Dietary fat intake and risk of stroke in male US healthcare professionals: 14 year prospective cohort study

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Abstract

Objective To examine the association between intake of total fat, specific types of fat, and cholesterol and risk of stroke in men.
Design and setting Health professional follow up study with 14 year follow up.
Participants 43 732 men aged 40-75 years who were free from cardiovascular diseases and diabetes in 1986.
Main outcome measure Relative risk of ischaemic and haemorrhagic stroke according to intake of total fat, cholesterol, and specific types of fat.
Results During the 14 year follow up 725 cases of stroke occurred, including 455 ischaemic strokes, 125 haemorrhagic stokes, and 145 strokes of unknown type. After adjustment for age, smoking, and other potential confounders, no evidence was found that the amount or type of dietary fat affects the risk of developing ischaemic or haemorrhagic stroke. Comparing the highest fifth of intake with the lowest fifth, the multivariate relative risk of ischaemic stroke was 0.91 (95% confidence interval 0.65 to 1.28; P for trend = 0.77) for total fat, 1.20 (0.84 to 1.70; P = 0.47) for animal fat, 1.07 (0.77 to 1.47; P = 0.66) for vegetable fat, 1.16 (0.81 to 1.65; P = 0.59) for saturated fat, 0.91 (0.65 to 1.28; P = 0.83) for monounsaturated fat, 0.88 (0.64 to 1.21; P = 0.25) for polyunsaturated fat, 0.87 (0.62 to 1.22; P = 0.42) for *trans* unsaturated fat, and 1.02 (0.75 to 1.39; P = 0.99) for dietary cholesterol. Intakes of red meats, high fat dairy products, nuts, and eggs were also not appreciably related to risk of stroke.
Conclusions These findings do not support associations between intake of total fat, cholesterol, or specific types of fat and risk of stroke in men.

Introduction

Strong evidence indicates that type of dietary fat is more important than total fat intake in predicting risk of coronary heart disease, as different types of fat or fatty acids may play different or opposite roles. Monounsaturated and polyunsaturated fats seem to have beneficial effects, but saturated fat and *trans* unsaturated fatty acids increase risk of coronary heart disease.[1] However, these associations do not seem to apply to stroke. Previous studies have even suggested an inverse relation between saturated fat or *trans* unsaturated fat intake and risk of stroke,[2 3] but the mechanisms remain unclear. Although epidemiological studies indicated beneficial effects of some specific fatty acids such as long chain omega 3 polyunsaturated fatty acid, α linolenic acid, and linoleic acid on ischaemic stroke,[4–6] few studies have directly related intake of dietary fat to risks of subtypes of stroke, and the results have been inconsistent. We prospectively examined the associations between intakes of total fat and specific types of fat and the risk of subtypes of stroke in the health professional follow up study.

Methods

Study population

The health professional follow up study is a cohort of 51 529 male US healthcare professionals, aged 40-75 years in 1986, who responded to a mailed questionnaire including a comprehensive survey of diet, lifestyle characteristics, and medical history. Non-dietary variables are updated every other year and dietary information every four years. For this analysis, we followed participants from 1986 to 2000. We excluded men who at baseline reported a previous diagnosis of cardiovascular diseases or diabetes mellitus. We also excluded men who had incomplete information (≥ 70 blanks out of 131 listed food items) or implausible total daily energy intake (≤ 800 or ≥ 4200 kcal (≤ 3.34 or ≥ 17.56 MJ). A total of 43 732 men remained in the analyses. The response to the questionnaires constituted the participants' informed consent

Dietary assessment

We assessed dietary intake by using semiquantitative food frequency questionnaires in 1986, 1990, and 1994.[7] We asked participants to record the frequency of consumption of specified portions of each selected food during the previous year by using one of nine options ranging from "never or < 1/month" to "≥ 6/day." We also inquired about types of fat, oil, or margarine used in food preparation and at the table. We obtained values for the amounts of nutrients, including specific types of fat, in foods from the Harvard University food composition database, which was updated over time with data from the US Department of Agriculture, manufacturers, and published reports. We based values for total *trans* isomer contents in food in part on analyses by Enig et al and Slover

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et al.[8 9] To assess the effects of food groups rich in fat or cholesterol, we defined red meat as beef, pork, or lamb as a main dish; beef, pork, or lamb as a sandwich or mixed dish; hamburgers; hot dogs; processed meat; and bacon. We defined high fat dairy food as whole milk, ice cream, hard cheese, butter, and sour cream.

