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SYSTEMATIC REVIEW

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Abbreviated dual antiplatelet therapy in patients undergoing percutaneous coronary intervention: a systematic review and meta-analysis of randomized controlled trials

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Abstract

Background Dual antiplatelet therapy (DAPT), combining aspirin and a P2Y12 receptor inhibitor, is a standard post-percutaneous coronary intervention (PCI) treatment to reduce thrombosis and ischemic events. However, the optimal DAPT duration remains unclear, with concerns about bleeding risks associated with long-term potent P2Y12 inhibitors. This systematic review and meta-analysis investigates the safety and efficacy of shortened DAPT regimens.

Methods A comprehensive search of PubMed, Scopus, and EMBASE identified randomized controlled trials (RCTs) comparing conventional DAPT (≥ 12 months) and abbreviated DAPT (≤ 3 months) post-PCI. Primary outcomes were 1-year all-cause mortality and bleeding, assessed using the Bleeding Academic Research Consortium (BARC) classification. Secondary outcomes included cardiovascular mortality, non-fatal myocardial infarction (MI), stroke, and major adverse cardiovascular events (MACE). Risk of bias was assessed with the Cochrane tool, and meta-analyses used random-effects models.

Results Forty studies involving 54,233 participants were included. Abbreviated DAPT significantly reduced all-cause mortality (RR: 0.90, 95%CI: 0.82–0.98) and bleeding (BARC 3 or 5: RR: 0.77, 95%CI: 0.60–0.97). No significant differences were observed in cardiovascular mortality, stroke, non-fatal MI, revascularization, or in-stent thrombosis. Subgroup analyses showed lower mortality with 1-month DAPT and reduced bleeding in patients with high bleeding risk, acute coronary syndrome (ACS), and complex PCI.

Conclusions Abbreviated DAPT post-PCI is associated with lower all-cause mortality and bleeding without compromising ischemic protection, supporting its use in specific patient populations. Individualized DAPT durations should be considered to balance bleeding and ischemic risks.

Keywords Acute coronary syndrome, Dual antiplatelet therapy, P2Y12 receptor inhibitor, Percutaneous coronary intervention

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Introduction

The combination of aspirin and a P2Y12 receptor inhibitor, also known as dual antiplatelet therapy (DAPT), is the cornerstone of post-percutaneous coronary intervention (PCI) medical treatment administered to reduce the risk of thrombosis and other ischemic cardiovascular events [1]. However, the optimal duration of post-PCI DAPT is still under question. Current guidelines emphasize a patient-centered approach in selecting the duration of DAPT, balancing ischemic and bleeding risks based on individual patient profiles. While traditional recommendations favored 12 months of DAPT for ACS and at least 6 months for non-ACS PCI, emerging evidence and expert consensus support more flexible, risk-adapted durations [1–4]. The long-term use of potent P2Y12 inhibitors has been lately associated with a higher risk of bleeding [5, 6], casting doubt on the traditional DAPT strategies.

The safety and efficacy of DAPT de-escalation strategies have recently been investigated in randomized clinical trials (RCTs). In these regimens, the administration of aspirin plus P2Y12 inhibitors is downgraded to monotherapy with a P2Y12 inhibitor after 1 to 3 months [7–12]. Despite evidence in favor of short duration vs conventional DAPT in terms of fewer side effects and non-inferior efficacy, the evidence is still limited. Herein, we conducted a systematic review and meta-analysis of RCTs to shed light on safety and efficacy of shortened DAPT following PCI.

Methods

This systematic review and network meta-analysis followed the guidelines set out by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [13]. The protocol for this analysis was submitted to the PROSPERO online database and assigned a registration ID CRD42024543394.

Search strategy, selection criteria and data extraction

A comprehensive and organized search strategy was developed and carried out in PubMed, Scopus, and EMBASE from the beginning of their records up to January 2024 (Supplemental Table 1). Additionally, reference lists of relevant studies and reviews were examined for possible inclusions.

All Randomized Controlled Trials (RCTs) that compared the following two DAPT strategies in patients who had undergone PCI were included: conventional DAPT strategy (defined as continuing DAPT for at least 12 months followed by single anti-platelet treatment, either Aspirin or a P2Y12inhibitor, for the remainder of the follow-up) and abbreviated DAPT strategy (defined as up to maximum 3 months of DAPT followed by single anti-platelet treatment, either Aspirin or a P2Y12inhibitor, for the remainder of the follow-up). Studies involving timing strategies that did not match our previously mentioned criteria, observational and non-comparative studies, conference abstracts, reviews, non-English language, and animal studies were excluded. Studies with pre-specified subgroup analysis of RCTs that met the inclusion criteria were also eligible for inclusion.

Data collection and extraction process involved importing the findings of the systematic search into Rayyan web application (Rayyan, Cambridge, MA, United States of America) [14]. Two researchers (H.R. and E.K), separately examined the titles and abstracts of the obtained citations to determine which studies were eligible. The full texts of the selected citations were then individually assessed by the same two investigators. Discrepancies were resolved through discussion and consensus, with a third reviewer consulted when necessary. This process ensured a high level of consistency and accuracy in the extracted data.

In the next step, data from the citations that remained on the final list after the full text review were collected by the same two authors, who also cross-verified each other's work to ensure consistency. Data from these studies were extracted using a standardized data collection sheet in Microsoft Excel (Microsoft Corporation, Redmond, WA, United States). The extracted data encompassed various variables, including author names, publication years, study designs, sample sizes, DAPT strategy durations, type of P2Y12 inhibitor used, follow-up duration, participant ages, gender distribution, type of subgroup analyzed in the study, and data regarding primary and secondary outcomes.

Outcomes

Our primary efficacy outcome was 1-year all-cause mortality as it was reported in more studies and it had the least amount of missing data. For primary safety outcome we evaluated data regarding bleeding in the first follow-up year as reported based on Bleeding Academic Research Consortium (BARC) classification. In short, BARC classification divides bleeding episodes into 5 distinct types where each type categorizes bleeding according to its severity and type of therapeutic actions needed (with type 1 being the least serious type of bleeding and type 5 being the most serious and life-threatening type) [15]. Secondary efficacy outcomes included cardiovascular mortality, non-fatal Myocardial Infarction (MI), stroke, target vessel revascularization, any coronary revascularization, in-stent thrombosis and composite MACE outcomes (with different definitions across different studies, but mostly consisting of composite of

all-cause mortality, non-fatal MI, need for revascularization and stroke).

Risk of bias assessment

Version 2.0 of Cochrane Risk of Bias Assessment Tool for Randomized Trials (RoB2) was used to assess the quality of the RCT included in the study [16]. Two authors (F.J and M.M) independently assessed and assigned stars to each included study in each of the five domains of RoB2 questionnaire, all disagreements in this step were resolved by the way of consensus.

Statistical analysis

All outcomes reported in our study were binary, therefore, they were reported as percentages (number) and in order to combine treatment effect estimates, the relative risk for each outcome was calculated and then pooled using the inverse-variance weighting method. As it was anticipated that significant heterogeneity would be present between studies, a random effects model was utilized to estimate and compare treatment effect sizes. Heterogeneity was objectively assessed using the Higgins & Thompson's I2 statistic and Cochrane's Q [17, 18]. We used the Egger test to formally investigate reporting bias. This test examines the symmetry of funnel plots. If the test results were not statistically significant, it was determined that the risk of reporting bias was minimal [19]. For outcomes where there were more than 10 studies available, funnel plots were also drawn. To perform sensitivity analysis of our outcome results, we gathered data from pre-specified subgroup studies of each main trial and pooled sub-group analysis was performed. Also, leave one out analysis was performed to uncover any source of heterogeneity. Meta-regression for evaluation of primary outcome was performed for four baseline characteristics that had the least amount of missing data. All statistical analyses were conducted using the R software (R for Windows, version 4.1.3, Vienna, Austria) [20] and R Studio version 1.1.463 (Posit PBC, Boston, MA, United States), utilizing packages tidyverse, meta and robvis [20–22].

