



Medi-Cal Rx

Aspirin for Primary Prevention of Cardiovascular Disease

May 28, 2024

Disclaimer: These articles are the result of analyses carried out by the Medi-Cal Drug Use Review (DUR) Program and are not official policies of the Department of Health Care Services (DHCS).

Learning Objectives

- Review recommendations from the United States Preventive Services Task Force (USPSTF) on the use of aspirin for primary prevention of cardiovascular disease (CVD).
- Explain how the 10-year CVD risk score can be used to distinguish between individuals who likely will or will not benefit from aspirin for primary prevention of CVD.
- Identify risk factors for bleeding, including medications and medical conditions.

Key Points

- CVD is the leading cause of death in California and the United States.
- The American College of Cardiology/American Heart Association (ACC/AHA) and the USPSTF provide recommendations on the use of aspirin for primary prevention of CVD.
- The 2022 USPSTF recommendations on the use of aspirin for primary prevention of CVD state the following:
 - For adults 60 years of age or older, aspirin is not recommended for primary prevention of CVD as the risks of bleeding outweigh the benefit.
 - For adults 40-59 years of age, providers should calculate 10-year risk using the ACC/AHA Pooled Cohort Equations (PCE) via the [ASCVD Risk Estimator Plus](#) and assess the patient's risk for bleeding. Aspirin can be considered for individuals with a 10-year CVD risk greater than 10% who are not at increased risk for bleeding.
- In January 2024, the AHA launched the [PREVENT™ Online Calculator](#) to estimate 10-year and 30-year CVD risk for primary prevention patients between 30-79 years of age. Compared to previous calculators, the updated tool considers broader measures of health and a longer horizon for risk.
- Aspirin is on the *Medi-Cal Rx Contract Drugs List* (CDL) and is available to Medi-Cal members with a prescription.

Background

CVD, which includes coronary heart disease, stroke, and heart failure, is a significant health problem in California, accounting for more than 84,000 deaths and 126,000 hospitalizations statewide in 2022.^{1,2} Interventions that target cardiovascular risk factors can significantly reduce CVD-related morbidity and mortality, as modifiable risk factors account for up to 90% of the risk of cardiovascular events.³ Periodic risk assessment offers an opportunity for health care providers to identify potential preventative measures that can reduce an individual's cardiovascular risk, including lifestyle modifications and pharmacotherapy.⁴

Primary prevention of CVD includes several strategies that aim to lower an individual's modifiable risk, including lipid lowering, blood pressure management, and the use of low-dose aspirin. Aspirin irreversibly inhibits platelet function, which both reduces the risk of thrombosis and increases the risk of major bleeding, particularly in the gastrointestinal tract. Although there is strong evidence supporting the use of aspirin to reduce morbidity and mortality in individuals with established CVD, the use of aspirin for primary prevention of CVD is more controversial due to inconsistent evidence regarding the magnitude of benefit in this population when compared with the risks of bleeding.^{4,5}

The USPSTF provides recommendations for prevention of several chronic conditions, including the use of aspirin for primary prevention of CVD. In 2022, the USPSTF published an update to its 2016 recommendations on [Aspirin Use to Prevent Cardiovascular Disease](#) based on a systematic review of 13 clinical trials (n = 134,470) and a microsimulation modeling study. Most trials studied low-dose aspirin (100 mg per day or less), and the patient population typically ranged from 53 to 74 years of age.^{5,6}

The 2022 USPSTF recommendations apply to adults 40 years of age or older who do not have pre-existing CVD and who are not at an increased risk for bleeding. The USPSTF provides the following recommendations divided by age group:

- For adults 40-59 years of age with a 10% or greater 10-year CVD risk, aspirin can be considered for primary prevention.
- For adults 60 years of age or older, aspirin is not recommended for primary prevention of CVD as the risk of bleeding outweighs the benefit of therapy.
- Adults of any age who are at risk for bleeding should not be initiated on aspirin for primary prevention.

