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META-ANALYSIS

Efficacy and Safety Outcomes of Short Duration Antiplatelet Therapy with Early Cessation of Aspirin Post Percutaneous Coronary Intervention: A Systematic Review and Meta-analysis

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Abstract: ***Background*:** The optimal duration of dual antiplatelet therapy is a matter of ongoing research. Clinical studies are assessing the optimal duration with the most favourable risk to benefit ratio. The efficacy of P2Y12 receptor inhibitors comparable to aspirin in preventing recurrent ischaemic events in patients with coronary artery diseases.

***Objectives*:** To investigate the outcomes of short-duration dual antiplatelet therapy after PCI with early discontinuation of aspirin while maintaining patients on P2Y12 inhibitor through systematic review and meta-analysis of available literature.

***Methods*:** We systematically searched PubMed, Cochrane Central Register of Controlled Trials (CENTRAL), and ClinicalTrials.gov. We included randomized controlled studies that measured clinical outcomes of efficacy (mortality and ischaemic events) and safety (bleeding) of short and standard-duration dual antiplatelet therapy. The protocol of this study was registered in the international prospective register of systematic reviews PROSPERO registry (CRD42020171468).

***Results*:** Four randomized controlled trials were included; GLOBAL LEADERS, SMART-CHOICE, STOPDAPT-2, and TWILIGHT. The total number of patients was 29,089. The safety outcomes showed a significant reduction in major bleeding events with short-duration dual antiplatelet therapy; the risk ratio was 0.61 (95% CI 0.38-0.99; z=2,00, p=0.05). There was no difference between short and standard-duration dual antiplatelet therapy regarding efficacy outcomes (all-cause death, major adverse cardiovascular events, myocardial infarction, stroke, and stent thrombosis).

***Conclusion*:** Short-duration dual antiplatelet therapy followed by P2Y12 inhibitor monotherapy after PCI is a feasible option and can be adopted, especially in patients with a high risk of bleeding.

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1. INTRODUCTION

The use of dual antiplatelet therapy (DAPT) is one of the significant advances in the management of ischaemic heart diseases since the introduction of percutaneous coronary intervention (PCI). By combining both aspirin and one of the P2Y12 receptor inhibitors, dual antiplatelet therapy (DAPT) has led to major reductions in the rate of recurrent ischemic events and, more importantly, coronary stent thrombosis [1-3]. However, the occurrence of bleeding remains the main concern with the use of combined antiplatelet therapy [4, 5].

The optimal duration of DAPT is a matter of ongoing research. Clinical studies are assessing the optimal duration with the most favourable risk to benefit ratio. The European

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Society of Cardiology recommends DAPT to be continued for one year in patients with the acute coronary syndrome, whether treated invasively or conservatively. However, in high bleeding risk patients, discontinuation of P2Y12 inhibitors can be considered after six months. In patients with stable ischaemic heart disease, the recommended DAPT duration with the use of contemporary drug-eluting stents is six months after PCI and only three months in patients with bleeding concerns [6].

The P2Y12 receptor inhibitors have comparable efficacy to aspirin in preventing recurrent ischaemic events in patients with coronary artery diseases [7, 8]. Early discontinuation of aspirin after PCI was assessed in several studies in patients with atrial fibrillation who need concurrent anticoagulation after PCI [9-12], but this approach has not been widely adopted yet.

This study aims to examine the outcomes associated with short-duration DAPT after PCI with early discontinuation of aspirin while maintaining P2Y12 inhibitor. We conducted a rigorous systematic review and meta-analysis of the literature to assess the relevant clinical outcomes.

2. METHODS

We followed the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) reporting guide- lines in preparing this systematic review and meta-analysis [13]. The protocol of this study was registered in the international prospective register of systematic reviews PROS- PERO registry (CRD42020171468).

2.1. Search Strategy

We systematically searched the databases of PubMed, Cochrane Central Register of Controlled Trials (CENTRAL), and ClinicalTrials.gov. We used the following keywords and subject headings in the search: percutaneous coronary intervention, dual antiplatelet therapy, drug-eluting stent, and aspirin. We restricted the search only to studies published in English after 1995.

Randomized-controlled trials investigating early discontinuation of aspirin following short-duration DAPT after PCI in adult participants (age ≥ 18 years) were included in this meta-analysis. The intervention group was identified as patients who received short-duration DAPT consisting of aspirin and P2Y12 inhibitor for less than 6 months followed by P2Y12 inhibitor only. The control group received standard duration DAPT for more than 6 months. We only included studies that measured clinical outcomes of efficacy (mortality and ischaemic events) and safety (bleeding).

We excluded all non-randomized studies, studies with short-duration DAPT followed by aspirin only, and studies with standard or longer duration of DAPT.

The safety endpoint used for this analysis was Bleeding Academic Research Consortium (BARC) type 3 or 5 bleeding [14]. The efficacy endpoints included all-cause mortality, Major Adverse Cardiovascular Events (MACE), myocardial infarction (MI), stroke, and stent thrombosis.

2.2. Extraction of Data

Two reviewers screened the title and abstract of all retrieved articles. Full text of relevant articles was re viewed. Two independent reviewers extracted data from selected studies that met the inclusion criteria. Disagreements or inconsistencies at any step were reviewed and resolved by a third reviewer. We extracted the trial characteristics (trial registration number, year of the publication, number of participants, follow-up duration, number of participating centres, and location), patient characteristics (mean age, comorbidities including hypertension and DM; and percentages of stable ischaemic heart disease and acute coronary syndrome) and outcome measures (efficacy and safety endpoints) from all studies consistent with the inclusion criteria. We used the Cochrane Collaboration's tool for assessing the risk of bias to evaluate the quality of the included studies.

