
<td>0.81</td>
</tr>
<tr>
<td><strong>Red Meat Intake</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>2308</td>
<td>1972</td>
<td>2301</td>
<td>2029</td>
<td>2080</td>
<td></td>
</tr>
<tr>
<td>Events, n</td>
<td>116</td>
<td>102</td>
<td>148</td>
<td>134</td>
<td>133</td>
<td></td>
</tr>
<tr>
<td>HR (95%CI)*</td>
<td>1 (ref)</td>
<td>1.19 (0.91, 1.56)</td>
<td>1.45 (1.11, 1.90)</td>
<td>1.34 (1.00, 1.79)</td>
<td>1.41 (1.02, 1.95)</td>
<td>0.05</td>
</tr>
</tbody>
</table>

*adjusted for age, sex, race, study center, total energy intake, smoking, cigarette years, education, systolic blood pressure, use of antihypertensive medication, HDLc, total cholesterol, use of lipid lowering medication, body mass index, waist-to-hip ratio, alcohol intake, sports-related physical activity, leisure-related physical activity, carbohydrate intake, fiber intake, fat intake, magnesium intake, and vital exhaustion score.
<table>
<thead>
<tr>
<th></th>
<th>Q 1</th>
<th>Q 2</th>
<th>Q 3</th>
<th>Q 4</th>
<th>Q 5</th>
<th>P_trend</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Processed Meat</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>2333</td>
<td>2731</td>
<td>1838</td>
<td>2427</td>
<td>2272</td>
<td></td>
</tr>
<tr>
<td>Hemorrhagic Stroke</td>
<td>Events, n</td>
<td>14</td>
<td>27</td>
<td>16</td>
<td>29</td>
<td>28</td>
</tr>
<tr>
<td>HR (95%CI)*</td>
<td>1 (ref)</td>
<td>1.56 (0.78, 3.12)</td>
<td>1.45 (0.69, 3.03)</td>
<td>1.54 (0.76, 3.12)</td>
<td>1.67 (0.80, 3.51)</td>
<td>0.24</td>
</tr>
<tr>
<td>Ischemic Stroke</td>
<td>Events, n</td>
<td>108</td>
<td>132</td>
<td>103</td>
<td>94</td>
<td>161</td>
</tr>
<tr>
<td>HR (95%CI)*</td>
<td>1 (ref)</td>
<td>1.03 (0.79, 1.35)</td>
<td>1.00 (0.75, 1.33)</td>
<td>0.80 (0.60, 1.06)</td>
<td>1.20 (0.90, 1.61)</td>
<td>0.09</td>
</tr>
<tr>
<td><strong>Red Meat</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>2510</td>
<td>2115</td>
<td>2506</td>
<td>2212</td>
<td>2258</td>
<td></td>
</tr>
<tr>
<td>Hemorrhagic Stroke</td>
<td>Events, n</td>
<td>22</td>
<td>23</td>
<td>17</td>
<td>28</td>
<td>24</td>
</tr>
<tr>
<td>HR (95%CI)*</td>
<td>1 (ref)</td>
<td>1.12 (0.60, 2.09)</td>
<td>1.00 (0.52, 1.92)</td>
<td>1.50 (0.79, 2.83)</td>
<td>1.13 (0.53, 2.45)</td>
<td>0.58</td>
</tr>
<tr>
<td>Ischemic Stroke</td>
<td>Events, n</td>
<td>111</td>
<td>86</td>
<td>146</td>
<td>130</td>
<td>125</td>
</tr>
<tr>
<td>HR (95%CI)*</td>
<td>1 (ref)</td>
<td>1.13 (0.85, 1.49)</td>
<td>1.44 (1.09, 1.90)</td>
<td>1.33 (0.99, 1.79)</td>
<td>1.47 (1.06, 2.05)</td>
<td>0.01</td>
</tr>
<tr>
<td><strong>Red Meat &amp; Processed Meat</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>2379</td>
<td>2290</td>
<td>2314</td>
<td>2289</td>
<td>2329</td>
<td></td>
</tr>
<tr>
<td>Hemorrhagic Stroke</td>
<td>Events, n</td>
<td>19</td>
<td>18</td>
<td>21</td>
<td>26</td>
<td>30</td>
</tr>
<tr>
<td>HR (95%CI)*</td>
<td>1 (ref)</td>
<td>0.87 (0.43, 1.74)</td>
<td>1.19 (0.61, 2.31)</td>
<td>1.29 (0.64, 2.60)</td>
<td>1.45 (0.66, 3.17)</td>
<td>0.17</td>
</tr>
<tr>
<td>Ischemic Stroke</td>
<td>Events, n</td>
<td>88</td>
<td>110</td>
<td>137</td>
<td>120</td>
<td>143</td>
</tr>
<tr>
<td>HR (95%CI)*</td>
<td>1 (ref)</td>
<td>1.22 (0.91, 1.63)</td>
<td>1.41 (1.05, 1.89)</td>
<td>1.14 (0.83, 1.58)</td>
<td>1.35 (0.95, 1.93)</td>
<td>0.16</td>
</tr>
<tr>
<td><strong>Poultry</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>1663</td>
<td>3163</td>
<td>1344</td>
<td>3176</td>
<td>2255</td>
<td></td>
</tr>
<tr>
<td>Hemorrhagic Stroke</td>
<td>Events, n</td>
<td>18</td>
<td>30</td>
<td>16</td>
<td>36</td>
<td>14</td>
</tr>
<tr>
<td>HR (95%CI)*</td>
<td>1 (ref)</td>
<td>0.85 (0.47, 1.52)</td>
<td>1.16 (0.60, 2.23)</td>
<td>0.95 (0.52, 1.74)</td>
<td>0.56 (0.26, 1.20)</td>
<td>0.30</td>
</tr>
<tr>
<td>Ischemic Stroke</td>
<td>Events, n</td>
<td>93</td>
<td>158</td>
<td>63</td>
<td>177</td>
<td>107</td>
</tr>
<tr>
<td>HR (95%CI)*</td>
<td>1 (ref)</td>
<td>0.94 (0.72, 1.23)</td>
<td>0.85 (0.62, 1.16)</td>
<td>0.92 (0.70, 1.21)</td>
<td>0.94 (0.70, 1.27)</td>
<td>0.92</td>
</tr>
<tr>
<td><strong>Dairy</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>2367</td>
<td>2299</td>
<td>2326</td>
<td>2259</td>
<td>2350</td>
<td></td>
</tr>
<tr>
<td>Hemorrhagic Stroke</td>
<td>Events, n</td>
<td>29</td>
<td>26</td>
<td>18</td>
<td>17</td>
<td>24</td>
</tr>
</tbody>
</table>

