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Dietary fibre and coronary heart disease, stroke and cardiovascular disease mortality in the UK Women's Cohort Study

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Abstract

Objectives and Background: Dietary fibre has been associated with improvements in key risk factors for cardiovascular disease (CVD). Prior research has focussed more on CVD development in men and our aim was therefore to explore the association between dietary fibre intake and CVD mortality using data from the United Kingdom Women's Cohort Study (UKWCS).

Methods and results: Dietary fibre intake from 31,036 women was calculated both as non-starch polysaccharide (NSP) and using the Association of Official Analytical Chemist (AOAC) method from food-frequency questionnaires. Participants were free from history of CVD at baseline and mean age at recruitment was 51.8 years (standard deviation 9.2). Mortality records for participants were linked from national registry data and 258 fatal CVD cases (130 stroke, 128 coronary heart disease (CHD)) were observed over an average follow-up period of 14.3 years.

Total dietary fibre (NSP/AOAC) or fibre from different food sources were not associated with reduced fatal CHD, stroke or CVD risk in the full sample. For every 6g/day increase in NSP, the hazard ratio (HR) was 0.91 (95% Confidence Interval (CI) 0.76 to 1.08) or for every 11g/day increase in fibre assessed as AOAC, the HR was 0.92 (95% CI 0.80 to 1.05). Sensitivity analyses suggest a possible protective association for cereal sources of fibre on fatal stroke risk in overweight women, 0.80 (95% CI 0.65 to 0.93) $p < 0.01$ and for fibre density and fatal stroke in women free of hypertension or angina 0.83 (95% CI 0.70 to 0.99) $p = 0.04$

Conclusions: In the UKWCS, a sample of health-conscious women, greater dietary fibre intake may confer no additional cardiovascular benefit, in terms of mortality, but may contribute to lower fatal stroke risk in those free of cardiovascular risk factors (hypertension/angina) or overweight women who consume greater cereal fibre.

Key words: Cardiovascular diseases, Coronary heart disease; Stroke; Diet; Fibre; Epidemiology

Background

Cardiovascular disease (CVD) accounts for almost half of all deaths across Europe and is the main cause of disease burden [1]. Although women typically experience CVD events later in life than men [2, 3], the annual mortality burden for coronary heart disease (CHD) and stroke in women is estimated to be greater than that in men, at around 597,000 compared to 548,000 cases within the European Union [4]. Rates of CVD are in decline in many developed European countries [1] and incidence rates are also declining in the United Kingdom (UK), [1, 5] a fall which has been attributed to improvements in risk factors for CVD, by means of lifestyle improvements [6].

Dietary fibre and wholegrain foods have long been proposed to confer protection against coronary heart disease [7] or more generally CVD [8]. Reviews of observational studies and pooling projects support the protective associations [9-11] and many potential mechanisms for the actions of fibre molecules have been highlighted through clinical trials. Plausible mechanisms for CVD risk reduction include, among others, the formation of viscous gels by soluble fibre molecules which both slow gastric emptying, leading to greater satiety and therefore less food consumption and lower obesity and also inhibit absorption of other nutrients, attenuating postprandial rises in glucose and lipids [12, 13]. Soluble fibre and resistant starch are additionally fermented in the large bowel, producing short-chain fatty-acids which are believed to inhibit hepatic cholesterol synthesis, leading to lower serum cholesterol levels [14-16].

The physiological consequences of diets with high fibre content may depend on the types of fibre and the food source [17] and so it is pertinent to explore sources of fibre as this could further explain the relationships between fibre intake and CVD risk. A number of observational studies have examined the relationship between dietary fibre and risk of myocardial infarction, stroke or CVD [18-20], with some additionally studying different types or sources of fibre [17, 21].

Gender differences in CVD mortality rates or lifecourse disease trends exist [4, 2], indicating the importance in exploring preventative strategies separately between the sexes. Given that 'most CVD in women is preventable' [22, 3], the current work utilises dietary data from middle-aged women and explore fatal CVD risk in relation to total fibre intake as well as exploring major food sources of fibre, in order to characterise potentially beneficial dietary behaviour.

Method

Study design and population

Recruitment and characteristics of cohort participants have been detailed previously [23]. In the mid 1990's, over 61,000 women were contacted and 35,691 (>58%) replied, forming the United Kingdom Women's Cohort Study (UKWCS). At baseline, participants completed a self-administered food frequency questionnaire (FFQ) and also provided further dietary, lifestyle and health information.

Assessment of baseline variables

Weight and height data were self-reported. Physical activity was calculated as metabolic equivalent tasks (METs) and was derived from a question "In a typical week during the last 12 months, how many hours did you spend on the following activities: housework, do-it-yourself, gardening, walking, cycling, other physical activity". The time spent on each activity per week was multiplied by the published met values [24] to derive physical activity level in METs per week. United Kingdom National Statistics-Socio-Economic Classification (NS-SEC) was used to define class and women were grouped either as 1) managerial/ professional, 2) Intermediate, 3) Routine/ manual. Ethnicity data were collected but not used in analyses as greater than 99% of study participants were white.

Dietary information

A validated 217-item FFQ was completed at baseline and included commonly consumed food items. Participants were asked to indicate their intake by ticking an appropriate consumption category (from 10 choices) such as 'once per day' or '2-3 times per week'. Energy intake from carbohydrates, fat and protein (kcal/day) and alcohol intake (g/day) were derived from FFQ responses.

Non-starch polysaccharide (NSP) intake values were estimated using data from McCance & Widdowson's *The Composition of Foods* (5th edition).[25] In the FFQ, a number of fruit items were under the heading 'seasonal' and participants were asked to mark the consumption of these foods when they were seasonally available. The number of months these items were available was taken into account when nutrient intakes were calculated.

NSP estimates from specific food sources were also generated and included fibre from the following foods: total cereal foods, breakfast cereals, vegetables (excluding potatoes), fruit, legumes and nuts/seeds.

Fibre intake was also calculated using the Association of Official Analytical Chemists (AOAC) method. As British nutrient tables do not include AOAC values for all foods, estimates were sought from a number of sources in the following order of preference (values in brackets indicate the proportion of data identified from each source): British reference values (7%) [26]; a review article (12%) [12]; European databases (11%) [27]; United States Department of Agriculture databank (46%) [28]; food packaging labels (18%); recipe calculation (6%).

Values for soluble and insoluble fibre were obtained from British food composition tables [29-33] for 90% of food items and were generated by mapping values from other foods where the estimates did not exist.

Mortality data

Mortality data are available from baseline for participants whom provided sufficient information for their records to be traced through the national death registry (98% of baseline participants were traced to allow linkage). Deaths were classified using International Classification of Disease (ICD) 9th edition and 10th edition codes. Fatal cerebrovascular events were identified with codes 430 to 438 or I60 to I698 and fatal heart disease events with codes 410 to 4149 or I20 to I259. CVD cases were classed as either a cerebrovascular or heart disease case.

Statistical analysis

Baseline participants not providing sufficient data to allow linkage to national death records were excluded from analyses. Also excluded were those women who died within one year of baseline, women self-reporting prior history of strokes, heart attacks, cancer or diabetes mellitus type 2, and those with implausible total energy intakes (outside the range 500 to 6000kcal/day or 2.1 to 25.1MJ/day). Those with missing data for self-reported prior history of disease were assumed to have no prior history.

Survival analyses were conducted using Cox proportional hazards regression, weighted by the inverse of the probability of being sampled to take into account the large proportion of vegetarians in this cohort. The time variable used in the models was time in the study (person years), calculated from the date of questionnaire receipt until either date of death or the censor date.