2.3. Statistical Analysis

The comparison of the clinical outcomes of the short-duration versus standard DAPT was analyzed by calculating the risk ratios and 95% confidence interval. A random-effect model was used to address the expected heterogeneity in the studied populations, types of P2Y12 inhibitors used, and the duration of treatment and follow-up. We assessed the heterogeneity of the studies with the Chi X2 test and Higgins I^2 statistics. The I^2 value less than 25% was considered low, 25-50% was considered to be moderate, and values more than 50% were deemed to show a high probability of hetero geneity. A *p*-value of less than 0.05 was considered statistically significant. The assessment of publication bias using funnel plot tests was not done due to the small number of studies included in the analysis (less than 10) that limits the power of any test to detect real bias. The Cochrane Collaboration Review Manager (RevMan) [Computer program]; Version 5.3, was used to undertake the statistical analysis.

3. RESULTS

A total of 4 randomized controlled clinical trials investigating short-duration DAPT with early cessation of aspirin (Fig. **1**) were included in the meta-analysis. These are GLOBAL LEADERS [15], SMART-CHOICE [16], STOP-DAPT-2 [17] and TWILIGHT [18] trials.

The total number of patients enrolled in the included studies was 29,089 (14,530 in the short DAPT arm and 14,559 in the standard DAPT arm). The basic characteristics of the four studies are shown in Table **1**, and the main outcome measures applied in the studies are shown in Table **2**. The clinical presentation of the patients was stable ischaemic heart disease in 14,095 (48.45%) patients and ACS in 14,990 (51.53%) patients. The duration of follow-up was 12-24 months in all studies.

All studies assessed the outcomes of using short-duration DAPT (≤ 3 months aspirin and P2Y12 inhibitor) followed by P2Y12 inhibitor monotherapy against standard duration DAPT (12 months aspirin and P2Y12 inhibitor). The duration of DAPT in the short arm was 1 month in both

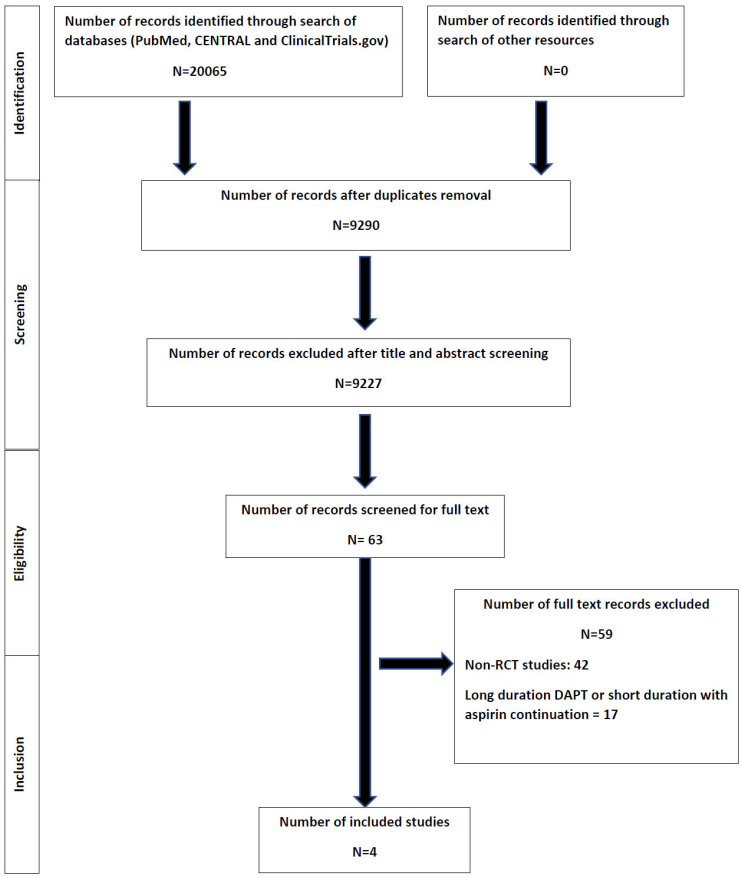


Fig. (1). Flow chart of the identification and screening process.

Table 1. Trial-specific characteristics.

Characteristics	Global Leaders	Smart-Choice	STOPDAPT-2	Twilight
Year	2018	2019	2019	2019
Patient no.	15,968	2993	3045	7119
Female (%)	3714 (23·3%)	795 (26.6%)	672 (22.3%)	1698 (23.8%)
Mean age	64·5 years	64.0 years	68.6 years	65.0 years
Study design	Multicentre, open-label, randomized superiority trial (18 countries)	Multicentre, open-label, non-inferiority, randomized trial (Korea)	Multicentre, open-label, randomized clinical trial (Japan)	Multicentre, double-blind, randomized, trial (11 countries)
Patient group Acute Coronary Syndrome Stable Ischaemic Heart Disease	7487/15968 (46.9%) 8481/15968 (53.1%)	1741/2993 (58.2%) 1250/2993 (41.8%)	1148/3009 (38.1%) 1861/3009 (61.9%)	4614/7119 (64.8%) 2503/7119 (35.2%)
Commodities Hypertension Diabetes Mellitus	11715/15914 (73.6%) 4038/15957 (25.3%)	1840/2993 (61.4%) 1122/2993 (37.5%)	2221/3009 (73.9) 1159/3009 (38.5%)	5154/7119 (72.3%) 2620/7119 (36.8%)
Stent type	Biolimus A9-eluting stent	Xience Prime, Xience Expedition, Xience Alpine, Promus Element, Promus Premier, SYNERGY or Orsiro	-	-
Follow-up duration	2 years	1 year	1 year	1 year
Type of analysis	Intention to treat	Intention-to-treat and per-protocol	Intention-to-treat and per-protocol	Intention-to-treat and per-protocol
Trial registration Number	NCT01813435	NCT02079194	NCT02619760	NCT02270242

Table 2. Trial-specific reported outcome measures and endpoints.

