Intake of dietary fats and colorectal cancer risk: Prospective findings from the UK Dietary Cohort Consortium

Christina C Dahm[a1*], Ruth H Keogh[ab], Marleen AH Lentjes[a], Elizabeth A Spencer[c], Tim J Key[c], Darren C Greenwood[d], Janet E Cade[d], Victoria J Burley[d], Martin J Shipley[e], Eric J Brunner[e], Alison M Stephen[f], Gita Mishra[g], Diana Kuh[g], Ian S Fentiman[h], Ian R White[b], Robert Luben[i], , Kay Tee Khaw[ai], Sheila A Rodwell (Bingham)[a]†.

[a] Medical Research Council Centre for Nutritional Epidemiology in Cancer Prevention and Survival, Department of Public Health and Primary Care, University of Cambridge, Cambridge CB1 8RN, United Kingdom

[b] MRC Biostatistics Unit, Institute of Public Health, University of Cambridge, Cambridge CB2 0SR, United Kingdom

[c] Cancer Epidemiology Unit, University of Oxford, Oxford OX3 7LF, UK

[d] Centre for Epidemiology & Biostatistics, Level 8, Worsley Building, University of Leeds, Leeds LS2 9JT, United Kingdom

[e] Department of Epidemiology and Public Health, University College London, London WC1E 6BT, United Kingdom

[f] MRC Human Nutrition Research, Elsie Widdowson Laboratory, Cambridge CB1 9NL, United Kingdom

[g] MRC Unit for Lifelong Health and Ageing, Department of Epidemiology and Public Health, University College London, 33 Bedford Place, London WC1B 5JU, United Kingdom

[h] Academic Oncology Unit, Guy's Hospital, London, SE1 9RT, United Kingdom

[i] Department of Public Health and Primary Care, University of Cambridge, Cambridge, CB1 8RN, United Kingdom

[1]Present address: Department of Cardiology, Aalborg Hospital, Aarhus University Hospital, Aalborg, Denmark and Department of Epidemiology, School of Public Health, Aarhus University, Aarhus, Denmark

†Deceased

*Corresponding author:

Department of Epidemiology, School of Public Health, Aarhus University, Bartholins Allé 2, DK-8000 Aarhus, Denmark

Email: ccd@soci.au.dk

Tel: +45 8942 6090

Fax: +45 8613 1580

Abstract

Introduction Epidemiologic evidence for an association between colorectal cancer (CRC) risk and total dietary fat, saturated fat (SF), monounsaturated fat (MUFA) and polyunsaturated fat (PUFA) is inconsistent. Previous studies have used food frequency questionnaires (FFQ) to assess diet, but data from food diaries may be less prone to severe measurement error than data from FFQ.

Methods We conducted a case–control study nested within seven prospective UK cohort studies, comprising 579 cases of incident CRC and 1996 matched controls. Standardized dietary data from 4-7 day food diaries and from FFQ were used to estimate odds ratios for CRC risk associated with intake of fat and subtypes of fat using conditional logistic regression. We also calculated multivariate measurement error corrected odds ratios for CRC using repeated food diary measurements.

Results We observed no associations between intakes of total dietary fat or types of fat and CRC risk, irrespective of whether dietary data were obtained using food diaries or FFQ.

Conclusion Our results do not support the hypothesis that intakes of total dietary fat, SF, MUFA or PUFA are linked to risk of CRC.

Keywords:
Colorectal cancer
Prevention of cancer
Epidemiology
Dietary fats
Diet records

Introduction

It has been suggested that dietary fat intake is directly linked to an increased risk of colorectal cancer through mechanisms such as increased secretion of bile acids, which leads to irritation of the bowel wall and increased cellular turnover [1]. Fat is also the major component of energy-dense diets, contributing to obesity, which is linked to incidence of gastrointestinal cancers, such as colorectal, oesophageal and stomach cancer, as well as endometrial, prostate and postmenopausal breast cancers [2]. However epidemiologic evidence directly linking dietary fat intake to colorectal cancer (CRC) is limited [2-4], and evidence from prospective studies on the effects of total fat, saturated fat, monounsaturated fat (MUFA) and polyunsaturated fat (PUFA) is inconsistent [5-7]. Previous studies have used food frequency questionnaires (FFQ) to assess diet, and data from FFQ may be subject to systematic measurement error according to participant age, sex and body mass index (BMI) [8-10]. Data from food diaries are more highly correlated with biomarker data [11], and may be less prone to severe measurement error than data from FFQ [12]. Here we present results from a nested matched case-control study of the association between total dietary fat, saturated fat, MUFA and PUFA intakes and colorectal cancer risk, utilizing pooled standardized diet diary data from the MRC Centre for Nutritional Epidemiology in Cancer Protection and Survival (CNC) UK cohort consortium, which comprises seven cohorts and a total cohort size of 153,000 UK individuals.

