



Pharmaceutical Assistance
Contract for the Elderly



Balanced information for better care

Aggregating the latest evidence on antiplatelet agents



The role of aspirin in primary prevention has changed

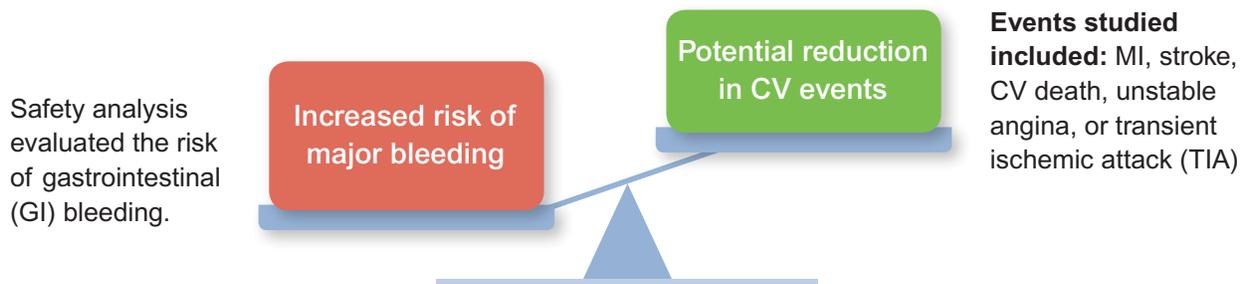
Recent landmark studies cast doubt on its usefulness in preventing cardiovascular events in healthier patients.

TABLE 1. Summary of large, long-term randomized controlled trials (RCTs) published in 2018 for aspirin vs. placebo for prevention of cardiovascular events¹⁻³

RCT Name	Patient Population	Size	Follow-up	Mean age	Relative CV effect	Relative risk of major bleeding
ASPREE	Healthy older adults	19,114	4.7 years (median)	74	No difference	38% increase
ARRIVE	"Moderate" CV risk	12,546	5 years (median)	64	No difference	>2-fold increase
ASCEND	Diabetes	15,480	7.4 years (mean)	63	12% decrease (NNT 91)	29% increase (NNH 111)

Aspirin significantly adds to the risk of bleeding.

