Stroke, food groups, and dietary patterns: a systematic review

Ayesha Sherzai, Lauren T Heim, Cassaundra Boothby, and A Dean Sherzai

Stroke is the fourth leading cause of mortality in the United States, yet it is 80% preventable by addressing lifestyle factors including nutrition. Evaluating the impact of nutrition at the food group and dietary pattern level will provide greater insight into the role of nutrition in stroke. For this purpose, a review of the literature was conducted using the PubMed, Web of Science, and CINAHL Plus online databases. While fruits, vegetables, and soy demonstrated a protective effect, variable findings were observed for fish, animal products, and whole grains. Adherence to DASH, Mediterranean, and prudent dietary patterns reduced the risk of stroke, whereas the Western dietary pattern was associated with increased stroke risk. Low-fat diet was not found to have a protective effect. Additional epidemiological evidence is needed to elucidate the impact of specific dietary patterns and food groups on stroke. Future research should consider developing dietary recommendations for stroke prevention, which are based on clinical trials and have an emphasis on food groups and dietary patterns that are palatable to the general public.

INTRODUCTION

Stoke places a tremendous burden on the healthcare system worldwide. In the United States, it is the 4th leading cause of mortality, with an estimated 795,000 incident strokes each year.¹,² As age is one of the main risk factors for stroke, and with the elderly population expected to double to more than 70 million by the year 2030, reducing the incidence of stroke has become a central healthcare policy concern.³ Treatment costs associated with chronic disease constitute three-fourths of US healthcare expenditures, and of this, $400 billion per year is spent on heart disease and stroke.⁴ It is, thus, imperative to identify and implement healthcare policies that can reduce the risk of stroke.

Risk factors associated with stroke have been divided into two main categories – non-modifiable and modifiable. Advanced age, gender, race, and genetic susceptibility are the most prominent non-modifiable risk factors, while lifestyle risk factors such as diet, exercise, and use of tobacco and alcohol are considered modifiable risk factors.⁵ By addressing the modifiable risk factors, it is estimated that stroke prevalence can be reduced by as much as 80%.⁶ Thus, primary prevention of stroke takes central importance.

Substantial research has been done over the past decades in order to advance understanding of stroke mechanisms and therapies. Despite a large body of data supporting specific pharmaceutical agents, such as antiplatelets, antithrombotics, and statins, as preventive measures in stroke, diet remains a focus of extensive epidemiological research for stroke prevention. The association between nutrients and stroke has been extensively investigated, yet findings are inconclusive and conflicting at best.⁷ There is some evidence that nutrients such as potassium may reduce stroke risk by modulating oxidative processes and blood pressure, yet other nutrients such as calcium, magnesium, total fat and fat subtypes,
animal protein, and antioxidants have demonstrated limited and inconsistent evidence related to vascular diseases. Indeed, randomized controlled trials on the long-term effects of nutrients on morbidity and mortality are lacking, because of a number of difficulties, all of which may be due to the complex nature of dietary intake and the synergistic dynamics of nutrients. First, at the individual level, caloric intake remains relatively stable, and changes in dietary habits generally occur with the substitution of macronutrients, such as replacement of high-carbohydrate foods with high-protein and low-fat foods. Additionally, foods contain intricate combinations of nutrients that are likely to be interactive, which makes it difficult to attribute outcomes to specific dietary constituents. Finally, variations in the bioavailability of nutrients may exist due to differences in the quality and metabolism of nutrients obtained from foods, as opposed to nutrients obtained from supplements.

The shift in approach from evaluating specific nutrients to exploring whole dietary patterns has recently been investigated in the study of risk factors for cardiovascular disease (CVD) and some chronic neurological diseases. In the Mediterranean Diet, Cardiovascular Risks and Gene Polymorphisms (Medi-RIVAGE) study, a 9% reduction in CVD risk factors among subjects on a low-fat diet and 15% reduction among subjects consuming a Mediterranean diet were observed. Scarmeas et al. demonstrated that adherence to a Mediterranean diet significantly reduced the risk of Alzheimer’s disease in a 4-year follow-up. Vegetarian diets have also revealed benefits in relation to CVD. A collaborative analysis of five prospective cohorts found a 34% reduction in mortality from ischemic heart disease among lacto-ovo vegetarians and a 26% reduction in vegans. This approach of looking at food groups and dietary patterns and their relationship to disease is also believed to be applicable to stroke. Thus, the objective of the present review was to present current research regarding the relationship between food groups, dietary patterns, and stroke.

LITERATURE SEARCH METHODS

A review of the PubMed, Web of Science, and CINAHL Plus databases was conducted to identify epidemiological studies concerning stroke, food groups, and dietary patterns (Figure 1). Initial search terms included “stroke” and “diet.” From these results, a search of the following medical subject headings terms was conducted: “stroke” combined with “diabetes,” “dietary patterns,” “vegetarian,” “meat,” “soy,” “fruit,” “vegetables,” “dairy,” “eggs,” “fish,” “DASH diet,” “Mediterranean diet,” “prudent diet,” and “whole grain.” Studies, in which CVD disease outcomes were assessed cumulatively, as opposed to individual disease risk assessment, were not included. References from pertinent articles were examined to ensure that no study was unintentionally excluded. An identical search process was carried out among all three databases, starting with PubMed. Subsequent query of CINAHL and Web of Science databases generated only duplicates and a few additional studies that were not relevant. In all, 34 studies met the inclusion criteria. Table 1 summarizes the results.