Methods

Participants and data collection

The UK Dietary Cohort Consortium was established to investigate associations between dietary intake, assessed by prospective 4-7 day food diaries, and cancer risk. The participating cohorts are EPIC-Norfolk, EPIC-Oxford, Guernsey Study, Medical Reseach Council National Survey of Health and Development (MRC NSHD), Oxford Vegetarian Study, the UK Women's Cohort Study (UKWCS) and Whitehall II, and the design, selection of controls, methods of pooling and standardization of dietary data have been described in detail elsewhere [13]. Briefly, CRC case status was defined using codes C18-20 from the 10th Revision of the International Statistical Classification of Diseases, Injuries and Causes of Death [14]. Case patients were individuals who were free of cancer (except non-melanoma skin cancer) at the time of

diary completion and who developed colorectal cancer at least 12 months after the date of diary commencement and before the end of the study period. They were matched on sex, age at enrolment (± 3 years) and month of diary completion (± 3 months) within their respective cohort to four controls each, with the exception of some cases from EPIC-Oxford, the Guernsey Study and the Oxford Vegetarian Study (2 controls), and some from UKWCS (5 controls). Participants with baseline cancers were excluded. Each cohort collected dietary information using 4-day (Guernsey, Oxford Vegetarian Study, UKWCS), 5-day (MRC NSHD) or 7-day food diaries (EPIC-Norfolk, EPIC-Oxford, Whitehall II), either at recruitment or during a subsequent survey. Participants were asked to record all the foods and drinks they consumed, usually within times of day presented in the food diary (e.g. before breakfast; breakfast; mid-morning), and with photographs showing servings of representative food items to aid estimation of portion sizes [15,16]. Information on age, sex, height, weight, smoking, education, socio-economic status, use of hormone replacement therapy among women, physical activity, family history of colorectal cancer and use of aspirin was collected either in interviews or in questionnaires administered prior to completion of the food diary. In most of these cohorts, FFQ were administered prior to diary data collection, and were available for analysis from most participants in EPIC-Norfolk, EPIC-Oxford, UKWCS and Whitehall II (Table 1).

The majority of data from the diet diaries were coded using the DINER/DINERMO system, although 51 of the 125 UKWCS diaries were coded and processed using DANTE [17], and MRC NSHD diaries were coded and processed using DIDO [18]. In these studies the coding systems were compared with DINER in 100 diaries. Fat and energy measures did not differ significantly for DANTE, and their geometric means differed by 14% and 8% between DIDO and DINER; this was attributed to DIDO portion sizes being more appropriate for that study's timeframe.

Statistical analysis

Conditional logistic regression models were used to calculate odds ratios (ORs) and 95% confidence intervals (95% CI) for colorectal cancer according to sex-specific quintiles of % energy from dietary fat, saturated fat, MUFA or PUFA intake based on the distribution of intakes among controls. The OR per increase in quintile was calculated by assigning a score to each quintile, then using the score as a continuous variable. The models were adjusted for height (m), weight (kg), smoking

(never, former, current), physical activity (inactive, moderately inactive, moderately active, active), education (no formal qualifications, schooling up to age 16 [UK: General Certificate of Secondary Education or equivalent], schooling up to to age 18 [UK: A levels or equivalent], university degree), social class (I = professional occupations; II = managerial and technical occupations; III-NM = skilled occupations, nonmanual; III-M = skilled occupations, manual; IV = partly skilled occupations; V = unskilled occupations), energy intake not from fat (MJ), fibre intake (g/day) and alcohol intake (g/day).