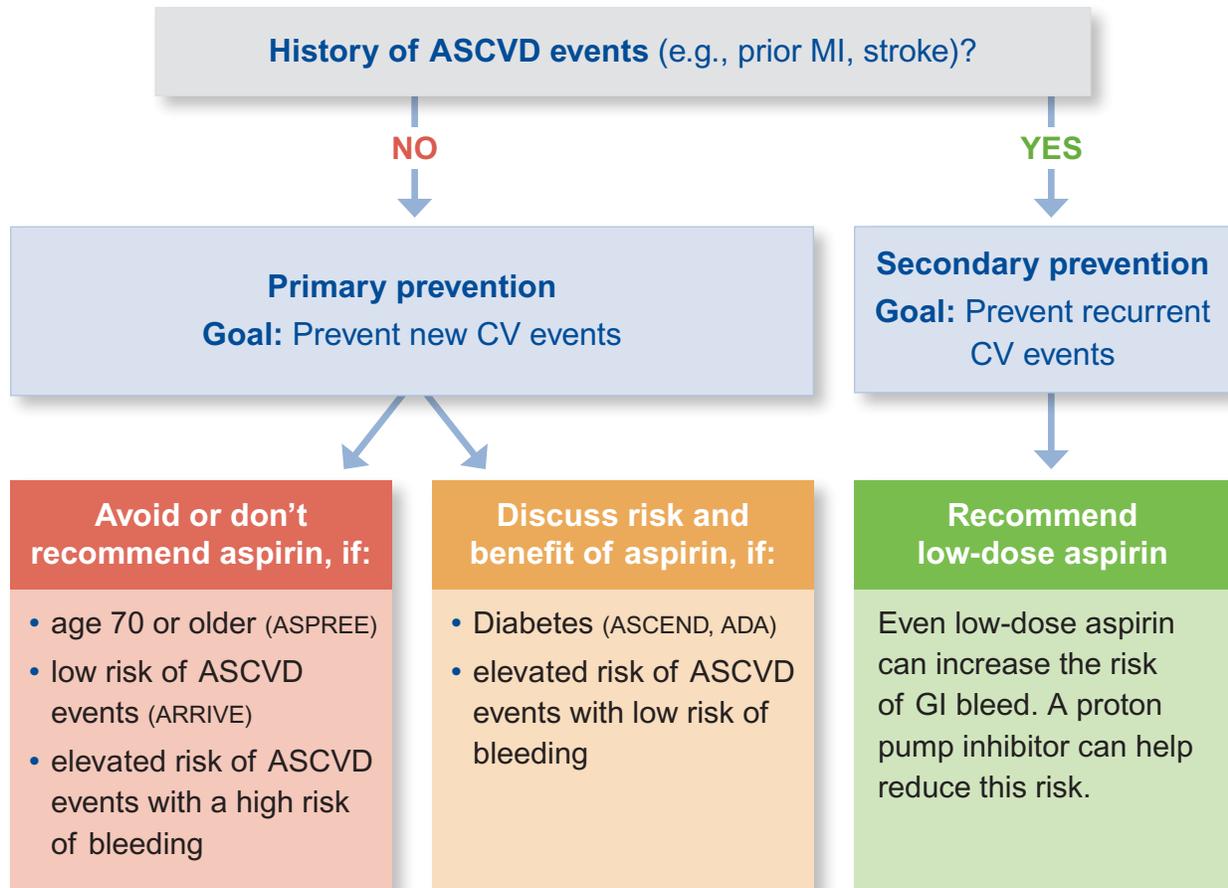
FIGURE 1. Balancing the risks of low-dose aspirin therapy with the benefit of CV event reduction



This risk is magnified in patients already at an increased risk of bleeding, such as those with anemia, on chronic steroids, or with a history of gastrointestinal bleeding.

So now, when should aspirin be used?

FIGURE 2. Recommendations for when aspirin can help based on level of risk¹⁻⁴



A given patient's risk of ASCVD events can be calculated using the ASCVD Risk Estimator Plus. Elevated risk is "intermediate risk" or higher in the tool. Visit AlosaHealth.org/Antiplatelet for links to this and other tools.



A low dose (81 mg) is best when aspirin is indicated.

