Nutrition and the risk of stroke

Graeme J Hankey

Poor nutrition in the first year of a mother’s life and undernutrition in utero, infancy, childhood, and adulthood predispose individuals to stroke in later life, but the mechanism of increased stroke risk is unclear. Overnutrition also increases the risk of stroke, probably by accelerating the development of obesity, hypertension, hyperlipidaemia, and diabetes. Reliable evidence suggests that dietary supplementation with antioxidant vitamins, B vitamins, and calcium does not reduce the risk of stroke. Less reliable evidence suggests that stroke can be prevented by diets that are prudent, aligned to the Mediterranean or DASH (Dietary Approaches to Stop Hypertension) diets, low in salt and added sugars, high in potassium, and meet, but do not exceed, energy requirements. Trials in progress are examining the effects of vitamin D and marine omega-3 fatty acid supplementation on incidence of stroke. Future challenges include the need to improve the quality of evidence linking many nutrients, foods, and dietary patterns to the risk of stroke.

Introduction

Between 1970 and 2008, the incidence of stroke in high-income countries fell by 42%, from 163 (95% CI 98–227) to 94 (72–116) per 100 000 person years.1 This decline coincided with increased public awareness of the dangers to health posed by high blood pressure, high blood cholesterol, and cigarette smoking, and reduced prevalence of these risk factors in the population.2 By contrast, between 1970 and 2008, the incidence of stroke in low-income and middle-income countries increased by more than 100%, from 52 (95% CI 33–71) to 117 (79–156) per 100 000 person years.1 This increase coincided with food and lifestyle changes arising from industrialisation and urbanisation.3

Modernisation, overconsumption of calories, and increased prevalence of obesity, metabolic syndrome, and type 2 diabetes mellitus threaten to stem the decline of stroke incidence in high-income countries and to accelerate the increase in stroke incidence in low-income and middle-income countries.4–7 Accurately assessing and understanding the role of nutrition in the causes and consequences of stroke will be crucial in developing and implementing strategies to minimise the global burden of stroke.8–12 The aim of this Review is to examine the evidence linking nutrition and diet to the risk of stroke.

Nutritional status

What is malnutrition?

Malnutrition has no universally accepted definition but describes a deficiency, excess, or imbalance in a wide range of nutrients, resulting in a measurable adverse effect on body composition, function, and clinical outcome.8 Undernutrition describes a long-standing deficiency of essential nutrients, most commonly energy (kJ or calories) and protein,9 whereas overnutrition describes an excess intake of nutrients (most commonly saturated fats and carbohydrates) for metabolic and health requirements.

How is nutritional status assessed?

Nutritional assessment is not standardised. The simplest measure of nutritional status is bodyweight, but it can be confounded by height and ethnic origin, and, in severe protein malnutrition, by fluid retention due to hypoalbuminaemia.

Body fat content is estimated by body mass index (BMI), which is a measure of weight in kilograms divided by the square of height in metres.13 Adults with a BMI of 18·5–24·9 kg/m² are categorised as being of normal weight, individuals with a BMI of 25·0 to 29·9 kg/m² as overweight, and those with a BMI of 30 kg/m² or more as obese.13 A drawback of this measure is that different ethnic groups have different proportions of fat to lean tissue at equivalent BMIs.14

Other measures of nutritional status include indicators of visceral adiposity, such as the waist-to-hip ratio, waist-to-height ratio, and waist circumference,15 and indicators of protein status, such as serum albumin and prealbumin concentrations.16–20

How common is malnutrition?

Undernutrition is common, under-recognised, and undertreated. In the UK, about 5% of the population have a BMI of below 18·5 kg/m².21 In UK hospitals, the prevalence of malnutrition is reported to range from 13% to 40%.18,21 The prevalence of undernutrition increases at least two times in the elderly and in those with chronic disease, and three times in people living in institutional care, such as survivors of stroke.19,20

The elderly are especially prone to deficiencies of specific micronutrients such as folate.22 Malnutrition is also common in situations of poverty, social isolation, and substance misuse.

An estimated 1·46 billion adults and 170 million children worldwide are now classified as overweight, including 502 million adults who are obese.5 In the USA, two-thirds of adults are overweight and one-third obese,5,23 and the incidence and prevalence of being overweight or obese in children and adults are increasing.5,23–25

Is malnutrition a risk factor for stroke?

The methods used to investigate the effects of nutritional factors on the risk of stroke have limitations (panel 1),7 and the results of such studies should be interpreted with caution, bearing in mind the criteria that need to be fulfilled to establish a causal association between a risk factor and disease.26,27
Undernutrition

Mother and fetus

Observational studies suggest that poor nutrition in the first year of a woman’s life leads to deformity of the bony pelvis.\(^{30,31}\) During subsequent pregnancy in adulthood, a flat pelvis impairs the mother’s ability to sustain growth of the placenta and fetus, as manifest by lower placental weight, smaller head circumference, and lower birthweight of the baby.\(^{30,31}\) In turn, these factors seem to be associated with an increased risk of stroke in the mother’s offspring.\(^{30,31}\) The mechanism by which poor maternal nutrition and poor growth in utero might increase the risk of stroke could be linked to hypertension and raised plasma fibrinogen concentrations in adulthood, and a permanent adverse effect on vascular structure and function.\(^{30,31}\)

Children

Observational evidence suggests that poor growth in childhood due to poor nutrition is associated with an increased risk of stroke in later life.\(^{30,31}\) Table 1 shows that for every one SD decrease in the difference between bodyweight at 2 years and that predicted from birthweight, the hazard ratio for stroke in adulthood increased by about 18% (hazard at 2 years and that predicted from birthweight, the hazard ratio per 1 SD decrease in the difference between bodyweight at different ages during childhood, the hazard ratio for stroke increased by 4–20% (table 2).\(^{30,31}\) These data suggest that biological vulnerability to stroke begins during early life and develops throughout the lifespan to increase risk of stroke later in life. This hypothesis is supported by observational data showing a 25% higher incidence of stroke among US adults who had lived as children in the southeastern states, or so-called stroke belt, of the USA, where stroke mortality rates are highest.\(^{30,31}\)

Adults

Few data correlate undernutrition in adulthood with risk of stroke. A collaborative analysis of 57 prospective studies in which 894,576 adults were followed up for a mean of 13 years (deaths during the first 5 years were excluded to limit reverse causality) showed that, in the lower range (15–25 kg/m²), each 5 kg/m² lower BMI was associated with a non-significant trend towards an increase in stroke mortality by 9% (hazard ratio 1.09, 95% CI 0.97–1.22).\(^{30,31}\) The association was stronger for haemorrhagic stroke (1.32, 1.00–1.72) than for ischaemic stroke (1.15, 0.91–1.47) but was not significant.\(^{30,31}\)

Among 8920 individuals with renal impairment who started renal dialysis, undernourishment, low bodyweight, and low serum albumin at baseline were independent, significant predictors of incident stroke after a median follow-up of 3.1 years.\(^{30,31}\)

