CANADIAN STROKE BEST PRACTICE RECOMMENDATIONS

Secondary Prevention of Stroke

Seventh Edition, 2020

Evidence Table: *Lifestyle & Risk Factor Management (Healthy Balanced Diet)*

Gladstone D, Poppe A (Writing Group Chairs)
on Behalf of the Canadian Stroke Best Practice Recommendations
Secondary Prevention of Stroke Writing Group and in collaboration with the Canadian Stroke Consortium

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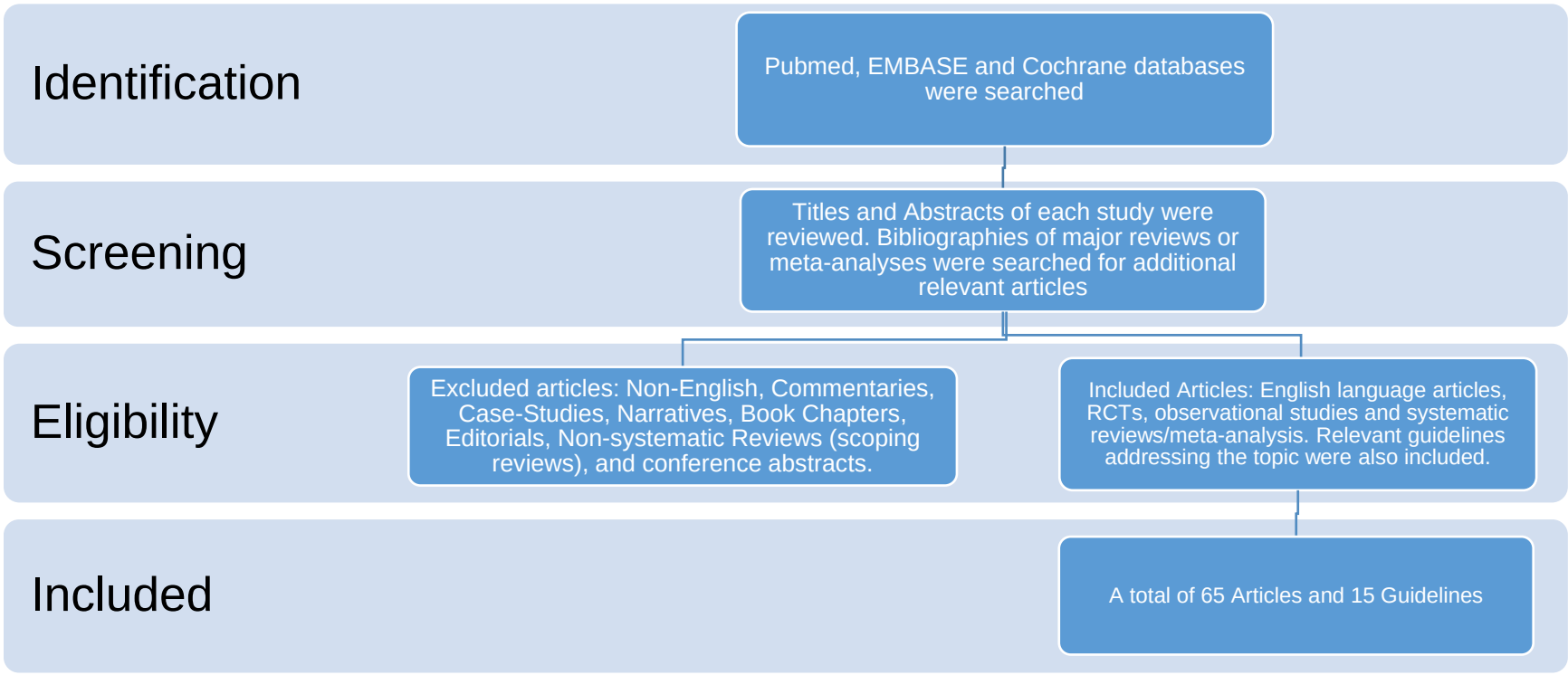
Search Strategy



Pubmed, EMBASE and the Cochrane Central Register of Controlled Trials databases were search using the terms (“Stroke” and “lifestyle” or “diet” or “sodium” or dietary patterns” or “fat” or “dietary supplements” or “vitamins”). Titles and abstract of each article were reviewed for relevance. Bibliographies were reviewed to find additional relevant articles. Articles were excluded if they were: non-English, commentaries, case-studies, narrative, book chapters, editorials, non-systematic review, or conference abstracts. Additional searches for relevant best practice guidelines were completed and included in a separate section of the review.

Published Guidelines

Guideline	Recommendations
Nardocci M, Polsky J, Moubarac JC. How ultra-processed foods affect health in Canada. Report prepared for Heart and Stroke. Montréal: TRANSNUT, Department of Nutrition, University of Montreal; June 2019.	Overall, the evidence provided in this report strongly supports recommendations in the newly revised 2019 Canada's Food Guide to "cook more often" and to choose fresh or minimally processed food on a daily basis. The evidence from this report and a growing number of international studies suggests that the adverse effects of ultra-processed foods on diet and health go well beyond their content of "risk" nutrients and importantly—as shown in this and previous reports—include the displacement of nutritious whole or minimally processed foods and dishes from the diet.
Risk reduction of cognitive decline and dementia: WHO guidelines. Geneva: World Health Organization; 2019. Licence: CC BY-NC-SA 3.0 IGO	The Mediterranean-like diet may be recommended to adults with normal cognition and mild cognitive impairment to reduce the risk of cognitive decline and/or dementia. Quality of evidence: moderate Strength of the recommendation: conditional A healthy, balanced diet should be recommended to all adults based on WHO recommendations on healthy diet. Quality of evidence: low to high (for different dietary components) Strength of the recommendation: conditional Vitamins B and E, polyunsaturated fatty acids and multi-complex supplementation should not be recommended to reduce the risk of cognitive decline and/or dementia. Quality of evidence: moderate Strength of the recommendation: strong
Arnett DK, Blumenthal RS, Albert MA, Buroker AB, Goldberger ZD, Hahn EJ, Himmelfarb CD, Khera A, Lloyd-Jones D, McEvoy JW, Michos ED, Miedema MD, Muñoz D, Smith SC Jr, Virani SS, Williams KA Sr, Yeboah J, Ziaeian B. **2019 ACC/AHA guideline on the primary prevention of cardiovascular disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines.** ***Circulation.* 2019;000:exxx–exxx. DOI: 10.1161/CIR.0000000000000678** **(selected)**	A diet emphasizing intake of vegetables, fruits, legumes, nuts, whole grains, and fish is recommended to decrease ASCVD risk factors. COE I; LOE B-R.
Tobe SW, Stone JA, Anderson T, et al. Canadian Cardiovascular Harmonized National Guidelines Endeavour (C-CHANGE)	**Primary prevention** To prevent hypertension and reduce blood pressure in hypertensive adults, consider reducing sodium intake toward 2000 mg (5 g of salt or 87 mmol of sodium) per day.

Guideline	Recommendations
guideline for the prevention and management of cardiovascular disease in primary care: 2018 update. ***CMAJ* 2018; 190: E1192-e206** **(selected)**	We suggest that all individuals be encouraged to moderate energy (caloric) intake to achieve and maintain a healthy body weight and adopt a healthy dietary pattern to lower their risk of cardiovascular disease: • Mediterranean dietary pattern • Portfolio dietary pattern • DASH dietary pattern • Dietary patterns high in nuts (≥ 30 g/d) • Dietary patterns high in legumes (≥ 4 servings/wk) • Dietary patterns high in olive oil (≥ 60 mL/d) • Dietary patterns rich in fruits and vegetables (≥ 5 servings/d) • Dietary patterns high in total fibre (≥ 30 g/d); and whole grains (≥ 3 servings/d) • Low glycemic load or low glycemic index dietary patterns • Vegetarian dietary patterns **Secondary prevention** Persons at risk of stroke and patients who have had a stroke should be assessed for vascular disease risk factors, lifestyle management issues (diet, sodium intake, exercise, weight, alcohol intake, smoking) and use of oral contraceptives or hormone replacement therapy. Persons at risk of stroke should receive information and counselling about possible strategies to modify their lifestyle and risk factors. Referrals to appropriate specialists should be made where required. They may provide more comprehensive assessments and structured programs to manage specific risk factors
Nerenberg KA, Zarnke KB, Leung AA, Dasgupta K, Butalia S, McBrien K, Harris KC, Nakhla M, Cloutier L, Gelfer M, Lamarre-Cliche M. **Hypertension Canada's 2018 Guidelines for Diagnosis, Risk Assessment, Prevention, and Treatment of Hypertension in Adults and Children.** ***Can J Cardiol* 2018 May 1;34(5):506-25.** **(selected)**	I. Health behaviour management Guidelines D. Diet It is recommended that hypertensive patients and normotensive individuals at increased risk of developing hypertension consume a diet that emphasizes fruits, vegetables, low-fat dairy products, whole grain foods rich in dietary fibre, and protein from plant sources that is reduced in saturated fat and cholesterol (Dietary Approaches to Stop Hypertension diet) (Grade B). E. Sodium intake T o prevent hypertension and reduce BP in hypertensive adults, consider reducing sodium intake toward 2000 mg (5 g of salt or 87 mmol of sodium) per day (Grade A). F. Calcium and magnesium intake Supplementation of calcium and magnesium is not recommended for the prevention or treatment of hypertension (Grade B).

Guideline	Recommendations
	G. Potassium intake In patients not at risk of hyperkalemia, increase dietary potassium intake to reduce BP (Grade A).
Heart and Stroke Foundation of Canada Position Statement **Saturated fat, heart disease and stroke** **(selected)**	1. Eat a healthy balanced diet. • Consume a variety of natural/whole and minimally processed foods at every meal. • Eat more vegetables and fruit. Fill half your plate with vegetables and fruit at every meal. Buy fresh or frozen unsweetened fruit, or fruit canned in water without added/free sugars or artificial/non-caloric sweeteners. Buy fresh or frozen vegetables without added sauce, or canned vegetables with no added salt. • Choose whole grains. • Include a variety of proteins from various sources. These protein sources can include beans, lentils, legumes, nuts, lower fat dairy or dairy alternatives (without added/free sugars or artificial/non-caloric sweeteners), lean meats, poultry and fish. • Eat fewer highly processed foods which include highly refined foods, confectionaries, sugary drinks, processed meats, and snack foods. • Plan healthy snacks. Include foods from at least 2 food groups with 1-2 servings of vegetables or fruit at every snack. • Drink water to satisfy thirst. Avoid consumption of sugary drinks including soft drinks, sports drinks, fruit drinks, 100 per cent fruit juices, and ready-to-drink sweetened coffees and teas. • Learn what a recommended serving size looks like and choose healthy portions for meals and snacks.
Clinical Guidelines for Stroke Management 2017. Melbourne (Australia): National Stroke Foundation. Section 4 Secondary Prevention	**Diet** Practice point People with stroke or TIA should be advised to manage their dietary requirements in accordance with the Australian Dietary Guidelines. All stroke survivors should be referred to an Accredited Practising Dietitian who can provide individualised dietary advice.
Leung AA, Daskalopoulou SS, Dasgupta K, McBrien K, Butalia S, Zarnke KB, et al. for Hypertension Canada **Hypertension Canada's 2017 Guidelines for Diagnosis, Risk Assessment, Prevention, and Treatment of Hypertension in Adults,** ***Canadian Journal of Cardiology* 2017;33(5):557-576.**	**Primary Prevention (general)** D. Diet: It is recommended that hypertensive patients and normotensive individuals at increased risk of developing hypertension consume a diet that emphasizes fruits, vegetables, low-fat dairy products, whole grain foods rich in dietary fibre, and protein from plant sources that is reduced in saturated fat and cholesterol (Dietary Approaches to Stop Hypertension [DASH] diet. (Grade B). E. Sodium intake: To prevent hypertension and reduce BP in hypertensive adults, consider reducing sodium intake towards 2000 mg (5 g of salt or 87 mmol of sodium) per day (Grade A). F. Calcium and magnesium intake: Supplementation of calcium and magnesium is not recommended for the prevention or treatment of hypertension (Grade B). G. Potassium intake: In patients not at risk of hyperkalemia, increase dietary potassium intake to reduce BP (Grade A).

Guideline	Recommendations
American Academy of Family Physicians (AAFP). Summary of recommendations for clinical preventive services. Leawood (KS), 2017.	The AAFP recommends offering or referring adults who are overweight or obese and have additional cardiovascular disease (CVD) risk factors to intensive behavioral counseling interventions to promote a healthful diet and physical activity for CVD. (2014) (Grade: B recommendation). The AAFP recommends that primary care professionals individualize the decision to offer or refer adults without obesity who do not have hypertension, dyslipidemia, abnormal blood glucose, or diabetes to behavioral counseling to promote a healthful diet and physical activity. (2016) (Grade: C recommendation).
Intercollegiate Stroke Working Party. Royal College of Physicians. National Clinical guidelines for stroke. 5th Edition 2016, Edinburgh, Scotland	**Diet** A- People with stroke or TIA should be advised to eat an optimum diet that includes: − five or more portions of fruit and vegetables per day from a variety of sources; − two portions of oily fish per week (salmon, trout, herring, pilchards, sardines, fresh tuna). B- People with stroke or TIA should be advised to reduce and replace saturated fats in their diet with polyunsaturated or monounsaturated fats by: − using low-fat dairy products; − replacing butter, ghee and lard with products based on vegetable and plant oils; − limiting red meat intake, especially fatty cuts and processed meat. C- People with stroke or TIA who are overweight or obese should be offered advice and support to aid weight loss including adopting a healthy diet, limiting alcohol intake to 2 units a day or less and taking regular exercise. Targeting weight reduction in isolation is not recommended. D- People with stroke or TIA should be advised to reduce their salt intake by: − not adding salt to food at the table; − using little or no salt in cooking; − avoiding high-salt foods, e.g. processed meat such as ham and salami, cheese, stock cubes, pre-prepared soups and savoury snacks such as crisps and salted nuts. E- People with stroke or TIA who drink alcohol should be advised to limit their intake to 14 units a week, spread over at least three days. F- Unless advised to do so for other medical conditions, people with stroke or TIA should not routinely supplement their diet with: − B vitamins or folate; − vitamins A, C, E or selenium; − calcium with or without vitamin D.
Kernan WN, Ovbiagele B, Black HR, Bravata DM, Chimowitz MI, Ezekowitz MD, Fang MC, Fisher M, Furie KL, Heck DV, Johnston SC, Kasner SE, Kittner SJ, Mitchell PH, Rich MW, Richardson D, Schwamm LH, Wilson JA	**Diet** • It is reasonable to conduct a nutritional assessment for patients with a history of ischemic stroke or TIA, looking for signs of overnutrition or undernutrition (Class IIa; Level of Evidence C). New recommendation • Patients with a history of ischemic stroke or TIA and signs of undernutrition should be referred for individualized nutritional counseling (Class I; Level of Evidence B). New recommendation

Guideline	Recommendations
Guidelines for the prevention of stroke in patients with stroke and transient ischemic attack: a guideline for healthcare professionals from the American heart association/American stroke association. ***Stroke 2014*;45:2160-2236.**	• Routine supplementation with a single vitamin or combination of vitamins is not recommended (Class III; Level of Evidence A). New recommendation • It is reasonable to recommend that patients with a history of stroke or TIA reduce their sodium intake to less than ≈2.4 g/d. Further reduction to <1.5 g/d is also reasonable and is associated with even greater BP reduction (Class IIa; Level of Evidence C). New recommendation • It is reasonable to counsel patients with a history of stroke or TIA to follow a Mediterranean-type diet instead of a low-fat diet. The Mediterranean-type diet emphasizes vegetables, fruits, and whole grains and includes low-fat dairy products, poultry, fish, legumes, olive oil, and nuts. It limits intake of sweets and red meats (Class IIa; Level of Evidence C).
Meschia JF, Bushnell C, Boden-Albala B, Braun LT, Bravata DM, Chaturvedi S, Creager MA, Eckel RH, Elkind MSV, Fornage M, Goldstein LB, Greenberg SM, Horvath SE, Iadecola C, Jauch EC, Moore WS, Wilson JA; on behalf of the American Heart Association Stroke Council, Council on Cardiovascular and Stroke Nursing, Council on Clinical Cardiology, Council on Functional Genomics and Translational Biology, and Council on Hypertension. **Guidelines for the primary prevention of stroke: a statement for healthcare professionals from the American Heart Association/American Stroke Association.** ***Stroke*. 2014;45:3754–3832. (selected)**	1. Reduced intake of sodium and increased intake of potassium as indicated in the US Dietary Guidelines for Americans are recommended to lower BP (Class I; Level of Evidence A). 2. A DASH-style diet, which emphasizes fruits, vegetables, and low-fat dairy products and reduced saturated fat, is recommended to lower BP127,218 (Class I; Level of Evidence A). 3. A diet that is rich in fruits and vegetables and thereby high in potassium is beneficial and may lower the risk of stroke (Class I; Level of Evidence B). 4. A Mediterranean diet supplemented with nuts may be considered in lowering the risk of stroke (Class IIa; Level of Evidence B).
Eckel RH, Jakicic JM, Ard JD et al. **2013 AHA/ACC guideline on lifestyle management to reduce cardiovascular risk: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines.**	**Diet** Advise adults who would benefit from LDL–C lowering to: Consume a dietary pattern that emphasizes intake of vegetables, fruits, and whole grains; includes low-fat dairy products, poultry, fish, legumes, nontropical vegetable oils and nuts; and limits intake of sweets, sugar-sweetened beverages and red **meats (Level A recommendation),** a. Adapt this dietary pattern to appropriate calorie requirements, personal and cultural food preferences, and nutrition therapy for other medical conditions (including diabetes mellitus)**,** b. Achieve this pattern by following plans such as the DASH dietary pattern, the USDA Food Pattern, or the AHA Diet. Aim for a dietary pattern that achieves 5% to 6% of calories from saturated fat (Level A recommendation).

