Aspirin for the Prevention of Cardiovascular Disease: U.S. Preventive Services Task Force Recommendation Statement

U.S. Preventive Services Task Force*

Description: Update of the 2002 U.S. Preventive Services Task Force (USPSTF) recommendation about the use of aspirin for the prevention of coronary heart disease.

Methods: Review of the literature since 2002, focusing on new evidence on the benefits and harms of aspirin for the primary prevention of cardiovascular disease, including myocardial infarction and stroke. The new evidence was reviewed and synthesized according to sex.

Recommendations: Encourage men age 45 to 79 years to use aspirin when the potential benefit of a reduction in myocardial infarctions outweighs the potential harm of an increase in gastrointestinal hemorrhage. (A recommendation)

Encourage women age 55 to 79 years to use aspirin when the potential benefit of a reduction in ischemic strokes outweighs the potential harm of an increase in gastrointestinal hemorrhage. (A recommendation)

Evidence is insufficient to assess the balance of benefits and harms of aspirin for cardiovascular disease prevention in men and women 80 years or older. (I statement)

Do not encourage aspirin use for cardiovascular disease prevention in women younger than 55 years and in men younger than 45 years. (D recommendation)

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For author affiliation, see end of text.

* For a list of the members of the USPSTF, see the **Appendix** (available at www.annals.org).

The U.S. Preventive Services Task Force (USPSTF) makes recommendations about preventive care services for patients without recognized signs or symptoms of the target condition.

It bases its recommendations on a systematic review of the evidence of the benefits and harms and an assessment of the net benefit of the service.

The USPSTF recognizes that clinical or policy decisions involve more considerations than this body of evidence alone. Clinicians and policymakers should understand the evidence but individualize decision making to the specific patient or situation.

See also:

Print

Editorial comment. 414
Related articles 379, 405
Summary for Patients. I-37

Web-Only

Appendix
CME quiz
Conversion of graphics into slides
Downloadable recommendation summary
Audio summary

Summary of Recommendation and Evidence

The USPSTF recommends the use of aspirin for men age 45 to 79 years when the potential benefit due to a reduction in myocardial infarctions outweighs the potential harm due to an increase in gastrointestinal hemorrhage. See the Clinical Considerations section for discussion of benefits and harms. This is an A recommendation.

The USPSTF recommends the use of aspirin for women age 55 to 79 years when the potential benefit of a reduction in ischemic strokes outweighs the potential harm of an increase in gastrointestinal hemorrhage. See the Clinical Considerations section for discussion of benefits and harms. This is an A recommendation.

The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of aspirin for cardiovascular disease prevention in men and women 80 years or older. This is an I statement.

See the Clinical Considerations section for suggestions for practice regarding the I statement.

The USPSTF recommends against the use of aspirin for stroke prevention in women younger than 55 years and for myocardial infarction prevention in men younger than 45 years. This is a D recommendation.

Figure 1 (page 403) shows a summary of the recommendations and suggestions for clinical practice.

Table 1 describes the USPSTF grades, and **Table 2**

describes the USPSTF classification of levels of certainty of net benefit.

Rationale

Importance

Cardiovascular disease, including heart attack and stroke, is the leading cause of death in the United States.

Recognition of Risk Status

For many groups, available risk calculators can provide an accurate estimate of the risk for coronary heart disease events and strokes based on information about cardiovascular risk factors that include sex. See the Clinical Considerations section.

Benefits of Preventive Medication

The USPSTF found good evidence that aspirin decreases the incidence of myocardial infarction in men and ischemic strokes in women.

Harms of Preventive Medication

The USPSTF found good evidence that aspirin increases the incidence of gastrointestinal bleeding and fair evidence that aspirin increases the incidence of hemorrhagic strokes.

USPSTF Assessment

The USPSTF concludes that, for men age 45 to 79 years whose benefit due to a reduction in myocardial infarctions exceeds the harm because of an increase in gastrointestinal bleeding, there is high certainty that the net benefit is substantial.

The USPSTF concludes that, for women age 55 to 79 years whose benefit due to a reduction in ischemic stroke exceeds the harm because of gastrointestinal bleeding, there is high certainty that the net benefit is substantial.

The USPSTF concludes that, for men and women 80 years or older, the evidence is insufficient to assess the balance of benefits and harms.

The USPSTF concludes that, for men 44 years or younger and women 54 years or younger, the potential benefits of reducing myocardial infarction in men or ischemic stroke in women are small, and there is moderate certainty that the benefits do not outweigh harms.

