*British Journal of Nutrition* (2006), **96**, Suppl. 1, S46–S48
DOI: 10.1079/BJN20061700




# Fibre and colorectal cancer: a controversial question

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Since the 1970s it has been postulated that dietary fibre is a protective factor against colorectal cancer. Several epidemiological studies have been performed following different designs (correlation studies, case–control, cohort) and overall they have supported the hypothesis of a benefit of dietary fibre. However, a few intervention trials have not demonstrated the preventive role of dietary fibre on the occurrence of adenomatous colorectal polyps. Nevertheless, there are multiple animal experimental studies that support the role of fibre in the prevention of colorectal cancer. In the present review, the most important contributions to this controversial question are revised. Finally, it is recommended to continue encouraging an increase in the daily consumption of fibre, since it probably plays an important role in the prevention of colorectal cancer, together with other beneficial effects.

**Colorectal cancer: Fibre: Prevention of cancer**

The importance of fibre for the prevention of several diseases was demonstrated by Denis Burkitt at the start of the 1970s. In 1971, he published a paper in the journal *Cancer* which highlighted that low fibre intake was a risk factor for the development of colorectal cancer (Burkitt, 1971). Since then several epidemiological studies, mostly retrospective, have pointed out the same observation. Moreover, it is worth noting that current recommendations for the prevention of colorectal cancer elaborated by several scientific societies highlight the importance of increasing the consumption of dietary fibre. Many experimental studies have also demonstrated the hypothesis of the protective role of fibre in colorectal cancer. However, some cohort studies as well as some intervention trials on colorectal adenomas and cancer cast doubt on the role of fibre in the prevention of this neoplasia. Therefore, nowadays there is certain controversy about an issue that seemed resolved after 30 years of investigation. In the present review the topic is briefly revised, emphasizing the contribution of the most recent studies.

## Epidemiological studies

Burkitt collected data on dietary habits, characteristics of the faeces and incidence of cancer in several populations from developed and developing countries. He described a high incidence of colorectal cancer, lower faeces weight and longer transit time in those populations that consumed a more processed diet. Moreover, he pointed out the changes in colorectal cancer incidence in migrant populations. These data suggested a relationship between diet and colorectal cancer but due to the observational condition of those studies a causal association could not be elucidated.

### *Ecological studies and temporal trends*

Ecological studies, also known as correlation studies, analyse the possible positive or negative association between risk factors and incidence or mortality due to different diseases in several countries or in different regions within the same country. A negative correlation between the consumption of fibre, especially from cereals, and colorectal cancer has been demonstrated in a number of studies (American Gastroenterological Association, 2000). However, this correlation is weakened when results are adjusted for different confounders, such as consumption of meat or fat.

Another way of analysing epidemiological data is to look at dietary changes in a population over time and to associate these changes with cancer incidence or mortality during the same period of time. Studies carried out in Japan and the USA showed that colon cancer mortality has increased during the twentieth century, whereas fibre consumption has decreased.

### *Case–control studies*

This type of study compares past consumption of a specific dietary component, in this case fibre, in colorectal cancer patients with a comparable sample of individuals without cancer. There are several meta-analyses that have evaluated the results of case–control studies. One of these meta-analyses evaluated twenty-three case–control studies (Trock *et al.* 1990). Out of them, fifteen demonstrated an inverse relationship, either moderate or high, between fibre consumption and the presence of colorectal cancer. Six studies showed an arguable protective effect, since the statistical significance was lost after adjusting results. Among the twenty-three studies, only two did not show a protective effect of fibre. Sixteen studies were selected out of the twenty-three, as they provided sufficient data for a whole analysis. It was observed that a diet rich in fibre achieved a 43 % decrease in the risk of colorectal cancer (odds ratio = 0·57; 95 % CI 0·50, 0·64). Another study analysed results of thirteen case–control studies carried out in several countries with very different dietary patterns (Howe *et al.*

