

Aspirin for All???

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Bottom Line at the Top: People at increased risk for cardiovascular disease who have minimal risk of excessive bleeding should take 81-100 mg of aspirin a day for prevention. Follow the guidelines concerning risk in the last paragraph of this article. Ignore sensational news drawing medical conclusions if the study didn't include people like you.

Atherosclerosis is the major cause of cardiovascular disease, including heart attacks and stroke. It is a chronic disease, in which cholesterol oxidation and microscopic blood vessel damage cause inflammation, thickening and clots in the artery wall.

Platelets normally circulate in blood to keep us from bleeding to death by forming clumps that initiate clotting. However, in response to arterial micro-trauma, clumping platelets add to the blood vessel wall thickening that closes them off.

Aspirin has remarkable anti-inflammatory and anti-clotting effects. It does this by inhibiting production of certain inflammatory factors, including thromboxane. Thromboxane made in platelets triggers clumping when it is time to clot. Aspirin irreversibly blocks platelet thromboxane production, thereby inactivating a platelet's ability to clot for the lifetime of the platelet.

We know that low-dose aspirin reduces risk of atherosclerosis in arteries throughout the body, but by inhibiting clotting, aspirin also increases risks of large bruises and excessive bleeding even with minor nosebleeds, gastritis or skin cuts. Still, low dose aspirin (81-100 mg per day) is standard preventive treatment after a person has had a stroke or heart attack, even in those with very healthy

lifestyles, because the risk of dying from bleeding is less than that from cardiovascular events.

Current debate revolves around the issue of using aspirin to prevent a FIRST cardiovascular event. A recent study's results were published as three papers in the October 18, 2018 "New England Journal of Medicine" (NEJM)¹. Researchers compared 100 mg daily aspirin to placebo in 19,114 predominantly white Australians and Americans older than age 70 (age 65 for American Blacks and Hispanics) who had no known cardiovascular disease, dementia, disability, bleeding risk or chronic disease that might be fatal within 5 years. Only 4% smoked and 10% were diabetic. Most had hypertension and/or cholesterol problems, for which about one-third took medication.

After 4.7 years the aspirin group experienced slightly less death, dementia and disability, but at the expense of more major bleeding. At 4 years, aspirin takers started to have fewer cardiovascular events, but the difference didn't reach statistical significance, and benefit was completely offset by major bleeding. The authors conclude that aspirin has no net benefit in "an apparently healthy older population."

Unfortunately, some medical people freaked out after this study and threw the baby out with the bath water. **An editorial opined that "aspirin for primary prevention is dead."** People in all age groups and risk categories stopped taking their aspirin. All because a *single* study found that aspirin's benefit is offset by major bleeding in Caucasians who have made it to age 70 without significant disease. How irritating. Why should we extrapolate results of a study about healthy elderly white people to different racial groups and younger people who may not be so healthy and may have significant, as-yet unrealized vascular disease risk?

Diabetics are a special population in this regard. Their platelets clump more easily than normal, and they have multiple other cardiovascular disease risk factors. Cardiovascular events afflict diabetics twice as often as non-diabetics in any given age group, occurring at about the same rate as a non-diabetic who has already had a heart attack or stroke. Because of this, the American Diabetes Association (ADA) recommended in 1997 that all diabetics who have at least one additional heart disease risk factor take prophylactic low dose aspirin. Risk factors include overweight, particularly around the mid-section, high blood pressure, lipid abnormalities and smoking.

The ASCEND trial², published in 2018, addressed the need for aspirin in diabetics who don't necessarily have that second risk factor. It included 15,480 diabetics older than 39 years who had not yet been diagnosed with cardiovascular disease and didn't necessarily have another risk factor, though many did. Half took 100 mg aspirin and the other half took placebo. During an average 7.4 years of follow-up, cardiovascular events occurred in 8.5% of those who took aspirin, vs. 9.6% the placebo group. Major bleeding events occurred in 0.9% more aspirin-takers, and overall there was no difference in death rate between the groups.

ASCEND reaffirmed that aspirin prevents cardiovascular events in diabetics with or without other risk factors but concluded that the cardiovascular benefit was offset by major bleeding events. Since the numerical risks of cardiovascular benefit and major bleeding events are similar, in my opinion the choice about aspirin becomes a matter of which disease type the patient fears most.

Addressing people under age 70, the United States Preventative Services Task Force (USPSTF) recommendations about aspirin use, published just this month, *does not* universally pan preventive aspirin use³. Based on data from 11 randomized trials published between 1989 and 2014, the USPSTF recommends low-dose aspirin for 50 to 59 years old adults whose 10-year cardiovascular risk, taking into account a variety of risk factors, exceeds 10% and who are not at excess risk for bleeding. Risk factors include diabetes, high blood pressure, high cholesterol/lipid levels, tobacco use, obesity

and family history of cardiovascular disease. They concluded that people age 60-69 years with elevated cardiovascular risk are also likely to benefit from aspirin therapy, but the magnitude of benefit may be less than that for those in their fifties. About other age groups, they felt "the current evidence is insufficient to assess the balance of benefits and harms of initiating aspirin use for the primary prevention" in those younger than 50 and those older than 70 years.

- 1) Patrono C, et al. Low-Dose Aspirin for the Prevention of Atherothrombosis. NEJM 2005. 353;22:2373-83. Three studies with first author McNeil JJ, et al. Effect of Aspirin on Disability-free Survival in the Healthy Elderly, Effect of Aspirin on Cardiovascular Events and Bleeding in the healthy Elderly, and Effect of Aspirin on All-Cause Mortality in the Healthy Elderly. NEJM 2018. 379;16:1499-1528.
- 2) The ASCEND Study Collaborative Group. Effects of Aspirin for Primary Prevention in Persons with Diabetes Mellitus. NEJM 2018. 379;16:1529-1539.
- 3) www.uspreventiveservicestaskforce.org/Page/Document/RecommendationStatementFinal/aspirin-to-prevent-cardiovascular-disease-and-cancer