

Role of Total, Red, Processed, and White Meat Consumption in Stroke Incidence and Mortality: A Systematic Review and Meta-Analysis of Prospective Cohort Studies

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Background—Previous meta-analyses on meat intake and risk of stroke did not report the effect of white meat (poultry meat, excluding fish) and did not examine stroke incidence and mortality separately. We aimed to investigate the relationship of total (red and processed meat), red (unprocessed or fresh red meat), and processed (processed red meat) consumption along with white meat on risk of stroke incidence and mortality.

Methods and Results—Articles were identified from databases and reference lists of relevant studies up to October 28, 2016. We selected prospective cohort studies on meat consumption specified by types of meat and stroke incidence and mortality reporting relative risks and 95% confidence intervals. The pooled relative risk was estimated using the random-effects model. Based on the inclusion criteria, 10 articles containing 15 studies (5 articles with 7 studies including 9522 cases of stroke incidence and 254 742 participants and 5 articles with 8 studies containing 12 999 cases of stroke mortality and 487 150 participants) were selected for quantitative synthesis. The pooled relative risks (95% confidence intervals) for total, red, processed and white meat consumption and total stroke incidence were 1.18 (1.09–1.28), 1.11 (1.03–1.20), 1.17 (1.08–1.25), and 0.87 (0.78–0.97), respectively. Total meat consumption (0.97 [0.85–1.11]) and red meat consumption 0.87 (0.64–1.18) were not significantly associated with stroke-related death.

Conclusions—The relationship between meat intake and risk of stroke may differ by type of meat. Recommendations for replacing proportions of red and processed meats to white meat for the prevention of stroke may be considered in clinical practice. (*J Am Heart Assoc.* 2017;6:e005983. DOI: 10.1161/JAHA.117.005983.)

Key Words: cerebrovascular accident • cerebrovascular infarction • cerebrovascular ischemia • meat consumption

Cerebrovascular accidents are a serious health condition that causes disability and death among adults, with high disease burden in the world.^{1,2} Although variation in stroke incidence and burden may exist between high- and low-income countries, the prevalence of stroke (proportion of the population with history of stroke) and burden (disability-adjusted life-years lost) are increasing worldwide.³ Controlling for risk factors is needed to halt the increasing rates of stroke prevalence globally.⁴

Among the risk factors for stroke, dietary habit is one of the modifiable and self-manageable factors that should be a focus of public health intervention. Previous meta-analyses show that increased fruit and vegetable consumption is associated with a decreased risk of stroke,^{5–7} whereas high intake of red and processed meats is related to an increase in total stroke and ischemic stroke cases.^{8–11} Despite a recent transition to a higher proportion of white meat (poultry) intake, consumption of red and processed meats still

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Accompanying Tables S1 and S2 are available at <http://jaha.ahajournals.org/content/6/9/e005983/DC1/embed/inline-supplementary-material-1.pdf>

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Clinical Perspective

What Is New?

- The association of meat consumption with risk of stroke varies by types of meat.

What Are the Clinical Implications?

- Replacement of red and processed meats to white meat may be considered among patients at high risk for stroke, among the other lifestyle interventions.

constitutes the largest proportion of overall meat consumption and has been increasing in the United States and other developed countries.¹² One of the major problems currently with the recommendations for dietary protein in North America is that there is no clear distinction of fat content between red meat and white meat and fish.¹³ At present, evidence on the effects of meat consumption on risk of stroke accounting for nutritional properties of different types of meat is not entirely clear. Therefore, it is necessary to examine the association of consumption of different kinds of meat with incident stroke and stroke-related death before establishing nutrition intervention strategies.

Some methodological inconsistencies and issues limit previous meta-analyses of red meat and processed meat consumption that have reported a positive association with risk of stroke. Existing meta-analyses considered stroke mortality as fatal stroke incidence and combined the results,^{8,10,11} synthesized both out-of-date¹⁴ and most recent¹⁵ results from the same cohort (ie, Health Professionals Follow-Up Study) for analysis,¹¹ and performed subgroup analysis only by stroke subtypes.^{8,10} In addition, none of the previous meta-analyses addressed the relationship between white meat intake and risk of stroke. This meta-analysis aimed to update evidence on the association between total, red, and processed meat consumption, and white meat consumption on the risk of stroke and stroke-related death.

Methods

Study Strategy and Literature Search

We followed the MOOSE (Meta-Analysis of Observational Studies in Epidemiology) guideline for reporting the relevant items in this study.^{16,17} We conducted a literature search of PubMed, Embase, and Cochrane Library databases to identify relevant articles published through October 2016. In accordance with one review,¹⁸ we used a broad search term for “total, red, processed and white meat” (meats, meat product, meat products, red meat, red meats, beef, veal, goat, lamb, pork, mutton, sausage, sausages, ham, hams, pastrami,

bacon, bacons, salami, salamis, hot dog, hot dogs, animal food, animal foods, animal protein, animal proteins, diet, diets, dietary, white meat, poultry, chicken, duck, turkey, rabbit) in combination with “stroke” (stroke, ischemic stroke, hemorrhagic stroke, cerebrovascular disease, cerebrovascular attack, cerebral infarct, intracranial hemorrhage) to identify articles on total, processed, red and white meat consumption, and risk of stroke incidence and mortality. The full search strategy is shown in Table S1.

Two authors (K.K. and J.H.) independently conducted the selection procedure from the initial screening to select the articles included for this meta-analysis. The two authors (K.K. and J.H.) reviewed articles eligible for a full-text review and additional records were identified through the reference lists of relevant publications. Each article was evaluated based on the inclusion criteria. We conducted study selection procedures without any language restrictions. Any cases of disagreement between the 2 authors were resolved by consulting with the corresponding author (S.M.P.).

Study Selection

We selected prospective cohort studies with an assessment of meat intake and stroke incidence along with mortality comparing the highest versus the lowest categories. The following inclusion criteria were adopted for the final selection of studies used for this meta-analysis: (1) prospective cohort design (2) assessment of total, red, processed, and white meat consumption (3) outcome of the study of stroke and its subtypes or stroke-related death; and (4) reporting the outcome as relative risks (RRs) with 95% confidence intervals (CIs) in publication. In addition, we considered only the most recent publication eligible for inclusion if the studies were based on the same cohort.

Definition of the Types of Meat

The types of meat were assessed and classified by the following definition: (1) total meat: red meat and processed meat; (2) red meat: unprocessed or fresh red meat; (3) processed meat: processed meat or processed red meat; and (4) white meat: poultry meat only (fish excluded).

Definition of Stroke Incidence and Mortality

We defined stroke incidence as the first occurrence of stroke and stroke mortality as death caused by stroke.

Data Extraction and Quality Assessment

Two authors (K.K. and J.H.) independently reviewed selected articles and extracted the following information: last name of

the author; study year; country; population size; follow-up duration; amount of highest and lowest intake; type of meat consumption; number of stroke (and stroke subtypes) incidence and mortality; adjustment variables; and RRs and corresponding 95% CIs. The quality assessment of each study was performed using the Newcastle-Ottawa Scale for cohort studies.¹⁹ Scores ranged from 0 to 9 based on the 8-item instrument containing subject selection, comparability of subjects, and assessment of outcome/exposure. The quality assessment based on Newcastle-Ottawa Scale for cohort studies is presented in Table S2.

