Dietary Protein Sources and the Risk of Stroke in Men and Women

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Background and Purpose—Few dietary protein sources have been studied prospectively in relation to stroke. We examined the relationship between foods that are major protein sources and risk of stroke.

Methods—We prospectively followed 84 010 women aged 30 to 55 years at baseline and 43 150 men aged 40 to 75 years at baseline without diagnosed cancer, diabetes, or cardiovascular disease. Diet was assessed repeatedly by a standardized and validated questionnaire. We examined the association between protein sources and incidence of stroke using a proportional hazard model adjusted for stroke risk factors.

Results—During 26 and 22 years of follow-up in women and men, respectively, we documented 2633 and 1397 strokes, respectively. In multivariable analyses, higher intake of red meat was associated with an elevated risk of stroke, whereas a higher intake of poultry was associated with a lower risk. In models estimating the effects of exchanging different protein sources, compared with 1 serving/day of red meat, 1 serving/day of poultry was associated with a 27% (95% CI, 12%–39%) lower risk of stroke, nuts with a 17% (95% CI, 4%–27%) lower risk, fish with a 17% (95% CI, 0%–30%) lower risk, low-fat dairy with an 11% (95% CI, 5%–17%) lower risk, and whole-fat dairy with a 10% (95% CI, 4%–16%) lower risk. We did not see significant associations with exchanging legumes or eggs for red meat.

Conclusions—These data suggest that stroke risk may be reduced by replacing red meat with other dietary sources of protein. (Stroke. 2012;43:637-644.)

Key Words: diet ■ men ■ nutrition ■ stroke ■ women

A diet high in protein, compared isocalorically with one high in carbohydrate, lowers blood pressure, a major risk factor for stroke, and improves plasma lipids.1 Foods that are major protein sources vary greatly in their nonprotein constituents and thus may have different relationships to risk of stroke, but these relationships have not been closely examined. In a recent meta-analysis of 2 observational studies, red meat intake was not significantly associated with incident stroke, and the paucity of data were noted.2 Higher fish intake has been associated with a lower risk of ischemic stroke in men3 and thrombotic stroke in women.4 No significant associations were seen between intakes of eggs, nuts, or whole-fat dairy products and stroke risk.5,6 Understanding which protein-rich foods are associated with stroke risk is important because substituting one for another may be easier for individuals to accomplish than substituting one nutrient for another or one dietary pattern for another.

We have previously reported on the relation between major dietary protein sources and incident coronary heart disease in women.7 Higher intakes of red meat and whole-fat dairy products were associated with a higher risk of coronary heart disease, whereas higher intakes of nuts, fish, and poultry were associated with a lower risk. To better understand the relations between dietary protein sources and risk of stroke, we investigated these in 2 large prospective cohorts of men and women.

Materials and Methods

Study Populations

The Nurses’ Health Study (NHS) began in 1976 when 121 700 female registered nurses aged 30 to 55 years residing in the United States provided information on their medical history and lifestyle. The Health Professionals Follow-Up Study (HPFS) began in 1986 when 51 529 male dentists, pharmacists, optometrists, osteopaths, podiatrists, and veterinarians aged 40 to 75 years and residing in the United States provided information on their medical history and lifestyle. Every 2 years, follow-up questionnaires have been sent to update this information. In 1980, a 61-item food-frequency questionnaire (FFQ) was included to assess intake of specific foods in NHS. Expanded questionnaires updated dietary intake in 1986, 1990, 1994,
1998, and 2002. In 1986, a 131-item FFQ assessed intake of specific foods in HPFS and similar questionnaires were used to update dietary intake in 1990, 1994, 1998, 2002, and 2006. Like in our previous analysis, we excluded participants with excessive blank items on their baseline FFQ, implausibly low or high energy intake, and those with previously diagnosed cancer, diabetes, angina, myocardial infarction, stroke, or other cardiovascular disease (including a history of percutaneous coronary intervention or coronary artery bypass grafting). The final baseline populations consisted of 84 010 women and 43 150 men.

The study was approved by the Committee on the Use of Human Subjects in Research at Brigham and Women’s Hospital. Return of a questionnaire was considered to imply consent.

Ascertainment of Diet
To calculate intakes of specific protein sources, a commonly used unit or portion size for each food was specified on the FFQ and the participant was asked how often on average during the previous year he or she had consumed that amount with answers ranging from “never” to “≥6 times per day” (for portion sizes see online-only Data Supplement; http://stroke.ahajournals.org). The major contributors to protein intake reported on the FFQs included: unprocessed red meat (hamburger, beef, pork, and lamb), processed red meat (beef hot dog, processed meats such as bologna and salami, and bacon), poultry (chicken with and without skin, chicken sandwich, and chicken/turkey hot dog), whole-fat dairy (whole milk, ice cream, hard cheese, full fat cheese, cream, sour cream, cream cheese, butter), and low-fat dairy (skim/low-fat milk, 1% and 2% milk, yogurt, cottage and ricotta cheeses, low-fat cheese, sherteb). We also evaluated fish (canned tuna, dark and light flished fish, and breaded fish), eggs, nuts, and legumes (dry beans, peas, soy, and tofu). In sensitivity analyses, we evaluated total processed meat (processed red meat plus chicken/turkey hot dogs), poultry excluding chicken/turkey hot dogs, whole-fat dairy excluding ice cream, and low-fat dairy excluding sherteb. The reproducibility and validity of the FFQs in measuring food intake have been previously described.

Ascertainment of Stroke
When participants reported a stroke, we obtained permission to review their medical records. Stroke was classified as ischemic (thrombotic, embolic, or unspecified nonhemorrhagic), hemorrhagic, or of unknown type according to criteria in the National Survey of Stroke. Subarachnoid hemorrhages were distinguished from intraparenchymal hemorrhages. Nonfatal strokes for which confirmatory information was obtained by interview or letter but no medical records were available were designated as probable (223 of 1098 [20%] cases in men and 641 of 2153 [30%] cases in women). Deaths were identified from state vital records, the National Death Index, next of kin, or the postal system. Stroke was classified as ischemic (thrombotic, embolic, or unspecified nonhemorrhagic), and hemorrhagic. To compare with previous analyses, we evaluated the relation between fish intake less than once per month versus intake more than once per month and risk of stroke. Person-years of follow-up were calculated from the return of the baseline FFQ to the date of the first stroke event, death, or June 1, 2006 (NHS) or January 31, 2008 (HPFS), whichever came first. The relative risk (RR) was computed using a multivariable Cox proportional hazards regression model. The model was stratified on age (months) and calendar time (2-year time intervals) and included dietary protein sources (servings/day) and also intakes of total energy (kcal), cereal fiber (g/day), alcohol (g/day), fruit and vegetables (servings/day), transunsaturated fatty acids (g/day), and potential nondietary confounding variables, which were updated biennially: body mass index (10 categories), physical exercise (<3, 3–9, 9–18, 18–27, 27+ metabolic equivalents/week), cigarette smoking (never, past, current 1–14 cigarettes/day, current 14–25 cigarettes/day, current 25+ cigarettes/day), menopausal status in women (premenopausal, postmenopausal with no history of hormone replacement, postmenopausal with a history of hormone replacement, postmenopausal with current hormone replacement), parental history of early myocardial infarction (age <60 years), years of multivitamin use, vitamin E supplement use (yes/no), and aspirin use (yes/no). Neither the diagnoses of diabetes, hypertension, hypercholesterolemia, coronary artery bypass grafting/percutaneous coronary intervention, nor myocardial infarction nor use of medications prescribed to treat these conditions (including statins and β-blockers) were included in the multivariable models, because these may be considered intermediate outcomes on the causal pathway between diet and stroke. However, in sensitivity analyses, intermediate diagnoses were included. The median values for each quintile of cumulative average food intake were used as a single variable to test for linear trend across quintiles and to estimate the relative risk for a 1-serving/day increase in intake. RRs and SEs for each quintile from each cohort were pooled in fixed-effects models to calculate summary estimates.

