

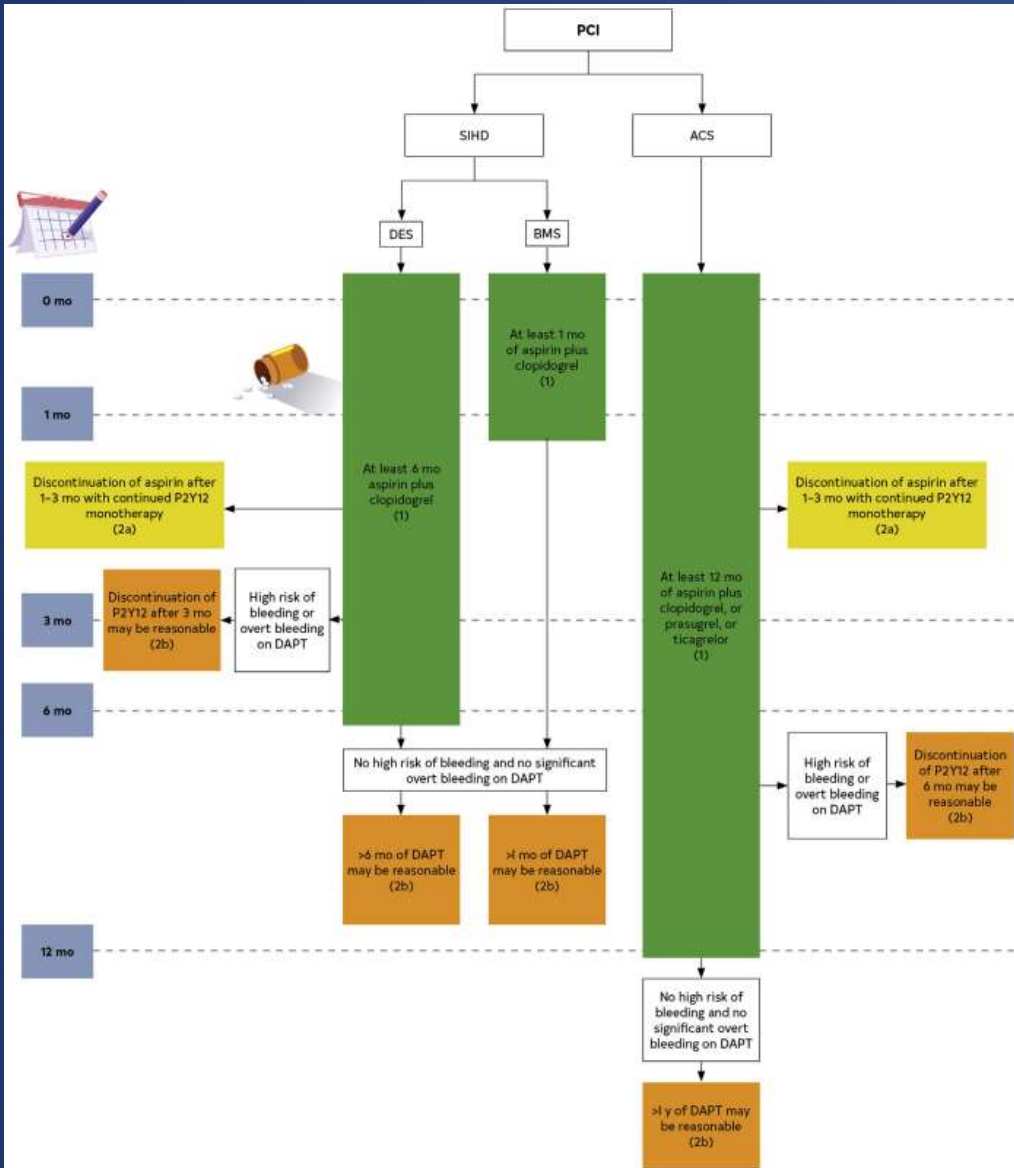
# Antiplatelet therapy

# Antiplatelet therapy

Recommendations for Aspirin and Oral P2Y12 Inhibitors in Patients Undergoing PCI  
 Referenced studies that support the recommendations are summarized in [Online Data Supplement 32](#).

COR	LOE	RECOMMENDATIONS
1	B-R	1. In patients undergoing PCI, a loading dose of aspirin, followed by daily dosing, is recommended to reduce ischemic events (1-4).*
1	B-R	2. In patients with ACS undergoing PCI, a loading dose of P2Y12 inhibitor, followed by daily dosing, is recommended to reduce ischemic events (5-15).
1	C-LD	3. In patients with SIHD undergoing PCI, a loading dose of clopidogrel, followed by daily dosing, is recommended to reduce ischemic events (8,12,15-19).
1	C-LD	4. In patients undergoing PCI within 24 hours after fibrinolytic therapy, a loading dose of 300 mg of clopidogrel, followed by daily dosing, is recommended to reduce ischemic events (5).
2a	B-R	5. In patients with ACS undergoing PCI, it is reasonable to use ticagrelor or prasugrel in preference to clopidogrel to reduce ischemic events, including stent thrombosis (6,14,20).
2b	B-R	6. In patients <75 years of age undergoing PCI within 24 hours after fibrinolytic therapy, ticagrelor may be a reasonable alternative to clopidogrel to reduce ischemic events (21).
3: Harm	B-R	7. In patients undergoing PCI who have a history of stroke or transient ischemic attack, prasugrel should not be administered (6).

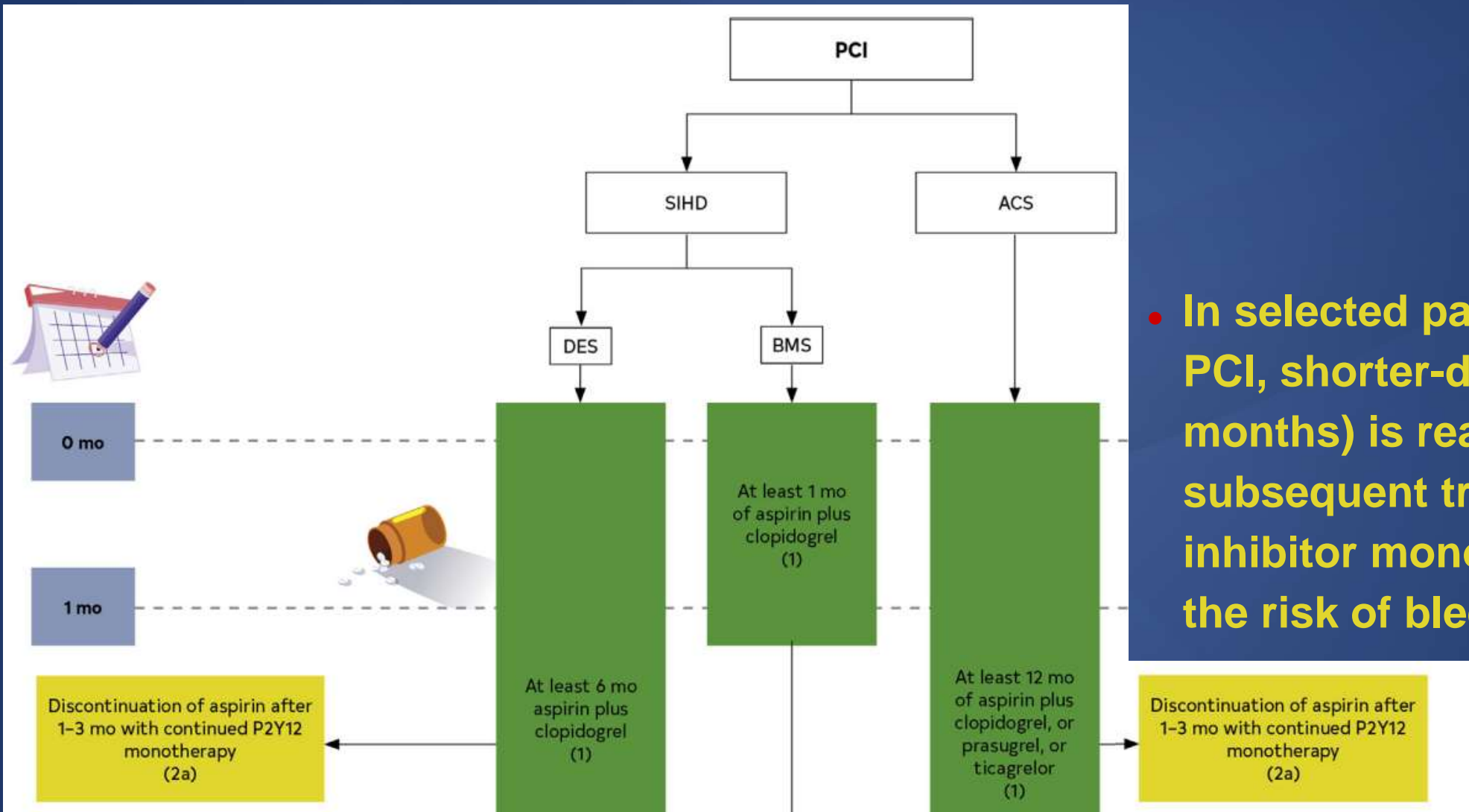
# Antiplatelet therapy



- In selected patients undergoing PCI, shorter-duration DAPT (1-3 months) is reasonable, with subsequent transition to P2Y12 inhibitor monotherapy to reduce the risk of bleeding events (2a).

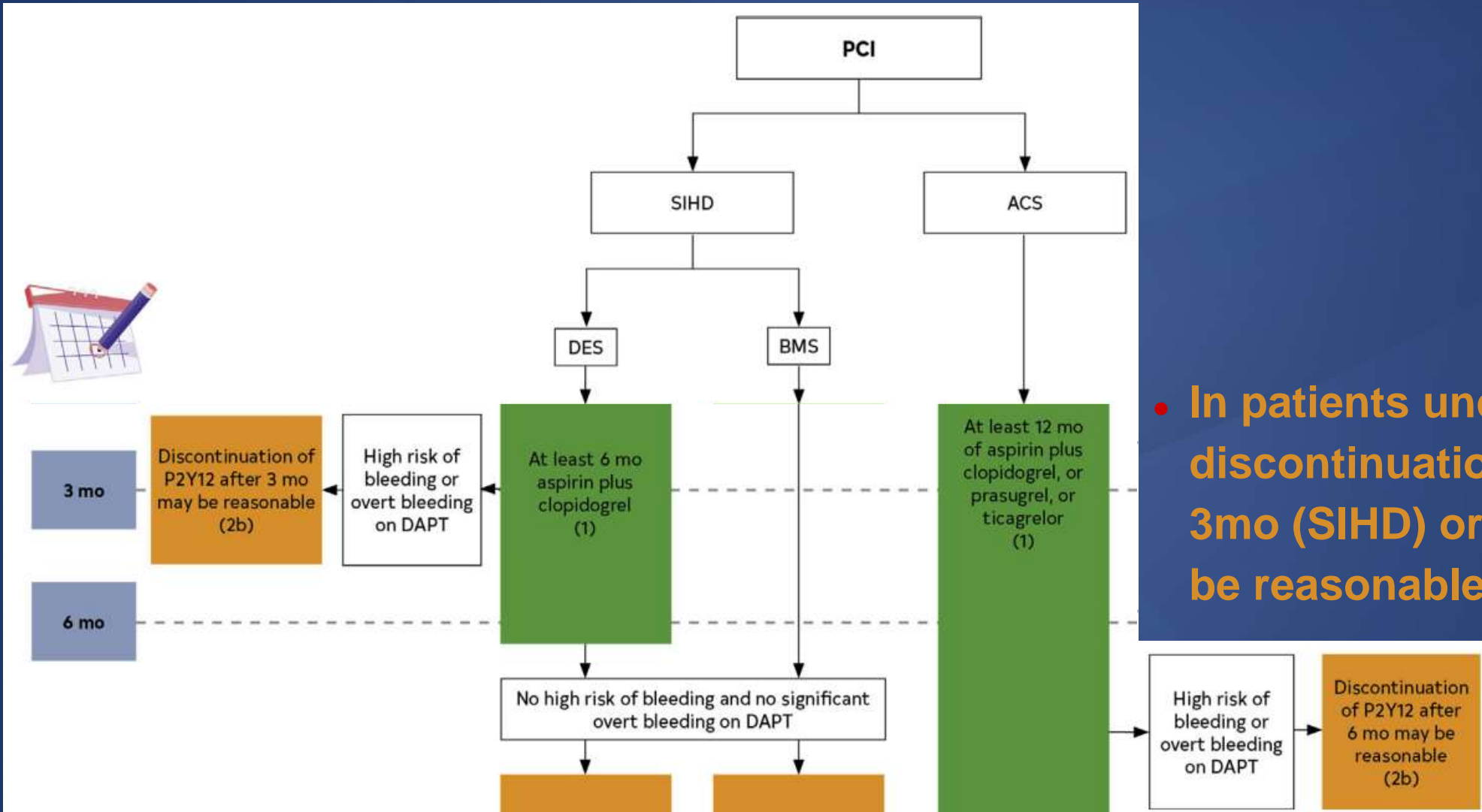
- In patients undergoing PCI, discontinuation of P2Y12 after 3mo (SIHD) or 6mo (ACS) may be reasonable (2b).

# Antiplatelet therapy



- In selected patients undergoing PCI, shorter-duration DAPT (1-3 months) is reasonable, with subsequent transition to P2Y12 inhibitor monotherapy to reduce the risk of bleeding events (2a).

# Antiplatelet therapy

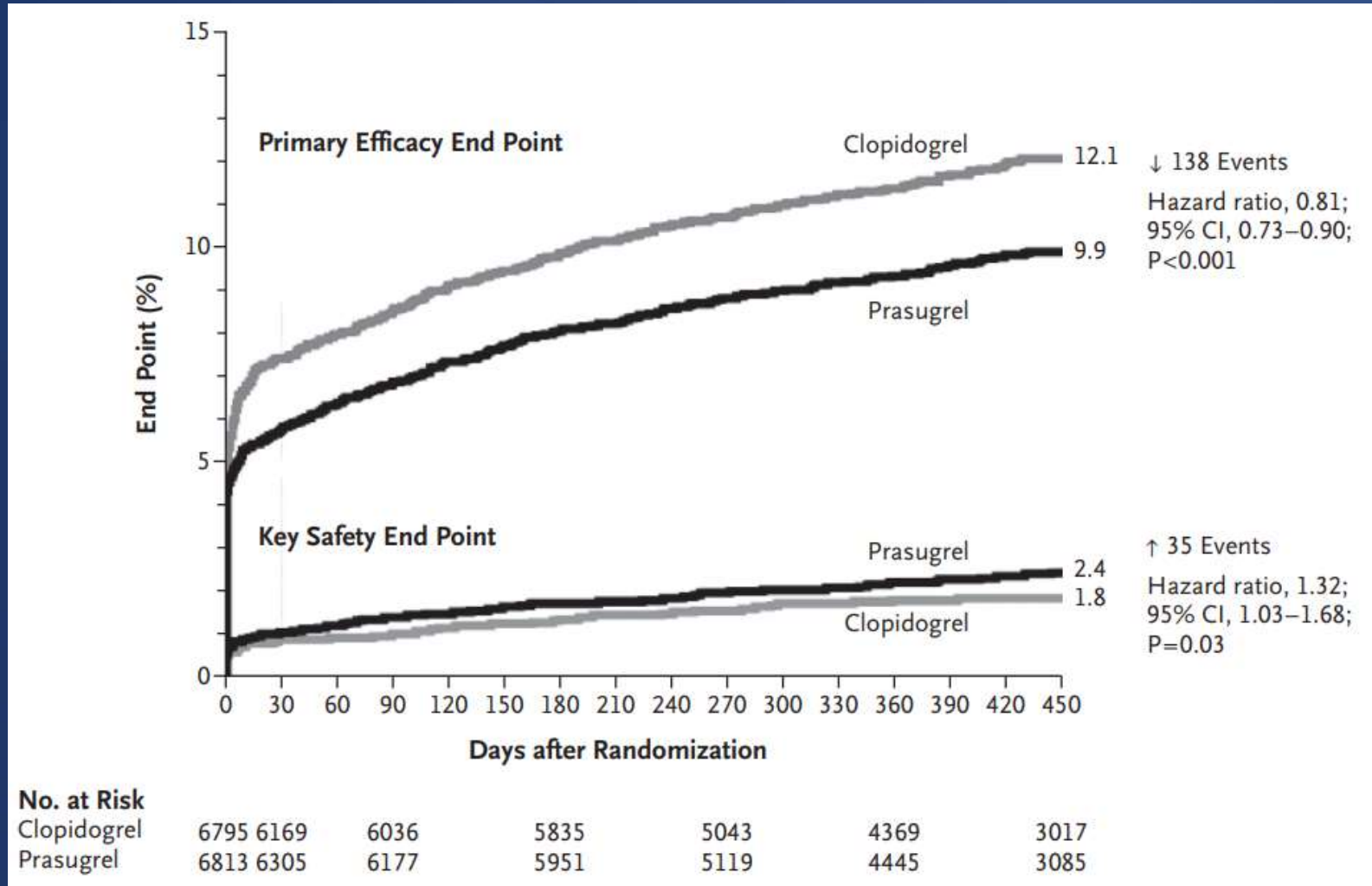


- In patients undergoing PCI, discontinuation of P2Y12 after 3mo (SIHD) or 6mo (ACS) may be reasonable (2b).



# TRITON-TIMI 38 Trial

## Prasugrel vs. Clopidogrel in patients with ACS



- The primary efficacy end point was death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke.
- The key safety end point was major bleeding.

# TRITON-TIMI 38 Trial

## Prasugrel vs. Clopidogrel in patients with ACS

**Table 2.** Major Efficacy End Points in the Overall Cohort at 15 Months.\*

End Point	Prasugrel (N=6813) <i>no. of patients (%)</i>	Clopidogrel (N=6795) <i>no. of patients (%)</i>	Hazard Ratio for Prasugrel (95% CI)	P Value†
Death from cardiovascular causes, nonfatal MI, or nonfatal stroke (primary end point)	643 (9.9)	781 (12.1)	0.81 (0.73–0.90)	<0.001
Death from cardiovascular causes	133 (2.1)	150 (2.4)	0.89 (0.70–1.12)	0.31
Nonfatal MI	475 (7.3)	620 (9.5)	0.76 (0.67–0.85)	<0.001
Nonfatal stroke	61 (1.0)	60 (1.0)	1.02 (0.71–1.45)	0.93
Death from any cause	188 (3.0)	197 (3.2)	0.95 (0.78–1.16)	0.64
Death from cardiovascular causes, nonfatal MI, or urgent target-vessel revascularization	652 (10.0)	798 (12.3)	0.81 (0.73–0.89)	<0.001
Death from any cause, nonfatal MI, or nonfatal stroke	692 (10.7)	822 (12.7)	0.83 (0.75–0.92)	<0.001
Urgent target-vessel revascularization	156 (2.5)	233 (3.7)	0.66 (0.54–0.81)	<0.001
Death from cardiovascular causes, nonfatal MI, nonfatal stroke, or rehospitalization for ischemia	797 (12.3)	938 (14.6)	0.84 (0.76–0.92)	<0.001
Stent thrombosis‡	68 (1.1)	142 (2.4)	0.48 (0.36–0.64)	<0.001

# TRITON-TIMI 38 Trial

## Prasugrel vs. Clopidogrel in patients with ACS

**Table 3.** Thrombolysis in Myocardial Infarction (TIMI) Bleeding End Points in the Overall Cohort at 15 Months.\*

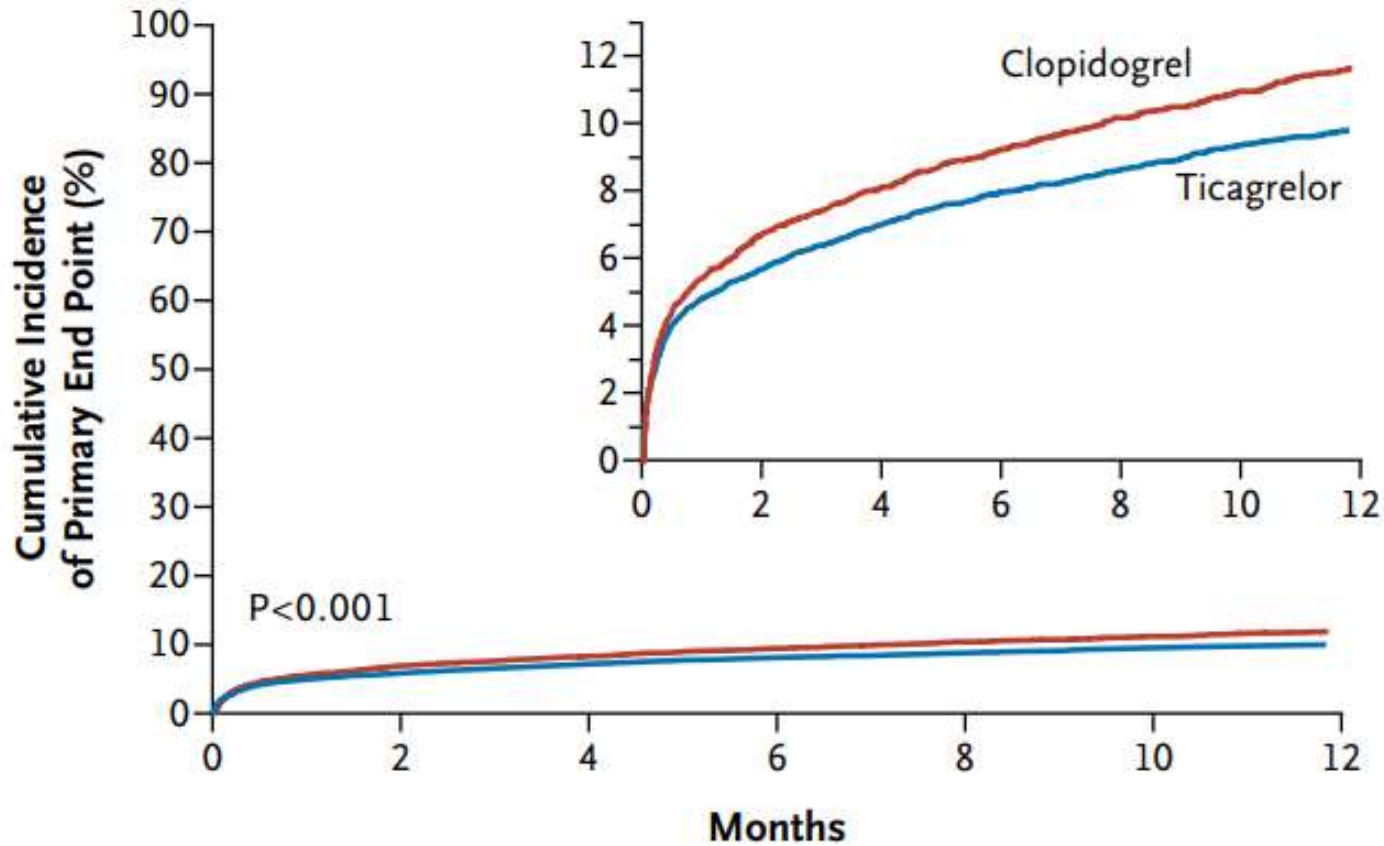
End Point	Prasugrel (N=6741)	Clopidogrel (N=6716)	Hazard Ratio for Prasugrel (95% CI)	P Value
	<i>no. of patients (%)</i>			
Non-CABG-related TIMI major bleeding (key safety end point)	146 (2.4)	111 (1.8)	1.32 (1.03–1.68)	0.03
Related to instrumentation	45 (0.7)	38 (0.6)	1.18 (0.77–1.82)	0.45
Spontaneous	92 (1.6)	61 (1.1)	1.51 (1.09–2.08)	0.01
Related to trauma	9 (0.2)	12 (0.2)	0.75 (0.32–1.78)	0.51
Life-threatening†	85 (1.4)	56 (0.9)	1.52 (1.08–2.13)	0.01
Related to instrumentation	28 (0.5)	18 (0.3)	1.55 (0.86–2.81)	0.14
Spontaneous	50 (0.9)	28 (0.5)	1.78 (1.12–2.83)	0.01
Related to trauma	7 (0.1)	10 (0.2)	0.70 (0.27–1.84)	0.47
Fatal‡	21 (0.4)	5 (0.1)	4.19 (1.58–11.11)	0.002
Nonfatal	64 (1.1)	51 (0.9)	1.25 (0.87–1.81)	0.23
Intracranial	19 (0.3)	17 (0.3)	1.12 (0.58–2.15)	0.74
Major or minor TIMI bleeding	303 (5.0)	231 (3.8)	1.31 (1.11–1.56)	0.002
Bleeding requiring transfusion§	244 (4.0)	182 (3.0)	1.34 (1.11–1.63)	<0.001
CABG-related TIMI major bleeding¶	24 (13.4)	6 (3.2)	4.73 (1.90–11.82)	<0.001

Stephen D. Wiviott et al. N Engl J Med. 2007;357:2001-15.



# PLATO Trial

## Ticagrelor vs. Clopidogrel in patients with ACS



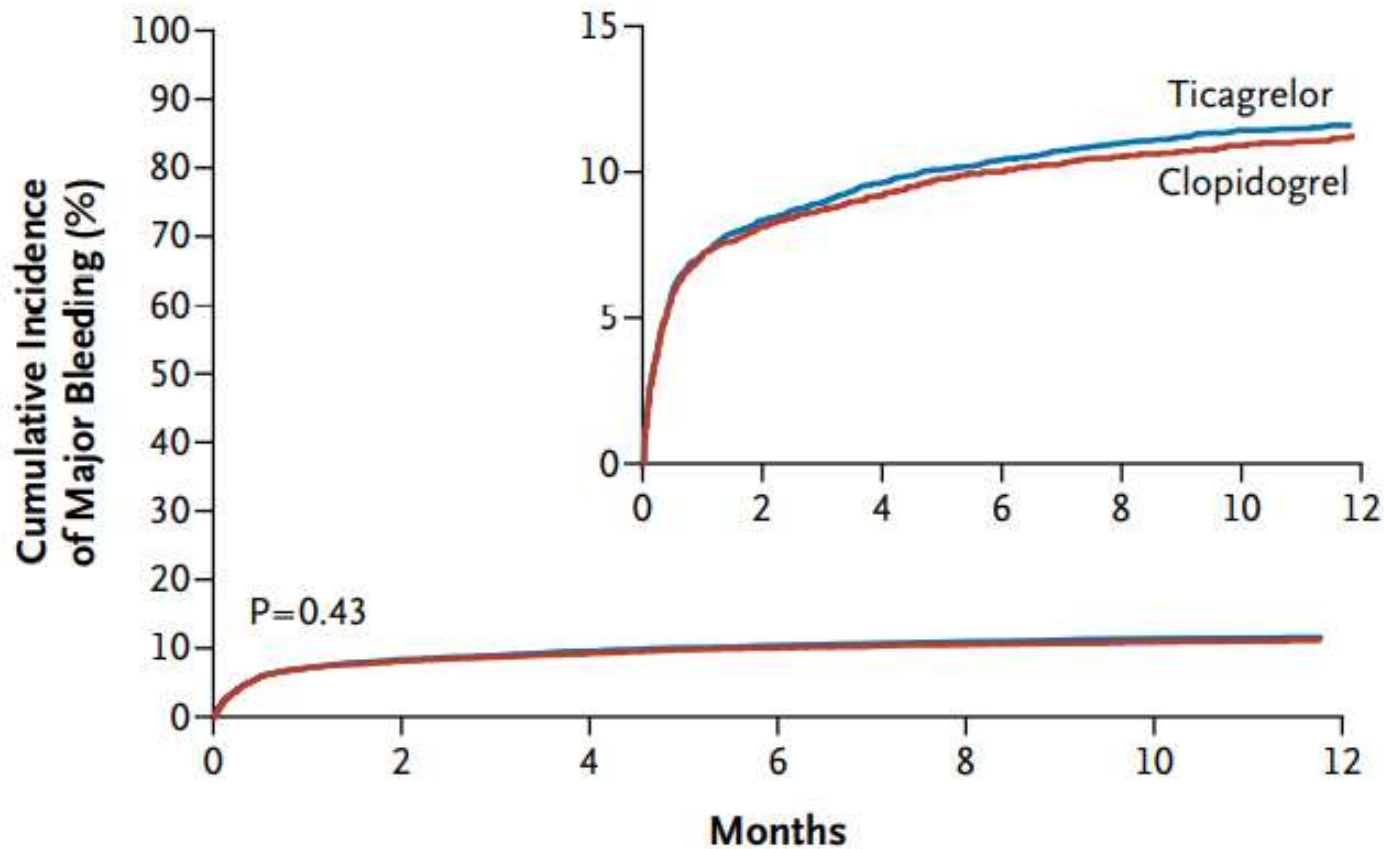
### No. at Risk

Ticagrelor	9333	8628	8460	8219	6743	5161	4147
Clopidogrel	9291	8521	8362	8124	6650	5096	4047

- The primary end point - a composite of death from vascular causes, myocardial infarction, or stroke – occurred significantly less often in the ticagrelor group than in the clopidogrel group (9.8% vs. 11.7% at 12months; hazard ratio, 0.84; 95% confidence interval, 0.77 to 0.92;  $P < 0.001$ ).

# PLATO Trial

## Ticagrelor vs. Clopidogrel in patients with ACS



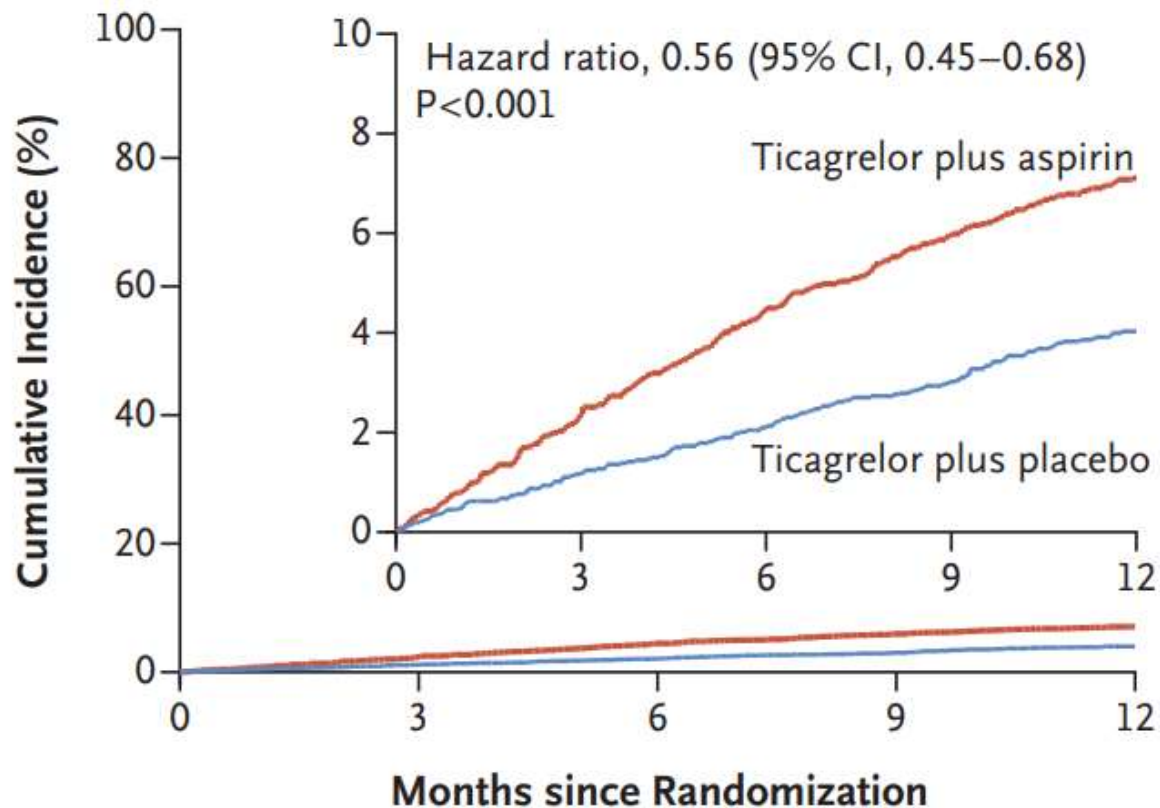
### No. at Risk

Ticagrelor	9235	7246	6826	6545	5129	3783	3433
Clopidogrel	9186	7305	6930	6670	5209	3841	3479

- The time was estimated from the first dose of the study drug in the safety population. The hazard ratio for major bleeding, defined according to the study criteria, for the ticagrelor group as compared with the clopidogrel group was 1.04 (95% confidence interval, 0.95 to 1.13).

