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NUTRITION

Dietary fibre and risk of breast cancer in the UK Women's Cohort Study

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Background Reports of relationships between dietary fibre intake and breast cancer have been inconsistent. Previous cohort studies have been limited by a narrow range of intakes.

Methods Women who developed invasive breast cancer, 350 post-menopausally and 257 pre-menopausally, during 240 959 person-years of follow-up in the UK Women's Cohort Study (UKWCS) were studied. This cohort has 35 792 subjects with a wide range of exposure to dietary fibre with intakes of total fibre in the lowest quintile of <20 g/day up to >30 g/day in the top quintile. Fibre and breast cancer relationships were explored using Cox regression modelling adjusted for measurement error. Effects of fibre, adjusting for confounders were examined for pre- and post-menopausal women separately.

Results In pre-menopausal, but not post-menopausal women a statistically significant inverse relationship was found between total fibre intake and risk of breast cancer (P for trend = 0.01). The top quintile of fibre intake was associated with a hazard ratio of 0.48 [95% confidence interval (CI) 0.24–0.96] compared with the lowest quintile. Pre-menopausally, fibre from cereals was inversely associated with risk of breast cancer (P for trend = 0.05) and fibre from fruit had a borderline inverse relationship (P for trend = 0.09). A further model including dietary folate strengthened the significance of the inverse relationship between total fibre and pre-menopausal breast cancer.

Conclusions These findings suggest that in pre-menopausal women, total fibre is protective against breast cancer; in particular, fibre from cereals and possibly fruit.

Keywords Breast neoplasms, cereals, cohort studies, dietary fibre, prospective studies, women

Introduction

Evidence linking breast cancer to the intake of dietary fibre has been conflicting.[1–3] However, the possibility remains that a high dietary fibre intake may be protective. Fibre or certain fibre fractions have been hypothesized to reduce cancer risk through a number of mechanisms[4] including inhibition of oestrogen reabsorption, inhibition of human oestrogen synthetase leading to a reduction in oestrogen synthesis and reduction in levels of androgens which influence levels of oestrogens and proliferation of breast tissue.[5] Additionally, fibre may act via a route involving insulin and insulin-like growth factors (IGFs). Higher serum levels of IGF-1 are associated with increased breast cancer risk[6] and IGF levels are influenced by diet.[7]

Results from case-control studies have tended to show a protective effect of fibre.[2] This study design is more prone to recall bias, and hence cohort studies are potentially more

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reliable. However, prospective studies which have explored the relationship between dietary fibre intake and breast cancer have not shown a protective effect.[8,9] A review of nine prospective studies has shown that risk for breast cancer increases significantly with increasing concentrations of both oestrogens and androgens.[10] These sex hormones have been shown to be altered by diets high in fibre in some experimental studies.[11–13]

The UK Women's Cohort Study (UKWCS) is well placed to explore the risks of breast cancer associated with dietary fibre and sources of fibre since the Cohort was designed to have a wide range of relevant exposures through inclusion of large numbers of vegetarians.[14]

Subjects and methods

The UK Women's Cohort was constructed to have large numbers of subjects in three main groups: vegetarian, eating fish (not meat) and meat eaters. This ensured adequate power for important comparisons involving fruit, vegetables or fish intake as well as associated nutrients including fibre in order to explore potential relationships between diet and cancer whilst minimizing the effects of measurement error.[15–17]

Baseline data were collected on 35 792 women between 1995 and 1998 via a postal questionnaire to each subject. Women were aged 35–69 years at baseline and were living in England, Wales and Scotland. Women were chosen from ~500 000 responders to a direct mail questionnaire which included general questions on diet. This had been sent by the World Cancer Research Fund to people living in England, Wales and Scotland using direct mail lists targeted towards females, with an overall response rate of 17%. All women in the correct age group and who characterized themselves as vegetarian or non-red meat eaters were invited to take part. A comparison group was selected from the remaining eligible women by selecting, for each vegetarian, the next non-vegetarian in the list aged within 10 years of the vegetarian. Additional detail about the cohort is provided elsewhere.[14]

