

Aspirin to prevent cardiovascular events: Weighing risks and benefits

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Principal Source: U.S. Preventive Services Task Force. Aspirin for the prevention of cardiovascular disease: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med.* 2009;150:396-404.

Cardiovascular disease (CVD) is the leading cause of death in the United States, accounting for >50% of all deaths. In persons age >40, the lifetime risk of death from CVD is 2 in 3 for men and more than 1 in 2 for women.¹ Persons with severe mental illness have nearly twice the risk of death from CVD compared with the general population, which may be attributed to:

- lifestyle factors, including poor diet, lack of exercise, and tobacco dependence²
- antipsychotic medications, which have been shown to increase the risk of CVD³
- lower likelihood of undergoing cardiovascular procedures—including percutaneous transluminal coronary angioplasty and coronary artery bypass graft surgery—after myocardial infarction (MI).⁴

Psychiatrists are often the primary contact for patients with mental illness, giving us an opportunity to collaborate with primary care physicians and apply preventative measures that can reduce illness and improve patients' morbidity and mortality. In addition to evaluating patients for possible hypercholesterolemia and diabetes, adding daily aspirin for primary preven-

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tion of heart attacks and strokes is an easily implementable option that could make a real difference in their health and quality of life.

New aspirin recommendations

The U.S. Preventive Services Task Force (USPSTF) found evidence that daily aspirin decreases the incidence of MI in men and ischemic strokes in women.¹ However, total mortality for either gender was not significantly reduced.⁵ The USPSTF's updated recommendations reflect results of the Women's Health Study⁶ with different guidelines for men and women.

The USPSTF recommends daily aspirin

Practice Points

- Consider **discussing or recommending daily aspirin** for men age 45 to 79 and women age 55 to 79 who are at risk for CVD, such as those who smoke or have diabetes.
- **Psychiatric patients are at higher risk of CVD** and often face systemic barriers to medical care. Collaborate with primary care physicians to determine which patients are good candidates for daily aspirin therapy.
- In psychiatric patients, watch for a **potential drug-drug interaction** between aspirin and valproate and increased risk of bleeding with selective serotonin reuptake inhibitors.
- Aspirin is associated with **increased risk of serious gastrointestinal (GI) bleeding**, hematuria, easy bruising, and epistaxis. Risk factors for GI bleeding include upper GI pain, history of GI ulcers, nonsteroidal anti-inflammatory drug (NSAID) use, alcohol dependence, and other anticoagulant use.



Robert M. McCarron, DO
Series Editor

Table 1

USPSTF recommendations for daily aspirin use in primary prevention of cardiovascular disease

| Population | Recommendation |
|-----------------------------|---|
| Men age 45 to 79 | Encourage aspirin use when potential benefit due to a reduction in myocardial infarctions outweighs potential increased risk of GI bleeding |
| Women age 55 to 79 | Encourage aspirin use when potential benefit of a reduction in ischemic strokes outweighs potential increased risk of GI bleeding |
| Men age <45 | Do not recommend aspirin use for cardiovascular prevention |
| Women age <55 | Do not recommend aspirin use for cardiovascular prevention |
| Men and women age ≥80 years | Insufficient evidence to make recommendations |

GI: gastrointestinal; USPSTF: U.S. Preventive Services Task Force
Source: Reference 1

Clinical Point

Contrary to popular belief and marketing, enteric-coated tablets do not seem to reduce the risk of bleeding

for men age 45 to 79 and for women age 55 to 79 when the benefits of decreased MI for men and ischemic strokes for women outweigh the risks of increased GI bleeding (Table 1).¹ This grade A recommendation means there is high certainty of substantial net benefit.

Aspirin is not recommended for patients age ≥80 because of insufficient evidence of harm or benefit. The risks of MI in men age <45 and stroke in women age <55 are low, and daily aspirin generally is not indicated.

Optimal aspirin dose is unclear. The USPSTF recommends approximately 75 mg/d (effectively 81 mg/d or 1 “baby aspirin” in most U.S. settings). Higher aspirin doses might not be more effective for primary prevention and could increase the risk of GI bleeding. Note that some patients with a history of cardiovascular or cerebrovascular events might receive higher aspirin doses for secondary prevention of additional injury.

Risk assessment. In addition to age, other risk factors for CVD include:

- diabetes

- high total cholesterol (>240 mg/dL)
- low high-density lipoprotein cholesterol or so-called “good cholesterol” (<40 mg/dL for men, <50 mg/dL for women)
- hypertension
- smoking
- family history.

Several online tools—based on data from the Framingham Heart Study and other cohorts—can help estimate a patient’s CVD risk (see *Related Resources, page 63*), or consult with your patient’s primary care physician.