-	Global Leaders	Smart-Choice	Stopdate-2	Twilight
DAPT regimen: Experimental *vs.* Control	Aspirin and ticagrelor (1month) *vs.* Aspirin and clopidogrel or tica-grelor (12months)	Aspirin and (clopidogrel or prasugrel or ticagrelor) (3 months) *vs.* Aspirin and (clopidogrel or prasugrel or ticagrelor) (12-months)	Aspirin and clopidogrel or prasugrel (1 month) *vs.* Aspirin and clopidogrel (12 months) ACS: aspirin and prasugrel for 1 month then aspirin and clopidogrel for 12 months	Aspirin and ticagrelor (3 months) *vs.* Aspirin and ticagrelor (15 months)
Post-DAPT regimen: Experimental *vs.* Control	Ticagrelor (23 months) *vs.* Aspirin (12 months)	P2Y21 inhibitor *vs.* Aspirin (indefinite)	Clopidogrel (5 years) *vs.* Aspirin (5 years)	Ticagrelor and placebo (12 months) then standard of care *vs.* standard of care
Primary endpoints	All-cause death or new Q-wave myocardial infarction	Composite of all-cause mortality, myocardial infarction, or stroke	Composite of cardiovascular death, myocardial infarction, definite stent thrombosis, ischemic or hemorrhagic stroke, or TIMI major or minor bleeding	BARC type 2, 3, or 5 bleeding
Secondary endpoints	*BARC grade 3 or 5 bleeding. *Composite endpoint of all-cause death, new Q-wave MI, or stroke. *Myocardial infarction. *Stroke. *Target vessel or any revascularization. *Definite stent thrombosis.	*All cause death *Myocardial infarction *Stroke *Cardiac death *Stent thrombosis *BARC type 2-5 *BARC 3 or 5	*Cardiovascular endpoint: composite of cardiovascular death, myocardial infarction, definite stent thrombosis; or ischaemic or hemorrhagic stroke. *Bleeding endpoint: TIMI major or mi-nor bleeding *Death *MI *Definite stent thrombosis *Probable or definite stent thrombosis *Stroke *Bleeding (TIMI, BARC, GUSTO, in-tracranial, gastrointestinal) *Death or myocardial infarction *Cardiovascular death or myocardial infarction *Major adverse cardiac events *Any coronary revascularization	*Death from any cause, nonfatal myocardial infarction, or nonfatal stroke *Death from cardiovascular causes, nonfatal myocardial infarc-tion, or nonfatal ischemic stroke *ALL cause death *Cardiovascular death *Myocardial infarction *Ischemic stroke *Bleeding: BARC type 3 or 5 TIMI (major or minor), GUSTO ,ISTCH *Stent thrombosis, definite or probable

GLOBAL LEADERS and STOPDAPT-2, and 3 months in both SMART-CHOICE and TWILIGHT trials. All studies discontinued aspirin after the indicated time and continued patients on P2Y12 inhibitor monotherapy in the interventional group. The type of P2Y12 inhibitor in the interventional group was ticagrelor in both GLOBAL LEADERS and TWILIGHT studies. For STOPDAPT-2, clopidogrel or prasugrel was used during the DAPT phase, and only clopidogrel was used during the monotherapy phase. In the SMART-CHOICE trial, the type of P2Y12 inhibitor was either clopidogrel, prasugrel, or ticagrelor.

We assessed the studies for the risk of bias and found them to be of high quality overall. The design of the study was open-label in the three (GLOBAL LEADERS, SMART-CHOICE, and STOPDAPT-2) trials, while the TWILIGHT study had a double-blind design. Event adjudication was performed by independent committees in all the studies except in the GLOBAL LEADERS.

To address the risk of bias, further sub-analysis was done by enrolling the GLASSY sub-study to replace the GLOBAL LEADERS trial [19]. The GLASSY sub-study evaluated the data of 7,585 patients (47.5% of the overall patients enrolled in the GLOBAL LEADERS trial) with 3,794 patients in the experimental arm and 3,791 patients in the control arm. The sub-study aimed to overcome significant limitations in the parent study by reporting the results through an independent clinical event committee to adjudicate investigator-reported outcomes. The protocol of the sub- study was similar with the experimental group received 1- month DAPT (aspirin plus ticagrelor) followed by 23--month ticagrelor monotherapy *vs*. the control group with 12--month DAPT followed by aspirin alone for 12 months. The efficacy primary endpoint was more inclusive in the sub-study and included a composite endpoint of death, MI, stroke, or urgent target vessel revascularization (TVR). Safety outcomes were analyzed as co-primary endpoints, while

in the parent study, safety outcomes were analyzed as secondary endpoints. The statistical analysis was designed for both non-inferiority and superiority targets. Data analysis provided data at 1, 12, and 24 months follow-up.

The secondary analysis was done at 12-month interval from all included studies. These data were available for the GLASSY sub-study but not the GLOBAL LEADERS trial.

3.1. Safety Endpoints

The risk of major bleeding was evaluated using different scores in the four trials. The Bleeding Academic Research Consortium (BARC) type 3 or 5 bleeding was the only score that was reported across all included studies and was therefore included in this meta-analysis. The analysis showed a higher bleeding rate in the standard DAPT group, but this did not reach statistical significance (Fig. **2A**). The BARC type 3 or 5 bleeding was 217/14530 in the short DAPT *vs*. 279/14559 in the control group. Risk ratio was 0.62 (95% CI 0.37-1.05; z=1.79, p=0.07). The risk of heterogeneity was high, with I^2=79%.

