Aspirin for Primary Prevention of CVD in HIV-infected patients: a CON viewpoint

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Disclosures

• None from industry

• Grant support from the National Institutes of Health (NIH)
Yes, HIV-infected individuals are at higher CVD Risk

Pathogenesis of atherothrombosis in HIV infection.

HIV infection itself
- Persistent immune activation and viral replication
- Microbial translocation
- Role of CMV

Inflammation
- Endothelial dysfunction
- Coagulation & platelet reactivity

Chronic immune system and endothelium activation
- Increased clotting
- Altered lipid metabolism
- Immunosenesence
- Macrophage/T cell arteries infiltration

Atherosclerosis in HIV patients
- Traditional risk factors
  - Smoking
  - Hypercholesterolaemia
  - Hypertriglyceridaemia
  - Cocaine abuse

HAART
Yes, HIV-infected individuals are at higher CVD Risk

From: *HIV Infection and the Risk of Acute Myocardial Infarction*


- Patients with HIV-infection (and no known CVD) had 50% increased risk of acute MI beyond that explained by recognized risk factors.

- But will treating with aspirin in primary prevention reduce that risk?

#Multivariate model adjusted for age, sex, race/ethnicity, HTN diabetes, lipids, smoking, statin use, HCV, eGFR, Hgb, BMI, history of cocaine or alcohol abuse
Aspirin therapy is underutilized in HIV-infected patients

• In an HIV-infected cohort, fewer than 1 in 5 received ASA for primary prevention of CVD indicated by USPSTF 2009 criteria

• Even when the focus was narrowed to patients at intermediate to high risk for events (10-year risk ≥10%), which constituted 50% of the study sample, only 22% were on ASA.

• Odds of ASA use did go up with increasing CVD risk factors

Univariate OR = 2.15; 95% CI: 1.57-2.95
Adjusted OR = 2.13; 95% CI: 1.51-2.99
Rates of acetylsalicylic acid (ASA) use in human immunodeficiency virus (HIV)-infected vs HIV-uninfected patients in overall group (A), low coronary heart disease (CHD) risk patients (B), and high CHD risk patients (C).
Aspirin therapy is underutilized in HIV-infected patients

- Decreased use of ASA among HIV-infected individuals could be relatively higher rates of conditions that might increase bleeding risk.

- Patients infected with HIV had higher rates of chronic liver disease, gastrointestinal bleed, and ulcer disease, any of which could represent a relative contraindication to ASA use.

- However, HIV status remained associated with decreased rates of ASA use when controlling for conditions that predispose to bleeding suggests that these factors alone are not likely to explain the lower rates of ASA use observed in HIV.
Here are the Randomized Controlled Trials of Aspirin for Primary Prevention Among HIV-Infected Individuals:
Here are the Randomized Controlled Trials of Aspirin for Primary Prevention Among HIV-Infected Individuals:

- Therefore, must extrapolate from primary prevention studies from general population.
Balance of Anticipated Benefits vs. Risks

CVD Prevention

Bleeding Risk
Aspirin in Primary Prevention

RR of MI Among Men

- BDT, 1988
- PHS, 1989
- TPT, 1998
- HOT, 1998
- PPP, 2001

Combined

RR = 0.68 (0.54-0.86)  
P=0.001

RR of Stroke Among Men

- BDT, 1988
- PHS, 1989
- TPT, 1998
- HOT, 1998
- PPP, 2001

Combined

RR = 1.13 (0.96-1.33)  
P=0.15

RR of MI Among Women

- HOT, 1998
- PPP, 2001
- WHS, 2005

Combined

RR = 0.99 (0.83-1.19)  
P=0.95

RR of Stroke Among Women

- HOT, 1998
- PPP, 2001

Combined

RR = 0.81 (0.69-0.96)  
P=0.01

Aspirin Better | Placebo Better

15-year follow-up of the Women’s Health Study

Over 27,000 healthy women randomized to alternate day dosing of 100 mg of aspirin vs Placebo

Conclusions Concurrent evaluation of the absolute effects on cancer, CVD and major gastrointestinal bleeding showed that alternate-day use of low-dose aspirin is ineffective or harmful in the majority of women in primary prevention. Selective treatment of women ≥65 years with aspirin may improve net benefit.

Trial registration number NCT00000479.