Food diary measurements of dietary intake are subject to within-person random error with respect to measuring long term intake, which results in attenuated OR estimates [19,20]. When repeat food diary measurements are available, regression calibration can be used to correct the OR estimates associated with intake [19,20]. We performed regression calibration using second 7-day food diaries available for 411 EPIC-Norfolk participants (130 cases, 281 controls). Let R_1 and R_2 denote two food diary measurements and T denote unobserved true intake. Under the classical measurement error assumption, $R_j = T + e_j$ (j = 1, 2), where errors e_j are uncorrelated with each other and with T. We fitted multivariate regression calibration models to give corrected odds ratio estimates assuming classical measurement error in diary measurements of intakes of percent energy from fat (total fat, saturated fat, MUFA, PUFA), non-fat energy, fibre, and alcohol, and adjusting for anthropometric and sociodemographic variables [19,20].

Two-sided P values less than 0.05 were considered statistically significant. Statistical analyses were done using Stata v.10 (StataCorp, Texas, USA) and R.

Results

579 CRC cases and 1996 matched controls were available for analysis (Table 1). There were no statistically significant differences in the means or distributions of any participant characteristics between cases and controls except for mean PUFA intake, which was higher among cases (not shown). When stratified by intake of types of fat as determined by food diaries, those in the highest quintiles of intake were generally younger, and consumed on average more energy but less fibre than those in the lowest quintiles (Table 2). Similar patterns were observed when stratifying by intake of types of fat determined by FFQ (not shown).

In age-adjusted analyses of risk of CRC, there was no clear evidence of an association between total fat intake and risk (Table 3). Adjustment for anthropometry, diet, smoking, physical activity or sociodemographics did not alter these results (Table 3). Similarly for intakes of saturated fat, MUFA and PUFA, age-adjusted analyses did not indicate an association between intake and CRC risk, and these results were not affected by further adjustment for anthropometry, diet, smoking, physical activity or sociodemographics (Table 3). When the analyses were repeated using dietary data from FFQ, similar results were observed (Table 3).

Multivariate regression calibration models were fitted using adjustments as in multivariable model 2 (Table 3). The corrected ORs (95% CIs) for SD increases in percent energy from total fat, saturated fat, MUFA and PUFA, corresponding to the uncorrected ORs in Table 3, were respectively 0.84 (0.65-1.10), 0.73 (0.56-0.97), 0.83 (0.65-1.07), 1.12 (0.88-1.43).

Discussion

In this prospective study of 579 incident CRC cases and 1996 matched controls, we observed no associations between intakes of total dietary fat or types of fat and colorectal cancer, irrespective of whether dietary data were obtained by using food diaries or by FFQ.

Validation studies involving recovery biomarkers suggest that food diary measurements may be subject to systematic error that depends on true intake and person-specific errors [21-23]. A previous study suggests that by ignoring systematic error we may under-correct for the effects of measurement error [13], hence the true ORs may be further from the null than suggested by the multivariate regression calibration which assumed classical measurement error.

Strengths of our study include its prospective design, which avoided the problems of recall bias and selection bias; standardized food diary data entry; the range of intake of fat; and the availability of repeated measurements which enabled use of regression calibration to correct for measurement error.

This study has limitations. While most food diary data were entered in the DINER processing program, some food diaries from UKWCS and all food diaries from MRC NSHD had previously been entered into other systems. Not all of the participating studies used 7-day food diaries, but 4-day diaries showed good agreement with longer diaries for averaged nutrient intakes in our data. Some of the

participating cohorts recorded self-reported anthropometric data, while in other cohorts these data were recorded by trained interviewers. Each of these points may have introduced measurement error into our study.

Previous studies on total fat intake and CRC risk have found conflicting evidence of an association [3-7,24], and while the recent WCRF report concluded that 'foods containing animal fats' were possible causes of CRC [2], this has been contested [25]. Evidence of associations between saturated fat, MUFA, PUFA, or PUFA subtypes such as n-3 or n-6 fatty acids, with CRC risk are similarly inconclusive [5-7,26]. It is possible that an underlying association between dietary fat intake and CRC risk may be obscured by measurement error in dietary assessment, and there is evidence for this in breast cancer [27,28]. However, our results using nutrient data derived from 4-7 day food diaries show no evidence of an association between dietary fat and CRC risk (Table 3), and are thus in agreement with both our own results determined using FFQ data from the same participants (Table 3), and with the recent WCRF/AICR report [2].

Conflict of Interest Statement:
The authors have no conflict of interest.