However, in the secondary analysis, the results of the GLASSY sub-study of the GLOBAL LEADERS trial were included instead. The safety outcomes showed a significant reduction of major bleeding events with short DAPT (124/10344 with short DAPT *vs*. 186/10362 with standard DAPT), risk ratio was 0.61 (95% CI 0.38-0.99; z=2,00, p=0.05). The risk of heterogeneity was moderate, I2=71% (Fig. **3A**).

3.2. Efficacy Endpoints

We analyzed the data of the efficacy outcomes represented by the ischaemic events rate in relation to the duration of the DAPT. The meta-analysis was conducted for the endpoints of all-cause death, MACE, myocardial infarction, stroke, and stent thrombosis (Fig. **2B-F**).

Regarding all-cause mortality, there was no significant difference between short DAPT (300/14530) and standard DAPT (334/14559) (Fig. **2B**), the risk ratio was 0.90 (95% CI 0.77-1.05; z=1.35, p=0.18) with a low risk of heterogeneity, (I^2=0%).

The rate of MACE was not significantly different between the two groups (568/14530 with short DAPT *vs*. 625/14559 with standard DAPT) (Fig. **2C**), a risk ratio of 0.91 (95% CI 0.81-1.02; z=1.69, p=0.09), with a low risk of heterogeneity, (I^2=0%).

Similarly, no significant difference was found for myocardial infarction (367/14530 with short DAPT *vs*. 373/14559 with standard DAPT (Fig. **2D**), a risk ratio of 0.99 (95% CI 0.86-1.14; z=0.19, p=0.85), with a low risk of heterogeneity, I^2=0%.

For stroke, the rate in each group was similar 115/14530 with short DAPT *vs*. 111/14559 with standard DAPT (Fig. **2E**), risk ratio 1.14 (95% CI 0.65-1.98; z=0.45, p=0.65), with a high risk of heterogeneity I^2=59%. The rate of stent thrombosis was also comparable, 85/14530 with short DAPT and 86/14559 with standard DAPT (Fig. **2F**), a risk ratio of 0.98 (95% CI 0.73-1.33, z=0.13, p=0.90), with low risk of heterogeneity, I^2=0%.

The outcomes of the efficacy were similar in the secondary analysis with no difference for all-cause death, MACE, MI, stroke, and stent thrombosis between the two groups (Fig. **3A-F**).

3.3. Subgroup Analysis

A subgroup analysis was conducted analyzing the bleeding rate and MACE rate in patients presenting with acute coronary syndrome and stable ischaemic heart disease. The GLASSY sub-study, SMART CHOICE, and TWILIGHT trials only provided data for bleeding events for these subgroups at 1-year follow-up.

In the ACS patients, the bleeding rate showed a highly significant difference between the short DAPT *vs*. standard DAPT, with a risk ratio 0.59 (95% CI 0.47-0.74; z=4.56, p=0.00001) (Fig. **4A**). The risk of heterogeneity was low, I2=10%. For the major adverse cardiovascular events, no significant difference was found between short DAPT and standard DAPT arms (Fig. **4B**), risk ratio 0.87 (95% CI 0.75-1.02; z=1.75, p=0.08). The risk of heterogeneity was low, I^2=0%.

In stable ischaemic heart disease patients, there was no significant difference in the rate of bleeding between short and standard DAPT (Fig. **5A**), risk ratio 0.88 (95% CI 0.55-1.41; z=0.51. p=0.61), the heterogeneity risk was moderate, I2=69%. The rate of major adverse cardiovascular events between both arms showed no significant difference (Fig. **5B**). The risk ratio 0.91 (95% CI 0.70-1.18; z=0.74, p=0.46). The risk of heterogeneity was moderate, I2=29%.

4. DISCUSSION

The current meta-analysis assesses short-duration DAPT with early cessation of aspirin *versus* standard DAPT followed by aspirin alone. There are four major randomized controlled clinical trials enrolled in the analysis. The findings of this meta-analysis show a favourable risk-benefit ratio of stopping aspirin early after PCI and continuing P2Y12 inhibitor only.

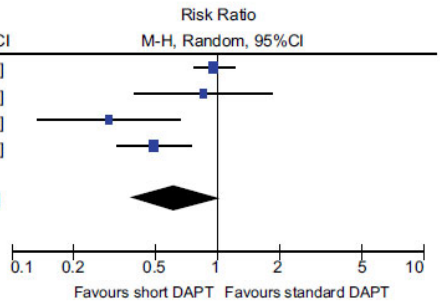
In terms of safety, there is a statistically significant reduction of major bleeding rate with short-duration DAPT followed by P2Y12 inhibitor monotherapy. The results indicate that early discontinuation of aspirin may provide an advantage to patients in lowering the mortality and morbidity secondary to bleeding.

Regarding the efficacy, short-duration DAPT followed by P2Y12 inhibitor monotherapy is non-inferior in comparison with standard DAPT regimen. There is no significant difference in ischaemic endpoints after PCI, including overall mortality, ischaemic MACE, MI, stroke, and stent thrombosis between the two regimens.

