

# Aspirin for the Primary Prevention of Cardiovascular Events: Recommendation and Rationale

U.S. Preventive Services Task Force\*

This statement summarizes the recommendation of the third U.S. Preventive Services Task Force (USPSTF) for aspirin for the primary prevention of cardiovascular events, as well as the supporting scientific evidence. The complete information on which this statement is based, including evidence tables and references, can be found in a companion article in this issue. Copies of this document, the summary of the evidence, and the systematic evidence review can be obtained through the USPSTF Web site ([www.ahrq](http://www.ahrq.gov/clinic/uspstfix.htm)

[.gov/clinic/uspstfix.htm](http://www.ahrq.gov/clinic/uspstfix.htm)) and in print through the Agency for Healthcare Research and Quality Publications Clearinghouse (800-358-9295).

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See related article on pp 161-172 and editorial comment on pp 155-156.

\* For a list of the members of the U.S. Preventive Services Task Force, see the Appendix.

## SUMMARY OF THE RECOMMENDATION

The U.S. Preventive Services Task Force (USPSTF) strongly recommends that clinicians discuss aspirin chemoprevention with adults who are at increased risk for coronary heart disease (see Clinical Considerations). Discussions with patients should address both the potential benefits and harms of aspirin therapy. This is a **grade A recommendation**. (See Appendix Table 1 for a description of the USPSTF classification of recommendations.)

*The USPSTF found good evidence that aspirin decreases the incidence of coronary heart disease in adults who are at increased risk for heart disease. It also found good evidence that aspirin increases the incidence of gastrointestinal bleeding and fair evidence that aspirin increases the incidence of hemorrhagic strokes. (See Appendix Table 2 for a description of the USPSTF classification of levels of evidence.) The USPSTF concluded that the balance of benefits and harms is most favorable in patients at high risk for coronary heart disease (those with a 5-year risk  $\geq 3\%$ ) but is also influenced by patient preferences.*

## CLINICAL CONSIDERATIONS

Decisions about aspirin therapy should take into account overall risk for coronary heart disease. Risk assessment should include asking about the presence and severity of the following risk factors: age, sex, diabetes, elevated total cholesterol levels, low levels of high-density lipoprotein cholesterol, elevated blood pressure, family history (in younger adults), and smoking. Tools that incorporate specific information on multiple risk factors

provide more accurate estimation of cardiovascular risk than categorizations based simply on counting the numbers of risk factors ([www.med-decisions.com](http://www.med-decisions.com)) (1).

Men older than 40 years of age, postmenopausal women, and younger persons with risk factors for coronary heart disease (for example, hypertension, diabetes, or smoking) are at increased risk for heart disease and may wish to consider aspirin therapy. The Table shows how estimates of the type and magnitude of benefits and harms associated with aspirin therapy vary with an individual's underlying risk for coronary heart disease. Although balance of benefits and harms is most favorable in high-risk persons (those with a 5-year risk  $\geq 3\%$ ), some persons at lower risk may consider the potential benefits of aspirin to outweigh the potential harms.

Discussions about aspirin therapy should focus on potential coronary heart disease benefits, such as prevention of myocardial infarction, and potential harms, such as gastrointestinal and intracranial bleeding. Discussions should take into account individual preferences and risk aversions concerning myocardial infarction, stroke, and gastrointestinal bleeding. Although the optimal timing and frequency of discussions related to aspirin therapy are unknown, reasonable options include every 5 years in middle-aged and older persons or when other cardiovascular risk factors are detected.

Most participants in the primary prevention trials of aspirin therapy have been men between 40 and 75 years of age. Current estimates of benefits and harms may not

**Table. Estimates of Benefits and Harms of Aspirin Given for 5 Years to 1000 Persons with Various Levels of Baseline Risk for Coronary Heart Disease\***

Benefits and Harms	Baseline Risk for Coronary Heart Disease over 5 Yearst		
	1%	3%	5%
Total mortality	No effect	No effect	No effect
Coronary heart disease events, <i>n</i>	1–4 avoided	4–12 avoided	6–20 avoided
Hemorrhagic strokes, <i>n</i> ‡	0–2 caused	0–2 caused	0–2 caused
Major gastrointestinal bleeding events, <i>n</i> §	2–4 caused	2–4 caused	2–4 caused

\* Estimates are based on a relative risk reduction of 28% for coronary heart disease events in aspirin-treated patients and assume that risk reductions do not vary significantly by age. Adapted from reference 2.

