Review: aspirin reduces CAD events in people with no history of cardiovascular disease, but it increases gastrointestinal bleeding


QUESTION: What are the benefits and harm of aspirin use to prevent coronary artery disease (CAD) events in people with no history of cardiovascular disease?

Data sources
Studies were identified by searching Medline (1966 to May 2001), reviewing bibliographies of relevant studies and systematic reviews, and contacting experts.

Study selection
Randomised controlled trials (RCTs) of aspirin related benefits were selected if they compared aspirin with placebo or no aspirin; included participants with no history of cardiovascular disease; had a duration ≥ 1 year; and assessed myocardial infarction (MI), stroke, and mortality. Case control studies, RCTs, and systematic reviews of aspirin related harm were selected if they assessed haemorrhagic stroke or gastrointestinal (GI) bleeding.

Data extraction
Data were extracted on study year and location, duration of treatment, patient characteristics, aspirin dosage, control condition, and additional treatments. Quality of trials was assessed on the basis of methods of randomisation, blinding, analysis by intention to treat, follow up, and crossover of assigned interventions.

Main results
5 RCTs (n=53035) were included in the meta-analysis: the British Male Doctors’ Trial, the Physicians’ Health Study (PHS), the Thrombosis Prevention Trial (TPT), the Hypertension Optimal Treatment Trial, and the Primary Prevention Project. Most participants were men (78%) and were middle aged, trial duration ranged from 3 to 7 years, and aspirin dosage was < 162 mg/day in 4 trials and 500 mg/day in 1 trial. Study quality was high overall. Meta-analyses showed that aspirin reduced the combined outcome of non-fatal MI or death from CAD but did not differ from the control intervention for CAD mortality alone, all cause mortality, or stroke. Previous meta-analyses that included the 5 trials showed that aspirin increased the risk for a major GI bleeding event but did not differ from the control intervention for haemorrhagic stroke (table).

Conclusions
In people with no history of cardiovascular disease, aspirin reduces the risk for overall coronary artery disease events but does not affect the risk for coronary artery disease mortality, all cause mortality, or stroke. The risk for gastrointestinal bleeding is increased, but the risk for haemorrhagic stroke is not.

<table>
<thead>
<tr>
<th>Outcomes at 3 to 7 years</th>
<th>Weighted event rates</th>
<th>Aspirin</th>
<th>Control</th>
<th>RRR (95% CI)</th>
<th>NNT (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total coronary events</td>
<td>1.9%</td>
<td>2.4%</td>
<td>28%</td>
<td>(13 to 39)</td>
<td>150 (105 to 324)</td>
</tr>
<tr>
<td>CAD mortality</td>
<td>0.67%</td>
<td>0.63%</td>
<td>13%</td>
<td>(9 to 30)</td>
<td>Not significant</td>
</tr>
<tr>
<td>All-cause mortality</td>
<td>3.5%</td>
<td>3.4%</td>
<td>7%</td>
<td>(2 to 16)</td>
<td>Not significant</td>
</tr>
<tr>
<td>Stroke</td>
<td>1.4%</td>
<td>1.3%</td>
<td>2%</td>
<td>(15 to 23)</td>
<td>Not significant</td>
</tr>
<tr>
<td>Major gastrointestinal bleeding</td>
<td>0.8%</td>
<td>0.48%</td>
<td>69%</td>
<td>(40 to 109)</td>
<td>302 (193 to 528)</td>
</tr>
<tr>
<td>Haemorrhagic stroke</td>
<td>0.22%</td>
<td>0.17%</td>
<td>40%</td>
<td>(10 to 100)</td>
<td>Not significant</td>
</tr>
</tbody>
</table>

*Abbreviations defined in glossary; RRR, RRI, NNT, NNH, and CI calculated from data in article by using a random effects model.

COMMENTARY
The meta-analysis by Hayden et al provides the rationale behind the recent US Preventive Services Task Force (USPSTF) recommendation supporting the use of aspirin for primary prevention of cardiovascular events in high risk patients.1–3 The authors used data from 5 RCTs to construct a model of the estimated benefits and harm of aspirin for patients at different 5 year risks for CAD events. In patients with a 5 year risk ≤ 1%, the harm of treatment outweighed the benefits; for those with a 5 year risk ≥ 3%, the benefits exceeded the harm. Neither mortality nor stroke was reduced. Patients benefited from a reduction in MI, which was balanced by increases in GI bleeding and haemorrhagic stroke. The studies reviewed had limited power to detect increases in haemorrhagic stroke.

It makes sense that patients at higher risk are more likely to benefit from aspirin treatment, as has been shown for secondary cardiovascular disease prevention.1 However, we share the authors’ concerns about extrapolating data from the population studied to high risk groups. For example, in the TPT, older patients did not benefit from aspirin, whereas younger patients did; aspirin benefited those with a systolic blood pressure (SBP) < 130 mm Hg but not those with SBP > 145 mm Hg. In the PHS, aspirin benefited those with lower cholesterol concentrations more than those with higher concentrations.1 However, these are subgroup analyses and may not be valid. Furthermore, we do not know if we can extrapolate these results to women.

The new USPSTF recommendation on aspirin for primary prevention should be placed in the context of primary prevention of cardiovascular disease through smoking cessation, dietary modification, and treatment of hypertension and hyperlipidaemia. These measures may be more important because they are well proved, do not increase risk for bleeding, and are associated with lower numbers needed to treat.2 Meera Jain, MD Mark Rosenberg, MD Providence Portland Medical Center, Portland, Oregon, USA