Shaded = harms outweigh benefits

Estimated MIs prevented and estimated harms of using aspirin for 10 years in a hypothetical cohort of 1000 men. Estimates are based on age and 10-year CHD risk. CHD = coronary heart disease; GI = gastrointestinal; MI = myocardial infarction.
Estimated number of strokes prevented and estimated harms of using aspirin for 10 years in a hypothetical cohort of 1000 women on the basis of age and 10-year stroke risk. GI = gastrointestinal.

Shaded = harms outweigh benefits
USE OF ASPIRIN FOR PRIMARY PREVENTION IN OTHER HIGH RISK GROUPS
Low dose ASA for primary prevention among pts with type 2 diabetes: 2008 JPAD RCT

**Primary End Point: Total Atherosclerotic Events According to the Treatment Groups**

Log-Rank Test, $P = 0.16$
HR (95% CI): 0.80 (0.58–1.10)

<table>
<thead>
<tr>
<th>Years</th>
<th>Nonaspirin Group (n)</th>
<th>Aspirin Group (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1277</td>
<td>1262</td>
</tr>
<tr>
<td>1</td>
<td>1220</td>
<td>1210</td>
</tr>
<tr>
<td>2</td>
<td>1165</td>
<td>1159</td>
</tr>
<tr>
<td>3</td>
<td>1117</td>
<td>1095</td>
</tr>
<tr>
<td>4</td>
<td>813</td>
<td>806</td>
</tr>
<tr>
<td>5</td>
<td>135</td>
<td>140</td>
</tr>
</tbody>
</table>

Ogawa H et al. JAMA 2008 (300) 18; 2134-2141
ASA and diabetes: 2008 JPAD RCT:
Primary end point if 65 years or older

Ogawa H et al. JAMA 2008 (300) 18; 2134-2141
ASA, diabetes, and PAD: the POPADAD trial (2008)

1276 adults age >40 with diabetes and ABI <0.99, but no clinical CVD

RCT of ASA 100 mg/d vs. placebo ± antioxidant in 2 x 2 factorial design

Median followup 6.7 yrs

Belch J et al. BMJ 2008
Asymptomatic “PAD” and diabetes
ASA ineffective

POPADAD Belch J et al.  BMJ 2008
Aspirin for primary prevention of cardiovascular events in people with diabetes: meta-analysis of randomised controlled trials

Giorgia De Berardis, research officer, Michele Sacco, research officer, Giovanna F M Strippoli, editor and regional coordinator of the Cochrane Renal Group, Fabio Pellegrini, senior biostatistician, Giusi Graziano, biostatistician, Gianni Tognoni, institute director, Antonio Nicolucci, department head

De Berardis G et al. BMJ 2009; 399
### Meta-analysis in primary prevention for diabetics 2009

ASA and diabetes: Major CV events

<table>
<thead>
<tr>
<th>Major cardiovascular events</th>
<th>Aspirin (No of events/No in group)</th>
<th>Control or placebo (No of events/No in group)</th>
<th>Relative risk (95% CI)</th>
<th>Relative risk (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>JPAD(^{10})</td>
<td>68/1262</td>
<td>86/1277</td>
<td>0.80 (0.59 to 1.09)</td>
<td></td>
</tr>
<tr>
<td>POPADAD(^{9})</td>
<td>105/638</td>
<td>108/638</td>
<td>0.97 (0.76 to 1.24)</td>
<td></td>
</tr>
<tr>
<td>WHS(^{8})</td>
<td>58/514</td>
<td>62/513</td>
<td>0.90 (0.63 to 1.29)</td>
<td></td>
</tr>
<tr>
<td>PPP(^{22})</td>
<td>20/519</td>
<td>22/512</td>
<td>0.90 (0.50 to 1.62)</td>
<td></td>
</tr>
<tr>
<td>ETDRS(^{21})</td>
<td>350/1856</td>
<td>379/1855</td>
<td>0.90 (0.78 to 1.04)</td>
<td>0.90 (0.81 to 1.00)</td>
</tr>
<tr>
<td>Total</td>
<td>601/4789</td>
<td>657/4795</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

De Berardis G et al. BMJ 2009; 399
2010 AAA Trial: No Benefit of Aspirin in Patients with Asymptomatic PAD

