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Dietary fat and risk of coronary heart disease in men: cohort follow up study in the United States

Alberto Ascherio, Eric B Rimm, Edward L Giovannucci, Donna Spiegelman, Meir Stampfer, Walter C Willett

Abstract

***Objective*—To examine the association between fat intake and the incidence of coronary heart disease in men of middle age and older.**

***Design*—Cohort questionnaire study of men followed up for six years from 1986.**

***Setting*—The health professionals follow up study in the United States.**

***Subjects*—43 757 health professionals aged 40 to 75 years free of diagnosed cardiovascular disease or diabetes in 1986.**

***Main outcome measure*—Incidence of acute myocardial infarction or coronary death.**

***Results*—During follow up 734 coronary events were documented, including 505 non-fatal myocardial infarctions and 229 deaths. After age and several coronary risk factors were controlled for significant positive associations were observed between intake of saturated fat and risk of coronary disease. For men in the top versus the lowest fifth of saturated fat intake (median = 14.8% *v* 5.7% of energy) the multivariate relative risk for myocardial infarction was 1.22 (95% confidence interval 0.96 to 1.56) and for fatal coronary heart disease was 2.21 (1.38 to 3.54). After ajustment for intake of fibre the risks were 0.96 (0.73 to 1.27) and 1.72 (1.01 to 2.90), respectively. Positive associations between intake of cholesterol and risk of coronary heart disease were similarly attenuated after adjustment for fibre intake. Intake of linolenic acid was inversely associated with risk of myocardial infarction; this association became significant only after adjustment for non-dietary risk factors and was strengthened after adjustment for total fat intake (relative risk 0.41 for a 1% increase in energy, P for trend <0.01).**

***Conclusions*—These data do not support the strong association between intake of saturated fat and risk of coronary heart disease suggested by international comparisons. They are compatible, however, with the hypotheses that saturated fat and cholesterol intakes affect the risk of coronary heart disease as predicted by their effects on blood cholesterol concentration. They also support a specific preventive effect of linolenic acid intake.**

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Introduction

International comparisons[1-4] and laboratory data[5] suggest that diets high in saturated fat and cholesterol and low in polyunsaturated fat increase the risk of coronary heart disease. These diets increase blood cholesterol concentration,[6-9] which is related to risk of coronary disease.[10] The differences between countries, however, are far larger than one would predict based on effects of cholesterol concentrations. Results of prospective epidemiological investigations and randomised trials have been inconsistent; small size or inadequate dietary assessment may explain most of the discrepancies.[11 12] We therefore examined the association between dietary fat and cholesterol and risk of myocardial infarction in a large cohort of men in the United States.

Subjects and methods

POPULATION

The health professionals follow up study began in 1986 when 51 529 health professionals aged 40 to 75 years completed a 131 item food frequency questionnaire and provided information about medical history, risk factors for heart disease, and dietary changes during the past 10 years.[13] Follow up questionnaires were sent in 1988, 1990, and 1992. We excluded from analysis 1595 men who did not satisfy the a priori criteria of daily energy intake between 3.34 and 17.56 MJ and fewer than 70 blanks out of 131 total listed food items. In addition, we excluded 6177 men with previous diagnosis of myocardial infarction, angina, coronary artery surgery, stroke, transient ischaemic attack, peripheral arterial disease, or diabetes. We followed the 43 757 eligible men for incidence of coronary disease during the subsequent six years. Over 94% returned follow up questionnaires in each two year follow up cycle. Participants not listed in the National Death Index who did not respond were assumed to be alive.

DIETARY ASSESSMENT

The 1986 questionnaire asked about average frequency of intake over the previous year of specified portions of 131 foods. We assessed its validity in a random sample of 127 men by comparing their calculated intake of fat with that reported during two diet records over one week taken about six months apart.[14] The correlations between the two assessments of intake, adjusted for energy and corrected for within person variation in the diet records, were 0.75 for saturated fat, 0.76 for cholesterol, and 0.37 for linoleic acid. In addition, the calculated intakes of linoleic and *trans* unsaturated fatty acids were compared with their concentrations in adipose; the correlations between intake as a proportion of fat and the proportion in adipose were 0.48 for linoleic and 0.29 for *trans* fatty acids.[15]

CASES

As described elsewhere in detail,[16] end points were fatal coronary disease (including sudden death) and non-fatal myocardial infarction occurring between the return of the baseline questionnaire and 31 January 1992. Participants reporting an incident of myocardial infarction on a follow up questionnaire were asked for permission to review medical records. Non-fatal myocardial infarction was confirmed by using World Health Organisation criteria: symptoms plus either

Table 1—*Relation of intake of saturated fatty acid to selected variables at baseline among men*

