Aspirin in Cardiovascular Disease: A Double-Edged Sword for Prevention

Aspirin, a medication that has been a staple in medicine cabinets for over a century, continues to be a topic of significant interest in the field of cardiovascular health. Its role in both primary and secondary prevention of atherosclerotic cardiovascular disease (ASCVD) is well-documented, yet nuanced. Atherosclerotic cardiovascular disease, which includes coronary artery disease, cerebrovascular disease, and peripheral artery disease, is the leading cause of death In the United States and most developed countries. It is rapidly becoming the leading cause of death in the world. The totality of evidence from basic research, clinical investigations, observational studies, and randomized trials has provided strong support for the benefit of aspirin in the secondary prevention of ASCVD yet has also shown a lack of benefit for primary prevention of ASCVD. We will discuss the current understanding and recommendations regarding aspirin use for ASCVD prevention, including the latest 2022 guidelines from the U.S. Preventive Services Task Force (USPSTF).

Understanding Atherosclerotic Cardiovascular Disease

Atherosclerotic cardiovascular disease encompasses a range of conditions caused by the buildup of atherosclerotic plaques within the arterial walls. These plaques can lead to events such as myocardial infarction (heart attack), ischemic stroke, and peripheral artery disease. The prevention of these events is categorized into primary and secondary prevention:

- Primary Prevention: Measures taken to prevent the first occurrence of ASCVD in individuals at risk.

- Secondary Prevention: Strategies aimed at preventing recurrent events in individuals with established ASCVD.

Current Guidelines and Evidence

- 2022 USPSTF Guidelines: The USPSTF now recommends not initiating low-dose aspirin for the primary prevention of ASCVD in adults aged 60 years or older as there is a lack of net benefit and as risk may outweigh benefit. For adults aged 40-59 years who have a 10% or greater 10-year cardiovascular risk, the decision to start low-dose aspirin should be an individual one. The USPSTF guidelines are based on evidence from 13 studies that suggest that aspirin provides a small benefit for select patients ages 40 to 59, and no net benefit (with potential for harm) for patients aged 60 or older.

- 2019 ACC/AHA guidelines recommend a highly individualized approach. Aspirin (75-100 mg daily) may be considered for primary prevention in adults aged 40-70 who are at high risk for ASCVD but not at increased risk for bleeding. For adults over 70 or those at low ASCVD risk, routine aspirin use is generally not recommended. Overall, the American College of Cardiology recommends aspirin should be used infrequently in the primary prevention of ASCVD because of the lack of net benefit.

- Estimating Risk: To calculate the 10-year ASCVD risk, clinicians use the American College of Cardiology/American Heart Association risk estimator which accounts for age, sex, blood pressure, lipids, diabetes mellitus, and tobacco use, but not family history. Also utilized is the newer American Heart Association PREVENT calculator which also accounts for obesity, kidney function, urine protein levels and level of diabetes control. Conditions which generally carry a 10% or greater 10-year ASCVD risk include diabetes and chronic kidney disease.

ASPIRIN IN PRIMARY PREVENTION

TABLE 1
Summary of 3 large trials on daily aspirin therapy for primary prevention

Trial	Population	Findings
ASCEND[4]	15,480 patients with diabetes and no prior CVD history	Therapy resulted in a 12% reduction in myocardial infarction and ischemic stroke Therapy resulted in a 30% increased risk for a major bleeding event, especially prominent in patients age 60 or older
ARRIVE[5]	12,546 patients with mean 17% 10-year CVD risk	No significant benefit in CVD prevention with therapy compared with placebo Twofold increase in gastrointestinal bleeding seen in aspirin therapy group
ASPREE[6,7]	19,114 patients, average age 74	Therapy provided no benefit in preventing first nonfatal cardiovascular event or death Therapy showed a 30% increased risk of major nonfatal hemorrhage, particularly in upper-gastrointestinal bleeds and intracranial hemorrhage

ARRIVE = Aspirin to Reduce Risk of Initial Vascular Events; ASCEND = A Study of Cardiovascular Events in Diabetes; ASPREE = Aspirin in Reducing Events in the Elderly; CVD = cardiovascular disease

- Risk-Benefit Balance: The benefits of aspirin for primary prevention must be weighed against its potential risks, particularly gastrointestinal bleeding and hemorrhagic stroke. Recent large-scale studies, such as the ASPREE (Aspirin in Reducing Events in the Elderly) and ARRIVE (Aspirin to Reduce Risk of Initial Vascular Events) trials, have shown no benefit and that the risk of bleeding may outweigh the cardiovascular benefits in low-risk populations. The ASCEND trial also showed that, even in diabetics without known ASCVD, risks outweighed benefits of aspirin for primary prevention.

Aspirin for Secondary Prevention

In contrast to primary prevention, the role of aspirin in secondary prevention is well-established and supported by robust evidence. For individuals with a history of ASCVD, aspirin significantly reduces the risk of subsequent cardiovascular events.

The following groups or patients with established cardiovascular disease, or at high risk, benefit from aspirin for the prevention or new cardiovascular events:

- Patients with acute coronary artery syndromes such as acute myocardial infarction (MI) or unstable angina

- Patients with acute occlusive stroke

- Patients with stable CVD, such as those with stable coronary artery disease (including those who have undergone re-vascularization with coronary artery bypass graft surgery), stable peripheral artery disease, or carotid artery disease

- Patients who have undergone coronary artery stenting

Key Points:

- Standard of Care: Aspirin remains a cornerstone of secondary prevention therapy. It is recommended for almost all patients with a history of myocardial infarction, stents, ischemic stroke, or established peripheral artery disease unless contraindications exist.

- Dosage: The typical dosage for secondary prevention is 81 mg daily, which balances efficacy with the risk of adverse effects. Higher doses have not shown additional benefit and may increase the risk of bleeding.

- Combination Therapy: In certain high-risk patients, dual antiplatelet therapy (DAPT), which includes aspirin and a P2Y12 inhibitor (such as clopidogrel), may be indicated, particularly following acute coronary syndromes or stent placement. This combination, however, is usually limited to a specific duration to mitigate bleeding risk.

Patient Communication

- Informed Decision-Making: Patients should be fully informed about the benefits and risks associated with aspirin therapy. Shared decision-making is essential, particularly for primary prevention.

- Lifestyle Modifications: Aspirin should be viewed as an adjunct to, not a replacement for, lifestyle modifications and other medical therapies aimed at reducing cardiovascular risk. Encouraging a heart-healthy diet, regular physical activity, smoking cessation, and management of hypertension, diabetes, and hyperlipidemia are foundational steps.

Conclusion

Aspirin's role in cardiovascular disease prevention requires careful consideration of individual patient profiles. While its benefits in secondary prevention are unequivocal, the decision to use aspirin for primary prevention should be made on a case-by-case basis, guided by a thorough risk assessment, patient preferences, and current guidelines. For patients aged 60 or older, the USPSTF now advises against initiating aspirin therapy for primary prevention as there is a lack of net benefit and as the risk of harm may outweigh benefit. ACC/AHA guidelines also advise avoiding aspirin for primary prevention in patients aged 70 or older. Evidence from studies additionally suggests that aspirin provides only a small benefit for select patients ages 40 to 59. In general, current guidelines advise patients over 40 and without high ASCVD risk, diabetes, chronic kidney disease, or known vascular disease to avoid aspirin for primary prevention. As always, ongoing research and emerging evidence will continue to refine our approach.