

Dietary fibre and risk of colorectal cancer in the Breast Cancer Detection Demonstration Project (BCDDP) follow-up cohort

Volker Mai, Andrew Flood, Ulrike Peters, James V Lacey Jr, Catherine Schairer and Arthur Schatzkin

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Background The hypothesis that increased intake of dietary fibre lowers the risk of colorectal cancer (CRC) has recently been weakened by results from cohort and intervention studies that did not detect such an association. We investigated the association between dietary fibre intake and risk of CRC in a cohort of women that prospectively answered a food frequency questionnaire (FFQ).

Methods We studied 45 491 women in the Breast Cancer Detection Demonstration Project (BCDDP) follow-up cohort. A 62-item FFQ was administered from 1987 and 1989 to assess dietary intake. Participants received follow-up questionnaires (in 1992–1995 and 1995–1998) on which they reported incident cancers. Cases were also identified through searches of the National Death Index and state cancer registries. Cox proportional hazard regression was used to generate risk ratios and 95% CI for quintiles of total fibre intake and fibre subtypes.

Results During a mean follow-up time of 8.5 years we identified 487 colorectal cancer cases. The 10th and 90th percentiles of dietary fibre intake were 5.4 g and 18.2 g respectively. For total fibre we observed no association with colorectal cancer (fifth versus first quintile, RR = 0.94, 95% CI: 0.71–1.23). Analyses by subgroup of fibre and by anatomical subsite did not reveal any stronger inverse associations.

Conclusions Within a cohort of older women characterized by a relatively low fibre intake, there was little evidence that dietary fibre intake lowers the risk of colorectal cancer.

Keywords Cancer, cohort, colon, dietary fibre, nutrition, rectum

Colorectal cancer (CRC) is the second most common cancer (excluding non-melanoma skin cancer) in the US and the fourth most common cause of death from cancer worldwide. Epidemiological studies suggest that environmental factors contribute to the aetiology of colorectal cancer. Burkitt proposed an association between high fibre intake and colorectal cancer (CRC) based on the low age-adjusted rates of CRC reported in various rural regions in Africa.¹ Due to the observations that rural Africans (1) eat a diet rich in fibre from unrefined grains and/or leafy vegetables and (2) defecate stools that are bulkier, softer and less odorous than the stools of Westerners, he proposed a protective effect of fibre on CRC.

Several epidemiological studies, especially ecologic and case-control studies, have shown an inverse association between

dietary fibre and colorectal cancer. However, recent prospective studies like the Nurse's Health Study² and a study of a Swedish mammography-screening cohort³ reported no relation between fibre intake and colon cancer incidence. Furthermore, increased dietary fibre intake did not reduce colorectal adenoma recurrence in three recent clinical trials.^{4–6}

We evaluated the association between total dietary fibre intake and incident CRC in a cohort of 45 491 women that had previously participated in the Breast Cancer Detection Demonstration Project (BCDDP). We also analysed the data for associations between source of fibre (fruits, vegetables, beans, grains) and cancer by location (colon, rectum, descending and sigmoid colon, and caecum and ascending colon).

Subjects and Methods

Study population

The BCDDP was a breast cancer-screening programme conducted by the National Cancer Institute (NCI) and the American Cancer Society. The project enrolled 283 222 women and ran

Division of Cancer Epidemiology and Genetics, National Cancer Institute, Bethesda, MD, 20892, USA.

Correspondence: Volker Mai, Division of Epidemiology and Preventive Medicine, University of Maryland School of Medicine, 10 South Pine St, MSTF-934, Baltimore, MD 21201, USA. E-mail: vmai@epi.umaryland.edu

from 1973 through 1980 at 29 screening centres in 27 cities across the US. The BCDDP follow-up cohort was established in 1979 from a subset of women enrolled in the original BCDDP.⁷ The follow-up study comprised all 4275 women from the BCDDP who had been diagnosed with primary breast cancer, all 25 114 women who had undergone a breast biopsy that indicated benign breast disease, and all 9628 women who had been recommended for breast biopsy or breast surgery but who did not have the procedure. In addition, the follow-up cohort included 25 165 women with no history of breast disease who were matched with the breast cancer and benign breast disease subjects on age, time of study entry, ethnicity, screening centre, and length of participation.

The BCDDP follow-up study has proceeded in several phases beginning with baseline interviews between 1979 and 1981. A total of 61 429 of the invited women (96%) gave informed consent and completed the baseline questionnaire, which was updated annually for up to 6 years by telephone interviews. Participants completed additional mailed questionnaires during three separate follow-up periods: 1987–1989, 1992–1995, and 1995–1998. We contacted non-responders with additional mailings and phone calls. Each follow-up questionnaire updated existing data, collected information about additional presumed risk factors, and provided self-reports of any newly diagnosed cancers.

