# Modulation of DAPT duration: risk-benefit of 1-year DAPT

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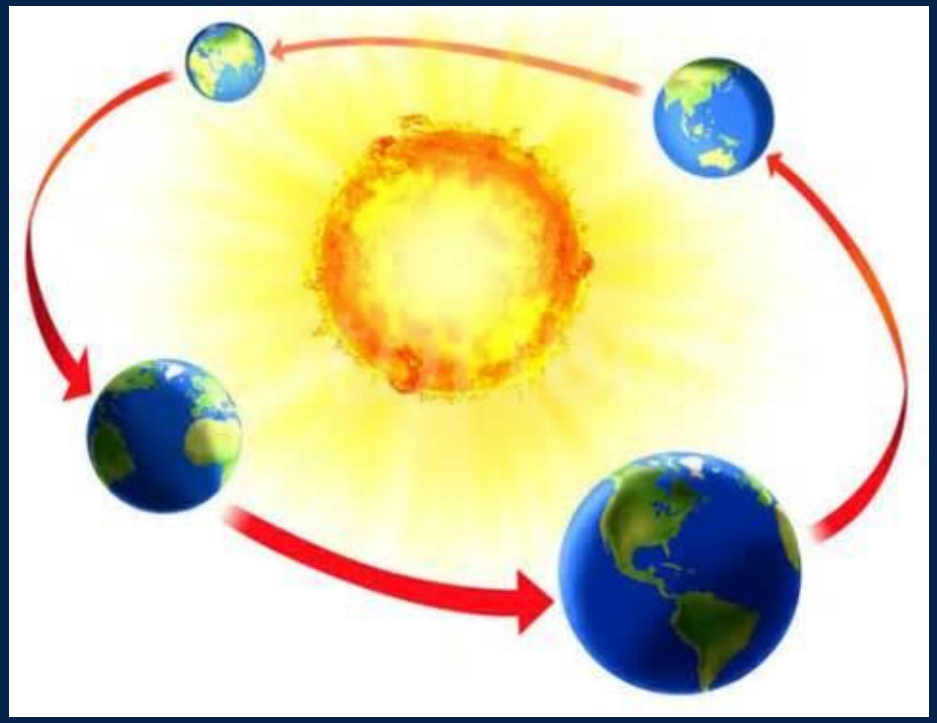
# Defining the problem: old strategies versus new strategies

1-year DAPT

Clopdigrel + asa



Potent DAPT + ASA

# Trials on 1-year DAPT with clopidogrel

## ≤6 months vs 1 year (n=13)

- STOP DAPT
- STOP DAPT ACS
- MASTER DAPT
- SMART CHOICE
- RESET
- OPTIMIZE
- REDUCE
- SMART DATE
- EXCELLENT
- ISAR SAFE
- SECURITY
- I LOVE IT
- IVUS XPL

3 RCT: 1 month vs 1 year

4 RCT: 3 months vs 1 year

6 RCT 6 months vs 1 year

## 1 year vs > 1 year (n=4)

- DAPT trial
- DES LATE
- ARCTIC INTERRUPTION
- OPTIDUAL

# Risk-Benefit of 1-Year DAPT After DES Implantation in Patients Stratified by Bleeding and Ischemic Risk

**IPD meta-analysis with 7 RCTs and 15,083 patients**

***Palmerini et al; JACC 2021***

Articles

Platelet reactivity and clinical outcomes after coronary artery implantation of drug-eluting stents (ADAPT-DES): a prospective multicentre registry study

Summary

Background The relation between platelet reactivity and stent thrombosis, major bleeding, and other adverse events after coronary artery implantation of drug-eluting stents has been incompletely characterised. We aimed to determine the relation between platelet reactivity during dual therapy with aspirin and clopidogrel and clinical outcomes after successful coronary drug-eluting stent implantation.

Methods ADAPT-DES was a prospective, multicentre registry of patients successfully treated with one or more drug-eluting stents and given aspirin and clopidogrel at 126 US and European hospitals. We assessed platelet reactivity in these patients after successful percutaneous coronary intervention using VerifyNow point-of-care assays, and assigned different cutoffs to define high platelet reactivity. The primary endpoint was definite or probable stent thrombosis; other endpoints were all-cause mortality, myocardial infarction, and clinically relevant bleeding. We did a prespecified adjusted multivariable analysis to determine the relation between platelet reactivity and subsequent adverse events. This study is registered with ClinicalTrials.gov, number NCT00809731.

Findings Between Jan 7, 2009, and Sept 16, 2010, 8583 patients were prospectively recruited at 31 sites, of which 8582 were eligible. At 1-year follow-up, stent thrombosis had occurred in 78 (1·0%) patients, myocardial infarction in 283 (3·3%), clinically relevant bleeding in 531 (6·2%), and death in 312 (3·6%) patients. High platelet reactivity on clopidogrel was strongly related to stent thrombosis (adjusted HR 2·08 [95% CI 1·13–3·83], p=0·019) and myocardial infarction (adjusted HR 1·42 [1·00–2·02], p=0·05), was inversely related to bleeding (adjusted HR 0·73 [0·63–0·85], p<0·0001), but was not related to mortality (adjusted HR 1·08 [0·78–1·49], p=0·65). High platelet reactivity on aspirin was not significantly associated with stent thrombosis (adjusted HR 1·46 [0·80–2·65], p=0·22), myocardial infarction, or death, but was inversely related to bleeding (adjusted HR 0·81 [0·66–0·98], p=0·03).

Interpretation The findings from this study emphasise the counterbalancing effects of haemorrhagic and ischaemic complications after stent implantation, and suggest that tailor drugs or tailored strategies for the use of more potent agents must be developed if the benefits of greater platelet inhibition in patients with cardiovascular disease are to be realised.

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Introduction

The occurrence of stent thrombosis after coronary artery implantation of drug-eluting stents is associated with high rates of myocardial infarction and death.[1] Dual antiplatelet therapy with aspirin and an adenosine diphosphate (ADP) receptor inhibitor is presently recommended for at least 1 year after drug-eluting stent implantation since most episodes of stent thrombosis have occur within this period.[2] Aspirin inhibits cyclo-oxygenase-1, a key enzyme involved in the conversion of arachidonic acid to thromboxane A2, an important agonist that amplifies platelet aggregation. Clopidogrel, the most widely used ADP-receptor inhibitor, undergoes a two-step metabolic transformation before binding to the platelet P2Y12 ADP receptor.[3] The conversion of clopidogrel to its active metabolite is regulated by the CYP450 system, and the presence of genetic polymorphisms partly determines the extent to which clopidogrel inhibits ADP-induced platelet activation.[4] Results from pharmacodynamic studies in patients treated with clopidogrel have shown wide variability in platelet responsiveness, and high platelet reactivity on clopidogrel has been linked to stent thrombosis and adverse cardiovascular events after stenting.[5–7] Variability in platelet responsiveness in aspirin has also been described, although its association with cardiac events and stent thrombosis is less clear.[8–10]

Previous studies examining the relation between platelet reactivity and stent thrombosis have been limited in size, and have often enrolled a stable, elective population in whom event rates were low.[6] Additionally, the effect of platelet reactivity on major bleeding, the



**Ischemic risk score**

| Variable | Category | Score |
|---|---|---|
| Platelet reactivity units | ≤208 | 0 |
| | >208 | 1 |
| Anemia (hemoglobin <12 mg/dL) | No | 0 |
| | Yes | 2 |
| Chronic kidney disease | No | 0 |
| | Yes | 2 |
| Peripheral artery disease | No | 0 |
| | Yes | 1 |
| Complex coronary artery disease | No | 0 |
| | Yes | 1 |
| Current smoker | No | 0 |
| | Yes | 2 |
| Diabetes | No | 0 |
| | Yes | 3 |
| Prior PCI | No | 0 |
| | Yes | 1 |
| Prior CABG | No | 0 |
| | Yes | 2 |
| ACS | No | 0 |
| | Yes | 3 |