- N=3,350 Scottish patients with ABI ≤ 0.95 and no PAD sx randomized to 100 mg aspirin vs. placebo
- 1° endpoint fatal + nonfatal coronary event or stroke, revascularization
- Mean 8.2 years of follow-up
- No difference in 1° composite endpoint fatal + nonfatal coronary event or stroke, revascularization
- Low overall event rate compared to historical PAD cohorts (12.7% at 5 years)
  - Is this really a PAD cohort?
- Trend toward bleeding requiring hospitalization in aspirin group

Fowkes FGR, et al. JAMA 2010;303:841.
2010 Aspirin and PAD Meta-analysis:
Aspirin Monotherapy

*published before AAA trial

N=3,019 patients (ASA alone), 1° composite endpoint CV death, MI, Stroke

<table>
<thead>
<tr>
<th>Source</th>
<th>Total No. of Patients</th>
<th>No. of Events/Total No. of Patients</th>
<th>Weight, %</th>
<th>RR (95% CI)</th>
<th>Favors Aspirin</th>
<th>Favors Control</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Composite cardiovascular end points</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Beil et al,9 2008</td>
<td>105/638</td>
<td>108/638</td>
<td>48.7</td>
<td>0.97 (0.76-1.24)</td>
<td>-</td>
<td>-</td>
<td>.82</td>
</tr>
<tr>
<td>Catalano et al,21 2007</td>
<td>7/185</td>
<td>19/181</td>
<td>19.2</td>
<td>0.36 (0.16-0.84)</td>
<td>-</td>
<td>-</td>
<td>.02</td>
</tr>
<tr>
<td>Hess et al,30 1990</td>
<td>3/80</td>
<td>3/80</td>
<td>7.3</td>
<td>1.00 (0.21-4.81)</td>
<td>-</td>
<td>-</td>
<td>&lt;.99</td>
</tr>
<tr>
<td>Green et al,36 1982</td>
<td>0/16</td>
<td>0/17</td>
<td>0.0</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Harjola et al,27 1981</td>
<td>0/100</td>
<td>3/100</td>
<td>2.3</td>
<td>0.14 (0.01-2.73)</td>
<td>-</td>
<td>-</td>
<td>.20</td>
</tr>
<tr>
<td>Ehresmann et al,24 1977</td>
<td>0/215</td>
<td>0/213</td>
<td>0.0</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Hess and Keil-Kuri,29 1975</td>
<td>5/92</td>
<td>6/84</td>
<td>12.2</td>
<td>0.76 (0.24-2.40)</td>
<td>-</td>
<td>-</td>
<td>.64</td>
</tr>
<tr>
<td>Hess and Keil-Kuri,29 1975</td>
<td>4/42</td>
<td>2/40</td>
<td>6.7</td>
<td>1.90 (0.37-9.83)</td>
<td>-</td>
<td>-</td>
<td>.44</td>
</tr>
<tr>
<td>Zekert-36 1975</td>
<td>1/148</td>
<td>3/150</td>
<td>3.8</td>
<td>0.34 (0.04-3.21)</td>
<td>-</td>
<td>-</td>
<td>.34</td>
</tr>
<tr>
<td>Total</td>
<td>125/1516</td>
<td>144/1503</td>
<td>0.75 (0.48-1.18)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>.21</td>
</tr>
</tbody>
</table>

36% reduction in non-fatal stroke (P=0.04)

No statistically significant benefit for primary composite outcome!

2012 Meta-analysis of aspirin for primary prevention of CVD

Reduction in non-fatal MI and total CVD, but 31% increased risk of major bleeding

Figure: Effect of aspirin on vascular and nonvascular outcomes or death. CHD indicates coronary heart disease; CVD, cardiovascular disease; and MI, myocardial infarction.
2014 Meta-analysis: Aspirin therapy versus placebo or control for primary prevention of CVD.

NNT to prevent 1 major CVD event over a mean f/u of 6.8 years = 284.
NNH to cause 1 major bleeding = 299.