The validity of the food frequency questionnaire has been evaluated in a subcohort. After adjustment for energy and de-attenuation for within person variation, the Pearson correlation between the questionnaire and the average of two single week diet records six months apart was 0.67 for total fat, 0.75 for

Table 1 Relative risks of stroke (95% confidence intervals) according to fifths of total fat, specific types of fat, dietary cholesterol, and Keys score

	Fifths of nutrient intake					
	1	2	3	4	5	P for trend
Total fat						
Median intake (g/day)	54	64	70	77	86	—
Ischaemic stroke:						
No of cases	89	87	91	97	91	—
Adjusted for age and smoking	1.0	0.96 (0.72 to 1.29)	0.97 (0.72 to 1.30)	1.04 (0.78 to 1.39)	0.93 (0.68 to 1.25)	0.91
Multivariate*	1.0	0.93 (0.68 to 1.26)	1.02 (0.74 to 1.39)	1.02 (0.74 to 1.42)	0.91 (0.65 to 1.28)	0.77
Haemorrhagic stroke:						
No of cases	18	30	28	23	26	—
Adjusted for age and smoking	1.0	1.66 (0.93 to 2.98)	1.50 (0.83 to 2.71)	1.23 (0.66 to 2.30)	1.32 (0.71 to 2.45)	0.73
Multivariate*	1.0	1.76 (0.95 to 3.25)	1.49 (0.79 to 2.83)	1.18 (0.60 to 2.35)	1.16 (0.58 to 2.32)	0.83
Animal fat						
Median intake (g/day)	25	33	39	45	54	—
Ischaemic stroke:						
No of cases	80	90	95	88	102	—
Adjusted for age and smoking	1.0	1.07 (0.78 to 1.45)	1.13 (0.84 to 1.53)	1.05 (0.77 to 1.43)	1.16 (0.86 to 1.58)	0.55
Multivariate*	1.0	1.14 (0.83 to 1.56)	1.12 (0.81 to 1.55)	1.04 (0.74 to 1.46)	1.20 (0.84 to 1.70)	0.47
+ vegetable fat†	1.0	1.11 (0.81 to 1.53)	1.10 (0.79 to 1.52)	1.02 (0.72 to 1.44)	1.15 (0.80 to 1.65)	0.61
Haemorrhagic stroke:						
No of cases	21	21	25	35	23	—
Adjusted for age and smoking	1.0	0.95 (0.52 to 1.77)	1.14 (0.63 to 2.06)	1.61 (0.92 to 2.82)	1.01 (0.54 to 1.90)	0.45
Multivariate*	1.0	0.95 (0.50 to 1.79)	1.12 (0.60 to 2.10)	1.49 (0.80 to 2.78)	0.90 (0.45 to 1.81)	0.90
+ vegetable fat†	1.0	0.92 (0.49 to 1.74)	1.08 (0.58 to 2.04)	1.44 (0.77 to 2.70)	0.86 (0.42 to 1.77)	0.99
Vegetable fat						
Median intake (g/day)	20	26	30	34	42	—
Ischaemic stroke:						
No of cases	94	105	96	70	90	—
Adjusted for age and smoking	1.0	1.18 (0.89 to 1.56)	1.11 (0.83 to 1.47)	0.82 (0.60 to 1.12)	0.98 (0.74 to 1.31)	0.27