*HR* (Hazard Ratio) and 95% CI (Confidence Interval)
<table>
<thead>
<tr>
<th></th>
<th>HR (95%CI)</th>
<th>1 (ref)</th>
<th>1.14 (0.67, 1.94)</th>
<th>0.72 (0.39, 1.33)</th>
<th>0.65 (0.33, 1.28)</th>
<th>1.16 (0.59, 2.28)</th>
<th>0.91</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ischemic Stroke</td>
<td>Events, n</td>
<td>139</td>
<td>128</td>
<td>107</td>
<td>121</td>
<td>103</td>
<td></td>
</tr>
<tr>
<td></td>
<td>HR (95%CI)</td>
<td>1 (ref)</td>
<td>1.07 (0.83, 1.36)</td>
<td>0.79 (0.60, 1.04)</td>
<td>0.98 (0.75, 1.29)</td>
<td>0.80 (0.58, 1.09)</td>
<td>0.11</td>
</tr>
<tr>
<td>High-Fat Dairy</td>
<td>n</td>
<td>2298</td>
<td>2335</td>
<td>2547</td>
<td>2173</td>
<td>2248</td>
<td></td>
</tr>
<tr>
<td>Hemorrhagic Stroke</td>
<td>Events, n</td>
<td>27</td>
<td>20</td>
<td>23</td>
<td>22</td>
<td>22</td>
<td>0.11</td>
</tr>
<tr>
<td></td>
<td>HR (95%CI)</td>
<td>1 (ref)</td>
<td>0.89 (0.50, 1.57)</td>
<td>0.90 (0.50, 1.62)</td>
<td>0.88 (0.49, 1.60)</td>
<td>0.53 (0.28, 1.03)</td>
<td></td>
</tr>
<tr>
<td>Ischemic Stroke</td>
<td>Events, n</td>
<td>114</td>
<td>112</td>
<td>144</td>
<td>117</td>
<td>111</td>
<td></td>
</tr>
<tr>
<td></td>
<td>HR (95%CI)</td>
<td>1 (ref)</td>
<td>1.07 (0.83, 1.39)</td>
<td>1.20 (0.92, 1.56)</td>
<td>1.07 (0.81, 1.41)</td>
<td>1.00 (0.75, 1.33)</td>
<td>0.72</td>
</tr>
<tr>
<td>Low-Fat Dairy</td>
<td>n</td>
<td>3130</td>
<td>1649</td>
<td>2181</td>
<td>2439</td>
<td>2202</td>
<td></td>
</tr>
<tr>
<td>Hemorrhagic Stroke</td>
<td>Events, n</td>
<td>44</td>
<td>23</td>
<td>9</td>
<td>20</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td></td>
<td>HR (95%CI)</td>
<td>1 (ref)</td>
<td>1.22 (0.72, 2.06)</td>
<td>0.75 (0.41, 1.39)</td>
<td>0.85 (0.45, 1.60)</td>
<td>1.05 (0.53, 2.09)</td>
<td>0.60</td>
</tr>
<tr>
<td>Ischemic Stroke</td>
<td>Events, n</td>
<td>176</td>
<td>94</td>
<td>118</td>
<td>114</td>
<td>96</td>
<td></td>
</tr>
<tr>
<td></td>
<td>HR (95%CI)</td>
<td>1 (ref)</td>
<td>1.23 (0.96, 1.58)</td>
<td>1.05 (0.81, 1.36)</td>
<td>1.09 (0.83, 1.42)</td>
<td>0.90 (0.66, 1.23)</td>
<td>0.23</td>
</tr>
<tr>
<td>Fish &amp; Seafood</td>
<td>n</td>
<td>2076</td>
<td>3227</td>
<td>1795</td>
<td>2092</td>
<td>2411</td>
<td></td>
</tr>
<tr>
<td>Hemorrhagic Stroke</td>
<td>Events, n</td>
<td>21</td>
<td>32</td>
<td>18</td>
<td>20</td>
<td>23</td>
<td></td>
</tr>
<tr>
<td></td>
<td>HR (95%CI)</td>
<td>1 (ref)</td>
<td>1.07 (0.61, 1.87)</td>
<td>0.94 (0.50, 1.76)</td>
<td>0.87 (0.47, 1.64)</td>
<td>0.85 (0.44, 1.66)</td>
<td>0.51</td>
</tr>
<tr>
<td>Ischemic Stroke</td>
<td>Events, n</td>
<td>94</td>
<td>174</td>
<td>91</td>
<td>115</td>
<td>124</td>
<td></td>
</tr>
<tr>
<td></td>
<td>HR (95%CI)</td>
<td>1 (ref)</td>
<td>1.07 (0.84, 1.37)</td>
<td>0.96 (0.72, 1.26)</td>
<td>1.00 (0.77, 1.32)</td>
<td>0.95 (0.71, 1.26)</td>
<td>0.51</td>
</tr>
<tr>
<td>Eggs</td>
<td>n</td>
<td>2077</td>
<td>2127</td>
<td>2885</td>
<td>3189</td>
<td>1322</td>
<td></td>
</tr>
<tr>
<td>Hemorrhagic Stroke</td>
<td>Events, n</td>
<td>20</td>
<td>10</td>
<td>23</td>
<td>42</td>
<td>19</td>
<td></td>
</tr>
<tr>
<td></td>
<td>HR (95%CI)</td>
<td>1 (ref)</td>
<td>0.72 (0.35, 1.48)</td>
<td>0.97 (0.52, 1.79)</td>
<td>1.47 (0.80, 2.67)</td>
<td>1.41 (0.77, 2.57)</td>
<td>0.02</td>
</tr>
<tr>
<td>Ischemic Stroke</td>
<td>Events, n</td>
<td>103</td>
<td>84</td>
<td>147</td>
<td>181</td>
<td>83</td>
<td></td>
</tr>
<tr>
<td></td>
<td>HR (95%CI)</td>
<td>1 (ref)</td>
<td>0.82 (0.61, 1.09)</td>
<td>1.06 (0.82, 1.37)</td>
<td>0.97 (0.74, 1.28)</td>
<td>1.05 (0.80, 1.38)</td>
<td>0.61</td>
</tr>
<tr>
<td>Nuts &amp; Peanut Butter</td>
<td>n</td>
<td>1951</td>
<td>2842</td>
<td>2363</td>
<td>2183</td>
<td>2262</td>
<td></td>
</tr>
<tr>
<td>Hemorrhagic Stroke</td>
<td>Events, n</td>
<td>21</td>
<td>30</td>
<td>15</td>
<td>28</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td></td>
<td>HR (95%CI)*</td>
<td>1 (ref)</td>
<td>1.38 (0.78, 2.46)</td>
<td>0.79 (0.39, 1.57)</td>
<td>1.44 (0.78, 2.68)</td>
<td>1.17 (0.59, 2.31)</td>
<td>0.67</td>
</tr>
<tr>
<td>----------------</td>
<td>--------------</td>
<td>---------</td>
<td>-------------------</td>
<td>-------------------</td>
<td>-------------------</td>
<td>-------------------</td>
<td>------</td>
</tr>
<tr>
<td>Ischemic Stroke</td>
<td>Events, n</td>
<td>111</td>
<td>128</td>
<td>125</td>
<td>116</td>
<td>118</td>
<td></td>
</tr>
<tr>
<td></td>
<td>HR (95%CI)*</td>
<td>1 (ref)</td>
<td>0.75 (0.58, 0.98)</td>
<td>1.09 (0.84, 1.42)</td>
<td>1.00 (0.76, 1.31)</td>
<td>1.01 (0.76, 1.34)</td>
<td>0.36</td>
</tr>
</tbody>
</table>