Dietary assessment

The 62-item Block/NCI food frequency questionnaire (FFQ) was included in the 1987–1989 questionnaire. This FFQ, which captures usual dietary intake over the previous year, has been described and evaluated elsewhere.⁸ Estimates of daily nutrient intake, including dietary fibre, were calculated by software specifically designed for this FFQ.⁹ Fibre subtypes were calculated based on the food source of the fibre and separated into fruit, vegetable, bean, and grain fibre.

Analytical cohort

We excluded women who did not complete a 1987–1989 questionnaire ($n = 9740$), and women with a CRC diagnosed before the 1987–1989 questionnaire ($n = 479$). In order to avoid inclusion of unrealistic dietary intake data we also excluded women who skipped more than 30 items on their FFQ or reported a calculated energy intake outside the range of 400–3800 kcal per day ($n = 5647$). For this analysis we also excluded subjects who reported consuming more than 16 servings of fruit or vegetables per day ($n = 72$). The final analytical cohort consisted of 45 491 individuals.

The follow-up period for each subject extended from the completion date for the 1987–1989 questionnaire until the date of the earliest of the following events: death; colorectal cancer diagnosis; completion of 1995–1998 questionnaire; or study end-date. For subjects who did not complete questionnaires subsequent to the 1987–1989 questionnaire and who were not identified as deceased the study end-date was calculated as follows: the end-date of the follow-up period was the date of last contact during 1995–1998 for subjects who were contacted. For those who could not be contacted, the end-date of the follow-up period was calculated as the date their last questionnaire was completed plus the average cohort follow-up time subsequent to that questionnaire. We were able to follow-up

90.8% of the final cohort through 1995–1998, meaning that they either answered the 1995–1998 questionnaire or were identified as dead.

Case ascertainment

We defined cases as all invasive carcinomas of the colon or rectum. Cases were identified through self-reports from the 1993–1995 and 1995–1998 questionnaires. Pathology reports were sought from all self-reported colorectal cancers. We obtained pathology reports for 245 of 311 (79%) self-reported CRC. Due to the high confirmation rate for the subjects for which we were able to obtain both pathology and self-reports (94%), we decided to include self-reported CRC from subjects from whom we were unable to obtain medical records. Subjects whose pathology reports contradicted their self-reports were excluded as cases in the analyses unless state cancer registry data confirmed the self-report. We identified additional cases from pathology reports of other self-reported medical conditions ($n = 17$). We also included cases that were identified by the National Death Index ($n = 107$) and by state cancer registries ($n = 66$). The additional cases identified through state cancer registries were not previously identified from self-reports, path reports, and death certificates. Of the cohort members, 71% resided in states that had cancer registries and provided access to their files. All identified cases were verified by manually matching the identifiers from the state cancer registry file with the identifiers in the BCDDP follow-up cohort file. Our final cohort yielded 487 cases; 308 of these were verified by secondary sources.

Statistical analysis

We used Cox proportional hazards (proc PHREG in SAS version 6.12) with age as the underlying time metric (adjusted by left truncation) to generate rate ratios (RR). We also applied a spline modelling approach to examine the data on a continuous scale without linearity assumptions. The knots in the model were set as the 10th, 30th, 50th, 70th, and 90th percentiles, corresponding to the medians of the five intake quintiles.

Total dietary fibre intake was expressed in terms of grams of dietary fibre per 1000 kcals of total energy intake per day. Similarly, intakes for fibre subgroups were calculated as grams of fibre from fruits, vegetables, grains, and beans per 1000 kcals. We created specific fibre intake groups for fruit fibre, vegetable fibre, grain fibre, and bean fibre by calculating the fibre content of each food item assigned to a specific fibre intake group and multiplying this value by the amount of the food consumed.

Covariates such as usual alcohol intake, smoking history (ever/never), BMI (body mass index, weight in kg/height in m^2), physical activity (average weekday activity in metabolic equivalent time), and level of education (high school graduate or less/at least some college) were ascertained from the 1987–1989 questionnaire. History of non-steroidal anti-inflammatory drug (NSAID) use was assessed with the 1993–1995 questionnaire and classified as yes/no with respect to ever having been a regular user, defined as taking at least one tablet weekly over a period of at least one year (excluding Tylenol).