A- Major bleeding

Study or Subgroup	Short duration DAPT Events	Total	Standard duration DAPT Events	Total	Weight	Risk Ratio M-H, Random, 95%CI
GLOBAL LEADERS	163	7980	169	7988	32.5%	0.97 [0.78,1.19]
SMART-CHOICE	12	1495	14	1498	19.7%	0.86 [0.40,1.85]
STOPDAPT-2	8	1500	27	1509	19.3%	0.30 [0.14,0.65]
TWILIGHT	34	3555	69	3564	28.4%	0.49 [0.33,0.74]
Total (95%CI)		14530		14559	100.0%	0.62 [0.37,1.05]
Total events	217		279			

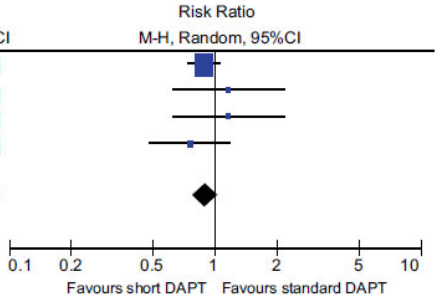
Heterogeneity: Tau^2=0.21 ; Chi^2=14.49, df=3 (P=0.002); I^2=79%
Test for overall effect: Z=1.79 (P=0.07)



B- All-cause death

Study or Subgroup	Short duration DAPT Events	Total	Standard duration DAPT Events	Total	Weight	Risk Ratio M-H, Random, 95%CI
GLOBAL LEADERS	224	7980	253	7988	75.7%	0.89 [0.74,1.06]
SMART-CHOICE	21	1495	18	1498	6.1%	1.17 [0.63,2.19]
STOPDAPT-2	21	1500	18	1509	6.1%	1.17 [0.63,2.19]
TWILIGHT	34	3555	45	3564	12.1%	0.76 [0.49,1.18]
Total (95%CI)		14530		14559	100.0%	0.90 [0.77,1.05]
Total events	300		334			

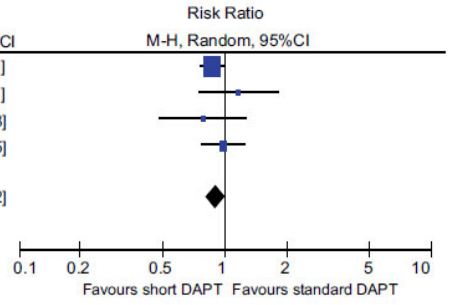
Heterogeneity: Tau^2=0.00 ; Chi^2=1.97, df=3 (P=0.58); I^2=0%
Test for overall effect:Z= 1.35 (P=0.18)



C- Major Adverse Cardiovascular Events (MACE)

Study or Subgroup	Short duration DAPT Events	Total	Standard duration DAPT Events	Total	Weight	Risk Ratio M-H, Random, 95%CI
GLOBAL LEADERS	362	7980	416	7988	65.5%	0.87 [0.76,1.00]
SMART-CHOICE	42	1495	36	1498	6.4%	1.17 [0.75,1.81]
STOPDAPT-2	29	1500	37	1509	5.3%	0.79 [0.49,1.28]
TWILIGHT	135	3555	137	3564	28.8%	0.99 [0.78,1.25]
Total (95%CI)		14530		14559	100.0%	0.91 [0.81,1.02]
Total events	568		626			

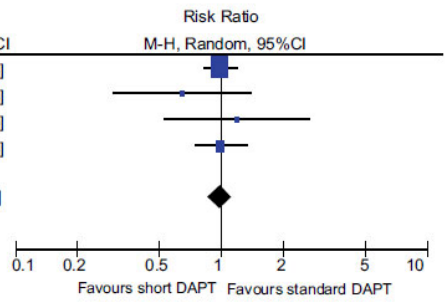
Heterogeneity: Tau^2=0.00; Chi^2=2.45, df=3 (P=0.48); I^2=0%
Test for overall effect:Z= 1.69 (P=0.09)



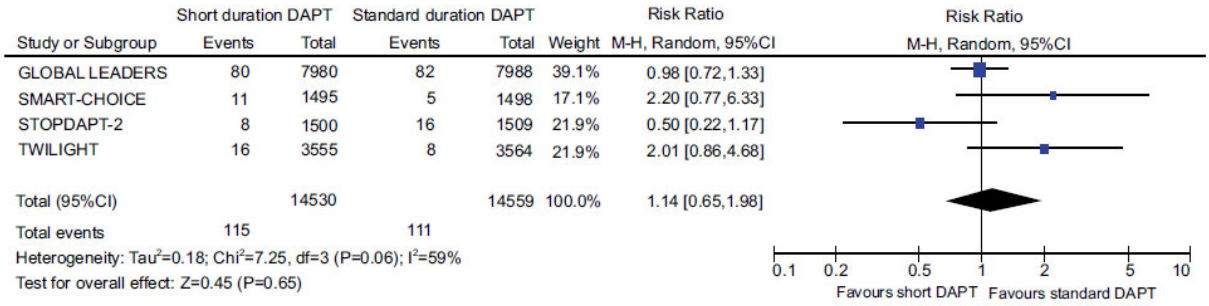
D- Myocardial infarction

Study or Subgroup	Short duration DAPT Events	Total	Standard duration DAPT Events	Total	Weight	Risk Ratio M-H, Random, 95%CI
GLOBAL LEADERS	248	7980	250	7988	67.6%	0.99 [0.84,1.18]
SMART-CHOICE	11	1495	17	1498	3.5%	0.65 [0.30,1.38]
STOPDAPT-2	13	1500	11	1509	3.2%	1.19 [0.53,2.65]
TWILIGHT	95	3555	95	3564	25.7%	1.00 [0.76,1.33]
Total (95%CI)		14530		14559	100.0%	0.99 [0.86,1.14]
Total events	367		373			

Heterogeneity: Tau^2=0.00; Chi^2=1.41, df=3 (P=0.70); I^2=0%
Test for overall effect: Z=0.19 (P=0.85)



