

Low dose aspirin did not prevent cancer in healthy women

Cook NR, Lee IM, Gaziano JM, *et al*. Low dose aspirin in the primary prevention of cancer: the Women's Health Study: a randomized controlled trial. *JAMA* 2005;**294**:47–55.

Clinical impact ratings GP/FP/Primary care ★★★★★☆☆ IM/Ambulatory care ★★★★★☆☆ Internal medicine ★★★★★☆☆

Q In healthy women ≥ 45 years of age, how effective is aspirin in preventing cancer?

METHODS

-  **Design:** randomised placebo controlled trial (Women's Health Study [WHS], a randomised 2 × 2 factorial trial).
-  **Allocation:** concealed.*
-  **Blinding:** blinded {participants, healthcare providers, data collectors, and outcome assessors}†.*
-  **Follow up period:** mean 10.1 years.
-  **Setting:** {a mail-based trial in female healthcare professionals in the US}†.
-  **Participants:** 39 876 women ≥ 45 years of age (mean age 55 y) without a history of cancer (except non-melanoma skin cancer), cardiovascular disease, or other major chronic illness and no history of adverse effects to aspirin who were not taking aspirin or non-steroidal anti-inflammatory drugs more than once per week; not taking anticoagulants or corticosteroids; or individual supplements of vitamin A, vitamin E, or β carotene more than once per week.
-  **Intervention:** aspirin (100 mg every other d) (n = 19 934) or matching placebo (n = 19 942).
-  **Outcomes:** total invasive cancer, excluding non-melanoma skin cancer. Secondary outcomes were breast, colorectal, and lung cancer.
-  **Patient follow up:** 97% for morbidity and 99% for mortality (intention to treat analysis).

*See glossary.

†Information provided by author.

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MAIN RESULTS

Aspirin and placebo groups did not differ for incidence of total invasive cancer (table). Groups also did not differ for incidence of breast, colorectal, or lung cancer (table). Group did not differ for total cancer mortality or site specific cancer mortality except for lung cancer mortality, which showed a reduction with aspirin (0.3% v 0.4%; relative risk 0.70, 95% CI 0.50 to 0.99).

CONCLUSION

In healthy women ≥ 45 years of age, low dose aspirin did not prevent total cancer or breast, colorectal, or other cancers.

Abstract and commentary also appear in ACP Journal Club.

Commentary

Two studies by Cook *et al* and Lee *et al* complete the reporting of primary outcomes from the Women's Health Study, a trial of low dose aspirin and high dose α tocopherol in the primary prevention of CVD and cancer in generally healthy female health care professionals. The 10 year results were fairly convincingly negative, with no hint of a benefit for either intervention in the primary end points. So many comparisons were made examining secondary outcomes and subgroups that caution is needed in interpreting any of these marginally significant findings, such as vitamin E reducing CV death or aspirin increasing cancer in never smokers.

The question then becomes, to whom and to what interventions do these results apply? Although all healthy women in the healthcare professions ≥ 45 years of age were eligible, only 10% of the participants were > 65 years. Thus, it may be hard to apply these results to older women. Subgroup analysis suggested a benefit in the older age group with both vitamin E and low dose aspirin¹ in the prevention of CVD. Doses of aspirin higher than the 100 mg every other day that was tested in the study by Cook *et al* might decrease the incidence of colorectal cancer^{2,3} but would be expected to carry greater toxicity. The finding that α tocopherol supplements had no benefit or might even increase mortality⁴ is at odds with well established epidemiological data regarding diets high in vitamin E, including α tocopherol and other antioxidants. Postulated causes include the displacement of other antioxidants, such as γ tocopherol by α tocopherol supplements.⁵ The observational epidemiological data also reflect uncontrolled confounding by other factors (eg, healthy diet).

Commentary continued on next page.

Aspirin v placebo to prevent total invasive cancer and breast, colorectal, and lung cancer at mean 10.1 years*

Outcomes	Aspirin	Placebo	RRI (95% CI)	NNH
Total invasive cancer	7.2%	7.2%	1.0% (-8 to 6)	Not significant
			RRR (CI)	NNT
Total cancer death	1.4%	1.5%	5.0% (-11 to 19)	Not significant
Breast cancer	3.1%	3.1%	2.0% (-9 to 13)	Not significant
Colorectal cancer	0.7%	0.7%	3.0% (-24 to 23)	Not significant
Lung cancer	0.5%	0.6%	22% (-3 to 41)	Not significant

*Abbreviations defined in glossary; RRI, RRR, NNH, NNT, and CI calculated from data in article.