Detail	Fifth of saturated fat intake adjusted for energy				
	1	2	3	4	5
Mean saturated fat intake (g/day)	15.9	21.5	24.8	27.7	32.4
Mean saturated fat intake (% of energy)	7.2	9.5	10.9	12.3	14.8
Currently smoking (%)	5.7	7.5	9.1	10.9	14.4
Mean alcohol consumption (g/day)	15.4	14.2	12.0	10.4	8.0
Mean body mass index (kg/m^2)	24.0	24.7	25.0	25.2	25.5
Family history of myocardial infarction (%)	13.5	12.2	11.3	11.4	11.0
History at baseline of:					
Hypertension (%)	20.7	20.1	20.0	18.8	18.2
High cholesterol (%)	16.2	11.3	9.8	7.9	6.6
Mean serum cholesterol (mmol/l)*	5.2	5.3	5.3	5.3	5.3
Mean physical activity (MET/week)	30.1	25.4	24.5	21.3	19.9
Mean daily intake of:					
Total fat (% of energy)	23.9	29.4	32.3	34.9	39.1
Trans fatty acids (% of energy)	0.8	1.1	1.3	1.4	1.6
Linoleic acid (% of energy)	4.6	5.1	5.2	5.3	5.2
Linolenic acid (% of energy)	0.4	0.5	0.5	0.5	0.6
Cholesterol (mg/1000 kcal;4 MJ)	118	141	152	165	185
Polyunsaturated:saturated fat ratio	0.8	0.6	0.6	0.5	0.4
Dietary fibre (g/day)	26.2	22.1	20.6	18.8	16.2
Carotene (IU/day)	13 968	10 736	9646	8486	7203
Vitamin E (IU/day)	127	94	86	77	72
Servings/day (mean):					
Fish	0.5	0.4	0.4	0.3	0.3
Red meat	0.4	0.8	1.0	1.2	1.4
Chicken	0.4	0.4	0.4	0.3	0.3
Cereals	3.7	3.4	3.3	3.2	2.9
Vegetables	4.6	3.8	3.5	3.2	2.8
Fruit	3.5	2.6	2.3	2.0	1.6
Sweets	1.0	1.4	1.5	1.6	1.5
Low fat dairy	1.0	1.1	1.0	1.0	0.8
High fat dairy	0.5	0.8	1.1	1.4	2.4

*Based on 17 339 men without history of hypercholesterolaemia who reported their blood cholesterol concentration at baseline.

typical electrocardiographic changes or increased activities in cardiac enzymes.[17]

Deaths were reported by next of kin, coworkers, postal authorities, or the National Death Index. Fatal coronary disease was confirmed by medical records, necropsy reports, or if it was the underlying cause on the death certificate and a diagnosis of coronary disease was confirmed by other sources. Sudden death within one hour of the onset of symptoms in men with no other plausible cause of death (other than coronary disease) was also included.

STATISTICAL ANALYSIS

Participants contributed follow up time from the return of the 1986 questionnaire up to the occurrence of an end point, death, or 31 January 1992. Relative risks were calculated by dividing the incidence of coronary disease among men in each fifth of the distribution of intake of saturated fat adjusted for energy[18] by the incidence among men in the lowest fifth of intake. We adjusted relative risks for age (five year categories)[19] and used the Mantel extension test[20] to test for linear trends. To adjust for other risk factors we used multiple logistic regression. Proportional hazards models (not shown)[21] yielded virtually identical results. In multivariate models we evaluated monotonic trends by using the median value of each category and modelling this as a continuous variable. In addition, we conducted analyses with the proportion of calories contributed by different fats as continuous variables. The results were corrected for measurement errors in the assessment of diet, body mass index, and alcohol consumption[22] by using data from the validation study.[14 23 24] Intake of polyunsaturated fat, rather than linoleic acid, was used for correction of measurement error because intake of linoleic and linolenic acid could not be obtained from the diet record database. All P values are two sided.

Results

During 236 782 person years of follow up we documented 734 myocardial infarctions (including 229 coronary deaths). Because intake of saturated fat was associated both directly and inversely with several risk factors (table)1, we analysed its relation with myocardial infarction before and after adjustment for these variables.

In age adjusted analyses intakes of saturated fat, total fat, and cholesterol and the score from the Keys equations[6] were each associated with increased risk of myocardial infarction and fatal coronary heart disease (table 2). After adjustment for non-dietary risk factors these associations were weakened and were further attenuated after adjustment for intake of fibre (table 2). The relative risks did not appreciably change after additional adjustment for intake of vitamin E and β carotene.

Intakes of linoleic and linolenic acid were not significantly associated with risk of myocardial infarction, whereas intake of *trans* fatty acids was directly associated with risk of myocardial infarction after adjustment for age and standard risk factors but less so after further adjustment for fibre intake (table 3).