The sample was divided into five approximately equal groups for every fibre exposure and risk in each increasing intake group was generated by comparison to the lowest, reference category. Linear trend was tested using increments which approximately matched the mean difference in fibre intake between the fifths, to reflect the increase trend within this sample. Selection of confounding variables to adjust for in models was undertaken in the first instance using a directed acyclic graph to identify the minimal sufficiency set of adjustments [34], to avoid issues of over adjustment. Chi² tests, analysis of variance and correlation between the selected adjustments was also undertaken in order to identify potentially collinear associations, again avoiding potential over adjustment of confounders. Results are presented for models adjusted only for age or additionally for BMI (kg/m²), calories from carbohydrate, fat and protein (kcal/day), ethanol intake (g/day), METS (1kcal/kg/hour), smoking status (current vs. not current smoker) and socio-economic status (professional or managerial/ intermediate/ routine or manual). The results presented for fibre density exposures do not include adjustment for energy intake, although models including this adjustment were also conducted, as suggested for nutrient density analyses by Willet and Stampfer [35]. Results were not appreciably different than fibre density models without this additional adjustment (data not shown).

An intermediate model was also created which did not include BMI or energy intake, as these represent one causal pathway for the action of dietary fibre. In the interest of brevity, results from these models are not presented, as did not differ substantially from the fully adjusted model, but are mentioned in the results and discussion sections. BMI was additionally explored through subgroup analyses since greater BMI has been independently associated with CHD risk[36, 37] and may modify the effect of fibre. Overweight and obese participants (BMI >25kg/m²) were grouped due to insufficient case numbers in either group separately.

Saturated fat intake correlated highly with energy intake (0.76) and this was therefore not included in models to avoid masking potentially beneficial effects of fibre. Menopausal status was not included as an adjustment as is functionally related to age but instead was explored through subgroup analyses because of its proposed independent association with CVD risk, possibly via influencing lipid changes[38], and therefore its potential as an effect modifier. Too few cases existed in the pre-menopausal women to allow analysis with this sub-group.

The presence of existing angina or hypertension was also considered an effect modifier and explored in subgroup analyses.

For primary analyses (full sample) a 2-sided p-value ≤ 0.05 was considered statistically significant but to acknowledge issues with multiple testing, for subgroup analyses the accepted p-value was reduced to ≤ 0.01 . Stata version 11.0 [39] was used for all data manipulation and analyses.

Ethical approval

At inception of the UK Women's Cohort study in 1993, in the absence of a more centralised system, individual ethical approval was sought and obtained from 174 local ethics committees across the UK. Approval was granted from each local authority for the study to trace participants for events such as cancer, death and other disease outcomes. Study ethical approval is now overseen by the National Research Ethics Committee- Yorkshire and the Humber, Leeds East and specific approval for this follow-up work was granted in December 2011.

Results

In total, 31,036 women free of history of stroke or heart attacks were followed for a median of 14.3 years, interquartile range (IQR) 1.4 years. The cause of death was attributed to stroke in 130 participants and to CHD in 128 participants. Table 1 details characteristics and cardiovascular risk factors in cases and non-cases. As expected, the non-cases were younger, BMI was lower, and a smaller proportion were current smokers and red meat-eaters.

Ethanol intake was markedly lower for the CHD cases, 1.2g/day (IQR 7.2) compared to both stroke cases, 5.0g/day (IQR12.2) and the non-cases 5.5g/day (IQR11.6). The socio-economic and education profile was higher for non-cases and personal history of angina or hypertension was lower. Other lifestyle and dietary fibre variables were comparatively similar for cases and non-cases.

Table 2 shows descriptive characteristics across increasing fibre intake groups (sample split into fifths based on NSP intake). Age varies little across groups but BMI decreases with greater intake and both physical activity level and energy intake are higher with increasing fibre intake categories. Fewer meat-eaters and more

vegetarians were categorised in the higher intake groups and more smokers existed in the lower intake groups. Additionally, the education and socio-economic profile improved with increased levels of fibre intake.

Hazard ratios (HR) and 95% confidence intervals (CI) for CHD, stroke and CVD mortality in relation to increasing fifths of the various fibre exposures are presented along with HRs for the linear associations in age-adjusted and fully adjusted models (Table 3). Full adjustment for confounders tended to attenuate associations. Compared to the intermediate models (not adjusted for BMI or energy intake), fully adjusted results indicated stronger associations between exposures and outcomes, especially for stroke. For example, HRs for the age-adjusted, intermediate and fully-adjusted models for stroke risk and greater cereal fibre intake in those with BMI $\geq 25\text{kg/m}^2$ were respectively, 0.87 (0.74 to 1.03) $p=0.10$, 0.88 (0.75 to 1.03) $p=0.12$ and 0.80 (0.65 to 0.93) $p<0.01$.

Total fibre, soluble and insoluble fibre

Adjustment for lifestyle characteristics tended to attenuate HRs but all remained non-significant, indicating no evidence of an association between fibre intake and CHD, stroke or CVD, in the full sample of women. Total fibre intake assessed as NSP, AOAC or fibre density did not appear to be associated with risk of CHD, stroke or CVD (Table 3). For stroke risk in the fully-adjusted model, significantly protective associations were seen in some AOAC fibre quintile comparisons but this did not remain significant for the linear relationship per 11g/day increase 0.86 (95% CI 0.86 to 1.08, $p=0.19$).

In a healthy sub-sample of women, who were free of hypertension or angina at baseline ($n=26,143$) 69 stroke cases were observed and a protective association was seen for both NSP and AOAC fibre density and stroke risk (data not shown in tables). For every 2g/1000kcal/day increase in NSP fibre, risk was reduced by 17%, HR 0.83 (95% CI 0.70 to 0.99) $p=0.04$ and by 18% for every 3g/1000kcal/day increase in AOAC fibre, HR 0.82 (95% CI 0.68 to 0.99) $p=0.04$. However, these results did not quite reach the pre-specified 1% significance level which had been set and so must be interpreted with caution because of the greater chance for type I error or false positive findings. For total fibre intake there was no evidence of an association in the post-menopausal subgroup or subgroups split based on BMI.

There was no evidence of any association between soluble or insoluble fibre intake and risk of fatal CHD, stroke or CVD. This remained the case in subgroup analyses.

Food sources of fibre

Similar to total fibre intake, food sources of fibre were not significantly associated with fatal CHD, stroke or CVD risk in fully adjusted models using the full sample. One or two quintile comparisons were statistically significantly associated, but this did not carry through to the linear test. Stroke risk was reduced by 55% for the highest group compared to the lowest intake for fibre from nuts and seeds [Q5: HR 0.45 (95% CI 0.23 to 0.85) $p=0.01$] but for every 0.2g/day increase in intake, the association was not statistically significant [HR 0.92 (95% CI 0.83 to 1.02) $p=0.13$].

In sensitivity analyses, there was no evidence of an association between total CVD risk and any of the food sources of fibre. There was also no evidence of associations between CHD and stroke with fibre from breakfast cereals, fruit, vegetables or legume (subgroup data not shown).

In women whose baseline BMI was $\geq 25\text{kg/m}^2$ ($n=11,331$) 45 stroke cases were observed. Risk of fatal stroke appeared to be significantly reduced with greater intake of fibre from nuts and seeds. With every 0.2g/day increase, risk was reduced by 32% [HR 0.68 (95% CI 0.48 to 0.98) $p=0.04$] but again, this result did not reach the 1% pre-specified significance criterion. However, stroke risk was significantly reduced with greater cereal fibre intake in women whose baseline BMI was $\geq 25\text{kg/m}^2$ [HR 0.80 (95% CI 0.65 to 0.93) $p<0.01$].

Discussion

In this prospective study of healthy females, there was no evidence of any associations between total fibre intake or fibre from certain food sources and risk of fatal CHD, stroke or CVD in analyses of the full sample. Results suggest that greater intake of cereal sources of fibre in those with higher BMI may be associated with reduced stroke risk.

Hazard ratios for both stroke and CVD decreased with greater intake of fibre from nuts and seeds and for both outcomes, risk was significantly reduced in the highest group compared to the lowest consumers. However, the evidence for a linear relationship was lacking, perhaps because fibre intake from nut and seed sources was relatively low and protective associations may only become apparent with intakes at sufficiently high levels.

In the healthy subgroup of participants, that is those free of hypertension and angina, there appeared to be a protective association with fibre density and fatal stroke risk. This had not been observed when those with hypertension or angina were combined in the full sample, suggesting greater fibre density may prevent CVD development in those who are healthy, rather than halt or reverse disease development in those already displaying risk factors.