# TWILIGHT Trial

## Ticagrelor with or without Aspirin in High-Risk patients after PCI



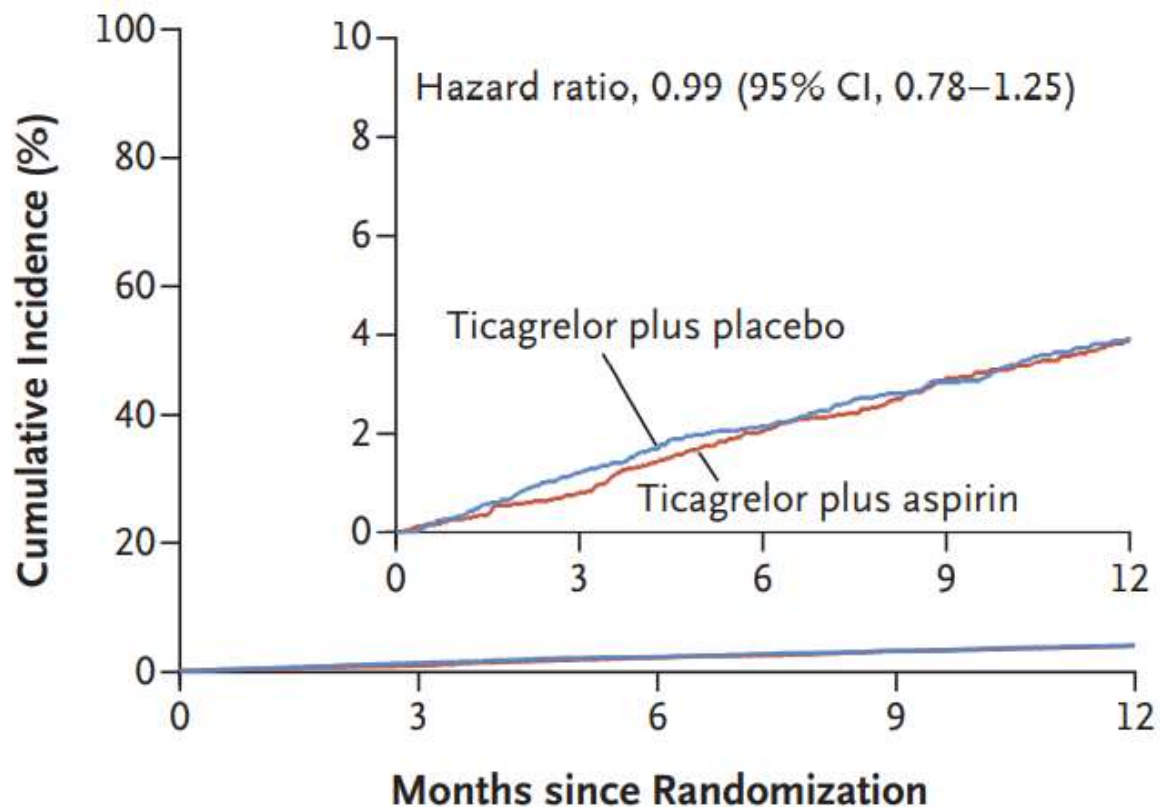
- Kaplan-Meier Estimates of the Incidence of BARC Type 2, 3, or 5 Bleeding 1 Year
- The hazard ratio shown is for ticagrelor plus placebo versus ticagrelor plus aspirin. Bleeding Academic Research Consortium (BARC) types range from 0 (no bleeding) to 5 (fatal bleeding).

### No. at Risk

Ticagrelor plus aspirin	3564	3454	3357	3277	3213
Ticagrelor plus placebo	3555	3474	3424	3366	3321

# TWILIGHT Trial

## Ticagrelor with or without Aspirin in High-Risk patients after PCI



### No. at Risk

Ticagrelor plus aspirin	3515	3466	3415	3361	3320
Ticagrelor plus placebo	3524	3457	3412	3365	3330

- Kaplan-Meier Estimates of the Incidence of Death from Any Cause, Nonfatal MI, or Nonfatal Stroke 1 Year
- The per-protocol population included patients who underwent randomization and had no major deviations from the protocol. The hazard ratio shown is for ticagrelor plus placebo versus ticagrelor plus aspirin.



# TWILIGHT Trial

## Ticagrelor with or without Aspirin in High-Risk patients after PCI

**Table 2. Bleeding and Ischemic Events 1 Year after Randomization.\***

Variable	Ticagrelor plus Placebo (N=3555)	Ticagrelor plus Aspirin (N=3564)	Hazard Ratio (95% CI)†	P Value
	no. of patients (%)‡			
<b>Bleeding end points</b>				
Primary end point: BARC type 2, 3, or 5§	141 (4.0)	250 (7.1)	0.56 (0.45–0.68)	<0.001¶
BARC type 3 or 5§	34 (1.0)	69 (2.0)	0.49 (0.33–0.74)	
TIMI minor or major	141 (4.0)	250 (7.1)	0.56 (0.45–0.68)	
GUSTO moderate or severe	26 (0.7)	49 (1.4)	0.53 (0.33–0.85)	
ISTH major	39 (1.1)	72 (2.1)	0.54 (0.37–0.80)	
<b>Ischemic end points</b>				
Death from any cause, nonfatal myocardial infarction, or nonfatal stroke	135 (3.9)	137 (3.9)	0.99 (0.78–1.25)	<0.001
Death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal ischemic stroke	126 (3.6)	130 (3.7)	0.97 (0.76–1.24)	
Death from any cause	34 (1.0)	45 (1.3)	0.75 (0.48–1.18)	
Death from cardiovascular causes	26 (0.8)	37 (1.1)	0.70 (0.43–1.16)	
Myocardial infarction	95 (2.7)	95 (2.7)	1.00 (0.75–1.33)	
Ischemic stroke	16 (0.5)	8 (0.2)	2.00 (0.86–4.67)	
Stent thrombosis, definite or probable	14 (0.4)	19 (0.6)	0.74 (0.37–1.47)	

- Among high-risk patients who underwent PCI and completed 3 months of dual antiplatelet therapy, ticagrelor monotherapy was associated with a lower incidence of clinically relevant bleeding than ticagrelor plus aspirin, with no higher risk of death, myocardial infarction, or stroke.

# DAPT Duration After Implantation of DES

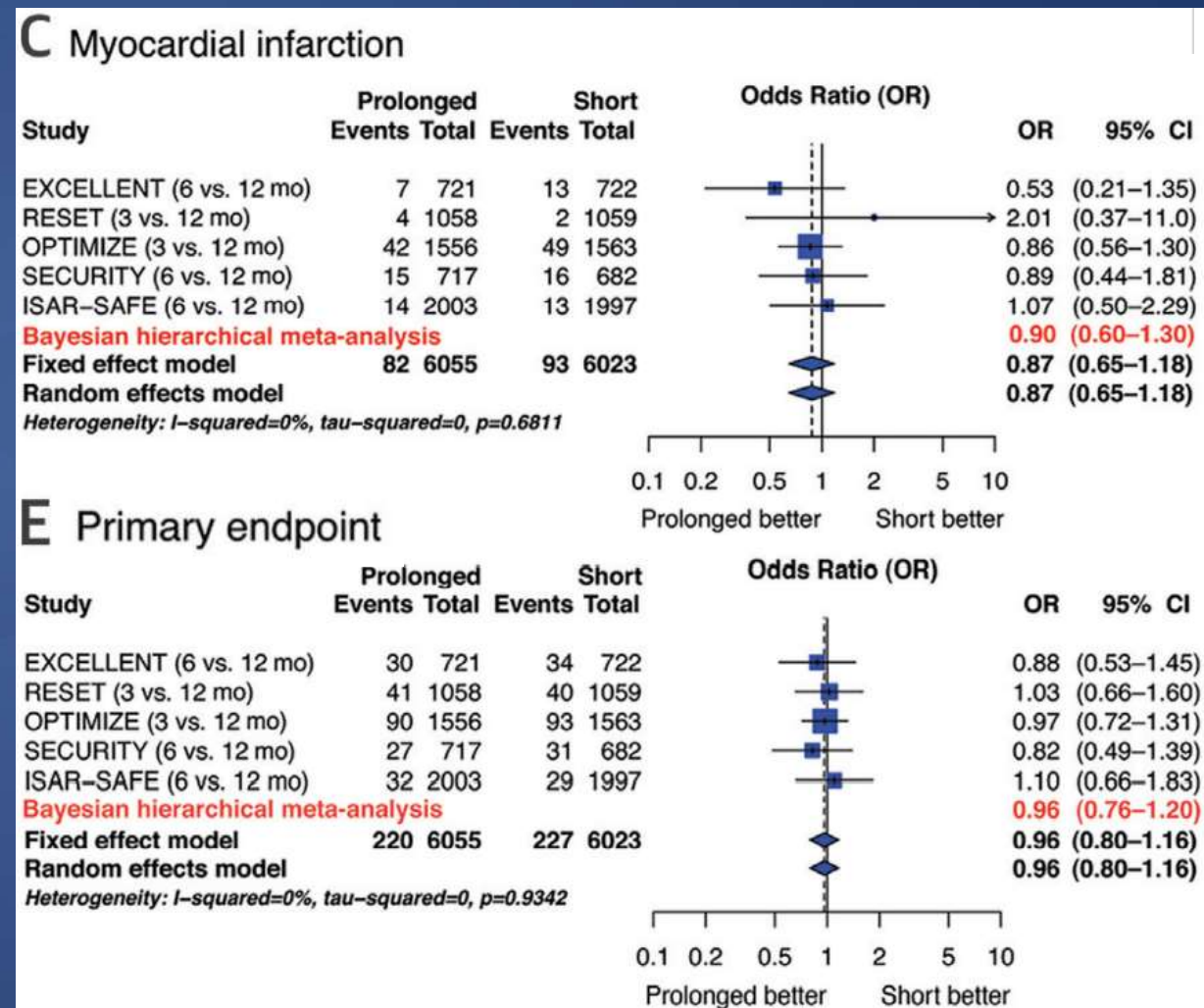
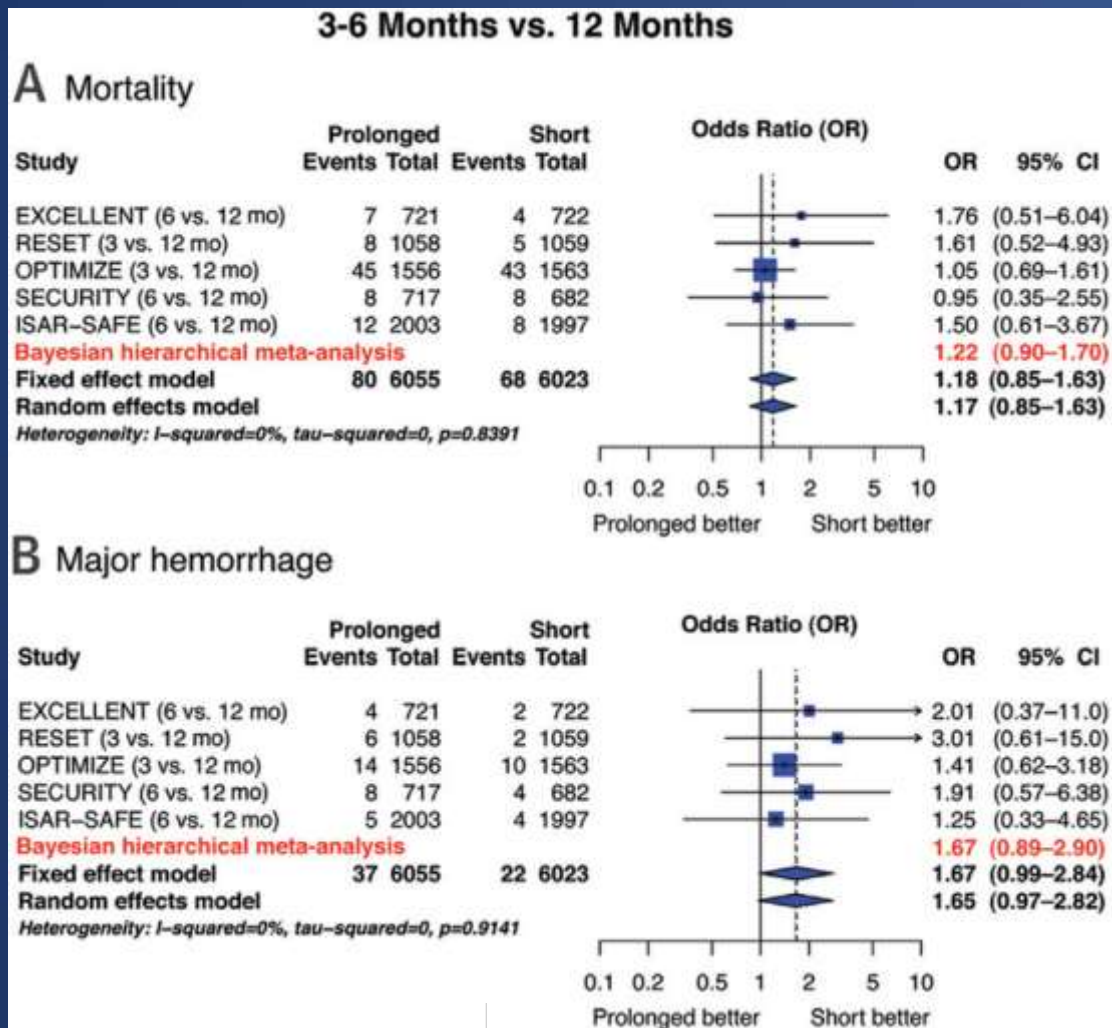
# DAPT Duration After Implantation of DES

Study	Year*	Trial Completion	Primary Study Endpoint	Trial Design and Outcome	Expected Event Rate in Control Group (%)	Observed Event Rate in Control Group (%)	Proportion With Newer-Generation DES (%)
DES LATE (12 vs. 36 mo) (13)	2010	Extension of ZEST-LATE and REAL-LATE (12)	Cardiac death, MI, or stroke <24 h	Superiority not shown	2.7	2.6	30
PRODIGY (6 vs. 24 mo) (14,15)	2012	Enrollment completed	Death, MI, or stroke	Superiority not shown	8.0	10.1	67
EXCELLENT (6 vs. 12 mo) (16)	2012	Enrollment completed	Cardiac death, MI, or ischemia-driven TVR	Noninferiority confirmed	10.0	4.5	75
RESET (3 vs. 12 mo) (17)	2012	Enrollment completed	Cardiac death, MI, ST, revasc, or bleeding	Noninferiority confirmed	10.5	4.7	85
OPTIMIZE (3 vs. 12 mo) (18)	2013	Enrollment completed	NACCE-death, MI, stroke, or bleed	Noninferiority confirmed	9.0	6.0	100
ARCTIC Interruption (12 vs. 18 mo) (19)	2014	Extension of ARCTIC (39)	Death, MI, ST, stroke, or urgent TVR	Superiority not shown	6.0	4.0	63
SECURITY (6 vs. 12 mo) (20)	2014	Stopped after 1,399 enrolled of 2,740 planned	Cardiac death, MI, ST, or stroke	Noninferiority confirmed	4.5	4.5	100
ITALIC (6 vs. 24 mo) (21)	2015	Stopped after 2,031 enrolled of 2,475 planned	Death, MI, urgent TVR, stroke, or major bleeding	Noninferiority confirmed	3.0	1.5	100
ISAR-SAFE (6 vs. 12 mo) (22)	2015	Stopped after 4,005 enrolled of 6,000 planned	Death, MI, ST, stroke, or TIMI major bleed	Noninferiority confirmed	10.0	1.5	72
DAPT (12 vs. 30 mo) (23)	2015	Enrollment completed	Coprietary: ST and MACCE	Superiority shown	0.5/2.9	0.5/2.4	59
OPTIDUAL (12 vs. 48 mo) (24)	2015	Stopped after 1,385 enrolled of 1,966 planned	Death, MI, stroke, or major bleed	Superiority not shown	7.0	7.5	59



# DAPT Duration After Implantation of DES

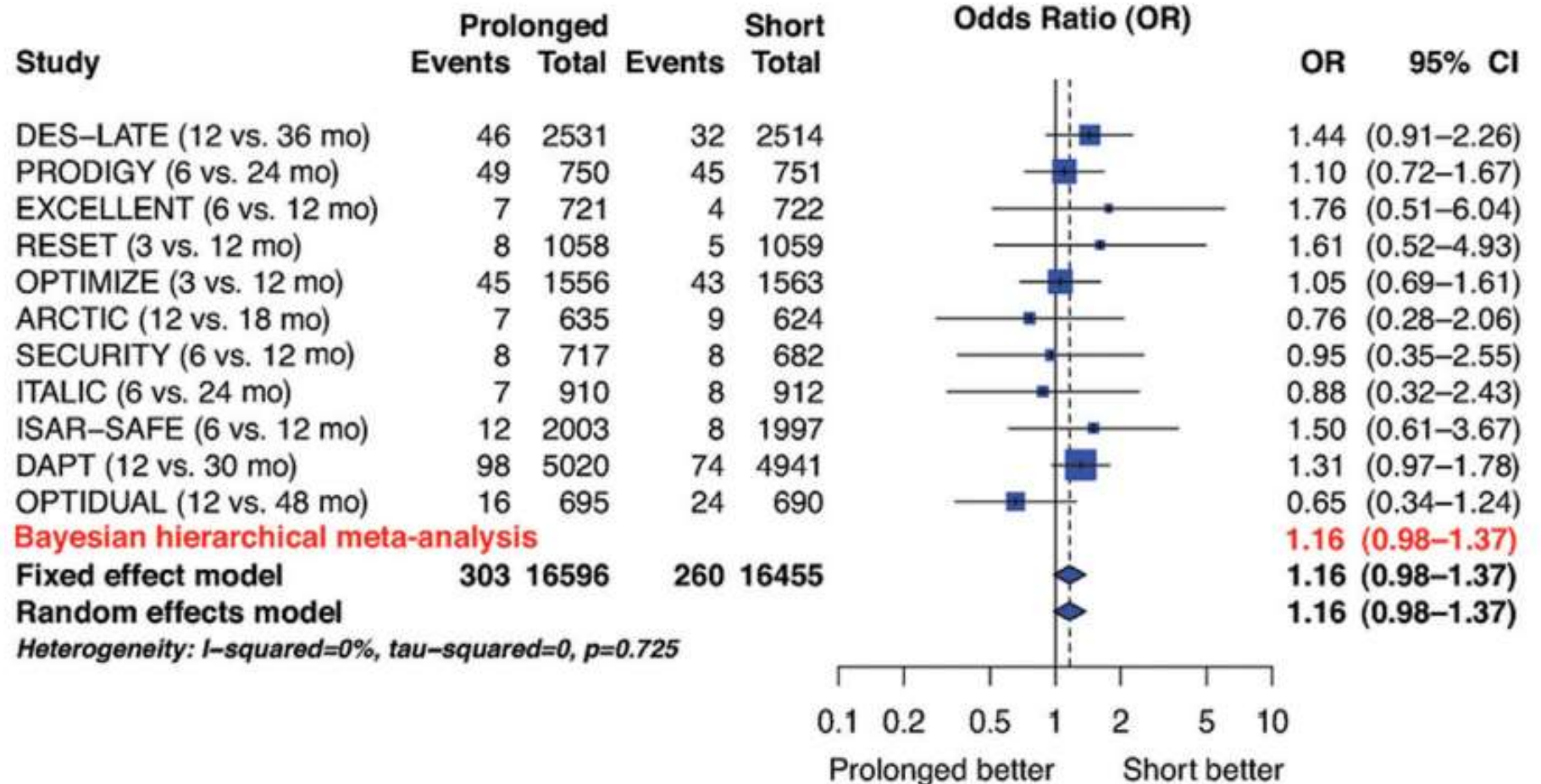
## Forest Plot of Endpoints After 12 Months Versus Shorter Courses





# DAPT Duration After Implantation of DES

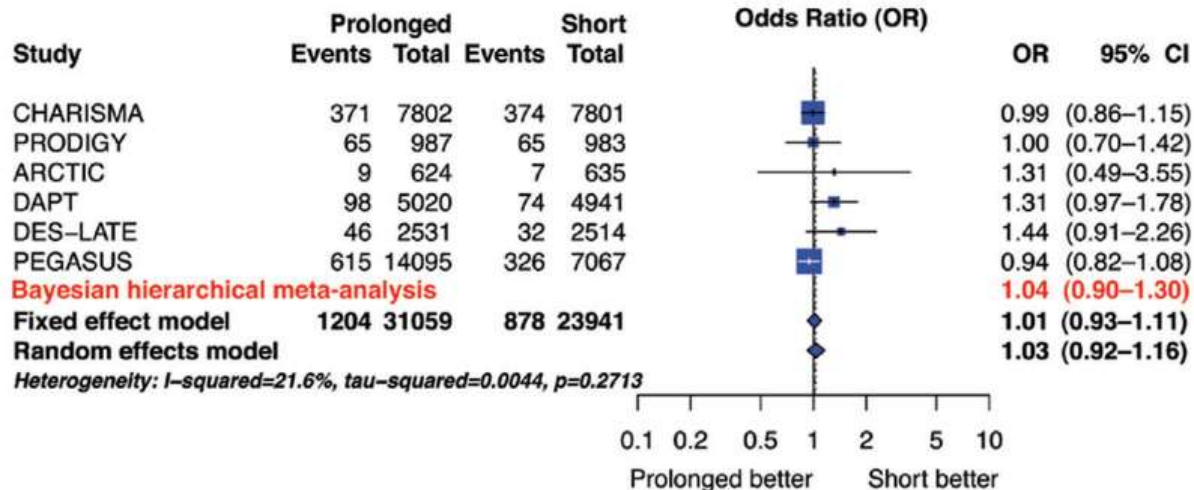
**FIGURE 3** Forest Plot of Mortality Rates in 11 RCTs After Stent Implantation



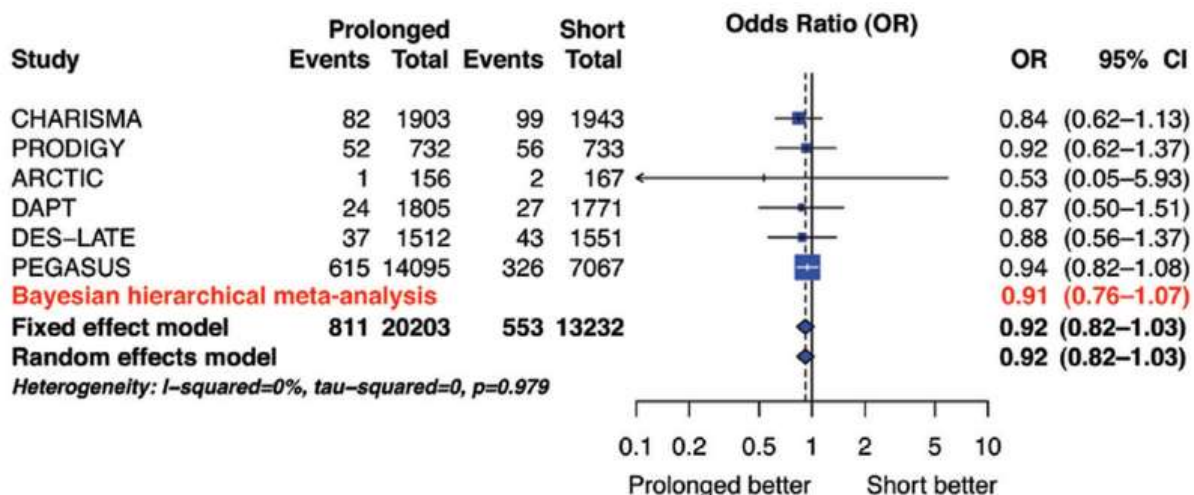
# DAPT Duration After Implantation of DES

All-Cause Mortality Rate in All Patients (A) and in Those With (B) and Without (C) A Prior History of ACS

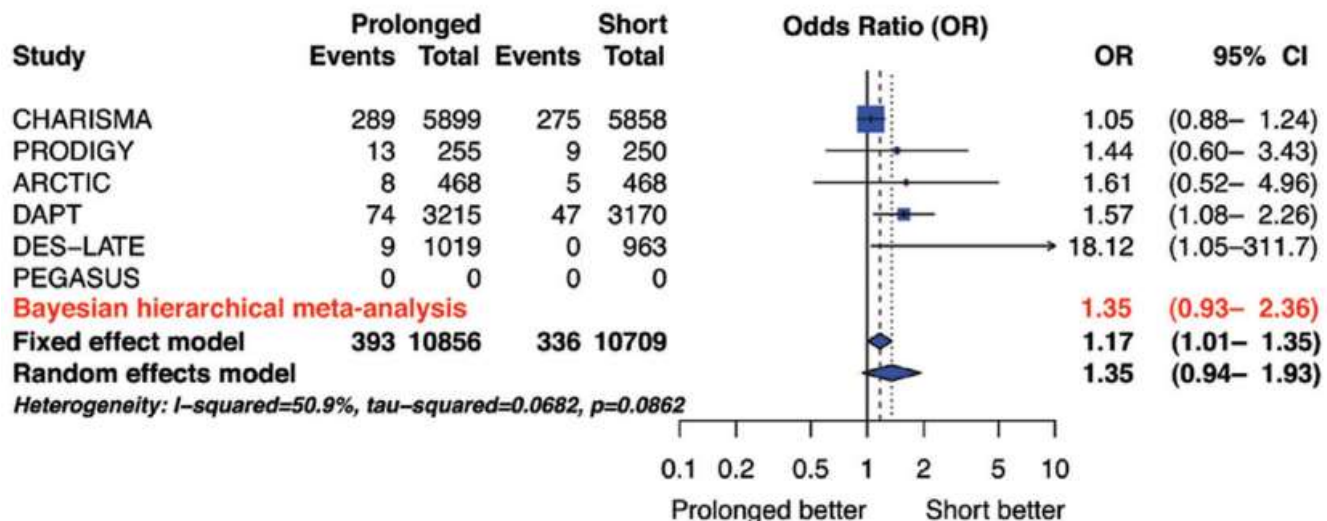
## A Overall



## B History of Acute Coronary Syndromes

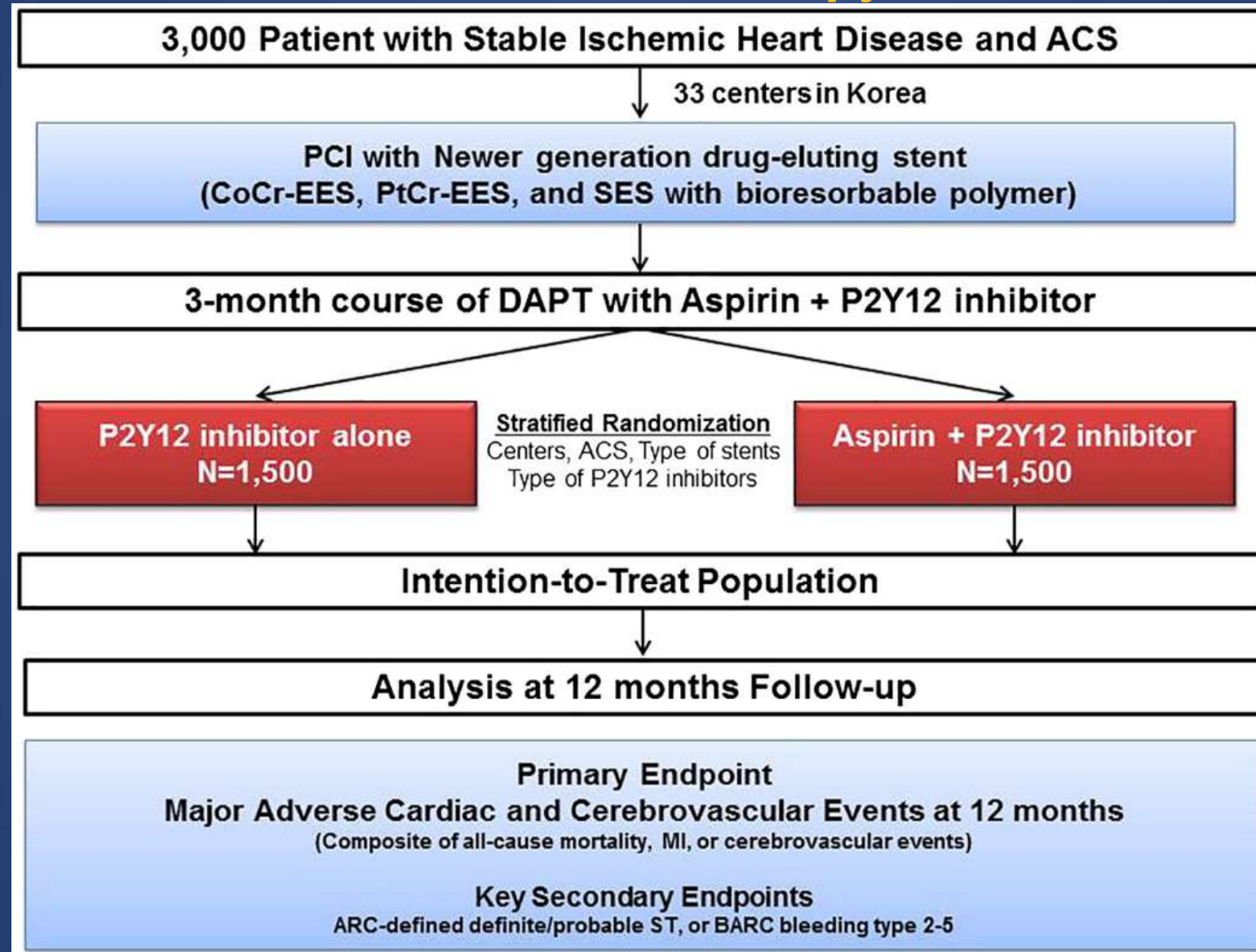


## C No History of Acute Coronary Syndrome



# SMART-CHOICE Trial

## Effect of P2Y12 Inhibitor Monotherapy vs DAPT after PCI

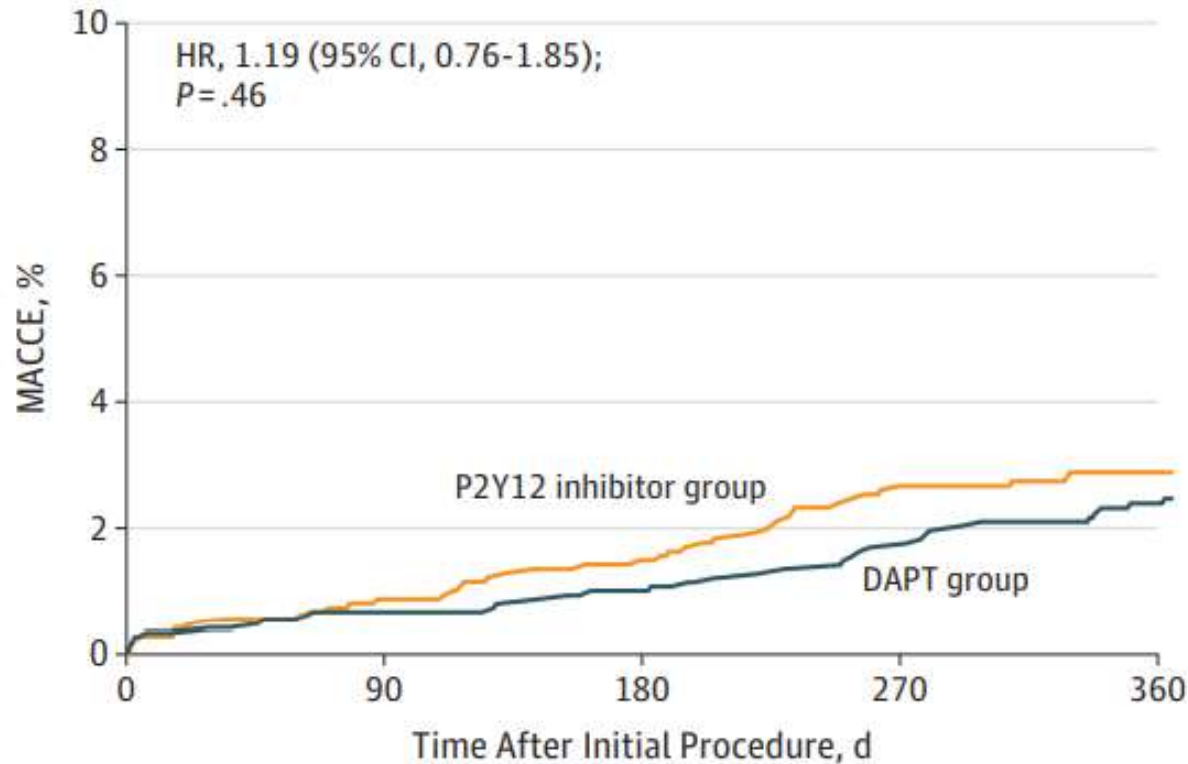




# SMART-CHOICE Trial

## Effect of P2Y12 Inhibitor Monotherapy vs DAPT after PCI

**A** Composite events (primary outcome)



No. at risk	0	90	180	270	360
DAPT	1498	1471	1454	1436	1220
P2Y12 inhibitor	1495	1456	1430	1402	1202