**Legumes**

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>2767</th>
<th>2771</th>
<th>828</th>
<th>2853</th>
<th>2382</th>
<th>0.36</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemorrhagic Stroke</td>
<td>Events, n</td>
<td>26</td>
<td>28</td>
<td>4</td>
<td>31</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td></td>
<td>HR (95%CI)*</td>
<td>1 (ref)</td>
<td>1.08 (0.61, 1.92)</td>
<td>1.18 (0.63, 2.23)</td>
<td>0.79 (0.41, 1.52)</td>
<td>0.98 (0.50, 1.95)</td>
<td>0.44</td>
</tr>
<tr>
<td>Ischemic Stroke</td>
<td>Events, n</td>
<td>109</td>
<td>139</td>
<td>43</td>
<td>162</td>
<td>145</td>
<td></td>
</tr>
<tr>
<td></td>
<td>HR (95%CI)*</td>
<td>1 (ref)</td>
<td>1.07 (0.82, 1.40)</td>
<td>1.15 (0.86, 1.53)</td>
<td>1.24 (0.94, 1.64)</td>
<td>1.33 (0.99, 1.80)</td>
<td>0.05</td>
</tr>
</tbody>
</table>

* Model 2 adjusted for age, sex, race, study center, total energy intake, smoking, cigarette years, education, systolic blood pressure, use of antihypertensive medication, HDLc, total cholesterol, use of lipid lowering medication, body mass index, waist-to-hip ratio, alcohol intake, sports-related physical activity, leisure-related physical activity, carbohydrate intake, fiber intake, fat intake and magnesium intake.
**Supplemental Table IV. Association of major dietary protein sources (in quintiles & quartiles) with stroke incidence by sex, ARIC 1987 – 2011**

