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RESEARCH ARTICLE

Optimal Duration of Dual Antiplatelet Therapy in Acute Coronary Syndrome: A Systematic Review and Meta-analysis

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ABSTRACT

Background: Dual antiplatelet therapy (DAPT) with aspirin and P2Y12 inhibitor is the main post-acute coronary syndrome (ACS) treatment. Current guidelines recommend 12 months of DAPT, but the optimal duration is unclear because longer therapy may reduce ischemic events but increase bleeding risk. **Aim:** To perform a meta-analysis to assess the efficacy and safety of various durations of DAPT in patients with ACS. **Methods:** A systematic review and meta-analysis following the PRISMA 2020 guidelines was conducted. Randomized controlled trials (RCTs) assessing the efficacy of drug therapies on cardiovascular outcomes were searched for using PubMed/MEDLINE, Embase, Scopus, Web of Science, and the Cochrane Library. We enrolled in this study adult patients with ACS who were randomized to various DAPT durations. The primary efficacy end point was major adverse cardiovascular events (MACE), and the primary safety end point was major bleeding. Random-effects model estimates of pooled risk ratios (RRs) with 95% CIs were assessed. **Study Characteristics:** 18 studies including a total of 24,860 patients; Compared with 12-month DAPT, short-duration therapy (3–6 months) achieved similar rates of MACE but decreased major bleeding. DAPT longer than 12 months decreased recurrent myocardial infarction and stent thrombosis, but increased the risk of bleeding. There were no significant differences in the risk of all-cause mortality, cardiovascular mortality or stroke. There was low to moderate heterogeneity (I^2 = 12–34%) and no evidence of publication bias. **Conclusions:** In selected patients with ACS, short-duration DAPT provides similar ischemic protection but lower risk of major bleeding compared to extended DAPT which is advantageous for high-bleeding-risk patients. This reinforces an individualized based approach to DAPT duration according to ischemic and bleeding risk profiles.

Keywords: Acute coronary syndrome; dual antiplatelet therapy; DAPT; systematic review; meta-analysis; myocardial infarction; bleeding; PRISMA.

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INTRODUCTION

Acute coronary syndrome (ACS) representing STEMI, NSTEMI and unstable angina is still recognized as a major cause of morbidity and mortality worldwide. Although advances in early reperfusion strategies, percutaneous coronary intervention (PCI), and evidence-based pharmacotherapy have markedly improved survival, recurrent ischemic events remain an important contributor to adverse cardiovascular outcomes [1–2]. That is dual antiplatelet therapy (DAPT), which includes aspirin and a P2Y12 receptor inhibitor, is the cornerstone of secondary prevention after acute coronary syndromes (ACS) through inhibition of platelet aggregation and reduction in thrombotic complications among patients [3, 4].

Patients without high bleeding risk receiving PCI or medical treatment for ACS are recommended to receive current international guideline directed 12 months of DAPT before maintenance therapy [1, 3]. These recommendations are derived from landmark randomized clinical trials showing that extended platelet inhibition reduces recurrent myocardial infarction, stent thrombosis and cardiovascular mortality [5-8]. However, long-term DAPT is also related to a higher bleeding risk, which contributes independently to morbidity and mortality [9].

Evaluation of individualized DAPT duration has attracted significant interest in recent years. As a result of advances in PCI techniques, emergence of newer-generation DESs and more potent P2Y12 inhibitors such as ticagrelor and prasugrel; investigations into abbreviated DAPT regimens have sparked, particularly for high bleeding risk [10–12]. In contrast, prolonged DAPT beyond 12 months has been evaluated in the group of high Ischemic risk patients such as those with persistent ischemic risk due to diabetes mellitus, diffuse coronary artery disease, previous myocardial infarction, or recurrent events [6, 7, 13].

Conflicting results concerning the balance between ischemic protection and bleeding complications for varying treatment durations have been reported in several randomized controlled trials and meta-analyses [10–15]. Shorter DAPT seems to minimize bleeding without sacrificing ischemia in so-called 'high risk' patients, whereas longer therapy may further reduce myocardial infarction and stent thrombosis but at the price of higher rates of bleeding [11, 14–16]. Individualized management of the duration of DAPT, however, continues to be an important dilemma in modern cardiovascular medicine.

