Meta-analysis/Systematic review

Early aspirin withdrawal with P2Y12 inhibitor monotherapy vs. standard dual antiplatelet therapy in patients undergoing percutaneous coronary intervention for acute coronary syndromes: a meta-analysis of randomised controlled trials

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Abstract

Introduction: Dual antiplatelet therapy (DAPT) with aspirin and a P2Y12 inhibitor is the standard antiplatelet strategy following percutaneous coronary intervention (PCI) in patients with acute coronary syndromes (ACS). Prolonged aspirin exposure, however, increases the risk of bleeding, prompting evaluation of early aspirin discontinuation.
Material and methods: We performed a systematic search of RCTs comparing abbreviated DAPT followed by P2Y12 inhibitor monotherapy with DAPT in this population. Six RCTs involving 18,794 patients were included.
Results: This strategy showed no significant difference compared with DAPT in the risk of major adverse cardiac and cerebrovascular events, all-cause death, cardiovascular death, myocardial infarction, and stroke. It was associated with significantly lower risk of clinically relevant bleeding (RR = 0.48), major bleeding (RR = 0.44), and net adverse events (RR = 0.80). However, the risk of stent thrombosis was higher with this strategy (RR = 1.83).
Conclusions: Abbreviated DAPT followed by P2Y12 monotherapy maintains efficacy and lowers bleeding, with increased stent thrombosis risk.

Key words: P2Y12 inhibitor monotherapy, dual antiplatelet therapy, aspirin withdrawal, percutaneous coronary intervention, acute coronary syndrome.

Introduction

Acute coronary syndrome (ACS) remains a major global health problem, contributing substantially to cardiovascular morbidity and mortality [1]. Cardiovascular disease accounts for approximately one-third of all deaths worldwide, with ischaemic heart disease causing roughly 7.5 million deaths annually [2, 3]. ACS and sudden cardiac death together are responsible for nearly 1.8 million deaths each year [2]. Short-term outcomes remain concerning, with 30-day mortality approaching 9% for myocardial infarction and higher rates for ST elevation myocardial infarction (STEMI) [4, 5]. Long-term risk is also substantial; large cohort studies report 5-year composite rates of cardiovascular death, reinfarction, or stroke exceeding 30%, with younger adults and older frail patients both demonstrating elevated risk despite contemporary therapy [6, 7].

Following percutaneous coronary intervention (PCI) for ACS, international guidelines recommend intensive antithrombotic therapy alongside comprehensive secondary prevention. Dual antiplatelet therapy (DAPT) remains the standard of care, consisting of aspirin indefinitely plus a P2Y12 inhibitor for 12 months after stent implantation, unless bleeding risk is high [8, 9]. In patients with high bleeding risk, DAPT duration may be shortened to 1-6 months, followed by single antiplatelet therapy (SAPT) with either aspirin or a P2Y12 inhibitor [10, 11]. Moreover, recent trials demonstrate that P2Y12 inhibitor monotherapy following 1 month of DAPT lowers bleeding risk without increasing major adverse cardiovascular and cerebrovascular events (MACCE), informing updated recommendations [12–14].

Despite growing evidence supporting P2Y12 inhibitor monotherapy as a strategy to reduce bleeding after PCI, uncertainty remains regarding its efficacy and safety compared with standard DAPT in patients with ACS. Individual trials are often limited by sample size, follow-up duration, or heterogeneity in study populations and treatment protocols, making it challenging to draw definitive conclusions. To address these gaps, we conducted a meta-analysis of randomized controlled trials comparing abbreviated DAPT followed by P2Y12 inhibitor monotherapy with conventional DAPT in patients undergoing PCI for ACS, with the aim of providing comprehensive evidence to inform clinical decision-making.

Methods

This systematic review and meta-analysis followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [15]. The review protocol was registered in the Prospero database (CRD420261279180). Ethical approval and informed consent were not applicable for this study.

Data sources and search strategy

Two authors (M.A and E.Z) independently searched PubMed/Medline, Google Scholar, and the Cochrane Library to identify RCTs comparing P2Y12 monotherapy with DAPT following PCI. The search covered all available literature in the database from inception to December 2025. Manual screening of reference lists of relevant articles was performed to identify additional studies. The search strategy included terms and medical subject headings such as ("aspirin withdrawal" OR "P2Y12 monotherapy" OR "ticagrelor monotherapy" OR "clopidogrel monotherapy" OR "prasugrel monotherapy") AND ("dual antiplatelet therapy" OR DAPT) AND ("PCI" OR "percutaneous coronary intervention"). The detailed search strategies for each database are provided in Supplementary Table SI.

Study selection and eligibility criteria

Search results were imported into Rayyan software, and duplicates were detected. After resolving the duplicates, two authors (K.S and A.R) independently screened the titles and abstracts for eligibility. Full texts of potentially relevant articles were sought and assessed according to inclusion criteria. Any conflicts were resolved by discussion or consultation with a third reviewer (EZ).

Studies were included if they: (1) were randomised controlled trials (RCTs); (2) included adult participants diagnosed with acute coronary syndromes who underwent successful PCI; (3) evaluated abbreviated DAPT followed by aspirin withdrawal and continuation of P2Y12 monotherapy as the intervention; and (4) compared this strategy with continued DAPT consisting of aspirin plus a P2Y12 inhibitor.

Studies were excluded if they: (1) were non-randomised, observational studies, retrospective analyses, pooled analyses, case reports, conference abstracts, or letters; and (2) included animal studies or trials conducted in healthy participants.

Data extraction, outcomes, and quality assessment

Two authors (A.M and U.A) independently extracted data from the included trials. Extracted information comprised trial name, publication year, intervention type, sample size, patient demographics (age, sex, body mass index), left ventricular ejection fraction, comorbid conditions, and the specific type of ACS at clinical presentation, alongside relevant outcome data.

The primary outcomes were MACCE and clinically relevant bleeding. Secondary outcomes included major bleeding, all-cause death, cardiovascular death, myocardial infarction, stent thrombosis, stroke, target-vessel revascularisation, and net adverse events.

