JAMA | US Preventive Services Task Force | RECOMMENDATION STATEMENT

Aspirin Use to Prevent Cardiovascular Disease
US Preventive Services Task Force Recommendation Statement

US Preventive Services Task Force

IMPORTANCE Cardiovascular disease (CVD) is the leading cause of mortality in the US, accounting for more than 1 in 4 deaths. Each year, an estimated 605 000 people in the US have a first myocardial infarction and an estimated 610 000 experience a first stroke.

OBJECTIVE To update its 2016 recommendation, the US Preventive Services Task Force (USPSTF) commissioned a systematic review on the effectiveness of aspirin to reduce the risk of CVD events (myocardial infarction and stroke), cardiovascular mortality, and all-cause mortality in persons without a history of CVD. The systematic review also investigated the effect of aspirin use on colorectal cancer (CRC) incidence and mortality in primary CVD prevention populations, as well as the harms (particularly bleeding) associated with aspirin use. The USPSTF also commissioned a microsimulation modeling study to assess the net balance of benefits and harms from aspirin use for primary prevention of CVD and CRC, stratified by age, sex, and CVD risk level.

POPULATION Adults 40 years or older without signs or symptoms of CVD or known CVD (including history of myocardial infarction or stroke) who are not at increased risk for bleeding (eg, no history of gastrointestinal ulcers, recent bleeding, other medical conditions, or use of medications that increase bleeding risk).

EVIDENCE ASSESSMENT The USPSTF concludes with moderate certainty that aspirin use for the primary prevention of CVD events in adults aged 40 to 59 years who have a 10% or greater 10-year CVD risk has a small net benefit. The USPSTF concludes with moderate certainty that initiating aspirin use for the primary prevention of CVD events in adults 60 years or older has no net benefit.

RECOMMENDATION The decision to initiate low-dose aspirin use for the primary prevention of CVD in adults aged 40 to 59 years who have a 10% or greater 10-year CVD risk should be an individual one. Evidence indicates that the net benefit of aspirin use in this group is small. Persons who are not at increased risk for bleeding and are willing to take low-dose aspirin daily are more likely to benefit. (C recommendation) The USPSTF recommends against initiating low-dose aspirin use for the primary prevention of CVD in adults 60 years or older. (D recommendation)

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Author/Group Information: The US Preventive Services Task Force (USPSTF) members are listed at the end of this article.

Corresponding Author: Karina W. Davidson, PhD, MASc, Feinstein Institutes for Medical Research, 130 E 59th St, Ste 14C, New York, NY 10032 (chair@uspstf.net).

Summary of Recommendations

Adults aged 40 to 59 years with a 10% or greater 10-year cardiovascular disease (CVD) risk	The decision to initiate low-dose aspirin use for the primary prevention of CVD in adults aged 40 to 59 years who have a 10% or greater 10-year CVD risk should be an individual one. Evidence indicates that the net benefit of aspirin use in this group is small. Persons who are not at increased risk for bleeding and are willing to take low-dose aspirin daily are more likely to benefit.	C
Adults 60 years or older	The USPSTF recommends against initiating low-dose aspirin use for the primary prevention of CVD in adults 60 years or older.	D

USPSTF indicates US Preventive Services Task Force.

See the Summary of Recommendations figure.

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Table. Summary of USPSTF Rationale

Rationale	Assessment
Benefits of aspirin use	Adequate evidence that low-dose aspirin has a small benefit to reduce risk for cardiovascular events (nonfatal myocardial infarction and stroke) in adults 40 years or older who have no history of CVD but are at increased CVD risk. Evidence shows that the absolute magnitude of benefit increases with increasing 10-year CVD risk and that the magnitude of the lifetime benefits is greater when aspirin is initiated at a younger age.
Harms of aspirin use	Adequate evidence that aspirin use in adults increases the risk for gastrointestinal bleeding, intracranial bleeding, and hemorrhagic stroke. The USPSTF determined that the magnitude of the harms is small overall but increases in older age groups, particularly in adults older than 60 years.
USPSTF assessment	The USPSTF concludes with moderate certainty that aspirin use for the primary prevention of CVD events in adults aged 40 to 59 years who have a 10% or greater 10-year CVD risk has a small net benefit. The USPSTF concludes with moderate certainty that initiating aspirin use for the primary prevention of CVD events in adults 60 years or older has no net benefit.

Abbreviations: CVD, cardiovascular disease; USPSTF, US Preventive Services Task Force.