The UK Dietary Cohort Consortium at the MRC Centre for Nutritional Epidemiology in Cancer Prevention and Survival is funded by the Medical Research Council. The cohort studies included in this consortium received funding from: British Heart Foundation; Cancer Research UK; Department of Health, UK; Food Standards Agency, UK; Lloyds TSB Foundation for the Channel Islands; Medical Research Council, UK; the Stroke Association, UK, and the World Cancer Research Fund.

Table 1. Cohort descriptions*

Cohort	Year of diary completion	Last follow-up date	No. of cases	No. of controls	No. with FFQ	Mean age at baseline, y (SD)
EPIC-Norfolk	1993–1998	31.12.2006	318	1272	1542	64.0 (7.9)
EPIC-Oxford	1993–1998	31.12.2004	121	280	401	61.6 (10.6)
Guernsey Study	1987–1991	31.12.2003	28	55	N/A	59.3 (10.2)
MRC NSHD	1989	31.12. 2006	7	28	N/A	43 (0.0)
Oxford Vegetarian Study	1985–1987	31.12.2004	31	70	N/A	54.4 (14.0)
UKWCS	1999–2003	31.12.2006	25	100	124	63.1 (8.9)
Whitehall II	1991–1993	30.09.2005	49	191	238	53.4 (5.8)

*EPIC = European Prospective Investigation into Cancer and Nutrition; MRC NSHD = Medical Research Council National Survey of Health and Development; UKWCS = UK Women's Cohort Study. N/A = not available

Table 2 Baseline characteristics by sex-specific quintile of total fat and types of fat intake (%energy) from food diaries. Values are % or mean (SD) as appropriate. (579 cases, 1996 controls)*

	Total Fat				Saturated fat				MUFA				PUFA			
	Q1	Q3	Q5	p value	Q1	Q3	Q5	p value	Q1	Q3	Q5	p value	Q1	Q3	Q5	p value
Mean (% energy)	26.3	34.3	42.0		8.8	12.9	17.9		8.7	11.7	14.7		4.3	6.3	9.6	
	(3.2)	(0.8)	(2.6)		(1.5)	(0.4)	(2.0)		(1.2)	(0.3)	(1.1)		(0.6)	(0.3)	(1.5)	
N (case/control)	118/399	106/399	124/400		121/392	104/394	112/394		115/392	115/394	110/394		105/392	126/394	121/394	
Sex (male; %)	48.9	48.7	46.8	0.9	49.3	46.8	48.4	0.9	49.5	47.4	47.6	0.9	50.1	45.8	48.2	0.9
Mean Age (y)	62.6	61.8	61.1	0.06	61.6	61.5	62.9	0.05	62.3	62.5	61.4	0.3	64.4	61.8	60.4	<0.001
	(8.8)	(9.2)	(10.7)		(9.6)	(9.2)	(9.7)		(9.1)	(9.2)	(10.0)		(8.4)	(9.0)	(10.5)	
Mean BMI (kg/m^2)	25.8	26.1	25.8	0.7	25.6	26.4	25.6	0.004	25.7	26.0	26.1	0.5	26.2	26.0	25.4	0.004