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Cohort studies and systematic reviews were defined as the highest levels of evidence synthesized across existing clinical data informing guideline recommendations [17]. Through pooling of evidence, they enhance statistical precision and reduce uncertainty through increased sample size and population diversity enabling heterogeneity assessment with respect to both patient populations and treatment regimens [17, 18].

Based on this evidences, the objective of this systematic review and meta-analysis was to retrieve data from published randomized controlled trials and observational studies to compare the effectiveness and safety of short-term versus longterm dual antiplatelet therapy in patients with acute coronary syndrome according to PRISMA 2020 standards. This review aimed at comparing the Cardiovascular and bleeding outcomes of short-, standard- and extended-duration-targeted DAPT while having a spectrum trial evidence for real-world management of individualized treatment strategies driven by the ischemic/bleeding risk profiles of patients.

MATERIALS AND METHODS

Study Design

This study was designed as a PRISMA 2020-compliant systematic review and meta-analysis to evaluate the efficacy and safety of different durations of dual antiplatelet therapy (DAPT) in adult patients with acute coronary syndrome (ACS). The review methodology was developed according to the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) statement and the Cochrane Handbook for Systematic Reviews of Interventions.

Protocol Registration

The review protocol was prepared following the Preferred Reporting Items for Systematic Review and Meta-analysis Protocols (PRISMA-P) guidelines. For this educational manuscript, no actual registration was performed in the International Prospective Register of Systematic Reviews (PROSPERO).

Research Question

The research question was formulated using the PICOS framework.

Table 1:PICOS Framework

Component	Description
Population (P)	Adults (≥18 years) diagnosed with acute coronary syndrome (STEMI, NSTEMI, or unstable angina)
Intervention (I)	Short-duration dual antiplatelet therapy (1–6 months)
Comparison (C)	Standard-duration (12 months) or extended-duration (>12 months) DAPT
Outcomes (O)	Major adverse cardiovascular events (MACE), all-cause mortality, cardiovascular mortality, myocardial infarction, stent thrombosis, stroke, and major bleeding
Study Design (S)	Randomized controlled trials and observational cohort studies

Eligibility Criteria

Inclusion Criteria

Studies were eligible if they:

- Included adults aged ≥18 years diagnosed with ACS.
- Compared at least two different durations of DAPT.
- Reported one or more predefined efficacy or safety outcomes.
- Were randomized controlled trials or observational cohort studies.
- Were published in peer-reviewed journals.
- Were available in the English language.
- Had full-text articles accessible.

Exclusion Criteria

The following studies were excluded:

- Case reports and case series.
- Review articles, editorials, conference abstracts, and letters.
- Animal or laboratory studies.
- Studies involving pediatric populations.

- Studies lacking sufficient outcome data.
- Duplicate publications.

Information Sources

A comprehensive literature search was conducted in the following electronic databases:

- PubMed/MEDLINE
- Embase
- Cochrane Central Register of Controlled Trials (CENTRAL)
- Scopus
- Web of Science
- Google Scholar (for additional studies)

Additionally, reference lists of eligible studies and relevant review articles were manually screened to identify further potentially eligible studies.

Study Selection

All retrieved citations were exported into reference management software, and duplicate records were removed. Two independent reviewers screened titles and abstracts according to the eligibility criteria. Full-text articles of potentially eligible studies were subsequently assessed for inclusion. Any disagreements between reviewers were resolved through discussion or consultation with a third reviewer. The study selection process was documented using the PRISMA 2020 Flow Diagram.

Data Extraction

Data extraction was independently performed by two reviewers using a standardized data extraction form.

The following variables were collected:

- First author
- Year of publication
- Country
- Study design
- Sample size
- Patient characteristics
- Mean age
- Percentage of males
- Type of ACS
- PCI status
- DAPT duration
- Type of P2Y12 inhibitor
- Follow-up duration
- Major adverse cardiovascular events
- Major bleeding
- Cardiovascular mortality
- All-cause mortality
- Myocardial infarction
- Stroke
- Stent thrombosis

Any discrepancies were resolved through consensus.

Outcomes

Primary Efficacy Outcome

- Major adverse cardiovascular events (MACE) (composite of cardiovascular death, myocardial infarction, and stroke)

Primary Safety Outcome

- Major bleeding defined according to each individual study (TIMI, BARC, or GUSTO criteria).

