The Prudent Prescriber

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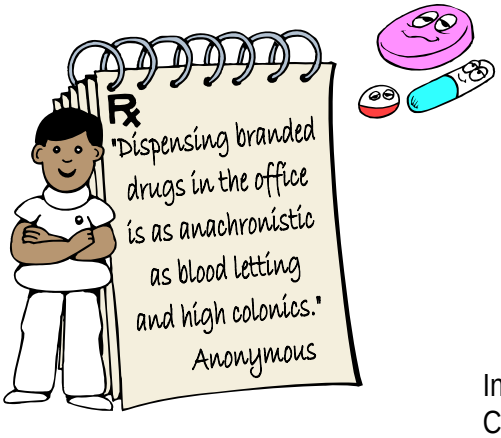


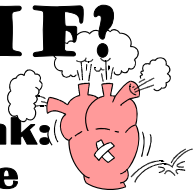
Pharm Reps ≠ Rational Prescribing
(PR) (RP)

Primary Prevention with Low Dose Aspirin
Time to Rethink the 2016 USPSTF Recommendations?
or
NNT Strikes again

In 2016, the USPSTF modified their low dose aspirin CV/CRC prophylaxis recommendations for healthy adults:

1. Patients age <50: Unable to evaluate benefits versus risks. (I recommendation)
2. Patients age 50-59: Highest benefit group for daily low-dose aspirin (81mg) if ASCVD risk is greater than 10%, as benefits outweigh the harms if they do not have any other factors that would predispose them to bleeding. In addition, this group is more likely to experience benefit for CRC prevention due to life expectancy if they are willing to comply with daily aspirin therapy. (B recommendation)
3. Patients age 60-69: Likely to benefit from aspirin therapy if ASCVD risk score is 10% or higher, as they are still expected to have a favorable benefit versus risk outlook. However, this group is less likely to experience benefit in regards to CRC prevention. (C recommendation)
4. Patients age 70 or greater: Unable to evaluate benefits versus risks. (I recommendation)

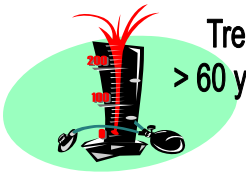
CHF?



Think:
Ace
Aldactone
B-blocker
Dig
Diuretic

Avoid these expensive "me-too" drugs:

Intermezzo
Vimovo
Livalo
Gralise
Viibyrd
Edarbi
Daliresp



Treat patients > 60 years to 150/90

Antibiotics do NOT help acute bronchitis

ß-blockers in post-MI save lives

Pill splitters save BIG

NOW AVAILABLE ON THE GENERIC MARQUEE

Viagra→sildenafil
Effient→prasugel
Strattera→atomoxetine
Asacol HD→mesalamine DR
Pristiq→desvenlafaxine

In 2018, three large (12,000 -19,000 patients) randomized controlled studies shed doubt on the Task Force recommendations. All three studies compared 100mg aspirin or placebo daily and measured CV endpoints over 4.8-7.4 years. All three studies excluded patients with known cardiovascular and cerebrovascular disease and those with increased bleeding risk.

Study	Reference	N	Age	% women	Follow up	Endpoints
ASPREE	N Engl J Med 2018; 379 (16): 1509-18	19,114	>70 yrs Mean age 74	56% 11% DM 8.7% non-white	4.7 years	Death Disability Dementia Fatal CAD Nonfatal MI Stroke Hosp CHF
ASCEND	N Engl J Med 2018; 379 (16):1529-1539	15,480 also got either omega-3 fatty acid or placebo	>40 yrs DM (94% type2)	37% 96% white	7.4 years Amazing 99% followup at 7.4 years	Vascular death; Nonfatal MI; Nonfatal ischemic stroke;
ARRIVE	Lancet 2018; 392(10152):1036-1046 Bayer sponsor	12,526 No DM	Men> 55 yrs With 10-20% risk of CV event	Women > 60 yrs With 10-20% risk of CV event	5.0 years	Death MI Stroke CV death Unstable angina TIA

ASPREE

The goal of the ASPREE trial (two papers in the same journal, crunching the same numbers in slightly different fashions) was to evaluate low-dose aspirin compared with placebo among healthy elderly patients.