	(3.8)	(3.7)	(4.2)		(4.0)	(4.1)	(3.8)		(3.9)	(3.8)	(4.1)		(4.1)	(3.7)	(4.3)	
Physical activity (%)																
Inactive	30.3	32.1	38.3	0.3	27.5	31.7	37.6	0.2	30.3	30.2	37.1	0.5	34.2	34.1	32.7	0.7
Moderately inactive	34.2	33.2	27.0		37.0	30.1	28.9		3454	34.0	27.6		33.1	31.6	31.9	
Moderately active	18.7	20.6	20.0		20.9	22.7	20.0		18.9	21.4	21.1		18.0	22.0	20.7	
Active	16.8	14.1	14.7		14.7	15.5	13.6		16.4	14.4	14.3		14.7	12.3	14.8	
Education level (%)																
No formal	37.9	41.3	40.2	0.5	35.4	44.1	38.2	0.3	33.9	41.8	42.0	0.06	42.7	40.1	37.9	0.3
GCSE	15.4	14.5	16.3		15.8	14.8	16.3		15.5	16.6	14.7		12.9	16.5	14.3	
A Level	30.7	26.1	24.6		29.5	27.3	28.4		31.6	28.1	24.6		30.0	26.5	26.3	
Degree level	16.1	18.1	22.0		19.2	13.8	17.2		19.1	13.5	18.8		14.4	16.9	21.6	
Current Smoking (%)	8.4	5.9	12.9	0.002	8.0	6.5	14.1	0.001	8.9	5.8	12.1	0.04	11.3	8.0	10.7	0.5
Aspirin use (yes; %)	15.6	11.6	8.0	0.02	15.0	9.7	10.8	0.02	15.2	10.7	8.7	0.05	15.6	11.1	9.9	0.03
Social class																
I	9.2	11.2	10.5	0.4	10.7	9.3	11.8	0.6	11.2	11.6	9.2	0.8	10.8	9.4	11.1	0.6
II	43.4	41.3	42.7		45.1	39.5	39.3		43.7	39.8	39.8		38.1	42.3	40.1	
IIINM	19.8	19.4	18.9		17.9	19.8	21.2		19.7	18.2	20.1		19.3	17.6	20.5	
IIIM	14.3	16.3	15.0		15.0	19.2	13.2		14.1	17.6	16.1		16.5	16.2	16.5	
IV	9.8	7.9	10.3		9.1	8.9	10.9		9.3	9.6	11.5		10.2	12.0	9.8	
V	3.7	3.9	2.7		2.3	3.4	3.6		2.1	3.3	3.1		5.1	2.7	2.1	
Total energy (MJ/day)	7.44	8.30	8.81	<0.001	7.60	8.13	8.82	<0.001	7.44	8.25	8.75	<0.001	7.91	8.14	8.56	<0.001
	(2.06)	(2.10)	(2.28)		(2.12)	(2.04)	(2.32)		(2.08)	(2.16)	(2.23)		(2.32)	(2.04)	(2.14)	
Non-fat energy	5.47	5.45	5.10	<0.001	5.47	5.31	5.26	0.1	5.44	5.41	5.15	0.001	5.42	5.34	5.32	0.8
(MJ/day)	(1.50)	(1.38)	(1.32)		(1.51)	(1.31)	(1.41)		(1.50)	(1.40)	(1.30)		(1.52)	(1.33)	(1.33)	
Fibre intake (g/day)	17.3	15.6	14.0	<0.001	18.2	15.2	13.6	<0.001	17.3	15.5	14.1	<0.001	14.7	15.1	16.8	<0.001
	(7.4)	(5.2)	(5.7)		(7.5)	(4.9)	(5.1)		(7.3)	(5.6)	(5.0)		(5.8)	(5.0)	(6.6)	
Alcohol intake (g/day)	16.2	11.8	8.7	<0.001	15.1	10.7	9.8	<0.001	16.5	11.4	9.2	<0.001	14.3	12.4	9.1	<0.001
	(24.2)	(16.8)	(11.8)		(22.5)	(15.4)	(14.1)		(24.5)	(14.8)	(12.9)		(23.1)	(15.9)	(13.0)	