Multivariate*	1.0	1.22 (0.91 to 1.62)	1.23 (0.91 to 1.66)	0.83 (0.60 to 1.16)	1.07 (0.77 to 1.47)	0.66
+ animal fat†	1.0	1.22 (0.91 to 1.62)	1.24 (0.92 to 1.67)	0.84 (0.60 to 1.18)	1.09 (0.78 to 1.51)	0.79
Haemorrhagic stroke:						
No of cases	25	23	27	27	23	—
Adjusted for age and smoking	1.0	0.96 (0.54 to 1.69)	1.16 (0.68 to 2.00)	1.17 (0.68 to 2.04)	0.95 (0.53 to 1.69)	0.83
Multivariate*	1.0	1.01 (0.56 to 1.82)	1.20 (0.68 to 2.13)	1.25 (0.70 to 2.25)	0.87 (0.46 to 1.63)	0.80
+ animal fat†	1.0	1.00 (0.56 to 1.80)	1.20 (0.67 to 2.13)	1.24 (0.68 to 2.24)	0.86 (0.45 to 1.64)	0.80
Saturated fat						
Median intake (g/day)	17	21	24	26	31	—
Ischaemic stroke:						
No of cases	81	92	95	88	99	—
Adjusted for age and smoking	1.0	1.10 (0.82 to 1.49)	1.15 (0.86 to 1.54)	1.01 (0.75 to 1.38)	1.08 (0.80 to 1.46)	0.65
Multivariate*	1.0	1.16 (0.85 to 1.59)	1.19 (0.86 to 1.65)	1.08 (0.77 to 1.52)	1.16 (0.81 to 1.65)	0.59
+ poly, mono, *trans*†	1.0	1.24 (0.87 to 1.76)	1.26 (0.84 to 1.88)	1.13 (0.73 to 1.76)	1.21 (0.75 to 1.97)	0.63
Haemorrhagic stroke:						
No of cases	18	24	34	26	23	—
Adjusted for age and smoking	1.0	1.30 (0.71 to 2.39)	1.86 (1.05 to 3.31)	1.36 (0.73 to 2.54)	1.15 (0.60 to 2.19)	0.63
Multivariate*	1.0	1.27 (0.66 to 2.42)	1.74 (0.93 to 3.26)	1.34 (0.68 to 2.66)	0.99 (0.48 to 2.04)	0.85
+ poly, mono, *trans*†	1.0	1.30 (0.64 to 2.64)	1.93 (0.91 to 4.08)	1.56 (0.67 to 3.67)	1.17 (0.45 to 3.07)	0.83
Monounsaturated fat						
Median intake (g/day)	20	24	27	30	34	—
Ischaemic stroke:						
No of cases	90	82	91	99	93	—
Adjusted for age and smoking	1.0	0.88 (0.65 to 1.18)	0.99 (0.74 to 1.33)	1.06 (0.80 to 1.41)	0.88 (0.66 to 1.19)	0.96
Multivariate*	1.0	0.89 (0.65 to 1.21)	1.03 (0.75 to 1.42)	1.03 (0.74 to 1.42)	0.91 (0.65 to 1.28)	0.83
+ poly, sat, *trans*†	1.0	0.85 (0.59 to 1.22)	1.01 (0.67 to 1.53)	1.06 (0.67 to 1.68)	1.00 (0.58 to 1.70)	0.85
Haemorrhagic stroke:						
No of cases	22	27	25	23	28	—
Adjusted for age and smoking	1.0	1.22 (0.70 to 2.15)	1.14 (0.64 to 2.02)	1.04 (0.57 to 1.87)	1.14 (0.64 to 2.03)	0.82
Multivariate*	1.0	1.23 (0.68 to 2.22)	1.00 (0.54 to 1.88)	0.91 (0.47 to 1.75)	0.95 (0.49 to 1.83)	0.62
+ poly, sat, *trans*†	1.0	0.96 (0.48 to 1.93)	0.69 (0.30 to 1.56)	0.61 (0.24 to 1.55)	0.68 (0.24 to 1.96)	0.40