RESULTS

Fruits and vegetables

Six prospective cohort studies have examined the relationship between fruit and vegetable intake and risk of stroke. The risk of ischemic stroke with fruit and vegetable intake was evaluated jointly among 75,596 women aged 34–59 years from the Nurses’ Health Study (NHS), who were followed for 14 years, and 38,683 men aged 40–75 years from the Health Professionals’ Follow-up Study (HPFS), who were followed for 8 years. Ischemic stroke was documented among 366 women and 204 men. An inverse relationship was detected among the group in the highest quintile of fruit and vegetable consumption (RR, 0.69; 95% confidence interval [CI], 0.52–0.92). In particular, high consumption of cruciferous vegetables, green leafy vegetables, citrus fruits, and vitamin C-rich fruits carried the lowest risk for both cohorts, with sig-
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<td>Joshipura et al. (1999)</td>
<td>Prospective cohort, 8 years</td>
<td>NHS, 14-y follow-up; HPFS, 8-y follow-up</td>
<td>75,596 females from NHS, age range: 34–59 y; 38,683 males from HPFS, age range: 40–75 y</td>
<td>Total and individual fruit and vegetable intake, and subtypes: fruits (citrus fruits, citrus fruit juices), Vegetables (cruciferous, green leafy), legumes, potatoes, vitamin C-rich fruits and vegetables</td>
<td>Ischemic stroke</td>
<td>↓ risk with cruciferous and green leafy vegetables, citrus- and vitamin C-rich associated with lower risk in both cohorts; no inverse association with potatoes and legumes</td>
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<td>Johnsen et al. (2003)</td>
<td>Prospective cohort, 4 years</td>
<td>Danish Diet, Cancer and Health Study</td>
<td>54,504 males and females</td>
<td>Total and individual fruit and vegetable intake</td>
<td>Ischemic stroke</td>
<td>↓ risk with ↑ fruit intake; no association with vegetable intake</td>
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<td>Mizrahi et al. (2009)</td>
<td>Prospective cohort, 24 years</td>
<td>Finnish Mobile Clinic Health Examination Survey</td>
<td>3,962 females and males; age range: 40–74</td>
<td>Plant food (fruits, berries, vegetables, and cereals)</td>
<td>Cerebrovascular disease, total stroke (acute, subarachnoid hemorrhages, other undefined), ischemic, IH</td>
<td>↓ risk of cerebrovascular disease, IH, and ischemic stroke in men only with fruit intake (especially citrus); no association with total vegetable or cereal consumption; ↓ risk of CVD, ischemic stroke, and IH with cruciferous vegetable intake</td>
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<tr>
<td>Gillman et al. (1995)</td>
<td>Prospective cohort, 20 years</td>
<td>Framingham Study</td>
<td>832 males; age range: 45–65 y</td>
<td>Total fruits and vegetables</td>
<td>Complete stroke (ischemic and hemorrhagic), TIA</td>
<td>↓ risk of all stroke and subtypes and TIA with 3 servings/day of fruits and vegetables</td>
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<td>Sauvaget et al. (2003)</td>
<td>Prospective cohort, 18 years</td>
<td>Hiroshima/Nagasaki Life Span Study, Japan</td>
<td>14,966 males and 23,471 males and females; mean age at baseline: females:5.8, males:5.4</td>
<td>Fruits and green-yellow vegetables</td>
<td>Total stroke, subtypes (cerebral hemorrhage, cerebral infarction)</td>
<td>↓ risk of death from total stroke and subtypes with daily fruits and green-yellow vegetables</td>
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<td>Rodriguez et al. (1998)</td>
<td>Ecological</td>
<td>Spain’s provincial vital statistics</td>
<td>CVD mortality of 50 provinces from Spanish vital statistics. Age-standardized CVD mortality rates calculated at provincial level for 1975–1979 and 1989–1993, for ages 45 to 79, European population deemed as standard. Diet information from 1964 (21,000 families) and 1980 (25,000 families) Household Budget Surveys</td>
<td>Life style factors including fish, fruit, and wine consumption</td>
<td>CVD mortality</td>
<td>↓ risk of mortality from total stroke, total CVD, and total mortality with ↑ fruit intake; ↓ total CVD mortality risk with vegetable intake; ↓ risk of other CVD, total CVD, and total mortality with ↑ bean intake</td>
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<td>Nagura et al. (2009)</td>
<td>Prospective cohort, 13 years</td>
<td>Japan Collaborative Cohort Study</td>
<td>25,206 males, 34,279 females; age range: 40–79 y</td>
<td>Fruit, vegetable and beans</td>
<td>Total stroke and subtypes (hemorrhagic and ischemic), CHD, other CVD, total CVD</td>
<td>↓ risk of mortality from total stroke, total CVD, total mortality with ↑ fruit intake; ↓ total CVD mortality risk with vegetable intake; ↓ risk of other CVD, total CVD, and total mortality with ↑ bean intake</td>
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<td>Park et al. (2010)</td>
<td>Case-control</td>
<td>Patients from Hanyang University Seoul Hospital, Korea</td>
<td>Cases: 69 first-event strokes, mean age 57.9; Controls: 69, mean age 57.4</td>
<td>Fruits and vegetables and their constituent nutrients (8 vitamins, macron, folate, calcium, potassium, zinc, retinol carotene, vitamin C, vitamin E), total fat, plant fat, animal protein, plant protein, total protein, fiber, carbohydrates, energy, iron, sodium, phosphorous</td>
<td>Stroke</td>
<td>↓ risk with higher intakes of vegetables and B complex vitamins; no association found with fruit and antioxidant intake</td>
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<tr>
<td>Caicoya (2002)</td>
<td>Case-control</td>
<td>Asturias, Spain</td>
<td>440 stroke cases and 473 controls; age range: 40–85 y</td>
<td>Fish and omega-3 PUFA</td>
<td>Total, subarachnoid hemorrhage, intraparenchymal hemorrhage, cerebral infarct, stroke of unknown origin</td>
<td>↑ risk of cerebral infarct, but not superficial cerebral infarct or intraparenchymal hemorrhage with ↑ fish consumption</td>
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<tr>
<td>Reference</td>
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<td>Wernberg et al. (2007)13</td>
<td>Nested case-control</td>
<td>Community intervention program on CVD and diabetes and the WHO MONICA Study, northern Sweden</td>
<td>369 cases, 738 matched controls (mean age for both cases and controls: males 54.6, females 55.4)</td>
<td>Fish (total, fatty, lean), fatty acid consumption and erythrocyte mercury levels</td>
<td>Total, ischemic, and hemorrhagic stroke</td>
<td>Significant risk difference between males and females; significant ↑ risk in males and non-significant ↓ risk in females with increasing fish intake</td>
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<tr>
<td>Jamrozik et al. (1994)23</td>
<td>Population-based case control</td>
<td>Perth Community Stroke Study, Western Australia</td>
<td>536 cases, 1,441 gender- and age-matched eligible controls</td>
<td>Lifestyle risk factors (alcohol, tobacco, hypertension, claudication, diabetes mellitus, previous MI, stroke or TIA, aspirin use, consumption of meat, salt, fish, margarine, and food preparation</td>
<td>First-ever strokes, ischemic, primary IH, and all strokes combined</td>
<td>↓ risk of first-ever stroke and hemorrhagic stroke with fish intake of &gt;2 times/month; ↑ risk of all strokes combined and first-ever strokes with meat intake &gt;4 times/week; ↓ risk of all strokes combined, first-ever strokes, and ischemic stroke with reduced-fat or skim milk intake</td>
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<td>Iso et al. (2001)17</td>
<td>Prospective cohort, 14 years</td>
<td>NHS</td>
<td>79,839 females; age range: 34–59 y</td>
<td>Fish and omega-3 PUFA</td>
<td>Total stroke and stroke subtypes</td>
<td>↓ risk of thrombotic infarction total stroke with intake ≥2 times/week; no association with hemorrhagic stroke</td>
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<tr>
<td>Montonen et al. (2009)27</td>
<td>Prospective cohort, 28 years</td>
<td>Finnish Mobile Clinic Health Examination Survey, Finland</td>
<td>3,958 males and females; age range: 40–79 y</td>
<td>Fish (total, salted, smoked, other smoked or salted)</td>