<table>
<thead>
<tr>
<th></th>
<th>Q 1</th>
<th>Q 2</th>
<th>Q 3</th>
<th>Q 4</th>
<th>Q 5</th>
<th>p-trend</th>
<th>P for Interaction**</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Processed Meat</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Females</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Events, n</td>
<td>1076</td>
<td>1819</td>
<td>756</td>
<td>1598</td>
<td>1232</td>
<td>0.20</td>
<td></td>
</tr>
<tr>
<td>HR (95%CI)*</td>
<td>1 (ref)</td>
<td></td>
<td>1.31 (0.91, 1.87)</td>
<td>1.10 (0.72, 1.69)</td>
<td>0.81 (0.54, 1.23)</td>
<td>1.29 (0.85, 1.97)</td>
<td>0.39</td>
</tr>
<tr>
<td><strong>Males</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Events, n</td>
<td>1257</td>
<td>912</td>
<td>1082</td>
<td>829</td>
<td>1040</td>
<td>0.06</td>
<td></td>
</tr>
<tr>
<td>HR (95%CI)*</td>
<td>1 (ref)</td>
<td></td>
<td>0.76 (0.52, 1.11)</td>
<td>0.91 (0.64, 1.29)</td>
<td>0.92 (0.64, 1.31)</td>
<td>1.20 (0.83, 1.72)</td>
<td>0.06</td>
</tr>
<tr>
<td><strong>Red Meat</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Females</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Events, n</td>
<td>1400</td>
<td>1198</td>
<td>1272</td>
<td>1296</td>
<td>1315</td>
<td>0.24</td>
<td></td>
</tr>
<tr>
<td>HR (95%CI)*</td>
<td>1 (ref)</td>
<td></td>
<td>1.19 (0.83, 1.70)</td>
<td>1.23 (0.84, 1.78)</td>
<td>1.47 (1.01, 2.14)</td>
<td>1.22 (0.80, 1.87)</td>
<td>0.34</td>
</tr>
<tr>
<td><strong>Males</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Events, n</td>
<td>1110</td>
<td>917</td>
<td>1234</td>
<td>916</td>
<td>943</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HR (95%CI)*</td>
<td>1 (ref)</td>
<td></td>
<td>1.07 (0.73, 1.57)</td>
<td>1.52 (1.07, 2.18)</td>
<td>1.32 (0.99, 1.96)</td>
<td>1.65 (1.06, 2.56)</td>
<td>0.02</td>
</tr>
<tr>
<td><strong>Red Meat &amp; Processed Meat</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Females</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Events, n</td>
<td>1346</td>
<td>1282</td>
<td>1266</td>
<td>1282</td>
<td>1305</td>
<td>0.11</td>
<td></td>
</tr>
<tr>
<td>HR (95%CI)*</td>
<td>1 (ref)</td>
<td></td>
<td>1.23 (0.84, 1.78)</td>
<td>1.38 (0.94, 2.02)</td>
<td>1.09 (0.72, 1.66)</td>
<td>1.19 (0.75, 1.89)</td>
<td>0.86</td>
</tr>
<tr>
<td><strong>Males</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Events, n</td>
<td>1033</td>
<td>1008</td>
<td>1048</td>
<td>1007</td>
<td>1024</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Poultry</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Females</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Events, n</td>
<td>835</td>
<td>1706</td>
<td>631</td>
<td>1943</td>
<td>1366</td>
<td>0.56</td>
<td></td>
</tr>
<tr>
<td>Events, n</td>
<td>53</td>
<td>86</td>
<td>26</td>
<td>114</td>
<td>70</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>HR (95%CI)</td>
<td>1 (ref)</td>
<td>0.71 (0.50, 1.00)</td>
<td>0.65 (0.41, 1.05)</td>
<td>0.75 (0.53, 1.07)</td>
<td>0.79 (0.53, 1.17)</td>
<td>0.88</td>
</tr>
<tr>
<td>------------------------</td>
<td>-----------</td>
<td>---------</td>
<td>------------------</td>
<td>------------------</td>
<td>------------------</td>
<td>------------------</td>
<td>------</td>
</tr>
<tr>
<td>Males n</td>
<td>828</td>
<td>1457</td>
<td>713</td>
<td>1233</td>
<td>889</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Events, n</td>
<td>58</td>
<td>99</td>
<td>50</td>
<td>94</td>
<td>49</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HR (95%CI) *</td>
<td>1 (ref)</td>
<td>1.14 (0.81, 1.60)</td>
<td>1.06 (0.73, 1.53)</td>
<td>1.04 (0.72, 1.51)</td>
<td>0.91 (0.61, 1.36)</td>
<td>0.42</td>
<td></td>
</tr>
<tr>
<td>Dairy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Females n</td>
<td>1289</td>