Benefits and Risks of Aspirin for Primary Prevention of CVD

The USPSTF analysis found that aspirin used for primary prevention in individuals at increased CVD risk was associated with a significant reduction in major cardiovascular events but did not reduce mortality. Although aspirin prevented cardiovascular events in this population, a pooled-analysis of 10 trials (n = 119,130) found a 58% increased risk of gastrointestinal bleeds and a pooled-analysis of 11 trials (n = 134,470) showed an increase in non-fatal intracranial bleeds. The final recommendations are based on a microsimulation model which found a

modest net benefit for adults 40-59 years of age with a 10-year CVD risk greater than 10% but no net benefit for individuals older than 60 years of age, regardless of 10-year risk score.⁵

Estimating Risk of CVD

A baseline CVD risk estimation establishes an initial reference point that can be used to guide discussions between the patient and provider about potential risk-lowering interventions, including the use of aspirin. When considering aspirin for primary prevention, the USPSTF encourages providers to start by estimating the patient's cardiovascular risk using a validated CVD risk calculator such as the ACC/AHA PCE. Providers can utilize the ACC's [ASCVD Risk Estimator Plus](#) to estimate a patient's 10-year cardiovascular risk based on the 2013 ACC/AHA PCE and approximate the potential benefit of specific risk-lowering interventions (including aspirin).^{4,5}

In January 2024, the AHA introduced the [PREVENT™ Online Calculator](#) as an update to the 2013 ACC/AHA PCE for estimating CVD risk. The PREVENT™ Online Calculator equations are based on a significantly larger data set and reflect important changes to the current understanding of CVD prevention, including the addition of new variables such as cardiovascular-kidney-metabolic health and social deprivation index, removal of race as a risk determinant, ability to perform sex-specific risk estimation, and incorporating risk for heart failure. Using the PREVENT™ Online Calculator, providers can predict 10- and 30-year risk of CVD for adults 30-79 years of age. The ACC/AHA recently noted that although there is no formal guidance yet for use of the PREVENT™ Online Calculator, providers can expect it to be incorporated into upcoming guidelines for CVD prevention.⁷

Although risk calculators provide a valuable initial assessment of CVD risk, it is important to individualize the decision to start aspirin according to the patient's preferences, presence of risk-enhancing factors, and the patient's risk for bleeding. For adults at borderline (5% to <7.5%) and intermediate ($\geq 7.5\%$ to <20%) risk, the ACC/AHA recommends that providers consider risk-enhancing factors including family history of early coronary artery disease, elevations in inflammatory and lipoprotein biomarkers, and medical conditions such as familial hypercholesterolemia, chronic kidney disease, metabolic syndrome, and chronic inflammatory conditions. Providers can refer to the *2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease* for a complete list of risk enhancing factors and additional guidance on CVD risk estimation.⁴

Assessing Risk for Bleeding

Aspirin increases the risk for major bleeding through inhibition of prostaglandins that are required for clotting and protection of the gastrointestinal tract from stomach acid. Data suggests that the increased incidence of bleeding associated with aspirin usually occurs within six months after initiating aspirin, and that aspirin does not have a differential relative bleeding risk based on age, sex, presence of diabetes, level of CVD risk, or race or ethnicity. Although the increase in relative risk does not appear to differ based on age, the absolute incidence of

bleeding with or without aspirin increases with age, and more so in adults 60 years of age or older.^{4,5}

Before initiating aspirin therapy, providers should perform a bleeding risk assessment that incorporates patient-specific risk factors such as history of gastrointestinal bleed, peptic ulcer disease, if the individual is older than 70 years of age, thrombocytopenia, and current use of nonsteroidal anti-inflammatory drugs (NSAIDs), steroids, or anticoagulants.^{4,5}

Table 1. Risk Factors for Bleeding

Category	Risk Factors
Medical History	<ul style="list-style-type: none"> • Coagulopathy • Gastrointestinal disorders (particularly peptic ulcer disease) • Liver or kidney disease • Thrombocytopenia • Anemia • History
Current Medications	<ul style="list-style-type: none"> • NSAIDs • Corticosteroids • Anticoagulants and antiplatelets • Selective
Other	<ul style="list-style-type: none"> • Male sex • Individual is older than 70 (strongest risk factor for bleeding) • Smoking