Clinical Considerations

Patient Population Under Consideration

These recommendations apply to adult men and women without a history of coronary heart disease or stroke.

Assessment of Risk for Cardiovascular Disease

Men

The net benefit of aspirin depends on the initial risk for coronary heart disease events and gastrointestinal bleeding (1). Thus, decisions about aspirin therapy should consider the overall risks for coronary heart disease and gastrointestinal bleeding.

Risk assessment for coronary heart disease should include ascertainment of risk factors: age, diabetes, total cholesterol levels, high-density lipoprotein cholesterol levels, blood pressure, and smoking. Available tools provide estimations of cor-

Figure 2. **Estimated MIs prevented and estimated harms of using aspirin for 10 years in a hypothetical cohort of 1000 men.**

As indicated, the estimated number of MIs prevented varies with 10-year CHD risk. The estimated harms of using aspirin vary with age. Therefore, both 10-year CHD risk and age must be considered when determining whether the potential harms of aspirin use outweigh the potential benefit in terms of MIs prevented. The shaded areas indicate the combinations of 10-year CHD risk and age for which the number of harms (GI bleeding and hemorrhagic stroke) are greater than or approximately equal to the number of MIs prevented.*

Variable	Estimated MIs Prevented (per 1000 Men), *n*		
	Age 45–59 Years	Age 60–69 Years	Age 70–79 Years
10-year CHD risk			
1%	3.2	3.2	3.2
2%	6.4	6.4	6.4
3%	9.6	9.6	9.6
4%	12.8	12.8	12.8
5%	16	16	16
6%	19.2	19.2	19.2
7%	22.4	22.4	22.4
8%	25.6	25.6	25.6
9%	28.8	28.8	28.8
10%	32	32	32
11%	35.2	35.2	35.2
12%	38.4	38.4	38.4
13%	41.6	41.6	41.6
14%	44.8	44.8	44.8
15%	48	48	48
16%	51.2	51.2	51.2
17%	54.4	54.4	54.4
18%	57.6	57.6	57.6
19%	60.8	60.8	60.8
20%	64	64	64
	Estimated Harms, *n*		
Type of event			
GI bleeding	8	24	36
Hemorrhagic stroke	1	1	1

* Calculations of estimated benefits and harms rely on assumptions and are by nature somewhat imprecise. Estimates of benefits and harms, especially at the borders of the shaded and unshaded areas, should be considered in the full context of clinical decision making and used to stimulate shared decision making. The calculations in the table are based on the following assumptions: that there is a 32% risk reduction of MIs with regular aspirin use (3) and that gastrointestinal bleeding includes serious hemorrhage, perforation, or other complications leading to hospitalization or death. The harm of GI bleeding in the table assumes that the risk for GI bleeding increases with age and that the men are not taking nonsteroidal anti-inflammatory drugs, do not have upper GI pain, or do not have a history of GI ulcer (2).

Estimates are based on age and 10-year CHD risk. CHD = coronary heart disease; GI = gastrointestinal; MI = myocardial infarction.

onary heart disease risk (such as the calculator available at http://healthlink.mcw.edu/article/923521437.html).

Figure 2 (2, 3) shows the estimated number of myocardial infarctions prevented according to coronary heart disease risk level for men age 45 to 79 years—the age range with the potential for substantial net benefit from the use of aspirin. It also shows that the coronary heart disease risk level at which the absolute number of myocardial infarctions prevented by the use of aspirin is greater than the absolute number of gastrointestinal bleeding episodes and hemorrhagic strokes caused by aspirin therapy increases with age. The estimates in **Figure 2** were developed assuming that the men are not currently taking nonsteroidal anti-inflammatory drugs (NSAIDs) and are without other conditions that increase the risk for gastrointestinal bleeding (see below). Furthermore, the decision about the exact level of risk at which the potential benefits outweigh potential harms is an individual one. Some men may decide that avoiding a myocardial infarction is of great value and that having a gastrointestinal bleeding event is not a major problem. This group would probably decide to take aspirin at a lower coronary heart disease risk level than men who are more afraid of gastrointestinal bleeding. Men who have a high likelihood of benefiting with little potential for harm should be encouraged to consider aspirin. Conversely, aspirin use should be discouraged among men who have little potential of benefiting from the therapy or have a high risk for gastrointestinal bleeding.