To examine for potential effect modification of the association between stroke risk and total red meat intake by adiposity, we stratified our multivariate model on body mass index (<25 versus ≥25 kg/m2) and, separately, tested the significance of an interaction with a likelihood ratio test comparing the model with the interactions terms to the model with only the main effects. Most study participants were white, precluding evaluation of potential differences by race. To evaluate the relation between a change in red meat intake with the risk of stroke, we created “change” variables equal to the simple updated red meat intake (intake reported during each questionnaire year) minus the baseline red meat intake and then included these variables, plus baseline intake, in our multivariate model. To estimate the relative risk of total stroke associated with substituting 1 serving/day of 1 major protein source for another, we fit a multivariable proportional hazards model including all major protein sources entered as continuous variables (servings/day) and potential confounding variables. The difference in the coefficients for 2 protein sources, plus their covariance, was used to estimate the RR and CI for the substitution.

Results
During 2,041,679 person-years of follow-up from 1980 through 2006 in the NHS, and 833,660 person-years of follow-up from 1986 through 2008 in the HPFS, we documented 1397 strokes (including 165 intraparenchymal hemorrhages, 829 ischemic strokes, 53 subarachnoid hemorrhages, and 350 of unspecified type) in men and 2633 strokes (including 235 intraparenchymal hemorrhages, 1383 ischemic strokes, 240 subarachnoid hemorrhages, and 775 of unspecified type) in women. Characteristics of the study...
participants during follow-up, averaged according to proportion of person-time in each quintile of intake, are shown in Table 1. High red meat consumption was associated with a higher rate of smoking, lower physical activity, increased intake of transfat, and decreased intakes of vitamin E and multivitamins in both men and women. The major groups of protein sources were not highly correlated with each other (see Data Supplement).

In multivariable analyses adjusted for dietary and nondietary cardiovascular disease risk factors, high intake of red meat was associated with a higher risk of total stroke (Table 2). Both processed and unprocessed red meat were significantly associated with risk; the association with processed meat was stronger in men and the association with unprocessed red meat was stronger in women but, for both foods, a test of heterogeneity by sex was not significant. Controlling for intermediate outcomes did not materially change these results (see Data Supplement). Poultry and nut consumption were associated with a lower total stroke risk in women, and poultry consumption was associated with a lower risk in the pooled analysis. We did not observe a significant association between intake of fish, dairy, eggs, or legumes and risk of stroke. A trend toward reduced risk was observed with fish intake more than once per month compared with less than once per month or never (RR in men, 0.85; 95% CI, 0.63–1.15; RR in women, 0.83; 95% CI, 0.65–1.06). Risk seen with total processed meat, poultry excluding chicken/turkey hot dogs, whole-fat dairy excluding ice cream, and low-fat dairy excluding sherbet were similar to main findings for processed red meat, poultry, whole-fat dairy, and low-fat dairy. All findings were generally similar when ischemic and hemorrhagic strokes were separately evaluated (Table 3; Data Supplement). We did not observe significant effect modification of red meat intake and stroke risk by body mass index in either men or women.

We observed a significant reduction in risk of stroke among men and women who lowered their consumption of red meat intake from baseline. Compared with those with an increase of 0.6 servings/day during follow-up, men with the greatest decrease (median for quintile of change, 0.93 servings/day) had a 0.79 (95% CI, 0.62–0.99) risk. Compared to those with an increase of 0.3 servings/day, women with the greatest decrease (median for quintile of change, 1.16 servings/day) had a risk of 0.84 (95% CI, 0.72–0.99). The pooled risk for men and women was 0.83 (95% CI, 0.72–0.94). Results were in a similar direction when the analysis was restricted to only those participants with the highest red meat intake at baseline, although findings were not statistically significant.


<table>
<thead>
<tr>
<th>Quintiles</th>
<th>Red Meat</th>
<th>Poultry</th>
<th>Fish</th>
<th>Red Meat</th>
<th>Poultry</th>
<th>Fish</th>
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<td>First</td>
<td>0.30</td>
<td>32.0</td>
<td>36</td>
<td>26</td>
<td>9.5</td>
<td>3.0</td>
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<tr>
<td>Third</td>
<td>1.03</td>
<td>34.0</td>
<td>37.5</td>
<td>34.5</td>
<td>35.0</td>
<td>35.0</td>
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<tr>
<td>Fifth</td>
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<td>33</td>
<td>32.5</td>
<td>32.0</td>
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<td>26</td>
<td>27</td>
<td>26</td>
<td>26</td>
<td>26</td>
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<td>6</td>
<td>9</td>
<td>5</td>
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<td>11</td>
<td>10</td>
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<td>History of high blood pressure, %</td>
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<td>34</td>
<td>30</td>
<td>34</td>
<td>37</td>
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<td>40</td>
<td>34</td>
<td>40</td>
<td>45</td>
<td>34</td>
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<td>N/A</td>
<td>N/A</td>
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<td>Aspirin use at least once per wk, %</td>
<td>36</td>
<td>37</td>
<td>30</td>
<td>31</td>
<td>37</td>
<td>35</td>
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<td>Multivitamin use, y</td>
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<td>8.5</td>
<td>7.7</td>
<td>7.4</td>
<td>8.3</td>
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<td>19</td>
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<td>Alcohol, g/d</td>
<td>9</td>
<td>12</td>
<td>13</td>
<td>11</td>
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<td>11</td>
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<td>Activity, METS/wk</td>
<td>38</td>
<td>34</td>
<td>34</td>
<td>31</td>
<td>35</td>
<td>38</td>
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<td>Calories, kcal/d</td>
<td>1685</td>
<td>1924</td>
<td>2408</td>
<td>1814</td>
<td>1972</td>
<td>2178</td>
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<tr>
<td>Cereal fiber, g/d</td>
<td>8.1</td>
<td>6.3</td>
<td>5.0</td>
<td>6.3</td>
<td>6.6</td>
<td>6.5</td>
</tr>
<tr>
<td>Transunsaturated fat, g/d</td>
<td>2.3</td>
<td>3.1</td>
<td>3.4</td>
<td>3.2</td>
<td>2.9</td>
<td>2.7</td>
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</table>

METS indicates metabolic equivalents; N/A, not applicable.

