

# Fiber supplementation increased the risk for recurrent adenomas, and calcium supplementation did not prevent recurrence

Bonithon-Kopp C, Kronborg O, Giacosa A, Räth U, Faivre J, for the European Cancer Prevention Organisation Study Group. Calcium and fibre supplementation in prevention of colorectal adenoma recurrence: a randomised intervention trial. *Lancet*. 2000 Oct 14;356:1300-6.

**QUESTION**

In patients with colorectal adenomas, does supplementation with ispaghula husk or calcium prevent adenoma recurrence?

**DESIGN**

Randomized (allocation concealed\*), blinded (patients, clinical staff, and investigators),\* placebo-controlled trial with 3-year follow-up.

**SETTING**

21 centers in 10 countries (Belgium, Denmark, France, Germany, Ireland, Israel, Italy, Portugal, Spain, and the United Kingdom).

**PATIENTS**

665 patients who were 35 to 75 years of age, had a complete index colonoscopy showing  $\geq 2$  adenomas or 1 adenoma of  $> 5$  mm in diameter, and did not have a debilitating or life-threatening disease. Exclusion criteria were history of large-bowel disease, contraindications to calcium or fiber, or inability or unwillingness to stop current fiber or calcium supplementation. 552 patients (83%, mean age 59 y, 64% men) completed the 3-year follow-up.

**INTERVENTION**

After stratification by center, patients were allocated to 1 of 3 groups: elemental calcium, given at 2 g of calcium gluconolactate and carbonate in a water solution twice daily ( $n = 176$ ); ispaghula husk, given as 3.5 g of orange-flavored effervescent granules dissolved in water ( $n = 198$ ); or placebo that either matched the elemental calcium or the ispaghula husk ( $n = 178$ ).

**MAIN OUTCOME MEASURE**

New adenomas at the 3-year colonoscopy.

**MAIN RESULTS**

Patients in the fiber group had a 45% increase in recurrent adenomas relative to the placebo group at 3 years  $\{P = 0.04\}^\dagger$  (Table). The difference between the calcium and placebo groups was not statistically significant (Table).

**CONCLUSIONS**

In patients with adenomas, supplementation with ispaghula husk increased the risk for recurrent adenoma. Calcium supplementation did not prevent adenomas.

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\*See Glossary.

$\dagger P$  value calculated from data in article.

**Supplementation with calcium or ispaghula husk (fiber) vs placebo for preventing recurrent adenomas $\ddagger$**

Outcome at 3 y	Comparison	Event rates	RRI (95% CI)	NNH (CI)
Recurrent adenomas	Fiber vs placebo	29% vs 20%	45% (1 to 109)	12 (6 to 340)
	Calcium vs placebo	16% vs 20%	21% (-23 to 50)	Not significant

$\ddagger$ Abbreviations defined in Glossary; RRI, RRR, NNH, NNT, and CI calculated from data in article.

**COMMENTARY**

The tendency to develop colorectal cancer is largely acquired, although genes play a role in some people. Age-adjusted incidence rates vary 10- to 15-fold throughout the world, and people who move from low- to high-incidence areas, such as North America and Europe, acquire higher rates during their lifetimes. Observational studies suggest that calcium and fiber are protective along with other factors (1), but this has been difficult to confirm because of the limitations of observational studies, especially the lack of ability to measure long-term dietary exposure.

The randomized trial by Bonithon-Kopp and colleagues ought to settle the matter. But does it? The trial has limitations, which are common even in the best preventive trials. The results are imprecise because enrollment was less than the investigators had planned. The main outcome event was recurrence of adenomas, but a different set of factors may govern their growth, evolution to cancer, and distant spread. Many participants did not cooperate with their assigned treatment, leaving room for systematic differences among compared

groups despite initial randomization. Finally, 3 years of follow-up is a short time in the natural history of this cancer, which usually takes at least 10 years to develop. With this study, the benefits of calcium supplementation look more promising, whereas fiber supplementation looks less promising. But that is a matter for investigators in this difficult field to tackle. Clinicians should still advise patients to consume  $\geq 5$  vegetables and fruits, a multivitamin, and calcium supplements each day. This practice not only may help prevent colorectal cancer but also is advisable for many other health reasons.

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**Reference**

1. Tomeo CA, Colditz GA, Willett WC, et al. Harvard Report on Cancer Prevention. Volume 3: Prevention of colon cancer in the United States. *Cancer Causes Control*. 1999;10:167-80.