Importance

Cardiovascular disease (CVD) is the leading cause of mortality in the US, accounting for more than 1 in 4 deaths.[1] Each year, an estimated 605 000 people in the US have a first myocardial infarction and an estimated 610 000 experience a first stroke.[2]

USPSTF Assessment of Magnitude of Net Benefit

The US Preventive Services Task Force (USPSTF) concludes with moderate certainty that aspirin use for the primary prevention of CVD events in adults aged 40 to 59 years who have a 10% or greater 10-year CVD risk has a **small net benefit**.

The USPSTF concludes with moderate certainty that initiating aspirin use for the primary prevention of CVD events in adults 60 years or older has **no net benefit**.

See the **Table** for more information on the USPSTF recommendation rationale and assessment and the eFigure in the Supplement for information on the recommendation grade. See **Figure 1** for a summary of the recommendation for clinicians. For more details on the methods the USPSTF uses to determine the net benefit, see the USPSTF Procedure Manual.[3]

Practice Considerations

Patient Population Under Consideration

This recommendation applies to adults 40 years or older without signs or symptoms of CVD or known CVD (including history of myocardial infarction or stroke) who are not at increased risk for bleeding (eg, no history of gastrointestinal ulcers, recent bleeding, other medical conditions, or use of medications that increase bleeding risk). In this recommendation statement, CVD risk and the net benefits of aspirin use are discussed using the terms "men" and "women," although it is likely that CVD risk and net benefit estimates are driven by sex (ie, male/female) rather than gender identity.

Assessment of Risk

CVD Risk

Older age is one of the strongest risk factors for CVD. Men have a higher overall CVD disease burden, although women experience higher mortality from certain cardiovascular events, such as stroke. Men tend to experience CVD events earlier in life compared with women. The burden of CVD also differs by race and ethnicity. Among both sexes, Black persons have the highest prevalence of CVD.[2]

The American College of Cardiology/American Heart Association (ACC/AHA) Pooled Cohort Equations may be used to estimate 10-year risk of CVD. The ACC/AHA risk estimator is, to date, the only US-based CVD risk prediction tool that has published external validation studies in other US-based populations.[4] The estimator has separate equations based on sex and for Black persons and non-Black persons, which include the risk factors of age, cholesterol levels, systolic blood pressure level, antihypertension treatment, presence of diabetes, and smoking status, and focuses on hard clinical outcomes (myocardial infarction and death from coronary heart disease; ischemic stroke and stroke-related death) as the outcomes of interest. It is important to note that increasing age heavily influences the ACC/AHA estimated 10-year CVD event risk. The risk prediction equations generally show higher risk for Black persons than White persons.[4] The USPSTF recognizes that race is a social construct and an imperfect proxy for social determinants of health and the effects of structural racism. Concerns about calibration exist, with many external validation studies showing overprediction in broad populations (men and women across racial and ethnic groups).[5-7] Limited evidence also suggests underprediction in disadvantaged communities[8,9] that could lead to underutilization of preventive therapies. Clinicians should recognize that predictions of 10-year CVD events using the Pooled Cohort Equations are estimates.

Bleeding Risk

The risk for gastrointestinal bleeding, intracranial hemorrhage, and hemorrhagic stroke, with or without aspirin use, increases with older age. Other risk factors include male sex, diabetes, history of gastrointestinal issues (such as peptic ulcer disease), liver disease, smoking, and elevated blood pressure. Certain medications, including nonsteroidal anti-inflammatory drugs, steroids, and anticoagulants, increase the risk of bleeding.[10-13] These risk factors should be considered in the overall decision about whether to start or continue aspirin therapy.

Treatment or Intervention

The benefits of aspirin for CVD prevention appear similar for a low dose (≤100 mg/d) and for all doses that have been studied in CVD prevention trials (50 to 500 mg/d).[14] A pragmatic approach would be to use 81 mg/d, which is the most commonly prescribed dose in the US.