Again, 10% relative reduction in MACE at expense of 55% increase in major bleeds

http://127.0.0.1:8081/plosone/article?id=info:doi/10.1371/journal.pone.0090286
2014 – the Japanese Primary Prevention Project (JPPP)

Ikeda et al. JAMA 2014

Patients aged 60–85 years
- Hypertension
- Dyslipidemia
- Diabetes mellitus (one or more condition)

1007 clinics (all 47 prefectures)

1:1 randomization

Eligible ✓

Enteric-coated aspirin 100 mg/day

No aspirin

Ongoing medications to control underlying disease(s)
2014 JPPP Primary endpoint: Kaplan–Meier estimate

Ikeda et al. JAMA 2014

p = 0.544
HR 0.94 (95% CI: 0.77–1.15)

<table>
<thead>
<tr>
<th>Time to event (years)</th>
<th>Proportion of patients with primary endpoint event (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Aspirin</td>
</tr>
<tr>
<td>0</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td></td>
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<tr>
<td>5</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td></td>
</tr>
<tr>
<td></td>
<td>No aspirin</td>
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<tr>
<td>0</td>
<td></td>
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<td>1</td>
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<tr>
<td>5</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td></td>
</tr>
</tbody>
</table>

| Number at risk         | Aspirin    | 7220 | 7021 | 6771 | 6583 | 6322 | 3639 | 169 |
|                       | No aspirin | 7244 | 7073 | 6861 | 6645 | 6359 | 3711 | 182 |
A Proposed Practical Stepwise Approach to the Use of Aspirin in Primary CV Prevention

Step 1: Assess 10 year risk of major CV events

- <10%
  - Stop

- 10-20%
  - Go ahead with caution

- >20%
  - Proceed

Step 2: History of bleeding without reversible causes, concurrent use of other medications that increase bleeding risk

Consider family history of GI (especially colon) cancer / patient values and preferences

Low-dose aspirin
Relationships Between Magnitude of Antithrombotic Benefit and of Bleeding Risk Connected With the Use of Aspirin, and Absolute Cardiovascular Risk, in Various Subsets of Subjects in Primary Prevention

Red arrow denotes the area where benefit likely equals risk, yellow area denotes area of prescription uncertainty, and green arrow denotes the area where benefit most likely exceeds risk.

From: Aspirin Therapy in Primary Cardiovascular Disease Prevention: A Position Paper of the European Society of Cardiology Working Group on Thrombosis

J Am Coll Cardiol. 2014;64(3):319-327. doi:10.1016/j.jacc.2014.03.049
Benefits and Risks of Low-Dose Aspirin in Primary Prevention Trials

NNT=500-1,000
NNH=500-1,000
Consider aspirin on an individual basis, after evaluating potential benefits and risks

NNT=?
NNH=?
Need for new trials:
ASCEND
ACCEPT-D
ASPREE
ARRIVE

NNT=≤100
NNH=500-1,000
Use aspirin routinely unless contraindicated
Don’t use aspirin as primary prevention for heart disease and stroke, FDA warns

The risks associated with taking aspirin outweigh the benefits, if you have no history of cardiovascular disease

SARAH GRAY
However, in 2015, USPSTF Updated their ASA Recommendations (Draft)

<table>
<thead>
<tr>
<th>Population</th>
<th>Recommendation</th>
<th>Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults ages 50 to 59 years</td>
<td>The USPSTF recommends low-dose aspirin use for the primary prevention of cardiovascular disease (CVD) and colorectal cancer in adults ages 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>
</tr>
<tr>
<td>Adults ages 60 to 69 years</td>
<td>The decision to use low-dose aspirin to prevent CVD and colorectal cancer in adults ages 60 to 69 years who have a greater than 10% 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 use low-dose aspirin.</td>
<td>C</td>
</tr>
<tr>
<td>Adults younger than age 50 years</td>
<td>The current evidence is insufficient to assess the balance of benefits and harms of aspirin use to prevent CVD and colorectal cancer in adults younger than age 50 years.</td>
<td>I</td>
</tr>
<tr>
<td>Adults age 70 years and older</td>
<td>The current evidence is insufficient to assess the balance of benefits and harms of aspirin use to prevent CVD and colorectal cancer in adults age 70 years and older.</td>
<td>I</td>
</tr>
</tbody>
</table>

Use the 2013 ACC/AHA Pooled Cohort Equation for hard CVD
## 2015 USPSTF Update:
Estimated Lifetime events for WOMEN on ASA