Statistical Analysis

We transformed hazard ratios, RRs, and standard errors (calculated from corresponding 95% CIs) by taking their natural logarithms.²⁰ The pooled RRs and 95% CIs were calculated from a random-effects model based on the Der Simonian and Laird method²¹ to account for variation and statistical heterogeneity between the studies. Assessment of heterogeneity between the studies was based on Cochran Q test and Higgin I^2 statistic.²² Egger test was performed to check for a publication bias.²³ $P < 0.1$ from Q test and I^2 value $> 50\%$ were determined as substantial heterogeneity. The significance

cutoff P value for the Egger test was set to 0.1. We conducted subgroup analyses to assess the associations between types of meat consumption and stroke incidence and mortality by various characteristics of the studies (number of cases, follow-up duration, sex, stroke subtypes, and adjustment variables ranging from sociodemographic status to health behavior and health status) to account for heterogeneity among the studies. All statistical analyses were conducted with Stata version 14.0 (StataCorp). Unless otherwise specified, P values were 2-sided. $P < 0.05$ was considered statistically significant.

Results

Study Selection and Characteristics of the Studies

An initial search identified a total of 2074 articles. In addition, we included 13 articles from the reference lists of relevant studies. After removing duplicates, a total of 1681 articles were remaining and 25 articles were eligible for a full-text review after excluding articles with irrelevant titles and abstracts. After the full-text review, we excluded 15 articles: 5 articles because they assessed overall dietary pattern instead of meat, 5 articles because they focused on the

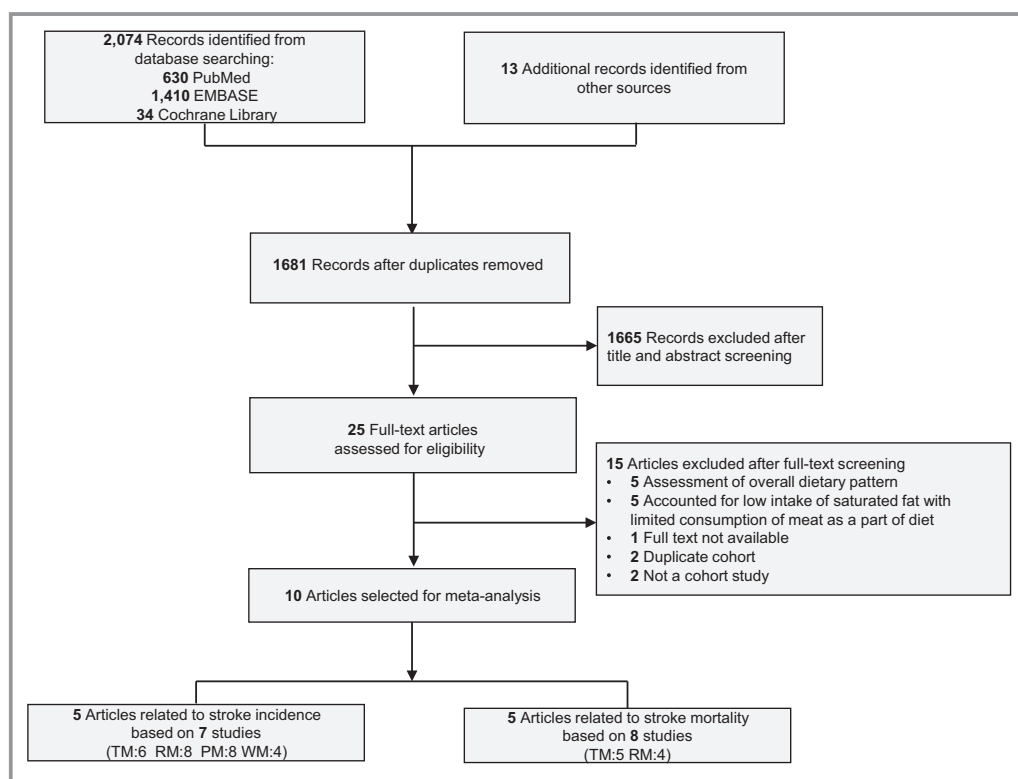


Figure 1. Flow diagram for identification and study selection. PM indicates processed meat; RM, red meat; TM, total meat; WM, white meat. The numbers in parentheses refer to the number of comparisons within the studies according to types of meat.

Mediterranean diet, 1 article because full text was not available, 2 articles because of a duplicate cohort, and 2 articles because of a case-control design. Finally, a total of 10 articles containing 15 cohort studies published until October 2016 were included in this meta-analysis. Five articles included 7 studies on total (6 comparisons), red (8 comparisons), processed (8 comparisons), and white meat (4 comparisons) consumption and stroke incidence and the other 5 articles contained 8 studies on total (5 comparisons) and red (4 comparisons) meat intake and stroke mortality. Data on 254 742 participants with 9522 stroke incidents and 487 150 participants with 12 999 cases of stroke mortality were quantitatively synthesized. A PRISMA(Preferred Reporting Items for Systematic reviews and Meta-Analyses)^{16,17} flow chart for the study selection is presented in Figure 1. Characteristics of the selected studies for this meta-analysis are summarized in Table 1.^{15,24–32}

Pooled Analysis and Heterogeneity

Figure 2^{15,24–26,30} demonstrates the adjusted RRs (95% CIs) for each study and the pooled RRs (95% CIs) comparing the highest versus the lowest category of each type of meat consumption. Cochran I^2 values are presented along with heterogeneity P value for the pooled analysis for each type of meat. Overall, the results of pooled analyses indicate that total (RR, 1.18; 95% CI, 1.09–1.28 [$I^2=0.00$]), red (RR, 1.11; 95% CI, 1.03–1.20 [$I^2=0.00$]), and processed (RR, 1.17, 95% CI, 1.08–1.25 [$I^2=0.00$]) meat intake is associated with an increase of stroke incidence, whereas white meat (RR, 0.87; 95% CI, 0.78–0.96 [$I^2=0.00$]) consumption is related to a reduction of stroke incidence. However, consumption of total (RR, 0.97; 95% CI, 0.85–1.11 [$I^2=0.00$]) and red meat (RR, 0.87; 95% CI, 0.64–1.18 [$I^2=70.9$]) were not significantly associated with stroke mortality. The association between total and red meat consumption and stroke mortality is shown in Figure 3.^{27–29,31,32}

Total meat consumption and stroke incidence and mortality

Four articles containing 6 comparisons with reporting data on a total of 213 722 participants were included in the meta-analysis of total meat consumption and stroke incidence.^{15,24–26} The estimated RRs and 95% CIs of total meat intake and stroke incidence comparing the highest versus the lowest category is shown in Figure 2. The results suggest that consumption of total meat is significantly associated with a 9% to 28% increased risk of stroke. No heterogeneity was found among the 6 comparisons ($I^2=0.00$). The meta-analysis of total meat consumption and mortality from stroke were based on 3 articles with 5 comparisons and a total of

313 596 participants.^{27–29} No evidence of an association between total meat intake and stroke mortality was found (RR,0.97; 95% CI, 0.85–1.11 [$I^2=0.00$]).

Red meat consumption and stroke incidence and mortality

The combined results from 5 articles^{15,24–26,30} with 8 comparisons (254 742 participants) on red meat intake and stroke incidence comparing the highest versus the lowest category show that red meat consumption is linked to an increase of 3% to 20% stroke incidence. Among these 8 comparisons, we did not detect any heterogeneity ($I^2=0.00$). The association between red meat consumption and stroke-related death was assessed based on 3 articles^{27,31,32} containing 4 comparisons (260 579 participants) comparing the highest versus the lowest categories. Although we found no association between red meat consumption and stroke mortality (RR, 0.87; 95% CI, 0.64–1.18 [$I^2=70.9$]), heterogeneity reached statistical significance.

Processed meat consumption and stroke incidence

The relationship between processed meat consumption and risk of stroke was investigated, with 5 articles consisting of 8 comparisons and a total of 254 742 participants.^{15,24–26,30} The meta-analysis for processed meat intake and stroke incidence comparing the highest versus the lowest category showed that processed meat consumption is related to an 8% to 25% elevated stroke risk. There was no heterogeneity among the 8 studies ($I^2=0.00$).