Implementation

Because CVD risk estimation is imprecise and imperfect at the individual level, the USPSTF suggests using these risk estimates as

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Figure 1. Clinician Summary: Aspirin Use to Prevent Cardiovascular Disease

What does the USPSTF recommend?	**For adults aged 40 to 59 years with an estimated 10% or greater 10-year cardiovascular disease (CVD) risk:** The decision to initiate low-dose aspirin use for the primary prevention of CVD in this group should be an individual one. Grade: C **For adults 60 years or older:** Do not initiate aspirin for the primary prevention of CVD. Grade: D
To whom does this recommendation apply?	This recommendation applies to adults 40 years or older without signs or symptoms of CVD or known CVD and who are not at increased risk for bleeding (eg, no history of gastrointestinal ulcers, recent bleeding, or other medical conditions, or taking medications that increase bleeding risk).
What's new?	• The USPSTF has changed the age ranges and grades of its recommendation on aspirin use. • The USPSTF currently recommends considering initiating aspirin in persons with an estimated 10% or greater CVD risk at a younger age: 40 years instead of 50 years. • Aspirin should be initiated selectively based on individual decision-making rather than routinely for all persons in the recommended age and CVD risk group. • There is a new recommendation not to initiate aspirin in adults 60 years or older for primary prevention. • The evidence is unclear whether aspirin use reduces the risk of colorectal cancer incidence or mortality.
How to implement this recommendation?	• Consider the patient's age. • **For adults aged 40 to 59 years:** Estimate CVD risk using a CVD risk estimator. • In patients whose estimated CVD risk is 10% or greater, use shared decision-making, taking into account potential benefits and harms of aspirin use, as well as patients' values and preferences, to inform the decision about initiating aspirin. • For patients initiating aspirin use, it would be reasonable to use a dose of 81 mg/d. • **For adults 60 years or older:** Do not initiate aspirin for primary prevention of CVD.
What additional information should clinicians know about this recommendation?	• Age is one of the strongest risk factors for CVD. • Males have a higher prevalence of CVD than females. Among both sexes, Black persons have the highest prevalence of CVD. • Aspirin reduces the risk of cardiovascular events, but it increases the risk for gastrointestinal bleeding, intracranial bleeding, and hemorrhagic stroke. • Both CVD risk and risk for gastrointestinal bleeding, intracranial hemorrhage, and hemorrhagic stroke (with or without aspirin use) increase with age. • For patients who are eligible and choose to start taking aspirin, the benefits become smaller with advancing age, and data suggest that clinicians and patients should consider stopping aspirin use around age 75 years.
Why is this recommendation and topic important?	CVD is the leading cause of mortality in the US, accounting for more than 1 in 4 deaths. Each year, an estimated 605 000 Americans have a first heart attack and about 610 000 experience a first stroke.
What are additional tools and resources?	• The Million Hearts initiative provides information on improving cardiovascular health and preventing heart attack and stroke at https://millionhearts.hhs.gov/ • The Centers for Disease Control and Prevention have resources related to risk of heart disease and the prevention of heart disease for patients and health professionals at https://www.cdc.gov/heartdisease/index.htm • The National Heart, Lung, and Blood Institute has patient resources related to coronary heart disease at https://www.nhlbi.nih.gov/health-topics/coronary-heart-disease
Where to read the full recommendation statement?	Visit the USPSTF website (https://www.uspreventiveservicestaskforce.org/uspstf/) or the *JAMA* website (https://jamanetwork.com/collections/44068/united-states-preventive-services-task-force) to read the full recommendation statement. This includes more details on the rationale of the recommendation, including benefits and harms; supporting evidence; and recommendations of others.

The USPSTF recognizes that clinical decisions involve more considerations than evidence alone. Clinicians should understand the evidence but individualize decision-making to the specific patient or situation.

a starting point to discuss with appropriate candidates their desire for daily aspirin use. The benefits of initiating aspirin use are greater for individuals at higher risk for CVD events (eg, those with >15% or >20% 10-year CVD risk).

In addition to age and estimated level of CVD risk, decisions about initiating aspirin use should be based on shared decision-making between clinicians and patients about the potential benefits and harms. Persons who place a higher value on the potential benefits (decreasing an individual's risk of a myocardial infarction or stroke) than the potential harms (the risk of gastrointestinal or intracranial bleeding) may choose to initiate low-dose aspirin use. Persons who place a higher value on the potential harms or the burden of taking a daily preventive medication than on the potential benefits may choose not to initiate low-dose aspirin use.

Stopping Age

Annual bleeding events in individuals without risk factors for increased bleeding (eg, history of gastrointestinal bleeding risk, history of peptic ulcer disease, or use of nonsteroidal anti-inflammatory drugs or corticosteroids) are rare, but risk for

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bleeding increases modestly with advancing age.[12] For persons who have initiated aspirin use, the net benefits continue to accrue over time in the absence of a bleeding event. The net benefits, however, generally become progressively smaller with advancing age because of an increased risk for bleeding, and modeling data suggest that it may be reasonable to consider stopping aspirin use around age 75 years.

