

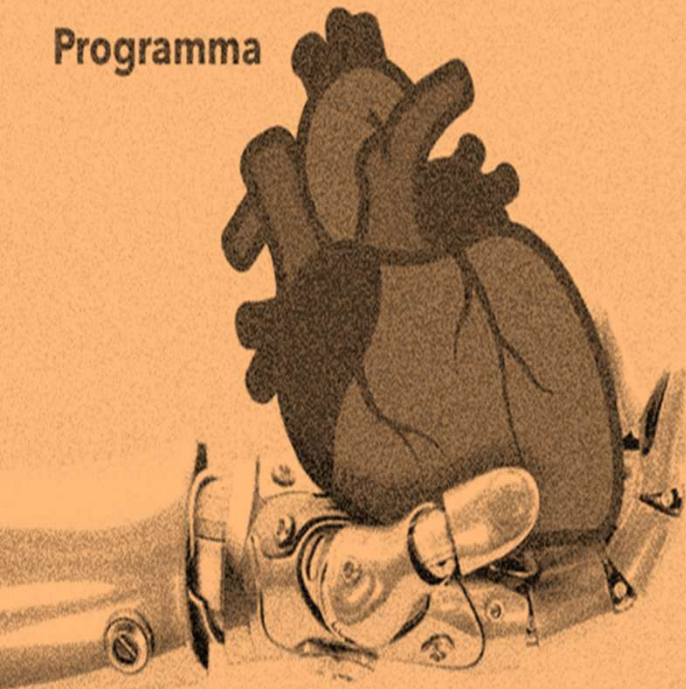
17° Meeting



# CardioLUCCA

Heart Brings Heart 2023

Programma



## Gli inibitori P2Y<sub>12</sub> sono superiori all'aspirina?



**Ugo Limbruno**

*UO Cardiologia, Grosseto*

# Acute

Clopidogrel+ Rivaroxaban  
(ATLAS-ACS)

Short vs Long DAPT  
(n TRIALS)

Clopidogrel  
(CURE)

Ticagrelor  
(PLATO)

Prasugrel  
(TRITON)

# Coronary Syndrome

Clopidogrel  
(CHARISMA)

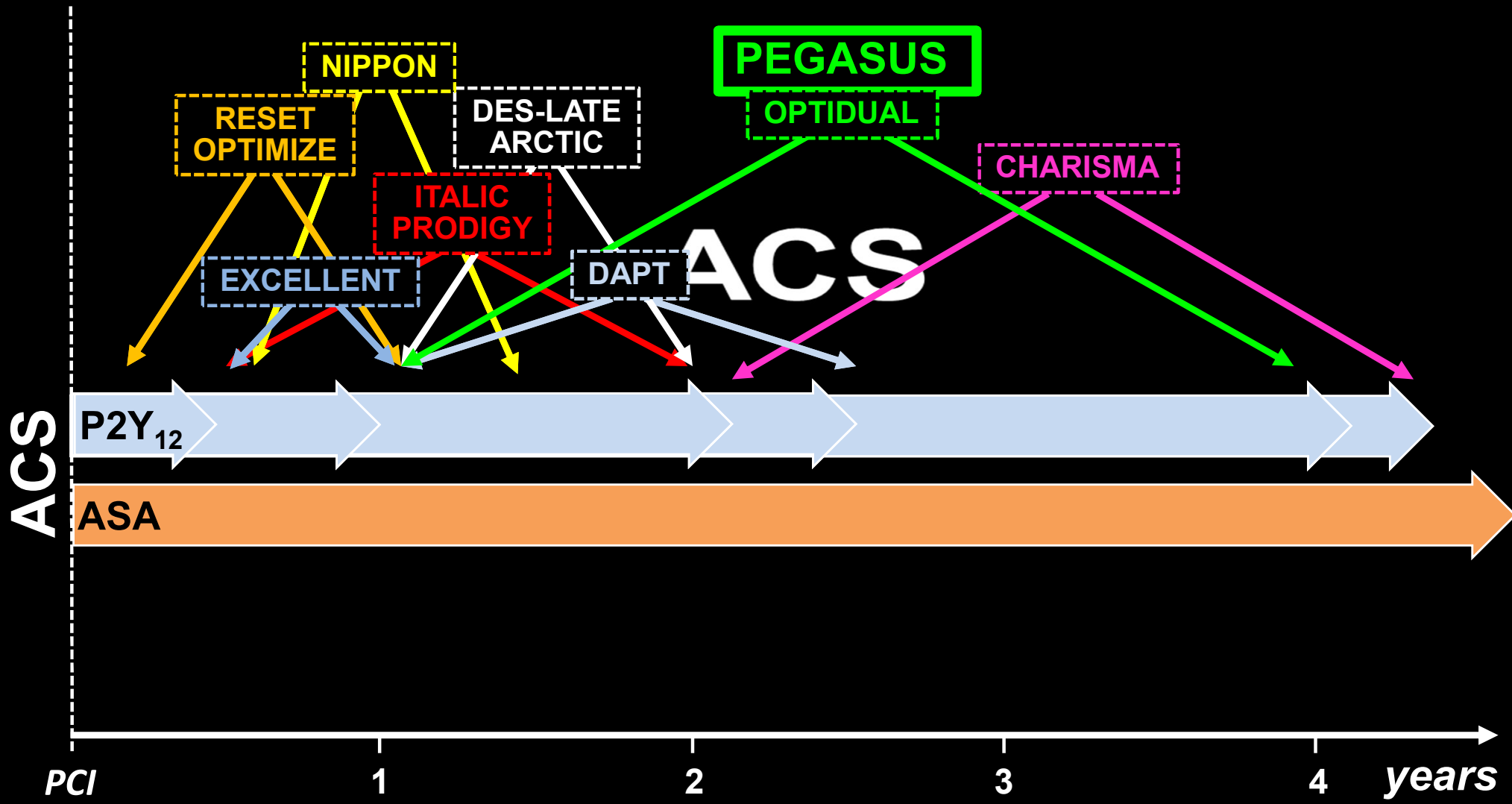
Clopidogrel  
(DAPT trial)

Ticagrelor  
(PEGASUS)

Rivaroxaban  
(COMPASS)

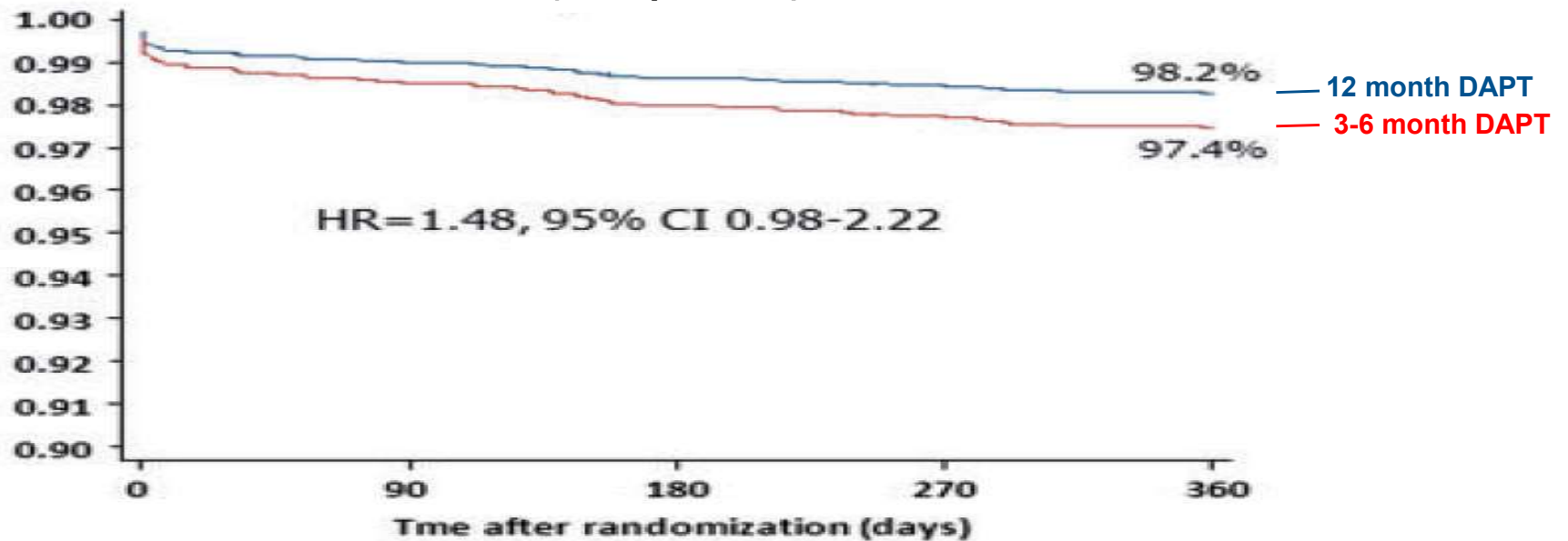


# Chronic



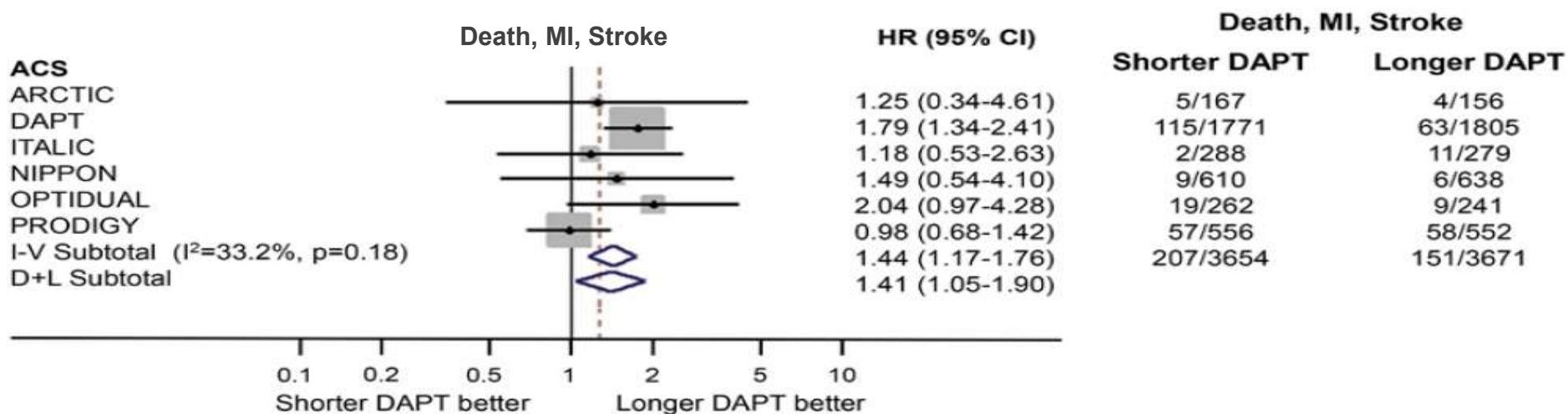
**Three, six, or twelve months of dual antiplatelet therapy after DES implantation in patients with or without acute coronary syndromes: an individual patient data pairwise and network meta-analysis of six randomized trials and 11 473 patients**