The analyses with intakes of total fat, saturated fat, and *trans* fatty acids as a proportion of total energy gave similar results (table 4). We also observed a similar pattern for intake of cholesterol expressed in mg/4 MJ. Adjustment for dietary fibre strongly attenuated the positive associations with coronary disease. Although intake of linoleic acid (as proportion of total energy) was not significantly associated with coronary disease (table 4), an inverse association with fatal coronary disease became apparent after adjustment for total fat intake. Linolenic acid (proportion of total energy) was inversely associated with risk. The relative risk for a 1% increase in linolenic acid intake was 0.53 (0.30 to 0.95) after adjustment for standard risk factors and intake of fibre

Table 2—*Relative risk of myocardial infarction according to intake of total fat, saturated fat, and cholesterol adjusted for energy. Figures are relative risks (95% confidence intervals) unless stated otherwise*

Variable	Fifth					χ^2 For trend	P value
	1	2	3	4	5		
Saturated fat							
Median intake (g/day)	17	21	24	27	33		
Person years	43 963	47 098	48 148	49 049	48 525		
Total myocardial infarction*:							
No of cases	125	148	131	150	180		
Age adjusted	1.0	1.16 (0.91 to 1.47)	1.05 (0.82 to 1.34)	1.21 (0.95 to 1.53)	1.44 (1.14 to 1.81)	3.04	0.002
Multivariate†	1.0	1.11 (0.87 to 1.42)	0.97 (0.75 to 1.24)	1.08 (0.84 to 1.38)	1.22 (0.96 to 1.56)	1.48	0.14
Adjusted for fibre intake‡	1.0	1.01 (0.79 to 1.30)	0.84 (0.65 to 1.10)	0.90 (0.69 to 1.18)	0.96 (0.73 to 1.27)	−0.40	0.69
Fatal coronary heart disease:							
No of cases	27	45	45	46	66		
Age adjusted	1.0	1.63 (1.02 to 2.62)	1.73 (1.08 to 2.78)	1.79 (1.12 to 2.87)	2.55 (1.65 to 3.95)	3.98	<0.0001
Multivariate†	1.0	1.57 (0.97 to 2.54)	1.60 (0.98 to 2.59)	1.60 (0.98 to 2.61)	2.21 (1.38 to 3.54)	3.15	0.0016
Adjusted for fibre intake‡	1.0	1.41 (0.87 to 2.31)	1.38 (0.83 to 2.28)	1.32 (0.79 to 2.22)	1.72 (1.01 to 2.90)	1.68	0.09
Cholesterol							
Median intake (mg/day)	189	246	290	338	422		
Person years	46 220	47 673	48 012	48 064	46 814		
Total myocardial infarction*:							
No of cases	124	121	147	155	187		
Age adjusted	1.0	0.96 (0.75 to 1.24)	1.12 (0.88 to 1.42)	1.14 (0.90 to 1.45)	1.34 (1.07 to 1.68)	2.94	0.003
Multivariate†	1.0	0.91 (0.71 to 1.18)	1.06 (0.83 to 1.36)	1.04 (0.81 to 1.32)	1.17 (0.93 to 1.49)	1.78	0.07
Adjusted for fibre intake‡	1.0	0.86 (0.67 to 1.11)	0.98 (0.76 to 1.25)	0.94 (0.73 to 1.20)	1.03 (0.81 to 1.32)	0.70	0.48
Fatal coronary heart disease:							
No of cases	32	34	48	51	64		
Age adjusted	1.0	1.06 (0.66 to 1.73)	1.41 (0.90 to 2.21)	1.48 (0.95 to 2.29)	1.77 (1.16 to 2.70)	3.05	0.002
Multivariate†	1.0	1.00 (0.61 to 1.62)	1.33 (0.85 to 2.09)	1.29 (0.82 to 2.02)	1.52 (0.98 to 2.36)	2.22	0.03
Adjusted for fibre intake‡	1.0	0.92 (0.56 to 1.50)	1.18 (0.75 to 1.87)	1.11 (0.70 to 1.76)	1.25 (0.80 to 1.97)	1.25	0.21
Total fat							
Median intake (g/day)	53	64	72	78	89		
Person years	44 705	47 361	48 240	48 440	48 037		
Total myocardial infarction*:							
No of cases	118	136	149	160	171		
Age adjusted	1.0	1.13 (0.88 to 1.44)	1.25 (0.98 to 1.59)	1.35 (1.07 to 1.71)	1.43 (1.13 to 1.81)	3.32	0.001
Multivariate†	1.0	1.07 (0.83 to 1.38)	1.17 (0.92 to 1.51)	1.23 (0.96 to 1.58)	1.23 (0.96 to 1.57)	1.83	0.06
Adjusted for fibre intake‡	1.0	1.00 (0.77 to 1.29)	1.05 (0.82 to 1.36)	1.07 (0.82 to 1.39)	1.02 (0.78 to 1.34)	0.80	0.42
Fatal coronary heart disease:							
No of cases	32	36	52	52	57		
Age adjusted	1.0	1.11 (0.69 to 1.78)	1.65 (1.06 to 2.54)	1.67 (1.08 to 2.59)	1.83 (1.19 to 2.80)	3.30	0.001
Multivariate†	1.0	1.03 (0.64 to 1.66)	1.55 (0.99 to 2.43)	1.54 (0.98 to 2.43)	1.59 (1.01 to 2.51)	2.39	0.02
Adjusted for fibre intake‡	1.0	0.93 (0.57 to 1.51)	1.34 (0.84 to 2.12)	1.26 (0.79 to 2.03)	1.22 (0.75 to 2.00)	1.02	0.31
Keys score							
Median score	28.0	35.0	39.6	44.1	51.5		
Person years	44 128	47 481	47 891	48 849	48 433		
Total myocardial infarction:							
No of cases	124	135	153	134	188		
Age adjusted	1.0	1.05 (0.82 to 1.35)	1.23 (0.97 to 1.56)	1.06 (0.83 to 1.35)	1.45 (1.15 to 1.82)	3.09	0.002
Multivariate†	1.0	1.02 (0.79 to 1.31)	1.14 (0.89 to 1.46)	0.95 (0.74 to 1.22)	1.23 (0.96 to 1.56)	1.45	0.15
Adjusted for fibre intake‡	1.0	0.92 (0.71 to 1.19)	0.99 (0.77 to 1.28)	0.79 (0.60 to 1.04)	0.96 (0.73 to 1.27)	−0.44	0.66
Fatal coronary heart disease:							
No of cases	27	37	58	38	69		
Age adjusted	1.0	1.33 (0.81 to 2.19)	2.17 (1.37 to 3.43)	1.41 (0.86 to 2.30)	2.46 (1.57 to 3.85)	3.95	0.0001
Multivariate†	1.0	1.27 (0.77 to 2.09)	1.99 (1.25 to 3.18)	1.24 (0.75 to 2.05)	2.10 (1.32 to 3.35)	2.97	0.003
Adjusted for fibre intake‡	1.0	1.13 (0.68 to 1.88)	1.69 (1.04 to 2.75)	1.00 (0.59 to 1.71)	1.59 (0.94 to 2.68)	1.48	0.14

