What is the Optimal Duration of DAPT after PCI/DES?

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Disclosures

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- Daiichi-Sankyo - Merck
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- Medtronic - Boston Scientific
- Biomet - CSI

Consulting/Advisory Boards

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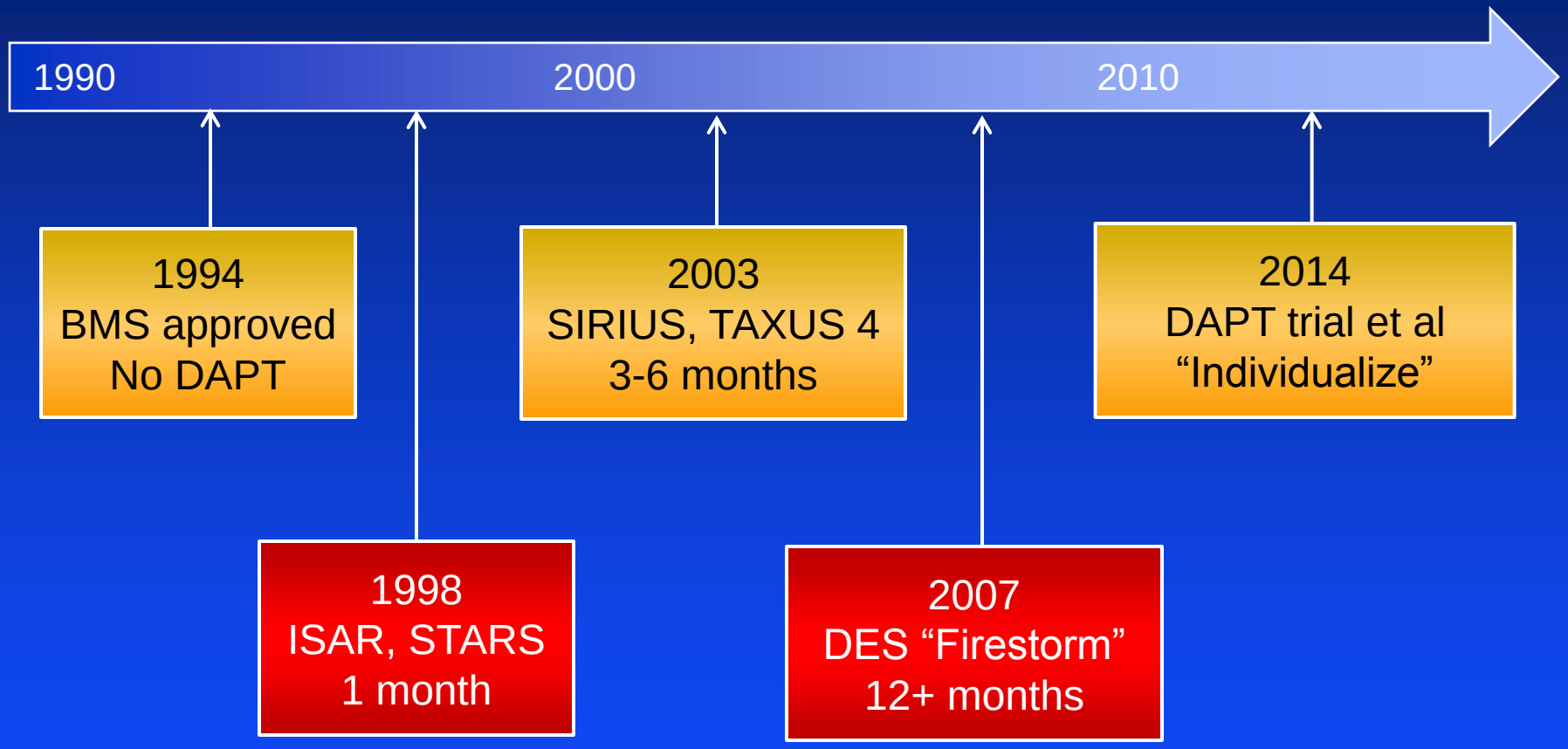
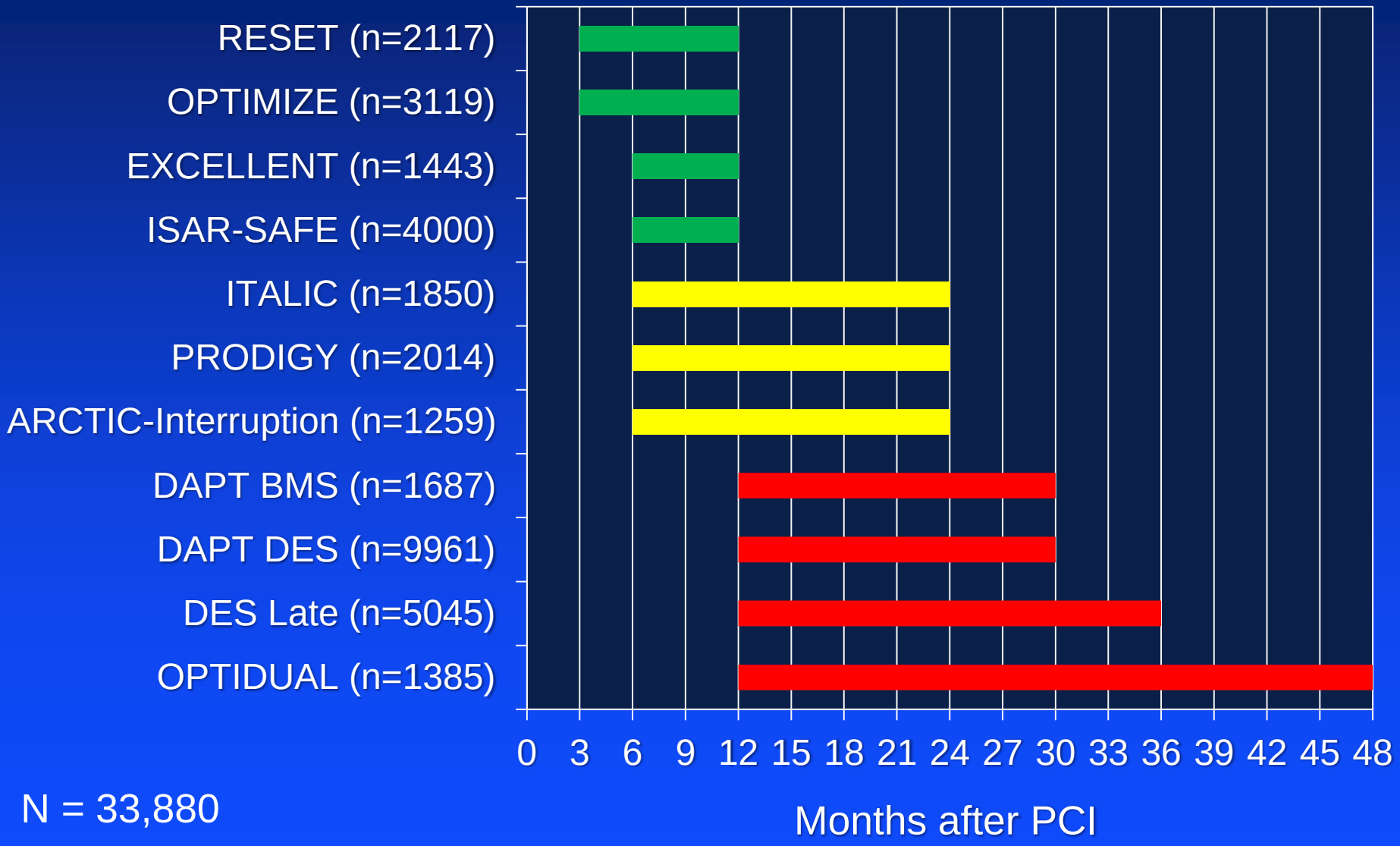
- Edwards Lifesciences - Cardinal Health

