



## Original Article

# Provision of a DAPT Score to Cardiologists and Extension of Dual Antiplatelet Therapy Beyond 1 Year After ACS: Randomized Substudy of the Prospective Canadian ACS Reflective II Study

Yaron Arbel, MD,<sup>a</sup> Ashish D. Patel, MD,<sup>b,o</sup> Shaun G. Goodman, MD, MSc,<sup>b,c</sup> Mary K. Tan, MSc,<sup>c</sup> Neville Suskin, MBChB, MSc,<sup>d</sup> Robert S. McKelvie, MD, PhD,<sup>d</sup> Andrew L. Mathew, MD,<sup>d,e</sup> Firas Ahmed, MD,<sup>e</sup> Sohrab Lutchmedial, MDCM,<sup>f</sup> Payam Dehghani, MD,<sup>g</sup> Andrea J. Lavoie, MD,<sup>g</sup> Thao Huynh, MD, MSc, PhD,<sup>h</sup> Shahar Lavi, MD,<sup>i</sup> Razi Khan, MD,<sup>j</sup> Andrew T. Yan, MD,<sup>b</sup> Christopher B. Fordyce, MD, MHS, MSc,<sup>k</sup> Michael Heffernan, MD, PhD,<sup>l</sup> Sean Jedrzkiewicz, MD,<sup>l</sup> Mina Madan, MD, MHS,<sup>m</sup> Shaheeda Ahmed, MD,<sup>m</sup> Colin Barry, MD,<sup>f</sup> Jean-Pierre Dery, MD,<sup>n</sup> and Akshay Bagai, MD, MHS;<sup>b</sup> for the Canadian ACS Reflective II

### Investigators

<sup>a</sup> Department of Cardiology, Tel Aviv Medical Center, Tel Aviv, affiliated to the Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel; <sup>b</sup> St. Michael's Hospital, University of Toronto, Toronto, Ontario, Canada; <sup>c</sup> Canadian Heart Research Centre, Toronto, Ontario, Canada; <sup>d</sup> St Joseph's Health Care London, Western University, London, Ontario, Canada; <sup>e</sup> London Health Sciences Centre, London, Ontario, Canada; <sup>f</sup> New Brunswick Heart Centre, Saint John, New Brunswick, Canada; <sup>g</sup> Saskatchewan Health Authority, University of Saskatchewan, Regina, Saskatchewan, Canada; <sup>h</sup> McGill University Health Centre, Montreal, Québec, Canada; <sup>i</sup> University Hospital, Western University, London, Ontario, Canada; <sup>j</sup> Royal Columbian Hospital, New Westminster, British Columbia, Canada; <sup>k</sup> Division of Cardiology, University of British Columbia, Vancouver, British Columbia, Canada; <sup>l</sup> Halton Healthcare, Oakville Hospital, Oakville, Ontario, Canada; <sup>m</sup> Schulich Heart Centre, Sunnybrook Health Sciences Centre, University of Toronto, Toronto, Ontario, Canada; <sup>n</sup> Institut Universitaire de Cardiologie et de Pneumologie de Québec, Québec City, Québec, Canada; <sup>o</sup> Mackenzie Health, Richmond Hill, Ontario, Canada

### ABSTRACT

**Background:** Extension of dual antiplatelet therapy (DAPT) beyond 1 year after acute coronary syndrome is associated with a reduction in ischemic events but also increased bleeding. The DAPT score identifies individuals likely to derive overall benefit or harm from DAPT extension. We sought to evaluate the impact of providing the DAPT score to treating physicians on the decision to extend DAPT beyond 1 year after non–ST-segment elevation myocardial infarction.

### RÉSUMÉ

**Introduction :** La prolongation de la bithérapie antiplaquettaire au-delà d'un an après un syndrome coronarien aigu est associée à la réduction des accidents ischémiques, mais aussi à l'augmentation des hémorragies. Le score de bithérapie antiplaquettaire permet de déterminer les individus susceptibles d'obtenir des avantages globaux ou des inconvénients de la prolongation de la bithérapie antiplaquettaire. Nous avons cherché à évaluer les répercussions de

Guidelines for the treatment of patients with non–ST-segment elevation myocardial infarction (NSTEMI), including those undergoing percutaneous coronary

intervention (PCI), recommend dual antiplatelet therapy (DAPT) with aspirin and a P2Y<sub>12</sub> receptor inhibitor for the first 12 months to reduce the incidence of coronary ischemic events, including reinfarction and stent thrombosis.<sup>1,2</sup> Prior studies and meta-analyses suggest that a longer duration of DAPT beyond 12 months after an acute coronary syndrome is associated with reduction in ischemic coronary events but also with increased bleeding events.<sup>3-5</sup> Thus, the decision to extend DAPT beyond 1 year requires individualization, balancing patients' risks of ischemic events and bleeding.<sup>6-8</sup> Various clinical scores have exist to help physicians decide on whether the individual patient's benefit of extended DAPT

Received for publication June 15, 2021. Accepted July 18, 2021.

**Ethics Statement:** Research reported has adhered to the relevant ethical guidelines.

Corresponding author: Dr Akshay Bagai, Terrence Donnelly Heart Centre, St Michael's Hospital, 30 Bond St, Toronto, Ontario Canada. Tel.: +1-416-864-5783; fax: +1-416-864-5989.