The quality of included trials was assessed using the Cochrane Risk of Bias 2 (RoB 2) tool, evaluating domains such as randomisation, deviations from intended interventions, missing outcome data, outcome measurement, and selective reporting [16]. Studies were rated as low risk, some concerns, or high risk. Traffic-light and summary plots were created using the Robvis visualisation tool [17]. The certainty of evidence for each outcome was assessed using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach. Evidence was rated as high, moderate, low, or very low certainty based on considerations of risk of bias, inconsistency, indirectness, imprecision, and publication bias.

Statistical analysis

Statistical analyses were carried out using Review Manager (RevMan) version 5.4 (The Nordic Cochrane Centre, Copenhagen, Denmark). For each outcome, effect sizes were summarised as risk ratios (RRs) with 95% confidence intervals (CIs). To account for the variability among studies, a random-effects model using the DerSimonian and Laird method was applied [18]. Forest plots were generated to illustrate the combined estimates. Heterogeneity across studies was measured using the I^2 statistic, with values of 25–50%, 50–75%, and above 75% considered low, moderate, and high, respectively. A *p*-value below 0.05 was considered statistically significant.

Results

The literature search across databases identified 11,754 studies. After removing 5223 duplicates, the remaining studies were screened by their titles and abstracts. This was followed by a full text review of 42 records. Finally, 6 trials met the inclusion criteria and were included in our review [12–14, 19–21]. The detailed selection process is illustrated in the PRISMA flow diagram (Supplementary Figure S1).

All included studies were RCTs published between 2020 and 2025. Each trial compared abbreviated DAPT followed by P2Y12 inhibitor monotherapy versus standard DAPT over a follow-up duration of 12 months. Three trials evaluated ticagrelor monotherapy, one assessed clopidogrel, one allowed either prasugrel or ticagrelor, and one included ticagrelor, clopidogrel, or prasugrel as the $P2Y_{12}$ inhibitor. A total of 18,794 patients were included (monotherapy: 9384; DAPT: 9410) in the pooled analysis. Overall, 77.3% of the patients were male and 22.7% were female. The mean age of the participants was 62.2 ±11.5 years. Study details and baseline characteristics of the included trials are summarised in Table I. There were some concerns in the risk of bias across all included trials due to deviations from the intended intervention (Domain 2) (Supplementary Figures S2 and S3).

Outcomes

MACCE

All included studies reported MACCE at 12-month follow-up. Definitions of MACCE varied across trials (Supplementary Table SII). There was no statistically significant difference in the risk of MACCE between abbreviated DAPT followed by P2Y12 inhibitor monotherapy and standard DAPT (RR = 1.03; 95% CI: 0.82–1.30; I^2 = 48%; p = 0.78; Figure 1 A).

Subgroup analysis according to the type of P2Y12 inhibitor suggested a significant difference in treatment effect across agent classes (p for subgroup differences = 0.02; Supplementary Figure S4). In the ticagrelor subgroup, abbreviated DAPT followed by ticagrelor monotherapy was associated with a numerically lower but non-significant risk of MACCE compared with standard DAPT (RR = 0.84; 95% CI: 0.66–1.07). In contrast, clopidogrel monotherapy showed a numerically higher but non-significant risk of MACCE, based on a single study (RR = 1.49; 95% CI: 0.99–2.24). Similarly, trials that included multiple P2Y12 inhibitors showed a numerically higher, but not statistically significant, risk of MACCE with abbreviated DAPT followed by P2Y12 inhibitor monotherapy compared with standard DAPT (RR = 1.22; 95% CI: 0.96–1.55).

Subgroup analysis according to the timing of aspirin withdrawal did not demonstrate a significant difference in treatment effect (p for subgroup differences = 0.15; Supplementary Figure S6). In the single study in which aspirin was discontinued within 1 month after PCI, abbreviated DAPT followed by P2Y12 inhibitor monotherapy was associated with a numerically higher but non-significant risk of MACCE compared with standard DAPT (RR = 1.27; 95% CI: 0.98–1.65). Among studies in which aspirin was discontinued after more than 1 month, there was no significant difference in the risk of MACCE between treatment strategies (RR = 0.97; 95% CI: 0.74–1.26).

Clinically relevant bleeding

Five out of six included trials reported clinically relevant bleeding, defined as TIMI minor or major/BARC types 2, 3, or 5. Abbreviated DAPT followed by P2Y12 inhibitor monotherapy was associated with a significantly lower risk of clinically rele-

Table I. Study details and baseline characteristics of the included trials

Clinical characteristic

Study	Year	Intervention	Control	Sample size, *n*		Age (mean ± SD)		Males, *n* (%)		BMI [kg/m^2]		LVEF (%)		Dyslipidaemia, *n* (%)	
				Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control
TICO	2020	Ticagrelor monotherapy (90 mg twice daily) after 3-month DAPT	ticagrelor-based 12-month DAPT	1527	1529	61.0 ±11.0	61.0 ±11.0	1204 (79)	1224 (80)	24.9 (3.2)	24.9 (3.3)	NR	NR	924 (61)	922 (60)
STOPDAPT-2	2022	Clopidogrel monotherapy after 1 to 2 months DAPT	Clopidogrel-based 12-month DAPT	2058	2078	67.0 ±11.9	66.6 ±11.9	1631 (79.3)	1649 (79.4)	24.1 ±3.7	24.2 ±3.5	56.7 ±10.6	56.9 ±10.5	1373 (66.7)	1391 (66.9)
T-PASS	2024	Ticagrelor Monotherapy (90 mg twice daily) after 1 month DAPT	Ticagrelor-based 12-month DAPT	1426	1424	61 ±10	61 ±10	1193 (84)	1181 (83)	25.1 ±3.6	25.0 ±3.5	NR	NR	1048 (74)	1058 (74)
ULTIMATE-DAPT	2024	Ticagrelor Monotherapy (90 mg twice daily) after 1 month DAPT	Ticagrelor-based 12-month DAPT	1700	1700	62 ±11.87	62 ±11.13	1264 (74.4)	1257 (73.9)	NR	NR	60.67 ±7.42	61.33 ±6.68	1178 (69.3)	1157 (68.1)
NEO-MINDSET	2025	Prasugrel (5/10 mg once daily) or ticagrelor (90 mg twice daily) monotherapy	Prasugrel or ticagrelor-based 12-month DAPT	1712	1698	59.5 ±10.9	59.8 ±10.7	1210 (70.7)	1201 (70.7)	27.6 ±4.5	27.5 ±4.4	NR	NR	464 (27.1)	452 (26.6)
TARGET-FIRST	2025	P2Y12 inhibitor (prasugrel, ticagrelor, or clopidogrel) monotherapy after 1 month DAPT	12-month DAPT	961	981	61.0 ±10.8	61.0 ±10.5	738 (76.8)	784 (79.9)	26.7 ±4.7	27.4 ±4.4	NR	NR	271 (28.2)	269 (27.4)