White meat consumption and stroke incidence

For white meat, the pooled results from 2 articles^{15,26} consisted of 4 comparisons (138 761 participants) comparing the highest versus the lowest categories and indicated that consumption of white meat is associated with a 4% to 22% decrease in stroke risk without any heterogeneity among studies ($I^2=0.00$).

Subgroup Analysis

The results from subgroup analyses for the studies on stroke incidence and mortality from stroke for each type of meat are presented in Tables 2 through 6, respectively. Most of the results were consistent across the subgroups defined by factors described in the Methods section.

Total, red, and processed meat consumption and stroke incidence

Studies containing a small number of cases (<2000 cases) and longer follow-up duration (≥ 20 years) showed a stronger

Table 1. Characteristics of the Cohort Studies Included in the Quantitative Analysis of Total, Red, Processed, and White Meat Consumption and Risk of Stroke Incidence and Mortality

Study	Country	Study Name	Follow-Up Duration, y	Study Population (Baseline Age)	Type of Stroke and No. of Cases	Range of Meat Intake: Highest vs Lowest	Adjusted RR (95% CI) for Strokes	Adjustment
Stroke incidence								
1. Larsson 2011 ²⁵	Sweden	Swedish Mammography Cohort	10.4	34 670 Women (49–83 y)	1680 Total strokes, 1310 CIs, 154 ICHs, 79 SAHs 137 nonspecific	Total red meat: ≥86.0 g/d vs <36.5 g/d Fresh red meat: ≥48.8 g/d vs <16.5 g/d Processed meat: ≥41.3 g/d vs 12.1 g/d	TS: 1.12 (0.95–1.31) IS: 0.74 (0.45–1.12) TS: 1.07 (0.91–1.23) HS: 0.85 (0.54–1.34) TS: 1.18 (1.00–1.38) HS: 0.91 (0.60–1.39)	Age, smoking, education, BMI, total physical activity, history of diabetes mellitus or hypertension, aspirin use, family history of MI, and intake of total energy, alcohol, coffee, fish, fruits, and vegetables
2. Larsson 2011 ²⁴	Sweden	The Cohort of Swedish Men	10.1	40 291 Men (45–79 y)	2409 Total strokes, 1849 ISS, 350 HSS	Total red meat: ≥136.2 g/d vs <62.5 g/d Fresh red meat: ≥83.1 g/d vs <33.5 g/d Processed meat: ≥57.1 g/d vs 20.1 g/d	TS: 1.15 (1.00–1.33) HS: 1.57 (1.09–2.25) TS: 1.07 (0.93–1.24) HS: 1.27 (0.90–1.80) TS: 1.23 (1.07–1.40) HS: 1.39 (0.97–1.99)	Age, smoking, education, BMI, total physical activity, history of diabetes mellitus or hypertension, aspirin use, family history of MI, and intake of total energy, alcohol, coffee, fish, fruits, and vegetables
3. Bernstein 2012 ¹⁵	United States	HFPS (Health Professionals Follow-Up Study)	22	43 150 Men (40–75 Years)	1397 Total strokes, 829 ISS, 165 ICHs, 53 SAHs	Total red meat: 2.29 servings/d vs 0.30 servings/d Fresh red meat: 1.11 servings/d vs 0.14 servings/d Processed red meat: 0.71 servings/d vs 0.03 servings/d White meat: 0.72 g/d vs 0.14 g/d	TS: 1.28 (1.02–1.61) HS: 1.07 (0.55–2.08) IS: 1.31 (0.97–1.77) TS: 1.11 (0.88–1.39) HS: 0.70 (0.36–1.37) IS: 1.23 (0.91–1.67) TS: 1.27 (1.03–1.55) HS: 1.47 (0.80–2.72) IS: 1.31 (1.00–1.71) TS: 0.97 (0.81–1.17) HS: 0.66 (0.37–1.18) IS: 1.07 (0.84–1.37)	Age, time period, BMI, smoking, physical exercise, parental history of early MI, menopausal status (including hormone replacement), multivitamin use, vitamin E supplement use, aspirin use, total energy, cereal fiber, alcohol, trans-fat, fruit and vegetables, other protein sources, and history of MI, coronary artery bypass surgery, or percutaneous coronary intervention, angina, diabetes mellitus, hypertension, and hypercholesterolemia
4. Bernstein 2012 ¹⁵	United States	NHS (Nurses' Health Study)	26	84 010 Women (30–55 y)	2663 Total strokes, 1383 ISS, 235 ICHs, 240 SAHs	Total red meat: 1.92 servings/d vs 0.44 servings/d Fresh red meat: 1.08 servings/d vs 0.28 servings/d	TS: 1.19 (1.00–1.41) HS: 1.30 (0.72–2.34) IS: 1.16 (0.92–1.48) TS: 1.19 (1.02–1.40) HS: 0.93 (0.54–1.60) IS: 1.30	Age, time period, BMI, smoking, physical exercise, parental history of early MI, menopausal status (including hormone replacement),

Continued

Table 1. Continued

Study	Country	Study Name	Follow-Up Duration, y	Study Population (Baseline Age)	Type of Stroke and No. of Cases	Range of Meat Intake: Highest vs Lowest	Adjusted RR (95% CI) for Strokes	Adjustment
5. Haring 2015 ²⁶	United States	ARIC (Atherosclerosis Risk in Communities Study)	22.7	11 601 Men and women (45–64 y)	699 Total stroke	<p>servings/d</p> <p>Processed red meat: 0.64 servings/d vs 0.05 servings/d</p> <p>White meat: 0.54 g/d vs 0.14 g/d</p> <p>Red and processed meats: 0.25 servings/d vs 1.90 servings/d</p> <p>Red meat: 0.14 servings/d vs 1.08 servings/d</p> <p>Processed meat: 0 servings/d vs 1.07 servings/d</p> <p>White meat 0.8 servings/d vs 0.07 servings/d</p>	<p>(1.03–1.63)</p> <p>TS: 1.10 (0.95–1.27) HS: 0.94 (0.56–1.57) IS: 1.07 (0.87–1.31)</p> <p>TS: 0.82 (0.71–0.94) HS: 0.79 (0.51–1.24) IS: 0.78 (0.64–0.95)</p> <p>Men TS: 1.62 (1.03–2.57) Women TS: 1.1 (0.75–1.89)</p> <p>Men and women: HS: 1.45 (0.66–3.17) IS: 1.35 (0.95–1.93)</p> <p>Men TS: 1.65 (1.06–2.56) Women TS: 1.22 (0.80–1.87)</p> <p>Men and women HS: 1.13 (.53–2.45) IS: 1.47 (1.06–2.05)</p> <p>Men TS: 1.20 (0.83–1.72) Women TS: 1.29 (0.85–1.97)</p> <p>Men and women HS 1.67 (0.80–3.51): IS: 1.20 (0.90–1.61)</p> <p>Men TS: 0.91 (0.61–1.36) Women TS: 0.79 (0.53–1.17)</p> <p>Men and women HS: 0.56 (0.26–1.20) IS: 0.94 (0.70–1.27)</p>	<p>multivitamin use, vitamin E supplement use, aspirin use, total energy, cereal fiber, alcohol, trans-fat, fruit and vegetables, other protein sources, and history of MI, coronary artery bypass surgery or percutaneous coronary intervention, angina, diabetes mellitus, hypertension, and hypercholesterolemia</p> <p>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, BMI, waist to hip ratio, alcohol intake, sports-related physical activity, leisure-related physical activity, carbohydrate intake, fiber intake, fat intake, and magnesium intake</p>