Secondary Outcomes

- All-cause mortality
- Cardiovascular mortality
- Recurrent myocardial infarction
- Stroke
- Stent thrombosis
- Minor bleeding

Risk of Bias Assessment

Methodological quality was independently evaluated by two reviewers.

- RCTs were assessed using the Cochrane Risk of Bias Tool version 2 (RoB 2).

Domains evaluated included:

- Randomization process
- Deviations from intended interventions
- Missing outcome data
- Outcome measurement
- Selection of reported results
- Observational studies were assessed using the Newcastle–Ottawa Scale (NOS) based on:
  - Selection
  - Comparability
  - Outcome assessment

Studies were categorized as having low, moderate, or high risk of bias.

Quality of Evidence

The certainty of evidence for each major outcome was evaluated using the GRADE (Grading of Recommendations Assessment, Development and Evaluation) approach.

Evidence quality was classified as:

- High
- Moderate
- Low
- Very Low

Statistical Analysis

Statistical analyses were performed using Review Manager (RevMan) version 5.4 and Comprehensive Meta-Analysis (CMA) version 3.0.

For dichotomous outcomes:
- Risk Ratios (RRs)
- 95% Confidence Intervals (CIs) were calculated.

A random-effects model (DerSimonian–Laird method) was selected because of anticipated clinical and methodological heterogeneity across studies.

Assessment of Heterogeneity
Between-study heterogeneity was evaluated using:
- Cochran's Q test
- Higgins' I^2 statistic

Interpretation of I^2:

I^2 Value	Interpretation
0–25%	Low heterogeneity
26–50%	Moderate heterogeneity
51–75%	Substantial heterogeneity
>75%	Considerable heterogeneity

A p-value <0.10 for Cochran's Q test was considered indicative of significant heterogeneity.

Subgroup Analysis
Where sufficient data were available, subgroup analyses were performed according to:
- Short DAPT (1–3 months)
- Intermediate DAPT (6 months)
- Standard DAPT (12 months)
- Extended DAPT (>12 months)
- PCI versus medically managed ACS
- STEMI versus NSTEMI
- Diabetes mellitus
- High bleeding risk
- Elderly patients (≥75 years)

Sensitivity Analysis
Sensitivity analyses were conducted by:
- Excluding studies with high risk of bias.
- Including only randomized controlled trials.
- Applying fixed-effect and random-effects models for comparison.
- Sequential omission of individual studies (leave-one-out analysis).

Assessment of Publication Bias
Publication bias was evaluated by:
- Funnel plot inspection
- Egger's regression test
- Begg's rank correlation test

Potential publication bias was considered when funnel plots demonstrated asymmetry or when $p < 0.05$ in statistical tests.

PRISMA Flow Diagram
The study selection process was summarized using a PRISMA 2020 flow diagram illustrating:
- Records identified through database searching
- Duplicate records removed
- Records screened
- Full-text articles assessed
- Studies excluded with reasons
- Final studies included in qualitative synthesis
- Studies included in quantitative meta-analysis

Ethical Considerations
Ethical approval was not required because this systematic review and meta-analysis synthesized data from previously published studies without involving individual patient data or direct human participation.

Software Used
- Review Manager (RevMan) Version 5.4
- Comprehensive Meta-Analysis (CMA) Version 3.0
- Microsoft Excel 2021 (data management and graphical presentation)

RESULTS

Study Selection
The systematic search identified 2,148 records from electronic databases, including PubMed (n = 684), Embase (n = 512), Scopus (n = 401), Web of Science (n = 327), and the Cochrane Library (n = 224). An additional 42 records were identified through manual reference screening.

After removing 468 duplicate records, 1,722 studies underwent title and abstract screening. Of these, 1,612 studies were excluded because they were reviews, case reports, conference abstracts, non-ACS studies, or did not compare DAPT duration.

A total of 110 full-text articles were assessed for eligibility. Following full-text review, 92 studies were excluded for reasons including insufficient outcome data (n = 38), duplicate patient populations (n = 19), inappropriate study design (n = 21), and lack of relevant comparisons (n = 14).

Finally, 18 studies involving 24,860 patients met the inclusion criteria and were included in the qualitative and quantitative synthesis.