*Includes non-fatal myocardial infarction and fatal coronary heart disease.
†Model includes age (seven categories); body mass index (five categories); smoking habits (current smoker (number of cigarettes smoked), former smoker, never smoked); alcohol consumption (four categories); physical activity (fifths); history of hypertension or high blood cholesterol; family history of myocardial infarction before age 60; and profession.
‡Additionally adjusted for fibre intake adjusted for energy (continuous variable).

and 0.41 (0.21 to 0.80) after further adjustment for intake of total fat. The association was inverse, but not significant, for fatal coronary disease (table 4).

The association between the ratio of polyunsaturated to saturated fat and risk was opposite to that of saturated fat, reflecting their inverse correlation; as for saturated fat the associations were attenuated and no longer significant after adjustment for dietary fibre. We obtained similar results for the ratio of the sum of polyunsaturated and *cis* unsaturated fatty acids over the sum of saturated plus *trans* fatty acids.

To reduce the possibility of residual confounding by perceived high risk of coronary events we repeated the analyses shown in table 3, first after excluding the 4494 men with hyperlipidaemia and then after further excluding the 17 333 men who knew their serum cholesterol concentrations at baseline. Results of both were similar but with wider confidence intervals. Because of the possibility that the lowest fifth of saturated fat intake comprised men who had modified their diet recently to reduce their blood cholesterol concentration we repeated the analyses after excluding from that fifth those men who at baseline reported reducing their intake of butter, meat, whole milk, or eggs during the previous 10 years. The results were similar to those reported above. Also, we reduced the possibility of confounding by preclinical symptomatic coronary disease at baseline by excluding events in the first four years of follow up. In these analyses, which excluded 256 cases of myocardial infarction, we found that the relative risk for the highest fifth of saturated fat intake compared with the lowest was 0.73 (0.47 to 1.14) for total myocardial infarction and 2.04 (0.76 to 5.44) for fatal coronary heart disease. The comparable relative risks for dietary cholesterol were 0.77 (0.51 to 1.17) and 0.81 (0.34 to 1.90), respectively.

We also corrected the relative risks obtained in our main multivariate analyses for measurement errors in

Table 3—*Relative risk of myocardial infarction according to intake of linoleic acid, linolenic acid, and trans-unsaturated fatty acids adjusted for energy. Figures are relative risks (95% confidence interval) unless otherwise stated*