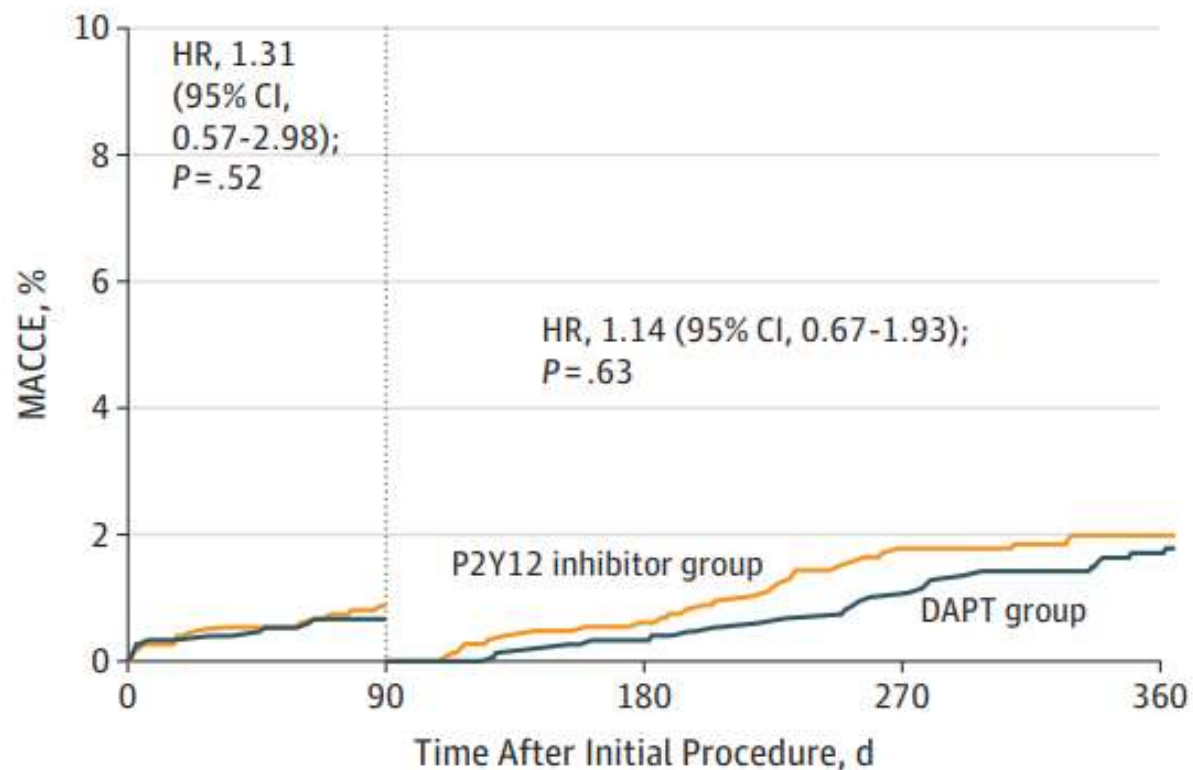
- Results of the analysis of the primary end point of major adverse cardiovascular and cerebrovascular events (a composite of death, myocardial infarction, or stroke) at 12 months.
- Cumulative rates of MACCE at 12 months were 2.9% for the P2Y12 inhibitor monotherapy group and 2.5% for the DAPT group (difference, 0.4%;  $P = .007$  for noninferiority of P2Y12 monotherapy)



# SMART-CHOICE Trial

## Effect of P2Y12 Inhibitor Monotherapy vs DAPT after PCI

**B** Landmark analysis of composite events

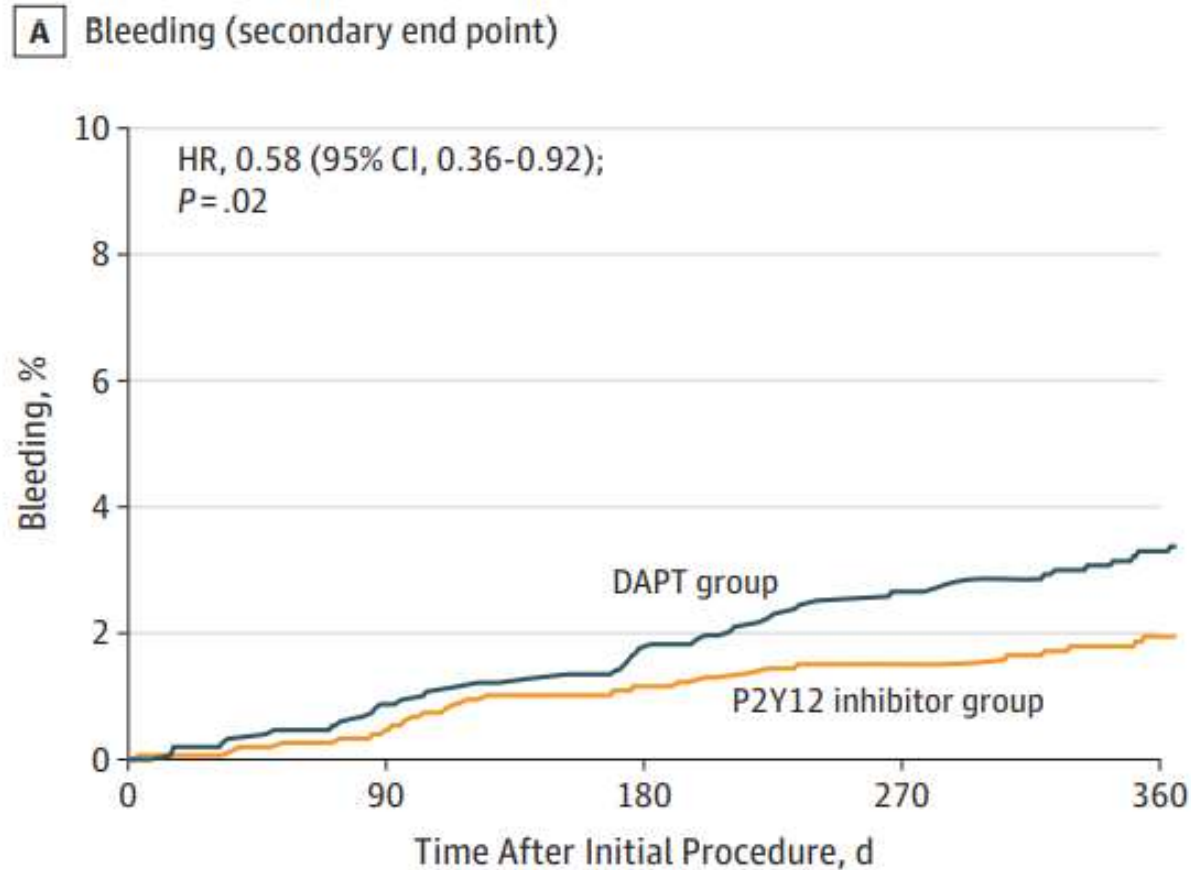


No. at risk	0	90	180	270	360
DAPT	1498	1471	1454	1436	1220
P2Y12 inhibitor	1495	1456	1430	1402	1202

- Results of the landmark analysis at 3 months (the point after which one group received P2Y12 inhibitor only and the other received DAPT) for the primary end point.
- The risk of MACCE between 3 and 12 months was not significantly different between the group (hazard ratio, 1.14; 95% CI, 0.67-1.93; P = .63)

# SMART-CHOICE Trial

## Effect of P2Y12 Inhibitor Monotherapy vs DAPT after PCI

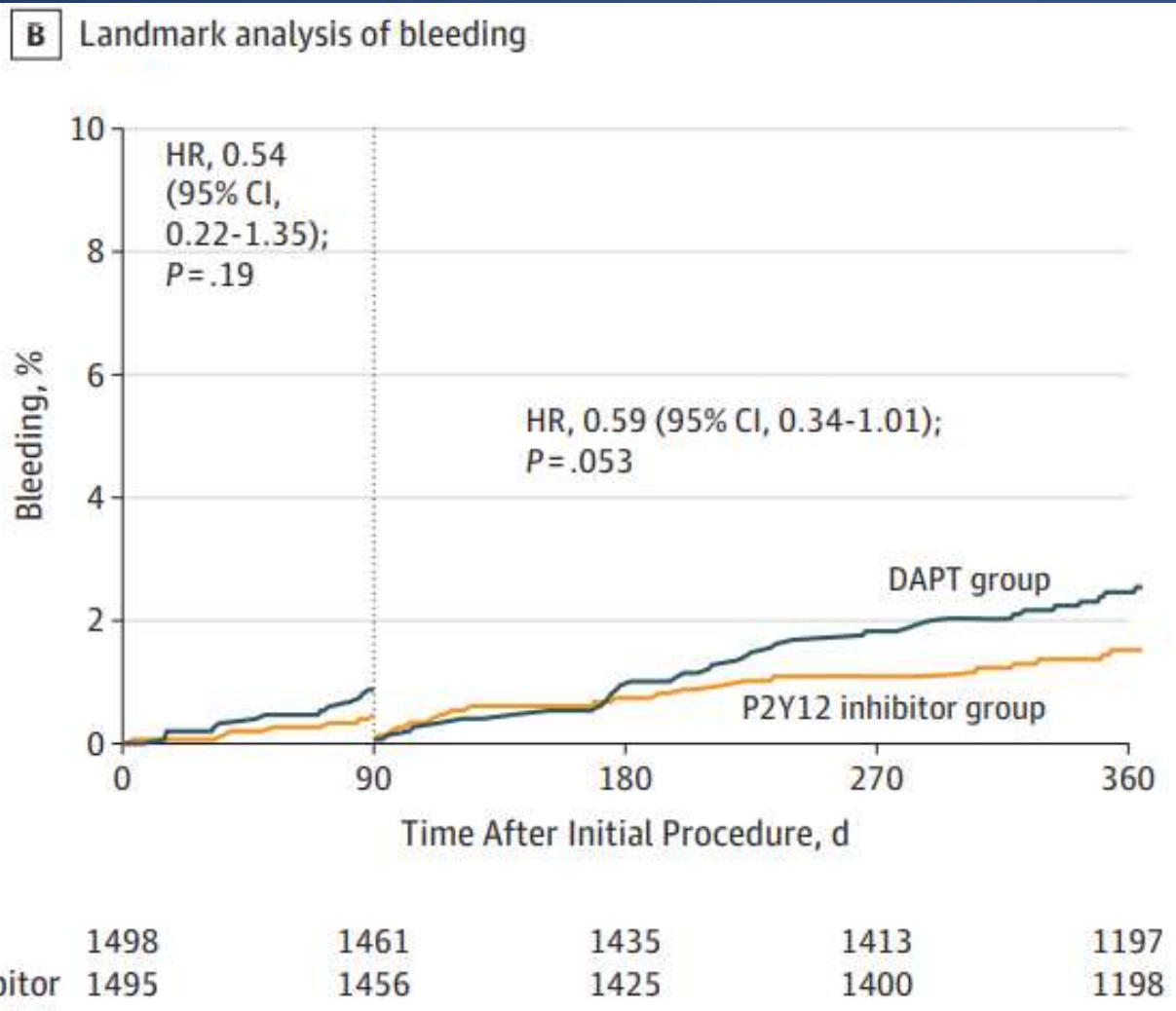


No. at risk					
DAPT	1498	1461	1435	1413	1197
P2Y12 inhibitor	1495	1456	1425	1400	1198

- Results of the analysis of the bleeding at 12 months.
- The rate of bleeding was significantly lower in the P2Y12 inhibitor monotherapy group than in the DAPT group (2.0% vs 3.4%; hazard ratio, 0.58 ; 95% CI, 0.36-0.92; P = .02)

# SMART-CHOICE Trial

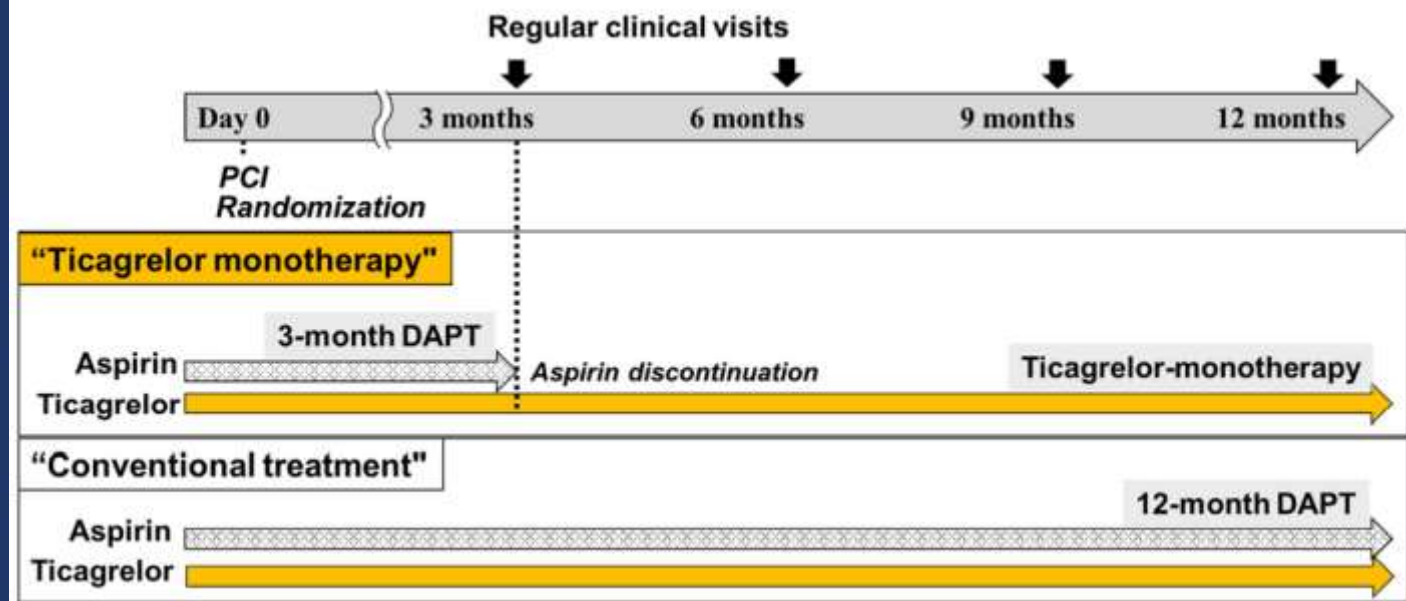
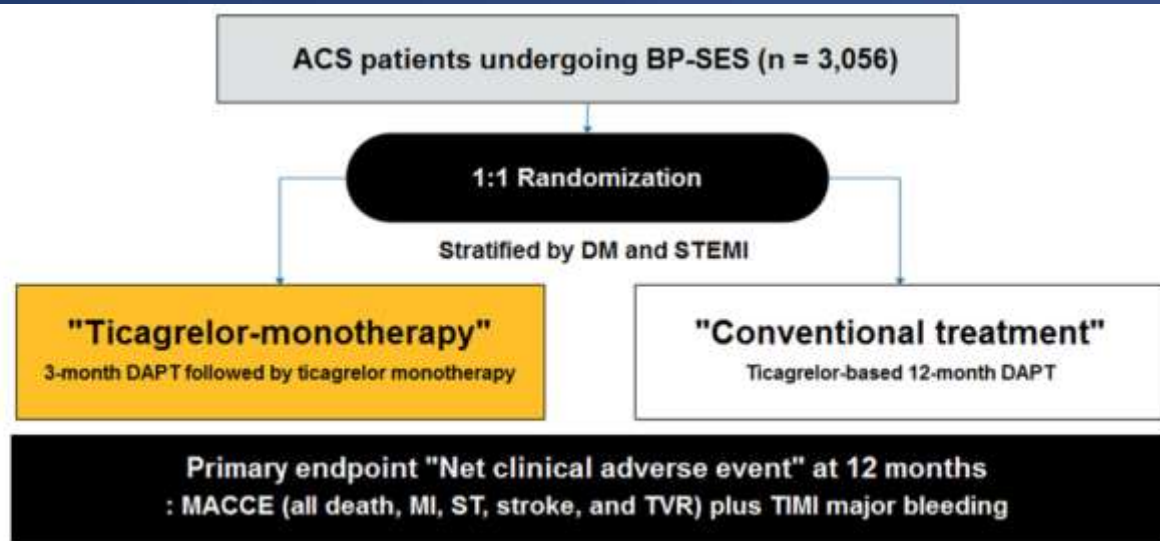
## Effect of P2Y12 Inhibitor Monotherapy vs DAPT after PCI



- Results of the landmark analysis at 3 months (the point after which one group received P2Y12 inhibitor only and the other received DAPT) for bleeding.
- There was no significant difference in the risk of bleeding between the groups in the post hoc 3-month landmark analysis (hazard ratio, 0.59; 95% CI, 0.34-1.01;  $P = 0.053$ )

# TICO Trial

## Effect of Ticagrelor mono vs Ticagrelor with Aspirin in patients with ACS

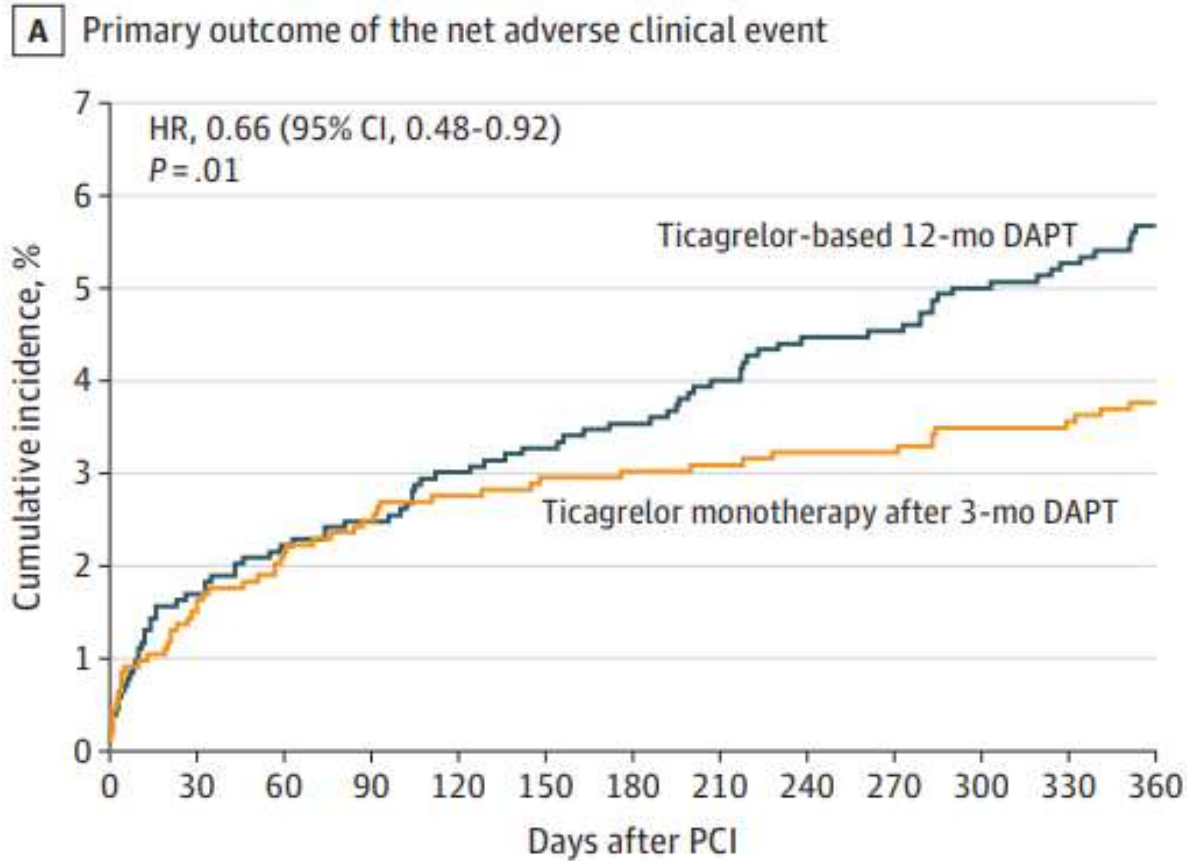


- The primary outcome  
A 1-year net adverse clinical event;  
a composite of major bleeding and  
adverse cardiac and  
cerebrovascular events (death, MI,  
stent thrombosis, stroke, or TVR)



# TICO Trial

## Effect of Ticagrelor mono vs Ticagrelor with Aspirin in patients with ACS



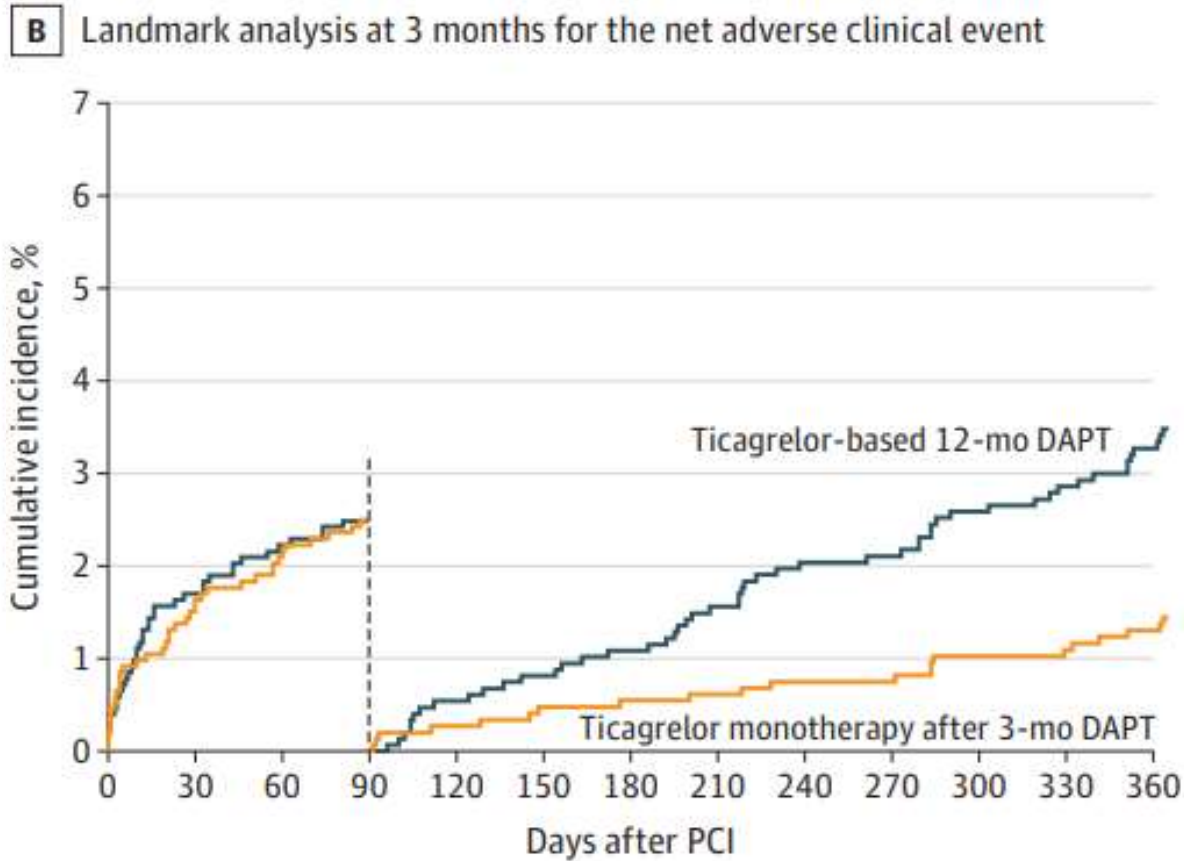
No. at risk

12-mo DAPT	1529	1500	1489	1481	1466	1460	1455	1442	1432	1430	1423	1418	1407
3-mo DAPT	1527	1498	1483	1471	1462	1456	1452	1442	1437	1437	1432	1430	1424

- The primary outcome of a net adverse clinical event occurred in 59 patients (3.9%) receiving ticagrelor monotherapy after 3-month DAPT and in 89 patients (5.9%) receiving ticagrelor-based 12-month DAPT (absolute difference, -1.98% [95% CI, -3.50% to -0.45%]; HR, 0.66 [95% CI, 0.48 to 0.92]; P = .01)

# TICO Trial

## Effect of Ticagrelor mono vs Ticagrelor with Aspirin in patients with ACS



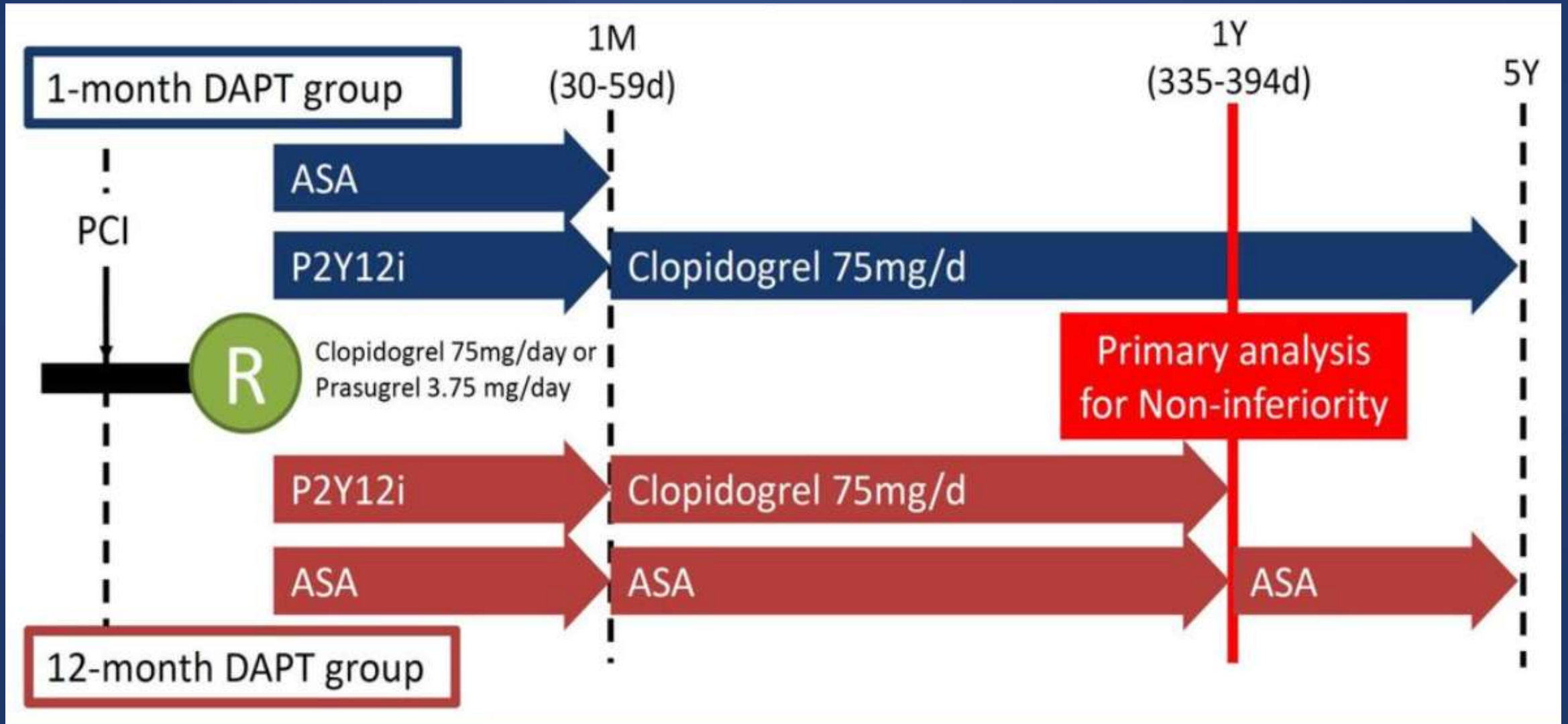
No. at risk

12-mo DAPT	1529	1500	1489	1481	1466	1460	1455	1442	1432	1430	1423	1418	1407
3-mo DAPT	1527	1498	1483	1471	1462	1456	1452	1442	1437	1437	1432	1430	1424

- On prespecified 3-month landmark analyses between 3 and 12 months, a net adverse clinical event occurred in 21 patients (1.4%) receiving ticagrelor monotherapy after 3-month DAPT and in 51 patients (3.5%) receiving ticagrelor-based 12-month DAPT (HR, 0.41 [95% CI, 0.25 to 0.68];  $P = 0.001$ )

# STOPDAPT-2 Trial

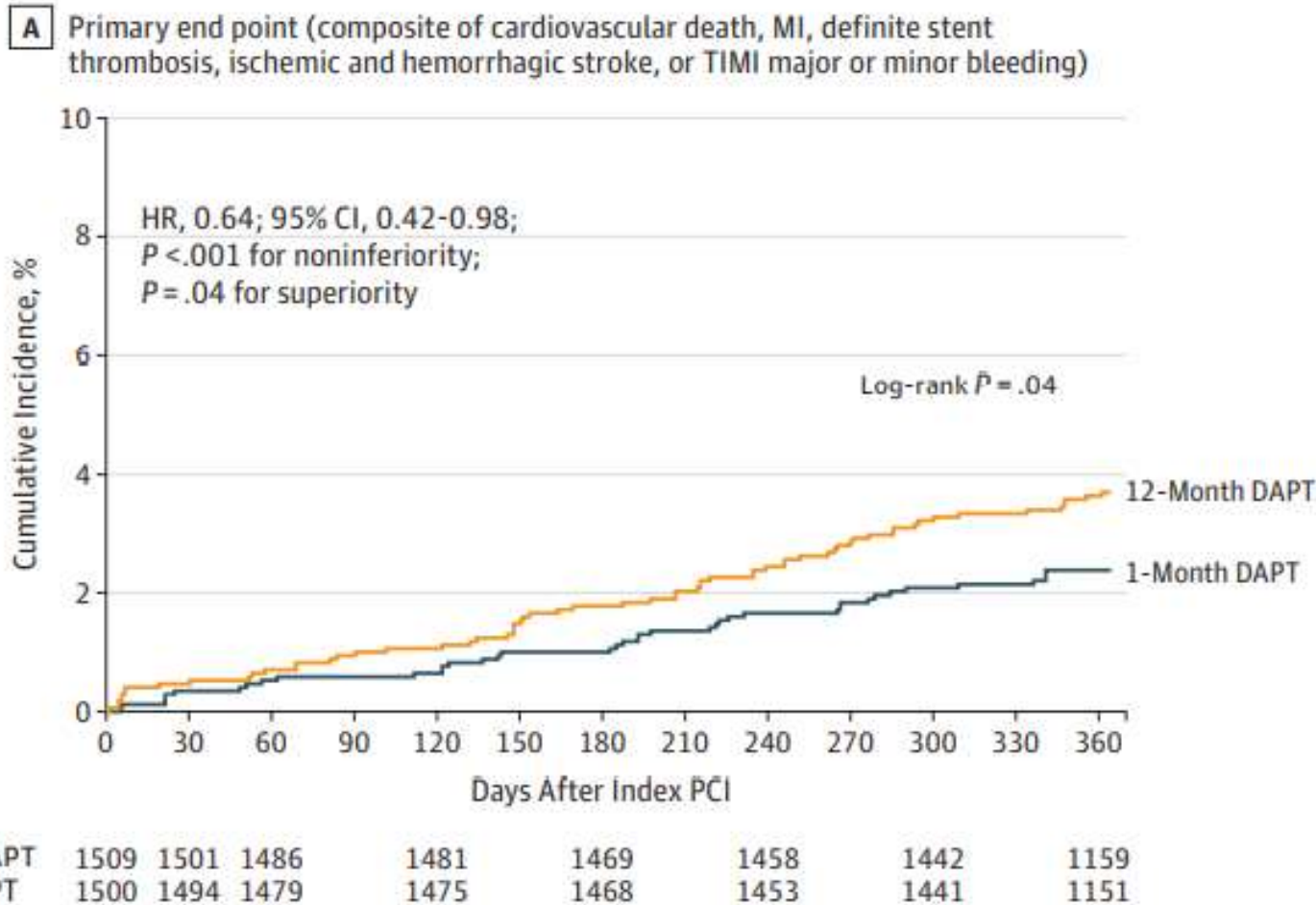
Effect of 1M DAPT followed by clopidogrel vs 12M DAPT after PCI



