Author's response to reviews

**Title:** Dietary Fiber Showed no Preventive Effect from Colon and Rectal Cancers in Japanese with Low Fat Intake

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PDF covering letter
Dietary Fiber Showed no Preventive Effect against Colon and Rectal Cancers in Japanese with Low Fat Intake: An Analysis from the Results of Nutrition Surveys from 23 Japanese prefectures

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Abstract

Background. Since Fuchs’ report in 1999, the reported protective effect of dietary fiber from colorectal carcinogenesis has led many researchers to question its real benefit. The aim of this study is to evaluate the association between diet, especially dietary fiber and fat and colorectal cancer in Japan.

Methods. A multiple regression analysis (using the stepwise variable selection method) was performed using the standardized mortality ratios (SMRs) of colon and rectal cancer in 23 Japanese prefectures as objective variables and dietary fiber, nutrients and food groups as explanatory variables.

Results. As for colon cancer, the standardized partial correlation coefficients were positively significant for fat (1.13, \(P=0.000\)), seaweeds (0.41, \(P=0.026\)) and beans (0.45, \(P=0.017\)) and were negatively significant for vitamin A (-0.63, \(P=0.003\)), vitamin C (-0.42, \(P=0.019\)) and yellow-green vegetables (-0.37, \(P=0.046\)) (Table 3). For rectal cancer, the standardized partial correlation coefficient in fat (0.603, \(P=0.002\)) was positively significant. Dietary fiber was not found to have a significant relationship with either colon or rectal cancers.

Conclusions. This study failed to show any protective effect of dietary fiber in
subjects with a low fat intake (Japanese) in this analysis, which supports Fuchs’ findings in subjects with a high fat intake (US Americans).

Key words: Colorectal cancer, dietary fiber, dietary fat, multiple regression analysis
INTRODUCTION

It is currently believed that dietary fiber and dietary fat are the most significantly associated dietary factors in colorectal carcinogenesis (1-3). Current epidemiological evidence would suggest that dietary fat is a more significant risk factor for colorectal cancer than the evidence indicating dietary fiber to be a preventative factor (1-4). Furthermore, since Fuchs’ report (5) in 1999, the reported protective effect of dietary fiber on colorectal carcinogenesis has led many researchers to question its real benefit. However, care should be taken in ascertaining the effect of dietary factors in carcinogenesis, including colorectal carcinogenesis, as the protective effects of dietary factors on carcinogenesis may not only be based upon the balance of the overall diet, but also on the interaction of specific dietary components, such as dietary fiber, nutrients and other foods. Furthermore, Fuchs’ results generated many points of controversy against the study, such as the inaccuracy of the dietary survey (using a food-frequency questionnaire); the basic values for fiber may not merit such analysis (the data on fiber are drawn from a 1976 article by Southgate et al., which gives fiber values for a limited number of foods in the United Kingdom); and the possible effect of fiber consumed early in life on the risk of colorectal cancer cannot be ruled
out; no assessment of colonic function was taken into consideration (so the Fuchs’ article leaves unchallenged the evidence that bulkier stools and faster transit through the gut reduce the risk of colorectal cancer) (6) and so on. It is thus logical to attempt to extend Fuchs’ cohort study to include Japanese subjects, whose intake of fat is lower than the US subjects, and to see if the study arrives at the same conclusions. Furthermore, care should be taken in estimating the result of intervention studies (7, 8), and further studies are thus required in other national groups.

As a nation, Japan is unique in that accurate regional dietary data are available, because many prefectures have periodically performed dietary surveys using similar methods. Japan is therefore an appropriate model to analyze geographically the relationship between dietary habit and colorectal cancer.

To evaluate the association between diet and colorectal cancer, we examined the correlation between dietary intake around 1990 and the standardized mortality ratios (SMRs) of colon and rectal cancer between 1995 and 1997 in 23 Japanese prefectures.
MATERIALS AND METHODS

Intake of dietary fiber and nutrients

We collected reports on the intake of food groups and nutrients (using the weighing method) in 23 prefectures, representing 50% of all 47 prefectures in Japan (Figure 1). These surveys were performed in 1987 and 1991. The number of survey subjects and the population in each prefecture in 1995 varied from 162 to 3,057, and from 816,008 to 11,734,920, respectively (Table 1). There were small differences in the mean ages (46.3 – 54.1 years old) and the male to female ratios (0.78-1.00) among the 23 selected prefectures.

The dietary survey was performed as follows. A staff dietitian demonstrated the survey methods and procedures to the housewife or whoever usually cooked in the family. The responsible person in each household weighed and recorded the cooked dishes and the ingredients for each dish, the amount consumed and any left uneaten, and the approximate proportions by which the family members shared each dish or food. The type and amount of foods eaten outside the home were also recorded as meals taken by each individual.

Nutrients included fat, carbohydrate, protein, vitamins (A, B₁, B₂ and C),
and mineral intake (iron); food included 20 major food groups (rice, barley, wheat, seeds, potatoes, confectionaries, beans, fruits, yellow-green vegetables, other vegetables, pickles, mushrooms, seaweeds, meat, egg, oil, milk, fish, juice and alcoholic drink in addition to other foods). The daily dietary fiber intake per capita was calculated from the food intake from each individual nutrition survey by substituting the dietary fiber content in each food (measurement value), obtained by the modified Prosky AOAC method (9) and the modified Southgate method (10). We calculated the different components under each method: the water-soluble and insoluble fibers from the modified Prosky AOAC method, and cellulose, hemicellulose and lignin from the modified Southgate method.

