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## CORRESPONDENCE

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## High-Fiber Diet and Colorectal Adenomas

*To the Editor:* I am concerned that the report by Schatzkin and colleagues (April 20 issue)<sup>1</sup> may lead many people to conclude erroneously that **diet** does not affect susceptibility to colon cancer, even though the hypothesis was not adequately tested. According to Table 3 of the report, dietary fat decreased from 35.6 percent at randomization to 23.8 percent at four years in the intervention group and from 36.0 to 33.9 percent in the control group. Consumption of red meat decreased from 93.2 to 74.5 g per day in the intervention group and from 97.9 to 94.9 g per day in the control group. However, plasma total cholesterol decreased only from 5.30 to 5.27 mg per deciliter in the intervention group and from 5.29 to 5.27 mg per deciliter in the control group (log-transformed values); these decreases represent 2 percent and 1 percent in the absolute cholesterol concentrations, respectively. Reductions of this magnitude in the intake of dietary fat and red meat in the intervention group (if they really occurred) should have caused a greater reduction in the plasma total cholesterol level — in any event, greater than that in the control group, which did not occur. Also, weight was essentially unchanged in both groups.

The logical conclusion is that the patients in the intervention group were actually consuming a **diet** very similar to that of the control group. This would not be surprising, since it is difficult to motivate people to make and maintain dietary changes in large-scale studies, and it is equally difficult to obtain accurate dietary information in clinical trials. But it is as erroneous to claim that dietary fat and cholesterol intake have no effect on colon cancer as it is to say that they have no effect on plasma total cholesterol.

It is a great disservice for the authors to conclude, "In summary, our study provided no evidence that a **diet** low in fat and high in fiber, fruits, and vegetables reduces the risk of recurrent colorectal adenomas." When headlines to this effect appeared widely in the media, they left many people with the

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belief that **diet** makes no difference, whereas, in fact, we do not yet know whether this is true.

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## References

1. Schatzkin A, Lanza E, Corle D, et al. Lack of effect of a low-fat, high-fiber **diet** on the recurrence of colorectal adenomas. *N Engl J Med* 2000;342:1149-1155.[[Abstract/Full Text](#)]

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*To the Editor:* The findings reported by Schatzkin et al. may reflect the failure of **dietary** counseling to produce a change in **diet** more than the lack of effect of **dietary** change on the recurrence of adenomas. The objective, or measured, data in Table 3 show very little change in comparison with the changes in reported **dietary** information. In particular, the reported caloric intake decreased by 102 and 71 kcal per day in the intervention and control groups, respectively. These reductions should have resulted in substantial weight loss, unless there were concomitant decreases in the expenditure of calories. Reductions in activity are plausible in patients in the age group represented by the study sample. However, such changes in activity should have been similar in the two groups, yet there was still a difference between the groups of 31 kcal per day in the change in the reported caloric intake. This difference in caloric intake would be expected to result in a difference in weight between the groups of about 12 lb (5.5 kg) over a period of four years.<sup>1</sup> The absolute difference, 2.5 lb (1.1 kg), is less than a quarter of that predicted by the **dietary** history. Thus, the patients in the intervention group may have overreported their compliance with the counseling they were given.

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## References

1. Rolls BJ, Bell EA. **Dietary** approaches to the treatment of obesity. *Med Clin North Am* 2000;84:401-418.[[Medline](#)]

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*To the Editor:* Most of the explanations for the disappointing results of the studies reported by Schatzkin et al.<sup>1</sup> and Alberts et al.<sup>2</sup> are noted in the accompanying editorial by Byers.<sup>3</sup> One question has not been addressed: Was compliance with the regimen sufficiently ascertained? In both studies, the assessment of compliance relied mainly on the study participants, who either returned cereal boxes and recorded supplement consumption on a calendar,<sup>2</sup> or reported daily intake of food and supplements.<sup>1</sup>

The incidence of some adverse gastrointestinal effects can be considered an independent marker of compliance with the use of the high-fiber supplement in the study by Alberts et al.; the incidence was significantly higher in the high-fiber group than in the low-fiber group. Thus, in this study, one can say that insoluble fiber alone does not account for all the effects that have been attributed to a diet high in fruit and vegetables in observational studies and has no short-term benefit in reducing the risk of colorectal adenoma.

