

# A diet low in fat and high in fiber, fruits, and vegetables did not reduce the recurrence of colorectal adenomas

Schatzkin A, Lanza E, Corle D, et al., and the Polyp Prevention Trial Study Group. Lack of effect of a low-fat, high-fiber diet on the recurrence of colorectal adenomas. *N Engl J Med*. 2000 Apr 20;342:1149-55.

## QUESTION

Does a diet that is low in fat and high in fiber, fruits, and vegetables reduce the rate of recurrent colorectal adenomas?

## DESIGN

Randomized {allocation concealed\*}†, blinded (outcome assessor)\*, controlled trial with 4-year follow-up.

## SETTING

8 clinical centers in the United States.

## PATIENTS

2079 adults  $\geq 35$  years of age who had had  $\geq 1$  histologically confirmed colorectal adenoma removed in the 6 months before the study. Exclusion criteria were history of colorectal cancer, surgical resection of adenomas, bowel resection, the polyposis syndrome, inflammatory bowel disease,  $> 150\%$  of recommended weight, use of lipid-lowering drugs, or condition or dietary restrictions that would limit compliance with the protocol. Follow-up was 92%.

## INTERVENTION

1037 participants were allocated to an intervention group and were given a diet

low in fat (20% of total calories), high in dietary fiber (18 g/1000 kcal), and high in fruits and vegetables (3.5 servings/1000 kcal) and nutrition and behavior-modification counseling by nutritionists. 1042 participants were allocated to a control group and were given a standard brochure on healthy eating; this group was asked to follow their usual diet.

## MAIN OUTCOME MEASURE

The recurrence of colorectal adenomas between 1 and 4 years was identified by colonoscopy. Secondary outcomes were the number, size, and histologic features of the detected adenomas and colorectal cancer.

## MAIN RESULTS

Analysis was by intention to treat. Participants in the intervention group had greater reductions in percentage of fat intake as total calories (absolute difference in change between groups, 9.7%; 95% CI 9.0% to 10.3%), greater increases in dietary fiber intake (absolute difference in change between groups, 6.9 g/1000 kcal; CI 6.4 to 7.3 g/1000 kcal), and greater increases in fruit and vegetable intake (absolute difference in change between groups, 1.13 serv-

ings/1000 kcal; CI 1.04 to 1.21 servings/1000 kcal) than did those in the control group. The intervention and control groups did not differ for rates of having  $\geq 1$  recurrent colorectal adenoma (39.7% vs 39.5%,  $P = 0.98$ ),  $\geq 1$  adenoma with a diameter  $\geq 1$  cm (4.9% vs 5.6%,  $P = 0.57$ ),  $\geq 1$  advanced adenoma (6.3% vs 7.0%,  $P = 0.60$ ), or colorectal cancer (1% vs 0.4%,  $P = 0.19$ ). Among those with recurrent colorectal adenomas, no difference existed for the mean number of adenomas in the intervention and control groups (1.85 vs 1.84,  $P = 0.93$ ).

## CONCLUSION

A diet that is low in fat and high in fiber, fruits, and vegetables did not reduce the rate of recurrent colorectal adenomas.

*Source of funding: National Cancer Institute.*

*For correspondence: Dr. A. Schatzkin, Chief, National Cancer Institute, EPS Room 7032, Bethesda, MD 20892-7232, USA. FAX 301-496-6829.* ■

\*See Glossary.

†Information provided by author.

## COMMENTARY

In developed countries, colon cancer is a common disease. Observational studies have shown that dietary factors may be causally associated with the risk for colon cancer. Specifically, epidemiologic studies have shown an increased risk for colon cancer with a diet high in fat and red meat and low in fiber, fresh fruits, and vegetables. Insoluble fiber is believed to protect the colon by absorbing carcinogens (1). Therefore, a strong rationale exists to evaluate dietary interventions in persons at risk for colon cancer.

Randomized controlled trials commonly examine the prevention of colonic adenomas (adenomatous polyps). Acceptance of these lesions as a surrogate end point for developing carcinoma is based on the observation that cancer almost always arises from preexisting polyps. Persons with benign polyps, especially those that are  $> 1$  cm in diameter or that show villous architecture, have an increased risk. Use of this outcome is efficient; fewer patients are required to detect a treatment effect than if cancer was selected for evaluation. However, this assumes that interventions that reduce polyp formation necessarily prevent cancer. Although this assumption may not inevitably be the case, the

approach is sensible given the existing data. Therefore, the results of the 2 large randomized controlled trials—one by Schatzkin and colleagues and the other by Alberts and colleagues—that evaluated the effect of dietary interventions on the formation of adenomatous polyps are of great interest.

Both studies were meticulously done. Schatzkin and colleagues randomized  $> 2000$  patients, 90% of whom underwent 2 colonoscopies over a 4-year period. Compliance with the low-fat, high-fiber, and high fruit and vegetable intake diet was excellent. Although self-reporting is a subjective measure of dietary compliance, the higher serum carotenoid level and the trend toward lower weight in the intervention group confirm that patients assigned to active treatment were compliant. No beneficial effect of therapy was observed; the lower boundary of the 95% confidence interval for the observed difference in polyp formation (0.2%) was consistent with only a potential 4% improvement over the control group. Moreover, more cases of colon cancer were observed in the intervention group.