**Bleeding risk score**

| Variable | Category | Score |
|---|---|---|
| Platelet reactivity units | Low (<95) | 1 |
| | Optimal (95–208) | 0 |
| | High (>208) | -1 |
| Oral anticoagulant therapy | No | 0 |
| | Yes | 4 |
| Anemia (hemoglobin <12 mg/dL) | No | 0 |
| | Yes | 3 |
| Chronic kidney disease | No | 0 |
| | Yes | 2 |
| Age (years) | <65 | 0 |
| | 65–75 | 2 |
| | >75 | 3 |
| Body mass index (kg/m²) | <25 | 1 |
| | 25–35 | 0 |
| | ≥35 | 2 |

EXCELLENT
ITALIC
NIPPON
OPTIMIZE
PRODIGY
RESET
SECURITY

Low IR

Intermediate IR

High IR

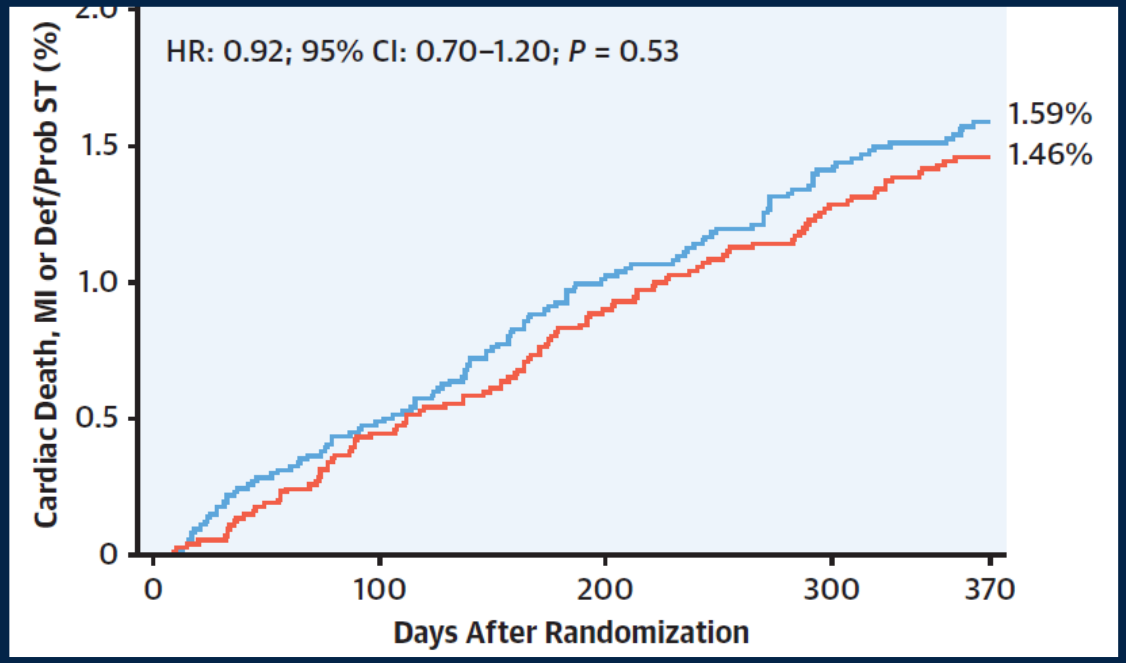
3/6-month vs 1-year DAPT

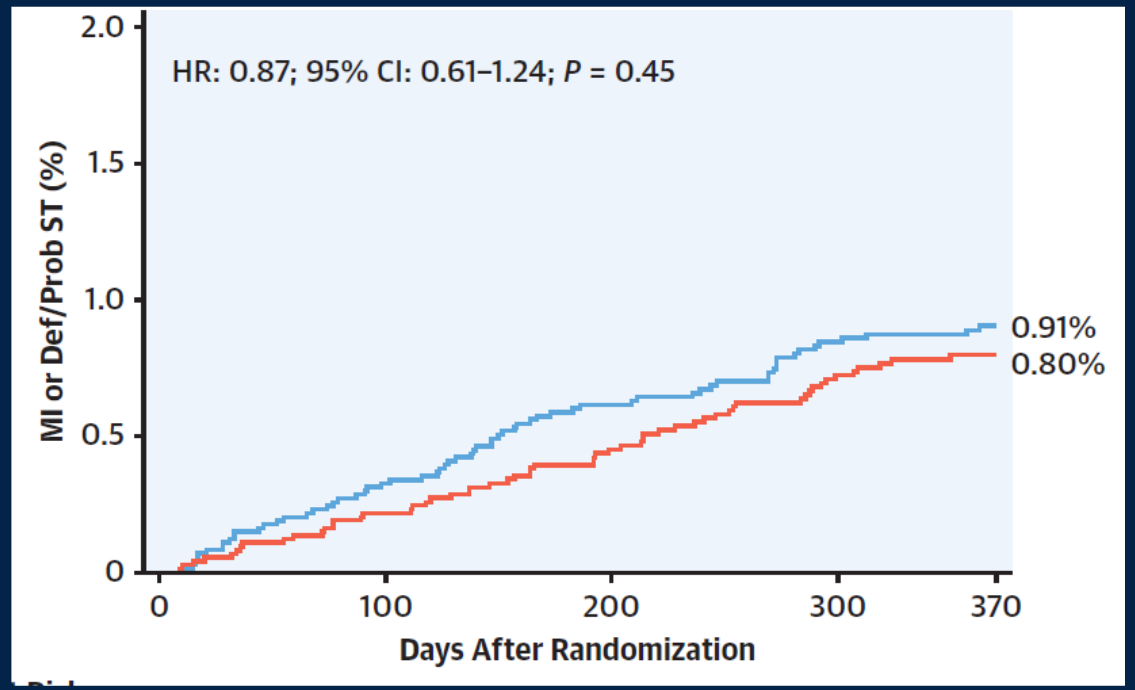
Low BR

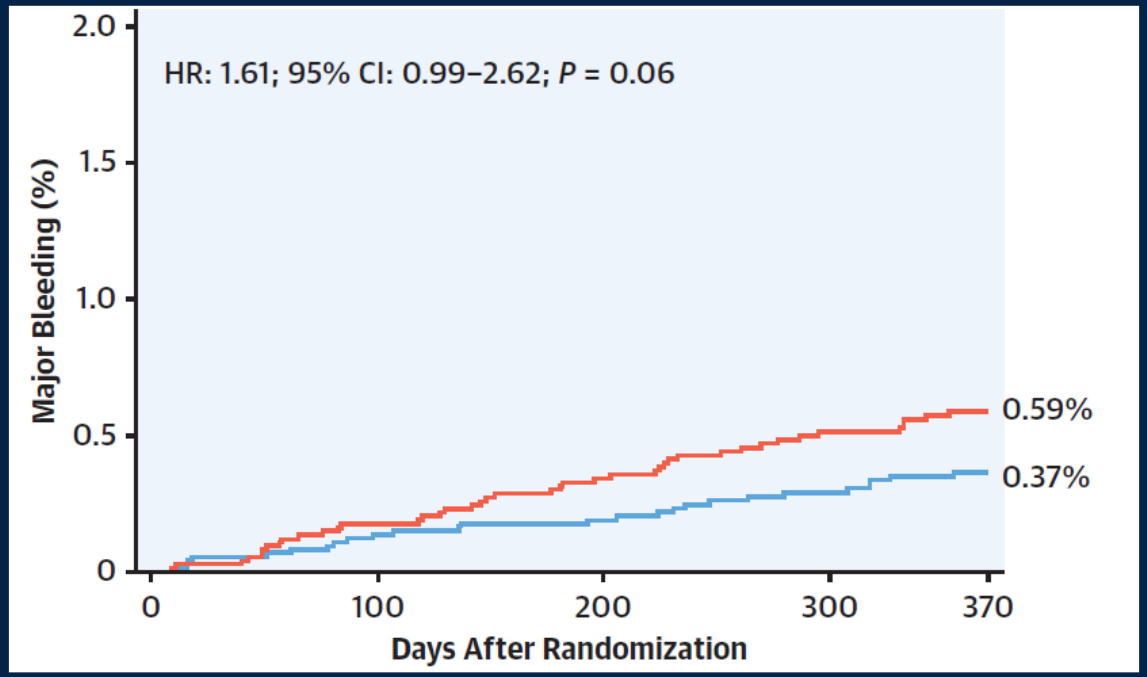
Intermediate BR

High BR

3/6-month vs 1-year DAPT



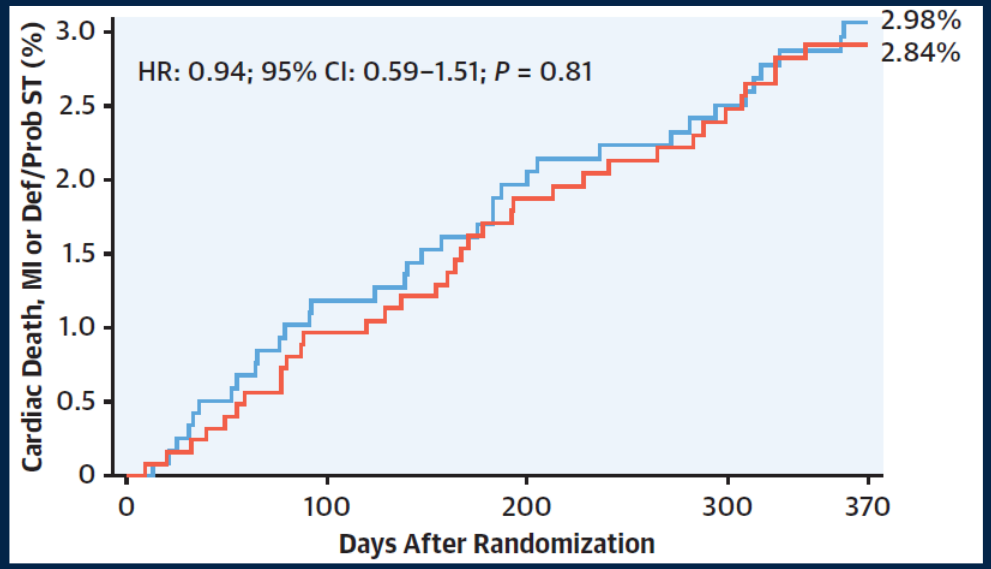



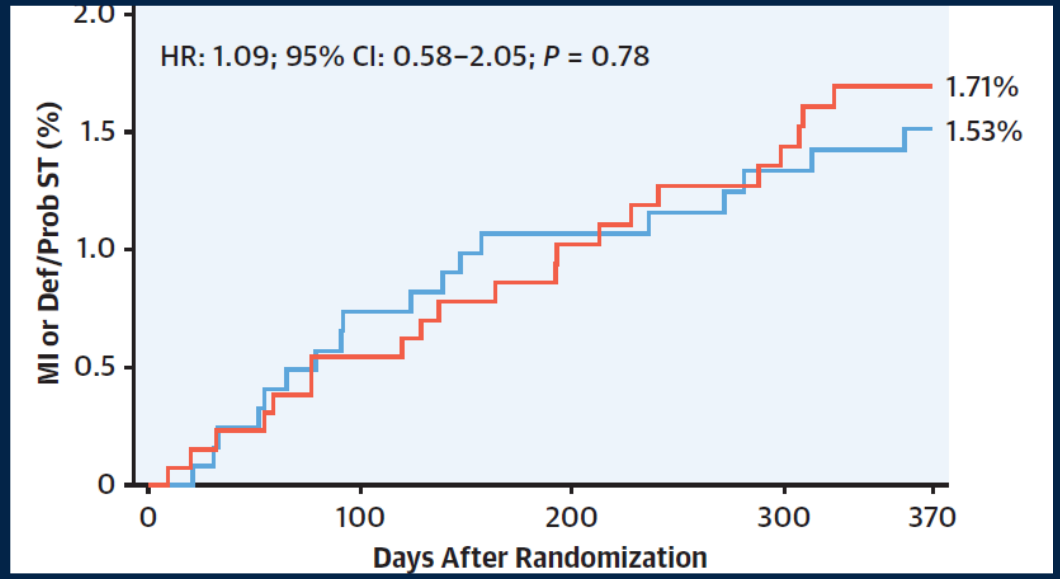

**IPD of 7 RCT**
**15,083 patients**

*Palmerini et al; JACC 2021*

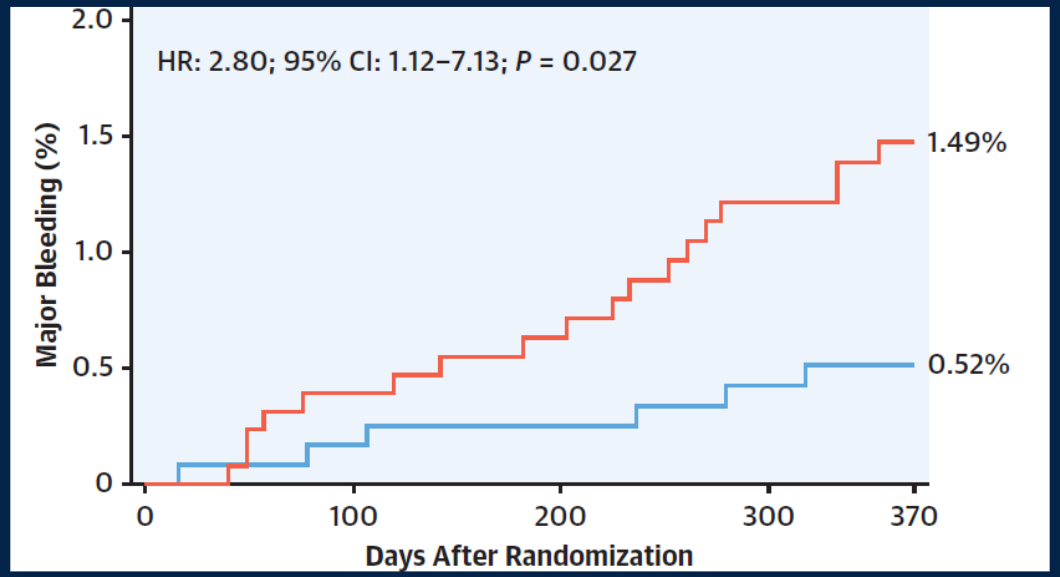
≤6-Month DAPT
1-Year DAPT

# HBR patients in IPD dataset: bleeding score≥4



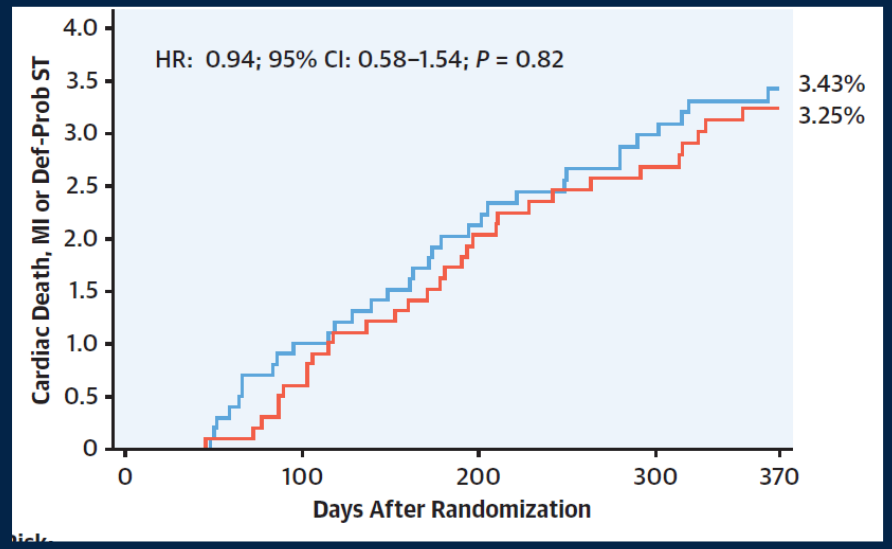