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1992). There were more than 5000 cases with colorectal cancer and more than 10 000 controls. In this work, a dose–response relationship was observed. Division into quintiles of fibre consumption showed an inverse effect on the risk of colorectal cancer: as the consumption of fibre was raised, the protective effect increased significantly. All studies were analysed together and individuals whose daily consumption of fibre was above 28 g showed a 50 % decrease in the risk of colorectal cancer (relative risk = 0·51; 95% CI 0·42, 0·59) after adjusting for several confounders compared with those with a consumption below 11 g. This study has been criticized because it did not evaluate the heterogeneity of the different studies included in the analysis (Friedenreich *et al.* 1994). After correction for this heterogeneity, the estimate of risk was closer to one. The same authors, as well as re-evaluating the previous study, carried out another meta-analysis including four new case–control studies in addition to the previously mentioned thirteen studies. Individuals consuming more than 27 g fibre daily showed a 50 % decrease in the risk of colorectal cancer when compared with individuals whose daily consumption was lower than 11 g fibre. Overall, it can be stated that case–control studies show a protective effect of high fibre consumption on colorectal cancer.

### *Cohort studies*

Longitudinal studies evaluate the diet of a large group of individuals over a period of time. During this period several people will develop adenomatous polyps of the colon or colorectal cancer. Possible differences between the diet of individuals with adenomatous polyps of the colon or colorectal cancer and the diet of people without such complications are analysed. Results of longitudinal studies are not conclusive. Initial studies showed an inverse relationship between fibre consumption and colorectal cancer, but recent studies do not show any effect (American Gastroenterological Association, 2000; Sengupta *et al.* 2001). In the present review, only a few selected studies are presented. One of the first studies was carried out in Japan: more than 250 000 people over the age of 40 years were followed for 13 years. In this study, it was observed that colorectal cancer mortality decreased as the consumption of rice and wheat increased, with a relative risk of 0·6 in those consuming high amounts of fibre compared to those with a lower consumption. The Cancer Prevention Study II was conducted in the USA with the participation of more than a million people. In this study, an inverse relation between fibre consumption and colorectal cancer mortality was observed, with a reduction in mortality of 30 % in the group consuming high amounts of fibre compared to the group that consumed less. More than 100 000 women were followed up in the Nurses' Health Study. This study has not shown any effect of fibre consumption on the reduction of either colorectal cancer or other colorectal adenoma incidence.

### *Intervention studies*

Intervention studies are the preferred studies to demonstrate an aetiological association between a studied variable and a certain effect. In this case, the studied variable is fibre consumption and the effect is the occurrence of colorectal cancer. The carcinogenic process is very long. Due to this fact, studies whose endpoint is cancer are very complex. To cope with this problem, studies have been conducted with patients at high risk of colorectal cancer. Intermediate markers and biomarkers such as adenoma, cell proliferation markers, mitotic index, etc. have also been utilized. Overall, studies carried out under such conditions could not support the hypothesis of the protective role of fibre. Studies have been performed with patients with a family history of adenomatous polyps without significant effects of fibre supplements on the reduction of adenoma occurrence. Other intervention studies were carried out with patients with colorectal adenoma after endoscopic polypectomy, i.e. the colon was free of polyps. Patients were randomly assigned into two groups: one group received fibre supplements whereas the other received placebo supplements. Recurrence of adenomas after 1-year intervention was measured. Several studies following this design could not demonstrate any effect of fibre supplements on the decrease of adenoma recurrence (Alberts *et al.* 2000; Bonithon-Kopp *et al.* 2000; Schatzkin *et al.* 2000; Jacobs *et al.* 2002). The coincidence in publication dates of several of these articles caused controversy in the media.

## Animal experimental studies

Experimental models of colorectal carcinogenesis facilitate the analysis of the risk associated with dietary components. This allows for the analysis of the effect of dietary fibre alone or in combination with other dietary components, as well as the analysis of different types of diets. Experimental models permit animals with colon cancer to be obtained rapidly and different studies to be performed that would not be possible in human subjects for ethical reasons. However, results of animal studies are difficult to extrapolate to man. Most of the studies about colonic carcinogenesis have been performed in rats and mice, with a digestive system and a diet different from those of man. In colorectal cancer, the carcinogens used do not form part of a normal human diet. Doses of fibre are also higher than normal human consumption. Despite this, it is believed that experimental models of colorectal cancer in animals are useful tools to study the role of fibre in the carcinogenesis of this type of tumour. Overall, these studies have demonstrated a protective effect of fibre, especially for not very fermented fibre, such as cellulose and wheat fibre, whereas soluble fibre such as guar and starch can strengthen the effect of carcinogens (Sengupta *et al.* 2001). Table 1 summarizes the fibre effect according to the different types of studies.