Watanabe et al., JAMA 2019;321:2414

# STOPDAPT-2 Trial

## Effect of 1M DAPT followed by clopidogrel vs 12M DAPT after PCI

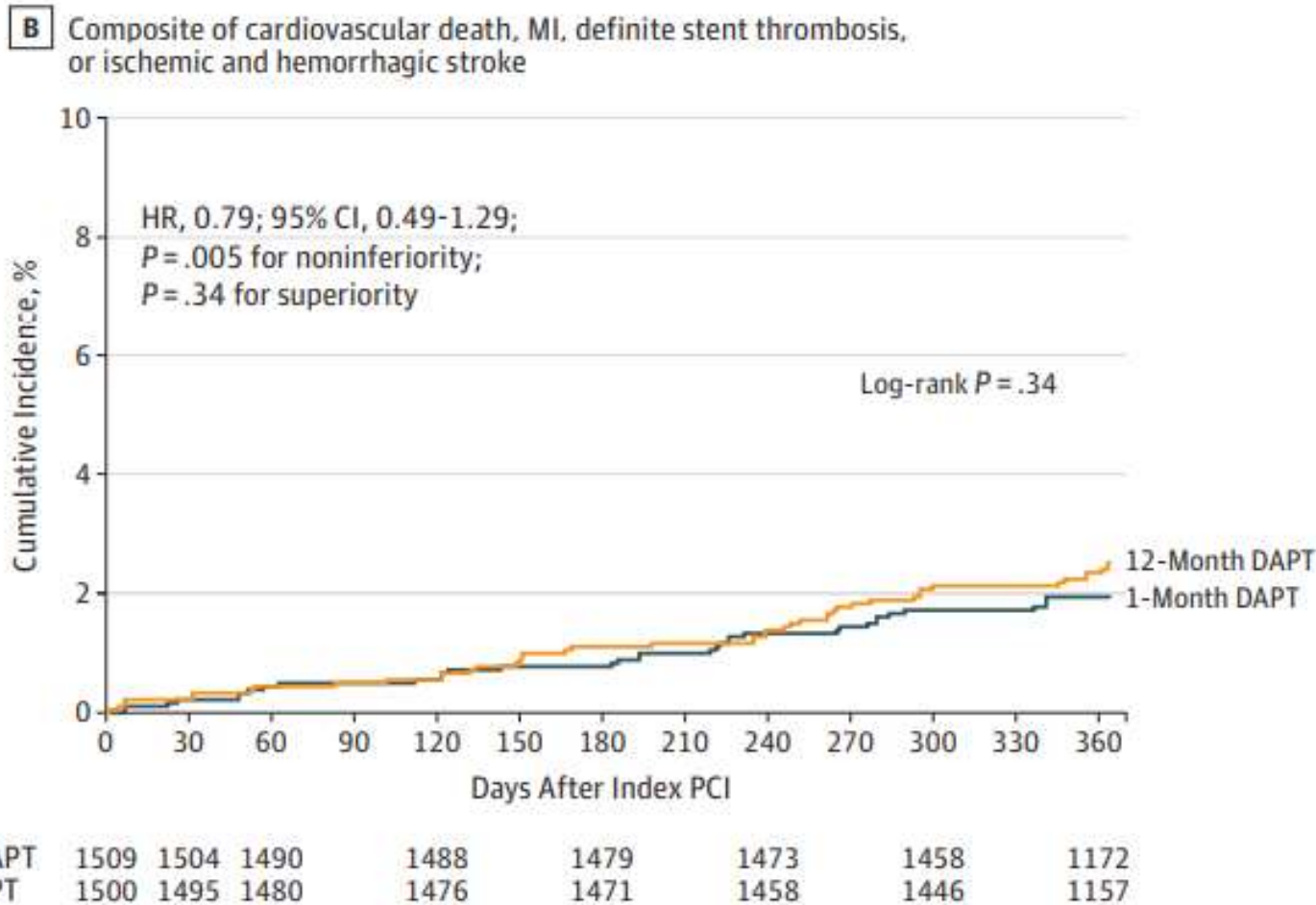


- The primary end point occurred in 35 patients (2.36%) in the 1M DAPT
- occurred in 55 patients (3.70%) in the 12M DAPT
- 1M DAPT to 12M DAPT (absolute difference, -1.34% [95% CI, -2.57% to -0.11%]; HR, 0.64 [95% CI, 0.42-0.98];  $P < .001$  for noninferiority;  $P = .04$  for superiority)



# STOPDAPT-2 Trial

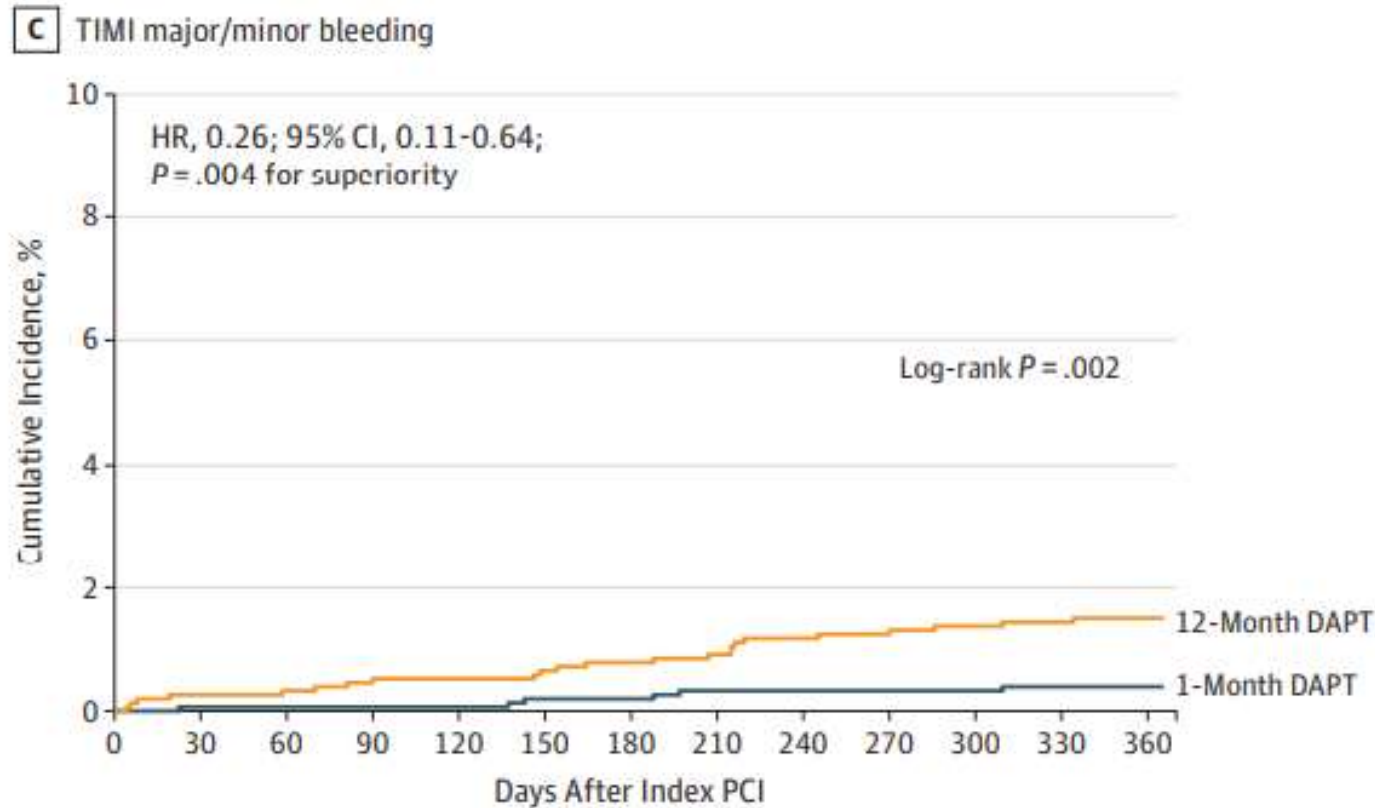
## Effect of 1M DAPT followed by clopidogrel vs 12M DAPT after PCI



- For the major secondary cardiovascular end point
- 1M DAPT to 12M DAPT (1.96% vs 2.51%; absolute difference, -0.55% [95% CI, -1.62% to -0.52%]; HR, 0.79 [95% CI, 0.49-1.29]; P = .005 for noninferiority; P = .34 for superiority)

# STOPDAPT-2 Trial

## Effect of 1M DAPT followed by clopidogrel vs 12M DAPT after PCI

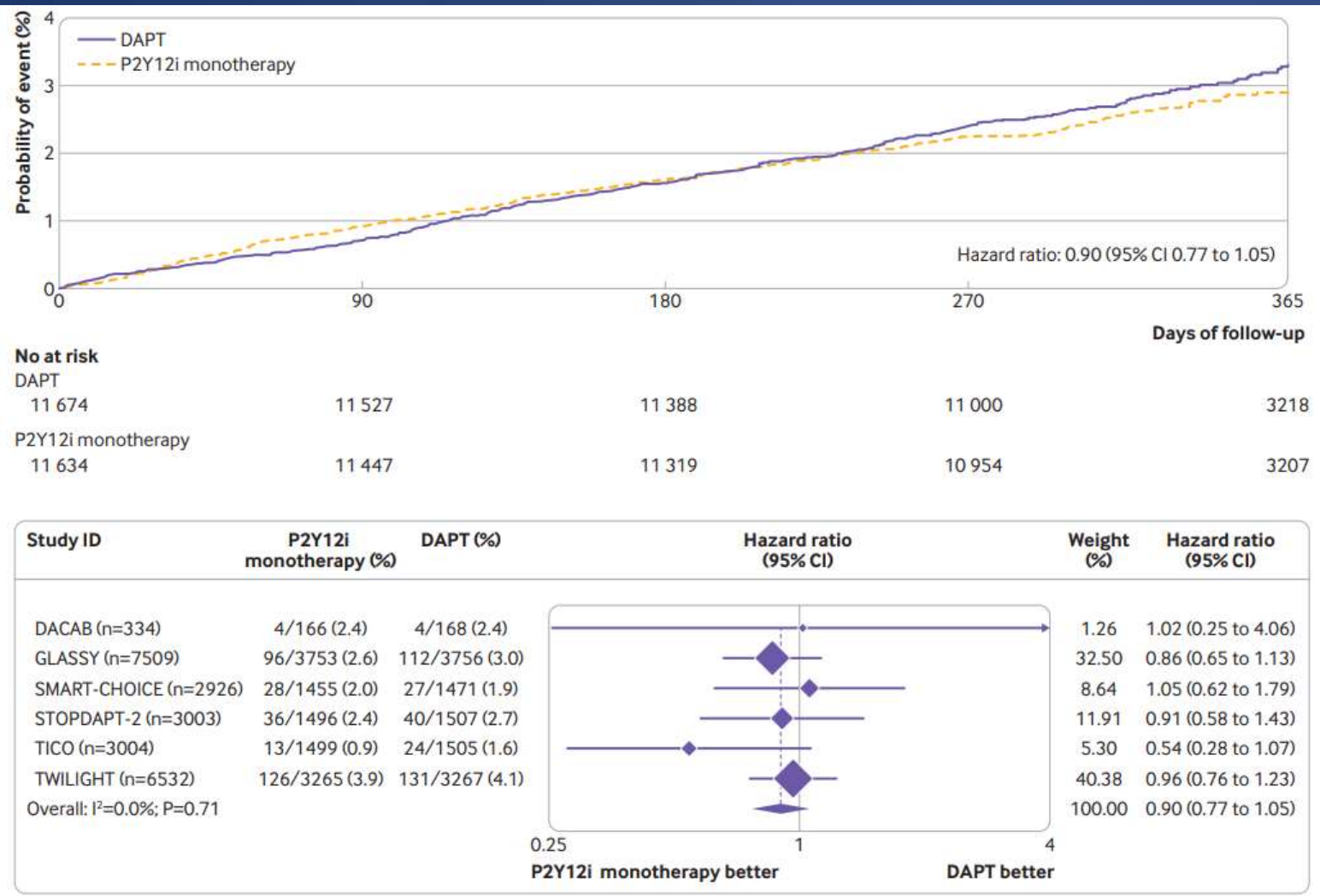


No. at risk	0	30	60	90	120	150	180	210	240	270	300	330	360
12-month DAPT	1509	1504	1491		1487	1480	1471	1462		1457		1180	
1-month DAPT	1500	1495	1483		1481	1477	1467	1457					1166

- For the major secondary bleeding end point
- 1M DAPT to 12M DAPT (0.41% vs 1.54%; absolute difference, -1.13% [95% CI, -1.84% to -0.42%]; HR, 0.26 [95% CI, 0.11-0.64];  $P = .004$ )

# P2Y12 inhibitor monotherapy or DAPT after PCI

## : Individual patient level meta-analysis of RCTs



- For primary endpoint of all cause death, myocardial infarction, or stroke in intention to treat population.

Fig 1 | Hazard ratios for individual trials and for pooled population and Kaplan-Meier estimates for primary endpoint of all cause death, myocardial infarction, or stroke in intention to treat population. Kaplan-Meier curves and hazard ratios from one step, fixed effect meta-analysis (top) and two step, fixed effect meta-analysis (bottom). DAPT=dual antiplatelet therapy; P2Y12i=P2Y<sub>12</sub> inhibitor monotherapy

# P2Y12 inhibitor monotherapy or DAPT after PCI

## : Individual patient level meta-analysis of RCTs

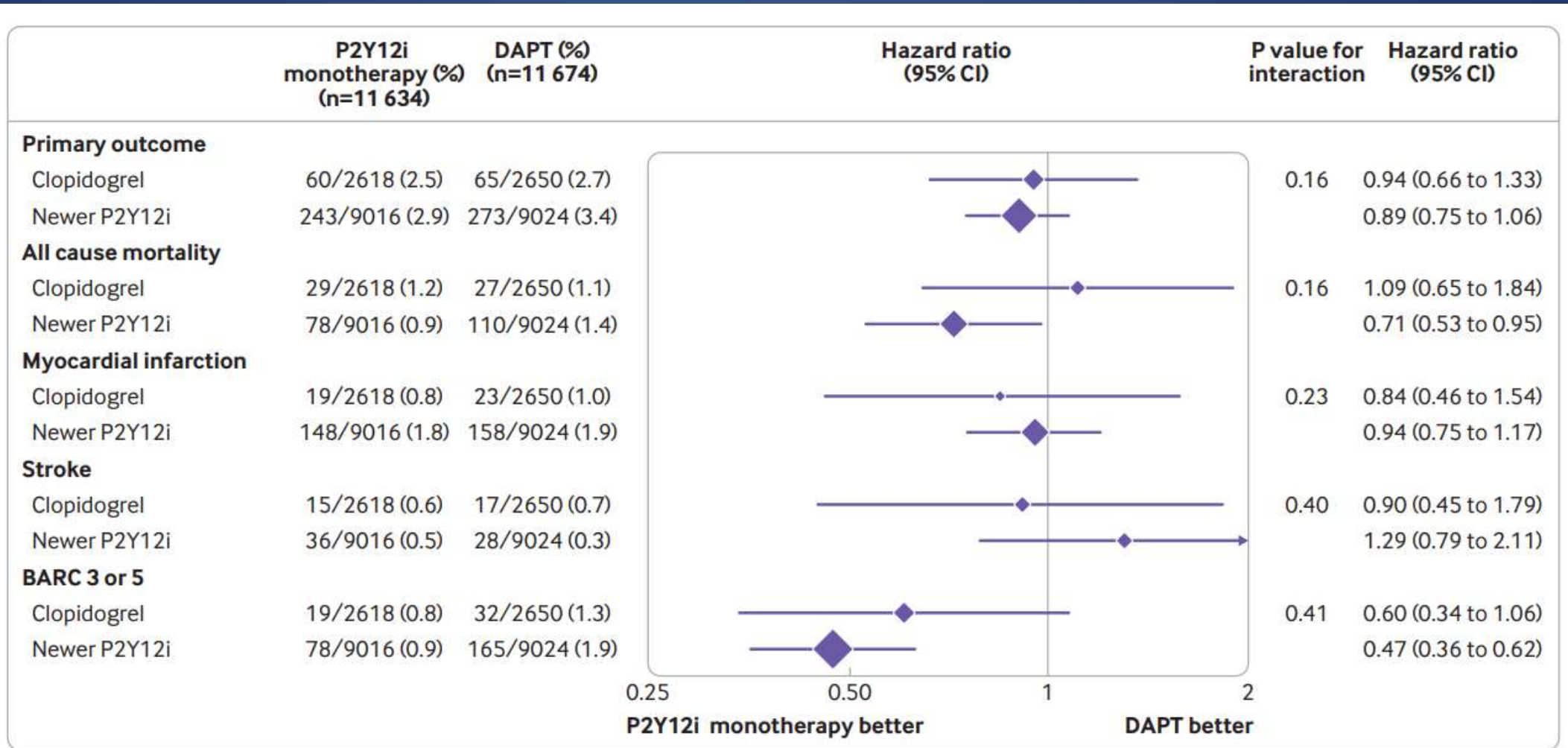
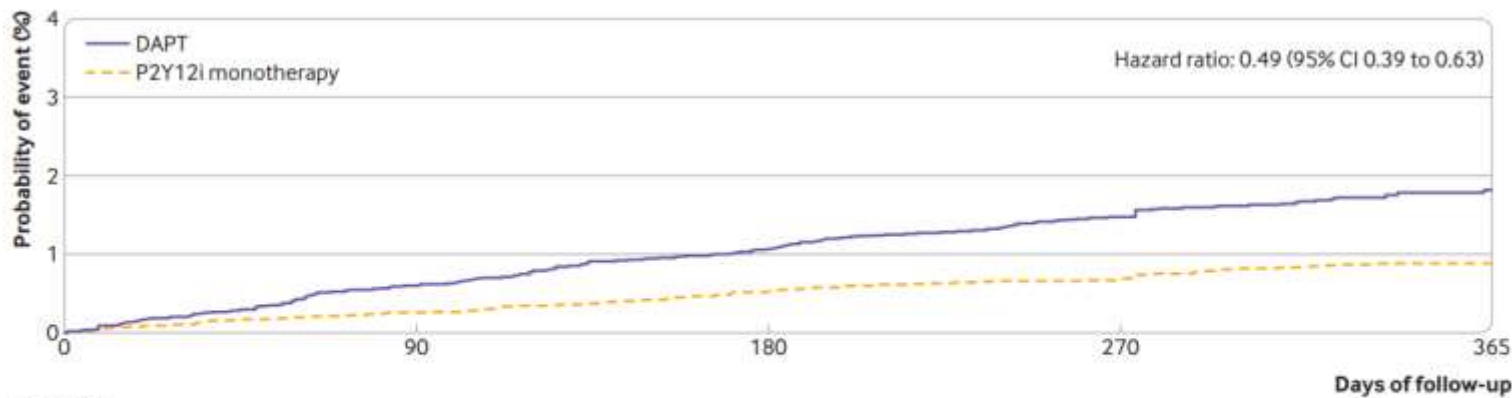


Fig 4 | Primary endpoint or its components and key safety endpoint stratified by use of clopidogrel or newer P2Y<sub>12</sub> inhibitors in experimental arm of intention to treat population. BARC=Bleeding Academy Research Consortium; DAPT=dual antiplatelet therapy



# P2Y12 inhibitor monotherapy or DAPT after PCI

## : Individual patient level meta-analysis of RCTs



No at risk	0	90	180	270	365
DAPT	11 674	11 511	11 382	11 006	3243
P2Y12i monotherapy	11 634	11 487	11 380	11 033	3270

- For safety endpoint of BARC type 3 or type 5 in intention to treat population.

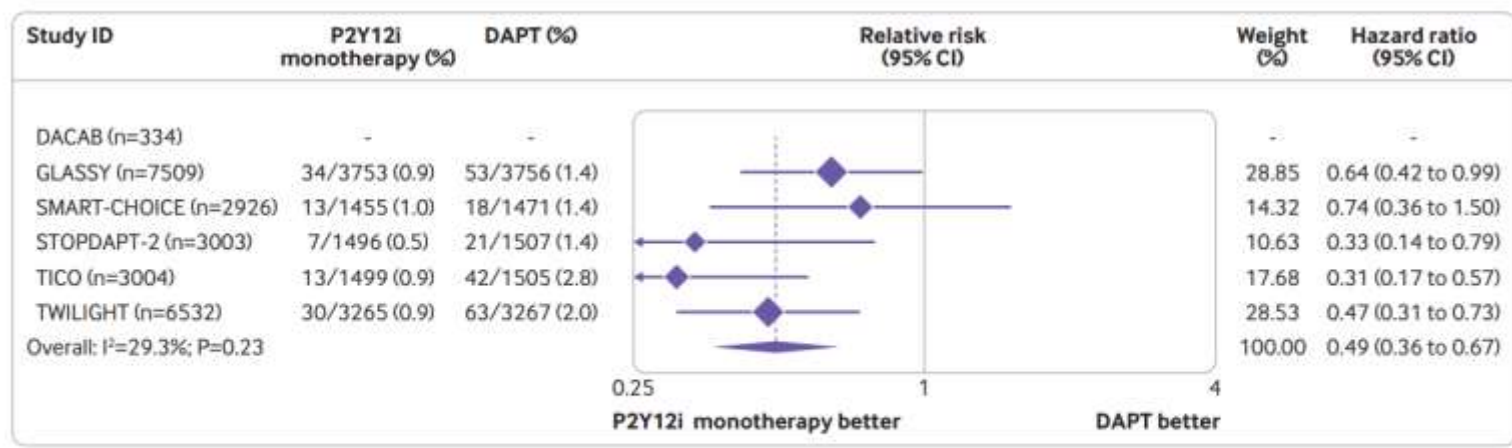


Fig 5 | Hazard ratios for individual trials and for pooled population and Kaplan-Meier estimates for key safety endpoint of Bleeding Academic Research Consortium (BARC) type 3 or type 5 bleeding in intention to treat population. Kaplan-Meier curves and hazard ratios from one step, fixed effect meta-analysis (top) and two step, fixed effect meta-analysis (bottom). DAPT=dual antiplatelet therapy

# Aspirin versus Clopidogrel

# CAPRIE Trial

## Clonidogrel vs Aspirin in patients at risk of ischaemic events

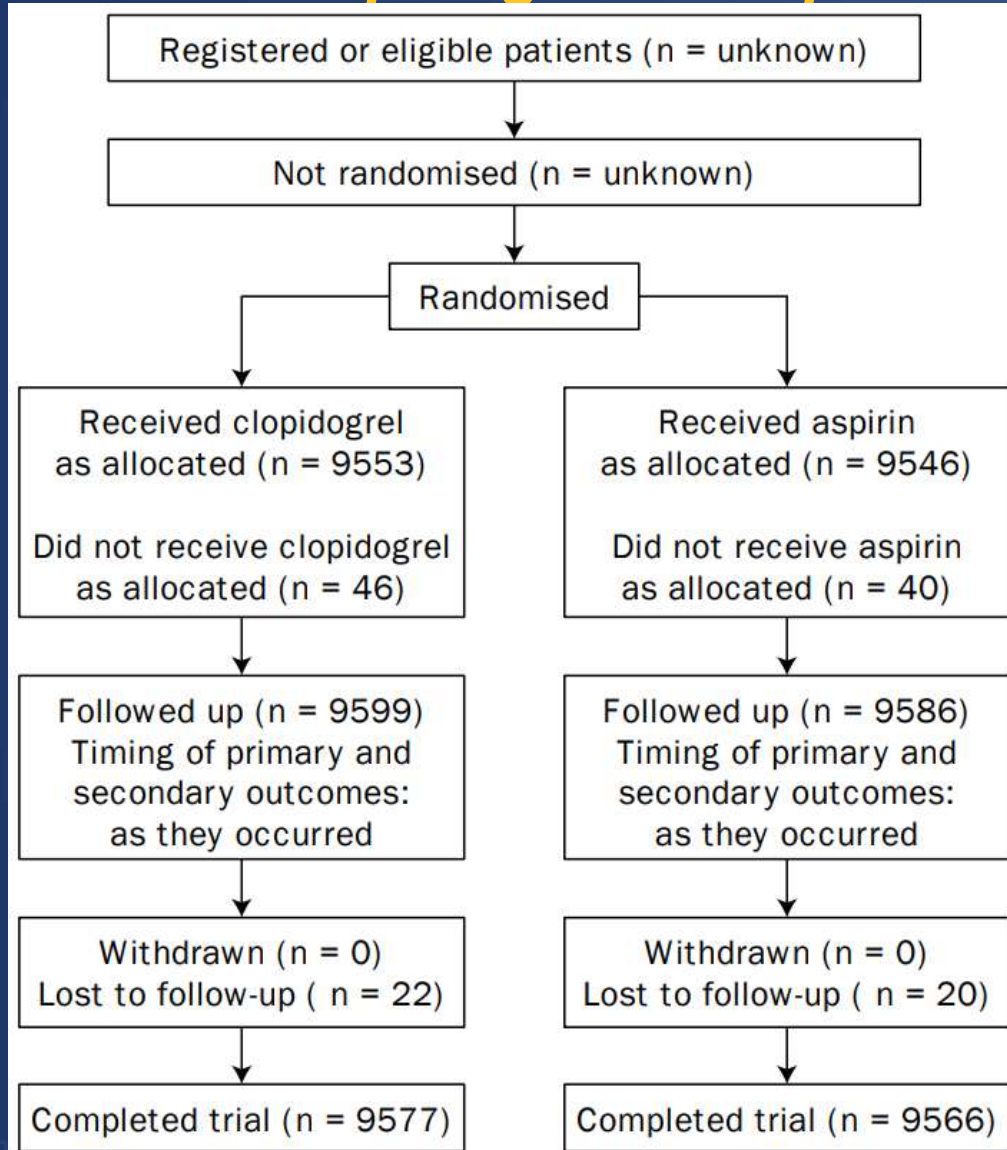


Figure 2: Participant progress through trial

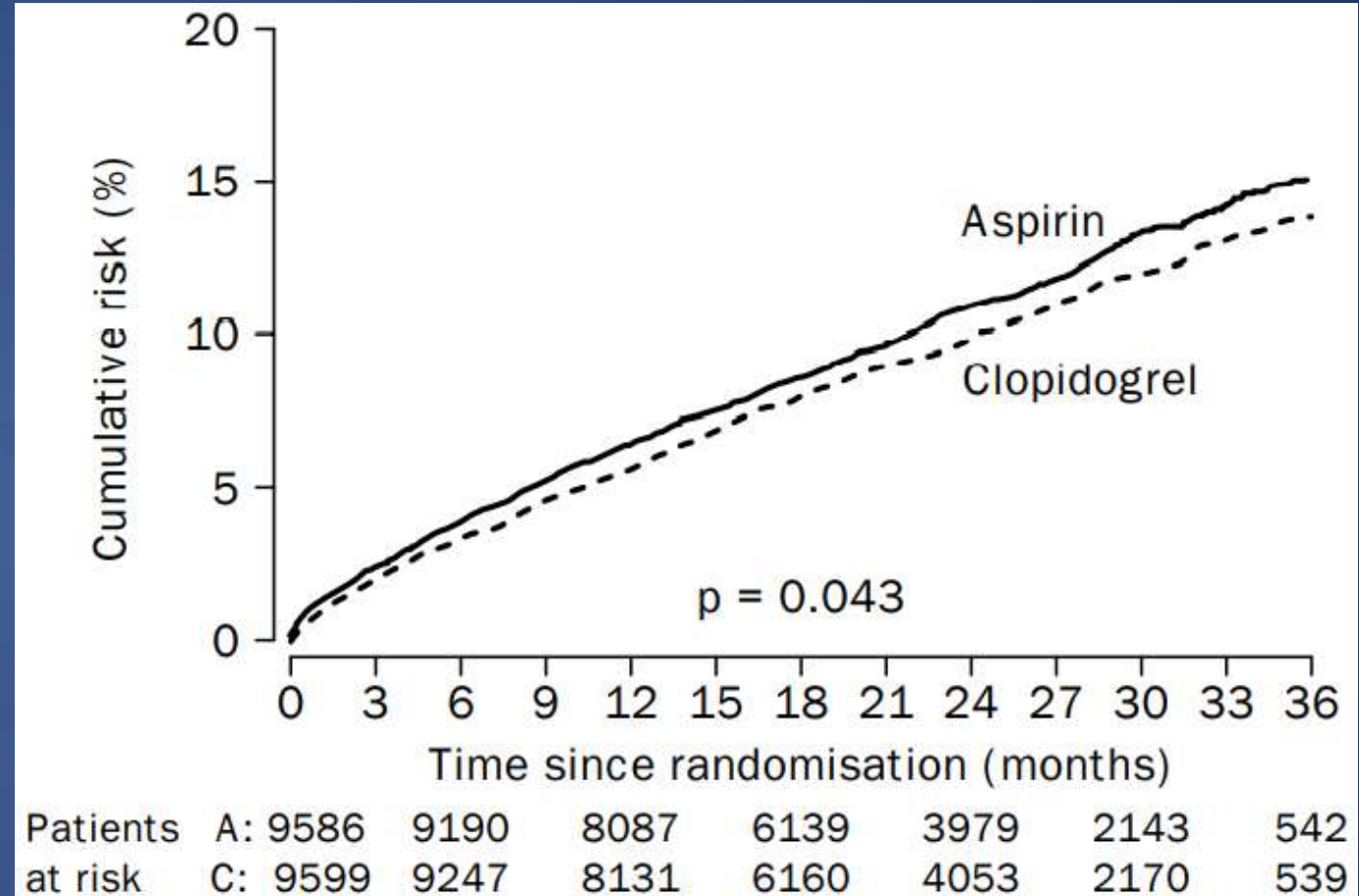


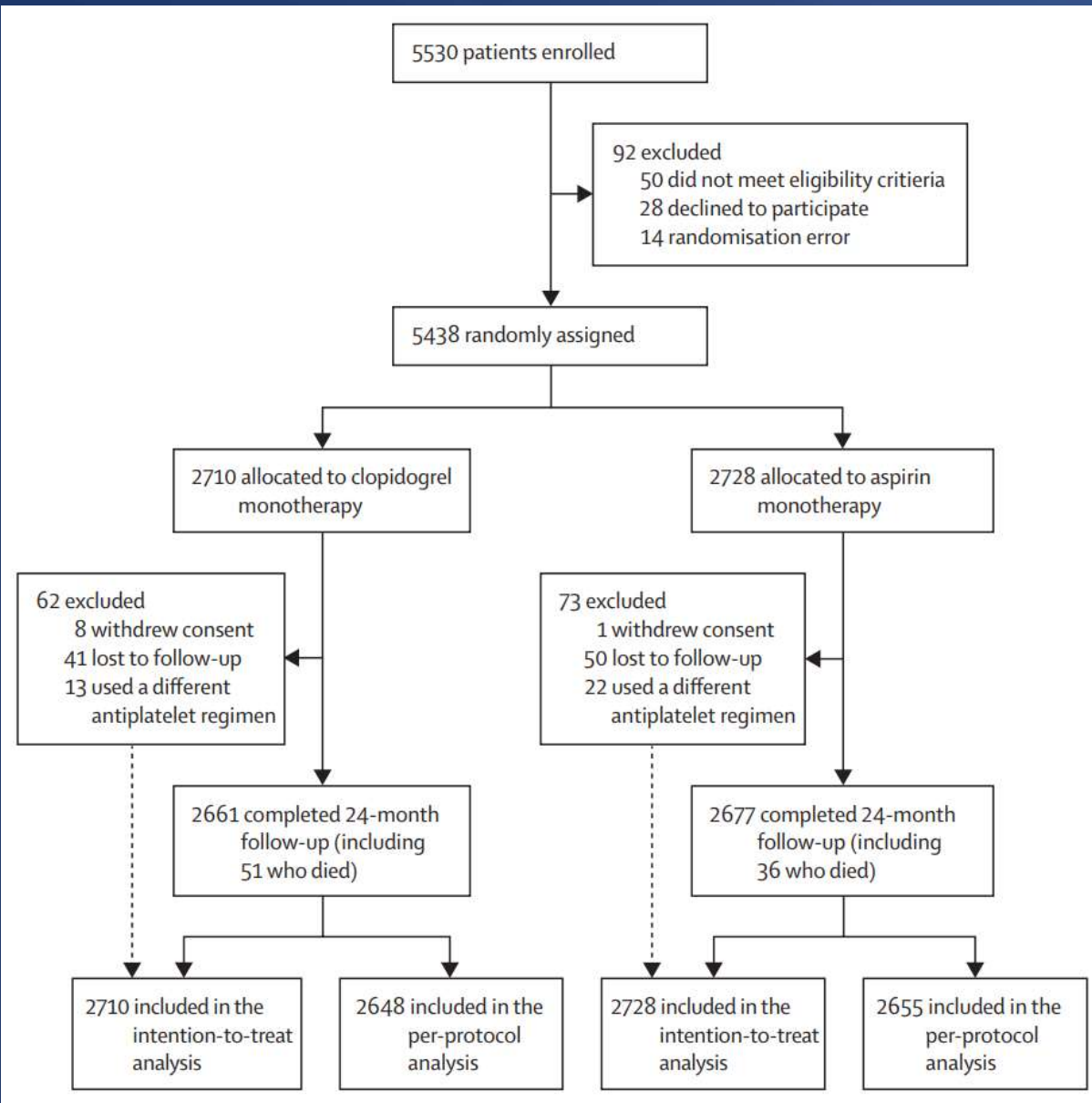
Figure 3: Cumulative risk of Ischaemic stroke, myocardial infarction, or vascular death

A=aspirin; C=clonidogrel.