† Nonfatal acute myocardial infarction and fatal coronary heart disease. Five-year risks of 1%, 3%, and 5% are equivalent to 10-year risks of 2%, 6%, and 10%, respectively.

‡ Data from secondary prevention trials suggest that increases in hemorrhagic stroke may be offset by reduction in other types of stroke in patients at very high risk for cardiovascular disease (≥10% 5-year risk).

§ Rates may be two to three times higher in persons older than 70 years of age.

be as reliable for women and older men. Although older patients may derive greater benefits because they are at higher risk for coronary heart disease and stroke, their risk for bleeding may be higher. Uncontrolled hypertension may attenuate the benefits of aspirin in reducing coronary heart disease.

The optimum dose of aspirin for chemoprevention is not known. Primary and secondary prevention trials have demonstrated benefits with a variety of regimens, including 75 mg/d, 100 mg/d, and 325 mg every other day. Dosages of approximately 75 mg/d seem to be as effective as higher doses; whether dosages below 75 mg/d are effective has not been established. Enteric-coated or buffered preparations do not clearly reduce adverse gastrointestinal effects of aspirin. Uncontrolled hypertension and concomitant use of other nonsteroidal anti-inflammatory agents or anticoagulants increase risk for serious bleeding.

**SCIENTIFIC EVIDENCE**

**Epidemiology and Clinical Background**

Cardiovascular disease, including ischemic coronary heart disease, stroke, and peripheral vascular disease, is the leading cause of death in the United States (3). Yearly, over 1 million Americans experience new or recurrent myocardial infarction or fatal coronary heart disease. Most events occur in older persons and those with recognized risk factors for cardiovascular disease, including high cholesterol level, high blood pressure, diabetes, or a history of smoking. The early-documented and clear success of aspirin in preventing further clinical disease in some patients with known heart disease (second-

ary prevention) raised interest in aspirin as a potential primary preventive intervention in men and women without known heart disease (4). Two early randomized trials of aspirin had conflicting results, however, and lacked sufficient power to estimate major harms, such as gastrointestinal bleeding and hemorrhagic stroke (5, 6). Thus, the role of aspirin in primary prevention has remained controversial. The new USPSTF recommendation incorporates additional data from three recent trials and provides more reliable estimates of both benefits and harms of aspirin in patients without known heart disease.

**Efficacy of Chemoprevention**

Five trials have examined the effects of daily or every-other-day aspirin for the primary prevention of cardiovascular events over periods of 4 to 7 years (7–9). Most participants were men older than 50 years of age. Meta-analysis of pooled data from all of the studies showed that aspirin therapy reduced the risk for coronary heart disease by 28% (summary odds ratio, 0.72 [95% CI, 0.60 to 0.87]). Summary estimates showed no significant effects of aspirin on total mortality (odds ratio, 0.93 [CI, 0.84 to 1.02]) and stroke (odds ratio, 1.02 [CI, 0.85 to 1.23]).

**Harms of Chemoprevention**

These five primary prevention trials, and a larger number of randomized, controlled trials of secondary prevention that enrolled patients with heart disease or stroke, demonstrate that aspirin increases rates of gastrointestinal bleeding. Estimated rates of major gastrointestinal bleeding episodes are approximately 2 to 4 per

1000 middle-aged persons (4 to 12 per 1000 for older persons) given aspirin for 5 years (10–12).

These controlled trials in primary and secondary prevention settings also suggest that aspirin increases rates of hemorrhagic strokes by a small amount (0 to 2 per 1000 persons given aspirin for 5 years) (5–7). Such estimates are less reliable than those of gastrointestinal bleeding because few strokes were reported in the trials.

