Aspirin

Role in Primary Prevention?

ASPREE
ASCEND
ARRIVE
73 year old man with hypertension, dyslipidemia, and diabetes, but no known CAD, comes in for annual exam. Based on recent ASPREE Investigator Group trial, adding 100 mg Aspirin to his regimen will:

A) Increase major hemorrhage risk and not change risk of cardiovascular (CV) disease
B) Increase major hemorrhage risk but lower risk of CV disease outcomes
C) Not change hemorrhage risk and reduce risk of CV disease
D) Have no effect on either major hemorrhage risk or CV disease
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Question 1

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ASPREE Investigator Group
NEJM Oct 2018
Primary Prevention Trial

• Age 70 (or 65 Black and Hispanic) and older
• No known cardiovascular disease, dementia or disability
• Randomized to 100 mg or placebo
• 19114 enrolled, medium 4.7 years follow up
• 2 CV risk factors 42%, 3-4 risk factors 25%
• Use of PPI on enrollment 25%
Cumulative Incidence Cardiovascular Disease

Hazard ratio, 0.95 (95% CI, 0.83–1.08)

<table>
<thead>
<tr>
<th>Years since Randomization</th>
<th>Aspirin</th>
<th>Placebo</th>
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<tbody>
<tr>
<td>0</td>
<td>9525</td>
<td>9589</td>
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<tr>
<td>1</td>
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<td>4</td>
<td>5827</td>
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<td>5</td>
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<td>3578</td>
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<tr>
<td>6</td>
<td>1234</td>
<td>1223</td>
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Cumulative Incidence Major Hemorrhage

Hazard ratio, 1.38 (95% CI, 1.18–1.62)
P<0.001

<table>
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<tr>
<td></td>
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<tr>
<td></td>
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<td>0.56</td>
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<tr>
<td></td>
<td>2</td>
<td>1.72</td>
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<tr>
<td></td>
<td>3</td>
<td>3.2</td>
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<td>4</td>
<td>5.0</td>
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<tr>
<td></td>
<td>5</td>
<td>7.1</td>
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No. at Risk

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<tr>
<th></th>
<th>9525</th>
<th>9337</th>
<th>9094</th>
<th>7833</th>
<th>5826</th>
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<th>1248</th>
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<tbody>
<tr>
<td>Aspirin</td>
<td>9589</td>
<td>9424</td>
<td>9192</td>
<td>7930</td>
<td>5935</td>
<td>3632</td>
<td>1244</td>
</tr>
<tr>
<td>Placebo</td>
<td></td>
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</table>
Effect of Aspirin on All Cause Mortality In The Healthy Elderly

ASPREE INVESTIGATOR GROUP
NEJM Oct 2018
Secondary end point of death analysis

- Higher all cause mortality seen among healthy older adults who received Aspirin vs. Placebo, primary cancer related deaths.
- “Result was unexpected and should be interpreted with caution.”
- Cancer related death 3.1% Aspirin Group, 2.3% Placebo Group, (Hazard ratio 1.31; 95% CI, 1.10-1.56)
60 yr old woman with Type II DM, hypertension, and obesity but no known CAD comes in for annual exam. Based on recently published ASCEND Study Group trial, adding 100 mg Aspirin will:

A) Decrease rate of gastrointestinal cancer
B) Decrease rate of overall cancer
C) Reduce rate of serious vascular event but increase major bleeding events
D) Increase major bleeding without changing rate of serious vascular events
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Primary Prevention in Diabetes