Recommendations from Other Societies

The 2019 ACC/AHA Guidelines on the Primary Prevention of Cardiovascular Disease also provides recommendations on the use of low-dose aspirin. Similarly to the USPSTF, ACC/AHA recommends against aspirin for primary prevention in individuals older than 70 years of age. The ACC/AHA guidance differs slightly from the USPSTF statement in recommending that aspirin therapy may be warranted for some individuals 60-70 years of age who are at high cardiovascular risk, particularly those with enhancing risk factors such as family history of early coronary artery disease, inability to achieve lipid or blood pressure targets, or elevated coronary artery calcium score. The ACC/AHA guideline does not make specific recommendations for these scenarios but encourages providers to assess an individual’s risk for CVD and bleeding in totality when determining if aspirin should be initiated for individuals 40-70 years of age.^{4,5,8}

As diabetes is a significant risk factor for development for CVD, the American Diabetes Association (ADA) recommends that providers consider low-dose aspirin for primary prevention in adults 50-70 years of age who have diabetes, are not at an increased risk for bleeding, and have at least one major CVD risk factor. Routine use of aspirin for primary

prevention was not recommended for individuals older than 70 years of age due to increased risk for bleeding in this population.⁹

Aspirin Use in the Medi-Cal Population

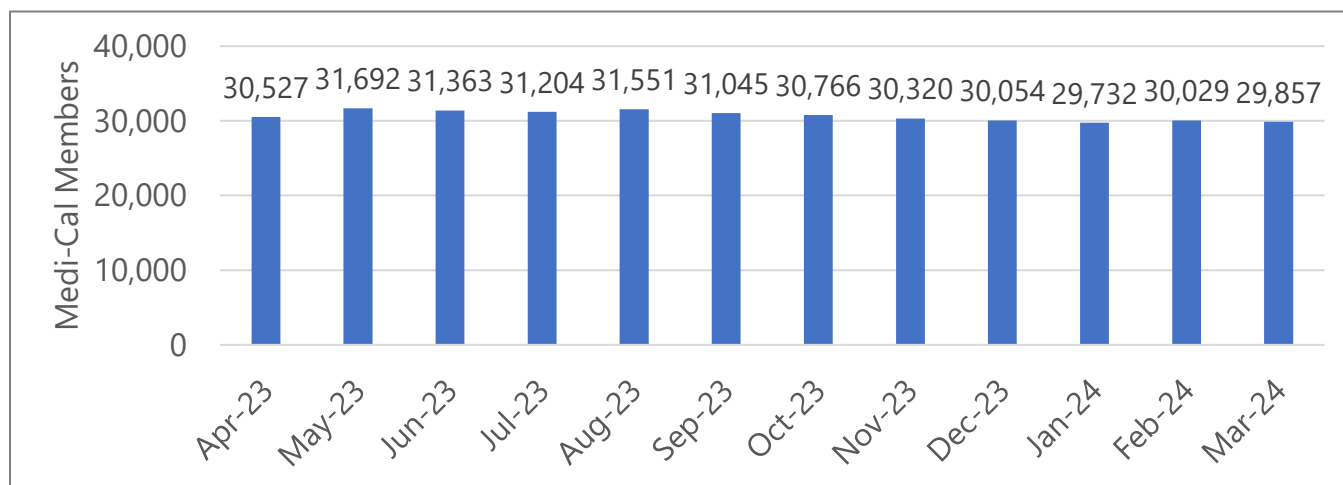
A retrospective administrative claims analysis was conducted to evaluate current aspirin use among Medi-Cal members with an increased risk of bleeding. All paid medical and pharmacy claims were reviewed for eligible Medi-Cal members with a date of service between April 1, 2023, and March 31, 2024. A 90-day lookback period was used to include any pharmacy claims paid before April 1, 2023, to account for any days' supply of aspirin that overlapped with the measurement year. Beneficiaries with dual eligibility for Medicare were excluded from the analysis, as there may be incomplete pharmacy claims data for these individuals.

Results

During the measurement year, a total of 263,054 Medi-Cal members 40 years of age or older had at least one paid claim for low-dose (81 mg) aspirin, with 10.1% (n = 26,612) 70 years of age or older. Of those members 70 years of age or older, almost half (40.9%; n = 10,885) were male and 64.3% (n = 17,126) had paid claims for low-dose aspirin for at least 180 days during the measurement year (median = 200 days), indicating long-term use of low-dose aspirin.

