2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease

A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines

Endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation, the American Geriatrics Society, the American Society of Preventive Cardiology, and the Preventive Cardiovascular Nurses Association

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This document was approved by the American College of Cardiology Clinical Policy Approval Committee, the American Heart Association Science Advisory and Coordinating Committee, and the American Heart Association Executive Committee in February 2019.

Supplemental materials are available with this article at
https://www.ahajournals.org/doi/suppl/10.1161/CIR.0000000000000678

The American Heart Association requests that this document be cited as follows: Arnett DK, Blumenthal RS, Albert MA, Buroker AB, Goldberger ZD, Hahn EJ, Himmelfarb CD, Khera A, Lloyd-Jones D, McEvoy JW, Michos ED, Miedema MD, Muñoz D, Smith SC Jr, Virani SS, Williams KA Sr, Yeboah J, Ziaeian B. 2019 ACC/AHA guideline on the primary prevention of cardiovascular disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation.* 2019;000:e●●●–e●●●. DOI: 10.1161/CIR.0000000000000678

This article has been copublished in the *Journal of the American College of Cardiology*.

(*Circulation.* 2019;000:e000–e000. DOI: 10.1161/CIR.0000000000000678)

Table of Contents

Top 10 Take-Home Messages for the Primary Prevention of Cardiovascular Disease

1. The most important way to prevent atherosclerotic vascular disease, heart failure, and atrial fibrillation is to promote a healthy lifestyle throughout life.
2. A team-based care approach is an effective strategy for the prevention of cardiovascular disease. Clinicians should evaluate the social determinants of health that affect individuals to inform treatment decisions.
3. Adults who are 40 to 75 years of age and are being evaluated for cardiovascular disease prevention should undergo 10-year atherosclerotic cardiovascular disease (ASCVD) risk estimation and have a clinician–patient risk discussion before starting on pharmacological therapy, such as antihypertensive therapy, a statin, or aspirin. In addition, assessing for other risk-enhancing factors can help guide decisions about preventive interventions in select individuals, as can coronary artery calcium scanning.
4. All adults should consume a healthy diet that emphasizes the intake of vegetables, fruits, nuts, whole grains, lean vegetable or animal protein, and fish and minimizes the intake of *trans* fats, processed meats, refined carbohydrates, and sweetened beverages. For adults with overweight and obesity, counseling and caloric restriction are recommended for achieving and maintaining weight loss.
5. Adults should engage in at least 150 minutes per week of accumulated moderate-intensity physical activity or 75 minutes per week of vigorous-intensity physical activity.
6. For adults with type 2 diabetes mellitus, lifestyle changes, such as improving dietary habits and achieving exercise recommendations, are crucial. If medication is indicated, metformin is first-line therapy, followed by consideration of a sodium-glucose cotransporter 2 inhibitor or a glucagon-like peptide-1 receptor agonist.
7. All adults should be assessed at every healthcare visit for tobacco use, and those who use tobacco should be assisted and strongly advised to quit.
8. Aspirin should be used infrequently in the routine primary prevention of ASCVD because of lack of net benefit.
9. Statin therapy is first-line treatment for primary prevention of ASCVD in patients with elevated low-density lipoprotein cholesterol levels (≥190 mg/dL), those with diabetes mellitus, who are 40 to 75 years of age, and those determined to be at sufficient ASCVD risk after a clinician–patient risk discussion.
10. Nonpharmacological interventions are recommended for all adults with elevated blood pressure or hypertension. For those requiring pharmacological therapy, the target blood pressure should generally be <130/80 mm Hg.

Preamble

Since 1980, the American College of Cardiology (ACC) and American Heart Association (AHA) have translated scientific evidence into clinical practice guidelines with recommendations to improve cardiovascular health. These guidelines, which are based on systematic methods to evaluate and classify evidence, provide a foundation for the delivery of quality cardiovascular care. The ACC and AHA sponsor the development and publication of clinical practice guidelines without commercial support, and members volunteer their time to the writing and review efforts.

Clinical practice guidelines provide recommendations applicable to patients with or at risk of developing cardiovascular disease (CVD). The focus is on medical practice in the United States, but these guidelines are relevant to patients throughout the world. Although guidelines may be used to inform regulatory or payer decisions, the goals are to improve quality of care and align with patients' interests. Guidelines are intended to define practices meeting the needs of patients in most but not all circumstances and should not replace clinical judgment.