Calculation of SMR of colon and rectal cancer

We used data from the National Vital Statistics (11) to record the number of deaths from colon cancer or rectal cancer between 1995 and 1997 in the 23 target prefectures. The SMRs from colon and rectal cancer, over the same period, by age group in all of Japan were also obtained from the Vital Statistics (12). The population by age group of each prefecture was obtained from the Japanese Census Report (12). The SMRs were calculated as an average for the three years.
Statistical analysis

A multiple regression analysis (based on the stepwise variable selection method) was carried out using the Statistical Package for the Social Sciences (SPSS), with the SMRs of colon cancer and rectal cancer as objective variables, and dietary fiber, nutrients and food groups as explanatory variables. A probability value ($P$) of less than 0.05 ($P < 0.05$) was considered to be significant.
RESULTS

SMRs of colon and rectal cancers and dietary intake

In general, intakes of dietary fiber and nutrients were slightly higher in northeastern Japan than in southwestern Japan (Table 2) and the SMRs of colon and rectal cancers were also slightly higher in northeastern than in southwestern Japan (Table 1).

Result of multiple regression analysis

As for colon cancer, the standardized partial correlation coefficients were positively significant for fat (1.13, \( P=0.000 \)), seaweeds (0.41, \( P=0.026 \)) and beans (0.45, \( P=0.017 \)) and were negatively significant for vitamin A (-0.63, \( P=0.003 \)), vitamin C (-0.42, \( P=0.019 \)) and yellow-green vegetables (-0.37, \( P=0.046 \)) (Table 3). For rectal cancer, the standardized partial correlation coefficient in fat (0.603, \( P=0.002 \)) was positively significant. Dietary fiber was not seen to have a significant relationship with either colon or rectal cancers.

DISCUSSION

Assuming that diet is a factor involved in the development of colon and rectal
cancers, any dietary-related effect would be expected to become apparent after a certain latent period, the duration of which is however unknown. Furthermore, the period between the development of colon and rectal cancers and death due to these disease is also unknown. For this study, the authors essentially defined the period in which dietary intake is able to have an influence on death from colon cancer as approximately 10 years. This is a limitation of this study, because it is clear that 10 years is too short. Furthermore, there were differences in the survey year among the 23 prefectures examined up to a maximum of 4 years. This is also a potential limitation.

From the previous case-control and cohort studies in Japan concerning fiber source foods and their preventive effect on colon and rectal cancer, three reports showed significant preventive effects in vegetables and fruits from a total of nine reports, and two out of five reports on rice showed a preventive effect. As for beans or seaweeds, one and two reports from respective totals of five and three showed significant preventive effects (13). Only two reports from Ohta and colleagues examined the relationship of pure dietary fiber on colorectal cancer or colon polyps. The authors reported that dietary fiber intakes in patients with colorectal cancer and colon polyp were higher than those in controls (10, 14). On the other hand, one report
from a total of five on dietary fat showed a promoting effect. As mentioned above, there are not many studies which show significant relationships between the effects of either dietary fiber or fat on colorectal cancer in Japan.

In this study, it was shown that there were significant relationships between fat intake and colon and rectal cancers, but no relationship between dietary fiber intake and colon or rectal cancers, thus demonstrating that the promoting effect of dietary fat was greater than the protective effect of dietary fiber. Furthermore, seaweeds and beans also demonstrated a carcinogenic promoting relationship with colon cancer even though these are well known as a source of dietary fiber. Hence, our data failed to show any protective effect of dietary fiber on colorectal carcinogenesis in subjects in the low fat intake group (Japanese; 25% in 1977-1978 and 29% in 1994-1995 in men and women, respectively)(15) in this analysis, while Fuchs showed the same result in subjects in the high fat intake group (US subjects; 42% and 40% in 1977-1978 and 34% and 32% in 1994-1995 in men and women, respectively)(16). However, we could not divide the total fat intake into animal fat and plant fat, so that it is unclear which type of fat has more influence on these cancers.

On the other hand, vitamin A (including carotenes)(17,18) and vitamin C
are believed to offer beneficial dietary factors against colorectal cancer through their anti-oxidative action, though the preventive effects of these dietary factors have not been reported in Japan. In this study, we also obtained similar results, even though the correlation coefficients were lower than those of fat.

The current results revealed that the number of nutrients and food groups that were significantly related with colon cancer was greater than those related to rectal cancer. This would suggest that colon cancer is affected by environmental factors, including the dietary factor, more than rectal cancer.
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REFERENCES


17. RG Ziegler, AF Subar, NE Craft, G Ursin, BI Patterson, BI Graubard. Dose β -carotene explain why reduced cancer risk is associated with vegetables and fruit intake? *Cancer Res* 1992 52(Supple): 2060s-2066s


Figure legends

Figure 1:

Location of the 23 prefectures selected. Target prefectures are shown in black.