*Mean values given for continuous variables, percentages of population given for dichotomous variables, and nutrients are calorie-adjusted by the residual method.
Table 2. Relative Risk and 95% CI for Total Stroke by Quintiles of Intake of Dietary Protein Sources Among 43 150 US Men and 84 010 US Women*†

<table>
<thead>
<tr>
<th>Quintiles</th>
<th>First</th>
<th>Second</th>
<th>Third</th>
<th>Fourth</th>
<th>Fifth</th>
<th>P for Trend</th>
<th>RR for 1 Serving/D</th>
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<td>Total red meat</td>
<td></td>
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<tr>
<td>Men</td>
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</tr>
<tr>
<td>Servings/d</td>
<td>0.30</td>
<td>0.68</td>
<td>1.03</td>
<td>1.46</td>
<td>2.29</td>
<td></td>
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<tr>
<td>Multivariable RR</td>
<td>1.00</td>
<td>0.98 (0.81–1.18)</td>
<td>1.08 (0.89–1.32)</td>
<td>1.24 (1.01–1.52)</td>
<td>1.28 (1.02–1.61)</td>
<td>0.01</td>
<td>1.15 (1.03–1.27)</td>
</tr>
<tr>
<td>Women</td>
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<tr>
<td>Servings/d</td>
<td>0.44</td>
<td>0.74</td>
<td>1.00</td>
<td>1.32</td>
<td>1.92</td>
<td></td>
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</tr>
<tr>
<td>Multivariable model</td>
<td>1.00</td>
<td>1.12 (0.99–1.26)</td>
<td>1.11 (0.97–1.27)</td>
<td>1.17 (1.01–1.36)</td>
<td>1.19 (1.00–1.41)</td>
<td>0.07</td>
<td>1.11 (0.99–1.24)</td>
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<tr>
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<tr>
<td>Multivariable model</td>
<td>1.00</td>
<td>1.08 (0.97–1.19)</td>
<td>1.10 (0.99–1.23)</td>
<td>1.19 (1.06–1.34)</td>
<td>1.22 (1.07–1.40)</td>
<td>&lt;0.01</td>
<td>1.13 (1.04–1.22)</td>
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<tr>
<td>Servings/d</td>
<td>0.03</td>
<td>0.14</td>
<td>0.21</td>
<td>0.39</td>
<td>0.71</td>
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<tr>
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<td>1.01 (0.84–1.21)</td>
<td>0.91 (0.75–1.10)</td>
<td>1.12 (0.92–1.36)</td>
<td>1.27 (1.03–1.55)</td>
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<td>1.53 (1.16–2.01)</td>
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<tr>
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<tr>
<td>Servings/d</td>
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<td>0.23</td>
<td>0.35</td>
<td>0.64</td>
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<td>0.98 (0.87–1.11)</td>
<td>1.06 (0.93–1.21)</td>
<td>1.09 (0.95–1.24)</td>
<td>1.10 (0.95–1.27)</td>
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<td>1.19 (0.95–1.50)</td>
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<td>1.23 (1.00–1.51)</td>
<td>1.11 (0.88–1.39)</td>
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<td>1.09 (0.98–1.21)</td>
<td>1.05 (0.94–1.17)</td>
<td>1.16 (1.03–1.31)</td>
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(Continued)
Table 2. Continued

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<td>0.04</td>
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<td>0.14</td>
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<td>0.14</td>
<td>0.17</td>
<td>0.24</td>
<td>0.43</td>
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<td>1.05 (0.94–1.16)</td>
<td>1.06 (0.95–1.19)</td>
</tr>
</tbody>
</table>

RR indicates relative risk; CI, confidence interval.

*Median values shown for quintiles of servings/d.
†Multivariable model stratified on age (mo) and time period (13 periods in Nurses’ Health Study, 11 in Health Professionals Follow-Up Study) and includes: body mass index (10 categories), cigarette smoking (never, past, current 1–14 cigarettes/d, current 14–25 cigarettes/d, current 25+ cigarettes/d), physical exercise (3, 3–9, 9–18, 18–27, 27+/H11021 metabolic equivalents/wk), parental history of early myocardial infarction (age <60 y), menopausal status in women (premenopausal, postmenopausal with no history of hormone replacement, postmenopausal with history of hormone replacement, postmenopausal with current hormone replacement), multivitamin use (quintiles of y), vitamin E supplement use (yes/no), aspirin use at least once per wk (yes/no), total energy (quintiles of kcal), cereal fiber (quintiles of g/d), alcohol (quintiles of g/d), transfat (quintiles of g/d), fruit and vegetables (quintiles of servings/d), and other protein sources (quintiles of servings/d).
In estimating the effect of substituting 1 protein source for another, we combined data for men and women because we did not observe significant between-study heterogeneity (Q statistic probability value < 0.05 for substitutions). When compared with 1 serving/day of red meat, 1 serving/day of poultry, nuts, fish, or dairy was associated with a decreased risk of stroke (Figure). When compared with 1 serving/day of red meat, 1 serving/day of poultry was associated with a 27% (95% CI, 12–39%) lower risk of stroke, nuts with a 17% (95% CI, 4–27%) lower risk, fish with a 17% (95% CI, 0–30%) lower risk, low-fat dairy with an 11% (95% CI, 5–17%) lower risk, and whole-fat dairy with a 10% (95% CI, 4–16%) lower risk.

### Discussion

We observed that higher consumption of red meat was associated with a higher risk of stroke; both processed and unprocessed red meat contributed to this excess incidence. Poultry intake was associated with a lower risk. These associations were independent of other major protein sources, fruits, and vegetables as well as of other stroke risk factors. Compared with red meat, intake of poultry, nuts, and both whole-fat and low-fat dairy was associated with a lower risk.

Earlier studies have found an increased risk of stroke with red meat intake with as little as 1 serving per day.6,12,13 In a recent meta-analysis, intake of both unprocessed and processed red meat was associated with a nonsignificant mod-

### Table 3. Pooled RR and 95% CI for Stroke Subtypes by Quintiles of Intake of Dietary Protein Sources Among 43,150 US Men and 84,010 US Women*

<table>
<thead>
<tr>
<th>Protein Source</th>
<th>Quintiles</th>
<th>RR for 1 Serving/D</th>
<th>P for Trend</th>
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<td><strong>Total red meat</strong></td>
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<tr>
<td>Hemorrhagic</td>
<td>First</td>
<td>1.00 (0.92–1.17)</td>
<td>1.24 (0.87–1.76)</td>
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<tr>
<td>Ischemic</td>
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<td>1.00 (0.93–1.23)</td>
<td>1.09 (0.94–1.27)</td>
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<td>Processed red meat</td>
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<tr>
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<td>1.08 (0.76–1.53)</td>
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<td>0.99 (0.86–1.15)</td>
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<td>Unprocessed red meat</td>
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<tr>
<td>Hemorrhagic</td>
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<td>1.00 (0.71–1.41)</td>
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<tr>
<td>Ischemic</td>
<td></td>
<td>1.00 (1.06–1.41)</td>
<td>1.15 (0.99–1.34)</td>
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<td>Poultry</td>
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<tr>
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<td>First</td>
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<td>0.89 (0.66–1.22)</td>
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<tr>
<td>Ischemic</td>
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<td>1.00 (0.88–1.17)</td>
<td>0.90 (0.79–1.03)</td>
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<tr>
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<td>First</td>
<td>0.80 (0.58–1.09)</td>
<td>0.71 (0.51–1.00)</td>
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<tr>
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<td>0.95 (0.82–1.11)</td>
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<tr>
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<tr>
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<td>0.96 (0.83–1.11)</td>
<td>1.03 (0.89–1.20)</td>
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</table>

RR indicates relative risk; CI, confidence interval.

