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Antiplatelet Dilemma: Clopidogrel or Aspirin for Long-Term Cardiovascular Protection after Dual Antiplatelet Therapy Following PCI

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Systematic review & meta-analysis · 6 studies (2 RCTs, 4 cohorts) · 14,992 patients

Aspirin vs clopidogrel monotherapy after DAPT

1 Background & aim

After percutaneous coronary intervention (PCI), patients take dual antiplatelet therapy (DAPT) for 6–12 months and then continue lifelong monotherapy. Aspirin has been the default, but clopidogrel may offer better ischaemic protection with less gastrointestinal injury.

AIM To compare long-term aspirin and clopidogrel monotherapy after DAPT in patients who underwent PCI.

RR > 1 = higher risk with aspirin (favours clopidogrel)

2 Methods

Search PubMed, Scopus and Web of Science from inception to January 2025; PRISMA and Cochrane Handbook

Eligibility RCTs and cohort studies of clopidogrel vs aspirin monotherapy after DAPT post-PCI

Outcomes Primary: MACE. Secondary: TIMI and BARC bleeding, GI bleeding, mortality, stroke, MI, TVR, stent thrombosis

Analysis RevMan; pooled risk ratios; fixed effect unless $I^2 \geq 50\%$; leave-one-out sensitivity and subgroup analysis by design

Quality RoB 2 for the 2 RCTs (low risk); Newcastle–Ottawa for the 4 cohorts (all high quality)

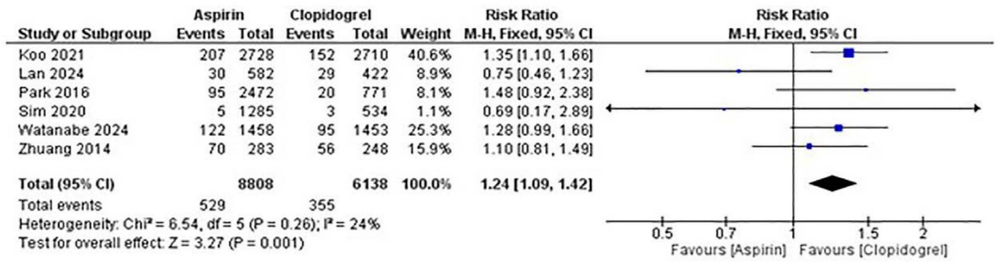
2,531 identified → 1,146 screened → 10 full text → 6 included

3 Results — forest plots

Risk ratios, aspirin vs clopidogrel

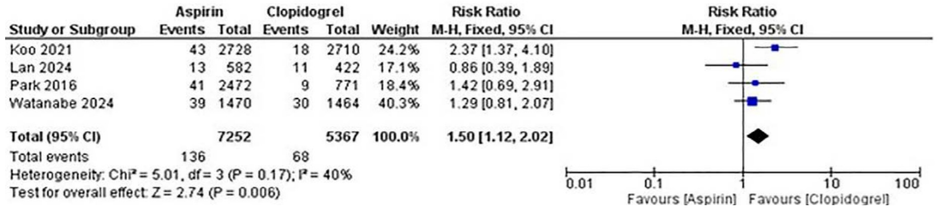
MACE — primary outcome (6 studies)

RR 1.24 (1.09–1.42) · P = 0.001



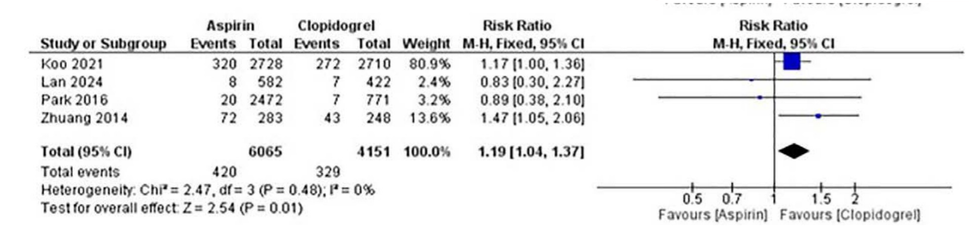
Stroke (any type)

RR 1.50 (1.12–2.02) · P = 0.006



Gastrointestinal bleeding

RR 1.19 (1.04–1.37) · P = 0.01



4 All pooled outcomes

Outcome (aspirin vs clopidogrel)	RR [95% CI]	P	I^2
MACE (primary)	**1.24 [1.09, 1.42]**	0.001	24%
Stroke (any)	**1.50 [1.12, 2.02]**	0.006	40%
Ischaemic stroke	**1.56 [1.03, 2.38]**	0.04	0%
Haemorrhagic stroke	**2.06 [1.06, 3.98]**	0.03	72%
Myocardial infarction	1.25 [0.98, 1.57]	0.07	—
Target vessel revascularisation	1.06 [0.77, 1.47]	0.72	—
Stent thrombosis	1.36 [0.58, 3.21]	0.48	—
Major bleeding (TIMI)	0.86 [0.61, 1.23]	0.42	18%
Minor bleeding (TIMI)	**1.57 [1.06, 2.34]**	0.03	75%
GI bleeding	**1.19 [1.04, 1.37]**	0.01	0%
BARC 2, 3 or 5	0.98 [0.57, 1.71]	0.95	80%
BARC 3 or 5	0.96 [0.58, 1.58]	0.86	67%
All-cause mortality	0.93 [0.76, 1.12]	0.43	45%
Cardiovascular mortality	1.21 [0.91, 1.60]	0.19	27%

5 Subgroups & robustness

By design: clopidogrel was superior in the RCT subgroup (MACE RR 1.32, 1.13–1.55) but comparable in cohorts (P = 0.49); the same pattern was seen for MI.

Sensitivity:
Watanabe 2024 (1-month DAPT) drove the BARC bleeding heterogeneity.

Limitations:
mixed RCT and cohort designs; DAPT duration 1–18 months; nearly all patients East Asian (high CYP2C19 loss-of-function prevalence); aggregate data only.

6 Conclusions

1. **Efficacy:** clopidogrel lowered MACE and stroke (ischaemic and haemorrhagic).
2. **Safety:** no excess major bleeding or mortality; more GI bleeding on aspirin.
3. **Practice:** individualise by CYP2C19 status, bleeding risk and cost.

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Published as: Moawad MHED et al. Antiplatelet dilemma. Medicine 2026;105:9(e47773). Abbreviations: MACE, major adverse cardiovascular events; DAPT, dual antiplatelet therapy; TIMI/BARC, bleeding scales; RR, risk ratio. No funding · No conflicts of interest.