### Draft: Table 1. Lifetime Events* in Women Taking Aspirin

<table>
<thead>
<tr>
<th>CVD Risk</th>
<th>MIs Prevented</th>
<th>Ischemic Strokes Prevented</th>
<th>CRC Cases Prevented</th>
<th>Serious GI Bleeding Caused</th>
<th>Hemorrhagic Strokes Caused</th>
<th>Net Life-Years Gained</th>
<th>Quality-Adjusted Life-Years Gained</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ages 50 to 59 years</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10%</td>
<td>14.8</td>
<td>13.7</td>
<td>13.9</td>
<td>20.9</td>
<td>3.5</td>
<td>21.9</td>
<td>62.1</td>
</tr>
<tr>
<td>15%</td>
<td>15.0</td>
<td>14.3</td>
<td>13.5</td>
<td>20.0</td>
<td>3.4</td>
<td>33.4</td>
<td>71.6</td>
</tr>
<tr>
<td>20%</td>
<td>15.2</td>
<td>14.4</td>
<td>13.2</td>
<td>18.4</td>
<td>2.9</td>
<td>46.3</td>
<td>83.3</td>
</tr>
<tr>
<td><strong>Ages 60 to 69 years</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10%</td>
<td>10.1</td>
<td>11.6</td>
<td>10.5</td>
<td>23.0</td>
<td>3.2</td>
<td>-1.2</td>
<td>28.4</td>
</tr>
<tr>
<td>15%</td>
<td>11.0</td>
<td>12.9</td>
<td>9.3</td>
<td>21.6</td>
<td>3.4</td>
<td>1.7</td>
<td>32.4</td>
</tr>
<tr>
<td>20%</td>
<td>11.1</td>
<td>13.0</td>
<td>9.7</td>
<td>21.7</td>
<td>3.3</td>
<td>4.8</td>
<td>36.0</td>
</tr>
</tbody>
</table>

*Per 1,000 persons.

Note: A complete set of results are available in the decision analysis report.28

**Abbreviations:** CVD=cardiovascular disease; CRC=colorectal cancer; GI=gastrointestinal; MI=myocardial infarction.
## 2015 USPSTF Update: Estimated Lifetime events for MEN on ASA

### Draft: Table 2. Lifetime Events* in Men Taking Aspirin

<table>
<thead>
<tr>
<th>CVD Risk</th>
<th>Mls Prevented</th>
<th>Ischemic Strokes Prevented</th>
<th>CRC Cases Prevented</th>
<th>Serious GI Bleeding Caused</th>
<th>Hemorrhagic Strokes Caused</th>
<th>Net Life-Years Gained</th>
<th>Quality-Adjusted Life-Years Gained</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ages 50 to 59 years</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10%</td>
<td>22.5</td>
<td>8.4</td>
<td>13.9</td>
<td>28.4</td>
<td>2.3</td>
<td>33.3</td>
<td>58.8</td>
</tr>
<tr>
<td>15%</td>
<td>26.7</td>
<td>8.6</td>
<td>12.1</td>
<td>26.0</td>
<td>2.8</td>
<td>39.5</td>
<td>64.4</td>
</tr>
<tr>
<td>20%</td>
<td>28.6</td>
<td>9.2</td>
<td>12.2</td>
<td>24.8</td>
<td>2.1</td>
<td>60.5</td>
<td>83.4</td>
</tr>
<tr>
<td><strong>Ages 60 to 69 years</strong></td>
<td></td>
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<td></td>
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<tr>
<td>10%</td>
<td>15.9</td>
<td>6.6</td>
<td>11.2</td>
<td>31.4</td>
<td>3.1</td>
<td>-2.0</td>
<td>18.0</td>
</tr>
<tr>
<td>15%</td>
<td>18.6</td>
<td>8.0</td>
<td>10.4</td>
<td>29.8</td>
<td>2.4</td>
<td>9.6</td>
<td>30.9</td>
</tr>
<tr>
<td>20%</td>
<td>20.1</td>
<td>8.4</td>
<td>9.1</td>
<td>26.7</td>
<td>2.7</td>
<td>11.6</td>
<td>31.8</td>
</tr>
</tbody>
</table>
From: An Analysis of Calibration and Discrimination Among Multiple Cardiovascular Risk Scores in a Modern Multiethnic Cohort

Calibration and Discrimination Among CVD Risk Scores


Overestimation in MESA cohort

Men (n=1,961)

Hosmer–Lemeshow calibration plots for men (n = 1961). ACC = American College of Cardiology; AHA = American Heart Association; ASCVD = atherosclerotic cardiovascular disease; ATPIII = Adult Treatment Panel III; CHD = coronary heart disease; CVD = cardiovascular disease; FRS = Framingham risk score; RRS = Reynolds Risk Score.
Limitations of ASA Primary Prevention Studies so far