Shared decision making should be encouraged with men for whom the potential benefits and risks for serious bleeding are more closely balanced (**Figure 3**). This discussion should explore the potential benefits and harms and patient preferences. As the potential benefit increases above potential harms, the recommendation to take aspirin should become stronger.

Evidence on the benefits in men younger than 45 years is limited, and the potential benefit in this age group is probably low because the risk for myocardial infarction is very low.

Figure 3. **10-year CHD risk levels at which the number of cardiovascular disease events prevented is closely balanced to the number of serious bleeding events.**

Shared decision making is strongly encouraged with persons whose risk is close to (either above or below) these estimates of 10-year risk levels. As the potential cardiovascular disease reduction benefit increases above harms, the recommendation to take aspirin should become stronger.

Men		Women	
Age	10-Year CHD Risk, %	Age	10-Year Stroke Risk, %
45–59 y	≥4	55–59 y	≥3
60–69 y	≥9	60–69 y	≥8
70–79 y	≥12	70–79 y	≥11

CHD = coronary heart disease.

Women

The net benefit of aspirin depends on the initial risks for stroke and gastrointestinal bleeding. Thus, decisions about aspirin therapy should consider the overall risk for stroke and gastrointestinal bleeding.

Risk factors for stroke include age, high blood pressure, diabetes, smoking, a history of cardiovascular disease, atrial fibrillation, and left ventricular hypertrophy. Tools for estimation of stroke risk are available (such as the calculator available at www.westernstroke.org/PersonalStrokeRisk1.xls).

Figure 4 shows the estimated number of strokes prevented according to stroke risk level in women age 55 to 79 years—the age range for which evidence shows that there could be substantial potential net benefit of aspirin use. It also shows that the stroke risk level at which the absolute number of strokes prevented is greater than the absolute number of gastrointestinal bleeding events caused increases with age. The estimates in **Figure 4** were developed assuming that women are not currently taking NSAIDs and are without other conditions that increase the risk for gastrointestinal bleeding (see the Risk for Gastrointestinal Bleeding section). Furthermore, the decision about the exact stroke risk level at which the potential benefits outweigh harms is an individual one. Some women may decide that avoiding a stroke is of great value but experiencing a gastrointestinal bleeding event is not a major problem. These women would probably decide to take aspirin at a lower stroke risk level than those who are more afraid of a bleeding event. Women who have little potential of benefiting from aspirin therapy or have a high risk for gastrointestinal bleeding should be discouraged from taking aspirin.

Shared decision making should be encouraged with women for whom the potential benefits and risks for serious bleeding are more closely balanced (**Figure 3**). This discussion should explore potential benefits and harms and patient preferences. As the potential stroke reduction benefit increases above the potential harms, the recommendation to take aspirin should become stronger.

Evidence on benefits in women younger than 55 years is limited, and the potential benefit in this age group is probably low because the risk for stroke is very low.

Assessment of Risk for Gastrointestinal Bleeding

Evidence shows that the risk for gastrointestinal bleeding with and without aspirin use increases with age (2, 4). For the purposes of making this recommendation, the USPSTF considered age and sex to be the most important risk factors for gastrointestinal bleeding. Other risk factors for bleeding include upper gastrointestinal tract pain, gastrointestinal ulcers, and NSAID use. Nonsteroidal anti-inflammatory drug therapy combined with aspirin approximately quadruples the risk for serious gastrointestinal bleeding compared with the risk with aspirin alone. The rate of serious bleeding in aspirin users is approximately 2

to 3 times greater in patients with a history of a gastrointestinal ulcer. Men have twice the risk for serious gastrointestinal bleeding than women (2, 4). These risk factors increase the risk for bleeding substantially and should be considered in the overall decision about the balance of benefits and harms of aspirin therapy. Enteric-coated or buffered preparations do not clearly reduce the adverse gastrointestinal effects of aspirin. Uncontrolled hypertension and concomitant use of anticoagulants also increase the risk for serious bleeding.

Treatment

The optimum dose of aspirin for preventing cardiovascular disease events is not known. Primary prevention trials have demonstrated benefits with various regimens, including dosages of 75 and 100 mg/d and 100 and 325 mg every other day. A dosage of approximately 75 mg/d seems as effective as higher dosages. The risk for gastrointestinal bleeding may increase with dose.

Intervention Intervals

Although the optimal timing and frequency of discussions related to aspirin therapy are unknown, a reasonable option might be every 5 years in middle age and later and also whenever other cardiovascular risk factors are detected.