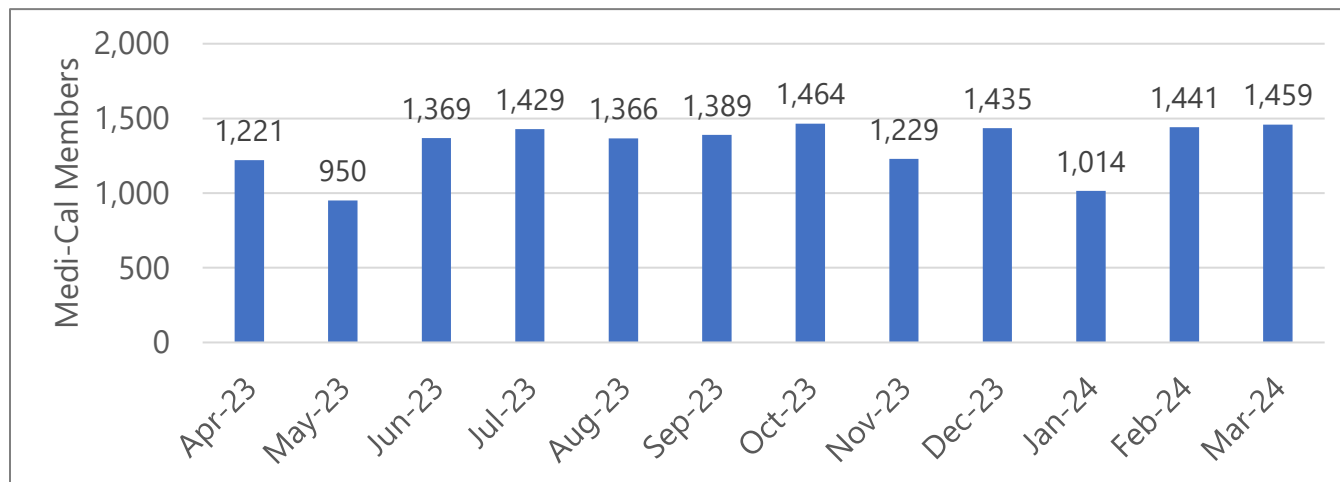
Claims data were reviewed for additional risk factors for bleeding, including concomitant use of low-dose aspirin and nonselective NSAIDs during the previous 90 days (**Figure 1**) and history of peptic ulcer disease and a paid claim for aspirin (**Figure 2**).

Figure 1. Medi-Cal Members with Paid Claims for Both Nonselective NSAIDs and Low-Dose Aspirin (81 mg/day) during the Previous 90 Days, by Month



As shown in **Figure 1**, while the number of members with concomitant use of low-dose aspirin and nonselective NSAIDs has decreased slightly over the measurement year, there are still enough members with paid claims for both medications that Medi-Cal providers may benefit from educational outreach on this topic.

Figure 2. Medi-Cal Members with a History of Peptic Ulcer Disease and a Paid Claim for Aspirin, by Month



Similarly, **Figure 2** shows another opportunity for educational outreach, as members with a history of peptic ulcer disease with paid claims for aspirin have remained relatively constant over the measurement year.

Conclusion/Discussion

Guidelines from USPSTF, ACC/AHA, and ADA all encourage a patient-centered approach and shared decision-making when considering initiating aspirin for primary prevention. If aspirin is initiated, providers should inform patients of the risk for bleeding and review the signs and symptoms of bleeding. Providers can refer to the [Let's Talk About It: Starting Aspirin to Prevent Heart Disease and Stroke](#) discussion guide created by USPSTF when talking with patients about the benefits and risks of starting aspirin for primary prevention of CVD.

Clinical Recommendations

- For all adults 40-60 years of age who do not have CVD, providers should complete an initial CVD risk estimation using a validated risk calculator such as the [ASCVD Risk Estimator Plus](#) or the [PREVENT™ Online Calculator](#).
- For adults 40-60 years of age with a 10% or greater 10-year CVD risk who are not at an increased risk of bleeding, initiation of low-dose aspirin daily can be considered after performing a risks and benefits assessment of the individual patient.
- For adults 60 years of age or older, the USPSTF recommends against routine initiation of aspirin therapy for primary prevention due to concerns for bleeding risks and lack of net benefit.
- In adults 50-70 years of age with diabetes who are not at increased risk of bleeding and have at least one major CVD risk factor, the ADA recommends that providers consider low-dose aspirin for primary prevention.