M Gent et al. Lancet. 1996 Nov 16;348(9038):1329-39.

# HOST-EXAM Trial

## Aspirin vs Clopidogrel for chronic maintenance monotherapy after PCI



- **Participants**

- **≥ 20 years old**

- **underwent PCI with DES and maintained DAPT without any**

- **clinical events within 6-18 months after PCI**

- **exclusion) any ischaemic and major bleeding complications (non-fatal MI, any repeat revascularization, readmission due to cardiac cause, and major bleeding**



# HOST-EXAM Trial

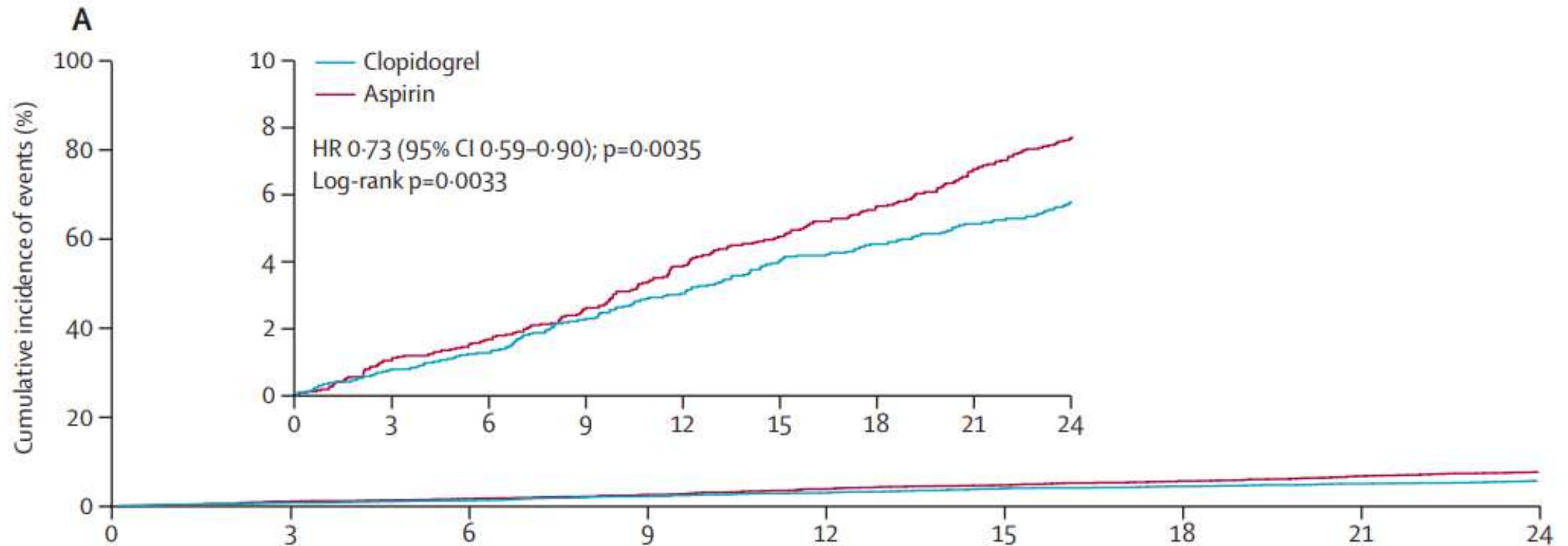
## Aspirin vs Clopidogrel for chronic maintenance monotherapy after PCI

	Clopidogrel (n=2710)	Aspirin (n=2728)	Hazard ratio (95% CI)*	p value
Primary composite endpoint†	152 (5.7%)	207 (7.7%)	0.73 (0.59-0.90)	0.003
Thrombotic composite endpoint‡	99 (3.7%)	146 (5.5%)	0.68 (0.52-0.87)	0.003
Any bleeding (BARC type ≥2)§	61 (2.3%)	87 (3.3%)	0.70 (0.51-0.98)	0.036
All-cause death¶	51 (1.9%)	36 (1.3%)	1.43 (0.93-2.19)	0.101
Cardiac death	19 (0.7%)	14 (0.5%)	1.37 (0.69-2.73)	0.374
Non-cardiac death	32 (1.2%)	22 (0.8%)	1.47 (0.85-2.52)	0.167
Non-fatal myocardial infarction	18 (0.7%)	28 (1.0%)	0.65 (0.36-1.17)	0.150
Stroke	18 (0.7%)	43 (1.6%)	0.42 (0.24-0.73)	0.002
Ischaemic stroke	14 (0.5%)	26 (1.0%)	0.54 (0.28-1.04)	0.064
Haemorrhagic stroke	4 (0.2%)	17 (0.6%)	0.24 (0.08-0.70)	0.010
Readmission due to ACS	66 (2.5%)	109 (4.1%)	0.61 (0.45-0.82)	0.001
Major bleeding (BARC type ≥3)	33 (1.2%)	53 (2.0%)	0.63 (0.41-0.97)	0.035
Any revascularisation	56 (2.1%)	69 (2.6%)	0.82 (0.57-1.16)	0.261
Target lesion revascularisation	24 (0.9%)	36 (1.4%)	0.67 (0.40-1.12)	0.130
Target vessel revascularisation	37 (1.4%)	48 (1.8%)	0.78 (0.50-1.19)	0.245
Definite or probable stent thrombosis	10 (0.4%)	16 (0.6%)	0.63 (0.29-1.39)	0.251
Any minor gastrointestinal complications	272 (10.2%)	320 (11.9%)	0.85 (0.72-1.00)	0.048

# HOST-EXAM Trial

## Aspirin vs Clopidogrel for chronic maintenance monotherapy after PCI

- A) The cumulative incidence of the primary endpoint, consisting of all-cause death, non-fatal MI, stroke, readmission due to ACS, and major bleeding (BARC 3 or more) complications



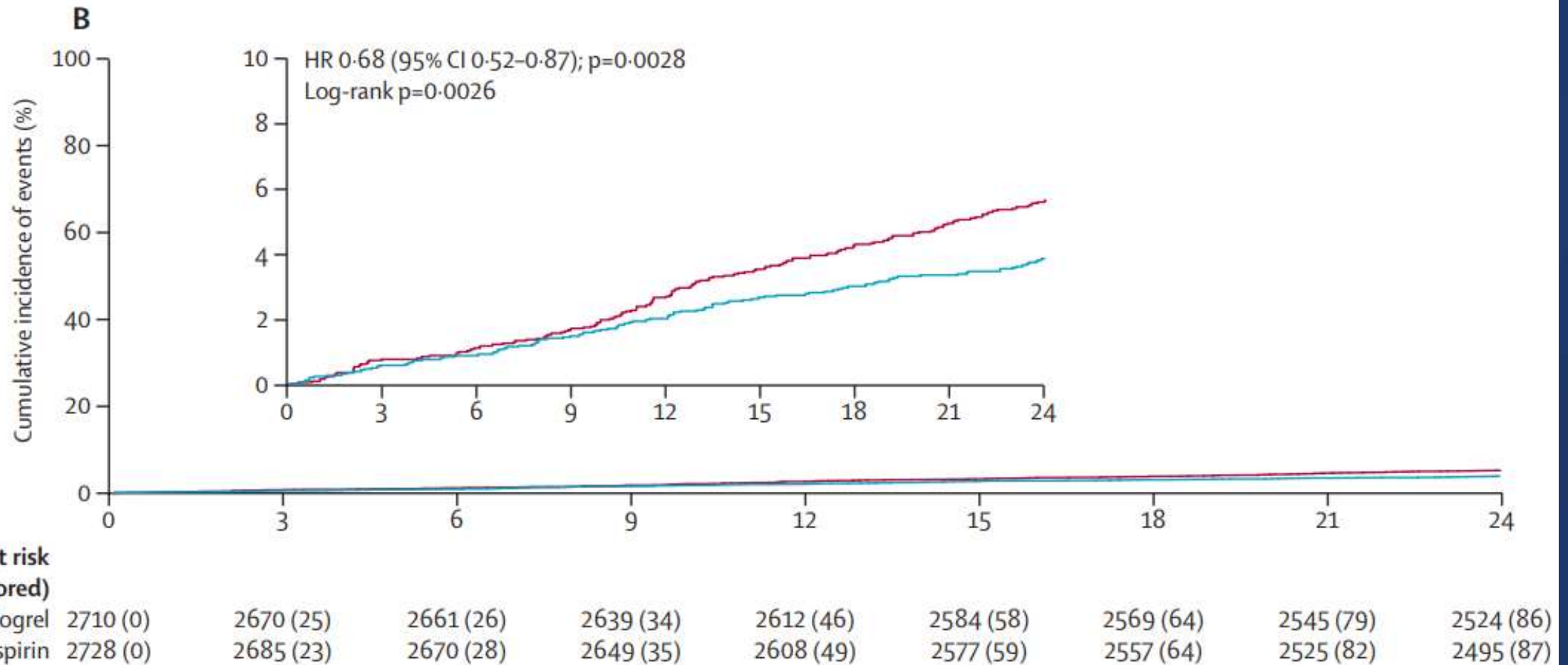
Number at risk  
(number censored)

Clopidogrel	2710 (0)	2667 (22)	2654 (22)	2626 (24)	2597 (33)	2565 (41)	2549 (43)	2521 (54)	2500 (58)
Aspirin	2728 (0)	2677 (23)	2657 (26)	2629 (31)	2585 (40)	2555 (48)	2531 (49)	2493 (64)	2456 (66)

# HOST-EXAM Trial

## Aspirin vs Clopidogrel for chronic maintenance monotherapy after PCI

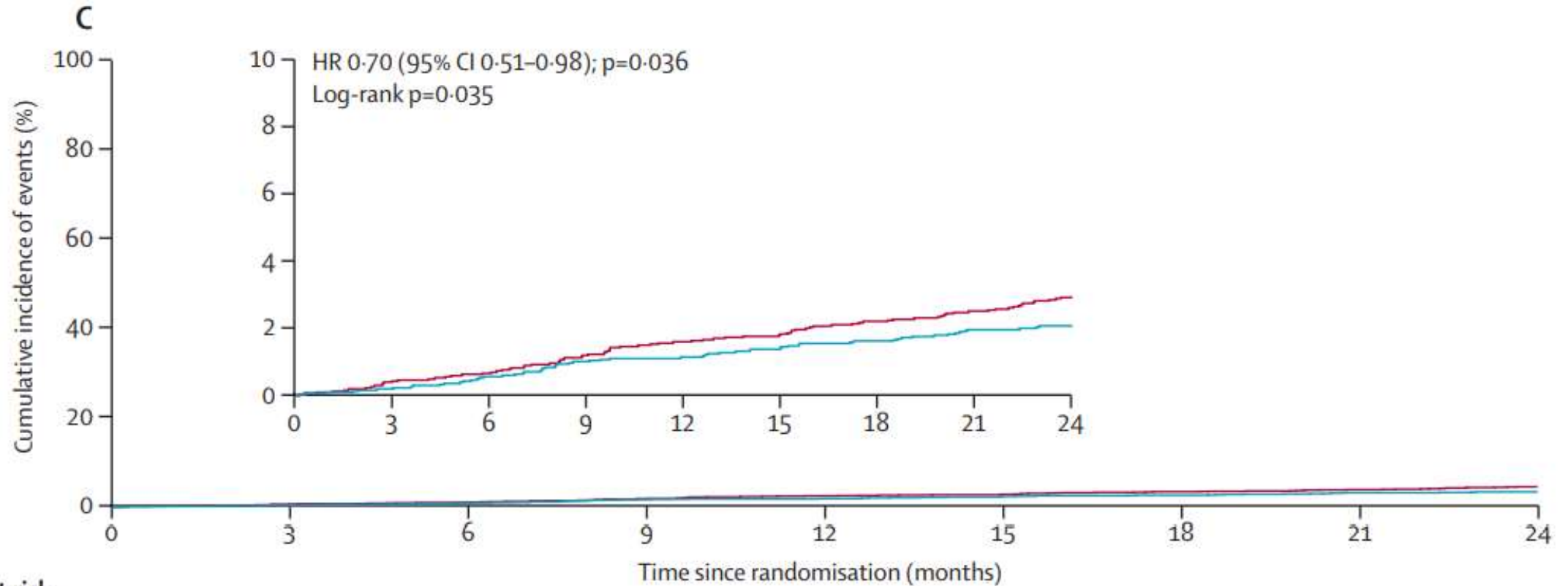
- B) The cumulative incidence of the secondary composite thrombotic endpoint, consisting of cardiac death, non-fatal MI, ischaemic stroke, readmission due to ACS, or definite or probable stent thrombosis



# HOST-EXAM Trial

## Aspirin vs Clopidogrel for chronic maintenance monotherapy after PCI

- C) The cumulative incidence of any bleeding events.



Number at risk  
(number censored)

Clopidogrel	2710 (0)	2676 (28)	2664 (29)	2643 (37)	2621 (56)	2597 (72)	2585 (77)	2556 (98)	2542 (105)
Aspirin	2728 (0)	2690 (26)	2677 (31)	2653 (39)	2626 (54)	2610 (65)	2595 (67)	2572 (85)	2547 (93)

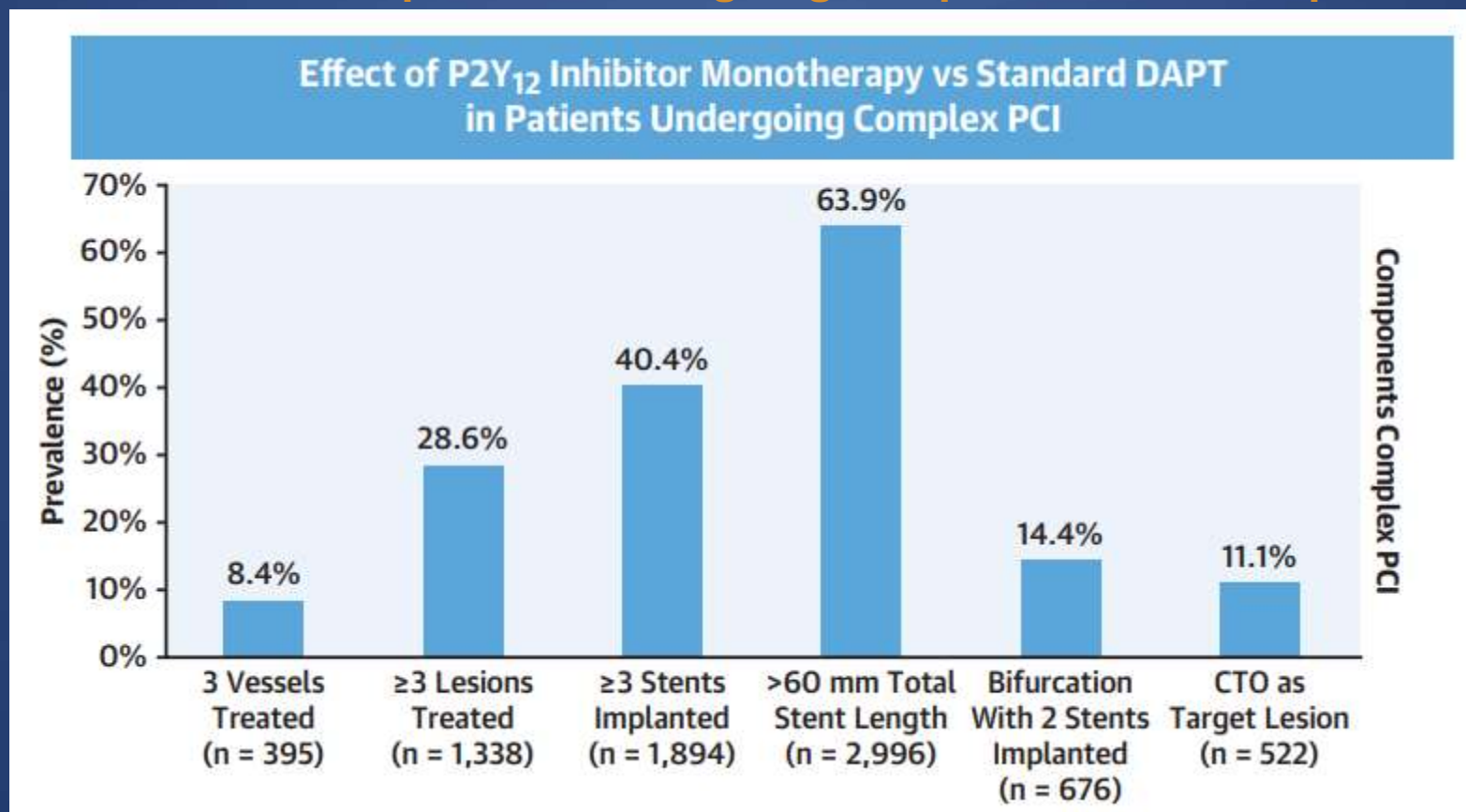


# P2Y12 Inhibitor Monotherapy or DAPT after Complex PCI: Sidney-2 Meta-Analysis of RCTs.

- Safety and efficacy with P2Y12 inhibitor monotherapy after initial period of DAPT(1 to 3 months)

versus

Standard DAPT in patients undergoing complex and noncomplex PCI



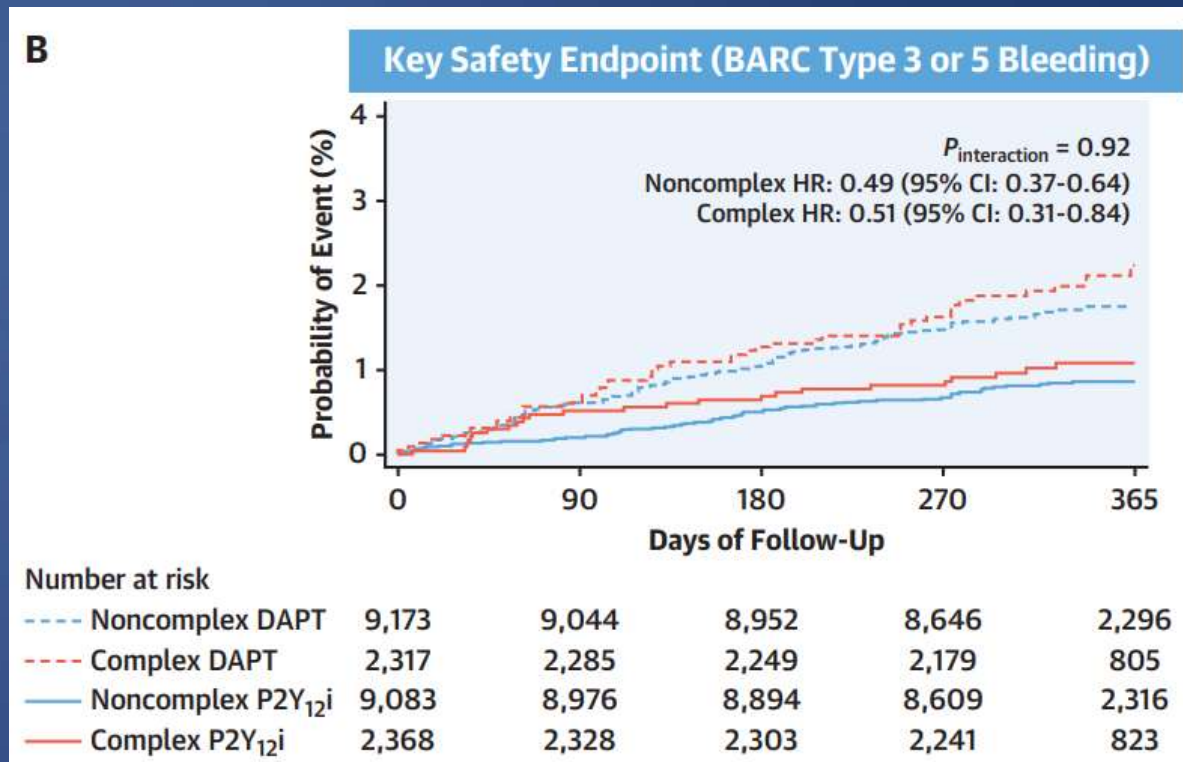
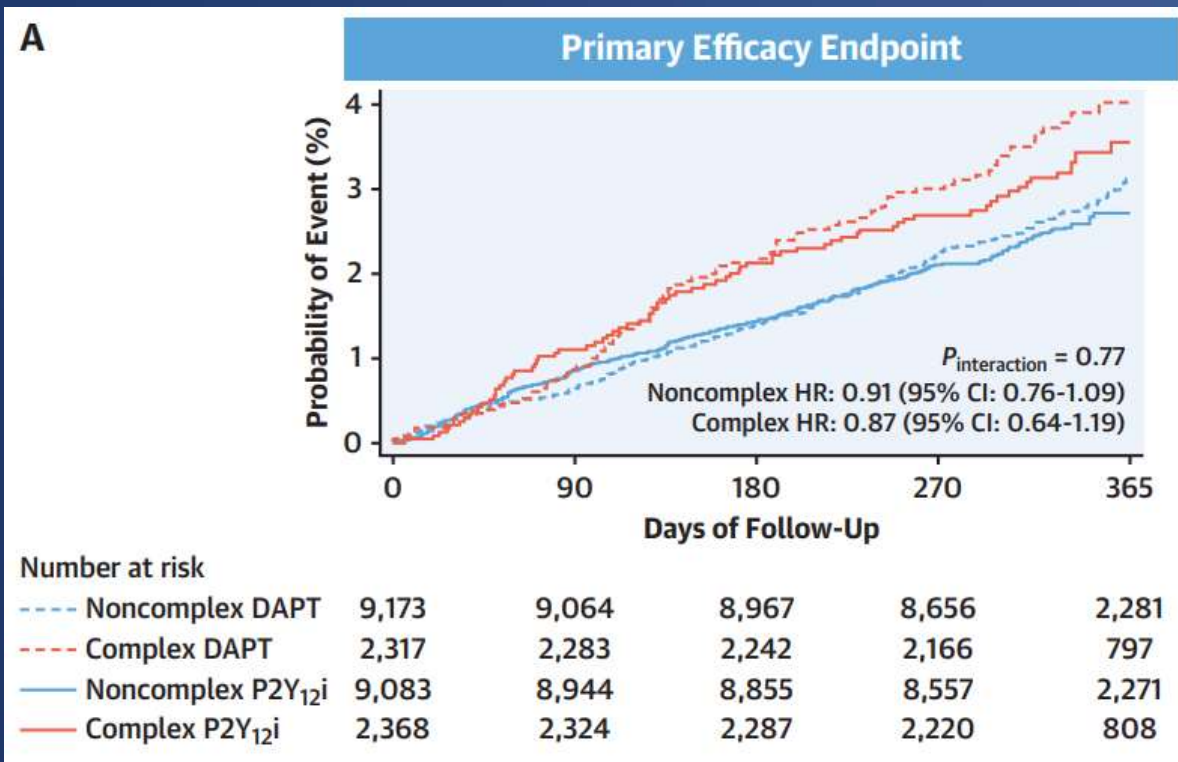
# P2Y12 Inhibitor Monotherapy or DAPT after Complex PCI: Sidney-2 Meta-Analysis of RCTs.

- A) Primary Efficacy Endpoint

(All-cause death, MI, and Stroke)

- B) Key Safety Endpoint

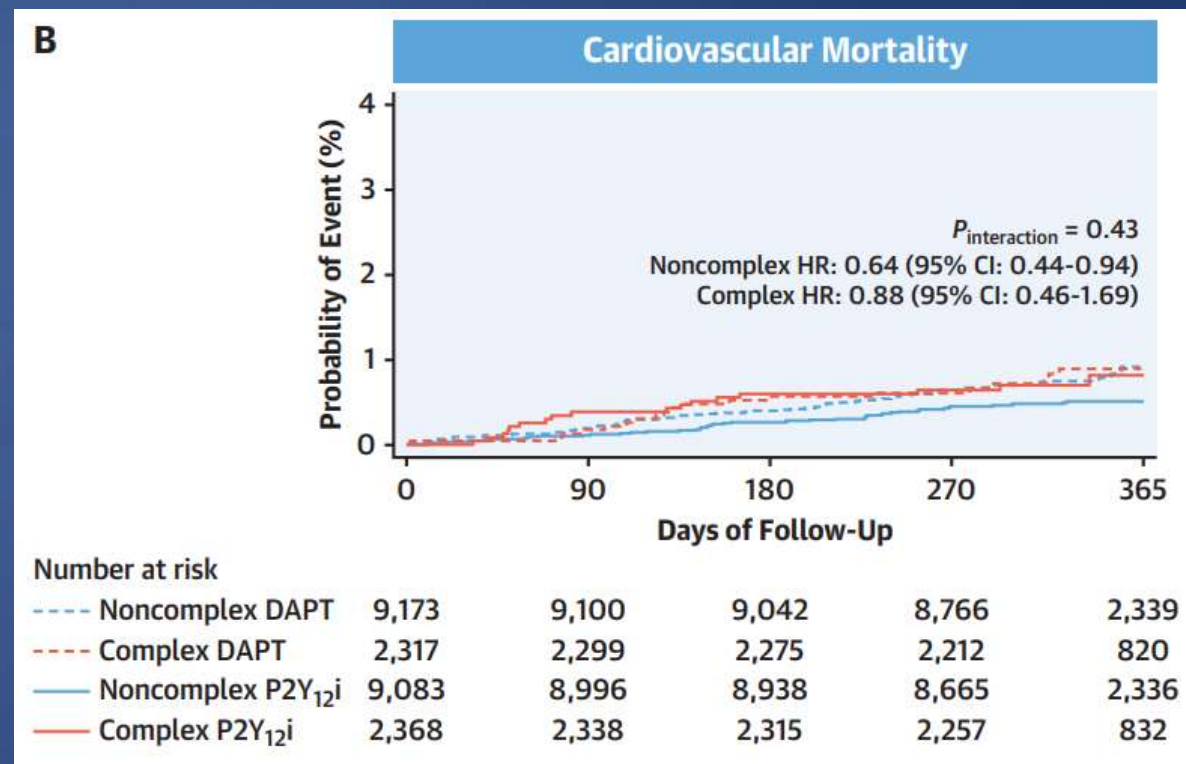
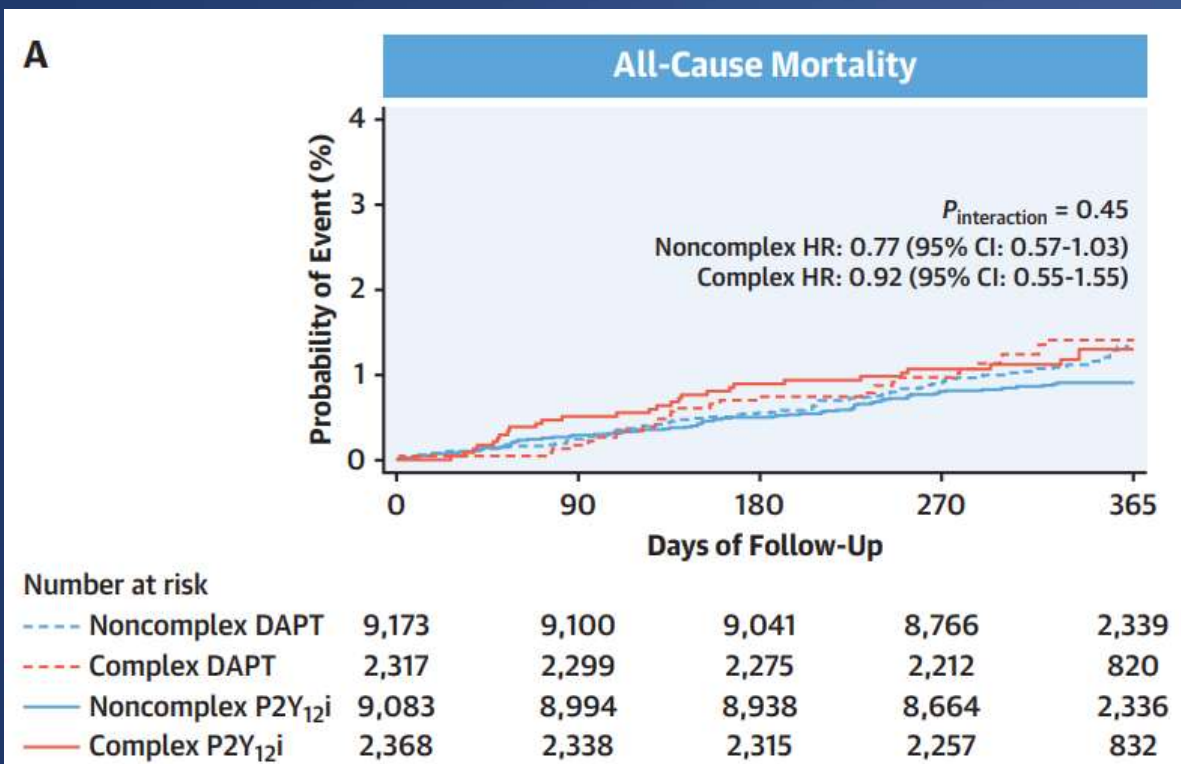
(BARC Type 3 or 5 Bleeding)