Suggestions for Practice Regarding the I Statement

The incidence of myocardial infarction and stroke is high in persons 80 years or older, and thus the potential benefit of aspirin is large. The relationship between increasing age and gastrointestinal bleeding is also well established, and thus the potential harms are also large. The net benefit of aspirin use in persons older than 80 years is probably best in those without risk factors for gastrointestinal bleeding (other than older age) and in those who could tolerate a gastrointestinal bleeding episode (for example, those with normal hemoglobin levels, good kidney function, and easy access to emergency care). Clinicians should inform patients about the adverse consequences of gastrointestinal bleeding because they might be mitigated by a patient's early recognition of the signs and symptoms of bleeding (dark stools, vomiting blood, bright red blood per rectum, syncope, and lightheadedness). If clinicians decide to prescribe aspirin in adults older than 80 years, they should do so only after a discussion with the patient that includes the potential harms and uncertain benefits.

Useful Resources

The USPSTF made recommendations on other interventions for the primary and secondary prevention of cardiovascular disease, including recommendations on screening for abdominal aortic aneurysm, carotid artery stenosis, coronary heart disease, high blood pressure, lipid disorders, and peripheral arterial disease. These are available at www.preventiveservices.ahrq.gov.

Figure 4. **Estimated number of strokes prevented and estimated harms of using aspirin for 10 years in a hypothetical cohort of 1000 women on the basis of age and 10-year stroke risk.**

As indicated, the estimated number of strokes avoided varies with 10-year stroke risk. The estimated harms of using aspirin vary with age. Therefore, both 10-year stroke risk and age must be considered when determining whether the potential harms of aspirin use outweigh the potential benefit in terms of strokes prevented. The shaded areas indicate the combinations of 10-year stroke risk and age for which the number of harms (GI bleeding) are greater than the number of strokes prevented.*

Variable	Estimated Strokes Prevented (per 1000 Women), *n*		
	Age 55–59 Years	Age 60–69 Years	Age 70–79 Years
10-year stroke risk			
1%	1.7	1.7	1.7
2%	3.4	3.4	3.4
3%	5.1	5.1	5.1
4%	6.8	6.8	6.8
5%	8.5	8.5	8.5
6%	10.2	10.2	10.2
7%	11.9	11.9	11.9
8%	13.6	13.6	13.6
9%	15.3	15.3	15.3
10%	17	17	17
11%	18.7	18.7	18.7
12%	20.4	20.4	20.4
13%	22.1	22.1	22.1
14%	23.8	23.8	23.8
15%	25.5	25.5	25.5
16%	27.2	27.2	27.2
17%	28.9	28.9	28.9
18%	30.6	30.6	30.6
19%	32.3	32.3	32.3
20%	34	34	34
	Estimated Harm, *n*		
Type of event			
GI bleeding	4	12	18

* Calculations of estimated benefits and harms rely on assumptions and are by nature somewhat imprecise. Estimates of benefits and harms, especially at the borders of the shaded and unshaded areas, should be considered in the full context of clinical decision making and used to stimulate shared decision making. The calculations in the table are based on the following assumptions: that there is a 17% risk reduction of strokes with regular aspirin use (3) and that gastrointestinal bleeding includes serious hemorrhage, perforation, or other complications leading to hospitalization or death. Harm of GI bleeding in the table assumes that risk for GI bleeding increases with age and that the women are not taking nonsteroidal anti-inflammatory drugs, do not have upper GI pain, or do not have a history of GI ulcer (2). "Strokes prevented" is the net reduction of strokes, which includes a decrease in ischemic strokes and a small increase in hemorrhagic strokes.

GI = gastrointestinal.

DISCUSSION

Burden of Disease

Cardiovascular disease is the leading cause of death in the United States—it is the underlying or contributing cause in approximately 58% of deaths. In 2003, 1 of every 3 adults had some form of cardiovascular disease. In adults

older than 40 years, the lifetime risk is 2 in 3 for men and more than 1 in 2 for women.

Scope of Review

In 2002, the USPSTF strongly recommended that clinicians discuss the use of aspirin with adults who have an increased risk for coronary heart disease (5). In ensuing years, the results of the WHS (Women's Health Study) were published. The current USPSTF review focused on new evidence on the benefits and harms of aspirin for the primary prevention of cardiovascular disease. The evidence was reviewed and synthesized according to sex, because available evidence suggested that aspirin may have differential benefits and harms in men and women.