Overnutrition

Obesity is associated with an increased risk of stroke, whether measured by BMI, waist-to-hip ratio, waist-to-
Table 3: Risk factors for stroke

<table>
<thead>
<tr>
<th>Prevalence</th>
<th>Odds ratio (99% CI)</th>
<th>Population attributable risk (99% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>History of hypertension</td>
<td>32%</td>
<td>56%</td>
</tr>
<tr>
<td>No regular physical activity</td>
<td>88%</td>
<td>92%</td>
</tr>
<tr>
<td>Waist-to-hip ratio (tertile 3 vs tertile 1)</td>
<td>33%</td>
<td>41%</td>
</tr>
<tr>
<td>Apolipoprotein B/A1 ratio (tertile 3 vs tertile 1)</td>
<td>33%</td>
<td>47%</td>
</tr>
<tr>
<td>Current smoking</td>
<td>24%</td>
<td>36%</td>
</tr>
<tr>
<td>Unhealthy diet risk score (tertile 3 vs tertile 1)</td>
<td>30%</td>
<td>35%</td>
</tr>
<tr>
<td>Cardiac causes*</td>
<td>5%</td>
<td>12%</td>
</tr>
<tr>
<td>Diabetes</td>
<td>12%</td>
<td>19%</td>
</tr>
<tr>
<td>Depression</td>
<td>14%</td>
<td>20%</td>
</tr>
<tr>
<td>Psychosocial stress</td>
<td>15%</td>
<td>20%</td>
</tr>
<tr>
<td>Alcohol intake &gt;30 drinks per month</td>
<td>11%</td>
<td>16%</td>
</tr>
</tbody>
</table>

Multivariable model adjusted for age, sex, and region. Risk factors for all stroke in 3000 patients with acute first stroke (within 5 days of symptom onset) compared with 3000 controls with no history of stroke who were matched with cases for age and sex, and who were assessed in 22 countries between 2007 and 2010 in the INTERSTROKE study.45

Table 2: Association of low bodyweight at birth, during infancy, and in childhood (poor growth) with an increased risk of stroke in later life

<table>
<thead>
<tr>
<th>SD decrease in weight at different ages</th>
<th>Hazard ratio (95% CI) for stroke per one unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 years</td>
<td>1.10 (1.01–1.20)</td>
</tr>
<tr>
<td>1 year</td>
<td>1.15 (1.05–1.27)</td>
</tr>
<tr>
<td>2 years</td>
<td>1.20 (1.10–1.32)</td>
</tr>
<tr>
<td>7 years</td>
<td>1.14 (1.03–1.27)</td>
</tr>
<tr>
<td>15 years</td>
<td>1.04 (0.94–1.16)</td>
</tr>
</tbody>
</table>

Data from Osmond and colleagues.21

23 kg/m².23 Each unit increase in BMI is associated with an increase in the adjusted risk of stroke by about 6% (relative risk 6%, 95% CI 4–8).30 Among adults who are overweight or obese (BMI 25–50 kg/m²), each 5 kg/m² increase in BMI is associated with about 40% higher mortality from stroke (hazard ratio 1.39, 95% CI 1.31–1.48).31

Individuals with a waist-to-hip ratio in the highest tertile (>0.96 in men and >0.93 in women) have a 65% increased risk of stroke (odds ratio 1.65, 99% CI 1.36–1.99) compared with individuals in the lowest tertile (<0.91 in men and <0.86 in women).32 The population attributable risk of stroke associated with an increased waist-to-hip ratio is 26.5% (99% CI 18.8–36.0; table 3).33

Although BMI, waist-to-hip ratio, and waist circumference do not meaningfully improve prediction of stroke risk when added to causal risk factors such as systolic blood pressure and history of diabetes, excess adiposity remains a major modifiable determinant of these causal risk factors.33 Hence, controlling adiposity is likely to help prevent stroke.33,34

Which nutrients affect the risk of stroke?

Antioxidant vitamins

Many nutrients can affect the risk of stroke (panel 2). The oxidation hypothesis of atherosclerosis—that oxidation of low-density lipoprotein (LDL) cholesterol (lipid peroxidation) allows it to accumulate in artery walls and promote atherosclerosis84—prompted several studies of antioxidant vitamins in the prevention of stroke and death.

A meta-analysis of 68 randomised trials of antioxidant supplements versus placebo in 232,605 participants showed that overall, antioxidants had no effect on mortality (relative risk 1.02, 95% CI 0.98–1.06).45 However, multivariate meta-regression analyses showed that low-bias risk trials (as defined by adequate generation of treatment allocation sequence, allocation concealment, masking, and follow-up) were significantly associated with mortality.45 In 47 low-bias trials with 180,938 participants, the antioxidant supplements significantly increased mortality (relative risk 1.04, 95% CI 1.02–1.08), especially exposure to vitamin A (1.16, 1.10–1.24), β-carotene (1.07, 1.02–1.11), and vitamin E (1.04, 1.01–1.07); vitamin C (1.06, 0.94–1.20) and selenium (0.90, 0.80–1.02) had no significant effect on mortality.45

Vitamin A and β-carotene

β-carotene, the biologically active metabolite of vitamin A, did not affect stroke rates in 82,483 participants enrolled in three randomised trials (odds ratio 1.0, 95% CI 0.91–1.09),48 but did increase all-cause mortality in 138,113 participants in eight randomised trials (1.07, 1.02–1.11) and cardiovascular mortality among 131,551 participants in six randomised trials (1.10, 1.03–1.17).47

Vitamin C

Vitamin C is a water-soluble antioxidant in plasma that helps regenerate oxidised vitamin E. Although observational studies suggest that increased dietary intake and plasma concentrations of vitamin C are associated independently with reduced rates of stroke,49–51 large randomised trials show no benefit of vitamin C supplementation in preventing stroke and other clinical outcomes.52–54

Vitamin E

Vitamin E is a lipid-soluble antioxidant that increases the resistance of LDL cholesterol to oxidation, reduces proliferation of smooth muscle cells, and reduces adhesiveness of platelets to collagen. This vitamin inhibits lipid peroxidation by scavenging reactive oxygen species and preserving cell membranes.55

In 2010, a meta-analysis of seven randomised trials with 116,567 individuals revealed that vitamin E had no effect on risk of incident total stroke (relative risk 0.98, 95% CI 0.91–1.05) but increased the risk of incident haemorrhagic stroke (1.22, 1.00–1.48) and reduced the
risk of incident ischaemic stroke (0.90, 0.82–0.99). Heterogeneity among the studies was not evident ($I^2=12.8\%$; $p$ for heterogeneity=0.33). However, in 2011, an updated meta-analysis of 13 randomised trials of vitamin E in 166,282 participants showed no significant benefit in the prevention of stroke of any type (relative risk 1.01, 95% CI 0.96–1.07), ischaemic stroke (1.01, 0.94–1.09), or haemorrhagic stroke (1.12, 0.94–1.33). Significant heterogeneity among the studies was not evident ($p$ for heterogeneity=0.37).