**Myocardial Infarction and Stent Thrombosis  
(ACS patients)**



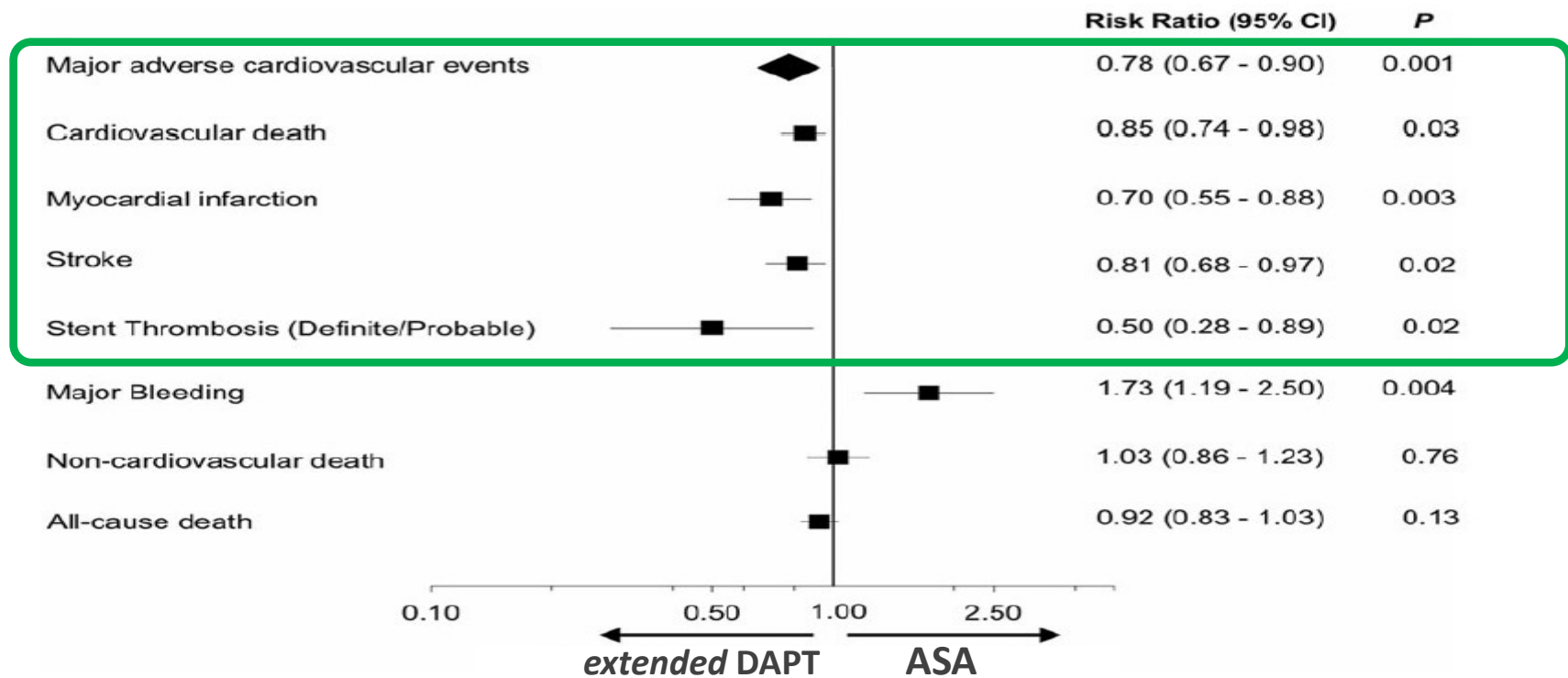
ORIGINAL ARTICLE

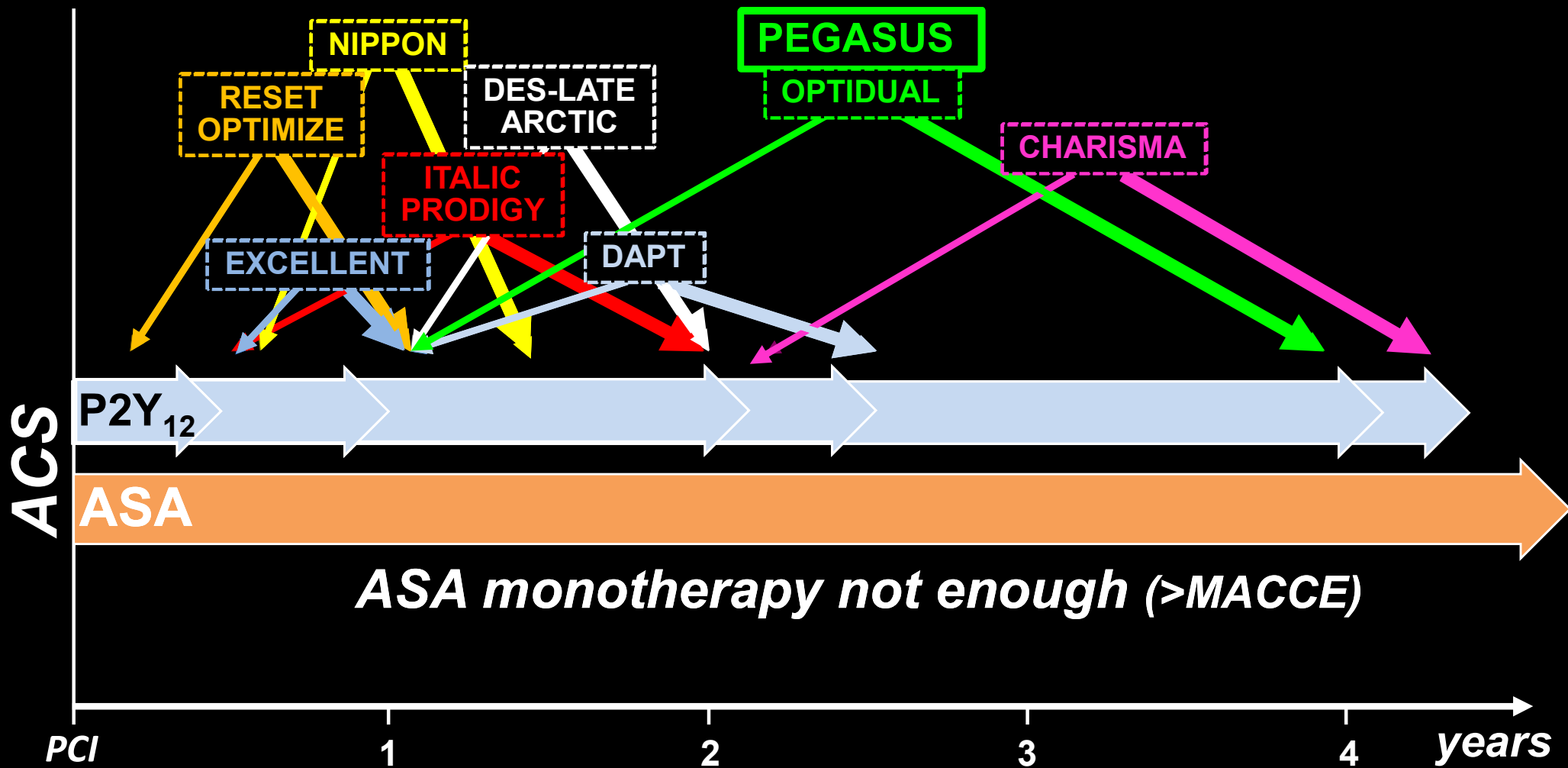
**Risk-Benefit Profile of Longer-Than-1-Year Dual-Antiplatelet Therapy Duration After Drug-Eluting Stent Implantation in Relation to Clinical Presentation**  
**A Pairwise Meta-Analysis of 6 Trials and 21 457 Patients**