History of DAPT after PCI/Stenting

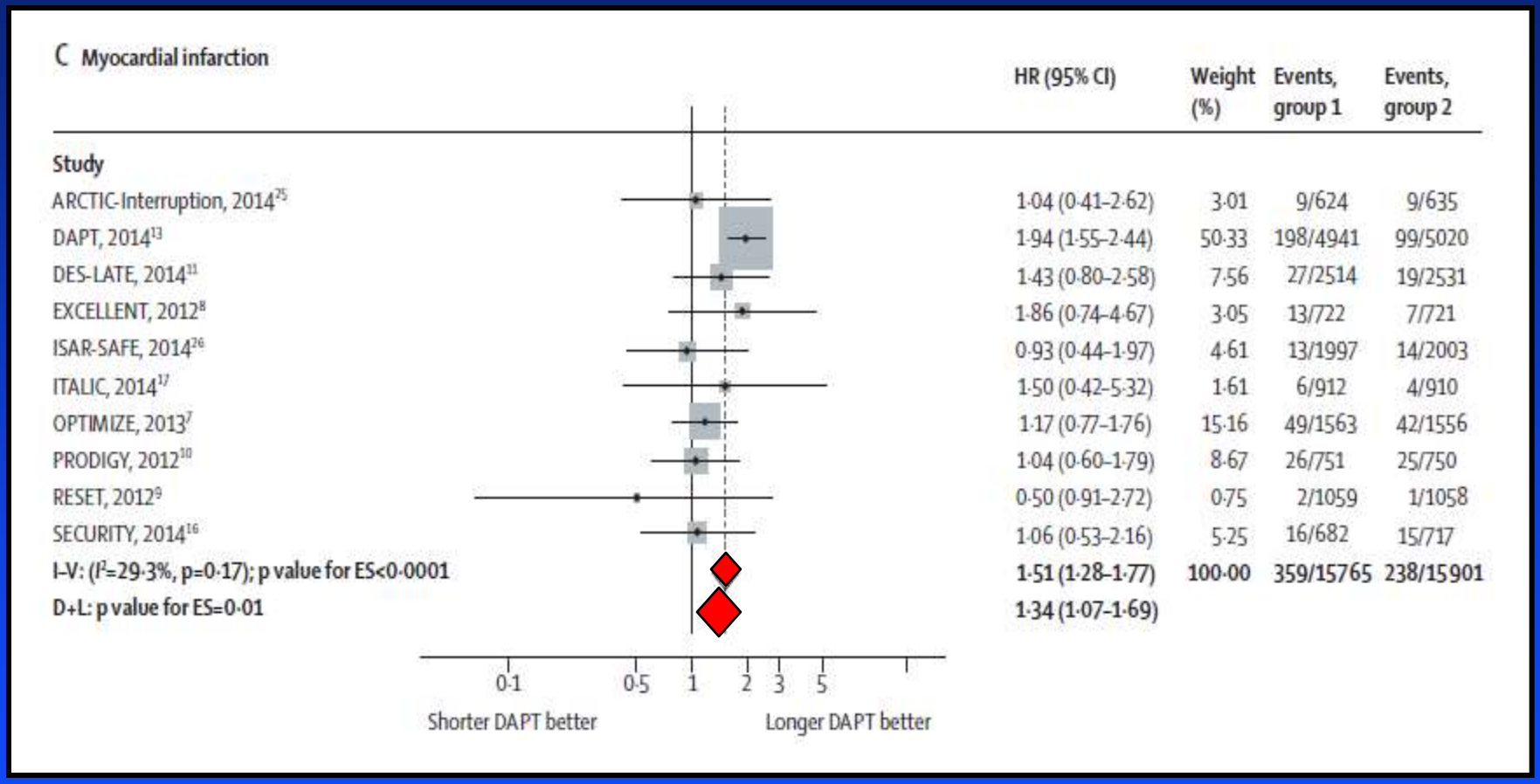


11 RCTs of DAPT Duration after Stenting



N = 33,880

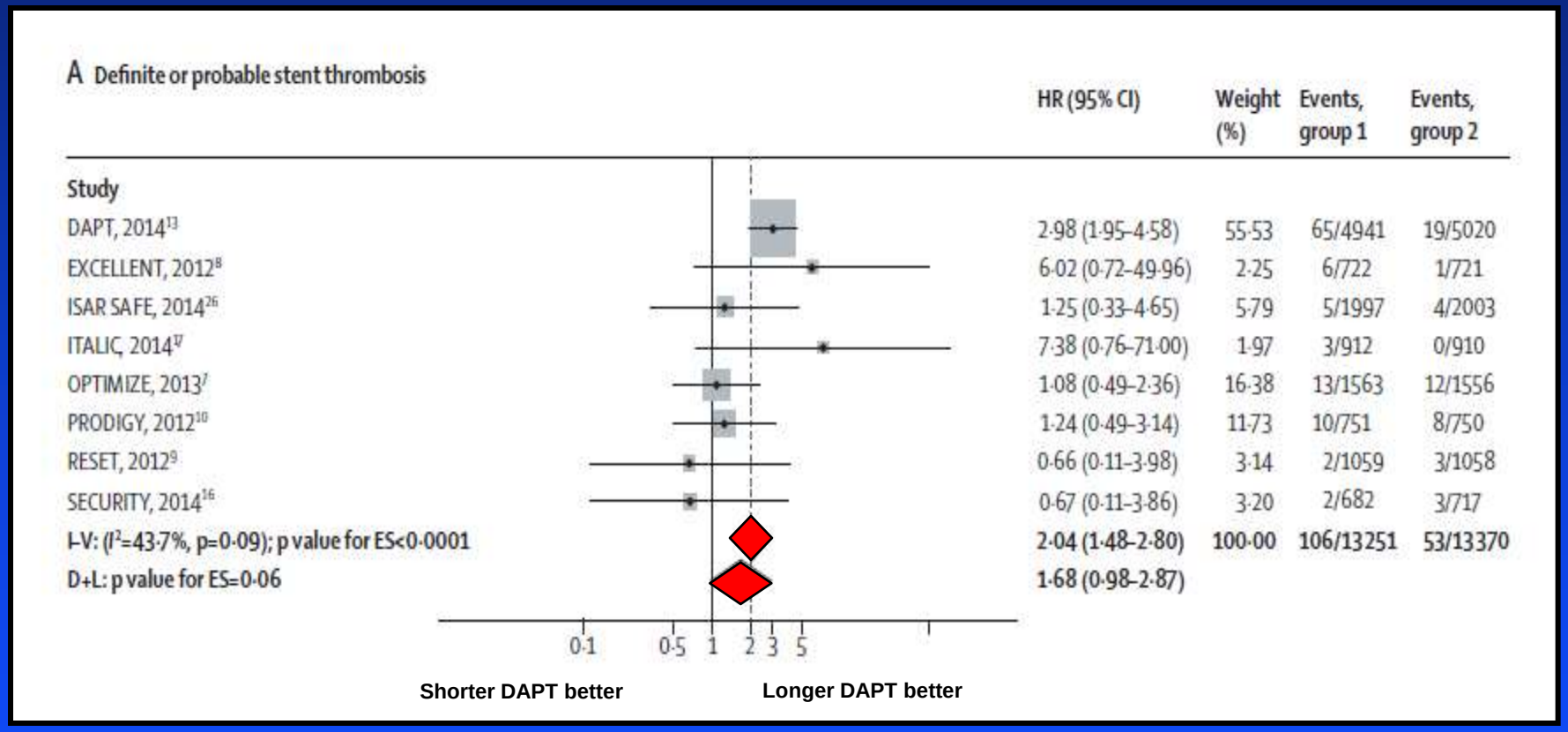
Long vs. Short DAPT: AMI



* Network meta-analysis of 10 RCTs of DAPT duration

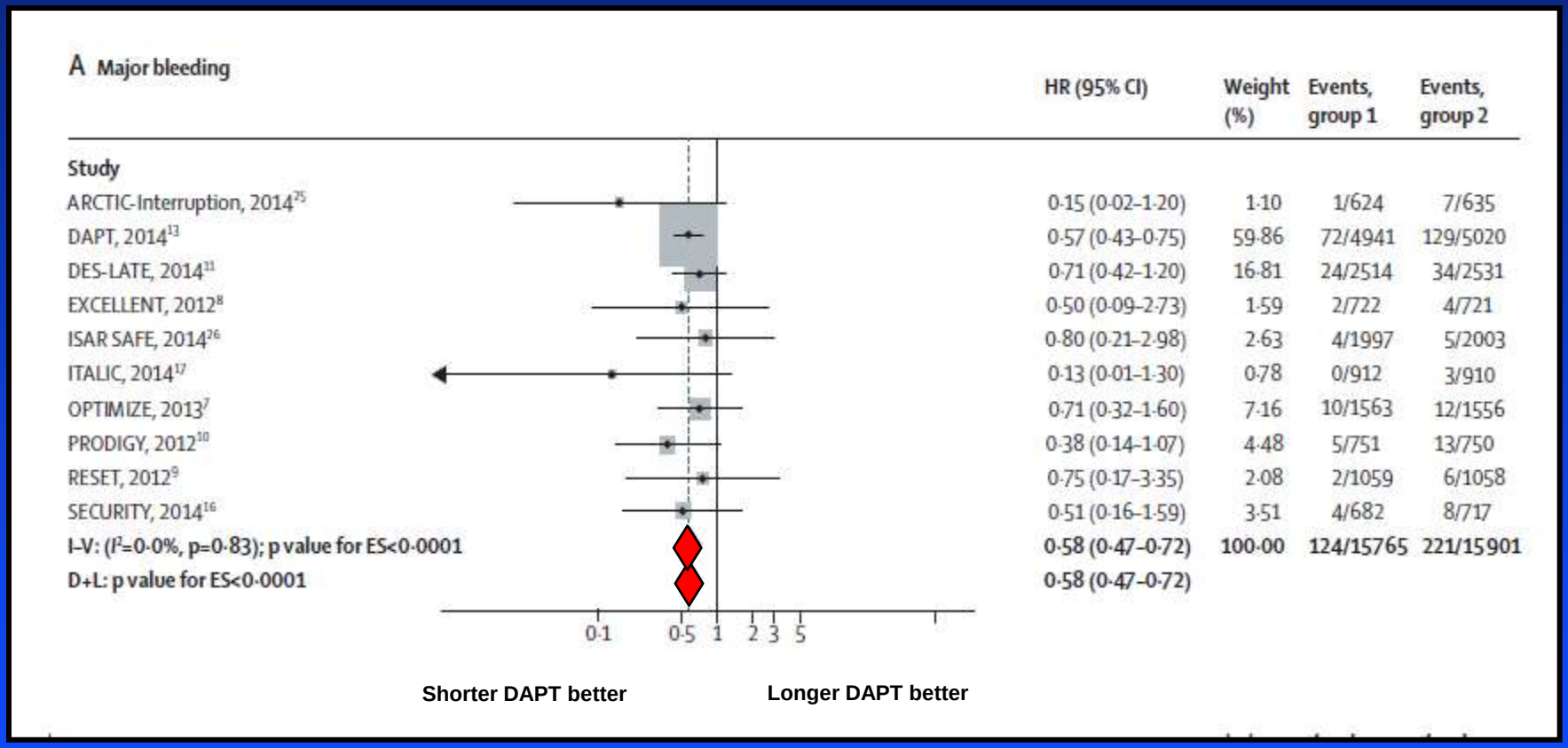
Palmerini T, et al. Lancet 2015;385:2371-82