*(continued on page 21)*

# A high-fiber cereal supplement did not prevent the recurrence of colorectal adenomas

Alberts DS, Martínez ME, Roe DJ, et al., and the Phoenix Colon Cancer Prevention Physicians' Network. Lack of effect of a high-fiber cereal supplement on the recurrence of colorectal adenomas. *N Engl J Med.* 2000 Apr 20;342:1156-62.

## QUESTION

Does a dietary supplement with wheat-bran fiber reduce the rate of recurrent colorectal adenomas?

## DESIGN

Randomized {allocation concealed\*}†, blinded (physicians, participants, and outcome assessors),\* controlled trial.

## SETTING

22 health care centers in the metropolitan area of Phoenix, Arizona, United States.

## PARTICIPANTS

1429 adults between 40 and 80 years of age (mean age 66 y, 66% men) who had had  $\geq 1$  colorectal adenoma that measured  $\geq 3$  mm in diameter at colonoscopy and had been removed within 3 months before recruitment; a Southwest Oncology Group performance status of 0, 1, or 2; adequate nutritional status; and normal renal and liver function. Exclusion criteria were invasive cancer in the previous 5 years, history of colon resection,  $\geq 2$  first-degree relatives

with colorectal cancer, severe metabolic disorders or other severe illnesses, or dietary fiber intake  $> 30$  g/d. Follow-up was 91%.

## INTERVENTION

After a 6-week run-in period, participants were allocated to receive a high-fiber supplement, 13.5 g/d (high-fiber group,  $n = 802$ ), or a low-fiber supplement, 2 g/d (low-fiber group,  $n = 627$ ), of wheat-bran cereal.

## MAIN OUTCOME MEASURES

Presence of  $\geq 1$  new colorectal adenoma, identified at the time of follow-up colonoscopy, and adverse events.

## MAIN RESULTS

Analysis was by intention to treat. The daily mean total fiber intake (from the wheat-bran cereal supplement and other sources) was 27.5 g for the high-fiber group and 18.1 g for the low-fiber group. The median follow-up time was 34 months for the high-fiber group and 36 months for the low-fiber group. The

high- and low-fiber groups did not differ for the rates of having  $\geq 1$  recurrent colorectal adenoma (47% vs 51%,  $P = 0.13$ ) or for the mean number of recurrent colorectal adenomas (0.61 vs 0.57,  $P = 0.93$ ). The high-fiber supplement was associated with a greater rate of mild gastrointestinal adverse effects (nausea, abdominal pain, diarrhea, intestinal gas, and abdominal bloating;  $P < 0.01$ ) but not with a greater rate of constipation than was the low-fiber supplement.

## CONCLUSION

A dietary supplement of wheat-bran fiber did not reduce the rate of recurrent colorectal adenomas.

*Sources of funding: National Cancer Institute and the Kellogg Company.*

*For correspondence: Dr. D. S. Alberts, Arizona Cancer Center 2964, 1515 North Campbell Avenue, P.O. Box 245024, Tucson, AZ 85724, USA. FAX 520-626-2445.* ■

\*See Glossary.

†Information provided by author.

## COMMENTARY (continued from page 20)

Alberts and colleagues evaluated the efficacy of a wheat-bran fiber supplement in 1429 patients who were at risk for polyp recurrence. Again, no beneficial effect of this intervention was identifiable on polyp or cancer formation. Although patients were preselected for tolerance of the fiber supplement, more gastrointestinal symptoms occurred in the intervention group.

Collectively, these 2 studies provide strong evidence that dietary interventions are ineffective in preventing the recurrence of adenomas. Nevertheless, these results do not necessarily mean that diet does not play a role in the development of cancer. Because exposure to carcinogens occurs over years, the experimental paradigm used in these trials may not be adequate to evaluate the role of fiber as a protective factor. Unfortunately, evaluation of long-term dietary interventions by randomized controlled trials is not practical.

Of interest, pharmacologic interventions may succeed where diets fail. Nonsteroidal anti-inflammatory drugs, most notably the cyclo-

oxygenase (COX)-2 inhibitors, have shown promising results in preventing polyp formation in patients with hereditary polyposis (2).

Although high-fiber, low-fat diets may have other benefits, this strategy will not prevent colonic polyp formation in patients who are at risk for recurrence.

Brian Feagan, MD  
University of Western Ontario  
London, Ontario, Canada

## References

1. Kritchevsky D. Protective role of wheat bran fiber: preclinical data. *Am J Med.* 1999;106:28S-31S.
2. Stockbrugger RW. Nonsteroidal anti-inflammatory drugs (NSAIDs) in the prevention of colorectal cancer. *Eur J Cancer Prev.* 1999;9(Suppl 1):S21-5.