The reasons for the discrepancy in findings for the effect of vitamin E on the pathological subtypes of stroke in the two meta-analyses might be the inclusion of six additional trials, longer follow-up data from one shared trial, and perhaps (although not stated) recurrent as well as incident strokes in the updated meta-analysis.

**B vitamins**

Increased serum concentrations of total homocysteine have been associated independently with an increased risk of stroke. Heterogeneity among the studies was not evident ($I^2=45\%$; $p$ for heterogeneity=0.33). However, in 2011, an updated meta-analysis of 13 randomised trials of vitamin E in 166,282 participants showed no significant benefit in the prevention of stroke of any type (relative risk 1.01, 95% CI 0.96–1.07), ischaemic stroke (1.01, 0.94–1.09), or haemorrhagic stroke (1.12, 0.94–1.33). Significant heterogeneity among the studies was not evident ($p$ for heterogeneity=0.37).

The reasons for the discrepancy in findings for the effect of vitamin E on the pathological subtypes of stroke in the two meta-analyses might be the inclusion of six additional trials, longer follow-up data from one shared trial, and perhaps (although not stated) recurrent as well as incident strokes in the updated meta-analysis.

### Panel 2: Effects of nutrients on the risk of stroke

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>Effects on Stroke</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antioxidant vitamins</strong></td>
<td></td>
</tr>
<tr>
<td>Vitamin A</td>
<td>Supplementation increases all-cause mortality.</td>
</tr>
<tr>
<td>β-carotene</td>
<td>Supplementation increases cardiovascular and all-cause mortality and does not prevent stroke.</td>
</tr>
<tr>
<td>Vitamin C</td>
<td>Supplementation does not prevent stroke.</td>
</tr>
<tr>
<td>Vitamin E</td>
<td>Supplementation increases all-cause mortality and does not prevent stroke.</td>
</tr>
<tr>
<td><strong>B vitamins (folic acid)</strong></td>
<td>Supplementation does not prevent stroke in populations with high folate intake; deficiency could be a causal and treatable risk factor for stroke in regions of low folate intake.</td>
</tr>
<tr>
<td><strong>Vitamin D</strong></td>
<td>Deficiency is associated with hypertension, cardiovascular disease, and stroke. Supplementation is not proven to prevent cardiovascular events. Randomised trials investigating vitamin D supplementation are in progress.</td>
</tr>
<tr>
<td><strong>Salt</strong></td>
<td>Supplementation by 5 g per day is associated with a 23% (95% CI 6–43) increased risk of stroke. Reduction in salt intake is not proven to reduce stroke. Reduction by 2 g per day reduces cardiovascular events by 20% (95% CI 1–36); reduction also lowers blood pressure.</td>
</tr>
<tr>
<td><strong>Potassium</strong></td>
<td>Supplementation by 1 g per day is associated with an 11% (95% CI 3–17) reduction in the risk of stroke; supplementation is not proven to prevent stroke. Supplementation by 0.8 g per day reduces blood pressure by 5/3 mm Hg.</td>
</tr>
</tbody>
</table>

**Calcium**

Supplementation by more than 0.5 g per day does not prevent stroke, might increase the risk of stroke, and can increase the risk of myocardial infarction by 31% (95% CI 2–67). Although homocysteine can be lowered by up to 25% (95% CI 1–15), but in one randomised trial it did not reduce stroke risk (hazard ratio 1.04, 95% CI 0.62–1.75).

**Fats**

Total fat

High intake is not associated with increased risk of stroke. Reduced intake does not reduce risk of stroke.

Trans fats

High intake is not associated with increased risk of stroke.

Saturated fats

High intake is not associated with increased risk of stroke.

**Marine n-3 polyunsaturated fats**

Supplementation reduces cardiovascular events and death by 8% (95% CI 1–15), but in one randomised trial it did not reduce stroke risk (hazard ratio 1.04, 95% CI 0.62–1.75). Randomised trials of folic acid versus control showed no effect of supplementation with folic acid on all stroke mortality. High intake is associated with increased stroke mortality.

**Fibre**

High intake is associated with reduced blood pressure, blood glucose, and LDL-cholesterol.

**Proteins**

High intake is not associated with risk of stroke.
In individuals who are folate-replete, vitamin B12 is an important determinant of total homocysteine, and subclinical vitamin B12 deficiency is not uncommon. Subgroup analyses from randomised trials raise the hypothesis that use of high doses of vitamin B12 in people who are folate-replete but vitamin B12 deficient could substantially lower total homocysteine and risk of stroke. This hypothesis requires confirmation a priori in clinical trials.

Vitamin D
Observational studies report an association between 25-hydroxyvitamin D and an increased incidence of hypertension, carotid artery atherosclerosis, and cardiovascular disease, including stroke. Although randomised trials show that vitamin D supplementation lowers blood pressure and improves endothelial function in the short term, two trials showed no significant effect on cardiovascular events of vitamin D supplementation at moderate to high doses (relative risk 0.90, 95% CI 0.83–0.97). If causal, the association might be mediated by lowered blood pressure, serum-lipid concentrations, and observational studies (relative risk 0.78, 95% CI 0.73–0.85). Potassium
An observational study of 38772 older women (mean age 61·6 years in 1986) reported that subsequent mortality was increased significantly in users of multivitamins (hazard ratio 1.06, 95% CI 1.02–1.10; absolute risk increase 2.4%, folic acid (1.15, 1.00–1.32; 5.9%), vitamin B6 (1.10, 1.01–1.21; 4.1%), iron (1.10, 1.03–1.17; 3.9%), magnesium (1.08, 1.01–1.15; 3.6%), zinc (1.08, 1.01–1.15; 3.0%), and copper (1.45, 1.20–1.75; 18.0%), and decreased in users of calcium (0.91, 0.88–0.94; 3.8%). These results and the effects on risk of stroke and its subtypes require confirmation by randomised trials. Salt
Most adult populations around the world have average daily salt intakes of higher than 6 g, and many in eastern Europe and Asia of more than 12 g, mostly from processed foods. Observational studies show that sustained high daily salt intake of 5 g on average (86 mmol [one teaspoon]) is associated with a 23% greater risk of stroke (pooled relative risk 1.23, 95% CI 1.06–1.43) and a 17% greater rate of total cardiovascular disease (relative risk 1.17, 1.02–1.34). No data on stroke subtypes were available but a large prospective, community-based, case-control study reported that adding salt to food not only independently increased the odds of all stroke (odds ratio 1.5, 95% CI 1.0–2.3), but that most of the effect was driven by an increase in odds of haemorrhagic stroke (3.5, 95% CI 1.6–7.6). Indeed, about 20% (95% CI 1–38) of all primary intracerebral haemorrhages were attributable to adding salt to food. A meta-analysis of six randomised trials showed that a reduction in dietary salt intake by 2·0–2·3 g (half a teaspoon) per day was associated with a reduction in cardiovascular events by 20% (relative risk 0.80, 95% CI 0.64–0.99). However, no randomised trials of the effect of salt reduction on risk of stroke or its pathological and aetiological subtypes have been done.