E- Stroke



F- Stent thrombosis

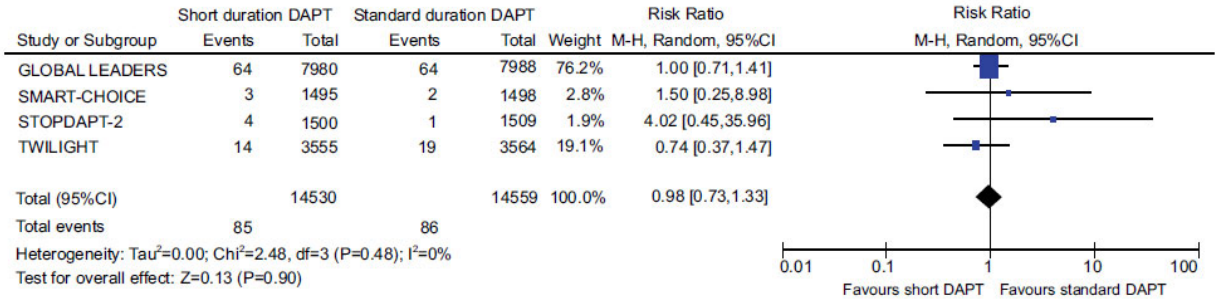
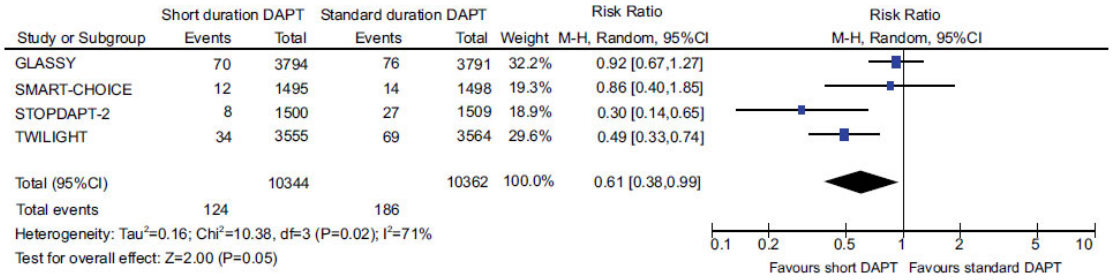
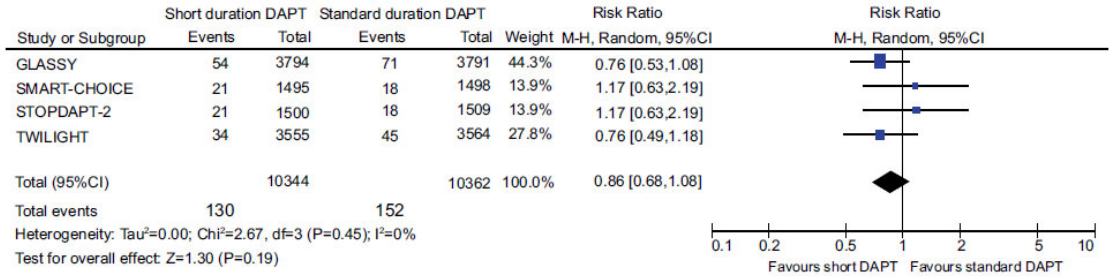


Fig. (2). (**C-F**) Forest plot for major bleeding [a], all-causes death, MACE [b], myocardial infarction, stroke and stent thrombosis. (**A**): BARC type 3 to 5 bleeding. (**B**): Major Adverse Cardiovascular Events (composite of all-cause mortality, myocardial infarction, or stroke).