Recommendations for guideline-directed management and therapy, which encompasses clinical evaluation, diagnostic testing, and both pharmacological and procedural treatments, are effective only when adopted by both practitioners and patients. Adherence to recommendations can be enhanced by shared decision-making between clinicians and patients, with patient engagement in selecting interventions on the basis of individual values, preferences, and associated conditions and comorbidities.

The ACC/AHA Task Force on Clinical Practice Guidelines strives to ensure that the guideline writing committee includes requisite expertise and is representative of the broader medical community by selecting experts from a broad array of backgrounds, representing different geographic regions, sexes, races, ethnicities, intellectual perspectives/biases, and scopes of clinical practice. The ACC and AHA have rigorous policies and methods to ensure that documents are developed without bias or improper influence. The complete policy on relationships with industry and other entities (RWI) can be found at: https://www.acc.org/guidelines/about-guidelines-and-clinical-documents/relationships-with-industry-policy.

Beginning in 2017, numerous modifications to the guidelines have been and continue to be implemented to make guidelines shorter and enhance "user friendliness." Guidelines are written and presented in a modular knowledge chunk format, in which each chunk includes a table of recommendations, a brief synopsis, recommendation-specific supportive text and, when appropriate, flow diagrams or additional tables. Hyperlinked references are provided for each modular knowledge chunk to facilitate quick access and review. More structured guidelines—including word limits ("targets") and a web guideline supplement for useful but noncritical tables and figures—are 2 such changes. This Preamble is an abbreviated version, with the detailed version available at: https://www.ahajournals.org/doi/suppl/10.1161/CIR.0000000000000678

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4.6. Aspirin Use

Recommendations for Aspirin Use Referenced studies that support recommendations are summarized in Online Data Supplements 17 and 18.		
COR	**LOE**	**Recommendations**
IIb	**A**	**1. Low-dose aspirin (75-100 mg orally daily) might be considered for the primary prevention of ASCVD among select adults 40 to 70 years of age who are at higher ASCVD risk but not at increased bleeding risk (S4.6-1–S4.6-8).**
III: Harm	**B-R**	**2. Low-dose aspirin (75-100 mg orally daily) should not be administered on a routine basis for the primary prevention of ASCVD among adults >70 years of age (S4.6-9).**
III: Harm	**C-LD**	**3. Low-dose aspirin (75-100 mg orally daily) should not be administered for the primary prevention of ASCVD among adults of any age who are at increased risk of bleeding (S4.6-10).**

Synopsis

For decades, aspirin has been widely administered for ASCVD prevention. By irreversibly inhibiting platelet function, aspirin reduces risk of atherothrombosis but also increases risk of bleeding, particularly in the gastrointestinal tract (S4.6-11). Aspirin is well established for secondary prevention of ASCVD (S4.6-12) and is widely recommended for this indication (S4.6-13). However, in primary prevention, aspirin use is more controversial. Because persons without prior ASCVD are inherently less likely to have future ASCVD events than are those with a prior history, it is more challenging for clinicians and patients to balance benefits and harms of prophylactic aspirin for primary prevention. This uncertainty is reflected in international guidelines, where, for example, aspirin is not recommended in European guidelines for primary ASCVD prevention (S4.6-13) but is recommended in prior U.S. guidelines for selected primary prevention for adults who have elevated risk of ASCVD based on traditional risk factors (S4.6-14, S4.6-15). Adding to this controversy are more recently conducted primary-prevention trials that, in contrast to older trials (S4.6-12), have shown less overall benefit of prophylactic aspirin alongside coadministration of contemporary ASCVD preventive treatments, such as evidence-based hypertension and cholesterol therapies (S4.6-5–S4.6-9, S4.6-16, S4.6-17).

Recommendation-Specific Supportive Text

1. To balance the benefits and risks, prior U.S. guidelines have recommended prophylactic aspirin only in the setting of elevated ASCVD risk (e.g., as calculated by risk estimators like the PCE or based on the presence of specific ASCVD risk factors) (S4.6-14, S4.6-18). Meta-regression analyses of historical trials show that observed ASCVD risk tracks reasonably well with baseline-estimated ASCVD risk (S4.6-19). In contrast, observed bleeding risk on aspirin is less well correlated with baseline-estimated ASCVD risk (S4.6-19). (A nonexhaustive list of scenarios associated with increased risk of bleeding includes: a history of previous gastrointestinal bleeding or peptic ulcer disease or bleeding from other sites, age >70 years, thrombocytopenia, coagulopathy, CKD, and concurrent use of other medications that increase bleeding risk, such as nonsteroidal anti-inflammatory drugs, steroids, direct oral anticoagulants, and warfarin.) In this context, post hoc study of older trials suggests that the benefit–risk ratio for prophylactic aspirin generally becomes more favorable at >10% estimated 10-year ASCVD risk (S4.6-15, S4.6-19). However, the relative benefits of aspirin, specifically in preventing nonfatal MI and perhaps stroke (with a trend to lower mortality) have been less evident in more recent trials (S4.6-9, S4.6-16, S4.6-17, S4.6-20). Similarly, in these recent trials, the estimated ASCVD risk has generally exceeded the actual risk observed during follow-up (S4.6-17). These recent data are the rationale for