vant bleeding compared with standard DAPT (RR = 0.48; 95% CI: 0.39–0.58; I^2 = 10%; p < 0.001; Figure 1 B).

Subgroup analysis according to the type of P2Y12 inhibitor did not demonstrate a significant difference in treatment effect across agent classes (p for subgroup differences = 0.45; Supplementary Figure S5). In the ticagrelor subgroup, abbreviated DAPT followed by ticagrelor monotherapy was associated with a significantly lower risk of clinically relevant bleeding compared with standard DAPT (RR = 0.51; 95% CI: 0.40–0.66). Similarly, clopidogrel monotherapy was associated with a significant reduction in clinically relevant bleeding based on a single study (RR = 0.41; 95% CI: 0.20–0.83). Trials that included multiple P2Y12 inhibitors also demonstrated a significant reduction in clinically relevant bleeding with abbreviated DAPT followed by P2Y12 inhibitor monotherapy compared with standard DAPT (RR = 0.39; 95% CI: 0.26–0.57).

Subgroup analysis according to the timing of aspirin withdrawal did not demonstrate a significant difference in treatment effect (p for subgroup differences = 0.23; Supplementary Figure S7). In the single study in which aspirin was discontinued within 1 month after PCI, abbreviated DAPT followed by P2Y12 inhibitor monotherapy was associated with a significant reduction in clinically relevant bleeding compared with standard DAPT (RR = 0.39; 95% CI: 0.26–0.57). Among studies in which aspirin was discontinued after more than 1 month, abbreviated DAPT followed by P2Y12 inhibitor monotherapy was also associated with a significant reduction in clinically relevant bleeding compared with standard DAPT (RR = 0.51; 95% CI: 0.41–0.63).

Comorbid conditions												Clinical presentation					
Hypertension, *n* (%)		Diabetes, *n* (%)		Current smoker, *n* (%)		Chronic kidney disease, *n* (%)		Previous MI, *n* (%)		Previous PCI, *n* (%)		STEMI, *n* (%)		NSTEMI, *n* (%)		Unstable angina, *n* (%)	
Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control
760 (50)	781 (51)	418 (27)	417 (27)	555 (36)	587 (38)	292 (19)	328 (22)	64 (4)	49 (3)	135 (9)	127 (8)	546 (36)	557 (36)	539 (35)	488 (32)	442 (29)	484 (32)
1396 (67.8)	1414 (68.1)	608 (29.5)	621 (29.9)	718 (34.9)	702 (33.8)	68 (3.3)	70 (3.4)	135 (6.6)	109 (5.3)	225 (10.9)	202 (9.7)	1179 (74.7)	1145 (72.8)	399 (25.3)	427 (27.2)	480 (23.3)	506 (24.4)
669 (47)	679 (48)	422 (30)	408 (29)	557 (39)	537 (38)	118 (8)	104 (7)	27 (2)	25 (2)	92 (7)	92 (7)	572 (40)	578 (41)	507 (36)	485 (34)	347 (24)	361 (25)
1058 (62.2)	1063 (62.5)	540 (31.8)	531 (31.5)	486 (28.6)	482 (28.4)	119 (7)	129 (7.6)	143 (8.4)	156 (9.2)	171 (10.1)	174 (10.2)	487 (28.7)	461 (27.1)	545 (32.1)	531 (31.2)	668 (39.3)	708 (41.7)
1093 (63.8)	1090 (64.2)	459 (26.8)	477 (28.1)	597 (36.1)	588 (36)	NR	NR	171 (10)	162 (9.5)	142 (8.3)	142 (8.4)	1058 (61.8)	1061 (62.5)	527 (30.8)	512 (30.2)	127 (7.4)	125 (7.4)
367 (38.2)	384 (39.1)	135 (14)	146 (14.9)	402 (41.9)	410 (41.8)	15 (1.6)	21 (2.1)	NR	NR	NR	NR	482 (50.2)	497 (50.7)	479 (49.8)	484 (49.3)	0	0

Major bleeding

All included studies reported major bleeding defined as TIMI major or BARC types 3 or 5. Abbreviated DAPT followed by P2Y12 inhibitor monotherapy was associated with a significantly lower risk of major bleeding compared with standard DAPT (RR = 0.44; 95% CI: 0.34–0.57; I^2 = 0%; p < 0.001; Figure 1 C).

All-cause death

All included studies reported all-cause death. There was no statistically significant difference in all-cause death between abbreviated DAPT followed by P2Y12 inhibitor monotherapy and standard DAPT (RR = 1.12; 95% CI: 0.88–1.43; I^2 = 0%; p = 0.35; Figure 1 D).

Cardiovascular death

All included studies reported cardiovascular mortality. There was no statistically significant difference in cardiovascular death between abbreviated DAPT followed by P2Y12 inhibitor monotherapy and standard DAPT (RR = 1.03; 95% CI: 0.75–1.42; I^2 = 0%; p = 0.86; Figure 1 E).

