A systematic review of the studies that evaluate the performance of the DAPT score

Chun Shing Kwok1,2 | Chun Wai Wong1,2 | Vinayak Nagaraja1,2 | Mamas A. Mamas1,2

1Keele Cardiovascular Research Group, Keele University, Stoke-on-Trent, UK
2Department of Cardiology, Royal Stoke University Hospital, Stoke-on-Trent, UK

Correspondence
Chun Shing Kwok, Keele Cardiovascular Research Group, Keele University, Stoke-on-Trent, UK.
Email: shingkwok@doctors.org.uk

Funding Information
The PhD tuition of CSK is funded by Biosensors International. No extramural funding was used to support this work.

Abstract

Background: The Dual Antiplatelet Therapy (DAPT) score was derived to determine which patients may benefit from prolonged DAPT therapy after 12 months based on the balance between ischaemic and bleeding events. Several studies have attempted to validate the score with inconsistent findings.

Methods: We conducted a systematic review of the studies that evaluated the DAPT score in PCI populations. A search was performed on MEDLINE and EMBASE and two independent reviewers reviewed the search results for study inclusion and extracted data from studies which met the inclusion criteria. Data are presented in tables and narrative synthesis was performed.

Results: A total of 13 studies were included in this review. The study designs included post hoc analysis of randomised trials, prospective cohorts, retrospective cohorts and a case-control study. In the derivation/validation study, the c-statistic for ischaemic and bleeding outcomes were 0.64/0.70 and 0.68/0.64, respectively. Among the validation studies, the C-statistics for composite outcomes ranged from 0.53 to 0.71 for ischaemic outcomes and 0.49 to 0.71 for bleeding outcomes. Only one study randomised patients with high DAPT score to different combinations of antiplatelet after 1 year of DAPT and found that continuation of DAPT was associated with fewer deaths because of myocardial infarction, but more bleeding.

Conclusions: While not designed for this purpose many studies have shown that the DAPT score has modest predictive value for ischaemic and bleeding outcomes. A prospective randomised controlled trial is needed to evaluate the clinical benefits of utilising the DAPT score in guiding continued DAPT therapy beyond 1 year.

1 | INTRODUCTION

Coronary revascularisation by percutaneous coronary intervention (PCI) requires a period of treatment with dual antiplatelet therapy (DAPT). DAPT is necessary to reduce stent thrombosis when the stent has not completely endothelialised,1 but prolonged antiplatelet therapy increases the propensity to bleed. While there is recent evidence that ≤6 months of DAPT therapy could be considered for most patients with DES,2 there is a population who may benefit from prolonged DAPT therapy as secondary prevention of ischaemic events. In order to better characterise the ideal duration of DAPT therapy several studies have been conducted.3-7 The DAPT trial was one of these studies which randomised patients to 12 or 30 months of DAPT therapy after DES4 and the authors have subsequently derived a DAPT score based on the trial results.8

This is an open access article under the terms of the Creative Commons Attribution NonCommercial License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited and is not used for commercial purposes.

© 2020 The Authors. International Journal of Clinical Practice published by John Wiley & Sons Ltd
The DAPT score was designed to determine whether patients would benefit from continuation of DAPT therapy beyond 12 months based on the balance between ischaemic and bleeding risk. It considers nine variables: age, cigarette smoking, diabetes mellitus, myocardial infarction at presentation, prior PCI or myocardial infarction, paclitaxel-eluting stent, stent diameter <3 mm, congestive heart failure or left ventricular ejection fraction <30% and vein graft stent and was first validated using data from the PROTECT trial which randomised patients to Endeavour vs Cypher drug eluting stent. In the derived model a DAPT score of ≥2 suggests that patients would gain benefit from prolonged DAPT therapy while a low score supports discontinuation of DAPT therapy after 12 months. The model is important because it is described in the ACC/AHA guidelines on the duration of dual antiplatelet therapy and is one of the recommended risk scores for DAPT duration decision making in the European cardiology guidelines.

Since the publication of the DAPT score several studies have been published evaluating its performance in predicting adverse events in several PCI populations and some report that it has modest predictive value, whereas others suggest that it is a poor predictor of adverse events. To better understand the utility of the DAPT score as a risk stratification tool, we conducted a systematic review of the literature.

2 | METHODS

We conducted a systematic review of the literature to evaluated the available published evidence on the DAPT score and clinical outcomes for patients.

This review has the objective to study the evidence evaluating the DAPT score in patients undergoing PCI, and determine whether the DAPT score was evaluated according to the purpose that it was initially developed for. We included published articles evaluating the DAPT score and articles that provided quantitative results showing how classification of patients using the DAPT score was associated with clinical outcomes for patients. Clinical outcomes were defined by mortality, ischaemic events (myocardial infarction and stent thrombosis), bleeding events and composite outcomes such as major adverse cardiovascular events or major adverse cardiac and cerebrovascular events.