<td>Cerebrovascular disease, IH, subarachnoid hemorrhage, thrombosis or emboli</td>
<td>Risk of total stroke with tuna fish and ↓ risk with fried fish; no association with hemorrhagic stroke</td>
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<tr>
<td>Mozaffarian et al. (2005)28</td>
<td>Prospective cohort, 12 years</td>
<td>Cardiovascular Health Study</td>
<td>4,775 males and females; age range: 65–98 y</td>
<td>Fish (tuna/other broiled or baked fish, fried fish/fish sandwich)</td>
<td>Total stroke, hemorrhagic, and ischemic</td>
<td>↓ risk of total stroke with tuna fish and ↑ risk with fried fish; no association with hemorrhagic stroke</td>
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<tr>
<td>Myint et al. (2006)29</td>
<td>Prospective cohort, 8.5 years</td>
<td>EPIC-Norfolk Study</td>
<td>24,312 males and females; age range: 40–79 y</td>
<td>Total fish, white fish, oily fish, shellfish, fish roe</td>
<td>Total stroke</td>
<td>No association</td>
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<tr>
<td>He et al. (2002)30</td>
<td>Prospective cohort, 12 years</td>
<td>HPFS</td>
<td>43,671 males; age range: 40–75 y</td>
<td>Fish consumption, omega-3 intake</td>
<td>Total stroke, hemorrhagic, and ischemic</td>
<td>↓ risk of ischemic stroke with ≥1 intake episode/month; no association with hemorrhagic stroke</td>
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<tr>
<td>Gillum et al. (1996)31</td>
<td>Longitudinal cohort, 12 years</td>
<td>NHANES I Epidemiologic Follow-Up Study</td>
<td>5,192 (4,410 white persons, 782 black persons); age range: 45–74 y</td>
<td>Fish</td>
<td>Total stroke</td>
<td>↓ risk with ≥1 serving/week in white females and any consumption among blacks; no association in males</td>
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<tr>
<td>Orencai et al. (1996)14</td>
<td>Prospective cohort, 12 years</td>
<td>Chicago Western Electric Study</td>
<td>2,107 males; age range: 40–55 y</td>
<td>Fish</td>
<td>Total stroke mortality</td>
<td>↑ risk of death with ≥35 g/day intake</td>
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<tr>
<td>Keli et al. (1994)32</td>
<td>Prospective cohort, 15 years</td>
<td>The Zutphen Study, Netherlands</td>
<td>552 males; age range: 50–69 y</td>
<td>Fish</td>
<td>Total stroke (fatal and non-fatal)</td>
<td>↓ risk with 1 serving/week</td>
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<tr>
<td>Liang et al. (2009)33</td>
<td>Hospital-based case-control</td>
<td>Southern China</td>
<td>374 incident ischemic stroke cases and 464 controls</td>
<td>Soy foods (total, dried soybean, tofu, soymilk)</td>
<td>Ischemic stroke</td>
<td>↓ risk of ischemic stroke with increased total soy foods, dried soybean, tofu, and soymilk</td>
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<tr>
<td>Kokubo et al. (2007)34</td>
<td>Prospective cohort, 12.5 years</td>
<td>Japan Public Health Center-Based Study</td>
<td>40,462 males and females; age range: 40–59 y at baseline</td>
<td>Soy and isoflavone</td>
<td>Myocardial infarction and cerebral infarction</td>
<td>↓ in ischemic stroke, myocardial infarction and CVD with soy and isoflavone intake among females (prominent in postmenopausal); no association in males</td>
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<tr>
<td>Sawagat et al. (2003)35</td>
<td>Prospective cohort, 16 years</td>
<td>Hisshima/Nagasaki Life Span Study</td>
<td>15,350 males (mean age: 54 y) and 24,999 females (mean age: 58 y)</td>
<td>Animal products (beef/pork, chicken, ham, sausage, milk, dairy products, eggs, fish, and broiled fish)</td>
<td>Stroke mortality (SH, IH, cerebral infarct, other cerebrovascular disease)</td>
<td>↑ in ischemic stroke, myocardial infarction and CVD with soy and isoflavone intake among females (prominent in postmenopausal); no association in males</td>
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<tr>
<td>He et al. (2003)36</td>
<td>Prospect cohort, 14 years</td>
<td>HPFS</td>
<td>43,732; age range: 40–75 y</td>
<td>Total fat, cholesterol, types of fat, intake of red meat, nuts, eggs and high-fat dairy products</td>
<td>Ischemic and hemorrhagic stroke</td>
<td>Yes association</td>
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<td>Study</td>
<td>Design</td>
<td>Study Population</td>
<td>Eggs Consumption and Outcomes</td>
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<td>Djoussé et al. (2008)</td>
<td>Prospective cohort, 20 years</td>
<td>Physicians’ Health Study 21,327 males; age range: 40–85 y at baseline</td>
<td>Incident myocardial infarction, total, hemorrhagic and ischemic stroke, and all-cause mortality</td>
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<td>Qureshi et al. (2007)</td>
<td>Prospective cohort, 20 years</td>
<td>NHANES 13,586 males and females; age range: 24–74 y</td>
<td>Total stroke, ischemic stroke, coronary artery disease, mortality</td>
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<tr>
<td>Hu et al. (1999)</td>
<td>Prospective cohort, 20 years</td>
<td>HPFS and NHS 37,851 males (age range: 40–75 y) and 80,082 females (age range: 34–69 y)</td>
<td>Total ischemic, and hemorrhagic stroke, CHD</td>
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<tr>
<td>Elwood et al. (2005)</td>
<td>Prospective cohort, 20 years</td>
<td>Caerphilly cohort study, Southern Whales ATBC, Finland 66.5 males; age range: 45–59 y</td>
<td>Ischemic heart disease and ischamic stroke</td>
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<tr>
<td>Larson et al. (2009)</td>
<td>Prospective cohort, 13.6 years</td>
<td>Prospctive cohort, 13.6 years</td>
<td>Dairy foods (total dairy, low-fat milk, whole milk, sour milk, yogurt, cheese, cream, ice cream, butter)</td>
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<tr>
<td>Liu et al. (2000)</td>
<td>Prospective cohort, 12 years</td>
<td>NHS 75,221 females; age range: 38–63 y</td>
<td>Ischemic stroke</td>
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<tr>
<td>Steffen et al. (2003)</td>
<td>Prospective cohort, 11 years</td>
<td>ARIC 15,792 males and females; age range: 45–64 y at baseline</td>
<td>Total mortality, CAD and ischemic stroke incidence</td>
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<tr>
<td>Fung et al. (2008)</td>
<td>Prospective cohort, 24 years</td>
<td>NHS 88,517 females; age range: 34–59 y</td>
<td>Total CHD, nonfatal CHD, fatal CHD, total stroke, ischemic stroke, hemorrhagic stroke</td>
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<tr>
<td>Fung et al. (2004)</td>
<td>Prospective cohort, 14 years</td>
<td>NHS 71,768 females; age range: 38–63 y</td>
<td>Total stroke, ischemic stroke, and hemorrhagic stroke</td>
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<tr>
<td>Fung et al. (2009)</td>
<td>Prospective cohort, 20 years</td>
<td>NHS 74,486 females; age range: 38–63 y</td>
<td>Total CHD, nonfatal CHD, fatal CHD, total stroke, ischemic stroke, hemorrhagic stroke, nonfatal stroke, fatal stroke</td>
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<tr>
<td>Howard et al. (2006)</td>
<td>Randomized controlled trial, 8.1 years</td>
<td>Women’s Health Initiative Dietary Modification Trial, US 48,835 postmenopausal females; age range: 50–79 y</td>
<td>Low-fat dietary pattern</td>
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**Abbreviations:** ARIC, Atherosclerosis Risk in Communities; ATBC, Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study; CHD, coronary heart disease; CVD, cardiovascuar disease; EPIC-Norfolk, European Prospective Investigation into Cancer; HPFS, Health Professionals’ Follow-Up Study; IHD, intracerebral hemorrhage; MONICA, Multinational Monitoring of Trends and Determinants in Cardiovascular Disease study; NHANES, National Health and Nutrition Examination Survey; NHS, Nurses’ Health Study; PUFA, polyunsaturated fatty acid; TIA, transient ischemic attack; WHO, World Health Organization; y, years.
nificance remaining intact after adjustment for potential confounders. Similar results were seen for total fruits and total vegetables when computed separately. Potatoes and legumes, when analyzed individually, did not show inverse associations with risk of ischemic stroke.\textsuperscript{12}