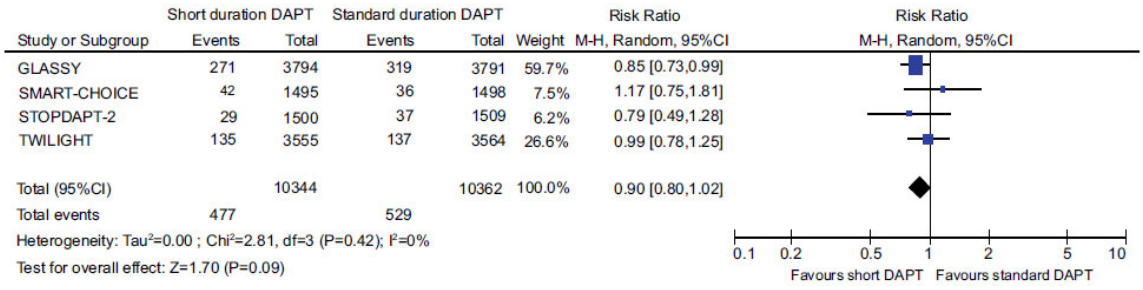
A. Major bleeding



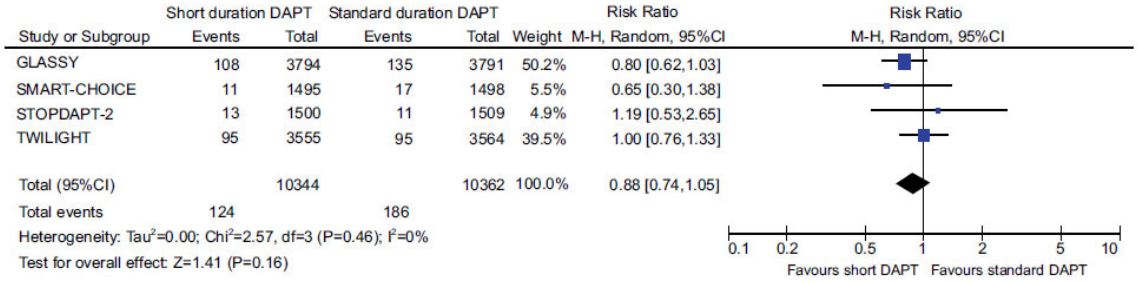
B. All-cause death



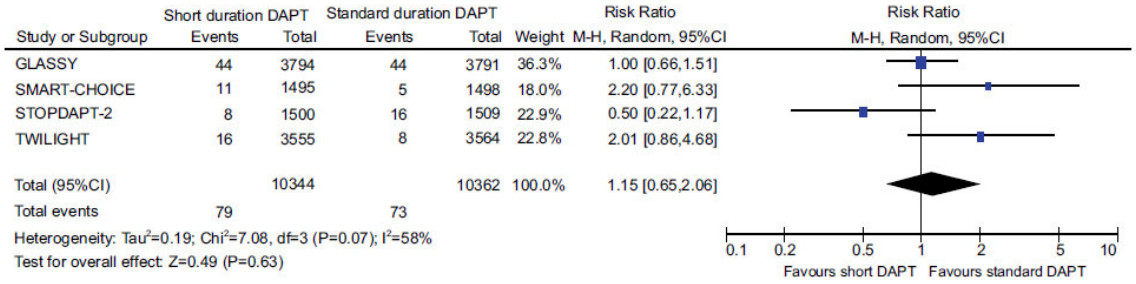
C. Major Adverse Cardiovascular Events (MACE)



D. Myocardial infarction



E. Stroke



F. Stent thrombosis

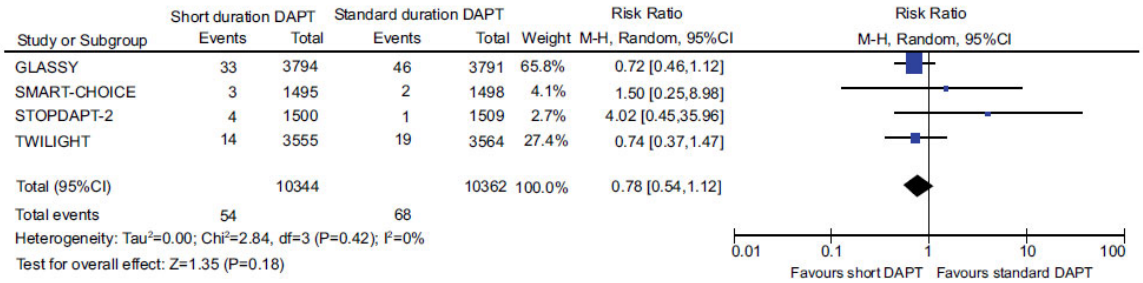


Fig. (3). Forest plot for major bleeding, all-causes death, MACE, myocardial infarction, stroke and stent thrombosis using GLASSY sub-study of GLOBAL LEADERS trial.

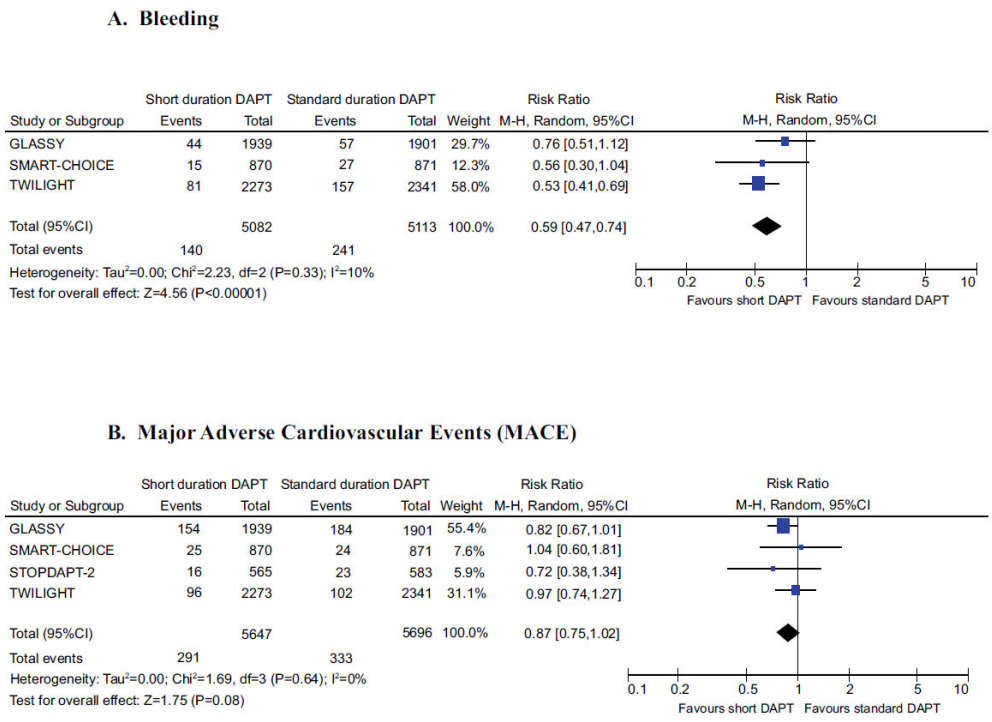


Fig. (4). Forest plot for bleeding events and major adverse cardiovascular events in the subgroup of acute coronary syndrome patients using GLASSY sub-study of GLOBAL LEADERS trial.