Effectiveness of Risk Assessment and Preventive Medication

A tool for predicting coronary heart disease events has been developed on the basis of Framingham Heart Study data. This tool uses sex, age, smoking, diabetes, blood pressure, and cholesterol levels as risk factors for coronary heart disease (6). A tool to calculate the risk for stroke has also been developed on the basis of Framingham data. Hypertension was shown to be the major risk factor for stroke in the Framingham study. Other risk factors that were shown to be associated with an increased risk for stroke and are included in the tool are age, sex, diabetes, smoking, known cardiovascular disease, atrial fibrillation, and left ventricular hypertrophy (7).

Several randomized, controlled trials (RCTs) reviewed for the 2002 USPSTF recommendation showed a reduction in myocardial infarctions in men. Most of the participants in the trials were white men. Only 2 of these studies included women, and no substantial reduction in coronary heart disease events occurred in women in these studies. Since the last USPSTF review, new evidence from the WHS and a meta-analysis suggests differential effects of aspirin by sex: Men derive benefit in the reduction of myocardial infarctions, and women derive benefit in the reduction of ischemic strokes (3, 8).

The WHS was a double-blind RCT that evaluated the risks and benefits of aspirin in the primary prevention of cardiovascular disease (8). The WHS randomly assigned 39 876 female health professionals to aspirin, 100 mg every other day, or placebo. The mean follow-up was 10.1 years. The WHS reported benefit with aspirin use in stroke reduction (relative risk [RR], 0.83 [95% CI, 0.69 to 0.99]). Specifically, investigators reported reduction in ischemic strokes (RR, 0.76 [CI, 0.63 to 0.93]) and found no significant benefit in reduction of combined cardiovascular events (strokes, myocardial infarctions, or death from either cause), myocardial infarctions, death from cardiovascular disease, or all-cause mortality.

A recent meta-analysis reported on the sex-specific benefits of aspirin in 51 342 women and 44 114 men enrolled in 6 primary prevention trials, including the WHS (3). The number of participants in the studies ranged from 2540 to 39 876. Mean age was 53 to 61.5 years, and the dosage of aspirin ranged from 100 mg every other day to 500 mg/d; 3 trials had a placebo control group, 3 studied health professionals, and 3 included participants with 1 or more risk factor for cardiovascular disease. In the meta-analysis, aspirin use in women was associated with significant reductions in cardiovascular events (strokes, myocardial infarctions, or death from either cause) (odds ratio [OR], 0.88 [CI, 0.79 to 0.99]) and ischemic strokes (OR, 0.76 [CI, 0.63 to 0.93]); there was no significant benefit in the reduction of myocardial infarctions or cardiovascular disease mortality. In men, aspirin use was associated with a significant reduction in cardiovascular events (OR, 0.86 [0.78 to 0.94]) and myocardial infarctions (OR, 0.68 [0.54 to 0.86]); there was no significant benefit in the reduction of ischemic stroke or cardiovascular disease mortality. There was no significant reduction in total mortality with aspirin use either in men or in women.

Potential Harms of Risk Assessment and Preventive Medication

Using aspirin for the primary prevention of cardiovascular disease events increases the risk for major bleeding events in men and women. In the meta-analysis discussed earlier, hemorrhagic strokes were statistically significantly increased in men but not in women.

The WHS reported harms of aspirin use in the primary prevention of cardiovascular events (8). Gastrointestinal bleeding, peptic ulcers, self-reported hematuria (blood in the urine), easy bruising, and epistaxis (nosebleeds) were significantly more common in women assigned to aspirin therapy than in women assigned to placebo. In each group, approximately equal numbers reported any gastrointestinal symptom. Serious gastrointestinal bleeding (requiring transfusion) were more common in the aspirin group: 127 in the aspirin group and 91 in the placebo group (RR, 1.40 [CI, 1.07 to 1.83]). Five deaths due to gastrointestinal bleeding occurred in the study. Of these, 3 were in the placebo group and 2 were in the aspirin group. Hemorrhagic strokes were not statistically significantly increased in the aspirin group (RR, 1.24 [CI, 0.82 to 1.87]).

The sex-specific meta-analysis of RCTs described above reported adverse events with aspirin use in the primary prevention of cardiovascular events in 51 342 women and 44 114 men (3). Major bleeding events were increased in persons taking aspirin compared with persons not taking aspirin (OR, 1.68 [CI, 1.13 to 2.52] in women and 1.72 [CI, 1.35 to 2.20] in men). The odds of hemorrhagic strokes were not significantly increased in women (OR, 1.07 [CI, 0.42 to 2.69]) but were significantly increased in men (OR, 1.69 [CI, 1.04 to 2.73]).