# P2Y12 Inhibitor Monotherapy or DAPT after Complex PCI: Sidney-2 Meta-Analysis of RCTs.

- A) All-Cause Mortality

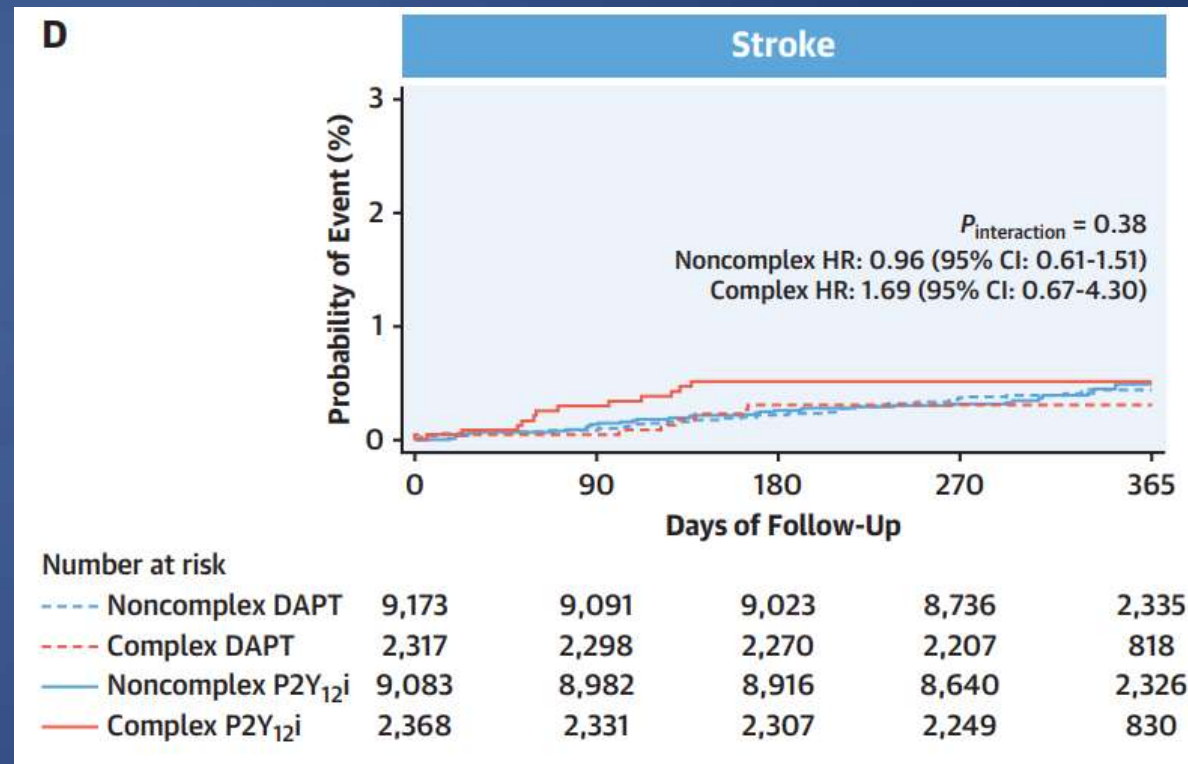
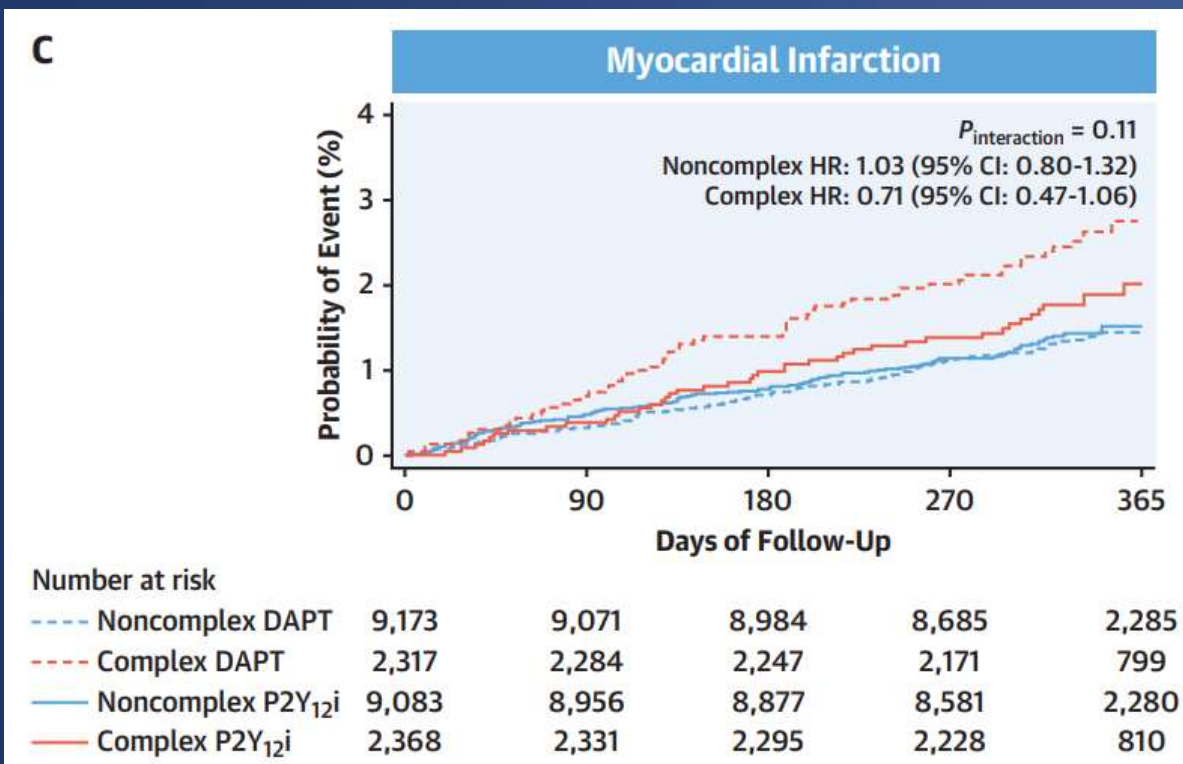
- B) Cardiovascular Mortality



# P2Y12 Inhibitor Monotherapy or DAPT after Complex PCI: Sidney-2 Meta-Analysis of RCTs.

## C) Myocardial Infarction

## D) Stroke

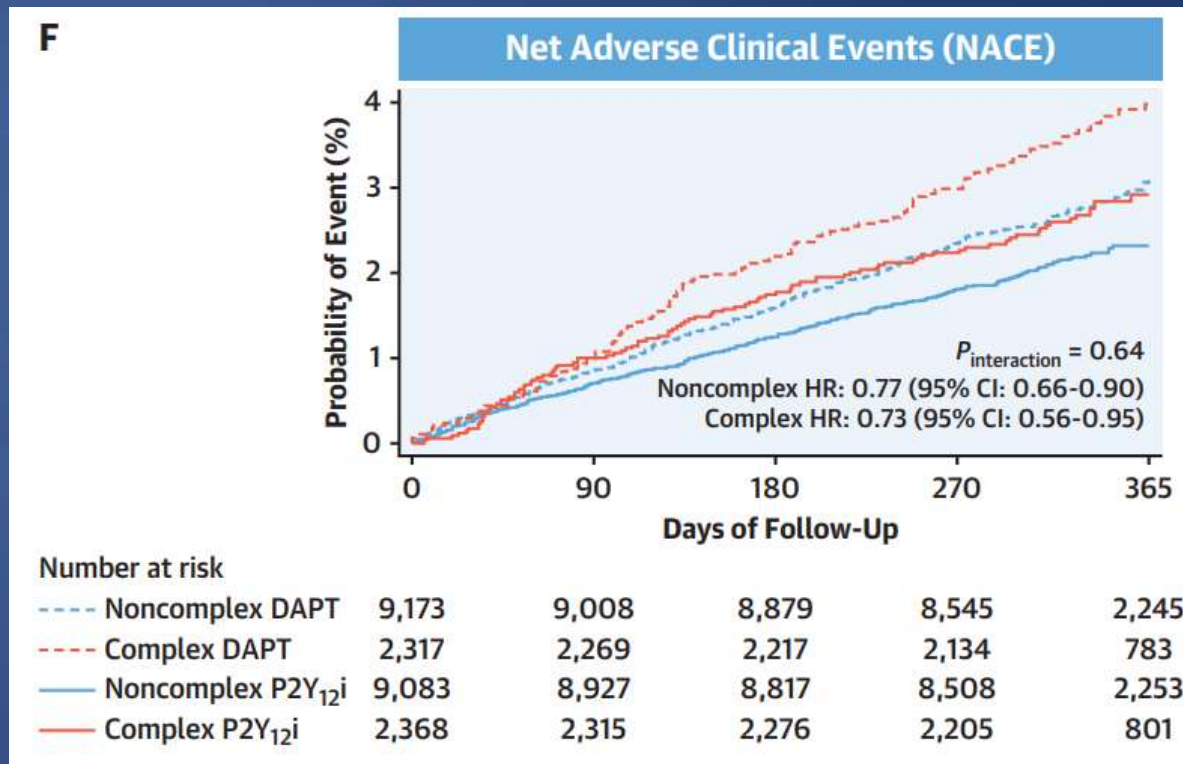
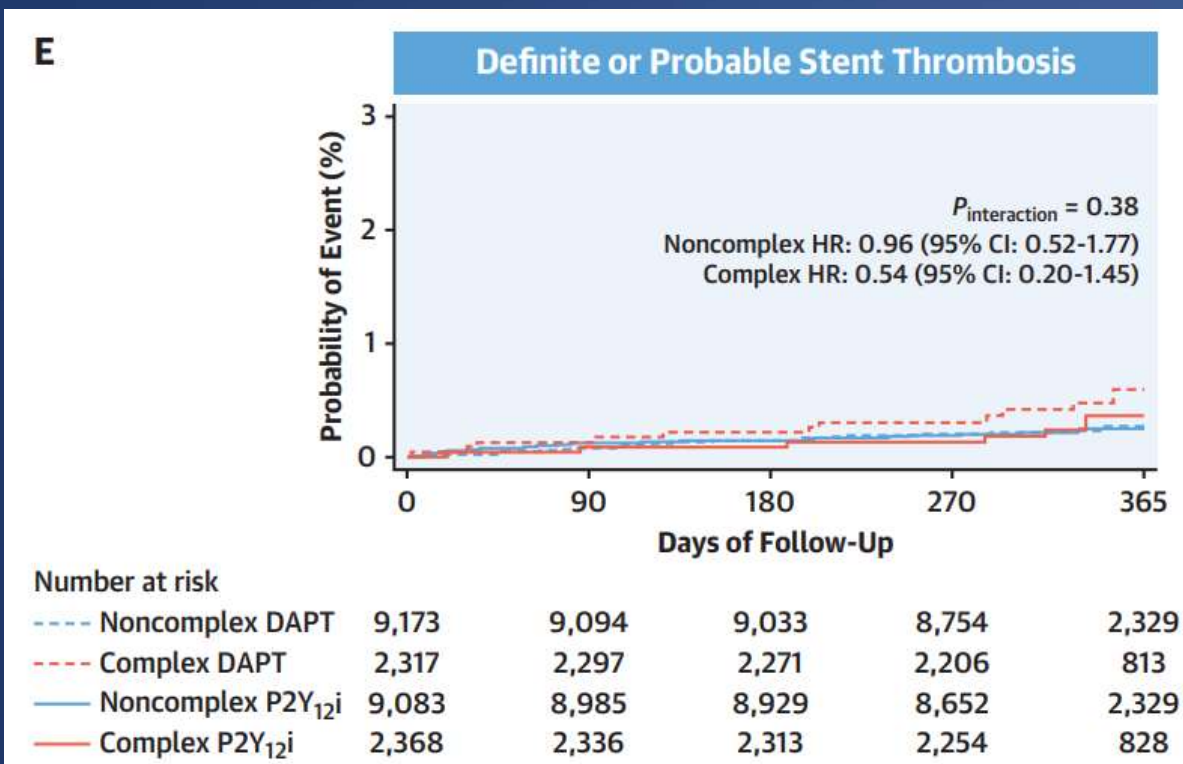




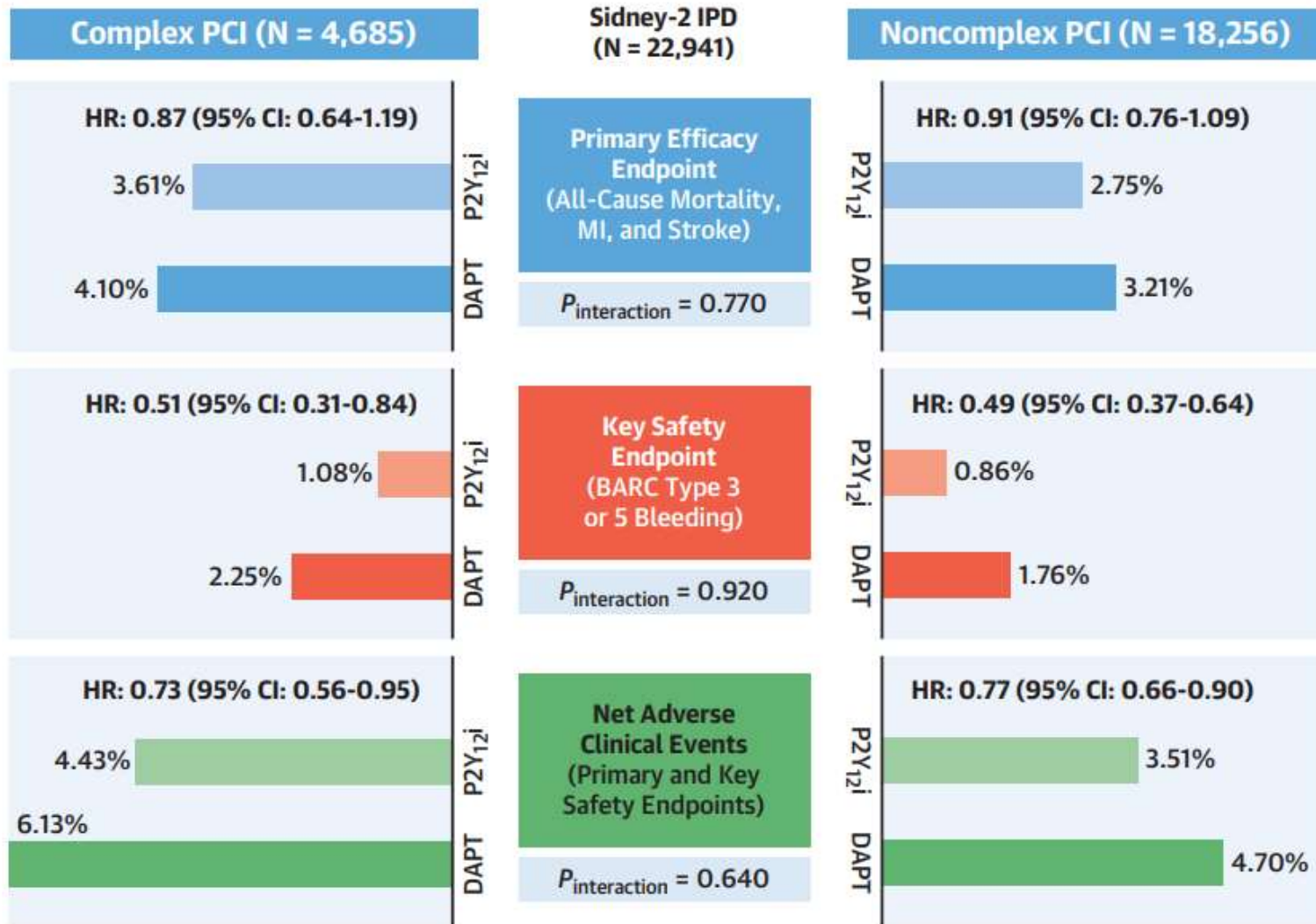
# P2Y12 Inhibitor Monotherapy or DAPT after Complex PCI: Sidney-2 Meta-Analysis of RCTs.

- E) Definite or Probable Stent Thrombosis

- F) Net Adverse Clinical Events (NACE)



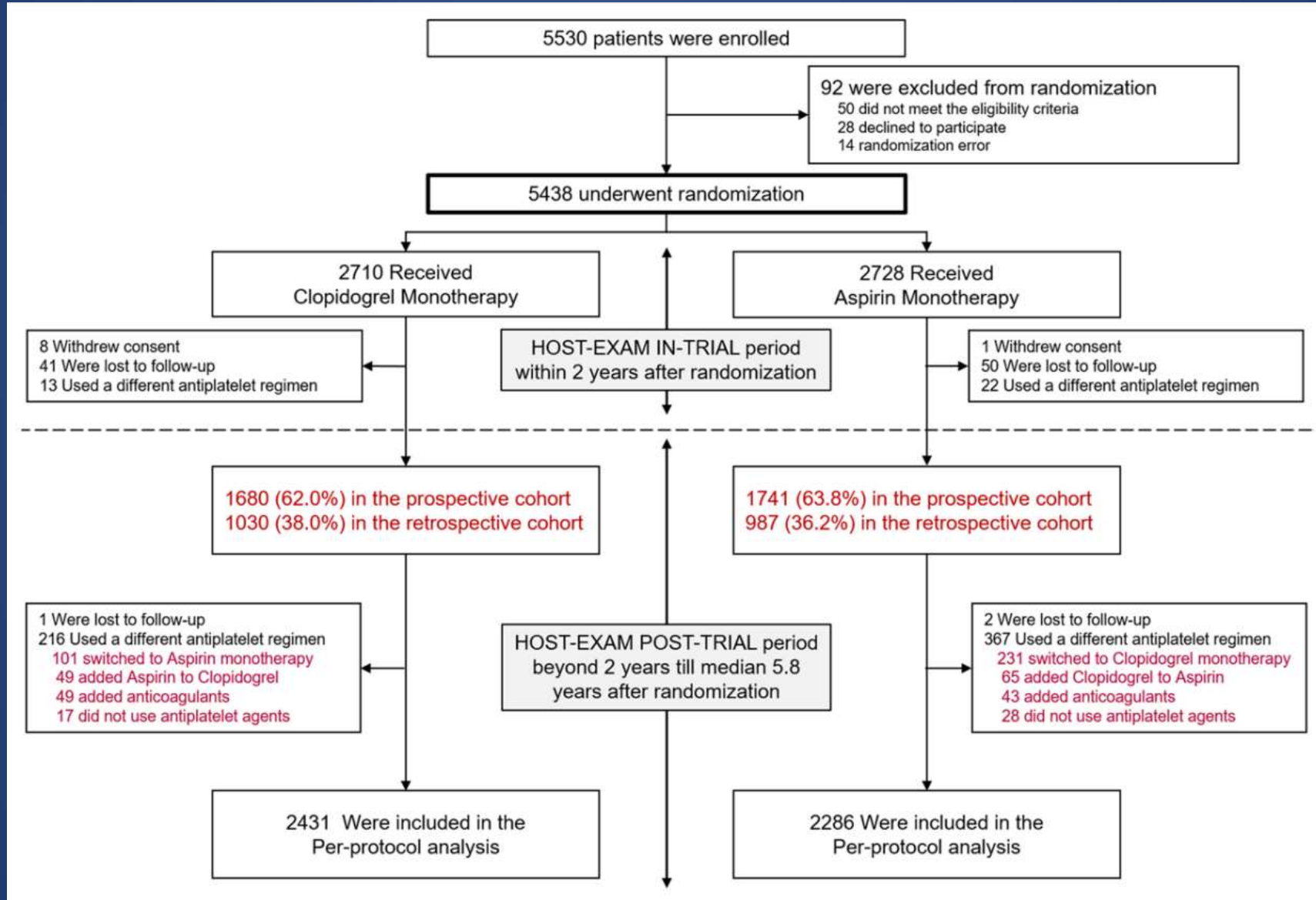
# P2Y12 Inhibitor Monotherapy or DAPT after Complex PCI: Sidney-2 Meta-Analysis of RCTs.



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

# HOST-EXAM Extended Study

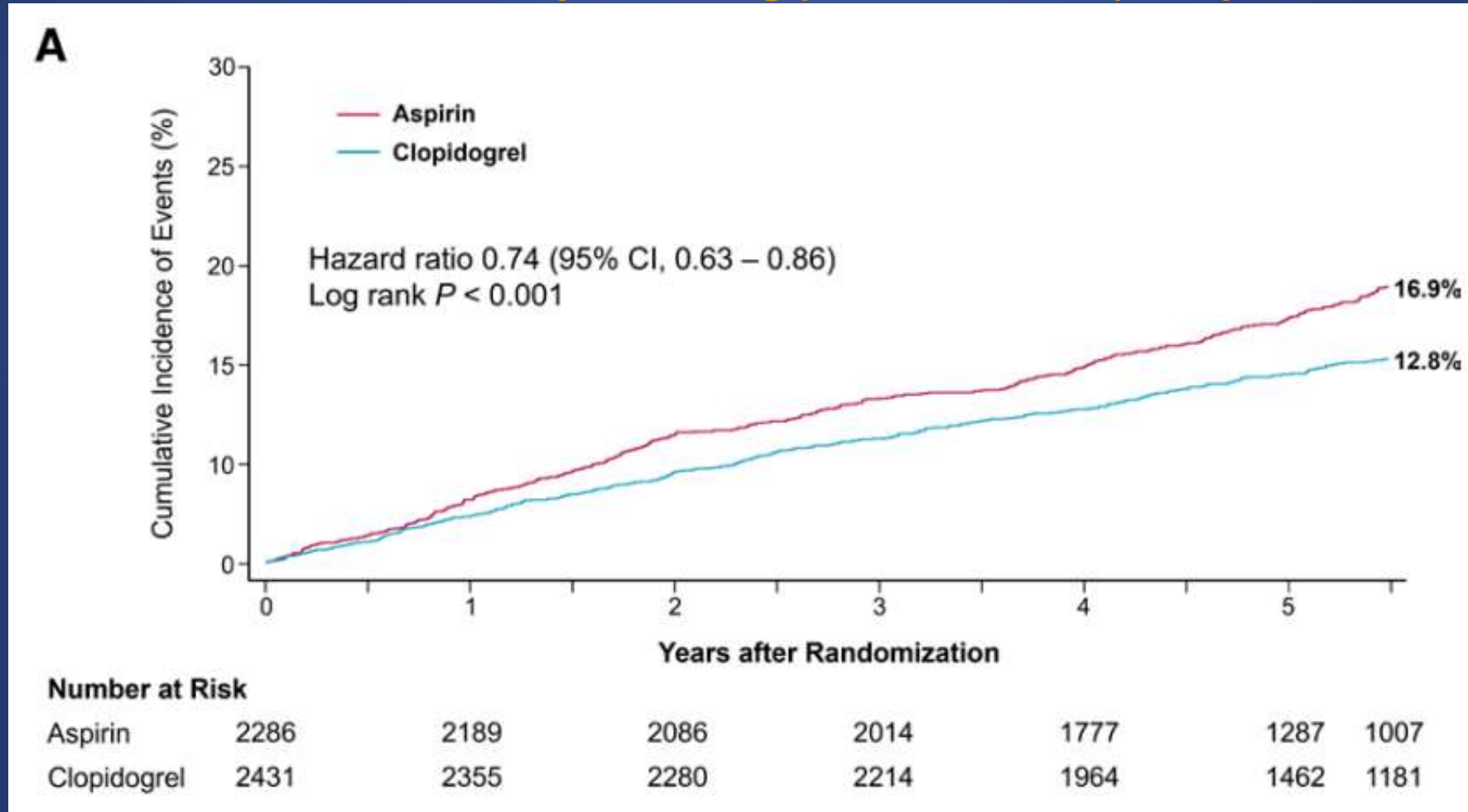
## Aspirin vs Clopidogrel for long term maintenance monotherapy after PCI



# HOST-EXAM Extended Study

## Aspirin vs Clopidogrel for long term maintenance monotherapy after PCI

- A) The cumulative incidence of the primary endpoint, consisting of all-cause death, non-fatal MI, stroke, readmission due to ACS, and major bleeding (BARC 3 or more) complications

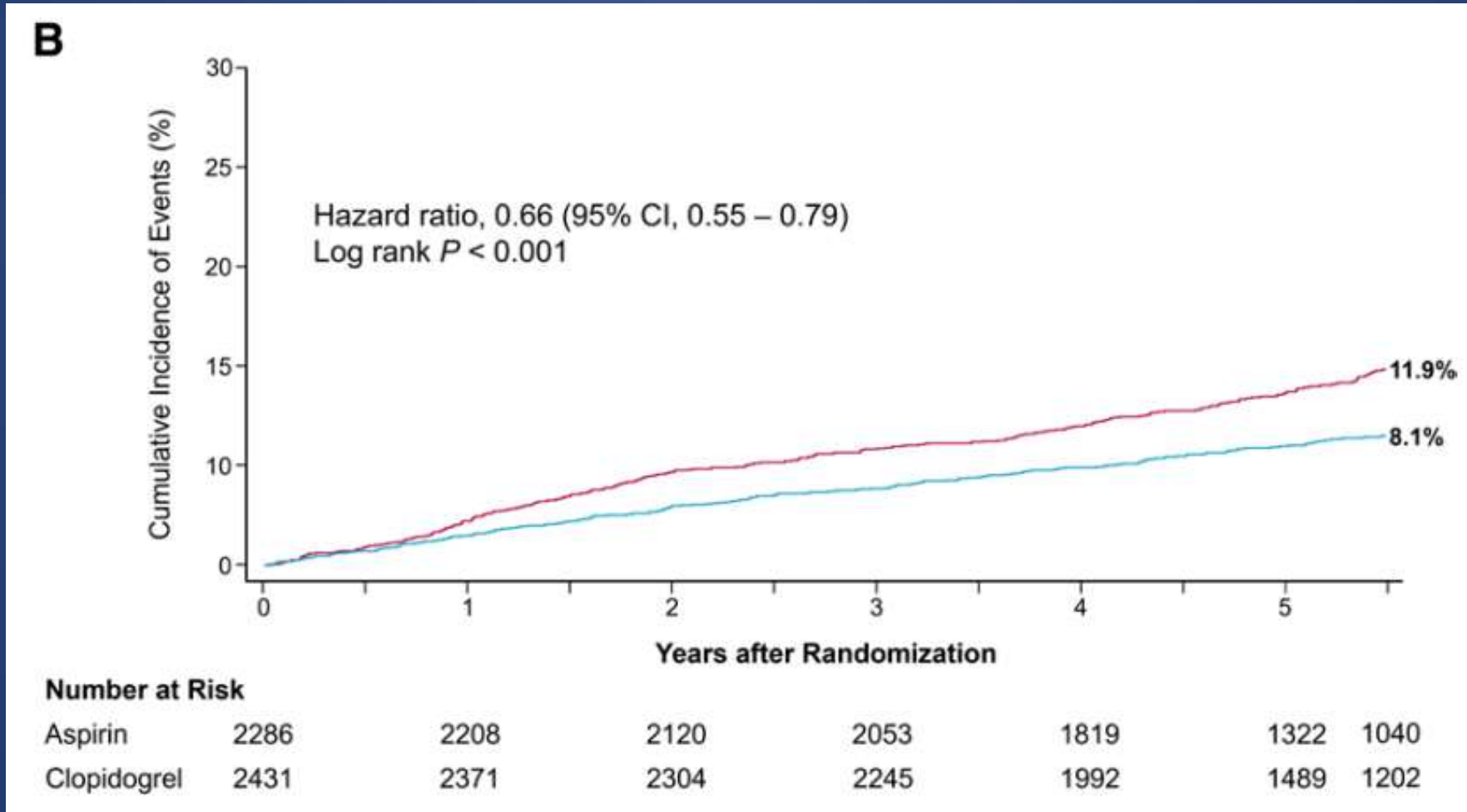




# HOST-EXAM Extended Study

## Aspirin vs Clopidogrel for long term maintenance monotherapy after PCI

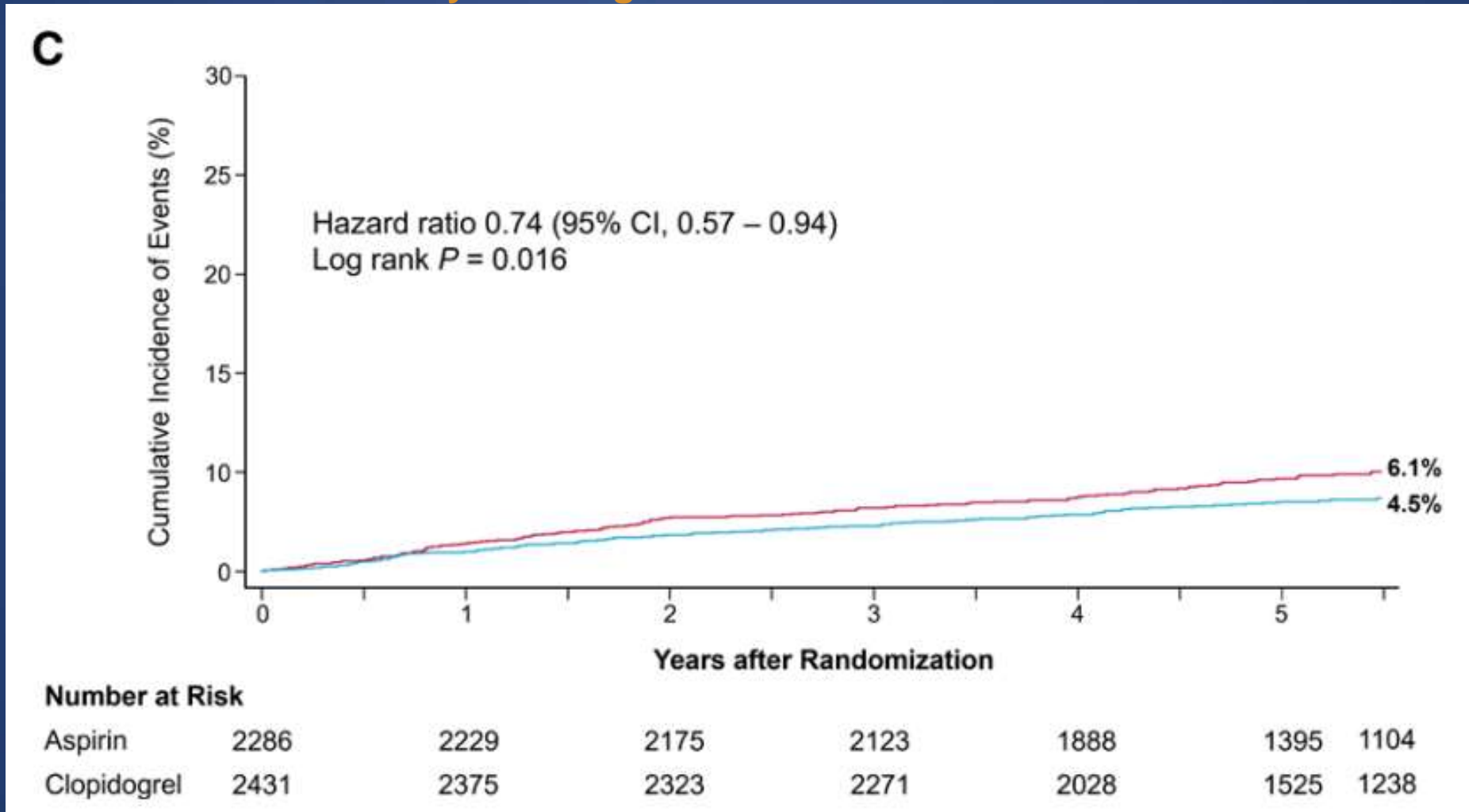
- B) The cumulative incidence of the secondary composite thrombotic endpoint, consisting of cardiac death, non-fatal MI, ischaemic stroke, readmission due to ACS, or definite or probable stent thrombosis



# HOST-EXAM Extended Study

## Aspirin vs Clopidogrel for long term maintenance monotherapy after PCI

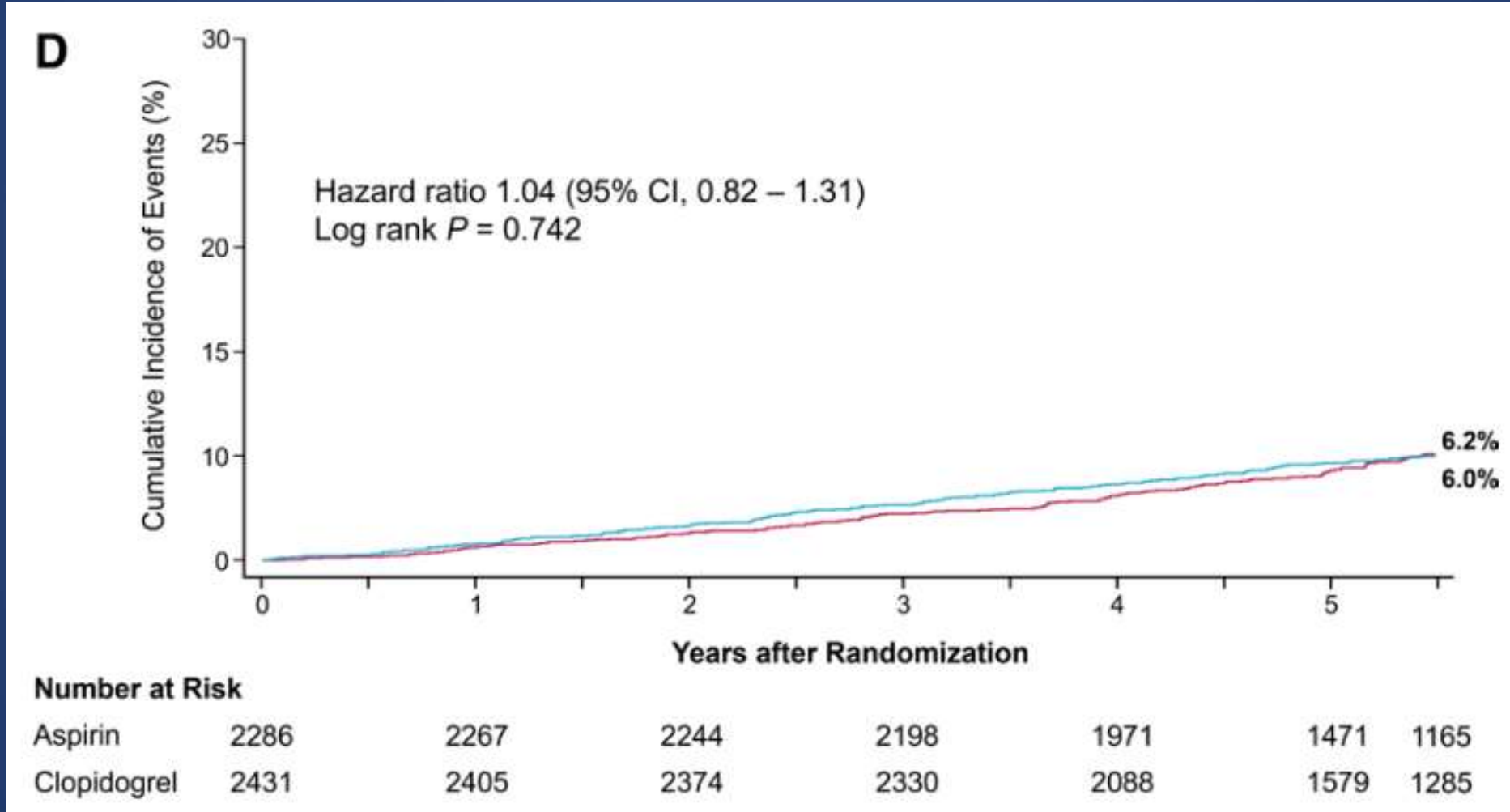
- C) The cumulative incidence of any bleeding events.