We evaluated possible confounders by adding known risk factors individually and simultaneously to the unadjusted model. Covariates evaluated in multivariate models included NSAID-use, smoking, education, BMI, red meat intake, percentage of calories from fat, vitamin D intake, alcohol intake,

and physical activity. We adjusted for energy using the nutrient density method, in which dietary fibre is expressed as grams per 1000 kcal, in all models. In addition, total energy intake was included as a covariate in some models (standard model).¹⁰ Standard multivariate models that included total energy intake showed associations similar to the ones observed in nutrient density models.

We analysed the association between fibre subgroups and CRC by modelling each subgroup in a substitution model (total dietary fibre included in the model) and an addition model (all other fibre subgroups individually included in the model). In addition models, fibre subgroups other than the one under investigation are held constant; in substitution models, an increase in the fibre intake from one subgroup is accompanied by a decrease in the combined intake from the other subgroups. We also analysed the effects of dietary fibre intake on CRC by anatomical subsite (colon, rectum, descending and sigmoid colon, and caecum and ascending colon) for cases for which this information was available. Finally, we performed analyses stratified by categories of a number of covariates, including BMI, NSAID-use, calcium intake, and fat intake.

Results

During an average follow-up of 8.5 years we observed a total of 386 186 total person years. Table 1 shows characteristics of study subjects in quintiles of dietary fibre density intake. The mean total fibre intakes for the first and fifth quintiles were 7.1 and 16.7 g/day/1000 kcal respectively. Subjects in the highest quintile of fibre intake were slightly older, had a lower BMI, consumed fewer total calories, dietary calcium, and less alcohol and were less often smokers than subjects in the lowest quintile.

The RR for the quintiles of dietary fibre intake are shown in Table 2. The RR for the fifth versus the first quintile of total fibre/1000 kcal intake was 0.94 (95% CI: 0.71–1.23) in the unadjusted and 0.94 (95% CI: 0.70–1.26) in the fully adjusted model. There was no evidence of a linear dose-response

relationship. Excluding 76 cases that were diagnosed during the first 2 years of follow-up did not alter the results. The spline-model results also did not suggest a relationship between dietary fibre intake and colorectal cancer. The stratified analyses showed small inverse but non-significant associations between dietary fibre and CRC in the strata with the highest BMI, the highest percentage of calories from fat, and among NSAID non-users, but there was little systematic evidence of effect modification.

We calculated risk ratios for the fifth versus the first quintile of intake for specific fibre subgroups (fibre from fruits, vegetables, beans, grains, and all combinations) in addition, as well as substitution models that were adjusted for total calorie intake, NSAID-use, and smoking status. These subgroup analyses did not reveal any fibre source that conferred a statistically significant risk reduction for CRC. Fibre from beans exhibited the strongest association (RR = 0.84; 95% CI: 0.63–1.1) (Table 2).

The analysis of the associations between total dietary fibre intake and fibre intake from various sources with cancer of the colon, rectum, descending and sigmoid colon, and caecum and ascending colon did not show a statistically significant association between dietary fibre intake and cancer incidence for any of these subsites (data not shown).

Discussion

We did not observe a significant inverse association between fibre intake and CRC. If there is a true inverse association between dietary fibre intake and colorectal cancer, these results and those from some recent prospective studies could be due to several factors including: (1) the limited dietary fibre intake range that is observed in the BCDDP as well as in other Western cohorts, (2) misclassification of true fibre intake due to mis-reporting and a limited ability to evaluate long-term dietary exposure, (3) little information on the physiologically relevant fibre subgroups, and (4) limited power to determine an association between dietary fibre and CRC at specific anatomical subsites.

Table 1 Characteristics of study subjects (means and percentages) by quintiles (Q1–Q5) of fibre density intake (gramme of fibre/day/1000 kcal) in the Breast Cancer Detection Demonstration Project follow-up study

N = 45 491	Q1	Q2	Q3	Q4	Q5
Fibre (g/day)	7.1	9.7	11.3	12.8	16.7
Fibre (g/1000 kcal)	4.9	7.2	8.8	10.7	14.8
Fibre from fruits (g/1000 kcal)	0.5	1.2	1.9	2.9	5.4
Fibre from vegetables (g/1000 kcal)	1.0	1.7	2.3	3.0	4.9
Fibre from beans (g/1000 kcal)	0.1	0.3	0.6	1.1	2.5
Fibre from grains (g/1000 kcal)	1.3	2.2	3.0	4.0	6.6
Age (years)	60.4	61.2	62.0	62.6	63.0
Energy (kcal/day)	1445	1344	1280	1198	1126
Body mass index (kg/m ²)	25.1	24.9	24.7	24.5	24.1
Smoking (% ever)	50	44	41	41	39
Non-steroidal anti-inflammatory drugs (% reg. users)	38	40	39	39	38
Follow-up (years)	8.5	8.5	8.5	8.5	8.5
Dietary calcium (mg/day)	713	694	682	655	625
Alcohol (g/day)	6.6	4.3	3.7	3.0	2.1