*nutrient data for saturated fat, MUFA and PUFA were missing in MRC NSHD leaving 572 cases, 1968 controls.

Quintile cutpoints were as follows: total fat (% energy), men 29.8, 33.1, 35.8, 39.1; women 29.7, 32.8, 35.7, 39.0; saturated fat (% energy), men 10.7, 12.3, 13.8, 15.6; women 10.3, 12.1, 13.7, 15.7; MUFA (% energy), men 10.2, 11.3, 12.3, 13.6; women 9.9, 10.2, 11.3, 12.3, 13.6; PUFA (% energy), men 5.0, 5.9, 6.7, 7.9; women 4.9, 5.9, 6.8, 8.1.

Table 3. Odds ratios (ORs) and 95% CIs for CRC risk across sex-specific quintiles of daily total fat and types of fat intake (% energy) from diaries (579 cases, 1996 controls) and FFQ (496 cases, 1809 controls) †

	Quintile of intake								
Model	1	2	3	4	5	Per quintile*	P trend*	Per SD**	p value
Food Diary									
Total Fat									
Mean (SD)	26.3 (3.2)	31.4 (0.9)	34.3 (0.8)	37.3 (1.0)	42.0 (2.6)				
N (case/control)	118/399	109/399	106/399	122/399	124/400				
Age adjusted	1.00 (ref)	0.97 (0.72-1.31)	0.90 (0.67-1.23)	1.05 (0.77-1.42)	1.02 (0.76-1.38)	1.01 (0.95-1.08)	0.7	1.00 (0.90-1.10)	0.9
Multivariable 1‡	1.00 (ref)	0.96 (0.71-1.30)	0.90 (0.66-1.22)	1.04 (0.77-1.41)	0.99 (0.73-1.34)	1.01 (0.94-1.08)	0.9	0.98 (0.89-1.09)	0.8
Multivariable 2§	1.00 (ref)	1.06 (0.75-1.50)	0.91 (0.64-1.30)	1.21 (0.86-1.72)	0.83 (0.57-1.20)	0.98 (0.90-1.06)	0.6	0.94 (0.83-1.06)	0.3
SF									
Mean (SD)	8.8 (1.5)	11.4 (0.5)	12.9 (0.4)	14.6 (0.6)	17.9 (2.0)				
N (case/control)	121/392	124/392	104/394	111/394	112/394				
Age adjusted	1.00 (ref)	1.02 (0.76-1.37)	0.85 (0.63-1.17)	0.91 (0.67-1.24)	0.88 (0.65-1.20)	0.96 (0.90-1.03)	0.3	0.96 (0.88-1.05)	0.4
Multivariable 1	1.00 (ref)	1.00 (0.75-1.35)	0.83 (0.61-1.14)	0.90 (0.66-1.22)	0.86 (0.63-1.17)	0.96 (0.90-1.03)	0.2	0.95 (0.87-1.04)	0.3
Multivariable 2	1.00 (ref)	0.99 (0.71-1.40)	0.81 (0.56-1.16)	0.81 (0.56-1.16)	0.73 (0.49-1.07)	0.92 (0.84-1.00)	0.05	0.88 (0.78-1.00)	0.05
MUFA									
Mean (SD)	8.7 (1.2)	10.6 (0.4)	11.7 (0.3)	12.8 (0.4)	14.7 (1.1)				
N (case/control)	115/392	110/394	115/394	122/394	110/394				
Age adjusted	1.00 (ref)	0.96 (0.71-1.30)	1.03 (0.76-1.40)	1.04 (0.77-1.41)	0.88 (0.64-1.20)	0.99 (0.92-1.06)	0.8	0.98 (0.90-1.08)	0.7
Multivariable 1	1.00 (ref)	0.97 (0.71-1.31)	1.03 (0.76-1.40)	1.04 (0.77-1.41)	0.88 (0.64-1.20)	0.98 (0.92-1.05)	0.6	0.97 (0.89-1.06)	0.5
Multivariable 2	1.00 (ref)	0.94 (0.66-1.34)	1.05 (0.74-1.48)	1.02 (0.71-1.44)	0.71 (0.49-1.04)	0.95 (0.87-1.03)	0.2	0.93 (0.82-1.05)	0.2
PUFA									
Mean (SD)	4.3 (0.6)	5.4 (0.3)	6.3 (0.3)	7.3 (0.4)	9.6 (1.5)				
N (case/control)	105/392	100/394	126/394	120/394	121/394				
Age adjusted	1.00 (ref)	0.86 (0.62-1.18)	1.10 (0.81-1.49)	1.06 (0.78-1.44)	1.07 (0.78-1.44)	1.04 (0.97-1.11)	0.3	1.09 (0.99-1.20)	0.09
Multivariable 1	1.00 (ref)	0.85 (0.62-1.16)	1.10 (0.81-1.49)	1.04 (0.76-1.41)	1.06 (0.78-1.46)	1.03 (0.96-1.11)	0.4	1.09 (0.98-1.20)	0.1
Multivariable 2	1.00 (ref)	0.75 (0.52-1.08)	1.04 (0.73-1.46)	1.04 (0.73-1.47)	0.98 (0.68-1.43)	1.03 (0.95-1.12)	0.5	1.08 (0.95-1.22)	0.2
FFQ									