Continued

Table 1. Continued

Study	Country	Study Name	Follow-Up Duration, y	Study Population (Baseline Age)	Type of Stroke and No. of Cases	Range of Meat Intake: Highest vs Lowest	Adjusted RR (95% CI) for Strokes	Adjustment
6. Amiano 2016 ³⁰	Spain	EPIC (the Spanish cohort of the European Prospective Investigation into Cancer and Nutrition)	12	15 490 Men (29–69 y)	373 Stroke, 302 ISs, 42 HS, 17 SAHs, 12 mixed or unspecified	Unprocessed red meat: <24.3 g/d vs ≥86 g/d Processed meat: <21.5 g/d vs 72.6 g/d	TS: 0.81 (0.54–1.21) IS: 0.80 (0.51–1.25) TS: 0.92 (0.64–1.32) IS: 0.86 (0.57–1.29)	Age, center, total energy, BMI, waist circumference, smoking status, smoking before age 20, recreational physical activity, educational level, alcohol consumption, use of vitamin supplements (ATC code A11), use of antithrombotic or antihemorrhagic agents (ATC code B01/B02), use of cardiovascular drugs (ATC code C01–C10), use of salicylic acid or derivatives (ATC code N02BA), incident acute myocardial infarction cases, diabetes mellitus, self-reported diseases (hypertension, hyperlipidemia), percentage of energy from carbohydrates, protein and fats, and intake of vegetables, fruit, dairy products, and fish
7. Amiano 2016 ³⁰	Spain	EPIC (the Spanish cohort of the European Prospective Investigation into Cancer and Nutrition)	12	25 530 Women (29–69 y)	301 Stroke, 229 ISs, 37 HS, 25 SAHs, 10 mixed or unspecified	Unprocessed red meat: 11.1 g/d vs ≥52.4 g/d Processed red meat: <12 g/d vs ≥46 g/d	TS: 1.21 (0.79–1.85) IS: 1.24 (0.74–2.05) TS: 0.81 (0.51–1.27) IS: 0.82 (0.47–1.42)	Age, center, total energy, BMI, waist circumference, smoking status, smoking before age 20, recreational physical activity, educational level, alcohol consumption, use of vitamin supplements (ATC code A11), use of antithrombotic or antihemorrhagic agents (ATC code B01/B02), use of cardiovascular drugs (ATC code C01–C10), use of salicylic acid or derivatives (ATC code N02BA), incident acute MI cases, diabetes mellitus, self-reported

Continued

Table 1. Continued

Study	Country	Study Name	Follow-Up Duration, y	Study Population (Baseline Age)	Type of Stroke and No. of Cases	Range of Meat Intake: Highest vs Lowest	Adjusted RR (95% CI) for Strokes	Adjustment
Stroke mortality								
1.	Japan	Life Spain Study	16	37 130 Men and women (34–103 y)	1462 Total stroke-related deaths	Red meat: never vs almost daily Processed meat: never vs almost daily	TS: 1.01 (0.73–1.38) TS: 0.90 (0.61–1.33)	Age, sex, city, radiation dose, BMI, smoking, alcohol, education, and history of diabetes mellitus or hypertension
2.	United States	WHIO (Women's Health Initiative Observational Study)	8	87 025 Women (50–79 y)	1049 IS-related deaths	Total red meat: per 1 serving/d Red meat: per 1 serving/d	IS: 0.94 (0.75–1.23) IS: 1.13 (0.95–1.34)	Age, race, education, family income, years as a regular smoker, hormone replacement therapy use, total metabolic equivalent task h/wk, alcohol intake, history of coronary heart disease, history of atrial fibrillation, history of diabetes mellitus, aspirin use, use of antihypertensive medication, use of cholesterol-lowering medication, BMI, systolic blood pressure, total energy intake, dietary vitamin E, fruits and vegetable intake, fiber intake
3.	Japan	JACC (the Japan Collaborative Cohort Study for Evaluation of Cancer Risk)	18	20 466 men (40–79 y)	1317 total stroke-related death	Total meat 77.6 g/d vs 10.4 g/d	TS: 1.10 (0.84–1.43)	Age, BMI, ethanol intake, perceived mental stress, walking time, sports participation time, year of education, history of hypertension and diabetes mellitus, total energy, and energy-adjusted food (rice, fish, soy, vegetables, and fruits) intakes

Continued

Table 1. Continued

Study	Country	Study Name	Follow-Up Duration, y	Study Population (Baseline Age)	Type of Stroke and No. of Cases	Range of Meat Intake: Highest vs Lowest	Adjusted RR (95% CI) for Strokes	Adjustment
4. Nagano 2012 ²⁸	Japan	JACC (the Japan Collaborative Cohort Study for Evaluation of Cancer Risk)	18	31 217 Women (40–79 y)	1368 Total stroke-related death	Total meat 59.9 g/d vs 7.5 g/d	TS: 0.91 (0.70–1.19)	Age, BMI, ethanol intake, perceived mental stress, walking time, sports participation time, y of education, history of hypertension and diabetes mellitus, total energy and energy-adjusted food (rice, fish, soy, vegetables, and fruits) intakes
5. Sharma 2013 ²⁹	United States	The Multiethnic Cohort	7.5 to	78 844 Men (45–75 y)	434 Total stroke-related death	Total meat >7.3 servings/d vs 0 to 2.5 servings/d	TS: 0.87 (0.57–1.34)	Ethnicity, time in study, y of education, energy intake, smoking, BMI, physical activity, history of diabetes mellitus, and alcohol intake
6. Sharma 2013 ²⁹	United States	The Multiethnic Cohort	7.5	96 044 Women (45–75 y)	426 total stroke-related death	Total meat >7.3 servings/d vs 0 to 2.5 servings/d	TS: 1.06 (0.69–1.65)	Ethnicity, time on study, y of education, energy intake, smoking, BMI, physical activity, history of diabetes mellitus, and alcohol intake
7. Takata 2013 ³²	China	SMHS (Shanghai Men's Health Study)	5.5	61 483 Men (40–74 y)	2733 Total stroke-related deaths	Red meat 126 g/d vs 21.4 g/d White meat 22.3 g/d vs 11.9 g/d	HS: 0.71 (0.43–1.20) IS: 1.22 (0.69–2.15) HS: 0.89 (0.56–1.40) IS: 0.92 (0.54–1.57)	Age, total caloric intake, income, occupation, education, comorbidity index, physical activity level, total vegetable intake, total fruit intake, fish intake, red meat or poultry intake where appropriate, smoking history, consumption of alcohol
8. Takata 2013 ³²	China	SWHS (Shanghai Women's Health Study)	11.2	74 941 Women (40–70 y)	4210 Total stroke-related deaths	Red meat 103.4 g/d vs 16.5 g/d White meat: 19.9 g/d vs 11.9 g/d	HS: 0.57 (0.37–0.87) IS: 0.84 (0.55–1.26) HS: 1.20 (0.79–1.80) IS: 1.04 (0.69–1.56)	Age, total caloric intake, income, occupation, education, comorbidity index, physical activity level, total vegetable intake, total fruit intake, fish intake, red meat or poultry intake where appropriate, smoking history, consumption of alcohol

ATC indicates anatomic therapeutic chemical; BMI, body mass index; CI, confidence intervals; HS, hemorrhagic stroke; IS, ischemic stroke; MI, myocardial infarction; RR, relative risk; SAH, subarachnoid hemorrhage; TS, total stroke.