<td>1328</td>
<td>1276</td>
<td>1276</td>
<td>1312</td>
<td></td>
<td>0.68</td>
</tr>
<tr>
<td>Events, n</td>
<td>85</td>
<td>82</td>
<td>48</td>
<td>68</td>
<td>66</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HR (95%CI) *</td>
<td>1 (ref)</td>
<td>1.08 (0.79, 1.47)</td>
<td>0.59 (0.41, 0.86)</td>
<td>0.88 (0.62, 1.25)</td>
<td>0.85 (0.57, 1.26)</td>
<td>0.28</td>
<td></td>
</tr>
<tr>
<td>Males n</td>
<td>1078</td>
<td>971</td>
<td>1050</td>
<td>983</td>
<td>1038</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Events, n</td>
<td>77</td>
<td>72</td>
<td>74</td>
<td>67</td>
<td>60</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HR (95%CI) *</td>
<td>1 (ref)</td>
<td>1.18 (0.85, 1.64)</td>
<td>0.98 (0.70, 1.39)</td>
<td>0.98 (0.68, 1.41)</td>
<td>0.89 (0.59, 1.34)</td>
<td>0.33</td>
<td></td>
</tr>
<tr>
<td>High-Fat Dairy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Females n</td>
<td>1374</td>
<td>1233</td>
<td>1580</td>
<td>1009</td>
<td>1285</td>
<td></td>
<td>0.67</td>
</tr>
<tr>
<td>Events, n</td>
<td>69</td>
<td>67</td>
<td>93</td>
<td>56</td>
<td>64</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HR (95%CI) *</td>
<td>1 (ref)</td>
<td>1.27 (0.91, 1.79)</td>
<td>1.37 (0.97, 1.93)</td>
<td>1.21 (0.83, 1.77)</td>
<td>1.08 (0.74, 1.59)</td>
<td>0.69</td>
<td></td>
</tr>
<tr>
<td>Males n</td>
<td>924</td>
<td>1102</td>
<td>967</td>
<td>1164</td>
<td>963</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Events, n</td>
<td>67</td>
<td>62</td>
<td>72</td>
<td>81</td>
<td>68</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HR (95%CI) *</td>
<td>1 (ref)</td>
<td>0.84 (0.60, 1.18)</td>
<td>0.98 (0.69, 1.38)</td>
<td>0.96 (0.68, 1.35)</td>
<td>0.78 (0.54, 1.13)</td>
<td>0.39</td>
<td></td>
</tr>
<tr>
<td>Low-Fat Dairy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Females n</td>
<td>1623</td>
<td>1157</td>
<td>1102</td>
<td>1341</td>
<td>1258</td>
<td></td>
<td>0.78</td>
</tr>
<tr>
<td>Events, n</td>
<td>89</td>
<td>83</td>
<td>56</td>
<td>60</td>
<td>61</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HR (95%CI) *</td>
<td>1 (ref)</td>
<td>1.60 (1.16, 2.21)</td>
<td>1.33 (0.94, 1.89)</td>
<td>0.97 (0.67, 1.42)</td>
<td>1.07 (0.71, 1.62)</td>
<td>0.18</td>
<td></td>
</tr>
<tr>
<td>Males n</td>
<td>1507</td>
<td>492</td>
<td>1079</td>
<td>1098</td>
<td>944</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Events, n</td>
<td>124</td>
<td>34</td>
<td>70</td>
<td>71</td>
<td>51</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HR (95%CI) *</td>
<td>1 (ref)</td>
<td>0.94 (0.66, 1.33)</td>
<td>0.79 (0.56, 1.10)</td>
<td>1.09 (0.78, 1.52)</td>
<td>0.80 (0.53, 1.19)</td>
<td>0.43</td>
<td></td>
</tr>
<tr>
<td>Fish &amp; Seafood</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Females n</td>
<td>1445</td>
<td>1255</td>
<td>1028</td>
<td>1350</td>
<td>1403</td>
<td></td>
<td>0.74</td>
</tr>
<tr>
<td>Events, n</td>
<td>71</td>
<td>74</td>
<td>52</td>
<td>79</td>
<td>73</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HR (95%CI) *</td>
<td>1 (ref)</td>
<td>1.33 (0.94, 1.86)</td>
<td>1.12 (0.78, 1.62)</td>
<td>0.98 (0.68, 1.42)</td>
<td>0.99 (0.66, 1.49)</td>
<td>0.36</td>
<td></td>
</tr>
<tr>
<td>Males n</td>
<td>631</td>
<td>1972</td>
<td>767</td>
<td>742</td>
<td>1008</td>
<td></td>
<td></td>
</tr>
<tr>
<td>---------</td>
<td>-----</td>
<td>------</td>
<td>-----</td>
<td>-----</td>
<td>------</td>
<td>---</td>
<td></td>
</tr>
<tr>
<td>Events, n</td>
<td>41</td>
<td>129</td>
<td>56</td>
<td>52</td>
<td>72</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HR (95%CI)*</td>
<td>1 (ref)</td>
<td>0.88 (0.65, 1.21)</td>
<td>0.83 (0.58, 1.19)</td>
<td>0.98 (0.69, 1.39)</td>
<td>0.92 (0.65, 1.31)</td>
<td>0.97</td>
<td></td>
</tr>
</tbody>
</table>