the lower COR for prophylactic aspirin in the present guideline (Class IIb) and the removal of a specific PCE risk threshold as an inclusion criterion for aspirin consideration. These changes reflect the need to instead consider the totality of available evidence for ASCVD risk [inclusive, where appropriate, of risk-enhancing factors, such as strong family history of premature MI, inability to achieve lipid or BP or glucose targets, or significant elevation in coronary artery calcium score (S4.6-21)] and to also tailor decisions about prophylactic aspirin to patient and clinician preferences. Depending on risk factors present, a given patient and his/her clinician may decide that lowering the risk of MI (which has potentially serious long-term consequences not captured by clinical trials of 5 to 10 years' duration) is worth a slight excess risk of serious bleeding. Recent trials show that absolute risk for ASCVD events typically exceeds that of bleeding and, although the gap of relative benefit to relative harm for aspirin has narrowed, the number needed to treat to prevent an ASCVD event remains lower than the number needed to harm to cause bleeding. Others may feel that the benefit of prophylactic aspirin is comparable to the risk and may instead choose to focus on optimal control of other modifiable ASCVD risk factors. Therefore, a Class IIb recommendation remains more suitable than a Class III recommendation for adults 40 to 70 years of age. Given the narrow overall balance between benefits and harms of prophylactic aspirin, there is limited justification to use aspirin at doses >100 mg daily for primary prevention. Indeed, meta-analyses suggest that the ASCVD risk benefit for low-dose aspirin is equivalent to that for high-dose aspirin, but the bleeding risk is higher with high-dose aspirin. Recent observational studies motivate future research on the personalization of prophylactic aspirin dose according to patient-specific factors (e.g., weight) (S4.6-22), though we note that, regarding weight specifically, there was no evidence low-dose aspirin was any more effective in low-weight individuals than in high-weight individuals in the more recently published ASCEND (A Study of Cardiovascular Events iN Diabetes) trial (S4.6-16), trial. Most importantly, recent clinical trials also teach us that low-dose prophylactic aspirin may be best justified among persons at high ASCVD risk who cannot achieve optimal control of other ASCVD risk factors (S4.6-23).

2. Prophylactic aspirin in primary-prevention adults >70 years of age is potentially harmful and, given the higher risk of bleeding in this age group, difficult to justify for routine use (S4.6-9). In addition, for adults <40 years of age, there is insufficient evidence to judge the risk–benefit ratio of routine aspirin for the primary prevention of ASCVD. However, one caveat is that, although routine use is not recommended in these settings, there is also insufficient evidence to comment on whether there may be select circumstances in which physicians might discuss prophylactic aspirin with adults <40 years of age or >70 years of age in the context of other known ASCVD risk factors (e.g., strong family history of premature MI, inability to achieve lipid or BP or glucose targets, or significant elevation in coronary artery calcium score). As inferred from the first recommendation, there is also no justification for the routine administration of low-dose aspirin for the primary prevention of ASCVD among adults at low estimated ASCVD risk. For example, in the recent ARRIVE (A Randomized Trial of Induction Versus Expectant Management) trial, observed average 10-year ASCVD risk was <10%, and the overall benefits of prophylactic aspirin by intention-to-treat were negligible (S4.6-17).
3. The accumulated trial and observational data to date support avoiding prophylactic aspirin in the setting of known risk factors for increased bleeding outcomes (S4.6-10). A nonexhaustive list of conditions associated with increased bleeding risk includes: a history of previous gastrointestinal bleeding or peptic ulcer disease or bleeding at other sites, age >70 years, thrombocytopenia, coagulopathy, CKD, and concurrent use of other medications that increase bleeding risk, such as nonsteroidal anti-inflammatory drugs, steroids, direct oral anticoagulants, and warfarin (S4.6-10).