Long vs. Short DAPT: Stent Thrombosis



Palmerini T, et al. Lancet 2015;385:2371-82

Long vs. Short DAPT: Major Bleeding



Palmerini T, et al. Lancet 2015;385:2371-82

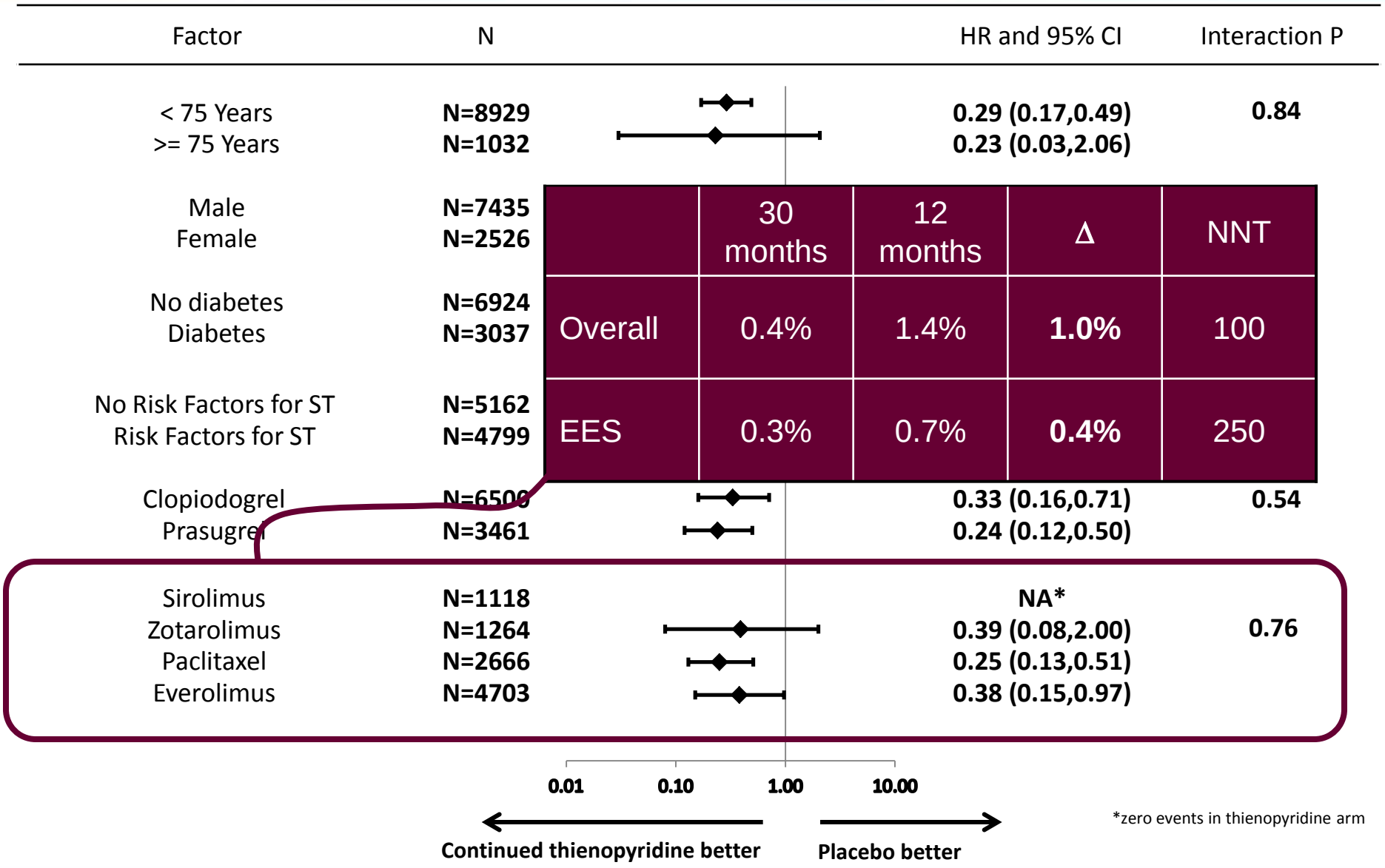
DAPT Duration Issues

- Does type of stent matter?
- Is 30 months “enough”?
- Based on the available data, how should we individualize care?