Results

Study outlines and baseline characteristics

A total of 4893 studies were identified through a systematic search. After removing duplicates, 3184 studies underwent title/abstract evaluation, and 86 full-texts were further assessed for eligibility. A total of 40 studies that met all inclusion criteria of this meta-analysis were finally included; of these, 12 studies were RCTs comparing abbreviated DAPT with conventional DAPT (Fig. 1). The remaining were studies with pre-specified subgroup analysis of the included RCTs, focusing on analyzing reference cohorts regarding gender, age, body mass index

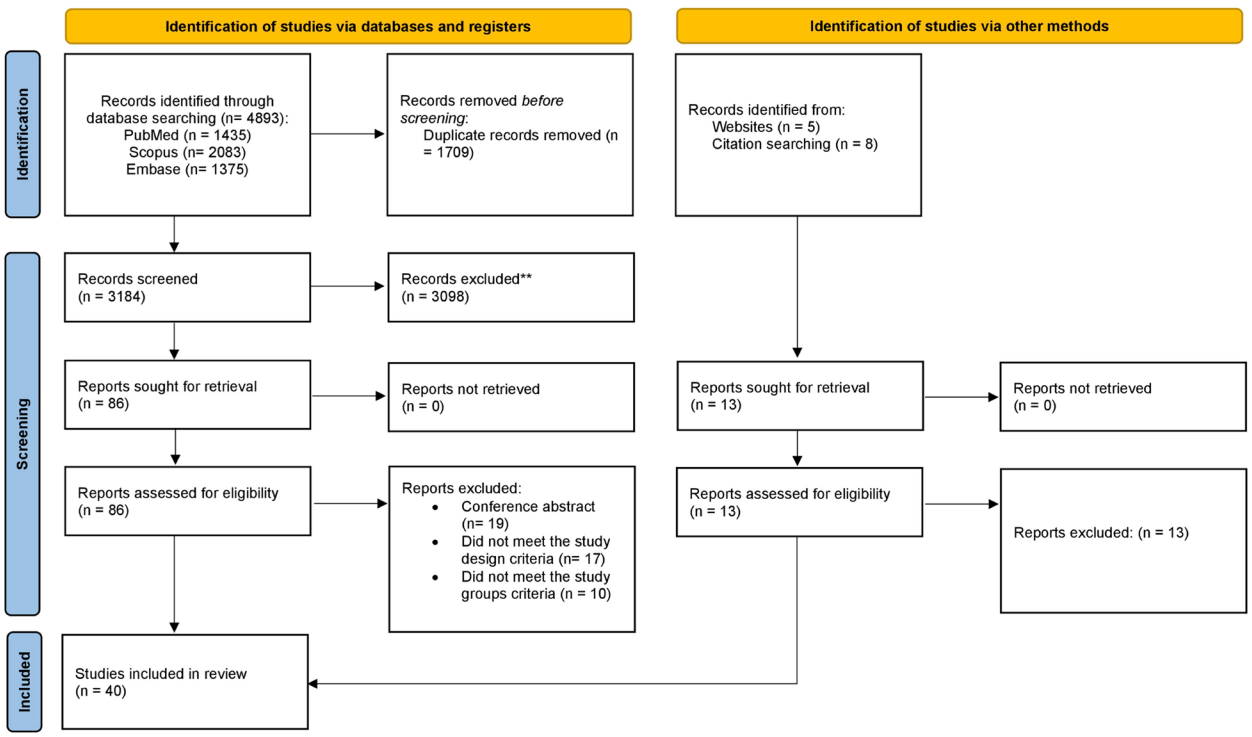

Fig. 1 PRISMA flow diagram

(BMI), ACS, diabetes mellitus (DM), complex PCI, high bleeding risk (HBR) status, and chronic kidney disease (CKD). Additionally, subgroup analyses were performed specifically for patients with HBR and those without.

All studies were conducted between 2012 and 2024, comprising 54,233 participants (27,136 randomized to conventional DAPT and 27,097 randomized to abbreviated DAPT) with a mean age of 61.45 years, and 75% were male. Six trials compared 3-month DAPT with 12-month DAPT [11, 23–27], four trials compared 1-month DAPT with 12-month DAPT [28–31], one trial compared 3-month DAPT with 15-month DAPT [32], and one trial compared 1-month Prasugrel monotherapy with 1-month DAPT [12]. All trials were multi-centric, with follow-up periods ranging from 1 month in the STOPDAPT-3 trial [12] to 5 years in the STOPDAPT-2 trial [31]. The baseline characteristics and main findings of the included studies are summarized in Table 1.

Quality assessment

We assessed the methodological quality of the included studies using the Cochrane Collaborative Assessment Tool. Our studies were generally assessed as having a moderate risk of bias overall. Supplemental Fig. 1 shows the methodological quality assessment results of each included RCT.

All-cause mortality

Thirteen studies reported the rate of all-cause mortality. Abbreviated DAPT significantly reduced all-cause mortality compared to conventional DAPT (RR: 0.90, 95%CI: 0.82–0.98, I^2: 0%) (Fig. 2A). Subgroup analysis by DAPT duration indicated that 1-month DAPT was associated with slightly lower all-cause mortality compared to conventional DAPT (RR: 0.89, 95%CI: 0.80–0.99, I^2: 0%), while no significant difference was found between 3-month DAPT and conventional DAPT (RR: 0.91, 95%CI: 0.75–1.11, I^2: 0%) (Fig. 2B). Further subgroup analyses based on demographics (gender, BMI, elderly), comorbidities (ACS, CKD, DM), PCI complexity, and HBR status did not reveal significant differences (Fig. 2C). The subgroup analysis for HBR vs. non-HBR patients showed that abbreviated DAPT was associated with no statistically significant difference in mortality risk between HBR and non-HBR patients (HBR: RR = 1.11, 95% CI: 0.84–1.48 vs. non-HBR: RR = 0.87, 95% CI: 0.80–0.94) (Supplemental Fig. 3).

Cardiovascular mortality

Abbreviated DAPT was not significantly associated with a reduced risk of CV mortality compared to conventional DAPT (RR: 0.88, 95%CI: 0.76–1.02, I^2: 0%) (Fig. 2D). Subgroup analysis based on DAPT duration showed no statistically significant differences in CV mortality: 1-month DAPT (RR: 0.87, 95%CI: 0.73–1.04, I^2: 0%) and 3-month DAPT (RR: 0.91, 95%CI: 0.70–1.18, I^2: 0%) (Supplemental Fig. 3). Moreover, the risk of CV mortality was comparable between abbreviated and conventional DAPT in all other subgroup analyses, except for a 49% lower risk observed in women who underwent abbreviated DAPT (RR: 0.51, 95%CI: 0.28–0.92, I^2: 0%) (Supplemental Figs. 4, 5).

Stroke

Based on 11 studies involving 58174 patients, there was no statistically significant difference in stroke rates between abbreviated DAPT and conventional DAPT (RR: 0.93, 95%CI: 0.79–1.10, I^2: 0%) (Fig. 3A). Subgroup analysis by DAPT duration also showed no significant difference in stroke rates: 1-month DAPT (RR: 0.89, 95%CI: 0.74–1.07, I^2: 0%) and 3-month DAPT (RR: 1.14, 95%CI: 0.78–1.67, I^2: 0%) (Supplemental Fig. 6). Furthermore, additional subgroup analyses revealed no significant differences in stroke risk across various pre-specified subgroups (Supplemental Figs. 7, 8).

