Aspirin Therapy in Primary Prevention of ASCVD

**PROBLEM**

- The use of aspirin in primary prevention of atherosclerotic cardiovascular disease (ASCVD) has faced increasing controversy.
- A recently published four-trial series evaluating the use of aspirin therapy in the primary prevention of ASCVD has yielded potential challenges to decades-old research as reflected in the current U.S. Preventive Services Task Force guidelines.
  - In three of the four trials, aspirin failed to show benefit of primary cardiovascular prevention, while suggesting potential harm including higher all-cause mortality and major hemorrhage with reduced disability-free survival.
  - A fourth trial showed modest reduction in serious vascular events which were “largely counterbalanced” by the observed rate of major bleeding events within the trial.

**SOLUTION**

- Low-dose aspirin SHOULD NOT be routinely administered for primary prevention of ASCVD to individuals >70 years of age and those at increased risk of bleeding irrespective of age (risk may outweigh benefit), or <40 years of age (insufficient data for determining risk-to-benefit).
- Low-dose aspirin MAY be considered for primary prevention of ASCVD among adults aged 40-70 years who possess higher ASCVD risk but remain at low probability for bleeding events.

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### LOW-DOSE ASPIRIN USE IN PRIMARY PREVENTION OF ASCVD

<table>
<thead>
<tr>
<th>Study</th>
<th>Patient Population</th>
<th>Benefit</th>
<th>Harm (Aspirin vs. Placebo)</th>
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</thead>
<tbody>
<tr>
<td>ASCEND</td>
<td>Diabetes without ASCVD</td>
<td>↓In MACE 8.5% vs. 9.6% (rate ratio 0.88, CI 0.79-0.97)</td>
<td>↑Risk of major bleeding 4.1% vs. 3.2% (rate ratio 1.29, CI 1.09-1.52)</td>
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<tr>
<td>ASPREE</td>
<td>Elderly: ≥70 years of age OR ≥65 years of age (Blacks and Hispanics)</td>
<td>No reduction all-cause mortality 5.9% vs. 5.2% (HR 1.14, CI 1.01-1.29) No reduction in MACE† 4.7% vs. 4.9% (HR 0.95, CI 0.83-1.08)</td>
<td>↑Risk of major hemorrhage 3.8% vs. 2.8% (HR 1.38, CI 1.18-1.62)</td>
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<tr>
<td>ARRIVE</td>
<td>Men ≥ 55 or women ≥60 years of age with moderate ACC/AHA 10-year ASCVD Risk Score (20-30%)</td>
<td>No reduction in MACE† 4.29% vs. 4.48% (HR 0.96, CI 0.81-1.13)</td>
<td>↑Risk of gastrointestinal bleeding 0.97% vs. 0.46% (HR 2.11, CI 1.36-3.28)</td>
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</tbody>
</table>

MACE: major adverse cardiac events; HR: hazard ratio; CI: confidence interval
† A pre-specified secondary endpoint
§ Per protocol population analysis = incidence of fatal and non-fatal myocardial infarction

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### PREVENT POTENTIAL ERRORS

- If your patient is taking aspirin and does not have a history of ASCVD, calculate their ASCVD risk, reevaluate the need (considering other known ASCVD risk factors such as strong family history of premature myocardial infarction, inability to meet lipid or blood pressure targets, and/or significant elevation in coronary calcium score), and have a risk-to-benefit discussion.
- Primary ASCVD prevention should focus on lifestyle modifications, adequate physical activity, tobacco cessation, weight management, and appropriate control of blood pressure and low-density lipoprotein cholesterol.

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