Table 2 Relative risk of colorectal cancer by quintile of fibre intake

	Quintiles				
	1	2	3	4	5
Total fibre					
Range in g/1000 kcal	<6.3	6.3–7.99	8–9.69	9.7–11.99	>12
No. of cases	99	92	72	113	111
RR unadjusted (95% CI)	1.00	0.88 (0.66–1.16)	0.65 (0.48–0.88)	0.99 (0.75–1.30)	0.94 (0.71–1.23)
RR fully adjusted ^a (95% CI)	1.00	0.90 (0.67–1.19)	0.67 (0.49–0.91)	1.00 (0.76–1.33)	0.94 (0.70–1.26)
Fruit fibre					
Range in g/1000 kcal	<0.90	0.90–1.57	1.57–2.37	2.37–3.57	>3.57
No. of cases	90	95	96	86	120
RR unadjusted (95% CI)	1.00	0.98 (0.74–1.31)	0.96 (0.72–1.28)	0.83 (0.61–1.12)	1.10 (0.83–1.46)
Vegetable fibre					
Range in g/1000 kcal	<1.44	1.44–1.99	1.99–2.59	2.59–3.48	>3.48
No. of cases	101	86	103	100	97
RR unadjusted (95% CI)	1.00	0.85 (0.64–1.13)	1.01 (0.77–1.34)	0.96 (0.72–1.26)	0.92 (0.69–1.21)
Bean fibre					
Range in g/1000 kcal	<0.20	0.20–0.47	0.47–0.81	0.81–1.38	>1.38
No. of cases	116	95	91	93	92
RR unadjusted (95% CI)	1.00	0.84 (0.64–1.11)	0.83 (0.63–1.09)	0.84 (0.64–1.11)	0.84 (0.63–1.10)
Grain fibre					
Range in g/1000 kcal	<1.80	1.80–2.58	2.58–3.46	3.46–4.75	>4.75
No. of cases	90	101	79	106	111
RR unadjusted (95% CI)	1.00	1.09 (0.82–1.45)	0.82 (0.60–1.10)	1.04 (0.78–1.38)	1.02 (0.76–1.37)

^a Adjusted for non-steroidal anti-inflammatory drugs, smoking, alcohol, calcium, vitamin D, red meat, height, body mass index, education.

The mean total dietary fibre intake in the highest quintile of fibre density intake was only 16.7 g/day, well below recommended minimum intake levels of 25–30 g/day. The original hypothesis that increased dietary fibre intake was associated with lower CRC was based on daily intakes of approximately 70 g.¹ It would be informative to investigate the effects of dietary fibre intake in populations that consume dietary fibre in amounts larger than those in typical Western cohorts.

Dietary fibre information derived from a 62-item FFQ may contain considerable errors, which would tend to attenuate true fibre-CRC associations. Because dietary habits might have changed prior to and after assessment, one-time administration of the FFQ might not accurately reflect long-term exposure. Our FFQ was designed to assess recent diet. If participation in the BCDDP programme caused study participants to alter their dietary habits, such that the FFQ responses no longer accurately reflected the fibre intake that was biologically relevant to colorectal carcinogenesis (a form of exposure misclassification), then we might have failed to observe a true association.

We note, however, that other cohort studies based on the administration of larger FFQ at multiple times also show null results for fibre and CRC.^{2,3} Moreover, some of these studies do observe protective associations between fibre intake and other chronic diseases^{11–13} (though we cannot rule out the possibility that these modest inverse associations are the attenuated products of even more substantial inverse relations). Our observational results, like those of other recent cohort studies, are consistent with the results of recent polyp trials in which increased dietary

fibre intake (as supplement or food) did not reduce colorectal adenoma recurrence.^{4–6} However, because there are potential limitations to both the observational studies (dietary measurement error, for example) and the trials (short follow-up in only those with previous adenomas), it would be premature to consider the issue resolved.