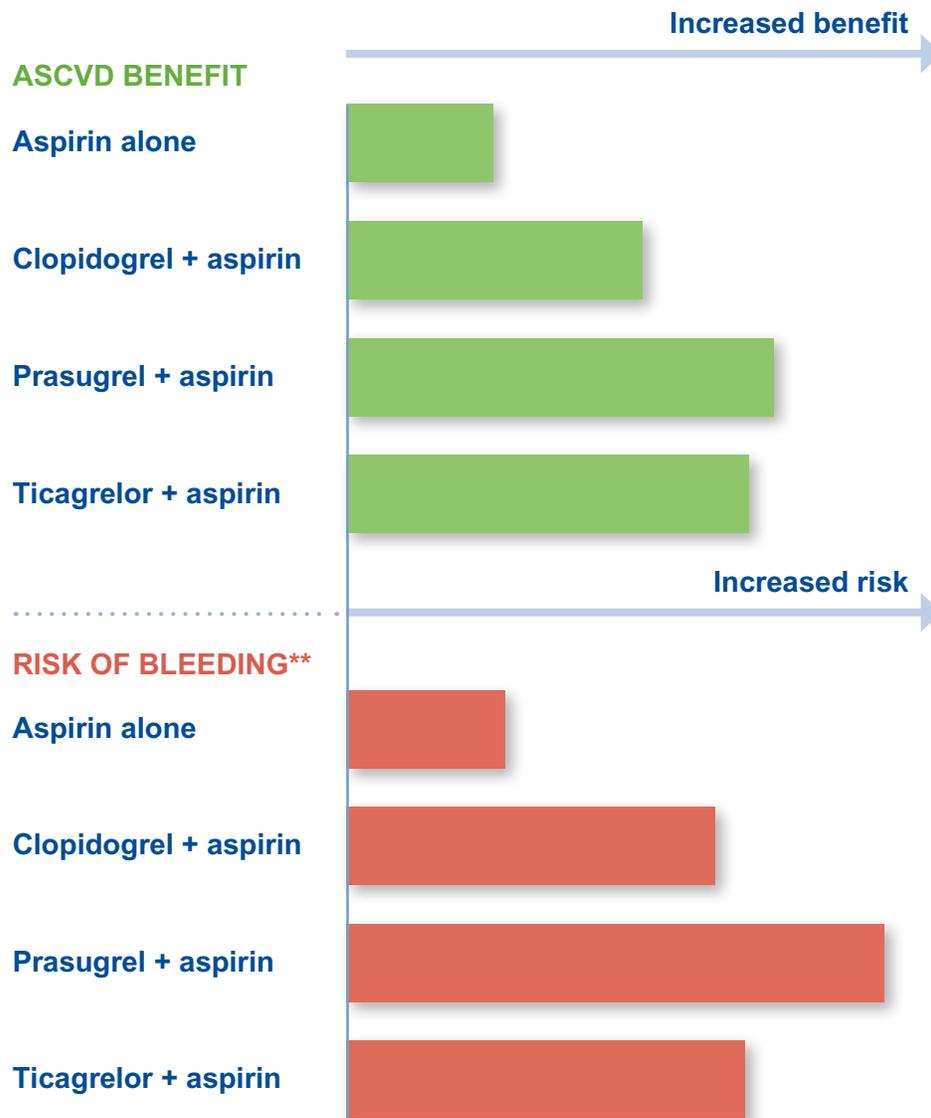


Some patients may require an additional antiplatelet medication, especially those who have had a stent or MI.



Doubling down: the risks and benefits of dual antiplatelet therapy (DAPT)

FIGURE 3. Using two different antiplatelet drugs can confer greater protection from CV events compared to aspirin alone in patients with acute coronary symptoms (ACS*), but with a greater risk of bleeding.⁵⁻⁸



*ACS includes MI, both with ST-segment elevation (STEMI) and without (NSTEMI-ACS), and unstable angina.