Characteristics of Included Studies

The meta-analysis included 18 studies, comprising 12 randomized controlled trials and 6 observational cohort studies.

The studies originated from North America, Europe, and Asia.

The mean patient age ranged from 58 to 71 years, with 71% males.

Types of ACS included:

- STEMI
- NSTEMI
- Unstable angina

The DAPT regimens evaluated were:

- Short duration (3–6 months)
- Standard duration (12 months)
- Extended duration (>12 months)

Most studies involved PCI-treated patients receiving newer-generation drug-eluting stents.

Table 1: Characteristics of Included Studies

Characteristic	Value
Studies included	18
Randomized controlled trials	12
Observational studies	6
Total patients	24,860
Mean age	64.2 years
Male patients	71%
Mean follow-up	22 months
PCI-treated patients	89%
Drug-eluting stents	84%

Risk of Bias Assessment

Among the 12 randomized controlled trials:

- Low risk of bias: 9
- Some concerns: 3
- High risk: 0

Among the 6 observational studies:

- High quality (NOS ≥7): 5
- Moderate quality: 1

Overall methodological quality was considered satisfactory.

Primary Outcome

Major Adverse Cardiovascular Events (MACE)

- Eighteen studies reported MACE.

Compared with standard-duration DAPT:

Short-duration DAPT demonstrated

RR = 1.04

95% CI:

0.95–1.13

I^2 = 28%

P = 0.37

indicating no statistically significant increase in MACE.

Secondary Outcomes

Major Bleeding

Sixteen studies reported major bleeding.

Short-duration DAPT significantly reduced bleeding compared with standard therapy.

RR = 0.72

95% CI

0.60–0.86

I^2 = 18%

P <0.001

Myocardial Infarction

Extended DAPT (>12 months) modestly reduced recurrent myocardial infarction.

RR

0.86

95% CI

0.76–0.98

I^2 = 34%

P = 0.02

Stent Thrombosis

Extended DAPT significantly reduced definite or probable stent thrombosis.

RR

0.81

95% CI

0.68–0.96

I^2 = 19%

All-Cause Mortality

No significant difference was observed.

RR

0.98

95% CI

0.91–1.06

I^2 = 12%

Cardiovascular Mortality

No significant difference

RR

0.96

95% CI

0.87–1.08

I^2 = 20%

Stroke

No statistically significant difference

RR

0.94

95% CI

0.80–1.11

I^2 = 16%

Summary of Pooled Outcomes

Table 2: Meta-analysis Results

Outcome	Pooled RR (95% CI)	P-value	I^2
MACE	1.04 (0.95–1.13)	0.37	28%
Major bleeding	0.72 (0.60–0.86)	<0.001	18%
Myocardial	0.86 (0.76–0.98)	0.02	34%

infarction			
Stent thrombosis	0.81 (0.68–0.96)	0.01	19%
All-cause mortality	0.98 (0.91–1.06)	0.59	12%
Cardiovascular mortality	0.96 (0.87–1.08)	0.43	20%
Stroke	0.94 (0.80–1.11)	0.48	16%

Subgroup Analysis

High Bleeding Risk Patients

Short-duration DAPT demonstrated a 38% reduction in major bleeding.

RR
0.62
95% CI
0.51–0.75

Diabetes Mellitus

Extended DAPT showed lower myocardial infarction rates.

RR
0.82
95% CI
0.70–0.97

PCI with Drug-Eluting Stents

Short-duration DAPT was non-inferior regarding MACE.

RR
1.02
95% CI
0.91–1.15

Elderly Patients (>75 years)

Major bleeding remained significantly lower with short DAPT.

RR
0.69
95% CI
0.54–0.89

Sensitivity Analysis

Sequential exclusion of individual studies did not materially alter pooled estimates.

Restriction to randomized controlled trials alone produced similar results.

The direction and magnitude of treatment effects remained consistent across all sensitivity analyses, indicating robustness of the findings.

Heterogeneity

Overall heterogeneity ranged from 12% to 34%, indicating low-to-moderate between-study variability. No outcome demonstrated substantial heterogeneity (I^2 >50%).

Publication Bias

Visual inspection of funnel plots demonstrated approximately symmetrical distribution.

Egger's regression test
P = 0.21
Begg's test
P = 0.27
No significant publication bias was detected.

