Dual Antiplatelet Therapy for Coronary Artery Disease

(Modified September 2023)

Antiplatelet therapy is often used in patients with coronary artery disease (CAD). The chart below provides **oral** antiplatelet regimen options and durations for CAD indications, including stents. For antiplatelet dosing, cost, and other pertinent information, see our chart, *Comparison of Oral Antiplatelets*. Intravenous antiplatelet agents or anticoagulants may also be indicated acutely but are not included in this document.

Indication	**Antiplatelet Regimen Options**	**Duration** **Note**: low-dose aspirin is almost always continued indefinitely in CAD.[1]
ACS treated with stent (BMS or DES) *Continued…*	• Aspirin plus ticagrelor (*Brilinta*)[e] (reasonable to use in preference to aspirin plus clopidogrel, except in patients ≥75 years of age undergoing PCI within 24 hours post-fibrinolysis)[2] **OR** • Aspirin plus prasugrel (*Effient*)[e] (reasonable to use in preference to aspirin plus clopidogrel if patient does not have a history of TIA or stroke). Caution if <60 kg or ≥75 years of age.[2] **OR** • Aspirin plus clopidogrel[2] See **footnote a** regarding aspirin dosing. Note: Ticagrelor or prasugrel prevent about one CV event for every 50 patients treated for one year vs clopidogrel,[7,8] but consider cost and side effects.	• DAPT for at least 12 months (see **footnote c**), then aspirin indefinitely (DES or BMS).[2,24] (see **footnote d**) • Weigh bleeding risk vs thrombosis risk when choosing DAPT duration.[2] o Consider using a bleeding risk calculator. See links in **footnote f**. o There is less data for abbreviated regimens (DAPT ≤6 months) after complex PCI: ≥three vessels/stents/lesions; bifurcation with two stents; total stent length >60 mm, or chronic total occlusion as target lesion.[18] o Studies of abbreviated regimens included few STEMI patients and were underpowered to show differences in stent thrombosis.[2,17] • Abbreviated regimens to reduce bleeding risk [Evidence level B-1]. Unless otherwise noted, studies included ACS and non-ACS patients: o P2Y12 inhibitor plus aspirin for one month, then monotherapy (non-inferior to continuation of DAPT for at least two months in patients with **high bleeding risk** [Precise DAPT ≥25] treated with sirolimus *Ultimaster* stent; clopidogrel was most commonly used).[17] o Ticagrelor plus aspirin for three months, then ticagrelor monotherapy (see **footnote d**) (safer and as effective as one year of DAPT in patients with **high bleeding or ischemic risk** treated with DES).[4] o Ticagrelor plus aspirin for one month, then ticagrelor monotherapy (see **footnote d**) (safety/efficacy similar to one year of DAPT in patients with biolimus A9 stent).[14] o Ticagrelor plus aspirin for three months , then ticagrelor monotherapy (see **footnote d**) (safety/efficacy superior to one year of DAPT in **ACS** treated with sirolimus *Orsiro* stent).[15]

Indication	**Antiplatelet Regimen Options**	**Duration** **Note**: low-dose aspirin is almost always continued indefinitely in CAD.[1]
ACS treated with stent (BMS or DES), continued		○ Clopidogrel plus aspirin for three months, then clopidogrel monotherapy (see **footnote d**) (noninferior [for major CV events] to one year of DAPT in patients with DES).[5] ○ Clopidogrel plus aspirin for one to two months, then clopidogrel monotherapy (see **footnote d**) reduced bleeding events, but noninferior for CV events vs one-year of DAPT in **ACS** treated with CoCr-EES stent).[23] • If at high risk of bleeding or severe bleeding complication (e.g., oral anticoagulant, major intracranial surgery), or if significant overt bleeding occurs, it may be reasonable to discontinue the P2Y12 inhibitor (clopidogrel, prasugrel, or ticagrelor) after six months and continue aspirin monotherapy.[1,2] • **Surgical considerations**: delay elective noncardiac surgery for 30 days after BMS placement, and preferably for six months (may consider after three months) after DES placement. Continue aspirin, if possible, and restart P2Y12 inhibitor (i.e., clopidogrel, prasugrel, or ticagrelor) as soon as possible post-op. Consider risk/benefit, with input from all treating clinicians, when making decisions regarding surgery and antiplatelet therapy.[1]
ACS, medically treated (no fibrinolysis, no revascularization)	• Aspirin plus ticagrelor (*Brilinta*)[e] (reasonable to use in preference to aspirin plus clopidogrel in NSTE-ACS)[1] **OR** • Aspirin plus clopidogrel[1] See **footnote a** regarding aspirin dosing. Note: Ticagrelor prevents about one CV event for every 50 patients treated for one year vs clopidogrel,[7] but consider cost and side effects.	• DAPT for at least 12 months, then aspirin indefinitely.[1,24] (see **footnote d**) ○ If not at high bleeding risk (e.g., no history of bleeding on DAPT, no coagulopathy, no oral anticoagulant use), longer-duration DAPT may be reasonable (e.g., up to 36 months).[1,24]