This result however did not reach the pre-specified 1% level of statistical significance, which was set for subgroup analyses, to acknowledge the issue of conducting multiple tests. The risk of Type I error, or false positive findings, is even greater in subgroup analyses, where sample sizes are diminished. The possible protective effect of fibre density in those without key CVD risk factors should be further explored in cohorts with larger case numbers.

Weakening of associations in the fully-adjusted models compared to age-adjusted indicate that the adjustments do indeed contribute to increase risk. However, results suggest the mechanism for the action of fibre may not be via influencing energy intake and ultimately BMI as adjustment for these did not attenuate, but strengthened HRs.

Average NSP intake in the UKWCS, assessed by FFQ, was around 24g/day, much higher than the 18g/day NSP intake found in another UK cohort, where diet was also assessed by FFQ [40]. A Finnish study of male smokers reported mean NSP intake closer to the UKWCS intake, at around 25g/day [41]. Mean AOAC fibre intake in the Nurses' Health Study was around 15g/day, drastically lower than the 36g/day AOAC fibre intake observed here [42]. The high intakes in this cohort, by comparison to representative study populations from the UK or United States, could simply reflect the healthy characteristics of participants here and the large proportion of vegetarians in the UKWCS. In addition to this, greater intake levels may also result from the large number of individual fruit and vegetable items listed on the FFQ, causing participants to over-estimate their intake of these foods and leading to inflated fibre values. Effects of systematic bias do not hinder the ability to identify important associations in epidemiologic research [35] are lessened through categorising participants into intake fifths.

A recent study from the European Prospective Investigation into Cancer and Nutrition (EPIC) observed contrasting results to ours and report a protective association between total fibre intake and total CVD mortality [43]. However, the definition for CVD mortality differed from the UKWCS and included any cardiovascular-related death rather than coronary plus stroke events. Another contrasting observation from EPIC was for cereal

fibre intake; greater intake was associated with risk reduction but, similar to the UKWCS, this was not the case for fruit or vegetable fibre intake [43]. Fatal CHD risk within EPIC was also reduced with greater total fibre intake [11]. However, one study focusing on just the UK data from the pooled EPIC study found that fibre assessed using food diaries was protectively associated with risk, but this was not the case for fibre calculated from FFQs [40], mirroring our results. In this UK EPIC study, there was also no evidence of an association between cereal, fruit or vegetable fibre but intakes here had been assessed with weighed food diaries [40].

Systematic reviews and data pooling projects for dietary fibre and CVD or CHD report protective associations for dietary fibre intake[10, 9, 44]. These reviews examined both incidence and mortality data together but it is possible the underlying pathology for incident events may differ from fatal events. However, other prospective studies reporting fatal CVD or CHD events also tend to observe protective associations both in men and women [45-47, 17, 21, 48] with one exception being the Australian Blue Mountain Eye study which did not report a protective association for total fibre and fatal CVD[49].

The picture for incident stroke risk is less consistent than CHD and CVD, whereby some studies report no evidence of protective associations with increased fibre intake[42, 18] and several observe protective associations [20, 41, 50]. Few studies report fatal stroke events and total fibre intake but a lack of association was reported in one Japanese cohort for both men and women[45] and a cohort from the US [18]. Additionally fatal stroke risk was not associated with greater cereal fibre intake in an Australian cohort [51].

Considering the existing evidence from observational studies and meta-analyses together, there appears to be an inverse association between total dietary fibre and both incident and fatal CVD or CHD risk, contrasting observations in the UKWCS. Our lack of evidence for a protective association for total fibre and stroke mortality risk mirrors observations from other cohorts but does not elucidate possible reasons for the protective associations observed for stroke risk in some subgroup analyses.

Recent work suggests that it may be the deceleration in rates of male CHD mortality and not an acceleration in females which explains the imbalance between sexes[2]. Additionally, the suggestions that changing hormone levels through menopause were responsible for this increased risk are disputed in a recent and comprehensive narrative synthesis of the menopause and CHD which indicates that age-related changes in weight, blood pressure, cholesterol and waist, determine hormonal changes and the age of menopause and not vice versa [52].

A systematic review of observational studies also indicated risk of CVD was not greater in

postmenopausal compared to premenopausal women after controlling for age and smoking, although there was a high degree of heterogeneity between the pooled studies[53]. Despite the lack of an apparent increase in heart disease mortality in women at menopausal ages, risk continued to increase exponentially throughout all ages[2] highlighting the importance of establishing potentially protective lifestyle habits. Strengths of this study include that this is a large prospective cohort that has been followed up for a relatively long period of time. The cohort was designed to allow exploration of disease in relation to healthy dietary characteristics by recruiting a large proportion of health conscious individuals. Diet was also assessed using a tool which had been validated for use in the sample.

Results were weighted to reduce the impact of data from vegetarian participants as a much greater proportion exist in this sample than the general population, meaning risk estimates are more applicable to the general population. However, the sample includes women who are generally well-educated, middle-class and are reasonably healthy and therefore, the generalisability of findings to other populations is unknown.

One limitation in dietary assessment is that diets may change over time but only diet assessed at baseline was considered in this analysis. However, some work using a sub-sample of cohort participants assessed 5-years after baseline indicated moderate stability in dietary pattern classification.[54] Other shortcomings in dietary assessment using FFQs are issues with measurement error and the tendency to over-estimate consumption of certain foods like fruit and vegetables.[55]

Uncontrolled confounding is a limitation with observational work,[56] meaning some other lifestyle or dietary factor, not adequately controlled for or accounted for in models, could explain observations. Therefore evidence from randomised controlled trials would be required to confirm associations as causal. Another problem with observational work of this kind is the inability to distinguish single nutrient specific end-points from other nutrients which are highly correlated.[57] Here it is not possible to identify whether fibre from a specific food is related to end-points or whether intake of the whole food, with associated nutrients, is responsible.

The use of only mortality data is a limitation as non-fatal cases are unidentified and misclassified as non-cases. Case numbers are also limited by using only mortality data, especially for sensitivity analyses. The lack of consideration for the time-frame of exposure and disease development in prospective work has been criticised [56] but case numbers here were too few to explore this.

Conclusions

Greater total dietary fibre intake may confer no additional cardiovascular benefit in already health-conscious women but may contribute to lower stroke risk in those free of cardiovascular risk factors (hypertension/angina). Cereal fibre may contribute to lower stroke risk specifically in women with higher BMI and there are suggestions that fibre from nuts and seeds may contribute to lower stroke risk in women free of CVD risk factors. There was no suggestion of protective associations for other sources of fibre for stroke risk reduction or for any food source of fibre with fatal CHD or CVD.

Further observational work will ideally include incidence data to boost statistical power. Experimental studies should contribute towards explaining observations from this and other cohort studies through exploring possible mechanisms underlying the relationship between CVD risk factors, BMI and the different types of fibre or sources of fibre.

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Competing interests

One author (DET) is in receipt of a studentship from Kellogg Marketing and Sales Company (UK) Ltd. One author is in receipt of an unrelated project grant from Danone (DCG). No other competing interests declared.