A search of MEDLINE and EMBASE was performed in August 2019 with the terms ‘DAPT score’ on OVID. We included published articles evaluating the DAPT score and clinical outcomes for patients. Conference abstracts were excluded because the contents lacked sufficient detail to extract information about study methodology. There was no restriction based on the study design, population evaluated and language of publication. Two independent reviewers (CSK and VN) reviewed the titles and abstract for the search results for potential studies to be included. Full manuscripts of potentially relevant studies were retrieved and two independent reviewers (CSK and CWW) extracted data into tables for each included study. Data were collected on the study design, country of evaluation, year, number of participants, age, percentage of male patients, population and inclusion criteria. Important methodology on timing of follow up, use of DAPT, outcome definitions and results were also collected and summarised in Tables. The results were evaluated by narrative synthesis. We used a modified version of the Ottawa-Newcastle Scale to perform a quality assessment of the included studies.

3 | RESULTS

Our search of MEDLINE and EMBASE yielded 81 results (Figure 1). After detailed review of titles and abstracts and full manuscripts of potentially relevant papers a total of 13 studies were included.

The description of included studies are shown in Table 1. There was one randomised controlled trial and seven post hoc analysis of randomised controlled trials. There were two prospective cohort studies, three retrospective cohort studies and one case-control studies. These were undertaken in the United States, Mexico, Germany, Italy, Sweden, China and Japan. The sample size of the included studies varied from 225 in a small randomised controlled trial to 41 101 patients in the Swedish National Registry. The mean age of participants in the studies ranged from 58.3 to 73 years and majority of patients were men. The studies included were either of populations of ACS or both stable ischaemic coronary disease and ACS.

The study quality assessment is shown in Supplementary Table 1. In general, the cohorts were representative of PCI cohort and ascertainment of exposure (DAPT score) and clinical outcomes were reliable with <10% lost to follow up or missing data.
The studies which validated the DAPT score are shown in Table 2. The data from the ADAPT-DES registry reported that the DAPT score better predicted ischaemic outcomes (myocardial infarction and stent thrombosis, C-statistic 0.71) compared with bleeding outcomes (C-statistic 0.62) at 12-24 months follow up in a cohort where more than half of patients continued DAPT beyond 12 months. The case-control study by Godschalk et al reported a C-statistic of 0.64 for the DAPT score and very late stent thrombosis. Among Chinese patients in the Song et al study, the DAPT score had poor predictive value for major adverse cardiovascular events (stent thrombosis and myocardial infarction, c-statistic 0.53) and major bleeding (c-statistic 0.56). The Harrell’s c-statistic for DAPT score was 0.58 for myocardial infarction and stent thrombosis and 0.49 for fatal or major bleeding from the Swedish National Registry. Considering a high (≥2) DAPT score compared with low (<2) DAPT score there was increased risk of ischaemic events (HR 1.33 95%CI 1.02-1.73, c-statistic 0.591) and reduced risk of bleeding (HR 0.37 95% CI 0.22-0.63, c-statistic 0.794). The derivation study using data from DAPT trial yielded a c-statistic of 0.70 for MI and stent thrombosis and 0.68 for bleeding events. The validation using data from the PROTECT trial yielded c-statistic of 0.64 for both ischaemic and bleeding outcomes. Finally, considering the high and low cutoffs for DAPT score data from the Japanese trials and cohort reported a significant increase in ischaemic outcomes with high DAPT score (1.5% vs 0.9%, P = .002), but not for bleeding (2.1% vs 2.7%, P = .07).

The description of other studies that evaluated the DAPT score is shown in Table 3. Considering data from the ISAR-SAFE trial which only followed up patients to 9 months the DAPT score did not differentiate patients with ischaemic and bleeding events. In addition, continued thienopyridine in patients with high DAPT score was associated with decreased myocardial infarction and stent thrombosis without significantly increasing bleeding while with low DAPT score continued thienopyridine increased bleeding without decreasing myocardial infarction or stent thrombosis. Post hoc analysis of the PRODIGY trial suggests that prolonged DAPT in patients with low DAPT score appears to be associated with harm from greater death and ischaemic events. Finally, another post hoc analysis of the DAPT trial data suggests that among patients with high DAPT score there was significant reductions in MI with continued thienopyridine at both 12-15 and 30-33 months, but less of a reduction for patients with low DAPT score.