E-mail: [akshay.bagai@unityhealth.to](mailto:akshay.bagai@unityhealth.to)

See page 1469 for disclosure information.

**Methods:** Moderate to high-risk non–ST-segment elevation myocardial infarction patients were enrolled from July 2016 to May 2018 in 13 Canadian hospitals by 52 cardiologists. Participating cardiologists were randomly assigned 1:1 to receive their individual patients' DAPT scores before the 1-year follow-up visit vs not receiving their patients' DAPT scores. Rates of DAPT extension were compared among the randomized groups.

**Results:** At 1 year, 370 of the 585 (63.2%) patients discharged on DAPT were receiving DAPT. Among patients on DAPT at 1 year, the median (25th, 75th percentile) DAPT score was 2 (1,3). DAPT was extended beyond 1 year in 36.2% randomly assigned to provision of DAPT score vs 35.7% in the control group ( $P = 0.93$ ). In the subgroup of patients with DAPT score  $\geq 2$ , DAPT extension was 49.5% in the DAPT score provision arm vs 40.4% in the control arm ( $P = 0.22$ ); among patients with DAPT score  $< 2$ , DAPT termination was 78.6% in the DAPT score provision arm vs 70.6% in the control arm ( $P = 0.26$ ) ( $P$  value for interaction = 0.1).

**Conclusions:** In this exploratory randomized trial, provision of the DAPT score to treating physicians had no impact on the duration of DAPT treatment beyond 1 year.

duration outweighs their bleeding risk. The DAPT score was the first such risk score, incorporating clinical and angiographic variables, and has been validated externally and recommended by the guidelines.<sup>9-13</sup> The Canadian Acute Coronary Syndrome (ACS) Reflective II Program was designed to determine the rates of DAPT at 1 year post-NSTEMI in real-world Canadian practice. We report the contemporary rates of DAPT use at 1 year in a moderate- to high-risk NSTEMI population and evaluate whether the rates of DAPT extension beyond 1 year can be affected by provision of DAPT score to treating physicians.

## Methods

### Data source and study population

The Canadian ACS Reflective II program was a prospective quality enhancement registry of NSTEMI patients enrolled in 13 hospitals by 52 cardiologists from July 2016 to May 2018.<sup>14</sup> Patient inclusion criteria were age  $\geq 18$  years, hospitalization with NSTEMI (positive biomarker[s] for myocardial necrosis), plus 1 indicator of moderate to high risk ( $\geq 1$  of the following criteria: ischemic ST-segment changes; age  $\geq 60$  years; previous myocardial infarction [MI] or coronary artery bypass grafting [CABG]; coronary artery disease with stenosis  $\geq 50\%$  in  $\geq 2$

l'obtention du score de bithérapie antiplaquettaire par les médecins traitants sur la décision quant à la prolongation de la bithérapie antiplaquettaire au-delà d'un an après l'infarctus du myocarde sans élévation du segment ST.

**Méthodes :** De juillet 2016 à mai 2018, 52 cardiologues de 13 hôpitaux du Canada ont inscrit des patients exposés à un risque modéré à élevé d'infarctus du myocarde sans élévation du segment ST. Nous avons réparti de façon aléatoire selon un rapport 1:1 les cardiologues participants qui recevaient les scores de bithérapie antiplaquettaire individuels de leurs patients avant la consultation de suivi après un an vs ceux qui ne recevaient pas les scores de bithérapie antiplaquettaire de leurs patients. Nous avons comparé les taux de prolongation de la bithérapie antiplaquettaire des groupes répartis de façon aléatoire.

**Résultats :** Après un an, 370 (63,2 %) patients sur 585 qui avaient eu à la sortie de l'hôpital une bithérapie antiplaquettaire recevaient la bithérapie antiplaquettaire. Parmi les patients qui prenaient la bithérapie antiplaquettaire après un an, le score médian de bithérapie antiplaquettaire (25<sup>e</sup>, 75<sup>e</sup> percentiles) était de 2 (1, 3). La bithérapie antiplaquettaire était prolongée au-delà d'un an chez 36,2 % des patients répartis de façon aléatoire qui avaient un score de bithérapie antiplaquettaire vs 35,7 % dans le groupe témoin ( $P = 0,93$ ). Dans le sous-groupe de patients qui avaient un score de bithérapie antiplaquettaire  $\geq 2$ , la prolongation de la bithérapie antiplaquettaire était de 49,5 % dans le bras qui avait un score de bithérapie antiplaquettaire vs 40,4 % dans le bras témoin ( $P = 0,22$ ); parmi les patients qui avaient un score de bithérapie antiplaquettaire  $< 2$ , la cessation de la bithérapie antiplaquettaire était de 78,6 % dans le bras qui avait un score de bithérapie antiplaquettaire vs 70,6 % dans le bras témoin ( $P = 0,26$ ) (valeur  $P$  pour l'interaction = 0,1).