Guideline	Recommendations
***J Am Coll Cardiol* 2014;63(25 Pt B):2960-2984.**	Reduce percent of calories from saturated fat (Level A recommendation). Reduce percent of calories from *trans* fat *(Level A recommendation)* Advise adults who would benefit from BP lowering to: Consume a dietary pattern that emphasizes intake of vegetables, fruits, and whole grains; includes low-fat dairy products, poultry, fish, legumes, nontropical vegetable oils and nuts; and limits intake of sweets, sugar-sweetened beverages and red **meats (Level A recommendation),** a. Adapt this dietary pattern to appropriate calorie requirements, personal and cultural food preferences, and nutrition therapy for other medical condition**s (including diabetes mellitus), b** Achieve this pattern by following plans such as the DASH dietary pattern, the USDA Food Pattern, or AHA diet. Reduce sodium intake (Level A recommendation) a. Consume no more than 2,400 mg of sodium/day b. Further reduction of sodium intake to 1,500 mg/day is desirable since it is associated with even greater reduction in BP c. Reduce intake by at least 1,000 mg/day since that will lower BP, even if the desired daily sodium intake is not yet achieved Combine the DASH dietary pattern with lower sodium intake.
Perk J, De BG, Gohlke H, Graham I, Reiner Z, Verschuren WM, et al. **European Guidelines on cardiovascular disease prevention in clinical practice (version 2012): the Fifth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of nine societies and by invited experts).** ***Atherosclerosis* 2012; 223:1–68.** **(selected)**	**Nutrition** A healthy diet is recommended as being the cornerstone of CVD prevention. Class I; Level B; GRADE Strong

Guideline	Recommendations
The European Stroke Organisation (ESO) Executive Committee and the ESO Writing Committee **Guidelines for Management of Ischaemic Stroke and Transient Ischaemic Attack 2008** ***Cerebrovasc Dis 2008*;25:457–507**	**Diet** • A diet low in salt and saturated fat, high in fruit and vegetables and rich in fibre is recommended (Class III, Level B) Weight Management • Subjects with an elevated body mass index are recommended to take a weight-reducing diet (Class III, Level B) **Vitamin and Supplements** • Antioxidant vitamin supplements are not recommended (Class I, Level A)
Additional Resources	
English C, MacDonald-Wicks L, Patterson A, Attia J, Hankey GJ. **The role of diet in secondary stroke prevention.** ***Lancet Neurol.* 2020 Dec 18:S1474-4422(20)30433-6.**	**Summary of findings and suggested guidance for clinical practice** **i) People at risk of stroke to prevent first stroke (suggested guidance)** Folic acid supplementation: People at risk of stroke living in areas of low folate fortification should be advised to take low-dose folic acid supplements (0·5–5·0 mg/day) with or without low-dose vitamin B_{12} (≤0·05 mg/day) Vitamin D supplements: People at risk of stroke should not be advised to take vitamin D supplements Vitamin B3 (niacin) supplements: People at risk of stroke should not be advised to take vitamin B3 (niacin) supplements Omega-3 fatty acids: People at risk of stroke should not be advised to take omega-3 supplements High intakes of fruit and vegetables: People at risk of stroke should be advised to increase fruit and vegetable consumption Low-fat diet: People at risk of stroke should not be advised to follow a low-fat diet Mediterranean-style diet: People at risk of stroke should be supported to follow a Mediterranean-style diet **ii) People with previous stroke or TIA or at risk of stroke to reduce blood pressure (suggested guidance)** Salt reduction: People with previous stroke should be supported to limit salt intake DASH-style diet: People at risk of stroke should be supported to follow a DASH-style diet

Evidence Tables

Diet & Stroke Risk

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
i) Studies primarily evaluating fruit and vegetable consumption					
Miller et al. 2017 **International** **Prospective study** ***Prospective Urban Rural Epidemiology (PURE) study***	NA	Persons aged 35–70 years, enrolled between Jan 1, 2003, and March 31, 2013) from 18, high, low and middle-income countries. Mean age was 50.3 years, 41.7% were men.	The dietary intakes of 135,335 individuals was recorded using validated food frequency questionnaires. Combined daily intakes of fruits vegetables and legumes were categorized as <1, 2-3, 3-4, 4-5, 5-6, 6-7, 7-8 and ≥8. Models were adjusted for age, sex, centre, energy intake, current smoker, diabetes, urban or rural location, physical activity, education level, and tertiles of white meat, red meat, and intake of breads, cereals, and vegetables.	**Primary outcomes:** Total mortality and major cardiovascular events (fatal CVD, non-fatal MI, stroke, and heart failure).	Median follow-up was 7.4 years. There were 4,784 major CVD events, 1,649 CVD deaths, and 5,796 total deaths Overall, mean fruit, vegetable, and legume intakes were 1·51 (SD 1·77), 2·01 (1·55), and 0·40 (0·48) servings per day, respectively. Combined intake was 3·91 (2·77) servings per day. Higher combined intakes of fruit, vegetables and legumes were associated with significant reductions in the risks of non-CVD deaths and total mortality only. The lowest level of risk for both outcomes was at intake levels of 3-4 servings per day (HR=0·77, 95% CI 0·66–0·89 and HR=0·78, 95% CI 0·69–0·88, respectively). *Fruit intake* The risks of CVD mortality, non-CVD mortality and total mortality were decreased significantly with increasing consumption of fruit (<3 serving/week vs. 3/week to <1 day vs. 1 to <2/day, 2 to <3/day and >3 per day) *Vegetable intake* The risks of none of the outcomes were reduced significantly with increasing intake of vegetables (<3 serving/week vs. 3/week to <1 day vs. 1 to <2/day, 2 to <3/day and >3 per day) *Legume intake* The risks of non-CVD mortality and total mortality were decreased significantly with increasing

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					consumption of legumes (<1/month, 1/month to <1/week, 1/week to <3/week, 3/week to <1/day and >1/day).
Du et al. 2016 China Kadoorie Biobank Study **China** **Prospective study**	NA	512,891 non-disabled adults, aged 35-74 years, who were recruited from the general population, from 10 regional study sites between 2004-08. Persons with a history of CVD or antihypertensive treatment were excluded. Mean age at admission was 50.5 years, 58.8% were women. Mean BMI was 23.5	Baseline surveys were conducted to collect information on diet and lifestyle factors. A physical exam was also conducted to obtain data on blood pressure, random blood sugar, height and weight. A food frequency questionnaire was used to collect information on 12 major food groups, including the average daily number of servings of fruit consumed over the past 12 months. Response categories were daily, 4-6/week, 1-3/week, monthly and never/rarely. A portion of the participants were resurveyed in 2008 and 2013.	**Primary outcomes:** Cardiovascular death, major coronary events ++nonfatal MI, hemorrhagic and ischemic stroke Analysis was adjusted for education, ETOH consumption, smoking, physical activity, survey season, and consumption of other dietary components, and were stratified by age, sex and region.	During 3.2 million person-years of follow-up, there were 14,579 ischemic strokes and 3,523 hemorrhagic strokes. The incidence rates of ischemic and hemorrhagic stroke (no./1,000 person-years) among the fruit consumption categories were: Never/rarely: 7.58/2.05 Monthly: 4.75/1.48 1-3 days/week: 3.88/1.00 4-6 days/week: 3.42/0.74 Daily: 5.17/0.47 Compared with rarely/never category, the consumption of any level of fruit consumption was associated with a significantly reduced risk of ischemic stroke. The reduction was dose-dependent, with daily consumption associated with the lowest risk (HR=0.75 vs. 0.79, 0.73 and 0.90 in descending order for the remaining categories. Compared with rarely/never category, the consumption of any level of fruit consumption was associated with a significantly reduced risk of hemorrhagic stroke. The greatest reduction in risk was associated with the daily consumption category (HR=0.64). In descending order, the HRs associated with the remaining 3 consumption categories were 0.76, 0.81 and 0.86, respectively.
Feigin et al. 2016 **International** **Retrospective study**	NA	Population-based data from 188 countries from 1990 to 2013.	Data from the Global Burden of Disease Study 2013 was used to estimate the population-attributable fraction (PAF) of stroke-related disability-adjusted life-years (DALYs) associated with 17 potentially modifiable risk	**Primary outcome**: Stroke burden (expressed as DALYs)	**Fruits** Globally, 35.6% (95% uncertainty interval 26.5%-42.0%) of the stroke burden was attributed to diets low in fruit. In high income countries, 24.3% (95% uncertainty interval 16.0%-29.7%) of the stroke burden was attributed to diets low in fruits.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
			factors (including diets low in fruits and vegetables) in high-income countries and low-income and middle-income countries. Diets low in fruits were defined as consumption of <200 g/day. Diets low in vegetables were defined as consumption of <350 g/day.		**In Canada, 20.4% (95% uncertainty interval 9.7%-31.5%) of the stroke burden was attributed to diets low in fruits** Globally, during the study period, there was an increase of 22.9% (95% UI 18.8%-24.3%) in the burden of stroke related to diets low in fruits. **Vegetables:** Globally, 20.0% (95% uncertainty interval 17.0%-22.4%) of the stroke burden was attributed to diets low in vegetables. In high income countries, 20.9% (95% uncertainty interval 18%-22.5%) of the stroke burden was attributed to diets low in vegetables. **In Canada, 19.5% (95% uncertainty interval 14.4%-25.5%) of the stroke burden was attributed to diets low in vegetables.** Globally, during the study period, there was an increase of 23% (95% UI 22.7%, 23.3%) in the burden of stroke related to diets low in vegetables.
Hu et al. 2014 **China** **Systematic review & meta-analysis**	NA	20 prospective cohort studies including 760,629 participants.	The risk of stroke among the lowest vs. highest categories of fruit and vegetable intake in each study were pooled. Food frequency questionnaires were used to estimate fruit/veg intake in all studies, except 3. Most included studies adjusted for age, smoking, blood pressure, physical activity and BMI	**Primary outcome:** Stroke	The mean duration of follow-up ranged from 4-37 years, during which time there were 16,981 stroke events. The risk of stroke was significantly lower in the groups associated with the highest intake of fruits and vegetables. Total combined fruit and veg: RR=0.79, 95% CI 0.75-0.84 Fruit: RR=0.77, 95% CI 0.71-0.84 Vegetables: RR=0.86, 95% CI 0.79-0.93 For every increase of 200 g/day of vegetables, stroke risk was decreased by 11% (RR=0.89, 95% CI 0.81-0.98).

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					For every increase of 200 g/day of fruit, stroke risk was decreased by 32% (RR=0.68, 95% CI 0.56-0.82).
Sharma et al. 2013 **Canada** **Prospective cohort study**	NA	174,888 participants without a history of stroke (78,844 men, 96,044 women) aged 45 to 75 years across 5 ethnic groups. The average ages of women and men at study entry were 66 and 59 years, respectively. 10% of participants had a history of diabetes, 37% had a history of hypertension, 39% were current smokers and 19% had a BMI >30	A one-time quantitative food frequency questionnaire was used to estimate daily number of servings of fruit and vegetable consumed. An individual's daily consumption was then compared with the USDA's food pyramid. Based on caloric intake, the recommendations for vegetables range from 3-5 servings/day and 2-4 servings/day for fruit. Compliance was categorized as adherent vs. non-adherent (<100% vs. ≥100%) of the daily servings of fruits and vegetables of the recommended number of servings based of age and caloric intake level.	**Primary outcome:** Fatal stroke Analyses were adjusted for: age, time in study, education, energy intake, smoking status, other dietary components, BMI, physical activity, alcohol intake, history of diabetes	At the end of follow-up (8 years), there were 860 fatal strokes. The average number of daily vegetable servings for all men and those who died of stroke were 4.5±2.8 and 4.3±2.7. The average number of daily fruit servings for all men and those who died of stroke were 3.0±2.6 and 3.2±2.5. The average number of daily vegetable servings for all women and those who died of stroke were 4.6±2.9 and 4.2±2.6. The average number of daily fruit servings for all women and those who died of stroke were 3.5±2.9 and 3.4±2.6. The risk of stroke mortality was not associated with adherence to USDA dietary recommendations for fruits or vegetables. **Men (434 fatal strokes)** Vegetables: adjusted RR (adherent vs. non-adherent) =0.99, 95% CI 0.81-1.22 Fruit: adjusted RR=1.13, 95% CI 0.92-1.37 **Women (426 fatal strokes)** Vegetables: adjusted RR=0.84, 95% CI 0.68-1.04 Fruit: adjusted RR=0.97, 95% CI 0.75-1.19
He et al. 2006 **UK** **Systematic review & meta-analysis**	NA	8 cohort studies including 257,551 participants. Data from the Nurses' Health Study, the Health Professionals' Follow-up Study, NHANES I, Danish Diet, Cancer and Health Study, Life Span Study and ARIC studies, were included.	Fruit and vegetable consumption was standardized among studies and comprised 3 categories of daily intake: <3 servings, 3-5 servings and >5 servings, based on a serving size of 77 grams of vegetables and 80 g of fruit.	**Primary outcome:** Risk of stroke Most of the included studies, adjusted risk estimates for: age, sex, smoking, alcohol intake, education, BMI, physical activity, total energy intake, blood pressure, history of diabetes,	Over an average of 13 years of follow-up, there were 4,917 stroke events. Increasing servings of fruits and vegetables/day was associated with a significantly decreased risk of stroke (compared with <3 servings) 3-5 servings/day: adjusted RR=0.89, 95% CI 0.83-0.97 >5 servings/day: adjusted RR=0.74, 95% CI 0.69-0.79.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
				cholesterol, consumption of fats and animal products	In subgroup analysis, the protective effect remained significant regardless of sex (male vs. female), duration of follow-up (<10 vs. ≥10 years), and dietary assessment method (food frequency questionnaire vs. other method). The protective effect was significant for ischemic stroke at both intake levels, but was only significant for the highest intake of fruit/veg for hemorrhagic stroke. The protective effect was significant for fruit consumption at both intake levels, but was only significant for the highest intake for vegetable consumption.
ii) Studies evaluating fat consumption					
Dehghan et al. 2017 **Canada** **Prospective study *Prospective Urban Rural Epidemiology (PURE) study***	NA	Persons aged 35–70 years, enrolled between Jan 1, 2003, and March 31, 2013) from 18, high, low and middle-income countries. Mean age was 50.3 years, 41.7% were men.	The dietary intakes of 135,335 individuals was recorded using validated food frequency questionnaires. Intakes of nutrients (CHO, fats and protein) were categorized into quintiles based on percentage of energy provided by nutrients. Models were adjusted for age, sex, education, waist-to-hip ratio, smoking, physical activity, diabetes, urban or rural location, and energy intake.	**Primary outcomes:** Total mortality and major cardiovascular events (fatal CVD, non-fatal MI, stroke, and heart failure).	Median follow-up was 7·4 years. On average, 61.2% of energy was derived from CHO, 23.5% from fat and 15.2% from protein. During follow-up, there were 5,796 deaths and 4,784 major CVD events (2,143 MI and 2,234 strokes). The risks of all mortality and non-CVD mortality were significantly increased in persons consuming higher amounts of CHO (Q5 vs Q1: HR=1·28, 95% CI 1·12–1·46 and HR=1·36, 95% CI 1·16–1·60, respectively). The risk of the other primary outcomes was not increased or decreased significantly with increasing CHO intake. The risks of all mortality, non-CVD mortality and stroke were significantly decreased in persons consuming higher amounts of fat (Q5 vs Q1: HR=0.77, 95% CI 0.67-0.87, HR=0.70, 95% CI 0.60-0.82, and HR= 0·82, 95% CI 0·68–1·00, respectively). The risk of the other primary outcomes was not increased or decreased significantly.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					The risks of all mortality, stroke and non-CVD mortality were significantly decreased in persons consuming higher amounts of saturated fat, while the risks of mortality and non-CVD mortality were significantly reduced in persons consuming higher amounts of mono and polyunsaturated fats. The authors concluded the findings do not support the current recommendation to limit total fat intake to less than 30% of energy and saturated fat intake to less than 10% of energy.
Kiage et al. 2014 **USA** **Prospective cohort study**	NA	17,107 participants, ≥45 years, without a previous history of stroke included in the REGARDS study. Mean age was 65 years	Consumption of trans fat intake was assessed using the self-administered Block 1998 food-frequency questionnaire at baseline and categorized into quintiles. The relationship between incident stroke and trans-fat consumption was examined.	**Primary outcome:** Incident stroke, ischemic stroke Models were adjusted for age, sex, smoking status, race, region, alcohol use, education, waist circumference, physical activity, diabetes, ischemic heart disease, hypertension, heart failure, kidney failure, medications, total energy intake, and intakes of saturated fat, monounsaturated fat, polyunsaturated fat, and protein	Median duration of follow-up was 6.8 years, during which time there were 479 incident strokes. In the fully adjusted model, the overall risks of stroke and ischemic stroke were not significantly increased (HR=1.07, 95% CI 0.97-1.18 and HR=1.06, 95% CI 1.18). There was a significant sex interaction (p=0.06), therefore results for men and women were reported separately. Men: All stroke HR=1.14, 95% CI 1.02-1.28; ischemic stroke HR=1.13, 95% CI 1.00-1.28 Women: All stroke HR=0.93, 95% CI 0.79-1.11; ischemic stroke HR=0.93, 95% CI 0.77-1.12
De Oliveira Otto et al. 2012 **USA** **Prospective cohort study *Multi-Ethnic Study of Atherosclerosis (MESA)***	NA	5,209 persons aged 45-84 years, without clinical CVD, recruited from 6 US communities. Mean age was approx. 62 years	Baseline 120-item FFQs were conducted and used to estimate saturated fat levels from various foods (dairy, meat, butter, and plants). The relationship between saturated fat (SF) and the development of CVD was examined.	**Primary outcome:** Cardiovascular disease The model was adjusted for age, sex, race-ethnicity, energy intake, location (field centre), education, active and sedentary leisure activities, alcohol intake, smoking dietary supplements, cholesterol-lowering medications,	There were 316 new cases of CVD identified during 10-year follow-up (36,364 person-years). For each 5 g/d increase in SF, the risk of CVD was significantly higher or lower depending on the food source Total SF: HR=0.86, 95% CI 0.75-0.97, p=0.02 Dairy SF: HR=0.79, 95% CI 0.68-0.92, p<0.01 Meat SF: 1.26, 95% CI 1.02-1.54, p=0.03 Butter SF: 0.87, 95% CI 0.66-1.15, p=0.33 Plant SF: HR=1.00, 95% CI 0.50-2.01, p=0.99 Mixed sources: HR=1.01, 95% CI 0.77-1.32, p=0.96