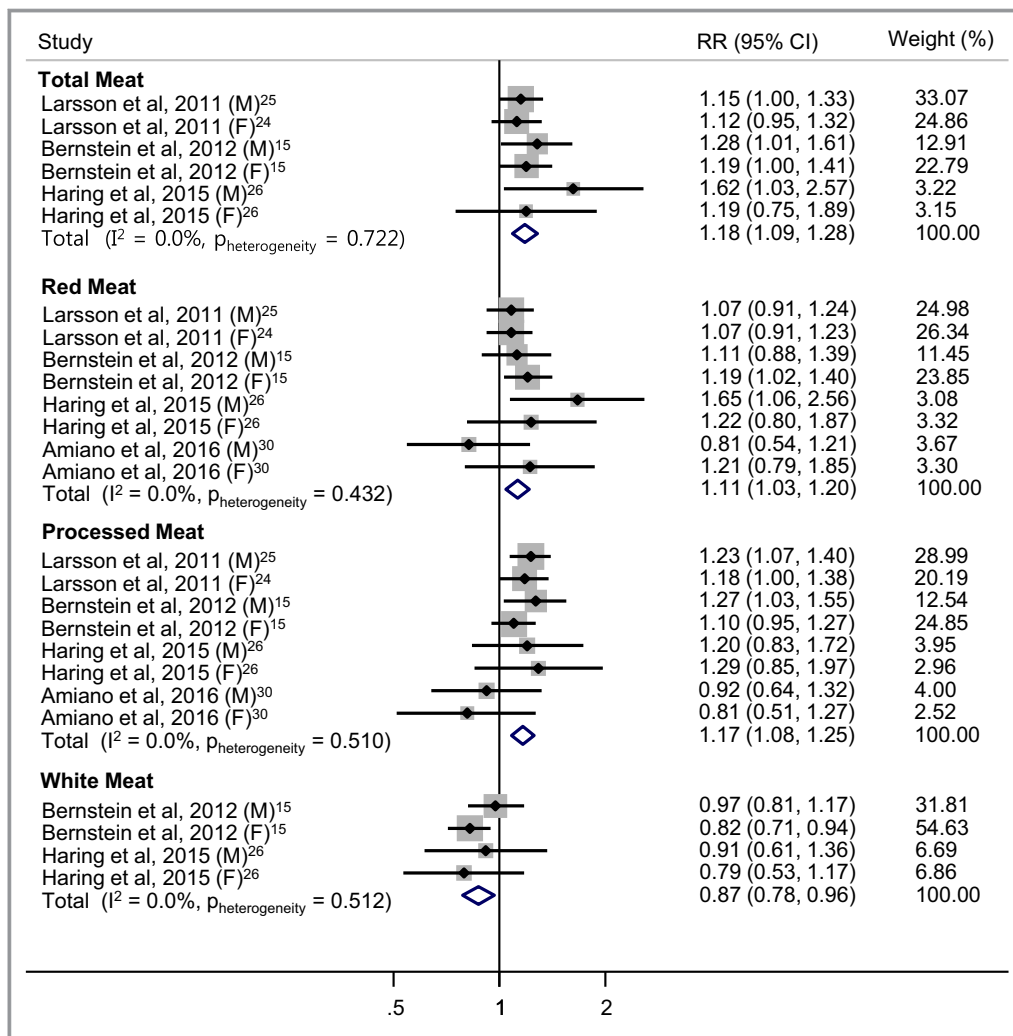


Figure 2. Relative risk (RR) ratios of total, red, processed, and white meat consumption and total incidence in stroke (highest vs lowest category). Weights are assigned from random-effects model. CI indicates confidence interval; F, female; M, male.

association of total, processed, and red meat consumption and stroke incidence compared with other studies. In general, studies with male participants showed a stronger association of total and processed meat intake and risk of stroke. Total meat consumption was associated with hemorrhagic stroke (RR, 1.41; 95% CI, 1.08–1.84 [$I^2=0.00$]), but no significant association was found between total meat consumption and ischemic stroke (RR, 1.16; 95% CI, 0.94–1.43 [$I^2=40.6$]). A positive association between total meat consumption and stroke incidence was found regardless of sex, number of cases, and follow-up duration. When we stratified the analysis by adjustment variables, studies that adjusted for family history of myocardial infarction, fruit and vegetable intake, and use of aspirin showed a statistically significant relationship between total meat intake and risk of stroke compared with other studies that did not include those as adjustment variables.

Red meat consumption was associated with ischemic stroke (RR, 1.24; 95% CI, 1.05–1.46 [$I^2=17.7$]) but not with

hemorrhagic stroke (RR, 1.11; 95% CI, 0.89–1.38 [$I^2=0.00$]). Studies adjusted for family history of myocardial infarction and use of aspirin and vitamin supplements showed a statistically significant association between consumption of red meat and risk of stroke. Processed meat consumption was linked to neither ischemic (RR, 1.10; 95% CI, 0.96–1.27 [$I^2=11.4$]) nor hemorrhagic stroke (RR, 1.19; 95% CI, 0.95–1.49 [$I^2=8.10$]). Studies adjusted for family history of MI, fruit and vegetable intake, and use of aspirin showed a statistically significant association between processed meat intake and stroke incidence compared with other studies.

Total and red meat consumption and stroke mortality

No statistically significant association between total and red meat consumption and stroke mortality was found in subgroup analysis by number of cases, follow-up duration, and adjustment variables.