Indication	**Antiplatelet Regimen Options**	**Duration** **Note**: low-dose aspirin is almost always continued indefinitely in CAD.[1]
STEMI, treated with fibrinolysis	• Aspirin plus clopidogrel[1] See **footnote a** regarding aspirin dosing.	• DAPT for at least 14 days, but ideally for at least 12 months, then aspirin indefinitely.[1] (see **footnote d**) o If not at high bleeding risk (e.g., no history of bleeding on DAPT, no coagulopathy, no oral anticoagulant use), longer-duration DAPT may be reasonable.[1]
Stable ischemic heart disease treated with stent (BMS or DES) *Continued…*	• Aspirin plus clopidogrel[1] See **footnote a** regarding aspirin dosing.	• **BMS**: DAPT for at least one month, then aspirin indefinitiely.[2] (see **footnote d**) o If not at high bleeding risk (e.g., no history of significant overt bleeding on DAPT, no coagulopathy, no oral anticoagulant use), longer-duration DAPT may be reasonable.[1,2] • **DES**: DAPT for at least six months (see **footnote b**), then aspirin indefinitely.[1,24] (see **footnote d**) • Weigh bleeding risk vs thrombosis risk when choosing DAPT duration.[2] o Consider using a bleeding risk calculator. See links in **footnote f**. o Abbreviated regimens (DAPT ≤6 months) are riskier after complex PCI: ≥three vessels/stents/lesions; bifurcation with two stents; total stent length >60 mm, or chronic total occlusion as target lesion.[18] o Studies of abbreviated regimens were underpowered to show differences in stent thrombosis.[2,17] • Abbreviated regimens to reduce risk of bleeding [Evidence level B-1]. Unless otherwise noted, studies included ACS and non-ACS patients. o P2Y12 inhibitor plus aspirin for one month, then monotherapy (non-inferior to continuation of DAPT for at least two months in patients with **high bleeding risk** [Precise DAPT ≥25] treated with sirolimus *Ultimaster* stent; clopidogrel was most commonly used).[17] o Ticagrelor plus aspirin for three months, then ticagrelor monotherapy (see **footnote d**) (safer and as effective as one year of DAPT in patients with **high bleeding or ischemic risk** treated with DES).[4] o Ticagrelor plus aspirin for one month, then ticagrelor monotherapy (see **footnote d**) (safety/efficacy similar to one year of DAPT in patients with biolimus A9 stent).[14] o Clopidogrel plus aspirin for three months, then clopidogrel monotherapy (see **footnote d**) (noninferior [for major CV events] to one-year of DAPT in patients with DES).[5]