## 2,443 patients at HBR

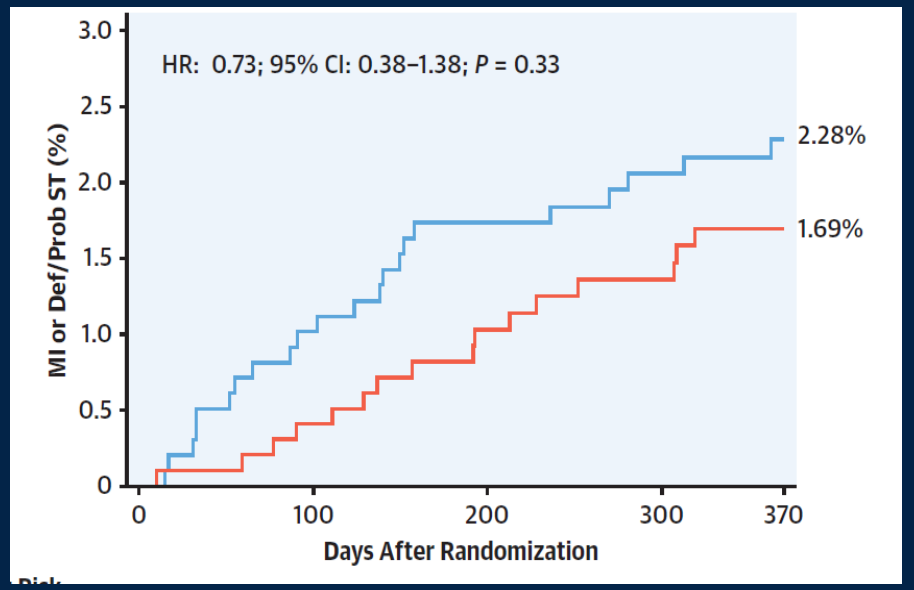



*Palmerini et al; JACC 2021*

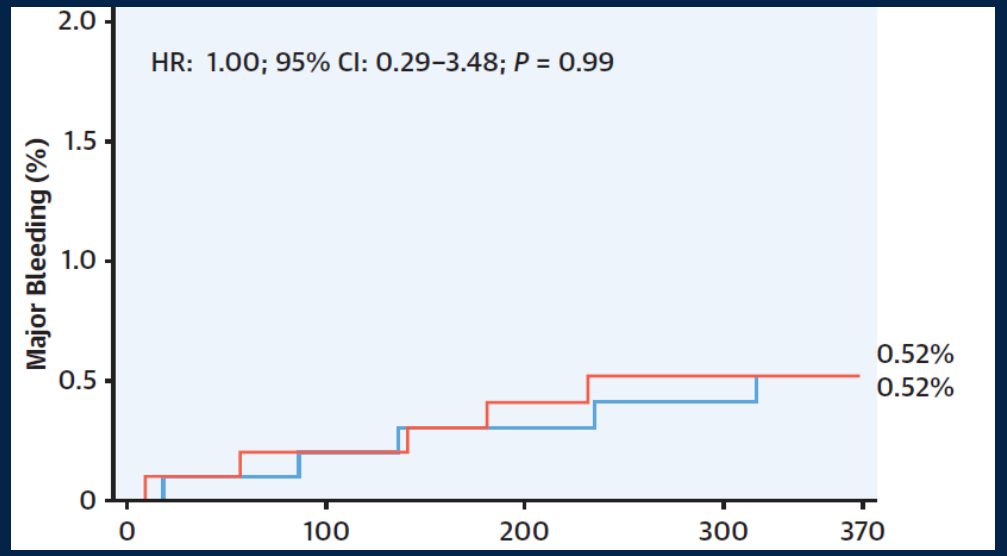
≤6-Month DAPT
1-Year DAPT

# HIR patients in IPD dataset: ischemic score≥7



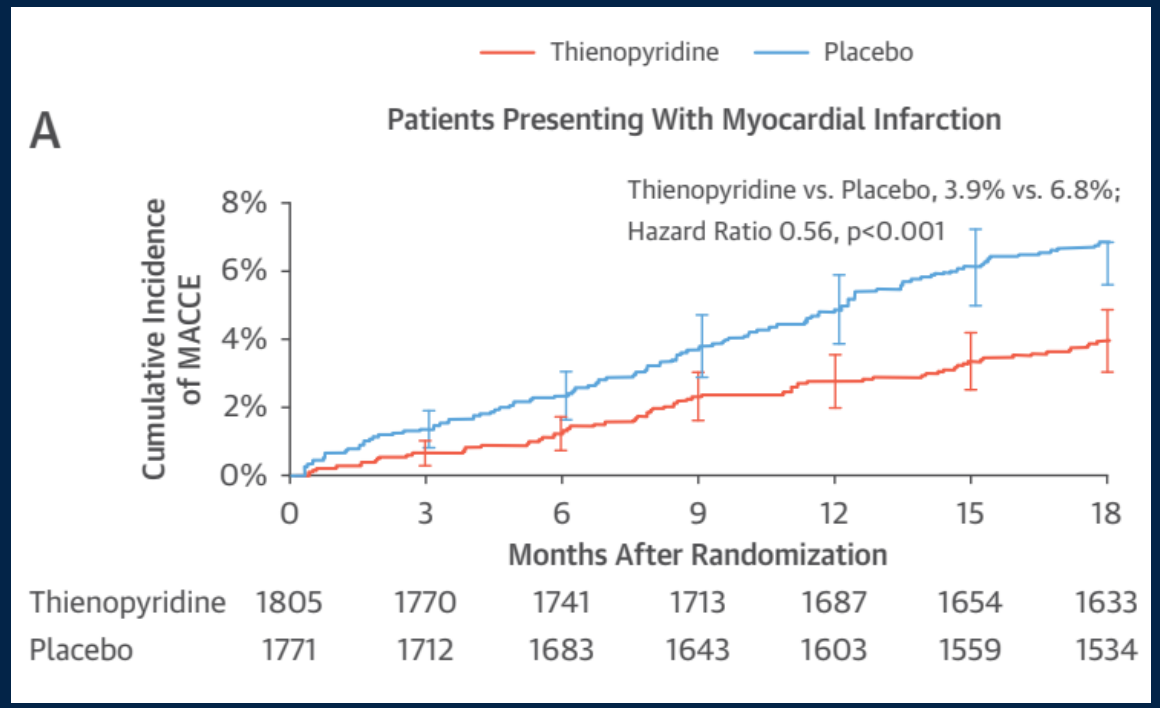

## 2,012 patients at HIR

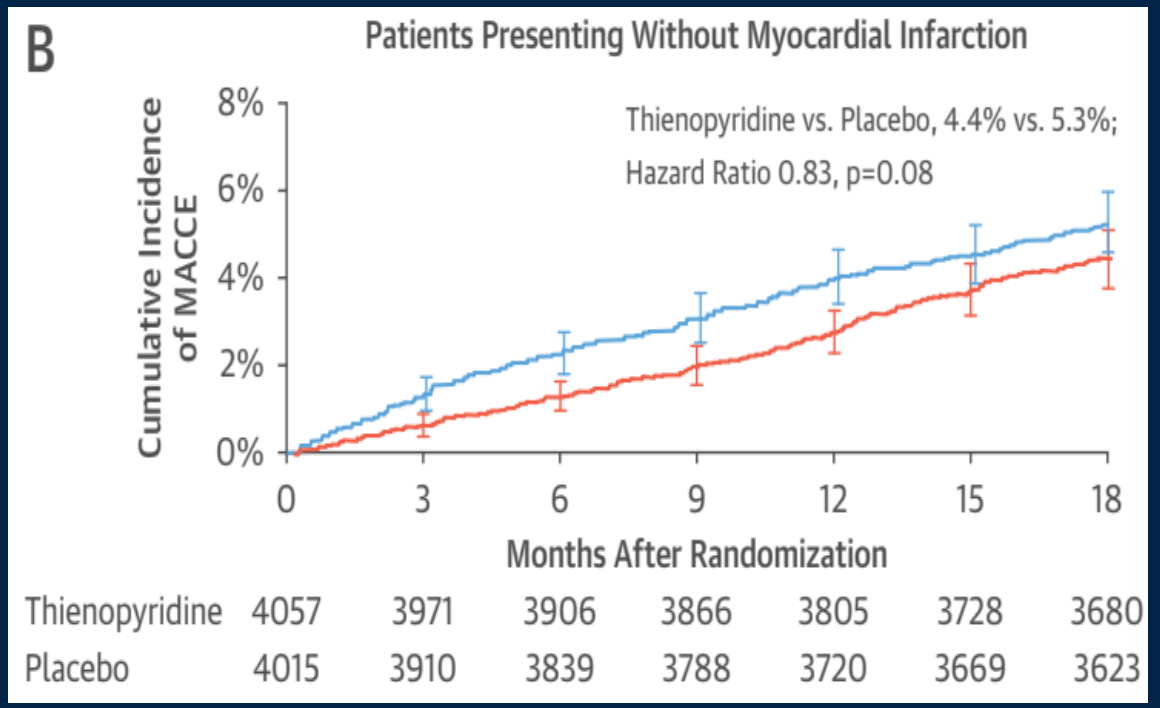



*Palmerini et al; JACC 2021*

≤6-Month DAPT
1-Year DAPT

# Twelve or 30 Months of Dual Antiplatelet Therapy after Drug-Eluting Stents

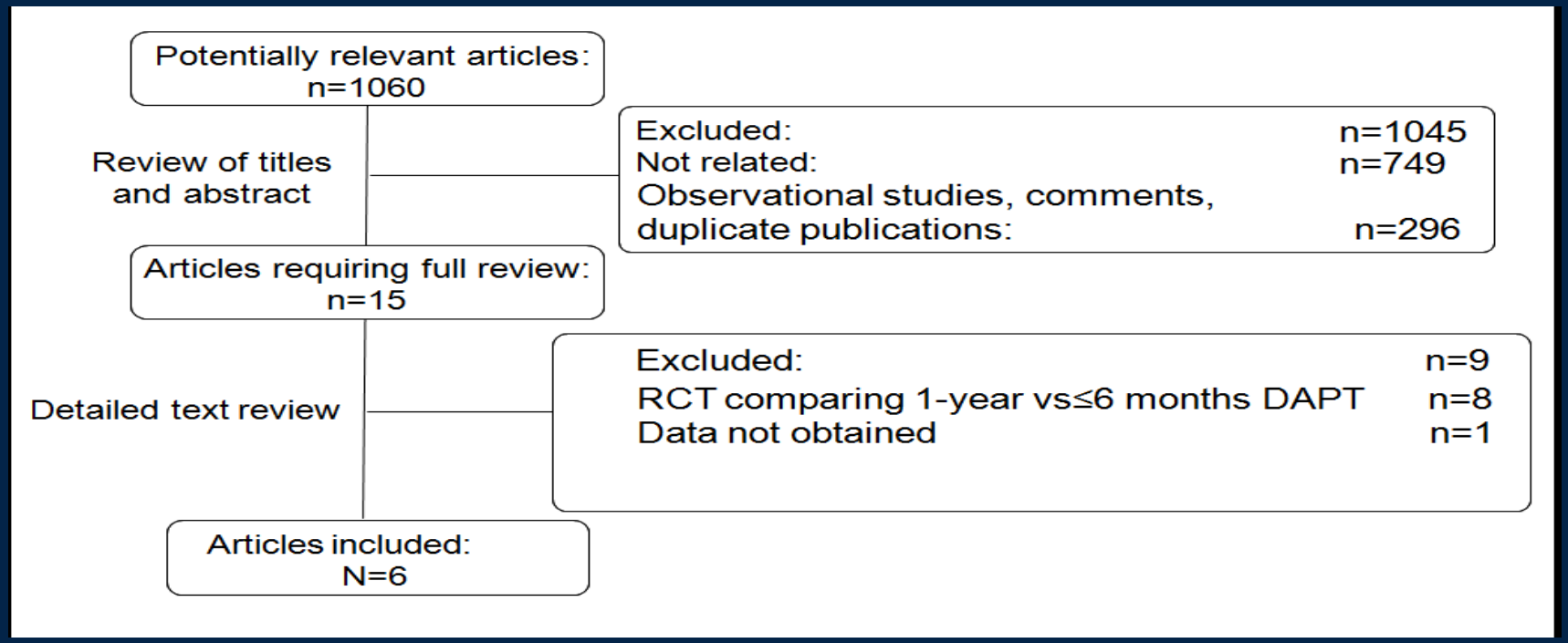