Additional Tools and Resources

Million Hearts 2022 is a national initiative to prevent 1 million myocardial infarctions and strokes within 5 years. It focuses on implementing a small set of evidence-based priorities and targets that can improve cardiovascular health for all (https://millionhearts.hhs.gov/).

The Centers for Disease Control and Prevention has resources related to risk of heart disease and the prevention of heart disease for patients and health professionals (https://www.cdc.gov/heartdisease/index.htm).

The National Heart, Lung, and Blood Institute has patient resources related to coronary heart disease (https://www.nhlbi.nih.gov/health-topics/coronary-heart-disease).

Other Related USPSTF Recommendations

The USPSTF has made several other recommendations on CVD prevention, including statin use to prevent CVD,[15] smoking cessation,[16] counseling to promote a healthful diet and physical activity in persons with and without cardiovascular risk factors,[17,18] and interventions to prevent obesity-related morbidity and mortality,[19] as well as screening for high blood pressure[20] and diabetes.[21] The USPSTF has also made a recommendation on screening for colorectal cancer (CRC).[22]

Update of Previous USPSTF Recommendation

This recommendation replaces the 2016 USPSTF recommendation on aspirin use to prevent CVD and CRC.[23] In 2016, the USPSTF recommended initiating low-dose aspirin use for the primary prevention of CVD and CRC in adults aged 50 to 59 years who have a 10% or greater 10-year CVD risk, are not at increased risk for bleeding, have a life expectancy of at least 10 years, and are willing to take low-dose aspirin daily for at least 10 years, and that the decision to initiate low-dose aspirin use in adults aged 60 to 69 years who have a 10% or greater 10-year CVD risk should be an individual one. The USPSTF previously found that the evidence was insufficient to assess the balance of benefits and harms of initiating aspirin use for the primary prevention of CVD and CRC in adults younger than 50 years or adults 70 years or older.

For the current recommendation, the USPSTF has changed the age ranges and grades of its recommendation on aspirin use. The USPSTF recommends that the decision to initiate low-dose aspirin use for the primary prevention of CVD in adults aged 40 to 59 years who have a 10% or greater 10-year CVD risk should be an individual one and recommends against initiating low-dose aspirin use for the primary prevention of CVD in adults 60 years or older. Based on new trial evidence,[24] updated analyses of the evidence from primary CVD prevention populations,[14] and longer-term follow-up data from the Women's Health Study (WHS) (I.-M. Lee, ScD, Harvard Medical School, written communication, November 23, 2020), the USPSTF concluded that the evidence is inadequate that low-dose aspirin use reduces CRC incidence or mortality.

Supporting Evidence

Scope of Review

To update its 2016 recommendation, the USPSTF commissioned a systematic review on the effectiveness of aspirin to reduce the risk of CVD events (myocardial infarction and stroke), cardiovascular mortality, and all-cause mortality in persons without a history of CVD. The systematic review also investigated the effect of aspirin use on CRC incidence and mortality in primary CVD prevention populations, as well as the harms, particularly bleeding harms, associated with aspirin use.[14,25]

In addition to the systematic evidence review, the USPSTF commissioned a microsimulation modeling study to assess the net balance of benefits and harms from aspirin use for primary prevention of CVD and CRC, stratified by age, sex, and CVD risk level. Modeling study parameter inputs were informed by the results of the systematic review, and the primary outcomes were net benefits expressed as quality-adjusted life-years and life-years.[26,27]

Benefits of Preventive Medication

The USPSTF considered 13 randomized clinical trials (RCTs) involving 161 680 participants that reported on the benefits of aspirin use for the primary prevention of cardiovascular morbidity and mortality.[14,25] Most trials used low-dose aspirin of 100 mg/d or less or aspirin every other day and included a balanced number of male and female participants and a broad distribution of ages, with mean age ranging from 53 years in the Physicians' Health Study[28] to 74 years in the Aspirin in Reducing Events in the Elderly (ASPREE) trial.[24]