ASCEND study collaborative
NEJM Oct 2018
Primary Prevention Trial

• Adults with DM over age 40
• Type 1 or Type 2 (94% Type 2 enrolled)
• No known CAD
• Excluded if clear contraindication to Aspirin
• Randomized to 100 mg Aspirin or Placebo
• 15,480 participants
• 7.4 years mean follow up
• 17% High vascular risk score, 43% Moderate vascular risk score
<table>
<thead>
<tr>
<th>Type of Event</th>
<th>Aspirin (N=7740)</th>
<th>Placebo (N=7740)</th>
<th>Rate Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vascular Outcomes</td>
<td>no. of participants with event (%)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Nonfatal myocardial infarction</td>
<td>191 (2.5)</td>
<td>195 (2.5)</td>
<td>0.98 (0.80–1.19)</td>
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<tr>
<td>Nonfatal presumed ischemic stroke</td>
<td>202 (2.6)</td>
<td>229 (3.0)</td>
<td>0.88 (0.73–1.06)</td>
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<tr>
<td>Vascular death excluding intracranial hemorrhage</td>
<td>197 (2.5)</td>
<td>217 (2.8)</td>
<td>0.91 (0.75–1.10)</td>
<td></td>
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<tr>
<td>Any serious vascular event excluding TIA</td>
<td>542 (7.0)</td>
<td>587 (7.6)</td>
<td>0.92 (0.82–1.03)</td>
<td></td>
</tr>
<tr>
<td>TIA</td>
<td>168 (2.2)</td>
<td>197 (2.5)</td>
<td>0.85 (0.69–1.04)</td>
<td></td>
</tr>
<tr>
<td>Any serious vascular event including TIA</td>
<td>658 (8.5)</td>
<td>743 (9.6)</td>
<td>0.88 (0.79–0.97)</td>
<td>0.01</td>
</tr>
<tr>
<td>Any arterial revascularization</td>
<td>340 (4.4)</td>
<td>384 (5.0)</td>
<td>0.88 (0.76–1.02)</td>
<td></td>
</tr>
<tr>
<td>Any serious vascular event or revascularization</td>
<td>833 (10.8)</td>
<td>936 (12.1)</td>
<td>0.88 (0.80–0.97)</td>
<td></td>
</tr>
<tr>
<td>Major Bleeding</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intracranial hemorrhage</td>
<td>55 (0.7)</td>
<td>45 (0.6)</td>
<td>1.22 (0.82–1.81)</td>
<td></td>
</tr>
<tr>
<td>Sight-threatening bleeding in eye</td>
<td>57 (0.7)</td>
<td>64 (0.8)</td>
<td>0.89 (0.62–1.27)</td>
<td></td>
</tr>
<tr>
<td>Serious gastrointestinal bleeding</td>
<td>137 (1.8)</td>
<td>101 (1.3)</td>
<td>1.36 (1.05–1.75)</td>
<td></td>
</tr>
<tr>
<td>Other major bleeding</td>
<td>74 (1.0)</td>
<td>43 (0.6)</td>
<td>1.70 (1.18–2.44)</td>
<td></td>
</tr>
<tr>
<td>Any major bleeding</td>
<td>314 (4.1)</td>
<td>245 (3.2)</td>
<td>1.29 (1.09–1.52)</td>
<td>0.003</td>
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65 yo man with ACC/AHA 10 year ASCVD risk score of 17 % comes in for routine follow up. According to the ARRIVE study, adding 100 mg aspirin will:

A) Lower risk of major cardiovascular events  
B) Lower risk of stroke  
C) Increase risk of gastrointestinal bleeding and epistaxis  
D) Not affect risk of gastrointestinal bleeding but increase risk of epistaxis
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Primary prevention for Moderate CV Risk

ARRIVE Executive Committee
Lancet Sept 2018
Primary Prevention for Moderate Risk Patients

Age 55 (men) or 60 (women) or older
Moderate cardiovascular risk
Hx GI bleeding, other bleeding, or DM excluded
Randomized to 100 mg Aspirin or Placebo
12,546 patients enrolled
5 year median follow up
Mean Framingham 10 year score 14%
Mean ACC/AHA 10 year ASCVD score 17%
Effect of aspirin on risks of vascular events and cancer according to bodyweight and dose: Analysis of individual patient data from randomized trials
Lancet
August 4, 2018

10 trials including 117,279 patients
Low dosage aspirin (75-100 mg) only effective in preventing vascular events in patients weighing less than 70 kg
High dosage aspirin (> 325 mg) reduced cardiovascular events only in patients weighing 70 kg or more
Aspirin mediated reduction in colon cancer also weight dependent