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Table 1 Relative risks of stroke (95% confidence intervals) according to fifths of total fat, specific types of fat, dietary cholesterol, and Keys score *contd*

	Fifths of nutrient intake					
	1	2	3	4	5	P for trend
Polyunsaturated fat						
Median intake (g/day)	10	11	13	14	17	—
Ischaemic stroke:						
No of cases	96	101	92	89	77	—
Adjusted for age and smoking	1.0	1.13 (0.85 to 1.50)	1.04 (0.78 to 1.39)	1.03 (0.77 to 1.38)	0.88 (0.65 to 1.19)	0.28
Multivariate*	1.0	1.14 (0.85 to 1.53)	1.11 (0.82 to 1.49)	0.99 (0.73 to 1.34)	0.88 (0.64 to 1.21)	0.25
+ mono, sat, *trans*†	1.0	1.15 (0.85 to 1.55)	1.11 (0.81 to 1.53)	0.98 (0.70 to 1.37)	0.86 (0.59 to 1.25)	0.26
Haemorrhagic stroke:						
No of cases	27	22	28	25	23	—
Adjusted for age and smoking	1.0	0.87 (0.50 to 1.52)	1.14 (0.67 to 1.93)	1.00 (0.58 to 1.73)	0.92 (0.53 to 1.59)	0.97
Multivariate*	1.0	0.85 (0.47 to 1.52)	1.12 (0.64 to 1.96)	1.02 (0.57 to 1.82)	0.86 (0.47 to 1.56)	0.75
+ mono, sat, *trans*†	1.0	0.89 (0.49 to 1.64)	1.20 (0.66 to 2.19)	1.09 (0.57 to 2.09)	0.95 (0.46 to 1.98)	0.99
***Trans* unsaturated fat**						
Median intake (g/day)	1.67	2.34	2.86	3.44	4.42	—
Ischaemic stroke:						
No of cases	91	93	83	97	91	—
Adjusted for age and smoking	1.0	1.01 (0.76 to 1.35)	0.90 (0.67 to 1.22)	1.10 (0.83 to 1.45)	0.93 (0.69 to 1.25)	0.79
Multivariate*	1.0	1.01 (0.75 to 1.37)	0.86 (0.62 to 1.19)	0.98 (0.71 to 1.35)	0.87 (0.62 to 1.22)	0.42
+ poly, mono, sat†	1.0	0.96 (0.70 to 1.33)	0.80 (0.57 to 1.14)	0.90 (0.63 to 1.29)	0.80 (0.54 to 1.17)	0.26
Haemorrhagic stroke:						
No of cases	18	29	22	22	34	—
Adjusted for age and smoking	1.0	1.66 (0.93 to 2.97)	1.20 (0.63 to 2.26)	1.24 (0.66 to 2.31)	1.78 (0.99 to 3.19)	0.16
Multivariate*	1.0	1.54 (0.83 to 2.87)	1.16 (0.59 to 2.27)	1.06 (0.53 to 2.15)	1.76 (0.90 to 3.45)	0.20
+ poly, mono, sat†	1.0	1.44 (0.76 to 2.73)	1.13 (0.55 to 2.30)	1.11 (0.53 to 2.36)	1.90 (0.90 to 3.98)	0.13
Cholesterol						
Median intake (mg/d)	189	239	278	321	398	—
Ischaemic stroke:						
No of cases	87	81	85	89	113	—
Adjusted for age and smoking	1.0	0.90 (0.67 to 1.23)	0.90 (0.67 to 1.22)	0.89 (0.65 to 1.20)	1.06 (0.79 to 1.41)	0.72
Multivariate*	1.0	0.97 (0.72 to 1.32)	0.85 (0.62 to 1.16)	0.82 (0.60 to 1.13)	1.02 (0.75 to 1.39)	0.99
+ poly, mono, sat, *trans*†	1.0	0.93 (0.68 to 1.27)	0.80 (0.57 to 1.10)	0.76 (0.54 to 1.06)	0.93 (0.66 to 1.30)	0.63
Haemorrhagic stroke:						
No of cases	24	19	25	24	33	—
Adjusted for age and smoking	1.0	0.77 (0.42 to 1.38)	0.95 (0.55 to 1.65)	0.82 (0.46 to 1.44)	1.10 (0.66 to 1.86)	0.51
Multivariate*	1.0	0.70 (0.37 to 1.32)	1.02 (0.57 to 1.83)	0.91 (0.50 to 1.65)	1.04 (0.58 to 1.88)	0.61
+ poly, mono, sat, *trans*†	1.0	0.66 (0.34 to 1.26)	0.99 (0.54 to 1.82)	0.90 (0.48 to 1.70)	1.16 (0.61 to 2.20)	0.37
Keys score‡						
Median score	27.0	33.1	37.0	41.0	47.4	—
Ischaemic stroke:						
No of cases	86	84	88	91	106	—
Adjusted for age and smoking	1.0	0.93 (0.69 to 1.25)	0.99 (0.73 to 1.33)	0.97 (0.72 to 1.30)	1.04 (0.77 to 1.39)	0.66
Multivariate*	1.0	0.92 (0.67 to 1.26)	0.96 (0.69 to 1.33)	0.96 (0.69 to 1.34)	1.04 (0.74 to 1.48)	0.71
Haemorrhagic stroke:						
No of cases	19	21	28	33	24	—
Adjusted for age and smoking	1.0	1.04 (0.55 to 1.94)	1.48 (0.83 to 2.65)	1.64 (0.92 to 2.92)	1.00 (0.52 to 1.92)	0.40
Multivariate*	1.0	1.12 (0.58 to 2.15)	1.46 (0.77 to 2.76)	1.59 (0.84 to 3.02)	1.07 (0.53 to 2.19)	0.68