# HOST-EXAM Extended Study

## Aspirin vs Clopidogrel for long term maintenance monotherapy after PCI

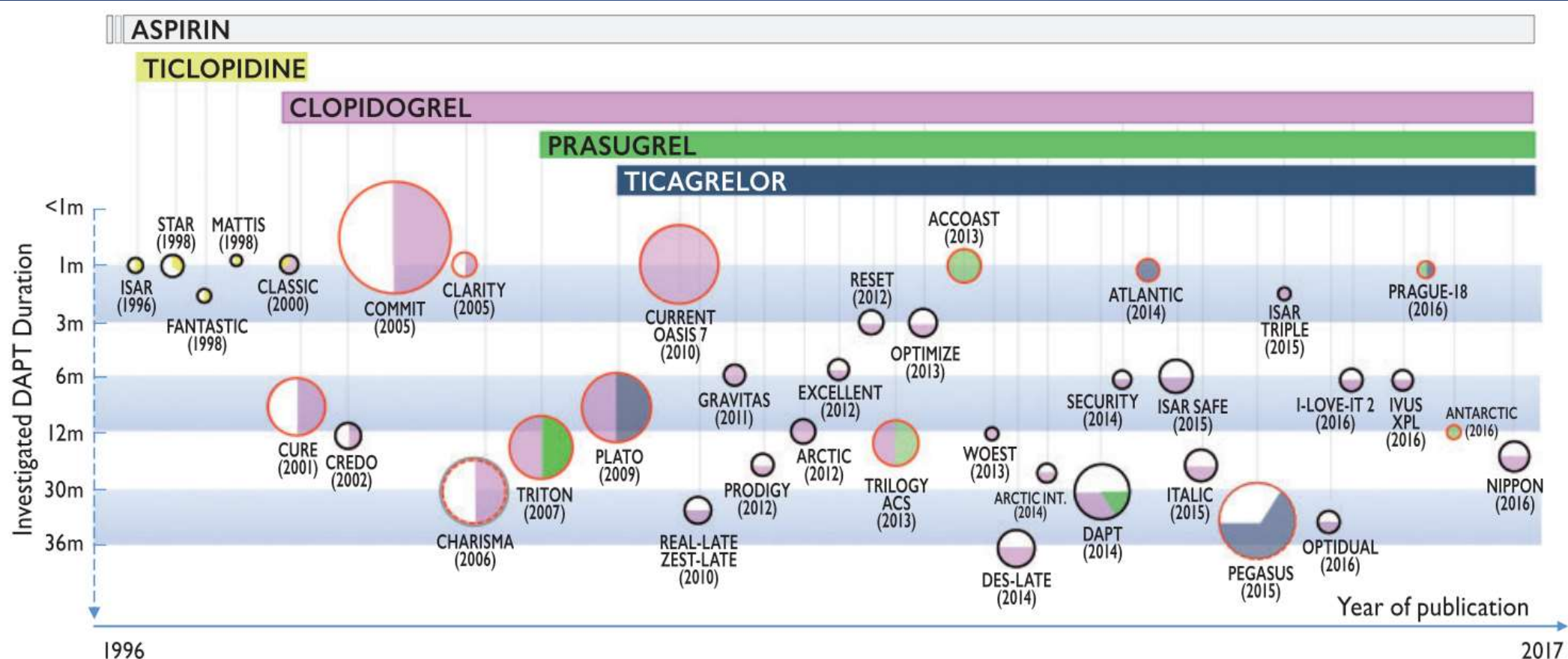
- D) The cumulative incidence of all-cause death.



# Antiplatelet Therapy in CAD

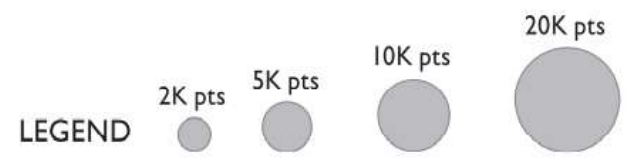


# Antiplatelet Therapy in CAD



Size of the circles denotes sample size

Perimeter of the circles denotes type of investigated population

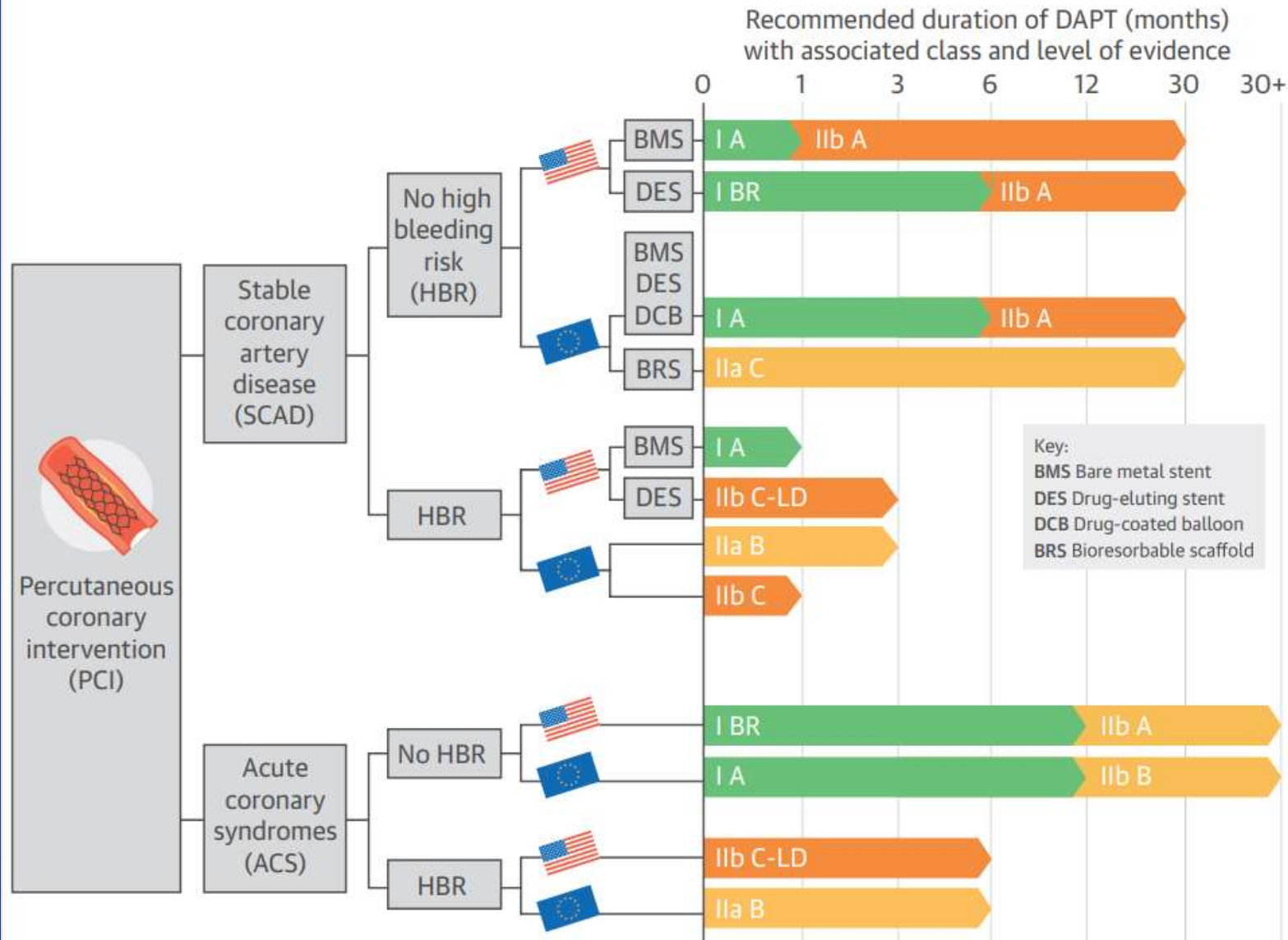


- Mixed clinical presentation at the time of stent implantation
- Acute coronary syndrome at presentation
- DAPT initiated in patients with prior myocardial infarction
- DAPT for primary prevention

©ESC 2017

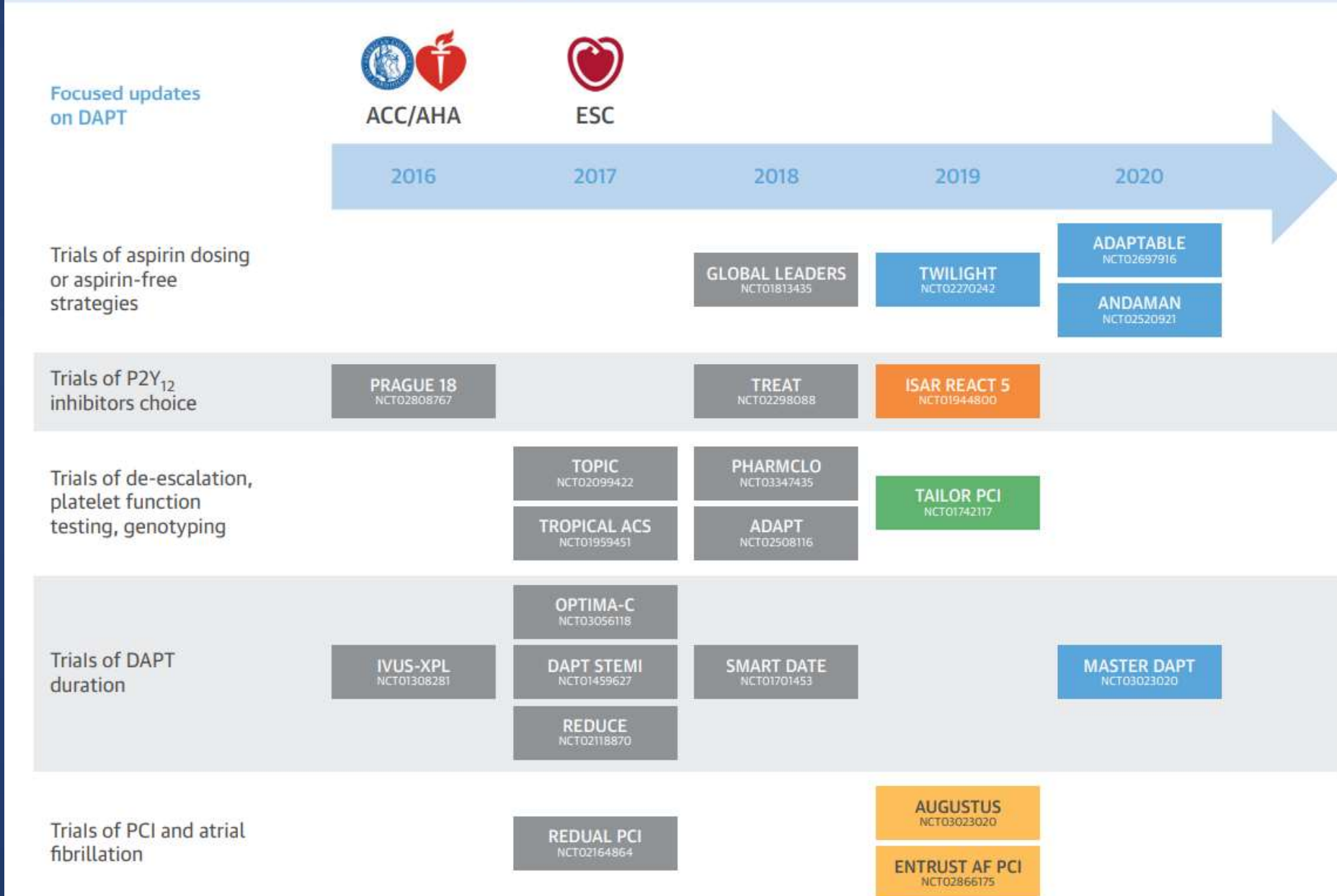
# Antiplatelet Therapy in CAD

**CENTRAL ILLUSTRATION** Recommendations for Dual Antiplatelet Therapy in Patients Undergoing Percutaneous Coronary Intervention



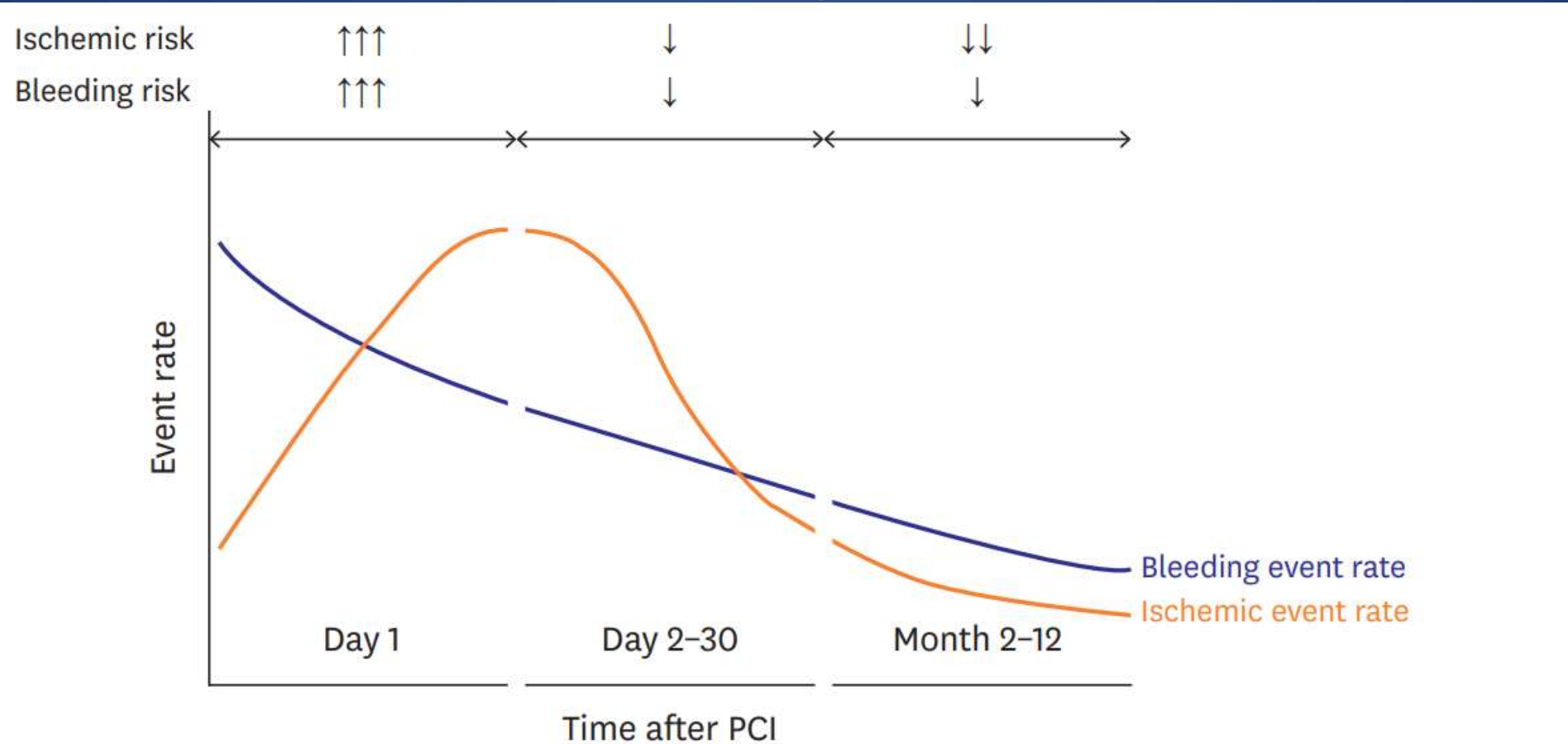
# Antiplatelet Therapy in CAD

**FIGURE 5** New Evidence and Ongoing Studies in the Field of DAPT



# TAILORED-CHIP Trial

## Tailored P2Y12 Strategy for CHIP patients



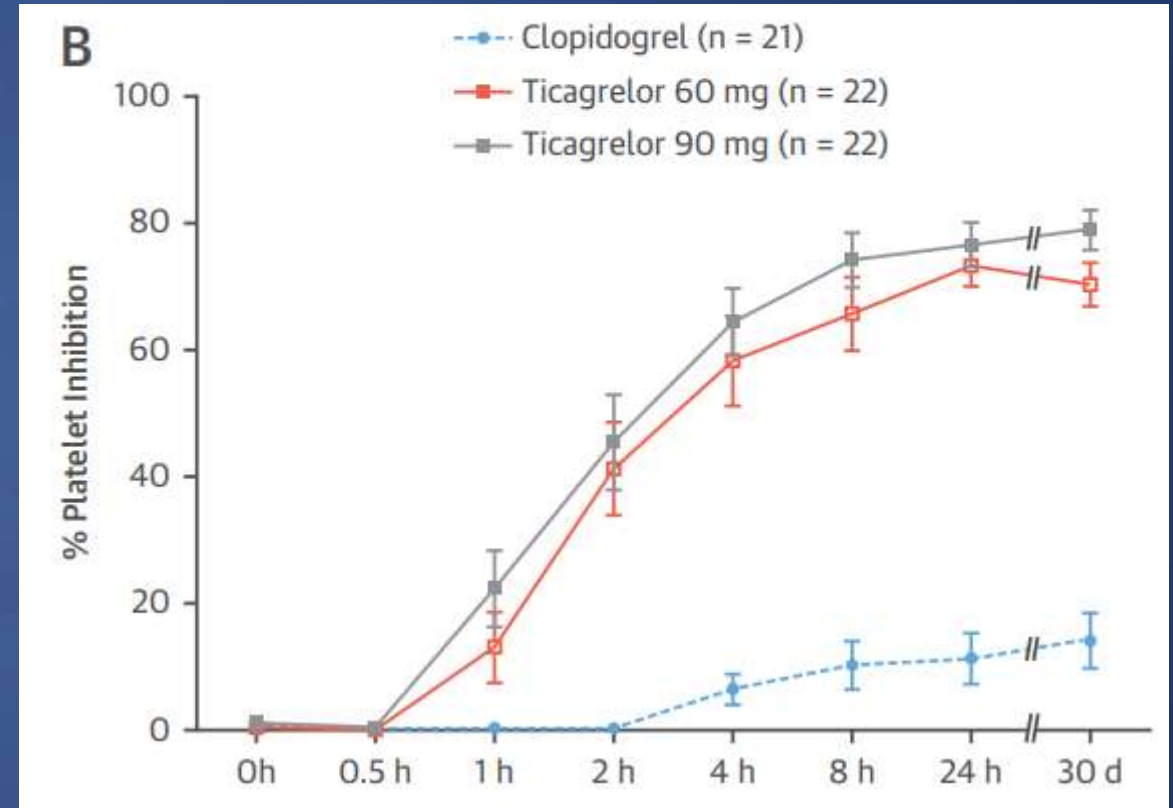
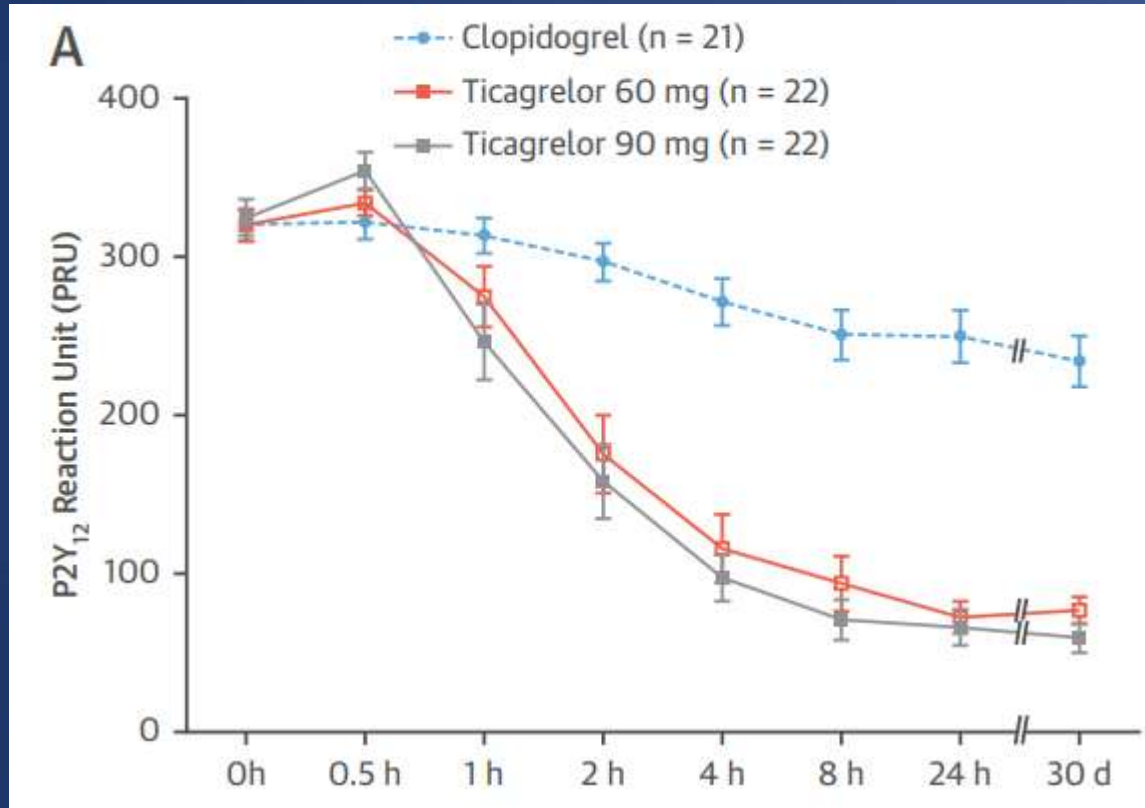
**Figure 1.** Timing of ischemic versus bleeding events after PCI. Ischemic and bleeding rates after PCI are displayed dependent on time. Whereas ischemic rates reach a plateau during the first month, bleeding rates steadily decline. In the second month, ischemic events substantially decrease resulting in an exuberant bleeding risk in the later phase post-PCI.

PCI = percutaneous coronary intervention.



# TAILORED-CHIP Trial

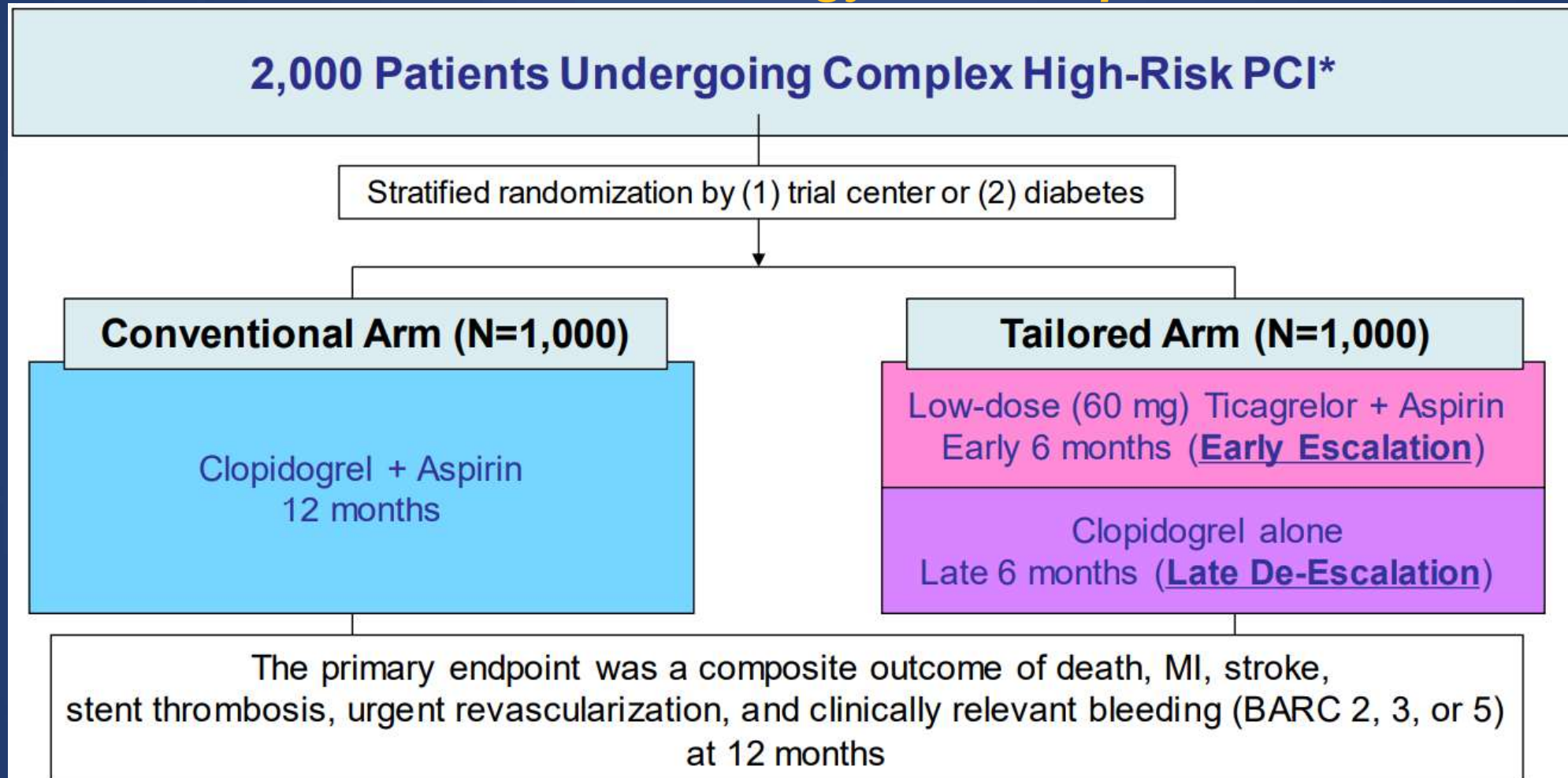
## Tailored P2Y<sub>12</sub> Strategy for CHIP patients



- Ticagrelor 60 mg might provide better safety and tolerability than ticagrelor 90 mg with similar efficacy in East Asian patients with ACS. From OPTIMA trial

# TAILORED-CHIP Trial

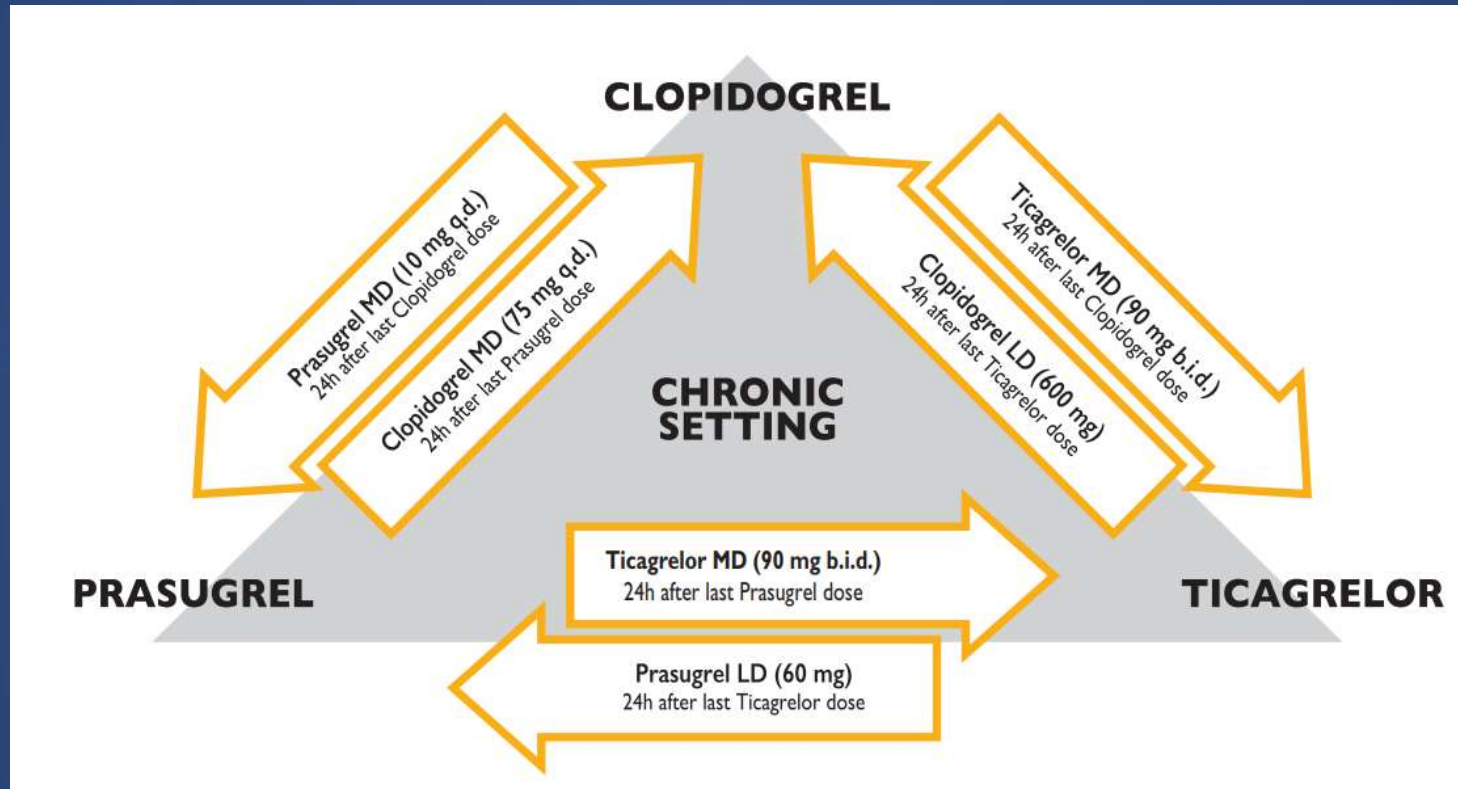
## Tailored P2Y12 Strategy for CHIP patients



### **\*Complex High-Risk PCI**

: Left main PCI, chronic total occlusion, bifurcation requiring two-stent technique, severe calcification, diffuse long lesion (lesion length  $\geq 30$ mm), multivessel PCI ( $\geq 2$  vessels requiring stent implantation),  $\geq 3$  requiring stents implantation,  $\geq 3$  lesions will be treated, predicted total stent length for revascularization  $>60$ mm, diabetes, CKD (Cr-clearance  $<60$ ml/min) or severe LV dysfunction (EF  $<40\%$ ).