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
				fruit/vegetable intake, vit D and PUFA	The pattern of risk was similar for each 5% increment of SF as a percentage of total energy intake. The substitution of 2% of energy from meat with energy from dairy products was associated with a significantly decreased risk of CVD (HR=0.75, 95% CI 0.63-0.91), while substitutions of butter and plant sources of SF were not. Across quintiles, there was an inverse association between dairy SF and CVD (Q5 vs. Q1; HR=0.56, 95% CI 0.38-0.82, p=0.01). There were no significant associations between any of the other sources of SF and CVD.
Siri-Tarino et al. 2010 **US** **Systematic review & meta-analysis**	NA	21 prospective cohort studies, including the results from 347,747 subjects. Stroke was the outcome in 8 of the included studies (n=179,436). In the stroke studies, participants ranged from 35-45 to 59-89 years at baseline. Studies included men only (n=4), women only (n=1) and both sexes (n=3)	Dietary fat intake was assessed using a food frequency questionnaire (n=4), 24-hour recall (n=3) and 1-day diet record (n=1). Diet was assessed only at baseline in 6 studies and 3 and 4 times at 2-4-year intervals in 2 studies.	**Primary outcome:** Stroke events: total stroke (n=2), ischemic stroke (n=3), hemorrhagic stroke (n=2), fatal stroke (n=1) Variables adjusted for included: age, sex (where applicable), energy intake, other dietary components, smoking status, alcohol intake, BMI, physical activity, hypertension or blood pressure, menopausal status (where applicable), other stroke risk factors, family history of stroke	The average duration of follow-up ranged from 8-23 years. There were 2,362 total stroke events. Fat intake: in studies that compared 1st and 5th quintile, (n=2) mean fat intakes were 20g vs.36g/day and 17g vs. 31 g/day. In studies that compared 1st and 4th quartile, (n=1) mean fat intake was 5.2g vs.17.1g/day. Fat comprised an average of 12.7% and 15% of total calories. Fat intakes for men and women were calculated separately in one study. Mean fat intake was 12.3% of total calories for men (1st quartile) compared with 22.3% in the 4th quartile. Results for women were similar. Fat intake was not reported in 2 studies. There was a significant reduction in the risk of hemorrhagic stroke in 2 studies, but there was a non-significant reduction for all other stroke events. Adjusted RR=0.81, 95% CI 0.62-1.05, p=0.11
Micha et al. 2010 **USA**	NA	20 studies (17 prospective cohort and 3 case-control) including 1,218,380 subjects who ranged in age from 15-55	Examination of red and processed meats.	**Primary outcomes:** Coronary heart disease (CHD), diabetes, stroke	Follow-up periods ranged from 3-18 years (4,381 to 856,539 person years). There were 2,280 stroke events.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Systematic review & meta-analysis		years to 46-103 years at baseline.	Most studies used validated food-frequency questionnaires.	Most studies adjusted for sociodemographic and disease risk factors	Mean (±sd) daily intakes (servings) from lowest to highest category of intake were: Red meat: 1.1±1.1 vs. 8.3±2.7 Processed meat: 0.4±0.8 vs. 5.7±3.9 Total: 1.8±1.7 vs. 10.5±4.2 The risk of stroke was evaluated as an outcome in 3 studies. There was no association between meat consumption and incident stroke. Red meat (100 g/day): RR=1.17, 95% CI 0.40 to 3.43 Results from 2 studies included. Processed meat (50 g/day): RR=1.14, 95% CI 0.94-1.39. Results from 2 studies included. Total meat (100 g/day); RR=1.24, 95% CI 1.08-1.43. Results from 2 studies included.
He et al. 2003 **USA** **Prospective cohort study**	NA	43,732 men aged 40-75 years included in the Health Professionals' follow-up study who were free of cardiovascular disease and diabetes at baseline	Dietary intake was assessed on 3 occasions using a semi quantitative food frequency questionnaire. There were 9 response categories ranging from <1/month to ≥6x/day. All dietary fat sources were collected.	**Primary outcome:** Fatal and non-fatal stroke Analysis were adjusted for: i) age and smoking and ii) multivariable (BMI, physical activity, history of hypertension, smoking status, aspirin use, alcohol intake, dietary intake and hypercholesterolemia)	During the 14-year follow-up period, there were 725 stroke events (ischemic n=455, hemorrhagic n=125, unknown etiology n=145). There were no associations between amount of total fat, source of fat (animal or vegetable), type of fat (saturated, unsaturated, monounsaturated, polyunsaturated, trans fat or cholesterol) or selected foods (red meat, high-fat dairy products, nuts or eggs) and incidence of ischemic or hemorrhagic stroke. For example, comparing lowest to highest quintile of fat intake in fully adjusted analyses: Total fat: RR (ischemic stroke) =0.91, 95% CI 0.65-1.28, p for trend=0.77.
iii) Studies evaluating dairy consumption					
Dehghan et al. 2018 **Canada** **Prospective study**	NA	136 384 persons aged 35-70 years from 21 countries enrolled between Jan 1, 2003, and July 14, 2018. Mean age was 50.1 years, 41.7% were men.	Habitual dietary intakes were recorded using validated FFQs. Dairy products included milk, yoghurt, cheese, yoghurt drinks, and mixed dishes prepared with dairy and included high-fat and low-	**Primary outcome:** Composite of mortality or major cardiovascular events (death from cardiovascular causes, non-fatal MI, stroke, or heart failure). **Secondary outcomes:**	Median duration of follow-up was 9.1 years. There were 10,567 (7·7%) persons who either died (n=6,796) or had major cardiovascular events (n=5,855; 4,796 non-cardiovascular deaths, 2,000 cardiovascular deaths, ,2594 MI, 2,718 strokes, and 516 cases of heart failure).

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Prospective Urban Rural Epidemiology (PURE) study			fat products. Intakes were categorized by quintiles (0 servings/day, <1/day, 1-2/day and >2/day).	Total mortality and major cardiovascular disease (fatal and nonfatal MI, fatal and non-fatal strokes, heart failure, and cardiovascular mortality). Models were adjusted for age, sex, education, urban or rural location, smoking status, physical activity, history of diabetes, family history of cardiovascular disease, family history of cancer, and quintiles of fruit, vegetable, red meat, starchy foods intake, and energy and centre.	Median daily servings of dairy products across quartiles were 0, 0.4, 1.4 and 3.2. Increasing intakes of dairy products were associated with significantly deceased risks of the composite outcome, total mortality (both CVD and non CVD causes), combined CVD and stroke, but not MI or heart failure. Compared with persons who consumed no dairy products, the risks of the primary outcome, total mortality and stroke were significantly reduced compared with persons who consumed >2 servings/day (HR= 0·84, 95% CI 0·75–0·94, HR= 0·83, 95% CI 0·72–0·96 and HR= 0·66, 95% CI 0·53–0·82, respectively). Increasing yogurt consumption was associated with the greatest reductions in risk of the composite outcome, total mortality and major CVD. Increasing consumption of whole-fat dairy was associated with significant reductions in risks of the composite outcome, total mortality and major CVD, whereas when high and low-fat dairy products were combined, there were no significant risk reductions.
Qin et al. 2015 **China** **Systematic review & meta-analysis**	NA	22 prospective studies with cohort sizes ranging from 1,529 to 223,170 including participants ≥18 years. Studies included both sexes (n=15), only men (n=3) and women only (n=4)	The association between risk of cardiovascular diseases and dairy consumption (with subgroup analyses for high fat, low fat yogurt, cheese and butter) was explored, by comparing the highest dairy consumer groups with the lowest (tertiles, quintiles). Dietary exposure was assessed using validated food frequency questionnaires (n=20	**Primary outcome:** Cardiovascular diseases (total), stroke, coronary heart disease	Duration of follow-up varied from 8-26 years Consumption of dairy products was associated with a significant reduction in the risk of total CVD (RR=0.88, 95% CI 0.81-0.96. Data from 9 studies), and stroke (RR=0.87, 95% CI 0.77-0.99. Data from 12 studies), but not CHD (RR=0.94, 95% CI 0.82-1.07. Data from 12 studies). In subgroup analysis of dairy types, only low-fat dairy significantly reduced the risk of stroke (RR=0.91, 95% CI 0.88-0.99).

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
			studies), a non-validated FFQ (n=1) and a 3day diet record (n=1) and most studies adjusted for potential confounders (age, gender, BMI, smoking, alcohol consumption, physical activity, energy and certain food intakes, and diseases related to CVD		
Hu et al. 2014 **China** **Systematic review & meta-analysis**	NA	15 prospective population-based studies (n=764,635) including men and women aged ≥30 years.	The association between risk of stroke and dairy consumption (total dairy, milk, and cheese, butter and cream) was explored, using a restricted cubic spline model with 3 knots (25 th, 50th and 75th percentiles). Dairy intake was estimated using a weighted 3-day diet record (n=1), a 7-day household inventory method (n=1) and self-administered food frequency questionnaires (n=13).	**Primary outcome:** Risk of stroke, stroke mortality Most studies adjusted for known stroke risk factors, BMI, energy and alcohol intake.	Mean duration of follow-up was >10 years. There was a total of 28,138 stroke events. Compared with the lowest dairy intake group, the highest group was associated with significantly reduced for risk of stroke (RR=0.80, 95% CI 0.76-0.84). Results from 11 studies included. Compared with the lowest dairy intake group, the highest group was associated with significantly reduced for risk of stroke mortality (RR=0.88, 95% CI 0.82-0.94). Compared with the lowest milk intake group, the highest group was not associated with a significantly reduced for risk of stroke (RR=0.91, 95% CI 0.82-1.01). Results from 10 studies were included. In subgroup analysis, fermented milk was associated with a reduced risk of stroke (RR=0.80, 95% CI 0.71-0.89. Results from 3 studies included. A non-linear dose-response relationship was observed between milk consumption and stroke risk whereby 200 mL/day was most protective (RR=0.82, 95% CI 0.79-0.86) Compared with the lowest cheese consumption group, the highest group was associated with significantly reduced for risk of stroke (RR=0.94, 95% CI 0.89-0.99). Results from 6 studies included.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					Butter and cream consumption was not associated with a significantly reduced risk of stroke.
De Oliveira Otto et al. 2013 **USA** **Prospective cohort study *Multi-Ethnic Study of Atherosclerosis (MESA)***	NA	2,837 persons aged 45-84 years, without clinical CVD, recruited from 6 US communities. Mean age was 61.5 years, 53% were women.	Plasma phospholipid fatty acids (14:0,15:0 and trans-16:1n7) were measured at baseline. Baseline 120-item FFQs were conducted and used to estimate saturated fat levels from various foods (dairy, meat, butter, and plants). The relationship between phospholipid fatty acids and saturated fat (SF) and the development of CVD was examined.	**Primary outcome:** Incident CVD Models were adjusted for age, sex, race/ethnicity, field center (6 sites), education, cigarette smoking, alcohol intake, physical activity, whole-fat dairy, processed and unprocessed meat, total energy intake, fiber and fruits and vegetables	There were 146 incident cases of CVD during 10-year follow-up (19,778 person years). Plasma phospholipid fatty acid 15:0 was most strongly correlated with the consumption of high-fat dairy. For each 1 standard deviation unit in 15:0 FA concentration, the risk of CVD was decreased significantly (HR=0.81, 95% CI 0.68-0.98). For each 1 standard deviation unit in 14:0 and trans-16:1n7 FA concentration, the risk of CVD was not decreased significantly (HR=1.02, 95% CI 0.87-1.20 and HR=0.97, 95% CI 0.82-1.13). Across quintiles, there was an inverse association between FA 15:0 and CVD risk (Q5 vs. Q1; HR=0.41,95% CI 0.22-0.78, p for trend=0.01).
Larsson et al. 2012 **Sweden** **Prospective cohort study**	NA	74,961 Swedish men and women, aged 45-83 years without a history of stroke, coronary heart disease or cancer at study baseline.	Participants completed a 350-item diet and lifestyle questionnaire. A 96-item food frequency questionnaire, with 8 response categories was used to estimated dairy consumption (milk, yogurt, cottage cheese, ice cream, crème fraiche)	**Primary outcome:** Incident stroke Analysis were adjusted for: i) age and sex and ii) multivariable (age, sex, smoking status, education, BMI, physical activity, history of hypertension, aspirin use, diabetes, family history, alcohol intake and other dietary components)	Mean duration of follow-up was 10.2 years. There were 4,089 new stroke incidents. Median total daily servings of dairy products for persons in the 1st and 5th quintiles were 2.3 and 9.3, respectively. Comparing the highest quintile with the lowest (reference): There was no association between consumption of dairy products and risk of stroke. Total dairy: RR=0.91, 95% CI 0.80-1.03. Full-fat dairy: RR=0.94, 95% CI 0.83-1.07 Cheese: RR=0.91, 95% CI 0.81-1.01 Consumption of low-fat dairy products was associated with a decreased risk of all stroke (RR=0.88, 95% CI 0.80-0.97) and ischemic stroke (RR=0.87, 95% CI 0.78-0.98)

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Soedamah-Muthu et al. 2011 **The Netherlands** **Systematic review & meta-analysis**	NA	17 studies including the results from 611,430 subjects. Mean age at baseline was 56±13 years. Studies included women only (n=3), men only (n=4) and both sexes (n=10)	Dairy consumption, including milk, cheese and yoghurt was estimated using validated food-frequency questionnaires and diet histories (n=11) and non-validated FFQs and questionnaires (n=6). Dairy servings were converted from servings to g/day using standard conversions	**Primary outcomes:** Cardiovascular disease, coronary heart disease, stroke, all-cause mortality Most studies adjusted for age, sex, smoking status, alcohol intake, BMI, traditional stroke risk factors and physical activity	The mean duration of follow-up was 14.0±6.0 years. Overall, mean milk intake/day was 266±210 mL. There was no association between intake of milk (200 mL/day) and all-cause mortality. RR=0.99, 95% CI 0.95-1.03. Results from 8 studies included. Stroke was an outcome in 6 studies (n=375,381). 15,554 fatal and non-fatal strokes occurred. Mean milk intake in stroke studies was 219 mL/day There was no association between intake of milk (200 mL/day) and stroke risk. RR=0.87, 95% CI 0.72-1.05.
iv) Studies evaluating whole grains/fiber					
Juan et al. 2017 **China** **Retrospective study**	NA	71,750 women from the Nurses' Health Study (NHS) and 42,823 men from the Health Professionals Follow-up Study (HPFS) without cardiovascular disease, diabetes mellitus, or cancer at baseline (1984 and 1986, respectively) through 2010. Mean age at baseline in the NHS was 50 years, and 53 years in the HPFS.	Semiquantitative FFQs were used to collect usual intake of whole grains and other dietary information every 4 year. Intakes of whole grains including whole grain cold breakfast cereal, dark bread, oatmeal, brown rice, popcorn, bran, and germ, were classified by quintiles.	**Primary outcome:** Ischemic stroke Analysis was adjusted for age, ethnicity, BMI, smoking status, alcohol intake, physical activity, multivitamin use, family history of MI, cancer, or diabetes mellitus, hypertension and high cholesterol at baseline, total energy intake, the modified alternative healthy eating index score, and menopausal status and postmenopausal hormone use women).	During 2,820,128 person-years of follow-up, there were 2,458 cases of ischemic stroke in the combined cohorts. Whole grain intakes NHS Q1 4.43g, Q2 10.10g, Q3 15.15g, Q4 21.46g, Q5 33.23g Whole grain intakes HPFS Q1 5.92g, Q2 14.47g, Q3 22.35g, Q4 31.5g, Q5 47.9g Compared with Q1 (reference), the risk of ischemic stroke was not significantly increased, compared with Q5 in either the NHS (HR=1.03, 95% CI 0.88-1.21) or the HPFS cohorts (HR=1.04, 95% CI 0.91-1.19). The risk was not significantly increased in the combined cohort (HR=1.04, 95% CI 0.91-1.19). When the 2 cohorts were combined, the risk of ischemic stroke was significantly lower in persons consuming >1 serving cold whole grain breakfast cereal/day compared with persons consuming <1 serving/day (HR=0.88, 95% CI 0.80–0.96).

