Low-dose aspirin prevents myocardial infarction and stroke and increases bleeding in people without known cardiovascular disease

Questions

In adults 40 years of age or older without known cardiovascular disease, does aspirin reduce the risk of myocardial infarction, stroke, death from cardiovascular disease, or death from all-causes? What is the risk of serious bleeding associated with aspirin use?

The research

2 systematic reviews, one focused on effectiveness of aspirin (11 studies, 118,445 people) and one on risk of bleeding associated with aspirin (10 studies). The review included studies that were published up to January 2015.

Who? People 40 years of age or older without known cardiovascular disease.

What? Aspirin was compared with no treatment or placebo.

Aspirin	vs	No treatment or placebo
Aspirin (at least 75 mg every other day) for 1 year or longer		Placebo is an inactive substance with no pharmacologic effect. It is used as a comparator to ensure the results obtained are due to the effect of the drug being tested and not due to the effect of “taking a medication”

What the researchers found

Risk of death from cardiovascular causes and all causes did not differ for people on aspirin compared with those who received no treatment. In most studies, the dose was ≤ 100 mg/day. When all doses of aspirin were considered (from 50 to 650 mg/day), aspirin reduced death from all causes but did not reduce nonfatal stroke.

Taking aspirin (≤ 100 mg/day) for 10 years would prevent a nonfatal myocardial infarction in 5

people out of 10,000 and nonfatal stroke in 4 people out of 10,000.

Taking aspirin (≤ 100 mg/day) for 10 years would cause major gastrointestinal bleeding in 3 people out of 10,000 and intracranial hemorrhage in 1 person out of 10,000.

The bottom line

In people without known cardiovascular disease, aspirin (≤ 100 mg/day) decreases nonfatal myocardial infarction and nonfatal stroke and increases gastrointestinal and intracranial hemorrhage compared with no treatment or placebo.

Summary of findings: Aspirin (≤ 100 mg/day) vs no treatment or placebo in people without known cardiovascular disease (primary prevention)

Outcomes (average follow-up 6 years)	Rate of events with aspirin	Rate of events with placebo or no treatment	Absolute effect of aspirin	Number of studies and quality of the evidence
Nonfatal myocardial infarction	0.22%	0.27%	About 5 fewer people out of 10,000 had a nonfatal myocardial infarction	8 studies (1 good quality, 7 fair quality)
Non-fatal stroke	0.24%	0.28%	About 4 fewer people out of 10,000 had non-fatal stroke	7 studies (1 good quality, 6 fair quality)
Cardiovascular disease mortality	0.21%	0.22%	No effect*	8 studies (1 good quality, 7 fair quality)
All-cause mortality	0.81%	0.86%	No effect*	8 studies (1 good quality 7 fair quality)
Major gastrointestinal bleeding	0.08%	0.05%	About 3 more people out of 10,000 had major gastrointestinal bleeding	9 studies (2 good quality, 7 fair quality)
Intracranial hemorrhage	0.06%	0.05%	About 1 more person out of 10,000 had intracranial hemorrhage	7 studies (2 good quality, 5 fair quality)

*Although the rates for the 2 groups look different, the differences were not statistically significant—this means that the difference could simply be due to chance rather than due to the different treatments.

This Evidence Summary is based on 2 systematic reviews:

Guirguis-Blake JM, Evans CV, Senger CA, O'Connor EA, Whitlock EP. ***Aspirin for the primary prevention of cardiovascular events: a systematic evidence review for the U.S. Preventive Services Task Force****. Ann Intern Med. 2016;164:804-13.*

Whitlock ET, Burda BU, Williams SB, Guirguis-Blake JM, Evans CV. ***Bleeding risks with aspirin use for primary prevention in adults: a systematic review for the U.S. Preventive Services Task Force.*** *Ann Intern Med. 2016;164: 826-35.*

Should people without known cardiovascular disease take aspirin to prevent cardiac events?

It is important to understand the net clinical benefit (i.e., the balance of benefits and harms) of aspirin in people without established cardiovascular disease.

Benefits: On average, 5 fewer nonfatal myocardial infarctions and 4 fewer nonfatal strokes per 10,000 adults who took aspirin (≤ 100 mg/day) for up to 10 years.

- The benefit occurs within the first 5 years of treatment.
- The baseline risk of cardiovascular disease varied between studies, which could affect the absolute benefit expected from aspirin.
- Firm conclusions could not be made about differences in the benefits of aspirin by characteristics such as age, sex, and diabetes.

Harms: **On average, 7 additional major gastrointestinal or extracranial bleeds and 3 hemorrhagic strokes per 10,000 adults who took aspirin (≤ 100 mg/ day) for up to 10 years.**

- The risk was highest in older patients and those previously admitted for a major bleeding event.
- Other important baseline characteristics that increased the risk of bleeding included male sex, diabetes, smoking, hypertension, obesity, and nonsteroidal anti-inflammatory drug use.
- Use of statins and proton-pump inhibitors reduced the risk of admission for major bleeding.

Overall, aspirin (100 mg/day) provides a small reduction in the risk of myocardial infarction and stroke at the expense of a similarly small increased risk of bleeding complications in adults without established cardiovascular disease. The variation in risk for the individual is impossible to calculate, but is probably very low—about 9996 patients in 10,000 will have no benefit from aspirin.

Use of low-dose aspirin for primary prevention may be beneficial for patients at high risk

of cardiovascular events, after individualized assessment of their cardiovascular disease risk (using validated risk prediction tools such as the Framingham Risk Score) and provided their bleeding risk is not increased.

What about aspirin for prevention in people with previous venous thromboembolism (VTE)?

In a meta-analysis of patients with a first episode of unprovoked VTE who completed anticoagulant therapy, aspirin reduced the risk of recurrent VTE by 2.4% per year and major vascular events by 3% per year, with a small increased risk of major bleeding of 0.1% per year.[1] Although aspirin is less effective than oral anticoagulants for secondary prevention of VTE, patients with a history of unprovoked VTE who have discontinued anticoagulant therapy may benefit from aspirin for the combined effect of preventing cardiovascular events and recurrent venous thromboembolism.

Doctor, should I take aspirin to reduce my chances of having a heart attack or stroke?

It depends on your risk of having a heart attack or stroke:

If you are at "average" risk, you will probably not benefit from taking aspirin because the trade-off between reducing your risk of death, heart attack, or stroke and increasing your risk of bleeding is about the same. If you previously had a clot in your veins, aspirin will reduce your risk of having another clot, which may shift the balance in favour of taking aspirin even if you are at average risk. If you are at higher risk, you would probably benefit from taking aspirin.

1. Simes J, Becattini C, Agnelli G; INSPIRE Study Investigators. Aspirin for the prevention of recurrent venous thromboembolism; the INSPIRE collaboration. Circulation. 2014;130:1062-71.

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Dr. Deborah Siegal graduated from Queen's University School of Medicine in 2009 and completed Internal Medicine and Hematology training at McMaster University. She holds a Master of Science degree in Pharmacology from the University of Toronto and is completing a Master of Science degree in Health Research Methodology at McMaster University. Dr. Siegal is currently a Clinical Scholar in the Division of Hematology and Thromboembolism at McMaster University. She received a Thrombosis Canada Research Fellowship Award in 2014 and a Canadian Institutes of Health Research Fellowship Award

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