Myocardial infarction (MI)

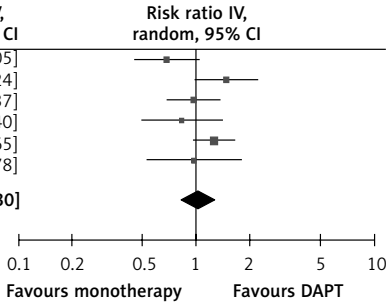
All included studies reported myocardial infarction. There was no statistically significant difference in the risk of MI between abbreviated DAPT followed by P2Y12 inhibitor monotherapy and standard DAPT (RR = 1.23; 95% CI: 0.87–1.76; I^2 = 29%; p = 0.24; Figure 2 A).

A. MACCE

Study or subgroup	P2Y12i Monotherapy Events	Total	DAPT Events	Total	Weight (%)	Risk ratio IV, random, 95% CI
TICO 2020	35	1527	51	1529	16.1	0.69 [0.45, 1.05]
STOPDAPT-2 2022	56	2058	38	2078	16.8	1.49 [0.99, 2.24]
ULTIMATE-DAPT 2024	61	1700	63	1700	19.8	0.97 [0.69, 1.37]
T-PASS 2024	26	1426	31	1424	12.7	0.84 [0.50, 1.40]
NEO-MINDSET 2025	119	1712	93	1698	24.4	1.27 [0.98, 1.65]
TARGET-FIRST 2025	20	961	21	981	10.2	0.97 [0.53, 1.78]
Total (95% CI)		**9384**		**9410**	**100.0**	**1.03 [0.82, 1.30]**
Total events	317		297			

Heterogeneity: $\tau^2 = 0.04$; $\chi^2 = 9.60$, $df = 5$ ($p = 0.09$); $I^2 = 48\%$

Test for overall effect: $Z = 0.28$ ($p = 0.78$)

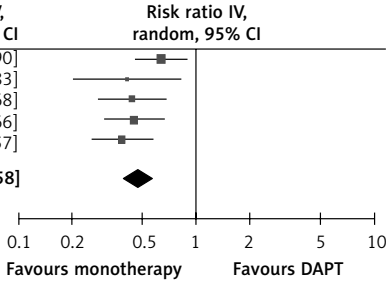


B. Clinically relevant bleeding

Study or subgroup	P2Y12i Monotherapy Events	Total	DAPT Events	Total	Weight (%)	Risk ratio IV, random, 95% CI
TICO 2020	53	1527	83	1529	29.3	0.64 [0.46, 0.90]
STOPDAPT-2 2022	11	2058	27	2078	7.7	0.41 [0.20, 0.83]
T-PASS 2024	28	1426	64	1424	18.5	0.44 [0.28, 0.68]
ULTIMATE-DAPT 2024	35	1700	78	1700	22.4	0.45 [0.30, 0.66]
NEO-MINDSET 2025	33	1712	85	1698	22.1	0.39 [0.26, 0.57]
Total (95% CI)		**8423**		**8429**	**100.0**	**0.48 [0.39, 0.58]**
Total events	160		337			

Heterogeneity: $\tau^2 = 0.01$; $\chi^2 = 4.44$, $df = 4$ ($p = 0.35$); $I^2 = 10\%$

Test for overall effect $Z = 7.37$ ($p < 0.00001$)

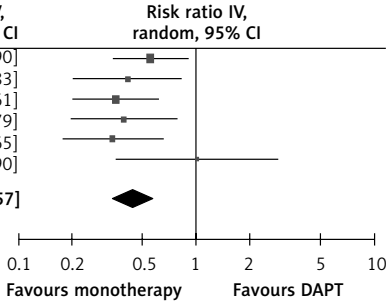


C. Major bleeding

Study or subgroup	P2Y12i Monotherapy Events	Total	DAPT Events	Total	Weight (%)	Risk ratio IV, random, 95% CI
TICO 2020	25	1527	45	1529	28.5	0.56 [0.34, 0.90]
STOPDAPT-2 2022	11	2058	27	2078	13.7	0.41 [0.20, 0.83]
T-PASS 2024	17	1426	48	1424	22.2	0.35 [0.20, 0.61]
ULTIMATE-DAFT 2024	11	1700	28	1700	13.8	0.39 [0.20, 0.79]
NEO-MINDSET 2025	12	1712	35	1698	15.7	0.34 [0.18, 0.65]
TARGET-FIRST 2025	7	961	7	981	6.1	1.02 [0.36, 2.90]
Total (95% CI)		**9384**		**9410**	**100.0**	**0.44 [0.34, 0.57]**
Total events	83		190			

Heterogeneity: $\tau^2 = 0.00$; $\chi^2 = 4.75$, $df = 5$ ($p = 0.45$); $I^2 = 0\%$

Test for overall effect: $Z = 6.20$ ($p < 0.00001$)

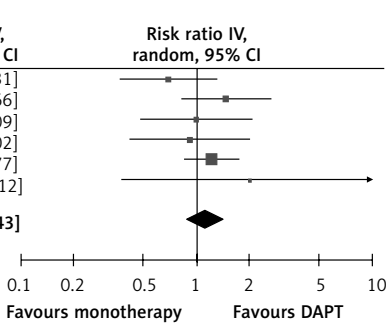


D. All-cause death

Study or subgroup	P2Y12i Monotherapy Events	Total	DAPT Events	Total	Weight (%)	Risk ratio IV, random, 95% CI
TICO 2020	16	1527	23	1529	14.9	0.70 [0.37, 1.31]
STOPDAPT-2 2022	28	2058	19	2078	17.8	1.49 [0.83, 2.66]
T-PASS 2024	14	1426	14	1424	11.0	1.00 [0.48, 2.09]
ULTIMATE-DAPT 2024	12	1700	13	1700	9.8	0.92 [0.42, 2.02]
NEO-MINDSET 2025	62	1712	50	1698	44.5	1.23 [0.85, 1.77]
TARGET-FIRST 2025	4	961	2	981	2.1	2.04 [0.37, 11.12]
Total (95% CI)		**9384**		**9410**	**100.0**	**1.12 [0.88, 1.43]**
Total events	136		121			