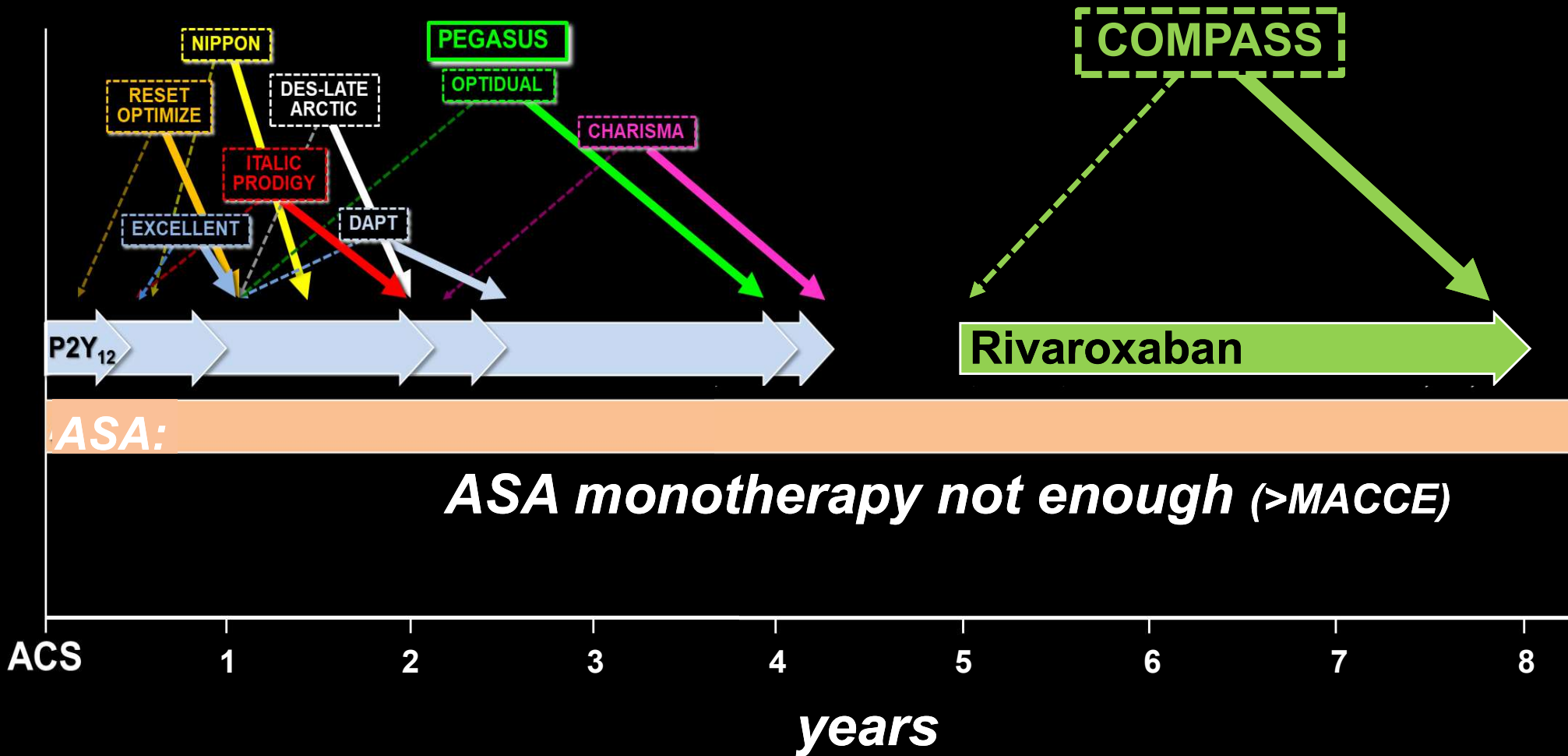


# Metanalysis extended vs standard DAPT (CHARISMA, PRODIGY, DES-LATE, ARCTIC, DAPT, PEGASUS)

## Patients with previous ACS



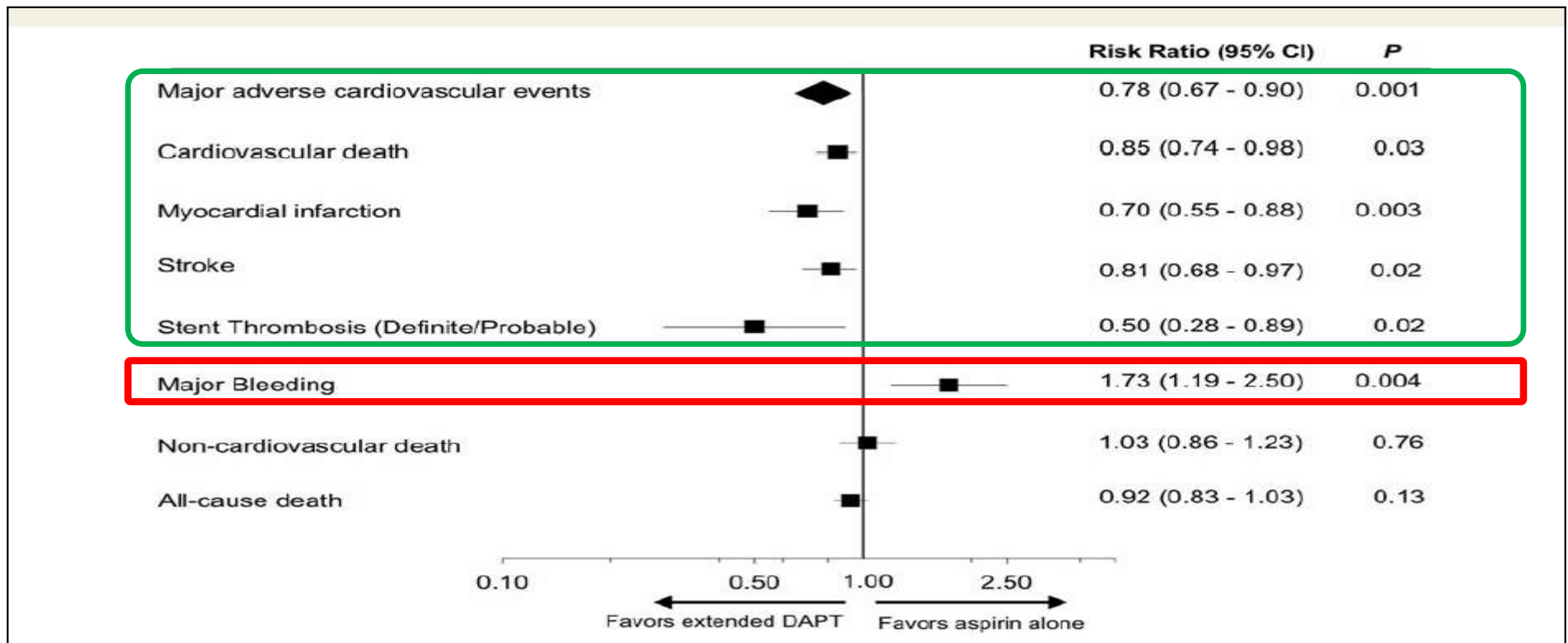






# Metanalysis extended vs standard DAPT (CHARISMA, PRODIGY, DES-LATE, ARCTIC, DAPT, PEGASUS)

## Patients with previous ACS



Udell et al, Eur Heart J 2016;37: 390–399

# DAPT trial: 12 vs 30 months DAPT

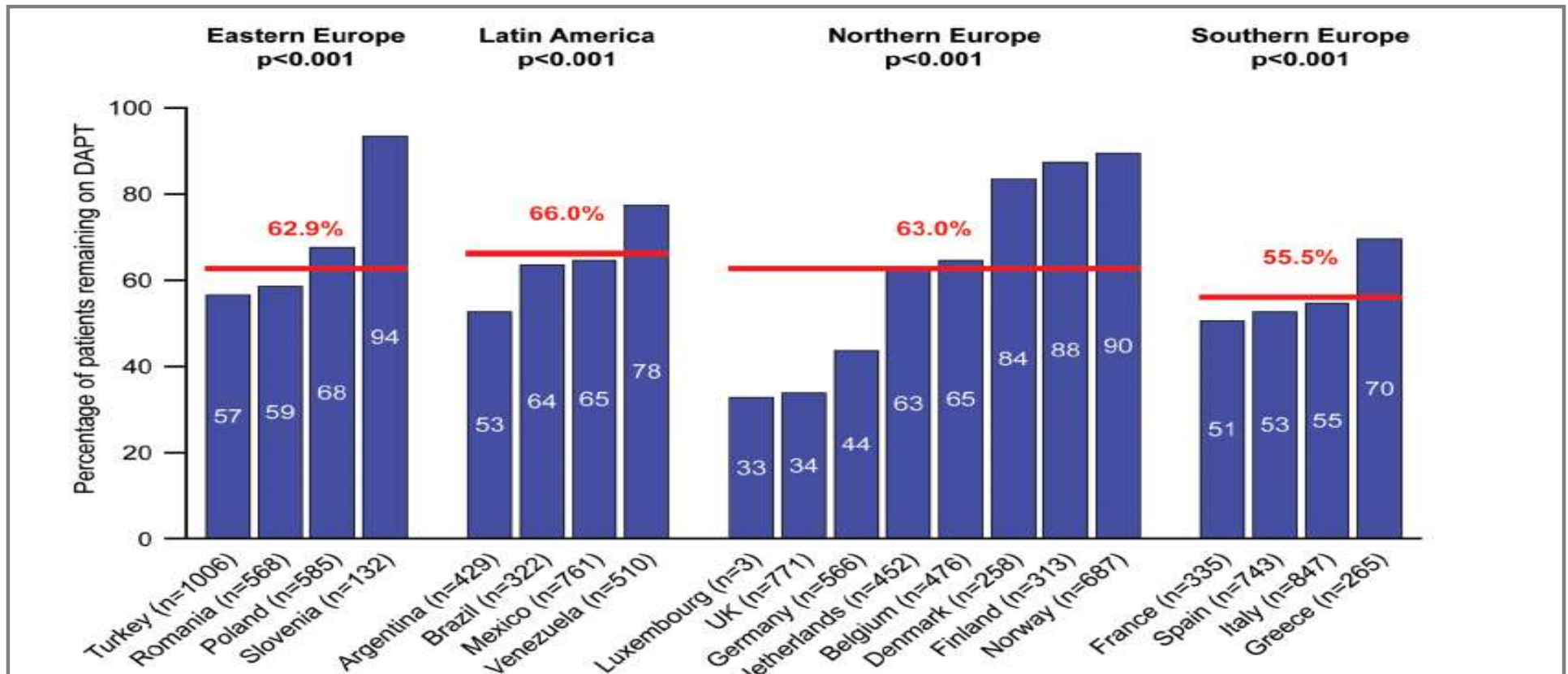
**Bleed (BARC 2-5) : + 93%**

**Table 2. Stent Thrombosis and Major Adverse Cardiovascular and Cerebrovascular Events.\***

Outcome	Continued Thienopyridine (N=5020)	Placebo (N=4941)	Hazard Ratio, Thienopyridine vs. Placebo (95% CI)†	P Value‡
	<i>no. of patients (%)</i>			
Stent thrombosis‡	19 (0.4)	65 (1.4)	0.29 (0.17–0.48)	<0.001
Definite	15 (0.3)	58 (1.2)	0.26 (0.14–0.45)	<0.001
Probable	5 (0.1)	7 (0.1)	0.71 (0.22–2.23)	0.55
Major adverse cardiovascular and cerebrovascular events§	211 (4.3)	285 (5.9)	0.71 (0.59–0.85)	<0.001
Death	98 (2.0)	74 (1.5)	1.36 (1.00–1.85)	0.05
Cardiac	45 (0.9)	47 (1.0)	1.00 (0.66–1.52)	0.98
Vascular	5 (0.1)	5 (0.1)	0.98 (0.28–3.39)	0.98
Noncardiovascular	48 (1.0)	22 (0.5)	2.23 (1.32–3.78)	0.002
Myocardial infarction	99 (2.1)	198 (4.1)	0.47 (0.37–0.61)	<0.001
Stroke	37 (0.8)	43 (0.9)	0.80 (0.51–1.25)	0.32
Ischemic	24 (0.5)	34 (0.7)	0.68 (0.40–1.17)	0.16
Hemorrhagic	13 (0.3)	9 (0.2)	1.20 (0.50–2.91)	0.68
Type uncertain	0	1 (<0.1)	—	0.32