The protective effect of fruit and vegetable consumption on risk of the ischemic stroke subtype was again investigated in the Danish Diet, Cancer and Health Study. During a 4-year follow-up, among 54,504 subjects, 266 cases of ischemic stroke were identified. A significant reduction in risk was observed with fruit intake (median intake, 673 g/day; RR, 0.60; 95% CI, 0.38–0.95; \( P \) for trend, 0.02). Similar patterns were seen for most fruits and vegetables, but risks remained significant for citrus fruits only. No clear association was found between total vegetable intake and stroke.\textsuperscript{13}

Mizrahi et al.\textsuperscript{14} studied the effects of plant food intake (fruit and berries, vegetables, and cereals) on the incidence of cerebrovascular disease and its subtypes (ischemic and hemorrhagic stroke) in a Finnish population — which is a population known for its low consumption of fruits and vegetables and high intake of whole-grain cereals. The cohort included 3,932 men and women between the ages of 40 and 74 years. A total of 625 cases of stroke were identified, of which 58 were caused by intracerebral hemorrhage (IH), 335 were ischemic strokes (thrombotic or embolic), and 232 were due to undefined cerebrovascular disease. An inverse relationship was detected between fruit consumption and incidence of cerebrovascular disease, ischemic stroke, and IH. The strongest association was found with citrus fruit, which was evident only among men in the group with the lowest quartile of fruit intake (0–12 g/day). An association between total vegetable consumption and risk of overall cerebrovascular disease could not be determined. Only higher cruciferous vegetable intake was associated with lower risk of cerebrovascular disease.\textsuperscript{14}

Between 1966 and 1969, the Framingham Study recruited 832 men, aged 45–65 years, who were free of CVD. During 20 years follow up, the study observed 97 incident strokes, 73 of which were complete strokes, and 24 transient ischemic attacks (TIA). Of the complete strokes, 61 cases were ischemic and 14 were hemorrhagic, with two individuals having both types of stroke. The study found that the risk ratio decreased with increasing fruit and vegetable consumption across all quintiles (\( P \) for trend, 0.01). A 22% decrease in the risk of all types of stroke and TIA was observed with every increment of three daily servings of fruits and vegetables (age-adjusted RR, 0.78; 95% CI, 0.62–0.98). This same reduction was also observed for age-adjusted total complete stroke (RR, 0.74; 95% CI, 0.57–0.96), ischemic stroke (RR, 0.76; 95% CI, 0.57–1.02), and hemorrhagic stroke (RR, 0.49; 95% CI, 0.25–0.95). With the exception of hemorrhagic stroke, very little deviation from these risks was observed with adjustment of other covariates.\textsuperscript{15}

Sauvaget et al.\textsuperscript{16} studied the effect of fruit and vegetable intake on total stroke mortality among participants in the Life Span Study. Stroke subtypes and gender were analyzed separately. The cohort consisted of 40,349 Japanese men and women who were followed for 18 years. A total of 1,926 stroke deaths were documented, with 920 ischemic strokes and 453 deaths due to IH. Consumption of green-yellow vegetables was associated with a 26% reduced risk of total death from stroke. The benefits of fruit and vegetable intake were seen equally for ischemic and hemorrhagic strokes, with 32% and 30% reduction in men and women, respectively, although not significant among men. Fruit consumption decreased the risk of total stroke, both infarction- and hemorrhage-related, by 35% in men and 25% in women.

The Japan Collaborative Cohort Study for Evaluation of Cancer Risk examined fruit, vegetable, and bean intake in relation to CVD in a population consisting of 25,206 men and 34,279 women aged 40–79 years who were followed for 13 years. Fruit, vegetable, and bean intake was recorded using a food frequency questionnaire (FFQ). During follow-up, the number of deaths recorded among men was 559 from total stroke, 258 from coronary heart disease, 1,207 from total CVD, and 4,514 from total mortality. Among women, 494 deaths occurred from total stroke, 194 from coronary heart disease (CHD), 1,036 from total CVD, and 3,092 from total mortality. There was an inverse relationship between fruit and mortality from total stroke (HR, 0.67; 95% CI, 0.55–0.81), total CVD (HR, 0.75; 95% CI, 0.66–0.85), and total mortality (HR, 0.86; 95% CI, 0.80–0.92) in the highest versus the lowest quartile of intake. An inverse association between vegetable intake and total CVD (HR, 0.88; 95% CI, 0.78–0.99) was observed. The same pattern was seen for bean intake, with inverse association with other CVD (HR, 0.79; 95% CI, 0.64–0.98), total CVD (HR, 0.84; 95% CI, 0.74–0.95), and total mortality (HR, 0.90; 95% CI, 0.84–0.96). After adjustment for other plant-based foods, the association of fruit consumption with mortality from total stroke, total CVD, and total mortality remained significant, but the associations of vegetables and beans with mortality risk diminished.\textsuperscript{17} A limitation of the study was noted to be low validity of the FFQ.

Ecological evidence also suggests a role of fruit in cerebrovascular disease. Artalejo-Rodriguez et al.,\textsuperscript{18} examined the distribution of CVD in different provinces of Spain, and the contributing factors responsible for the decrease in deaths due to cerebrovascular diseases during 1975–1993, as cerebrovascular disease was the leading cause of death in Spain. Changes in fruit, fish, and wine intake accounted for 22% of the decrease in cerebrovas-
cular disease mortality. Increased fruit and decreased wine consumption were significantly associated with decreased risk of cerebrovascular disease mortality ($P = 0.04$).