**Eggs**

| Females n | 1326 | 1337 | 1714 | 1613 | 490 | 0.47 |
| Events, n | 74  | 52   | 94   | 97   | 32  |     |
| HR (95%CI)* | 1 (ref) | 0.90 (0.63, 1.29) | 1.09 (0.79, 1.50) | 1.05 (0.72, 1.55) | 1.25 (0.90, 1.73) | 0.05 |

| Males n | 751 | 790 | 1171 | 1576 | 832 |  |
| Events, n | 47  | 40   | 75   | 121  | 67  |   |
| HR (95%CI)* | 1 (ref) | 0.65 (0.43, 1.00) | 0.96 (0.67, 1.37) | 0.95 (0.67, 1.35) | 0.90 (0.61, 1.32) | 0.82 |

**Nuts & Peanut Butter**

| Females n | 1195 | 1139 | 1719 | 1134 | 1294 | 0.01 |
| Events, n | 73  | 54   | 98   | 66   | 58   |     |
| HR (95%CI)* | 1 (ref) | 0.83 (0.59, 1.17) | 1.12 (0.82, 1.53) | 0.98 (0.69, 1.39) | 0.76 (0.52, 1.10) | 0.13 |

| Males n | 756 | 1703 | 644 | 1049 | 968 |  |
| Events, n | 57  | 101  | 40   | 75   | 77  |   |
| HR (95%CI)* | 1 (ref) | 0.83 (0.60, 1.17) | 0.91 (0.61, 1.36) | 1.12 (0.78, 1.62) | 1.35 (0.92, 1.99) | 0.01 |

**Legumes***

| Females n | 1740 | 1642 | 1702 | 1397 | 0.50 |
| Events, n | 72  | 83   | 100  | 94   |     |
| HR (95%CI)* | 1 (ref) | 1.12 (0.81, 1.55) | 1.27 (0.92, 1.75) | 1.35 (0.95, 1.92) | 0.13 |

| Males n | 1027 | 1129 | 1595 | 1369 |  |
| Events, n | 59  | 81   | 106  | 104  |   |
| HR (95%CI)* | 1 (ref) | 1.16 (0.83, 1.62) | 1.21 (0.84, 1.73) | 1.31 (0.88, 1.94) | 0.25 |

*adjusted for age, sex, race, study center, total energy intake, smoking, cigarette years, education, systolic blood pressure, use of antihypertensive medication, HDLc, total cholesterol, use of lipid lowering medication, body mass index, waist-to-hip ratio, alcohol intake, sports-related physical activity, leisure-related physical activity, carbohydrate intake, fiber intake, fat intake, and magnesium intake.