Mauri et al, N Engl J Med 2014;371:2155-66

## Use of DAPT >1 year: country variability



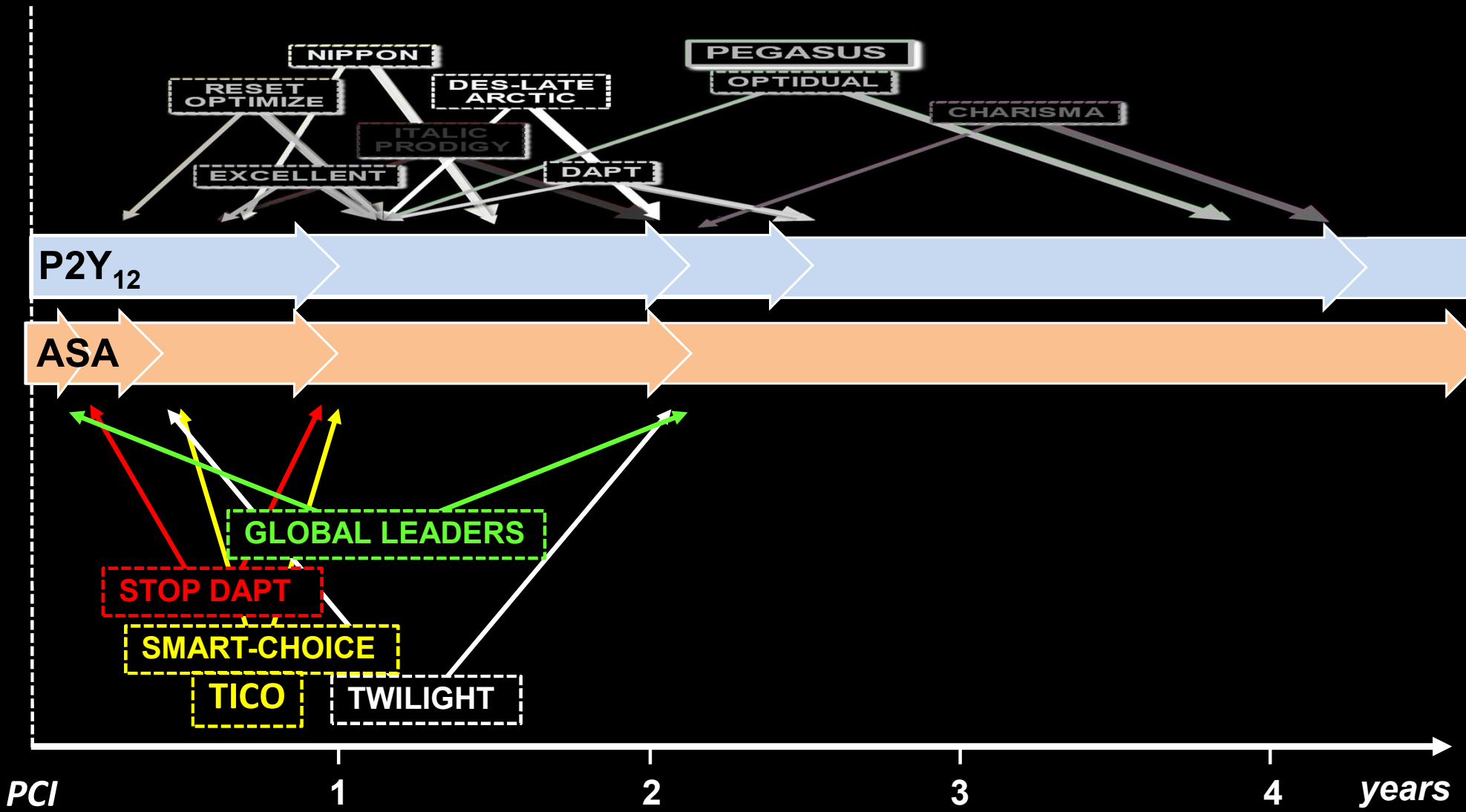


American Heart Journal  
Volume 158, Issue 4, October 2009



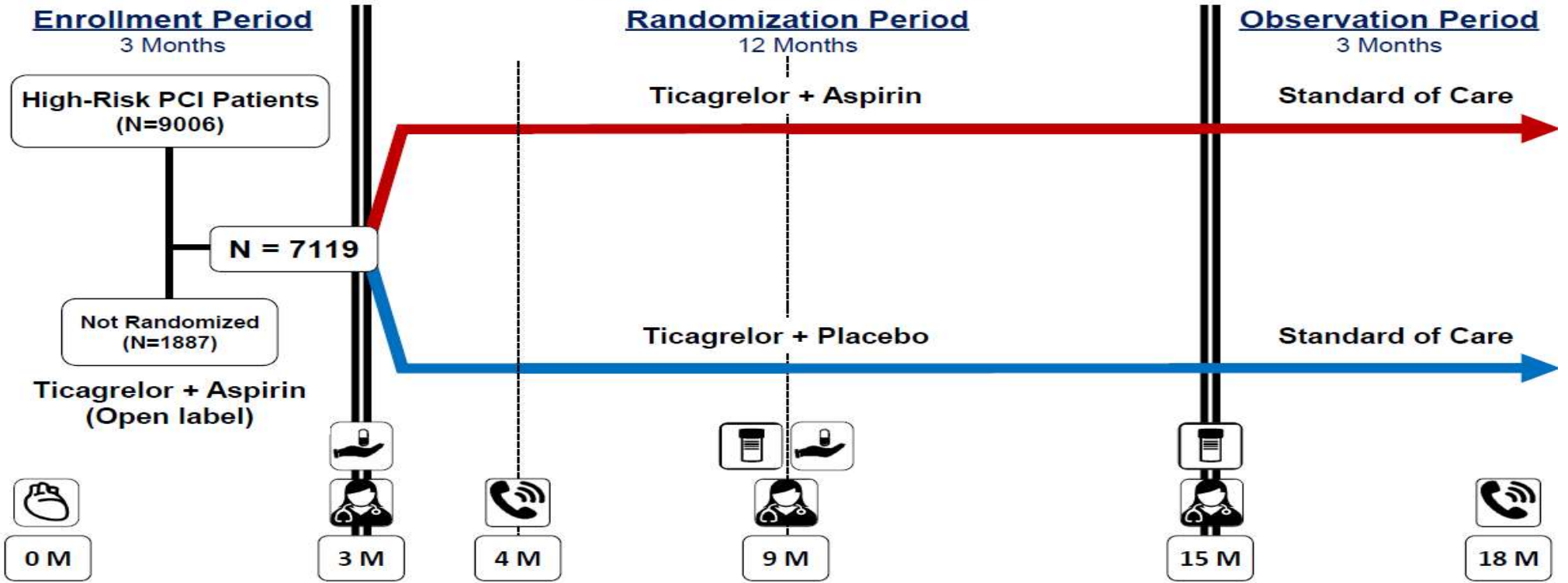
# Are we sure we have taken the best from clopidogrel?

Bernardo Cortese MD , Andrea Picchi MD, Andrea Micheli MD,  
Ugo Limbruno MD, PhD