**DISCUSSION**

The results of this systematic review are that many of the studies evaluating the DAPT score are not assessing its utility for its intended purpose. Most studies have shown that the performance of the DAPT score for ischaemic and bleeding outcomes are modest at best, but the score was designed for a different purpose of determining if DAPT should be continued beyond 1 year by balancing the net gain/net harm between bleeding and ischaemic risk. In the derivation and validation study, the c-statistic for ischaemic and bleeding outcomes were 0.64/0.70 and 0.68/0.64, respectively. Among the validation studies the C-statistics for composite outcomes ranged from 0.53 to 0.71 for ischaemic outcomes and 0.49 to 0.71 for bleeding outcomes. Validation studies have shown that patients with high DAPT score benefit from prolonged DAPT therapy. Future prospective randomised controlled trials should focus on whether outcomes associated with DAPT regimes guided by DAPT score are superior to those from a one size fits all regime.

An important consideration of the review is that even though the methodology of the DAPT score derivation and validation was clearly reported, many of the subsequently published studies used methods and reporting that differed from the original studies. The original studies reported c-statistics for their model and yet some of the validation type studies reported hazard ratios and event rates.
| Study ID  | Study design       | Countries          | Year       | No. patients | Mean age | % male | Population                                           | Inclusion criteria                                                                 |
|----------|--------------------|--------------------|------------|--------------|----------|--------|-----------------------------------------------------|------------------------------------------------------------------------------------|
| Peng 2019 | RCT                | China              | 2016       | 225          | 57.8     | 58.2   | Patients with ACS at the General Hospital of Western Theater Command of the Chinese PLA | Patients with ACS                                                                  |
| Brener 2018 | Prospective cohort study | USA and Germany    | 2008-2010  | 5397         | Median 59.0 DAPT ≥ 2, 670 DAPT < 2 | 73.7   | ADAPT-DES registry                                  | 1-y event-free survival after DES for stable ischaemic disease and ACS patients |
| Godschalk 2018 | Case-control study | Netherlands        | 2007-2014  | 310          | 58       | 80.3   | Dutch stent thrombosis study                       | Cases of very late stent thrombosis (1 y post implantation) were matched to patients with PCI with stent implantation without stent thrombosis with stable ischaemic disease and ACS patients |
| Long 2018  | Retrospective cohort study | China              | 2012-2013  | 359          | 59.4     | 77.4   | Patients with ACS at Xiangya Hospital in China       | Patients with ACS                                                                  |
| Song 2018  | Retrospective cohort study | China              | 2013       | 6088         | 58.3     | 76.9   | Patients with ACS undergoing emergent of elective PCI at Fu Fai Hospital | Patients with ACS                                                                  |
| Ueda 2018  | Retrospective cohort study | Sweden              | 2006-2014  | 41 101       | 65.8     | 73.4   | Swedish Coronary Angiography and Anioplasty Registry | All PCI procedures in Sweden                                                        |
| Veron-Esquivel 2018 | Prospective cohort study | Mexico              | 2010-2016  | 230          | 63.6     | 78.0   | Patients with AMI at Hospital Espanol in Mexico City | Patients with AMI                                                                  |
| Yoshikawa 2018 | Post hoc analysis of RCT and registry | Japan              | 2005-2011  | 12 223       | 68.5     | 74.8   | CREDO-Kyoto Registry Cohort-2, RESET trial and NEXT trial | Patients with stable ischaemic disease and ACS                                      |
| Harada 2017 | Post hoc analysis of RCT | International 40 study centres | 2008-2014  | 3976         | Median 62 DAPT ≥ 2, 70 DAPT < 2 | 80.6   | ISAR-SAFE trial                                     | Patients with DES randomised to 6 or 12 mo of DAPT with stable ischaemic disease and ACS patients |