Table 1 Baseline characteristics for fatal stroke, or CHD cases and non-cases

		<i>Fatal Stroke</i>	<i>Fatal CHD</i>	<i>No fatal stroke or CHD</i>
Number of cases/ non-cases		130	128	30778
Age (years)		67.3 (11.4)	65.8 (10.5)	50.3 (14.1)
BMI (kg/m ²)		24.1 (5.1)	24.6 (6.2)	23.6 (4.7)
Smoking status (%)	Current smoker	22 (18)	24 (20)	3228 (11)
	Former smoker	27 (22)	43 (35)	9123 (30)
	Never smoker	76 (60)	56 (45)	17545 (59)
Vegetarian status (%)	Meat-eater	93 (72)	92 (72)	19616 (63)
	Poultry-eater	6 (5)	6 (5)	862 (3)
	Fish-eater	12 (9)	13 (10)	3938 (13)
	Vegetarian	19 (14)	17 (13)	6363 (21)
Socio-economic status (%)	Professional/ managerial	71 (58)	63 (52)	19214 (64)
	Intermediate	38 (31)	48 (40)	8198 (27)
	Routine and manual	13 (11)	10 (8)	2722 (9)
	No formal record	37 (36)	38 (37)	4469 (15)
Highest educational achievement (%)	O-level (16years old)	20 (20)	25 (24)	8909 (32)
	A-level (18years old)	22 (22)	17 (16)	7039 (25)
	Degree	23 (22)	24 (23)	7834 (28)
Menopausal status (%)	Postmenopausal	100 (78)	94 (78)	10657 (35)
	Premenopausal	9 (7)	6 (5)	12808 (42)
	Perimenopausal/ insufficient data	19 (15)	21(17)	6838 (23)
Self-reported angina at baseline (%)	Yes	6 (5)	11 (10)	374 (1)
	No	104 (95)	99 (90)	28421 (99)
Self-reported hypertension at baseline (%)	Yes	48 (41)	46 (39)	4596 (16)
	No	69 (59)	73 (61)	24768 (84)
Ethanol (g/day)		5.0 (12.2)	1.2 (7.2)	5.5 (11.6)
Physical activity (METS)		14.3 (13.9)	12.3 (12.6)	14.5 (13.2)
Energy intake (kcal)		2175 (1010)	2215 (864)	2187 (863)
NSP (g/day)		23.0 (14.5)	23.3 (12.1)	23.8 (12.4)
NSP density (g/1000kcal/day)		11.1 (4.6)	11.0 (5.0)	11.0 (4.2)
AOAC fibre (g/day)		36.1 (22.0)	34.8 (17.1)	36.7 (18.9)
AOAC fibre density (g/1000kcal/day)		17.1 (6.9)	16.3 (6.9)	16.9 (6.2)
Soluble fibre (g/day)		9.6 (5.6)	9.6 (4.7)	10.4 (5.0)
Insoluble fibre (g/day)		14.9 (10.7)	14.4 (9.0)	15.3 (8.9)
NSP within Foods (g/day)	Total fruit	4.2 (4.8)	3.9 (3.5)	4.2 (3.9)
	Vegetables	4.5 (3.6)	5.0 (4.2)	4.9 (3.7)
NSP within Foods (g/day)	Total cereal foods	7.2 (7.0)	7.5 (7.3)	7.6 (7.0)
	Breakfast cereals	2.1 (3.3)	1.7 (3.8)	1.8 (3.6)
	Nuts & Seeds	0.07 (0.17)	0.06 (0.22)	0.08 (0.29)
	Legumes	0.8 (1.0)	0.9 (0.9)	1.1 (1.3)

Values are medians (IQR) or counts (%).

Table 2: Baseline characteristics with increasing NSP intake

	<i>1st fifth</i>	<i>2nd fifth</i>	<i>3rd fifth</i>	<i>4th fifth</i>	<i>5th fifth</i>	
Number of participants, n	6207	6207	6207	6207	6208	
Stroke mortality cases, n	37	21	21	22	24	
CHD mortality cases, n	26	30	20	26	17	
Total CVD mortality cases, n	63	51	41	48	41	
NSP (g/day)	14.2 (3.9)	19.5 (2.3)	23.8 (2.3)	29.1 (3.1)	38.3 (8.6)	
NSP density (g/1000kcal/day)	8.2 (2.9)	10.0 (3.0)	11.0 (3.2)	12.1 (3.4)	13.8 (3.8)	
AOAC fibre (g/day)	21.9 (6.0)	30.1 (3.9)	36.7 (4.2)	44.6 (5.3)	58.8 (13.8)	
Soluble fibre (g/day)	6.5 (1.9)	8.8 (1.6)	10.5 (1.9)	12.5 (2.2)	16.3 (4.3)	
Insoluble fibre (g/day)	8.4 (2.7)	12.2 (2.0)	15.3 (14.3)	19.0 (2.6)	25.6 (6.2)	
Age (years)	50.0 (13.8)	50.2 (14.1)	50.6 (14.0)	50.1 (14.4)	50.7 (14.5)	
BMI (kg/m ²)	24.0 (5.1)	23.8 (4.8)	23.6 (4.5)	23.3 (4.5)	23.1 (4.3)	
Smoking status (%)	Current smoker	1075 (18)	701 (12)	545 (9)	489 (8)	464 (8)
	Former smoker	1751 (29)	1831 (30)	1843 (30)	1904 (31)	1864 (31)
	Never smoker	3189 (53)	3507 (58)	3658 (61)	3652 (61)	3671 (61)
Vegetarian status (%)	Meat-eaters	4830 (78)	4382 (71)	4107 (66)	3527 (56)	2955 (48)
	Poultry-eaters	129 (2)	143 (2)	174 (3)	191 (3)	237 (4)
	Fish-eaters	429 (7)	629 (10)	760 (12)	949 (15)	1196 (19)
	Vegetarian	819 (13)	1053 (17)	1167 (19)	1540 (25)	1820 (29)
Socio-economic status (NSSEC %)	Professional/managerial	3711 (61)	3784 (62)	3889 (64)	3945 (65)	4019 (66)
	Intermediate	1759 (29)	1708 (28)	1672 (27)	1607 (27)	1538 (25)
	Routine and manual	589 (10)	597 (10)	525 (9)	514 (8)	520 (9)
Highest educational achievement (%)	No formal record	1096 (19)	911 (16)	862 (15)	791 (14)	884 (16)
	O-level (16years old)	1925 (34)	1788 (31)	1821 (32)	1715 (30)	1705 (30)
	A-level (18years old)	1283 (23)	1397 (25)	1436 (25)	1516 (27)	1446 (25)
	Degree	1367 (24)	1566 (28)	1602 (28)	1690 (29)	1656 (29)
Menopausal status (%)	Postmenopausal	2123 (35)	2094 (34)	2198 (36)	2172 (36)	2264 (37)
	Premenopausal	2543 (42)	2653 (43)	2534 (41)	2598 (42)	2495 (41)
	Not-applicable	1432 (23)	1375 (23)	1391 (23)	1338 (22)	1342 (22)
Ethanol (g/day)	5.7 (13.1)	5.6 (12.2)	5.8 (11.6)	5.4 (11.0)	4.8 (10.7)	
Physical activity (METS)	12.3 (12.2)	13.6 (12.2)	14.4 (12.6)	15.2 (12.8)	17.0 (14.8)	
Energy intake (MJ/day)	6.9 (2.4)	8.1 (2.4)	9.09 (2.6)	10.1 (2.9)	12.0 (3.7)	

Values are medians (IQR) or counts (%).

Table 3 Total dietary fibre intake, fibre from food sources and cardiovascular mortality risk