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					Increasing bran intake was also associated with a significantly reduced risk of ischemic stroke.
Larsson & Wolk 2014 **Sweden** **Prospective study**	NA	69,677 participants from 2 large population-based studies (Swedish Mammography Cohort and Cohort of Swedish Men), aged ≥18 years, free of CVD, cancer and diabetes at baseline.	A 96-item food frequency questionnaire (FFQ) with 8 response categories was used to estimate dietary fiber intake (fruits, vegetables and cereal grains) at baseline. Associations with incident stroke and dietary fiber (quintiles) were examined, adjusting for potential confounders (sex, age, education, family history of MI before age 60, smoking, physical activity, BMI, diabetes, HTN, aspirin use, total energy and alcohol use)	**Primary outcomes:** Total stroke, ischemic stroke and ICH	Mean duration of follow-up was 10.3 years. There were 3680 incident strokes. Mean fiber intake/day was 25.6 g (women) and 23.4 g (men). The risk of all stroke was significantly lower among persons in the highest total fiber intake group (Q5), compared with Q1: RR=0.90, 95% CI 0.81-0.99). p for trend=0.03. The risk of all stroke was not significantly lower among persons in the highest cereal fiber group (Q5), compared with Q1: RR=0.94, 95% CI 0.84-1.04). p for trend=0.42 The risk of all stroke was significantly lower among persons in the highest fruit fiber group (Q5), compared with Q1: RR=0.85, 95% CI 0.77-0.95). p for trend=0.007 The risk of all stroke was significantly lower among persons in the highest vegetable fiber group (Q5), compared with Q1: RR=0.90, 95% CI 0.82-1.00). p for trend=0.12. Only vegetable fiber was associated with a significantly reduced risk of cerebral infarction (Q5 vs. Q1 (RR=0.77-0.98) p for trend=0.06. Increasing fiber intake (total, cerebral fruit or vegetable) was not associated with significant reduction in the risk of ICH.
Mellen et al. 2008 **USA**	NA	7 studies (288,376 subjects). Age at baseline ranged from 38-50 years (youngest) to 63-84 years (oldest). Studies included women	Whole grain intake was measured using food frequency questionnaires (servings/day or week grams/day) (n=6) and a	**Primary outcomes:** Incident coronary heart disease, CHD death, incident stroke, stroke death, cardiovascular death.	Follow-up ranged from 6-14 years. Median intake of grains (servings/day) for persons in the lowest and highest quantiles were 0.2 vs. 2.5.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Systematic review & meta-analysis		only (n=2), men only (n=2) and both sexes (n=3).	3-day day food intake record (n=1)	Most common covariates adjusted for in analyses were age, sex, smoking blood pressure, BMI, physical activity and total energy intake	There was no association between incidence of stroke and whole grain intake. RR=0.83, 95% CI 0.68-1.02. Results from 4 studies included. CVD events were significantly lower for persons consuming higher amounts of whole grains. RR=0.79, 95% CI 0.73-0.85.
v) Studies evaluating fish consumption					
Abdelhamid et al. 2018 **UK** **Cochrane review**	25 trials were considered to be at low risk for bias	79 RCTs (n=112,059) including participants ≥18 years, at any risk for cardiovascular disease, including those with a history of cardiovascular events.	Trials compared fish-based (as oily fish or supplements, n=71) and plant-based (n=8) sources of omega-3 fatty acids vs. no supplementation or lower levels, which were provided for ≥12 months. Duration of supplementation in trails ranged from 12 to 72 months.	**Primary outcomes:** All-cause mortality, cardiovascular mortality, cardiovascular events, stroke, coronary heart disease events/mortality **Secondary outcomes:** Major adverse cardiovascular events, body weight, lipids **Safety outcomes:** Bleeding, pulmonary embolus or DVT	33 of the trials were secondary prevention, 46 trials were of primary prevention. The risk of all-cause mortality was not reduced significantly with long-chain (LC) omega-3 fatty acids (i.e. fish-based). RR=0.98, 95% CI 0.93 to 1.03. The results from 39 trials included. There were no significant effects based on dose, source, duration of supplementation or statin use. The risks of cardiovascular mortality and cardiovascular events were not reduced significantly with LC omega-3 fatty acids. RR=0.95, 95% CI 0.87 to1.03 and RR=0.99, 95% CI, 94 to 1.04, respectively. The results from 25 and 38 trials included. The risk of stroke was not reduced significantly with LC omega-3 fatty acids. RR=1.06, 95% CI 0.96 to 1.16. The results from 28 trials included. There was no significant effect of supplementation by stroke type (ischemic, hemorrhagic or TIA), or when used for primary or secondary prevention. The risk of major adverse cardiovascular events was not reduced significantly with LC omega-3 fatty acid supplementation. There were no significant changes in measures of body weight between groups. LC omega-3 fatty acids was associated with some improvements in serum lipid profiles. The risk of bleeding or pulmonary embolus or DVT were not increased with LC omega-3 fatty acid supplementation.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					Supplementation with plant-based sources of omega-3 fatty acids did not reduce the risks of all-cause, cardiovascular mortality, cardiovascular events or stroke.
Xun et al. 2012 **USA** **Systematic review & meta-analysis**	NA	16 prospective studies including 402,127 adult participants. 8 studies included men and women, 5 included only men and 3 included only women.	Studies were included if fish consumption and stroke risk was assessed, with the lowest category of fish consumption serving as the reference group. Frequency of intake was obtained using self-administered questionnaires or by interview in the majority of studies.	**Primary outcome:** Stroke incidence All studies adjusted for age, sex, smoking, blood pressure and most studies also controlled for alcohol consumption, lipids, BMI or obesity diabetes, physical activity and other dietary factors. Some studies adjusted for other factors such as aspirin use and education	Mean duration of follow-up ranged from 8.5-28 years (mean 12.8). There were 10,568 stroke events. The risk of stroke was inversely associated with fish consumption. Compared with those that consumed fish never or <1 a month: 1-3x/month: HR= 0.97, 95% CI 0.87-1.08 1/week: HR= 0.86, 95% CI 0.80-0.93 2-4x/week: HR= 0.91, 95% CI 0.85-0.98 ≥5/week: HR= 0.87, 95% CI 0.79-0.96 The pattern of results was similar for ischemic stroke. There was no reduced risk associated with hemorrhagic stroke. Compared with fish consumption of less than once a month, the risk of stroke was significantly reduced for consumption of 2-4x/week (HR=0.91, 95% CI 0.85-0.98).
Larson & Orsini 2011 **Sweden** **Systematic review & meta-analysis**	NA	15 prospective studies including 383,838 adult participants. 8 studies included men and women, 4 included only men and 3 included only women.	Studies were included if at least 3 categories of fish consumption were used.	**Primary outcome:** Stroke incidence or mortality All studies adjusted for age, smoking, and history of hypertension or measured blood pressure, while most studies also controlled for alcohol consumption, BMI or obesity diabetes, physical activity and other dietary factors	Mean duration of follow-up ranged from 4-28 years. There were, 9360 stroke events. The risk of stroke was significantly decreased for a 3-serving/week increase in fish consumption (RR=0.94, 95% CI 0.89-0.99). Compared with the lowest consumption group, the risk of stroke was significantly decreased in the highest fish intake group (RR=0.88, 95% CI 0.81-0.96).
vi) Studies evaluating egg consumption					
Zhong et al. 2019 **USA**	NA	29,615 participants from 6 cohort studies (Atherosclerosis Risk in Communities [ARIC]	The association between increased consumption of cholesterol (per 300 mg/day increments) and	**Primary outcomes:** Incident CVD and all-cause mortality	Median duration of follow-up was 17.5 years.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Pooled analysis of cohort studies		Study, Coronary Artery Risk Development in Young Adults [CARDIA] Study, Framingham Heart Study [FHS], Framingham Offspring Study [FOS], Jackson Heart Study [JHS] and the Multi-Ethnic Study of Atherosclerosis [MESA]). Mean age was 51.6 years at baseline, 44.9% were men.	0.5 eggs/day, and the development of incident CVD was examined. The model was adjusted for age, sex, race/ ethnicity, education, total energy, smoking status, physical activity, alcohol intake (and use of hormone therapy.		Median dietary cholesterol consumption was 241 mg per day (IQR, 164-350). Mean ± SD was 285± 184 mg per day. Median egg consumption was 0.14 per day (IQR, 0.07- 0.43). Mean was 0.34±0.46 per day. For each 300 mg chol consumed/day, the risk of incident CVD was significantly increased (HR=1.17, 95% CI 1.09-1.26) or an absolute risk difference of 3.24% (95% CI 1.39% to 5.08%). The association was no longer significant after adjusting for the consumption of eggs, unprocessed red meat, and processed meat. The association between dietary cholesterol consumption (per 300 mg/day) and incident CVD was stronger in participants with BMI < 25 and in those with higher lipid levels. For each 300 mg chol consumed/day, the risk of all-cause mortality was significantly increased (HR=1.18, 95% CI 1.10-1.26) or an absolute risk difference of 4.43% (95% CI 2.51% to 6.36%). The association was no longer significant after adjusting for egg consumption. The risk of stroke for each 300 mg chol/day was significantly increased (HR=1.26, 95% CI 1.09-1.46). The association between dietary cholesterol consumption (per 300 mg/day) and all-cause mortality was stronger in women and in those who consumed a high-fat diet. For each 0.5 egg consumed/day, the risk of incident CVD was significantly increased (HR=1.06, 95% CI 1.03-1.10) or an absolute risk difference of 1.11% (95% CI 0.32% to 1.89%). The association was stronger in women and in those with higher lipid levels.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					The risk of stroke for each 0.5 egg consumed daily was significantly increased (HR=1.11, 95% CI 1.03-1.18). For each 0.5 egg consumed/day, the risk of all-cause mortality was significantly increased (HR=1.08, 95% CI 1.04-1.11) or an absolute risk difference of 1.93% (95% CI 1.10% to 1.76%). The association was stronger in women and in those with higher lipid levels.
Xu et al. 2019 **China** **Prospective study and updated meta-analysis**	NA	28,024 participants without CVD included in the Guangzhou Biobank Cohort Study from 2003-2008. Mean age at baseline was approximately 62 years, 28% were men.	Participants were asked how many eggs they had consumed daily over the past 7 days based on a validated FFQ. Models were adjusted for sex, age, education, occupation, family income, smoking status, physical activity, alcohol drinking, self-rated health and chronic disease history (diabetes, hypertension and dyslipidemia)	**Primary outcomes:** All-cause mortality and CVD death	Mean duration of follow-up was 9.8 years. 21% of participants did not consume eggs, while 44%, 22%, 5% and 8% had consumed 1–2, 3–4, 5–6 and 7+ eggs over the past 7 days, respectively. Compared with the lowest level of egg consumption (<1/day) no level of increased egg consumption was not associated with significantly increased risks of all-cause mortality, CVD, ischemic heart disease, all stroke, ischemic stroke, hemorrhagic stroke or ischemic heart disease/ischemic stroke. When including the results of the present study in an updated systematic review, the risk of stroke was significantly decreased in 436,088 participants in 9 trials when comparing more frequent vs. less frequent egg consumption (7+eggs/week vs. <1 egg/week). HR=0.91, 95% CI 0.85-0.98. 7+ eggs/week was not associated with significantly increased risks of all-cause mortality (HR 1.09, 95% CI 0.997–1.200, n=4 studies) or IHD (HR 0.97, 95% CI 0.90–1.05, n=9 studies)
Alexander et al. 2016 **USA**	NA	7 prospective studies, including 308,000 participants, published between 1982 and 2014.	The summary relative risk estimates (SRREs) of the primary outcome associated with high (1 daily) vs. low consumption (<2/week) of eggs, were calculated.	**Primary outcomes:** Coronary heart disease and stroke	Mean duration of follow-up ranged from 6 to 26 years. Higher egg consumption was associated with a reduced risk of stroke (SSRE=0.88, 95% CI, 0.81–0.97). consuming up to 3.5 eggs per week was

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Systematic review & meta-analysis					associated with statistically significant reductions in risk of total stroke. There was no significant dose-response relationship for egg consumption and stroke identified using meta-regression. Higher egg consumption was not associated with an increased risk of CHD (SSRE=0.97, 95% CI, 0.88–1.07).
vii) Studies evaluating dietary patterns					
Adjibade et al. 2019 **France** **Prospective study**	NA	6,011 participants ≥60 years, without subjective memory complaints (SMC) recruited from the general population by a vast multimedia campaign. Mean age was 64.4 years.	The association between adherence to the MIND diet (a combination of the Mediterranean Diet and DASH diet) and SMC, measured by the Cognitive Difficulties Scale (CDS) was examined. Adherence to the MIND diet was assessed by a series of 24-hour recalls (baseline and twice annually). Adherence was scored 1-15, with higher scores indicating greater adherence. The CDS is a 37-item questionnaire with scores ranging from 0 and 148 points, with a higher score indicating more frequent and severe cognitive difficulties. CDS scores were converted to binary variables (low level of complaints vs a high level) using a cut-off value of 43.	**Primary outcome:** Risk of SMC Models were adjusted for age, sex, marital status, educational level, occupational categories, household income, energy intake without alcohol, number of recording days, and inclusion month	Mean duration of follow-up was 6.1 years. There were 1,053 (17.5%) cases of SMC. Of these, 15.7% were among persons aged 60-69 years and 30.6% were among persons aged ≥70 years. Overall, the risk of SMCs was not significantly lower among persons in the highest vs. lowest tertile, nor was it reduced in Q2 vs. Q1 (ref). Among persons aged 60-69 years (n=5,270), the risk of SMC was not reduced significantly in comparisons of Q3 vs. Q1 and Q2 vs. Q1 Among persons aged ≥70 years (n=741), the risk of SMC was significantly reduced (Q3 vs. Q1; HR= 0.69, 95% CI 0.47- 0.99). Each one-point increase in the MIND diet score was associated with a 14% reduction in the risk of SMC. (HR=0.86, 95% CI 0.77-0.96). There was no significant reduction in SMC comparing Q2 vs. Q1: HR= 0.76, 95% CI 0.56- 1.04.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Akbaraly et al. 2019 **France** **Prospective study**	NA	8,225 participants aged 35 to 55 years working in 20 London-based departments, without dementia, recruited between 1991-1993. Mean age was 50.2 years. 69.1% were men.	The results from a 127-item FFQ were categorized according to the Alternative Healthy Eating Index (AHEI). Dietary intake was assessed during 1991-1993, 1997-1999, and 2002-2004, with scores ranging from 0 to 110, with higher scores representing a healthier diet. The association between dietary patterns, derived from AHEI scores (classified by tertiles) and the development of dementia was examined. Dietary patterns included *healthy* (high intakes of vegetables, fruits, and fish) and *western* (high consumption of fried food, processed and red meat, pies, chocolate and sweets, high-fat dairy products, and refined grains). An AHEI score was developed for each of these 2 patterns.	**Primary outcome:** Incident dementia (ICD-10) **Secondary outcome:** Cognitive decline from 1997-1999 and 2015-2016. A global cognitive score was calculated based on measures of memory, executive function, and fluency	At the end of follow-up (March 31, 2017), the mean age of the participants was 74.2 years. Median duration of follow-up was 24.8 years. There were 344 cases of incident dementia. During the entire follow-up period, the incidence rates (per 1,000-person years) for dementia by AHEI tertiles were: Worst: (range, 22.0 to 48.0 points) 1.76 (95% CI, 1.47 to 2.12) Intermediate: (range, 48.5 to 57.0 points), 1.80 (95% CI, 1.50 to 2.15) Best: AHEI (range, 57.5 to 91.0 points), 1.81 (95% CI, 1.50 to 2.17). The risk of dementia was not significantly reduced among patients in the intermediate and best groups compared with the worst (HR=0.95, 95% CI 0.73-1.23 and HR=0.93, 95% CI 0.71-1.22), adjusting for age, sex, race/ethnicity, total energy intake, sociodemographic, health behavioral, and health factors. No significant differences in the risks of dementia were noted between the worst and the intermediate and best tertiles of AHEI scores during follow up from 1994-1997 and 2002-2004. The same patterns were noted for AHEI scores based on both healthy and western style diet patterns. Per each 10-point increment in better diet scores was not associated with a significant decrease in the risk of dementia when assessed in 1991-1993, 1997-1999, or 2002-2004. There was no association between cognitive decline and diet quality.
Lim et al. 2019 **USA**	NA	548,845 individuals aged 50-71 years included in the National Institutes of	The modifying effect of a Mediterranean diet was examined in relation to	**Primary outcomes:** Mortality associated with cardiovascular disease,	Duration of follow-up was 17 years. There were 5,592 CVD deaths.

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Prospective cohort study		Health–American Association for Retired Persons Diet and Health Study, who responded to a postal questionnaire in 1995. Mean age was 62.2 years, 59.1% were men.	the association between air pollution and cardiovascular and cerebrovascular mortality. Using the responses from a 124-item FFQ, an alternative Mediterranean diet (aMED) score (1-9, with higher scores indicating greater adherence) was developed to assess adherence to a Mediterranean diet. Scores were arranged into quintiles. Exposures to fine particulate matter ($PM_{2.5}$) and nitrogen dioxide (NO_2) were estimated from prediction models using data from satellites and governmental agencies.	cerebrovascular disease, ischemic heart disease and cardiac arrest	The risk of CVD mortality was increased significantly with increasing exposure to $PM_{2.5}$ (HR per 10 $\mu g/m^3$ =1.16, 95% CI 1.04–1.30), but not NO_2 (HR per 10 ppb= 1.05, 95% CI 0.99–1.10). The risk of CVD mortality associated with $PM_{2.5}$ was highest in the lowest (i.e lowest adherence) aMED quintile (HR=1.26, 95% CI 1.05-1.52) and lowest in the highest (i.e highest adherence) aMED quintile (HR= 0.95, 95% CI 0.79-1.14). p for interaction <0.01. The risks of cardiovascular and ischemic heart disease related mortality were increased significantly with increasing exposures to both $PM_{2.5}$ and NO_2. Increasing adherence to a Mediterranean diet attenuated the risks (p for interactions were <0.01). There was no association between exposure to either $PM_{2.5}$ or NO_2 and mortality associated with cardiac arrest.
McEvoy et al. 2019 **UK** ***Coronary Artery Risk Development in Young Adults (CARDIA) Study***	NA	2,621 participants, recruited in 1984, from 4 urban areas in the USA, who were 19-30 years, Mean age at baseline was 25.2 years, 43% were men.	The association between 3 heart healthy dietary patterns including the Mediterranean diet (MedDiet), Dietary Approaches to Stop Hypertension (DASH) and CARDIA A Priori Diet Quality Score (APDQS) and mid-life cognitive performance was examined. Low, medium and high diet quality scores were compiled for each diet pattern. Dietary intake was assessed at 3	**Primary outcome:** Changes in cognitive function	Higher mean MedDiet and APDQS scores were associated with better cognitive function at 25 years. Each 1-point standard deviation increase in MedDiet score was associated with improved overall cognition (β= 0.08, 95% CI 0.05 to 0.10), after adjusting for sex, age, race, education, smoking, BMI, diabetes mellitus, physical activity, and total energy intake. Each 1-point standard deviation increase in APDQS score was associated with improved overall cognition (β= 0.09, 95% CI 0.0 to 0.12), adjusting for same variables.