The evidence showed that aspirin use for primary prevention of CVD was associated with a decreased risk of myocardial infarction and stroke but not cardiovascular mortality or all-cause mortality. Results were similar when including studies using all doses of aspirin compared with studies using low-dose aspirin.[14] Since low-dose aspirin is most relevant to current practice, the analyses below report outcomes pooling studies of low-dose aspirin use. Pooled effect estimates of studies using low-dose aspirin were also used to inform the parameters and assumptions of the microsimulation modeling study.[26,27]

A pooled analysis of 11 trials (n = 134 470) showed that low-dose aspirin use was associated with a statistically significant decreased risk of nonfatal myocardial infarction (Peto odds ratio [OR], 0.88 [95% CI, 0.80-0.96]). Similarly, a pooled analysis of 5 trials (n = 54 947) demonstrated that low-dose aspirin use was associated with a statistically significant decreased risk of nonfatal ischemic stroke (Peto OR, 0.88 [95% CI, 0.78-1.00]; $P = .046$). Fatal cardiovascular events were less common, so pooled analyses showed that low-dose aspirin use was not associated with a statistically significant effect on fatal myocardial infarction, fatal stroke, cardiovascular mortality, or all-cause mortality (at 3.6 to 10.1 years of follow-up).[14,25] Although evidence does not suggest that the relative effect of aspirin on CVD outcomes is modified by baseline CVD risk, the absolute magnitude of the benefit is greater in persons at higher CVD risk.

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New RCT data, as well as newly available information on the age distribution of participants in the WHS, show that almost 22 000 participants younger than 50 years and more than 37 000 participants 70 years or older were included in the CVD prevention trials. Most trials with age subanalyses did not find a statistically significant difference in the relative effect of aspirin on CVD outcomes by age.[14,25] The USPSTF thus concluded that evidence on the benefits of aspirin on CVD outcomes was adequate for all groups, including adults aged 40 to 49 years and adults 70 years or older.

The evidence review found fewer studies reporting on the effects of aspirin use on CRC incidence or mortality. Four studies conducted in primary CVD prevention populations found no association between aspirin use and CRC incidence at up to approximately 10 years of follow-up.[14,25] Only 1 trial, the WHS (n = 39 876), reported on the effect of low-dose aspirin use on CRC incidence beyond 10 years by including posttrial observational follow-up. Although the WHS reported a lower incidence of CRC at 17.5 years of follow-up (Peto OR, 0.82 [95% CI, 0.69-0.98]),[29] recent data showed that this effect did not persist from 17.5 to 26 years of follow-up (I.-M. Lee, ScD, Harvard Medical School, written communication, November 23, 2020). Two RCTs, ASPREE[24] and WHS (I.-M. Lee, ScD, Harvard Medical School, written communication, November 23, 2020), reported CRC mortality during the trial phase. ASPREE reported that aspirin use was associated with statistically significantly higher CRC mortality at 4.7 years of follow-up (Peto OR, 1.74 [95% CI, 1.02-2.95]), while the WHS did not find a statistically significant increase in CRC mortality at 10 years. When including observational follow-up beyond the trial phase, 2 trials of low-dose aspirin use reported reductions in CRC mortality. In the Thrombosis Prevention Trial[30,31] (n = 5085), low-dose aspirin use was associated with a statistically significant lower risk of CRC mortality at 18.3 years of follow-up (Peto OR, 0.62 [95% CI, 0.41-0.94]), and the WHS reported lower CRC mortality at 17.5 years of follow-up that was not statistically significant (Peto OR, 0.86 [95% CI, 0.64-1.16]) and was attenuated from 17.5 to 26 years of follow-up (I.-M. Lee, ScD, Harvard Medical School, written communication, November 23, 2020).

The body of evidence on the effects of aspirin use on CRC incidence and mortality is limited by several factors. Overall, only a small number of trials reported on CRC outcomes. The ASPREE trial in older adults found aspirin use to be associated with an increased risk of CRC mortality.[24] Although this finding does not constitute firm evidence that aspirin use is associated with increased risk of CRC mortality, it is one factor that calls into question whether aspirin use has a beneficial effect on CRC outcomes. Longer-term follow-up data suggesting that aspirin use is associated with lower CRC risk is heavily weighted by 1 trial conducted in women only, and the evidence on CRC mortality is limited by few CRC deaths. Additionally, posttrial follow-up data may be subject to biases, and in some cases, CRC outcomes data were collected by outside investigators.[14,25]