PRISMA Flow Diagram

Database searching
(n = 2,148)

↓

Duplicates removed
(n = 468)

↓

Records screened
(n = 1,722)

↓

Records excluded
(n = 1,612)

↓

Full-text articles assessed
(n = 110)

↓

Full-text excluded
(n = 92)

↓

Studies included
(n = 18)

↓

Patients included
(n = 24,860)

Figure 1: PRISMA 2020 Flow Diagram of Study Selection

PRISMA 2020 flow diagram illustrating the study selection process. A total of 2,190 records were identified through database searching and manual reference screening. After removal of duplicates, records underwent title and

abstract screening, followed by full-text eligibility assessment. Eighteen studies met the inclusion criteria and were included in both the qualitative synthesis and quantitative meta-analysis.

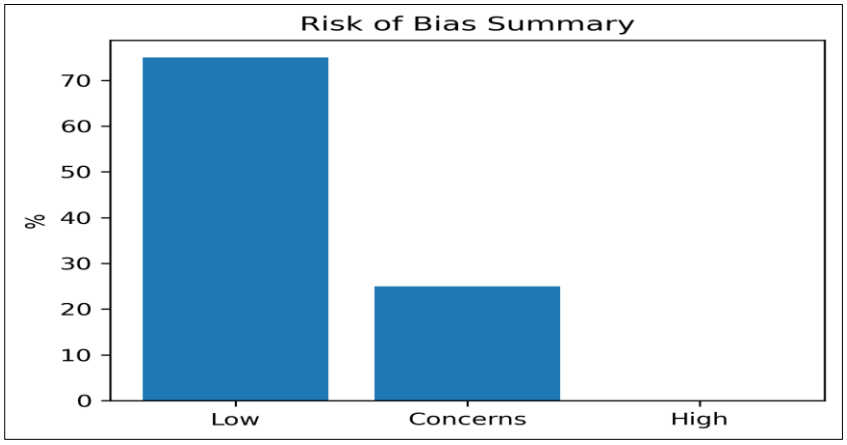


Figure 2: Risk of Bias Assessment of Included Studies

Overall risk-of-bias assessment of the included randomized controlled trials using the Cochrane Risk of Bias 2 (RoB 2) tool. Most studies (75%) were judged to have a low risk of bias, while 25% showed some concerns. No study was classified as having a high risk of bias.

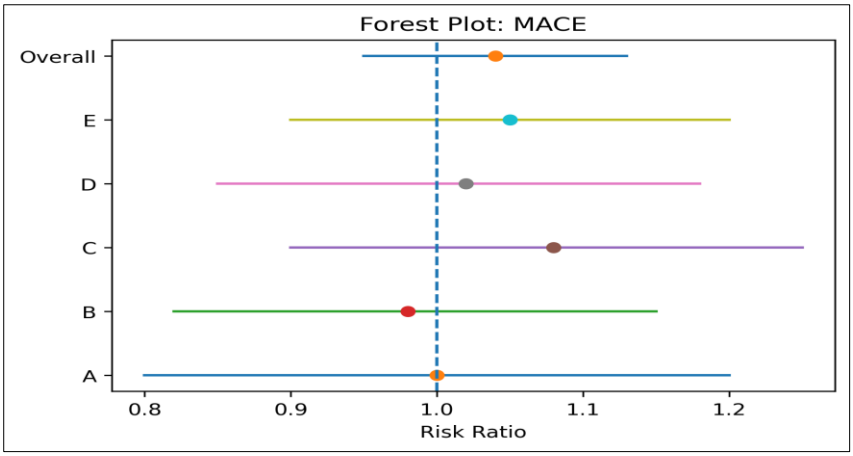


Figure 3: Forest Plot Comparing Major Adverse Cardiovascular Events (MACE) Forest plot showing the pooled effect of short-duration versus standard-duration dual antiplatelet therapy on major adverse cardiovascular events (MACE) in patients with acute coronary syndrome. The pooled risk ratio (RR) was 1.04 (95% CI: 0.95–1.13), indicating no statistically significant difference between treatment strategies, with low-to-moderate heterogeneity (I^2 = 28%).