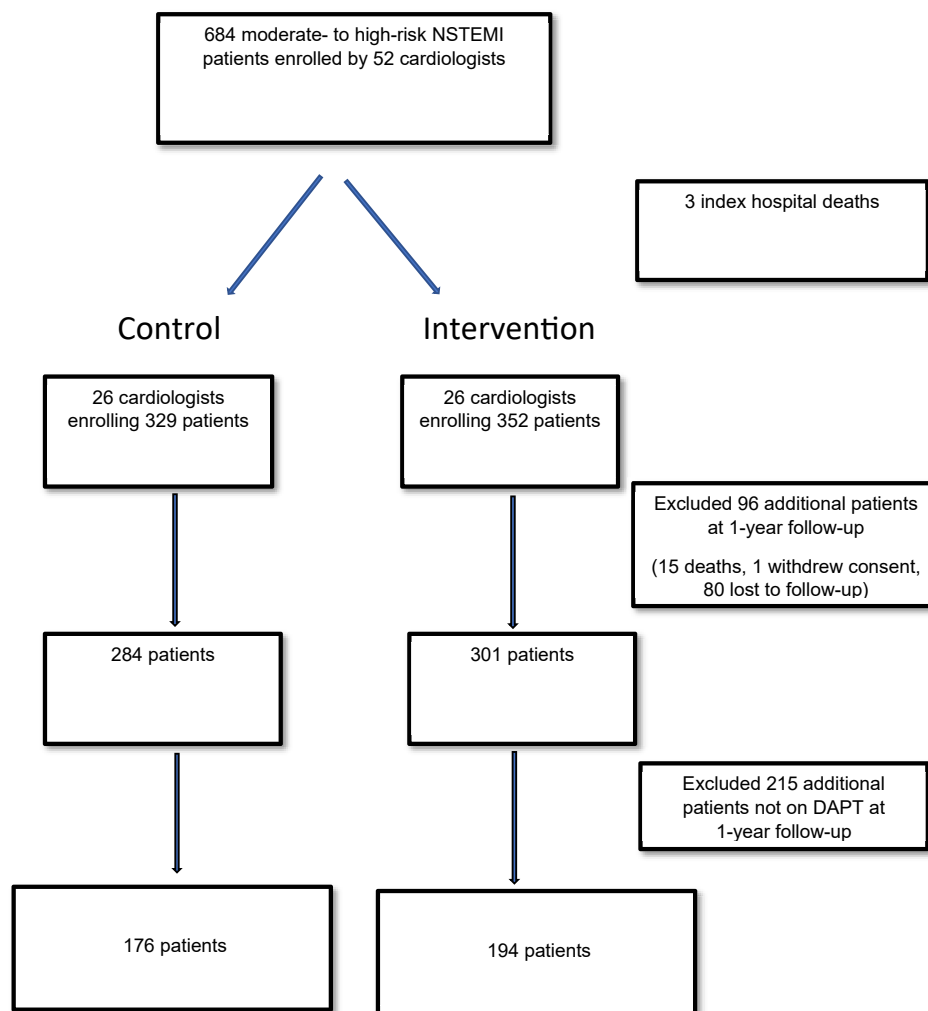
**Conclusions :** Dans cet essai exploratoire à répartition aléatoire, l'obtention du score de la bithérapie antiplaquettaire par les médecins traitants n'a pas engendré de répercussions sur la durée de la bithérapie antiplaquettaire au-delà d'un an.

vessels; previous ischemic stroke, transient ischemic attack, carotid stenosis of  $\geq 50\%$ , or cerebral revascularization; diabetes mellitus; peripheral arterial disease; or chronic renal dysfunction with creatinine clearance  $< 60$  mL/min/1.73m<sup>2</sup>). Exclusion criteria included STEMI, unstable angina (ie, ACS without positive cardiac biomarkers for myocardial necrosis), and ongoing participation in a research study in which the oral antithrombotic therapy (antiplatelet and/or anticoagulant) was unknown or not approved for clinical use. All treatment decisions during index hospitalization and postdischarge were made by the treating physicians.

We collected data on demographics, key presenting symptoms, clinical diagnosis, prior medical history, in-hospital management (including medical and revascularization therapies), in-hospital and discharge pharmacotherapies, and 1-year clinical outcomes and treatment. Patients provided informed consent, and each hospital research ethics board provided study approval.

### DAPT score

The DAPT score is composed of clinical and angiographic variables. The following variables are given 1 point each: myocardial infarction at presentation, prior myocardial infarction or PCI, diabetes mellitus, stent diameter  $< 3$  mm, active smoking, and paclitaxel-eluting stent; 2 points each for



**Figure 1.** Cohort flowchart. DAPT, dual antiplatelet therapy; NSTEMI, non–ST-segment elevation myocardial infarction.

history of congestive heart failure/low ejection fraction and saphenous vein graft intervention; -1 point for age 65 to < 75 years; and -2 points for age  $\geq 75$  years.<sup>6</sup> The sum of all variables is calculated, and a DAPT score of  $\geq 2$  is considered beneficial to extend DAPT for 18 months (beyond the initial 12 months) with a number needed to treat to prevent ischemic events of 34 and number needed to harm to cause bleeding of 272. Extension of DAPT for 18 months beyond the initial 12 months in patients with DAPT score < 2 has a number needed to harm of 64 and a number needed to treat of 153, favoring cessation of DAPT at 12 months.<sup>6</sup>

### Study intervention

This was an exploratory cluster-randomized study, and the treating cardiologists were randomly assigned to 1 of 2 groups: (1) DAPT score provided a month before the 1-year visit (intervention group) for each of their enrolled patients and (2) DAPT score not provided before the 1-year visit (control group) for their enrolled patients. Participating cardiologists were randomly assigned in a 1:1 ratio, regardless of the number of patients enrolled by the physician and location of

their treating hospital (Fig. 1). Physicians were randomly assigned after all their patients were enrolled. All participating cardiologists were included, and the intervention (DAPT score provided vs not prior to the 1-year patient follow-up visit) was applied to all of their enrolled patients on DAPT at 1 year.