DAPT Trial Issues

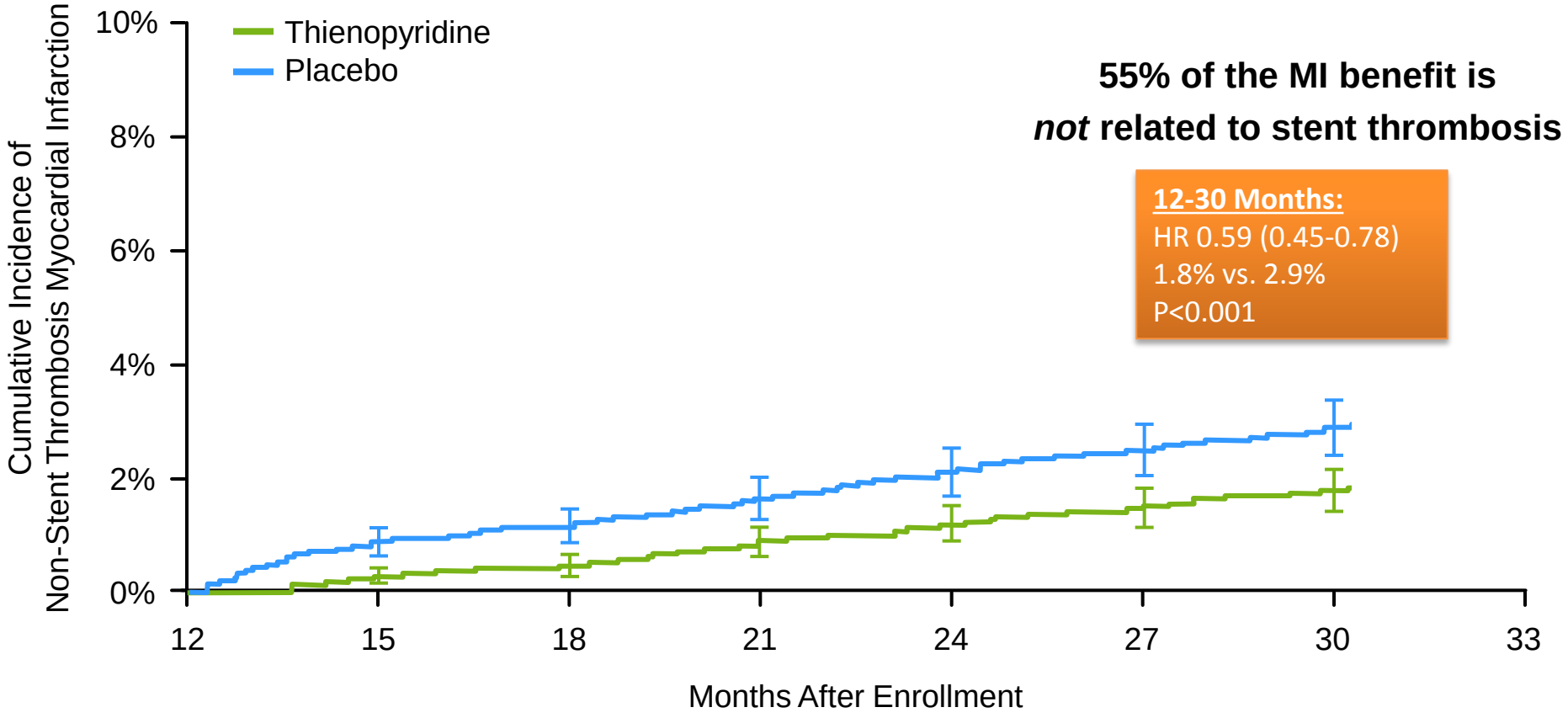
- Does type of stent matter?
- Is 30 months “enough”?
- Based on the DAPT results, how should we individualize care?

Consistency of Treatment Effect Stent Thrombosis (12-30 Months)



	30 months	12 months	Δ	NNT
Overall	0.4%	1.4%	**1.0%**	100
EES	0.3%	0.7%	**0.4%**	250

Non-Stent Thrombosis Myocardial Infarction



55% of the MI benefit is *not* related to stent thrombosis

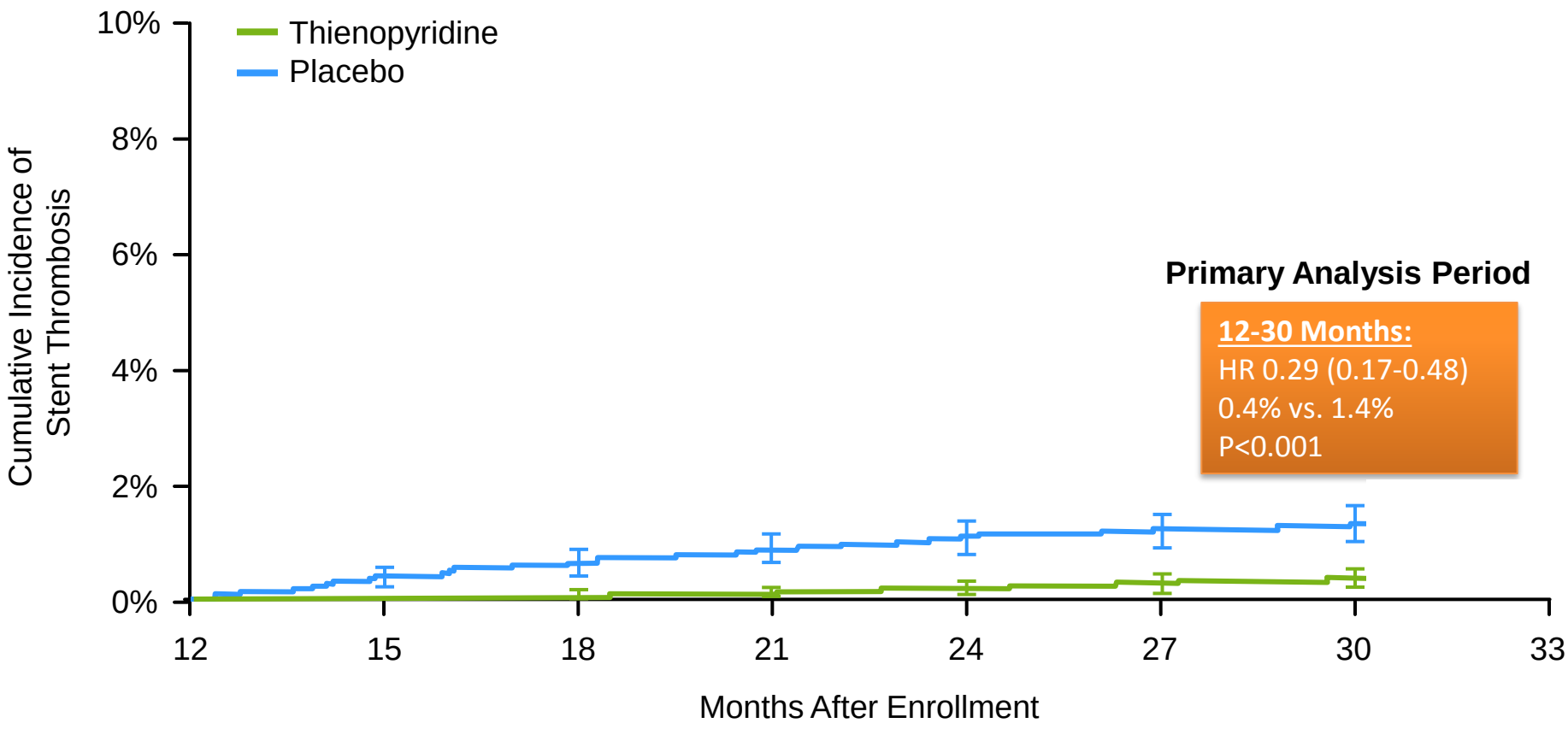
12-30 Months:
HR 0.59 (0.45-0.78)
1.8% vs. 2.9%
P<0.001