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			examinations (baseline and years 7 and 20). A composite cognitive function score was computed using the results from assessments of verbal learning and memory, processing speed and executive function, and assessed at years 25 and 30.		Higher DASH scores were not associated with changes in cognition. Compared with low diet quality scores, medium and high MedDiet and APDQS diet scores were associated with reduced odds of cognitive decline, defined as ≥1 SD (3.9 points) below the population mean Montreal Cognitive Assessment score (24.0) at 30 years. DASH scores were not associated with protection from cognitive decline.
Tong et al. 2019 **UK** **Prospective cohort study *EPIC-Oxford***	NA	48,188 participants, aged 35-59 years, recruited from 1993 and 2001 with no history of cardiovascular disease. Mean age was approximately 44.7 years, >75% were women	On the basis of 4 questions about consumption of meat, fish, dairy products, and eggs, collected at baseline and around 2010, participants were classified into three distinct diet groups: meat eaters (those who consumed meat, regardless of whether they consumed fish, dairy, or eggs; n=24,428), fish eaters (consumed fish but no meat; n=7,506), and vegetarians including vegans (n=16, 254). The baseline questionnaire also included a semiquantitative 130-item FFQ, which asked about dietary intake over the past year.	**Primary outcomes:** Ischemic heart disease, stroke Analyses were adjusted for year of recruitment (per year), education, Townsend deprivation index, smoking alcohol consumption, dietary supplement use and oral contraceptive and hormone replacement therapy use in women.	Duration of follow-up was 18.1 years. There were 2,820 cases of ischaemic heart disease and 1,072 cases of total stroke (519 ischaemic stroke and 300 haemorrhagic stroke). Using meat eaters as the reference group, the risk of acute MI was not reduced significantly in fish eaters or vegetarians (HR=1.00, 95% CI 0.78 to 1.26 and HR=0.89, 95% CI 0.73 to 1.09, respectively). The risk of ischemic heart disease was significantly lower in fish eaters and vegetarians (HR=0.87, 95% CI 0.77 to 0.99 and HR=0.78, 95% CI 0.70 to 0.87, respectively). Using meat eaters as the reference group, the risk of total stroke was increased significantly in vegetarians (HR=1.20, 95% CI 1.02 to 1.40), but not in fish eaters (HR=1.14, 95% CI 0.94 to 1.38). The risk of ischemic stroke was not increased significantly in either fish eaters or vegetarians, but the risk of hemorrhagic stroke was increased significantly in vegetarians (HR=1.43, 95% CI 1.08 to 1.90). There were no significant differences in risks when vegans and vegetarians were analyzed separately. Vegetarian diets were associated with 10 fewer cases of ischaemic heart disease per 1,000

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					population over 10 years than meat eaters, while vegetarian diets were associated with 3 more cases of total stroke.
Estruch et al. 2018 (re-analysis of original data) **Spain** **RCT** ***Prevención con Dieta Mediterránea Trial (PREDIMED)***	CA: ☑ Blinding: Patient ☒ Assessor ☑ ITT: ☑	7,447 men (aged 55 to 80 years) and women (aged 60 to 80 years) with no cardiovascular disease with either type 2 diabetes mellitus or at least three major risk factors: smoking, hypertension, elevated LDL cholesterol levels, low HDL cholesterol levels, overweight or obesity, or a family history of premature coronary heart disease. Mean age: 67 years, 57% women.	Participants were randomized (1:1:1) to a **Mediterranean diet** supplemented with extra-virgin olive oil (EVOO), a Mediterranean diet supplemented with mixed nuts, or a control diet (advice to reduce dietary fat). A 137-item food frequency questionnaire and a 14-item questionnaire were used to assess adherence to a Mediterranean diet at baseline and yearly thereafter.	**Primary outcome:** Major cardiovascular events (myocardial infarction, stroke, or death from cardiovascular causes) **Secondary outcomes:** Changes in blood pressure, body weight, adiposity measures, blood sugar, lipids	The median duration of follow-up was 4.8 years. The mean scores for adherence to the Med diet (0=no adherence, 14=maximum adherence) across groups were 8.7 (2 study diet groups) and 8.4 for the control group. Participants in the two Mediterranean-diet groups significantly increased their weekly servings of fish (by 0.3 servings), legumes (by 0.4 servings), olive oil and nuts compared with the control group. The crude event rates/1,000-person yrs for the primary outcome were significantly lower for the 2 Med diets: EVOO: 8.1, nuts: 8.0, control 11.2. Compared with the control diet, the risk of the primary outcome was significantly reduced. EVOO: adj HR=0.69, 95% CI 0.53–0.91, p<0.01 Nuts: adj HR=0.72, 95% CI 0.54–0.95, p=0.03 The crude event rates/1,000-person yrs for stroke were significantly lower for the 2 Med diets: EVOO: 4.1, nuts: 3.1, control 5.9. Compared with the control diet, the risk of stroke was significantly reduced. EVOO: adj HR=0.65, 95% CI 0.44–0.95, p=0.04 Nuts: adj HR=0.54, 95% CI 0.35–0.82, p=0.006 There were no significant reductions associated with the Med diet for MI, death from cardiovascular causes, or death from any cause. No interactions were observed in subgroups analyses: sex, diabetes, age (<70 vs. ≥70 yrs), hypertension, dyslipidemia, smoking, family history of CHF).

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					The results were similar after the omission of 1,588 participants whose study-group assignments were known or suspected to have departed from the protocol, which was the reason for the reanalysis of the 2013 initial report.
Feng et al. 2018 **China** **Systematic review & meta-analysis**	Newcastle Ottawa Scale scores ranged from 7-9. All studies were considered to be of good quality	12 prospective cohort studies including 548,632 participants. 2 studies included all women, 2 included all men. The remainder included both men and women. 5-38% had hypertension. Mean ages ranged from 20 to 79 years.	The association between adherence to the **DASH diet** (obtained through analysis of food frequency questionnaires, from which a DASH diet score was estimated), and stroke risk was examined. The most common factors controlled for in the studies were age, sex, smoking, alcohol use, BMI and energy intake	**Primary outcome:** Stroke incidence	Duration of follow-up ranged from 5.7 to 24 years. Higher adherence to the DASH diet significantly reduced the risk of stroke (RR=0.88, 95% CI 0.83-0.93). Each 4-point increment in DASH score conferred a risk reduction of 4% (RR= 0.96, 95% CI 0.94–0.97) in total stroke events
McEvoy et al. 2017 **USA** **Cross-sectional study**	NA	5,907 community-dwelling older adults selected from the Health & Retirement Study. Mean age was 67.8 years, 60% were women.	The association between the Mediterranean diet (MedDiet) and the Mediterranean-DASH diet Intervention for Neurodegeneration Delay (MIND diet) and cognition was examined. Adherence to dietary patterns was determined from food frequency questionnaires using criteria determined a priori to generate diet scores for the Med-Diet (range 0–55) and MIND diet (range 0–15). Cognitive performance was measured using a composite test score of	**Primary outcome:** Global Cognition scores (Impaired cognitive performance, defined as more than1 SD [4.3 points] below the mean global cognitive score)	Impaired cognition was found in 831 (14%) participants. In the fully adjusted model (sex, age, race, education, current smoking, total wealth, obesity [BMI ≥30], hypertension, diabetes mellitus, physical inactivity, depression score, and total energy intake), persons with mid MedDiet scores (Q2) had lower odds of poor cognitive performance than those with low scores (Q1: OR = 0.85, 95% CI 0.71–1.02, P = .08). Persons with high MedDiet scores (Q3) had significantly lower odds of having poor cognitive performance than those with the lowest scores (OR = 0.65, 95% CI 0.52–0.81, P < .001). Results were similar for individuals with mid (OR = 0.85, 95% CI 0.70–1.03, P = .10) and high (OR = 0.70, 95% CI 0.56–0.86, P = .001) MIND diet scores. In fully adjusted linear models, each 1 SD increase (5.4 units) in MedDiet was associated with 15%

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			global cognitive function (range 0–27). Linear regression was used to compare cognitive performance according to tertiles of dietary pattern.		lower odds of poor cognitive performance (OR = 0.85, 95% CI 0.78–0.93, P < .001) Each 1 SD increase (1.8 units) in MIND diet was associated with 14% lower odds of poor cognitive performance (OR = 0.86, 95% CI 0.79–0.94, P < .001).
O'Donnell et al. 2016 **Canada (International)** **INTERSTROKE Phase 2** **Case-control study**	NA	Participants were recruited from 32 countries from 2007-2015. Cases were 13,447 persons admitted to hospital within 5 days of first acute stroke and 72 hours of admission to hospital (77% ischemic stroke, 23% ICH). Mean age was 62.2 years. 40.4% of cases were women. 13,472 controls were matched for age and sex and were recruited from the community or hospitals (in-patient or outpatient, unrelated to treatment for stroke or TIA)	All key vascular risk factors (hypertension, DM, smoking, waist-to-hip ratio, diet, physical activity, alcohol intake, psychosocial factors, cardiac causes and ApoB:ApoA1) were collected using questionnaires, physical examinations and blood and urine samples. A modified version of the Alternative Healthy Eating Index (mAHEI) was used to measure diet quality. Higher mAHEI scores reflect better diet quality (higher intakes of fruits/vegetables, whole grains, polyunsaturated fatty acids, nuts, and long chain omega-3 fats and low intakes of red/processed meats, refined grains, and sugar sweetened drinks). The score was based on dietary patterns identified using a 19-item qualitative food group frequency questionnaire.	The odds of all stroke, ischemic stroke and intracerebral hemorrhagic stroke (ICH) and population attributable risk (PAR)	Dietary risk factor scores were presented as tertiles, with T1 representing the highest risk. **T2 vs. T1** All stroke: OR=0.77, 99% CI 0.69-0.86, Ischemic stroke: OR=0.75, 99% CI 0.66-0.85 ICH: OR=0.80, 99% CI 0.68-0.94 **T3 vs. T1** All stroke: OR=0.60, 99% CI 0.53-0.67; PAR 23.2%, 99% CI 18.2-28.9% Ischemic stroke: OR=0.59, 99% CI 0.52-0.68; PAR 22.4%, 99% CI 17.0-29.0 ICH: OR=0.61, 99% CI 0.50-0.74; PAR 24.5%, 99% CI 16.5-34.8% The results were similar for men and women in subgroup analysis (T1+T2 vs. T3 PAR: men 23.5%, 99% CI 17.4-31.0% and women PAR 22.9%, 99% CI 15.3-32.7%)
Morris et al. 2015	NA	960 participants from the Memory and Aging	The association between adherence to the MIND	**Primary outcome:**	Mean duration of follow-up was 4.7 years.

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USA **Prospective study**		Project (MAP), which included residents of >40 retirement communities and senior public housing units in the Chicago area. Persons were free of dementia at baseline but those with mild cognitive impairment were included. Mean age was 81.4 years, 75% were women.	diet (by tertile) and DASH diets and overall cognitive performance, assessed across 5 cognitive domains was examined.	Decline in cognitive performance	In a model adjusted for age, sex, MIND diet score, sex, education, participation in cognitive activities, APOE ε4 (any ε4 allele), smoking history (current, past, and never), physical activity hours per week, total energy intake, time and interaction terms between time and each model covariate, higher adherence to the MIND diet was associated with a significantly slower rate of cognitive decline (global cognition, episodic memory, semantic memory, perceptual organization, perceptual speed and working memory). Compared to the decline rate of participants in the lowest tertile of scores, the rate for participants in the highest tertile was substantially slower. The difference in rates was the equivalent of being 7.5 years younger.
O'Donnell et al. 2010 **Canada (International)** **INTERSTROKE** **Phase 1** **Case-control study**	NA	Participants were recruited from 22 countries from 2007-2010. Cases were 3,000 persons admitted to hospital within 5 days of acute stroke (78% ischemic stroke, 22% ICH). Mean age was 61 years. 37% of cases were women. 3,000 controls were matched for age and sex and were recruited from the community or hospitals (in-patient or outpatient, unrelated to treatment for stroke or TIA)	All key vascular risk factors (hypertension, DM, smoking, waist-to-hip ratio, BMI, physical activity, alcohol intake, psychological stress, depression, diet) were collected using questionnaires, physical examinations and blood and urine samples. A diet risk score was used to estimate the progression from healthy to unhealthy diet. The score was based on dietary patterns identified using a 19-item qualitative food group frequency questionnaire.	**Primary outcomes:** The odds of all stroke, ischemic stroke and intracerebral hemorrhagic stroke (ICH) and population attributable risk (PAR) Results were adjusted for age, sex, and region	Dietary risk factor scores were presented as tertiles, with T1 representing the lowest risk. **T2 vs. T1** All stroke: adjusted OR=1.35, 99% CI 1.12-1.61, PAR 18.8%, 99% CI 11.2-29.7% Ischemic stroke: adj OR=1.29, 99% CI 1.06-1.57 ICH: adj OR=1.53, 99% CI 1.13-2.08 **T3 vs. T1** All stroke: adj OR=1.35, 99% CI 1.11-1.64 Ischemic stroke: adj OR=1.34, 99% CI 1.09-1.65 ICH: adj OR=1.41, 99% CI 1.01-1.97 Increased consumption of fruits was associated with a decreased risk of stroke: adj OR (T3 vs. T1) =0.61, 99% CI 0.66-0.91. Increased consumption of vegetables was not associated with a decreased risk of stroke: adj OR (T3 vs. T1) =0.91, 99% CI 0.75-1.00.
Larsson et al. 2016	NA	74,404 men and women, aged 45-83 years from 2	Dietary intake during the previous years was	**Primary outcome:** Stroke incidence	Mean duration of follow-up was 11.9 years.

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Sweden **Prospective study**		population-based cohort studies (Cohorts of Swedish men and Swedish Mammography), with no prior history of stroke. Mean age was 60 years, 54% men	assessed using a 96-item FFQ. Adherence to the DASH diet was evaluated using an adaptation of the Fung score (7 minimal adherence to 35 maximum adherence) and scores arranged by quartiles.		There were 3,896 ischemic strokes, 560 ICHs and 176 SAHs during 882,727 person-years follow-up. The risk of stroke was adjusted for age, sex, education, family history of MI before 60 years, smoking status, aspirin use, exercise BMI, HTN, high chol, diabetes, atrial fibrillation and total energy and alcohol. **Ischemic stroke** Men DASH score of 7-18 was reference category 19-21: RR=0.93, 95% CI 0.83-1.04 21-23: RR=0.92, 95% CI 0.82-1.03 24-35: RR=0.89, 95% CI 0.78-1.01 p for trend 0.06 Women DASH score of 7-18 was reference category 19-21: RR=0.86, 95% CI 0.75-1.00 21-23: RR=0.87, 95% CI 0.75-1.01 24-35: RR=0.80, 95% CI 0.69-0.92 p for trend 0.0005 The risks of ICH and SAH were not decreased among men or women with higher adherence to a DASH diet.
Tsivgoulis et al. 2015 **Greece** **Prospective cohort study**	NA	20,197 participants, aged ≥45 years, without previous history of stroke, enrolled in the REGARDS study. Mean age was 65 years, 44% were male.	A self-administered 98-item food frequency questionnaire (FFQ) was obtained at baseline. Adherence to the Mediterranean diet was based on the MeD score, with scores of 0-3 (low), med (4-5) and high (6-9). The association between incident stroke and Mediterranean diet adherence was examined	**Primary outcome:** Incident ischemic and hemorrhagic stroke	Mean duration of follow-up was 6.5 years. There were 565 strokes (2.8%) The mean MeD score was 4.4. The risk of stroke was significantly reduced among participants with high MeD scores (vs. low MeD) in the fully adjusted model (age, race, region, sex, income, education, smoking, energy intake, sedentary behaviour, medication, BMI, waist circumference, DM, HTN and blood pressure); HR=0.79, 95% CI 0.65-0.96, p=0.00164.