• Overestimation of CVD risk by FRS and ACC/AHA Risk Estimators in Modern Cohorts like MESA

• CVD event rate lower than expected in these primary prevention trials
  – likely due to background additional therapy like statin use
  – CVD event rates declining overall in US population
  – Not same risk as older historical cohorts

• Therefore trials may be underpowered to confirm ASA benefit in primary prevention

• Larger primary prevention trials on-going likely will guide future guidelines
ON-GOING ASPIRIN PRIMARY PREVENTION TRIALS
Ongoing ASA Studies among Diabetics

ASCEND
  UK
  ASA 100 mg and Omega-3 vs placebo (2 x 2 factorial design)
  Randomized double blind for 5 years
  10,000+ patients > 40 yrs

ACCEPT – D
  Italy
  ASA 100 mg + simvastatin 20-40 mg vs. simva alone
  Randomized open for 5 years
  5170 patients > 50 yrs
Ongoing Studies of ASA in older high risk patients

• ARRIVE
  – 12,000 pts from 7 countries
  – in middle-age and older patients with multiple cardiovascular risk factors, 10-year CHD risk of 10-20%
  – ASA 100 mg vs. placebo

• ASPREE
  – 19,000 individuals over age 70 (non-minorities) and >65 yrs (minorities)
  – US and Australia
  – Free of dementia, disability, and CVD
  – ASA 100 mg vs placebo
Do we need a “REPRIEVE”-like Trial for Aspirin?

- REPRIEVE:
  - Investigators plan to randomize 6,500 HIV-infected participants age 40 to 75 years who would not meet current national guidelines for statin therapy to either a daily dose of pitavastatin or a placebo while continuing with antiretroviral therapy.
  - Will follow the participants for up to six years, assessing for major adverse cardiovascular events, such as heart attacks and strokes.
CAN WE USE SUBCLINICAL ATHEROSCLEROSIS IMAGING TO REFINE RISK PREDICTION?
• 4229 participants from Multi-Ethnic Study of Atherosclerosis (MESA) not on aspirin at baseline and without DM
• Followed for median 7.6 yrs
• Assumed an 18% relative reduction in CHD event rate with ASA therapy.
• Applied that to observed events in groups categorized by their baseline coronary artery calcium (CAC) scores
Estimated risk/benefit of aspirin in primary prevention by coronary artery calcium score in Multi-Ethnic Study of Atherosclerosis (MESA) participants. *Coronary heart disease (CHD) risk was calculated using the Framingham Risk Score.
In meantime while waiting on-going studies, should we use Aspirin in Primary CVD Prevention for HIV-infected patients?

- Current data shows lack of significant benefit in some high risk groups (DM, asymptomatic PAD)
- Lack of primary prevention ASA guidelines specific for HIV-infected patients
- Which risk estimator do we use for HIV patients?
  - FRS, ACC/AHA Pooled Cohort Equation, DAD
- Management of other CVD risk factors may be more important
  - Encourage healthy lifestyle
  - Smoking cessation
  - BP control
  - Control hyperglycemia
  - Statin use for higher risk primary prevention
In meantime, should we use Aspirin in Primary Prevention for HIV?

- Some higher risk primary prevention may still benefit
  - USPSTF says age 50-69 if 10-year risk >10% and no increased risk of bleeding
  - Consider in those with a positive FH of premature thrombosis/CHD or FH of colon cancer
  - Consider for higher-risk diabetics (not all)
  - Consider using CAC to refine ASCVD risk when risk is uncertain
    - Caveat: HIV more like to have non-calcified plaque

- A detailed clinician-patient risk discussion is warranted before initiating ASA therapy
  - discuss potential for benefits to patient vs. safety risks
  - Review other meds, consider issues of polypharmacy
  - Note that Enteric Coated Aspirin does not reduce GI bleeding!
Summary of Con View Point

• In primary prevention, aspirin is of uncertain net value as the reduction in occlusive events needs to be weighed against the increase in major bleeds.

• This is compounded when we treat with other risk-lowering drugs
The ABCDE Approach

A | Assessment of Risk
   | Aspirin for high risk
B | Blood pressure
C | Cholesterol
   | Cigarette Smoking Cessation
D | Diabetes Prevention
   | Diet
E | Exercise
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