*Pooled multivariable models are stratified on age (mo) and time period (13 periods in Nurses’ Health Study, 11 in Health Professionals Follow-Up Study) and include: body mass index (10 categories), cigarette smoking (never, past, current 1–14 cigarettes/d, current 14–25 cigarettes/d, current ≥ 25 cigarettes/d), physical exercise (3, 3–9, 9 –18, 18 –27, 27+ metabolic equivalents/wk), parental history of early myocardial infarction (age < 60 y), menopausal status in women (premenopausal, postmenopausal with no history of hormone replacement, postmenopausal with history of hormone replacement, postmenopausal with current hormone replacement), multivitamin use (quintiles of y), vitamin E supplement use (yes/no), aspirin use at least once per wk (yes/no), total energy (quintiles of kcal), cereal fiber (quintiles of g/d), alcohol (quintiles of g/d), transfat (quintiles of g/d), fruit and vegetables (quintiles of servings/d), and other protein sources (quintiles of servings/d).
estly increased risk of total stroke (14% and 17%). However, only 2 studies had separated unprocessed from processed red meat, and the meta-analysis included a total of 1700 cases. Our findings, with more than twice the number of cases included in the meta-analysis, are largely in agreement with earlier findings on the association between red meat and ischemic stroke. Fish intake has been associated with a lower risk of stroke in some studies but not all. We did not observe a statistically significant association between fish intake and stroke risk. Poultry intake was more strongly associated with lower stroke risk than was fish intake, especially among women, for ischemic stroke, and when substituted for red meat; substituting poultry for fish was also associated with a trend toward a lower stroke risk (RR, 0.89; 95% CI, 0.68–1.16). Both whole-fat dairy and low-fat dairy were associated with lower stroke risk when substituted for red meat. The caloric content for a 1-ounce serving of mixed nuts is 168 kcal and for a cooked or broiled 15% fat hamburger patty is 192 kcal. Three slices of cooked, broiled, or pan-fried bacon has 129 kcal and a cup of plain low-fat yogurt has 154 kcal. Thus, substituting nuts or yogurt for bacon at breakfast, for example, or yogurt or nuts in a salad for a hamburger at lunch or dinner could maintain energy balance.

Multiple mechanisms might mediate the relationship between protein sources and stroke risk. A diet high in protein, when compared with a diet high in carbohydrates, may lower blood pressure, a major risk factor for stroke, and improve plasma lipids. Prior analyses from our group found that a lower intake of total animal protein was associated with a higher risk of hemorrhagic stroke in women but not in men. However, this mechanism alone would not account for the different associations of various protein sources with stroke risk. A lower intake of saturated fat has been associated with a trend toward higher stroke risk in some but not all studies, perhaps mediated by low total serum cholesterol levels, reduced platelet aggregation, increased vascular fragility, and increased risk for hemorrhage. Such mechanisms could partly explain, for example, why dairy foods were associated with a lower stroke risk. In a recent meta-analysis of prospective cohort studies, higher milk intake was associated with a nonsignificant trend toward lower stroke risk (per 200 mL/day; RR, 0.87; 95% CI, 0.72–1.05); insufficient data were available to separately evaluate low-fat versus whole-fat milk. In contrast, through its effects on blood pressure, sodium may account for part of the association seen between processed red meat and ischemic stroke risk. Heme iron, found in processed and unprocessed red meat, has been associated with coronary heart disease and diabetes. Higher intakes of potassium, magnesium, and calcium have been associated with reduced stroke risk; ≥1 of these nutrients may help explain the reduction in risk seen when dairy products are substituted for red meat. The reasons for risk reduction seen with higher poultry intake, especially when compared with fish, are not certain, but we note that processing and cooking methods for poultry likely differ from other protein sources, as does the nutrient content, and higher poultry intake was associated with lower stroke risk in earlier studies.

Figure. RR and 95% CI for stroke associated with substitution of dietary protein sources. Q statistic probability value for between-study heterogeneity (null hypothesis is that there is no heterogeneity) for estimate of effect of substitutions >0.05; RR and 95% CI for substitutions not shown here: poultry for fish: 0.89 (0.68–1.16); nuts for fish: 0.99 (0.80–1.23); nuts for poultry: 1.11 (0.90–1.37). RR indicates relative risk.
intake has been associated with lower risk of coronary heart disease. Compared with red meat, poultry has lower amounts of heme iron and higher amounts of polyunsaturated fat.

Our analysis has important strengths and limitations. We separately examined total, hemorrhagic, and ischemic stroke outcomes. We accounted for other lifestyle factors and dietary habits over time to minimize effects of time-dependent confounding. The long cohort follow-up with updated dietary data, high follow-up rate, and large number of participants provided power to detect clinically relevant differences in risks. Although we reduced measurement error in these prospective studies by the use of repeated assessment of diet, some error is inevitable. However, this error should be independent of stroke and would likely lead to an underestimate of the true associations. Misclassification of dietary covariates could create bias in unpredictable directions. The ability to control for known cardiovascular disease risk factors, assessed repeatedly during follow-up, in multivariable models reduced bias, but we cannot exclude the possibility of residual and unmeasured confounding.

Conclusions

In conclusion, greater red meat consumption was associated with a higher risk of stroke. Compared with the same number of servings per day of red meat, consumption of poultry, nuts, or dairy products was associated with lower risk. Similar to what we have observed for coronary heart disease, shifting sources of protein in the US diet may contribute to the prevention of stroke.

Sources of Funding

This study was supported by grant P01CA087969 from the National Institutes of Health, Department of Health and Human Services. A.M.B. was supported through the Harvard Human Nutrition Program.

Disclosures

D.M. received research grants for studying the effects of diet on cardiometabolic diseases from the National Institutes of Health; the Searle Scholar Award from the Searle Funds at The Chicago Community Trust; the Genes and Environment Initiative at the Harvard School of Public Health; and the Gates Foundation/World Health Organization Global Burden of Diseases, Injuries, and Risk Factors Study; and from GlaxoSmithKline, Sigma Tau, Pronova, and the National Institutes of Health for an investigator-initiated, not-for-profit clinical trial of fish oil and post-surgical complications. He also received ad hoc travel reimbursement and/or honoraria for research presentations from the Chicago Council, International Life Sciences Institute, Aramark, Unilever, SPRIM, Nutrition Impact, Norwegian Seafood Export Council, United Nations Food and Agricultural Organization, World Health Organization, US Food and Drug Administration, and several universities. He received ad hoc consulting fees from Foodminds and royalties from UpToDate for an online chapter on fish oil. Harvard University has filed a provisional patent application that has been assigned to Harvard University, listing D.M. as a coinventor to the US Patent and Trademark Office for use of transpalmitoleic acid to prevent and treat insulin resistance, Type 2 diabetes, and related conditions.