| Piccolo 2017 | Post hoc analysis of RCT | Italy               | 2006-2008  | 1970         | 67.9     | 76.7   | PRODIGY trial                                      | Patients with PCI randomised to clopidogrel 6 or 24 mo with stable ischaemic disease and ACS patients |
| Stefanescu 2017 | Post hoc analysis of RCT | International 452 sites in 11 countries | 2009-2014  | 11 648       | 61.3     | 74.9   | DAPT study for derivation                          | Patients with stable ischaemic disease and ACS                                      |
| Kereiakes 2016 | Post hoc analysis of RCT | International 452 sites in 11 countries | 2009-2011  | 11 648       | 61.3     | 74.9   | DAPT study                                         | After 12 mo of DAPT for PCI, patients with AMI and no AMI compared                 |
| Yeh 2016   | Post hoc analysis of trial | International      | 2009-2014  | 11 648       | 61.3     | 74.9   | DAPT study for derivation                          | Patients with stable ischaemic disease and ACS                                      |
| Study ID     | Follow up and exclusion for events within 12 mo | DAPT during follow up | Ischaemia definition | Ischaemia | Bleeding definition | Bleeding |
|--------------|-----------------------------------------------|-----------------------|----------------------|-----------|---------------------|----------|
| Brener 2018  | 12-24 mo with exclusion of death, ischaemic, bleeding events within the first 12 mo | 51.2% continued DAPT, 36.8% monotherapy, 12.0% no antiplatelet, 3.7% warfarin | MI or ST | Sensitivity 57%, specificity 58%, PPV 1.9%, NPV 99%, C-statistic 0.71 | Clinically relevant bleeding meeting major criteria of GUSTO/ACUITY scales and other bleeding requiring medical attention similar to BARC types 2 to 5 | Sensitivity 41%, specificity 57%, PPV 2.2%, NPV 98%, C-statistic 0.62 |
| Godschalk 2018 | 4.7 y, no 1-y event-free period | Unclear | Very late ST | Sensitivity 69.2%, specificity 54.1%, PPV 59.8%, NPV 64.0%, AUC 0.64 | -- | -- |
| Song 2017    | 12-24 mo with exclusion of death, stent thrombosis, myocardial infarction and major bleeding events within 1 y | Patients recommended lifelong aspirin and minimum of 12 mo clopidogrel, but not clear to what extent stayed on DAPT | Coronary thrombotic event defined by definite or probable stent thrombosis or myocardial infarction | Stent thrombosis C-statistic 0.56, coronary thrombotic event C-statistic 0.53, MACE C-statistic 0.53, MACCE C-statistic 0.47 | BARC type 2, 3 or 5 bleed | Major bleeding C-statistic 0.56, any clinically relevant bleeding C-statistic 0.71 |
| Ueda 2018    | 12-30 mo with exclusion of death, stent thrombosis, myocardial infarction, revascularisation, stroke or major bleeding within 12 mo | Unclear | MI or ST, MACCE | Ischaemic prediction model 0.67, MI or stent thrombosis Harrell's c-statistic 0.58, MACE Harrell's c-statistic 0.54 | Fatal or major bleeding or bleeding requiring hospitalisation | Bleeding prediction model 0.67. Fatal or major bleeding Harrell's c-statistic 0.49 or fatal or major bleeding or bleeding requiring hospitalisation Harrell's c-statistic 0.48 |
| Veron-Esquivel 2018 | Median follow up 31 mo, patients must have had 12 mo follow up, but did not exclude for events | Unclear | Ischaemic event | HR 1.33 (1.02-1.73), P = .033, C-statistic 0.591 | Bleeding event | HR 0.37 (0.22-0.63), P < .001, c-statistic 0.794 |
| Yeh 2016 (DAPT study) | 12-30 mo excluded patients with ischaemic and bleeding events | Proportion of patients on DAPT between 12-30 mo was 50.3% | MI or stent thrombosis | C-statistic ischaemic model: 0.70 95% CI 0.68-0.73 | Moderate to severe bleeding by GUSTO criteria. | C-statistic bleeding model: 0.68 95% CI 0.65-0.72. |
| Yeh 2016 (PROTECT) | 12-30 mo excluded patients with ischaemic and bleeding events | Proportion of patients on DAPT therapy at 1 y 87%, 2 y 37% and 3 y 30% | MI or stent thrombosis | C-statistic ischaemic model: 0.64 95% CI 0.58-0.70 | Moderate to severe bleeding by GUSTO criteria | C-statistic bleeding model: 0.64 95% CI 0.55-0.73 |
| Yoshikawa 2017 | 13-36 mo excluded patients with death, ischaemia and bleeding before 13 mo | On DAPT at 13 mo 76.7% (9371/12223) | Composite of MI and definite/probably ST | Ischaemic outcome high DS 1.5% low 0.9%, log-rank P = .002 | Moderate or severe bleeding by GUSTO | High DS vs low DS 2.1% vs 2.7%, log-rank P = .07 |
### TABLE 3 
Other studies that evaluate the DAPT score

