



Q/What are the benefits and risks of daily low-dose aspirin for primary prevention of CV events?

EVIDENCE-BASED ANSWER

A ONE NONFATAL MYOCARDIAL INFARCTION (MI) will be avoided for every 126 to 138 adults who take daily aspirin for 10 years (strength of recommendation [SOR]: A, systematic reviews and meta-analyses of multiple randomized controlled trials [RCTs]).

Taking low-dose aspirin for primary prevention shows no clear mortality ben-

efit. A benefit for primary prevention of stroke is less certain. Although no evidence establishes increased risk of hemorrhagic stroke from daily low-dose aspirin, one gastrointestinal hemorrhage will occur for every 72 to 357 adults who take aspirin for longer than 10 years (SOR: A, systematic reviews and meta-analyses of multiple RCTs and cohort studies).

Evidence summary

A 2013 systematic review of RCTs, systematic reviews, and meta-analyses examined the prophylactic use of low-dose aspirin for the primary prevention of cardiovascular disease (CVD) among adults 18 years and older.¹ Twenty-seven papers met inclusion criteria; the total number of patients wasn't reported.

A composite finding of nonfatal MI, nonfatal stroke, and CVD death indicated a number needed to treat (NNT) of 138 over 10 years of therapy (relative risk [RR]=0.90; 95% confidence interval [CI], 0.85-0.96). CVD death wasn't disaggregated from this composite, but an analysis of all-cause mortality didn't reach statistical significance (RR=0.94; 95% CI, 0.88-1.00). RR for nonfatal stroke alone also wasn't disaggregated.

Risk of gastrointestinal (GI) bleeding was found to be a number needed to harm (NNH) of 108 over 10 years (RR=1.37; 95% CI, 1.15-1.62) whereas risk of hemorrhagic stroke didn't reach statistical significance (RR=1.32; 95% CI, 1.00-1.74). This population-level review didn't report disaggregated findings by age or baseline atherosclerotic cardiovascular disease (ASCVD) risk.

Another review finds benefit only for prevention of nonfatal MI

A 2016 systematic review included 2 good-quality and 9 fair-quality RCTs evaluating the benefits of low-dose aspirin compared with placebo or no treatment for primary prevention of CVD events in 118,445 patients ages 40 years and older.² The review found benefit only for nonfatal MI, with an NNT of 126 over 10 years (RR=0.78; 95% CI, 0.71-0.87). There was no change in RR for nonfatal stroke (RR=0.95; 95% CI, 0.85-1.06); negligible impact on all-cause mortality (RR=0.95; 95% CI, 0.89-0.99); and no statistically significant benefit for CVD-specific mortality (RR=0.94; 95% CI, 0.86-1.03).

Aspirin carries risk of GI hemorrhage, but not hemorrhagic stroke

A companion 2016 systematic review of 16 RCTs, cohort studies, and meta-analyses evaluated the risk of serious bleeding in patients using low-dose aspirin for primary prevention of either CVD or cancer.³ The review (number of patients not reported) found that estimated excess bleeding events differed substantially depending on varying

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sources for baseline bleeding rates in aspirin nonusers.

The most conservative comparison yielded an NNH of 72 over 10 years of therapy (1.39 excess major GI bleeding events per 1000 person-years, 95% CI, 0.70-2.28). Comparison with other baseline bleeding rates in trial data yielded less risk of harm, with an NNH of 357 over 10 years (0.28 excess major GI bleeding events per 1000 person-years; 95% CI, 0.14-0.46). Excess risk for hemorrhagic stroke was not statistically significant (0.32 excess events per 1000 person-years; 95% CI, -0.05 to 0.82).

Recommendations

The US Preventive Services Task Force gives a Grade B recommendation (recommended, based on moderate to substantial benefit) to the use of aspirin to prevent CVD among adults ages 50 to 59 years with an ASCVD risk $\geq 10\%$ who don't have increased bleeding risk and are capable of 10 years of pharmacologic adherence with a similar expected longevity.⁴ The Task Force assigns a Grade C recommendation (individual and professional choice) to patients 60 to 69 years of age with the same constellation of risk factors and health status. Insufficient evidence was available to make recommendations for other age cohorts.

The American College of Chest Physicians recommends 75 to 100 mg of aspirin daily for adults 50 years or older who have moderate to high CV risk, defined as $\geq 10\%$.⁵

A working group of the European Society of Cardiology (ESC) released a statement in 2014 recommending aspirin for primary prevention in adults with a CV risk $\geq 20\%$ and no risk factors for bleeding. For patients with a CVD risk between 10% and 20%, the ESC recommends deferring to patient preference.⁶

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