A study of very large databases of users and nonusers of aspirin and NSAIDs reported higher rates of excess serious gastrointestinal bleeding with aspirin use in people with the following factors: male sex, upper gastrointestinal pain, and a history of a gastrointestinal ulcer (2, 4). In

women younger than 60 years without these risk factors, the excess number of serious gastrointestinal bleeding episodes associated with aspirin use is 0.4 per 1000 person-years. The rate is 0.8 per 1000 person-years for women with a history of upper gastrointestinal pain and 2.4 to 4.0 per 1000 person-years for women with a history of a gastrointestinal ulcer. In men younger than 60 years without these risk factors, the excess number of serious gastrointestinal bleeding episodes associated with aspirin use is 0.8 per 1000 person-years. The rate is 1.6 per 1000 person-years for men with a history of upper gastrointestinal pain and 4.8 to 8.0 per 1000 person-years for men with a history of gastrointestinal ulcer. As discussed above, gastrointestinal bleeding risk increases with age. In women without risk factors for gastrointestinal bleeding, the rate of excess serious bleeding associated with aspirin is 1.2 per 1000 person-years at 60 to 69 years, 1.8 per 1000 person-years at 70 to 79 years, and 3 per 1000 person-years at 79 years or older. In men, these numbers are 2.4, 3.6, and 6 per 1000 person-years, respectively. The use of NSAIDs approximately triples or quadruples these rates (2).

Estimate of Magnitude of Net Benefit

Aspirin use for the primary prevention of cardiovascular disease provides more benefits than harms in men or women whose risk for myocardial infarction or ischemic stroke, respectively, is high enough to outweigh the risk for gastrointestinal hemorrhage. In men similar to those enrolled in the RCTs, the number needed to treat to prevent 1 myocardial infarction over 5 years of aspirin use is 118, whereas the number needed to treat to cause 1 major bleeding event is 303 over 5 years of aspirin use and 769 to cause 1 hemorrhagic stroke. The balance of benefits and harms varies by coronary heart disease risk and risk for gastrointestinal bleeding. For a hypothetical group of 1000 men younger than 60 years with a 6% 10-year baseline risk for myocardial infarction, aspirin use will prevent approximately 19 myocardial infarctions and cause approximately 1 hemorrhagic stroke and 8 major bleeding events (**Figure 2**). The USPSTF concluded with high certainty that the net benefit is substantial in men at increased risk for myocardial infarctions and not at increased risk for serious bleeding.

In women similar to those enrolled in the RCTs, the number needed to treat to prevent 1 ischemic stroke with 5 years of aspirin use is 417, and the number needed to treat to cause 1 major bleeding event is 392 over 5 years of aspirin use. The balance of benefits and harms varies by stroke risk and risk for a bleeding event. In a hypothetical group of 1000 women younger than 60 years with a 6% 10-year risk for stroke, aspirin use will prevent approximately 10 strokes and cause approximately 4 major bleeding events (**Figure 4**). The estimates of the number of major bleeding events were assumed to be stable within age strata with respect to increases in baseline stroke risk. The USPSTF concluded with high certainty that the net benefit is substantial for women at increased risk for stroke and not at increased risk for serious bleeding.

How Evidence Fits With Biological Understanding

Platelet adhesion and activation is part of the complex process of arterial thrombosis that may lead to vascular occlusion and subsequent myocardial infarctions and strokes. Aspirin is thought to be useful for the primary and secondary prevention of cardiovascular events because of its inhibition of platelet aggregation mediated through the permanent inactivation of cyclooxygenases (9).

The epidemiology of cardiovascular disease events differs for men and women. Men have a higher risk for coronary heart disease and tend to have these events at a younger age than women. After age 40 years, men have a 49% lifetime risk for a coronary heart disease event. Women older than 40 years have a 32% risk. The median age of first myocardial infarction is 65.8 years in men and 70.4 years in women. However, women are more likely to die of a myocardial infarction; 38% of women die within 1 year of a first event versus 25% of men. This is probably partly because of the older age in women at first event (7, 10).

