The role of aspirin for primary prevention of cardiovascular events in the elderly – insights from the ASPREE Trial

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Geriatrics EBM Presentation
Acetylsalicylic Acid

- Irreversible Acetylation of COX1 at low concentration – COX2 at higher doses
- Inhibits Platelet activation/aggregation
  - Reduced production of Thromboxane A2
- Complex Modulation of Systemic Inflammatory Mileau [1]
Research Question

- Is there sufficient Evidence to support aspirin use for primary prophylaxis of MI in the elderly?
Literature Search Strategy

Search Criteria
NCBI Pubmed Database
USPSTF Guidelines

Search Terms
(Aspirin) AND Geriatric
AND aged[MeSH] – 196
Studies Via Pubmed

13 Systematic Review
Articles with META
Analysis
General Primary Prevention
Reduced MI but No clear role in prevention of Stroke or CVD mortality [2]

Table 1. Pooled Estimates for All Included Trials and Trials With Aspirin Doses of ≤100 mg/d

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Studies, k</th>
<th>Participants, n</th>
<th>Mantel-Haenszel Fixed-Effects RR (95% CI)</th>
<th>$\hat{\rho}^2$, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonfatal MI</td>
<td>10</td>
<td>114,734</td>
<td>0.78 (0.71-0.87)</td>
<td>61.9</td>
</tr>
<tr>
<td>Nonfatal stroke</td>
<td>10</td>
<td>99,655</td>
<td>0.95 (0.85-1.06)</td>
<td>25.1</td>
</tr>
<tr>
<td>CVD mortality</td>
<td>11</td>
<td>118,445</td>
<td>0.94 (0.86-1.03)</td>
<td>8.8</td>
</tr>
<tr>
<td>All-cause mortality</td>
<td>11</td>
<td>118,445</td>
<td>0.94 (0.89-0.99)</td>
<td>0</td>
</tr>
<tr>
<td>CVD = cardiovascular disease; MI = myocardial infarction; RR = relative risk.</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Population</td>
<td>Recommendation</td>
<td>Grade (What's This?)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>------------------------------------------------------</td>
<td>---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
<td>---------------------</td>
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</tr>
<tr>
<td>Adults aged 50 to 59 years with a ≥10% 10-year CVD risk</td>
<td>The USPSTF recommends initiating low-dose aspirin use for the primary prevention of cardiovascular disease (CVD) and colorectal cancer (CRC) in adults aged 50 to 59 years who have a 10% or greater 10-year CVD risk, are not at increased risk for bleeding, have a life expectancy of at least 10 years, and are willing to take low-dose aspirin daily for at least 10 years.</td>
<td>B</td>
<td></td>
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<tr>
<td>Adults aged 60 to 69 years with a ≥10% 10-year CVD risk</td>
<td>The decision to initiate low-dose aspirin use for the primary prevention of CVD and CRC in adults aged 60 to 69 years who have a 10% or greater 10-year CVD risk should be an individual one. Persons who are not at increased risk for bleeding, have a life expectancy of at least 10 years, and are willing to take low-dose aspirin daily for at least 10 years are more likely to benefit. Persons who place a higher value on the potential benefits than the potential harms may choose to initiate low-dose aspirin.</td>
<td>C</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adults younger than 50 years</td>
<td>The current evidence is insufficient to assess the balance of benefits and harms of initiating aspirin use for the primary prevention of CVD and CRC in adults younger than 50 years.</td>
<td>I</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adults aged 70 years or older</td>
<td>The current evidence is insufficient to assess the balance of benefits and harms of initiating aspirin use for the primary prevention of CVD and CRC in adults aged 70 years or older.</td>
<td>I</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Subgroup Analyses suggest CVD benefits in Elderly

Several Studies offer post hoc and pre-specified subgroup analysis that suggests benefits of aspirin are greatest in older populations [4-6]

E.g. Woman’s Health Trial – Women 65+ are only subgroup with reduced CV events [4]

Not all studies show a statistically significant relationship, cutoffs are inconsistent and these studies are not designed to interrogate elderly populations specifically.
ASPREE Trial [7-9]

- Randomized Multi-center placebo controlled Trial With Multi Year Follow-up
- Patients >/= 65 yo
- 19k participants
- Well randomized, adherence assessed pre-enrollment
- Includes patients with medical comorbidity but not overt disease
- Followed Patients until Death/Disability Median 4.7 yrs
- Relatively low previous aspirin users on enrollment so cannot address benefits/risks of long term therapy.
No change in composite endpoints
Increased risk of serious hemorrhage
No Differences in Cardiovascular Events

<table>
<thead>
<tr>
<th>End Point</th>
<th>Overall (N=19,114)</th>
<th>Aspirin (N=9525)</th>
<th>Placebo (N=9589)</th>
<th>Hazard Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>no. of participants with event</td>
<td>no. of participants with event</td>
<td>rate per 1000 person-yr</td>
<td>no. of participants with event</td>
</tr>
<tr>
<td>Cardiovascular disease†</td>
<td>922</td>
<td>448</td>
<td>10.7</td>
<td>474</td>
</tr>
<tr>
<td>Major adverse cardiovascular event‡</td>
<td>701</td>
<td>329</td>
<td>7.8</td>
<td>372</td>
</tr>
<tr>
<td>Fatal cardiovascular disease§</td>
<td>159</td>
<td>78</td>
<td>1.8</td>
<td>81</td>
</tr>
<tr>
<td>Hospitalization for heart failure</td>
<td>171</td>
<td>88</td>
<td>2.1</td>
<td>83</td>
</tr>
<tr>
<td>Fatal or nonfatal myocardial infarction</td>
<td>355</td>
<td>171</td>
<td>4.0</td>
<td>184</td>
</tr>
<tr>
<td>Fatal or nonfatal ischemic stroke¶</td>
<td>315</td>
<td>148</td>
<td>3.5</td>
<td>167</td>
</tr>
</tbody>
</table>
Summary

Aspirin has a beneficial profile for reducing nonfatal MI but not all cause or CV mortality in general.

Primary prophylaxis is not likely to result in decreased cardiovascular mortality, or all cause mortality/disability.

Aspirin use is significantly associated with serious hemorrhage.

Conclusions

• Starting aspirin in an elderly individual without overt cardiovascular disease is potentially inappropriate.
• Whether or not to continue aspirin for primary prophylaxis after long term use for primary prophylaxis is unclear and should involve shared decision making and appropriate clinical judgement.
"When I feel a headache coming on, I find the best thing is to buy stock in two aspirin companies and go right to bed."
References

1. **Modes of action of aspirin-like drugs.**
   PMID:2997778

2. **Aspirin for the Primary Prevention of Cardiovascular Events: A Systematic Evidence Review for the U.S. Preventive Services Task Force.**
   Guirguis-Blake JM, Evans CV, Senger CA, O'Connor EA, Whitlock EP.
   PMID: 27064410


4. **A randomized trial of low-dose aspirin in the primary prevention of cardiovascular disease in women.**
   Ridker PM, Cook NR, Lee IM, Gordon D, Gaziano JM, Manson JE, Hennekens CH, Buring JE.
   PMID: 15753114

5. **Final report on the aspirin component of the ongoing Physicians' Health Study.**
   Steering Committee of the Physicians' Health Study Research Group.
   PMID: 2664509
References (continued)