***Yeh et al et al; JACC 2016***

# 1-year or less versus longer than 1-year DAPT in patients stratified by clinical presentation

**Aggregate data based meta-analysis including 6 RCTs and 21,457 patients**
**14,132 patients with SIHD and 7,325 patients with ACS**
**Median follow up of 19.5 months**

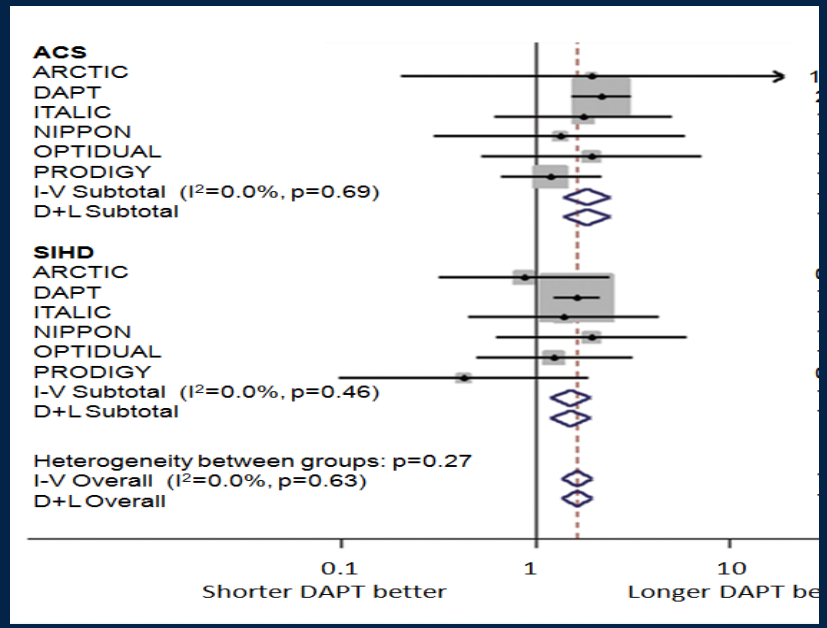



**1 year vs > 1 year (n=6)**

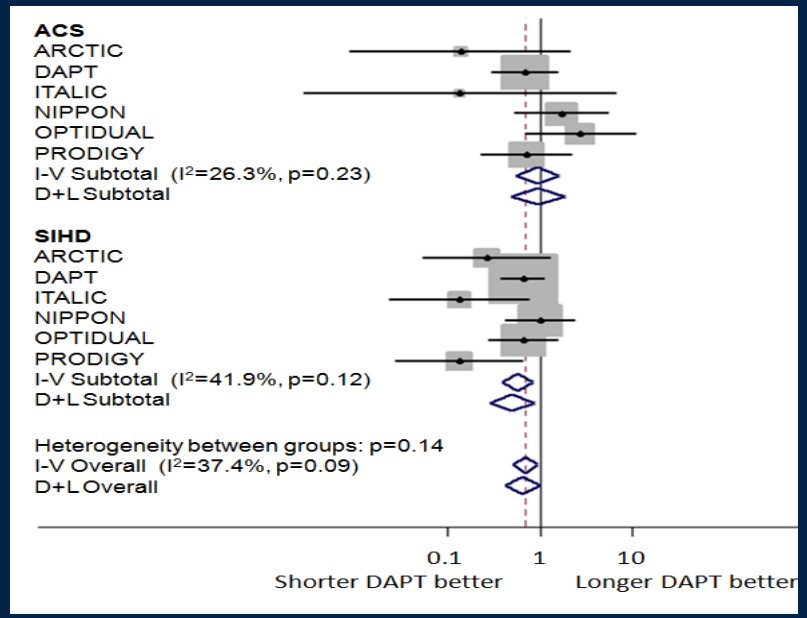
- **DAPT trial**
- **DES LATE**
- **ARCTIC INTERRUPTION**
- **OPTIDUAL**
- **ITALIC**
- **PRODIGY**