Although incidence rates of stroke are higher in men than in women, more women die of stroke than men because of their longer life expectancy. According to Framingham data, the 10-year risk for initial ischemic stroke at age 55 years is 1.8% for women and 2.4% for men. At age 65 years, the risk increases to 3.9% in women and 5.8% in men. The lifetime risk for ischemic stroke is greater in women than in men from age 55 to 75 years (approximately 17% to 18% in women and 13% to 14% in men). After age 75 years, the lifetime risk decreases to 14% in women and 8% in men.

The underlying biological reasons for these differences in epidemiology and aspirin effect are not understood.

Recommendations of Others

In 2006, the American Diabetes Association and the American Heart Association jointly recommended aspirin therapy (75 to 162 mg/d) for primary prevention of heart disease for persons with diabetes who are older than 40 years or who have additional risk factors for cardiovascular disease and no contraindications to aspirin therapy (11). Along with the American Stroke Association, the American Heart Association further recommended the use of aspirin for cardiovascular prophylaxis among persons whose risk is sufficiently high for the benefits to outweigh the risks associated with treatment (a 10-year risk for cardiovascular events of 6% to 10%). For the primary prevention of stroke, they recommended against aspirin in men and stated that aspirin can be useful for primary prevention of stroke in women whose risk is sufficiently high for the benefits to outweigh the harms of treatment (12).

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Disclaimer: Recommendations made by the USPSTF are independent of the U.S. government. They should not be construed as an official position of the Agency for Healthcare Research and Quality or the U.S. Department of Health and Human Services.

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Requests for Single Reprints: Reprints are available from the USPSTF Web site (www.preventiveservices.ahrq.gov).

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Figure 1. **Aspirin for the prevention of cardiovascular disease: clinical summary of a U.S. Preventive Services Task Force recommendation statement.**

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USPSTF

ASPIRIN FOR THE PREVENTION OF CARDIOVASCULAR DISEASE
CLINICAL SUMMARY OF U.S. PREVENTIVE SERVICES TASK FORCE RECOMMENDATION

Population	Men Age 45–79 Years	Women Age 55–79 Years	Men Age <45 Years	Women Age <55 Years	Men and Women Age ≥80 Years
Recommendation	Encourage aspirin use when potential CVD benefit (MIs prevented) outweighs potential harm of GI hemorrhage	Encourage aspirin use when potential CVD benefit (strokes prevented) outweighs potential harm of GI hemorrhage	Do not encourage aspirin use for MI prevention	Do not encourage aspirin use for stroke prevention	No Recommendation
	Grade: A		Grade: D		Grade: I (insufficient evidence)

How to Use This Recommendation

Shared decision making is strongly encouraged with individuals whose risk is close to (either above or below) the estimates of 10-year risk levels indicated below. As the potential CVD benefit increases above harms, the recommendation to take aspirin should become stronger.

To determine whether the potential benefit of MIs prevented (men) and strokes prevented (women) outweighs the potential harm of increased GI hemorrhage, both 10-year CVD risk and age must be considered.

Risk Level at Which CVD Events Prevented (Benefit) Exceeds GI Harms			
Men		Women	
Age	10-Year CHD Risk	Age	10-Year Stroke Risk
45–59 years	≥4%	55–59 years	≥3%
60–69 years	≥9%	60–69 years	≥8%
70–79 years	≥12%	70–79 years	≥11%

The table above applies to adults who are not taking NSAIDs and who do not have upper GI pain or a history of GI ulcers. NSAID use and history of GI ulcers increase the risk for serious GI bleeding events considerably and should be considered in determining the balance of benefits and harms.

NSAID use combined with aspirin use approximately quadruples the risk for serious GI bleeding events compared with the risk with aspirin use alone. The rate of serious bleeding in aspirin users is approximately 2 to 3 times greater in patients with a history of GI ulcers.

Risk Assessment

For men: Risk factors for CHD include age, diabetes, total cholesterol level, HDL cholesterol level, blood pressure, and smoking.
CHD risk estimation tool: http://healthlink.mcw.edu/article/923521437.html

For women: Risk factors for ischemic stroke include age, high blood pressure, diabetes, smoking, history of CVD, atrial fibrillation, and left ventricular hypertrophy.
Stroke risk estimation tool: www.westernstroke.org/PersonalStrokeRisk1.xls

Relevant Recommendations from the USPSTF

The USPSTF has made recommendations on screening for abdominal aortic aneurysm, carotid artery stenosis, CHD, high blood pressure, lipid disorders, and peripheral arterial disease. These recommendations are available at www.preventiveservices.ahrq.gov.