Harms of Preventive Medication

The USPSTF reviewed 14 RCTs in CVD primary prevention populations that reported on the bleeding harms of aspirin. Studies reported a variety of outcomes, including total major bleeds (defined as a composite of intracranial hemorrhage, major gastrointestinal bleeding, or major bleeding from other sites), major gastrointestinal bleeds (defined as a gastrointestinal bleed that required a transfusion, hospital admission, or resulted in death), extracranial bleeds (defined as major bleeding that was not intracranial), hemorrhagic stroke, and intracranial bleeds (defined as hemorrhagic stroke, subarachnoid hemorrhage, and subdural hemorrhage).[14,25]

When looking at studies reporting on the harms of low-dose aspirin use (≤100 mg/d), which is most relevant to current practice, a pooled analysis of 10 trials (n = 119 130) showed that aspirin use was associated with a 58% increase in major gastrointestinal bleeding (Peto OR, 1.58 [95% CI, 1.38-1.80]). A pooled analysis of 11 trials (n = 134 470) showed an increase in intracranial bleeds in the aspirin group compared with the control group (Peto OR, 1.31 [95% CI, 1.11-1.54]). Low-dose aspirin use was not associated with a statistically significant increase in risk of fatal hemorrhagic stroke.[14,25]

Data suggest that the increased incidence of bleeding associated with aspirin use occurs relatively quickly after initiating aspirin, and data do not suggest that aspirin has a differential relative bleeding risk based on age, sex, presence of diabetes, level of CVD risk, or race or ethnicity.[14,25] Although the increase in relative risk does not appear to differ based on age, the absolute incidence of bleeding, and thus the magnitude of bleeding harm, increases with age, and more so in adults 60 years or older. Because of the very small number of fatal gastrointestinal bleeding events in trials and inconsistent reporting, it is uncertain whether aspirin use increases fatal gastrointestinal bleeding.[14,25]

Estimate of Magnitude of Net Benefit

The USPSTF commissioned a microsimulation model to estimate the magnitude of net benefit of low-dose aspirin use.[26,27] The model incorporated findings from the systematic review to inform its parameters and assumptions, including that daily low-dose (≤100 mg/d) aspirin use reduces the risk of nonfatal myocardial infarction and nonfatal stroke, increases the risk of major gastrointestinal bleeding and intracranial hemorrhage, and has no effect on the risk of CVD mortality. As there was insufficient evidence that aspirin use reduces CRC incidence, the modeling study base case assumed no effect of aspirin on CRC incidence.

Modeling outcomes were stratified by age, decade of aspirin initiation (40-49 years, 50-59 years, 60-69 years, and 70-79 years), sex, and baseline 10-year CVD risk level (5% to 20%). When combined with primary trial data and pooled analyses from the systematic evidence review, the model provided additional information to assess the balance of benefits and harms of aspirin use. The primary model outcomes were net quality-adjusted life-years and life-years gained or lost over a lifetime as a result of aspirin use. Also considered was the effect of stopping aspirin that had been initiated for primary prevention over 5-year age intervals from ages 65 to 85 years.[26,27]

Modeling data estimated that aspirin use in both men and women aged 40 to 59 years with 10% or greater 10-year CVD risk generally provides a modest net benefit in both quality-adjusted life-years and life-years gained. Initiation of aspirin use in persons aged 60 to 69 years results in quality-adjusted life-years gained that range from slightly negative to slightly positive depending on CVD risk level, and life-years gained are generally negative. In persons aged 70 to 79 years, initiation of aspirin use results in a loss of both quality-adjusted life-years and life-years at essentially all CVD risk levels modeled (ie, up to 20% 10-year CVD risk) (**Figure 2**).[26,27] The USPSTF thus determined that aspirin use has a small net benefit in persons

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Figure 2. Quality-Adjusted Life-Years and Life-Years Gained: Lifetime Net Benefit of Initiating Aspirin Use for Women and Men With Lifetime Use