### *Most recent contributions*

Several studies with new arguments over this controversy have been published more recently. The role of fibre on the occurrence of colorectal polyps has been evaluated in the study known as the

**Table 1.** Fibre and colorectal cancer: effect according to study type

| Type of study | Effect |
|---|---|
| Correlation | Inverse correlation |
| Case–control | Protective effect |
| Cohort | Contradictory results |
| Intervention trials | No effect observed |
| Experimental | Overall, protective effect |

Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial, carried out in the USA (Peters *et al.* 2003). The fibre consumption of more than 3500 patients with distal polyps was compared with the fibre intake of nearly 34 000 individuals without distal polyps. Participants whose fibre consumption was within the highest quintile showed 27 % fewer polyps (95 % CI 14, 38) than those individuals situated in the lowest quintile. The European Prospective Investigation into Cancer and Nutrition has recently published data about fibre consumption and colorectal cancer (Bingham *et al.* 2003). This study had a cohort of more than half a million people from ten European countries, and it involved nearly two million people-years of follow-up. During this follow-up period, 1065 cases of colorectal cancer were detected. Information about fibre consumption was obtained from a dietary questionnaire completed at the beginning of the study. Fibre intake was inversely related to colorectal cancer risk. Individuals in the highest quintile of fibre intake showed a risk of colorectal cancer of 0·75 (95 % CI 0·59, 0·95) in relation to individuals in the lowest quintile. After adjusting for further dietary components, the risk was 0·58 (95% CI 0·41, 0·85). According to the authors' interpretation, populations with a middle–low consumption of fibre could decrease the risk of colorectal cancer up to 40 % if fibre intake were doubled. Finally it is worth mentioning a Cochrane review published in 2004 on intervention studies with fibre to decrease the risk of adenomatous polyps. The conclusion of this study is that there is currently no evidence from randomized controlled trials to suggest that increased dietary fibre intake will reduce the incidence or recurrence of adenomatous polyps within a 2–4-year period (Asano & McLeod, 2004).

In order to correctly interpret all the available information, it should be taken into consideration that colorectal cancer is a complex disease that can appear in different locations from the caecaum to the rectum, that there are different hypotheses of carcinogenesis (from the sequence adenoma–carcinoma which explains most cases, to the carcinogenesis from flat polyps or that derived from inflammation in inflammatory bowel disease). Furthermore, it should be noted that there are different genetic mutations involved, from the mutation of the genes of family adenomatous polyposis to the instability of microsatellites related to mutations of repairing genes. On the other hand, some aspects of the intervention studies performed could explain why they did not demonstrate fibre effectiveness. Among these aspects we could mention that the type of fibre was not the most effective, the dose was not adequate to achieve an effect, the time of treatment and follow-up was not long enough and that there was a bias in the measurement of the effect. For all these, it can be hypothesized that the beneficial effects of fibre are produced on the most common type of cancer, located in the sigma, following the adenoma–carcinoma sequence and initiated after the loss of heterozygosity of the gene of the adenomatous polyposis family. From an epidemiological point of view, there are certain criteria to confirm the possible existence of an aetiological relationship between a factor and a studied effect (fibre and colorectal cancer). In this case consistency, strength of association, dose response, epidemiological coherence, analogy and biological plausibility are met. However, experimentation from human intervention studies and specificity are not fulfilled criteria.

Finally, it should be pointed out that a few scientific societies such as the European Cancer Prevention Consensus Panel still advise intake of fruit, vegetables and cereals as part of the recommended diet to decrease cancer risk. On the other hand, a high fibre intake is a good indicator of a healthy diet as it is associated with lower energy and fat intakes and has a beneficial effect on other prevalent diseases in Western countries (CVD, hypertension, hypercholesterolaemia, hyperglycaemia and constipation).

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