Non-fatal myocardial infarction

The incidence of non-fatal MI was comparable between patients receiving abbreviated DAPT and those receiving conventional regimen (RR: 0.97, 95%CI: 0.85–1.10, I^2: 19%) (Fig. 3B). These results remained consistent across different durations of abbreviated DAPT, including 1-month DAPT (RR: 0.95, 95%CI: 0.74–1.23, I^2: 62%) and 3-month DAPT (RR: 1.01, 95%CI: 0.84–1.22, I^2: 0%) (Supplemental Fig. 9). Subgroup analyses based on prespecified factors did not reveal any statistically significant difference in non-fatal MI rates between the two groups (Supplemental Figs. 10, 11).

Any revascularization

The rate of any revascularization was reported in six studies. Compared to conventional DAPT, abbreviated DAPT did not significantly reduce the risk of any revascularization (RR: 0.99, 95%CI: 0.89–1.10, I^2: 31%) (Figs. 3C). This trend remained consistent in the subgroup analysis of different abbreviated DAPT durations: 1-month DAPT (RR: 0.95, 95%CI: 0.88–1.04, I^2: 60%) and 3-month DAPT (RR: 1.06, 95%CI: 0.83–1.36, I^2: 0%) (Supplemental Fig. 12). Additionally, the risk of any revascularization was similar between abbreviated and conventional DAPT across subgroups defined by DM, ACS, HBR, and complex PCI (Supplemental Figs. 13, 14), with subgroup analysis showing no significant difference in pooled risk (P: 0.83).

Table 1 Characteristics of included randomized controlled trials

Study or subgroup, year	Country	Design	Follow-up duration	Study Population	Patients, *n*	Age (years)	Male (%)	Experimental therapy	Standard therapy	Included Sub-studies	Outcomes	Main Findings
RESET, 2012 [23]	Korea	Prospective, multicenter, open-label, randomized clinical trial	1 year	Patients with a diagnosis of angina or acute MI with more than 50% diameter stenosis	DAPT: 1058 Abbreviated DAPT: 1059	DAPT: 62.4 ± 9.8 Abbreviated DAPT: 62.4 ± 9.4	63.62	3 m DAPT (Aspirin + Clopidogrel)	12 m DAPT (Aspirin + Clopidogrel)	DM ACS	Primary endpoints: A composite of death from cardiovascular cause, MI, stent thrombosis, ischemia-driven target-vessel revascularization, or bleeding Secondary endpoints:: Each component of the primary composite endpoints	3-month DAPT was noninferior to the standard therapy with respect to the occurrence of the primary endpoint
OPTIMIZE, 2013 [24]	Brazil	Multicenter, open-label, active-controlled, non-inferiority, randomized clinical trial	1 year	Patients with stable coronary artery disease or history of low-risk ACS undergoing PCI with zotarolimus-eluting stents	DAPT: 1556 Abbreviated DAPT: 1563	DAPT: 61.9 ± 10.6 Abbreviated DAPT: 61.3 ± 10.4	63.28	3 m DAPT (Aspirin + Clopidogrel)	12 m DAPT (Aspirin + Clopidogrel)	-	Primary endpoints: NACCE (a composite of all-cause death, MI, stroke, or major bleeding specifically, major bleeding incorporated modified major REPLACE-2 and severe or life-threatening GUSTO) Secondary endpoints: MACE (a composite of all-cause death, MI, emergent coronary artery bypass graft surgery, or target lesion revascularization), target-lesion and target-vessel revascularization, definite or probable stent thrombosis and any bleeding, which included major bleeding plus bleeding events that did not meet criteria for either major or severe or life-threatening bleeding according to modified major REPLACE-2 and severe or life-threatening GUSTO criteria	3 months of DAPT was noninferior to 12 months for NACCE, without significantly increasing the risk of stent thrombosis

Table 1 (continued)

Study or subgroup, year	Country	Design	Follow-up duration	Study Population	Patients, *n*	Age (years)	Male (%)	Experimental therapy	Standard therapy	Included Sub-studies	Outcomes	Main Findings
GLOBAL LEADERS, 2018 [28]	Multinational	Multicenter, open-label, randomized superiority trial	2 years	Patients scheduled to undergo PCI for stable coronary artery disease or ACS	DAPT: 7988 Abbreviated DAPT: 7980	DAPT: 64.6 ± 10.3 Abbreviated DAPT: 64.5 ± 10.3	76.74	1 m DAPT (Aspirin + Ticagrelor) followed by 23 m Ticagrelor monotherapy	12 m DAPT (Aspirin + Clopidogrel [for patients with stable CAD] or Ticagrelor [for patients with ACS]) followed by 12 m Aspirin monotherapy	GLOBAL LEADERS, GLASS Substudy 2019 [33] GLOBAL LEADERS, Complex PCI (Serruys, 2019 [34]) GLOBAL LEADERS-BMI (Ono, 2020 [35]) GLOBAL LEADERS, DM-CKD (Gao-2020 [36]) GLOBAL LEADERS-ACS (Vranckx, 2021 [37])	Primary endpoints: A composite of all-cause death or new Q-wave MI Secondary endpoints: Bleeding events (BARC type 3 or 5), a composite endpoint of all-cause death, new Q-wave MI, or stroke; MI; stroke; target vessel or any revascularization; and definite stent thrombosis	Ticagrelor with aspirin for 1 month, followed by ticagrelor monotherapy for 23 months, did not demonstrate better outcomes compared to 12-month DAPT followed by aspirin monotherapy for another 12 months in preventing all-cause mortality or new Q-wave MI two years after PCI
TWILIGHT, 2019 [32]	Multinational	Multicenter, randomized, double-blind placebo controlled trial	1 year	High-risk patients undergoing PCI with DES who have completed a 3-month coarse of DAPT with aspirin and ticagrelor	DAPT: 3564 Abbreviated DAPT: 3555	DAPT: 65.1 ± 10.4 Abbreviated DAPT: 65.2 ± 10.3	76.14	3 m DAPT (Aspirin + Ticagrelor) followed by 12 m Ticagrelor monotherapy	15 m DAPT (Aspirin + Ticagrelor)	TWILIGHT—ACS (Baber, 2020 [38]) TWILIGHT—Complex PCI (Dangas, 2020 [39]) TWILIGHT -Gender (Vogel, 2021 [40]) TWILIGHT—CKD (Stefanini, 2021 [41]) TWILIGHT—HBR (Escaned, 2021 [42]) TWILIGHT—BMI (Kunadian, 2022 [43]) TWILIGHT—DM/CKD (Dehghani, 2022 [44])	Primary endpoints: Type 2, 3, or 5 BARC bleeding Secondary endpoints: Composite of all-cause death, nonfatal MI, nonfatal stroke; cardiovascular death, MI, ischemic stroke, definite or probable stent thrombosis, and all bleeding events, adjudicated according to the BARC, TIMI, and GUSTO, ISTH classifications	In high-risk patients undergoing PCI who have completed a 3-month coarse of DAPT, ticagrelor monotherapy resulted in lower incidence of clinically relevant bleeding compared to standard DAPT. While, there was no increased risk of death, MI, or stroke with ticagrelor monotherapy

Table 1 (continued)