In the study by Schatzkin et al., there were two independent markers of compliance: weight loss and serum total carotenoids. (The carotenoid values in Table 3 of their article appear to be 100 times the usual values.) Although significant, the changes were very small after four years, and it is unfortunate that no additional biologic markers were investigated and that such investigations were not performed more often. Thus, it is difficult to say that compliance was satisfactory.

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## References

1. Schatzkin A, Lanza E, Corle D, et al. Lack of effect of a low-fat, high-fiber diet on the recurrence of colorectal adenomas. *N Engl J Med* 2000;342:1149-1155. [[Abstract/Full Text](#)]
2. Alberts DS, Martínez ME, Roe DJ, et al. Lack of effect of a high-fiber cereal supplement on the recurrence of colorectal adenomas. *N Engl J Med* 2000;342:1156-1162. [[Abstract/Full Text](#)]
3. Byers T. Diet, colorectal adenomas, and colorectal cancer. *N Engl J Med* 2000;342:1206-1207. [[Full Text](#)]

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*To the Editor:* Is it possible that a high-fiber diet may be harmful? The main end point in both the study by Schatzkin et al. and the study by Alberts et al. was the recurrence of polyps, but an even more important consideration is the effect of a high-fiber diet on the occurrence of bowel cancer. In each study, there appeared to be more bowel cancers in the high-fiber group than in the low-fiber or control group: 10 cases as compared with 4 in the study by Schatzkin et al. and 7 cases as compared with 2 in the study by Alberts et al.

In the two studies, the risk ratios for bowel cancer in the high-fiber groups, as compared with the low-fiber and control groups, appear to be similar, and the characteristics of the patients in the two groups were similar. Therefore, we assessed the risk of bowel cancer in the high-fiber groups and in the low-fiber and control groups after combining the data from the two studies. We used the available information in the two studies to estimate the approximate number of person-years for the combined high-fiber groups and the combined low-fiber and control groups. We assumed that the combined high-fiber groups should have had the same frequency of bowel cancer as the combined low-fiber and control groups. However, the estimated number of expected cancers in the combined high-fiber groups was only 6.4, as compared with the observed number of 17, yielding a risk ratio of 2.6. This unexpected excess

number of bowel cancers after dietary modification appears to be significant at the 95 percent level. The surprising finding that the risk of bowel cancer is increased by a factor of two or three after dietary supplementation with fiber, if confirmed by a more detailed analysis of the combined sets of data, suggests that high-fiber diets may actually be harmful and should be avoided in patients with bowel polyps.

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*To the Editor:* Is it possible that in the study by Schatzkin et al. the choice of subjects for enrollment, all of whom had adenomas that were potential precursors of colorectal cancer, had a leveling effect on the variable potentially influenced by dietary change? Does the study ultimately demonstrate only that the dietary changes made, over a period of just four years, do not prevent the recurrence of adenomas or reduce the incidence of colorectal cancer in persons who already have a genetic (or other) predisposition to adenomas?

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*To the Editor:* Although the subjects in the intervention group in the study by Schatzkin et al. were given nutritional information and counseling in order to reach a goal of 20 percent of total calories from fat, the Methods section of the report does not state whether the subjects were encouraged to eat fish known to contain n-3 lipids. Table 3 of the article shows that the ratio of red meat to chicken and fish decreased in the intervention group. However, if the subjects ate more chicken, but not fish, then they still did not increase their dietary intake of n-3 lipids. Table 1 of the article shows data on current aspirin use and the serum levels of two nutrients, total carotenoids and  $\alpha$ -tocopherol, in the control and intervention groups, but serum n-3 lipids are not noted.

I think an assessment of n-3 lipids must be taken into account in evaluating the effects of dietary interventions on the rate of recurrence of colonic adenomas.

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The authors reply:

*To the Editor:* The Polyp Prevention Trial targeted total dietary fat. Because the ratio of dietary-fat subtypes did not change appreciably, it is not surprising that the difference in cholesterol reduction between the intervention and control groups was minimal.<sup>1</sup> As we stated in our report, our study could not rule out the possibility that greater reductions in fat and red meat or further increases in fiber and fruits and vegetables might be required to reduce the risk of colorectal neoplasia.