Poly=polyunsaturated fat; mono=monounsaturated fat; sat=saturated fat; *trans*=*trans* unsaturated fat.
*Adjusted for body mass index (<21, 21-22.9, 23-24.9, 25-29.9, or ≥30), physical activity (fifths), history of hypertension (yes or no), smoking status (never, past, and current with 1-14, 15-24, or ≥25 cigarettes/day), aspirin use (yes or no), multivitamin use (yes or no), and consumption of alcohol (0, 0.1-9.9, 10-19.9, 20-29.9, or ≥30g/day), potassium (fifths), fibre (fifths), and vitamin E (fifths), total servings of fruit and vegetables (fifths), total energy intake (continuous), and hypercholesterolaemia (yes or no) at baseline.
†Additional adjustments. All additional variables are fifths.
‡Keys score=1.26(2S-P)+1.5(square root (C)); S=percentages of total energy from saturated fat; P=percentages of total energy from polyunsaturated fat; C=daily cholesterol intake in mg/1000 kcal.

saturated fat, 0.37 for polyunsaturated fat, 0.68 for monounsaturated fat, and 0.76 for cholesterol.[10] In addition, a Spearman correlation of 0.34 was obtained for the comparison of intake of *trans* unsaturated fatty acids as a percentage of total fat calculated from the questionnaire with the *trans* isomer composition of adipose aspirates.[11]

Outcome assessment

We considered as endpoints all incident fatal and non-fatal strokes occurring between the return of the baseline questionnaire and 31 January 2000. A physician blinded to risk factor status reviewed participants' medical records, for which permission was obtained, when incident strokes were reported on a follow up questionnaire. Fatal stroke was reported by next of kin or colleagues or obtained from postal authorities or the national death index. All fatal cases have been confirmed by medical records, autopsy report, or death certificate. We classified cases into ischaemic (embolism or thrombosis), haemorrhagic (subarachnoid and intracerebral), or unknown type of stroke according to the criteria of the national survey of stroke.[12]

Statistical analyses

We calculated follow up time for each participant from the date of return of the first questionnaire to the date of the first stroke, death, or end of the follow up. We

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divided participants into fifths according to their intake of each type of fat. We calculated incidence rates as the number of events divided by the follow up time in each fifth. We estimated relative risks with rate ratios comparing the incidence of stroke in a particular fifth of dietary intake with that of the lowest fifth. To estimate age and smoking adjusted relative risks and 95% confidence intervals we used the Mantel-Haenszel method by stratifying data according to age (five year categories) and smoking status. To further adjust for other covariates we used Cox's proportional hazards models with age (months) as the time variable. In addition to determining the effects of each type of fat individually, we examined the possible confounding by intake of other fat subtypes in secondary analyses. Nutrient intakes were adjusted for energy by regression analysis or used as a nutrient density (nutrient/energy), and we included total energy intake in all regression models. We used the Mantel extension test to test for linear trends,[13] and we included the median values for each fifth in the model as a continuous variable.

To account for changes in diet during the follow up and to best represent long term intake, we used the cumulative average of nutrient intakes derived from all previous food frequency questionnaires. To determine the difference between long term and most recent fat intake, we used the baseline intake and the most recent intake in relation to incidence of stroke. The detail of this method has been previously described.[4] We used the Keys equation to predict serum cholesterol from dietary intake of cholesterol and saturated and polyunsaturated fat.[14] As participants were likely to change their diets after they developed some diseases or health conditions, we stopped updating individual dietary information if a participant had diabetes mellitus, coronary heart disease, transient ischaemic attack, peripheral arterial disease, or a diagnosis of hypercholesterolaemia.