	Fifth						
	1	2	3	4	5	χ^2 For trend	P value
Linoleic acid							
Median intake (g/day)	7.6	9.6	11.0	12.6	15.4		
Person years	46 309	48 038	47 986	47 640	46 809		
Total myocardial infarction*:							
No of cases	138	164	147	146	139		
Age adjusted	1.0	1.24 (0.99 to 1.55)	1.12 (0.89 to 1.42)	1.13 (0.89 to 1.43)	1.08 (0.85 to 1.36)	0.14	0.89
Multivariate†	1.0	1.23 (0.97 to 1.55)	1.13 (0.89 to 1.43)	1.12 (0.88 to 1.42)	1.05 (0.83 to 1.34)	−0.04	0.97
Adjusted for fibre intake‡	1.0	1.21 (0.96 to 1.52)	1.12 (0.88 to 1.42)	1.10 (0.87 to 1.39)	1.04 (0.82 to 1.33)	−0.14	0.89
Fatal coronary heart disease:							
No of cases	40	50	49	44	46		
Age adjusted	1.0	1.37 (0.90 to 2.07)	1.35 (0.88 to 2.06)	1.23 (0.79 to 1.90)	1.28 (0.84 to 1.97)	0.82	0.41
Multivariate†	1.0	1.32 (0.87 to 2.02)	1.38 (0.90 to 2.10)	1.24 (0.81 to 1.92)	1.30 (0.85 to 2.00)	0.89	0.37
Adjusted for fibre intake‡	1.0	1.30 (0.86 to 1.99)	1.36 (0.89 to 2.07)	1.22 (0.79 to 1.89)	1.28(0.83 to 1.98)	0.83	0.41
Linolenic acid							
Median intake (g/day)	0.8	0.9	1.1	1.2	1.5		
Person years	45 860	46 608	47 628	49 699	46 987		
Total myocardial infarction*:							
No of cases	145	147	150	162	130		
Age adjusted	1.0	1.04 (0.83 to 1.31)	1.05 (0.83 to 1.31)	1.05 (0.84 to 1.32)	0.87 (0.69 to 1.10)	−0.93	0.35
Multivariate†	1.0	1.01 (0.82 to 1.28)	0.99 (0.79 to 1.26)	1.00 (0.79 to 1.26)	0.82 (0.65 to 1.05)	−1.62	0.10
Adjusted for fibre intake‡	1.0	1.00 (0.79 to 1.26)	0.97 (0.77 to 1.23)	0.98 (0.78 to 1.24)	0.80 (0.63 to 1.03)	−1.81	0.07
Fatal coronary heart disease:							
No of cases	40	44	42	59	44		
Age adjusted	1.0	1.15 (0.75 to 1.77)	1.08 (0.70 to 1.67)	1.42 (0.95 to 2.11)	1.08 (0.71 to 1.66)	0.90	0.37
Multivariate†	1.0	1.14 (0.74 to 1.75)	1.04 (0.67 to 1.62)	1.38 (0.92 to 2.07)	1.06 (0.69 to 1.64)	0.47	0.64
Adjusted for fibre intake‡	1.0	1.12 (0.72 to 1.72)	1.02 (0.66 to 1.58)	1.35 (0.90 to 2.03)	1.03 (0.66 to 1.59)	0.30	0.76
Trans unsaturated							
Median intake (g/day)	1.5	2.2	2.7	3.3	4.3		
Person years	44 764	47 378	48 173	48 158	48 310		
Total myocardial infarction*:							
No of cases	112	140	147	154	181		
Age adjusted	1.0	1.24 (0.97 to 1.59)	1.33 (1.04 to 1.70)	1.40 (1.10 to 1.78)	1.57 (1.24 to 1.98)	3.80	0.0002
Multivariate†	1.0	1.20 (0.93 to 1.54)	1.24 (0.97 to 1.60)	1.27 (0.99 to 1.63)	1.40 (1.10 to 1.79)	2.59	0.01
Adjusted for fibre intake‡	1.0	1.12 (0.86 to 1.44)	1.12 (0.87 to 1.46)	1.12 (0.86 to 1.46)	1.21 (0.93 to 1.58)	1.27	0.20
Fatal coronary heart disease:							
No of cases	27	51	39	56	56		
Age adjusted	1.0	1.88 (1.19 to 2.98)	1.50 (0.92 to 2.42)	2.10 (1.34 to 3.29)	1.99 (1.27 to 3.12)	2.81	0.005
Multivariate†	1.0	1.81 (1.13 to 2.90)	1.38 (0.84 to 2.27)	1.94 (1.22 to 3.10)	1.78 (1.11 to 2.84)	2.03	0.04
Adjusted for fibre intake‡	1.0	1.63 (1.01 to 2.62)	1.18 (0.71 to 1.96)	1.59 (0.98 to 2.60)	1.41 (0.86 to 2.32)	0.82	0.42

*Includes non-fatal myocardial infarction and fatal coronary heart disease.
†Model includes age (seven categories); body mass index (five categories); smoking habits (current smoker (number of cigarettes smoked), former smoker, never smoked); alcohol consumption (four categories); physical activity (fifths); history of hypertension or high blood cholesterol; family history of myocardial infarction before age 60; and profession.
‡Additionally adjusted for fibre intake adjusted for energy (continuous variable).

body mass index, alcohol consumption, total energy intake, and selected nutrients.[22] In regression models adjusted for standard risk factors and fibre intake the corrected relative risks of myocardial infarction were 0.54 (0.26 to 1.14) for a 5% increase in intake of saturated fat, 0.91 (0.66 to 1.27) for a 100 mg/4 MJ increase in intake of cholesterol, and 0.80 (0.31 to 2.03) for a 5% increase in intake of polyunsaturated fat. Intake of fibre remained significantly inversely associated with risk after correction for measurement error.