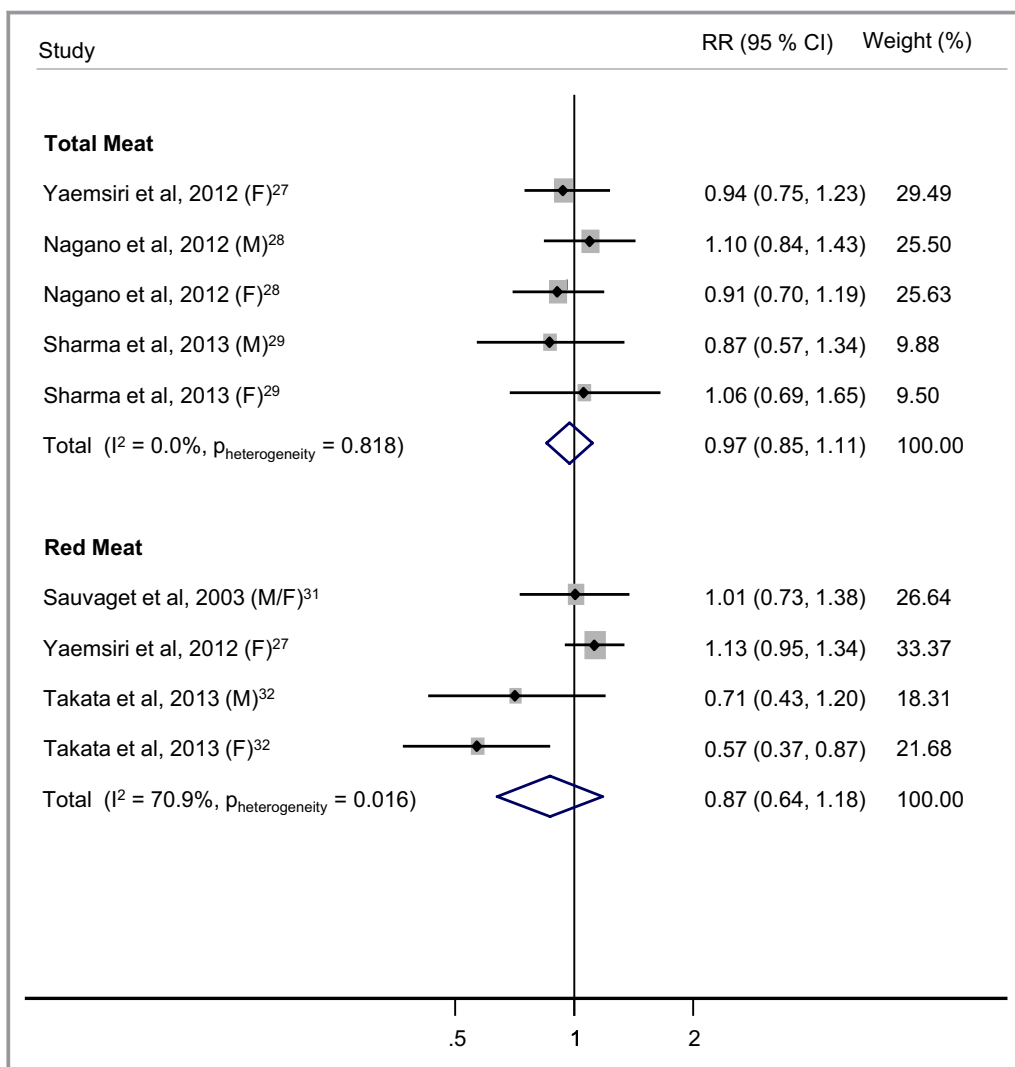


Figure 3. Total and red meat consumption and relative risk (RR) of stroke mortality (highest vs lowest category). Weights are assigned from random-effects model. CI indicates confidence interval; F, female; M, male.

Publication Bias and Quality Assessment

We did not detect any significant publication bias based on the Egger test except that the evaluation of total meat with stroke incidence reached the significance threshold. The *P* values from the Egger test for the articles related to meat consumption and stroke incidence were 0.10 for total meat, 0.59 for red meat, 0.30 for processed meat, and 0.903 for white meat. For the articles concerning meat consumption and stroke mortality, the *P* values from the Egger test were 0.95 for total meat and 0.11 for red meat. The average score for study quality assessed by the Newcastle-Ottawa Scale was 7.29 (range 7–8) for studies on meat consumption and stroke incidence and 6.87 (range 6–8) for those on stroke mortality (Table S2).

Discussion

The findings from this meta-analysis of prospective cohort studies suggest that higher consumption of total, red, and processed meats is associated with an 18%, 11%, and 17% increase in the risk of stroke, while higher intake of white meat is related to a 13% reduction in stroke incidence. We observed no association between total and red meat intake and mortality from stroke. In terms of stroke subtype, we found a significant association between red meat consumption and risk of ischemic stroke.

The underlying mechanisms for the increased risk of stroke associated with high red and processed meat consumption may relate to the nutritional content of meat. Red meat contains a large amount of saturated fats that can raise the

Table 2. Subgroup Analyses of the Studies on Total Meat Consumption and Stroke Incidence

Total Meat	Stroke Incidence			
	No.	RR (95% CI)	I^2 , %	P_h Value
Stroke subtype				
Ischemic	4	1.16 (0.94–1.43)	40.6	0.168
Hemorrhagic	4	1.41 (1.08–1.84)	0.00	0.783
Sex				
Male	3	1.22 (1.07–1.40)	12.5	0.319
Female	3	1.16 (1.03–1.30)	0.00	0.875
No. of cases				
<2000	4	1.19 (1.06–1.35)	0.00	0.424
≥2000	2	1.17 (1.04–1.30)	0.00	0.764
Follow-up duration				
<20 y	2	1.14 (1.02–1.26)	0.00	0.809
≥20 y	4	1.24 (1.09–1.41)	0.00	0.601
Adjustment variable				
Education				
Yes	4	1.15 (1.04–1.28)	0.00	0.514
No	2	1.22 (1.07–1.40)	0.00	0.706
Family history of MI				
Yes	4	1.17 (1.07–1.27)	0.00	0.808
No	2	1.34 (0.91–1.95)	26.6	0.243
Fruit and vegetable intake				
Yes	4	1.17 (1.07–1.27)	0.00	0.808
No	2	1.34 (0.91–1.95)	26.6	0.243
Fish intake				
Yes	2	1.14 (1.02–1.26)	0.00	0.809
No	4	1.24 (1.09–1.41)	0.00	0.601
Use of aspirin				
Yes	4	1.17 (1.07–1.27)	0.00	0.808
No	2	1.34 (0.91–1.95)	26.6	0.243
Use of vitamin supplements				
Yes	2	1.22 (1.07–1.40)	0.00	0.617
No	4	1.15 (1.04–1.28)	0.00	0.514

CI indicates confidence interval; P_h , P value for heterogeneity; RR, relative risk.

level of plasma cholesterol,³³ low-density lipoprotein cholesterol,³⁴ and triglycerides.³⁵ The artery-clogging effects of cholesterol and triglycerides may contribute to an interruption in blood flow to the brain and lead to stroke incidence. In addition, red meat is high in heme iron, which can catalyze oxidative reactions in biological systems.³⁶ Oxidative reactions can damage lipids, proteins, and DNA, increasing the risk of metabolic, neurologic, and cardiovascular diseases.^{37,38} According to one epidemiological study,³⁹ heme

Table 3. Subgroup Analyses of the Studies on Red Meat Consumption and Stroke Incidence

Red Meat	Stroke Incidence			
	No.	RR (95% CI)	I^2 , %	P_h Value
Stroke subtype				
Ischemic	5	1.24 (1.05–1.46)	17.7	0.302
Hemorrhagic	5	1.11 (0.89–1.38)	0.00	0.530
Sex				
Male	4	1.10 (0.91–1.32)	46.0	0.135
Female	4	1.14 (1.02–1.26)	0.00	0.770
No. of cases				
<2000	4	1.14 (0.99–1.30)	13.7	0.324
≥2000	4	1.10 (0.98–1.24)	13.9	0.323
Follow-up duration				
<20 y	4	1.06 (0.96–1.17)	0.00	0.550
≥20 y	4	1.20 (1.06–1.53)	0.00	0.481
Adjustment variable				
Education				
Yes	6	1.10 (0.98–1.23)	18.0	0.297
No	2	1.16 (1.02–1.33)	0.00	0.624
Family history of MI				
Yes	4	1.11 (1.02–1.20)	0.00	0.750
No	4	1.18 (0.88–1.57)	46.3	0.133
Fruit and vegetable intake				
Yes	6	1.10 (1.01–1.19)	0.00	0.605
No	2	1.41 (1.04–1.92)	0.00	0.334
Fish intake				
Yes	4	1.06 (0.96–1.17)	0.00	0.550
No	4	1.20 (1.06–1.35)	0.00	0.481
Use of aspirin				
Yes	4	1.11 (1.02–1.20)	0.00	0.750
No	4	1.18 (0.88–1.57)	46.3	0.133
Use of vitamin supplements				
Yes	4	1.13 (1.00–1.28)	4.70	0.369
No	4	1.11 (0.99–1.26)	20.0	0.290

CI indicates confidence interval; MI, myocardial infarction; P_h , P value for heterogeneity; RR, relative risk.

iron intake was related to a 16% increased risk of stroke (hazard ratio, 1.16; 95% CI, 1.03–1.31) when comparing the highest (≥2.34 mg/d) category with the lowest (<1.28 mg/d) category.