***Palmerini et al; Circ Cv Int 2019***

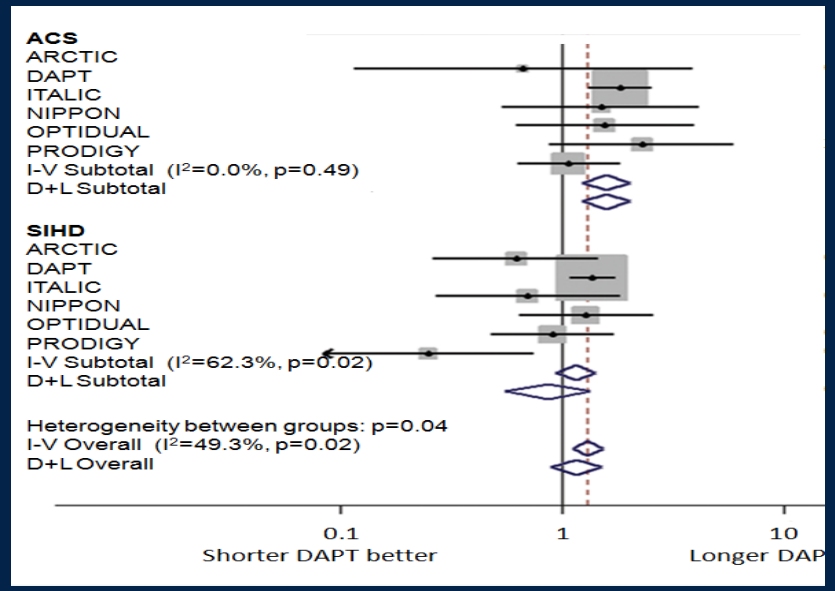
# Myocardial infarction



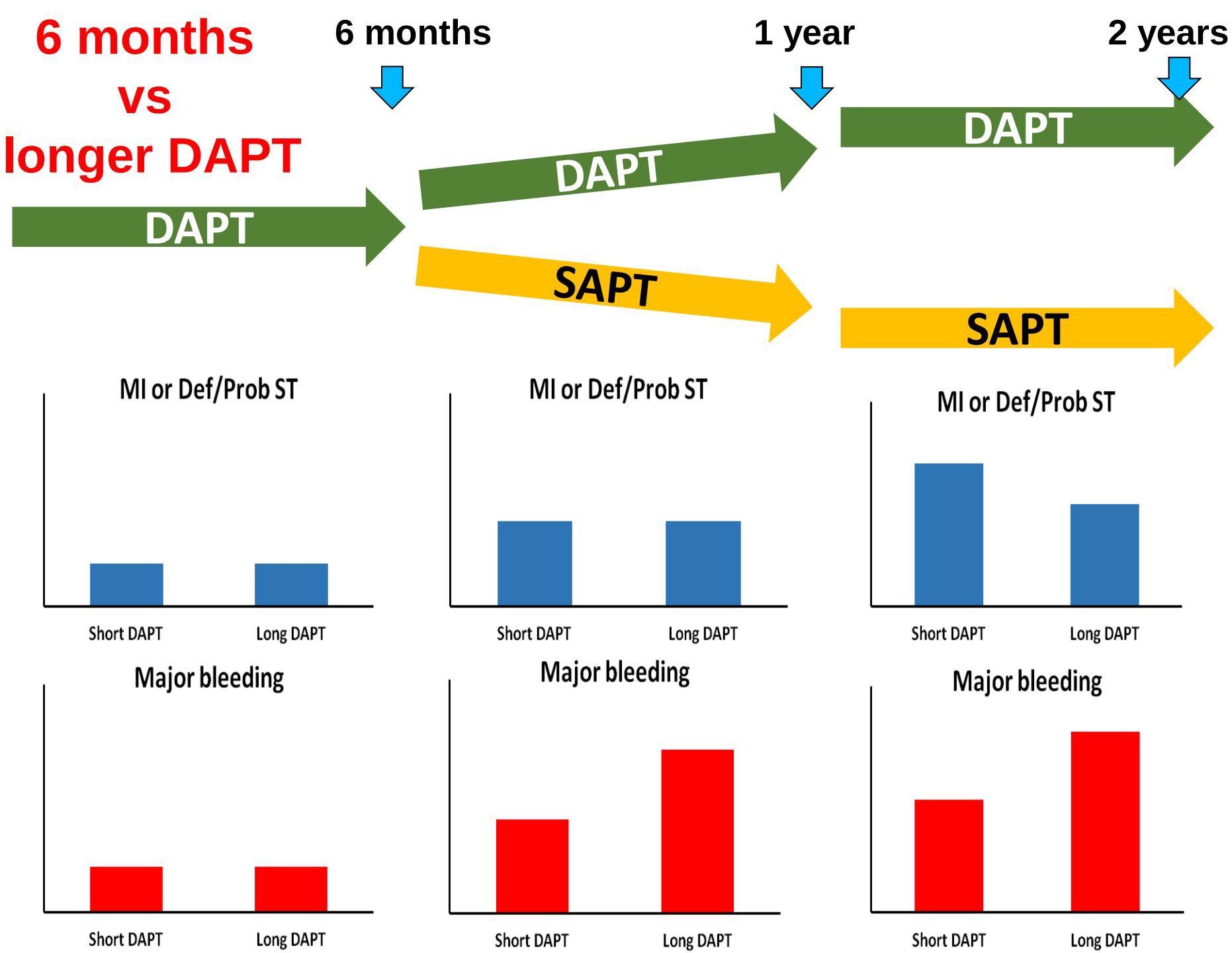

# Major bleeding




# MI and bleeding

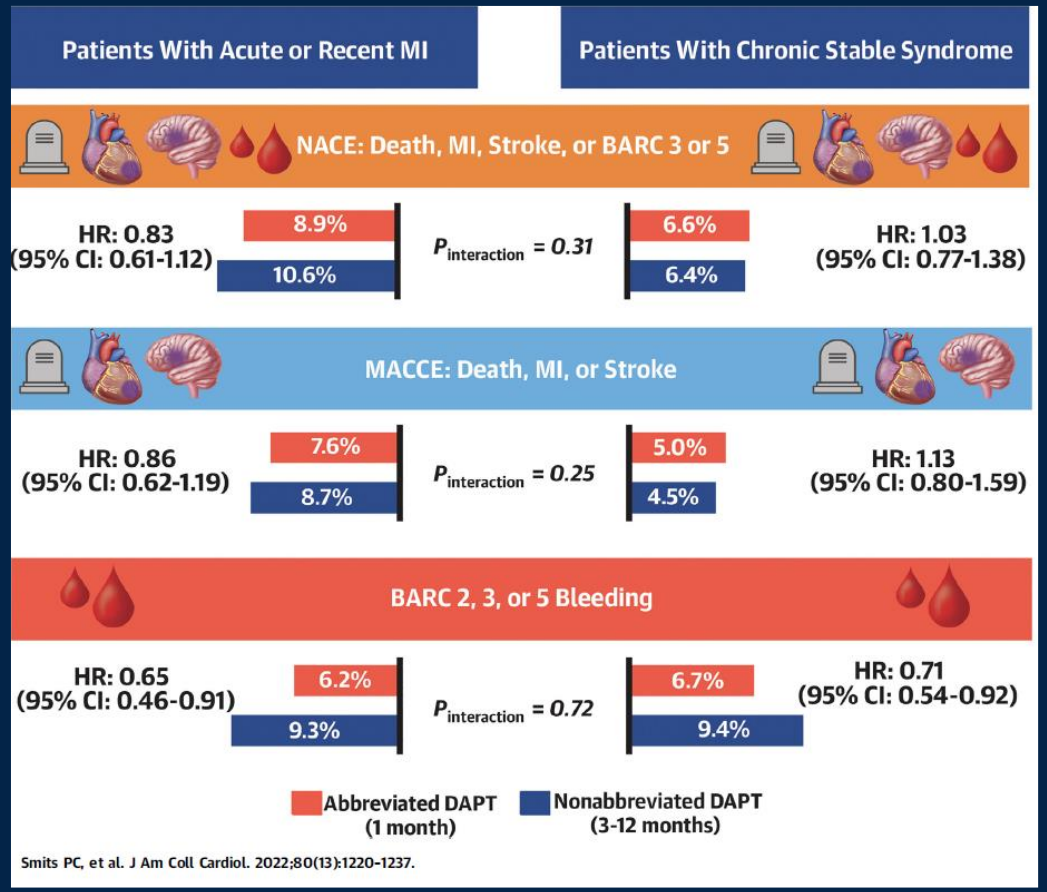



*Palmerini et al; Circ Cv Int 2019*

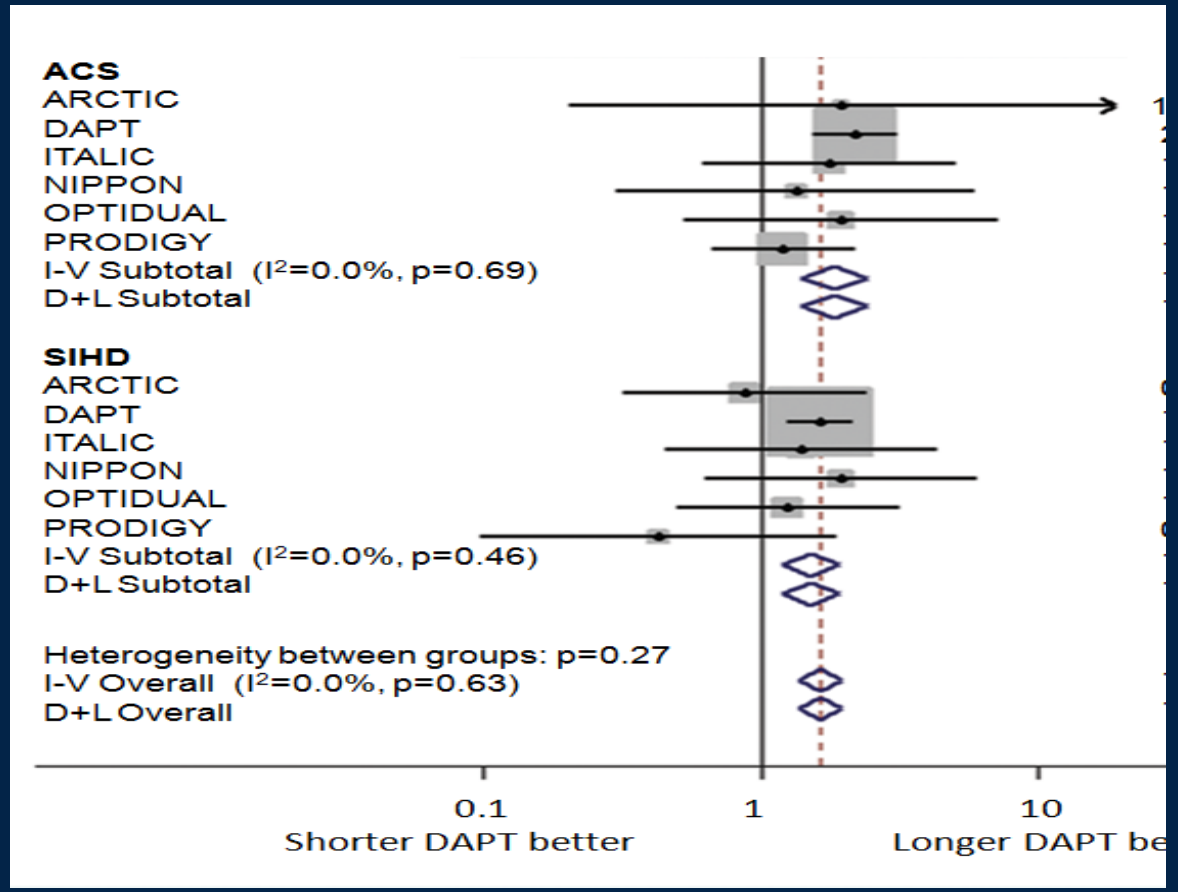

6 months
vs
longer DAPT
6 months
1 year
2 years
DAPT
DAPT
DAPT
SAPT
SAPT
MI or Def/Prob ST
Short DAPT
Long DAPT
MI or Def/Prob ST
Short DAPT
Long DAPT
MI or Def/Prob ST
Short DAPT
Long DAPT
Major bleeding