Heterogeneity: $\tau^2 = 0.00$; $\chi^2 = 4.14$, $df = 5$ ($p = 0.53$); $I^2 = 0\%$

Test for overall effect: $Z = 0.93$ ($p = 0.35$)



E. Cardiovascular death

Study or subgroup	P2Y12i Monotherapy Events	Total	DAPT Events	Total	Weight (%)	Risk ratio IV, random, 95% CI
TICO 2020	7	1527	12	1529	11.9	0.58 [0.23, 1.48]
STOPDAPT-2 2022	10	2058	10	2078	13.5	1.01 [0.42, 2.42]
T-PASS 2024	6	1426	9	1424	9.7	0.67 [0.24, 1.87]
ULTIMATE-DAFT 2024	8	1700	7	1700	10.1	1.14 [0.42, 3.14]
NEO-MINDSET 2025	42	1712	34	1698	51.6	1.23 [0.78, 1.92]
TARGET-FIRST 2025	3	961	2	981	3.2	1.53 [0.26, 9.14]
Total (95% CI)		**9384**		**9410**	**100.0**	**1.03 [0.75, 1.42]**
Total events	76		74			

Heterogeneity: $\tau^2 = 0.00$; $\chi^2 = 2.93$, $df = 5$ ($p = 0.71$); $I^2 = 0\%$

Test for overall effect: $Z = 0.18$ ($p = 0.86$)

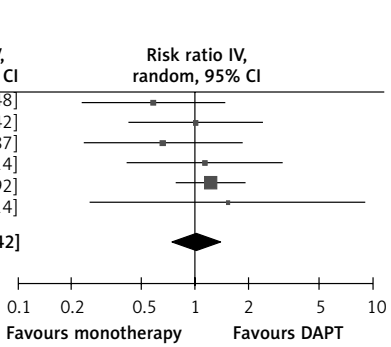


Figure 1. Forest plots for MACCE (**A**); clinically relevant bleeding (**B**); major bleeding (**C**); all-cause death (**D**); and cardiovascular death (**E**)

Stent thrombosis

All included studies reported stent thrombosis. Abbreviated DAPT followed by P2Y12 inhibitor monotherapy was associated with significantly higher risk of stent thrombosis compared with standard DAPT (RR = 1.83; 95% CI: 1.04–3.20; I^2 = 0%; p = 0.04; Figure 2 B).

Stroke

All included studies reported stroke. There was no statistically significant difference in the risk of stroke between abbreviated DAPT followed by P2Y12 inhibitor monotherapy and standard DAPT (RR = 1.00; 95% CI: 0.72–1.38; I^2 = 0%; p = 1.00; Figure 2 C).

Target-vessel revascularisation

All included studies reported target-vessel revascularisation. There was no statistically significant difference in the risk of target-vessel revascularisation between abbreviated DAPT followed by P2Y12 inhibitor monotherapy and standard DAPT (RR = 1.09; 95% CI: 0.79–1.49; I^2 = 28%; p = 0.61; Figure 2 D).

Net adverse events

Four out of six included trials reported net adverse events. Abbreviated DAPT followed by P2Y12 inhibitor monotherapy was associated with significantly lower risk of adverse events compared with standard DAPT (RR = 0.80; 95% CI: 0.68–0.94; I^2 = 42%; p = 0.007; Figure 2 E).

Discussion

In this systematic review and meta-analysis of six randomized controlled trials, comprising 18,794 patients undergoing PCI, we evaluated the safety and efficacy of abbreviated DAPT followed by aspirin withdrawal and continuation of P2Y12 inhibitor monotherapy compared with continued dual antiplatelet therapy over a 12-month follow-up. The pooled analysis demonstrated that this strategy was comparable to DAPT with respect to ischaemic efficacy, with no significant differences observed in MACCE, all-cause mortality, cardiovascular mortality, myocardial infarction, stroke, or target vessel revascularisation. Subgroup analyses further showed that the effect on MACCE differed significantly according to the type of P2Y12 inhibitor, with ticagrelor monotherapy demonstrating a numerically lower risk of MACCE, whereas clopidogrel monotherapy and mixed P2Y12 inhibitor regimens showed numerically higher but non-significant risks. In contrast, no significant interaction was observed according to the timing of aspirin withdrawal, with comparable MACCE rates whether aspirin was discontinued within 1 month or after more than 1 month. Importantly, early aspirin withdrawal was associated with a significant reduction in bleeding outcomes, including clinically relevant bleeding and major bleeding, translating into significantly lower risk of net adverse events overall. The reduction in clinically relevant bleeding was consistent regardless of P2Y12 inhibitor type and aspirin withdrawal timing. However, this bleeding benefit was accompanied by a statistically significant increase in the risk of stent thrombosis among patients receiving P2Y12 inhibitor monotherapy, highlighting the potential trade-off between bleeding reduction and thrombotic protection.

Consistent with our findings, accumulating evidence supports 1-3 months of DAPT followed by P2Y12 inhibitor monotherapy as a strategy to reduce bleeding without compromising ischaemic protection, and P2Y12 inhibitors appear preferable to aspirin as the single antiplatelet agent [22–25]. However, very early or immediate aspirin withdrawal remains experimental and is not yet supported as a replacement for guideline-recommended DAPT in patients with acute coronary syndromes [26]. Current international guidelines continue to recommend 6–12 months of DAPT after PCI for most patients, particularly those with ACS, while permitting shorter durations in individuals at higher bleeding-risk [27–30]. Notably, a network meta-analysis demonstrated that DAPT de-escalation strategies were associated with improved net clinical outcomes compared with continued potent P2Y12 monotherapy with similar bleeding and no clear ischaemic penalty [31]. Similarly, an individual patient-level meta-analysis of de-escalation trials in ACS reported reductions in both ischaemic and bleeding events compared with standard potent DAPT [32].