# At Risk								
Thienopyridine	5020	4920	4851	4792	4721	4641	4588	3066
Placebo	4941	4820	4751	4686	4607	4547	4491	3052

DAPT Trial Issues

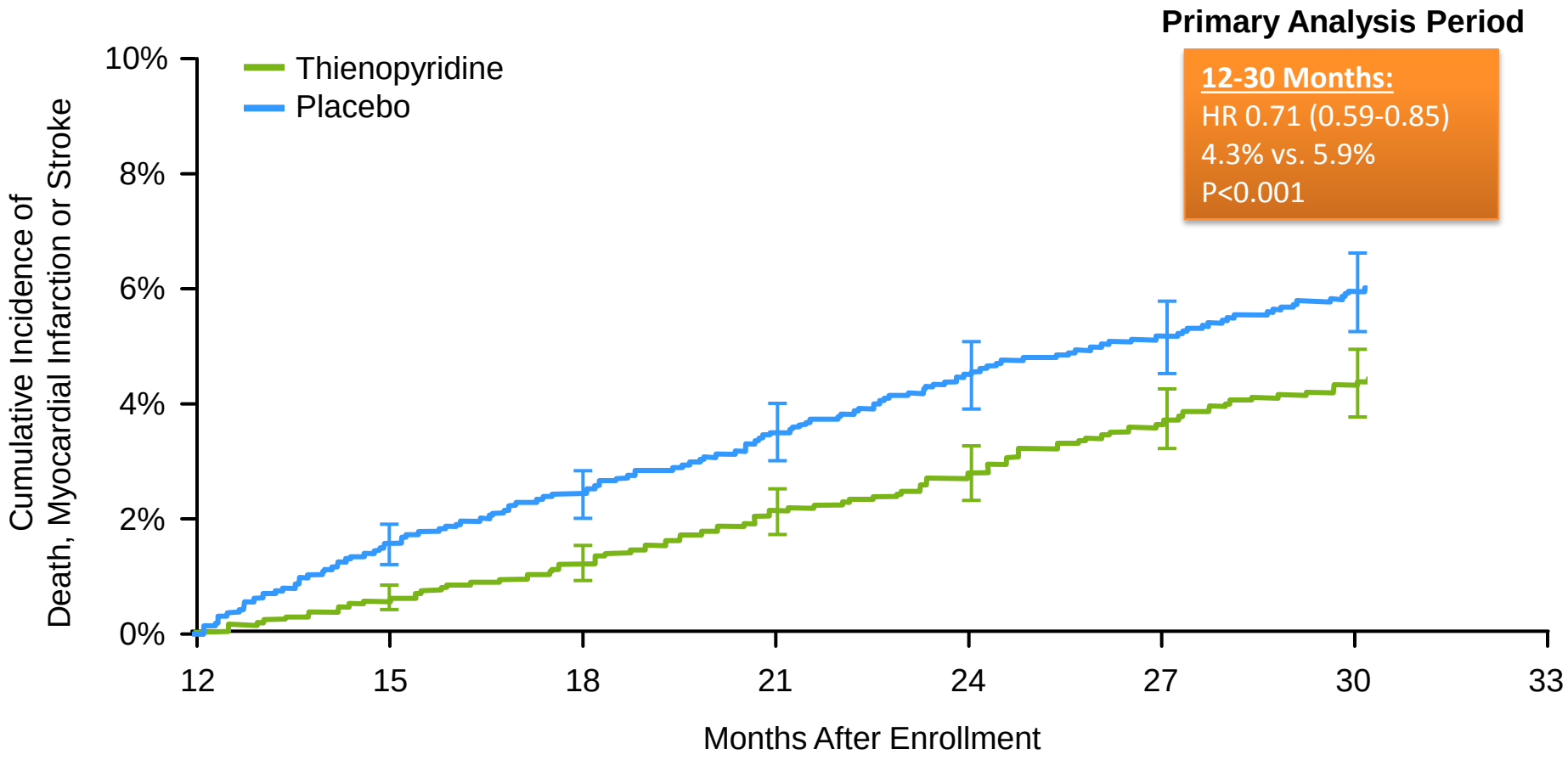
- Does type of stent matter?
- Is 30 months “enough”?
- Based on the DAPT results, how should we individualize care?

Co-Primary Effectiveness End Point
Stent Thrombosis



# At Risk								
Thienopyridine	5020	4934	4870	4828	4765	4686	4642	3110
Placebo	4941	4845	4775	4721	4651	4603	4556	3105

Co-Primary Effectiveness End Point MACCE

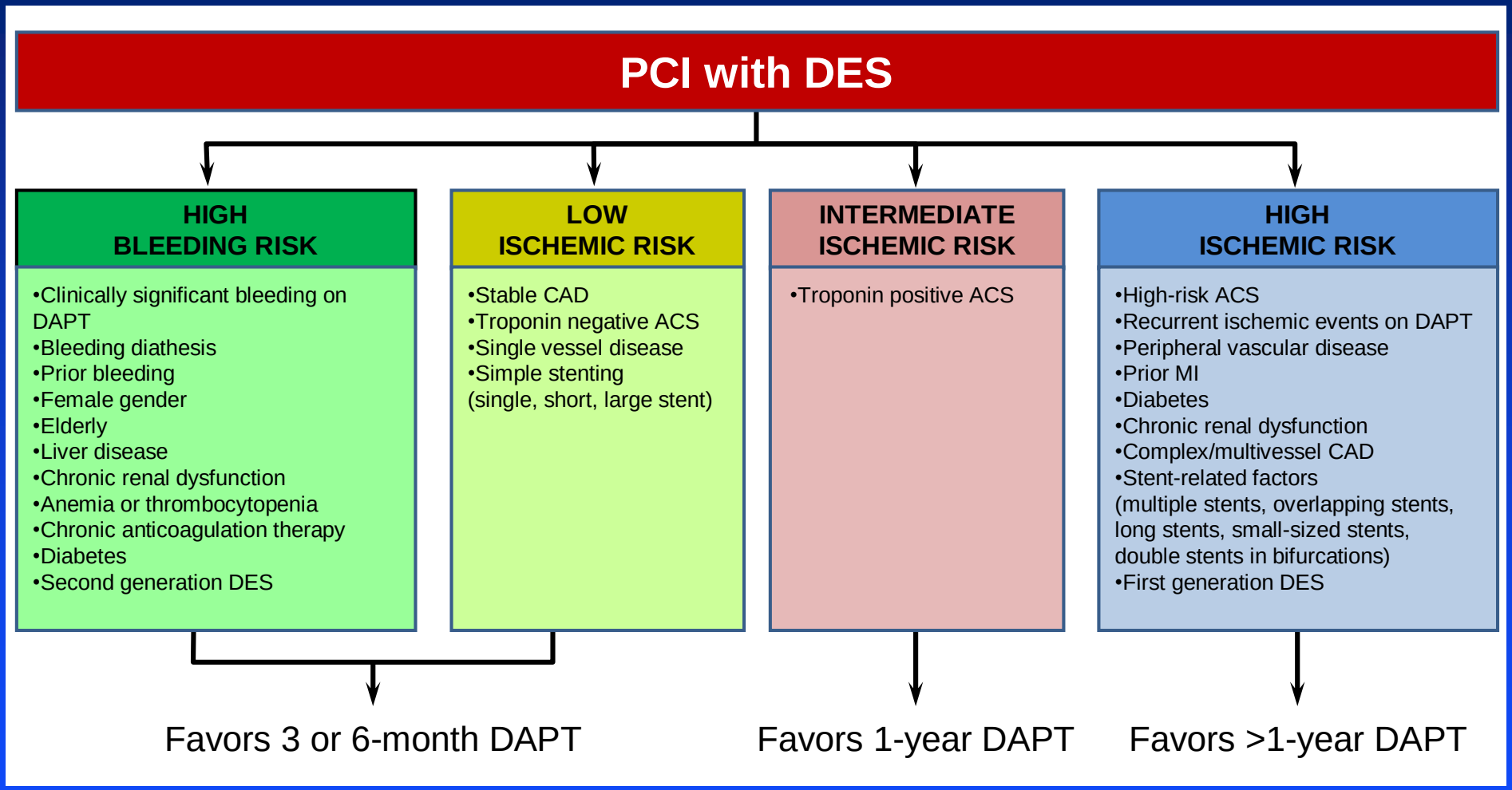


# At Risk								
Thienopyridine	5020	4917	4840	4778	4702	4611	4554	3029
Placebo	4941	4799	4715	4635	4542	4476	4412	2997

DAPT Trial Issues

- Does type of stent matter?
- Is 30 months “enough”?
- Based on the available data, how should we individualize care?