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					Each 1-point increase in MeD score was associated with a 5% reduction (95% CI 0-11%) in the risk of ischemic stroke. The risk of hemorrhagic stroke was not reduced significantly in participants with high MeD scores.
Naude et al. 2014 **South Africa** **Systematic review & meta-analysis**	>50% of trials were deemed to be at high risk of attrition bias, reporting bias or other bias	19 RCTs (n = 3,209) including persons who were overweight or obese (n=14), had diabetes, glucose intolerance or insulin resistance (n=5), cardiovascular conditions or risk factors (hypertension and dyslipidaemia). All trials included men and women with the exception of 2, which included only men. Sample sizes ranged from 36 to 811.	Trials compared low CHO diets with a balanced diet, as described by the British Dietetic Association. Low CHO diets included 8 trials with high protein, low CHO and 6 trials of high fat, low CHO . The intervention periods ranged from 12-104 weeks	**Primary outcomes:** Weight loss, markers of cardiovascular disease, including blood pressure, cholesterol *Stroke was not an outcome*	The percentage of total calories from CHO in the intervention group ranged from 4% to 40%. The corresponding figures for the control group were 52% to 60%. Control and intervention diets were isocaloric. *3-6 months* A low CHO diet was associated with a difference in weight loss of 0.74 kg (95% CI -1.59 to 0.01, p=0.05) in persons who were overweight/obese, but without diabetes. There were no significant differences between groups in mean changes in BMI, SBP/DBP, or chol (LDL, HDL, total chol or triglycerides) in persons who were overweight/obese, but without diabetes. In person who were overweight with diabetes, there were no significant mean differences between groups in mean weight loss, HbA1c, SBP/DBP, or chol (LDL, HDL, total chol or triglycerides) *1-2 years* A low CHO diet was associated with a difference in mean weight loss of 0.48 kg (95% CI -1.44 to 0.49, p=0.33) in persons who were overweight/obese, but without diabetes. There were no significant differences between groups in mean changes in SBP/DBP, BMI or chol (LDL, HDL, total chol or triglycerides) in persons who were overweight/obese, but without diabetes. In person who were overweight with diabetes, there were no significant differences between groups in

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					mean weight loss, HbA1c, SBP/DBP, chol (LDL, HDL, total chol or triglycerides)
Martınez-Gonzalez et al. 2014 **Spain** **Systematic review & meta-analysis**	NA	9 studies (3 case-control studies, 5 cohort studies and 1 RCT-PREDIMED) including participants with no previous history of CVD at baseline	The association between the consumption of olive oil and cardiovascular disease was explored. In all included studies, olive oil consumption was assessed using validated food frequency questionnaires. Repeated FFQs were repeated (yearly) in one study	**Primary outcome:** Coronary heart disease (CHD), stroke and CHD/stroke combined	In cohort studies, there were 543 cases of stroke reported during follow-up periods that ranged from 4.8-10.4 years. For each 25 g/day increase in olive oil consumption there was a significant reduction in the risk of stroke (RR=0.76, 95% CI 0.67-0.86, p<0.001). The results from 3 studies were included. For each 25 g/day increase in olive oil consumption there was a significant reduction in the risk of CHD and stroke combined (RR=0.82, 95% CI 0.70-0.96, p<0.001). The results from 9 studies were included.
Psaltopoulou et al. 2013 **Greece** **Systematic review & meta-analysis**	NA	22 studies examining the relationship between adherence to a Mediterranean diet and risk of stroke, cognitive impairment, Alzheimer's disease and depression. In the 11 studies that assessed stroke as outcome (9 cohort studies, n=162,092 and 2 case-control studies, n=297 cases, 296 controls) both males and females were recruited in 10 studies and the 11th was restricted to females. The age ranges were 23-66 (youngest) to 55-92 years (oldest. The minimum age of participants was 65 years in 3 studies and 60 years in 1 study.	Since different methods were used to assess adherence to the Mediterranean diet across studies, the method developed by Trichopoulou et al, (0-9) was used to standardize scores to represent low, medium and high adherence.	**Primary outcome:** Stroke	Length of follow-up in the cohort studies ranged from 4.1 to 20 years. **High adherence** to a Mediterranean diet was associated with reduced risk of total stroke and ischemic stroke. Overall: RR=0.71, 95% CI 0.57-0.89. Results from 11 trials included: Ischemic stroke: RR=0.52, 95% CI 0.28-0.96. Results from 5 studies included. Hemorrhagic stroke: RR=0.97, 95% CI 0.57-1.67. Results from 2 studies included. Non-fatal stroke: RR=0.48, 95% CI 0.14-1.71. Results from 2 studies included. Fatal stroke: RR=0.69, 95% CI 0.44-1.08. Results from 1 study included. **Moderate adherence** to a Mediterranean diet was not associated with reduced risk of total stroke. Overall: RR=0.90, 95% CI 0.81-1.00. Results from 11 trials included. Ischemic stroke: RR=0.91, 95% CI 0.74-1.13). Results from 6 studies included. Hemorrhagic stroke: RR= 0.91, 95% CI 0.72-1.16. Results from 3 studies included.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					Non-fatal stroke: RR=0.84, 95% CI 0.64-1.09. Results from 3 studies included. Fatal stroke: RR=1.12, 95% .0.86-1.46. Results from 2 study included.
Salehi-Abargouei et al. 2013 **Iran** **Systematic review & meta-analysis**	NA	6 studies that examined the relationship between the Dietary Approaches to Stop Hypertension (DASH)-style diet and cardiovascular disease were included. 4 studies included females only, 1 included only males and 1 included both sexes. Age range at baseline was 30.	All studies, except one identified 8 DASH components (fruits. Vegetable, nuts and legumes, whole grains, low-fat dairy, sodium, red and processes meats and sweetened beverages) and expressed the results as quintiles. No information provided on method used to collect dietary intake data or how diet was scored/ranked.	**Primary outcome:** Heart failure, cardiovascular deaths, coronary heart disease, stroke, stroke death. Most common covariates adjusted for in analyses were age, sex, smoking blood pressure, BMI, physical activity and total energy intake, menopausal status.	Follow-up ranged from 7-24 years. DASH diet was protective for all outcomes. When highest concordance groups were compared with lowest: RR (stroke)=0.81, 95% CI 0.72-0.92, p<0.001. Results from 3 studies included. High adherence to a DASH diet was protective for the development of CVD. RR=0.80, 95% CI 0.74-0.86. Results from 6 studies included
Misirli et al. 2012 **Greece** **Prospective cohort study**	NA	23,601 adults who were participants in the Greek cohort of the EPIC study, free of cancer and CVD at baseline	Dietary intake was assessed using a validated semi quantitative FFQ including 150 items. Adherence to the Mediterranean diet was assessed using the 10-point scale developed by Trichopoulou et al. (0-9) with higher scores indicating better adherence. Scores of 0-3 (low), med (4-5) and high (6-9). Associations between adherence to a Mediterranean diet and CVD were examined with adjustment for sex, age, education, smoking status, BMI,	**Primary outcomes:** CVD, mortality-associated CVD, all stroke, ischemic and hemorrhagic stroke	The median duration of follow-up was 10.6 years. There was a total of 395 CV events and 196 deaths. Compared with the reference category (diet scores 0-3), scores of 4-5 and 6-9 were associated with significantly reduced risk of CVD (HR=0.80, 95% CI 0.64-1.00 and HR=0.72, 95% CI 0.54-0.97, respectively). Each 2-point increase in diet scores was associated with a significant decrease in incident CVD (HR=0.85, 95% CI 0.74-0.96). There were no associated reductions in the risk of CV-associated mortality. Compared with the reference category (diet scores 0-3), scores of 4-5 and 6-9 were not associated with significantly reduced risk of stroke. Ischemic stroke (n=95) HR=0.77, 95% CI 0.50-1.21 and 0.54, 95% CI 0.29-1.01 Hemorrhagic stroke (n=59) HR=1.25, 95% CI 0.69-2.26 and HR=0.86, 95% CI 0.40-1.87.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
			physical activity, hypertension, diabetes, and total energy intake		Dietary components that were associated with reduction in the risk of incident CVD were vegetables, legumes and monounsaturated oils
Agnoli et al. 2011 **Italy** **Cohort Study**	NA	40,681 men and women aged 35-74 years with no history of stroke, MI, hyperlipidemia, diabetes, and those following a special diet for hypertension.	Dietary intake data was collected using a semi-quantitative FFQ. This information was used to develop a score to assess adherence to 4 different dietary eating patterns, Healthy Eating Index (HEI-2005), Dietary Approaches to Stop Hypertension (DASH), Greek Mediterranean Index and the Italian Mediterranean Index.	**Primary outcomes:** All stroke, hemorrhagic and ischemic stroke. Dietary scores of the 4 diet types were expressed as tertiles (T1, T2, T3). Analysis was adjusted for sex, smoking status, education, non-alcoholic energy intake, and BMI.	There were 178 strokes during the follow-up of 7.9 years. The risk of all stroke was significantly reduced for the Italian Mediterranean Diet pattern (T1 vs. T2 HR=0.68, 95% CI 0.48-0.94 & T1 vs. T3 HR=0.47, 95% CI 0.30-0.75, p=0.001). The risk of ischemic stroke was significantly reduced for the HEI-2005, DASH and Italian Mediterranean diet, while no diet pattern was protective for hemorrhagic stroke.
Fung et al. 2004 **USA** **Prospective Cohort study**	NA	71,768 women enrolled in the Nurses' Health Study aged 38-63 years, without CVD or diabetes.	Dietary intake data was collected every 2-4 years from 1984-1998 using a 116-item food-frequency questionnaire. The FFQ had 9 response categories, which were the assembled into 36-42 food groups. Dietary patterns were identified using factor analysis. Two dietary eating patterns were compared, the "prudent diet", characterized by higher intakes of fruits, vegetables, legumes, fish, and whole grains, and the "Western" pattern, characterized by higher intakes of red and processed meats, refined	**Primary outcome:** Incidence of stroke (total, ischemic, hemorrhagic). Analysis was adjusted for; i) age and energy adjusted and ii) fully adjusted-age, smoking status, BMI, menopausal status, aspirin use, energy intake, alcohol intake, physical activity	Over the 14 years of follow-up, there were 791 incident strokes (476 ischemic and 189 hemorrhagic). Comparing the 5th with the 1st quintile, the **prudent diet** was associated with a trend towards lower risk of stroke in the fully adjusted analyses. All stroke: RR=0.78, 95% CI 0.61-1.01, p for trend=0.13. Ischemic stroke: RR=0.74, 95% CI 0.54-1.02, p for trend=0.13. Hemorrhagic stroke: RR=1.01, 95% CI 0.47-1.30, p for trend=0.51. Comparing the 5th with the 1st quintile, the Western diet was associated with an increased risk of stroke in the fully adjusted analyses. All stroke: RR=1.58, 95% CI 1.15-2.15, p for trend=0.0002.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
			grains, and sweets and desserts.		Ischemic stroke: RR=1.56, 95% CI 1.05-2.33, p for trend=0.02. Hemorrhagic stroke: RR=1.63, 95% CI 0.86-3.090, p for trend=0.098.

Vitamin B Supplementation to Reduce Risk of Recurrent Stroke

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Hankey et al. 2010 **International** **RCT** ***VITAmins TO Prevent Stroke (VITATOPS)***	CA: ☑ Blinding: Patient ☑ Assessor ☑ ITT: ☑	8,164 patients with recent stroke or TIA (within previous 7 months) recruited from 20 countries from 1998-2008. Mean age was 62.6 years, 64% were men, 71% ischemic stroke, 17% TIA, 10% ICH or SAH	Patients were randomized 1:1 to receive B vitamins (2 mg folic acid, 25 mg vitamin B_6, and 0.5 mg vitamin B_{12}) or placebo for the duration of the trial	**Primary outcome:** Composite of non-fatal stroke, non-fatal MI, or death from any vascular causes **Secondary outcome:** Stroke (non-fatal or fatal), MI non-fatal or fatal), death from any vascular cause, death from any cause, revascularisation procedures, the composite of non-fatal stroke, non-fatal MI, and death from any vascular cause, and revascularisation procedures of the coronary, cerebral, or peripheral circulation	Median duration of follow-up was 3.4 years. (14,182 person-years). There was a borderline reduction in the risk of the composite outcome in the vitamin B group (15% vs. 17%, RR=0.91, 95% CI 0.82-1.00, p=0.05, absolute risk reduction of 1.56%, 95% CI -0.01-3.16). There were no significant interactions based on subgroup analyses (age, sex, ethnicity, clinical stroke syndrome, stroke pathology, stroke cause, stroke severity, baseline blood creatinine, total homocysteine, and vitamin B12 status). The risk of stroke or stroke/MI or death was not reduced significantly with vitamin B supplementation (9% vs. 10%, RR=0.92, 95% CI 0.81-1.06, p=0.25 and 21% vs. 22%, RR=0.96, 95%CI 0.88-1.04, p=0.26). The risk of fatal or nonfatal stroke was not reduced significantly with vitamin supplementation (9% vs. 10%, RR=0.92, 95% CI 0.81-1.06, p=0.25) At the end of follow-up, the mean total homocysteine concentration was significantly lower in the supplement group 10.5 vs. 14.3 μmol/L, p<0.0001.
Toole et al. 2004	CA: ☑	3,680 patients, recruited from 1997-2002, ≥35 years with non-disabling	Patients were randomized 1:1 to receive high-dose B	**Primary outcome:** Recurrent cerebral infarction	Mean duration of follow-up was 20.3 months.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
USA **RCT** ***Vitamin Intervention for Stroke Prevention (VISP)***	Blinding: Patient ☑ Assessor ☑ ITT: ☑	ischemic stroke (mRS ≤3), occurring ≤120 days previously, with a total homocysteine level ≥25th percentile. Mean age was 66.3 years, 62.5% men. Mean baseline total homocysteine level at randomization was 13.4 µg	vitamins (25 mg B_6, 0.4 mg B_{12}, and 2.5 mg folic acid) or low-dose B vitamins (200 µg B_6, 6 µg B_{12}, and 20 µg folic acid), for the duration of the trial	**Secondary outcome:** Coronary heart disease (CHD), death	There were 148 cases of ischemic stroke in the low-dose group vs. 152 in the high-dose group. There was no significant difference between groups in the relative 2-year risk (8.1% vs. 8.4%, RR=1.0, 95% CI 0.8-1.3). There were 18 cases of fatal or disabling ischemic stroke in the low-dose group vs. 12 in the high-dose group. There was no significant difference between groups in the relative 2-year risk (1.0% vs. 1.2%, RR=1.1, 95% CI 0.6-1.2). There were no significant reductions in the risks of ischemic stroke or CHD; or ischemic stroke, CHD or death associated with high-dose supplementation. Mean total homocysteine fell over the study for patients in both groups, but the decrease at 2 years was greater by 2.3 µg in the high-dose group. There were no significant differences in minor adverse events between groups. There was a significant association between baseline homocysteine levels (classified as low, medium and high) and stroke recurrence in the low-dose group (p=0.02), but not in the high-dose group (p=0.24). When analyzed as a continuous variable, a 3-µmol/L lower total homocysteine level was associated with a 10% lower risk of stroke (p=0.05)
Spence et al. 2005 **Canada** **Sub-group analysis of VISP trial**	NA	2,155 patients hypothesized to benefit the most from vitamin therapy (GFR > 10th percentile for calculated GFR [>46.18] and with serum B12 levels 25th to 95th percentiles (250 to 637 pmol/L). Mean age	As above	**Primary outcome:** Recurrent cerebral infarction **Secondary outcome:** Coronary heart disease (CHD), death	The subgroup included 58.6% of patients randomized. The risk of ischemic stroke was not reduced significantly among patients in the high-dose group in either unadjusted or adjusted analysis (age, sex, BP, smoking and vit B_{12} level) adj HR=0.91, 95% CI 0.67-1.24, p=0.56.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
		was 66 years, 63% male. Mean baseline total homocysteine level at randomization was 12.6 µg.			The risk of the combined outcome of stroke and CHD was not reduced significantly among patients in the high-dose group in either unadjusted or adjusted analysis (adj HR=0.84, 95% CI 0.66-1.06, p=0.14. The risk of the combined outcome of stroke, death and CHD was reduced significantly among patients in the high-dose group in the unadjusted analysis (HR=0.79, 95% CI 0.63-1.00, p=0.049), but not in the adjusted analysis (HR=0.80, 95% CI 0.63-1.01, p=0.056). Patients with a baseline B_{12} level ≥ the median, randomized to high-dose group vitamin had the best overall outcome, and those with B12 <the median randomized to the low-dose group had the worst (p<0.02 for combined stroke, death, and coronary events and p<0.03 for stroke and coronary events).

Interventions to Increase Fruit & Vegetable Consumption

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Hartley et al. 2013 **UK** **Cochrane review**	NA	10 RCTs including 1,730 adults who were at increased risk for stroke because of dyslipidemia, smoking or hypertension. Studies in which 25% of subjects had CVD at baseline (including those who had experienced a previous MI, stroke or had angina) and where more than 25% of the	Interventions included: i) specific dietary advice to increase fruit and vegetable consumption (n=4) and ii) the provision of fruit and vegetables (n=6), to increase consumption. Treatment interventions included the consumption of: 25 g/day of soy (n=1), 130 g/day of cooked pinto beans (n=1), half a grapefruit	**Primary outcome:** Systolic & diastolic blood pressure (SBP, DBP), serum cholesterol & triglycerides (TG). Due to short intervention and follow-up periods, stroke events were not reported.	**Advice to increase fruit and vegetables** Change in SBP from baseline: mean difference (MD) = -3.00, 95% CI -4.92, -1.09, p= 0.0021). Results from 2 trials included. Change in DBP from baseline: MD= -0.90, 95% CI -2.03, 0.24, p= 0.12. Results from 2 trials included. Change in total cholesterol from baseline: MD= -0.01, 95% CI -0.11, 0.09, p= 0.81. Results from 2 trials included. Change in TG from baseline: MD= 0.10, 95% CI -0.06, 0.27, p= 0.20. Results from 3 trials included.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
		participants had type 2 diabetes, were excluded. Four of the 10 trials recruited only female participant. Participants included: women with metabolic syndrome (n=2), healthy post-menopausal women with a family history of breast cancer (n=1), obese individuals (n=1), patients with a history of colorectal adenomatous (n=1), pre-metabolic or healthy individuals (n=1), healthy individuals (n=3).	three times a day (n=1), addition of raw garlic on a sandwich (n=1) a high tomato diet (n=1) and 750 mL/week (n=1) In trials that provided additional fruits and vegetables, the intervention period lasted 3 or 6 months with final assessment at the end of the intervention period. In trials that provided dietary advice, the treatments ranged from a single session to 4 sessions with a dietitian with follow-up of 6 or 12 months. None of the included studies had interventions that provided fruit and vegetables and gave advice.		**Provision of fruits and vegetables** Change in SBP from baseline: mean difference (MD) = 1.00, 95% CI 0.45, 1.55, p= 0.0038). Results favour control condition. Results from 1 trial included. Change in DBP from baseline: MD= 1.50, 95% CI 1.18, 1.82, p<0.0001. Results favour control condition. Results from 1 trial included. Change in total cholesterol from baseline: MD= -0.10, 95% CI -0.24, 0.04 p= 0.17. Results from 2 trials included. Change in TG from baseline: MD= % -0.01, 95% CI 0.03, 0.01, p= 0.32. Results from 3 trials included.
Howard et al. 2006 **USA** **RCT**	CA: ☑ Blinding: Patient ☒ Assessor ☑ ITT: ☑	48,835 postmenopausal women, aged 50 to 79 years (mean=62.3 years) whose dietary intake of fat was ≥32% of total calories at baseline. Exclusions: prior breast or colorectal cancer, other cancers except nonmelanoma skin cancer, medical conditions with predicted survival less than 3 years, type I diabetes,	Participants were randomized to the intervention group (n=19,541) or control group (n=29,294) Participants in the intensive behavior modification group participated in 18 group sessions during the first year and quarterly sessions thereafter, designed to reduce total fat intake to 20% of calories and increase intakes of	**Primary outcome:** Fatal and nonfatal coronary heart disease (CHD), fatal and nonfatal stroke, and total CVD (combined CHD and stroke).	Mean follow-up was 8.1 years. By year 6, relative to those in the control group, participants in the intervention group had reduced their mean fat intake by 8.2%, saturated fat intake by 2.9% and had increased their daily fruit and veg consumption by an average of 1.1 servings. At 3 years, relative to those in the control group, participants in the intervention group had significantly reduced their mean BMI (-0.49), diastolic blood pressure (mean -0.31 mm Hg), total chol (mean -3.26 mg/dL) and increased total carotenoids (mean 0.04 µg/mL).