| Study ID | Study description | Results | Interpretation |
|----------|-------------------|---------|----------------|
| Peng 2019<sup>21</sup> | All PCI patients high (≥2) DAPT score were randomised to 100 mg aspirin or 100 mg aspirin/clopidogrel 75 mg or aspirin 100 mg/clopidogrel 50 mg after 12 mo of DAPT. | For control, high and low dose clopidogrel, Cardiovascular death: 2.7% vs 1.3% vs 1.3%, P = .78 Death caused by MI: 6.7% vs 0% vs 1.3%, P = .03 Stroke: 1.3% vs 0% vs 0%, P = .37 Stent thrombosis: 5.3% vs 2.7% vs 1.3%, P = .36 Target lesion revascularisation: 5.3% vs 1.3% vs 1.3%, P = .21 Bleeding by BARC type 1:1.3% vs 8.0% vs 2.6%, P = .09 Bleeding by BARC type 2: 2.7% vs 4.0% vs 1.3%, P = .44 Bleeding by BARC type 1 + 2: 2.7% vs 12.0% vs 3.9%, P = .04 Bleeding by BARC type 3: 3.0% vs 1.3% vs 0%, P = .34 | Among patients with high DAPT score use of high doses of aspirin/clopidogrel is associated with fewer deaths because of MI, but more BARC type 1+2 bleeding |
| Long 2018<sup>20</sup> | Retrospective cohort with ACS Risk of triple-vessel disease per 1-point increment of DAPT score | Unadjusted OR 1.43 95% CI 1.19-1.72 Adjusted OR 1.51 95% CI 1.19-1.91 | DAPT score is associated with triple-vessel disease and can be improved with adjustment. |
| Harada 2017<sup>15</sup> | PCI patients with 6 or 12 mo of DAPT who were followed up at 9 mo for ischaemic and bleeding events | High (≥2) vs low (<2) DAPT score: All-cause death, MI, definite ST, stroke: 1.8% vs 1.2%, P = .11 All-cause death, MI: 1.5% vs 0.9%, P = .08 All-cause death: 0.8% vs 0.3%, P = .07 MI: 0.9% vs 0.5%, P = .19 Definite/probable ST: 0.3% vs 0.2%, P = .33 TIMI major/minor bleeding: 0.4% vs 0.6%, P = .49 TIMI major bleeding: 0.3% vs 0.2%, P = .76 | DAPT score does not differentiate ischaemic and bleeding events at 9 mo |
| Piccolo 2017<sup>22</sup> | PCI patients randomised to 6 or 24 mo of DAPT | For high (≥2) vs low (<2) DAPT score: Events for 24 mo DAPT subgroup (n = 987): Death, MI or CVA: 2.4% vs 9.8% Death: 2.3% vs 6.3% Cardiac death: 0.9% vs 2.7% MI: 2.3% vs 3.2% Cardiac death, MI or CVA: 2.8% vs 7.4% Death or MI: 3.9% vs 8.0% Cardiac death or MI: 2.6% vs 5% Definite ST: 0.9% vs 0.2% Definite or probable ST: 1.2% vs 0.6% Definite, probable or possible ST: 1.6% vs 2.5% MI or definite/probable ST: 2.3% vs 3.3% Events for ≤6 mo DAPT subgroup (n = 983): Death, MI or CVA: 6.2% vs 6.8% Death: 3.2% vs 5.0% Cardiac death: 2.1% vs 2.5% MI: 2.9% vs 2.1% Cardiac death, MI or CVA: 4.8% vs 5.0% Death or MI: 6.0% vs 6.6% Cardiac death or MI: 4.6% vs 4.2% Definite ST: 1.2% vs 0.2% Definite or probable ST: 1.9% vs 0.4% Definite, probable or possible ST: 4.1% vs 2.8% MI or definite/probable ST: 2.9% vs 2.1% Events for combined DAPT cohort (n = 1970): Death, MI or CVA: 5.0% vs 9.8% Death: 2.9% vs 6.8% Cardiac death: 1.5% vs 3.1% MI: 2.5% vs 3.2% Cardiac death, MI or CVA: 3.6% vs 7.2% Death or MI: 4.8% vs 8.7% Cardiac death or MI: 3.4% vs 5.4% Definite ST: 1.0% vs 0.2% Definite or probable ST: 1.5% vs 0.6% Definite, probable or possible ST: 2.7% vs 3.2% MI or definite/probable ST: 2.5% vs 3.2% | Prolonged DAPT in low DAPT score patients is associated with harm from greater death and ischaemic events, but whether prolonged DAPT benefits patients with high DAPT score requires further studies |

(Continues)
and log-rank test which makes it challenging to determine how comparable the results are to the derivation study.\textsuperscript{14,15,22} While it is novel to look at a different PCI cohort such as patients who were only followed up for 9 months,\textsuperscript{15} the score was not designed for these patients, as patients were only included in the DAPT trial if they had not experienced clinical events for 12 months. An interesting Chinese study evaluated 225 patients with a high DAPT score and randomised these patients to aspirin 100 mg monotherapy, aspirin 100 mg/clopidogrel 75 mg and aspirin 100 mg/clopidogrel 50 mg.\textsuperscript{21} This study found that patients with high DAPT score did benefit from prolonged DAPT through a reduction in myocardial infarction, but they reported more bleeding events.