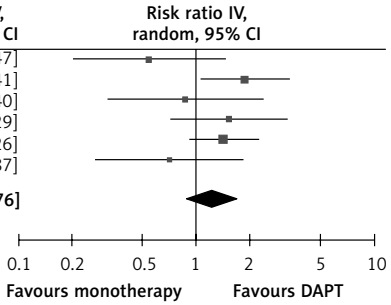
In the present meta-analysis, rates of MACCE were comparable with P2Y12 inhibitor monotherapy and standard DAPT over 12 months, indicating preserved ischaemic efficacy following aspirin withdrawal. Notably, subgroup analyses suggested that treatment effects may vary according to the specific P2Y12 inhibitor used, with ticagrelor showing a numerically favourable ischaemic profile, whereas clopidogrel and mixed regimens did not demonstrate a similar trend. Although these findings should be interpreted cautiously because several subgroup estimates were based on single studies, they are directionally consistent with prior ACS-specific analyses demonstrating more favourable ischaemic outcomes with ticagrelor-based monotherapy [33]. By contrast, the timing of aspirin withdrawal did not significantly modify the effect on MACCE, suggesting that ischaemic outcomes were similar whether aspirin was

A. Myocardial infarction

Study or subgroup	P2Y12i Monotherapy Events	Total	DAPT Events	Total	Weight (%)	Risk ratio IV, random, 95% CI
TICO 2020	6	1527	11	1529	10.4	0.55 [0.20, 1.47]
STOPDAPT-2 2022	32	2058	17	2078	22.5	1.90 [1.06, 3.41]
T-PASS 2024	7	1426	8	1424	10.1	0.87 [0.32, 2.40]
ULTIMATE-DAPT 2024	17	1700	11	1700	16.0	1.55 [0.73, 3.29]
NEO-MINDSET 2025	45	1712	31	1698	30.0	1.44 [0.92, 2.26]
TARGET-FIRST 2025	7	961	10	981	11.0	0.71 [0.27, 1.87]
Total (95% CI)		**9384**		**9410**	**100.0**	**1.23 [0.87, 1.76]**
Total events	114		88			

Heterogeneity: $\tau^2 = 0.06$; $\chi^2 = 7.03$, $df = 5$ ($p = 0.22$); $I^2 = 29\%$

Test for overall effect: $Z = 1.16$ ($p = 0.24$)

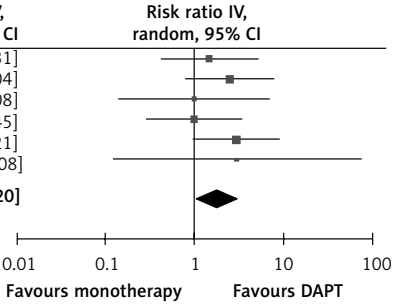


B. Stent thrombosis

Study or subgroup	P2Y12i Monotherapy Events	Total	DAPT Events	Total	Weight (%)	Risk ratio IV, random, 95% CI
TICO 2020	6	1527	4	1529	19.8	1.50 [0.42, 5.31]
STOPDAPT-2 2022	10	2058	4	2078	23.5	2.52 [0.79, 8.04]
T-PASS 2024	2	1426	2	1424	8.2	1.00 [0.14, 7.08]
ULTIMATE-DART 2024	5	1700	5	1700	20.6	1.00 [0.29, 3.45]
NEO-MINDSET 2025	12	1712	4	1698	24.7	2.98 [0.96, 9.21]
TARGET-FIRST 2025	1	961	0	981	3.1	3.06 [0.12, 75.08]
Total (95% CI)		**9384**		**9410**	**100.0**	**1.83 [1.04, 3.20]**
Total events	36		19			

Heterogeneity: $\tau^2 = 0.00$; $\chi^2 = 2.48$, $df = 5$ ($p = 0.78$); $I^2 = 0\%$

Test for overall effect $Z = 2.10$ ($p = 0.04$)

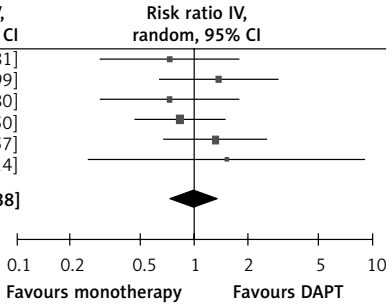


C. Stroke

Study or subgroup	P2Y12i Monotherapy Events	Total	DAPT Events	Total	Weight (%)	Risk ratio IV, random, 95% CI
TICO 2020	8	1527	11	1529	12.7	0.73 [0.29, 1.81]
STOPDAPT-2 2022	15	2058	11	2078	17.4	1.38 [0.63, 2.99]
T-PASS 2024	8	1426	11	1424	12.7	0.73 [0.29, 1.80]
ULTIMATE-DART 2024	20	1700	24	1700	30.2	0.83 [0.46, 1.50]
NEO-MINDSET 2025	20	1712	15	1698	23.6	1.32 [0.68, 2.57]
TARGET-FIRST 2025	3	961	2	981	3.3	1.53 [0.26, 9.14]
Total (95% CI)		**9384**		**9410**	**100.0**	**1.00 [0.72, 1.38]**
Total events	74		74			

Heterogeneity: $\tau^2 = 0.00$; $\chi^2 = 2.86$, $df = 5$ ($p = 0.72$); $I^2 = 0\%$

Test for overall effect: $Z = 0.00$ ($p = 1.00$)