Excess salt intake might increase cardiovascular and stroke risk by increasing blood pressure and causing fibrosis in the heart, kidneys, and arteries. Reducing dietary salt intake by 6 g a day reduces systolic and diastolic blood pressure by 4 and 2 mm Hg, respectively, in people without hypertension, 7 and 4 mm Hg, respectively, in those with hypertension, and 23 and 9 mm Hg, respectively, in people with resistant hypertension. Sodium reduction by 6 g per day also blunts the age-related rise in blood pressure by about 0·5 mm Hg per year. The response of blood pressure to sodium reduction is direct and progressive, but non-linear; decreasing sodium intake by about 0·9 g per day causes a greater reduction in blood pressure when the starting sodium intake is about 2·3 g per day than when it is about 3·5 g per day. A higher potassium intake of 42 mmol/L (1·64 g) per day was associated with a 21% reduced risk of stroke after 5–19 years of follow-up of 247 510 adults in 11 observational studies (relative risk 0·79, 95% CI 0·60–0·90). For every increase in potassium intake by 1 g per day, the risk of stroke decreased by 11% (relative risk 0·89, 95% CI 0·83–0·97). If causal, the association might be mediated by lowered blood pressure; increasing potassium intake by 20 mmol (0·78 g) or more per day lowers blood pressure by an average of 4·9 mm Hg systolic blood pressure and 2·7 mm Hg diastolic blood pressure in patients with hypertension. Randomised trials are needed to establish the independent effects of long-term increases in dietary potassium intake on stroke risk, but are unlikely to be undertaken because of technical difficulties and possible ethical constraints.

Calcium
Many guidelines recommend adequate calcium intake as part of the prevention or treatment of osteoporosis, despite the fact that calcium supplements only marginally reduce the risk of fracture. Interventional studies show that calcium supplements improve some risk factors for stroke such as blood pressure, bodyweight, and serum-lipid concentrations, and observational studies...
suggest that high calcium intake might protect against stroke.\textsuperscript{66-69} However, a recent observational study of 34670 women reported that increasing calcium intake was not associated with altered risk of any stroke or ischaemic stroke, but was associated with an increased risk of haemorrhagic stroke (for highest vs lowest tertile; adjusted relative risk 2.04, 95% CI 1.24–3.35).\textsuperscript{69} Randomised trials have shown that, after a median of 3.6 years (IQR 2.7–4.3), calcium supplementation (≥500 mg per day), without co-administered vitamin D, is associated with a significant increase in myocardial infarction (hazard ratio 1.31, 1.02–1.67) and a trend towards an increase in stroke (1.20, 0.96–1.50).\textsuperscript{69}

Co-administration of calcium plus vitamin D supplements for an average of 6.2 years was associated with an increased risk of stroke (relative risk 1.20, 95% CI 1.00–1.43), myocardial infarction (1.21, 1.01–1.44), and the composite of myocardial infarction or stroke (1.16, 1.02–1.32) among 20090 individuals in three placebo-controlled trials.\textsuperscript{70} Some studies do not distinguish between calcium taken alone and calcium co-administered with vitamin D. An analysis of such studies showed that calcium alone or calcium plus vitamin D increased the risk of stroke (hazard ratio 1.19, 95% CI 1.02–1.39), myocardial infarction (1.26, 1.07–1.47), and the composite of stroke or myocardial infarction (1.17, 1.05–1.31) over a mean follow-up of 5-9 years in 24869 people in six randomised trials.\textsuperscript{70} These data suggest that treating 1000 people with calcium or calcium and vitamin D for 5 years would cause an additional six myocardial infarctions or strokes and prevent three fractures. However, methodological caveats exist that limit the conclusiveness of this evidence. Furthermore, when calcium and vitamin D supplements are used as an adjunct to bisphosphonates in the treatment of osteoporosis, no adverse effect on cardiovascular safety and survival occurs.\textsuperscript{111,112} Randomised trials of the effects of calcium, with or without vitamin D, on the risk of stroke, its pathological and aetiological subtypes, and other vascular and non-vascular outcomes are warranted.

Fats
An observational study of 43732 men in the USA showed that, compared with the lowest quintile, the risk of ischaemic stroke over 14 years of follow-up was not increased in those in the highest quintile for intake of total fat (adjusted relative risk 0.91, 95% CI 0.65–1.28; p for trend 0.77), animal fat (1.20, 0.84–1.70; p for trend 0.47), saturated fat (1.16, 0.81–1.65; p for trend 0.59), vegetable fat (1.07, 0.77–1.47; p for trend 0.66), dietary cholesterol (1.02, 0.75–1.39; p for trend 0.99), monosaturated fat (0.88, 0.64–1.21; p for trend 0.25), or transunsaturated fat (0.87, 0.62–1.22; p for trend 0.42).\textsuperscript{71} These findings are supported by a large randomised trial in which a reduction of mean total fat intake by 8–2% of energy intake over 8.1 years (mean) did not significantly reduce the risk of stroke (hazard ratio 1.02, 95% CI 0.90–1.15) in 48835 postmenopausal women.\textsuperscript{72} However, trends towards greater reductions in risk of coronary heart disease were seen with low intakes of trans fat and saturated fat,\textsuperscript{72} suggesting that the type of fats consumed might be more relevant for cardiometabolic health than the proportion of calories consumed from total fat.\textsuperscript{113,114}

Trans fatty acids
Consumption of industrially produced trans fatty acids from partially hydrogenated vegetable oils are the most potent fat-related risk factor for coronary heart disease.\textsuperscript{115,116} Although observational studies suggest no significant relation between trans fat consumption and risk of stroke,\textsuperscript{72} no reliable observational data or data from randomised trials on the association of trans fatty acids with stroke subtypes are available.

Saturated fatty acids
A meta-analysis of eight observational studies showed that intake of saturated fat in the highest quintile was not associated with an increased risk of stroke compared with intake in the lowest quintile (relative risk 0.81, 95% CI 0.62–1.05).\textsuperscript{72} Sufficient statistical power in these studies was not available to assess whether the observed associations between saturated fat intake and stroke risk were modified or confounded by the cardiometabolic effects of nutrients, such as refined carbohydrates, starches, and sugars, which might be exchanged for saturated fatty acids.\textsuperscript{113,117} Data on the relation between saturated fat intake and risk of subtypes of stroke were also restricted.