**P-value for the median trend*sex interaction term.

***Quartiles were used instead of quintiles due to an issue when stratifying by sex-specific quintiles (a lack of females in the middle quintile).
**Supplemental Table V. Association of major dietary protein sources (in quartiles) with incidence of silent cerebral infarcts, ARIC 1993-2006**

<table>
<thead>
<tr>
<th></th>
<th>Q 1</th>
<th>Q 2</th>
<th>Q 3</th>
<th>Q 4</th>
<th>p-trend</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Processed Meat</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>166</td>
<td>150</td>
<td>173</td>
<td>164</td>
<td></td>
</tr>
<tr>
<td>Events, n</td>
<td>32</td>
<td>23</td>
<td>37</td>
<td>35</td>
<td></td>
</tr>
<tr>
<td>OR (95%CI)*</td>
<td>1 (ref)</td>
<td>0.80 (0.44, 1.44)</td>
<td>1.26 (0.73, 2.18)</td>
<td>1.29 (0.73, 2.30)</td>
<td>0.16</td>
</tr>
<tr>
<td>OR (95%CI)**</td>
<td>1 (ref)</td>
<td>0.81 (0.43, 1.54)</td>
<td>1.20 (0.66, 2.22)</td>
<td>1.09 (0.56, 2.13)</td>
<td>0.46</td>
</tr>
<tr>
<td><strong>Red Meat</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>171</td>
<td>159</td>
<td>160</td>
<td>163</td>
<td></td>
</tr>
<tr>
<td>Events, n</td>
<td>35</td>
<td>34</td>
<td>30</td>
<td>28</td>
<td></td>
</tr>
<tr>
<td>OR (95%CI)*</td>
<td>1 (ref)</td>
<td>1.13 (0.66, 1.94)</td>
<td>0.94 (0.54, 1.64)</td>
<td>0.92 (0.51, 1.63)</td>
<td>0.60</td>
</tr>
<tr>
<td>OR (95%CI)**</td>
<td>1 (ref)</td>
<td>1.11 (0.62, 1.99)</td>
<td>0.93 (0.50, 1.72)</td>
<td>0.73 (0.35, 1.50)</td>
<td>0.29</td>
</tr>
<tr>
<td><strong>Red Meat &amp; Processed Meat</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>156</td>
<td>170</td>
<td>164</td>
<td>163</td>
<td></td>
</tr>
<tr>
<td>Events, n</td>
<td>28</td>
<td>37</td>
<td>30</td>
<td>32</td>
<td></td>
</tr>
<tr>
<td>OR (95%CI)*</td>
<td>1 (ref)</td>
<td>1.37 (0.78, 2.40)</td>
<td>1.14 (0.63, 2.04)</td>
<td>1.33 (0.73, 2.47)</td>
<td>0.53</td>
</tr>
<tr>
<td>OR (95%CI)**</td>
<td>1 (ref)</td>
<td>1.22 (0.66, 2.26)</td>
<td>1.09 (0.56, 2.13)</td>
<td>1.10 (0.51, 2.35)</td>
<td>0.97</td>
</tr>
<tr>
<td><strong>Poultry</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>168</td>
<td>134</td>
<td>180</td>
<td>171</td>
<td></td>
</tr>
<tr>
<td>Events, n</td>
<td>36</td>
<td>21</td>
<td>31</td>
<td>39</td>
<td></td>
</tr>
<tr>
<td>OR (95%CI)*</td>
<td>1 (ref)</td>
<td>0.69 (0.38, 1.25)</td>
<td>0.78 (0.45, 1.35)</td>
<td>1.16 (0.68, 1.97)</td>
<td>0.44</td>
</tr>
<tr>
<td>OR (95%CI)**</td>
<td>1 (ref)</td>
<td>1.08 (0.55, 2.06)</td>
<td>1.00 (0.54, 1.84)</td>
<td>1.93 (1.02, 3.67)</td>
<td>0.05</td>
</tr>
<tr>
<td><strong>Dairy</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>166</td>
<td>164</td>
<td>151</td>
<td>172</td>
<td></td>
</tr>
<tr>
<td>Events, n</td>
<td>39</td>
<td>26</td>
<td>32</td>
<td>30</td>
<td></td>
</tr>
<tr>
<td>OR (95%CI)*</td>
<td>1 (ref)</td>
<td>0.60 (0.34, 1.06)</td>
<td>0.84 (0.47, 1.49)</td>
<td>0.67 (0.37, 1.21)</td>
<td>0.27</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>----------------</td>
<td>------</td>
<td>------</td>
<td>------</td>
<td>------</td>
<td>------</td>
</tr>
<tr>
<td></td>
<td>1 (ref)</td>
<td>0.65 (0.35, 1.19)</td>
<td>0.95 (0.51, 1.80)</td>
<td>0.81 (0.41, 1.61)</td>
<td>0.68</td>
</tr>
<tr>
<td><strong>High-Fat Dairy</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>159</td>
<td>160</td>
<td>171</td>
<td>163</td>
<td></td>
</tr>
<tr>
<td>Events, n</td>
<td>30</td>
<td>26</td>
<td>34</td>
<td>37</td>
<td></td>