Indication	Antiplatelet Regimen Options	Duration **Note**: low-dose aspirin is almost always continued indefinitely in CAD.[1]
Stable ischemic heart disease treated with stent (BMS or DES), continued		○ Clopidogrel plus aspirin for one month, then clopidogrel monotherapy (see **footnote d**) (noninferior to one year of DAPT in patients with CoCr-EES stent).[6] • If at high risk of bleeding or severe bleeding complication (e.g., oral anticoagulant use, major intracranial surgery), or if significant overt bleeding occurs, it may be reasonable to discontinue clopidogrel after three months and continue aspirin monotherapy.[1,2] • **Surgical considerations**: delay elective noncardiac surgery for 30 days after BMS placement, and preferably for six months (may consider after three months) after DES placement. Continue aspirin, if possible, and restart clopidogrel as soon as possible post-op. Consider risk/benefit, with input from all treating clinicians, when making decisions regarding surgery and antiplatelet therapy.[1]
Stable ischemic heart disease, with **NO** history of ACS, stent, or CABG	• Aspirin monotherapy (do not use DAPT)[1,24] See **footnote a** regarding aspirin dosing.	• Indefinitely.[1,24]
Stable ischemic heart disease patient with history of MI one to three years prior	• DAPT[1] **OR** • Aspirin monotherapy[1] See **footnote a** regarding aspirin dosing.	• Reasonable to continue DAPT if not at high bleeding risk (e.g., no history of bleeding on DAPT, no coagulopathy, no oral anticoagulant use).[1] ○ DAPT with ticagrelor 60 mg twice daily is approved for use in this situation, based on results of the PEGASUS-TIMI 45 study.[1,12] Combo prevented a second MI in one in 139 patients treated over three years vs aspirin alone. Combo caused major bleeding in one in 81 patients. One in 27 patients discontinued ticagrelor due to shortness of breath. Patients in the study had relatively high cardiovascular risk and relatively low bleeding risk.[9] • If DAPT is not continued, continue aspirin monotherapy indefinitely.[1] (see **footnote d**)

Indication	Antiplatelet Regimen Options	Duration **Note**: low-dose aspirin is almost always continued indefinitely in CAD.[1]
CABG	Pre-CABG antiplatelet management for patients on DAPT: • **Elective CABG**: it is reasonable to stop clopidogrel for five days, ticagrelor for three days, and prasugrel for seven days pre-op.[2] • **Urgent CABG**: hold clopidogrel or ticagrelor for at least 24 hours pre-op.[2] • Continue aspirin until the time of surgery.[2]	Post-CABG antiplatelets: • If a patient being treated with DAPT **post-stent** undergoes CABG, resume P2Y12 inhibitor as soon as safe post-op for recommended duration (4 weeks to >12 months, as above).[1,10] Continue aspirin 100 to 325 mg daily, indefinitely.[2] (see **footnote d**) • If a post-ACS patient being treated with DAPT undergoes CABG, resume P2Y12 inhibitor as soon as safe post-op to complete the recommended DAPT duration, as above.[1] Continue aspirin 100 to 325 mg daily, indefinitely.[2] (see **footnote d**) • In CABG patients who present with ACS, DAPT with prasugrel or ticagrelor is reasonable (and preferred over clopidogrel), for at least 12 months.[1,3,e] Continue aspirin 100 to 325 mg daily, indefinitely.[2] (see **footnote d**) • In patients with stable ischemic heart disease, DAPT (with clopidogrel or ticagrelor) for 12 months post-CABG is reasonable to improve graft patency (most data with clopidogrel, off-pump).[2,e] Continue aspirin 100 to 325 mg daily, indefinitely.[2] (see **footnote d**) • If DAPT is not used, start aspirin 100 to 325 mg daily within six hours post-CABG and continue indefinitely.[2] Patients taking warfarin should use an aspirin dose of 75 to 162 mg daily.[3] Consider a dose of 325 mg once daily, for at least the first year, for patients not taking warfarin.[3,16] If aspirin cannot be used, clopidogrel 75 mg once daily, indefinitely, is a reasonable aspirin alternative.[3] (see **footnote d**)

a. The recommended aspirin dose is 81 mg (75 to 100 mg) daily when used as part of dual antiplatelet therapy or monotherapy for CAD.[1,24] Doses >81 mg daily may not be more effective, while causing more bleeding.[1] Use ticagrelor with aspirin 75 to 100 mg daily (Canada: 75 to 150 mg daily). Higher doses may reduce ticagrelor efficacy.[11,12]