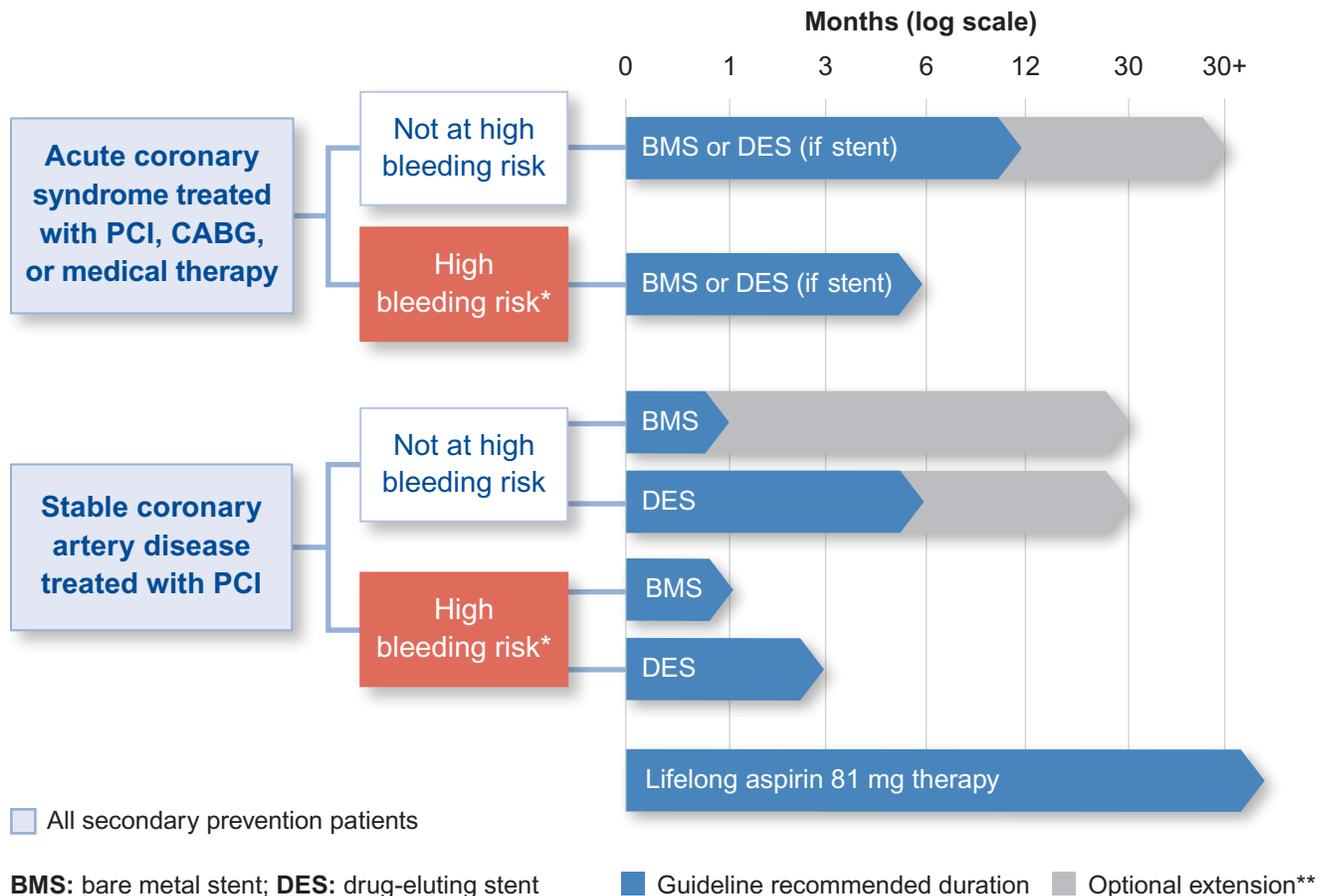
**Major bleeding includes fatal or disabling bleeding, signs of hemorrhage with a drop in hemoglobin of ≥ 5 g/dL, the need for transfusion of >2 units of blood, and/or non-surgical bleeding that results in death.

Prasugrel should be used only after percutaneous coronary intervention (PCI) and avoided in patients 75 and over.

Deciding when to stop multi-drug therapy

How long to continue DAPT depends on the reason for its use.

FIGURE 4. Recommended duration of DAPT by indication⁹⁻¹¹



****Optional extension in duration of therapy:** In patients without a high risk of bleeding who do not have another ASCVD event or a major bleed during the initial treatment period, the prescriber may opt to extend treatment up to 30 months if a stent was placed and possibly longer in patients after an MI.^{10,11} In patients with a second ASCVD event, the duration for DAPT should reset (i.e., another 12 months after an ACS event).

***Those at high bleeding risk** should be prescribed shorter courses (e.g., patients taking anticoagulants, or with thrombocytopenia or cancer).⁹

In general, DAPT therapy is not life-long, though aspirin is continued indefinitely.