				Total Fat					
Mean (SD)	24.4 (2.9)	30.0 (1.1)	33.2 (0.9)	36.2 (1.0)	41.2 (2.9)				
N (case/control)	96/361	101/362	101/362	110/362	88/362				
Age adjusted	1.00 (ref)	1.03 (0.74-1.42)	1.01 (0.73-1.40)	1.16 (0.84-1.59)	0.89 (0.64-1.25)	0.99 (0.92-1.07)	0.8	1.00 (0.90-1.11)	0.9
Multivariable 1	1.00 (ref)	1.03 (0.75-1.43)	1.02 (0.73-1.41)	1.17 (0.85-1.62)	0.90 (0.64-1.26)	0.99 (0.92-1.07)	0.9	1.00 (0.90-1.11)	0.9
Multivariable 2	1.00 (ref)	0.91 (0.63-1.32)	0.88 (0.61-1.27)	0.97 (0.68-1.40)	0.74 (0.50-1.09)	0.95 (0.87-1.04)	0.2	0.95 (0.84-1.07)	0.4
				SF					
Mean (SD)	8.0 (1.43)	10.6 (0.6)	12.2 (0.5)	14.1 (0.7)	17.5 (2.1)				
N (case/control)	101/361	106/362	100/362	102/362	87/362				
Age adjusted	1.00 (ref)	1.10 (0.79-1.53)	1.02 (0.73-1.42)	1.07 (0.78-1.48)	0.88 (0.63-1.23)	0.97 (0.90-1.05)	0.4	0.96 (0.88-1.06)	0.4
Multivariable 1	1.00 (ref)	1.11 (0.80-1.54)	1.03 (0.74-1.43)	1.07 (0.77-1.48)	0.89 (0.63-1.25)	0.97 (0.90-1.05)	0.5	0.96 (0.88-1.06)	0.5
Multivariable 2	1.00 (ref)	1.07 (0.74-1.55)	1.02 (0.70-1.48)	0.93 (0.63-1.37)	0.82 (0.55-1.21)	0.95 (0.87-1.03)	0.2	0.91 (0.81-1.04)	0.2
				MUFA					
Mean (SD)	7.9 (1.1)	10.0 (0.4)	11.3 (0.4)	12.6 (0.5)	14.7 (1.6)				
N (case/control)	96/361	101/362	109/362	92/362	98/362				
Age adjusted	1.00 (ref)	1.06 (0.77-1.46)	1.21 (0.87-1.69)	0.99 (0.71-1.39)	1.07 (0.76-1.50)	1.01 (0.93-1.09)	0.9	1.01 (0.93-1.10)	0.8
Multivariable 1	1.00 (ref)	1.05 (0.76-1.46)	1.21 (0.87-1.69)	1.01 (0.72-1.41)	1.08 (0.77-1.51)	1.01 (0.94-1.09)	0.8	1.01 (0.93-1.10)	0.8
Multivariable 2	1.00 (ref)	0.90 (0.62-1.29)	1.11 (0.76-1.60)	0.86 (0.59-1.25)	0.91 (0.62-1.34)	0.98 (0.90-1.07)	0.6	0.97 (0.85-1.10)	0.6
				PUFA					
Mean (SD)	3.9 (0.5)	5.0 (0.3)	6.0 (0.3)	7.2 (0.5)	9.8 (1.6)				
N (case/control)	96/361	99/362	92/362	105/362	104/362				
Age adjusted	1.00 (ref)	0.98 (0.71-1.36)	0.90 (0.65-1.26)	1.03 (0.75-1.43)	1.03 (0.75-1.43)	1.01 (0.94-1.09)	0.8	1.05 (0.96-1.16)	0.3
Multivariable 1	1.00 (ref)	0.98 (0.71-1.36)	0.90 (0.64-1.26)	1.02 (0.74-1.42)	1.02 (0.74-1.41)	1.01 (0.94-1.09)	0.8	1.05 (0.96-1.15)	0.3
Multivariable 2	1.00 (ref)	1.00 (0.70-1.42)	0.86 (0.60-1.25)	0.89 (0.62-1.28)	0.95 (0.66-1.37)	0.98 (0.90-1.06)	0.6	1.09 (0.95-1.25)	0.2

†Food diary nutrient data for saturated fat, MUFA and PUFA were missing in MRC NSHD leaving 572 cases, 1968 controls in Multivariable 1, and 436 cases, 1678 controls in Multivariable 2 for these exposures.

*using the score of the quintile.

** per SD (diary: 5.7% for total fat, 3.3% for saturated fat, 2.2% for MUFA, 2.0% for PUFA; FFQ: 6.0% for total fat, 3.2% for saturated fat, 2.5% for MUFA, 2.2% for PUFA)

‡ Multivariable 1 = adjusted for age, height, weight and non-fat energy (MJ) intake.

§ Multivariable 2 = 1+ fibre, alcohol, physical activity level, social class, educational level and smoking status (443cases, 1673 controls for diary; 420cases, 1615 controls for FFQ).

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