For the full recommendation statement and supporting documents, please go to www.preventiveservices.ahrq.gov.

CHD = coronary heart disease; CVD = cardiovascular disease; GI = gastrointestinal; HDL = high-density lipoprotein; MI = myocardial infarction; NSAID = nonsteroidal anti-inflammatory drug; USPSTF = U.S. Preventive Services Task Force.

Table 1. **What the USPSTF Grades Mean and Suggestions for Practice**

Grade	Definition	Suggestions for Practice
A	The USPSTF recommends the service. There is high certainty that the net benefit is substantial.	Offer/provide this service.
B	The USPSTF recommends the service. There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.	Offer/provide this service.
C	The USPSTF recommends against routinely providing the service. There may be considerations that support providing the service in an individual patient. There is moderate or high certainty that the net benefit is small.	Offer/provide this service only if other considerations support offering or providing the service in an individual patient.
D	The USPSTF recommends against the service. There is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits.	Discourage the use of this service.
I statement	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined.	Read the clinical considerations section of the USPSTF Recommendation Statement. If the service is offered, patients should understand the uncertainty about the balance of benefits and harms.

USPSTF = U.S. Preventive Services Task Force.

Table 2. **U.S. Preventive Services Task Force Levels of Certainty Regarding Net Benefit**

Level of Certainty*	Description
High	The available evidence usually includes consistent results from well-designed, well-conducted studies in representative primary care populations. These studies assess the effects of the preventive service on health outcomes. This conclusion is therefore unlikely to be strongly affected by the results of future studies.
Moderate	The available evidence is sufficient to determine the effects of the preventive service on health outcomes, but confidence in the estimate is constrained by such factors as: the number, size, or quality of individual studies inconsistency of findings across individual studies limited generalizability of findings to routine primary care practice lack of coherence in the chain of evidence. As more information becomes available, the magnitude or direction of the observed effect could change, and this change may be large enough to alter the conclusion.
Low	The available evidence is insufficient to assess effects on health outcomes. Evidence is insufficient because of: the limited number or size of studies important flaws in study design or methods inconsistency of findings across individual studies gaps in the chain of evidence findings that are not generalizable to routine primary care practice a lack of information on important health outcomes. More information may allow an estimation of effects on health outcomes.

* The U.S. Preventive Services Task Force (USPSTF) defines *certainty* as "likelihood that the USPSTF assessment of the net benefit of a preventive service is correct." The net benefit is defined as benefit minus harm of the preventive service as implemented in a general primary care population. The USPSTF assigns a certainty level based on the nature of the overall evidence available to assess the net benefit of a preventive service.

Appendix: U.S. Preventive Services Task Force

Members of the U.S. Preventive Services Task Force† are Ned Calonge, MD, MPH, *Chair* (Colorado Department of Public Health and Environment, Denver, Colorado); Diana B. Petitti, MD, MPH, *Vice Chair* (Arizona State University, Phoenix, Arizona); Thomas G. DeWitt, MD (Children's Hospital Medical Center, Cincinnati, Ohio); Leon Gordis, MD, MPH, DrPH (Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland); Kimberly D. Gregory, MD, MPH (Cedars-Sinai Medical Center, Los Angeles, California); Russell Harris, MD, MPH (University of North Carolina School of Medicine, Chapel Hill, North Carolina); George Isham, MD, MS (HealthPartners, Minneapolis, Minnesota, Michael L. LeFevre, MD, MSPH (University of Missouri School of Medicine, Columbia, Missouri); Carol Loveland-Cherry, PhD, RN (University of Michigan School of Nursing, Ann Arbor, Michigan); Lucy N. Marion, PhD, RN (Medical College of Georgia, Augusta, Georgia); Virginia A. Moyer, MD, MPH (Baylor College of Medicine, Houston, Texas); Judith K. Ockene, PhD (University of Massachusetts Medical School, Worcester, Massachusetts); George F. Sawaya, MD (University of California, San Francisco, San Francisco, California); Albert L. Siu, MD, MSPH (Mount Sinai Medical Center, New York, New York); Steven M. Teutsch, MD, MPH (Merck & Company, West Point, Pennsylvania); and Barbara P. Yawn, MD, MSPH, MSc (Olmsted Medical Center, Rochester, Minnesota).

†This list includes members of the Task Force at the time this recommendation was finalized. For a list of current Task Force members, go to www.ahrq.gov/clinic/uspstfab.htm.