Results

During the 14 year follow up we documented 725 cases, including 455 ischaemic strokes, 125 haemorrhagic strokes, and 145 strokes of unknown type. In both age and smoking adjusted analyses and multivariate analyses, intakes of total fat, animal fat, vegetable fat, saturated fat, monounsaturated fat, polyunsaturated fat, *trans* unsaturated fat, or cholesterol or the score from the Keys equation were not significantly associated with risk of ischaemic or haemorrhagic stroke. Also, none of the trends across fifths was statistically significant (table 1). After further adjustment for intakes of other fat subtypes, the results were not appreciably altered. In addition, none of the specific types of fat intake was significantly related to risk of total stroke (data not shown).

To evaluate the effects of long term and short term dietary intakes, we examined these associations by using baseline intakes and the most recent intakes separately. The multivariate estimations were similar to those obtained using cumulative average diet, and none of the associations was statistically significant (table 2).

We have reported earlier that intakes of long chain omega 3 fatty acids from seafood were inversely associated with ischaemic but not haemorrhagic stroke.[4] However, neither total omega 3 nor omega 6 polyunsaturated fatty acid intake was significantly related to ischaemic or haemorrhagic stroke in this study (data not shown).

We further evaluated risk of strokes according to consumption of selected foods rich in fat or cholesterol, including red meat, high fat dairy products, nuts, and eggs. We found no significant associations with ischaemic or haemorrhagic stroke (table 3).

Discussion

We observed no statistically significant associations in this large cohort between intake of total fat, specific types of fat, or cholesterol and risk of ischaemic, haemorrhagic, or total stroke. In addition, consumption of red meats, high fat dairy products, nuts, or eggs did not seem to be related to risk of stroke.

Strengths and weaknesses of the study

Our findings are unlikely to be explained by recall or selection bias, because of the prospective nature of the study design and minimal loss to follow up. The results are also unlikely to be due to confounding, as the rela-

Table 2 Relative risks of ischaemic stroke according to intakes of total energy, total fat, specific types of fat, and cholesterol as continuous variables in different models

Daily nutrient increment	Relative risk (95% CI)*
Total energy (400 kcal):	
Cumulative average diet	1.00 (0.92 to 1.08)
Most recent diet	1.01 (0.95 to 1.09)
Baseline diet	0.98 (0.91 to 1.05)
Total fat (10% of energy):	
Cumulative average diet	0.97 (0.80 to 1.17)
Most recent diet	0.97 (0.81 to 1.15)
Baseline diet	1.02 (0.87 to 1.21)
Animal fat (10% energy):	
Cumulative average diet	1.08 (0.88 to 1.32)
Most recent diet	1.03 (0.85 to 1.25)
Baseline diet	1.13 (0.94 to 1.36)
Vegetable fat (10% energy):	
Cumulative average diet	0.85 (0.67 to 1.09)
Most recent diet	0.92 (0.74 to 1.15)
Baseline diet	0.87 (0.70 to 1.09)
Saturated fat (10% energy):	
Cumulative average diet	1.10 (0.72 to 1.68)
Most recent diet	1.01 (0.68 to 1.52)
Baseline diet	1.24 (0.85 to 1.82)
Monounsaturated fat (10% of energy):	
Cumulative average diet	0.93 (0.61 to 1.43)
Most recent diet	0.99 (0.67 to 1.46)
Baseline diet	1.01 (0.68 to 1.48)
Polyunsaturated fat (5% of energy):	
Cumulative average diet	0.81 (0.57 to 1.15)
Most recent diet	0.83 (0.60 to 1.15)
Baseline diet	0.87 (0.63 to 1.20)
Trans unsaturated fat (2% of energy):	
Cumulative average diet	0.86 (0.55 to 1.32)
Most recent diet	1.04 (0.72 to 1.51)
Baseline diet	0.80 (0.53 to 1.22)
Cholesterol (200 mg/1000 kcal):	
Cumulative average diet	0.92 (0.62 to 1.36)
Most recent diet	0.84 (0.57 to 1.23)
Baseline diet	1.00 (0.70 to 1.39)

*Adjusted for covariates listed for multivariate model in table 1.