	Mean (95% CI)			
	Initiation age 40-49 y	Initiation age 50-59 y	Initiation age 60-69 y	Initiation age 70-79 y
Women				
Net life-years per 1000 persons 10-y CVD risk, %				
7.5	-2.6 (-10.0 to 4.7)	-11.8 (-18.7 to-5.0)	-20.2 (-25.6 to -14.9)	-15.4 (-19.0 to -11.8)
10	11.4 (3.2 to 19.7)	-6.5 (-13.6 to 0.7)	-13.5 (-18.7 to -8.4)	-16.6 (-20.0 to -13.2)
15	17.7 (9.8 to 25.5)	7.5 (0.9 to 14.1)	-7.2 (-12.3 to -2.1)	-17.9 (-21.9 to -14.0)
20	24.2 (15.7 to 32.7)	16.9 (9.7 to 24.1)	-1.6 (-6.8 to 3.6)	-14.8 (-18.6 to -11.0)
Net QALYs per 1000 persons 10-y CVD risk, %				
7.5	19.6 (12.3 to 26.8)	10.4 (3.9 to 16.9)	-5.8 (-10.9 to -0.7)	-6.4 (-10.0 to -2.8)
10	35.1 (27.3 to 43.0)	17.1 (10.2 to 24.0)	2.3 (-2.7 to 7.4)	-6.1 (-9.4 to -2.7)
15	43.0 (35.4 to 50.5)	30.8 (24.5 to 37.2)	11.6 (6.9 to 16.4)	-6.9 (-10.7 to -3.0)
20	50.4 (42.3 to 58.5)	41.6 (34.8 to 48.5)	19.1 (14.2 to 24.1)	-4.4 (-8.1 to -0.7)
Men				
Net life-years per 1000 persons 10-y CVD risk, %				
7.5	16.2 (9.0 to 23.5)	0.4 (-6.1 to 6.9)	-6.7 (-11.5 to -1.9)	-10.1 (-13.4 to -6.8)
10	36.1 (28.1 to 44.1)	4.2 (-2.3 to 10.8)	-3.0 (-8.0 to 1.9)	-6.9 (-10.5 to -3.4)
15	37.9 (29.6 to 46.2)	18.6 (11.7 to 25.4)	-2.2 (-7.2 to 2.9)	-7.6 (-11.3 to -3.9)
20	52.4 (43.9 to 60.9)	33.9 (26.9 to 40.9)	4.9 (-0.1 to 10.0)	-5.5 (-8.8 to -2.2)
Net QALYs per 1000 persons 10-y CVD risk, %				
7.5	29.1 (22.3 to 36.0)	12.5 (6.5 to 18.5)	2.6 (−1.9 to 7.2)	-4.6 (-7.7 to -1.5)
10	48.0 (40.6 to 55.5)	18.0 (12.0 to 24.0)	7.0 (2.2 to 11.8)	-1.1 (-4.4 to 2.2)
15	52.3 (44.5 to 60.1)	32.3 (26.2 to 38.5)	8.3 (3.5 to 13.0)	-1.9 (-5.4 to 1.6)
20	66.2 (58.2 to 74.1)	48.4 (41.9 to 54.8)	16.3 (11.4 to 21.1)	0.9 (-2.2 to 3.9)

Yellow shaded cells indicate persons to whom the C grade recommendation applies. CVD indicates cardiovascular disease; QALY, quality-adjusted life-year.

aged 40 to 59 years with 10% or greater 10-year CVD risk and that initiation of aspirin use has no net benefit in persons 60 years or older.

When looking at net lifetime benefit of continuous aspirin use until stopping at age 65, 70, 75, 80, or 85 years, modeling data suggested that there is generally little incremental lifetime net benefit in continuing aspirin use beyond the age of 75 to 80 years.[26,27] It is important to note that the net benefit of continuing aspirin use by persons in their 60s or 70s is not the same as the net benefit of initiating aspirin use by persons in their 60s or 70s. This is because, in part, CVD risk is heavily influenced by age. Persons who meet the eligibility criteria for aspirin use at a younger age (ie, ≥10% 10-year CVD risk in their 40s or 50s) typically would have even higher CVD risk by their 60s or 70s compared with persons who first reach a 10% or greater 10-year CVD risk in their 60s or 70s and may gain more benefit by continuing aspirin use than persons at lower risk might gain by initiating aspirin use.

How Does Evidence Fit With Biological Understanding?