### Statistical analysis

Among patients on DAPT at 1 year, we compared the proportion of patients with DAPT extension beyond 1 year between patients whose physicians received the DAPT score and those whose physicians did not receive the DAPT score. The decision for extending DAPT beyond 1 year was also compared separately among those with DAPT score  $\geq 2$  vs < 2. Categorical variables were summarized as percentages and were compared using  $\chi^2$  test, and continuous variables were reported as mean and standard deviation or median and interquartile range and were compared using *t* test or Kruskal-Wallis test, as appropriate.

The study was a cluster-randomized trial design, as the unit of randomization is physicians, whereas the outcomes pertain

**Table 1. Baseline characteristics**

	Total patients (n = 370)	No Provision of DAPT score (n = 176)	Provision of DAPT score (n = 194)	P value
Demographics				
Age, y*	67 (58, 74)	66 (58, 74)	67 (60, 74)	0.39
Age group				0.98
≥ 75	88 (23.8)	41 (23.3)	47 (24.2)	
65-74	126 (34.1)	60 (34.1)	66 (34.0)	
< 65	156 (42.2)	75 (42.6)	81 (41.8)	
Sex, male	255 (68.9)	117 (66.5)	138 (71.1)	0.33
Weight, kg*	83 (70, 94)	82 (71, 94)	84 (70, 94)	0.86
Medical history				
Diabetes	114 (30.8)	55 (31.3)	59 (30.4)	0.86
Hypertension	241 (65.3)	110 (62.5)	131 (67.9)	0.28
Dyslipidemia	213 (57.7)	102 (58.0)	111 (57.5)	0.93
Smoking, current or past	208 (56.2)	105 (59.7)	103 (53.1)	0.20
Prior myocardial infarction	79 (21.4)	41 (23.3)	38 (19.6)	0.38
Prior percutaneous coronary intervention	68 (18.4)	33 (18.8)	35 (18.0)	0.86
Prior CABG	34 (9.2)	20 (11.4)	14 (7.2)	0.17
Prior heart failure	14 (3.8)	6 (3.4)	8 (4.1)	0.72
Peripheral arterial disease	19 (5.1)	10 (5.7)	9 (4.6)	0.65
Atrial fibrillation	11 (3.0)	6 (3.4)	5 (2.6)	0.64
Prior stroke	21 (5.7)	8 (4.5)	13 (6.7)	0.37
Presentation characteristics				
Heart rate, bpm*	76 (66, 87)	76 (66, 86)	75 (66, 87)	0.88
Systolic blood pressure, mmHg*	140 (121, 160)	137 (120, 157)	144 (122, 163)	0.28
Killip class > 1	33 (9.0)	12 (6.9)	21 (11.0)	0.17
Cardiac arrest	5 (1.4)	2 (1.1)	3 (1.6)	1.00
ECG on presentation				
Transient ST-segment elevation	32 (8.6)	9 (5.1)	23 (11.9)	0.021
ST-segment depression	90 (24.3)	45 (25.6)	45 (23.2)	0.60
T wave inversion	80 (21.6)	43 (24.4)	37 (19.1)	0.21
Nonspecific ST and T wave abnormality	94 (25.4)	39 (22.2)	55 (28.4)	0.17
Normal (no ST segment or T wave abnormality)	104 (28.1)	58 (33.0)	46 (23.7)	0.048

CABG, coronary artery bypass grafting; DAPT, dual antiplatelet therapy; ECG, electrocardiogram.

\* Median (25th, 75th) percentiles; all others are presented as N (%).

to the patient level. Because patients enrolled within a given hospital could be more similar than patients across different hospitals, and at a hospital level physicians may tend to practice in a similar manner, we performed multilevel logistic regression models to assess for factors independently associated with DAPT extension beyond 1 year. The generalized estimating equations method with an exchangeable working correlation structure was used to account for the clustering effects of the correlated data with physicians and patients within the hospitals. The following variables were included: feedback groups, DAPT score, age, sex, diabetes, hypertension, history of smoking, prior MI, prior PCI, prior CABG, prior heart failure, atrial fibrillation, prior stroke, chronic kidney disease (defined as estimated glomerular filtration rate < 60 mL/min/1.73m<sup>2</sup>), peripheral arterial disease, PCI during index hospitalization, CABG during index hospitalization, PCI after discharge within 1 year of follow-up, ischemic events at baseline/follow-up, bleeding at baseline/follow-up, and oral anticoagulant use at baseline/follow-up. Adjusted odds ratio with 95% confidence intervals are presented. The randomization of treating cardiologists was added to the protocol after the observational component of the study had already begun, but before the first patient 1-year follow-up. Thus, the randomized component was exploratory and without a formal sample size estimation.

We undertook a post hoc sensitivity analysis to evaluate the impact of the intervention in patients who did not have atrial

fibrillation and were not receiving an oral anticoagulant. Statistical analyses were conducted using SAS 9.4 (SAS Institute, Cary, NC) program. Two-sided *P* values < 0.05 were considered statistically significant.