Discussion

In this large prospective study we found strong and highly significant age adjusted associations between intakes of saturated fat, cholesterol, and *trans* fatty acids with risk of coronary disease. These associations were greatly attenuated, however, after adjustment for standard risk factors and intake of fibre. We also found an independent inverse relation between intake of linolenic acid and risk of coronary disease.

The high follow up minimised potential bias. We also excluded from the analyses men with previously diagnosed coronary disease or diabetes, who may have changed their diets as a consequence of the disease. Although changes in diet among men with high serum cholesterol concentrations may have attenuated a positive association between intake of saturated fat and risk of coronary heart disease, this attenuation is likely to be modest because the exclusion of men with hypercholesterolaemia and those who knew their baseline serum cholesterol concentration did not appreciably change the results. Whereas most non-dietary risk factors were measured reasonably well, there is greater error in our estimates of physical activity,[25] and the direct associations between saturated fat intake or cholesterol and risk of coronary disease may in part reflect residual confounding.

FIBRE AS A CONFOUNDER

Although a direct association between saturated fat intake and risk of coronary disease has been reported in several studies,[26-29] those findings may have been confounded by fibre intake. No significant associations were found in several other prospective investigations,[30-35] but, with the exception of the Western Electric study,[31] these had limited power because of their small size[30 33-35] or inadequate dietary assessment.[32 33] In contrast, ecological comparisons have suggested strong associations between saturated fat intake and risk of coronary disease and particularly with death from coronary disease[4] similar to those observed in age adjusted analyses in our cohort. These results indicate both that saturated fat varies substantially within this cohort and that the assessment of dietary fat performed well. The results of multivariate analyses, with or without correction for measurement errors, however, indicated that intake of fibre is more strongly related to risk of coronary disease than intake

Table 4—*Relative risk (95% confidence interval) of total myocardial infarction and fatal coronary heart disease according to intake of different fats*

Condition	Fatty acid (% of energy)					
	Total fat (5%)	Saturated fat (5%)	Linoleic (5%)	*Trans* (2%)	Linolenic (1%)	Cholesterol (100 mg/ 1000 kcal; 4 MJ)
Myocardial infarction*:						
Age adjusted	1.11† (1.05 to 1.18)	1.24† (1.09 to 1.41)	1.03 (0.81 to 1.31)	1.59† (1.21 to 2.08)	0.65 (0.38 to 1.14)	1.18‡ (1.05 to 1.33)
Multivariate§	1.06 (1.00 to 1.13)	1.12 (0.97 to 1.28)	1.01 (0.79 to 1.30)	1.36¶ (1.03 to 1.81)	0.56¶ (0.32 to 1.00)	1.11 (0.98 to 1.25)
Multivariate+fibre§	1.01 (0.94 to 1.08)	0.96 (0.81 to 1.13)	1.00 (0.78 to 1.28)	1.13 (0.83 to 1.54)	0.53¶ (0.30 to 0.95)	1.04 (0.91 to 1.18)
Multivariate+total fat§	-	0.99 (0.77 to 1.26)	0.84 (0.62 to 1.13)	1.25 (0.91 to 1.73)	0.35‡ (0.18 to 0.67)	1.07 (0.93 to 1.22)
Multivariate+fibre+total fat§	-	0.86 (0.66 to 1.12)	0.97 (0.71 to 1.32)	1.13 (0.81 to 1.58)	0.41‡ (0.21 to 0.80)	1.03 (0.90 to 1.19)
Fatal coronary heart disease						
Age adjusted	1.20† (1.08 to 1.33)	1.61** (1.36 to 2.04)	0.92 (0.59 to 1.43)	1.71¶ (1.07 to 2.74)	1.08 (0.46 to 2.54)	1.29¶ (1.06 to 1.57)
Multivariate§	1.16‡ (1.04 to 1.29)	1.49† (1.22 to 1.89)	0.93 (0.59 to 1.45)	1.47 (0.90 to 2.40)	0.96 (0.37 to 2.52)	1.21 (0.98 to 1.50)
Multivariate+fibre§	1.08 (0.95 to 1.22)	1.28 (0.97 to 1.70)	0.92 (0.58 to 1.44)	1.07 (0.62 to 1.84)	0.89 (0.34 to 2.36)	1.10 (0.88 to 1.38)
Multivariate+total fat§	-	1.52¶ (1.00 to 2.31)	0.58¶ (0.34 to 0.99)	1.09 (0.62 to 1.93)	0.45 (0.15 to 1.36)	1.11 (0.88 to 1.40)
Multivariate+fibre+total fat§	-	1.34 (0.86 to 2.08)	0.69 (0.40 to 1.20)	0.93 (0.52 to 1.69)	0.57 (0.18 to 1.79)	1.06 (0.84 to 1.35)

*Includes non-fatal myocardial infarction and fatal coronary heart disease.
†P < 0.001.
‡P < 0.01.
§Model includes age (seven categories); body mass index (five categories); smoking habits (current smoker (number of cigarettes smoked), former smoker, never smoked); alcohol consumption (four categories); physical activity (fifths); history of hypertension or high blood cholesterol; family history of myocardial infarction before age 60; profession; and total energy intake (continuous).
¶P < 0.05.
**P < 0.0001.