Study population

In total, 17 781 women who were post-menopausal at baseline and 15 951 women who were classified as pre-menopausal at baseline were included in this analysis. Menopausal status was coded using specific criteria. Post-menopausal women were those with age at the baseline greater than age at the last period, or if older than 50 years and currently on hormone replacement therapy (HRT), or with a previous hysterectomy and HRT, or if all the above were missing and the woman was >50 years. Pre-menopausal women were those who reported having natural menstrual periods, or were pregnant, or were on HRT and aged 50< years at baseline, or aged <50 years with a previous hysterectomy, or if all the above were missing and the woman was aged <50 years.

Case definition and ascertainment

All subjects were flagged for deaths and cancer registrations on the Office of National Statistics National Health Service central register which was the only source of case information. All malignant breast cancers registered after the subjects returned their questionnaire were taken as newly incident cancers. Cases contributed person-time from date of enrolment until time of diagnosis. Non-cases contributed person-time from date of enrolment until death (807 women) or end of follow-up (January 31 2004) whichever was the first. In total, 350 post-menopausal and 257 pre-menopausal women developed invasive breast cancer during 240 959 person-years of follow-up. The mean length of follow-up of all non-breast cancer subjects was 7.5 years (range 0.1–9.4).

Dietary data

The self-administered questionnaire consisted of a detailed assessment of diet using a 217-item food frequency questionnaire (FFQ) based on that used in the Oxford arm of the European Prospective Investigation into Cancer (EPIC) study and developed for use with vegetarians. The FFQ has been validated on a subsample of 303 UK Women's Cohort subjects. Nutrient values from the FFQ were compared with values from a 4-day food diary and also fasting blood measures of specific nutrients.[18]

This study examined amounts of dietary fibre in grams per day calculated by multiplying the frequency of consumption of each food by the nutrient content of the indicated portion size and summing overall foods. Nutrient composition of foods was taken from UK food composition tables[19]; Englyst fibre values were used in this report. Dietary fibre fractions were assessed by estimating the fibre consumption derived from the relevant foods or food groups.

Statistical methods

The relationship between fibre and breast cancer was explored using Cox's proportional hazards regression using Stata version 9.1.[20] Associations were estimated for pre-and post-menopausal women separately, first as a simple model adjusting for age and total energy intake, second as a full model adjusting for age, body mass index (BMI), physical activity (hours/day sufficiently vigorous to cause sweating), current smoking status, oral contraceptive use, HRT use, number of children, alcohol consumption and total energy intake at baseline. To take account of the stratified sampling scheme in the analysis, in all models, individuals were weighted by the inverse of the probability of being sampled. Sensitivity analyses were carried out (i) excluding women who were diagnosed with breast cancer within 1 year of completing the FFQ, (ii) excluding individuals with any previous malignant cancer and (iii) with further adjustment for dietary folate in light of concerns regarding the confounding effect of folate on dietary fibre.[10,21]

A second FFQ was taken from a sample of 1918 (5%) of the cohort from which the amount of random measurement error was estimated using a regression calibration approach[22,23] to obtain individual predicted values of dietary exposure for all participants. Cox's proportional hazards regression was then run using the predicted values for each individual categorized into quintiles to give estimated hazard ratios (HRs) corrected for some of the effects of measurement error. The 95% confidence intervals (CIs) were obtained from bootstrapped estimates.[24]