## Results

Among the 684 patients enrolled in the study, 3 patients died in hospital. At 1 year of follow-up, 15 additional patients (2.2%) had died, 1 (0.1%) withdrew consent, and 80 patients (11.7%) did not have follow-up data. Among the remaining 585 patients, the 1-year incidence of reinfarction was 2.4%, stent thrombosis 0.7%, stroke 0.2%, major bleeding 1.2%, PCI 4.1%, and CABG 1.2%; 370 (63.2%) were still on DAPT at 1 year (35.4% clopidogrel, 63.5% ticagrelor, 1.1% prasugrel). Twenty-six cardiologists treating 194 patients were randomly assigned to the intervention group, and 26 cardiologists treating 176 patients were randomly assigned to the control group (Fig. 1). Patients in both groups were generally similar in their clinical characteristics (Table 1) as well as in-hospital procedures and events (Table 2), with the exception of more prevalent transient ST-elevation in the intervention group and use of ticagrelor at hospital discharge, which was greater in the control group (Table 2). During follow-up, there was no difference in ischemic or bleeding events or medication changes between the 2 groups (Table 2).

**Table 2. Index-hospital management and postdischarge events**

	Total (n = 370)	No provision of DAPT score (n = 176)	Provision of DAPT score (n = 194)	P value
<b>In-hospital procedures</b>				
Coronary angiography	317 (85.7)	141 (80.1)	176 (90.7)	0.0036
Percutaneous coronary intervention	302 (81.6)	149 (84.7)	153 (78.9)	0.15
Coronary artery bypass grafting	19 (5.1)	9 (5.1)	10 (5.2)	0.99
Left ventricular ejection fraction < 30%	11 (3.0)	6 (3.4)	5 (2.6)	0.54
<b>Drug-eluting stent*</b>				
Bare metal stent*	291 (96.4)	145 (97.3)	146 (95.4)	0.38
Smallest stent diameter, < 3 mm*	6 (2.0)	2 (1.3)	4 (2.6)	0.68
Vein graft intervention performed*	164 (54.8)	81 (54.4)	83 (55.3)	0.87
Vein graft intervention performed*	6 (2.0)	5 (3.4)	1 (0.7)	0.12
<b>Index-hospitalization events</b>				
Reinfarction	0	0	0	—
Stent thrombosis	2 (0.5)	2 (1.1)	0	0.23
Heart failure	16 (4.3)	6 (3.4)	10 (5.2)	0.41
Stroke	2 (0.5)	0	2 (1.0)	0.50
Major bleeding	2 (0.5)	1 (0.6)	1 (0.5)	1.00
Blood transfusion	6 (1.6)	3 (1.7)	3 (1.5)	1.00
Any ischemic event <sup>†</sup>	2 (1.1)	2 (1.1)	2 (1.0)	1.00
Bleeding event <sup>‡</sup>	6 (1.6)	3 (1.7)	3 (1.7)	1.00
Reinfarction, stent thrombosis, heart failure, stroke or major bleeding	21 (5.7)	9 (5.1)	12 (6.2)	0.66
<b>Medications at index hospital discharge/transfer</b>				
Ticagrelor	235 (63.5)	129 (73.3)	106 (54.6)	0.0002
Prasugrel	4 (1.1)	2 (1.1)	2 (1.0)	1.00
Clopidogrel	131 (35.4)	45 (25.6)	86 (44.3)	0.0002
Oral anticoagulant	13 (3.5)	7 (4.0)	6 (3.1)	0.64
<b>Events post discharge during 1-year follow-up</b>				
Any ischemic event during index hospitalization or during 1-year follow-up <sup>1</sup>	13 (3.5)	7 (4.0)	6 (3.1)	0.64
Bleeding event during index hospitalization or during 1-year follow-up <sup>2</sup>	10 (2.7)	4 (2.3)	6 (3.1)	0.75
Oral anticoagulant use at index hospital discharge or at 1-year follow-up	15 (4.1)	8 (4.6)	7 (3.6)	0.65

All data presented as n (%).

DAPT, dual antiplatelet therapy.

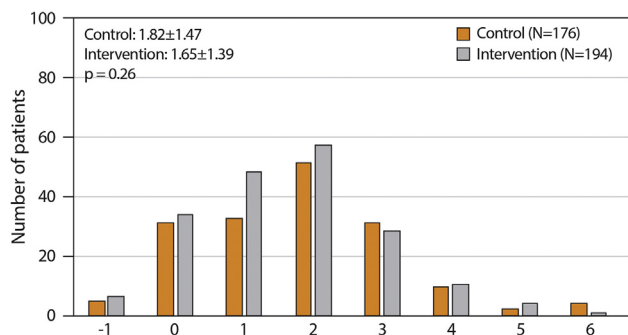
\* Among patients undergoing percutaneous coronary intervention.

<sup>†</sup> Any ischemic event includes myocardial reinfarction, stroke, or stent thrombosis.

<sup>‡</sup> Bleeding event includes major bleeding or blood transfusion.

### DAPT score and treatment decisions for extension of DAPT beyond 1 year

The DAPT scores were similar in the control and interventional groups ( $1.8 \pm 1.5$  vs  $1.7 \pm 1.4$ ;  $P = 0.26$ ; Fig. 2).