Polyunsaturated fatty acids
No reliable studies of the association between increased intake of polyunsaturated fatty acids and stroke risk have been done, but observational studies and randomised trials suggest that consumption of these fatty acids in place of saturated fatty acids reduces incidence of coronary heart disease.\textsuperscript{113,118} For each 5% of energy obtained from polyunsaturated fatty acids, instead of saturated fatty acids, the risk of coronary heart disease is reduced by 10% (relative risk 0.90, 95% CI 0.83–0.97).\textsuperscript{118} Marine-derived omega-3 (or n-3) polyunsaturated fatty acids
Human beings rely on direct dietary consumption of omega-3 polyunsaturated fatty acids, which include eicosapentaenoic acid (20:5 omega-3) and docosahexaenoic acid (22:6 omega-3) from oily fish such as salmon, herring, trout, and sardines.\textsuperscript{111} A meta-analysis of 11 randomised trials including 39044 patients showed that random allocation to the omega-3 fatty acids eicosapentaenoic acid or docosahexaenoic acid for 2.2 years (mean) significantly reduced cardiovascular deaths (odds ratio 0.87, 95% CI 0.79–0.95), sudden cardiac death (0.87, 0.76–0.99), all-cause mortality (0.92, 0.85–0.99), and non-fatal cardiovascular events (0.92, 0.85–0.99) compared with...
placebo. The effect could be mediated by an anti-arrhythmic effect or other beneficial effects on blood pressure, concentration of plasma triglycerides, and markers of thrombosis and inflammation.

However, a subsequent randomised trial showed that in 2501 patients with a history of myocardial infarction, unstable angina, or ischaemic stroke, random assignment to a daily dietary supplement containing omega-3 fatty acids (600 mg of eicosapentaenoic acid and docosahexaenoic acid at a ratio of 2:1) for a median of 4–7 years had no significant effect on stroke (hazard ratio 1·04, 95 CI% 0·62–1·75) or major vascular events (1·08, 0·79–1·47). The effect of treatment on stroke subtypes was not reported.

**Plant-derived omega-3 (n-3) polyunsaturated fatty acids**

The plant-derived n-3 polyunsaturated fatty acid α-linolenic acid is an essential fatty acid found mainly in vegetable oils such as soybean, canola, and flaxseed, and in walnuts. An observational study of 20069 Dutch adults showed that, compared with the bottom quintile (Q1) of α-linolenic acid intake (less than 1·0 g per day), participants in high quintiles (Q2–Q5) had a 35–50% lower risk of incident stroke; hazard ratios were 0·65 (0·43–0·97; Q2), 0·49 (0·31–0·76; Q3), 0·53 (0·34–0·83; Q4), and 0·65 (0·41–1·04; Q5) after 8–13 years of follow-up. These results need confirmation in randomised trials.

**Carbohydrates**

Like fat intake, carbohydrate intake in quantities that exceed energy requirements (positive energy imbalance) is a major determinant of weight gain and adiposity, and the quality of carbohydrate intake also affects metabolic health. Consumption of refined sugars in liquid form promotes weight gain. The glycaemic index is a measure of how much a standard quantity of food raises blood glucose levels compared with a standard quantity of glucose or white bread. The glycaemic load is a measure of the product of the glycaemic index of a food item and the available carbohydrate content of that item. Foods with a high glycaemic index, such as sugar-sweetened beverages and refined carbohydrates and starches, increase fasting blood glucose. Glycated proteins, and beverages and foods with high glycaemic load, including added sugars, increase bodyweight.

High carbohydrate intake from foods with a high glycaemic index, added sugars, and high dietary glycaemic load also leads to reduced intake of essential nutrients and has been associated with an increased risk of stroke mortality and coronary heart disease in women in observational studies. Replacement of saturated fats with carbohydrates that have a high glycaemic index is associated with an increased risk of myocardial infarction (hazard ratio for myocardial infarction per 5% increment of energy intake of carbohydrates 1·33, 95% CI 1·08–1·64).

Increased dietary fibre reduces blood pressure, blood glucose, serum triglycerides, and LDL cholesterol but no reliable data on its effect on risk of stroke and stroke subtypes are available.

**Protein**

Observational studies in Japan have shown that increased protein intake is associated with reduced risk of stroke. However, no significant association between total, animal, or vegetable protein and risk of stroke was reported in a cohort study of 43 960 men in the USA.

**Which foods and beverages affect the risk of stroke?**

Many foods and beverages affect the risk of stroke (panel 3). The INTERSTROKE study reported that, within food groupings (adjusted for age, sex, and region; tertile 3 vs tertile 1), increased consumption of fish (odds ratio 0·78, 99% CI 0·66–0·91) and fruit (0·61, 0·50–0·73) were associated with reduced risk of stroke.

**Fish**

Fish can be an excellent source of protein and the essential omega-3 fatty acids eicosapentaenoic acid and docosahexaenoic acid. A meta-analysis of 15 observational studies reported that an increase in consumption of three servings per week of fish was associated with a 6% (95% CI 1–11) lower risk of stroke. No significant heterogeneity among the studies was reported ($I^2$=25–7%). Some studies suggest that consumption of oily fish drives the inverse association between fish intake and stroke risk and others suggest that the consumption of lean fish (cod, sablefish, and fish fingers), but not other fish types (eg, salmon, white fish, and char, herring, or mackerel), is associated with a lower risk of stroke. The effect of the consumption of lean fish could be confounded by the fact that herring and salmon are commonly eaten salted in Sweden, thus affecting blood pressure levels.

Studies that have examined pathological subtypes of stroke suggest that fish consumption is associated with a lower risk of ischaemic stroke but not haemorrhagic stroke. However, no reliable data from randomised trials of the effect of fish consumption on the risk of stroke or its subtypes are available.

**Fruit and vegetables**

Increased fruit and vegetable intake (more than five servings per day) was associated with a lower risk of stroke than was intake of fewer than three servings per day (relative risk 0·74, 95% CI 0·69–0·79) and three to five servings per day (0·89, 0·83–0·97) in 237 551 individuals followed up for 13 years. However, vegetable intake alone was not associated with a reduced risk of stroke (odds ratio 0·91, 99% CI 0·75–1·05) in the INTERSTROKE study. If the association between fruit and vegetable intake is validated, the mechanism might be that consumption of...
five or more daily portions of fruit and vegetables reduces blood pressure by about 4.0 mm Hg (95% CI 2.0–6.0) systolic and 1.5 mm Hg (0.2–2.7) diastolic.126

Meats
A meta-analysis of observational studies including 152630 individuals showed that total meat consumption was associated with a 24% higher risk of ischaemic stroke per daily serving (relative risk 1.24, 95% CI 1.08–1.43).127 Among subtypes of meat, consumption of unprocessed red meats (which contain saturated fatty acids, cholesterol, and haem iron113) was not associated with a significant increase in risk of ischaemic stroke or total stroke mortality (relative risk per 100 g serving per day 1.17, 95% CI, 0.40–3.43) and nor was intake of processed meats (which contain high levels of salt and other preservatives;113 relative risk 1.14, 95% CI, 0.94–1.39).127 However, a recent large cohort study of 40 291 men reported that processed meat consumption was positively associated with an increased risk of stroke (multivariate relative risk for highest vs lowest quintiles 1.23, 95% CI 1.07 to 1.40) after a mean follow-up of 10.1 years.128 Further studies of meat consumption by subtype and risk of stroke by pathological and aetiological subtypes are needed.