### RECOMMENDATIONS OF OTHER ORGANIZATIONS

In 1994, the Canadian Task Force on Preventive Health Care concluded that the evidence was not strong enough to recommend for or against use of aspirin for primary prevention of heart disease in men or women and recommended that physicians and patients balance the reduced rate of nonfatal myocardial infarction against potential adverse effects (13). In 2000, the American Diabetes Association recommended that clinicians consider aspirin for primary prevention of heart disease in diabetic patients who are older than 30 years of age or have risk factors for cardiovascular disease and no contraindications to aspirin therapy (14). In 1997, the American Heart Association concluded that aspirin may be warranted for patients at high risk for myocardial infarction but that health care providers must consider a patient's particular cardiovascular risk profile, the demonstrated benefits of aspirin on reducing risk for a first myocardial infarction, and known and unknown side effects of aspirin (15). In 1998, the European Society of Cardiology recommended low-dose aspirin (75 mg) for patients with well-controlled hypertension and men at "particularly" high risk for coronary heart disease, but not for all persons at high risk (16).

### APPENDIX

Members of the U.S. Preventive Services Task Force are Alfred O. Berg, MD, MPH, *Chair* (University of Washington, Seattle, Washington); Janet D. Allan, PhD, RN, CS, *Vice-Chair* (University of Texas Health Science Center, San Antonio, Texas); Paul S. Frame, MD (Tri-County Family Medicine, Cohocton, New York, and University of Rochester, Rochester, New York); Charles J. Homer, MD, MPH (National Initiative for Children's Healthcare Quality, Boston, Massachusetts); Mark S. Johnson, MD, MPH (University of Medicine and Dentistry of New Jersey–New Jersey Medical School, Newark, New Jersey); Jonathan D. Klein, MD, MPH (University of Rochester School of Medicine, Rochester, New York); Tracy A. Lieu, MD, MPH (Harvard Pilgrim Health Care and Harvard Medical School, Bos-

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**Appendix Table 1. U.S. Preventive Services Task Force Grades and Recommendations\***

Grade	Recommendation
A	The USPSTF strongly recommends that clinicians routinely provide [the service] to eligible patients. <i>The USPSTF found good evidence that [the service] improves important health outcomes and concludes that benefits substantially outweigh harms.</i>
B	The USPSTF recommends that clinicians routinely provide [the service] to eligible patients. <i>The USPSTF found at least fair evidence that [the service] improves important health outcomes and concludes that benefits outweigh harms.</i>
C	The USPSTF makes no recommendation for or against routine provision of [the service]. <i>The USPSTF found at least fair evidence that [the service] can improve health outcomes but concludes that the balance of benefits and harms is too close to justify a general recommendation.</i>
D	The USPSTF recommends against routinely providing [the service] to asymptomatic patients. <i>The USPSTF found at least fair evidence that [the service] is ineffective or that harms outweigh benefits.</i>
I	The USPSTF concludes that the evidence is insufficient to recommend for or against routinely providing [the service]. <i>Evidence that the [service] is effective is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined.</i>

\* The U.S. Preventive Services Task Force (USPSTF) grades its recommendations according to one of five classifications (A, B, C, D, I) reflecting the strength of evidence and magnitude of net benefit (benefits minus harms).

**Appendix Table 2. U.S. Preventive Services Task Force Grades for Strength of Overall Evidence\***

Grade	Definition
Good	Evidence includes consistent results from well-designed, well-conducted studies in representative populations that directly assess effects on health outcomes
Fair	Evidence is sufficient to determine effects on health outcomes, but the strength of the evidence is limited by the number, quality, or consistency of the individual studies, generalizability to routine practice, or indirect nature of the evidence on health outcomes
Poor	Evidence is insufficient to assess the effects on health outcomes because of limited number or power of studies, important flaws in their design or conduct, gaps in the chain of evidence, or lack of information on important health outcomes

\* The U.S. Preventive Services Task Force (USPSTF) grades the quality of the overall evidence for a service on a three-point scale (good, fair, poor).

sylvania); Carolyn Westhoff, MD, MSc (Columbia University College of Physicians and Surgeons, New York, New York); and Steven H. Woolf, MD, MPH (Medical College of Virginia, Virginia Commonwealth University, Fairfax, Virginia).

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