References

Dietary Protein Sources and the Risk of Stroke in Men and Women
Adam M. Bernstein, An Pan, Kathryn M. Rexrode, Meir Stampfer, Frank B. Hu, Dariush Mozaffarian and Walter C. Willett

Stroke. 2012;43:637-644; originally published online December 29, 2011;
doi: 10.1161/STROKEAHA.111.633404

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Print ISSN: 0039-2499. Online ISSN: 1524-4628

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Supplemental Methods:

Serving Sizes of Major Protein Sources on Food Frequency Questionnaires in the Nurses’ Health Study, 1980-2002

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<td>2% milk</td>
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<td>Hard cheese</td>
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<td>1 slice or 1oz svg</td>
<td>1 slice or 1oz svg</td>
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<td>1 piece or slice</td>
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<td>1 sandwich</td>
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<td>* Other</td>
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<td>(sausage, kielbasa, et)</td>
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<td>Bacon</td>
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<tr>
<td>(stew, casserole, lasagna, etc)</td>
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<td></td>
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<tr>
<td>Beef, pork, lamb as main dish</td>
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<td>4-6oz</td>
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<td></td>
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<tr>
<td>(steak, roast, ham, etc.)</td>
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<tr>
<td>Pork as a main dish (eg, ham or chops)</td>
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<td></td>
<td></td>
<td>4-6oz</td>
<td>4-6oz</td>
<td>4-6oz</td>
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<tr>
<td>Beef or lamb as a main dish (eg, steak or roast)</td>
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<td>4-6oz</td>
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<td>Eggs</td>
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<td>Fish</td>
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<tr>
<td>* Canned tuna</td>
<td>3-5oz</td>
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<td>3-5oz</td>
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<tr>
<td>* Dark meat fish (mackerel, salmon, sardines, bluefish, swordfish)</td>
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<td>3-5oz</td>
<td>3-5oz</td>
<td>3-5oz</td>
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<tr>
<td>* Other fish (eg, Cod, Haddock, Halibut)</td>
<td>3-5oz</td>
<td>3-5oz</td>
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<td>3-5oz</td>
<td>3-5oz</td>
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<tr>
<td>* Breaded fish cakes, pieces, or fish sticks</td>
<td>3-5oz</td>
<td>3-5oz</td>
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<td>Nuts (incl. peanuts,)</td>
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<td>walnuts, other nuts)</td>
<td>or 1oz</td>
<td>or 1oz</td>
<td>or 1oz</td>
<td>or 1oz</td>
<td>or 1oz</td>
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<td>Beans or lentils, baked or dry</td>
<td>½ cup</td>
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<td>½ cup</td>
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<tr>
<td>String beans</td>
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<td>½ cup</td>
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<td>Peas</td>
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<tr>
<td>Soybeans or tofu</td>
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<td>3-4 oz</td>
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<td>Tofu, soy burger, or other soy protein</td>
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Supplemental Methods:

Serving Sizes of Major Protein Sources on Food Frequency Questionnaires in the Health Professionals’ Follow-up Study, 1986-2006

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<td>2% milk</td>
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<td>1% or 2% milk</td>
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<tr>
<td>Sour cream</td>
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<td>1 tbs</td>
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<tr>
<td>Sherbet or ice milk or frozen yogurt or non-fat ice cream</td>
<td>1 cup</td>
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<td>Yogurt</td>
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<td>Ice cream</td>
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<td>Cottage or ricotta cheese</td>
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<td>½ cup</td>
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<tr>
<td>Hard cheese</td>
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<td>Butter</td>
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<td>1 pat</td>
<td>1 pat</td>
<td>1 pat</td>
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<tr>
<td>Chicken or turkey w/o skin</td>
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<td>3oz</td>
<td>3oz</td>
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<td>Chicken or turkey sandwich</td>
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</tr>
<tr>
<td>* Other (sausage, kielbasa, et)</td>
<td>2oz or 2 small links</td>
<td>2oz or 2 small links</td>
<td>2oz or 2 small links</td>
<td>2oz or 2 small links</td>
<td>2oz or 2 small links</td>
<td>2oz or 2 small links</td>
</tr>
<tr>
<td>Bacon</td>
<td>2 slices</td>
<td>2 slices</td>
<td>2 slices</td>
<td>2 slices</td>
<td>2 slices</td>
<td>2 slices</td>
</tr>
<tr>
<td>Beef, pork, lamb sandwich or mixed dish (stew, casserole, lasagna, etc)</td>
<td>Not quantified</td>
<td>Not quantified</td>
<td>Not quantified</td>
<td>Not quantified</td>
<td>Not quantified</td>
<td>Not quantified</td>
</tr>
<tr>
<td>Beef, pork, lamb as main dish (steak, roast, ham, etc.)</td>
<td>4-6oz</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pork as a main dish (eg, ham or chops)</td>
<td>4-6 oz</td>
<td>4-6oz</td>
<td>4-6oz</td>
<td>4-6oz</td>
<td>4-6oz</td>
<td>4-6oz</td>
</tr>
<tr>
<td>Beef or lamb as a main dish (eg, steak or roast)</td>
<td>4-6 oz</td>
<td>4-6oz</td>
<td>4-6oz</td>
<td>4-6oz</td>
<td>4-6oz</td>
<td>4-6oz</td>
</tr>
<tr>
<td>Eggs</td>
<td>1 egg</td>
<td>1 egg</td>
<td>1 egg</td>
<td>1 egg</td>
<td>1 egg</td>
<td>1 egg</td>
</tr>
<tr>
<td>Fish</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>* Canned tuna</td>
<td>3-4oz</td>
<td>3-4oz</td>
<td>3-4oz</td>
<td>3-4oz</td>
<td>3-4oz</td>
<td>3-4oz</td>
</tr>
<tr>
<td>* Dark meat fish (mackerel, salmon, sardines, bluefish,</td>
<td>3-5oz</td>
<td>3-5oz</td>
<td>3-5oz</td>
<td>3-5oz</td>
<td>3-5oz</td>
<td>3-5oz</td>
</tr>
<tr>
<td>Food Item</td>
<td>Calories</td>
<td>Protein</td>
<td>Fat</td>
<td>Carbs</td>
<td>Sodium</td>
<td></td>
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<td>-----------------------------------------------</td>
<td>----------</td>
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<td>-------</td>
<td>--------</td>
<td></td>
</tr>
<tr>
<td>swordfish)</td>
<td>3-5 oz</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>* Other fish (eg, Cod, Haddock, Halibut)</td>
<td>3-5 oz</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>* Breaded fish cakes, pieces, or fish sticks</td>
<td>3-5 oz</td>
<td>1 svg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nuts (incl. peanuts, walnuts, other nuts)</td>
<td>Small packet or 1oz</td>
<td>Small packet or 1oz</td>
<td>Small packet or 1oz</td>
<td>Small packet or 1oz</td>
<td>Small packet or 1oz</td>
<td></td>
</tr>
<tr>
<td>Beans or lentils, baked or dry</td>
<td>½ cup</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>String beans</td>
<td>½ cup</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peas</td>
<td>½ cup</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Soybeans or tofu</td>
<td>3-4 oz</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tofu, soy burger, or other soy protein</td>
<td>Not quantified</td>
<td>Not quantified</td>
<td>Not quantified</td>
<td>Not quantified</td>
<td>Not quantified</td>
<td></td>
</tr>
</tbody>
</table>
Supplemental Methods:

Many previous prospective cohort studies have stopped updating a study participant’s diet when he or she developed an intermediate outcome on the causal pathway between diet and cardiovascular disease, such as diabetes, hypertension, hypercholesterolemia, angina, or coronary artery bypass surgery (CABG)/percutaneous coronary intervention (PCI). This has been done because changes in diet after these interim diagnoses or events may bias the diet-disease association; i.e., these diagnoses can be confounders. Rather than stop updating diet at all of these intermediates, we first assessed whether the occurrence of an intermediate outcome or event was associated with change in dietary protein intake. To do so, we fit multiple generalized linear models accounting for within-person repeated dietary measures. Three models were fit with data from the Nurses’ Health Study and three were fit with data from the Health Professionals’ Follow-Up Study. Within each Study, one model had as its continuous dependent variable the change in calorie-adjusted animal protein intake at each point in time (e.g., the “change” in animal protein intake in 1986 in the NHS was the calorie-adjusted 1984 intake subtracted from the calorie-adjusted 1990 intake), another model had as its continuous dependent variable the change in calorie-adjusted vegetable protein intake (defined in the same way as for animal protein), and a third model had as its outcome the change in calorie-adjusted red meat intake. The independent variables for each of the six models included binary indicators for a new diagnosis of each intermediate (yes/no for diabetes, hypertension, hypercholesterolemia, angina, or CABG/PCI), a binary indicator for a new diagnosis of cancer (yes/no), a binary indicator for a new diagnosis of myocardial infarction (yes/no), an indicator for the current follow-up cycle (ten 2-year follow-up cycles between 1986 and 2006), and interaction terms between the intermediate outcomes or cancer or myocardial infarction and the follow-up cycle. The correlation structure for the generalized linear models was autoregressive. From these models, we observed that new diagnoses of high cholesterol, high blood pressure, angina, and PCI/CABG were associated with statistically significant but very small changes in subsequent animal and vegetable protein intake (e.g., 0.1 to 1.2 g/day following diagnosis) and red meat intake (e.g., 0.01 to 0.1 servings/day following diagnosis) in men and women. As these diagnoses appeared to be only weak time-dependent confounders, and to avoid the potential for misclassification of each participant’s long-term diet by stopping the updating of diet at one of these diagnoses, we continued updating a study participant’s dietary intake throughout follow-up using data from all repeated FFQs.
Supplemental Tables:

Table S1. Spearman correlations between dietary protein sources in Health Professionals’ Follow-up Study

<table>
<thead>
<tr>
<th></th>
<th>Unprocessed red meat</th>
<th>Processed red meat</th>
<th>Poultry</th>
<th>Fish</th>
<th>Whole fat dairy</th>
<th>Low fat dairy</th>
<th>Eggs</th>
<th>Nuts</th>
<th>Legumes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unprocessed red meat</td>
<td>1.00</td>
<td>0.53</td>
<td>-0.01</td>
<td>-0.18</td>
<td>0.32</td>
<td>-0.01</td>
<td>0.32</td>
<td>0.08</td>
<td>0.08</td>
</tr>
<tr>
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<td>-0.06</td>
<td>-0.17</td>
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<td>-0.05</td>
<td>0.42</td>
<td>0.08</td>
<td>0.08</td>
<td>0.01</td>
</tr>
<tr>
<td>Poultry</td>
<td>1.00</td>
<td>0.33</td>
<td>-0.05</td>
<td>0.08</td>
<td>-0.02</td>
<td>0.06</td>
<td>0.15</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fish</td>
<td>1.00</td>
<td>-0.10</td>
<td>0.08</td>
<td>-0.07</td>
<td>0.10</td>
<td>0.16</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Whole fat dairy</td>
<td>1.00</td>
<td>-0.03</td>
<td>0.34</td>
<td></td>
<td>0.12</td>
<td>0.01</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low fat dairy</td>
<td>1.00</td>
<td></td>
<td>0.05</td>
<td>0.11</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eggs</td>
<td>1.00</td>
<td>0.07</td>
<td>0.02</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nuts</td>
<td>1.00</td>
<td></td>
<td>0.17</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Legumes</td>
<td>1.00</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tbody>
</table>
Table S2. Spearman correlations between dietary protein sources in Nurses’ Health Study

<table>
<thead>
<tr>
<th></th>
<th>Unprocessed red meat</th>
<th>Processed red meat</th>
<th>Poultry</th>
<th>Fish</th>
<th>Whole fat dairy</th>
<th>Low fat dairy</th>
<th>Eggs</th>
<th>Nuts</th>
<th>Legumes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unprocessed red meat</td>
<td>1.00</td>
<td>0.40</td>
<td>-0.03</td>
<td>-0.13</td>
<td>0.18</td>
<td>-0.10</td>
<td>0.19</td>
<td>0.03</td>
<td>0.13</td>
</tr>
<tr>
<td>Processed red meat</td>
<td></td>
<td>1.00</td>
<td>-0.10</td>
<td>-0.12</td>
<td>0.23</td>
<td>-0.14</td>
<td>0.26</td>
<td>0.01</td>
<td>0.06</td>
</tr>
<tr>
<td>Poultry</td>
<td>1.00</td>
<td></td>
<td>0.42</td>
<td>-0.04</td>
<td>0.19</td>
<td>0.04</td>
<td>0.09</td>
<td>0.13</td>
<td></td>
</tr>
<tr>
<td>Fish</td>
<td>1.00</td>
<td></td>
<td>-0.05</td>
<td>0.26</td>
<td>0.03</td>
<td>0.11</td>
<td>0.14</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Whole fat dairy</td>
<td></td>
<td></td>
<td>1.00</td>
<td>-0.13</td>
<td>0.19</td>
<td>0.12</td>
<td>0.06</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low fat dairy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.00</td>
<td>0.05</td>
<td>0.08</td>
<td></td>
<td>0.10</td>
</tr>
<tr>
<td>Eggs</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.00</td>
<td>0.07</td>
<td></td>
<td>0.07</td>
</tr>
<tr>
<td>Nuts</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.00</td>
<td></td>
<td>0.16</td>
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<tr>
<td>Legumes</td>
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<td></td>
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<td></td>
<td></td>
<td></td>
<td>1.00</td>
</tr>
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</table>
Table S3. RR and 95% CI for stroke by quintiles of intake of processed and unprocessed red meat *