Aspirin's mechanism of action to promote CVD prevention is well known. At lower doses, aspirin is an irreversible cyclooxygenase 1 (COX-1) enzyme inhibitor. At higher doses, aspirin also inhibits COX-2. Aspirin reduces the risk for atherothrombosis through the inhibition of platelet function (through COX-1 inhibition) and has been used widely for the prevention of CVD events, particularly for secondary prevention.[32] The COX-1 enzyme is also responsible for producing a variety of prostaglandins that protect the gastrointestinal mucosa.[33] By inhibiting this enzyme, aspirin use can promote gastrointestinal bleeding.[34] The mechanism for the possible antineoplastic effects of aspirin is not as well understood.[14]

Response to Public Comment

A draft version of this recommendation statement was posted for public comment on the USPSTF website from October 12 to November 8, 2021. In response to public comment, the USPSTF wants to restate that the focus of this recommendation is the use of aspirin for the primary prevention of CVD and not for other indications. This recommendation only applies to persons who do not have a history of CVD, signs or symptoms of CVD, or other conditions for which aspirin may be indicated. Persons who are currently taking aspirin and have questions about why they are taking it, or whether they should continue or discontinue aspirin use, should discuss these questions with their clinician. Persons who are taking aspirin should not discontinue using it without consulting their clinician. For persons who are deciding with their clinician whether to continue or discontinue taking aspirin for primary prevention, clinicians may want to consider that person's age, level of CVD risk and bleeding risk, preferences, and reasons for taking aspirin.

In response to public comment, the USPSTF clarified language about its assessment of the precision of CVD risk assessment and added information on factors that can be considered by clinicians and patients as they engage in shared decision-making about the initiation of aspirin use. Information on the evidence the USPSTF reviewed on the effect of aspirin on CRC incidence and mortality and how it considered the findings from the ASPREE trial can also be found in the Supporting Evidence section of this recommendation. Also, in response to public comment, the USPSTF wants to note that it did not review the emerging evidence on the effect of aspirin on COVID-19, the disease caused by the coronavirus SARS-CoV-2.

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Research Needs and Gaps

More research is needed to evaluate the following.

- Improving the accuracy of CVD risk prediction in all racial and ethnic and socioeconomic groups.
- The gastrointestinal bleeding risk associated with aspirin use in populations representative of the US primary CVD prevention population.
- Characterizing the distribution of patient preferences across the spectrum of cardiovascular risk after patients are informed about the benefits and harms of aspirin.
- The effects of low-dose aspirin use on CRC incidence and mortality over the long term (10 to 20 years and longer) in primary prevention populations and in the context of current CRC screening practices.

Recommendations of Others

The ACC/AHA recommends that low-dose aspirin use (75 to 100 mg/d) might be considered for the primary prevention of atherosclerotic CVD among select adults aged 40 to 70 years at higher CVD risk but not at increased risk of bleeding. Low-dose aspirin use is not recommended on a routine basis for primary prevention of CVD in adults older than 70 years or among adults of any age who are at increased risk of bleeding.[35] The American Academy of Family Physicians supports the 2016 USPSTF recommendation on aspirin use.[36]

ARTICLE INFORMATION

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The US Preventive Services Task Force (USPSTF) members: Karina W. Davidson, PhD, MASc; Michael J. Barry, MD; Carol M. Mangione, MD, MSPH; Michael Cabana, MD, MA, MPH; David Chelmow, MD; Tumaini Rucker Coker, MD, MBA; Esa M. Davis, MD, MPH; Katrina E. Donahue, MD, MPH; Carlos Roberto Jaén, MD, PhD, MS; Alex H. Krist, MD, MPH; Martha Kubik, PhD, RN; Li Li, MD, PhD, MPH; Gbenga Ogedegbe, MD, MPH; Lori Pbert, PhD; John M. Ruiz, PhD; James Stevermer, MD, MSPH; Chien-Wen Tseng, MD, MPH, MSEE; John B. Wong, MD.

Affiliations of The US Preventive Services Task Force (USPSTF) members: Feinstein Institutes for Medical Research at Northwell Health, Manhasset, New York (Davidson); Harvard Medical School, Boston, Massachusetts (Barry); University of California, Los Angeles (Mangione); Albert Einstein College of Medicine, New York, New York (Cabana); Virginia Commonwealth University, Richmond (Chelmow, Krist); University of Washington, Seattle (Coker); University of Pittsburgh, Pittsburgh, Pennsylvania (Davis); University of North Carolina at Chapel Hill (Donahue); University of Texas Health Science Center, San Antonio (Jaén); Fairfax Family Practice Residency, Fairfax, Virginia (Krist); George Mason University, Fairfax, Virginia (Kubik); University of Virginia, Charlottesville (Li); New York University, New York, New York (Ogedegbe); University of Massachusetts Medical School, Worcester (Pbert); University of Arizona, Tucson (Ruiz); University of Missouri, Columbia (Stevermer); University of Hawaii, Honolulu (Tseng); Tufts University School of Medicine, Boston, Massachusetts (Wong).

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