# Study Design

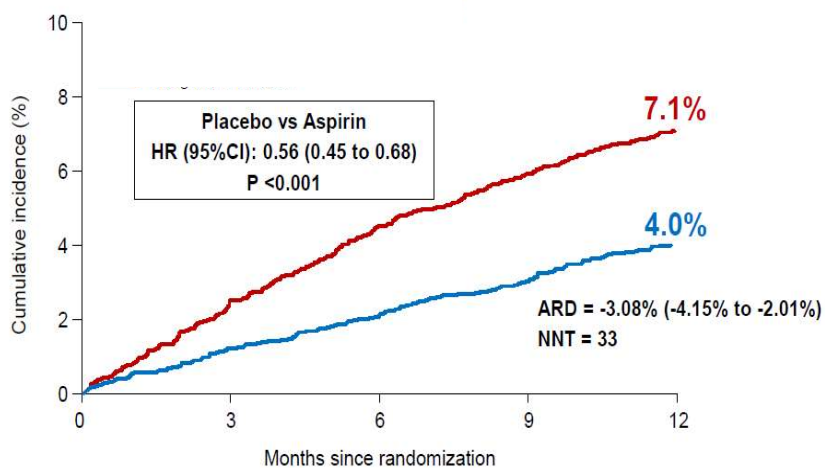




— Ticagrelor + ASA  
— Ticagrelor

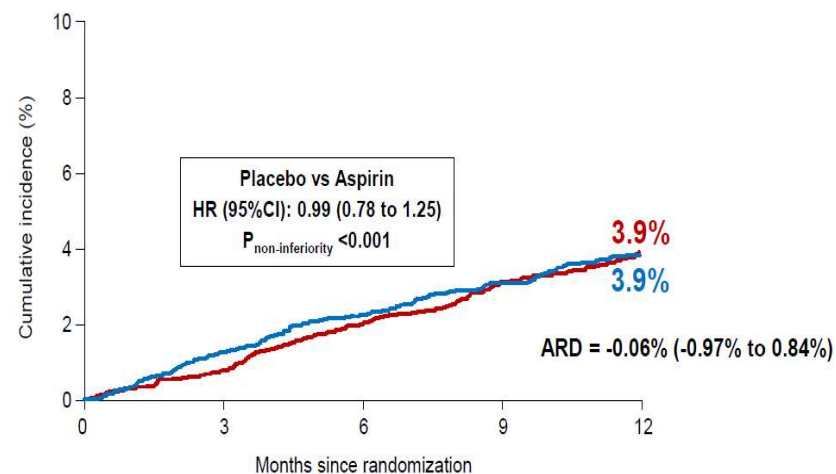
## BLEEDING

### Primary Endpoint: BARC 2, 3 or 5 Bleeding



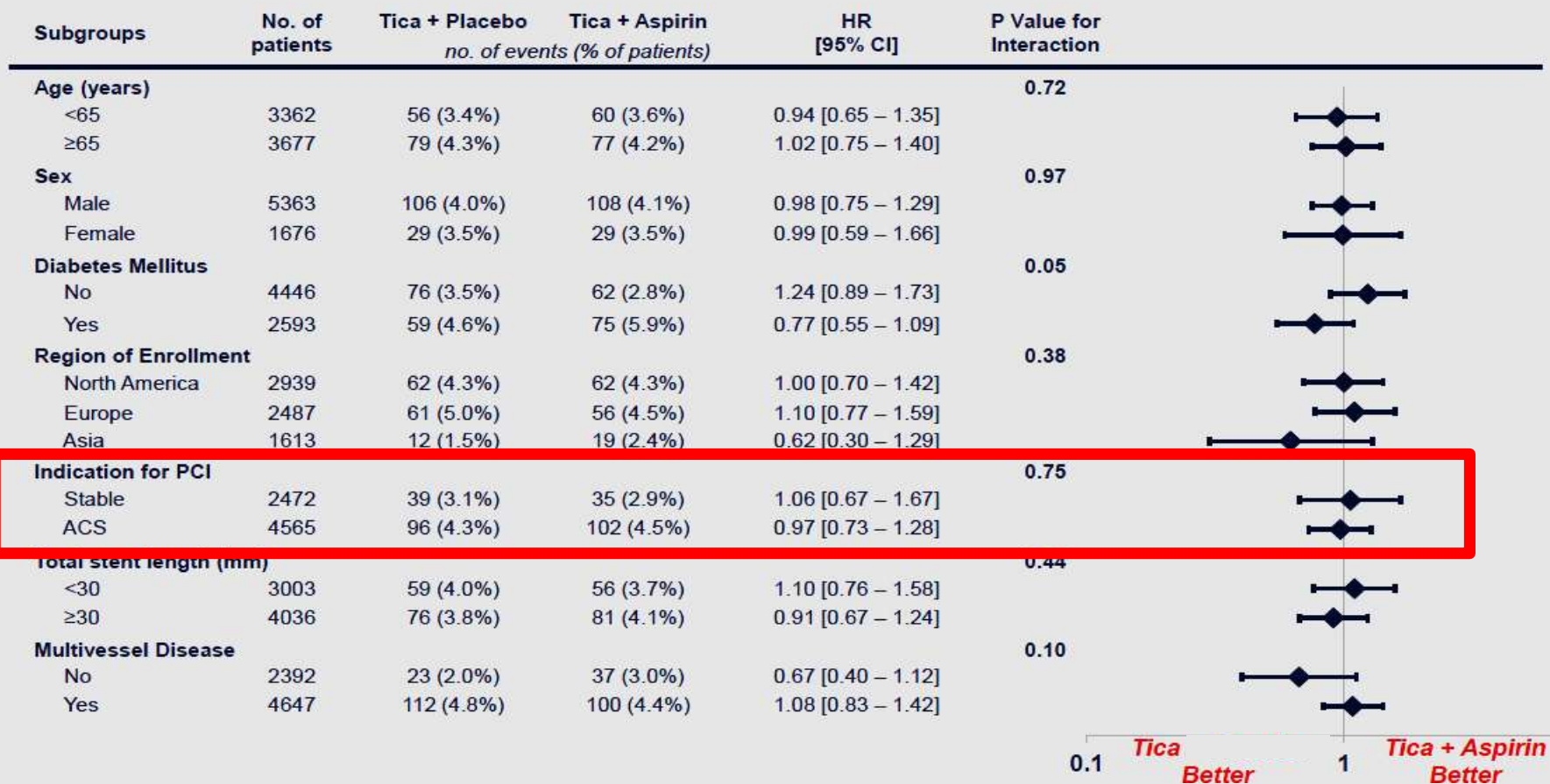
## MACCE

### Key Secondary Endpoint: Death, MI or Stroke





# MACCE





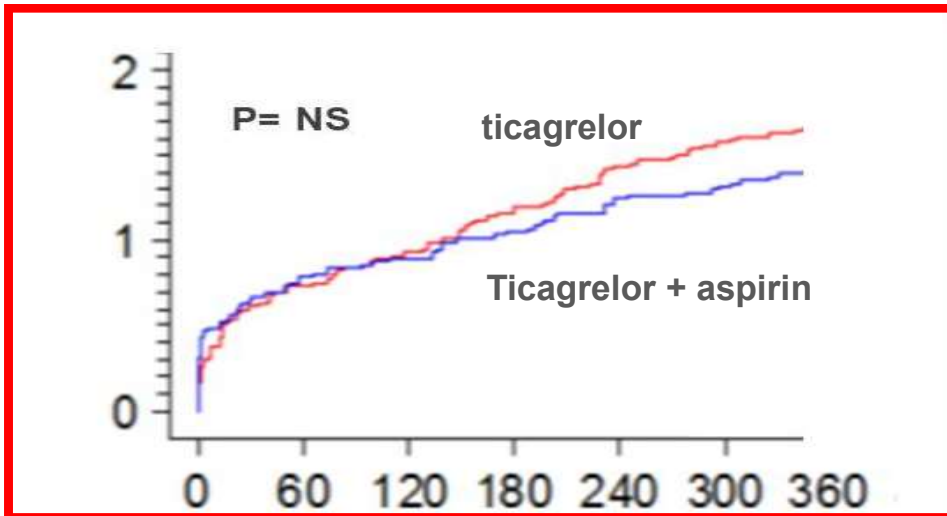


# BLEEDING

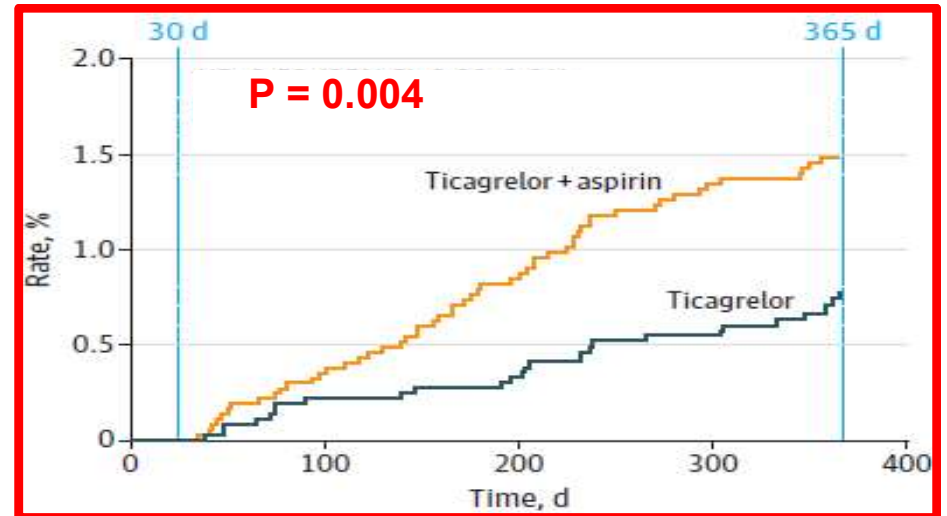
Subgroups	No. of patients	Tica + Placebo <i>no. of events (% of patients)</i>	Tica + Aspirin <i>no. of events (% of patients)</i>	HR [95% CI]	P Value for Interaction
<b>Age (years)</b>					0.67
<65	3400	59 (3.5%)	100 (6.0%)	0.59 [0.42 – 0.81]	
≥65	3719	82 (4.5%)	150 (8.2%)	0.54 [0.41 – 0.70]	
<b>Sex</b>					0.89
Male	5421	99 (3.7%)	178 (6.7%)	0.55 [0.43 – 0.70]	
Female	1698	42 (5.0%)	72 (8.6%)	0.57 [0.39 – 0.83]	
<b>Diabetes Mellitus</b>					0.23
No	4499	83 (3.8%)	164 (7.3%)	0.50 [0.39 – 0.66]	
Yes	2620	58 (4.5%)	86 (6.6%)	0.65 [0.47 – 0.91]	
<b>Region of Enrollment</b>					0.16
North America	2972	83 (5.7%)	126 (8.7%)	0.65 [0.49 – 0.85]	
Europe	2509	32 (2.6%)	79 (6.3%)	0.40 [0.27 – 0.61]	
Asia	1638	26 (3.2%)	45 (5.5%)	0.57 [0.35 – 0.92]	
<b>Indication for PCI</b>					0.03
Stable	2503	60 (4.8%)	75 (6.2%)	0.76 [0.54 – 1.06]	
ACS	4614	81 (3.6%)	175 (7.6%)	0.47 [0.36 – 0.61]	
<b>Total stent length (mm)</b>					0.06
<30	3036	64 (4.4%)	93 (6.1%)	0.70 [0.51 – 0.97]	
≥30	4082	77 (3.8%)	157 (7.9%)	0.47 [0.36 – 0.62]	
<b>Multivessel Disease</b>					0.74
No	2422	47 (4.1%)	94 (7.6%)	0.53 [0.37 – 0.75]	
Yes	4697	94 (4.0%)	156 (6.9%)	0.57 [0.44 – 0.74]	