- For adults 70 years of age or older, the ACC/AHA, ADA, and the USPSTF recommend against initiating aspirin for primary prevention, as the potential risks of bleeding outweigh the benefits of therapy in this group.
- Patients of any age who are at a high risk for bleeding should not be started on aspirin for primary prevention of CVD.
- In addition to age and an estimated 10-year CVD risk, the decision to initiate aspirin should be individualized based on the patient’s risk for bleeding, presence of risk-enhancing factors, and the patient’s preferences.
- The ACC/AHA and USPSTF recommend against initiating aspirin in patients with a history of gastrointestinal bleeding, peptic ulcer disease, current use of certain medications such as anti-inflammatory drugs, corticosteroids, and anticoagulants, older than 70 years of age, thrombocytopenia, and coagulopathies.
- If aspirin is prescribed, providers should counsel patients on the potential risks for bleeding, including monitoring for signs and symptoms of bleeding while on aspirin.
- Additional tools and resources for both patients and providers can be found on the following websites:
 - Through their [HeartBeatCA Program](#), the California Department of Public Health (CDPH) supports public health efforts in chronic disease prevention and management activities to improve the health and quality of life for Californians diagnosed with CVD, hypertension (HTN), and high blood cholesterol (HBC).
 - The [Million Hearts®](#) initiative provides information on improving cardiovascular health and preventing heart attack and stroke.
 - The Centers for Disease Control and Prevention (CDC) has resources related to the risk of heart disease and prevention of heart disease for both patients and professionals on their [Heart Disease](#) page.
 - The National Heart, Lung, and Blood Institute has patient resources related to coronary heart disease on their [Coronary Heart Disease](#) page.

References

1. Policy and Planning. 2024. [California Community Burden of Disease Engine](#). California Department of Public Health. Accessed: May 13, 2024.
2. National Center for Health Statistics. [Leading Causes of Death in 2021, California](#). Centers for Disease Control and Prevention. Accessed: May 13, 2024.
3. Adams ML, Grandpre J, Katz DL, Shenson D. The impact of key modifiable risk factors on leading chronic conditions. *Prev Med*. 2019 Mar;120:113-118. <https://doi.org/10.1016/j.ypmed.2019.01.006>. Accessed: May 13, 2024.
4. Arnett DK, Blumenthal RS, Albert MA, et al. 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;140:e596–e646. <https://doi.org/10.1161/CIR.0000000000000678>. Accessed: May 13, 2024.

5. U.S. Preventive Services Task Force. Aspirin Use to Prevent Cardiovascular Disease: U.S. Preventive Services Task Force Recommendation Statement. *JAMA*. 2022;327(16):1577-1584. <https://doi.org/10.1001/jama.2022.4983>. Accessed: May 13, 2024.
6. Bibbins-Domingo K and the U.S. Preventive Services Task Force. Aspirin Use for the Primary Prevention of Cardiovascular Disease and Colorectal Cancer: U.S. Preventive Services Task Force Recommendation Statement. *Ann Intern Med*. 2016;164(12):836-845. <https://doi.org/10.7326/M16-0577>. Accessed: May 13, 2024.
7. Khan SS, Matsushita K, Sang Y, et al. Development and Validation of the American Heart Association's PREVENT Equations. *Circulation*. 2024 Feb 6;149(6):430-449. <https://doi.org/10.1161/CIRCULATIONAHA.123.067626>. Accessed: May 13, 2024.
8. Mallick S, Shroff GR, Linzer M. Aspirin for primary prevention of cardiovascular disease: What do the current USPSTF guidelines say? *Cleve Clin J of Med*. 2023 May 1;90(5):287-291. <https://doi.org/10.3949/ccjm.90a.22087>. Accessed: May 13, 2024.
9. American Diabetes Association Professional Practice Committee. 10. Cardiovascular Disease and Risk Management: Standards of Care in Diabetes-2024. *Diabetes Care*. 2024 Jan 1;47(Suppl 1):S179-S218. <https://doi.org/10.2337/dc24-S010>. Accessed: May 13, 2024.