Dairy
The dairy products milk, cheese, and butter have a high saturated fat and calcium content that could increase the risk of stroke. However, a meta-analysis of six cohort studies showed that milk intake was not associated with risk of stroke (relative risk 0.87, 95% CI 0.72–1.05).129 A subsequent large cohort study of 40 291 men reported that processed milk intake was positively associated with an increased risk of stroke (multivariate relative risk for highest vs lowest quintiles 1.23, 95% CI 1.07 to 1.40) after a mean follow-up of 10.1 years.129 Further studies of meat consumption by subtype and risk of stroke by pathological and aetiological subtypes are needed.

Chocolate
Observational studies suggest that individuals with the highest levels of chocolate consumption have a 29% (95% CI 2–48) lower risk of stroke.130 If valid, the mechanism of this association might include antihypertensive, anti-inflammatory, antiatherogenic, and antithrombotic effects of cocoa.130

Coffee
A meta-analysis of 11 prospective studies of 479 689 participants in which three or more categories of coffee consumption were correlated with the subsequent occurrence of 10033 cases of stroke reported that moderate coffee consumption might have a weak non-linear inverse association with risk of stroke (p for non-linearity=0.005).131 Compared with no coffee consumption, the relative risks of stroke were 0.86 (95% CI 0.78–0.94) for two cups of coffee per day, 0.83 (0.74–0.92) for three to four cups per day, 0.87 (0.77–0.97) for six cups per day, and 0.93 (0.79–1.08) for eight cups per day. Marginal between-study heterogeneity was present.131

Panel 3: Effects of foods and beverages on the risk of stroke

Fish
Increased consumption by three servings per day is associated with a 6% (95% CI 1.11) lower risk of stroke.124

Fruit and vegetables
Consumption of more than five servings of fruit and vegetables per day is associated with a 26% (95% CI 21–31) lower risk of stroke.125 Consumption of more than five servings per day lowers blood pressure by 4.0/1.5 mm Hg.126

Meat
Total meat
Each daily serving is associated with a 24% (95% CI 8–43) increased risk of stroke.127

Unprocessed meat
Consumption is not a proven risk factor for stroke.127

Processed meat
Consumption was associated with an increased risk of stroke in one observational study but not in another.127

Dairy
Milk
Consumption is not associated with risk of stroke.129

Reduced-fat milk (vs full-strength milk)
Consumption is associated with lower risk of stroke.98

Chocolate
High consumption is associated with a 29% (95% CI 2–48) lower risk of stroke.130

Coffee
Moderate consumption (3–4 cups per day) is associated with a 17% (95% CI 8–26) lower risk of stroke.131,132

Tea
Moderate consumption (≥3 cups per day) is associated with a 21% (95% CI 15–27) lower risk of stroke.133

Sugar-sweetened beverages
High intake is associated with increased obesity, diabetes, metabolic syndrome, and coronary heart disease.134–136

Whole grains
High intake is associated with a 21% (95% CI 15–27) lower incidence of cardiovascular events.137

Rice
Intake is not associated with risk of stroke.138
The association between coffee consumption and pathological subtype of stroke was examined in a single cohort study of 34670 women, which reported that, after a mean follow-up of 10·4 years, consumption of at least one cup of coffee a day was associated with a lower risk of ischaemic stroke and subarachnoid haemorrhage but not haemorrhagic stroke compared with consumption of less than one cup of coffee a day.112

This association, if causal, is unlikely to be mediated by blood pressure because caffeine intake is not associated with a long-term increase in blood pressure compared with a caffeine-free diet or with decaffeinated coffee, despite the fact that caffeine intake of 200–300 mg produces an acute mean increase in blood pressure of 8·1 mm Hg (95% CI 5·7–10·6) systolic and 5·7 mm Hg (95% CI 4·1–7·4) diastolic for 3 h or more.109 The effect could be due to the action of the phenolic compounds in coffee, which might increase resistance of LDL cholesterol to oxidation.111

Although chronic coffee consumption is associated with a lower risk of stroke,111,112 some preliminary evidence suggests an acutely increased risk of ischaemic stroke in the hour after coffee intake (relative risk 2·0, 95% CI 1·4–2·8), especially in infrequent coffee drinkers (one cup or less a day).148 Because these results could mirror recall bias, they require confirmation.

Tea
A meta-analysis of nine observational studies of 194965 individuals reported that consumption of three or more cups of tea (green or black) a day was associated with a 21% (95% CI 15–27%) lower risk of stroke than in those who consumed less than one cup a day (P=23·8%).113 Population-based studies do not suggest that tea lowers blood pressure,149 but it might have a favourable effect on endothelial function and reduce the oxidation of LDL cholesterol.106,111

Sugar-sweetened beverages
High intake of sugar-sweetened beverages leads to lower intake of more healthy beverages and is associated with adiposity, and an increased incidence of diabetes mellitus, metabolic syndrome, and coronary heart disease.146–148 However, no reliable data exist that relate intake of sugar-sweetened beverages to incidence of stroke.

Whole grains
Whole grains comprise bran, germ, and endosperm from natural cereal.111 Bran contains soluble and insoluble dietary fibre, B vitamins, minerals, flavonoids, and tocothere; germ contains many fatty acids, antioxidants, and phytochemicals; and endosperm provides largely starch (carbohydrate polysaccharides) and storage proteins.150 Consumption of whole grains improves glucose-insulin homeostasis and endothelial function, and possibly reduces inflammation and improves weight loss.107

Increased whole grain intake (pooled average 2·5 servings a day vs 0·2 servings a day) was associated with a trend towards a lower risk of incident stroke events (odds ratio 0·83, 95% CI 0·68–1·02) and a significantly lower risk of cardiovascular disease events (0·79, 0·73–0·85) in seven observational studies whereas refined grain intake was not associated with incident cardiovascular disease events (1·07, 0·94–1·22).107

Rice
Rice intake was not associated with risk of stroke (adjusted hazard ratio per one SD increment of energy-adjusted risk intake 0·97, 95% CI 0·90–1·04) in a study that followed 83752 Japanese adults for a median of 14·1 years.108

Legumes
Legumes include beans, peas, chickpeas, and lentils; their independent effects on risk of stroke are unknown. However, randomised trials have shown that soy-containing foods produce a non-significant reduction in blood pressure by about 5·8 mm Hg systolic and 4·0 mm Hg diastolic,152 and isolated soy protein or isoflavones (phytoestrogens) lower diastolic blood pressure by 2 mm Hg and LDL cholesterol by 3%.215

Which dietary patterns affect the risk of stroke?
Dietary patterns can have various effects on risk of stroke (panel 4). Several studies have developed and assessed diet scores as a risk factor for stroke, often in conjunction with other lifestyle factors.45,154–156

Healthy versus unhealthy diets
In the Women’s Health Study of 37636 women aged 45 years or older, a healthy diet was defined as one high in cereal fibre, folate, and omega-3 fatty acids, with a high ratio of polyunsaturated to saturated fat, and low in trans fats and glycaemic load, but was unexpectedly associated with an increased risk of stroke over 10 years of follow-up.159

In the Nurses’ Health Study of 71243 women and the Health Professionals Follow-Up Study of 43685 men, a score within the top 40% of a healthy diet score (defined by high intakes of fruits, vegetables, soy, nuts, and cereal fibre; a high ratio of polyunsaturated to saturated fat, and low in trans fats and glycaemic load, but was unexpectedly associated with an increased risk of stroke over 10 years of follow-up.159