Principal Findings:

The primary outcome, all-cause death, dementia, or physical disability, was 21.5 events per 1,000 person-years in the aspirin group compared with 21.2 events per 1,000 person-years in the placebo group ($p = 0.79$). NNT=3333

Secondary outcomes:

- Major hemorrhage: 8.6 events per 1,000 person-years in the aspirin group vs. 6.2 events per 1,000 person-years in the placebo group ($p < 0.001$) NNH = 417
- All-cause mortality: 5.9% in the aspirin group vs. 5.2% in the placebo group ($p < 0.05$) NNH=143
- Cancer mortality: 3.1% in the aspirin group vs. 2.3% in the placebo group ($p < 0.05$) NNH=125

Interpretation:

Among healthy elderly patients, low-dose aspirin therapy was not beneficial. Compared with placebo, aspirin did not improve disability-free survival or reduce major adverse cardiovascular events at a median of 4.7 years. Aspirin was associated with a significant increase in major bleeding, which was attributed to excess intracranial and upper gastrointestinal bleeding. Aspirin was also associated with a slight increase in all-cause mortality, which was attributed to excess cancer mortality. Take the excess cancer and all-cause mortality results with a large grain of salt as these findings have not been previously reported.

ASCEND

The goal of the ASCEND trial was to study the benefits and harms of low dose aspirin in adults with diabetes mellitus.

Principal findings:

There was no statistical difference between groups in the original efficacy outcome of vascular death, nonfatal MI, and nonfatal ischemic stroke (7.0% with aspirin versus 7.6% with placebo). NNT =166 for 7.4 years.

As the trial was ongoing, the authors played down and dirty by adding TIA and revascularization to the original primary composite outcome. When you add TIA to the original composite, the difference between groups is statistically different. NNT= 90 for 7.4 years. When you add revascularization to the original composite, the difference between groups is also statistically different. NNT= 77 for 7 years.

Secondary outcomes:

- In the composite harm outcome, there was a significantly increased risk of major bleeding (4.1% with aspirin versus 3.2% with placebo). NNH = 111 for 7 years.
- There was no difference in the incidence of cancer including for gastrointestinal cancers.
- There were no significant differences between groups in all-cause mortality.

Interpretation:

The ASCEND aspirin trial, after some nefarious tomfoolery, showed that among diabetic patients, aspirin reduced the incidence of major adverse cardiovascular events (MACE); however, this was somewhat counterbalanced by an increase in major bleeding.

ARRIVE

The ARRIVE trial set out to look at low dose aspirin's benefits and harms in a population of men and women with moderate risk (10-20% 10 year risk) of heart disease. However, the event rate in the study was much lower than expected, probably making the study more representative of a low risk population.

Principal Findings:

The primary composite outcome, cardiovascular death, myocardial infarction, unstable angina, stroke, or TIA occurred in 4.29% of the patients in the aspirin group and 4.48% of the patients in the placebo group. p = 0.6038. NNT= 526.

Secondary outcomes:

- The overall incidence rate of serious adverse events was similar in both groups: 20.19% aspirin vs 20.89% placebo.
- There were no significant differences between groups in all-cause mortality.

Interpretation:

In what proved to be a cohort at low risk for cardiovascular disease, low-dose aspirin did not provide benefit for prevention of composite of cardiovascular outcomes. Nor did aspirin significantly harm this group.

My Take:

- ❖First, it should be clear that the data for using low-dose aspirin for secondary prevention of cardiovascular disease is on very solid footing. Keep doing it!
- ❖None of this discussion really touches on the USPSTF recommendations with respect to aspirin and prevention of colorectal cancer. Of note, the ASPREE trial showed a tiny increase in aspirin associated cancers and the ASCEND study showed no difference in malignancies between the aspirin and placebo groups.
- ❖For years, I quoted the 2009 Lancet study that became the basis of thennt.com proclamation that to prevent one CV "problem" 1,667 people would have to take low dose aspirin for one year and that 1 of every 3,333 patients would suffer major bleeding from doing so. The pattern of the results in the 2018 studies doesn't look much different.
- ❖The bottom line is that most average risk adults will not be either benefitted or harmed by taking low dose aspirin for 5-7 years.
- ❖The questions that remain:

  1) How many of us will consistently take aspirin for 5-7 years?

  2) Is the aspirin prophylaxis discussion worth the shared decision making time it takes or would patients benefit more by talking about the risks/benefits of screening mammography, Shingrix or "routine" lab work?
- ❖While millions of individuals use aspirin for primary prevention, this routine practice is now questioned in light of recent randomized trial data.