Low dose aspirin lowered stroke risk but not risks of MI or cardiovascular deaths in women

Ridker PM, Cook NR, Lee IM, *et al.* A randomized trial of low-dose aspirin in the primary prevention of cardiovascular disease in women. *N Engl J Med* 2005;**352**:1293–304.

Clinical impact ratings GP/FP/Primary care ★★★★★★☆ IM/Ambulatory care ★★★★★☆☆ Neurology ★★★★★★☆ Haematology ★★★★★★☆

Q Is low dose aspirin effective for the primary prevention of cardiovascular disease in women?

METHODS

Design: randomised, placebo controlled trial (Women's Health Study).

Allocation: {concealed*}†.

Blinding: blinded {healthcare providers, participants, data collectors, and outcome assessors}†.*

Follow up period: mean 10 years.

Setting: USA and Puerto Rico.

Participants: 39 876 women ⩾45 years of age (mean age 55 y) who had no history of coronary artery disease, cerebrovascular disease, cancer (except non-melanoma skin cancer), or other major chronic illness; contraindication to the study medications; were not taking aspirin, non-steroidal anti-inflammatory drugs, anticoagulants, or corticosteroids; and were not taking vitamin A or E, or ß carotene supplements more than once per week.

Intervention: aspirin, 100 mg every other day (n = 19 934) or placebo (n = 19 942).

Outcomes: first major cardiovascular event (non-fatal myocardial infarction, non-fatal stroke, or cardiovascular death); individual cardiovascular endpoints; and adverse events.

Patient follow up: 97% (intention to treat analysis).

*See glossary.
†Information provided by author.

MAIN RESULTS

The table shows the results.

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CONCLUSION

Low dose aspirin lowered risk of stroke but not risks of myocardial infarction or death from cardiovascular causes.

Abstract and commentary also appear in ACP Journal Club.

Commentary—continued from previous page

In 2002, the US Preventive Services Task Force concluded that good evidence existed to suggest that aspirin lowers the incidence of coronary artery disease in adults without previous symptomatic CVD.[4] This conclusion was based on a review of 5 randomised trials involving >50 000 persons. However, aspirin did not reduce stroke and the evidence was less certain for women because only 20% of trial participants were women.

The Women's Health Study randomised almost 40 000 initially healthy women and, in contrast to previous trials, aspirin did not reduce MI or death but lowered the incidence for ischaemic stroke and transient ischaemic attack. These benefits were partly counterbalanced by an increase in gastrointestinal ulcers and bleeding, highlighting the potential for toxicity even with low doses of alternate daily aspirin, and the importance of balancing risks and benefits when making decisions about the use of aspirin for primary prevention of CVD.

Controversy concerning apparent sex differences in the antiplatelet effects of aspirin is not new. Subgroup analyses from early randomised aspirin trials suggested that men, but not women, benefited from aspirin;[5 6] later, large trials and systematic reviews[3] confirmed a benefit in both. In the Women's Health Study, the low event rates and use of a potentially suboptimal aspirin dose may have contributed to the apparent lack of benefit of aspirin for preventing MI. However, lack of evidence of benefit is not the same as evidence of lack of benefit; the 95% CI of the risk estimates do not exclude a 16% reduction in MI or a 20% reduction in major CVD with aspirin treatment. Nevertheless, if a benefit exists, it is small in absolute terms.

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1 Patrono C, Coller B, FitzGerald GA, *et al. Chest* 2004;**126**:234S–64S.
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3 Antithrombotic Trialists' Collaboration. *BMJ* 2002;**324**:71–86.
4 US Preventive Services Task Force. *Ann Intern Med* 2002;**136**:157–60.
5 The Canadian Cooperative Study Group. *N Engl J Med* 1978;**299**:53–9.
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Aspirin *v* placebo for primary prevention of cardiovascular disease in women at mean 10 years*

Outcomes	Aspirin	Placebo	RRR (95% CI)	NNT (CI)
Major cardiovascular event†	2.4%	2.6%	9% (−3 to 20)	Not significant
Stroke	1.1%	1.3%	17% (1 to 31)	445 (227 to 103 77)
Cardiovascular death	0.60%	0.63%	5% (−22 to 26)	Not significant
Transient ischaemic attack	0.93%	1.2%	22% (6 to 36)	385 (216 to 1687)
			RRI (CI)	**NNH (CI)**
Fatal or non-fatal MI	0.99%	0.97%	2% (−16 to 25)	Not significant
Transfusion for GI bleed	0.6%	0.5%	40% (7 to 83)	554 (305 to 2751)

*GI = gastrointestinal; MI = myocardial infarction. Other abbreviations defined in glossary; RRR, RRI, NNT, NNH, and CI calculated from data in article.
†Major cardiovascular event = non-fatal myocardial infarction, non-fatal stroke, or death from cardiovascular causes.