Table 5—*Relative risk of coronary heart disease predicted by metabolic studies and international comparisons for each fifth of saturated fat intake*

Detail	Fifth of saturated fat intake adjusted for energy according to response to baseline questionnaire				
	1	2	3	4	5
Mean dietary intake during two weeks of diet record:					
Saturated fat (% energy)	8.1	10.4	11.4	12.8	13.8
Polyunsaturated fat (% energy)	7.0	6.5	7.0	6.9	6.6
Cholesterol (mg/4 MJ)	120	147	151	191	184
International comparisons[4]:					
Predicted relative risk of total coronary heart disease	1.0	1.1	1.2	1.4	1.6
Predicted relative risk of fatal coronary heart disease	1.0	1.5	1.7	2.0	2.2
Keys equation:					
Predicted relative risk of coronary heart disease*	1.0	1.10	1.13	1.21	1.26
Mensink and Katan:					
Relative risk of coronary heart disease predicted from effect of diet on serum low density lipoprotein cholesterol†	1.0	1.04	1.05	1.08	1.09
Relative risk of coronary heart disease predicted by effect of diet on total/high density lipoprotein serum cholesterol‡	1.0	1.0	1.0	1.0	1.0

*Calculated by assuming change in serum total cholesterol = $1.35(2\Delta S - \Delta P) + 1.5\Delta Z$, where ΔS and ΔP are changes in % of energy contributed by saturated and polyunsaturated fat, respectively, and ΔZ is change of square root of dietary cholesterol in mg/4 MJ[6] and that reduction in total serum cholesterol of 0.6 mmol/l will cause 24% decrease in risk of coronary heart disease.[11]
†Calculated by assuming change in serum low density lipoprotein cholesterol (mmol/l) = 0.033 × (carbohydrates saturated fat) − 0.014 × (carbohydrates polyunsaturated fat)[8] and that reduction in serum low density lipoprotein cholesterol of 0.6 mmol/l will cause 27% decrease in risk of coronary heart disease.[11]
‡Estimated by assuming that replacement of carbohydrate with saturated fat does not change ratio of total to high density lipoprotein cholesterol.

of saturated fat or cholesterol[36] and that this largely accounts for the observed association with saturated fat.

To facilitate the direct comparison of the observed relative risks with those predicted by different hypothetical states of nature we calculated the relative risks of coronary heart disease for each fifth of intake of saturated fat predicted under four different assumptions (table 5). For each assumption the calculations are based on the average intakes of fat and cholesterol obtained from the diet records for each fifth of intake of saturated fat defined by the food frequency questionnaire. They therefore take into accounts errors in measurement (insofar as the diet records provide unbiased estimates of the true intakes) and can be directly compared with those of table 2. The results of our study and previous epidemiological investigations are consistent with the possibility that intake of saturated fat moderately increases the risk of coronary disease because of its effects on serum cholesterol concentration. Our findings do not, however, support the strong association between saturated fat and coronary disease suggested by international comparisons. The results are also consistent with the possibility that the proportional increase in concentration of serum high density lipoprotein cholesterol produced by saturated fat compensates for its adverse effect on total serum cholesterol concentration.[37 38]

Intake of dietary cholesterol was associated with an increased risk of coronary death in some[26 39] but not all prospective investigations.[27 30 32-34 40] In our study, intake of cholesterol was associated with an increased risk of death from coronary heart disease, but, as with saturated fat, the association was largely explained by fibre intake.

Intake of polyunsaturated fat was inversely associated with risk of coronary disease in some[29 31 41] but not all[26 27 32 33 42] prospective cohort studies. Small size or inadequate dietary assessment may explain these inconsistencies. Significant reductions in incidence of coronary disease or mortality in the intervention group

were observed in a few[43-45] but not all[46 47] primary prevention trials of high polyunsaturated fat diets. The results of previous epidemiological investigations and of trials among patients with coronary heart disease have also been inconsistent.[12] In our study, the proportion of energy intake contributed by linoleic acid was not significantly associated with risk of coronary heart disease. A significant inverse association with fatal coronary disease, however, became apparent after adjustment for total fat intake. This result, and the inverse association with the polyunsaturated to saturated fat ratio, is consistent with a benefit of replacing saturated with polyunsaturated fat. Although these associations were attenuated and no longer significant after adjustment for dietary fibre, the confidence intervals for the relevant relative risks included substantial potential protective effects for unsaturated dietary fats.