Study or subgroup, year	Country	Design	Follow-up duration	Study Population	Patients, *n*	Age (years)	Male (%)	Experimental therapy	Standard therapy	Included Sub-studies	Outcomes	Main Findings
TICO, 2020 [25]	South Korea	Multicenter, randomized, unblinded trial	1 year	Patients who successful PCI for ACS (ST-elevation myocardial infarction, non-ST- elevation myocardial infarction, or unstable angina)	DAPT: 1529 Abbreviated DAPT: 1527	61	80	3 m DAPT (Aspirin + Ticagrelor) followed by Ticagrelor monotherapy	12 m DAPT (Aspirin + Ticagrelor)	TICO—DM (Yun, 2020 [45]) TICO—Age (Kim, 2021 [46]) TICO—ACS (Lee, 2021 [47]) TICO—HBR (Lee, 2022 [48]) TICO—Gender (Lee, 2023 [49]) TICO—BMI (Kim, 2023 [50])	Primary endpoints: NACE (a composite of major bleeding and adverse cardiac and cerebrovascular events) Secondary endpoints: major bleeding, MACCE, major or minor bleeding, death, MI, stent thrombosis, stroke, target-vessel revascularization, the composite of cardiac death or MI, and the composite of cardiac death, MI, stent thrombosis, or target-vessel revascularization	Comparing to 12-month DAPT, ticagrelor monotherapy after 3-month DAPT led to a slight yet statistically significant decrease in a composite outcome of major bleeding and cardiovascular events at 1 year
REDUCE, 2021 [26]	Multinational	Prospective, multicenter, open- label, randomized, clinical trial	2 years	ACS patients who were treated with the COMBO stent	DAPT: 745 Abbreviated DAPT: 751	60.94 ± 8.92	79.81	3 m DAPT (Aspirin + Prasugrel or Ticagrelor or Clopidogrel) followed by Aspirin monotherapy	12 m DAPT (Aspirin + Prasugrel or Ticagrelor or Clopidogrel)	REDUCE-Gender (Verdoia, 2021 [51]) REDUCE-DM (Vranken, 2022 [52])	Primary endpoints: A composite of all-cause mortality, MI, stent thrombosis, stroke, target vessel revascularization, and bleeding complications ((BARC II, III, V) Secondary endpoints:: Cardiovascular death or the individual components of the primary endpoint	ACS patients randomized to a 3-month DAPT strategy had similar outcomes to those on standard 12-month DAPT at a 2-year follow-up, for both ischemic events and bleeding complications, regardless of age (elderly or younger patients)

Table 1 (continued)

Study or subgroup, year	Country	Design	Follow-up duration	Study Population	Patients, *n*	Age (years)	Male (%)	Experimental therapy	Standard therapy	Included Sub-studies	Outcomes	Main Findings
SMARTCHOICE, 2022 [27]	Korea	Multicenter, randomized, open-label, noninferiority trial	3 years	Patients who had at least 1 stenosis of 50% or greater in a native coronary artery with a visually estimated diameter of 2.25 mm or larger and 4.25 mm or smaller that was suitable for PCI	DAPT: 1498 Abbreviated DAPT: 1495	DAPT: 64.6 ± 10.7 Abbreviated DAPT: 64.6 ± 10.7	73.43	3 m DAPT (Aspirin + Clopidogrel or Prasugrel or Ticagrelor) followed by P2Y12 inhibitor monotherapy	12 m DAPT (Aspirin + Clopidogrel or Prasugrel or Ticagrelor)	SMARTCHOICE -Complex PCI (Roh, 2021 [53]) SMARTCHOICE -Gender (Shin, 2023 [54])	Primary endpoints: MACCE (a composite of all-cause death, MI, or stroke) Secondary endpoints: The components of the primary endpoint, cardiac death, target-vessel revascularization, any revascularization, stent thrombosis, bleeding (BARC types 2–5), major bleeding (BARC types 3–5), and NACCE (a composite of all-cause death, MI, stroke, and BARC types 2–5 bleeding)	3-month DAPT followed by P2Y12 inhibitor monotherapy significantly decreased the rate of major bleeding over a 3-year follow-up period. However, there was no significant difference in the 3-year risk of ischemic cardiovascular events between the two groups
MASTERDAPT, 2023 [29]	Europe, South America, the Middle East, Asia, and Australia	Multicenter, randomized, open-label, noninferiority trial	15 months	HBR patients with acute or chronic coronary syndromes who underwent PCI	DAPT: 2295 Abbreviated DAPT: 2284	DAPT: 75.86 ± 8.80 Abbreviated DAPT: 76.06 ± 8.73	69.19	1 m DAPT (Aspirin + Clopidogrel or Prasugrel or Ticagrelor) followed by 11 m P2Y12 inhibitor monotherapy	12 m DAPT (Aspirin + Clopidogrel or Prasugrel or Ticagrelor)	Complex PCI (Valgimigli, 2022 [55]) Gender (Landi, 2024 [56])	Primary endpoints: NACE, MACCE, major or clinically relevant nonmajor bleeding (composite of type 2, 3, or 5 BARC bleeding) Secondary endpoints: The composite of cardiovascular death, MI, and stroke; The composite of cardiovascular death, MI, definite or probable stent thrombosis, The composite of stroke and transient ischemic attack; and all bleeding events, adjudicated according to the BARC, TIMI, and GUSTO classifications	At 15 months, there was no significant difference in the occurrence of NACE and MACCE between HBR patients who received abbreviated and standard DAPT. However, the risk of major or clinically relevant nonmajor bleeding was lower with abbreviated DAPT compared with standard therapy

Table 1 (continued)

Study or subgroup, year	Country	Design	Follow-up duration	Study Population	Patients, *n*	Age (years)	Male (%)	Experimental therapy	Standard therapy	Included Sub-studies	Outcomes	Main Findings
T-PASS, 2023 [30]	South Korea	Multicenter, randomized, open-label, noninferiority trial	1 year	Patients with ACS who had undergone DES implantation	DAPT: 1424 Abbreviated DAPT: 1426	61	83.39	< 1 month of DAPT (Aspirin + Ticagrelor) followed by Ticagrelor monotherapy	12 m DAPT (Aspirin + Ticagrelor)	-	Primary endpoints: A composite of all-cause death, myocardial infarction, stent thrombosis, stroke, and major bleeding Secondary endpoints: All-cause death, cardiovascular death, MI, stent thrombosis, stroke, major bleeding, minor or major bleeding, and MACE composed of cardiovascular death, myocardial infarction, stent thrombosis, and ischemia-driven target-vessel revascularization	In Patients with ACS who had undergone DES implantation, < 1 month of DAPT followed by ticagrelor monotherapy demonstrated superiority over 12-months DAPT for one-year composite outcome of death, MI, stent thrombosis, stroke, and major bleeding. This superiority was mainly due to a significant reduction in bleeding events
HOSTIDEA, 2023 [11]	South Korea	Multicenter, open-label, noninferiority, adjudicator-blinded randomized clinical trial	1 year	Patients with de novo stenotic lesions and without ST-segment–elevation MI suitable for DES implantation	DAPT: 1011 Abbreviated DAPT: 1002	65.7 ± 10.5	73.9	3 to 6 m DAPT (Aspirin + Clopidogrel or Prasugrel or Ticagrelor) followed by monotherapy (aspirin or clopidogrel for patients with SIHD; aspirin, clopidogrel, ticagrelor, or prasugrel for patients with ACS)	12 m DAPT (Aspirin + Clopidogrel or Prasugrel or Ticagrelor)	-	Primary endpoints: NACE, a composite of cardiac death, target vessel MI, clinically driven target lesion revascularization, stent thrombosis, or major bleeding (BARC 3 or 5) Secondary endpoints: Target lesion failure, a composite of cardiac death, target vessel MI, clinically driven target lesion revascularization, and major bleeding	3- to 6-month DAPT was noninferior to 12-month DAPT for NACE. There were no significant differences in target lesion failure or major bleeding between the 2 groups

Table 1 (continued)