DAPT Duration: How do we Decide?

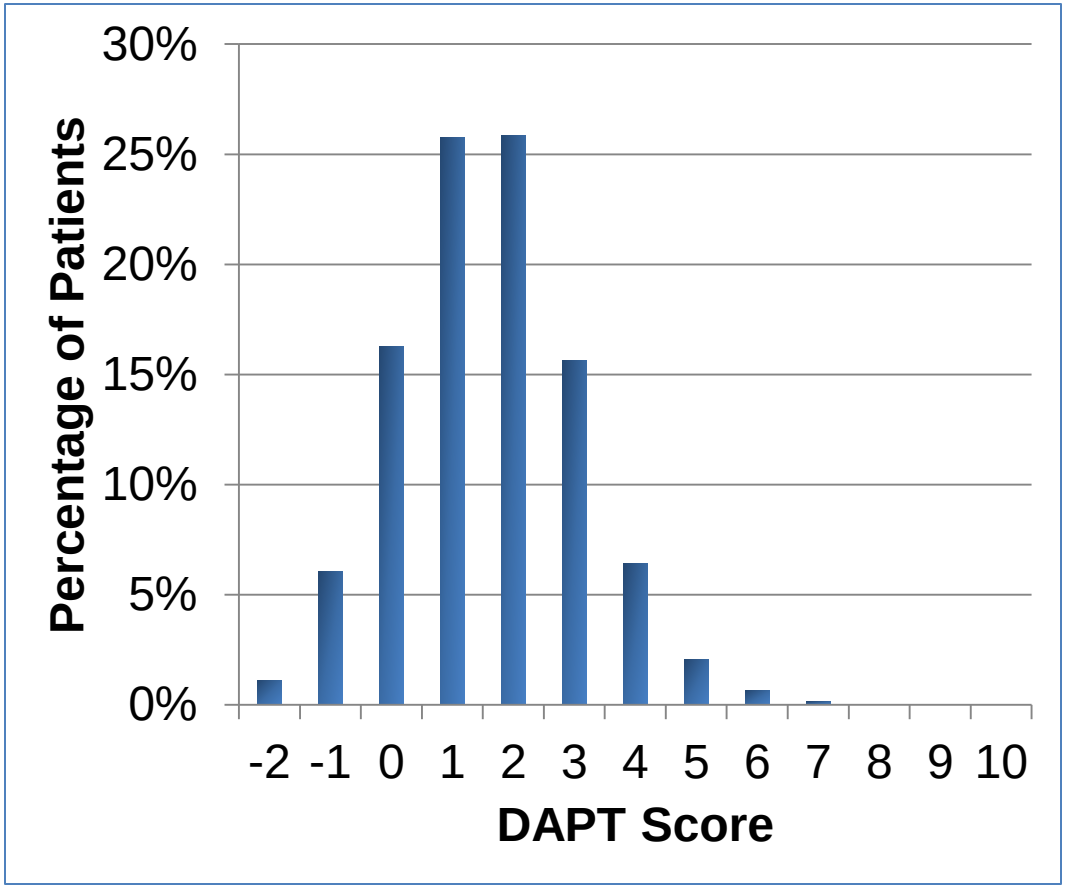


Palmerini T and Stone GW. EHJ 2016;37:353-64

The DAPT Score

Variable	Points
Patient Characteristic	
Age	
≥ 75	-2
65 - <75	-1
< 65	0
Diabetes Mellitus	1
Current Cigarette Smoker	1
Prior PCI or Prior MI	1
CHF or LVEF < 30%	2
Index Procedure Characteristic	
MI at Presentation	1
Vein Graft PCI	2
Stent Diameter < 3mm	1

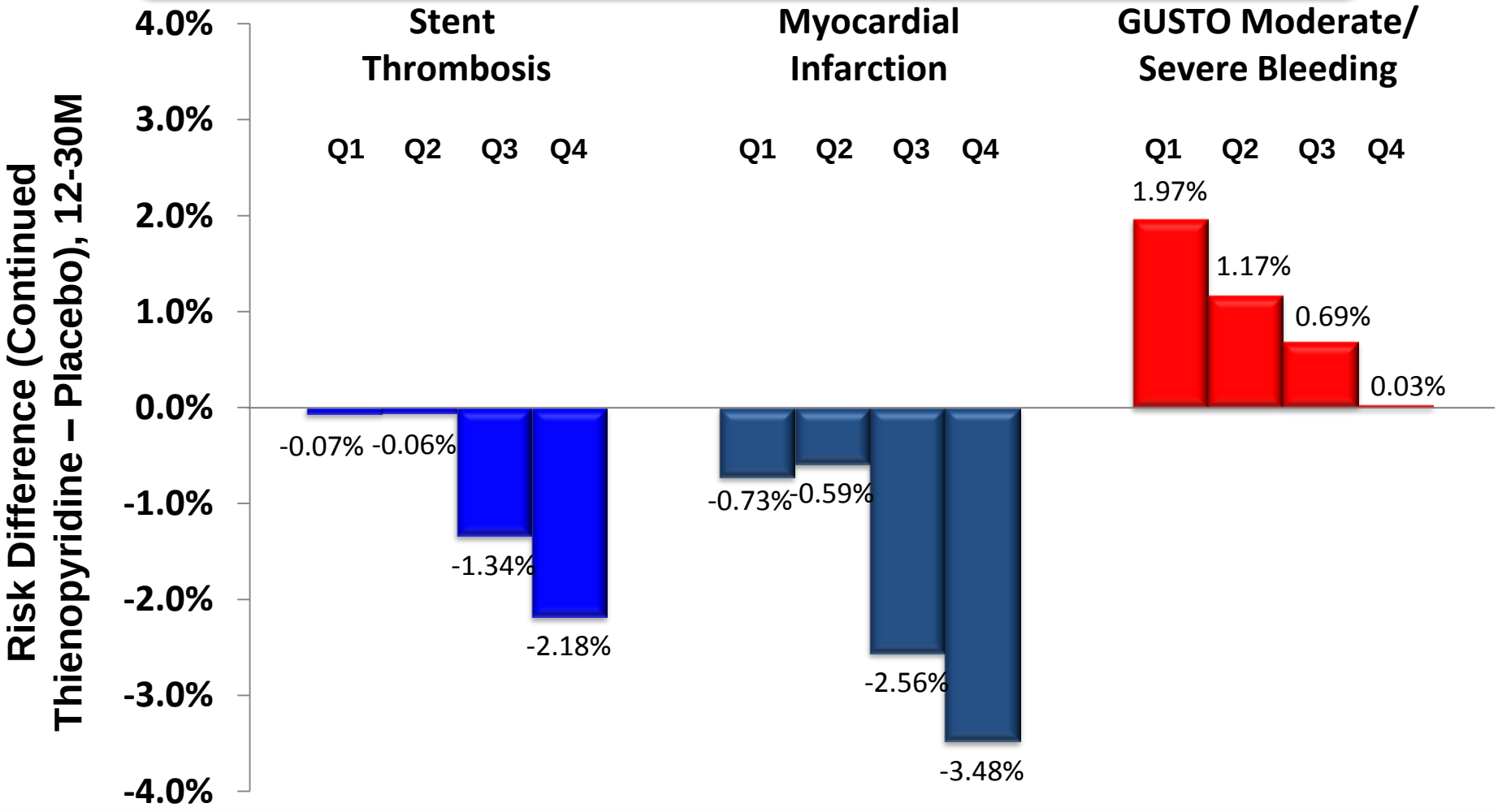
Distribution of DAPT Scores among all randomized subjects in the DAPT Study