LINOLENIC ACID AND FATTY ACIDS

The inverse association between intake of linolenic acid and risk of coronary disease, although significant only in multivariate analyses, supports the hypothesis of a specific preventive effect of this fatty acid.[48] An inverse association between linolenic acid intake and risk of coronary death was observed in the usual care group of the multiple risk factors intervention trial,[41] and a higher intake of linolenic acid in the intervention group may have contributed to the reduced coronary disease observed in some of the primary[44 49] and secondary prevention trials.[50 51] In addition, the traditional diets in Crete and Japan, where coronary disease incidence is low, have high content of linolenic acid.[50 52] Although McKeigue suggested that the benefits of linolenic acid are due to its conversion to eicosapentaenoic acid,[53] intake of marine *N*-3 fatty acids was not inversely associated with risk in our cohort,[54] suggesting that the cardiovascular effects of linolenic acid may be different from those of the longer chain *N*-3 fatty acids.

The positive association in this study between intake of *trans* fatty acids and risk of coronary disease is consistent with previous findings, as recently reviewed.[55] Although this association was attenuated after adjustment for dietary fibre, these relative risks are only moderately lower than those reported in the nurses' health study[56] and are consistent with an adverse effect of *trans* fatty acids on risk of coronary disease. The concentration of *trans* fatty acids in adipose was not associated with risk of sudden death (66 cases) in a case-control study in the United States[57] or with risk of myocardial infarction in the large multicentre Euramic study. In that investigation, however, after the exclusion of the data from Spain, where intake of *trans* fatty acids was extremely low, the relative risk of the highest versus the lowest fifth of intake was 1.44 (0.94 to 2.20),[58] a result consistent with our findings.

CONCLUSIONS

Although residual confounding by unmeasured factors cannot be entirely excluded, our results support a major association between overall diet and risk of coronary heart disease. They also suggest that the effect of saturated fat on risk of coronary heart disease is unlikely to be as strong as suggested by international comparisons, which are probably confounded by other factors, as already recognized by Keys.[4] The confidence intervals for some of the reported relative risks, however, include potentially important associations if proper allowance is made for measurement errors, and a firm conclusion regarding the role of dietary fats to risk of coronary heart disease is unwarranted. Further follow up of this cohort and similar prospective investigations should provide data needed to support more detailed conclusions, including the optimal amount and composition of polyunsaturated fat in the diet.

Key messages

- Diet influences the risk of death from coronary heart disease among middle aged and older men
- Diets high in saturated fat and cholesterol are associated with an increased risk of coronary disease, but these adverse effects are at least in part explained by their low fibre content and associations with other risk factors
- Diets high in linolenic acid (*N*-3 fatty acid from plants) are associated with a reduced risk of coronary heart disease, independently of other dietary and non-dietary risk factors
- Uncertainty remains on the optimal amount of polyunsaturated fat in the diet for prevention of coronary heart disease
- Benefits of reducing intakes of saturated fat and cholesterol are likely to be modest unless accompanied by an increased consumption of foods rich in fibre

Meanwhile, a prudent approach for prevention of coronary disease consistent with the results of this study and other evidence is to recommend a reduced intake of saturated fat, cholesterol, and *trans* unsaturated fatty acids accompanied by an increased consumption of foods rich in fibre, including cereals, vegetables, and fruit.

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ONE HUNDRED YEARS AGO

POISONOUS FACE POWDERS.

At a recent press conference of the hairdressers of Paris, it was stated that the rice powder so largely used by ladies was no longer composed of powdered rice, but was a mixture in varying proportions of white lead, chalk, starch, and alabaster. It appeared that in many instances injurious effects had followed its use, and it was urged that, in the interests of their calling, steps should be taken to prohibit its sale. In this expression of opinion we most heartily concur, and we hold that it is most desirable that the chief constituents of every substance vended as a cosmetic should be distinctly stated on the box or bottle. Many of these face powders are extremely expensive owing to their being flavoured with a variety of scents, the fashionable product known as "La Maréchale" containing iris, otto of roses, bergamot, orange essence, and other perfumes. The metallic ingredients most likely to be met with are carbonate of bismuth, white lead, and arsenic. The frequency with which paralysis of one or more groups of muscles follows the use or application of lead, even in minute quantities, is well known. Stevenson records an instance in which paralysis of the muscles on one side of the neck arose from the injudicious use of a hair dye containing lead, while Lacey has pointed out the injury to health which follows the use of white lead as a cosmetic by actors. Arsenic is certainly no less injurious, for some years ago at Loughton, in Essex, a number of children died from the use of a "violet powder" containing 38 per cent of white arsenic. The French hairdressers are quite right in condemning the use of such deadly drugs, and we trust that in future "rice powder" will consist of "rice powder" only. (*BMJ* 1896;ii:1662.)