Study or subgroup, year	Country	Design	Follow-up duration	Study Population	Patients, *n*	Age (years)	Male (%)	Experimental therapy	Standard therapy	Included Sub-studies	Outcomes	Main Findings
STOPDAPT-2, 2024 [31]	Japan	Prospective, multicenter, open-label, adjudicator-blinded randomized clinical trial	5 years	Patients who underwent successful PCI (ACS: 38.3%)	DAPT: 1486 Abbreviated DAPT: 1471	68.6 ± 10.7	77.7	1 m DAPT (Aspirin + Clopidogrel or Prasugrel) followed by Clopidogrel monotherapy	12 m DAPT (1 month Aspirin + Clopidogrel or Prasugrel followed by Aspirin + Clopidogrel)	STOPDAPT- HBR/complex PCI (Watanabe, 2023 [57]) STOPDAPT-2-DM (Yamamoto, 2023 [58]) STOPDAPT-2-ACS (Watanabe, 2022 [10])	Primary endpoints: A composite of cardiovascular outcomes (death from cardiovascular cause, MI, definite stent thrombosis, stroke including both ischemic and hemorrhagic) and bleeding outcomes defined as TIMI major or minor bleeding Secondary endpoints: The cardiovascular and bleeding components of the primary endpoint	Clopidogrel monotherapy, compared to the aspirin monotherapy, was found to be non-inferior but not superior for the primary endpoint. However, it demonstrated superiority for cardiovascular outcomes and showed no superiority for major bleeding. In the 1-year landmark analysis, clopidogrel showed a numerical advantage over aspirin for cardiovascular events, though this difference was not statistically significant, and there was no disparity in major bleeding
STOPDAPT-3, 2024 [12]	Japan	Prospective, multicenter, open-label, adjudicator-blinded randomized clinical trial	1 month	Patients with ACS regardless of HBR or non-ACS with HBR with minimal exclusion criteria	DAPT: 2982 No-aspirin: 2984	71.6 ± 11.7	76.6	1 m Prasugrel	1 m DAPT (Aspirin + Prasugrel)	STOPDAPT-3-HBR (Obayashi, 2024 [59])	Primary endpoints: BARC type 3 or 5, a composite of cardiovascular death, MI, definite stent thrombosis, or ischemic stroke Secondary endpoints: A composite of the coprimary bleeding and cardiovascular end points representing net adverse clinical outcomes	After 1 month, the no-aspirin group did not show superiority over the DAPT group for the primary bleeding endpoint. However, the no-aspirin group was considered non-inferior to the DAPT group for the primary cardiovascular endpoint. There were no differences in net adverse clinical outcomes or each component of the primary cardiovascular endpoint

Table 1 (continued)

Study or subgroup, year	Country	Design	Follow-up duration	Study Population	Patients, *n*	Age (years)	Male (%)	Experimental therapy	Standard therapy	Included Sub-studies	Outcomes	Main Findings
												between the two groups. However, the no-aspirin group had more cases of unplanned coronary revascularization and subacute definite or probable stent thrombosis compared to the DAPT group

Data are presented as mean ± standard deviation, median [interquartile range], or percentage. *PCI* Percutaneous coronary intervention, *ACS* Acute coronary syndrome, *DAPT* Dual antiplatelet therapy, *CAD* Coronary artery disease, *SAPT* Short antiplatelet therapy, *BMI* Body mass index, *DM* Diabetes mellitus, *CKD* Chronic kidney disease, *MI* Myocardial infarction, *BARC* Bleeding Academic Research Consortium, *TIMI* Thrombolysis in Myocardial Infarction, *GUSTO* Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries, *DES* Drug-eluting stent, *SIHD* Stable ischemic heart disease, *NACE* Net adverse clinical events, *HBR* High Bleeding Risk, *MACCE* Major adverse cardiac and cerebrovascular events, *REPLACE* Randomized Evaluation of PCI Linking Angiomax to Reduced Clinical Events, *CVA* Cerebrovascular accident, *NACCE* Net adverse clinical and cerebral events, *MACE* Major adverse cardiac events, *ISTH* International Society on Thrombosis or Haemostasis, *ARC* Academic Research Consortium

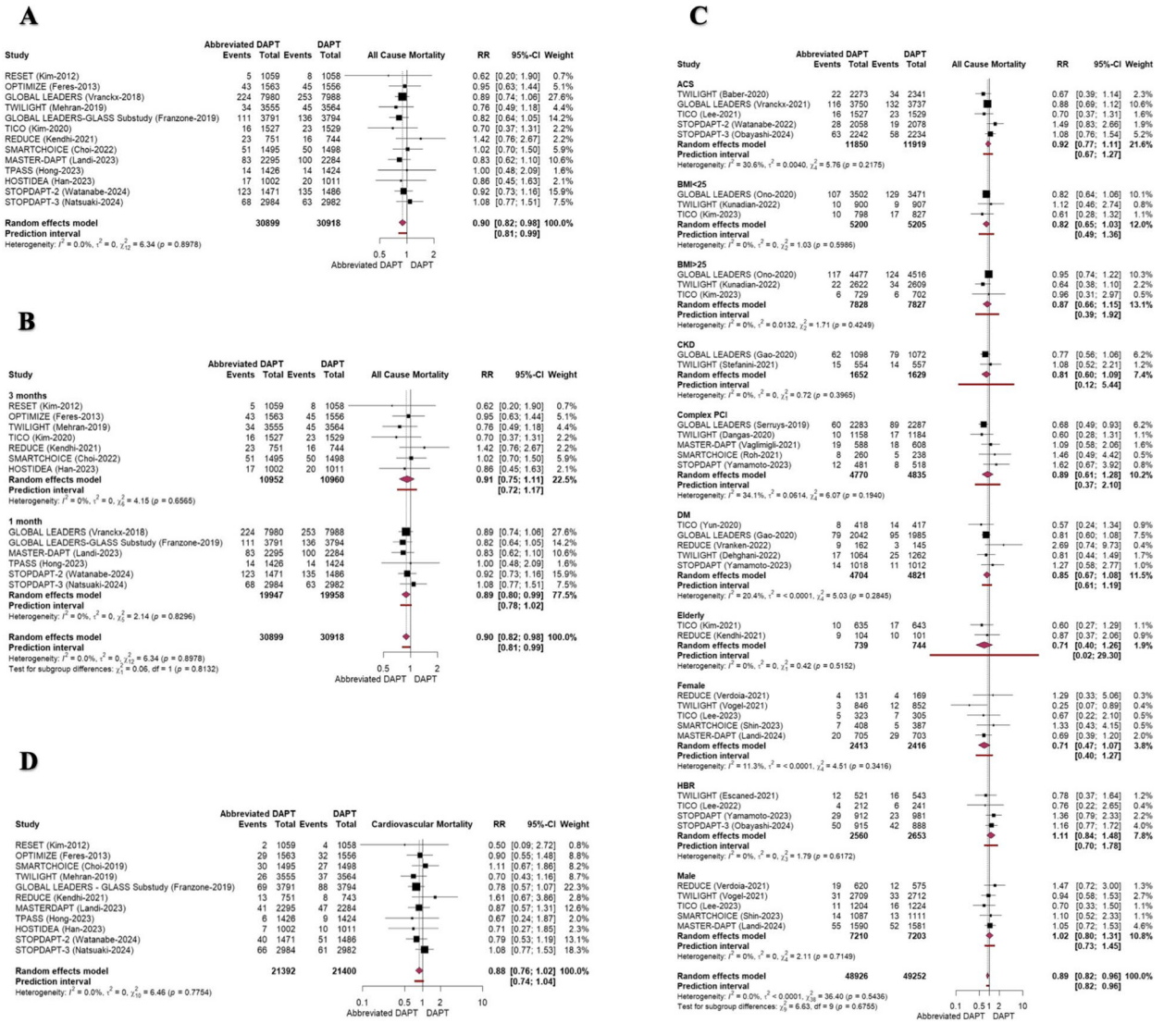

Fig. 2 *All-cause and Cardiovascular Mortality Outcomes:* **A** Forest plots representing the risk of all-cause mortality after abbreviated DAPT vs. conventional DAPT; **B** Forest plots representing the risk of all-cause mortality after 1- and 3-month abbreviated DAPT vs. conventional DAPT; **C** Forest plots representing the risk of all-cause mortality after abbreviated DAPT vs. conventional DAPT in pre-specified subgroups; **D** Forest plots representing the risk of cardiovascular mortality after abbreviated DAPT vs. conventional DAPT