An issue affecting the ischaemic and bleeding events in the period beyond 12 months after PCI is the therapy patients remain on. In many of the studies that have been used to ‘validate’ the DAPT score, patients may continue DAPT, monotherapy or be on no antiplatelet, which will alter the propensity for ischaemic and bleeding events. For example, in the ADAPT-DES study 51.2% continued thienopyridine, 36.8% had monotherapy, 12.0% had no antiplatelet and 3.7% had warfarin therapy.\textsuperscript{12} In Yoshikawa et al study 76.7% of patients remained on DAPT beyond 13 months.\textsuperscript{14} However, several of the included studies did not specify the treatment during the post-12-month period\textsuperscript{13,16,17} and in the Song et al study it was only mentioned that it was recommended that patients be on lifelong aspirin, but the proportion of patients taking lifelong aspirin was not reported. Understanding what antiplatelet regime patients were treated with beyond 12 months may provide insight as to why the DAPT score may or may not be correlated to ischaemic and bleeding events.

The DAPT score only randomised patients after 12 months of DAPT so patients must have had a 12-month period of event-free survival after PCI. In general, most studies did exclude patients who had death, ischaemic or bleeding events in the first 12 months. However, if the event rate in the first 12 months was high, then there may be fewer high-risk patients in the period beyond 12 months so there may be fewer events. This will be determined by the risk profile of the cohort studied. The event rate in the period beyond 12 months was highlighted as an important consideration in the study by Yoshikawa et al.\textsuperscript{14} If event rates are low in the period beyond 12 months then it makes demonstrating a statistical difference between low and high DAPT score more challenging. Moreover, the DAPT score is not designed to identify bleeding or ischaemic risk separately which the studies have done, but the net clinical gain between ischaemic and bleeding risk and continuation of DAPT.

The authors of the Swedish registry study raised a few important points in their published letter.\textsuperscript{25} They suggest that it is important for investigators proposing risk scores to (a) clearly outline how the score is designed to work (b) describe the assumptions for generalisability; and (c) if the calibration is included in these assumptions, properly perform and report the analysis. This is particularly important as validation studies should clearly know what they should do in order to best validate proposed scores.

The European guidelines for the duration of DAPT therapy have a section devoted to risk stratification tools for ischaemia and bleeding risks where both the PRECISE-DAPT score and DAPT score are both described and use of either risk score to evaluate the benefits and risks of different DAPT duration has a Class Ib recommendation.\textsuperscript{12} The PRECISE-DAPT score is very different from the DAPT score as its use is at the time of coronary stenting whereas the DAPT score was for patients after 12 months of uneventful DAPT.\textsuperscript{26} The only common variables in both scores is age and the PRECISE-DAPT score contains laboratory variables such as haemoglobin, white cell

\begin{table}
| Study ID   | Study description                                                                 | Results                                                                                                      | Interpretation                                                                 |
|------------|----------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------|
| Stefanescu 2017\textsuperscript{24} | Post hoc analysis of PCI patients in DAPT trial with continued thienopyridine vs placebo | DAPT (≥2) Risk of MI at 12-15 mo with continued thienopyridine vs placebo: 0.16% vs 0.51%, \( P < .001 \) Risk of MI at 30-33 mo with continued thienopyridine vs placebo: 0.43% vs 0.18%, \( P = .008 \) DAPT (<2) Risk of MI at 12-15 mo with continued thienopyridine vs placebo: 0.08% vs 0.24%, \( P = .01 \) Risk of MI at 30-33 mo with continued thienopyridine vs placebo: 0.16% vs 0.13%, \( P = .61 \) | Among patients with high DAPT score there was significant reductions in MI with continued thienopyridine at both 12-15 and 30-33 mo, but a less reduction for patients with low DAPT score |
| Kereiakes 2016\textsuperscript{19}  | Post hoc analysis of PCI patients in DAPT trial with consideration of any MI and no MI and continued thienopyridine vs placebo | DAPT ≥ 2, For continued thienopyridine vs placebo: MI/ST for any MI: 2.7% vs 6.0%, \( P < .001 \) MI/ST for no MI: 2.6% vs 5.2%, \( P = .002 \) Bleeding for any MI: 1.5% vs 1.1%, \( P = .24 \) Bleeding for no MI: 2.2% vs 2.0%, \( P = .68 \) DAPT < 2: For continued thienopyridine vs placebo: MI/ST for any MI: 2.1% vs 3.2%, \( P = .17 \) MI/ST for no MI: 1.5% vs 2.0%, \( P = .21 \) Bleeding for any MI: 3.2% vs 1.2%, \( P = .01 \) Bleeding for no MI: 2.9% vs 1.6%, \( P = .004 \) | Continued thienopyridine reduces MI/ST with DAPT ≥ 2 without increase in bleeding and increased risk of bleeding in DAPT < 2 and continued thienopyridine |
\end{table}
count and creatinine clearance, whereas the DAPT score has many variables that are fixed at time of PCI such as Placlitaxel-eluting stent, stent diameter <3 mm, stenting to vein graft, MI at presentation.