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
		many meals eaten away from home. Participants were well-matched for stroke risk factors. Current smokers 6.7%, hypertension 43%, hypercholesterolemia 12%, history of stroke or CVD <2%, metabolic syndrome 36%.	vegetables/fruits to 5 servings/d and grains to at least 6 servings/d. Additional individual contact through email or telephone was used to reinforce the message. Participants in the control group received healthy diet-related education materials only.		The intervention was not associated with a significant decrease in stroke risk. All stroke: HR=1.02, 95% CI 0.90-1.17 Fatal stroke: HR=0.94, 95% CI 0.65-1.35 Non-fatal stroke: HR=1.04, 95% CI 0.90-1.19 Ischemic stroke: HR=1.03, 95% CI 0.87-1.22 Hemorrhagic stroke: HR=0.88, 95%CI 0.64-1.20 Total CVD: HR=0.96, 95% CI 0.89-1.03 Losses to follow-up or withdrawals: intervention group n=917, control group n=1,163

Interventions to Decrease Fat Consumption

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Hooper et al. 2015 **UK** **Cochrane review**	NA	15 RCTs (59,000), including adults (≥18 years) at any risk of cardiovascular disease (with or without existing cardiovascular disease), who were taking/not taking lipid-lowering medication. .	Same approach as Hooper et al. 2012, with the focus on saturated fat. Interventions included dietary advice, supplementation of fats, oils or modified or low-fat foods, or a provided diet, vs. control group that could include usual diet, placebo or a control diet. Intended duration of the dietary intervention was at least two years	**Primary outcomes:** All-cause mortality, CVD mortality (deaths from MI, stroke, or sudden death), combined CVD events. **Secondary outcomes:** Additional health events	Following a reduced saturated fat diet was not associated with reductions in the risks of any of the outcomes except combined CV events. Total mortality: RR= 0.97, 95% CI 0.90-1.05, p=0.47, 55,858 participants, 11 RCTs. Mean duration of follow-up was 56 months. CV mortality: RR=0.95, 95% CI 0.80-1.12, p=0.5110 RCTs, 53,421 participants. Mean duration of follow-up was 53 months. All stroke: RR= 1.00, 95% CI 0.89 to 1.12, p=0.97 Results from 7 RCTs, 50,952 participants included. Mean duration of follow-up was 59 months. Non-fatal MI: RR= 0.95, 95% CI 0.80-1.13, p=0.57 7 RCTs, 52,834 participants. Mean duration of follow-up was 55 months.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					Combined CV events: RR=0.83, 95% CI 0.72-0.96, p=0.01. 11 RCTs, 53,300 participants. Mean duration of follow-up was 52 months
Hooper et al. 2012 **UK** **Cochrane review**	NA	48 RCTs, including adults (≥18 years) at any risk of cardiovascular disease (with or without existing cardiovascular disease). 9 studies recruited participants with cardiovascular disease, 12 recruited those at increased risk of CVD, 25 recruited those from the general population without specific CVD risk factors and 2 studies included participants at both high and low CVD risk.	Interventions to reduce or modify fat or cholesterol intake compared with usual diet and was at least 6 months in length. A low-fat diet was considered to be one that aimed to reduce fat intake to < 30% or more from fat, and at least partially replace the energy lost with carbohydrates (simple or complex), protein or fruit and vegetables. A modified fat diet was considered one that aimed to include 30% or more energy from total fats, and included higher levels of mono-unsaturated or poly-unsaturated fats than a 'usual' diet. Interventions included: provision of dietary advice (n=35), provision of dietary advice plus some dietary supplementation (e.g., oils or margarines, n=9), provision of most food eaten by participants (n=16)	**Primary outcomes** Total cardiovascular mortality and combined cardiovascular events	Following a reduced fat or modified fat diet was not associated with reductions in total mortality, or fatal/non-fatal stroke. Total mortality: RR=0.98, 95% CI 0.93- 1.04, p=0.53. Results from 21 trials (n=71,790) included. Stroke: RR= 0.99, 95% CI 0.89- 1.11, p=0.87 Results from 11 trials (n= 59,853) included Following a reduced fat or modified fat diet was associated with reductions total cardiovascular events (RR=0.86, 95% 0.77-0.96, p= 0.0068). Results from 21 trials (n= 65,508) included.

Effect of Dietary Sodium Reduction on Blood Pressure

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Hernandez et al. 2019 **USA** **Systematic review & meta-analysis**	Most trials were considered to have a low risk of bias There was low quality of evidence for SBP and DBP, using GRADE criteria	21 RCTs (15 in hypertensive (n=2016), 2 in normotensive (n=163) and 4 in mixed populations (n=5224). Mean age was 58.7 years.	Trials low-sodium salt substitutes (LSSS) vs. regular salt	**Primary outcome:** Systolic blood pressure (SBP), diastolic blood pressure (DBP), detected HTN, overall mortality, and stroke	Duration of follow-up ranged from 1week to 44 months. Salt substitutes significantly decreased SBP (MD −7.81mm Hg, 95% CI −9.47 to –6.15, p<0.00001, n=16 trials) and DBP (MD −3.96mm Hg, 95% CI −5.17 to –2.74, p<0.00001), n=15 trials). The effect was similar across hypertensive groups (hypertensive, normotensive and mixed), and duration of the intervention (≤ 3 vs. > 3 months). The use of salt substitutes did not significantly reduce the risk of HTN (RR= 0.88, 95%CI 0.75 to 1.03, p=0.11, 4 trials). Only 2 trials reported on the outcome of mortality and one reported on the risk of stroke. Salt substitutes were not associated with significant reductions in either outcome.
Aburto et al. 2013 **UK** **Systematic review & meta-analysis**	NA	56 studies were included (5,508 subjects), 1,478 with hypertension, and 3,263 without. 14 cohort studies and 5 RCTs examined all-cause mortality, CVD, stroke or CHD. 37 RCTs measured blood pressure, renal function or catecholamines	Cohort studies: measured sodium intake for a duration of at least 1 year and reported an outcome of interest. Duration of follow-up ranged from 3.8 to 22 years. RCTs: compared decreased sodium intake with higher sodium intake with a between-group difference of 40 mmol/day with a duration of 4 weeks to 36 months and measured sodium intake using 24-hour	**Primary outcome:** Blood pressure, all-cause mortality, CVD, stroke, CHD, adverse effects, catecholamine levels, renal function	SBP: Mean difference= -3.39, 95% CI -4.31 to -2.46 (results from 36 studies included). Significant reductions of -1.38 and -4.06 for subgroups of subjects without HTN and with HTN DBP: MD= -1.54, 95% CI -2.11 to -0.98 (results from 36 studies included). Significant reduction of -2.26 for subgroup of subjects with HTN In trials where the relative sodium reduction of subjects in the intervention group was <1/3 of the control group, (8 studies), there were significant reduction in both SBP (MD= -1.45, 95% CI -2.29 to -0.60) and DBP (MD= -0.74, 95% CI -1.28 to -0.19)

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
			urinary sodium excretion. Interventions included dietary advice, education, counselling, or provision of foods with a reduced sodium content		In trials where the relative sodium reduction of subjects in the intervention group was ≥1/3 of the control group, (30 studies), there were significant reduction in both SBP (MD= -3.79, 95% CI -4.82 to -2.75) and DBP (MD= -1.68, 95% CI -2.34 to -1.02). Both mean SBP and DBPs were significantly reduced in patients who were taking concomitant drug therapy (-4.55, 95% CI -6.59 to -2.51 and -2.05, 95% CI -3.19 to -0.91, 6 studies) and those not taking drugs (-3.66, 95% CI -4.85 to -2.47 and -1.70, 95% CI -2.37 to -1.04, 27 studies). Increased sodium intake was associated with an increased risk in all stroke (RR= 1.25, 95% CI 1.08 to 1.43, 10 studies) and combined fatal and non-fatal events (RR=1.13, 95% CI 1.01 to 1.26, 8 studies). The authors note that the findings related to stroke occurrence are based on studies of low and very low quality.
He et al. 2013 **UK & China** **Cochrane review**	NA	34 RCTs (n=3,230 subjects). 23 trials were a crossover and 11 were parallel group design. The mean age of participants ranged from 22 to 73 years. Subjects in 22 trials were hypertensive and in 12, were normotensive.	Comparison of trials in which subjects were randomized to a diet that moderately restricted sodium intake (2.3-7.0 g/day or 40-120 mmol/day urinary sodium excretion) or usual intake for a minimum of 4 weeks. Subjects could not receive additional pharmacological therapy for hypertension.	**Primary outcomes:** Change in systolic and diastolic blood pressure at end of treatment.	Study durations were 4 weeks (n=19), 5-8 weeks (n=10), 3-6 months (n=2).>6 months (n=3). **Overall** In subjects in the control group, the median 24-hour urinary sodium excretion was 160 (range: 125-200) mmol or the equivalent of 9.4 (range: 7.3-11.7) grams of salt intake/day. Median blood pressure at baseline was 141/86 mm Hg. The change in urinary sodium excretion from control condition to reduced salt intake was -75 (range: -40 to 118) mmol or a dietary reduction of 4.4 (range: 2.3-6.9) g/day. The mean change in SBP was -4.18 mm Hg (95% CI -5.18 to -3.18), p<0.01. Results from 35 trials included.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					The mean change in DBP was -2.06 mm Hg (95% CI -2.67 to -1.45), p<0.0001. Results from 37 trials included. In meta-regression, a 100 mmol reduction in 24-hour urinary sodium was associated with a 5.8 mm Hg decrease in SBP (95% CI 2.5-9.2), p<0.001. **Hypertension Trials** The median 24-hour urinary sodium excretion was 162 mmol (125-191 mmol) equivalent to a salt intake of 9.5 g/day. The median blood pressure was 148/93 mm Hg. The pooled estimate of the change in 24-hour sodium from the usual to the reduced salt intake was -75 mmol (range -53 to -117mmol) or -4.4 g/day (range (-3.1 to -6.8) grams Na /day. The mean change in SBP was -5.39 mm Hg (95% CI -6.62 to -4.150, p< 0.00001). Results from 21 trials included. The mean change in DBP was -2.82 mm Hg (95% CI -3.54 to -2.11), p<0.0001. Results from 23 trials included. In meta-regression, a 100 mmol reduction in 24-hour urinary sodium was associated with a 10.8 mm Hg decrease in SBP (95% CI 3.5-18.2), p<0.01. **Normotensive Trials** The median 24-hour urinary sodium excretion was 153 mmol (128-200 mmol) equivalent to a salt intake of 8.9 g/day. The median blood pressure was 148/93 mm Hg. The pooled estimate of the change in 24-hour sodium from the usual to the reduced salt intake was -75 mmol (range -40 to -118mmol) or -4.4 g/day (range (-2.3 to -6.89 grams Na /day

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					The mean change in SBP was -2.42 mm Hg (95% CI -3.56 to -1.29, p<0.0001). Results from 14 trials included. The mean change in DBP was -1.00 mm Hg (95% CI -1.85 to -0.15), p<0.0001). Results from 14 trials included.
Stolarz-Skrzypek et al. 2011 **Belgium** **Observational study**	NA	3,681 participants without cardiovascular disease (CVD), were included from the EPOGH and FLEMENGHO studies. Following ascertainment of the outcome portion of the study (described above), 2,856 participants agreed to the follow-up portion of the study and comprised a blood pressure cohort (1,499) and a hypertension cohort (2,096). All the participants in the hypertension cohort were normotensive. Mean age was 38.6 years. 54.1% were female. The mean age of participants in the blood pressure cohort was 38.3 years. 52.4% were female. 9.9% of participants had hypertension at baseline	Baseline measurements included blood pressure, 24-hour urine collection, weight, medical history, demographics. 1-3 follow-up visits were conducted.	**Primary outcomes:** Incident hypertension, changes in systolic blood pressure (SBP) and diastolic blood pressure (DBP)	Median follow-up was 6.5 years for participants of the hypertension cohort and 6.4 years for those in the blood pressure cohort. There were 552 cases of incident hypertension. There was no significant increase in the development of incident hypertension across sodium excretion tertiles (p=0.93) Low: adjusted HR=1.00 (95% CI 0.87 to 1.16) Medium: adjusted HR=1.02 (95% CI 0.89 to 1.16) High: adjusted HR= 0.98 (95% CI 0.86 to 1.12) In the blood pressure cohort, the mean annual change in SBP and DBP were 0.37 and 0.47 mm Hg (p<0.001 for both). Untreated HTN had increased from 9.9% to 19.9% at follow-up. Absolute SBP increased by 1.71 mm Hg /each 100 mmol/ day increment of urinary sodium excretion (95% CI 0.786-2.637, p<0.001). Absolute DBP increased by 0.379 mm Hg /each 100 mmol/ day increment of urinary sodium excretion (95% CI -0.313-1.070, p<0.12).
Whelton et al. 1998 **USA** **RCT** ***A Randomized Controlled Trial of Nonpharmacologic***	CA: ☑ Blinding: Patient ☒ Assessor ☑ ITT: ☑	975 healthy participants, aged 60 to 80 years, with SBP < 145 mmHg and DBP < 85 mmHg while taking a single antihypertensive medication or a single combination regimen consisting of a diuretic agent	390 nonobese participants were randomized to a 3-phase, (intensive, extended and maintenance) diet/exercise program, using small group and	**Primary outcome:** Occurrence of high blood pressure (SBP>190 mm Hg or DBP>110 mm Hg at a single visit), at one or more study follow-up visits, after withdrawal of antihypertensive	Withdrawal of antihypertensive agents was attempted after 3 months. At final follow-up, the mean reduction in SBP was greater for participants in the sodium reduction group compared with usual care (-3.4±0.8 vs. -0.8±0.8, p<0.001).

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Interventions in the Elderly (TONE)		and a non-diuretic agent. Individuals taking 2 antihypertensive medications were also eligible if they were successfully weaned off one of them during the screening phase. Mean age was 66 years, 53% male	individual counseling sessions or usual care. Participants in the intervention group learned about sources of sodium, sodium alternatives and ways to adapt a low-salt diet to their own lifestyle, with the goal of achieving and maintaining a dietary sodium intake of ≤80 mmol/day, measured by 24-hour urine collection. 585 obese participants were randomized to a reduced sodium intake and/or weight loss group	medication and a cardiovascular event Final follow-up was conducted at 30 months	At final follow-up, the mean reduction in DBP was greater for participants in the sodium reduction group compared with usual care (-1.9±0.5 vs. -0.8±0.5, p<0.001). Overall, the risk of the primary outcome over the study period was significantly lower among participants in the sodium reduction group (HR=0.69, 95% CI 0.59-0.81, p<0.001). Among the obese participants, the risk of the primary outcome over the study period was significantly lower among participants in the sodium reduction group (HR=0.70, 95% CI 0.57-0.87, p<0.001). There were 145 cardiovascular events over the study period, including 4 strokes and 17 TIAs. There were no differences between study groups in the risk of any of these events.

