

## Re-assessing aspirin: not so good for primary prevention?

**The clinical issue:** Aspirin has clear evidence and indications for preventing myocardial infarction (MI) and ischemic stroke in patients who already have cardiovascular disease (CVD). Current guidelines also recommend it for primary prevention in patients with CVD risk factors such as diabetes or hypertension. However, new evidence suggests that the benefits of aspirin for patients without established CVD may be modest, especially in light of its risks of bleeding.

**The new evidence:** Seshasai and colleagues conducted a meta-analysis of nine large, randomized controlled trials that compared aspirin to placebo in patients without CVD, many of whom had risk factors such as diabetes. Together, the trials included over 100,000 participants followed for an average of about 6 years.

Compared to placebo, patients who took aspirin were 10% less likely to have a CVD event (95% confidence interval [CI] 4% to 15%), mostly because of lower rates of non-fatal MI. Studies published after 2000 showed no evidence that aspirin was better than placebo for reducing non-fatal MI. Aspirin did not reduce the risk of death from cardiovascular disease or cancer. It did reduce death from non-cardiovascular causes by 8% (95%CI 0% to 15%), although this change was of borderline statistical significance. Aspirin did, however, increase the risk of serious bleeding (defined as bleeding that is fatal, intracranial, retinal, gastrointestinal, or requiring transfusion or hospitalization) by 31% (95%CI 14% to 50%).

The benefits of aspirin were greater for patients whose baseline risk of CVD was higher, although these patients also faced a greater risk of bleeding. Overall, 120 patients would need to be treated with aspirin for 6 years to prevent one CVD event. In contrast, for every 73 patients treated with aspirin, one would be harmed by a serious bleeding event.

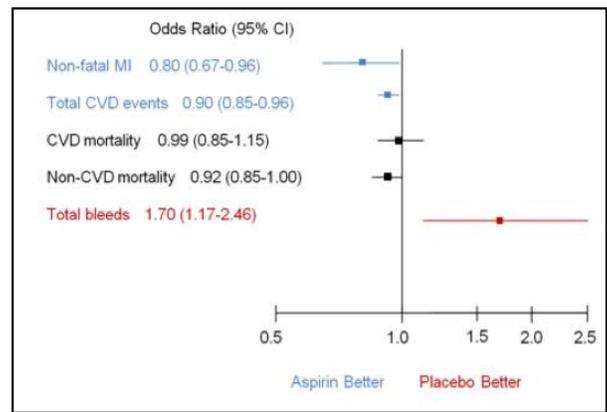
**Limitations:** The analysis did not quantify the specific risks and benefits of aspirin in individual subgroups, such as the elderly or those with peripheral artery disease or diabetes. The studies reviewed were too short to reliably evaluate cancer mortality outcomes.

**Bottom line:** In patients without prior CVD, the benefits of aspirin are more modest than previously thought, while the risks of therapy are substantial. The smaller benefit attributable to aspirin in more recent studies may be due to improvements in cholesterol and/or blood pressure management. As a result, the current evidence does not support the routine use of aspirin for primary prevention in low-risk patients.

**References:** 1. Seshasai SR, Wijesuriya S, Sivakumaran R, Nethercott S, Erqou S, Sattar N, Ray KK. Effect of Aspirin on Vascular and Nonvascular Outcomes: Meta-analysis of Randomized Controlled Trials. *Arch Intern Med.* 2012 Feb 13;172(3):209-16. 2. Mora S. Aspirin Therapy in Primary Prevention (comment). *Arch Intern Med.* 2012 Feb 13;172(3):217-8. 3. Guyatt GH, Akl EA, Crowther M et al, for the American College of Chest Physicians Antithrombotic Therapy and Prevention of Thrombosis Panel. Executive Summary: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest* February 2012 141:2 suppl 7S-47S.

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**These are general recommendations only; specific clinical decisions should be made by the treating physician based on an individual patient's clinical condition.**



Effect of aspirin on vascular and nonvascular outcomes in primary prevention patients. CVD, cardiovascular disease; and MI, myocardial infarction.

Figure adapted from *Effect of aspirin on vascular and nonvascular outcomes: Meta-analysis of randomized controlled trials.* *Arch Intern Med.* 2012; 172(3):209-216.