Recently, Park et al.\textsuperscript{19} examined the relationship between fruit and vegetable intake and stroke in a South Korean hospital-based case-control study among 69 new-onset stroke patients and 69 age-, gender-, and BMI-matched controls. After adjustment for age, sex, BMI, and family history of stroke, intakes of total fat, plant fat, calcium, potassium, vitamin B\textsubscript{1}, vitamin B\textsubscript{2}, vitamin B\textsubscript{6}, niacin, and folate were negatively correlated with the risk of stroke. Vegetable intake was associated with reduced risk of stroke after adjustment for confounding factors (seen in 4\textsuperscript{th} quartile of intake; OR, 0.311; 95% CI, 0.100–0.963; $P$ for trend, 0.043). Similar findings were reported for vitamin B complex (B\textsubscript{1}, B\textsubscript{2}, B\textsubscript{6}, niacin, and folate); however, they failed to detect a significant relationship between stroke risk and intake of grains, fruits (OR, 0.605; 95% CI, 0.197–1.852; $P$, 0.85), seafood, milk, and meat. In addition, there was a negative association between the risk of stroke and total fat, plant fat, calcium, potassium, vitamin B\textsubscript{1}, vitamin B\textsubscript{2}, vitamin B\textsubscript{6}, niacin, and folate, which remained significant after adjustment for confounding factors. Of note, the FFQ used to measure dietary intake had not been validated, and the possibility of omission in capturing the entire intake of nutrients was noted. Other limitations included low participation in the study and low intake of fruits among the participants, with an average of one serving per day, thus failing to specify the link between fruit intake and risk of stroke.\textsuperscript{19}

**Fish**

Eight prospective cohort and three case-control studies were identified that assessed the relationship between fish intake and stroke risk. Caicoya et al.\textsuperscript{20} examined the relationship between fish consumption and stroke among 440 incident cases of stroke and 437 controls (age range: 40–85 years) in the Asturias region of Spain. The highest quintile intake of fish was associated with significant increased risk of deep small cerebral infarct (OR, 3.21; 95% CI, 1.11–9.20) but was not associated with significant increased risk of superficial cerebral infarct (OR, 1.19; 95% CI, 0.57–2.48) or intraparenchymal hemorrhage (OR, 1.74; 95% CI, 0.72–4.17). Increasing intake of fish resulted in significant increased overall stroke risk when the highest and lowest quintiles of consumption (46 g/day versus 11 g/day) were compared (OR, 1.95; 95% CI, 1.14–3.33). Increasing fish consumption was also associated with increased risk of cerebral infarct (highest quartile of consumption, >46 g/day; OR, 1.98; 95% CI, 1.08–3.47).\textsuperscript{20}

Wennberg et al.\textsuperscript{21} conducted a nested case-control study in northern Sweden among 369 cases and 738 controls to investigate the relationship between fish intake and risk of stroke subtypes, and to determine the differences between men and women. Multivariate analysis indicated that increased fish intake was associated with increased risk of overall stroke in men (OR, 1.24; 95% CI, 1.01–1.51), with non-significant protection in women (OR, 0.90; 95% CI, 0.73–1.12). Based on fish subtype, ischemic stroke risk in men increased with fatty fish intake (OR, 1.25; 95% CI, 1.00–1.56) but decreased slightly in women (OR, 0.93; 95% CI, 0.74–1.17). Similar results were observed for hemorrhagic stroke and fatty fish intake (males: OR, 1.42; 95% CI, 0.71–2.85; females: OR, 0.28; 95% CI, 0.07–1.10).\textsuperscript{21}

A population-based case-control study conducted in Western Australia examined a number of lifestyle factors in relation to stroke, including fish intake. Multivariate analysis of 175 first-ever stroke cases and 553 controls indicated a significantly decreased risk of first-ever stroke (OR, 0.60; 95% CI, 0.6–0.99) when fish was consumed more than twice per month, and a significant protective effect for primary IH (OR, 0.42; 95% CI, 0.19–0.90) when fish was consumed more than twice per month. No significant association was observed for ischemic stroke.\textsuperscript{22} In a longitudinal study published by Gillum et al.,\textsuperscript{23} 3,192 adults from the National Health and Nutrition Examination Survey (NHANES), including 4,410 white and 782 black persons aged 45–74 years, were followed for 12 years. White women who consumed fish more than once per week had significantly lower risk of stroke as compared to women who never ate fish (RR, 0.55; 95% CI, 0.32–0.93). Black men and women also had significantly lower risk of stroke with any level of fish consumption (RR, 0.51; 95% CI, 0.30–0.88). Although lower risk was observed in white men who consumed fish more than once per week, the relationship was not significant (RR, 0.85; 95% CI, 0.49–1.46).\textsuperscript{23}

Three studies investigated the relationship between fish consumption and stroke risk among men. Orencia et al.\textsuperscript{24} conducted a study among 2,107 men, aged 40–55 years, from the Chicago Western Electric Study, who were followed prospectively for 30 years. The highest intake of fish (≥35 g/day) was associated with increased risk of fatal and non-fatal stroke (HR, 1.26; 95% CI, 0.74–1.16), whereas the lowest level of intake (1–17 g/day) was associated with slightly lower risk (HR, 0.98; 95% CI, 0.61–1.59). Although stroke incidence was highest in the group that consumed the most fish, results were not sufficiently significant to draw any conclusions. Information on stroke subtype was not available for a large proportion of study subjects; therefore, analysis according to stroke subtype could not be performed.\textsuperscript{24} Conversely, Keli et al.\textsuperscript{25} detected decreased stroke risk with at least one serving of...
fish per week in 552 males aged 50–69 years from the Zutphen Study Cohort in the Netherlands. High fish intake (>20 g/day) was associated with decreased risk of stroke (HR, 0.49; 95% CI: 0.24–1.01) as compared to those who consumed ≤20 g/day of fish. Analysis was performed by grouping subjects based on their report of fish intake at each follow-up period as “always eaters” and as “not-always eaters.” A lower, yet non-significant risk of stroke was observed among the “always eaters” as compared to the “not-always” eaters (OR, 0.71; 95% CI: 0.38–1.33).²⁵

He et al.²⁶ observed occasional fish intake to be associated with decreased risk of ischemic stroke, but not hemorrhagic stroke. The cohort consisted of 43,671 men from the HPFS, aged 40–75 years, who were followed for 12 years. Significant decreased risk of ischemic stroke was observed with consumption of fish 1–3 times per month (RR, 0.57; 95% CI, 0.35–0.95) and >5 times per week (RR, 0.54; 95% CI, 0.31–0.94).²⁶ Iso et al.²⁷ examined the relationship between fish intake and stroke risk specifically in elderly women. In that study, 79,839 females from the NHS, aged 34–59 years, were followed for 14 years. During follow-up, 574 incident strokes were documented, of which 119 were cases of subarachnoid hemorrhage, 62 intraparenchymal hemorrhage, and 303 ischemic stroke. Increased risk of stroke was observed with increasing fish consumption (1–3 times per month: RR, 0.93; 95% CI, 0.65–1.34; once per week: RR, 0.78; 95% CI, 0.55–1.12; 2–4 times per week: RR, 0.73; 95% CI, 0.47–1.14; greater than 5 times per week: RR, 0.48; 95% CI, 0.21–1.06; P for trend, 0.06). There was a significant relationship between thrombotic infarction and fish consumption greater than two times per week (HR, 0.73; 95% CI, 0.47–1.14; >5 times per week: HR, 0.48; 95% CI, 0.21–1.06; P for trend, 0.06). No significant correlation was found between fish consumption and hemorrhagic stroke.²⁷

