

Review: Aspirin reduces the incidence of coronary artery disease in persons at risk

Sanmuganathan PS, Ghahramani P, Jackson PR, Wallis EJ, Ramsay LE. Aspirin for primary prevention of coronary heart disease: safety and absolute benefit related to coronary risk derived from meta-analysis of randomised trials. *Heart*. 2001 Mar;85:265-71.

QUESTION

In persons at risk, what is the effectiveness of aspirin for primary prevention of coronary artery disease (CAD)?

DATA SOURCES

Randomized controlled trials from 1985 onward were identified by searching MEDLINE with the terms cardiovascular disease and aspirin. Meta-analyses and review articles were also scrutinized.

STUDY SELECTION

Studies were selected if they assessed the effectiveness of aspirin for primary prevention of CAD and assessed outcomes that included incidence of myocardial infarction (MI), stroke, all cardiovascular events (MI, stroke, and cardiovascular deaths), bleeding complications, and all-cause mortality.

DATA EXTRACTION

Data were extracted on study sample size, patient characteristics, key components of the intervention, duration of intervention, and outcomes.

MAIN RESULTS

4 trials (48 540 patients) were included in the meta-analysis. 25 133 patients received aspirin, and 23 407 received placebo. The incidence of MI and all cardiovascular events was higher in the placebo group than in the aspirin group (Table). The groups did not

differ for the incidence of stroke or all-cause mortality (Table). The incidence of bleeding complications was higher in the aspirin group than in the placebo group (Table). For patients with risk for CAD $\geq 1.5\%$ per year, treatment with aspirin for primary prevention was reported to be valuable and safe, with benefits likely to outweigh harms (Figure).

CONCLUSIONS

In persons at risk, aspirin reduces the incidence of coronary artery disease. This reduction is associated with an increase in the incidence of bleeding complications.

Source of funding: Not stated.

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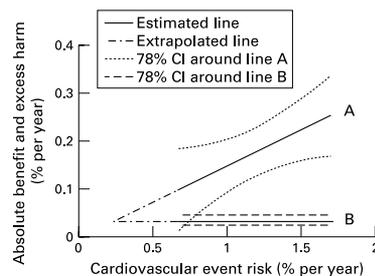


Figure. Absolute benefit (reduction in all cardiovascular events) (line A) and absolute harm (increase in major bleeds) (line B) from aspirin treatment, related to absolute cardiovascular event risk. The dotted lines show the 78% confidence regions. By extrapolation, benefit and harm from aspirin are equal when cardiovascular event risk is 0.22%/y, with an upper 95% confidence limit for this estimate at a cardiovascular event risk of approximately 0.8%/y. Reprinted with permission from BMJ Publishing Group.

Aspirin vs placebo for primary prevention of coronary artery disease*

Outcomes at 3.8 to 6.8 y	Weighted event rates		RRR (95% CI)	NNT (CI)
	Aspirin	Placebo		
Myocardial infarction	1.7%	2.4%	30% (20 to 38)	150 (113 to 224)
All cardiovascular events	4.5%	5.2%	13% (6 to 19)	149 (97 to 317)
All-cause mortality	3.2%	3.4%	6% (-3 to 14)	Not significant
			RRI (CI)	NNH (CI)
Stroke	1.5%	1.4%	5% (-22 to 9)	Not significant
Bleeding complications	1.0%	0.7%	63% (34 to 99)	375 (251 to 739)

*Abbreviations defined in Glossary; RRR, RRI, NNT, NNH, and CI calculated from data in original articles.

COMMENTARY

It is more difficult to assess treatment benefits with primary prevention than with secondary prevention because event rates are lower. This difficulty is shown again in the review by Sanmuganathan and colleagues of aspirin therapy for primary prevention of CAD events. The absolute benefit was a 0.15% reduction per year in myocardial infarction compared with an increased risk of 0.04% per year for major noncerebral hemorrhage (noncerebral bleeds causing death, transfusion, or operation) and 0.18% per year for nonminor hemorrhage (noncerebral bleeds not classified as minor). Differences in stroke or all-cause mortality were not statistically significant.

The 4 trials summarized in this paper have previously been reviewed in the sixth American College of Chest Physicians consensus conference on antithrombotic therapy (1). These authors recommended the use of 75 or 81 mg of aspirin daily for primary prevention because of lower stroke rates in the 2 trials that used this

dose compared with the 325-mg daily or every-other-day doses used in the other 2 trials. They also emphasized lowering the diastolic blood pressure below 85 mm Hg in patients receiving aspirin for primary prevention. Since the bleeding risk remains constant while the therapeutic benefit and the risk for cardiovascular events increase, treating higher-risk patients makes more clinical sense than does treating everyone. For risk assessment, the consensus conference authors emphasize older age and cardiac risk factors, whereas Sanmuganathan and colleagues offer a modified Sheffield table.

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Reference

1. Cairns JA, Theroux P, Lewis HD Jr, Ezekowitz M, Meade TW. Anti-thrombotic agents in coronary artery disease. *Chest*. 2001;119:228S-252S.