The average follow-up time of 8.5 years and the mean age of 62 years at the time of administration of the FFQ prohibit demonstrating the importance of diet early in life on carcinogenesis at advanced age. This is a limitation of most current prospective studies. Following many thousands of young people over several decades is a potential—though daunting—approach to this problem. Unfortunately the ability of FFQ to accurately assess early life diet is problematic.¹⁴

Difficulties with assessing dietary fibre intake are compounded by problems with defining substances that should be included as dietary fibre and measuring them accurately in foods. Various heterogeneous complex materials are included in any dietary fibre definition. Recently a panel convened by the Food and Nutrition Board at the Institute of Medicine suggested new definitions as follows: 1. *Dietary fibre* consists of non-digestible carbohydrates and lignin that are intrinsic and intact in plants, 2. *Added fibre* consists of isolated, non-digestible carbohydrates that have beneficial physiological effects in humans, and 3. *Total fibre* is the sum of *Dietary fibre* and *Added fibre*.¹⁵ If incorporated into food ingredient databases, these proposed definitions might be useful in quantifying dietary fibre in epidemiological studies, food labelling, and intake recommendations.

Many potential mechanisms have been proposed to explain the health-mediating effect of increased dietary fibre intake.^{16,17} For instance, fermentable fibre can be metabolized by the bacterial flora to short chain fatty acids. Butyrate has been especially shown to influence colorectal carcinogenesis. Furthermore, specific fermentable fibre has the potential to select for a beneficial composition of the flora by selectively enhancing the growth of bacterial groups that are associated with improved health including decreased CRC risk (such as certain Lactic acid bacteria and Bifidobacteria).¹⁸ Fermentation rates and bacterial growth are highest in the proximal colon and thus any beneficial effect of fermentable fibre might be limited to that anatomical site. Insoluble fibre might lower cancer risk by accelerating the fecal transit time, which in turn results in decreased exposure of the distal colon epithelium to fecal carcinogens. These few examples illustrate that most of the proposed beneficial effects of fibre are likely to be specific to the anatomical subsite and dependent on specific kinds of dietary fibre. However, our analyses did not reveal any fibre subgroup to be associated with colorectal cancer, nor was fibre associated with specific anatomical subsites. Due to the limited intake range of fibre subgroups in this cohort and the low number of cases for subsites, these analyses had little power to detect small associations. The dietary intake data from the 62-item FFQ did not allow us to separate fibre into soluble and insoluble fibre and thus we could not explore their specific associations with CRC. It would be important in subsequent epidemiological studies to collect data that allow for stratification by physiological property of the dietary fibre and by anatomical subsite (distal and proximal colon, rectum).

Some of the strengths of this study include the large sample size, large number of CRC cases, and the high follow-up proportion. We decided to include CRC cases that were identified through state cancer registries, even though 29% of the cohort members resided in states that did not have or did not give us access to their cancer registries. When we excluded cases that were identified through the state cancer registries only, the association between dietary fibre and CRC in the states that had cancer registries was very similar to the association observed in the entire cohort, indicating limited potential for bias due to the inclusion of the state cancer registries identified cases. Similarly,

exclusion of the 66 cases that were identified by self-reports only had minimal impact on the observed risk.

Early stages of CRC could influence the diet of affected subjects leading to a misclassification of their true long-term dietary exposure and a weakening of observed associations. The consistency of the results after exclusion of cases diagnosed during the first 2 years of follow-up suggests this as an unlikely problem in our study.

In summary, our study provides little evidence that dietary fibre reduces risk of CRC, though error in fibre assessment and limited intake range (for all and specific subgroups of fibre) may account for the null findings. We note that even if fibre intake should prove unrelated to colorectal carcinogenesis, there is evidence that increased fibre consumption is inversely related to the incidence of cardiovascular and other chronic diseases.

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KEY MESSAGES

- Increased dietary fibre intake might lower the risk for colorectal cancer.
- There was no evidence in our cohort of older women with overall low fibre intake that dietary fibre lowers the risk for colorectal cancer.

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Commentary: The rough world of nutritional epidemiology: Does dietary fibre prevent large bowel cancer?

Debbie A Lawlor and Andy R Ness

'Nutritional information seems awash with conflicting and contradictory messages, so it can be comforting to cling to advice that appears constant. One concept on which the nutritional cognoscenti are united is the value of eating a diet rich in fibre.'¹

This quote from a doctor writing in a British broadsheet newspaper illustrates many of the problems faced by nutritional epidemiologists and health practitioners who try to determine the health damaging and health promoting aspects of a population's diet and provide appropriate dietary advice to its members.¹ No doubt this doctor will be frustrated if he reads today's volume of the *International Journal of Epidemiology* (IJE) in which the findings of a prospective cohort study by Mai et al. suggest that diets rich in dietary fibre are not protective against colorectal cancer.²

Burkitt is credited with first proposing that dietary fibre was protective against colorectal cancer and other gastrointestinal problems including diverticular disease and appendicitis.^{3,4}

However, discussions about the value of white (of low fibre content) and brown (of high fibre content) bread date back to antiquity. Interestingly, Hippocrates, in the 5th century BC, believed white bread to be more nutritious:

'Wholemeal bread cleans out the gut and passes through as excrement. White bread is more nutritious as it makes less faeces.'⁵

In England the notion that wholemeal bread was good for health had emerged by the late 1500s, with Peter Stubbs writing in 1585

'doe we not see the poore man that eateth browne bread healthe fuller, stronger, fayrer complexioned and longer living than the other that faredaintelie every day.'⁶

In 1683 Tyron wrote a book about the value of wholemeal bread, stating that it was the most important way to a long and happy life.⁷ In the US in 1837 Sylvester Graham wrote on the importance of wholemeal bread as a natural food, and to this day wholemeal bread in the States is known as Graham bread.⁸

Wholemeal bread, known at that time in England as Graham bread, became popular among the upper classes, for the first time, when Queen Victoria took to eating it in 1847.⁵

Evidence from observational studies

The study by Mai *et al.* reported in this issue of the IJE examined the association between dietary fibre, estimated using a 62-item food frequency questionnaire, and colorectal cancer risk among 45 491 women who participated in the Breast Cancer Detection and Demonstration Project.² During a mean follow-up time of 8.5 years they observed no association between total dietary fibre and colorectal cancer; neither was there an association between specific types of dietary fibre and cancer nor between dietary fibre and cancer at different sites. Several limitations of this study may explain its null findings, and these are fully discussed by the authors. The mean fibre intake even amongst women in the highest quintile of intake in this study (16.7 g/day) was below the daily intakes recommended by US and UK advisory bodies (18–30 g/day),^{9,10} and considerably lower than the amounts that Burkitt first proposed were necessary to protect against cancer (70 g/day).⁴ Thus it may be that none of the women were consuming sufficient fibre to confer a protective effect. Misclassification may also have biased the results towards the null. Although there is debate about the validity of food frequency questionnaires, the degree of regression-dilution in estimating diet–disease outcomes may be considerable,^{11–14} and there were no repeat measures of dietary intake over the follow-up period.

A number of, largely hospital-based, case-control studies have found that dietary fibre is inversely associated with colorectal cancer,^{15,16} but the results from nested case-control studies or prospective cohort studies have been inconsistent, though results from three recent large studies, including that presented in today's IJE by Mai *et al.*, show no real benefit (Figure 1).^{17–24} The differences between these studies may be due to the heterogeneous nature of fibre and differences in the ways in which fibre has been measured in different studies. The strong inverse association found in the US health professionals study²⁰ was for cancers occurring within the first 2 years of dietary assessment and it is possible that some individuals who developed cancer already had symptoms at baseline and had adjusted their diets to relieve these. A longer, 6-year follow-up, of the same cohort found that the association was considerably weaker than that reported earlier.²¹ Although recent studies showing little or no protective effect of dietary fibre^{21–23} have been large and well-conducted, these null results may at least in part be explained by the low overall mean fibre intake in the study populations and regression-dilution bias as discussed above.

Evidence from randomized controlled trials

It is difficult to make sense of the findings from these observational studies. Dietary fibre may be protective but poor assessment tools and lack of repeat measures in most studies may bias the estimates towards the null. On the other hand it is possible that the protective effects in some studies are due to