Short DAPT
Long DAPT
Major bleeding
Short DAPT
Long DAPT
Major bleeding
Short DAPT
Long DAPT

# Conclusions

## HBR: 1 month DAPT




## HIR: >1year DAPT




*Palmerini et al; Circ Cv Int 2019*

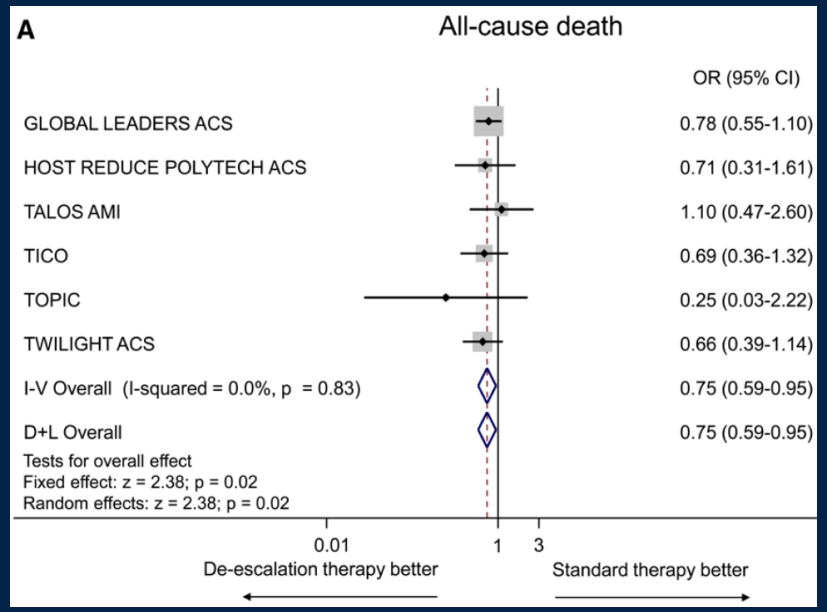
# 1-year DAPT with new strategies

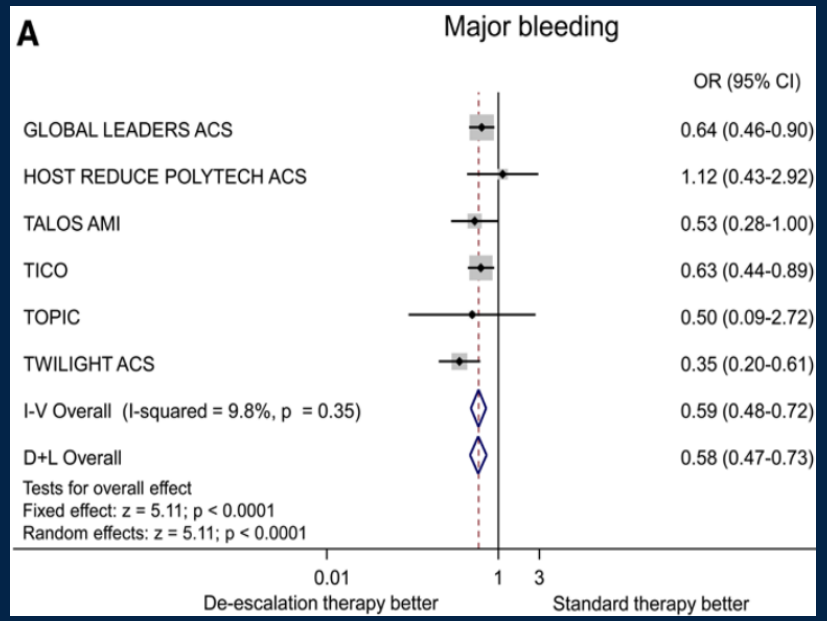
ORIGINAL ARTICLE

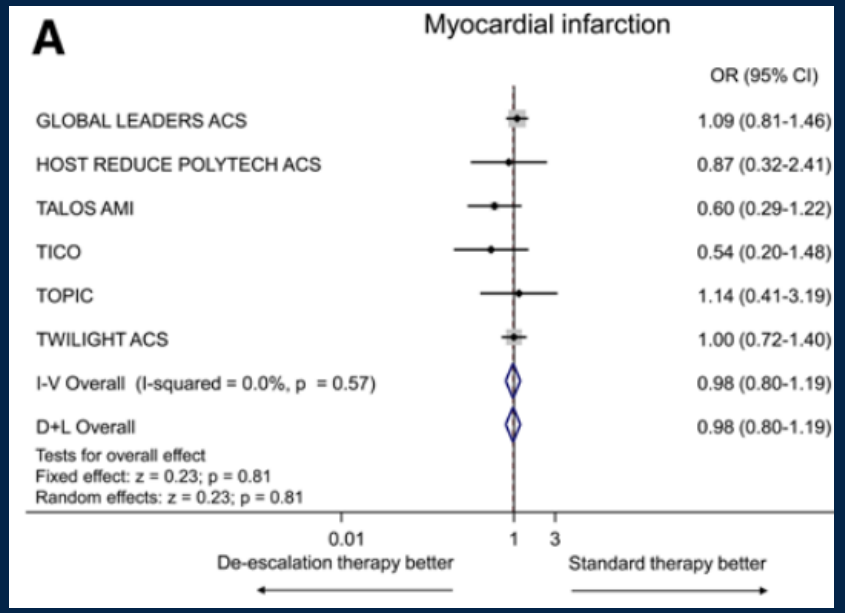
## Reduced Mortality With Antiplatelet Therapy Deescalation After Percutaneous Coronary Intervention in Acute Coronary Syndromes: A Meta-Analysis