**Figure 2.** Distribution of dual antiplatelet therapy (DAPT) scores.

DAPT was extended beyond 1 year in 35.9%; extension of DAPT beyond 1 year was 36.2% in the interventional group vs 35.7% in the control group ( $P = 0.93$ ; Table 3). In the subgroup of patients with DAPT score  $\geq 2$ , DAPT extension beyond 1 year was numerically but not statistically greater in the intervention group (49.5% vs 40.4%;  $P = 0.22$ ). In the subgroup analysis of patients with DAPT score  $< 2$ , discontinuation of DAPT was numerically but not statistically greater in the intervention group (78.6% vs 70.6%;  $P = 0.26$ ;  $P$  value for interaction = 0.1; Fig. 3). After excluding patients with prior atrial fibrillation and/or treatment with oral anticoagulation at discharge ( $n = 20$ ), the frequency of DAPT extension was similar in the interventional and control arms (35.6% vs 35.3%;  $P = 0.96$ ). After multivariable adjustment, PCI within 1 year after discharge was associated with DAPT extension beyond 1 year (adjusted odds ratio, 4.50; 95% confidence interval, 1.07-18.93;  $P = 0.04$ ; Table 4). The DAPT score itself or the provision of the DAPT score to treating cardiologists was not associated with DAPT extension

**Table 3. Decision to continue DAPT beyond 1 year**

	Total patients (n = 370)	No Provision of DAPT score (N = 176)	Provision of DAPT score (N = 194)	P value
DAPT score				0.39
≥ 2	208 (56.2)	103 (58.5)	105 (54.1)	
< 2	162 (43.8)	73 (41.5)	89 (45.9)	
Plan for DAPT beyond 1 year				0.93
Discontinue treatment	214/334 (64.1)	101/157 (64.3)	113/177 (63.8)	
Continue treatment	120/334 (35.9)	56/157 (35.7)	64/177 (36.2)	
Among patients with DAPT score ≥ 2				0.22
Discontinue treatment	100/182 (55.0)	53/89 (59.6)	47/93 (50.5)	
Continue treatment	82/182 (45.0)	36/89 (40.4)	46/93 (49.5)	
Among patients with DAPT score < 2				0.26
Discontinue treatment	114/152 (75.0)	48/68 (70.6)	66/84 (78.6)	
Continue treatment	38/152 (25.0)	20/68 (29.4)	18/84 (21.4)	

Data presented as n (%).

DAPT, dual antiplatelet therapy.

beyond 1 year. PCI after discharge was no longer associated with DAPT extension after excluding patients with atrial fibrillation and/or those treated with oral anticoagulant.

## Discussion

In a contemporary multicenter cohort study of moderate- to high-risk NSTEMI patients in Canada, providing a patient-specific DAPT score to treating physicians before their 1-year follow-up did not change the overall rates of DAPT extension beyond 1 year. To the best of our knowledge, this study is the first to report on the randomized provision of DAPT scores and its potential impact on DAPT extension.

Current Canadian antiplatelet guidelines recommend DAPT with aspirin and a P2Y<sub>12</sub> receptor inhibitor for the first 12 months after MI and to consider extending therapy in patients with high ischemic risk and low bleeding risk.<sup>2</sup> These guidelines are based on prior studies that reported reduction in ischemic events with DAPT extension beyond 1 year, albeit, with an increase in bleeding events. The DAPT study randomly selected 9,961 patients with a drug-eluting stent 1 year after PCI to an additional 18 months of DAPT (total of 30 months) vs cessation of DAPT with 18 months of placebo. Extended DAPT was associated with reduced risk of stent thrombosis and major cardiovascular and cerebrovascular events but with an increased risk of bleeding and all-cause death.<sup>4</sup> Meta-analyses of additional randomized studies found that extended DAPT therapy (up to 30-36 months) was associated with reduced long-term risk of stent thrombosis and recurrent myocardial infarction.<sup>5,15</sup> Unsurprisingly, these ischemic benefits with prolonged DAPT use were associated

with increased risk of bleeding. The DAPT score was developed to better discriminate patients that might derive ischemic benefit from DAPT extension beyond 1 year without increased bleeding risk.<sup>9,10</sup> The overall accuracy of the DAPT score is, however, limited with an area-under-the-curve of 0.7 in the original study<sup>9</sup> and 0.58 in a recent publication from a real-world registry.<sup>12</sup> This finding, therefore, may primarily explain the low impact of the provision of DAPT score on DAPT extension in this study.

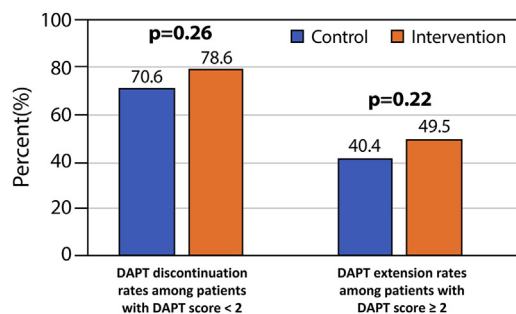
**Table 4. Factors associated with DAPT extension beyond 1 year**