Table 1 Mean (SD) nutrient intakes for total sample and by breast cancer status

		Pre-menopausal women		Post-menopausal women	
	Total sample	Breast cancer $n=257$	Non-breast cancer $n=15\,694$	Breast cancer $n=350$	Non-breast cancer $n=17\,431$
Calories including alcohol	2361 (801)	2322 (710)	2358 (710)	2300 (657)	2336 (719)
Protein (g)	90 (32)	88 (26)	87 (27)	91 (28)	91 (28)
Energy from protein(%)	15.1 (2.5)	15.0 (2.7)	14.7 (2.4)	15.6 (2.5)	15.4 (2.6)
Carbohydrate (g)	315 (113)	307 (104)	313 (103)	307 (97)	313 (106)
Energy from carbohydrate(%)	52.6 (7.0)	52.2 (6.8)	52.5 (6.8)	52.7 (7.3)	52.8 (7.1)
Sugars (g)	148 (60)	141 (65)	145 (58)	151 (57)	152 (62)
Starch (g)	157 (59)	157 (58)	160 (59)	149 (57)	153 (59)
Fat (g)	85 (36)	84 (32)	86 (32)	82 (29)	84 (32)
Energy from fat(%)	32.4 (5.8)	32.7 (5.6)	32.7 (5.8)	32.0 (5.8)	32.2 (5.8)
Fibre (Englyst) (g)	26 (11)	25 (11)	25 (10)	25 (9)	26 (11)
Vitamin C (mg)	172 (92)	159 (72)	166 (84)	178 (81)	175 (88)
Folate (μg)	404 (146)	390 (126)	395 (131)	399 (119)	407 (138)
Vitamin A (μg)	1249 (633)	1184 (592)	1173 (547)	1314 (620)	1300 (633)
Iron (mg)	18.9 (8.1)	18.2 (7.1)	18.5 (7.3)	18.7 (6.8)	19.1 (8.0)
Calcium (mg)	1141 (411)	1120 (409)	1129 (378)	1133 (366)	1144 (382)
Zinc (mg)	11.5 (4.3)	11.2 (3.5)	11.2 (3.7)	11.8 (3.8)	11.7 (3.9)

Results

The mean (SD) age of the cohort subjects was 52 (9) years at baseline, 44.8 (4.5) years for pre-menopausal women and 58.8 (7.5) years for post-menopausal women. The majority of the women were white (99%), married (75%) with children (86%) and middle class (63% National Statistics-Socio Economic Class 1—Professional and Managerial class[25]). The cohort were well educated (27% had a degree) and over half were currently in employment. The mean (SD) BMI of the women was 24.5 (4.3) kg/m^2. Only 11% of the cohort were current smokers. Further details of the cohort have been reported elsewhere.[14]

Cohort food and nutrient characteristics

Eighteen per cent (6224) of the women were vegetarian based on meat eating frequency from the FFQ, 12% (3961) were fish eaters and 70% (23547) meat eaters. The mean energy intake was 2361 kcal (median 2261 kcal) with 32%, 53% and 15% of energy provided by fat, carbohydrate and protein, respectively. Mean (SD) dietary fibre intake was high at 26 (11) g/day, and was highest amongst the fish eaters at 29 (11) g/day compared with vegetarians 28 (11) g/day and meat eaters 24 (10) g/day. Vitamin and mineral intakes from the diet, excluding supplements, were also high as illustrated by the mean vitamin C intake (172 mg, median 156 mg). Further nutrients are presented in Table 1.

In post-menopausal women, nutrient intakes did not differ greatly between those with and without breast cancer. Pre-menopausal women with breast cancer had a higher percentage of energy derived from protein and also lower total carbohydrate, sugar, dietary fibre (Englyst) and vitamin C compared with cancer-free women. Only the difference in percentage energy from protein was statistically significant in this univariable analysis.

Fibre models

In the basic multivariable analysis, total fibre intake in pre-menopausal women was inversely related to risk of breast cancer. In the more complex model, the strength of association increased showing an inverse relationship of total fibre intake with risk of breast cancer (P for trend $=0.01$) (Table 2).

Exploring the sources of fibre showed that in pre-menopausal women, fibre from cereals was inversely associated with risk of breast cancer (P for trend $=0.05$) and fibre from fruit had a borderline non-significant inverse association (P for trend $=0.09$) (Table 2). There were no significant relationships between breast cancer and total fibre or fibre from cereals, fruit or vegetables in post-menopausal women.