	Median intake (IQR)	Cases ¹	CHD		Cases ¹	Stroke		Cases ¹	Total CVD		
			Age-adjusted	Fully-adjusted ²		Age-adjusted	Fully-adjusted ²		Age-adjusted	Fully-adjusted ²	
NSP (g/day)	Q1	14.1 (3.9)	24	1	1	34	1	1	58	1	1
	Q2	19.4 (2.3)	28	0.99 (0.58, 1.68)	1.30 (0.76, 2.24)	21	0.61 (0.35, 1.04)	0.63 (0.35, 1.12)	49	0.78 (0.54, 1.14)	0.90 (0.61, 1.34)
	Q3	23.8 (2.3)	18	0.75 (0.42, 1.33)	0.93 (0.48, 1.82)	19	0.48 (0.27, 0.86)	0.48 (0.24, 0.93)	37	0.60 (0.40, 0.90)	0.66 (0.41, 1.06)
	Q4	29.1 (3.1)	26	0.84 (0.49, 1.45)	1.15 (0.61, 2.17)	21	0.57 (0.33, 0.99)	0.55 (0.39, 1.04)	47	0.69 (0.47, 1.02)	0.79 (0.51, 1.24)
	Q5	38.3 (8.6)	17	0.63 (0.34, 1.15)	0.89 (0.38, 2.08)	22	0.74 (0.44, 1.25)	0.61 (0.27, 1.36)	39	0.69 (0.47, 1.03)	0.74 (0.41, 1.33)
	Per 6g/day <i>p Trend</i>		113	0.92 (0.80, 1.05) 0.22	0.96 (0.79, 1.17) 0.69	117	0.95 (0.84, 1.07) 0.37	0.87 (0.73, 1.04) 0.13	230	0.93 (0.85, 1.02) 0.13	0.92 (0.80, 1.05) 0.20
AOAC (g/day)	Q1	21.0 (5.9)	27	1	1	35	1	1	62	1	1
	Q2	30.0 (3.4)	26	0.89 (0.52, 1.50)	1.18 (0.68, 2.03)	20	0.57 (0.33, 0.99)	0.59 (0.32, 1.06)	46	0.72 (0.49, 1.05)	0.84 (0.56, 1.25)
	Q3	36.8 (3.5)	18	0.72 (0.42, 1.26)	0.82 (0.43, 1.58)	20	0.50 (0.28, 0.87)	0.47 (0.25, 0.90)	38	0.60 (0.41, 0.89)	0.62 (0.39, 0.98)
	Q4	44.8 (4.8)	26	0.76 (0.44, 1.29)	0.99 (0.52, 1.86)	21	0.58 (0.34, 1.00)	0.54 (0.29, 1.00)	47	0.66 (0.45, 0.97)	0.72 (0.46, 1.13)
	Q5	63.0 (13.5)	16	0.56 (0.30, 1.02)	0.72 (0.28, 1.83)	21	0.69 (0.40, 1.16)	0.51 (0.21, 1.26)	37	0.63 (0.42, 0.93)	0.61 (0.32, 1.17)
	Per 11g/day <i>p Trend</i>		113	0.90 (0.76, 1.07) 0.23	0.96 (0.73, 1.26) 0.76	117	0.94 (0.81, 1.09) 0.42	0.86 (0.68, 1.08) 0.19	230	0.92 (0.82, 1.03) 0.15	0.91 (0.76, 1.08) 0.28
NSP density g/1000 kcal (4.2MJ)/day	Q1	7.4 (1.5)	29	1	1	27	1	1	56	1	1
	Q2	9.4 (0.8)	20	0.66 (0.38, 1.16)	0.85 (0.47, 1.52)	23	0.75 (0.43, 1.30)	0.81 (0.46, 1.44)	43	0.70 (0.47, 1.04)	0.83 (0.55, 1.24)
	Q3	11.0 (0.8)	22	0.72 (0.41, 1.25)	0.91 (0.51, 1.63)	19	0.64 (0.36, 1.15)	0.71 (0.39, 1.29)	41	0.68 (0.46, 1.02)	0.80 (0.53, 1.22)
	Q4	12.7 (1.0)	19	0.70 (0.40, 1.22)	0.74 (0.40, 1.38)	23	0.80 (0.46, 1.39)	0.79 (0.44, 1.44)	42	0.75 (0.51, 1.11)	0.77 (0.50, 1.19)
	Q5	15.4 (2.3)	23	0.84 (0.49, 1.43)	0.99 (0.55, 1.76)	25	0.82 (0.47, 1.43)	0.89 (0.49, 1.62)	48	0.83 (0.57, 1.22)	0.94 (0.62, 1.42)
	Per 2g/1000 kcal/day <i>p Trend</i>		113	0.98 (0.85, 1.14) 0.81	0.95 (0.86, 1.06) 0.89	117	0.92 (0.81, 1.04) 0.17	0.92 (0.80, 1.05) 0.21	230	0.95 (0.86, 1.05) 0.30	0.95 (0.86, 1.06) 0.37
AOAC density g/1000 kcal (4.2MJ)/day	Q1	11.3 (2.1)	31	1	1	28	1	1	59	1	1
	Q2	14.6 (1.2)	22	0.63 (0.37, 1.09)	0.76 (0.43, 1.33)	20	0.62 (0.25, 1.09)	0.65 (0.36, 1.16)	42	0.62 (0.42, 0.92)	0.70 (0.47, 1.05)
	Q3	16.9 (1.1)	21	0.70 (0.41, 1.19)	0.81 (0.46, 1.44)	21	0.64 (0.36, 1.12)	0.68 (0.38, 1.21)	42	0.67 (0.45, 0.99)	0.74 (0.49, 1.11)
	Q4	19.4 (1.4)	18	0.59 (0.33, 1.03)	0.68 (0.37, 1.25)	25	0.76 (0.44, 1.31)	0.84 (0.47, 1.49)	43	0.67 (0.45, 0.99)	0.76 (0.50, 1.15)
	Q5	24.3 (3.6)	21	0.73 (0.42, 1.25)	0.81 (0.45, 1.47)	23	0.75 (0.43, 1.31)	0.76 (0.42, 1.40)	44	0.74 (0.50, 1.09)	0.79 (0.52, 1.21)
	Per 3g/1000 kcal/day <i>p Trend</i>		113	0.98 (0.84, 1.15) 0.81	0.99 (0.84, 1.17) 0.92	117	0.92 (0.80, 1.05) 0.20	0.92 (0.80, 1.06) 0.24	230	0.95 (0.86, 1.05) 0.32	0.96 (0.86, 1.07) 0.42
Soluble fibre (g/day)	Q1	6.4 (1.6)	29	1	1	31	1	1	60	1	1
	Q2	8.6 (0.9)	24	0.88 (0.52, 1.47)	0.91 (0.52, 1.61)	27	0.80 (0.47, 1.36)	0.89 (0.50, 1.60)	51	0.84 (0.58, 1.22)	0.90 (0.60, 1.35)
	Q3	10.4 (0.9)	20	0.65 (0.37, 1.14)	0.88 (0.47, 1.62)	15	0.56 (0.31, 1.01)	0.52 (0.26, 1.03)	35	0.60 (0.40, 0.91)	0.68 (0.43, 1.08)
	Q4	12.5 (1.2)	21	0.64 (0.37, 1.11)	0.74 (0.37, 1.49)	26	0.85 (0.50, 1.43)	0.78 (0.40, 1.51)	47	0.74 (0.51, 1.08)	0.76 (0.47, 1.23)
	Q5	16.4 (3.8)	19	0.62 (0.35, 1.10)	0.76 (0.32, 1.80)	18	0.70 (0.40, 1.24)	0.60 (0.25, 1.43)	37	0.66 (0.44, 0.99)	0.68 (0.37, 1.25)
	Per 3g/day <i>p Trend</i>		113	0.87 (0.74, 1.03) 0.12	0.91 (0.69, 1.19) 0.47	117	0.95 (0.83, 1.10) 0.52	0.88 (0.70, 1.11) 0.29	230	0.91 (0.82, 1.02) 0.11	0.89 (0.75, 1.07) 0.22
Insoluble fibre (g/day)	Q1	8.4 (2.6)	26	1	1	32	1	1	58	1	1
	Q2	12.4 (1.6)	29	1.00 (0.60, 1.68)	1.29 (0.76, 2.19)	21	0.68 (0.39, 1.17)	0.73 (0.41, 1.32)	50	0.83 (0.57, 1.21)	0.98 (0.66, 1.46)
	Q3	15.3 (1.6)	15	0.64 (0.36, 1.14)	0.67 (0.35, 1.31)	19	0.56 (0.32, 1.00)	0.57 (0.30, 1.07)	34	0.60 (0.40, 0.90)	0.62 (0.39, 0.98)
	Q4	19.1 (2.2)	27	0.80 (0.47, 1.36)	1.09 (0.58, 2.06)	22	0.63 (0.36, 1.10)	0.69 (0.37, 1.28)	49	0.71 (0.49, 1.04)	0.87 (0.56, 1.36)
	Q5	25.6 (6.0)	16	0.57 (0.31, 1.05)	0.75 (0.33, 1.71)	23	0.83 (0.49, 1.41)	0.78 (0.37, 1.67)	39	0.71 (0.48, 1.05)	0.78 (0.45, 1.36)
	Per 4g/day <i>p Trend</i>		113	0.94 (0.82, 1.08) 0.38	1.00 (0.82, 1.20) 0.96	117	0.95 (0.85, 1.07) 0.40	0.90 (0.78, 1.05) 0.20	230	0.95 (0.87, 1.03) 0.23	0.95 (0.84, 1.07) 0.41

