



Rethinking daily aspirin for primary prevention

An updated meta-analysis of newer RCTs seems to settle the matter as to whether to use aspirin in individuals with no known history of atherosclerotic CVD.

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PRACTICE CHANGER

Do not routinely use aspirin for primary prevention of cardiovascular disease (CVD). There is no identifiable mortality benefit for those without established CVD—regardless of risk factors. And aspirin therapy increases the risk of major bleeding.

STRENGTH OF RECOMMENDATION

A: Based on a meta-analysis of 11 randomized trials involving 157,248 patients who received aspirin for primary prevention.¹

Mahmoud AN, Gad MM, Elgendy AY, et al. Efficacy and safety of aspirin for primary prevention of cardiovascular events: a meta-analysis and trial sequential analysis of randomized controlled trials. *Eur Heart J*. 2019;40:607-617.

ILLUSTRATIVE CASE

A 55-year-old man with well-controlled diabetes, hypertension, and sleep apnea arrives at your office for a routine annual physical. In reviewing his medications, you note that he takes a low-dose aspirin daily for “heart health.” He has no known cardiovascular disease (CVD). His calculated 10-year risk of a major cardiovascular event is 11%.

Should this patient continue taking a daily aspirin for primary prevention of CVD?

Many patients in the United States take aspirin for primary prevention of CVD as recommended by the US Preventive Services Task Force (USPSTF).² This recommendation was based on older studies of populations in which

smoking rates were higher and statin use was less common, leading to an overall higher risk of CVD.³ (The USPSTF is currently in the process of updating its recommendation.) More recent RCTs have been done in patients with a lower baseline risk of CVD, and these outcomes are more generalizable to today’s population. This new meta-analysis includes recent RCTs that evaluated whether there is value in using aspirin for the primary prevention of CVD.

STUDY SUMMARY

No reduction in risk, increased chance of bleeding

Mahmoud and colleagues conducted a meta-analysis of 11 randomized controlled trials that included 157,248 patients and assessed the efficacy and safety of aspirin for primary prevention of cardiovascular events.¹ The mean age of the total population was 61.3 years; 52% were women and 14% were smokers. The doses of aspirin used in most of the studies were ≤ 100 mg/d, although 2 of the studies examined doses that were higher. Patients were followed for a mean of 6.6 years. The primary efficacy outcome was all-cause mortality, and the primary safety outcome was major bleeding (as defined by each study). The secondary outcomes included cardiovascular mortality, fatal and nonfatal myocardial infarction (MI), and fatal and nonfatal ischemic stroke.

Aspirin did not lower all-cause mortality

➤ Review of current guidelines and studies regarding the use of aspirin for primary prevention of CVD shows that the tide has been turning against this practice.

(risk ratio [RR] = 0.98; 95% confidence interval [CI], 0.93-1.02) and was associated with an increased risk of major bleeding (RR = 1.47; 95% CI, 1.31-1.65; number needed to harm = 250) and intracranial hemorrhage (RR = 1.33; 95% CI, 1.13-1.58). Aspirin also had no effect on all-cause mortality in subgroup analyses of patients with diabetes mellitus or high cardiovascular risk (10-year risk > 7.5%). There was (again) an increased risk of major bleeding.

Aspirin had no effect on the secondary outcomes—with the exception of the incidence of MI (RR = 0.82; 95% CI, 0.71-0.94; number needed to treat = 333). However, this outcome was associated with considerable heterogeneity ($I^2 = 67%$), and the reduction was no longer evident after limiting the analysis to the more recent trials.

WHAT'S NEW?

Study is emblematic of a shift away from daily aspirin

Review of current guidelines and studies regarding the use of aspirin for primary prevention of CVD shows that the tide has been turning against this practice, but the change has been gradual. Newer studies—large RCTs such as ARRIVE (Aspirin to Reduce Risk of Initial Vascular Events) and ASCEND (A Study of Cardiovascular Events in Diabetes)—found no mortality benefit (all-cause or cardiovascular) from using aspirin in this context.

The USPSTF guidelines in 2016 recommended prescribing daily aspirin for adults ages 50 to 59 who have a > 10% 10-year CVD risk and discussing with adults ages 60 to 69 the risks and benefits of daily aspirin.²

The 2019 American College of Cardiology/American Heart Association guidelines state that aspirin should no longer be used routinely for primary prevention, given the lack of net benefit. Patients ages 40 to 70 who are not at increased risk of bleeding with a higher risk of CVD may be considered for daily low-dose aspirin. The guidelines also state that adults > 70 years or those with increased risk of bleeding should not be started on a daily aspirin.⁴

CAVEATS

Jury is still out regarding very high-risk patients

While the meta-analysis by Mahmoud and colleagues makes a good case for discontinuing aspirin for primary prevention in most patients, the data do not examine in detail whether there is a benefit in patients with very high risk (> 20%) for atherosclerotic CVD. More studies are needed before making recommendations for that specific subgroup.

CHALLENGES TO IMPLEMENTATION

Patients may not be eager to give up an accepted practice

Physicians have been recommending aspirin for primary prevention of CVD for decades and many patients, who purchase aspirin themselves, are vested in the notion that aspirin protects them. It will take time for this change in practice to be accepted. Some patients may continue taking aspirin despite recommendation to stop. Primary care physicians will need to educate patients and clearly explain the rationale for stopping daily aspirin. **JFP**

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