# Bleed (BARC 3-5)

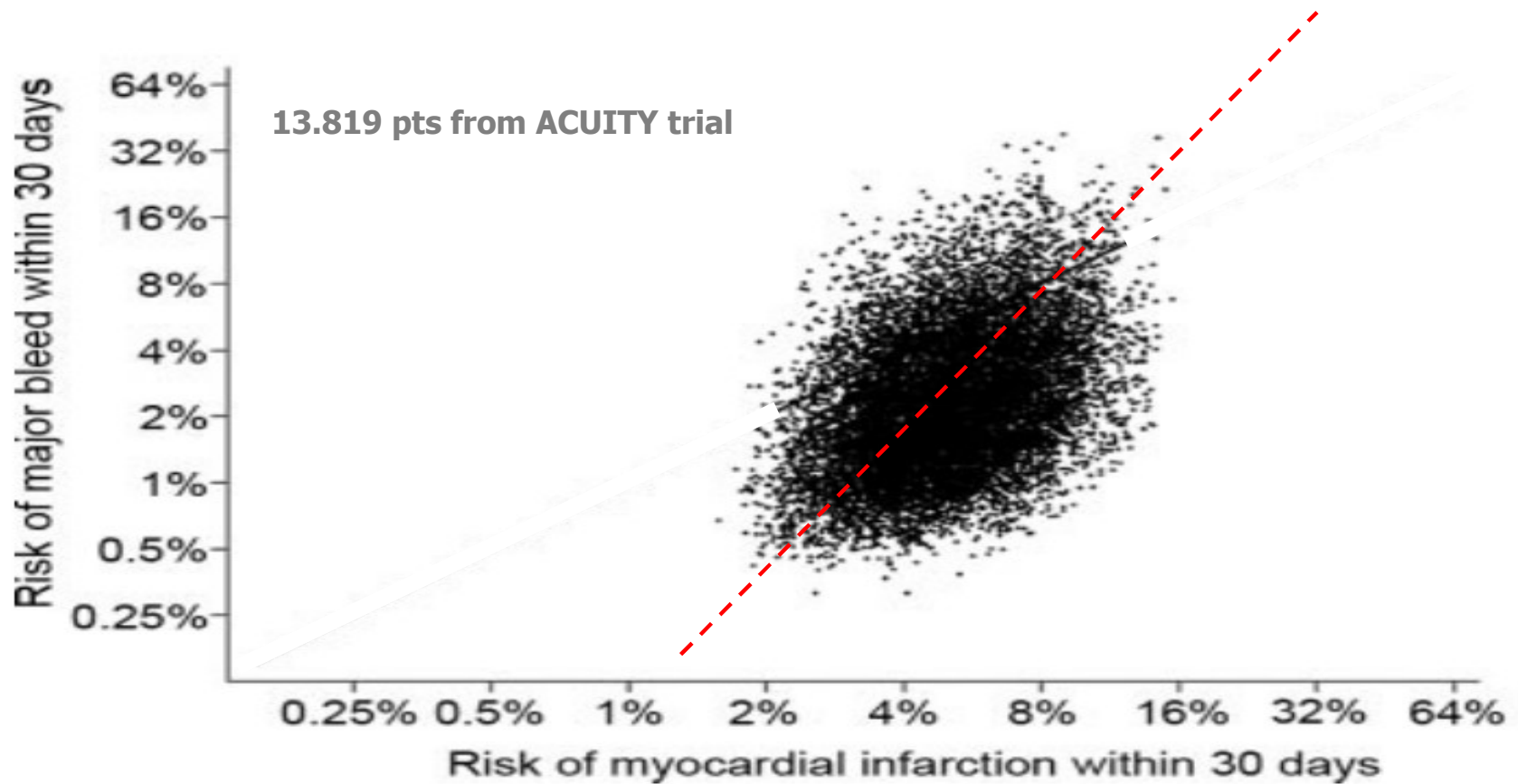
## Whole trial population



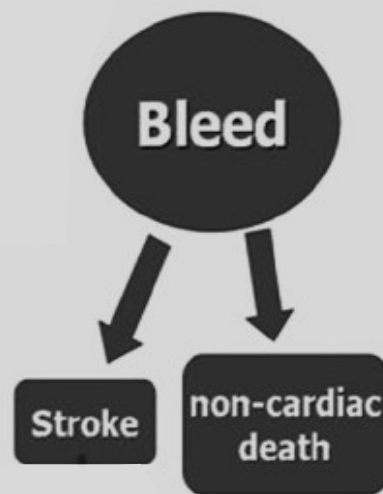
## ACS subgroup



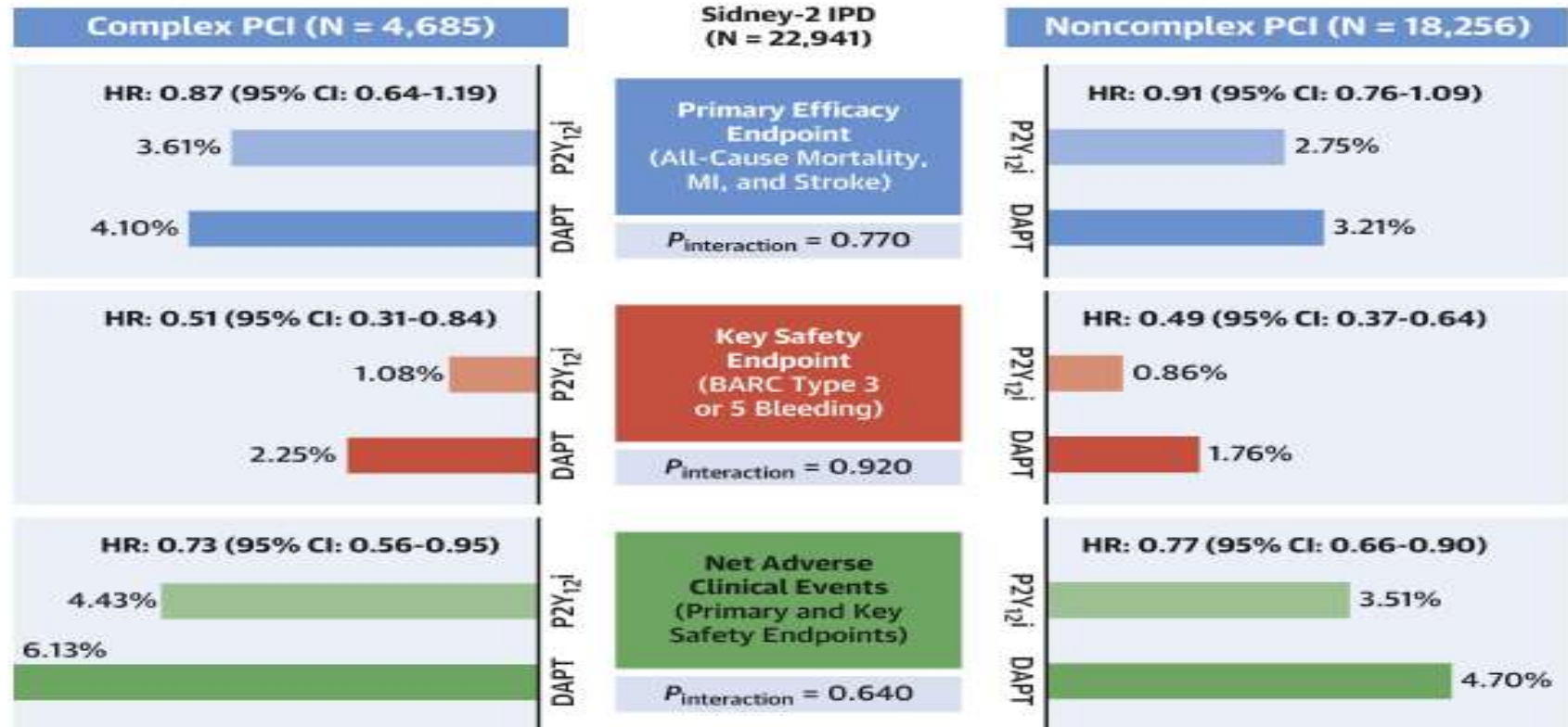
# Ischemic *vs* Bleeding risk







# CENTRAL ILLUSTRATION: P2Y<sub>12</sub> Inhibitor Monotherapy vs Standard DAPT After Complex PCI

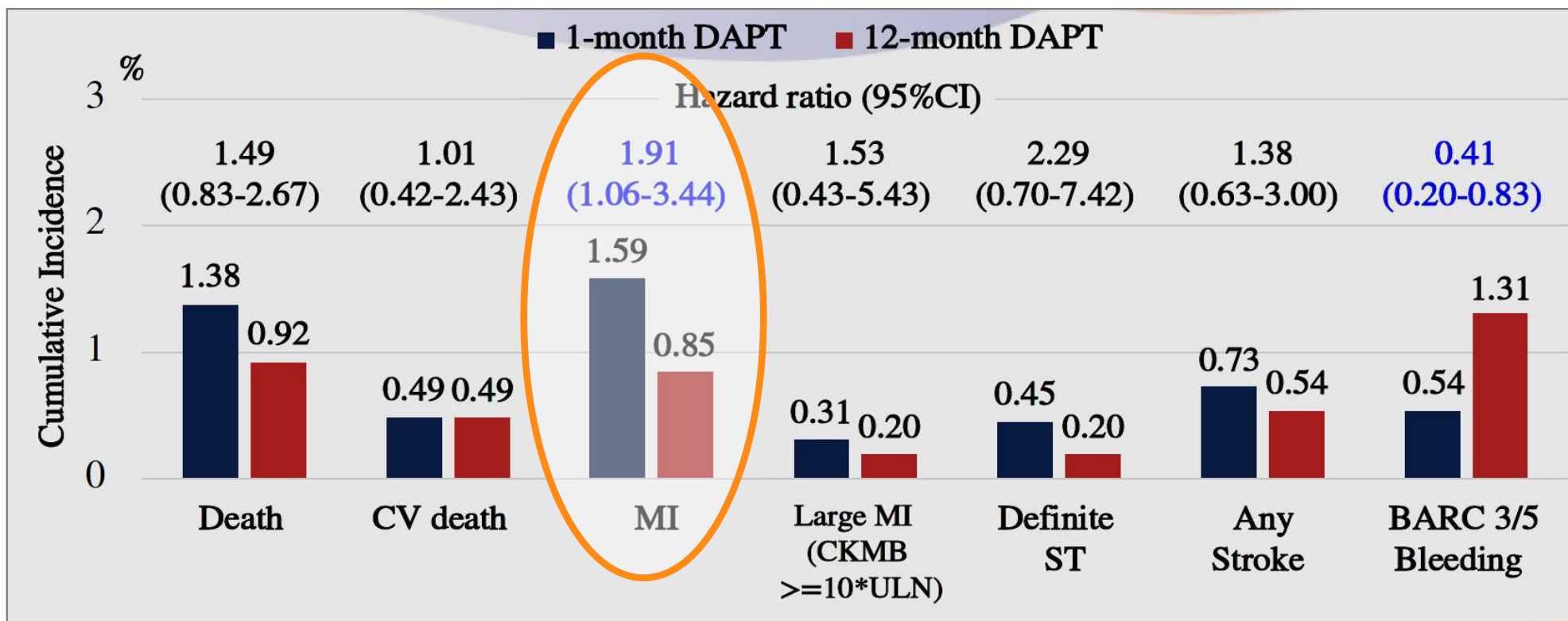


Gagnano F, et al. J Am Coll Cardiol. 2023;81(6):537-552.