Potential harm of aspirin. USPSTF considers age and gender the most important risk factors for GI bleeding. GI bleeding is defined as serious hemorrhage, perforation, or other complications that could lead to hospitalization or death. Other risk factors include:

- upper GI pain
- history of gastric or duodenal ulcers
- NSAID use
- heavy, regular alcohol consumption.

In general, men have twice the risk of GI bleeding compared with women.¹ The baseline number of GI bleeding events for individuals without a history of GI pain or bleeds taking daily aspirin is 4 per 10,000 person-years for women and 8 per 10,000 for men.¹ Patients with preexisting GI ulcers who receive daily aspirin have more than 2 to 3 times the baseline risk of serious GI bleeding.⁷ NSAIDs taken with daily as-

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Table 2

**Aspirin to prevent cardiovascular disease and stroke:
When benefits outweigh risks**

| Men | | Women | |
|----------|-------------------|----------|----------------------|
| Age | 10-year CVD risk* | Age | 10-year stroke risk* |
| 45 to 59 | ≥4% | 55 to 59 | ≥3% |
| 60 to 69 | ≥9% | 60 to 69 | ≥8% |
| 70 to 79 | ≥12% | 70 to 79 | ≥11% |

*Risk thresholds where aspirin should be started. Estimate risk using an online calculator based on the Framingham Heart Study at www.framinghamheartstudy.org/risk/coronary.html or consult with your patient's primary care physician
CVD: cardiovascular disease
Source: Reference 1

Clinical Point

Watch for a potential drug-drug interaction with valproate and a mildly increased risk of bleeding with SSRIs

pirin can quadruple the risk of GI bleeding compared with aspirin use alone, although antacid therapy can reduce this risk.⁸ Co-administered anticoagulants (eg, warfarin) also significantly increase the risk—especially when compliance with medication and monitoring is poor. Aspirin also increases the risk of hematuria, easy bruising, and epistaxis.

Because consuming >3 standard drinks a day also increases the risk of GI bleeding by up to 6 fold, patients with untreated chronic alcohol abuse or dependence might not be good candidates for daily aspirin therapy.⁹ Contrary to popular belief and pharmaceutical marketing, enteric-coated tablets do not seem to reduce the risk of bleeding because aspirin impacts platelet function, not the lining of the stomach.

Aspirin for psychiatric patients

Patients who have serious mental illness are at increased risk for CVD and often experience systemic barriers to receiving appropriate medical care.¹⁰ Psychiatrists can provide and advocate for primary care services for our patients, including daily aspirin use to prevent CVD when appropriate, and encourage a closer relationship with a

primary care physician before an adverse event occurs. Aspirin use in psychiatric patients is associated with:

- potential drug-drug interaction with valproate¹¹
- mildly increased risk of bleeding as a result of reduced platelet function with the use of selective serotonin reuptake inhibitors.¹²

Balancing benefits vs risks. The USPSTF recommendation assumes that the value of preventing 1 MI or stroke is roughly equivalent to (or slightly less than) the cost of 1 GI bleeding event caused by aspirin. For example, among 1,000 men age 45 to 79 who have a ≥4% risk of MI over 10 years, 12.8 MIs would be prevented for every 8 GI bleeds caused by aspirin by following the current recommendations.¹

The USPSTF guidelines are based on average levels of risk for age and gender. Some men age <45 may decide that it is more important to avoid a cardiovascular event rather than an episode of GI bleeding and might choose to begin daily aspirin. Aspirin use should be discouraged in most patients at high risk for GI bleeding. The point where the potential benefits outweigh the risks must be determined on an individual basis (*Table 2*).

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Related Resources

- National Cholesterol Education Program. Online heart attack risk assessment tool. <http://hp2010.nhlbihin.net/atp/iii/calculator.asp>.
- Framingham Heart study calculator. www.framinghamheartstudy.org/risk/coronary.html.
- National Cholesterol Education Program. www.nhlbi.nih.gov/health/public/heart/cholesterol/wyntk.htm#risk.
- Colorado Neurological Institute. Online stroke risk assessment tool. www.thecni.org/Public/CNICenters/StrokeCenter/StrokeRiskCalculator/index.cfm.
- Agency for Healthcare Research and Quality. Fact sheet on aspirin to prevent cardiovascular disease. www.ahrq.gov/clinic/cvd/aspprovider.htm.

Drug Brand Names

Valproate • Depacon
Warfarin • Coumadin

Disclosures

Dr. Xiong reports no financial relationship with any company whose products are mentioned in this article or with manufacturers of competing products.

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