The absolute difference in the change in caloric intake between the intervention and control groups was -25 kcal (95 percent confidence interval, -72 to 22). Therefore, the trial did not establish a significant between-group difference in the change in energy consumption. Moreover, the likelihood of underreporting of energy intake in dietary-intervention studies would explain, at least in part, the apparent discrepancy between changes in reported energy intake and observed weight loss in this and other dietary trials.<sup>2</sup>

We are conducting the type of observational analyses suggested by Dr. Davis. All such analyses, however, are subject to confounding: people who adhere to an intervention are often found to be systematically different from those who do not in ways that are related to the clinical outcome. We presented the results of an intention-to-treat analysis, which is an internationally accepted method of analysis.<sup>3</sup>

We did find significant net increases in lutein, alpha carotene, and beta carotene in the intervention group. The relatively small (though statistically significant) increase in carotenoids may reflect the facts that carotenoid-rich fruits and vegetables accounted for only about half the total increase in fruits and vegetables in the intervention group and that carotenoids from fruits and vegetables are substantially less bioavailable than those from supplements.<sup>4</sup> Dr. Gerber correctly points out two errors in the units of measurement for carotenoids in our article: in the third footnote to Table 1, the unit of measurement should be micromoles per liter, and in Table 3 it should be micrograms per deciliter.

If we eliminate the cancers diagnosed within the first year after enrollment, which were likely to have been present when the interventions began (six in the intervention group and two in the control group in our study, and three in the high-fiber group in the study by Alberts et al.), there were a total of nine cancers in the high-fiber groups and four in the control and low-fiber groups — not a statistically significant difference. A thorough investigation of the effects of fiber on the risk of colorectal cancer in intervention studies requires the pooling of data from all the trials that have looked at this issue.

We agree with Dr. Muller: our trial could not determine whether dietary modification affects the risk of colorectal adenoma in persons who have not had a previous adenoma.

In line with Dr. Duprey's suggestion, we will be analyzing the dietary data from our study for n-3 fatty acids. There was only a small, though statistically significant, difference in the consumption of fish between the intervention and control groups (21.5 and 18.6 g, respectively).

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## References

1. Hegsted DM, Kritchevsky D. Diet and serum lipid concentrations: where are we? *Am J Clin Nutr* 1997;65:1893-1896.[[Medline](#)]
2. Henderson MM, Kushi LH, Thompson DJ, et al. Feasibility of a randomized trial of a low-fat diet for the prevention of breast cancer: dietary compliance in the Women's Health Trial Vanguard Study. *Prev Med* 1990;19:115-133.[[Medline](#)]
3. Friedman LM, Furberg CD, DeMets DL. Fundamentals of clinical trials. Littleton, Mass.: PSG Publishing, 1981.
4. Van Het Hof KH, West CE, Weststrate JA, Hautvast JG. Dietary factors that affect the bioavailability of carotenoids. *J Nutr* 2000;130:503-506.[[Abstract/Full Text](#)]

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*To the Editor:* We agree with Dr. Gerber that the gastrointestinal side effects caused by the daily intake of 13.5 g of wheat-bran cereal are an independent marker of compliance with the use of the high-fiber supplement in our trial. In our phase 1 and 2 studies of interventions involving wheat-bran fiber, we documented that 13.5 g of this supplement per day could be taken with a reasonable level of compliance by older study participants for periods of a few months.<sup>1,2</sup> However, some older persons may not be able to tolerate high doses of wheat-bran fiber on a daily basis for several years.

Lowenfels and Maisonneuve argue that the high-fiber cereal promoted the development of colorectal cancer. However, our findings do not support this argument. Seven of the nine colorectal cancers that were detected occurred in members of the high-fiber group, but three of these seven cancers were diagnosed 8, 10, and 11 months after randomization; these cancers were probably missed at the qualifying colonoscopy (i.e., before the start of the intervention). Thus, only 4 of the 719 patients in the high-fiber group and 2 of the 584 in the low-fiber group had colorectal cancers that were detected at least 1 year after randomization (range, 19 to 39 months). The difference is not statistically significant.

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## References

1. Ho EE, Atwood JR, Benedict J, et al. A community-based feasibility study using wheat bran fiber supplementation to lower colon cancer risk. *Prev Med* 1991;20:213-225.[[Medline](#)]
2. Alberts DS, Ritenbaugh C, Story JA, et al. Randomized, double-blinded, placebo-controlled study of effect of wheat bran fiber and calcium on fecal bile acids in patients with resected adenomatous colon polyps. *J Natl Cancer Inst* 1996;88:81-92.[[Abstract/Full Text](#)]

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