The INTERSTROKE study46 identified an unhealthy diet as a significant risk factor for stroke (table 3). An unhealthy diet risk score was derived from a simple 19-item qualitative food-group-frequency questionnaire about consumption of meat, salty snacks, fried foods, fruits, green leafy vegetables, cooked vegetables, and other raw vegetables (a high score indicating a poorer...
Adherence to the Mediterranean diet was associated with a lower risk of stroke after 14 years of follow-up of 71 768 women (relative risk 0·78, 95% CI 0·61–1·01; comparing extreme quintiles) whereas a western diet, characterised by high intakes of red and processed meats, refined grains, and sweets and desserts, was associated with an increased risk of stroke (relative risk 1·58, 95% CI 1·15–2·15; comparing the highest with lowest quintiles of the western diet).156

The Mediterranean diet is more effective than a low-fat diet in reducing oxidised LDL concentrations and blood pressure152,153 and, in obese individuals, improving weight loss and lowering the ratio of total to high-density lipoprotein cholesterol.154

**Vegetarian diets**

Compared with typical western diets, vegetarian diets can reduce blood pressure but lactovegetarian (milk consumed) and vegan (no animal products consumed) diets have not been shown to reduce blood pressure, bodyweight, concentrations of blood lipids, or insulin resistance.113,166

Vegetarians might have improved survival compared with non-vegetarians but, if so, whether it is because the components of the diet (plant-based foods) replace unhealthy processed meats and other processed and fast foods or whether the diet is a marker of individuals (vegetarians) who might be more health conscious in other aspects of their lifestyle behaviours is unclear.

Panel 4: Effects of dietary patterns on the risk of stroke

<table>
<thead>
<tr>
<th>Dietary pattern</th>
<th>Effect on stroke risk</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Healthy diet</strong></td>
<td>High intake of a healthy diet was associated with an increased risk of stroke in one observational study154 and a reduced risk of stroke in another observational study155</td>
</tr>
<tr>
<td><strong>Unhealthy diet</strong></td>
<td>High intake of an unhealthy diet is associated with an increased risk of stroke and a population-attributable risk of stroke of 19% (99% CI 11–30)165</td>
</tr>
<tr>
<td><strong>Prudent diet</strong></td>
<td>In women, high intake of a prudent diet is associated with a lower risk of stroke than is low intake156</td>
</tr>
<tr>
<td><strong>Western diet</strong></td>
<td>In women, high intake of a western diet is associated with a higher risk of stroke than is low intake156</td>
</tr>
<tr>
<td><strong>DASH-style diet</strong></td>
<td>In women, high intake of a DASH-style diet is associated with a lower risk of stroke than is low intake157</td>
</tr>
<tr>
<td><strong>Mediterranean diet</strong></td>
<td>In women, high intake of a Mediterranean diet is associated with a lower risk of stroke (63,89) and all-cause mortality (46) than is low intake</td>
</tr>
<tr>
<td><strong>Vegetarian diet</strong></td>
<td>Effect on stroke risk is not known</td>
</tr>
<tr>
<td><strong>Japanese diet</strong></td>
<td>Effect on stroke risk is not known</td>
</tr>
</tbody>
</table>

DASH=Dietary Approaches to Stop Hypertension.
**Search strategy and selection criteria**

I searched PubMed articles published from 1970 to October, 2011, using the search terms “stroke”, “nutrition”, “undernutrition”, “overnutrition”, “nutrients”, “foods”, “diet”, “dietary patterns”, “overweight”, “obesity”, “mortality”, “prospective cohort studies”, “randomized controlled trial(s)”, “systematic review”, and “meta-analysis”. Articles were also identified through searches of reference lists and my own files. Studies were selected for inclusion on the basis of a judgment about the quality of the evidence according to four key elements: study design, study quality, consistency, and directness (ie, the extent to which the study participants, interventions, and outcome measures are similar to those of interest), as proposed by the Grading of Recommendations Assessment, Development and Evaluating (GRADE) working group. For each nutrient, food, or dietary pattern, only the studies with the highest level of evidence were included. If randomised trials had not been undertaken and only observational data were available, studies were included if they were prospective, population-based, and large, with standardised diagnostic criteria for stroke outcome events (and, ideally, also pathological and aetiological stroke subtypes), prolonged follow-up, and statistical adjustment for the effect of other potential prognostic variables by means of multiple regression analysis. Studies were excluded if serious limitations to study quality and major uncertainty about directness existed. Only articles published in English were included.

**Japanese diets**

Traditional Japanese diets, characterised by increased intake of fish, plant foods (soybean products, seaweeds, vegetables, fruits), and sodium (soy sauce and added salt), decreased intake of refined carbohydrates and animal fat (meats), and appropriate energy balance have been associated in ecological studies with some of the lowest rates of coronary heart disease in the world.123,168–171

In observational cohort studies, the Japanese dietary pattern has also been associated with a reduced risk of cardiovascular mortality (hazard ratio for the highest vs lowest quartile 0·73, 95% CI 0·59–0·90).172

However, the rates of stroke in Japan remain high, perhaps because of the greater relevance of hypertension to stroke than coronary heart disease, and the effect of the high sodium diet and, for men, high alcohol consumption in the Japanese population. By contrast, low saturated fat (meat) and high n3-polyunsaturated fat (fish) in the Japanese diet could contribute to the low prevalence of hypercholesterolaemia, which is more relevant to risk of coronary heart disease than to stroke.173

**Conclusions and future directions**

Many studies have assessed the associations between dietary exposures and stroke risk. The findings are diverse, mainly because most studies are epidemiological and prone to substantial methodological challenges of bias, confounding, and measurement error. Furthermore, most studies have classed stroke as a composite outcome, without distinguishing first-ever stroke from recurrent stroke, ischaemic stroke from haemorrhagic stroke (pathological stroke subtypes), ischaemic stroke due to large artery disease from that due to small artery disease and embolism from the heart (aetiological subtypes of ischaemic stroke), and haemorrhagic stroke due to hypertensive small vessel disease from its many other causes. Consequently, important potential effects of nutrients, foods, beverages, and dietary patterns on specific pathophysiological mechanisms of one stroke subtype could have been diluted and missed by assessing a single outcome of stroke. The same applies to nutritional factors; overall negative associations between total fat or total carbohydrate intake and stroke risk could mask important associations between specific subtypes of fat and subtypes of carbohydrate intake that influence health and stroke risk. These limitations have led one commentator to lament: “almost every nutritional ‘fact’ is in reality an opinion, often based on poor quality evidence.”174

However, the few randomised trials that have been undertaken provide more reliable conclusions than do previous epidemiological studies—that dietary supplementation with antioxidant vitamins, B vitamins, and calcium do not reduce the risk of stroke. Indeed, calcium might increase myocardial infarction, and β-carotene, vitamin A, and vitamin E might increase mortality. Less reliable observational data suggest that a lower risk of stroke could be associated with diets that are low in salt and added sugars, high in potassium, and contain the ingredients of a Mediterranean diet. The overall quality of an individual’s diet (ie, dietary pattern) and balance between energy intake and expenditure seem to be more important determinants of stroke risk than individual nutrients and foods.

