Does a Low Dose Aspirin Really Keep the Doctor Away?

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Objective
- Given a patient without established cardio- or cerebrovascular disease, discuss the role of low-dose aspirin for primary prevention

Mechanism for Prevention
- Vasodilation
- Platelet aggregation

Risk Factors for Cardiovascular Disease
- Age (per decade)
- Male sex
- DM
- Current smoker
- HTN (mean BP increase of 20 mmHg)
- Dyslipidemia
- BMI

Risk Factors for Bleeding
- Prior dyspepsia, PUD, or GI bleed
- Medications (NSAID, OAC, steroid)
- H. pylori infection
- History of heavy alcohol use
- Bleeding disorder
- Age, DM, smoking, HTN, BMI

Controversy? Comparing the Guidelines

Historical Evaluation
ATT Meta-analysis (2009)

- Analyzed 6 primary prevention trials and 16 secondary prevention trials
- Population:
  - Mostly healthy volunteers (67,086 patients)
  - Risk factors for CVD: HTN, dyslipidemia, DM, obesity, family history of CVD, elderly (28,784 patients)
- ASA dosing:
  - 75 mg daily (2 trials)
  - 100 mg daily (1 trial) and every other day (1 trial)
  - 325 mg every other day (1 trial)
  - 500 mg daily (1 trial)


Benefits vs Risk

- Any major coronary event:
  - 0.28 vs 0.34%/yr
  - 0.82 (0.75-0.90)

- Any stroke:
  - 0.20 vs 0.21%/yr
  - 0.95 (0.85-1.06)

- Any vascular death:
  - 0.19 vs 0.20%/yr
  - 0.97 (0.87-1.09)

- Any serious vascular event:
  - 0.51 vs 0.57%/yr
  - 0.88 (0.82-0.94)

- Major GI and other extracranial bleeds:
  - 0.10 vs 0.07%/yr
  - 1.54 (1.30-1.82)

NNT=3125*  
NNH=5681

* NNT based on any serious vascular event data as events/person years.


Updates Since ATT Meta-analysis

- Aspirin in Asymptomatic Atherosclerosis-AAA (2010)
  - 50-75 yo with ABI < 0.99 (mean 0.85)
  - ASA 100 mg daily vs placebo
  - Initial fatal or nonfatal coronary event, stroke, or revascularization: no difference
  - Bleeding: no difference
    - 2.0% vs 1.2% with major hemorrhage
  - 2 trials in diabetic patients
    - POPADAD
    - JPAD

Summary of Diabetic Trials

<table>
<thead>
<tr>
<th>Trial</th>
<th>Design</th>
<th>Population</th>
<th>Clinical Outcomes</th>
<th>Bleeding</th>
</tr>
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<tbody>
<tr>
<td>POPADAD</td>
<td>RCT, double blind, placebo controlled, multicenter</td>
<td>&gt;75 pts with DM and ABI 0.99 without CVD</td>
<td>No evidence of reduction in CV events or mortality</td>
<td>No difference in GI bleed (4.2% vs 4.7%) or GI symptoms (3.1% vs 3.6%)</td>
</tr>
<tr>
<td>JPAD</td>
<td>RCT, open label, multicenter</td>
<td>139 pts with DM 50-85 yrs 85 mg or 200 mg ASA daily vs placebo</td>
<td>Did not reduce risk of atherosclerotic events</td>
<td>No significant difference in hemorrhagic stroke and GIB</td>
</tr>
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Summary of Diabetic Trials

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<tr>
<td>POPADAD sub-group: Renal Disease</td>
<td>253 pts with DM 50-85 yrs 3 groups: eGFR &gt;90 ml/min/1.73m²  - eGFR 60-89 ml/min/1.73m²  - eGFR &lt;60 ml/min/1.73m²</td>
<td>Incidence of atherosclerotic events (fatal and nonfatal MI, stroke, and PAD) significantly lower in ASA group</td>
<td>Event rates low and not significant</td>
</tr>
<tr>
<td>JPAD sub-group: Hypertension</td>
<td>259 pts with DM 30-85 yrs 3 groups: - SBP &gt;140 mmHg and/or DBP &gt;90 mmHg  - SBP &lt;140 mmHg and/or DBP &lt;90 mmHg</td>
<td>ASA may reduce cardiovascular events in DM pts with higher blood pressure</td>
<td>Event rates low and not compared in the study</td>
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Nonfatal MI/Coronary and Stroke Events

Major GI Bleeding

Patient Case
• JP is a 55 y/o WM presents to your outpatient clinic asking about starting 81 mg ASA because he heard it will prevent a heart attack on Dr. Oz.
• PMH: HTN and PUD
• Non-smoker
• Medications: Lisinopril 10 mg daily, Pantoprazole 40 mg daily
• BP 142/88 mmHg Chol 192 mg/dL LDL 98 mg/dL HDL 47 mg/dL

Patient Case
• DJ is a 62 y/o WF was admitted to the hospital with hypertensive urgency and is being prepared for discharge after control of her BP.
• PMH: HTN, CKD (eGFR 65 ml/min/1.73m²), DM
• Non-smoker
• Medications: Lisinopril 40 mg daily, Furosemide 40 mg daily, Amlodipine 10 mg daily, Metformin 1000 mg BD
• BP 154/98 mmHg Chol 214 mg/dL LDL 130 mg/dL HDL 40 mg/dL

Patient Case
• Would you recommend ASA 81 mg daily?
  – Yes
  – No

Patient Case
• Would you recommend ASA 81 mg daily?
  – Yes
  – No
Take Home Points
- Heterogenous data
- Compare risk vs. benefit in each patient
- Overall recommendations

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<th>Recommendation</th>
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<tr>
<td>CVD risk high, bleed risk low</td>
<td>ASA 81 mg daily</td>
</tr>
<tr>
<td>CVD risk high, bleed risk high</td>
<td>ASA 81 mg daily with increased monitoring for bleeding</td>
</tr>
<tr>
<td>CVD risk moderate</td>
<td>Discussion with patient and evaluation of bleeding risks</td>
</tr>
<tr>
<td>CVD risk low</td>
<td>Do not give ASA, reassess regularly to determine risks</td>
</tr>
</tbody>
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Future Directions
- ASCEND
  - 2x2 comparison of pts ≥ 40 y/o with DM and no previous history of vascular disease
    - ASA 100 mg daily vs placebo + Omega-3 1 gm daily vs placebo
    - Non-fatal MI, non-fatal stroke, TIA, or vascular death
- ACCEPT-D
  - Open label trial of pts ≥ 50 y/o with DM on simvastatin
    - ASA 100 mg daily plus Simvastatin vs Simvastatin alone
    - Cardiovascular death, non-fatal MI, non-fatal stroke, and hospital admission for CV causes
- ASPREE
  - 19,000 men ≥ 70 y/o (≥65 y/o non-US minorities)
    - ASA 100 mg daily vs placebo
    - All cause mortality, dementia incidence, or physical disability

Questions?