</tr>
<tr>
<td>OR (95%CI)</td>
<td>1 (ref)</td>
<td>0.84 (0.46, 1.51)</td>
<td>1.12 (0.64, 1.96)</td>
<td>1.44 (0.82, 2.54)</td>
<td>0.09</td>
</tr>
<tr>
<td>OR (95%CI)</td>
<td>1 (ref)</td>
<td>0.94 (0.50, 1.76)</td>
<td>1.03 (0.57, 1.89)</td>
<td>1.42 (0.77, 2.62)</td>
<td>0.18</td>
</tr>
<tr>
<td><strong>Low-Fat Dairy</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>169</td>
<td>150</td>
<td>174</td>
<td>160</td>
<td></td>
</tr>
<tr>
<td>Events, n</td>
<td>43</td>
<td>31</td>
<td>24</td>
<td>29</td>
<td></td>
</tr>
<tr>
<td>OR (95%CI)</td>
<td>1 (ref)</td>
<td>0.72 (0.41, 1.24)</td>
<td>0.40 (0.22, 0.73)</td>
<td>0.55 (0.30, 1.00)</td>
<td>0.05</td>
</tr>
<tr>
<td>OR (95%CI)</td>
<td>1 (ref)</td>
<td>0.82 (0.44, 1.51)</td>
<td>0.44 (0.22, 0.86)</td>
<td>0.68 (0.32, 1.42)</td>
<td>0.25</td>
</tr>
<tr>
<td><strong>Fish &amp; Seafood</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>128</td>
<td>226</td>
<td>134</td>
<td>165</td>
<td></td>
</tr>
<tr>
<td>Events, n</td>
<td>30</td>
<td>44</td>
<td>29</td>
<td>24</td>
<td></td>
</tr>
<tr>
<td>OR (95%CI)</td>
<td>1 (ref)</td>
<td>0.84 (0.49, 1.44)</td>
<td>0.93 (0.50, 1.72)</td>
<td>0.60 (0.31, 1.12)</td>
<td>0.11</td>
</tr>
<tr>
<td>OR (95%CI)</td>
<td>1 (ref)</td>
<td>0.79 (0.45, 1.41)</td>
<td>1.00 (0.51, 1.93)</td>
<td>0.66 (0.32, 1.37)</td>
<td>0.33</td>
</tr>
<tr>
<td><strong>Eggs</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>177</td>
<td>140</td>
<td>187</td>
<td>149</td>
<td></td>
</tr>
<tr>
<td>Events, n</td>
<td>33</td>
<td>25</td>
<td>41</td>
<td>28</td>
<td></td>
</tr>
<tr>
<td>OR (95%CI)</td>
<td>1 (ref)</td>
<td>0.96 (0.53, 1.71)</td>
<td>1.22 (0.73, 2.07)</td>
<td>1.05 (0.59, 1.87)</td>
<td>0.55</td>
</tr>
<tr>
<td>OR (95%CI)</td>
<td>1 (ref)</td>
<td>0.88 (0.47, 1.64)</td>
<td>1.21 (0.69, 2.13)</td>
<td>0.89 (0.46, 1.69)</td>
<td>0.88</td>
</tr>
<tr>
<td><strong>Nuts &amp; Peanut Butter</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>176</td>
<td>159</td>
<td>159</td>
<td>159</td>
<td></td>
</tr>
<tr>
<td>Events, n</td>
<td>42</td>
<td>30</td>
<td>35</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>OR (95%CI)</td>
<td>1 (ref)</td>
<td>0.77 (0.44, 1.32)</td>
<td>0.90 (0.53, 1.53)</td>
<td>0.46 (0.25, 0.85)</td>
<td>0.04</td>
</tr>
<tr>
<td>OR (95%CI)</td>
<td>1 (ref)</td>
<td>0.76 (0.42, 1.36)</td>
<td>1.03 (0.57, 1.85)</td>
<td>0.49 (0.25, 0.97)</td>
<td>0.10</td>
</tr>
<tr>
<td>Legumes</td>
<td>n</td>
<td>134</td>
<td>213</td>
<td>148</td>
<td>158</td>
</tr>
<tr>
<td>------------------</td>
<td>-----</td>
<td>-----</td>
<td>-----</td>
<td>-----</td>
<td>-----</td>
</tr>
<tr>
<td>Events, n</td>
<td></td>
<td>26</td>
<td>47</td>
<td>24</td>
<td>30</td>
</tr>
<tr>
<td>OR (95%CI)*</td>
<td>1 (ref)</td>
<td>1.21 (0.70, 2.11)</td>
<td>0.85 (0.45, 1.60)</td>
<td>1.05 (0.57, 1.96)</td>
<td>0.78</td>
</tr>
<tr>
<td>OR (95%CI)**</td>
<td>1 (ref)</td>
<td>1.22 (0.68, 2.20)</td>
<td>1.01 (0.51, 2.00)</td>
<td>1.05 (0.50, 2.21)</td>
<td>0.89</td>
</tr>
</tbody>
</table>

*adjusted for age, sex, race, study center, and total energy intake

**adjusted for age, sex, race, study center, total energy intake, smoking, cigarette years, education, systolic blood pressure, use of antihypertensive medication, HDLc, total cholesterol, use of lipid lowering medication, body mass index, waist-to-hip ratio, alcohol intake, sports-related physical activity, leisure-related physical activity, carbohydrate intake, fiber intake, fat intake and magnesium intake