Furthermore, processed meat is often manufactured with the preservative sodium nitrate,⁴⁰ which elevates the risk of hypertension and consequently exerts negative effects on the cardiovascular systems.^{41–43} According to reviews, high blood

Table 4. Subgroup Analyses of the Studies on Processed Meat Consumption and Stroke Incidence

Processed Meat	Stroke Incidence			
	No.	RR (95% CI)	I^2 , %	P_h Value
Stroke subtype				
Ischemic	5	1.10 (0.96–1.27)	11.4	0.341
Hemorrhagic	5	1.19 (0.95–1.49)	8.10	0.360
Sex				
Male	4	1.21 (1.09–1.34)	0.00	0.480
Female	4	1.12 (1.01–1.24)	0.00	0.476
No. of cases				
<2000	4	1.22 (1.09–1.37)	0.00	0.943
≥2000	4	1.10 (0.96–1.26)	39.3	0.176
Follow-up duration				
<20 y	4	1.12 (0.95–1.31)	36.6	0.193
≥20 y	4	1.17 (1.05–1.30)	0.00	0.674
Adjustment variable				
Education				
Yes	6	1.16 (1.04–1.29)	0.60	0.412
No	2	1.16 (1.01–1.33)	20.8	0.261
Family history of MI				
Yes	4	1.18 (1.08–1.29)	0.00	0.595
No	4	1.05 (0.85–1.28)	6.00	0.363
Fruit and vegetable intake				
Yes	6	1.15 (1.05–1.26)	16.6	0.307
No	2	1.24 (0.94–1.63)	0.00	0.799
Fish intake				
Yes	4	1.12 (0.95–1.31)	36.6	0.193
No	4	1.17 (1.05–1.30)	0.00	0.674
Use of aspirin				
Yes	4	1.18 (1.08–1.29)	0.00	0.595
No	4	1.05 (0.85–1.28)	6.00	0.363
Use of vitamin supplements				
Yes	4	1.09 (0.94–1.27)	34.0	0.208
No	4	1.22 (1.09–1.37)	0.00	0.943

CI indicates confidence interval; MI, myocardial infarction; P_h indicates P value for heterogeneity; RR, relative risk.

pressure is a major risk factor for stroke; thus, lowering blood pressure can contribute to a reduction in stroke risk across different geographic regions and population groups.^{44,45} High blood pressure may contribute to an increased risk of stroke risk because of the elevated force placed on the walls of arteries, which facilitates damage and the accumulation of circulating particles.⁴⁶ However, regarding the possibility of the imprecision and variability of sodium nitrate concentration

Table 5. Subgroup Analyses of the Studies on Total Meat Consumption and Stroke Mortality

Total Meat	Stroke Mortality			
	No.	RR (95% CI)	I^2 , %	P_h Value
No. of cases				
<1000	2	0.96 (0.71–1.30)	0.00	0.526
≥1000	3	0.98 (0.84–1.14)	0.00	0.568
Follow-up duration				
<10 y	3	0.95 (0.78–1.15)	0.00	0.814
≥10 y	2	1.00 (0.83–1.21)	0.00	0.323
Adjustment variable				
Socioeconomic status				
Yes	1	0.94 (0.75–1.23)	NC	NC
No	4	0.99 (0.84–1.16)	0.00	0.697
History of hypertension				
Yes	2	1.00 (0.83–1.21)	0.00	0.323
No	3	0.95 (0.78–1.15)	0.00	0.814
Smoking				
Yes	2	0.96 (0.71–1.30)	0.00	0.526
No	3	0.98 (0.84–1.14)	0.00	0.568
Fruit and vegetable intake				
Yes	3	0.98 (0.84–1.14)	0.00	0.568
No	2	0.96 (0.71–1.30)	0.00	0.526

CI indicates confidence interval; NC, not calculable; P_h , heterogeneity P value; RR, relative risk.

in processed meat, the extent to which sodium nitrate in processed meat could induce high blood pressure and stroke needs to be examined in future studies.

In contrast to red and processed meats, white meat contains less heme iron and is high in polyunsaturated fat. A previous study showed that a diet consisting of polyunsaturated fats as the primary source of fatty acids can lower low-density lipoprotein cholesterol (LDL-C).⁴⁷ Compared with no change or an increase in low-density lipoprotein cholesterol, the lowering of low-density lipoprotein cholesterol was related to a decreased risk of stroke and coronary heart disease.⁴⁸ Despite this plausible mechanism, further studies are required to investigate the biological mechanism that can explain the protective effect of poultry meat consumption on stroke risk.

In our study, red meat consumption was associated with stroke incidence, not mortality. More than two thirds of stroke cases are ischemic strokes,^{49,50} and ischemic strokes are generally associated with lower mortality compared with hemorrhagic stroke because of the nature of their pathogenesis.⁵¹ The former occurs from a clotting in blood vessels,

Table 6. Subgroup Analyses of the Studies on Red Meat Consumption and Stroke Mortality

Red Meat	Stroke Mortality			
	No.	RR (95% CI)	I^2 , %	P_h Value
Follow-up duration				
<10 y	2	0.96 (0.62–1.48)	64.7	0.092
≥10 y	2	0.77 (0.44–1.35)	77.4	0.035
Adjustment variable				
Socioeconomic status				
Yes	3	0.80 (0.50–1.28)	80.6	0.006
No	1	1.01 (0.73–1.38)	NC	NC
History of hypertension				
Yes	1	1.01 (0.73–1.38)	NC	NC
No	3	0.80 (0.50–1.28)	80.6	0.006
Smoking				
Yes	3	0.76 (0.53–1.10)	57.3	0.096
No	1	1.13 (0.95–1.34)	NC	NC
Fruit and vegetable intake				
Yes	3	0.80 (0.50–1.28)	80.6	0.006
No	1	1.01 (0.73–1.38)	NC	NC

CI indicates confidence interval; NC, not calculable; P_h , heterogeneity P value; RR, relative risk.

whereas the latter occurs as a result of a rupture of blood vessels, which is fatal and may need additional clinical attention. In addition, considerable heterogeneity was found in the evaluation of red meat consumption and stroke mortality in this study. Given the limited number of published studies on meat consumption and stroke mortality, more studies are warranted to make a definite conclusion on this relationship.

Study Strengths and Limitations

There are several strengths in our study. By including only prospective cohort studies, we were able to minimize the effects from possible recall and selection. To our knowledge, our study is the first to examine stroke incidence and mortality separately and to include white meat, which were not considered in previous meta-analyses.^{8–11} Limitations of this meta-analysis also need to be addressed when interpreting the results. Because our meta-analysis was based on observational studies, we could not entirely eliminate the effect of confounding from unadjusted risk factors. Several previous researches reported that stroke incidence is greater among participants with a higher consumption of red and processed meats because they tend to have unhealthy behaviors and conditions.^{15,24,25} Although studies included

in this meta-analysis adjusted for major stroke risk factors such as hypertension, diabetes mellitus, smoking, obesity, and alcohol use, the effect of unadjusted risk factors still remain. Quantification of meat consumption through a self-reported survey in the selected studies may have led to a misclassification of the different types of meat caused by a measurement error. Because categorization of high versus low meat intake used to assess RR reflects characteristics of the population in each study, quantity of meat intake dividing high versus low consumption groups were not entirely consistent in the studies included in this meta-analysis. Therefore, further investigation should standardize the comparison between highest and lowest meat consumption and risk of stroke incidence and mortality to account for this variability.

In addition, the tendency to publish only positive results may have influenced the results of this meta-analysis. However, we found no evidence of publication bias in this study except for the results of total meat consumption and stroke incidence that met the threshold. Possible sources of this publication bias is the existence of unpublished studies in other continents since all of the data available for the evaluation of total meat consumption and stroke incidence were from Europe and North America. Further evaluation of publication bias on this result is required when more studies become available. In this study, we were not able to perform analyses on the associations between processed and white meat consumption and stroke mortality because of limitation of data. It is necessary to examine these relationships when relevant data are published in the future.