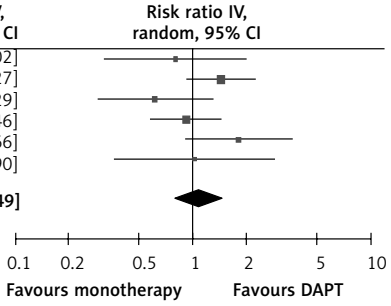


D. Target vessel revascularization

Study or subgroup	P2Y12i Monotherapy Events	Total	DAPT Events	Total	Weight (%)	Risk ratio IV, random, 95% CI
TICO 2020	8	1527	10	1529	9.7	0.80 [0.32, 2.02]
STOPDAPT-2 2022	46	2058	32	2078	27.4	1.45 [0.93, 2.27]
T-PASS 2024	11	1426	18	1424	13.8	0.61 [0.29, 1.29]
ULTIMATE-DART 2024	33	1700	36	1700	26.1	0.92 [0.57, 1.46]
NEO-MINDSET 2025	22	1712	12	1698	15.2	1.82 [0.90, 3.66]
TARGET-FIRST 2025	7	961	7	981	7.9	1.02 [0.36, 2.90]
Total (95% CI)		**9384**		**9410**	**100.0**	**1.09 [0.79, 1.49]**
Total events	127		115			

Heterogeneity: $\tau^2 = 0.04$; $\chi^2 = 6.90$, $df = 5$ ($p = 0.23$); $I^2 = 28\%$

Test for overall effect: $Z = 0.51$ ($p = 0.61$)



E. Net adverse events

Study or subgroup	P2Y12i Monotherapy Events	Total	DAPT Events	Total	Weight (%)	Risk ratio IV, random, 95% CI
TICO 2020	59	1527	89	1529	17.4	0.66 [0.48, 0.92]
ULTIMATE-DAPT 2024	97	1700	140	1700	24.1	0.69 [0.54, 0.89]
NEO-MINDSET 2025	145	1712	166	1698	28.9	0.87 [0.70, 1.07]
TARGET-FIRST 2025	144	961	157	981	29.5	0.94 [0.76, 1.15]
Total (95% CI)		**5900**		**5908**	**100.0**	**0.80 [0.68, 0.94]**
Total events	445		552			

Heterogeneity: $\tau^2 = 0.01$; $\chi^2 = 5.21$, $df = 3$ ($p = 0.16$); $I^2 = 42\%$

Test for overall effect: $Z = 2.71$ ($p = 0.007$)

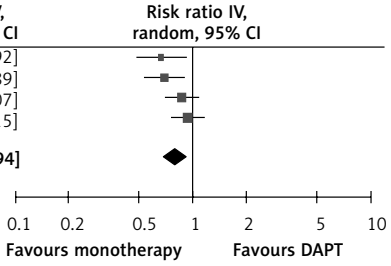


Figure 2. Forest plots for myocardial infarction (**A**); stent thrombosis (**B**); stroke (**C**); target vessel revascularisation (**D**); and net adverse events (**E**)

discontinued within 1 month or later. This finding aligns with prior meta-analyses, for example, Bianco *et al.* reported no significant difference in 1-year cardiovascular events between short-duration DAPT and conventional 12-month DAPT following PCI [34]. Similarly, a recent systematic review evaluating early aspirin discontinuation found that P2Y12 inhibitor monotherapy maintained ischaemic protection, with reported hazard ratios ranging from 0.54 to 1.14 across diverse PCI populations [22]. Multiple RCT-based meta-analyses, including those focused exclusively on ACS cohorts, have likewise demonstrated no excess risk of MACCE with P2Y12 inhibitor monotherapy following ≤ 3 months of DAPT compared with prolonged DAPT [35, 36]. Notably, in the OPT-BRISK trial, which enrolled patients with ACS at both high ischaemic and bleeding risk, extended clopidogrel monotherapy after an initial DAPT period was associated with a lower incidence of MACCE compared with continued DAPT [37]. Several earlier meta-analyses have also evaluated DAPT compared with P2Y12 inhibitor monotherapy after PCI in patients with acute coronary syndrome [38, 39]. Although some of these studies reported larger pooled sample sizes, this was largely attributable to the inclusion of subgroup analyses from broader randomised trials. In contrast, our meta-analysis included six dedicated randomised controlled trials that specifically enrolled and randomised patients with acute coronary syndrome, whereas earlier analyses included only four such trials. The availability of two additional ACS-specific randomised trials allowed us to provide a more contemporary and comprehensive assessment without relying on subgroup-derived data, which may be associated with greater uncertainty.

We observed no significant differences between groups in rates of MI, stroke, or target vessel revascularisation. This finding aligns with multiple meta-analyses demonstrating that P2Y12 inhibitor monotherapy following 1–3 months of DAPT is non-inferior to standard 12-month DAPT with respect to major ischaemic outcomes, including MI and stroke [23, 24, 30, 40]. Similarly, large trials such as the SMART-CHOICE and SHARE reported comparable rates of MI and stroke with short-duration DAPT followed by P2Y12 inhibitor monotherapy versus conventional DAPT [41, 42]. In more complex PCI populations, P2Y12 monotherapy after short DAPT has been associated with reduced MI without increases in stroke, death, or stent thrombosis [43]. Concordantly, prior meta-analysis by Bianco *et al.* found no significant differences in MI, stroke, or target vessel revascularisation [34]. Collectively, these data suggest that early aspirin withdrawal after an initial phase of DAPT does not appear to compromise composite ischaemic outcomes in appropriately selected patients undergoing PCI for ACS, although careful risk stratification remains essential.

Our analysis demonstrated that aspirin withdrawal with the continuation of P2Y12 inhibitor monotherapy was associated with a significant reduction in bleeding events, including both clinically relevant bleeding and major bleeding, compared with continued DAPT. This benefit was consistent across all examined subgroups. Clinically relevant bleeding was significantly reduced with ticagrelor monotherapy, clopidogrel monotherapy, and mixed P2Y12 inhibitor regimens, with no significant interaction by agent type. Similarly, significant reductions were observed both when aspirin was discontinued within 1 month and when discontinued after more than 1 month, indicating that the bleeding advantage of aspirin withdrawal was robust regardless of treatment strategy. This bleeding benefit aligns closely with prior evidence. Bianco *et al.* demonstrated significantly lower rates of major bleeding with short DAPT followed by P2Y12 inhibitor monotherapy compared with 12-month DAPT, reporting a reduction in BARC type 3-5 bleeding of approximately 30% [34]. Similarly, a recent meta-analysis by Singh *et al.* focusing on ACS populations found that early aspirin discontinuation reduced major bleeding by nearly 50% without compromising ischaemic outcomes [23]. The magnitude of bleeding reduction observed in our study is consistent with these reports and reflects the well-established contribution of aspirin to gastrointestinal and systemic bleeding risk following PCI.