Heilbrun 1989 Colon

Heilbrun 1989 Rectum

Willet 1990

Thun 1992 Women

Thun 1992 Men

Giovannucci 1992

Giovannucci 1994

Steinmetz 1994

Fuchs 1999

Terry 2001

Mai 2002

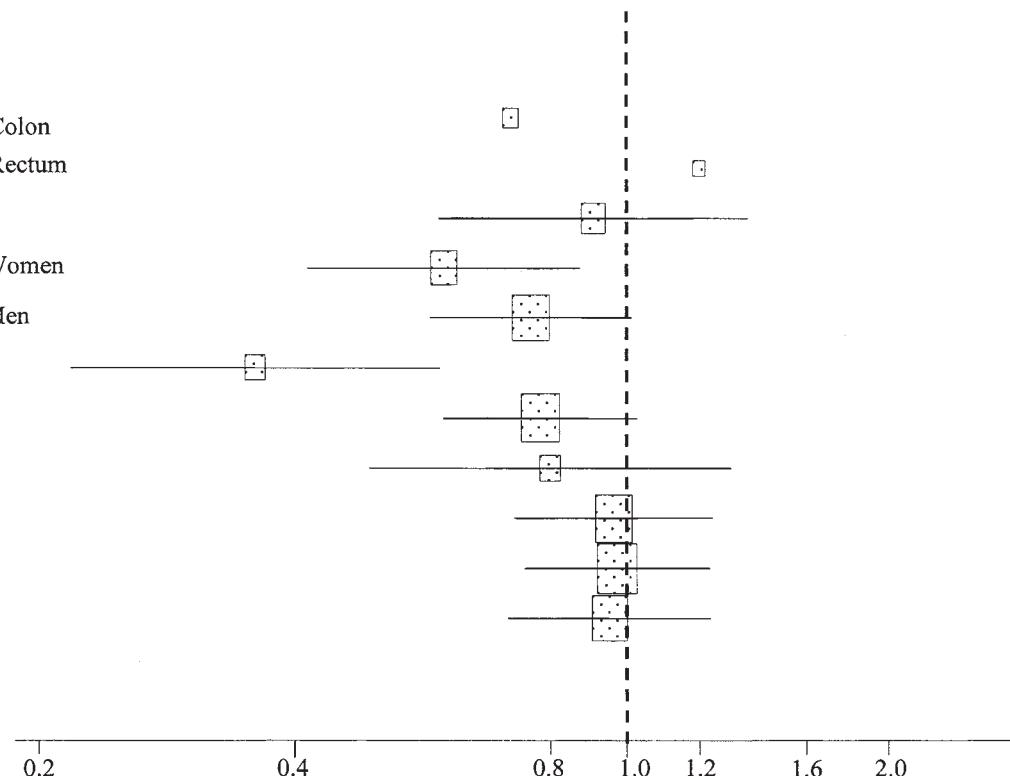


Figure 1 Relative risks (95% CI) comparing highest with lowest intakes of dietary fibre in nested case-control and prospective cohort studies. Produced using results from references 14–21

confounding. Randomized controlled trials could clarify this and are feasible. Dietary fibre intake can be substantially increased by simply adding a bran supplement to the diet or advising people to make simple changes such as switching to a high fibre breakfast cereal and changing to wholemeal bread, without the need for altering other aspects of the diet.²⁵ To date there have been five randomized trials of dietary fibre in high-risk patients—those with a previous history of an adenomatous polyp but no previous history of cancer.²⁶ None of these trials has found fibre to be effective at reducing the recurrence of polyps or the occurrence of colorectal cancer.²⁶ The follow-up time in these trials was 3–4 years and it is possible that a longer period is required for a protective effect to be detected. It is also possible that fibre may have a protective effect earlier in the disease process so that once adenomatous polyps have formed it is no-longer effective.

Mai *et al.* conclude that although their results suggest that fibre is not protective against bowel cancer the public should still be encouraged to consume a high fibre diet since there is good evidence that it is protective against cardiovascular and other chronic diseases.² However, if fibre really is protective against heart disease and cancers (the two biggest killers in the Western world) then one would expect it to have an important impact on all-cause mortality. To date randomized trials have found no evidence that dietary fibre confers any short-term benefit on all-cause mortality (Figure 2).^{27–29} Indeed, a large study on British men post myocardial infarction suggested, if anything, that mortality was higher among those allocated to dietary advice aimed at increasing fibre consumption.²⁷

Why was fibre thought to protect against colorectal cancer?

Burkitt's original hypothesis was that colorectal cancer, benign bowel tumours, diverticular disease, and appendicitis all shared a common aetiology: low levels of dietary fibre.^{3,4} This

suggestion was largely based on geographical comparisons. He noted that in the 1960s the age-standardized incidence rate for colorectal cancer among men aged 35–64 years varied from 3.5/100 000 in Uganda and 5.3/100 000 in Moçambique to 51.5/100 000 in Scotland and 51.8/100 000 in Connecticut, USA. Although Burkitt did not have data on dietary fibre intake for any of these countries his hypothesis was supported by his own knowledge of typical diets in Africa, Europe, and the US, and substantiated by his studies showing marked differences in bowel transit times between Africans and Europeans and in mean daily stool weight (500 g for African village children, 200 g for African children in missionary boarding schools, and 100 g for children in English boarding schools in one of Burkitt's studies).⁴ Further, he noted that African Americans had bowel cancer rates similar to those of European Americans, strongly suggesting environmental factors in its aetiology.

Epidemiologists are aware of the limitations of ecological studies and the need for individual-based analytical studies to provide good evidence of causation. At the same time, as Burkitt pointed out, and others have recently re-emphasized, explaining population differences in disease occurrences is also important.^{3,30} African populations today continue to experience lower levels of bowel cancer than Western populations,³¹ and the question remains as to whether this is due to differences in dietary patterns, and if so, what particular features of the diet are healthy or unhealthy.