Two additional studies examined the relationship between subtypes of stroke and different types of fish. Mozaffarian et al.²⁸ evaluated this relationship in an elderly cohort of 4,755 adults from the Cardiovascular Health Study (CHS), aged 65–98 years, who were followed for 12 years. The study found 626 incident strokes, 529 of which were ischemic. The subcategory of tuna/other fish was inversely correlated with total stroke (P, 0.04) and ischemic stroke (P, 0.02). The risk of ischemic stroke was 27% lower when fish was consumed 1–4 times per week (HR, 0.73; 95% CI, 0.55–0.98) and 30% lower when fish consumption totaled more than 5 times per week (HR, 0.70; 95% CI, 0.50–0.99) when compared with consumption of less than once per month. Conversely, the category of fried fish/fish sandwich was positively correlated with total stroke incidence (P, 0.006), and ischemic stroke incidence (P, 0.003). The risk for ischemic stroke was 44% higher when fried fish/fish sandwich consumption totaled more than once per week (HR, 1.44; 95% CI, 1.12–1.85) compared to once per month. No correlation between fish consumption and hemorrhagic stroke was observed.²⁸ Montonen et al.²⁹ studied fish subtype consumption and the risk of cerebrovascular disease. The study population consisted of 3,958 men and women, aged 40–79 years, from the Finnish Mobile Clinical Health Examination Survey cohort. In a 28-year follow-up, 659 incident cases of cerebrovascular disease occurred, including 80 IH, 364 thrombotic or embolic, 40 subarachnoid hemorrhage, and 175 unspecified cerebral strokes. The study found that total fish consumption did not predict risk of thrombotic, hemorrhagic, or total stroke. However, salted fish consumption, when compared with non-consumption, was associated with a significant increased risk of IH (RR, 1.98; 95% CI, 1.02–3.84).²⁹

Finally, a prospective cohort study consisting of 24,312 men and women aged 40–79 years was conducted on participants of the European Prospective Investigation into Cancer (EPIC) study in Norfolk, UK. FFQs were provided to the participants between 1993 and 1997, and participants were followed until 2004. The study recorded 421 incident strokes. No significant relationship was observed between total fish, shellfish, or fish roe consumption and stroke risk. Oily fish intake was lower among women who suffered from stroke (OR, 0.69; 95% CI, 0.51–0.94; P, 0.02).³⁰

**Soy**

Soy provides an abundance of nutrients including fiber, antioxidants, and phytochemicals and is an especially important food group in the vegetarian food guide pyramid.³¹³² Soy isoflavones can act as antioxidants, reducing the formation of oxidized lipoproteins like low-density lipoproteins. Two studies examined the relationship between soy and stroke. Liang et al.³³ studied soy consumption and its correlation with stroke incidence. The study population consisted of 374 ischemic stroke patients and 464 hospital-based controls. The mean weekly soy food intake was significantly lower in cases when compared to controls (P, 0.001). The highest tertiles of intake of dried soybeans (OR, 0.20; 95% CI, 0.09–0.48), tofu (OR, 0.56; 95% CI, 0.36–0.89), soymilk (OR, 0.18; 95% CI, 0.06–0.51), and total soy foods (OR, 0.23; 95% CI, 0.14–0.39) were each associated with significantly reduced risk of stroke after adjustment for confounders, as compared to the lowest tertiles of consumption.³³

A protective effect of soy and isoflavone intake against risk of ischemic stroke and myocardial infarction (MI) was also observed in a prospective study among 40,462 Japanese individuals. After an average 12.5 years of follow-up, 587 cerebral infarcts and 308 MIs occurred, with a combined mortality of 232 for MI and CI. Evalu-
ation of soy and isoflavone intake revealed a strong inverse association between risk of stroke and MI in women, primarily postmenopausal women, but no link was detected in men. For women, consumption five times per week, as compared to 0–2 times per week, was associated with significant reductions in risk of ischemic stroke (HR 0.64; 95% CI, 0.43–0.95), MI (HR 0.55; 95% CI, 0.26–1.09), and CVD (HR 0.31; 95% CI, 0.13–0.74) in multivariate analysis. A weak inverse association was identified between consumption of miso soup and beans and CVD mortality. The highest quintiles of isoflavone intake in women (37.7–73.1 mg/day) were linked to reduced risk of ischemic stroke (HR 0.35, 95% CI, 0.21–0.59), MI (HR 0.37; 95% CI, 0.14–0.98), and CVD mortality (HR 0.87; 95% CI, 0.29 to 2.52). The study failed to demonstrate a significant relationship between consumption of miso soup, beans, and isoflavones with stroke and MI among men.34

Whole grain

Liu et al.35 studied the relationship of whole-grain consumption and stroke in women. The study population consisted of 75,221 women in the United States, 38–63 years of age, who were participants in the NHS. Participants were followed over a period of 12 years. A significant inverse relationship between whole-grain consumption and ischemic stroke risk was observed across all quintiles of intake, which remained unchanged after adjustment for other CVD risk factors. Age-adjusted RRs for lowest to highest quintiles were as follows: RR 0.68 (95% CI, 0.49–0.94), RR 0.69 (95% CI, 0.51–0.95), RR (0.49; 95% CI, 0.35–0.69), and RR 0.57 (95% CI, 0.42–0.78, P 0.003 for trend). However, no association between total grain intake and ischemic stroke risk was observed.35

Steffen et al.36 examined intake of whole grains, refined grains, and incidence of ischemic stroke. A total of 15,792 subjects, aged 45–64 years, from the Atherosclerosis Risk in Communities Study (ARIC) were followed for 11 years. The study, however, failed to find any association between whole-grain intake, refined-grain intake, and stroke incidence.36

Animal products: meats, eggs, and dairy

The relationship between egg consumption and CVD is of interest due to the presence of both potentially harmful constituents (cholesterol) and healthful nutrients (B-vitamins, folate, and monounsaturated fatty acids) in this food. Three large prospective studies have examined this relationship. During a 20-year follow-up, the Physician’s Health Study (PHS), consisting of 21,327 male participants aged 40–85 years, found no association between stroke at any level of intake, after adjustment for age, BMI, smoking, and history of hypertension (consumption of 1 egg/week: HR, 0.96; 95% CI, 0.82–1.12; consumption of ≥7 eggs/week: HR, 1.06; 95% CI, 0.86–1.30).37 Similarly, a collaborative study including 37,851 men, aged 40–75 years, from the HPSF and 80,082 women, aged 34–59 years, from the NHS found no association between egg consumption and stroke risk. During an 8-year follow-up in the male cohort, 258 incident strokes occurred, and during a 14-year follow-up in the female cohort, 563 strokes occurred. Consumption of ≥1 egg/day was not associated with total stroke risk in multivariate analysis (men: RR, 1.07; 95% CI, 0.66–1.75; women: RR, 0.89; 95% CI, 0.60–1.31). Similar non-significant findings were observed for ischemic stroke (men: RR, 0.93; 95% CI, 0.46–1.87; women: RR, 0.81; 95% CI, 0.46–1.42) and hemorrhagic stroke (men: RR, 0.67; 95% CI, 0.22–2.07; women: RR, 1.07; 95% CI, 0.56–2.03).38 Finally, a 20-year follow-up study among 13,586 subjects, aged 24–74 years, from the NHANES-1 cohort, found no association between egg consumption in the highest quartile (>6 eggs/day) and ischemic stroke risk (RR, 0.9; 95% CI, 0.7–1.1) or all stroke risk (RR, 0.9; 95% CI, 0.7–1.1) after adjustment for age, gender, race/ethnicity, systolic blood pressure, diabetes mellitus, serum cholesterol, cigarette smoking, BMI, and educational status.39