<table>
<thead>
<tr>
<th>Quintiles</th>
<th>1st</th>
<th>2nd</th>
<th>3rd</th>
<th>4th</th>
<th>5th</th>
<th>P for trend</th>
<th>RR for 1 serving/day</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total Red Meat</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>1.00</td>
<td>0.97</td>
<td>1.07</td>
<td>1.20</td>
<td>1.25</td>
<td>0.02</td>
<td>1.14</td>
</tr>
<tr>
<td></td>
<td>(0.81,1.17)</td>
<td>(0.88,1.30)</td>
<td>(0.98,1.48)</td>
<td>(1.00,1.58)</td>
<td></td>
<td></td>
<td>(1.02,1.26)</td>
</tr>
<tr>
<td>Women</td>
<td>1.00</td>
<td>1.09</td>
<td>1.08</td>
<td>1.11</td>
<td>1.12</td>
<td>0.28</td>
<td>1.06</td>
</tr>
<tr>
<td></td>
<td>(0.97,1.23)</td>
<td>(0.94,1.23)</td>
<td>(0.95,1.28)</td>
<td>(0.94,1.33)</td>
<td></td>
<td></td>
<td>(0.95,1.19)</td>
</tr>
<tr>
<td>Pooled</td>
<td>1.00</td>
<td>1.05</td>
<td>1.08</td>
<td>1.14</td>
<td>1.17</td>
<td>0.01</td>
<td>1.10</td>
</tr>
<tr>
<td></td>
<td>(0.95,1.17)</td>
<td>(0.96,1.20)</td>
<td>(1.01,1.29)</td>
<td>(1.02,1.34)</td>
<td></td>
<td></td>
<td>(1.02,1.19)</td>
</tr>
<tr>
<td><strong>Processed Red Meat</strong></td>
<td></td>
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<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Men</td>
<td>1.00</td>
<td>0.98</td>
<td>0.89</td>
<td>1.09</td>
<td>1.23</td>
<td>&lt;0.01</td>
<td>1.48</td>
</tr>
<tr>
<td></td>
<td>(0.82,1.19)</td>
<td>(0.73,1.08)</td>
<td>(0.89,1.32)</td>
<td>(1.00,1.51)</td>
<td></td>
<td></td>
<td>(1.13,1.95)</td>
</tr>
<tr>
<td>Women</td>
<td>1.00</td>
<td>0.96</td>
<td>1.03</td>
<td>1.04</td>
<td>1.03</td>
<td>0.53</td>
<td>1.08</td>
</tr>
<tr>
<td></td>
<td>(0.85,1.08)</td>
<td>(0.91,1.18)</td>
<td>(0.91,1.18)</td>
<td>(0.89,1.19)</td>
<td></td>
<td></td>
<td>(0.86,1.35)</td>
</tr>
<tr>
<td>Pooled</td>
<td>1.00</td>
<td>0.97</td>
<td>0.99</td>
<td>1.05</td>
<td>1.09</td>
<td>0.02</td>
<td>1.23</td>
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<tr>
<td></td>
<td>(0.87,1.07)</td>
<td>(0.89,1.10)</td>
<td>(0.94,1.17)</td>
<td>(0.97,1.23)</td>
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<td></td>
<td>(1.03,1.46)</td>
</tr>
<tr>
<td><strong>Unprocessed Red Meat</strong></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>1.00</td>
<td>1.09</td>
<td>1.05</td>
<td>1.22</td>
<td>1.10</td>
<td>0.56</td>
<td>1.07</td>
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<tr>
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<td>(0.86,1.28)</td>
<td>(0.99,1.50)</td>
<td>(0.87,1.38)</td>
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<td>(0.86,1.33)</td>
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<tr>
<td></td>
<td></td>
<td>1.00</td>
<td>1.07</td>
<td>1.03</td>
<td>1.11</td>
<td>1.16</td>
<td>0.07</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(0.95,1.21)</td>
<td>(0.90,1.17)</td>
<td>(0.96,1.28)</td>
<td>(0.99,1.37)</td>
<td>(0.99,1.37)</td>
<td>(0.98,1.43)</td>
</tr>
<tr>
<td>Pooled</td>
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<td>1.00</td>
<td>1.08</td>
<td>1.04</td>
<td>1.14</td>
<td>1.14</td>
<td>0.08</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(0.97,1.19)</td>
<td>(0.93,1.16)</td>
<td>(1.02,1.28)</td>
<td>(1.00,1.30)</td>
<td>(1.00,1.30)</td>
<td>(0.98,1.31)</td>
</tr>
</tbody>
</table>

* Median values shown for quintiles of servings/day

† Multivariable model stratified on age (months) and time period (13 periods in NHS, 11 in HPFS) and includes: body mass index (10 categories), cigarette smoking (never, past, current 1-14 cig/day, current 14-25 cig/day, current 25+ cig/day), physical exercise (<3, 3-9, 9-18, 18-27, 27+ metabolic equivalents/week), parental history of early myocardial infarction (before age 60), menopausal status in women (pre-menopausal, postmenopausal with no history of hormone replacement, postmenopausal with history of hormone replacement, postmenopausal with current hormone replacement), multivitamin use (quintiles of yrs), vitamin E supplement use (yes/no), aspirin use at least once per week (yes/no), total energy (quintiles of Kcal), cereal fiber (quintiles of g/day), alcohol (quintiles of g/day), trans-fat (quintiles of g/day), fruit and vegetables (quintiles of servings/day), other protein sources (quintiles of servings/day), and history of myocardial infarction (yes/no), coronary artery bypass surgery or percutaneous coronary intervention (yes/no), angina (yes/no), diabetes (yes/no), hypertension (yes/no), and hypercholesterolemia (yes/no)

‡ Q statistic p value for between-study heterogeneity (null hypothesis is that there is no heterogeneity) for total red meat, processed meat, unprocessed meat > 0.05
Table S4: Relative Risks (RR) and 95% confidence intervals for hemorrhagic stroke in men and women by quintiles of intake of major sources of dietary protein *