Target vessel revascularization

No statistically significant difference was found between abbreviated and conventional DAPT regarding the occurrence of target vessel revascularization (RR: 0.94, 95%CI: 0.82–1.07, I^2: 12%) (Fig. 3D). Similarly, no difference was found in the risk of target vessel revascularization across different durations of abbreviated DAPT: 1-month DAPT (RR: 0.87, 95%CI:0.73–1.04, I^2: 39%) and 3-month DAPT (RR: 1.07, 95%CI: 0.88–1.30, I^2: 0%) (Supplemental Fig. 15). Subgroup analyses based on gender, BMI, elderly, HBR, and comorbidities such as ACS and DM revealed no significant difference in target vessel revascularization (Supplemental Figs. 16, 17).

In-stent thrombosis

The incidence of in-stent thrombosis was assessed in 13 studies, revealing no significant difference between abbreviated DAPT versus conventional DAPT (RR: 1.04, 95%CI: 0.87–1.23, I^2: 0%) (Fig. 4A). The risk of in-stent thrombosis with 1- or 3-month abbreviated DAPT regimens was comparable to conventional DAPT (RR: 0.97, 95%CI: 0.75–1.26, I^2: 0%; RR: 1.12, 95%CI: 0.87–1.44, I^2: 0%, respectively) (Supplemental Fig. 18). Subgroup analysis based on different characteristics and various comorbidities, yielded similar outcomes to the overall analysis (Supplemental Figs. 19, 20).

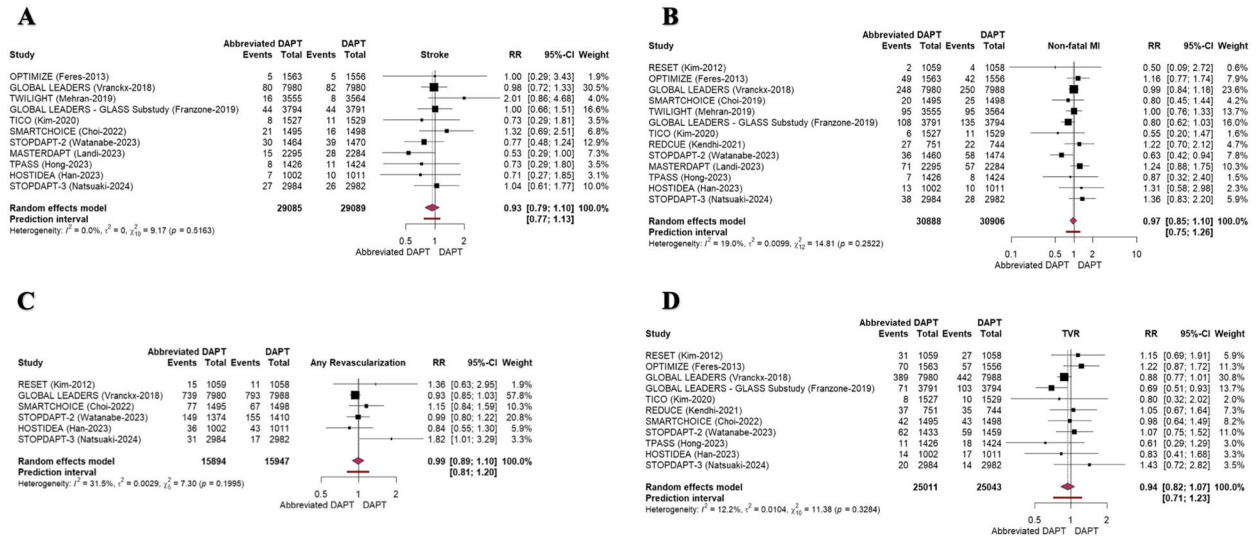

Fig. 3 *Ischemic Outcomes*: **A** Forest plots representing the risk of stroke after abbreviated DAPT vs. conventional DAPT; **B** Forest plots representing the risk of non-fatal MI after abbreviated DAPT vs. conventional DAPT; **C** Forest plots representing the risk of any revascularization after abbreviated DAPT vs. conventional DAPT; **D** Forest plots representing the risk of target vessel revascularization after abbreviated DAPT vs. conventional DAPT

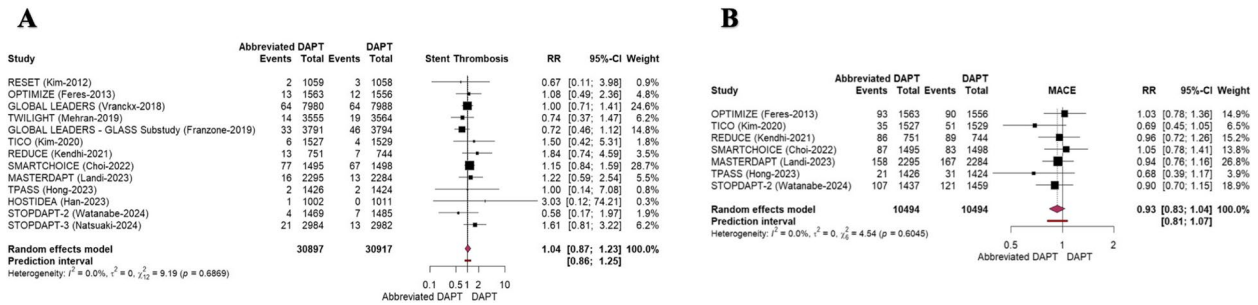

Fig. 4 **A** Forest plots representing the risk of in-stent thrombosis after abbreviated DAPT vs. conventional DAPT; **B** Forest plots representing the risk of MACE after abbreviated DAPT vs. conventional DAPT

MACE

No significant difference was found in the incidence of MACEs between patients receiving abbreviated DAPT and those receiving conventional DAPT (RR: 0.93, 95%CI: 0.83–1.04, I^2: 0%) (Figs. 4B). The risk of MACEs remained comparable across different durations of abbreviated DAPT, including 1-month (RR: 0.90, 95%CI: 0.77–1.05, I^2: 0%) and 3-month DAPT (RR: 0.96, 95%CI: 0.82–1.12, I^2: 0%) (Supplemental Fig. 21), with subgroup analysis showing no significant difference in pooled risk (*P*: 0. 56). Notably, abbreviated DAPT was associated with significantly lower risk of MACEs compared to conventional DAPT among patients undergoing complex PCI (RR: 0.84, 95%CI: 0.75–0.94, I^2: 0%); However, no difference was observed between the two regimens across other pre-specified subgroups (Supplemental Figs. 22, 23).

BARC

The incidence of BARC type 2 or 3 or 5 bleeding was reduced by 30% with abbreviated DAPT compared to conventional DAPT (RR: 0.70, 95%CI: 0.50–0.98, I^2: 88%). However, there was high heterogeneity among the seven studies reporting this outcome. Abbreviated DAPT also significantly lowered the risk of BARC 3 or 5 bleeding (RR: 0.77, 95%CI: 0.60–0.97, I^2: 67%). However, there was no significant difference in the rate of BARC type 2 (RR: 0.83, 95%CI: 0.68–1.01, I^2: 63%), BARC type 3 (RR: 0.98, 95%CI: 0.86–1.11, I^2: 0%), and BARC type 5 bleeding (RR: 1.01, 95%CI: 0.70–1.44, I^2: 20%) between abbreviated DAPT and conventional DAPT (Figs. 5).