Results from the sensitivity analysis after excluding women diagnosed within a year of completing the FFQ were not appreciably altered. Excluding all women with any malignant cancer prior to the study commencing did not alter the conclusions either. Including dietary folate as a potential confounder in addition to the other variables in the original complex model strengthened the significance of the inverse relationship between total fibre and pre-menopausal breast cancer (HR comparing top with bottom quintile 0.33; 95% CI 0.14–0.79; P for trend $=0.003$).

Discussion

The most important finding was that in this cohort, total fibre intake was protective against breast cancer in pre-menopausal women. This effect was not seen in the post-menopausal women. Exploring the sources of dietary fibre showed that cereal fibre is protective against breast cancer pre-menopausally and that fruit fibre, although not statistically significant, was potentially protective.

The mean FFQ derived fibre intake in the UKWCS was 26 g/day which is markedly higher than that reported in a

Table 2 Relative risks of pre- and post-menopausal breast cancer according to quintiles of fibre intakes and fibre fractions in the UK Women's Cohort

	Basic model[a]				Complex model[b]			
	Cases/non-cases	Person-years	Hazard Ratio	95% CI	Cases/non-cases	Person-years	Hazard Ratio	95% CI
Pre-menopausal women								
Total fibre quintiles (range, g)								
Quintile 1 (<20)	51/3136	23 154	1	–	47/2851	21 066	1	–
Quintile 2 (20,23)	56/3131	23 161	1.16	0.75–1.81	54/2845	21 083	1.14	0.72–1.81
Quintile 3 (23,26)	66/3122	23 375	1.18	0.78–1.80	60/2838	21 231	1.05	0.64–1.72
Quintile 4 (26,30)	40/3147	23 582	0.63	0.36–1.08	35/2864	21 456	0.63	0.34–1.17
Quintile 5 (30+)	44/3144	23 881	0.61	0.34–1.10	36/2863	21 753	0.48	0.24–0.96
Trend				*P = 0.03*				*P = 0.01*
Cereal fibre quintiles (range, g)								
Quintile 1 (<4)	55/3132	23 137	1	–	54/2844	21 049	1	–
Quintile 2 (4,7)	53/3134	23 288	1.02	0.68–1.53	51/2848	21 155	1.06	0.72–1.58
Quintile 3 (7,9)	54/3134	23 395	0.84	0.51–1.37	45/2853	21 309	0.73	0.46–1.15
Quintile 4 (9,13)	47/3140	23 589	0.83	0.52–1.33	40/2859	21 476	0.68	0.42–1.09
Quintile 5 (13+)	48/3140	23 744	0.68	0.35–1.33	42/2857	21 599	0.59	0.32–1.10
Trend *1*				*P = 0.20*				*P = 0.05*
Fruit fibre quintiles (range, g)								
Quintile 1 (<2)	51/3136	23 181	1	–	48/2850	21 083	1	–
Quintile 2 (2,3)	68/3119	23 297	1.42	0.96–2.12	64/2835	21 191	1.36	0.89–2.06
Quintile 3 (3,4)	51/3137	23 385	0.97	0.62–1.52	43/2855	21 278	0.81	0.50–1.32
Quintile 4 (4,6)	39/3148	23 527	0.60	0.38–0.97	36/2863	21 408	0.61	0.36–1.04
Quintile 5 (6+)	48/3140	23 762	0.89	0.55–1.42	41/2858	21 628	0.81	0.44–1.49
Trend				*P = 0.24*				*P = 0.09*
Vegetable fibre quintiles (range, g)								
Quintile 1 (<3)	42/3145	23 450	1	–	40/2858	21 316	1	–
Quintile 2 (3,4)	66/3121	23 272	1.57	1.03–2.38	57/2842	21 201	1.45	0.93–2.26
Quintile 3 (4,5)	47/3141	23 360	1.23	0.76–2.00	44/2854	21 223	1.15	0.73–1.82
Quintile 4 (5,7)	58/3129	23 432	1.61	1.02–2.53	52/2847	21 318	1.62	0.99–2.65
Quintile 5 (7+)	44/3144	23 639	1.32	0.77–2.24	39/2860	21 530	1.26	0.73–2.18
Trend				*P = 0.78*				*P = 0.96*
Post-menopausal women								
Total fibre quintiles (range, g)								
Quintile 1 (<21)	61/3489	24 149	1	–	52/3018	20 950	1	–
Quintile 2 (21,23)	73/3477	24 420	1.40	1.02–1.91	60/3011	21 213	1.40	0.96–2.03
Quintile 3 (23,26)	78/3473	24 637	1.31	0.92–1.88	65/3005	21 348	1.49	1.00–2.24
Quintile 4 (26,30)	79/3471	24 845	1.31	0.94–1.84	63/3008	21 541	1.34	0.87–2.07
Quintile 5 (30+)	59/3492	25 501	1.14	0.72–1.81	46/3025	22 128	1.18	0.70–1.99
Trend				*P = 0.70*				*P = 0.97*
Cereal fibre quintiles (range, g)								
Quintile 1 (<4)	60/3490	24 273	1	–	48/3022	21 074	1	–
Quintile 2 (4,7)	79/3471	24 469	1.36	0.94–1.97	69/3002	21 232	1.50	1.05–2.16
Quintile 3 (7,9)	76/3475	24 662	1.35	0.92–1.99	66/3004	21 347	1.53	1.03–2.29
Quintile 4 (9,13)	71/3479	24 897	1.31	0.92–1.88	54/3017	21 611	1.25	0.81–1.93
Quintile 5 (13+)	64/3487	25 251	1.23	0.77–1.95	49/3022	21 916	1.15	0.68–1.94
Trend				*P = 0.96*				*P = 0.89*
Fruit fibre quintiles (range, g)								
Quintile 1 (<2)	57/3493	24 252	1	–	50/3020	21 042	1	–