A Japanese study prospectively investigated the relationship between risk of stroke death and intake of animal products. Sauvaget et al.40 examined animal product consumption and stroke mortality in the Japanese Life Span Study, which consisted of 14,209 men and 22,921 women, aged 34–103 years. During 16 years of follow-up, 1,462 deaths occurred from stroke. Milk consumption was not associated with incident stroke mortality. However, the highest tertiles of intakes of eggs (HR, 0.70; 95% CI, 0.51–0.95), dairy products (HR, 0.73; 95% CI, 0.57–0.94), fish (HR, 0.71; 95% CI, 0.48–1.05), and broiled fish (HR, 0.60; 95% CI, 0.37–0.98) were inversely associated with stroke mortality. A composite measure of the same animal products also revealed a significantly inverse relationship with the highest intake level for total stroke (HR, 0.80; 95% CI, 0.68–0.93). The protective effect of the highest, as compared to the lowest, intake of these animal products was only significantly associated with cerebral hemorrhage (HR, 0.72; 95% CI, 0.53–0.98), not with cerebral infarct (HR, 0.84; 95% CI, 0.67–1.06). High intake of fish products was associated with a lower risk of IH (HR, 0.70; 95% CI, 0.54–0.92) and total stroke (HR, 0.85; 95% CI, 0.75–0.98) only. The study mentioned that a generally low consumption of animal products including eggs, dairy products, and fish in this population may contribute to the observed protective effect.40

Jamrozik et al.42 studied stroke type and associated lifestyle factors in a case-control setting that included meat intake. A total of 536 stroke cases were identified.
from a population-based registry in Western Australia, and the cases were matched for gender and birth year with 1–5 controls, depending on the type of stroke. Consumption of meat with a frequency greater than 4 times per week was positively correlated with risk of all strokes as well as first-incident strokes (multivariate OR for all strokes, 2.17; 95% CI, 1.33–3.53; OR for first-ever strokes, 2.30; 95% CI, 1.29–4.08). Finally, in addition to finding no statistical association of stroke risk with specific types of fat (total, animal, vegetable, saturated, monounsaturated, polyunsaturated, and trans fat) a study of 43,732 participants, aged 40–75 years, in the HPFS study found no association between stroke risk and intake of red meats, high-fat dairy products, nuts, or eggs. A few studies have investigated the impact of dairy products on stroke risk. In one study, baseline dietary information regarding milk consumption was gathered from a 7-day dietary record obtained from a subsample of male subjects, aged 45–59 years, from the Caerphilly cohort study in Southern Wales. During a 20-year follow-up, 54 ischemic stroke events occurred and there were 139 ischemic heart disease events. Compared to milk drinkers, non-milk drinkers were more likely to drink alcohol. As compared to subjects who consumed milk below the medium intake, those who drank milk at or above the medium intake were at lower risk of ischemic stroke (RR, 0.52; 95% CI, 0.27–0.99) after adjustments were made for age, smoking, total energy, and social class. Results were nearly the same for men who consumed whole milk at baseline (data not shown).

In a study by Larsson et al., specific dairy components were found to be associated with stroke risk. Consumption of milk and other dairy food was determined from a baseline FFQ among 26,556 Finnish male smokers, aged 50–69 years, from the Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study. Whole-milk intake was associated with increased risk of IH (RR, 1.41; 95% CI, 1.02–1.96) and yogurt intake with increased risk of subarachnoid hemorrhage (RR, 1.83; 95% CI, 1.29–2.80). The highest quintile of cream intake was associated with a slight decrease of cerebral infarct risk (RR, 0.81; 95% CI, 0.72–0.92) and IH (RR, 0.72; 95% CI, 0.52–1.00), yet no association was found for total dairy intake, ice cream, cheese, low-fat milk, butter or sour milk and stroke risk.

Prudent diet

Fung et al. prospectively examined the relationship between two dietary patterns, the prudent and the Western diet, in relation to stroke risk. A prudent diet is characterized by higher intakes of fruits, vegetables, whole grains, legumes, and fish, whereas a Western diet has higher intakes of red and processed meats, refined grains, and sweets. During follow-up, 791 strokes occurred, 476 of which were ischemic and 189 hemorrhagic. The Western diet was associated with an increased risk of ischemic stroke (RR, 1.56; 95% CI, 1.05–2.33; P, 0.02 for trend) and total stroke (RR, 1.58; 95% CI, 1.15–2.15; P, 0.0002 for trend). Conversely, the prudent diet was correlated with decreased incidence of total stroke (RR, 0.78; 95% CI, 0.61–1.01), and ischemic stroke (RR, 0.74; 95% CI, 0.54–1.02).

DASH diet

The DASH diet, which emphasizes high intake of fruits, vegetables, grains, low-fat dairy products, nuts, chicken, and fish and low intake of red meat, sweets, and refined carbohydrates, has demonstrated great efficacy in reducing blood pressure and low-density lipoproteins, which are known risk factors for CVD. Fung et al. also demonstrated the benefit of a DASH diet in relation to stroke risk. In that study, 88,517 female nurses from the NHS, aged 34–59 years, were followed for 24 years. During the follow-up period, there were 2,317 stroke cases, among which 1,242 were ischemic and 440 hemorrhagic. The highest quintile of adherence to the DASH diet was significantly associated with reduced risk of total stroke (RR, 0.82; 95% CI, 0.71–0.94) and for ischemic and hemorrhagic stroke (RR, 0.89; 95% CI, 0.73–1.07; RR, 0.86; 95% CI, 0.62–1.18, respectively), although these findings were not significant.

Mediterranean diet

The Mediterranean diet has also been shown to be effective in reducing risk and mortality for a number of chronic diseases including CVD, cancer, and neurodegenerative diseases. Fung et al. also studied the relationship between a Mediterranean diet and stroke mortality among 74,486 women, aged 38–63 years, from the NHS cohort. During the 20-year follow up, the study recorded 1,763 incident strokes, 959 of which were ischemic, 329 hemorrhagic, and 475 not clearly identified. Reduced risk of both CHD and stroke were observed for women in the top quintile of Mediterranean diet adherence as compared to the lowest quintile (RR for CHD, 0.71; 95% CI, 0.62–0.82; P for trend, 0.0001; RR for stroke, 0.87; 95% CI, 0.73–1.02; P for trend, 0.03). A similar reduction in risk was seen for both ischemic and hemorrhagic subtypes, but it was not statistically significant due to small numbers (low power).