Antiplatelet therapy for stroke

Acute

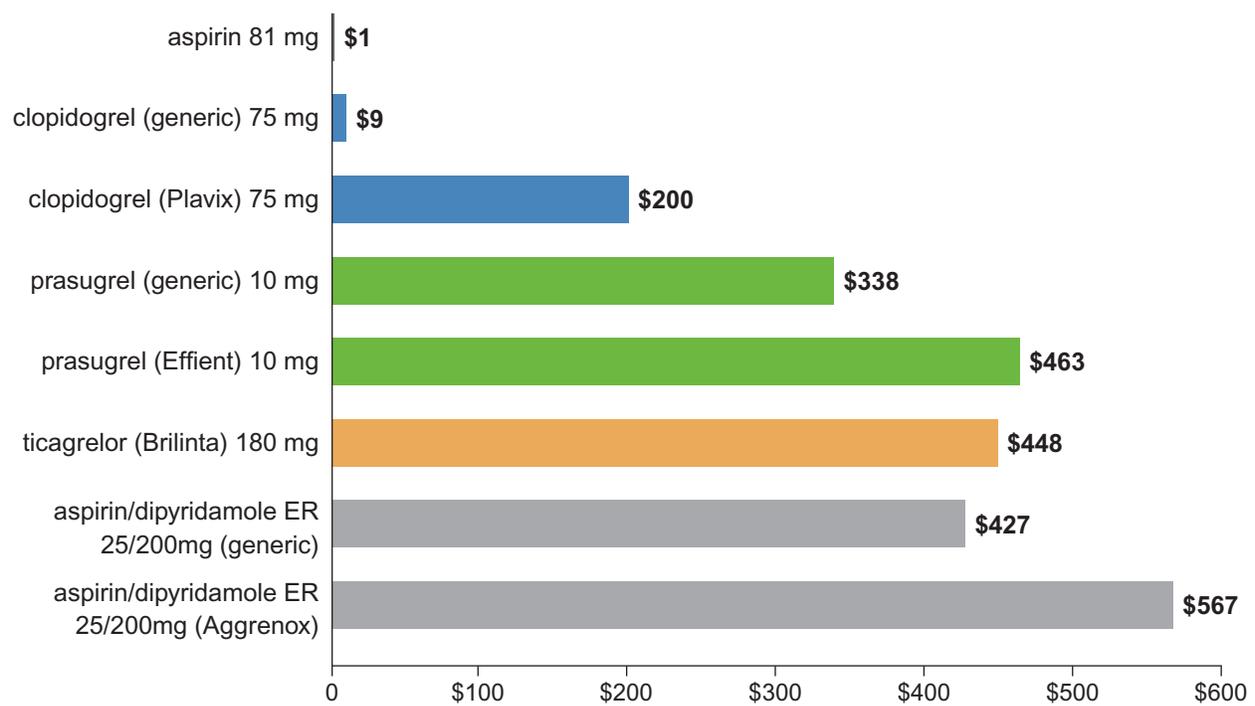
- Emerging evidence suggests **clopidogrel plus aspirin** reduces the risk of recurrent stroke, MI, or CV death in the short term (21 to 90 days immediately following an acute, minor stroke).^{12,13}

Longer-term

- Stop clopidogrel plus aspirin.**
 - Clopidogrel plus aspirin should be stopped after acute stroke management due to an increased risk of bleeding without a CV benefit in long-term therapy, compared to prescribing clopidogrel or aspirin alone.¹⁴
- Use clopidogrel alone or dipyridamole ER/aspirin.**
 - Dipyridamole ER/aspirin (Aggrenox) and clopidogrel alone provide similar CV benefit and risk of bleeding.¹⁵ Dipyridamole ER/aspirin can cause headache and may not be tolerated in some patients.
 - Low-dose (81 mg) aspirin can also be used to prevent CV events after a stroke.⁵

Prices

FIGURE 5. Cost of a 30-day supply of various antiplatelet medications



Prices from goodrx.com, June 2019. Listed doses are based on Defined Daily Doses by the World Health Organization and should not be used for dosing in all patients. All prices shown are for generics when available, unless otherwise noted. These prices are a guide; patient costs will be subject to copays, rebates, and other incentives.

Key points

- Aspirin is no longer recommended for the routine primary prevention of cardiovascular events in patients with low risk or who are over 70.
- There is good evidence favoring the use of DAPT (e.g., clopidogrel plus aspirin) following acute coronary syndromes or elective PCI.
- The duration of DAPT depends on the indication and patient characteristics, but is generally not life-long.
- Aspirin should be recommended indefinitely for secondary prevention in patients who have had CV events.
- Immediately following stroke, clopidogrel plus aspirin reduces ischemic risk in the short term, but should be discontinued after 21-90 days due to risk of bleeding in the longer term.
- Clopidogrel alone or aspirin plus dipyridamole are most effective in preventing CV events in the longer term after stroke.