Further research is needed to improve the quality of evidence relating to the association of many nutrients, foods, and dietary patterns with stroke risk. To establish a causative role for specific nutrients, foods, and dietary patterns in the pathogenesis of stroke, adequately powered, large randomised trials are needed in which the patient population and intervention are carefully described and the outcomes not only include all stroke but also distinguish first-ever and recurrent stroke, and pathological and aetiological subtypes of stroke. A large randomised trial is currently examining the effect of vitamin D and marine omega-3 fatty acid supplementation on incidence of stroke.175 To examine the effects of interactions between different genetic and environmental factors, large genetic epidemiological studies that minimise bias, confounding, measurement error, and random error are needed.

At a population level, the two main nutritional threats to global health and risk of stroke are over-consumption of calories and salt. These behaviours are a normal response by people to an abnormal environment.1 Our living environments have become more conducive to consumption of energy and less conducive to expenditure of energy in developed and increasingly in developing regions. Most of the salt in our diet is added to food before it is sold. If the environment is not changed to increase energy expenditure and to supply healthy food in appropriate, affordable, and accessible quantities, the obesity epidemic will not be reversed and, by 2050, 60% of...
men and 50% of women in the UK could be clinically obese.\textsuperscript{52} Unlike the tobacco and cardiovascular disease epidemic, the obesity and salt epidemics have not been reversed by public health interventions and policies aimed at individuals to change personal choice and behaviour.\textsuperscript{1,2,53–56} A whole-system approach, involving many sectors, is crucial to tackling the obesity and salt epidemics.\textsuperscript{3,5,7,21–110} Integrated action is required by national and local governments, industry and communities, and families and the societies in which they live. Potential policies include the following initiatives: to assess and understand the size and nature of the problem; to establish communication strategies to improve public knowledge about food and behaviours relating to food; to engage with the food industry to set fair and progressive standards and targets for nutrient contents in processed foods, food labelling, and market advertising; to implement multiple progressive interventions to change behaviours at all levels (individual, local, national, and global); and to serially monitor the effects of the above interventions.\textsuperscript{76–110}

Population-wide salt-reduction programmes that are led by governments and engage with industry to remove salt at its source could be highly cost effective. In the USA, modest, population-wide reductions in dietary salt of up to 3 g per day (1-2 g of sodium per day) are projected to reduce the annual number of new cases of stroke by 32,000 to 66,000, similar to the benefits of population-wide reductions in tobacco use, obesity, and cholesterol levels.\textsuperscript{31–111} The UK Government has accepted the challenge to set and enforce salt targets for foods.\textsuperscript{6,176} The potential effect of adopting a healthy diet policy on population health, agricultural production, trade, the global economy, and livelihoods is likely to be substantial in some countries,\textsuperscript{112} and the effects could be realised sooner than we think.\textsuperscript{195}

**Conflicts of interest**

I was the principal investigator of the VITAMins TO Prevent Stroke (VITATOPS) trial. I have received honoraria for serving on the executive committees of the AMADEUS trial (Sanofi-Aventis), ROCKET-AF trial (Johnson & Johnson), and BOREALIS trial (Sanofi-Aventis), the steering committee of the ACTIVE-W, ACTIVE-A, RE-LY, and AVERROES trials, and for speaking at sponsored scientific symposia and consulting on advisory boards for Bristol-Myers Squibb, Boehringer Ingelheim, Bayer, and Pfizer Australia.

**References**


Review


122 Larsson SC, Orsini N. Fish consumption and risk of stroke. A dose-response meta-analysis. Stroke 2011; published online Sept 8. DOI:10.1161/STROKEAHA.111.60319.


163 Fitó M, Guxens M, Corella D, et al, and the for the PREDEMEDI
Study Investigators. Effect of a traditional Mediterranean diet on
lipoprotein oxidation: a randomized controlled trial. Arch Intern Med
164 Shai I, Schwarzfuchs D, Henkin Y, et al, and the Dietary
Intervention Randomized Controlled Trial (DIRECT) Group. Weight
loss with a low-carbohydrate, Mediterranean, or low-fat diet.
165 Sciarrone SE, Strahan MT, Beilin LJ, Burke V, Rogers P, Rouse IR.
Ambulatory blood pressure and heart rate responses to vegetarian
166 Burke LE, Hudson AG, Warziski MT, et al. Effects of a vegetarian
diet and treatment preference on biochemical and dietary variables
in overweight and obese adults: a randomized clinical trial.
167 Key TJ, Fraser GE, Thorogood M, et al. Mortality in vegetarians and
non-vegetarians: a collaborative analysis of 8300 deaths among
76,000 men and women in five prospective studies.
168 Willcox BJ, Wilcox DC, Todonki H, et al. Caloric restriction, the
traditional Okinawan diet, and healthy aging: the diet of the world’s
longest-lived people and its potential impact on morbidity and life
169 Willcox DC, Wilcox BJ, Todonki H, Suzuki M. The Okinawan diet:
health implications of a low-calorie, nutrient-dense, antioxidant-rich
170 Oba S, Nagata C, Nakamura K, et al. Dietary glycemic index,
glycemic load, and intake of carbohydrate and rice in relation to risk
of mortality from stroke and its subtypes in Japanese men and
women. Metabolism 2010;59:1574–82.
171 Tada N, Maruyama C, Koba S, et al. Japanese dietary lifestyle and
172 Shimazu T, Kuriyama S, Hozawa A, et al. Dietary patterns and
cardiovascular disease mortality in Japan: a prospective cohort
173 Iso H. Lifestyle and cardiovascular disease in Japan.
174 Hawkes N. Take dietary truths with a pinch of salt. BMJ 2011;
343:d5346.
176 Cappuccio FP, Capewell S, Lincoln P, McPherson K. Policy options
to reduce population salt intake. BMJ 2011;343:d4995.
177 Campbell NRC, Legowski B, Legetic B. Mobilising the Americas for
178 Kopelman P. Symposium 1: Overnutrition: consequences and
179 Gortmaker SL, Swinburn BA, Levy D, et al. Changing the future of
180 Mozaffarian D, Capewell SU. United Nations’ dietary policies to
181 He FJ, MacGregor GA. A comprehensive review on salt and health
and current experience of worldwide salt reduction programmes.
J Hum Hypertens 2009;23:363–84.
effect of dietary salt reductions on future cardiovascular disease.
183 Appel LJ, Frohlich ED, Hall JE, et al. The importance of
population-wide sodium reduction as a means to prevent
cardiopulmonary disease and stroke: a call to action from the
184 Lock K, Smith RD, Dangour AD, et al. Health, agricultural, and
economic effects of adoption of healthy diet recommendations.
185 Capewell S, O’Flaherty M. Rapid mortality falls after risk-factor