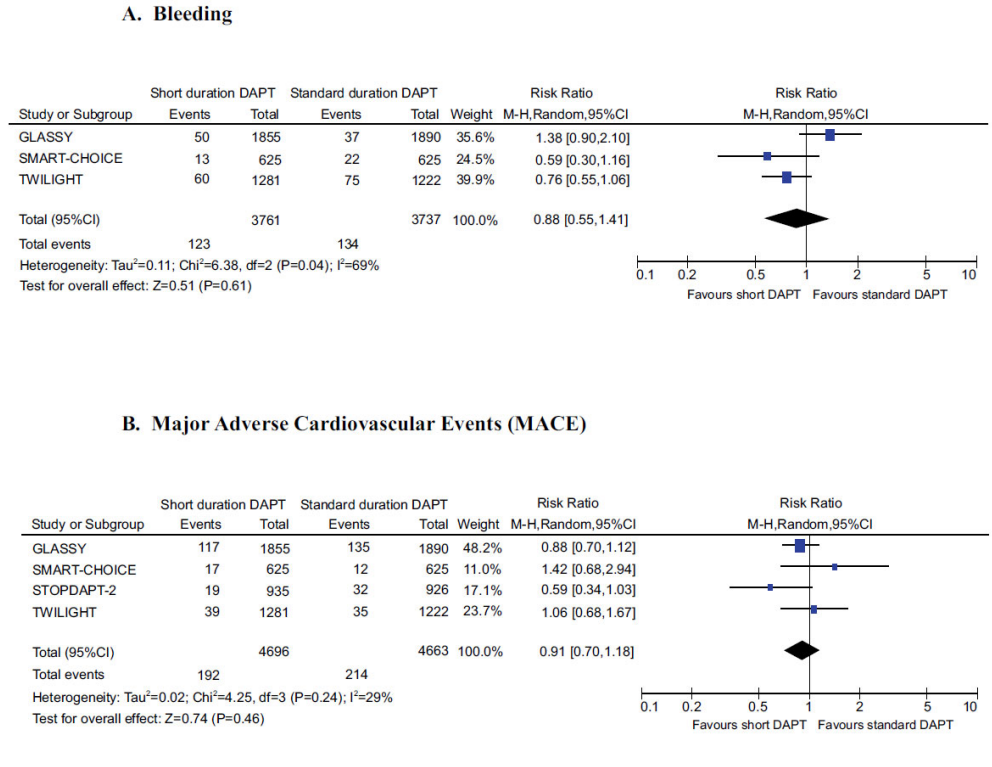


Fig. (5). Forest plot for bleeding events and major adverse cardiovascular events in the subgroup of stable ischaemic heart disease patients using GLASSY sub-study of GLOBAL LEADERS trial.

The major challenge in patients with coronary artery disease is balancing the risk of ischaemic events (cardiovascular mortality, recurrent ischaemia, and stent thrombosis) against the risk of bleeding due to pharmacotherapy. The advances in the technology of newer generation drug-eluting stents and the introduction of more potent P2Y12 inhibitors facilitate the testing of new regimens of dual antiplatelet therapy (DAPT). The optimal duration of DAPT is still debatable, especially in patients with a high risk of bleeding.

The concept of lowering the number of antiplatelet agents after PCI is attracting more attention. It has been investigated in an increasing number of studies in the last years. The results of our meta-analysis are consistent with other studies regarding the safety and efficacy of short-duration DAPT (≤ 6 months) [20-23].

Until recently, early discontinuation of aspirin was not considered as an option for patients treated with PCI. New data indicate cessation of aspirin can be possible in PCI patients with a history of atrial fibrillation and anticoagulant use [24].

The risk of bleeding after PCI can be high in a specific group of patients. In patients with acute coronary syndrome who received DAPT, the risk of bleeding was up to 13% 12 months after discharge from the hospital. Interestingly, the bleeding events can be recurrent in 26% of patients and continue even after cessation of P2Y12 inhibitors [25].

The subgroup analysis of ACS patients in this meat-analysis shows improved outcomes with the short-duration DAPT and P2Y12 inhibitor monotherapy. There is a highly significant reduction in bleeding events without any increase in the ischaemic outcomes in comparison with standard DAPT followed by aspirin.

Our results support the utility of short-duration DAPT followed by P2Y12 inhibitor monotherapy, especially with high bleeding risk, intolerance to aspirin, and in cases of emergency or urgent non-cardiac surgery with the need to stop DAPT early.

5. LIMITATIONS

The limitations of this meta-analysis are related to the differences in the endpoint definitions between the included trials. Secondly, the regimen of P2Y12 inhibitor varied between studies with ticagrelor used in both GLOBAL LEADERS and TWILIGHT, clopidogrel in STOPDAPT-2, and any P2Y12 inhibitor in SMART- CHOICE. Third, the enrolled patients' population varied in the studies with GLOBAL LEADERS and TWILIGHT trials, which enrolled multi--ethnic patients, whereas STOPDAPT-2 and SMART-CHOICE were restricted to Asian patients.

Fourth, high-risk patient representation differed across trials, with the TWILIGHT trial enrolling only patients with a high risk of ischaemia or bleeding (clinical or angiographic), with the majority of patients in the other three trials being at low to intermediate risk. The highest presentation of acute coronary syndrome was in TWILIGHT (64.8% of the total population), and the lowest was in STOPDAPT-2 (38.1%).

Another procedural difference across the trials was the high rate of intravascular imaging, with more than 80% of patients in STOPDAPT-2 and 25% in SMART-CHOICE having IVUS. On the other hand, in GLOBAL LEADERS and TWILIGHT, were not specified.

CONCLUSION

Short-duration DAPT followed by P2Y12 inhibitor monotherapy after PCI is a feasible option and can be adopted especially in patients with a high risk of bleeding. Further studies are required to confirm the advantages of early aspirin suspension in larger patients' cohorts.

LIST OF ABBREVIATIONS

ACS	=	Acute Coronary Syndrome
SIHD	=	Stable Ischaemic Heart Disease
MI	=	Myocardial Infarction
PCI	=	Percutaneous Coronary Intervention
DAPT	=	Dual Antiplatelet Therapy
MACE	=	Major Adverse Cardiovascular Events

CONSENT FOR PUBLICATION

Not applicable.

STANDARD OF REPORTING

PRISMA guidelines and methodologies were followed.

FUNDING

None.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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Declared none.

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