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Table 3 Relative risks of stroke (95% confidence intervals) according to categories of consumption of red meat, high fat dairy products, nuts, and eggs

	Frequency of intake					
	<1/week	1/week	2-4/week	5-6/week	≥1/day	P for trend
Red meats						
Ischaemic stroke:						
No of cases	21	21	124	62	227	—
Adjusted for age and smoking	1.0	0.87 (0.47 to 1.61)	1.04 (0.65 to 1.66)	0.89 (0.54 to 1.48)	1.04 (0.66 to 1.64)	0.64
Multivariate*	1.0	0.81 (0.43 to 1.49)	0.94 (0.59 to 1.52)	0.73 (0.44 to 1.22)	0.97 (0.60 to 1.55)	0.57
Haemorrhagic stroke:						
No of cases	4	4	29	24	64	—
Adjusted for age and smoking	1.0	0.96 (0.23 to 3.99)	1.40 (0.48 to 4.05)	1.76 (0.58 to 5.36)	1.56 (0.55 to 4.45)	0.14
Multivariate*	1.0	0.84 (0.20 to 3.49)	1.23 (0.42 to 3.57)	1.71 (0.58 to 5.06)	1.58 (0.55 to 4.55)	0.19
High fat dairy products						
Ischaemic stroke:						
No of cases	18	47	113	48	225	—
Adjusted for age and smoking	1.0	1.53 (0.88 to 2.66)	1.11 (0.67 to 1.84)	1.01 (0.58 to 1.76)	1.19 (0.73 to 1.94)	0.82
Multivariate*	1.0	1.50 (0.86 to 2.62)	1.03 (0.62 to 1.71)	0.88 (0.51 to 1.55)	1.23 (0.74 to 2.03)	0.38
Haemorrhagic stroke:						
No of cases	5	8	36	12	63	—
Adjusted for age and smoking	1.0	1.04 (0.34 to 3.19)	1.27 (0.49 to 3.28)	0.83 (0.28 to 2.52)	1.19 (0.47 to 3.01)	0.54
Multivariate*	1.0	0.86 (0.27 to 2.69)	1.25 (0.48 to 3.27)	0.87 (0.30 to 2.56)	1.22 (0.47 to 3.16)	0.53
Nuts						
Ischaemic stroke:						
No of cases	105	112	152	36	48	—
Adjusted for age and smoking	1.0	1.13 (0.87 to 1.48)	1.03 (0.80 to 1.32)	0.95 (0.65 to 1.40)	0.85 (0.61 to 1.20)	0.31
Multivariate*	1.0	1.09 (0.83 to 1.43)	1.01 (0.78 to 1.31)	0.95 (0.64 to 1.41)	0.88 (0.61 to 1.26)	0.30
Haemorrhagic stroke:						
No of cases	28	33	38	7	19	—
Adjusted for age and smoking	1.0	1.22 (0.74 to 2.02)	0.97 (0.60 to 1.57)	0.68 (0.30 to 1.57)	1.32 (0.74 to 2.37)	0.89
Multivariate*	1.0	1.29 (0.77 to 2.15)	1.05 (0.63 to 1.74)	0.74 (0.31 to 1.72)	1.29 (0.69 to 2.42)	0.82
Eggs						
Ischaemic stroke:						
No of cases	134	93	167	30	24	—
Adjusted for age and smoking	1.0	0.83 (0.64 to 1.08)	0.87 (0.69 to 1.09)	1.14 (0.76 to 1.70)	0.88 (0.56 to 1.37)	0.81
Multivariate*	1.0	0.83 (0.63 to 1.09)	0.86 (0.68 to 1.09)	1.23 (0.81 to 1.87)	1.09 (0.69 to 1.71)	0.35
Haemorrhagic stroke:						
No of cases	29	35	47	8	2	—
Adjusted for age and smoking	1.0	1.39 (0.85 to 2.28)	1.14 (0.73 to 1.81)	1.45 (0.68 to 3.09)	0.39 (0.10 to 1.59)	0.64
Multivariate*	1.0	1.47 (0.88 to 2.45)	1.17 (0.72 to 1.90)	1.54 (0.67 to 3.50)	0.32 (0.07 to 1.37)	0.34

*Adjusted for covariates listed for multivariate model in table 1.

tive risk estimates did not materially change after simultaneous adjustment for the potential confounding variables. However, as in any observational study, residual confounding from some unknown factors could not be excluded.