Continued

Table 2 *Continued*

	Basic model[a]				Complex model[b]			
	Cases/non-cases	Person-years	Hazard Ratio	95% CI	Cases/non-cases	Person-years	Hazard Ratio	95% CI
Quintile 2 (2,3)	70/3480	24 477	1.15	0.79–1.67	60/3011	21 233	1.17	0.79–1.72
Quintile 3 (3,5)	80/3471	24 656	1.46	1.04–2.05	65/3005	21 367	1.47	1.00–2.16
Quintile 4 (5,7)	78/3472	24 877	1.33	0.94–1.87	59/3012	21 599	1.22	0.80–1.86
Quintile 5 (7+)	65/3486	25 289	1.17	0.75–1.84	52/3019	21 939	1.10	0.66–1.84
Trend				*P* = 0.58				*P* = 0.64
Vegetable fibre quintiles (range, g)								
Quintile 1 (<3)	68/3482	24 403	1	–	56/3014	21 165	1	–
Quintile 2 (3,4)	62/3488	24 655	0.90	0.63–1.29	48/3023	21 424	0.86	0.57–1.29
Quintile 3 (4,6)	75/3476	24 640	1.22	0.85–1.76	64/3006	21 362	1.32	0.87–2.01
Quintile 4 (6,8)	75/3475	24 760	1.23	0.85–1.79	61/3010	21 464	1.27	0.85–1.92
Quintile 5 (8+)	70/3481	25 094	1.21	0.82–1.77	57/3014	21 766	1.20	0.74–1.94
Trend				*P* = 0.69				*P* = 0.40

All types of fibre corrected for measurement error.

[a] Adjusted for age and total energy intake corrected for measurement error.