We found that many studies used the C-statistic to evaluate the performance of the DAPT score. The interpretation of the C-statistic has been well defined by Bittl.\(^2\) In the editorial, a C-statistic of 0.50 has no discrimination—‘we might as well flip a coin’ and a C-statistic of >0.50-0.70 had poor or inadequate discrimination. The strength of discrimination was considered to be at the ‘low end of acceptable’ or adequate for C-statistic >0.70-0.80 while values >0.80-1.00 are considered excellent or outstanding. Considering this classification, the validation studies included in this review suggest that the DAPT score for composite outcomes has poor or inadequate discrimination to the low end of acceptable C-statistics.

The DAPT score has now been incorporated into guidelines to determine if DAPT therapy should be continued beyond 1 year. While we have shown that many studies have evaluated the DAPT score using appropriate methodologies to ascertain the score and associated outcomes, these studies are largely those which used the score for prediction rather than to determine continuation or discontinuation of therapy. The ideal study would be to randomise patients who have DAPT for 1 year without adverse events, to a DAPT score guided approach (vs clinician guided management) to determine if use of the DAPT score significantly improves clinical outcomes of patients. The only study that evaluates the value of the DAPT score in a randomised approach was that of Peng et al which only considered patients with high DAPT score and randomised these patients to aspirin or aspirin and clopidogrel at two different doses of clopidogrel and showed that high doses of aspirin and clopidogrel is associated with fewer deaths because of myocardial infarction, but is associated with more bleeding.

A key consideration of the external studies evaluating the DAPT score is that there is a difference between a score used to determine whether or not patients should be treated with prolonged DAPT after 12-month event-free survival and a score which discriminates ischaemic and bleeding events. To determine whether DAPT score predicts events one should consider a homogeneous cohort such as one where all patients discontinue DAPT after 12 months and then evaluated the ischaemic and bleeding events based on DAPT score.

There are several limitations in this review. First, there was significant methodological heterogeneity such that it was inappropriate to pool the results from multiple studies. Second, the DAPT score was designed to determine which patients benefit from prolonged DAPT therapy beyond 1 year and many of the studies use the score for prediction of ischaemic and haemorrhagic events rather than for its intended purpose to guide therapy decision. Finally, our review is based from publication level data, that as we have highlighted above is limited with lack of clarity particularly around anti-platelet regimes post 12-months in many of the studies assessed.

In conclusion, while many studies have been conducted to evaluate the DAPT score, there is not strong and consistent evidence that this score has the ability to discriminate ischaemic and bleeding events separately and should only be used for decisions concerning prolonged DAPT therapy for which it was designed. The current external validations studies suggest that the score has modest value at best for predicting ischaemic and bleeding outcomes.

**ACKNOWLEDGEMENT**

None.

**DISCLOSURES**

The authors declare that they have no conflict of interest.

**AUTHORS’ CONTRIBUTIONS**

CSK conceived of the study, performed the search and analysed the data. CSK and VN performed the screening of the search results for study inclusion. CSK and CWW extracted the data from included studies. CSK and MAM drafted the manuscript. All authors contributed in the writing of the manuscript. CSK is the guarantor.

**ORCID**

Chun Shing Kwok [https://orcid.org/0000-0001-7047-1586](https://orcid.org/0000-0001-7047-1586)