# Comparison of Clopidogrel Monotherapy After 1 to 2 Months of Dual Antiplatelet Therapy With 12 Months of Dual Antiplatelet Therapy in Patients With Acute Coronary Syndrome

The STOPDAPT-2 ACS Randomized Clinical Trial (4136 pts)





# Acute

Clopidogrel+ Rivaroxaban  
(ATLAS-ACS)

Short vs Long DAPT  
(n TRIALS)

Clopidogrel  
(CURE)

Ticagrelor  
(PLATO)

Prasugrel  
(TRITON)

# Coronary Syndrome

Clopidogrel  
(CHARISMA)

Clopidogrel  
(DAPT trial)

Ticagrelor  
(PEGASUS)

Rivaroxaban  
(COMPASS)



# Chronic

Articles

**A randomised, blinded, trial of clopidogrel versus aspirin in patients at risk of ischaemic events (CAPRIE)**

CAPRIE Steering Committee\*

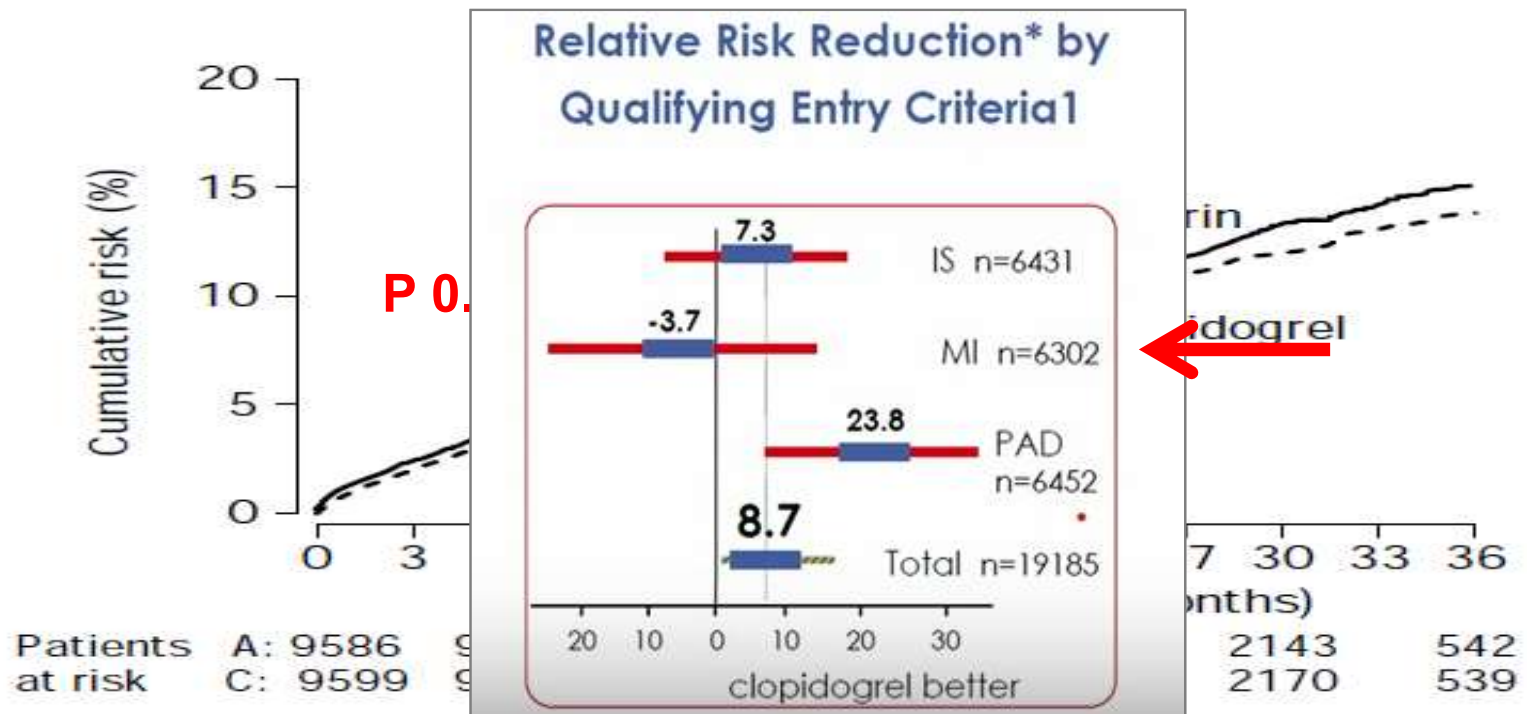


Figure 3: Cumulative risk of ischaemic stroke, myocardial infarction, or vascular death

# Study Design and Patient Population

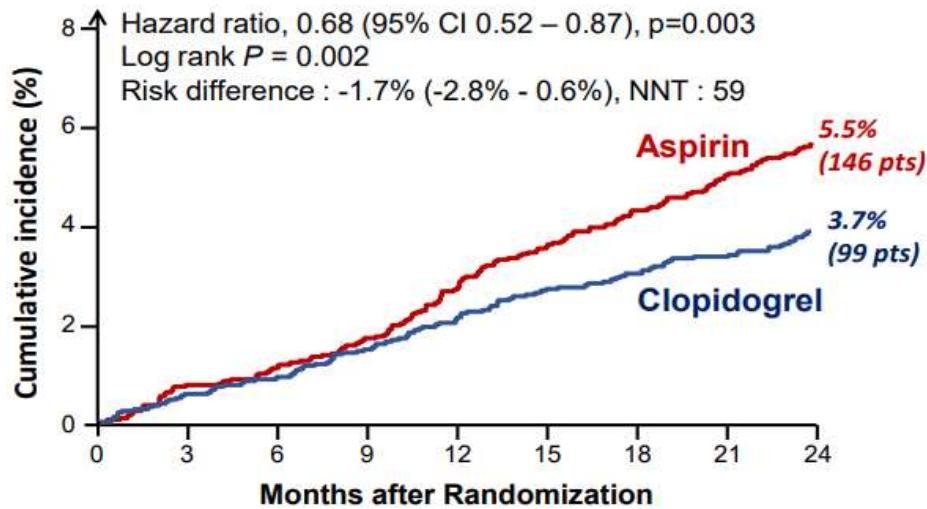


- 5,530 eligible patients screened, from 37 centers in Korea



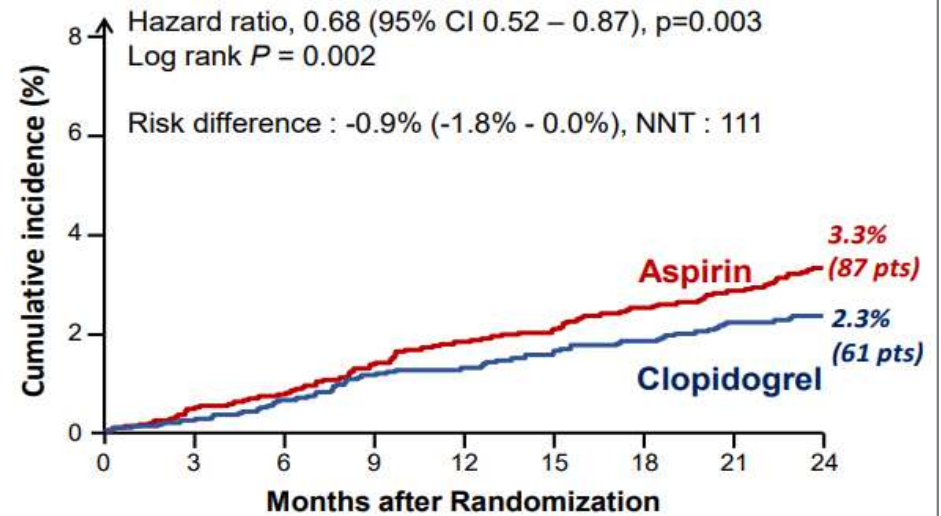
## Thrombotic composite outcome

(cardiac death, non-fatal MI, ischemic stroke, readmission due to ACS, and definite or probable stent thrombosis)

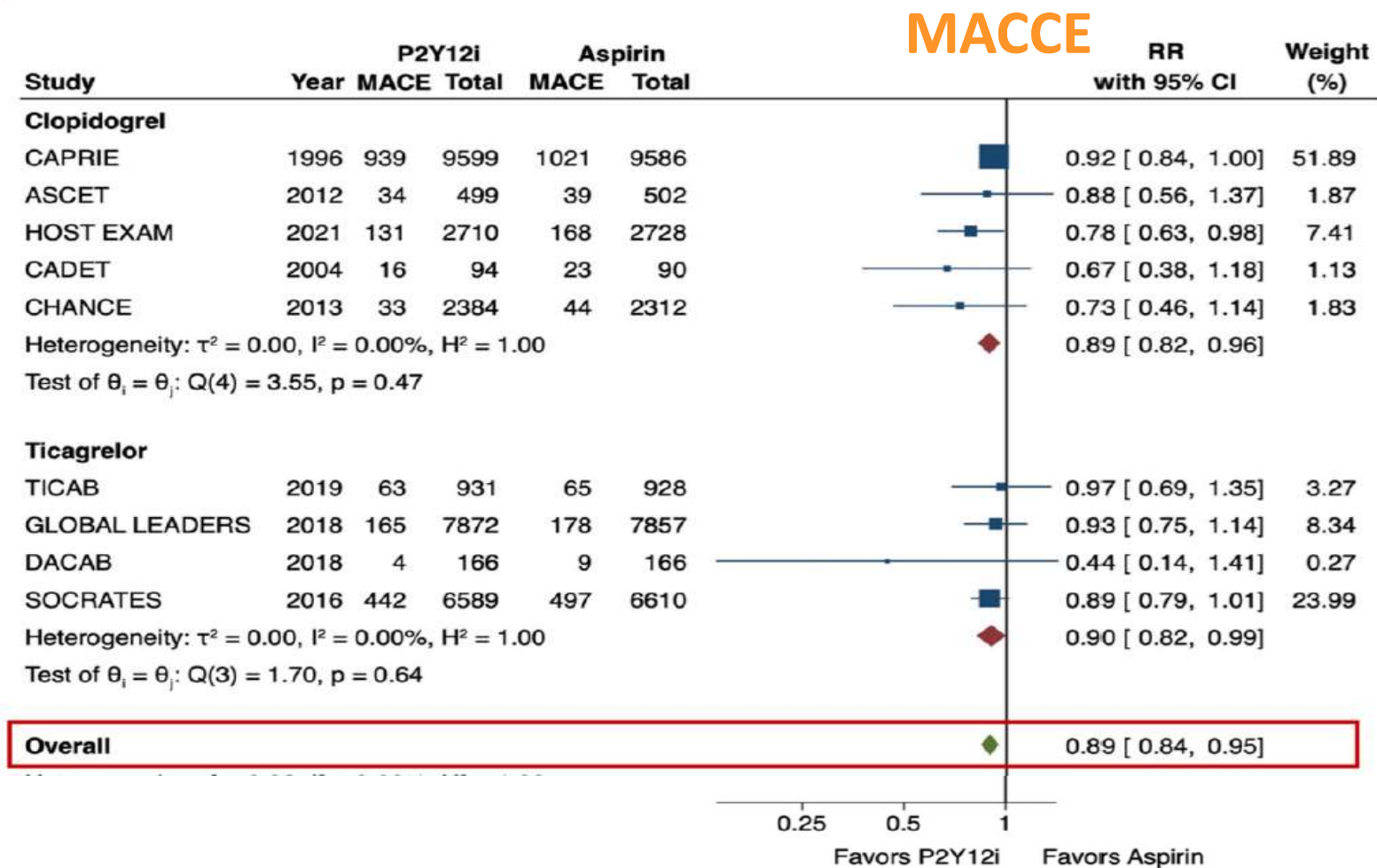


## Any bleeding

(BARC type ≥2 bleeding)