Many people believe that the dietary habits adopted by Western societies over the last 150 years make important contributions to colorectal and other cancers, hypertension, diabetes, and coronary heart disease. It has been suggested that humans evolved to consume a Paleolithic diet (high animal protein, high fibre, low refined carbohydrate), and that we are therefore genetically determined to eat diets very different to those of today's Western societies.³² Recent evidence has challenged the idea that Paleolithic diets were high in animal fat and protein but the fibre content is likely to have been high.^{33–35} However, the fibre in Paleolithic diets was certainly of plant origin rather than cereal fibre that has been the major source of dietary fibre in Western and African diets for several hundred years.^{33–35} To this extent the notion that we need to consume a diet closer to our earliest origins is not consistent with Burkitt's hypothesis which was based on dietary fibre derived largely from cereals.^{3,4} The differences in dietary fibre content noted by Burkitt continue to present times. The mean consumption of cereal and starchy foods in Sub-Saharan Africa and South Asia greatly exceed those of Europe, the US, Australia, and New Zealand. However, the consumption of fruit and vegetables is considerably lower in Sub-Saharan Africa and South Asia than it is in Western countries.³⁶ Ecological data does not, therefore, suggest that fibre or other nutrients from fruit and vegetables protect against bowel cancer. Further, large cohort studies, including results from the Breast Cancer Detection and Demonstration Project published elsewhere suggest that fruit and vegetable consumption does not protect against colon cancer.^{37–39}

Conclusions

Thus, although the ecological differences in bowel cancer rates and consumption of cereal based dietary fibre noted over 30 years

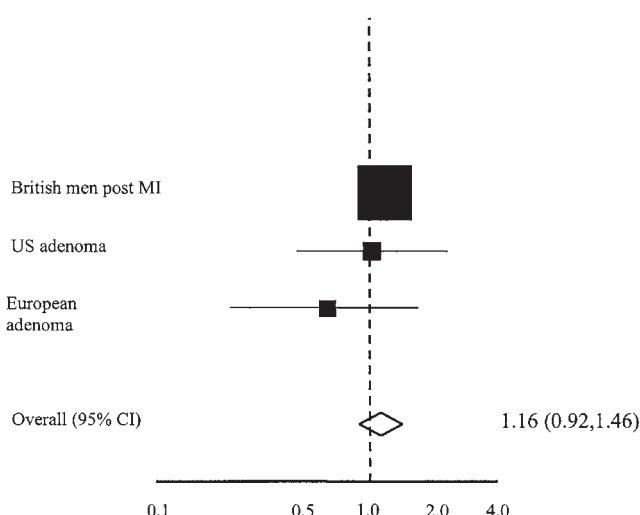


Figure 2 Pooled relative risk (95% CI) of all-cause mortality from randomized controlled trials of dietary fibre that reported on mortality

ago by Burkitt persist, recent evidence from prospective cohort studies and randomized controlled trials suggest that the two are not causally related. Examining ecological differences in disease can provide epidemiologists with clues as to the aspects of a population's habits that are health protective and those which are damaging to health. Further work is required to determine what aspect or aspects of African life styles protect from bowel cancer.

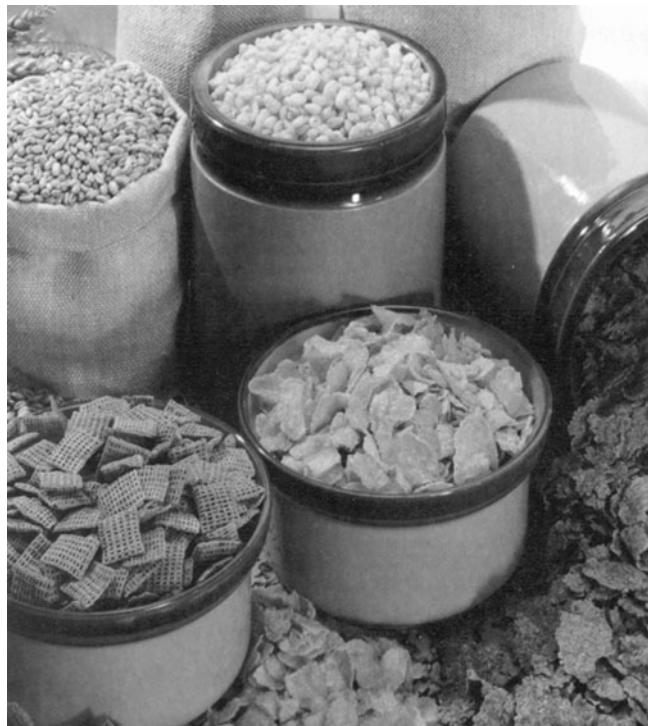
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High fibre cereals may not be all that good for you after all