More information is available at AlosaHealth.org/Antiplatelet

References:

(1) McNeil JJ, Wolfe R, Woods RL, et al. Effect of Aspirin on Cardiovascular Events and Bleeding in the Healthy Elderly. *N Engl J Med.* 2018;379(16):1509-1518. (2) Gaziano JM, Brotons C, Coppolecchia R, et al. Use of aspirin to reduce risk of initial vascular events in patients at moderate risk of cardiovascular disease (ARRIVE): a randomised, double-blind, placebo-controlled trial. *Lancet.* 2018;392(10152):1036-1046. (3) Bowman L, Mafham M, Wallendszus K, et al. Effects of Aspirin for Primary Prevention in Persons with Diabetes Mellitus. *N Engl J Med.* 2018;379(16):1529-1539. (4) Arnett DK, Blumenthal RS, Albert MA, et al. 2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease. *Circulation.* 2019;Cir0000000000000678. (5) Baigent C, Blackwell L, Collins R, et al. Aspirin in the primary and secondary prevention of vascular disease: collaborative meta-analysis of individual participant data from randomised trials. *Lancet.* 2009;373(9678):1849-1860. (6) Yusuf S, Zhao F, Mehta SR, Chrolavicius S, Tognoni G, Fox KK. Effects of clopidogrel in addition to aspirin in patients with acute coronary syndromes without ST-segment elevation. *N Engl J Med.* 2001;345(7):494-502. (7) Wiviott SD, Braunwald E, McCabe CH, et al. Prasugrel versus clopidogrel in patients with acute coronary syndromes. *N Engl J Med.* 2007;357(20):2001-2015. (8) Wallentin L, Becker RC, Budaj A, et al. Ticagrelor versus clopidogrel in patients with acute coronary syndromes. *N Engl J Med.* 2009;361(11):1045-1057. (9) Capodanno D, Alfonso F, Levine GN, Valgimigli M, Angiolillo DJ. ACC/AHA Versus ESC Guidelines on Dual Antiplatelet Therapy: JACC Guideline Comparison. *J Am Coll Cardiol.* 2018;72(23 Pt A):2915-2931. (10) Mauri L, Kereiakes DJ, Yeh RW, et al. Twelve or 30 Months of Dual Antiplatelet Therapy after Drug-Eluting Stents. *N Engl J Med.* 2014;371(23):2155-2166. (11) Bonaca MP, Bhatt DL, Cohen M, et al. Long-Term Use of Ticagrelor in Patients with Prior Myocardial Infarction. *N Engl J Med.* 2015;372(19):1791-1800. (12) Johnston SC, Easton JD, Farrant M, et al. Clopidogrel and Aspirin in Acute Ischemic Stroke and High-Risk TIA. *N Engl J Med.* 2018;379(3):215-225. (13) Powers WJ, Rabinstein AA, Ackerson T, et al. 2018 Guidelines for the Early Management of Patients With Acute Ischemic Stroke: A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association. *Stroke.* 2018;49(3):e46-e110. (14) Diener HC, Bogousslavsky J, Brass LM, et al. Aspirin and clopidogrel compared with clopidogrel alone after recent ischaemic stroke or transient ischaemic attack in high-risk patients (MATCH): randomised, double-blind, placebo-controlled trial. *Lancet.* 2004;364(9431):331-337. (15) Sacco RL, Diener HC, Yusuf S, et al. Aspirin and extended-release dipyridamole versus clopidogrel for recurrent stroke. *N Engl J Med.* 2008;359(12):1238-1251.

About this publication

These are general recommendations only; specific clinical decisions should be made by the treating clinician based on an individual patient's clinical condition. More detailed information on this topic is provided in a longer evidence document at AlosaHealth.org.



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