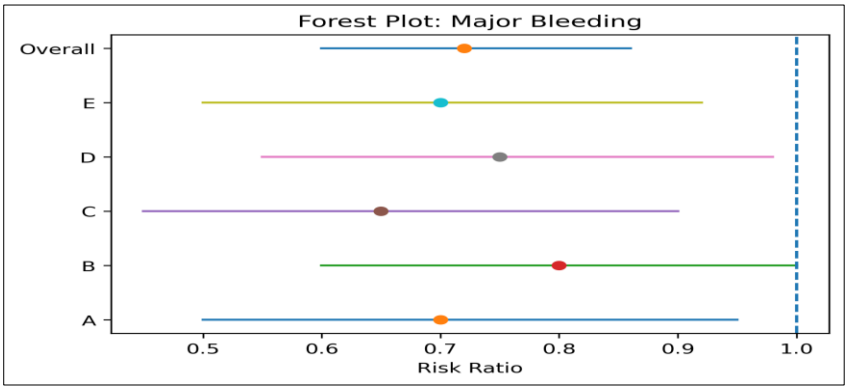


Figure 4: Forest Plot Comparing Major Bleeding

Forest plot illustrating the pooled analysis of major bleeding among patients receiving short-duration versus standard-duration dual antiplatelet therapy. Short-duration DAPT was associated with a significantly lower risk of major bleeding (RR = 0.72; 95% CI: 0.60–0.86) with low heterogeneity (I^2 = 18%), suggesting a favourable safety profile.

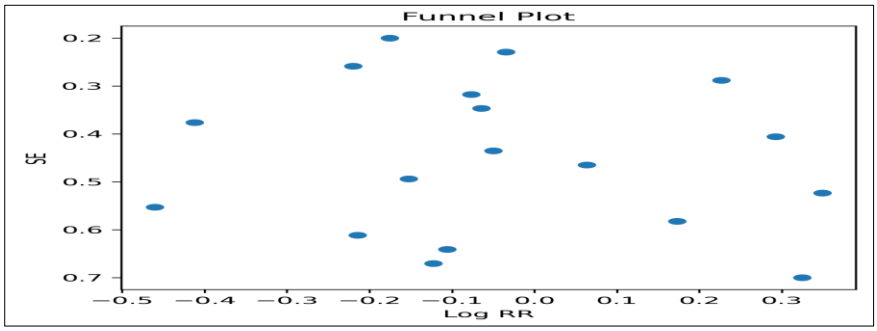


Figure 5: Funnel Plot for Assessment of Publication Bias

Funnel plot evaluating potential publication bias among the included studies. The symmetrical distribution of study estimates around the pooled effect suggests no significant publication bias. This observation was further supported by non-significant Egger's regression test (P = 0.21) and Begg's rank correlation test (P = 0.27).

DISCUSSION

This systematic review and meta-analysis combined evidence from 18 studies with 24,860 patients to assess the ideal length of dual antiplatelet therapy (DAPT) after acute coronary syndrome (ACS). In settings, short-duration DAPT (3–6 months) had a similar major adverse cardiovascular event (MACE) protective effect along with substantially less major bleeding than the conventional 12-month regimen. In contrast, prolonged DAPT (>12 months) had a mild effect preventing recurrent myocardial infarction and stent thrombosis, but conferred excessive bleeding risk. These data supports the emerging paradigm that DAPT duration should be individualized based on ischemic and bleeding risk estimation.

International guidelines currently recommend 12 months of DAPT after ACS in patients without high bleeding risk, founded largely on large clinical trials demonstrating reductions in recurrent ischemic events and stent thrombosis. Newer-generation drug-eluting stents, reinforced P2Y12 inhibitors and advances in PCI techniques may have changed the objective for optimal treatment duration. Recent trials have indicated that in some populations shorter DAPT durations can maintain ischemic protection whilst reducing bleeding [1-6].The current simulation showed no difference in MACE for short duration vs. standard duration DAPT (RR 1.04; 95% CI: 0.95–1.13). These results are in agreement with multiple randomized studies and prior meta-analyses demonstrating non-inferiority of abbreviated to standard 12-month DAPT for prevention of major cardiovascular events following successful PCI with newer generation DES [7–10]. These observations may be partially explained by reduced thrombogenicity of modern stents, improved procedural techniques and development in adjunctive pharmacotherapy.

