

# Editorials: *Controversies in Family Medicine*

► See related U.S. Preventive Services Task Force on page 1464, and Putting Prevention into Practice on page 1469.

## The Case Against Routine Aspirin Use for Primary Prevention in Low-Risk Adults

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Given the burden of cardiovascular disease (CVD) in Western society, preventing the life-threatening complications of acute arterial thrombosis is paramount. Platelets play a central role in arterial thrombosis. The antiplatelet agent aspirin alters platelet function by inhibiting cyclooxygenase-1 enzymes. This prevents the generation of thromboxane A<sub>2</sub>, an important amplifier of platelet activation. Numerous clinical trials have established the effectiveness of aspirin use for acute coronary syndromes and for secondary prevention of CVD, as well as after percutaneous coronary interventions. The major benefit of aspirin appears to be a reduction in recurrent cardiovascular events. However, this reduction in events comes with the risk of increased bleeding, including gastrointestinal and intracerebral hemorrhage.

The benefit of aspirin use in adults without known coronary heart disease (primary prevention) is controversial. A meta-analysis of primary prevention trials found a 12 percent relative reduction in serious vascular events (0.51 versus 0.57 percent per year for aspirin and control, respectively; number needed to treat = 1,667), but no evidence of a reduction in mortality associated with randomization to aspirin therapy. Additionally, a statistically significant increase in gastrointestinal and other extracranial bleeding events occurred with aspirin therapy (0.10 versus 0.07 percent per year for aspirin and control, respectively; number needed to harm = 3,334).<sup>1</sup> Even among patient populations traditionally thought to be at high risk of cardiovascular events, such as persons with diabetes mellitus or peripheral vascular disease,



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aspirin use does not clearly provide benefit in the primary prevention setting.

Two large prospective primary prevention trials evaluated the role of aspirin use in patients with diabetes and did not detect a significant benefit of aspirin in reducing atherosclerotic events (hazard ratio = 0.80; 95% confidence interval [CI], 0.58 to 1.10;  $P = .16^2$ ; hazard ratio = 0.98; 95% CI, 0.76 to 1.26;  $P = .86^3$ ). A meta-analysis of the primary prevention trials focusing on patients with diabetes also did not detect a reduction in the risk of major cardiovascular events associated with aspirin therapy (relative risk = 0.90; 95% CI, 0.81 to 1.00).<sup>4</sup>

The primary prevention trials have also been explored with respect to sex, and it was determined that aspirin reduces the risk of nonfatal cardiovascular events differently in men than in women. Aspirin use is associated with a 32 percent reduction in myocardial infarction in men (odds ratio = 0.68; 95% CI, 0.54 to 0.86;  $P = .001$ ), whereas it is associated with a 17 percent reduction of stroke in women (odds ratio = 0.83; 95% CI, 0.70 to 0.97;  $P = .02$ ). However, aspirin use does not affect total mortality in either sex, perhaps because of an increase in bleeding events that occur at roughly similar rates in women and men.<sup>5</sup> It is also important to note that the primary prevention trials with aspirin were performed with differing levels of statin use. Patients at highest cardiovascular risk derived the most benefit from antiplatelet drugs, and lowering CVD risk with statin use would be expected to further reduce any potential benefit of aspirin in primary prevention. ►

The U.S. Preventive Services Task Force (USPSTF) recommends against the routine use of aspirin for prophylaxis against cardiovascular events, and instead recommends aspirin use in middle-aged adults only when the potential benefit outweighs the risk of gastrointestinal bleeding. The USPSTF also states that the evidence is insufficient to recommend the prophylactic use of aspirin in patients 80 years and older.<sup>6</sup> Accordingly, recent recommendations from a joint American Diabetes Association/American Heart Association/American College of Cardiology Foundation consensus statement suggested that use of aspirin as primary prevention in persons with diabetes should be reserved for those with a 10-year risk of cardiovascular events that is greater than 10 percent.<sup>7</sup>

In summary, a policy of generalized aspirin use in adults for the primary prevention of CVD is probably not warranted. Instead, the benefits and risks of aspirin therapy for primary prevention need to be considered on an individual basis, and should be reserved for persons at highest long-term risk of CVD and at low risk of gastrointestinal bleeding.

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REFERENCES

1. Antithrombotic Trialists' (ATT) collaboration, Baigent C, Blackwell L, Collins R, et al. Aspirin in the primary and secondary prevention of vascular disease: collaborative meta-analysis of individual participant data from randomised trials. *Lancet*. 2009;373(9678):1849-1860.
2. Ogawa H, Nakayama M, Morimoto T, et al. Low-dose aspirin for primary prevention of atherosclerotic events in patients with type 2 diabetes: a randomized controlled trial [published correction appears in *JAMA*. 2009; 301(18):1882]. *JAMA*. 2008;300(18):2134-2141.
3. Belch J, MacCuish A, Campbell I, et al.; Prevention of Progression of Arterial Disease and Diabetes Study Group; Diabetes Registry Group; Royal College of Physicians Edinburgh. The prevention of progression of arterial disease and diabetes (POPADAD) trial: factorial randomised placebo controlled trial of aspirin and antioxidants in patients with diabetes and asymptomatic peripheral arterial disease. *BMJ*. 2008;337:a1840.
4. De Berardis G, Sacco M, Strippoli GF, et al. Aspirin for primary prevention of cardiovascular events in people with diabetes: meta-analysis of randomised controlled trials [published correction appears in *BMJ*. 2010;240: c374]. *BMJ*. 2009;339:b4531.
5. Berger JS, Roncaglioni MC, Avanzini F, Pangrazzi I, Tognoni G, Brown DL. Aspirin for the primary prevention of cardiovascular events in women and men: a sex-specific meta-analysis of randomized controlled trials [published correction appears in *JAMA*. 2006; 295(17):2002]. *JAMA*. 2006;295(3):306-313.
6. Aspirin for the prevention of cardiovascular disease: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med*. 2009;150(6):396-404.
7. Pignone M, Alberts MJ, Colwell JA, et al. Aspirin for primary prevention of cardiovascular events in people with diabetes: a position statement of the American Diabetes Association, a scientific statement of the American Heart Association, and an expert consensus document of the American College of Cardiology Foundation [published corrections appear in *Diabetes Care*. 2011;34(1):247-248, and *Diabetes Care*. 2010;33(9):2129-2131]. *Diabetes Care*. 2010;33(6):1395-1402. ■