In our study, we separately examined the association between consumption of total, red, processed, and white meats and risk of stroke and deaths from stroke. Previous meta-analyses that showed a positive association between total, red, and processed meat intake and risk of stroke have not distinguished stroke incidence from stroke mortality and synthesized the results from all studies. In our meta-analysis, we found no significant association between consumption of total and red meat and deaths from stroke. In terms of stroke subtype, previous meta-analyses indicated that there was no association between total, red, and processed meat intake and hemorrhagic stroke.^{8,10} However, the present meta-analysis shows that total meat consumption is significantly related to hemorrhagic stroke. Since more studies are included in our meta-analysis, our analysis had higher statistical power to assess the relationship between total meat intake and risk of hemorrhagic stroke.

Although our findings on the association between the high consumption of total, red, and processed meats and an increase in the risk of stroke events are consistent with previous studies, our meta-analysis has some additions to the

current topic that may have clinical importance. We found evidence that the consumption of white meat is related to a lower risk of stroke. Individuals who are at a higher risk of stroke who habitually consume red and processed meats should consider substituting a source of their protein intake to white meat.

Conclusions

High meat consumption, particularly red and processed meats, is associated with increased risk of stroke. In contrast, white meat consumption is associated with reduced risk of stroke. While no association was found between any meat consumption and stroke mortality, more studies are warranted to confirm this finding.

Author Contributions

K.K. conducted the systematic review, selected the studies for meta-analysis (cross-checked by J.H. and under the supervision of S.M.P.), and wrote the first draft of the article. J.H., S.A.L., S.O.K., H.L., N.K., J.K.L., and S.M.P. provided the important intellectual content for the draft. S.A.L., S.O.K., H.J.L., N.K., J.K.L., and S.M.P. supervised the meta-analysis and draft and critically revised the article.

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Disclosures

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SUPPLEMENTAL MATERIAL

Table S1. Search Strategy

<p>PudMed (https://www.ncbi.nlm.nih.gov/pubmed) 2016.10.07</p>	<p>((“meat”[tw] OR “meats”[tiab] OR “meat product”[tiab] OR “meat products”[tw] OR “red meat”[tw] OR “red meats”[tiab] OR beef[tiab] OR veal[tiab] OR goat[tiab] OR lamb[tiab] OR pork[tiab] OR mutton[tiab] OR sausage[tiab] OR sausages[tiab] OR ham[tiab] OR hams[tiab] OR pastrami[tiab] OR bacon[tiab] OR bacons[tiab] OR salami[tiab] OR salamis[tiab] OR “hot dog”[tiab] OR “hot dogs”[tiab] OR “animal food”[tiab] OR “animal foods”[tiab] OR “animal protein”[tiab] OR “animal proteins”[tiab] OR “diet”[tiab] OR “diets” [tiab] OR “dietary” [tiab] OR “white meat”[tiab] OR “poultry”[tiab] OR “chicken”[tiab] OR “duck”[tiab] OR “turkey”[tiab] OR “rabbit”[tiab]) AND ((“stroke”[tiab]) “Ischemic stroke”[tiab] OR “hemorrhagic stroke”[tiab] OR “cerebrovascular disease”[tiab] OR “cerebrovascular attack”[tiab] OR “cerebral infarct”[tiab] OR “intracranial hemorrhage”[tiab]))</p>
<p>EMBASE (http://www.embase.com/) 2016.10.07</p>	<p>(‘meat’:ab,ti OR ‘meats’:ab,ti OR ‘meat product’:ab,ti OR ‘meat products’:ab,ti OR ‘red meat’:ab,ti OR ‘red meats’:ab,ti OR ‘beef’:ab,ti OR ‘veal’:ab,ti OR ‘goat’:ab,ti OR ‘lamb’:ab,ti OR ‘pork’:ab,ti OR ‘mutton’:ab,ti OR ‘sausage’:ab,ti OR ‘sausages’:ab,ti OR ‘ham’:ab,ti OR ‘hams’:ab,ti OR ‘pastrami’:ab,ti OR ‘bacon’:ab,ti OR ‘bacons’:ab,ti OR ‘salami’:ab,ti OR ‘salamis’:ab,ti OR ‘hot dog’:ab,ti OR ‘hot dogs’:ab,ti OR ‘animal food’:ab,ti OR ‘animal foods’:ab,ti OR ‘animal protein’:ab,ti OR ‘animal proteins’:ab,ti OR ‘diet’:ab,ti OR ‘diets’:ab,ti OR ‘dietary’:ab,ti OR ‘white meat’:ab,ti OR ‘poultry’:ab,ti OR ‘chicken’:ab,ti OR ‘duck’:ab,ti OR ‘turkey’:ab,ti OR ‘rabbit’:ab,ti) AND (‘stroke’:ab,ti ‘Ischemic stroke’:ab,ti OR ‘hemorrhagic stroke’:ab,ti OR ‘cerebrovascular disease’:ab,ti OR ‘cerebrovascular attack’:ab,ti OR ‘cerebral infarct’:ab,ti OR ‘intracranial hemorrhage’:ab,ti)</p>
<p>Cochrane Library (http://www.cochranelibrary.com/) 2016.10.07</p>	<p>(‘meat’ OR ‘meats’ OR ‘meat product’ OR ‘meat products’ OR ‘red meat’ OR ‘red meats’ OR ‘beef’ OR ‘veal’ OR ‘goat’ OR ‘lamb’ OR ‘pork’ OR ‘mutton’ OR ‘sausage’ OR ‘sausages’ OR ‘ham’ OR ‘hams’ OR ‘pastrami’ OR ‘bacon’ OR ‘bacons’ OR ‘salami’ OR ‘salamis’ OR ‘hot dog’</p>

	OR 'hot dogs' OR 'animal food' OR 'animal foods' OR 'animal protein' OR 'animal proteins' OR 'diet' OR 'diets' OR 'dietary' OR 'white meat' OR 'poultry' OR 'chicken' OR 'duck' OR 'turkey' OR 'rabbit') AND ('stroke' OR Ischemic stroke' OR 'hemorrhagic stroke' OR 'cerebrovascular disease' OR 'cerebrovascular attack' OR 'cerebral infarct' OR 'intracranial hemorrhage')
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tw=Text Words, ab,ti/tiab=Title/Abstract

Table S2. Quality assessment of studies selected for final meta-analysis based on the Newcastle-Ottawa Scale

Studies (n =10)	Selection			Comparability			Outcome		Total score (0-9)
	Representativeness of the exposed cohort	Selection of the non exposed cohort	Ascertainment of exposure	Outcome of interest not present at start of study	Control for important factor or additional factor	Assessment of outcome	Follow-up long enough form outcomes to occur	Adequacy of follow up of cohorts	
Stroke Incidence									
1	Larsson et al, 2011 ¹	1	1	1	1	1	1	1	8
2	Larsson et al, 2011 ²	1	1	1	1	1	1	1	8
3	Bernstein et al, 2012 ³	0	1	1	1	1	1	1	7
4	Bernstein et al, 2012 ³	0	1	1	1	1	1	1	7
5	Haring et al, 2015 ⁴	1	1	1	0	1	1	1	7
6	Amiano et al, 2016 ⁵	1	1	1	0	1	1	1	7
7	Amiano et al, 2016 ⁵	1	1	1	0	1	1	1	7
Stroke Mortality									
8	Sauvaget et al, 2003 ⁶	0	1	1	1	1	1	1	7
9	Yaemsiri et al, 2012 ⁷	0	1	1	0	1	1	1	6
10	Nagano et al, 2012 ⁸	0	1	1	0	1	1	1	6
11	Nagano et al, 2012 ⁸	0	1	1	0	1	1	1	6
12	Sharma et al, 2013 ⁹	1	1	1	1	1	1	1	8
13	Sharma et al, 2013 ⁹	1	1	1	1	1	1	1	8
14	Takata et al, 2013 ¹⁰	1	1	1	0	1	1	1	7
15	Takata et al, 2013 ¹⁰	1	1	1	0	1	1	1	7

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