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FROM THE FAMILY PRACTICE INQUIRIES NETWORK

Which healthy adults should take aspirin?

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EVIDENCE-BASED ANSWER

In adults with no history of cardiovascular disease, aspirin reduces the risk of nonfatal myocardial infarction (MI). Aspirin prophylaxis does not decrease all-cause mortality, risk of fatal coronary heart disease, or risk of first stroke (strength of recommendation [SOR]: **A–**, based on multiple randomized controlled trials).

The benefits of aspirin use must be weighed against its potential risks, primarily gastrointestinal bleeding and cerebral hemorrhage. The benefit of aspirin increases with higher levels of cardiovascular risk, while the potential for harm remains relatively constant. Adults with a calculated 5-year coronary heart disease (CHD) event risk of 3% or greater should receive prophylaxis (SOR: **A**, based on multiple randomized controlled trials). The ideal dose of aspirin for prophylaxis is unknown, but it appears that low doses (75–81 mg/d) are as effective as higher doses.

EVIDENCE SUMMARY

The leading cause of morbidity and mortality in the United States is cardiovascular disease (ischemic CHD, stroke, peripheral vascular disease).[1] A meta-analysis of 5 placebo-controlled randomized controlled trials involving more than 50,000 patients free of CHD and stroke evaluated aspirin for primary prevention of cardiovascular disease. Since 3 of the trials excluded women, only 20% of the participants were female. The mean age of participants was 57 years.

The treatment groups took aspirin 75 to 500 mg/d for 3 to 7 years. The meta-analysis found that compared with placebo, aspirin significantly reduced total CHD events (odds ratio [OR]=0.72; 95% confidence interval [CI], 0.60–0.87).[2] Aspirin did not reduce coronary disease mortality (OR=0.87; 95% CI, 0.70–1.09); however, results from 1 study did achieve statistical significance (OR=0.64; 95% CI, 0.42–0.99).[3] No differences were found between aspirin-treated and control groups for all-cause mortality or ischemic stroke reduction.

Aspirin increased the risk of major gastrointestinal bleeding events by almost twofold (OR=1.70; 95% CI, 1.4–2.1). Three of the 5 trials showed no significant increase of intracranial hemorrhage event rates (OR=1.4; 95% CI, 0.9–2.0). Based on combined primary and secondary prevention trials, the risk of intracranial bleeding with aspirin is estimated at 0 to 2 events per 1000 patients per year.[2]

Although the ideal aspirin dosage is uncertain, lower dosages (75–81 mg/d) have been shown to be as beneficial as higher dosages, and may have fewer bleeding complications. Buffered and entericcoated formulations are no more protective than plain aspirin.[4]

In patients with no known cardiovascular disease, aspirin chemoprevention has been shown to decrease the risk of nonfatal MI and fatal CHD by 28%. At a 5-year CHD risk of 3%, the benefits of prophylaxis outweigh the harms (see **Table**) by 2 to 1—assuming the events of stroke, MI, and bleeding are considered roughly equivalent in severity. (A different threshold may be appropriate for patients that perceive 1 of these events as significantly more serious than the others.) Typical patients at a 3% or greater risk for cardiovascular disease include men aged >40 years, post-menopausal women, and younger persons with risk factors for CHD. Physicians determine cardiovascular risk from the presence and severity of risk factors: gender, age, blood pressure, lipid status, diabetes, and smoking status.

Simple risk-assessment tools based on Framingham data are available for computers and palmtop devices (eg, Heart to Heart CV Risk Assessment Calculator, **www.meddecisions.com**; National Institutes of Health, **www.nhlbi.nih.gov/health/prof/heart/**). Because only 2 trials included women, it is less clear whether both sexes benefit equally from aspirin prophylaxis.[1]

Net benefits and harms of aspirin prophylaxis, per 1000 patients

Outcome	Estimated 5-year risk for CHD event		
	1%	3%	5%
All-cause mortality	NS	NS	NS
CHD events avoided	3	8	14
Ischemic strokes avoided	NS	NS	NS
Hemorrhagic strokes	1	1	1
Major gastrointestinal bleeding	3	3	3

NS, not significant

RECOMMENDATIONS FROM OTHERS

The US Preventive Services Task Force recommends that clinicians discuss aspirin prophylaxis with adults at increased risk for CHD (defined as a 5-year risk of 3% or more). Discussion should include the potential

benefits and harms of aspirin therapy.[5]

The American Heart Association recommends low-dose aspirin in people at higher risk of coronary heart disease (especially those with a 10-year CHD risk of 10% or greater).[6] The European Society of Cardiology says there is evidence that low-dose aspirin can reduce the risk of cardiovascular events in asymptomatic high-risk people, such as those with diabetes or well-controlled hypertension, and in men at high multifactorial risk of cardiovascular disease.[7]

CLINICAL COMMENTARY

Aspirin: effective, safe, inexpensive—and it may prevent heart attacks

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Acetylsalicylic acid was first compounded in Germany by chemist Felix Hoffman in 1897. According to information from the Bayer Company, aspirin's cardioprotective effect was first recognized by Dr Lawrence Craven, a California general practitioner. He noted a decreased rate of heart attacks in patients taking this medication.

We now have evidence supporting Dr Craven's astute clinical observation. In adults with no history of cardiovascular disease, aspirin reduces the risk of nonfatal MI. For an individual at a 5-year CHD risk as low as 3%, the benefits of prophylaxis outweigh the harms. The leading cause of morbidity and mortality in the US is still cardiovascular disease. A simple, effective, safe, and inexpensive preventive measure like recommending aspirin has the potential to prevent heart attacks on a grand scale. A low-dose aspirin per day should be recommended for patients at risk for cardiovascular disease, including men aged >40 years, postmenopausal women, and younger persons with risk factors for CHD. As a 40-something male with a family history of cardiovascular disease reviewing this Clinical Inquiry, I will be taking my aspirin a day.

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