The food frequency questionnaire that we used in the dietary assessment has been previously evaluated as a reasonable reflection of long term diet, including fat intakes.[7] In addition, we reduced error in dietary assessment by using repeated measurements. The questionnaire's validity is further supported by the fact that it has predicted risk of coronary heart disease in this cohort.[15] Participants might change their diets after developing some diseases that predispose them to stroke. After the dietary recommendation in the past decades, the most likely changes would be reduction in total fat, saturated fat, and cholesterol intakes. These dietary changes would dilute a possible positive association between these nutrients and risk of stroke. To reduce bias from this source, we excluded men with cardiovascular diseases or diabetes mellitus at baseline and stopped updating individual dietary information once a participant reported any cardiovascular disease, diabetes, or hypercholesterolaemia during the follow up period. The fact that the associations remained similar when we used baseline diet, most recent diet, or cumulative average diet further suggested that the observed associations were unlikely to be substantially attenuated.

Ischaemic stroke

Saturated fat intake has been found to be positively related to carotid artery wall thickness, a marker of atherosclerosis and a potential risk factor for stroke.[16] Polyunsaturated fat intake was inversely associated with this marker. However, epidemiological data on dietary fat and risk of stroke have produced inconsistent results. Whereas saturated fat intake was positively correlated with total mortality from stroke in an ecological study,[17] and the results of several prospective studies have supported beneficial effects of long chain omega 3 polyunsaturated fatty acids, α linolenic acid, and linoleic acid on ischaemic stroke,[4–6] opposite results were reported from the Framingham heart study.[2] In that study total fat, saturated fat, and monounsaturated fat, but not polyunsaturated fat, were inversely associated with risk of ischaemic stroke.

Although ischaemic heart disease and stroke share many of the same risk factors, the association of blood cholesterol with stroke remains controversial. A meta-analysis including 45 prospective cohorts found no association between blood cholesterol and stroke.[18]

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What is already known on this topic

The associations between different types of fat and coronary heart disease do not seem to apply to stroke

Ecological data indicate that dietary fat intake is inversely related to risk of stroke

What this study adds

Intake of total fat, cholesterol, or major specific types of fat was not associated with risk of stroke

Consumptions of red meats, high fat dairy products, nuts, and eggs were also not appreciably related to risk of stroke

However, most studies did not distinguish ischaemic stroke from haemorrhagic stroke, which contributes approximately 20% of all strokes in Western countries, and this would probably dilute any association between blood cholesterol and ischaemic stroke. No significant association between reduction in blood cholesterol and risk of stroke was reported in an overview of trials of cholesterol lowering treatment involving more than 36 000 patients.[19] However, in recent trials of cholesterol lowering treatment in patients with cardiovascular disease, the incidence of stroke was reduced in the treated groups.[20] Overall, it seems that serum lipid concentration is not a strong predictor of total stroke, probably because a substantial proportion of ischaemic strokes are caused by embolism or other mechanisms that are not directly related to atherosclerosis. In addition, nitric oxide and inflammation may play important roles in the pathogenesis of ischaemic stroke,[21 22] and the findings of the beneficial effects of unsaturated fatty acids on ischaemic stroke may be in part due to their favourable effects on platelet aggregation and endothelial function.[4–6 23 24]

Haemorrhagic stroke

The association between dietary fat intake and risk of haemorrhagic stroke is far from clear. In the nurses' health study, Iso et al observed an inverse association between risk of intraparenchymal haemorrhagic stroke and intake of saturated fat or *trans* unsaturated fat but no associations with total fat, polyunsaturated fat, monounsaturated fat, or dietary cholesterol.[3] Although we did not observe any significant association between dietary fat intake and risk of haemorrhagic stroke, we could not exclude any important association because of the modest number of cases of haemorrhagic stroke. Further studies are needed.

Conclusion

Our findings from this large cohort of middle aged US male healthcare professionals without a history of cardiovascular disease or diabetes mellitus indicate that intakes of total fat, specific types of fat, or dietary cholesterol do not seem to be related to the development of stroke.

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