Total cereal fibre (g/day)	Q1	2.8 (1.4)	25	1	1	27	1	1	52	1	1
	Q2	5.1 (1.1)	18	0.70 (0.39, 1.26)	0.87 (0.46, 1.65)	21	0.86 (0.49, 1.53)	0.88 (0.48, 1.62)	39	0.78 (0.52, 1.17)	0.88 (0.56, 1.36)
	Q3	7.6 (1.4)	27	0.98 (0.58, 1.65)	1.11 (0.61, 2.04)	26	0.92 (0.53, 1.59)	0.95 (0.53, 1.71)	53	0.95 (0.65, 1.39)	1.04 (0.68, 1.58)
	Q4	10.7 (1.8)	19	0.59 (0.33, 1.06)	0.72 (0.36, 1.45)	21	0.72 (0.41, 1.28)	0.69 (0.37, 1.26)	40	0.65 (0.43, 0.98)	0.71 (0.44, 1.12)
	Q5	15.7 (4.5)	24	0.75 (0.43, 1.29)	1.06 (0.52, 2.15)	22	0.81 (0.46, 1.41)	0.77 (0.40, 1.50)	46	0.78 (0.52, 1.15)	0.91 (0.56, 1.48)
	Per 3g/day		113	1.00 (0.88, 1.14)	1.03 (0.89, 1.19)	117	0.96 (0.87, 1.07)	0.94 (0.83, 1.07)	230	0.98 (0.90, 1.07)	0.99 (0.89, 1.09)
	<i>p Trend</i>			0.99	0.71		0.48	0.34		0.67	0.77
Fibre from breakfast cereals (g/day)	Q1	0.05 (0.14)	23	1	1	20	1	1	43	1	1
	Q2	0.5 (0.4)	25	1.20 (0.68, 2.09)	1.11 (0.61, 2.03)	21	1.17 (0.63, 2.17)	1.24 (0.65, 2.35)	46	1.18 (0.78, 1.79)	1.16 (0.75, 1.80)
	Q3	1.8 (0.7)	16	0.75 (0.41, 1.40)	0.82 (0.42, 1.62)	23	1.04 (0.57, 1.92)	1.06 (0.56, 2.02)	39	0.89 (0.57, 1.36)	0.93 (0.80, 1.48)
	Q4	3.5 (0.7)	23	0.93 (0.52, 1.64)	1.04 (0.55, 1.69)	30	1.41 (0.80, 2.50)	1.45 (0.79, 2.68)	53	1.15 (0.77, 1.71)	1.22 (0.79, 1.90)
	Q5	7.6 (2.6)	26	0.91 (0.52, 1.59)	1.09 (0.58, 2.02)	23	1.06 (0.59, 1.91)	1.11 (0.59, 2.10)	49	0.98 (0.65, 1.46)	1.09 (0.70, 1.71)
	Per 2g/day		113	1.04 (0.93, 1.16)	1.04 (0.93, 1.17)	117	0.98 (0.89, 1.07)	0.97 (0.88, 1.07)	230	1.01 (0.93, 1.09)	1.01 (0.93, 1.09)
	<i>p Trend</i>			0.52	0.46		0.58	0.52		0.81	0.83
Fruit fibre (g/day)	Q1	1.4 (0.9)	26	1	1	27	1	1	53	1	1
	Q2	2.9 (0.7)	24	0.64 (0.38, 1.08)	0.83 (0.47, 1.47)	21	0.56 (0.32, 1.00)	0.69 (0.39, 1.23)	45	0.60 (0.41, 0.89)	0.76 (0.50, 1.14)
	Q3	4.2 (0.7)	23	0.55 (0.32, 0.95)	0.76 (0.42, 1.38)	25	0.69 (0.40, 1.17)	0.73 (0.41, 1.31)	48	0.61 (0.42, 0.90)	0.74 (0.49, 1.13)
	Q4	5.8 (1.1)	23	0.53 (0.31, 0.90)	0.74 (0.40, 1.36)	18	0.43 (0.23, 0.78)	0.50 (0.25, 0.97)	41	0.48 (0.32, 0.72)	0.61 (0.39, 0.96)
	Q5	9.5 (4.1)	17	0.38 (0.21, 0.69)	0.55 (0.28, 1.06)	26	0.72 (0.43, 1.22)	0.79 (0.42, 1.48)	43	0.54 (0.37, 0.80)	0.68 (0.43, 1.06)
	Per 2g/day		113	0.91 (0.75, 1.10)	0.98 (0.83, 1.17)	117	1.00 (0.90, 1.12)	1.02 (0.90, 1.15)	230	0.96 (0.87, 1.06)	1.00 (0.90, 1.11)
	<i>p Trend</i>			0.32	0.85		0.98	0.78		0.42	0.97
Vegetable fibre (g/day)	Q1	2.3 (0.9)	27	1	1	27	1	1	54	1	1
	Q2	3.7 (0.6)	23	0.79 (0.46, 1.36)	0.92 (0.52, 1.62)	25	1.11 (0.65, 1.90)	1.10 (0.63, 1.93)	48	0.94 (0.64, 1.37)	1.00 (0.67, 1.50)
	Q3	4.9 (0.7)	20	0.73 (0.42, 1.27)	0.82 (0.45, 1.50)	21	0.68 (0.37, 1.23)	0.76 (0.41, 1.41)	41	0.71 (0.47, 1.06)	0.78 (0.51, 1.20)
	Q4	6.6 (1.0)	17	0.57 (0.32, 1.03)	0.64 (0.35, 1.18)	27	0.90 (0.53, 1.55)	1.00 (0.57, 1.75)	44	0.73 (0.49, 1.08)	0.82 (0.54, 1.23)
	Q5	9.5 (3.0)	26	0.74 (0.44, 1.26)	0.95 (0.52, 1.74)	17	0.69 (0.39, 1.22)	0.58 (0.30, 1.11)	43	0.72 (0.49, 1.06)	0.75 (0.49, 1.17)
	Per 2g/day		113	0.92 (0.81, 1.05)	0.95 (0.83, 1.09)	117	0.94 (0.83, 1.06)	0.90 (0.79, 1.03)	230	0.93 (0.85, 1.01)	0.93 (0.84, 1.02)
	<i>p Trend</i>			0.21	0.50		0.30	0.11		0.10	0.21
Legume fibre (g/day)	Q1	0.2 (0.2)	25	1	1	31	1	1	56	1	1
	Q2	0.65 (0.20)	29	1.08 (0.65, 1.79)	1.35 (0.77, 2.37)	30	1.06 (0.64, 1.74)	1.11 (0.65, 1.89)	59	1.07 (0.75, 1.52)	1.22 (0.83, 1.79)
	Q3	1.11 (0.18)	28	1.12 (0.66, 1.89)	1.58 (0.90, 2.79)	23	0.93 (0.54, 1.61)	1.08 (0.62, 1.90)	51	1.02 (0.71, 1.49)	1.30 (0.87, 1.94)
	Q4	1.66 (0.39)	14	0.84 (0.46, 1.56)	1.09 (0.54, 2.21)	19	0.89 (0.50, 1.61)	1.05 (0.58, 1.90)	33	0.87 (0.57, 1.33)	1.07 (0.68, 1.69)
	Q5	3.6 (1.4)	17	1.01 (0.55, 1.85)	1.33 (0.65, 2.71)	14	1.01 (0.55, 1.86)	0.79 (0.37, 1.67)	31	1.01 (0.66, 1.55)	1.03 (0.62, 1.72)
	Per 1g/day		113	0.95 (0.82, 1.10)	1.01 (0.87, 1.17)	117	0.97 (0.82, 1.14)	0.87 (0.74, 1.04)	230	0.96 (0.86, 1.07)	0.94 (0.84, 1.06)
	<i>p Trend</i>			0.47	0.92		0.73	0.12		0.46	0.32
Fibre from nuts and seeds (g/day)	Q1	0 (0.01)	38	1	1	45	1	1	83	1	1
	Q2	0.06 (0.01)	25	0.83 (0.51, 1.36)	0.86 (0.51, 1.45)	26	0.96 (0.60, 1.53)	0.86 (0.52, 1.43)	51	0.89 (0.64, 1.26)	0.86 (0.60, 1.23)
	Q3	0.08 (0.05)	16	0.74 (0.42, 1.30)	0.84 (0.50, 1.53)	18	0.67 (0.38, 1.17)	0.63 (0.35, 1.13)	34	0.70 (0.47, 1.05)	0.72 (0.47, 1.10)
	Q4	0.27 (0.13)	17	0.67 (0.38, 1.21)	0.87 (0.47, 1.61)	14	0.49 (0.29, 0.94)	0.50 (0.26, 0.95)	31	0.58 (0.38, 0.90)	0.66 (0.42, 1.03)
	Q5	0.85 (0.91)	17	0.65 (0.37, 1.15)	0.84 (0.44, 1.59)	14	0.52 (0.29, 0.96)	0.45 (0.23, 0.85)	31	0.58 (0.39, 0.88)	0.61 (0.39, 0.96)
	Per 0.2g/day		113	0.97 (0.89, 1.06)	0.99 (0.90, 1.08)	117	0.93 (0.85, 1.02)	0.92 (0.83, 1.02)	230	0.95 (0.89, 1.02)	0.96 (0.89, 1.03)
	<i>p Trend</i>			0.51	0.76		0.13	0.13		0.16	0.25