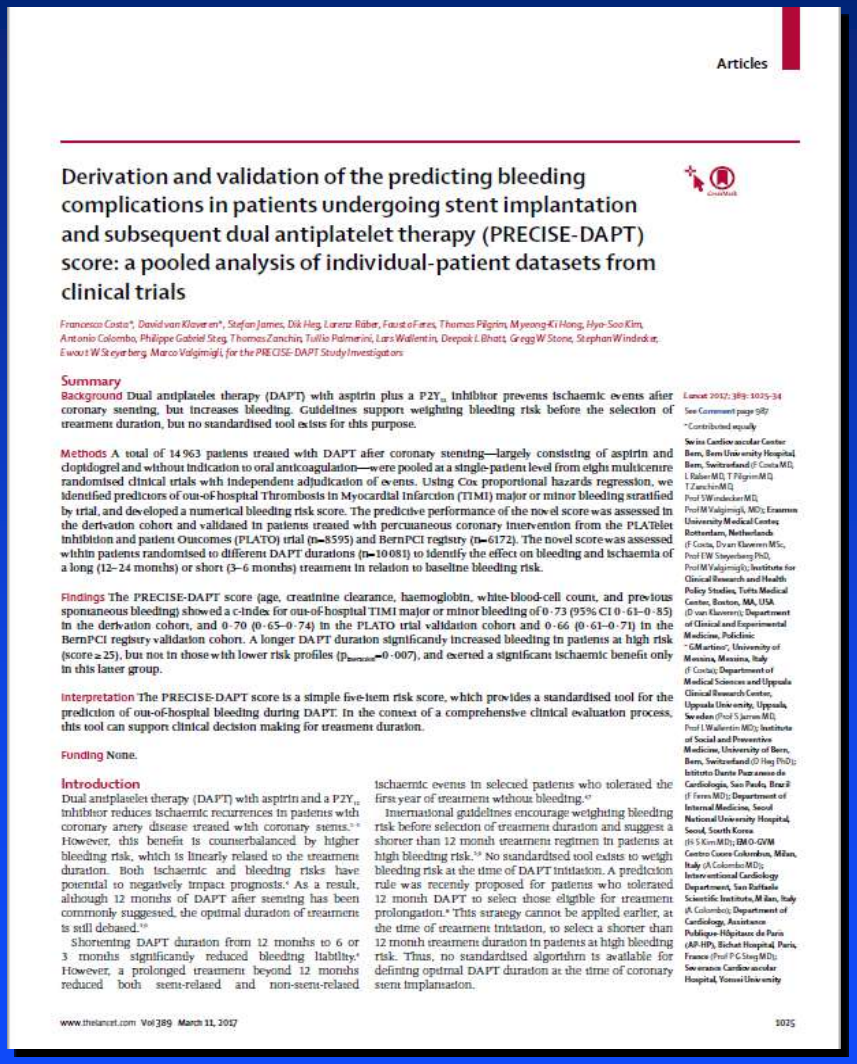
Continued Thienopyridine vs. PlaceboTreatment Effect by DAPT Score Quartile (N = 11,648)

DAPT STUDY

Q1 = DAPT Score -2 to 0
Q2 = DAPT Score 1
Q3 = DAPT Score 2
Q4 = DAPT Score > 2



PRECISE Risk Score



Articles

Derivation and validation of the predicting bleeding complications in patients undergoing stent implantation and subsequent dual antiplatelet therapy (PRECISE-DAPT) score: a pooled analysis of individual-patient datasets from clinical trials

Francesca Costa*, David van Klaveren*, Stefan James, Dik Heg, Lorenz Räber, Faisal Feres, Thomas Pilgrim, Myeong-Ki Hong, Hyo-Soo Kim, Antonio Colombo, Philippe Gabriel Steg, Thomas Zanchin, Tullio Palmerini, Lars Wallentin, Deepak L Bhatt, Gregg W Stone, Stephan Windecker, Ewout W Steyerberg, Marco Valgimigli, for the PRECISE-DAPT Study Investigators

Summary

Background Dual antiplatelet therapy (DAPT) with aspirin plus a $P2Y_{12}$ inhibitor prevents ischaemic events after coronary stenting, but increases bleeding. Guidelines support weighing bleeding risk before the selection of treatment duration, but no standardised tool exists for this purpose.

Methods A total of 14 963 patients treated with DAPT after coronary stenting—largely consisting of aspirin and clopidogrel and without indication to oral anticoagulation—were pooled at a single-patient level from eight multicentre randomised clinical trials with independent adjudication of events. Using Cox proportional hazards regression, we identified predictors of out-of-hospital Thrombosis in Myocardial Infarction (TIMI) major or minor bleeding stratified by trial, and developed a numerical bleeding risk score. The predictive performance of the novel score was assessed in the derivation cohort and validated in patients treated with percutaneous coronary intervention from the PLATelet inhibition and patient Outcomes (PLATO) trial (n=8595) and BernPCI registry (n=6172). The novel score was assessed within patients randomised to different DAPT durations (n=10 081) to identify the effect on bleeding and ischaemia of a long (12–24 months) or short (3–6 months) treatment in relation to baseline bleeding risk.

Findings The PRECISE-DAPT score (age, creatinine clearance, haemoglobin, white-blood-cell count, and previous spontaneous bleeding) showed a c-index for out-of-hospital TIMI major or minor bleeding of 0·73 (95% CI 0·61–0·85) in the derivation cohort, and 0·70 (0·65–0·74) in the PLATO trial validation cohort and 0·66 (0·61–0·71) in the BernPCI registry validation cohort. A longer DAPT duration significantly increased bleeding in patients at high risk (score ≥ 25), but not in those with lower risk profiles ($p_{interaction}$=0·007), and exerted a significant ischaemic benefit only in this latter group.

Interpretation The PRECISE-DAPT score is a simple five-item risk score, which provides a standardised tool for the prediction of out-of-hospital bleeding during DAPT. In the context of a comprehensive clinical evaluation process, this tool can support clinical decision making for treatment duration.

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See Comment page 987

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Introduction

Dual antiplatelet therapy (DAPT) with aspirin and a $P2Y_{12}$ inhibitor reduces ischaemic recurrences in patients with coronary artery disease treated with coronary stents.[1–3] However, this benefit is counterbalanced by higher bleeding risk, which is linearly related to the treatment duration. Both ischaemic and bleeding risks have potential to negatively impact prognosis.[4] As a result, although 12 months of DAPT after stenting has been commonly suggested, the optimal duration of treatment is still debated.[5,6]