A pre-specified analysis of bleeding endpoints was conducted based on the presence of ACS, PCI complexity, and HBR status. Among patients undergoing complex PCI, abbreviated DAPT resulted in lower rates of BARC 2 or 3 or 5 bleeding (RR: 0.56, 95%CI: 0.40–0.77, I^2: 0%),

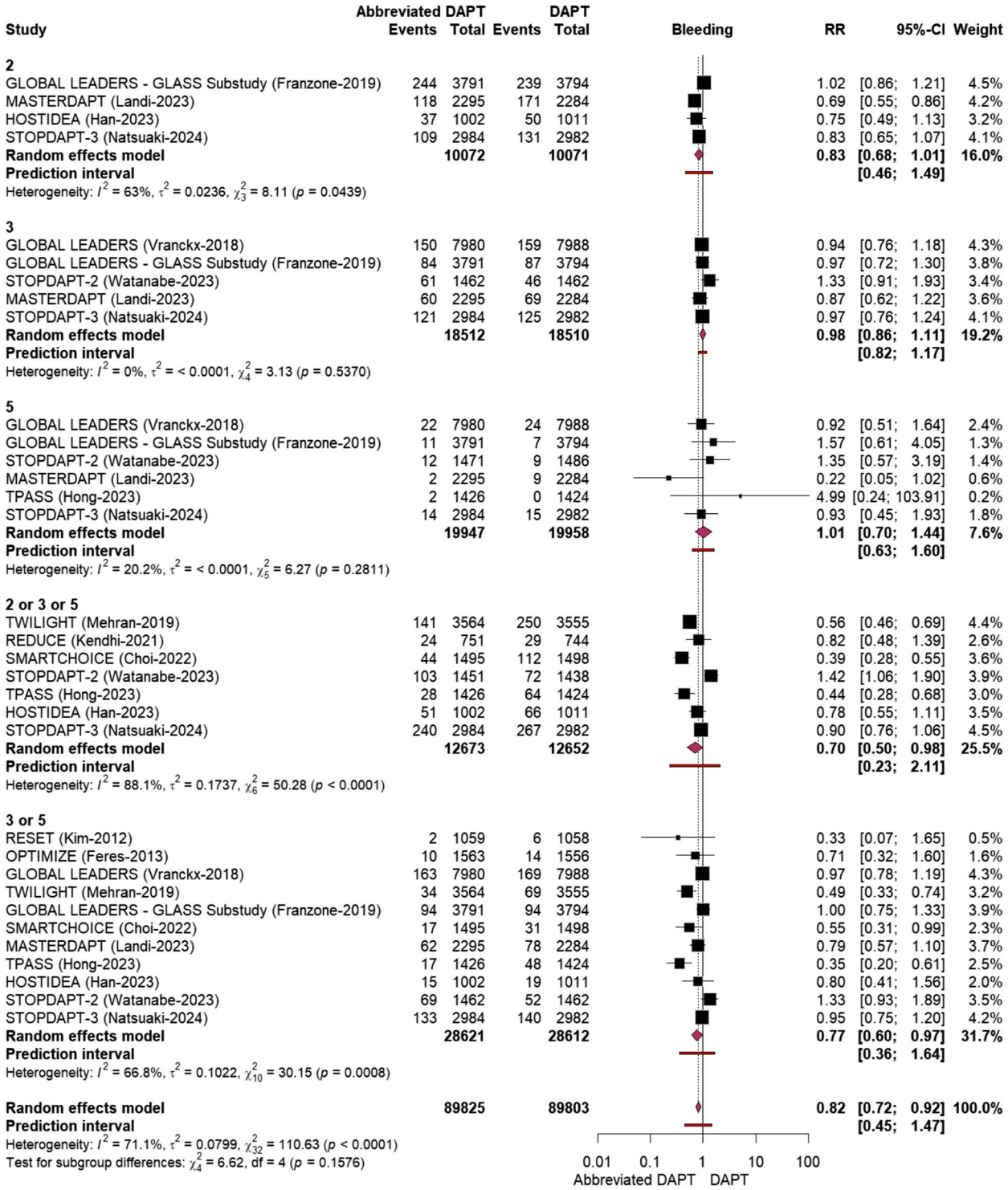

Fig. 5 Forest plots representing the risk of BARC after abbreviated DAPT vs. conventional DAPT

while the risk of BARC type 3, BARC type 5, and BARC 3 or 5 bleeding did not significantly differ in this population (Fig. 6A). In the ACS subgroup, abbreviated DAPT was associated with lower rates of BARC type 3 (RR: 0.55, 95%CI: 0.32–0.96, I^2: 55%) and BARC 3 or 5 bleeding (RR: 0.60, 95%CI: 0.39–0.94, I^2: 76%), with no significant

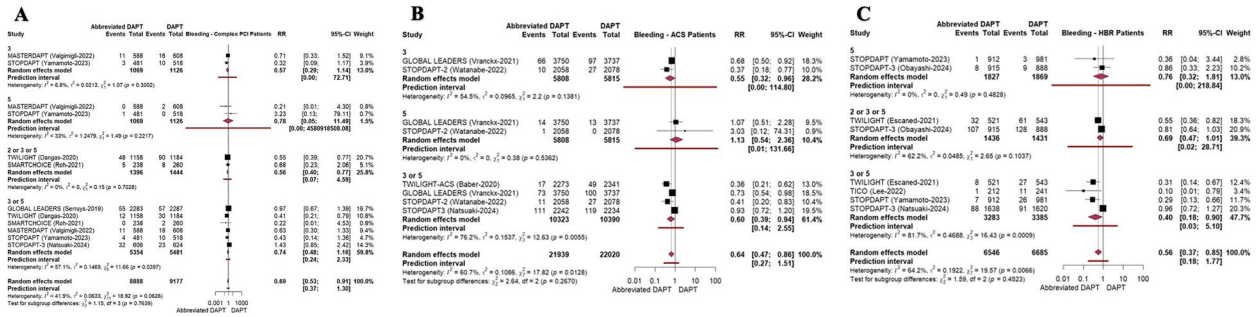

Fig. 6 *Bleeding Outcomes*: **A** Forest plots representing the risk of BARC after abbreviated DAPT vs. conventional DAPT in the complex PCI subgroup; **B** Forest plots representing the risk of BARC after abbreviated DAPT vs. conventional DAPT in the ACS subgroup; **C** Forest plots representing the risk of BARC after abbreviated DAPT vs. conventional DAPT in the HBR subgroup

differences in BARC type 5 bleeding (RR: 1.13, 95%CI: 0.54–2.36, I^2: 0%) (Figs. 6B). In the HBR subgroup analysis, there was a substantial reduction in the incidence of BARC 3 or 5 bleeding in HBR patients randomized to abbreviated DAPT compared with those randomized to conventional DAPT (RR: 0.40, 95%CI: 0.18–0.90, I^2: 82%). However, significant heterogeneity was observed among studies reporting this outcome in HBR patients. Furthermore, there were no significant differences between abbreviated DAPT and conventional DAPT in terms of BARC type 5 and BARC type 2 or 3 or 5 bleeding (RR: 0.76, 95%CI: 0.32–1.81, I^2: 0%; RR: 0.69, 95%CI: 0.47–1.01, I^2: 62%, respectively) (Figs. 6C).