¹Case numbers apply to fully-adjusted models. ²Adjustments include Age (years), BMI (kg/m²), calories from carbohydrate, fat and protein (kcal/day), ethanol intake (g/day), METS (1kcal/kg/hour), smoking status (current vs. not current smoker), socio-economic status (professional or managerial/ intermediate/ routine or manual). Note, adjustment for energy intake was not included in fibre density models.

References

1. Allender S, Scarborough P, Peto V, Rayner M, Leal J, Luengo-Fernandez R et al. European cardiovascular disease statistics Available online <http://www.heartstats.org/datapage.asp?id=7683> 2008.
2. Vaidya D, Becker DM, Bittner V, Mathias RA, Ouyang P. Ageing, menopause, and ischaemic heart disease mortality in England, Wales, and the United States: modelling study of national mortality data. *BMJ*. 2011;343:d5170.
3. Worrall-Carter L, Ski C, Scruth E, Campbell M, Page K. Systematic review of cardiovascular disease in women: assessing the risk. *Nurs Health Sci*. 2011;13(4):529-35. doi:10.1111/j.1442-2018.2011.00645.x.
4. Nichols M, Townsend N, Luengo-Fernandez R, Leal J, Gray A, Scarborough P et al. European Cardiovascular Disease Statistics. European Heart Network, Brussels, European Society of Cardiology, Sophia Antipolis. 2012.
5. Gale CP, Cattle BA, Woolston A, Baxter PD, West TH, Simms AD et al. Resolving inequalities in care? Reduced mortality in the elderly after acute coronary syndromes. The Myocardial Ischaemia National Audit Project 2003-2010. *Eur Heart J*. 2012;33(5):630-9. doi:10.1093/eurheartj/ehr381.
6. Unal B, Critchley JA, Capewell S. Explaining the decline in coronary heart disease mortality in England and Wales between 1981 and 2000. *Circulation*. 2004;109(9):1101-7. doi:10.1161/01.cir.0000118498.35499.b2.
7. Trowell H. Ischemic heart disease and dietary fiber. *Am J Clin Nutr*. 1972;25(9):926-32.
8. Erkkila AT, Lichtenstein AH, Erkkila AT, Lichtenstein AH. Fiber and cardiovascular disease risk: how strong is the evidence? *Journal of Cardiovascular Nursing*. 2006;21(1):3-8.
9. Mente A, de Koning L, Shannon HS, Anand SS, Mente A, de Koning L et al. A systematic review of the evidence supporting a causal link between dietary factors and coronary heart disease. *Archives of Internal Medicine*. 2009;169(7):659-69.
10. Pereira MA, O'Reilly E, Augustsson K, Fraser GE, Goldbourt U, Heitmann BL et al. Dietary fiber and risk of coronary heart disease: a pooled analysis of cohort studies. *Arch Intern Med*. 2004;164(4):370-6.
11. Crowe FL, Key TJ, Appleby PN, Overvad K, Schmidt EB, Egeberg R et al. Dietary fibre intake and ischaemic heart disease mortality: the European Prospective Investigation into Cancer and Nutrition-Heart study. *Eur J Clin Nutr*. 2012;66(8):950-6. doi:10.1038/ejcn.2012.51.
12. Lunn J, Buttriss JL. Carbohydrates and dietary fibre. *British Nutrition Foundation Nutrition Bulletin*. 2007;32:21-64.
13. James SL, Muir JG, Curtis SL, Gibson PR. Dietary fibre: a roughage guide. *Intern Med J*. 2003;33(7):291-6.
14. Slavin JL, Martini MC, Jacobs DR, Jr., Marquart L. Plausible mechanisms for the protectiveness of whole grains. *Am J Clin Nutr*. 1999;70(3 Suppl):459S-63S.
15. Brown L, Rosner B, Willett WW, Sacks FM. Cholesterol-lowering effects of dietary fiber: a meta-analysis. *Am J Clin Nutr*. 1999;69(1):30-42.
16. Coultate TP. Chapter 3 Polysaccharides. In: Coultate TP, editor. *Food The Chemistry of its components*. Cambridge: The Royal Society of Chemistry; 2009. p. 75.
17. Rimm EB, Ascherio A, Giovannucci E, Spiegelman D, Stampfer MJ, Willett WC. Vegetable, fruit, and cereal fiber intake and risk of coronary heart disease among men. *Journal of the American Medical Association*. 1996;275(6):447-51.
18. Bazzano LA, He J, Ogden LG, Loria CM, Whelton PK, National Health Nutrition Examination Survey. Dietary fiber intake and reduced risk of coronary heart disease in US men and women: the