**REFERENCES**

1. Cho MS, Park DW. Stent thrombosis and optimal duration of dual antiplatelet therapy after coronary stenting in contemporary practice. *Korean J Intern Med*. 2017;32:769-779.
2. Yin SHL, Xu P, Wang B, et al. Duration of dual antiplatelet therapy after percutaneous coronary intervention with drug-eluting stent: systematic review and network meta-analysis. *BMJ*. 2019;36:12222.
3. Valgimigli M, Campo G, Monti M, et al. Ferrari R Short- versus long-term duration of dual-antiplatelet therapy after coronary stenting: a randomized multicenter trial. *Circulation*. 2012;125:2015-2026.
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;371:2155-2166.
5. Schulz-Schüpke S, Byrne RA, Ten Berg JM et al. ISAR-SAFE: a randomized, double-blind, placebo-controlled trial of 6 vs. 12 months of clopidogrel therapy after drug-eluting stenting. *European Heart Journal*. 2015;36:1252-1263.
6. Collet JP, Silvain J, Barthélémy O, et al. Dual-antiplatelet treatment beyond 1 year after drug-eluting stent implantation (ARCTIC- Interruption): a randomised trial. *Lancet*. 2014;384:1577-1585.
7. Gwon HC, Hahn JY, Park KW, et al. Six-month versus 12-month dual antiplatelet therapy after implantation of drug-eluting stents: the Efficacy of Xience/Promus Versus Cypher to Reduce Late Loss After Stenting (EXCELLENT) randomized, multicenter study. *Circulation*. 2012;125:505-513.
8. Yeh RW, Secemsky DA, 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;315:1735-1749.
9. Wijns W, Steg PG, Mauri L, et al. Endeavour zotarolimus-eluting stent reduces stent thrombosis and improves clinical outcomes compared with cypher sirolimus-eluting stent: 4-year results of the PROTECT randomized trial. *Eur Heart J*. 2014;35:2812-2820.
10. Levine GN, Bates ER, Bittl JA, et al. 2016 ACC/AHA guidelines focused update on duration of dual antiplatelet therapy in patients with coronary artery disease. *J Am Coll Cardiol*. 2016;68:1082-1115.
11. 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;39:213-260.

12. Brener SJ, Kirtane AJ, Rinaldi MJ, et al. Prediction of ischemic and bleeding events using the dual antiplatelet therapy score in an unrestricted percutaneous coronary intervention population. Circ Cardiovasc Interv. 2018;11:e006853.

13. Veron-Esquivel D, Batiz-Armenta F, et al. Validation of DAPT score for prolonged dual antiplatelet therapy in acute myocardial infarction patients. Hellenic J Cardiol. 2019;60:296–302.

14. Yoshikawa Y, Shiomi H, Watanabe H, et al. Validating utility of dual antiplatelet therapy score in a large pooled cohort from 3 Japanese percutaneous coronary intervention studies. Circulation. 2018;137:551-562.

15. Harada Y, Michel J, Lohaus R, et al. Validation of the DAPT score in patients randomized to 6 or 12 months clopidogrel after predominantly second-generation drug-eluting stents. Thromb Haemost. 2017;117:1989-1999.

16. Ueda P, Jernberg T, James S, et al. External validation of the DAPT score in a nationwide population. J Am Coll Cardiol. 2018;72:1069-1078.

17. Wells GA, Shea B, O’Connell D, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analysis. http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp. Accessed July 12, 2020.

18. Godschalk TC, Gimbel ME, Nolet WW, et al. A clinical risk score to identify patients at high risk of very late stent thrombosis. J Interv Cardiol. 2018;31:159-169.

19. Kereiakes EJ, 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;67:2492-2502.

20. Long T, Peng L, Li F, et al. Correlation of DAPT score and PRECISE-DAPT score with the extent of coronary stenosis in acute coronary syndrome. Medicine. 2018;97:e12531.

21. Peng K, Wang Z, Wang Q, Yang D, Li D. Efficacy and safety of dual antiplatelet prolongation therapy after PCI in ACS patients guided by DAPT scoring system. Med J Chin PLA. 2019;33:37-41.

22. Piccolo R, Gargiulo G, Franzone A, et al. Use of the dual-antiplatelet therapy score to guide treatment duration after percutaneous coronary intervention. Ann Intern Med. 2017;167:17-25.

23. Song L, Guan C, Yan H, et al. Validation of contemporary risk scores in predicting coronary thrombotic events and major bleeding with acute coronary syndrome after drug-eluting stent implantation. Catheter Cardiovasc Interv. 2018;91:573-581.

24. Stefanescu Schmidt AC, Kereiakes DJ, Cutlip DE, et al. Myocardial infarction risk after discontinuation of thienopyridine therapy in the randomized DAPT study (dual antiplatelet therapy). Circulation. 2017;135:1720-1732.

25. Ueda P, Jernberg T, Varenhorst C. Reply: The DAPT Score in Sweden: Successful validation, flawed interpretation. J Am Coll Cardiol. 2019;73:114-115.

26. Costa F, van Klaveren D, James S, et al. Derivation and validation of the predicting bleeding complications in patients undergoing stent implantation and subsequent dual antiplatelet therapy (PRECISE-DAPT) score: a pooled analysis of individual-patient datasets from clinical trials. Lancet. 2017;389:1025-1034.

27. Bittl JA. A swing and a miss for the DAPT score. J Am Coll Cardiol. 2018;72:1079-1080.

How to cite this article: Kwok CS, Wong CW, Nagaraja V, Mamas MA. A systematic review of the studies that evaluate the performance of the DAPT score. Int J Clin Pract. 2020;74:e13591. https://doi.org/10.1111/ijcp.13591