**P2Y<sub>12</sub> inhibitor versus aspirin monotherapy for secondary prevention of cardiovascular events: meta-analysis of randomized trials**

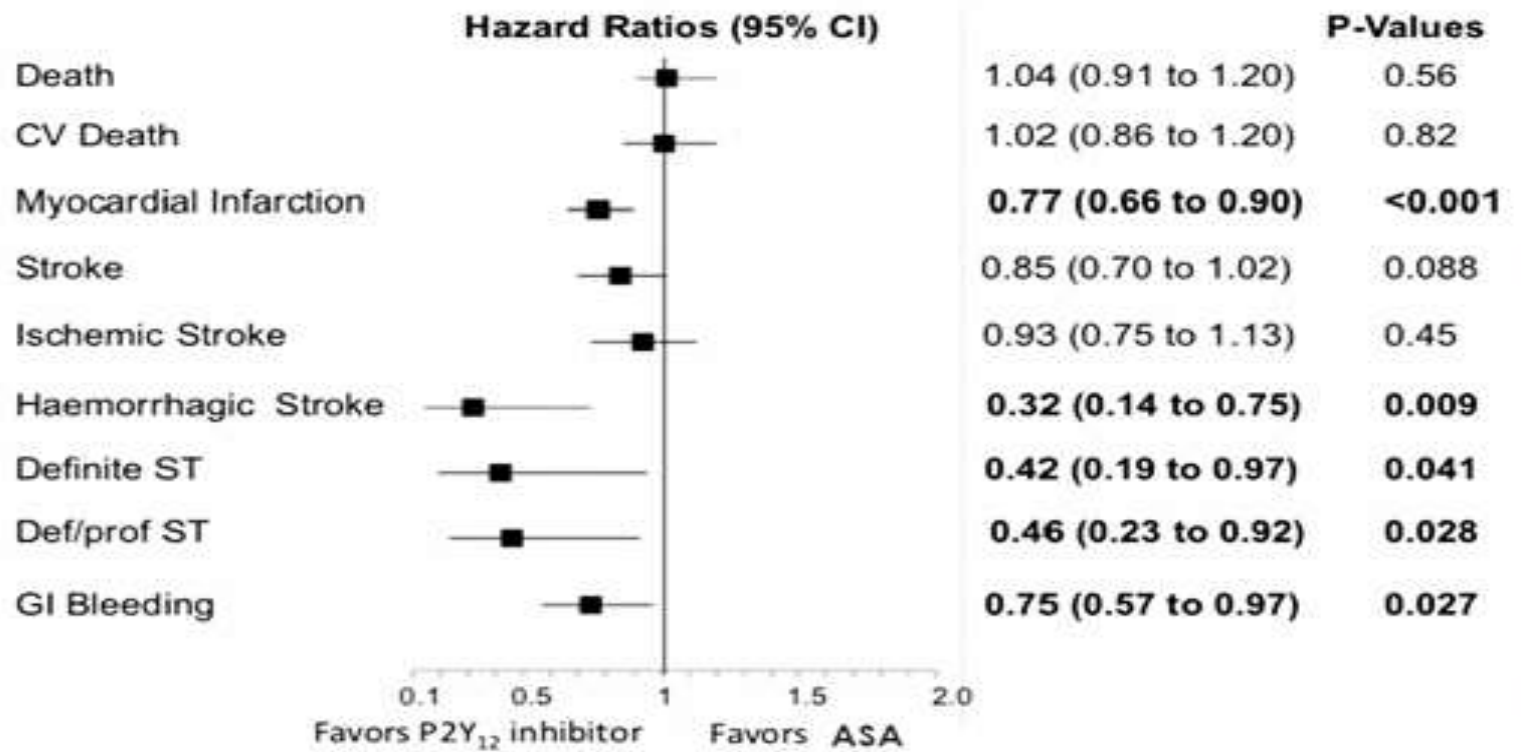


ESC 2022

Results from the PANTHER Trial

NEW INSIGHTS

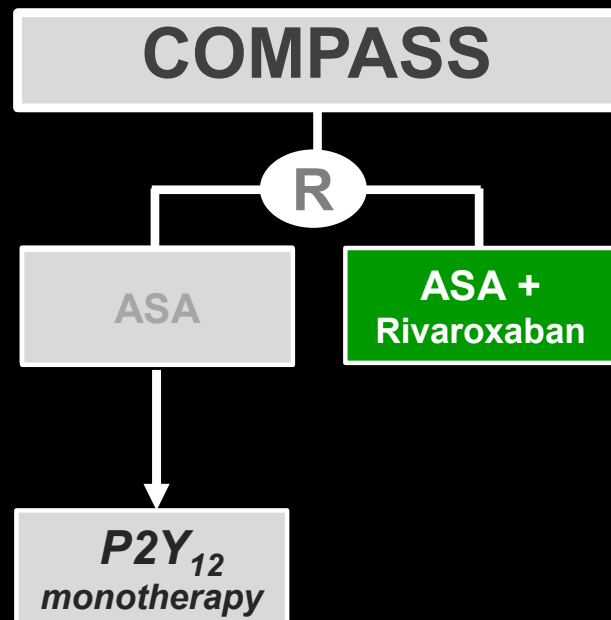
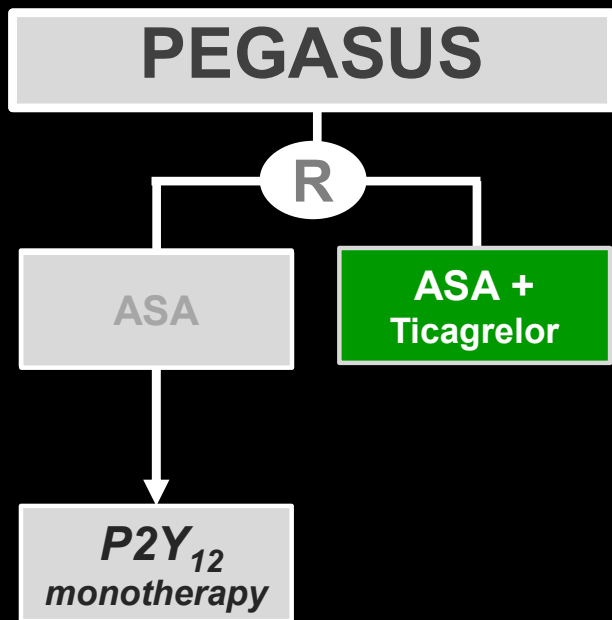
Prof Marco Valgimigli  
McMaster University, CA



# Conclusions

**ACS:**

**CCS:**



#AHA22

**Long Term Follow-Up  
of Aspirin vs. Clopidogrel Monotherapy  
in the Chronic Maintenance Period After PCI with DES  
: The Host-Exam Extended Study**

Hyo-Soo Kim, MD PhD

Seoul National University Hospital

Seoul, Korea

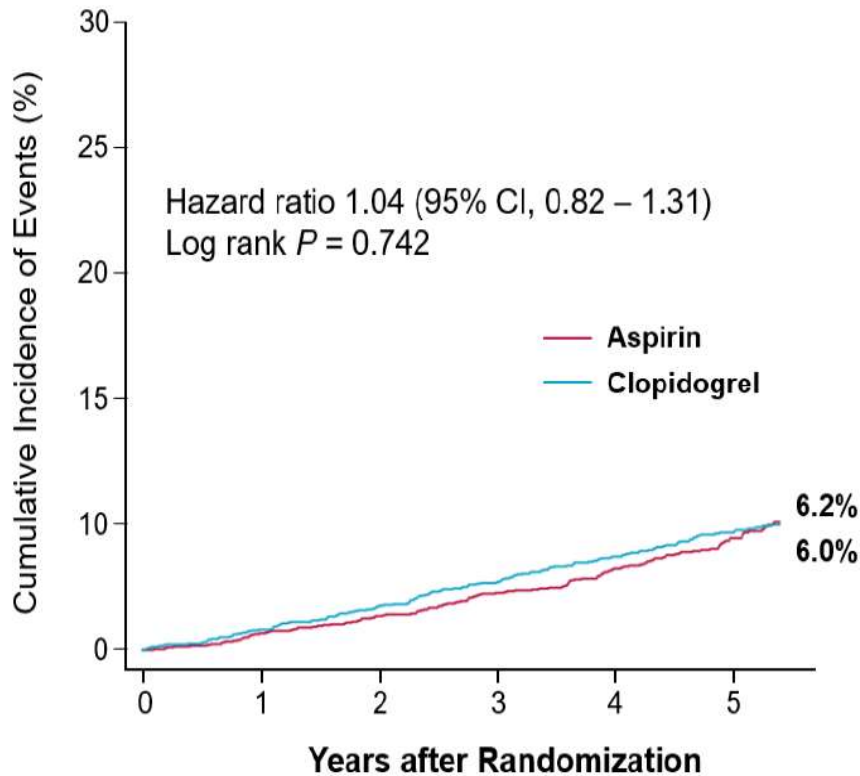


**American  
Heart  
Association.**



# Clinical Outcomes

## ▪ Mortality



### Number at Risk

	0	1	2	3	4	5
Aspirin	2286	2244	1971	1165		
Clopidogrel	2431	2374	2088	1285		

No. of patients	Clopidogrel (N=2431)	Aspirin (N=2286)	P value
<b>Total mortality</b>	<b>150 (6.2%)</b>	<b>136 (6.0%)</b>	<b>0.753</b>
<b>Cardiovascular cause</b>	<b>69 (2.8%)</b>	<b>71 (3.1%)</b>	<b>0.587</b>
Cardiac arrest	21	22	
Heart failure aggravation	5	3	
Cerebrovascular accident	7	3	
Unknown origin of death	36	43	
<b>Non-cardiovascular cause</b>	<b>81 (3.3%)</b>	<b>65 (2.8%)</b>	<b>0.334</b>
<b>Malignancy</b>	<b>34</b>	<b>29</b>	
- Gastrointestinal origin	15	12	
- Respiratory origin	8	11	
- Endocrinology origin	1	1	
- Genitourinary origin	4	3	
- Other	3	2	
- Unknown primary	3	0	
Infectious disease	4	5	
Suicide or Trauma	8	3	
Others	20	16	