<table>
<thead>
<tr>
<th>Quintiles</th>
<th>1st</th>
<th>2nd</th>
<th>3rd</th>
<th>4th</th>
<th>5th</th>
<th>P for trend</th>
<th>RR for 1 serving/day</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total Red Meat</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>1.00</td>
<td>1.03</td>
<td>0.93</td>
<td>1.14</td>
<td>1.07</td>
<td>0.61</td>
<td>1.08 (0.80,1.48)</td>
</tr>
<tr>
<td></td>
<td>(0.61,1.73)</td>
<td>(0.53,1.63)</td>
<td>(0.63,2.06)</td>
<td>(0.55,2.08)</td>
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<tr>
<td>Women</td>
<td>1.00</td>
<td>1.46</td>
<td>1.49</td>
<td>1.54</td>
<td>1.30</td>
<td>0.56</td>
<td>1.11 (0.78,1.60)</td>
</tr>
<tr>
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<td>(0.94,2.51)</td>
<td>(0.72,2.34)</td>
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</tr>
<tr>
<td><strong>Processed Red Meat</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>1.00</td>
<td>0.95</td>
<td>1.04</td>
<td>1.26</td>
<td>1.47</td>
<td>0.08</td>
<td>2.06 (0.92,4.62)</td>
</tr>
<tr>
<td></td>
<td>(0.55,1.67)</td>
<td>(0.59,1.84)</td>
<td>(0.72,2.21)</td>
<td>(0.80,2.72)</td>
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* Multivariable model stratified on age (months) and time period (13 periods in NHS, 11 in HPFS) and includes: body mass index (10 categories), cigarette smoking (never, past, current 1-14 cig/day, current 14-25 cig/day, current 25+ cig/day), physical exercise (<3, 3-9, 9-18, 18-27, 27+ metabolic equivalents/week), parental history of early myocardial infarction (before age 60), menopausal status in women (pre-menopausal, postmenopausal with no history of hormone replacement, postmenopausal with history of hormone replacement, postmenopausal with current hormone replacement), multivitamin use (quintiles of yrs), vitamin E supplement use (yes/no), aspirin use at least once per week (yes/no), total energy (quintiles of Kcal), cereal fiber (quintiles of g/day), alcohol (quintiles of g/day), trans-fat (quintiles of g/day), fruit and vegetables (quintiles of servings/day), and other protein sources (quintiles of servings/day)
Table S5: Relative Risks (RR) and 95% confidence intervals for ischemic stroke in men and women by quintiles of intake of major sources of dietary protein *

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### Whole-fat dairy

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### Low-fat dairy

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<td>(0.74,1.08)</td>
<td>(0.79,1.14)</td>
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</tr>
</tbody>
</table>

### Nuts

<table>
<thead>
<tr>
<th></th>
<th>Men</th>
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</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1.00</td>
<td>1.04</td>
<td>1.02</td>
<td>1.06</td>
<td>0.97</td>
<td>0.51</td>
<td>0.89</td>
</tr>
<tr>
<td></td>
<td>(0.83,1.31)</td>
<td>(0.81,1.28)</td>
<td>(0.85,1.32)</td>
<td>(0.77,1.22)</td>
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<td></td>
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</tr>
<tr>
<td>Women</td>
<td>1.00</td>
<td>0.92</td>
<td>0.98</td>
<td>1.01</td>
<td>0.96</td>
<td>0.98</td>
<td>0.99</td>
</tr>
<tr>
<td></td>
<td>(0.77,1.10)</td>
<td>(0.81,1.18)</td>
<td>(0.84,1.21)</td>
<td>(0.80,1.16)</td>
<td></td>
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</tr>
</tbody>
</table>

### Legumes
<p>| | | | | | | |</p>
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</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td>1.00</td>
<td>0.93</td>
<td>0.89</td>
<td>1.03</td>
<td>1.11</td>
<td>0.09</td>
</tr>
<tr>
<td></td>
<td>(0.74,1.16)</td>
<td>(0.70,1.12)</td>
<td>(0.82,1.30)</td>
<td>(0.88,1.41)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>1.00</td>
<td>0.98</td>
<td>1.14</td>
<td>1.04</td>
<td>1.16</td>
<td>0.12</td>
</tr>
<tr>
<td></td>
<td>(0.82,1.18)</td>
<td>(0.95,1.37)</td>
<td>(0.87,1.25)</td>
<td>(0.96,1.40)</td>
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</tbody>
</table>

* Multivariable model stratified on age (months) and time period (13 periods in NHS, 11 in HPFS) and includes: body mass index (10 categories), cigarette smoking (never, past, current 1-14 cig/day, current 14-25 cig/day, current 25+ cig/day), physical exercise (<3, 3-9, 9-18, 18-27, 27+ metabolic equivalents/week), parental history of early myocardial infarction (before age 60), menopausal status in women (pre-menopausal, postmenopausal with no history of hormone replacement, postmenopausal with history of hormone replacement, postmenopausal with current hormone replacement), multivitamin use (quintiles of yrs), vitamin E supplement use (yes/no), aspirin use at least once per week (yes/no), total energy (quintiles of Kcal), cereal fiber (quintiles of g/day), alcohol (quintiles of g/day), trans-fat (quintiles of g/day), fruit and vegetables (quintiles of servings/day), and other protein sources (quintiles of servings/day)
Abstract 6

Dietary Protein Sources and the Risk of Stroke in Men and Women

Adam M. Bernstein, MD, ScD; An Pan, PhD; Kathryn M. Rexrode, MD; Meir Stampfer, MD, DrPH; Frank B. Hu, MD, PhD; Dariush Mozaffarian, MD, DrPH; Walter C. Willett, MD, DrPH

(Stroke. 2012;43:637-644.)

Key Words: diet ■ men ■ nutrition ■ stroke ■ women

Clinical Sciences

남성과 여성에서 식이 단백질원(Protein Source)과
뇌졸중의 위험

Dietary Protein Sources and the Risk of Stroke in Men and Women

Adam M. Bernstein, MD, ScD; An Pan, PhD; Kathryn M. Rexrode, MD; Meir Stampfer, MD, DrPH; Frank B. Hu, MD, PhD; Dariush Mozaffarian, MD, DrPH; Walter C. Willett, MD, DrPH

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배경과 목적
식이 단백질원(protein sources)과 뇌졸중의 관계는 전향적으
로 연구된 적이 거의 없다. 우리는 주요 단백질원의 식품들과
뇌졸중의 위험 사이의 관계를 조사하였다.

방법
기준시점에 약, 당뇨, 심혈관질환을 진단받지 않은 30~55세
여성 84,010명과 40~75세 남성 43,150명을 전향적으로 추적
하였다. 식이는 표준화되고 검증된 설문지에 의해 반복적으로
평가되었다. 우리는 뇌졸중 위험 인자에 대해 보정된 비례위험
모형을 사용하여 단백질원과 뇌졸중의 발병을 사이의 연관 관
계를 조사하였다.

결과
여성과 남성 각각 26년, 22년의 추적기간 동안, 각각 2,633건, 1,397건의 뇌졸중이 확인되었다. 다변량분석에서, 붙은 살코기
(red meat)의 섭취는 뇌졸중의 위험을 높였고, 가금류(poul-
try)의 섭취는 위험을 낮추었다. 다른 단백질원으로 변경했을
경우의 효과분석 시 붙은 살코기 1그릇/일(serving/day)과 비
교하여 가금류의 1그릇/일은 뇌졸중의 위험을 27% (95% CI, 12~39%) 낮추었고, 전과류에서 17% (95% CI, 4~27%), 생선
류에서 17% (95% CI, 0~30%), 저지방 유제품에서 11% (95% CI, 5~17%), 전자(whole-fat) 유제품에서 10% (95% CI, 4~16%) 위험을 낮추었다. 붙은 살코기를 콘과나 계란으로 바
꾸었을 때는 유의성이 없었다.

결론
이러한 자료는 붙은 살코기를 다른 단백질 식이원으로 대체함
으로써 뇌졸중 위험을 줄일 수 있음을 시사한다.