Dietary Sodium Intake and Stroke Risk

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Mente et al. 2018 **International** ***Prospective Urban Rural Epidemiological study (PURE)***	NA	For this analysis, there were 95,767 participants from 369 communities for which blood pressure data were available and 82,544 from 255 communities for which cardiovascular outcomes were available. Participants were enrolled from 2003-2013.	Additional reporting from PURE study. Fasting urine was used to estimate 24 h sodium and potassium excretion, which was used as a surrogate for intake. Community-level associations between sodium and potassium intake and BP and cardiovascular diseases, was assessed.	**Primary outcomes:** Cardiovascular events (stroke, MI, heart failure or death)	Mean duration of follow-up was 8.1 years. During follow-up, 6,281 participants had a cardiovascular event or had died. There were 3,695 deaths, of which 3,543 were due to major cardiovascular events (MI n=1372, stroke n=1965, heart failure n=343, and cardiovascular death n=914). The mean community-level sodium intake was 4.77 g/day (range 3.22–7.52). Sodium intake was higher in communities from China (mean of 5.58 g/day). Overall, for each 1 g increase in estimated sodium intake, systolic BP increased by 2·86 mm Hg (95% CI 2·12–3·60, p<0·0001). In the highest sodium intake tertile, the association between community-level systolic BP and sodium intake was positive, large, and significant, but was inverse and non-significant in the communities with sodium intakes in the middle and lower tertiles. Potassium intake was not significantly associated with systolic or diastolic BP. There was a non-linear relationship between sodium intake and cardiovascular events. There was a significant inverse association in the lowest tertile of sodium intake (mean intake of 4.04 g/day) no association in the middle tertile (mean intake of 4.70 g/day), and a non-significant positive association in the highest tertile (mean intake of 5.75g/day). The association between sodium intake and stroke (in all countries with the exception of China) was also nonlinear, with a positive association found only among communities in

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					the highest tertile of sodium intake (>5·08 g/day) and no significant association found in the middle or lowest tertiles.
Feigin et al. 2016 **International** **Retrospective study**	NA	Population-based data from 188 countries from 1990 to 2013.	Data from the Global Burden of Disease Study 2013 was used to estimate the population-attributable fraction (PAF) of stroke-related disability-adjusted life-years (DALYs) associated with 17 potentially modifiable risk factors (including high-sodium diets, defined as > 5g/day) in high-income countries and low-income and middle-income countries.	**Primary outcome:** Stroke burden (expressed as DALYs)	Globally, 22.6% (95% uncertainty interval 12.5%-33.0%) of the stroke burden was attributed to diets high in sodium. In high income countries, 17.8% (95% uncertainty interval 9.2%-26.6%) of the stroke burden was attributed to diets high in sodium. **In Canada, 12.6% (95% uncertainty interval 4.6%-24.3%) of the stroke burden was attributed to diets high in sodium.** Globally, during the study period, there was an increase of 33.4% (95% UI 32.1%, 35.8%) in the burden of stroke related to high sodium diets.
Cook et al. 2014 **USA** **Prospective observational study**	NA	2,275 participants from Trials of Hypertension Prevention (TOHP) phases I and II, recruited over 1897-1995, aged 30-54 years, with prehypertension who received no active treatment (i.e. control group).	Associations between urinary sodium excretion, (averaged across 3-7, 24-hr urine collections) over the study period (18 months in TOHP I, 3-4 yrs TOHP II), and cardiovascular risk over 10-15 years of follow-up. Models were adjusted for age, sex, race other treatment assignments (Model 1) and additional confounders in Models 2 and 3.	**Primary outcome:** Cardiovascular disease or CVD-associated mortality	There were 193 CVD events or death (including 22 strokes). The reference category for sodium excretion was 3600-4800 mg/day. The risks of the primary outcome among the sodium excretion groups for Model 1 were: <2300 mg/day: HR=0.92, 95% CI 0.53-1.60 2300-<3600 mg/day: HR=0.80, 95% CI 0.56-1.13) ≥4800 mg/day: HR=1.11, 95% CI 0.75-1.64, p for trend =0.18. Per 1000 mg/day increase in sodium excretion HR=1.13, 95% CI 1.00-1.27, p=0.044.
Graudal et al. 2014 **Denmark** **Meta-analysis**	NA	23 cohort studies (n=274,683) including all individuals (healthy and those with diseases, all ages, sex and race). Studies in which participants had been advised to reduce their	The relationship between sodium intake and cardiovascular events was examined. Sodium intakes from participants in individual studies were classified	**Primary outcome:** All-cause mortality, cardiovascular disease events **Secondary outcomes:** Stroke, heart disease	Usual sodium intake was associated with a significantly lower risk of all-cause mortality compared with low-sodium intake (HR=0.91, 95% CI 0.82-0.99, p=0.04). Usual sodium intake was associated with a significantly lower risk of all-cause mortality and

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
		sodium consumption were excluded.	as low sodium (mean usual intake <115 mmol), usual sodium (mean daily intake of 115–215 mmol) and high sodium (mean daily intake >215 mmol). Sodium intake was assessed using 24-hour urine secretions, spot urine secretions, or dietary anamnesis (dietary recalls, food frequency questionnaires).	In most studies, analyses were adjusted for sex, age, body mass index, smoking, alcohol, diabetes, CVD, BP, HTN, use of diuretics, intake of total energy, potassium, cholesterol, and education.	cardiovascular events, combined compared with low-sodium intake (HR=0.90, 95% CI 0.82-0.99, p=0.02). Usual sodium intake was not associated with a lower risk of stroke events or stroke mortality, combined compared with low-sodium intake (HR=1.04, 95% CI 0.96-1.13, p=0.33). High-sodium intake was associated with a significantly higher risk of all-cause mortality compared with usual sodium intake (HR=1.16, 95% CI 1.03-1.30, p=0.01). High-sodium intake was associated with a significantly higher risk of all-cause mortality and cardiovascular events, combined compared with high-sodium intake (HR=1.12, 95% CI 1.02-1.24, p=0.02). High-sodium intake was associated with a significantly increased risk of stroke events or stroke mortality, combined compared with usual-sodium intake (HR=1.18, 95% CI 1.05-1.33, p=0.006
Mozaffarian et al. 2014 **International** **Survey data analysis**	NA	Data from national surveys, Cochrane reviews, prospective cohort studies, controlled trials, dietary recommendations and data from the Global Burden of Disease study were used.	Data from various sources were used to: estimate global sodium consumption, estimate the effects of reduced sodium intake on blood pressure, calculate the effects of blood pressure levels on mortality, establish a reference level for sodium intake, and to examine the relationship between CVD mortality and sodium intake above the reference level.	**Primary outcome:** CVD mortality	In 2010, the mean global level of sodium intake was estimated to be 3.95 g/day.99% of all adults in the world had estimated sodium intakes exceeding the WHO recommendations of 2.0 g/day. Mean global systolic blood pressure was 134, 95% CI 124-144 mm Hg. To estimate CVD mortality attributed to excessive sodium intake, a reference level of 2.0‡2.0 g sodium/day was used. Each reduction in sodium intake of 2.3 g/day was associated with a reduction of 3.82 mm Hg.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					Worldwide, an estimated 1.65, 95% CI 1.0-2.2 million deaths were attributed to sodium intake above the reference level, of which 685K (42%) were caused by stroke. 9.5% of all CVD was attributed to sodium consumption.
O'Donnell et al. 2014 **International** ***Prospective Urban Rural Epidemiological study (PURE)***	NA	156,424 participants aged 35-70 years, living in 17 countries, were recruited (starting in 2003) to the prospective Urban Rural Epidemiological (PURE) study. For this analysis, a morning midstream urine sample was available from 101,945 persons. Mean age was 51 years, 42.5% male, 41.5% of participants were hypertensive	The association between dietary sodium intake (estimated from urinary sodium and potassium excretion) and health outcomes was explored, adjusted for age, sex, education, ancestry (Asian vs. non-Asian), ETOH use (former vs. current vs. non), diabetes, BMI, history of CVD, and smoking status) in the primary analysis.	**Primary outcome:** Composite of death/major cardiovascular events Mean length of follow-up was 3.7 years.	The primary outcome occurred in 3317 (3.3%) participants. The reference category for estimated sodium excretion was 4.00-5.99 g/day. (x 2.5 to convert to estimated sodium intake). The risks of the primary outcome among the sodium excretion groups were: **<3.0 g/day: OR=1.27, 95% CI 1.12-1.44** 3.00-3.99 g/day: OR=1.01, 95% CI 0.93-1.09) 6.00-6.99 g/day: OR=1.05, 95% CI 0.94-1.17 **≥7.00 g/day: OR=1.15, 95% CI 1.02-1.30** The pattern of results was similar when additional confounders were controlled for (LD:HDL, dietary factors/blood pressure, excluding CVD at baseline, excluding cancer and restricted to very low-risk cohort). The risks of all-cause mortality among the sodium excretion groups were: **<3.0 g/day: OR=1.39, 95% CI 1.12-1.72** **3.00-3.99 g/day: OR=0.82, 95% CI 0.69-0.99** 6.00-6.99 g/day: OR=1.13, 95% CI 0.93-1.37 ≥7.00 g/day: OR=1.16, 95% CI 0.95-1.43 The risks of all stroke among the sodium excretion groups were: **<3.0 g/day: OR=1.38, 95% CI 1.15-1.66** 3.00-3.99 g/day: OR=1.09, 95% CI 0.96-1.24 6.00-6.99 g/day: OR=1.02, 95% CI 0.89-1.18 **≥7.00 g/day: OR=1.25, 95% CI 1.07-1.48**

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					Higher urinary potassium excretion (>3 g/day) was associated with reduced risks of all-cause mortality (OR= 0.62, 95% CI 0.49- 0.77), major cardiovascular events (OR= 0.87, 95% CI 0.72- 1.06) and cardiovascular death (OR= 0.48, 95% CI 0.32- 0.71). In subgroup analysis, the risk of the primary outcome was increased significantly for persons with HTN and estimated sodium excretion >6 g/day (OR= 1.17, 95% CI 1.04- 1.31) vs. no HTN and estimated sodium excretion > 6g/day (OR=0.89, 95% CI 0.78- 1.03), p for interaction=0.02. There were no other significant interactions among subgroups.
Stolarz-Skrzypek et al. 2011 **Belgium** **Observational study**	NA	3,681 participants without cardiovascular disease (CVD), who were included in the EPOGH and FLEMENGHO studies. The mean age of participants was 40.9 years. 52.7% were female. 25.8% had hypertension at baseline.	Baseline measurements included blood pressure, 24-hour urine collection, weight, medical history, demographics. 1-3 follow-up visits were conducted	**Primary outcome:** Mortality, fatal and non-fatal cardiovascular events	Median follow-up of 7.9 years. There were 219 deaths (84 cardiovascular and 135 noncardiovascular). Of these, there were 20 fatal and 13 non-fatal strokes. Across sodium excretion tertiles (low: mean 106 mmol, medium: mean 165 mmol, high: 250 mmol), there was no increased risk of all-cause mortality (p=0.10). Low: adjusted HR=1.14, (95% CI 0.87-1.50) Medium: adjusted HR=0.94 (95% CI 0.75-1.18) High: adjusted HR=1.06 (95% CI 0.84-1.33) There was a decrease in cardiovascular mortality with increasing sodium excretion (p=0.02) Low: adjusted HR=1.56 (95% CI 1.02-2.36), p=0.04 Medium: adjusted HR=1.05 (95% CI 0.72-1.53) High: adjusted HR=0.95 (95% CI 0.66-1.38) There was no increase in the risk of fatal/non-fatal stroke (p=0.64) Low: adjusted HR=1.07 (95% CI 0.57-2.00)

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					Medium: adjusted HR=1.29 (95% CI 0.75-2.200 High: adjusted HR=0.78 (95% CI 0.45-1.33) There was no increase in stroke mortality risk in subgroup analysis examining age (<60 years and ≥60 years)
Strazzullo et al. 2009 **Italy** **Systematic review & meta-analysis**	NA	13 prospective cohort studies (n=177,025) in which dietary sodium intake was estimated at baseline and subjects were followed for at least 3 years. 11 studies included both men and women while 2 only included men.	Sodium intake was estimated using a 24-hour recall (n=3), 24-hr urine collection (n=4), food frequency questionnaire (n=3), household survey questionnaire (n=1) and multiple methods (n=2).	**Primary outcome:** Risk of stroke, risk of cardiovascular disease. Classification of salt intake varied across studies (continuous variable, quartiles, quintiles), therefore, where possible, the authors compared "higher" versus "lower" intakes based on the categories in which salt intake differed by an average of 100 mmol (6 grams/day)	Follow-up ranged from 3.5 to 19 years. Higher salt intake was associated with increased risk of stroke (RR=1.23, 95% CI 1.06 to 1.43, p=0.007). Results from 10 studies included Higher salt intake was associated with a trend towards increased risk of cardiovascular disease (RR=1.14, 95% CI 0.99 to 1.32, p=0.07). Results from 9 studies included.

Interventions Designed to Reduce Sodium intake

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Adler et al. 2014 **UK** **Cochrane review**	NA	8 RCTs including 3 in healthy, normotensive individuals (n= 3518), 2 in persons with hypertension and 3 in mixed populations of normo- and hypertensives, who were both treated and untreated for HTN.	Trials examined interventions designed to reduce dietary salt intake, either by advice from health professionals (n=6) or provision of low-sodium salt substitution (n=2) versus usual care, control or placebo diet, or no intervention.	**Primary outcomes:** All-cause mortality, cardiovascular mortality, cardiovascular morbidity **Secondary outcomes:** Changes in SBP and DBP, urinary salt excretion (or other method of estimation of salt intake), Health-related quality of life	Dietary sodium reduction was not associated with a reduced risk of all-cause mortality at end of trial: RR= 0.96, 95% CI 0.83-1.10. (Results from 7 trials included). There was not associated risk reduction when trials of normotensive (n=3) or hypertensive (n=4) persons were examined separately. Dietary sodium reduction was not associated with a reduced risk of all-cause mortality at end of follow-up in trials of normotensive persons (RR= 0.90, 95% CI 0.58-1.40, results from 3 trials included), nor in trials with hypertensive persons (RR= 0.99, 95% CI 0.87-1.14, results from 5 trials included).

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
			Sodium reduction goals varied from 70-100 mmol/day urinary sodium	Trial durations ranged from 7 to 36 months with additional follow-up ranging from 30 months to 11.5 years.	Dietary sodium reduction was associated with a reduced risk of cardiovascular events at the end of follow-up: RR= 0.77, 95% CI 0.63-0.95. Results from 6 trials included). However, when the trials of normotensive and hypertensive persons were examined separately, there was a non-significant risk reduction. There was a significant reduction in SBP (mean difference= -1.79, 95% CI -3.23 to -0.36, results from 6 trials) and DBP (mean difference= -1.17,95% CI -2.08 to -0.2, results from 5 trials)
Taylor et al. 2011 **UK** **Systematic review & meta-analysis**	NA	7 RCTs (n=6,491) that included adults who were both normotensive and hypertensive. Mean age ranged from 39 to 75 years. In 2 studies 100% of subjects were male. Subjects were on antihypertensive medications in 3 trials.	Intervention group received group or individual counseling and behaviour change programs to reduce dietary sodium (n=6) or ate high potassium (low sodium) prepared foods. Average duration was 6 months (n=2), 18 months (n=1), 31 months (n=1), 36 months (n=20 and was unclear in one study. Sodium excretion goals were set at <70-100 mmol/day. Subjects in the control group did not receive dietary instruction (n=3) or were given general guidelines for healthy eating (n=1), attended group meetings without dietary counseling (n=1), received same dietary advice as subjects in treatment arm + additional 40 mmol	**Primary outcomes:** All-cause mortality at end of trial, cardiovascular disease, systolic blood pressure (SBP), diastolic blood pressure (DBP) Follow-up ranged from 6 months to 12.7 years.	All-cause mortality at end of trial: Among subjects who were normotensive at baseline: RR=0.67, 95% CI 0.40 to 1.12, p=0.13. Results from 3 trials included. Among subjects who were hypertensive at baseline: RR=0.97, 95% CI 0.83 to 1.13, p=0.72. Results from 2 trials included. All-cause mortality at end of follow-up: Normotensive: RR=0.90, 95% CI 0.58 to 1.40, p=0.64. Results from 3 trials included. Hypertensive: RR=0.96, 95% CI 0.83 to 1.11, p=0.61. Results from 3 trials included. CVD mortality at longest follow-up Normotensive: no data Hypertensive: RR=0.69, 95% CI 0.45 to 1.5, p=0.08. Results from 2 trials included. CVD events at longest follow-up Normotensive: RR=0.71, 95% CI 0.42 to1.20, p=0.20. Results from 2 trials included. Hypertensive: RR=0.84, 95% CI 0.57 to 1.23, p=0.38. Results from 2 trials included. SBP at end of trial

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
			sodium/day (n=1) or ate prepared foods containing usual salt (high sodium).		Normotensive: Mead difference= -1.11, 95% CI -2.34 to 0.11 mm Hg, p=0.007. Results from 3 trials included. Hypertensive: MD=-4.14, 95% CI -5.84 to -2.43 mm Hg, p<0.0001. Results from 2 trials included. DBP at end of trial Normotensive: MD= -0.80, 95% CI -1.37 to -0.23 mm Hg, p=0.006. Results from 3 trials included. Hypertensive: MD= -3.74, 95% CI -0.41 to 0.93 mm Hg, p=0.12. Results from 2 trials included. Urinary sodium was reduced by 34 mmol in normotensives and 39 mmol in hypertensives.
Hooper et al. 2004 **UK** **Cochrane review**	NA	11 RCTs including 3 trials in normotensives (n=2,326), 5 in untreated hypertensives (n=387) and 3 in treated hypertensives (n=801) Subjects in all studies were adult (≥16 years) Persons who were institutionalized, acutely ill or pregnant, were excluded. Most trials included both men and women.	Comparison of interventions designed to reduce dietary sodium intake that lasted at least 6 months compared with placebo or no intervention. Studies that included multiple risk factor intervention programs that included a salt reduction component, were excluded. Interventions: comprehensive diet and behavior change programs including individual or group counseling sessions, with provision of written materials, and/or instruction on reducing sodium in cooking or provision of low salt diets. Programs lasted several months. Treatment goals were urinary sodium	**Primary outcome:** Mortality, cardiovascular mortality, systolic blood pressure (SBP), diastolic blood pressure (DBP)	Follow-up ranged from 6 months to 7 years. At the end of follow-up, there were 17 deaths (1 from stroke) Mortality: RR= 0.90, 95% CI 0.36- 2.24, p=0.82. Results from 4 studies included. Cardiovascular mortality: RR= 0.82, 95% CI 0.56-1.21, p=0.32. Results from 2 studies included. SBP: Mean difference= -1.12, 95% CI -1.83, -0.41, p=0.0020. Results from 4 studies with 13 to 60 months of follow up were included. DBP: MD= -0.62, 95% CI -1.54, 0.31, p=0.19. Results from 4 trials with 13 to 60 months of follow up were included. Urinary sodium excretion. Mean difference= - 35.5 mmol/ 24 hours, 95% CI -47.2 to -23.9, p<0.0001. Results from 4 studies that assessed outcome 13 to 60 months following initiation of intervention were included.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
			excretion of 70-100 mmol/day.		

Abbreviations

ARR: absolute risk reduction	CA: concealed allocation	CI: confidence interval
HR: hazard ratio	ITT: intention-to-treat	NA: Not assessed
OR: odds ratio	RR: relative risk	RRR: relative risk reduction

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