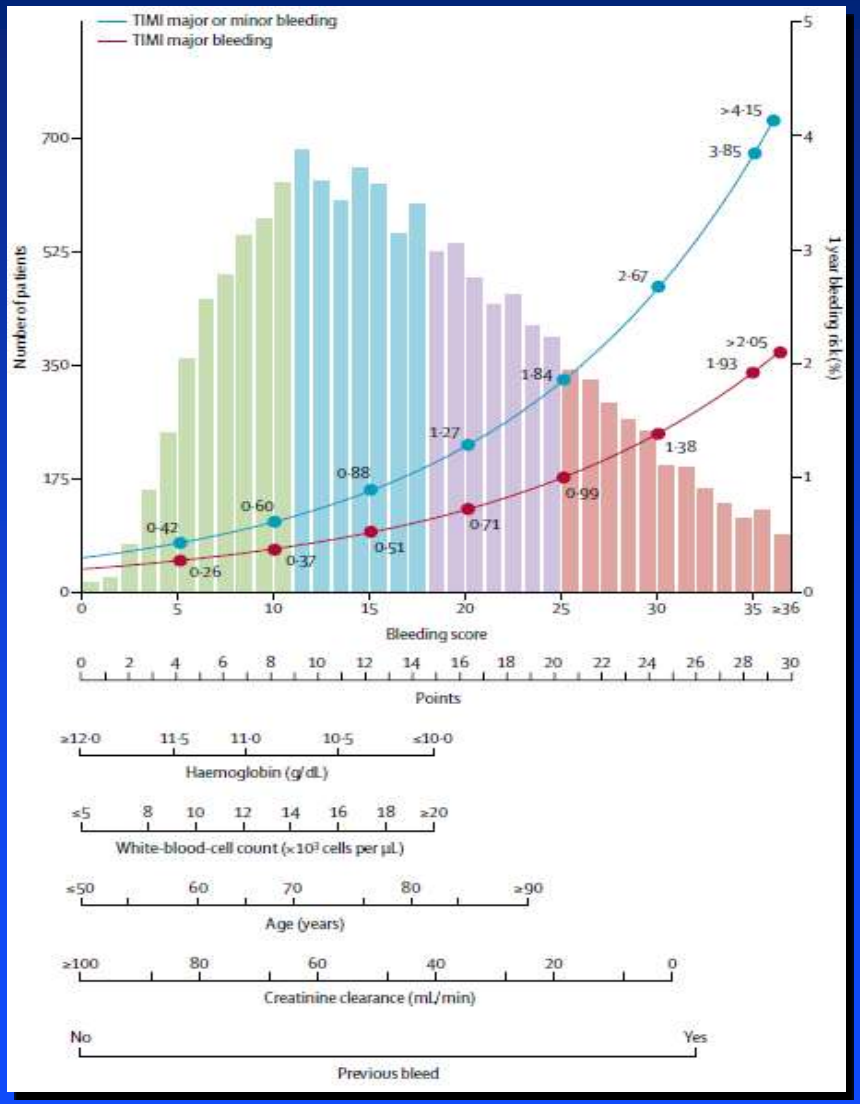
Shortening DAPT duration from 12 months to 6 or 3 months significantly reduced bleeding liability.[4] However, a prolonged treatment beyond 12 months reduced both stent-related and non-stent-related ischaemic events in selected patients who tolerated the first year of treatment without bleeding.[4,7]

International guidelines encourage weighing bleeding risk before selection of treatment duration and suggest a shorter than 12 month treatment regimen in patients at high bleeding risk.[5,8] No standardised tool exists to weigh bleeding risk at the time of DAPT initiation. A prediction rule was recently proposed for patients who tolerated 12 month DAPT to select those eligible for treatment prolongation.[9] This strategy cannot be applied earlier, at the time of treatment initiation, to select a shorter than 12 month treatment duration in patients at high bleeding risk. Thus, no standardised algorithm is available for defining optimal DAPT duration at the time of coronary stent implantation.

- Risk score to predict 1-year major bleeding on DAPT
- Developed using pooled data from 8 multicenter RCTs of varying DAPT duration
- Bleeding endpoint = TIMI major or minor bleeding between 7 days and 1 year after PCI
- Score based on patient characteristics available at time of index PCI procedure

Costa F, et al. Lancet 2017;389:1025-34

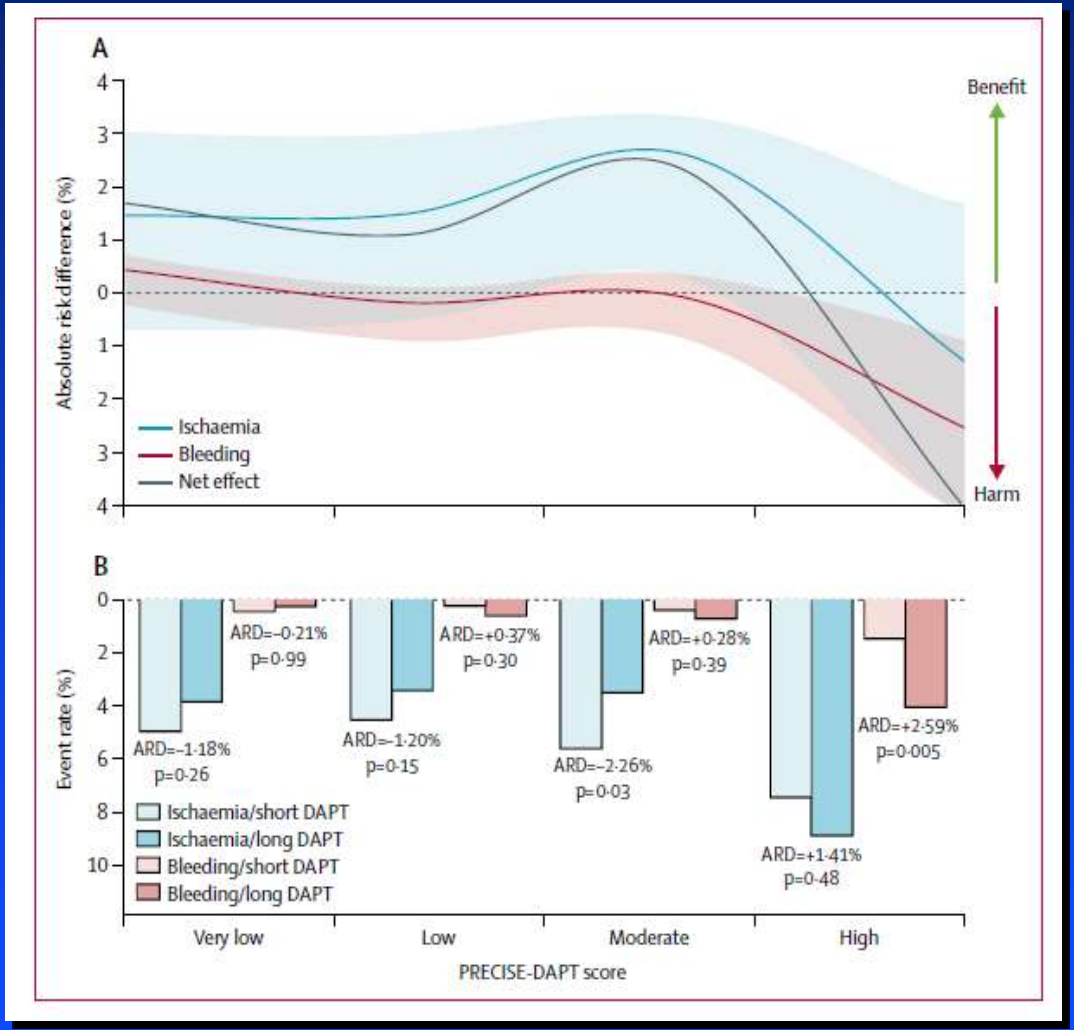
PRECISE Risk Score



- Score (range 0-100) includes 5 independent risk factors
  - *Hemoglobin* -- *WBC*
  - *Age* -- *CrCl*
  - *Prior bleeding*
- Top quartile (score >25) correlates with high risk of bleeding (2-4%/year)
- Available as web-based calculator (http://www.precisedaptscore.com/predapt/webcalculator.html) and phone app

Costa F, et al. Lancet 2017;389:1025-34

PRECISE Risk Score: Net Clinical Benefit



- Net benefit of long DAPT positive in first 3 quartiles and only harmful in top quartile

Risk Quartile	Net Clinical Benefit
1	+ 1.4%
2	+ 0.8%
3	+ 2.0%
4	- 1.2%

Costa F, et al. Lancet 2017;389:1025-34

Conclusions

- For most patients undergoing PCI with current-generation DES, 6-12 months of DAPT represents a reasonable balance between safety and efficacy
- For selected patients at very high risk of bleeding, shorter durations of DAPT (3-6 months) are likely sufficient
- For patients who present with ACS and have additional risk factors for recurrent events, longer term therapy (> 2 years) should be strongly considered as long as bleeding risk is not excessive
- Both the DAPT and PRECISE risk scores appear to be useful tools for identifying patients who should be treated with shorter or longer-term DAPT