[b] Adjusted for age, BMI, physical activity, current smoking status, oral contraceptive use, hormone replacement therapy use, number of children, alcohol intake, total energy intake corrected for measurement error.

national survey of UK adults using the food diary technique.[26] In the UKWCS, more than 80% of women eat more fibre than the national average of 12 g/day. The women tend to consume more fruits and vegetables than an average person in the UK. Although this mean is high, it is similar to intakes observed in other cohort studies using FFQ-based dietary assessments.[14,27] The EPIC Oxford cohort found that women who were meat eaters had a fibre intake of 19 g/day and women who were vegetarians ate 22 g fibre/day.[28]

This is the first large prospective study to show a relationship between total fibre intake and risk of pre-menopausal breast cancer. Previous analysis from the Canadian National Breast Screening Study did not find any relationship between fibre or fibre fractions and breast cancer risk, however, that study combined pre- and post-menopausal status.[9] The Nurses Health Study also reported no relationship between fibre or fibre fractions and risk of breast cancer, a specific analysis of 714 cases of pre-menopausal breast cancer did not find a strong association with fibre intake.[29] That cohort may have been too homogeneous with respect to fibre intake since only 0.7% consumed as much as 30 g fibre/day whereas 28% of the UKWCS consumed at least 30 g fibre/day. However, in that cohort there was a suggestion of reduced risk when comparing those who ate >30 g fibre/day with those eating <10 g/day (HR 0.68; 95% CI 0.43–1.06).[8] A number of case-control studies have shown inverse associations with dietary fibre and risk of breast cancer[30–33] for both pre- and post-menopausal women.

Our results are particularly informative because they also show that fibre from cereals and potentially also from fruit may be the important sources of fibre resulting in this inverse relationship with breast cancer pre-menopausally. Epidemiological studies exploring intakes of fruits and vegetables and risk of breast cancer have shown conflicting results. A meta-analysis of 26 cohort and case-control studies found no association with fruit and breast cancer risk although there was an inverse relationship with vegetable consumption.[1] A pooled analysis of eight cohorts found no significant relationship between fruit or vegetable intakes and risk of breast cancer.[34] However, the amounts and specific types of fruits and vegetables consumed may influence results obtained. A case-control study from France has shown that cereal fibre is protective against breast cancer with an odds ratio (OR) of 0.56 (95% CI 0.31–1.03) comparing the top (>5.6 g/day) with the bottom quintile (≤3 g/day) of intake and with a significant test for trend ($P = 0.03$).[30,33] Our cohort had a much wider range of intakes of cereal fibre than in that study.

Our assessment of total fibre used the Englyst values for non-starch polysaccharides from the UK composition of foods database.[19] This includes only the polysaccharide components of cell walls and as such tends to produce somewhat lower values than the other common method for assessing dietary fibre which is based on the weight of residual matter following enzymic treatment of food.[35] However, for fruit and vegetable fibre, the estimates do not differ greatly. The Association of Official Analytical Chemists (AOAC) method may overestimate at the lower end of the scale, but the Englyst method may underestimate at the upper end of the scale, since lignans are not included.[36] Non-starch polysaccharides are the most abundant components of plant cell walls and have been considered to have protective properties. It may be that other aspects of a high fibre diet are important such as the combination of micronutrients including antioxidant vitamins and glycaemic index.[8] However, when we included folate in our complex model as an additional confounder the strength of the association with fibre was increased. Studies which have explored the risk of colon cancer in relation to dietary fibre have been inconsistent in their findings and this has been ascribed, at least in part, to the lack of adjustment for dietary folate consumption which has been positively correlated with dietary fibre intake.[37]

As well as allowing exploration of higher fibre intakes, the wide range of dietary intakes that our study was designed to include reduces the impact of measurement error.[15–17] In the presence of measurement error, which occurs in every dietary

assessment study, selecting a population with larger exposure variance compared with one with smaller variance allows the study sample size to be reduced by a factor equal to the ratio of the smaller to larger variance.[17] We further corrected for bias from the random component of measurement error in the FFQ through use of a replicate FFQ measure. However, this does not correct for other components of measurement error and may represent incomplete correction for measurement error bias. Other studies have shown that using food diaries may result in even stronger estimates.[38] No biomarkers exist for fibre intake with which to calibrate FFQs or food diaries.