**Pairwise aggregate data meta-analysis**
**6 RCTs with 20,837 patients**
**Only ACS**
**Potent standard DAPT vs de-escalation**

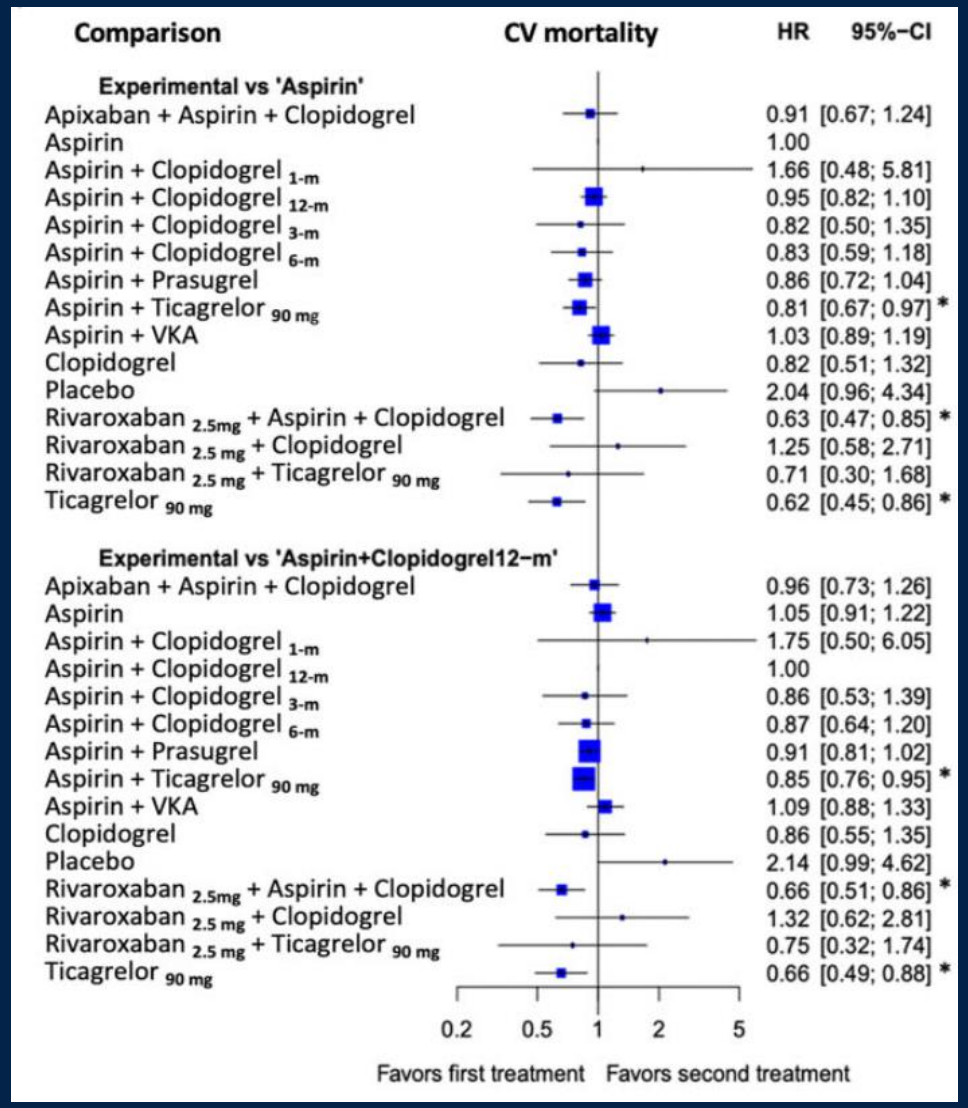
***Palmerini et al; Circ Cv Int 2022***

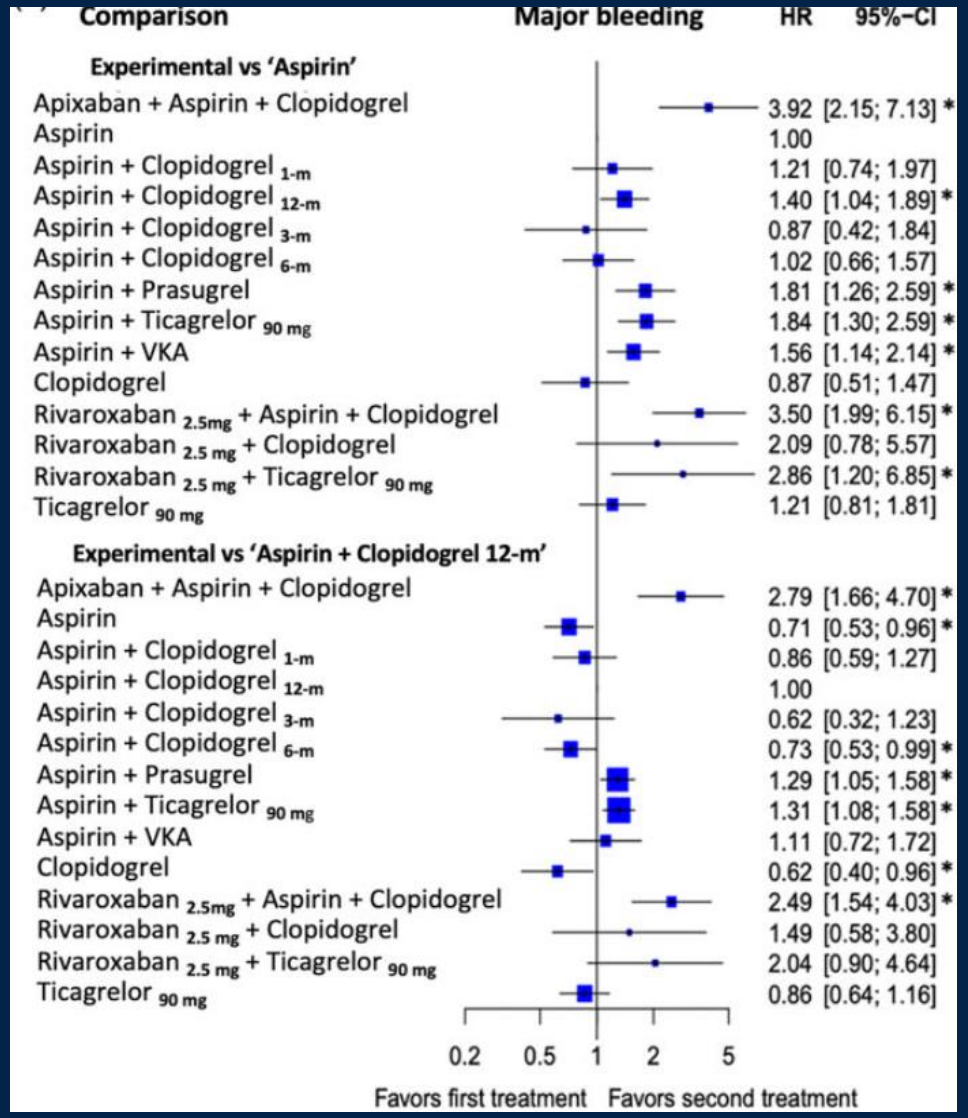


# NMA with 43 trials and 189,261 patients




*Navarese et al; EHJ Pharmacotherapy 2023*

# Conclusions

- A brief period of potent DAPT followed by ticagrelor monotherapy up to 1 year may provide the best safety and efficacy profile in patients with acute coronary syndromes