Aspirin for the Primary Prevention of Cardiovascular Events

Recommendations and Rationale

U.S. Preventive Services Task Force

This statement summarizes the current U.S. Preventive Services Task Force (USPSTF) recommendation for aspirin for the primary prevention of cardiovascular events and the supporting scientific evidence, and it updates the 1995 recommendations contained in the *Guide to Clinical Preventive Services*, second edition.[1] Explanations of the ratings and of the strength of overall evidence are given in Appendix A and Appendix B, respectively. The complete information on which this statement is based, including evidence tables and references, is available in the article Aspirin for the Primary Prevention of Cardiovascular Events[2] (which follows this recommendation). These documents, along with reprints, can be obtained through the USPSTF Web site (www.ahrq.gov/clinic/uspstfix.htm), through the National Guideline Clearinghouse™ (www.guideline.gov), or in print through the AHRQ Publications Clearinghouse (call 1-800-358-9295 or e-mail ahrqpubs@ahrq.gov).

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Summary of 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 (CHD) (see "Clinical Considerations"). Discussions with patients should address both the potential benefits and harms of aspirin therapy. **A recommendation.**

The USPSTF found good evidence that aspirin decreases the incidence of coronary heart disease in adults who are at increased risk for heart disease. They also found good evidence that aspirin increases the incidence of gastrointestinal bleeding and fair evidence that aspirin increases the incidence of hemorrhagic strokes. The USPSTF concluded that the balance of benefits and harms is most favorable in patients at high risk of CHD (5-year risk of greater than or equal to 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 (HDL) 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 (http://www.intmed.mcw.edu/clincalc/heartrisk.html).[3]
- **Men older than 40 years, postmenopausal women, and younger people with risk factors for coronary heart disease (eg, hypertension, diabetes, or smoking) are at increased risk for heart disease and may wish to consider aspirin therapy.**

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Table 1. Estimates of benefits and harms of aspirin therapy given for 5 years to 1,000 individuals with various levels of baseline risk for coronary heart disease*

Benefits and harms	Baseline risk for coronary heart disease over 5 years†		
	1%	3%	5%
Total mortality	No effect	No effect	No effect
CHD events†	1-4 avoided	4-12 avoided	6-20 avoided
Hemorrhagic strokes**	0-2 caused	0-2 caused	0-2 caused
Major gastrointestinal bleeding events++	2-4 caused	2-4 caused	2-4 caused

*These estimates are based on a relative risk reduction of 28% for coronary heart disease events in aspirin-treated patients. They assume risk reductions do not vary significantly by age.

†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 (CVD) (greater than or equal to 10% 5-year risk).

++ Rates may be 2 to 3 times higher in people older than 70 years.

Source: Hayden M, Pignone M, Phillips C, Mulrow C. Aspirin for the primary prevention of cardiovascular events: A summary of the evidence for the U.S. Preventive Services Task Force. *Ann Intern Med*. 2002;136:161-172.

Table 1 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 people (5-year risk greater than 3%), some people at lower risk may consider the potential benefits of aspirin to be sufficient 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 people 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 be as reliable for women and older men.
- **Although older patients may derive greater benefits because they are at higher risk for CHD and stroke, their risk for bleeding may be higher.**
- **Uncontrolled hypertension may attenuate the benefits of aspirin in reducing CHD.**
- **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 per day, 100 mg per day, and 325 mg every other day. Doses of approximately 75 mg per day appear as effective as higher doses; whether doses below 75 mg per day 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.[4] Yearly, over 1 million Americans experience new or recurrent myocardial infarction or fatal coronary heart disease. Most events occur in older people and those with recognized risk factors for cardiovascular disease, including high cholesterol, 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 (secondary prevention) raised interest in aspirin as a potential primary preventive intervention in men and women without known heart disease.[5] 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.[6,7] Thus, the role of aspirin in primary prevention has remained controversial. The new USPSTF recommendation incorporates additional data from 3 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.[6-10] Most participants were men older than 50 years. Meta-analysis of pooled data from all of the studies showed that aspirin therapy reduced the risk for CHD by 28% (summary odds ratio (OR), 0.72; 95% CI, 0.60 to 0.87). Summary estimates showed no significant effects of aspirin on total mortality (OR, 0.93; 95% CI, 0.84 to 1.02) and stroke (OR, 1.02; 95% CI, 0.85 to 1.23).

Harms of Chemoprevention

These 5 primary prevention trials, and a larger number of randomized controlled trials (RCTs) 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 1,000 middle-aged individuals (4 to 12 for older individuals) given aspirin for 5 years.[11-13]

These controlled trials in primary and secondary prevention settings also suggest that aspirin increases rates of hemorrhagic strokes by a small amount (0-2 per 1,000 individuals given aspirin for 5 years).[6-8] Such estimates are less reliable than those of gastrointestinal bleeding because few strokes were reported in the trials.

Recommendations of Others

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.[14] 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 or have risk factors for cardiovascular disease and no contraindications to aspirin therapy.[15] In 1997, the American Heart Association concluded that aspirin may be warranted for patients at high risk of 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 as well an unknown side effects of aspirin.[16] 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 individuals at high risk.[17]

References

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Appendix A
U.S. Preventive Services Task Force - Recommendations and Ratings

The Task Force grades its recommendations according to one of 5 classifications (A, B, C, D, I) reflecting the strength of evidence and magnitude of net benefit (benefits minus harms):

A. The USPSTF strongly recommends that clinicians routinely provide [the service] to eligible patients. *The USPSTF found good evidence that [the service] improves important health outcomes and concludes that benefits substantially outweigh harms.*

B. The USPSTF recommends that clinicians routinely provide [the service] to eligible patients. *The USPSTF found at least fair evidence that [the service] improves important health outcomes and concludes that benefits outweigh harms.*

C. The USPSTF makes no recommendation for or against routine provision of [the service]. *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.*

D. The USPSTF recommends against routinely providing [the service] to asymptomatic patients. *The USPSTF found at least fair evidence that [the service] is ineffective or that harms outweigh benefits.*

I. The USPSTF concludes that the evidence is insufficient to recommend for or against routinely providing [the service]. *Evidence that [the service] is effective is lacking, of poor quality, or conflicting and the balance of benefits and harms cannot be determined.*

Appendix B
U.S. Preventive Services Task Force - Strength of Overall Evidence

The USPSTF grades the quality of the overall evidence for a service on a 3-point scale (good, fair, poor):

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.

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