- National Health and Nutrition Examination Survey I Epidemiologic Follow-up Study. *Archives of Internal Medicine*. 2003;163(16):1897-904.
19. Akbaraly TN, Ferrie JE, Berr C, Brunner EJ, Head J, Marmot MG et al. Alternative healthy eating index and mortality over 18 y of follow-up: Results from the Whitehall II cohort. *Am J Clin Nutr*. 2011;94(1):247-53. doi:<http://dx.doi.org/10.3945/ajcn.111.013128>.
 20. Kokubo Y, Iso H, Saito I, Yamagishi K, Ishihara J, Inoue M et al. Dietary fiber intake and risk of cardiovascular disease in the Japanese population: The Japan Public Health Center-based study cohort. *European Journal of Clinical Nutrition*. 2011;65(11):1233-41. doi:<http://dx.doi.org/10.1038/ejcn.2011.100>.
 21. Streppel MT, Ocke MC, Boshuizen HC, Kok FJ, Kromhout D. Dietary fiber intake in relation to coronary heart disease and all-cause mortality over 40 y: the Zutphen Study. *Am J Clin Nutr*. 2008;88(4):1119-25.
 22. Mosca L, Banka CL, Benjamin EJ, Berra K, Bushnell C, Dolor RJ et al. Evidence-based guidelines for cardiovascular disease prevention in women: 2007 update. *J Am Coll Cardiol*. 2007;49(11):1230-50. doi:10.1016/j.jacc.2007.02.020.
 23. Cade JE, Burley VJ, Greenwood DC. The UK Women's Cohort Study: comparison of vegetarians, fish-eaters and meat-eaters. *Public Health Nutr*. 2004;7(7):871-8.
 24. Ainsworth B.E., Haskell W.L., Leon A.S., Jacobs D.R.Jr., Montoye H.J., Sallis J.F. et al. Compendium of physical activities: Classification of energy costs of human physical activities. *Medicine and Science in Sports and Exercise*. 1993;25:71-80.
 25. Holland B, Welch AA, Unwin ID, Buss DH, Paul AA, Southgate DAT. McCance & Widdowson's *The Composition of Foods*. Fifth ed. London: Royal Society of Chemistry and Ministry of Agriculture, Fisheries and Food.; 1991.
 26. Food Standards Agency. McCance and Widdowson's *The Composition of Foods*, 6th Summary Edition. Cambridge: Royal Society of Chemistry: 2002.
 27. EuroFIR. European Food Information Resource. EuroFIR eSearch Prototype [Accessed 11 May 2011]. Available from <http://esearch.eurofir.org/>. 2010.
 28. USDA. United States Department of Agriculture, Agricultural Research Service. USDA National Nutrient Database for Standard Reference, Release 23. Nutrient Data Laboratory Home Page [online]. [Accessed 11 May 2011]. Available from: <http://www.ars.usda.gov/ba/bhnrc/ndl>. 2010.
 29. Holland B, Unwin ID, Buss DH. *Cereals and cereal products: third supplement to McCance and Widdowson's the composition of foods*. Cambridge: Royal Society of Chemistry: 1988.
 30. Holland B, Unwin ID, Buss DH. *Milk products and eggs: fourth supplement to McCance and Widdowson's the composition of foods*. Cambridge: Royal Society of Chemistry: 1989.
 31. Holland B, Unwin ID, Buss DH. *Vegetables, herbs and spices: fifth supplement to McCance and Widdowson's the composition of foods*. Cambridge: Royal Society of Chemistry: 1991.
 32. Holland B, Unwin ID, Buss DH. *Fruit and nuts: first supplement to 5th edition of McCance and Widdowson's the composition of foods*. Cambridge: Royal Society of Chemistry: 1992.
 33. Holland B, Welch AA, Buss DH. *Vegetable dishes: second supplement to 5th edition of McCance and Widdowson's the composition of foods*. Cambridge: Royal Society of Chemistry: 1992.
 34. Greenland S, Pearl J, Robins JM. Causal diagrams for epidemiologic research. *Epidemiology*. 1999;10(1):37-48.
 35. Willett WW, Stampfer MJ. Implications of total energy intake for epidemiologic analyses. In: Willett WW, editor. *Nutritional Epidemiology*. Oxford: Oxford University Press; 1998. p. 273-300.
 36. Nordestgaard BG, Palmer TM, Benn M, Zacho J, Tybjaerg-Hansen A, Davey Smith G et al. The effect of elevated body mass index on ischemic heart disease risk: causal estimates from a Mendelian randomisation approach. *PLoS Med*. 2012;9(5):e1001212. doi:10.1371/journal.pmed.1001212.
 37. Logue J, Murray HM, Welsh P, Shepherd J, Packard C, Macfarlane P et al. Obesity is associated with fatal coronary heart disease independently of traditional risk factors and deprivation. *Heart*. 2011;97(7):564-8. doi:10.1136/hrt.2010.211201.

38. Matthews KA, Crawford SL, Chae CU, Everson-Rose SA, Sowers MF, Sternfeld B et al. Are changes in cardiovascular disease risk factors in midlife women due to chronological aging or to the menopausal transition? *J Am Coll Cardiol*. 2009;54(25):2366-73. doi:10.1016/j.jacc.2009.10.009.
39. Stata. *Stata Statistical Software: Release 11*. College Station, TX: StataCorp LP. 2009.
40. Ward HA, Keogh R, Lentjes M, Luben RN, Wareham NJ, Khaw KT. Fibre intake in relation to serum total cholesterol levels and CHD risk: A comparison of dietary assessment methods. *European Journal of Clinical Nutrition*. 2012;66(3):296-304. doi:<http://dx.doi.org/10.1038/ejcn.2011.184>.
41. Larsson SC, Mannisto S, Virtanen MJ, Kontto J, Albanes D, Virtamo J. Dietary fiber and fiber-rich food intake in relation to risk of stroke in male smokers. *European Journal of Clinical Nutrition*. 2009;63(8):1016-24.
42. Oh K, Hu FB, Cho E, Rexrode KM, Stampfer MJ, Manson JE et al. Carbohydrate intake, glycemic index, glycemic load, and dietary fiber in relation to risk of stroke in women. *American Journal of Epidemiology*. 2005;161(2):161-9.
43. Chuang S-C, Norat T, Murphy N, Olsen A, Tjønneland A, Overvad K et al. Fiber intake and total and cause-specific mortality in the European Prospective Investigation into Cancer and Nutrition cohort. *Am J Clin Nutr*. 2012;96(1):164-74.
44. Ye EQ, Chacko SA, Chou EL, Kugizaki M, Liu S. Greater whole-grain intake is associated with lower risk of type 2 diabetes, cardiovascular disease, and weight gain. *J Nutr*. 2012;142(7):1304-13. doi:10.3945/jn.111.155325.
45. Eshak ES, Iso H, Date C, Kikuchi S, Watanabe Y, Wada Y et al. Dietary fiber intake is associated with reduced risk of mortality from cardiovascular disease among Japanese men and women. *Journal of Nutrition*. 2010;140(8):1445-53.
46. Park Y, Subar AF, Hollenbeck A, Schatzkin A. Dietary fiber intake and mortality in the NIH-AARP diet and health study. *Archives of Internal Medicine*. 2011;171(12):1061-8. doi:<http://dx.doi.org/10.1001/archinternmed.2011.18>.
47. Pietinen P, Rimm EB, Korhonen P, Hartman AM, Willett WC, Albanes D et al. Intake of dietary fiber and risk of coronary heart disease in a cohort of Finnish men. The Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study. *Circulation*. 1996;94(11):2720-7.
48. Wolk A, Manson JE, Stampfer MJ, Colditz GA, Hu FB, Speizer FE et al. Long-term intake of dietary fiber and decreased risk of coronary heart disease among women. *Journal of the American Medical Association*. 1999;281(21):1998-2004.
49. Buyken AE, Flood V, Empson M, Rochtchina E, Barclay AW, Brand-Miller J et al. Carbohydrate nutrition and inflammatory disease mortality in older adults. *Am J Clin Nutr*. 2010;92(3):634-43.
50. Ascherio A, Rimm EB, Hernan MA, Giovannucci EL, Kawachi I, Stampfer MJ et al. Intake of potassium, magnesium, calcium, and fiber and risk of stroke among US men. *Circulation*. 1998;98(12):1198-204.
51. Kaushik S, Wang JJ, Wong TY, Flood V, Barclay A, Brand-Miller J et al. Glycemic index, retinal vascular caliber, and stroke mortality. *Stroke*. 2009;40(1):206-12.
52. Barrett-Connor E. Menopause, atherosclerosis, and coronary artery disease. *Curr Opin Pharmacol*. 2013. doi:10.1016/j.coph.2013.01.005.
53. Atsma F, Bartelink ML, Grobbee DE, van der Schouw YT. Postmenopausal status and early menopause as independent risk factors for cardiovascular disease: a meta-analysis. *Menopause*. 2006;13(2):265-79. doi:10.1097/01.gme.0000218683.97338.ea.
54. Greenwood DC, Gilthorpe MS, Golding C, Cade JE. Stability over time of dietary patterns in the UK Women's Cohort Study. . *Proceedings of the Nutrition Society*. 2003;62, 89A.
55. Cade J, Thompson R, Burley V, Warm D. Development, validation and utilisation of food-frequency questionnaires - a review. *Public Health Nutr*. 2002;5(4):567-87. doi:10.1079/phn2001318.
56. Willett WW. *Diet and Coronary Heart Disease*. In: Willett WW, editor. *Nutritional Epidemiology*. Second Edition ed. Monographs in Epidemiology and biostatistics, vol 30. Oxford: Oxford University Press; 1998. p. 414-66.

57. Bingham SA, Gill C, Welch A, Day K, Cassidy A, Khaw KT et al. Comparison of dietary assessment methods in nutritional epidemiology: weighed records v. 24 h recalls, food-frequency questionnaires and estimated-diet records. *Br J Nutr.* 1994;72(4):619-43.