Other dietary patterns

Research on low-fat diets, particularly low trans fats and cholesterol, and replacing saturated fats with polyunsatu-
rated and monounsaturated fats, have demonstrated reduced risk of cardiovascular disease. Howard et al.\(^49\) examined the impact of a low-fat dietary pattern on stroke risk and did not observe a protective effect. The population consisted of 48,835 post-menopausal women, aged 50–79 years, from the Women’s Health Initiative Randomized Controlled Dietary Modification Trial, who were randomly assigned to an intervention diet of total fat at 20% of caloric intake, increased fruits, vegetables, and grains. The control group was asked to follow the recommendations of the Dietary Guidelines for Americans. After a 6-year follow-up period, significant changes in dietary pattern among the intervention group were observed, namely, reduced intake of total fat, saturated fat, trans fat, monounsaturated fatty acids and polyunsaturated fatty acids, and increased intake of fiber, vegetables, fruits, whole grains, and soy. However, no association between the dietary intervention and either hemorrhagic or ischemic stroke was observed (HR, 0.90; 95% CI, 0.66–1.22 and HR, 1.01; 95% CI: 0.86–1.18, respectively).

**DISCUSSION**

The findings of this review indicate that stronger evidence exists supporting the benefits of certain dietary factors than others. For example, consumption of fruits and vegetables is protective against stroke, with consumption of three to five servings per day associated with reduced stroke risk compared to the consumption of less than three servings of fruit and vegetables per day. Despite their protective effect, however, research on the salutary effects of individual fruits and vegetables is less clear. Soy products appear to be protective against ischemic stroke in Japanese populations, but the numbers of such studies are too small to allow conclusions to be drawn regarding the different soy products and/or to extrapolate the results to other populations. Compliance with a DASH, Mediterranean, or a prudent diet was found to be associated with decreased stroke risk, while a predominantly Western diet was associated with increased stroke risk. Only one study assessed the association between low-fat diet and stroke risk, and no association was observed.

Evidence for other nutritional parameters and their relationship with stroke risk is not clear. An example is the relationship between fish intake and stroke risk. Consumption of fatty fish, such as tuna and other broiled fish, was generally associated with a decreased risk of ischemic stroke, with the protective effect more pronounced in women. Recently, methods of fish preparation have been better studied, and this has given us greater insight into stroke risk. Fried fish was associated with increased risk of total and ischemic stroke in one study, and salted fish was found to be significantly associated with increased risk of hemorrhagic stroke in another. There is a lack of consistent positive correlation between fish consumption and hemorrhagic stroke, primarily due to insufficient cases, and therefore, low statistical power. Indeed, the dissimilarities between the mechanisms of stroke subtypes may contribute to the differential outcomes, where one could foresee fish consumption affecting processes leading to ischemic stroke and not those related to hemorrhagic outcomes. Overall, the protective effect of fish is generally observed at moderate levels of intake, with higher levels being associated with increased risk of ischemic stroke, especially in men.

With the exception of eggs, which consistently showed no relation to stroke risk, the relation of other animal products such as dairy and meat and stroke has not been clearly elucidated. Finally, there is inadequate data related to the protective effect of cereals and whole-grain intake and risk of ischemic stroke, but in the studies performed to date, such associations remained significant after adjustment for confounding factors.

A limitation commonly mentioned in the studies reviewed was the inability to evaluate the relationship between subtypes of stroke and dietary factors. It was often cited that the limited number of hemorrhagic stroke cases resulted in inadequate power to perform the necessary analysis.\(^21,23,28,30,48\) However, due to the different pathophysiological mechanisms of stroke subtypes, and the unique risk factors involved, it is important to delineate the impact of dietary parameters on stroke types. For some dietary constituents, a biologic mechanism has been identified that is suggestive of their unique effects on stroke subtype risk. In the present review, moderate and high intakes of fatty fish were found to be associated with decreased risk of ischemic stroke,\(^26,27\) which is likely due to the atheromatous plaque-stabilizing quality of omega-3 fatty acids and their putative anticoagulant effects.\(^50,51\) That said, there is some evidence to suggest that the anticoagulant effect can only be observed at high levels of fatty fish intake, which may ultimately lead to an increased risk of hemorrhagic stroke.\(^52\) Additionally, some preliminary evidence suggests that specific amino acids, such as taurine and arginine, found in animal protein may modulate vasoactivity, resulting in reduced blood pressure.\(^52\) Therefore, low intakes of animal fat and protein may have a stronger association with IH as compared to ischemic stroke. Increased risk of IH has been observed among women in the NHS cohort who consume low levels of animal protein and saturated fat, with the latter among hypertensive women only.\(^53\)

A common challenge in attempting to explain nutrition-disease relationships based on epidemiological studies is the variations in the study populations, and caution in interpreting such results is imperative. Patterns
of food consumption, such as amount consumed, method of food preparation, seasonal variation in food intake, and other lifestyle factors, may modify the relationship between nutritional parameters and disease outcomes. For example, Sauve et al. found a protective effect of animal products on stroke mortality; yet this could be attributed to the generally low consumption of animal products, including eggs, dairy, and fish among the Japanese population studied. Similarly, investigators who examined fruit, vegetable, and whole-grain intake among a population of Finnish women, indicated consumption of these foods is generally lower among this group, which may influence the results. Food preparation, especially with fish, may modify the stroke relationship. In the study conducted among a cohort of women in Norfolk, United Kingdom, white fish was the predominantly consumed fish type. These fish were prepared with heavy processing and were not a significant source of omega-3 fatty acids, which are usually thought to be the protective agent in fish. Cross-sectional studies in the United States also indicate there is an influence of fish preparation on stroke risk. The Reasons for Geographic and Racial Differences in Stroke (REGARDS) study found that subjects living in the stroke belt region of the United States had a 50% higher mortality rate than those in the rest of the country. Individuals living in the stroke belt were more likely to consume more than 2 servings of fried fish per week and less likely to consume more than 2 servings of non-fried fish per week. African Americans living in this region were found to consume more fish per week than their white counterparts, yet a larger proportion of the fish was fried, and this group was at twice the risk for new-onset strokes in comparison to the white population in the United States.

Current evidence has shed some light on the benefit of food groups such as fruits and vegetables, fish, and specific dietary patterns in reducing stroke risk and mortality. However, further clarification is needed for other nutritional components including whole grains, animal products, soy, and other dietary patterns, especially vegetarianism. This review found a relatively strong protective effect of soy products among two Asian populations. Studying soy intake and stroke risk within populations, such as in the Adventist Health Study cohort, which has a high soy intake amongst its vegetarian group, would provide us with valuable information related to this relationship. Vegetarian diets have been shown to reduce the risk of hypertension, type II diabetes, ischemic heart disease, and some cancers, yet current evidence is limited for stroke risk.

CONCLUSION

Increasing dietary fruit and vegetable intake is expected to exert a protective effect against stroke. Further work is needed to elucidate the role of whole grains, animal products, and dietary patterns, especially vegetarian diets, and their effects on stroke. Due to the synergistic interaction of nutrients that make it difficult to pinpoint specific nutrients as risk factors for stroke, future research, particularly clinical trials, should also focus on developing stroke prevention recommendations based on food groups and dietary patterns that are palatable and understandable to the general public.

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REFERENCES