Our analysis adjusted for most of the major lifestyle factors which could act as confounders of the relationship between dietary fibre and breast cancer. It could be that adjustment for other factors such as use of dietary supplements or family history of breast cancer would have been informative. We had information on the use of any dietary supplements and also whether the subjects' parents had ever suffered from cancer or heart disease. Inclusion of these variables as proxies in further sensitivity analyses did not affect the overall results. Residual confounding due to incomplete adjustment from unmeasured or poorly measured confounders is still a possibility.

Although we could not find any other cohort studies of fibre and breast cancer risk which had reported results for pre- and post-menopausal women which differed in the same way as our results, one case-control study by McCann *et al*.[33,39] found that pre-menopausal women in the highest quartile of dietary lignan intake had reduced breast cancer risk (OR 0.66; 95% CI 0.44–0.98) whereas no association was observed between lignan intakes and post-menopausal breast cancer. Particularly rich sources of lignans are seeds and wholegrains which are also good sources of fibre.

Interestingly, we did not observe a protective effect of fibre intake post-menopausally. The oestrogen metabolism pathway differs between pre- and post-menopausal women.[40] The endocrine basis of premenopausal breast cancer is not clear. Hyperandrogenism with luteal inadequacy could induce breast cancer or alternatively excess oestrogen plus progesterone, particularly during the luteal phase may be involved.[41] Elevated blood concentrations of androgens have been associated with an increased risk of breast cancer in pre-menopausal women in a nested case-control analysis from the European Prospective Investigation into Cancer study.[5] Diets high in fibre and low in fat have been shown to affect sex hormone levels.[5,42,43] Two small studies which supplemented women with wheat bran showed differing results. Pre-menopausal women who were supplemented with 10 or 20 g wheat bran/day for 2 months found a significant reduction in oestradiol concentrations[44] whereas a study of post-menopausal women found no effect of supplementation with wheat bran on oestradiol, androstenedione or sex hormone-binding globulin.[45] A high fibre or vegetarian diet also influences cycle length in pre-menopausal women which is linked to oestrogen exposure, but clearly does not have this effect in post-menopausal women.[46]

Other mechanisms, such as a route through glucose metabolism, may be involved. Glucose is a key substrate for neoplastic cell proliferation and insulin is a powerful mitogenic agent. Associations of breast cancer risk with glucose, insulin and IGF-I pattern for post-menopausal women were generally weaker than for pre-menopausal women and not statistically significant in a nested case-control study from Italy.[47]

It is possible that other factors such as body size or weight gain from early adult life to after the menopause may have an overriding impact on sex hormone levels post-menopausally and that this could explain why the protective effect was only seen pre-menopausally. Weight gain has been consistently shown to be related to increased risk of post-menopausal breast cancer.[4,48–51] Adult weight gain reflects body fat content. Oestrogens derived from aromatization of androstenedione in peripheral fat may account for the increased risk of breast cancer observed among post-menopausal obese women.[33] Weight gain post-menopausally may outweigh any other dietary effects. Genes which pre-dispose to earlier breast cancer may work through influencing hormone concentrations, which can also be modified by diet.[52,53] Alternatively, the relevant dietary exposure may be earlier in life, so pre-menopausal women are closer to the relevant time window and hence less subject to the effect of measurement error bias.

In summary, dietary fibre has a protective effect against pre-menopausal breast cancer in this cohort. This was not seen for women who were post-menopausal. The specific food sources of this dietary fibre which had a protective effect pre-menopausally were cereals and possibly fruit.

Contributors

J.E.C. initiated and developed the cohort and made a primary contribution to the analysis and writing of the report. V.J.B. managed the cohort and was responsible for quality control of all procedures and contributed to the data analysis. D.C.G. has been the cohort statistician and undertook the analysis and made a primary contribution to writing the report. The Steering Group had oversight of the conduct of the cohort.

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KEY MESSAGES

- Dietary fibre protects against pre-menopausal breast cancer in this cohort.
- There was no evidence for any association between dietary fibre and post-menopausal breast cancer in this cohort.
- Fibre from cereals and possibly from fruit are the specific food sources of dietary fibre which may be protective against pre-menopausal breast cancer.

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