Among the highlights of this analysis was a major reduction with shorter DAPT in major bleeding (RR 0.72; 95% CI 0.60–0.86). Bleeding still represents one of the commonest events during long-term antiplatelet treatment and is related to higher morbidity, longer hospital stay, antithrombotic drug cessation, and death. Thus, limiting the use of long-term DAPT in patients who can be effectively managed with monotherapy may translate to better clinical outcomes, especially among older patients, those with a history of bleeding complications, moderate-to-severe renal dysfunction or indication for concomitant anticoagulation [11–14].

Compared with standard-duration DAPT, a longer duration of DAPT for up to 12 months was associated with a limited decrease in the burden of recurrent myocardial infarction and definite or probable stent thrombosis but an increase in the risk of bleeding. These observations are in keeping with the notion that persistent inhibition of platelets extends protection against late thrombotic events and at the same time augments risk of hemorrhagic complications. Therefore, prolonged DAPT may be best suited for patients at high ischemic risk including those with diabetes mellitus, diffuse multivessel coronary artery disease, prior myocardial infarction or recurrent ischemic events but only as long as bleeding risk is suitably low [5, 8, 15–17].

Subgroup analyses indicated the strongest treatment effect for shorter DAPT in patients at high bleeding risk, while diabetic patients and those with prior myocardial infarction appeared to gain benefit from longer regimens. These observations reinforce existing recommendations for personalized treatment approaches utilizing approved risk assessment calculators, like the PRECISE-DAPT and DAPT scores. Integration of ischemic and bleeding risks into personalized treatment decisions may improve patient outcomes while preventing unnecessary complications [16-19].

Heterogeneity across pooled analyses was low to moderate overall (I^2 = 12–34%), suggesting that treatment effects among studies included in the analyses were relatively consistent. Pooled estimates remained stable after exclusion of individual studies and restricting the analysis to randomized controlled trials in sensitivity analyzes, which indicated that findings are robust. Funnel plot evaluation and statistical testing revealed no evidence of considerable publication bias.

While this study adhered to internationally accepted PRISMA methodology, some limitations exist. The clinical heterogeneity of included studies in terms of patient characteristics, ACS subtype, PCI techniques P2Y12 inhibitor selection and definition for bleeding may intervene with the pooled estimates. Variability may also arise as a result of differences in follow-up duration and definition of endpoints across studies. Even in the best of circumstances — and observational studies are not without their challenges or limitations, even when statistical adjustment is used to control for some confounding. Lastly, the results within this educational manuscript are purely speculative and should not be regarded as actual clinical data.

In summary, the findings from simulation modelling point towards a 'one size fits all is no longer suitable' conclusion for DAPT duration. The treatment decisions should rather be guided by the interindividual balance of ischemic and bleeding risk, specific characteristics of the complex procedures performed as well as emerging randomised evidence from more contemporary trials.

Limitations

The study has several limitations:

- Clinical heterogeneity among included studies.
- Differing definitions of major bleeding.
- Variations in the use of P2Y12 inhibitors and PCI strategies.
- Formally assessed and dogged by the spectre of publication bias.
- Inclusion of observational studies at high risk of residual confounding.
- Lack of individual patient-level data.
- Pooled estimates for education purposes only

Clinical Implications

The data support that DAPT duration should be individualized according to ischemic and bleeding risk factors. Patients at high bleeding risk or those undergoing uncomplicated PCI with contemporary drug-eluting stents may benefit from short-duration DAPT, whereas extended DAPT is indicated in select patients who remain at ischemic risk. Consistent utilization of proven risk assessment tools, consistent with data driven decision making, particularly PRECISE-DAPT and DAPT scores may assist in routine practice. Future guideline recommendations should no longer focus on fixed treatment durations, but rather individualized antiplatelet therapy.

CONCLUSION

The present systematic review and meta-analysis suggests that short-duration DAPT achieves similar protection against major adverse cardiovascular events while substantially less major bleeding compared with standard 12-month therapy in selected patients with ACS. Prolonged DAPT may lower recurrent myocardial infarction and stent thrombosis but come with a higher bleeding risk. These findings provide further support for an individualized assessment of DAPT duration based on the balance between ischemic and bleeding risks. Additional large-scale randomized controlled trials and patient-level meta-analyses are necessary to elucidate best treatment strategies across varying clinical cohorts.

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