Sensitivity analysis

Supplemental Table 2 shows the sensitivity analysis using the leave-one-out analysis, which showed that removing none of the studies shows a significant difference in overall analysis. Meta-regression based on mean age, male percentage, DM, and hypertension was performed, as shown in Supplementary Figs. 24–27. As indicated, none of the variables had an association with all-cause mortality.

Publication bias

No significant publication bias was identified upon reviewing Begg's funnel plots and conducting Egger's test for all outcomes. The corresponding funnel plots are illustrated in Supplemental Figs. 28–33.

Discussion

This meta-analysis of RCTs evaluating abbreviated vs. conventional DAPT strategies following PCI revealed a favorable trend for shorter DAPT durations. While ischemic outcomes, including target vessel revascularization, any vessel revascularization, stroke, myocardial infarction, and in-stent restenosis, were comparable between the two strategies, abbreviated DAPT demonstrated significant advantages in terms of mortality and bleeding.

In terms of mortality, the study revealed a critical finding regarding all-cause mortality, which was significantly lower in the abbreviated DAPT group. It is noteworthy that in previous meta-analysis studies, all-cause mortality was not significantly different between conventional and abbreviated DAPT strategies [60, 61], our study provides a thought provoking benefit of the abbreviated DAPT strategy. This benefit was also observed in patients receiving DAPT for only one month, suggesting a potential opportunity worthwhile further investigation.

Current guidelines recommend DAPT duration for 6–12 months after PCI for the treatment of chronic coronary syndrome (CCS) and ACS [62–64]. However, in congruence with several meta-analyses in different populations after PCI, the similarity in ischemic outcomes across all subgroup analyses suggests that abbreviated DAPT does not compromise efficacy in preventing ischemic events [65–69].

To address the balance between bleeding and thrombosis, this meta-analysis further supports abbreviated DAPT, specifically showing fewer bleeding issues without compromising thrombosis.

Overt and severe bleeding (BARC 2, 3, 5) and severe bleeding (BARC 3, 5) were significantly reduced in the abbreviated DAPT group. These findings suggest that an abbreviated DAPT strategy may be associated with lower rates of bleeding events, particularly in certain subgroups of patients, which is in line with previous studies [65, 68]. Importantly, this benefit extended to patients at high bleeding risk, patients with complicated PCI, and those with acute coronary syndromes, demonstrating the safety and effectiveness of this strategy.

A prominent strength of our article lies in its comprehensive assessment of outcomes across the cardiometabolic disease spectrum. The effect on outcomes

was consistent across subgroup analysis, with the most intriguing findings below:

While previous guidelines recommend prolonged DAPT (3–6 months) for HBR patients [1, 62], this meta-analysis and several others [70–72] support abbreviated DAPT (1–3 months) as a safer alternative, reducing bleeding events without compromising ischemic protection. Additionally, the State-of-the-Art Review by Galli et al. suggested an individualized approach for DAPT strategy favoring the abbreviated DAPT approach [73].

Furthermore, optimal duration of DAPT in patients undergoing complex PCI remains under investigation, Apostolos et al. demonstrated that abbreviated DAPT significantly reduced the odds of major bleeding in patients undergoing complex PCI without increasing the ischemic events or mortality. Thus, it could be considered a safe and feasible option for such patients [69]. Moreover, it found that abbreviated DAPT was associated with lower MACE rates in this group, demonstrating its effectiveness in more complex scenarios [74, 75].

While concerns remain about increased ischemic events with abbreviated DAPT in ACS patients, Park et al. [76] suggest that abbreviated DAPT (1–3 months) offers similar ischemic protection with reduced bleeding risk compared to conventional DAPT (6–12 months). However, the most recent ACC guideline recommended that in ACS patients who are not at high bleeding risk, DAPT should be continued at least 1 year to reduce MACE. It is noteworthy that the 2025 ACC guideline also recommended an abbreviated DAPT strategy (after 1 month) as a logical approach in ACS patients with high bleeding risk with class of recommendation 2b [77].

This study observed a significant reduction in CV mortality among women receiving abbreviated DAPT. Given that several studies have introduced the female sex as a poor prognostic factor after PCI, probably due to older age and comorbidities [78–80] and different platelet reactivity and response to antiplatelet therapy in women compared to men [81], this gender-specific difference warrants further investigation, potentially concerning inherent dissimilarity in bleeding risk or DAPT response between men and women.

Furthermore, our analysis of secondary stenotic outcomes revealed minimal heterogeneity (I^2: 0–12%) regarding Cardiovascular mortality, stroke, in-stent thrombosis, and MACE across total and subgroup analysis, indicating highly consistent findings across included studies. However, non-fatal myocardial infarction showed low heterogeneity overall (I^2: 19%), with the 1-month DAPT subgroup demonstrating moderate heterogeneity (I^2: 62%). Additionally, any revascularization displayed moderate heterogeneity overall (I^2: 31%) with the 1-month DAPT subgroup demonstrating more heterogeneity (I^2: 60%). The aforementioned heterogeneity may reflect differences in study design or patient characteristics. However, sensitivity analyses confirmed that this variation does not materially affect the overall conclusion that abbreviated DAPT provides comparable protection against stenotic outcomes.

Our meta-analysis had some limitations, first, this is a study-level meta-analysis; thus, it was not feasible to perform a patient-level analysis. The different durations of follow-up and different P2Y12 inhibitors used across included RCTs may have affected the final results. Additionally, another possible limitation of our study may be attributable to the heterogeneity among patient populations and follow-up periods, differences in age mix, concomitant disorders, and gender ratio, which may affect the generalizability of our results. However, extensive sensitivity analyses and subgroup analysis were conducted to provide robustness of the results. Another limitation is that hazard ratios were not reported for all outcomes in the examined studies, preventing us from using HR as a consistent effect estimate to combine long-term statistics across studies. Furthermore, the term "complex PCI" encompasses a spectrum of PCI settings, making conducting sub-analyses for each definition impractical. Looking ahead, future studies should focus on overcoming these limitations. Specifically, the inconsistency in reporting HR should be addressed, as using HR would facilitate more robust comparisons across studies, particularly for long-term outcomes. Furthermore, conducting a network meta-analysis could provide more comprehensive insights by allowing the comparison of different treatment regimens, such as the duration of DAPT, even when these have not been directly compared in individual trials. This approach could yield more robust and generalized results, helping to clarify the optimal treatment strategies across varied patient populations and PCI settings.

Conclusion

In conclusion, an abbreviated DAPT strategy appears safe for patients undergoing PCI with less bleeding risks without compromising ischemic outcomes. In specific subgroups like females and complex PCI patients, individual patient characteristics and risk profiles should continue to guide clinical decision-making. The current evidence supports a move towards personalized antiplatelet therapy, where the duration of DAPT is tailored to each patient.

Supplementary Information

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Supplementary Material 1.

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Authors' contributions
H.R.S.: Supervision, data analysis and visualization, and drafting of the manuscript. E.K.: Title/abstract screening, full-text screening, data extraction, and drafting of the manuscript. M.M.: Title/abstract screening, full-text screening, and data extraction. F.J.E.: Title/abstract screening, full-text screening, and data extraction. A1.N.: Visualization and drafting of the manuscript. A2.N.: Visualization and drafting of the manuscript. H.R.: Title/abstract screening and full-text screening. P.K.: Supervision. K.M.A.: Supervision and review of the final manuscript. L.H.P.R.: Supervision and review of the final manuscript. W.S.A.: Supervision and review of the final manuscript. A.P.A.: Supervision and review of the final manuscript. K.H.: Conceptualization of the work, supervision and final approval of the manuscript.

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Declarations

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Consent for publication
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Competing interests
The authors declare no competing interests.

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