Variables	OR (95% CI)	P value
Provision of DAPT score (vs no provision of DAPT score)	1.25 (0.56, 2.80)	0.59
DAPT score (per unit increase)	0.95 (0.76, 1.18)	0.62
Age ≥ 75 vs < 65 years	0.64 (0.28, 1.47)	0.30
Age 65-74 vs < 65 years	0.58 (0.31, 1.09)	0.09
Female sex	1.22 (0.69-2.13)	0.49
Diabetes	1.21 (0.74-1.99)	0.45
Hypertension	0.99 (0.71-1.37)	0.93
Current or past smoker	1.02 (0.68-1.53)	0.93
Prior myocardial infarction	0.80 (0.43-1.48)	0.48
Prior PCI	1.73 (0.94-3.18)	0.08
Prior CABG	1.26 (0.62-2.56)	0.52
Prior stroke	1.46 (0.52-4.11)	0.47
Prior heart failure	0.51 (0.17-1.57)	0.24
Atrial fibrillation	2.15 (0.83-5.55)	0.11
Chronic kidney disease (eGFR < 60 mL/min/1.73m <sup>2</sup> )	1.15 (0.68-1.94)	0.61
Peripheral arterial disease	0.88 (0.26-3.05)	0.85
CABG during index hospitalization	0.95 (0.23-3.91)	0.95
PCI during index hospitalization	0.76 (0.39-1.50)	0.43
PCI post discharge within 1-year follow-up	4.50 (1.07-18.93)	0.04
Any ischemic event during index hospitalization or during 1-year follow-up*	5.08 (0.45-57.24)	0.19
Bleeding event during index hospitalization or during 1-year follow-up†	0.79 (0.22-2.82)	0.72
Oral anticoagulant use at index hospital discharge or at 1-year follow-up	1.08 (0.45-2.60)	0.86

CABG, coronary artery bypass grafting; CI, confidence interval; DAPT, dual antiplatelet therapy; eGFR, estimated glomerular filtration rate; OR, odds ratio; PCI, percutaneous coronary intervention.

\* Any ischemic event includes myocardial reinfarction, stroke, or stent thrombosis.

† Bleeding event includes major bleeding or blood transfusion.



**Figure 3.** Dual antiplatelet therapy (DAPT) extension/discontinuation rates.

The availability of the DAPT score did not result in universal or large influences in extension of DAPT. There may be several reasons for this finding. The accuracy characteristics of the DAPT score maybe perceived to be less than ideal, and it is possible that the physicians provided with patient-specific DAPT scores chose not to use this information. Secondly, the decision to extend or discontinue DAPT may have been influenced significantly by nuisance bleeding, information not captured in this study. Furthermore, despite the apparent benefits of extending DAPT post-MI, even when provided with estimated risk, physician inertia and patient preference may overwhelm other considerations for DAPT extension. Another consideration relates to patient access and drug cost; no provincial formulary in Canada covers long-term or reduced dose ticagrelor. Therefore, even if the treating physician recommended DAPT continuation, financial considerations may have been a barrier to continuation. Our findings are consistent with those of other cohorts in which provision of patient risk estimates and risk scores to physicians has not resulted in increase in optimal therapy. For example, in a primary prevention study in which physicians were randomly assigned to receive a 10-year coronary risk score or not for their individual patients, the intervention did not influence the rates of starting statin in patients with elevated lipids despite their at-risk status.<sup>16</sup>

### Limitations

Several limitations are noteworthy. First, physician participation in the study was voluntary, and patients had to provide informed consent for the use of their data; thus, our findings are not representative of the broader Canadian cardiologist and general NSTEMI population. Second, patients were not consecutively enrolled, in part because it was a requirement for the enrolling physician to be the primary cardiologist caring for the patient during the index hospitalization and as part of routine clinical practice at 1-year follow-up. Third, only 63.2% of patients with available data were on DAPT at 1 year, and as such our exploratory sample size was underpowered to detect a statistically significant difference in DAPT extension rates at 1 year overall and in the subgroup of patients with DAPT score  $\geq 2$  and  $< 2$ . Although we did observe that providing a DAPT score to treating physicians was associated with a numeric increase in DAPT extension among patients with DAPT score  $\geq 2$  and numeric increase in DAPT discontinuation among patients with DAPT score  $< 2$ , these post hoc findings require further assessment in larger, adequately powered trials. Fourth, although physicians were aware of the randomized allocation, randomization allocation was concealed at the patient level. Fifth, reasons for discontinuation of DAPT prior to 1 year and reasons for not following the DAPT score recommendation at 1 year were not collected. Lastly, the DAPT score was derived from a clinical trial cohort using older-generation stents and before the common use of ticagrelor in a NSTEMI population; thus, practicing physicians may question the contemporary relevance and applicability of the DAPT score.

### Conclusion

In Canadian practice, providing DAPT scores to physicians did not affect the overall rates of DAPT extension beyond 1 year.

### Funding sources

The ACS Reflective II was supported by the Canadian Heart Research Centre (CHRC) through an unrestricted investigator-initiated grant from AstraZeneca Canada (Mississauga, ON). The sponsor had no involvement in the study design, data collection, analysis, or interpretation of the data; in the writing of the report; or in the decision to submit the manuscript for publication.