Bleeding events after PCI are not benign, and they have been independently associated with increased mortality, recurrent ischaemic events, and prolonged hospitalisations, emphasising the clinical importance of strategies that improve safety [44–46]. Large meta-analysis of randomised trials have consistently shown a 40–50% relative reduction in major or clinically relevant bleeding with P2Y12 inhibitor monotherapy after 1–3 months of DAPT, including in ACS-specific analyses, while overall MACCE rates remain comparable to standard DAPT [24, 35, 36, 47]. Collectively, these findings support evolving guideline recommendations favouring abbreviated DAPT or aspirin-free strategies in patients at elevated bleeding risk, and reinforce that the principal clinical advantage of aspirin withdrawal lies in a meaningful reduction in bleeding without an apparent loss of overall ischaemic protection when applied in appropriately selected patients.

Our findings demonstrated no significant differences between P2Y12 inhibitor monotherapy and continued DAPT with respect to all-cause or cardiovascular mortality. These findings are

consistent with prior randomised evidence in ACS populations undergoing PCI. Available evidence has demonstrated that abbreviated DAPT (1–3 months) followed by P2Y12 inhibitor monotherapy does not increase the risk of all-cause or cardiovascular death compared with standard-duration DAPT, while substantially reducing bleeding events [23, 48]. In an ACS-focused meta-analysis by Laudani *et al.*, P2Y12 inhibitor monotherapy after short DAPT was associated with lower rates of major bleeding and net adverse clinical events, with neutral effects on mortality [40]. Similarly, a O'Donoghue *et al.*, in their meta-analysis including both ACS and stable coronary artery disease (CAD) patients, reported marked bleeding reductions without an excess of major adverse cardiovascular events or death, including in ACS subgroups [24]. In line with these findings, Bianco *et al.* similarly found no significant difference in mortality between the two strategies [34].

Unlike the marked and consistent reduction in bleeding risk observed with aspirin withdrawal, our analysis identified a statistically significant increase in stent thrombosis with abbreviated DAPT followed by P2Y12 inhibitor monotherapy. We consider this to be a clinically important safety signal rather than a secondary finding, given the potentially catastrophic consequences of stent thrombosis, including myocardial infarction and sudden cardiac death. This finding diverges from most prior meta-analyses, which have generally reported similar stent thrombosis rates between the two groups. For example, a meta-analysis by Giacoppo *et al.*, assessing short DAPT followed by P2Y12 inhibitor monotherapy, found no significant difference in stent thrombosis between regimens despite lower bleeding with monotherapy, suggesting that overall thrombotic risk may not universally rise with de-escalation [49]. Another meta-analysis by Nicolas *et al.* in complex PCI populations also highlighted that while bleeding was reduced, ischaemic risk including stent thrombosis was not consistently increased, emphasising the influence of patient and procedural characteristics on thrombotic outcomes [50]. However, this result should be interpreted cautiously because the absolute number of events was small, definitions of stent thrombosis varied across trials, and most events probably occurred during the first 1–3 months after PCI, when patients in the abbreviated DAPT arms were still receiving dual antiplatelet therapy rather than P2Y12 inhibitor monotherapy. Therefore, the observed increase cannot be attributed solely to aspirin withdrawal, although it remains an important consideration when applying aspirin-free strategies, particularly in patients at high thrombotic risk. Potential explanations include very early aspirin cessation, heterogeneity in stent platforms, variability in P2Y12 inhibitor potency (especially clopidogrel based strategies), and differences in trial populations, procedural factors, and stent characteristics that influence baseline thrombotic risk.

This meta-analysis has certain limitations. First, this was a study-level analysis, limiting adjustment for individual ischaemic and bleeding risk profiles. Second, heterogeneity in trial designs, including differences in timing of aspirin withdrawal, and the choice and potency of P2Y12 inhibitors, which may have influenced outcome estimates. Third, the finding of increased stent thrombosis should be interpreted cautiously because event rates were low, definitions varied across trials, and most events likely occurred during the initial 1–3 months when patients in the abbreviated DAPT arms were still receiving dual antiplatelet therapy. Fourth, follow-up was limited to 12 months across all studies, precluding assessment of longer-term ischemic and bleeding risks. Fifth, variability in stent platforms and procedural characteristics could not be fully accounted for. Finally, variability in MACCE definitions across trials, including differences in component endpoints such as the inclusion of major bleeding in one study, may limit the interpretability and comparability of the pooled MACCE outcome. These limitations highlight the need for large, well-powered, randomised trials with extended follow-up to better define optimal antiplatelet strategies after PCI.

In conclusion, in this systematic review and meta-analysis of 18,794 patients undergoing PCI, a strategy of abbreviated DAPT followed by aspirin withdrawal and continuation with $P2Y_{12}$ inhibitor monotherapy demonstrated comparable ischaemic efficacy to standard 12-month dual antiplatelet therapy, with no significant differences in MACCE, all-cause mortality, cardiovascular mortality, myocardial infarction, stroke, or target-vessel revascularisation. Importantly, this approach was associated with a substantial reduction in clinically relevant and major bleeding, resulting in a significantly lower risk of net adverse events. However, this bleeding benefit was accompanied by a modest but statistically significant increase in stent thrombosis, underscoring the need for careful patient selection. Overall, these findings suggest that early aspirin withdrawal may be a reasonable strategy in selected patients, particularly those at high bleeding risk, while highlighting the importance of individualised antiplatelet therapy and continued vigilance regarding thrombotic risk. Future studies should focus on refining patient selection, optimal timing of aspirin discontinuation, and the choice of $P2Y_{12}$ inhibitor to further optimise clinical outcomes.

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Ethical approval

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Conflict of interest

The authors declare no conflict of interest.

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