

some dietary supplements is expected to prevent 600 to 1200 cases of CAD and 250 to 500 CAD-related deaths each year.⁵

Practice implications: There have been no safe levels of trans fat consumption shown, and dietary trans fat and saturated fat intake should be reduced. Consumers should take advantage of the new labelling regulations and select

products that contain low levels of trans and saturated fats.

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IN THE LITERATURE

Do ASA and NSAIDs reduce the risk of colorectal cancer?

Chan AT, Giovannucci EL, Meyerhardt JA, et al. Long-term use of aspirin and nonsteroidal anti-inflammatory drugs and risk of colorectal cancer. *JAMA* 2005;294(8):914-23.

Background: Regular use of ASA in patients with a history of colorectal adenoma or cancer has been shown to reduce the risk of recurrent adenoma within 1–3 years.¹ Although 2 trials looking at the effect of ASA on colorectal cancer did not show a benefit after 5–10 years,^{2,3} it is unknown whether ASA taken for a longer duration, or at a different dose, would reduce the risk of colorectal cancer. It is also unclear

whether other NSAIDs would have similar protective effects.

Design: A prospective study involving 82 911 women enrolled in the Nurses' Health Study collected data from questionnaires biennially on ASA and other NSAID use and new cases of colorectal cancer from 1980 to June 2000. From the data collected, the mean ASA intake was calculated, and women were divided into groups of regular ASA users (2 or more 325-mg tablets per week) and nonregular users. Rates of colorectal cancer were calculated for each group by dividing the number of new cases of cancer by the number of person-years of ASA use. The investigators also collected data about gastrointestinal bleeding in participants.

Results: A total of 962 cases of colorectal cancer were found among the wo-

men during the 20 years of follow-up. Regular users of ASA had a lower risk of colorectal cancer than nonregular users. The reduced risk started after 10 years of regular use, and larger doses of ASA resulted in larger reductions in risk (Table 1, Table 2). Women who used more than 14 tablets of ASA per week for longer than 10 years had a 53% lower risk of colorectal cancer than those who did not use ASA (age-adjusted relative risk [RR] 0.47). A similar protective dose–response relation was found for NSAIDs: women who used NSAIDs regularly (2 or more tablets per week) had a 21% lower risk of colorectal cancer than nonregular users (adjusted RR 0.71, 95% confidence interval 0.64–0.97).

ASA and NSAID use were not related to reduced number of rectal cancers, and lower doses of ASA (50 mg/d) did not lower the risk of colon cancer.

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Table 1: Trend in relative risk of colorectal cancer by duration of regular ASA use*

Years of regular ASA use	Adjusted RR (95% CI)†
0	1.0
1-5	1.04 (0.88-1.24)
6-10	0.89 (0.74-1.08)
11-20	0.67 (0.54-0.85)
> 20	0.68 (0.54-0.85)

Note: RR = relative risk, CI = confidence interval. *Regular ASA use is defined as 2 or more 325-mg tablets per week. †p for trend < 0.001. See Table 2 footnote for definition of multivariate adjustment.

Table 2: Trend in relative risk of colorectal cancer by ASA dose

No. of 325-mg ASA tablets per wk	Adjusted relative risk (95% CI)*	
	All women with colorectal cancer†	Women with history of ASA use ≥ 10 yr†
0	1.0	1.0
0.5-1.5	1.10 (0.92-1.31)	0.94 (0.79-1.13)
2-5	0.89 (0.73-1.10)	0.74 (0.59-0.93)
6-14	0.78 (0.62-0.97)	0.81 (0.63-1.05)
> 14	0.68 (0.49-0.95)	0.51 (0.33-0.80)

Note: CI = confidence interval.

*Adjusted for age, smoking before age 30, body mass index, regular vigorous exercise, colorectal cancer in a parent or sibling, history of polyp, postmenopausal hormone use, current multivitamin use, frequency of beef, pork or lamb as a main dish per week, alcohol consumption, and folate and calcium intake. †p for trend < 0.001.

The incidence of major gastrointestinal bleeding events related to ASA use was also dose-related: it varied from 7.7 cases per 10 000 women who did not use ASA to 15.7 per 10 000 women taking 14 or more tablets of ASA per week. For NSAID users, the rate of gastrointestinal bleeds was 19.1 per 10 000 women taking 14 NSAID tablets per week, compared with 10.1 per 10 000 non-NSAID users.

Commentary: The study builds on previous work on the impact of ASA on neoplasia, showing that longer duration, and larger doses, of ASA are required to produce a protective effect against colorectal cancer. It shows that NSAIDs also reduce the risk of colorectal cancer. Like recent findings reported from the Women's Health Study,³ low doses of ASA (50 mg/d) were not effective at reducing the risk of colorectal cancer. Although this

study involved only women, previous reports have shown a protective effect of ASA in men.⁴

Practice implications: The main practical problem with the study's findings is that most of the benefit is achieved at high doses of ASA and NSAIDs. The doses of ASA are considerably higher than those currently recommended for the prevention of cardiovascular disease and may increase the risk of gastrointestinal bleeding. The findings suggest that if 10 000 women take more than 14 tablets of ASA a week, 1 or 2 cases of colorectal cancer may be prevented over a year. However, that same dose of ASA may also cause 8 cases of bleeding severe enough to require hospital admission or blood transfusion.

Therefore, the practical application of high-dose ASA therapy is limited in day-to-day practice. Most people are unable to take ASA or NSAIDs at the

high doses shown in the study to be effective in preventing colorectal cancer.

Because many of ASA's toxic effects, including gastrointestinal bleeding, are dose-dependent, further research is needed into the risk-benefit profile of ASA and other NSAIDs for chemoprevention in different risk groups.

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