### Disclosures

Y.A. receives speaking/consulting honoraria from Boehringer Ingelheim, Sanofi, Medison, Medtronic, Novartis, and NovoNordisk. S.G.G. receives research grant support (eg, steering committee or data and safety monitoring committee) and/or speaker/consulting honoraria (eg, advisory boards) from Amgen, AstraZeneca, Bayer, Boehringer Ingelheim, Bristol Myers Squibb, CSL Behring, Daiichi-Sankyo/American Regent, Eli Lilly, Esperion, Ferring Pharmaceuticals, GlaxoSmithKline, HLS Therapeutics, Janssen/Johnson & Johnson, Merck, Novartis, Novo Nordisk A/C, Pendopharm, Pfizer, Regeneron, and Sanofi, Servier. S.G.G. also receives salary support/honoraria from the Heart and Stroke Foundation of Ontario/University of Toronto (Polo) Chair, Canadian Heart Research Centre and MD Primer, Canadian VIGOUR Centre, Cleveland Clinic Coordinating Center for Clinical Research, Duke Clinical Research Institute, New York University Clinical Coordinating Centre, and PERFUSE Research Institute. S.L. receives speaking/consulting honoraria from AstraZeneca, Bayer, and Servier. C.G. receives grants and speaking/consulting fees from Bayer and speaking/consulting fees from Novo Nordisk, Boehringer Ingelheim, Sanofi, Pfizer, Amgen, and Novartis. M.M. receives consulting fees from Bayer, Amgen, Sanofi, Bristol Myers Squibb/Pfizer, Novartis, and Pendopharm. M.H. receives Speaking/consulting honoraria and research support from Amgen, AstraZeneca, Bayer, Boehringer Ingelheim, HLS Therapeutics, Bristol Myers Squibb/Pfizer, Novartis, and Servier. S.J. receives research support from AstraZeneca, Bayer, Bristol-MeyersSquibb/Pfizer, Novartis, and Servier. A.B. receives speaking/consulting honoraria (eg, advisory boards) from AstraZeneca, Bayer, Boehringer Ingelheim, HLS Therapeutics, Bristol Myers Squibb/Pfizer, and Servier. The rest of the authors have no conflicts to disclose.

### References

1. Knuuti J, Wijns W, Saraste A, et al. 2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes: The Task Force for the diagnosis and management of chronic coronary syndromes of the European Society of Cardiology (ESC). *Eur Heart J* 2019.
2. Mehta SR, Bainey KR, Cantor WJ, et al. 2018 Canadian Cardiovascular Society/Canadian Association of Interventional Cardiology focused update of the guidelines for the use of antiplatelet therapy. *Can J Cardiol* 2018;34:214-33.
3. Bonaca MP, Bhatt DL, Cohen M, et al. Long-term use of ticagrelor in patients with prior myocardial infarction. *N Engl J Med* 2015;372:1791-800.
4. 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;371:2155-66.

5. Udell JA, Bonaca MP, Collet JP, et al. Long-term dual antiplatelet therapy for secondary prevention of cardiovascular events in the subgroup of patients with previous myocardial infarction: a collaborative meta-analysis of randomized trials. *Eur Heart J* 2016;37:390-9.
6. Costa F, Van Klaveren D, Feres F, et al. Dual antiplatelet therapy duration based on ischemic and bleeding risks after coronary stenting. *J Am Coll Cardiol* 2019;73:741-54.
7. Angoulvant D, Genet T, Ivanov F. Optimizing DAPT duration in high-risk patients after coronary stent implantation: bleeding risk takes it all. *J Am Coll Cardiol* 2019;73:755-7.
8. Elliott J, Kelly SE, Bai Z, et al. Optimal Duration of dual antiplatelet therapy following percutaneous coronary intervention: an umbrella review. *Can J Cardiol* 2019;35:1039-46.
9. Yeh RW, Secemsky EA, Kereiakes DJ, et al. Development and validation of a prediction rule for benefit and harm of dual antiplatelet therapy beyond 1 year after percutaneous coronary intervention. *JAMA* 2016;315:1735-49.
10. Kereiakes DJ, Yeh RW, Massaro JM, et al. DAPT score utility for risk prediction in patients with or without previous myocardial infarction. *J Am Coll Cardiol* 2016;67:2492-502.
11. Witberg G, Zusman O, Yahav D, Perl L, Vaknin-Assa H, Kornowski R. Meta-analysis of studies examining the external validity of the DAPT score. *Eur Heart J Cardiovasc Pharmacother* 2020;6:285-91.
12. Ueda P, Jernberg T, James S, et al. External validation of the DAPT score in a nationwide population. *J Am Coll Cardiol* 2018;72:1069-78.
13. Valgimigli M, Bueno H, Byrne RA, et al. 2017 ESC focused update on dual antiplatelet therapy in coronary artery disease developed in collaboration with EACTS: The Task Force for dual antiplatelet therapy in coronary artery disease of the European Society of Cardiology (ESC) and of the European Association for Cardio-Thoracic Surgery (EACTS). *Eur Heart J* 2018;39:213-60.
14. Patel A, Goodman SG, Tan M, et al. Contemporary use of guideline-based higher potency P2Y12 receptor inhibitor therapy in patients with moderate-to-high risk non-ST-segment elevation myocardial infarction: Results from the Canadian ACS reflective II cross-sectional study. *Clin Cardiol* 2021;44:839-47.
15. Palmerini T, Benedetto U, Bacchi-Reggiani L, et al. Mortality in patients treated with extended duration dual antiplatelet therapy after drug-eluting stent implantation: a pairwise and Bayesian network meta-analysis of randomised trials. *Lancet (London, England)* 2015;385:2371-82.
16. Jacobson TA, Gutkin SW, Harper CR. Effects of a global risk educational tool on primary coronary prevention: the Atherosclerosis Assessment Via Total Risk (AVIATOR) study. *Curr Med Res Opin* 2006;22:1065-73.