Aim
Dual antiplatelet therapy (DAPT) consists of administering two different types of antiplatelet drugs — a P2Y12 inhibitor in combination with acetylsalicylic acid. DAPT helps to reduce the risk of thrombosis and vascular events in patients who have undergone percutaneous coronary intervention (PCI) with stent insertion; however, it also results in an increased bleeding risk.

The objective of this Health Technology Assessment was to evaluate the clinical benefits and harms, as well as the cost-effectiveness, of extended DAPT beyond 12 months compared with the standard DAPT duration (six to 12 months) in clinically relevant subgroups of patients who recently underwent PCI with stenting. Three different P2Y12 inhibitors were considered: clopidogrel, prasugrel, and ticagrelor.

Conclusions and Results
Findings from eight randomized controlled trials involving 25,982 participants suggest that extended DAPT (mostly involving clopidogrel) reduces the risk of myocardial infarction (MI); relative risk [RR], 0.58; 95% confidence interval [CI], 0.48 to 0.70) and stent thrombosis (RR, 0.38; 95% CI, 0.21 to 0.67) but increases the risk of bleeding (Global Use of Strategies to Open Occluded Arteries [GUSTO] moderate bleeding [RR, 1.68; 95% CI, 1.22 to 2.30]; GUSTO moderate or severe bleeding [RR, 1.57; 95% CI, 1.17 to 2.11]).

The economic analysis found that extended DAPT was dominant, with small lifetime incremental benefits (0.0160 quality-adjusted life-years) and savings (C$707), and most benefits occurring after discontinuation of extended DAPT. Patients with prior MI, acute coronary syndrome, no diabetes, or younger than 75 years may benefit most from extended DAPT.

It was concluded that the use of extended DAPT may lead to small lifetime benefits and cost savings. Patient characteristics may influence these results, which suggests the need for careful patient selection for extended DAPT.

Recommendations
The CADTH Canadian Drug Expert Committee (CDEC) recommends that a P2Y12 inhibitor (clopidogrel, prasugrel, or ticagrelor) be reimbursed for use beyond 12 months in combination with acetylsalicylic acid in patients who have undergone PCI with drug-eluting stent insertion. The decision to extend DAPT should account for whether the potential benefits (i.e., reduced risk of thrombotic and vascular events post-PCI) outweigh the risks (i.e., increased bleeding risks) based on individual patient characteristics.

Because evidence comparing the different P2Y12 inhibitors was limited, CDEC further recommends that the selection of which P2Y12 inhibitor (clopidogrel, prasugrel, or ticagrelor) be made at the discretion of the treating physician, based on the individual characteristics and risk profile of each patient.

Methods
CADTH undertook a systematic review of randomized clinical trials in addition to a cost-utility analysis comparing standard-duration (six to 12 months) DAPT with extended-duration (beyond 12 months) DAPT following PCI with stent insertion. Key outcomes were evaluated for all patients who received PCI with stent insertion, as well as for clinically relevant subgroups (i.e., patients who have had a prior MI, those with acute coronary syndrome at presentation, those with diabetes, those who smoke, and those older or younger than 75 years). CDEC then developed recommendations based on the findings from CADTH’s report and consultations with clinical experts and other stakeholder groups.

Further Research or Reviews Required
To further inform clinical and policy decisions, additional research may be warranted to clearly determine whether certain patient subgroups could benefit more from extended DAPT than other subgroups. Further research may also be warranted to determine the comparative clinical effectiveness of the different P2Y12 inhibitors when used for extended DAPT.

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