b. **Stable ischemic heart disease** treated with stent (DES): If not at high bleeding risk (e.g., no history of bleeding on DAPT, no coagulopathy, no oral anticoagulant use), longer-duration DAPT may be reasonable.[1] However, longer durations do not seem to reduce CV events and may increase bleeding risk.[13]

c. **ACS** treated with stent: If **NOT** at high bleeding risk (e.g., no history of bleeding on DAPT, no coagulopathy, no oral anticoagulant use), longer-duration DAPT may be reasonable (e.g., up to 36 months).[1,24] The **DAPT risk calculator** (http://tools.acc.org/DAPTriskapp/#!/content/calculator/) can help identify patients who might benefit from DAPT continuation beyond one year.

d. Increasing evidence supports clopidogrel over aspirin for long-term maintenance monotherapy.[19-21] Post DES (12+/- 6 months), use of clopidogrel instead of aspirin for ~6 years reduces BARC ≥2 bleeding (NNT = 63), ACS readmission (NNT = 33), any revascularization (NNT = 63), and stroke (NNT =72).[19] In patients with CAD, a meta-analysis found that clopidogrel was more effective than aspirin for reducing a composite endpoint of CV death, MI, and stroke (NNT = 133), with similar major bleeding risk. The primary endpoint was largely driven by a reduction in MI.[25]
e. De-escalation from ticagrelor or prasugrel to clopidogrel is often necessary due to cost, side effects, or poor adherence.[22] Clopidogrel can be started 24 hours after the last dose of prasugrel or ticagrelor.[22] Patients switched from ticagrelor to clopidogrel (or from prasugrel to clopidogrel <30 days post-event/stent) should generally be given a loading dose of clopidogrel 600 mg x 1, but skipping the loading dose and starting with clopidogrel 75 mg once daily is an option, especially if the patient is being switched due to bleeding or if de-escalation is >30 days after the event/PCI.[22]
f. Bleeding risk calculator links: Precise DAPT: http://www.precisedaptscore.com/predapt/; Academic Research Consortium High Bleeding Risk evaluator: https://www.cerc-europe.org/arc-hbr-high-bleeding-risk-evaluator/.

Abbreviations: ACS = acute coronary syndrome (i.e., NSTE-ACS or STEMI); BMS = bare metal stent; BARC = Bleeding Academic Research Consortium; CABG = coronary artery bypass graft; CAD = coronary artery disease; CoCR-EES = cobalt-chromium-everolimus-eluting stent; CV = cardiovascular; DAPT = dual antiplatelet therapy; DES = drug-eluting stent; MI = myocardial infarction; NSTE-ACS = non-ST-elevation acute coronary syndrome; P2Y12 inhibitor = clopidogrel, prasugrel, or ticagrelor; PCI = percutaneous coronary intervention; STEMI = ST-elevation MI; TIA = transient ischemic attack.

Levels of Evidence

In accordance with our goal of providing Evidence-Based information, we are citing the **LEVEL OF EVIDENCE** for the clinical recommendations we publish.

Level	Definition	Study Quality
A	Good-quality patient-oriented evidence.*	1. High-quality randomized controlled trial (RCT) 2. Systematic review (SR)/Meta-analysis of RCTs with consistent findings 3. All-or-none study
B	Inconsistent or limited-quality patient-oriented evidence.*	1. Lower-quality RCT 2. SR/Meta-analysis with low-quality clinical trials or of studies with inconsistent findings 3. Cohort study 4. Case control study
C	Consensus; usual practice; expert opinion; disease-oriented evidence (e.g., physiologic or surrogate endpoints); case series for studies of diagnosis, treatment, prevention, or screening.	

***Outcomes that matter to patients** (e.g., morbidity, mortality, symptom improvement, quality of life).

[Adapted from Ebell MH, Siwek J, Weiss BD, et al. Strength of Recommendation Taxonomy (SORT): a patient-centered approach to grading evidence in the medical literature. *Am Fam Physician* 2004;69:548-56. https://www.aafp.org/afp/2004/0201/p548.pdf.]

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