# P2Y12 inhibitor: Switching Ticagrelor to Clopidogrel at 6 month



**“At 24 hours from last dose of ticagrelor, clopidogrel 600 mg loading dose should be given”**

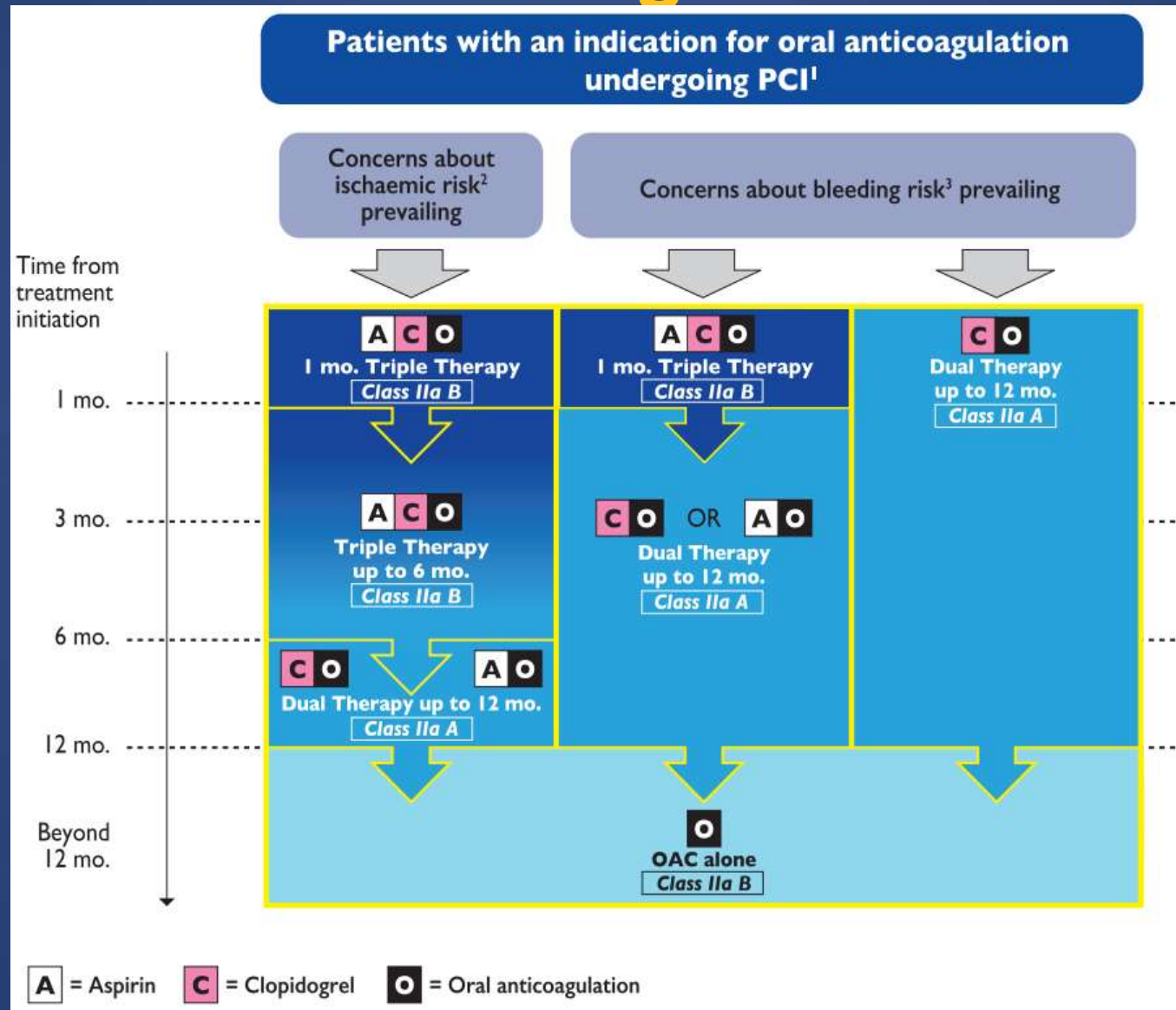
# Antiplatelet Therapy in Patients with Anticoagulation



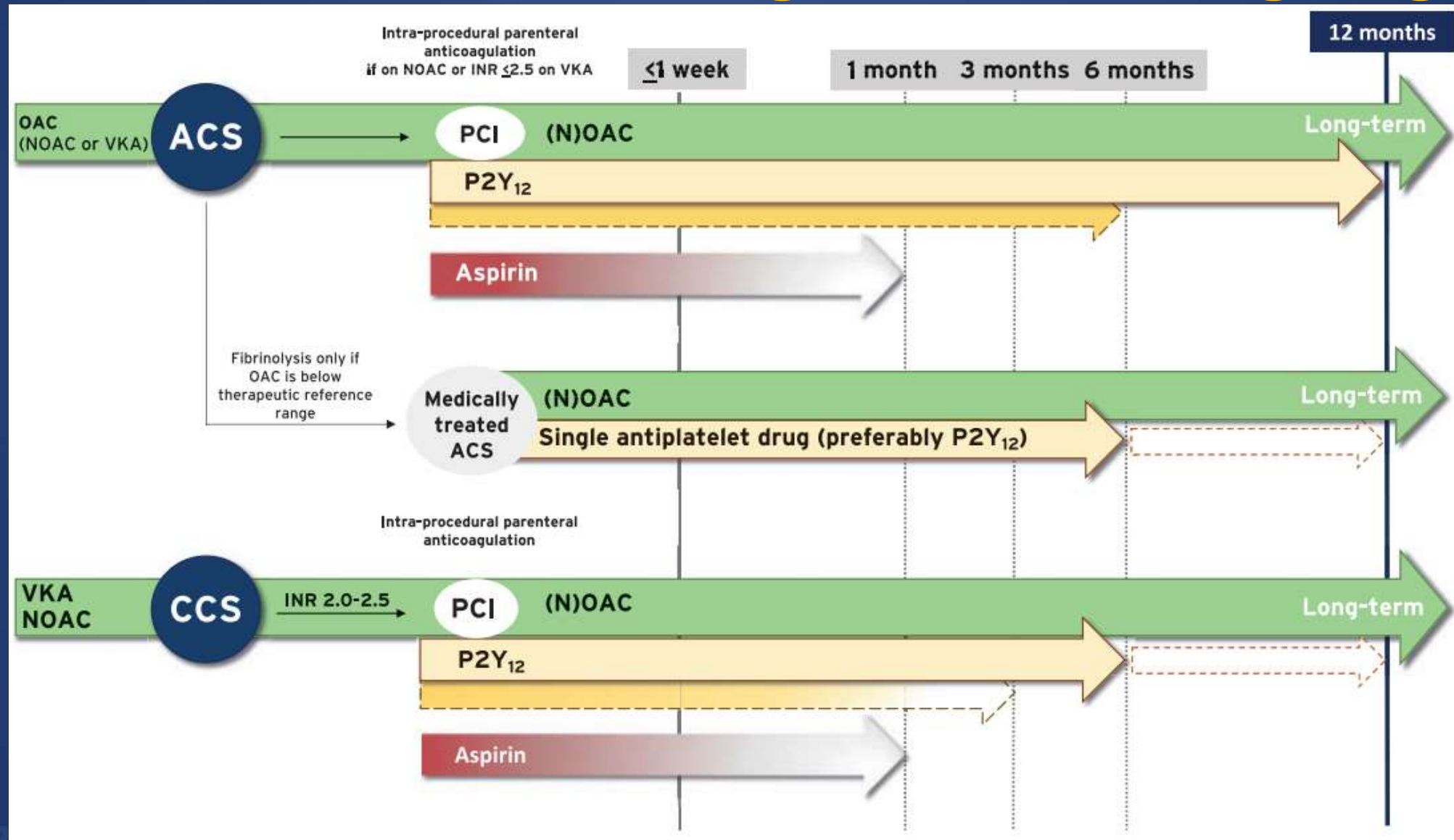
# Antiplatelet Therapy in Patients with an Indication for Oral Anticoagulation Undergoing PCI

COR	LOE	RECOMMENDATIONS
1	B-R	1. In patients with atrial fibrillation who are undergoing PCI and are taking oral anticoagulant therapy, it is recommended to discontinue aspirin treatment after 1 to 4 weeks while maintaining P2Y12 inhibitors in addition to a non-vitamin K oral anticoagulant (rivaroxaban, dabigatran, apixaban, or edoxaban) or warfarin to reduce the risk of bleeding (1-7).
2a	B-R	2. In patients with atrial fibrillation who are undergoing PCI, are taking oral anticoagulant therapy, and are treated with DAPT or a P2Y12 inhibitor monotherapy, it is reasonable to choose a non-vitamin K oral anticoagulant over warfarin to reduce the risk of bleeding (1,3,4).

# Antiplatelet Therapy in Patients with an Indication for Oral Anticoagulation Undergoing PCI



# Antiplatelet Therapy in Patients with an Indication for Oral Anticoagulation Undergoing PCI





# Antiplatelet Therapy in Patients with an Indication for Oral Anticoagulation Undergoing PCI

## THROMBOTIC RISK FACTORS

- Diabetes mellitus requiring therapy
- Prior ACS/recurrent myocardial infarction
- Multivessel CAD
- Concomitant PAD
- Premature CAD (occurring at age of <45 y) or accelerated CAD (new lesion within 2 years)
- CKD (eGFR <60 mL/min)
- Clinical presentation (ACS)
- Multivessel stenting
- Complex revascularisation (left main stenting, bifurcation lesion stenting, chronic total occlusion intervention, last patent vessel stenting)
- Prior stent thrombosis on antiplatelet treatment
- Procedural factors (stent expansion, residual dissection, stent length, etc.)

## BLEEDING RISK FACTORS

- Hypertension
- Abnormal renal or liver function
- Stroke or ICH history
- Bleeding history or bleeding diathesis (e.g., anaemia with haemoglobin <110 g/L)
- Labile INR (if on VKA)
- Elderly (>65 years)
- Drugs (concomitant OAC and antiplatelet therapy, NSAIDs), excessive alcohol consumption

## STRATEGIES TO REDUCE BLEEDING ASSOCIATED WITH PCI

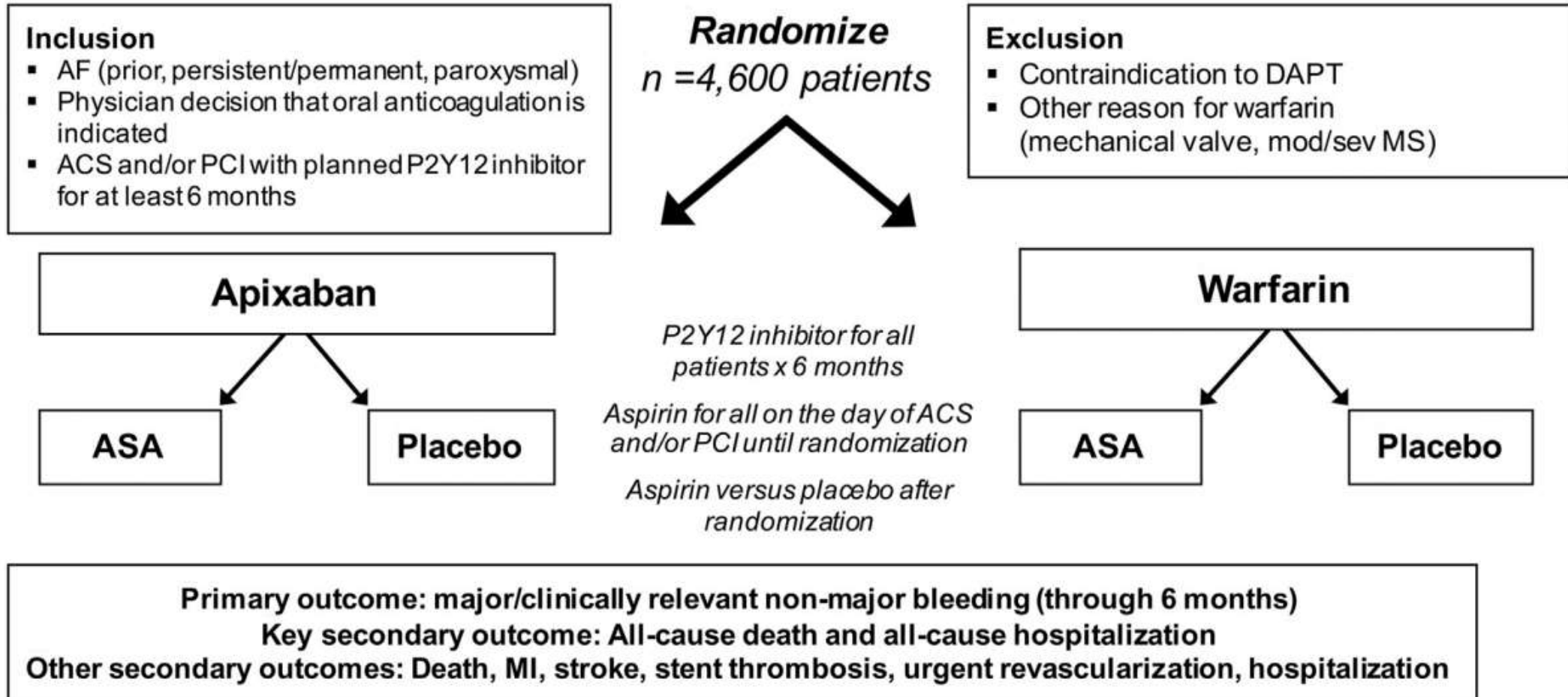
- Radial artery access
- PPIs in patients taking DAPT who are at increased risk of bleeding (e.g., the elderly, dyspepsia, gastro-oesophageal reflux disease, Helicobacter pylori infection, chronic alcohol use)
- Non-administration of unfractionated heparin in patients on VKA with INR >2.5
- Pre-treatment with aspirin only, add a P2Y<sub>12</sub> inhibitor when coronary anatomy is known or if STEMI
- GP IIb/IIIa inhibitors only for bailout or periprocedural complications
- Shorter duration of combined antithrombotic therapy



# AUGUSTUS Trial

## Antithrombotic Therapy after ACS or PCI in Atrial Fibrillation

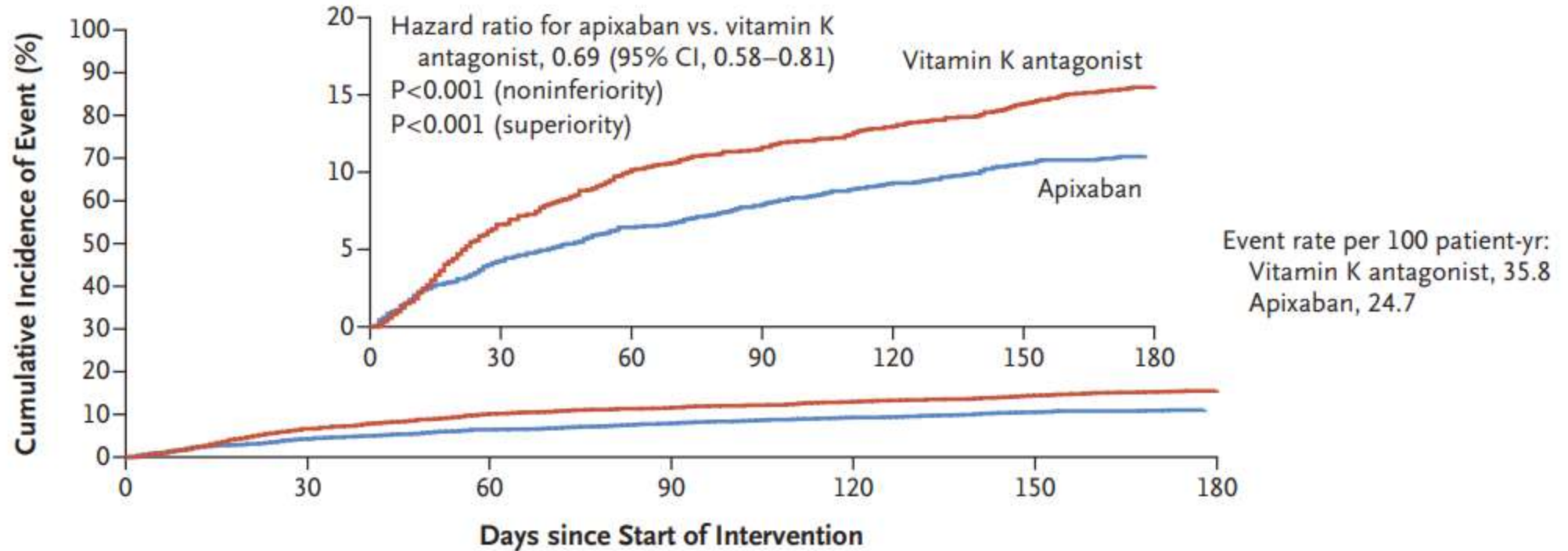
### Apixaban Versus Warfarin in Patients with AF and ACS and/or PCI: The AUGUSTUS Trial



# AUGUSTUS Trial

## Antithrombotic Therapy after ACS or PCI in Atrial Fibrillation

### A Primary Outcome — Apixaban vs. Vitamin K Antagonist



#### No. at Risk

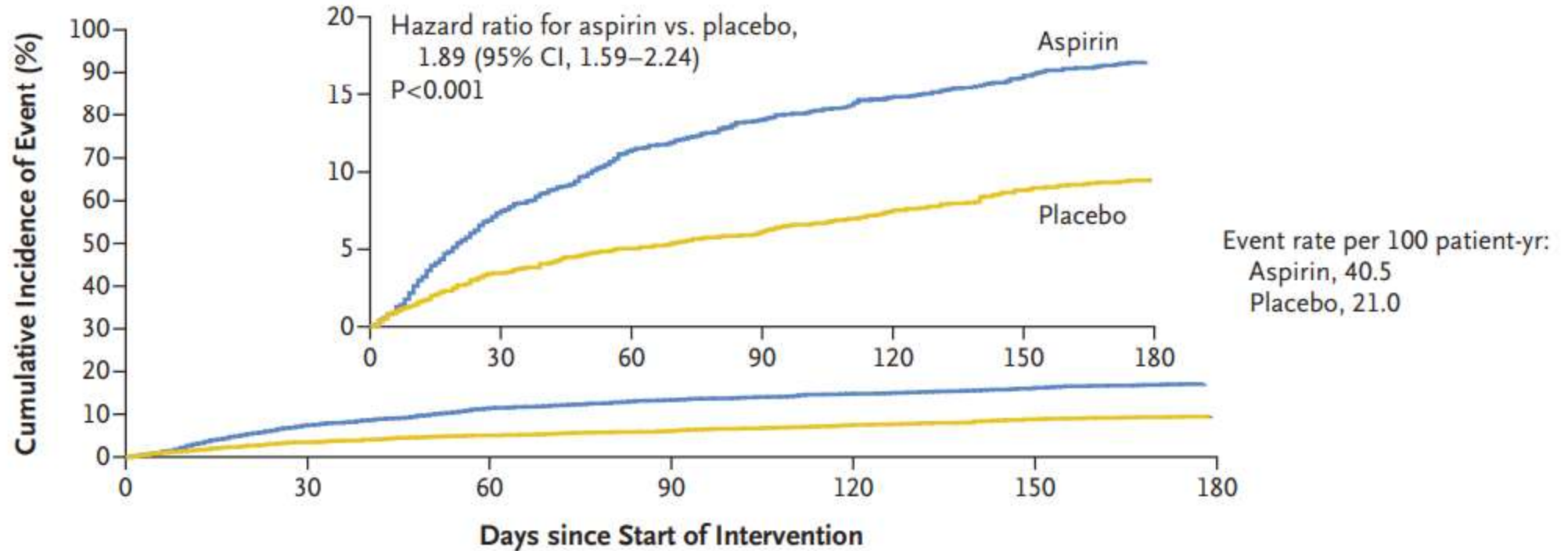
Vitamin K antagonist	2259	1984	1861	1795	1736	1686	1079
Apixaban	2290	2110	2019	1957	1902	1858	1037

- Primary outcome was major or clinically relevant nonmajor bleeding defined by the International Society on Thrombosis and Haemostasis.

# AUGUSTUS Trial

## Antithrombotic Therapy after ACS or PCI in Atrial Fibrillation

### B Primary Outcome — Aspirin vs. Placebo



#### No. at Risk

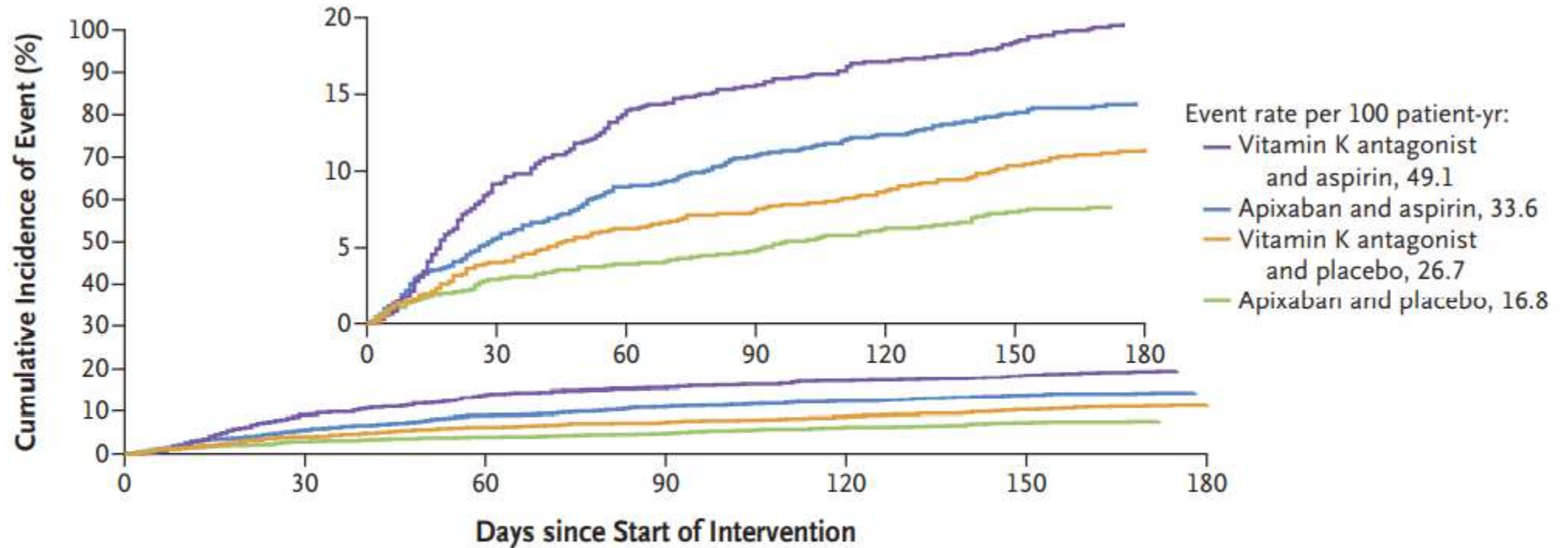
Aspirin	2277	2003	1863	1789	1717	1674	962
Placebo	2279	2095	2006	1941	1880	1824	1079

- Primary outcome was major or clinically relevant nonmajor bleeding defined by the International Society on Thrombosis and Haemostasis.

# AUGUSTUS Trial

## Antithrombotic Therapy after ACS or PCI in Atrial Fibrillation

C Primary Outcome, According to Intervention Combination



**No. at Risk**

Vitamin K antagonist and aspirin	1123	962	881	838	800	776	467
Apixaban and aspirin	1145	1036	975	937	903	880	485
Vitamin K antagonist and placebo	1126	1007	947	917	883	851	528
Apixaban and placebo	1143	1075	1044	1007	975	947	536

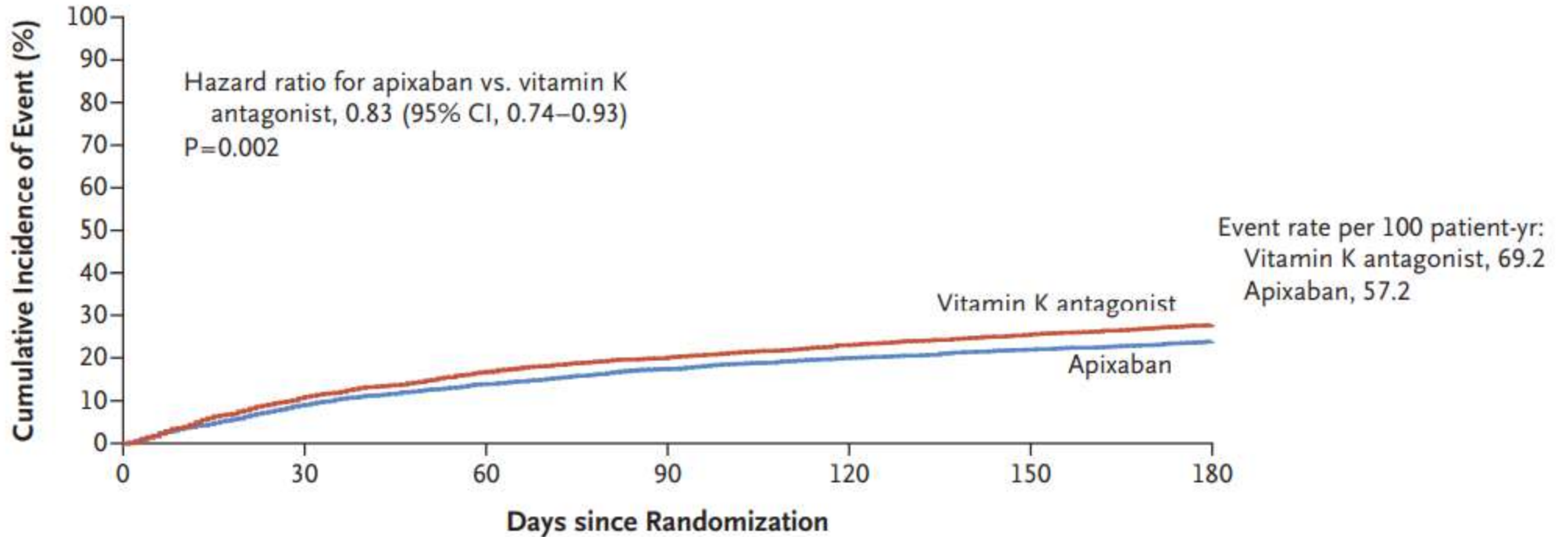
Primary outcome was major or clinically relevant nonmajor bleeding defined by the International Society on Thrombosis and Haemostasis.



# AUGUSTUS Trial

## Antithrombotic Therapy after ACS or PCI in Atrial Fibrillation

### A Death or Hospitalization — Apixaban vs. Vitamin K Antagonist



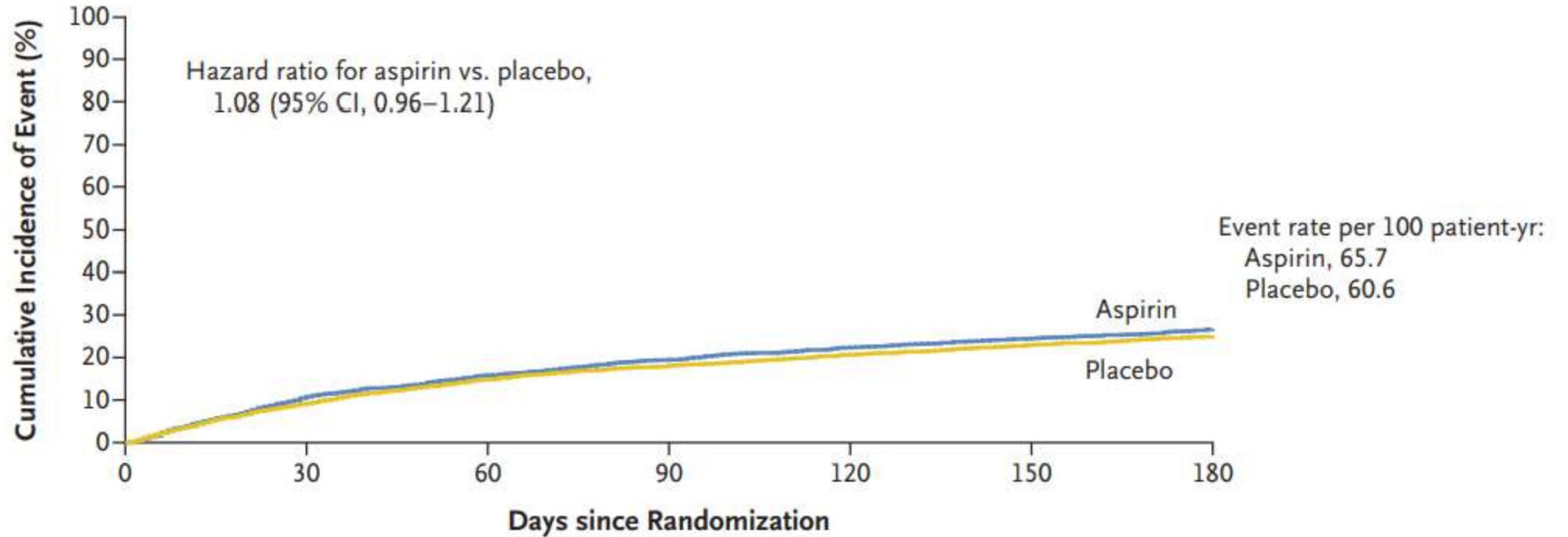
#### No. at Risk

Vitamin K antagonist	2308	2035	1885	1805	1732	1673	1001
Apixaban	2306	2090	1965	1881	1821	1772	947

# AUGUSTUS Trial

## Antithrombotic Therapy after ACS or PCI in Atrial Fibrillation

### B Death or Hospitalization — Aspirin vs. Placebo



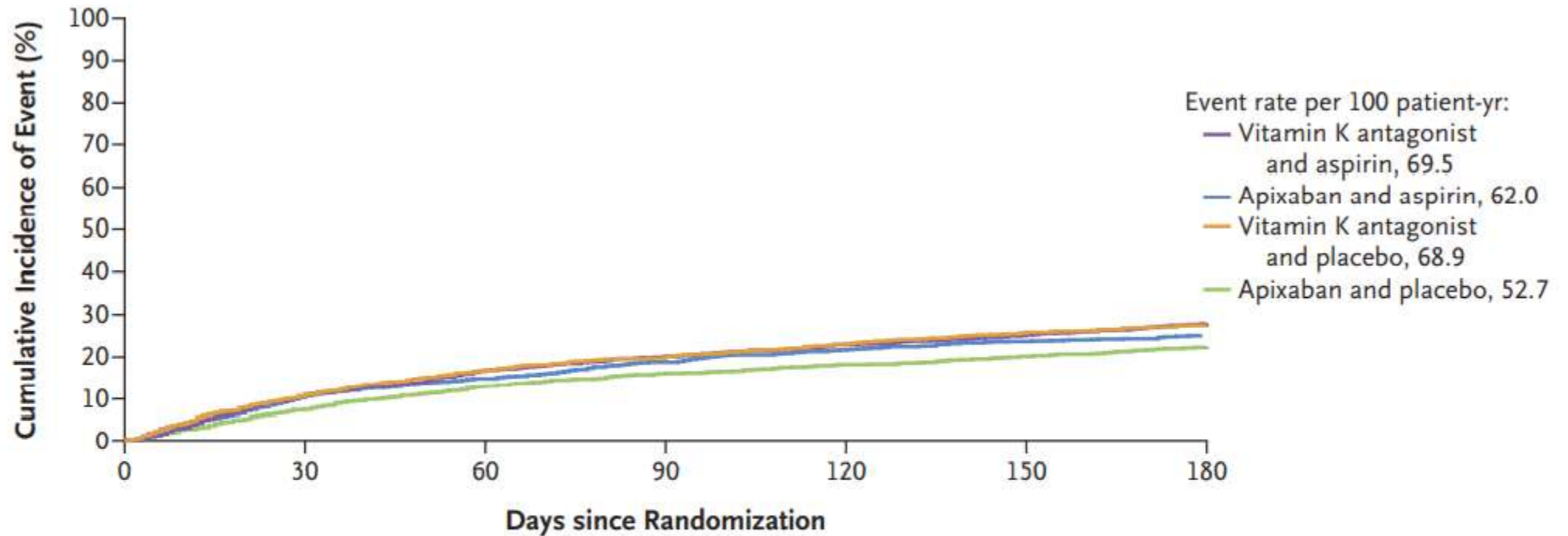
#### No. at Risk

Aspirin	2307	2042	1909	1822	1752	1699	951
Placebo	2307	2083	1941	1864	1801	1746	997

# AUGUSTUS Trial

## Antithrombotic Therapy after ACS or PCI in Atrial Fibrillation

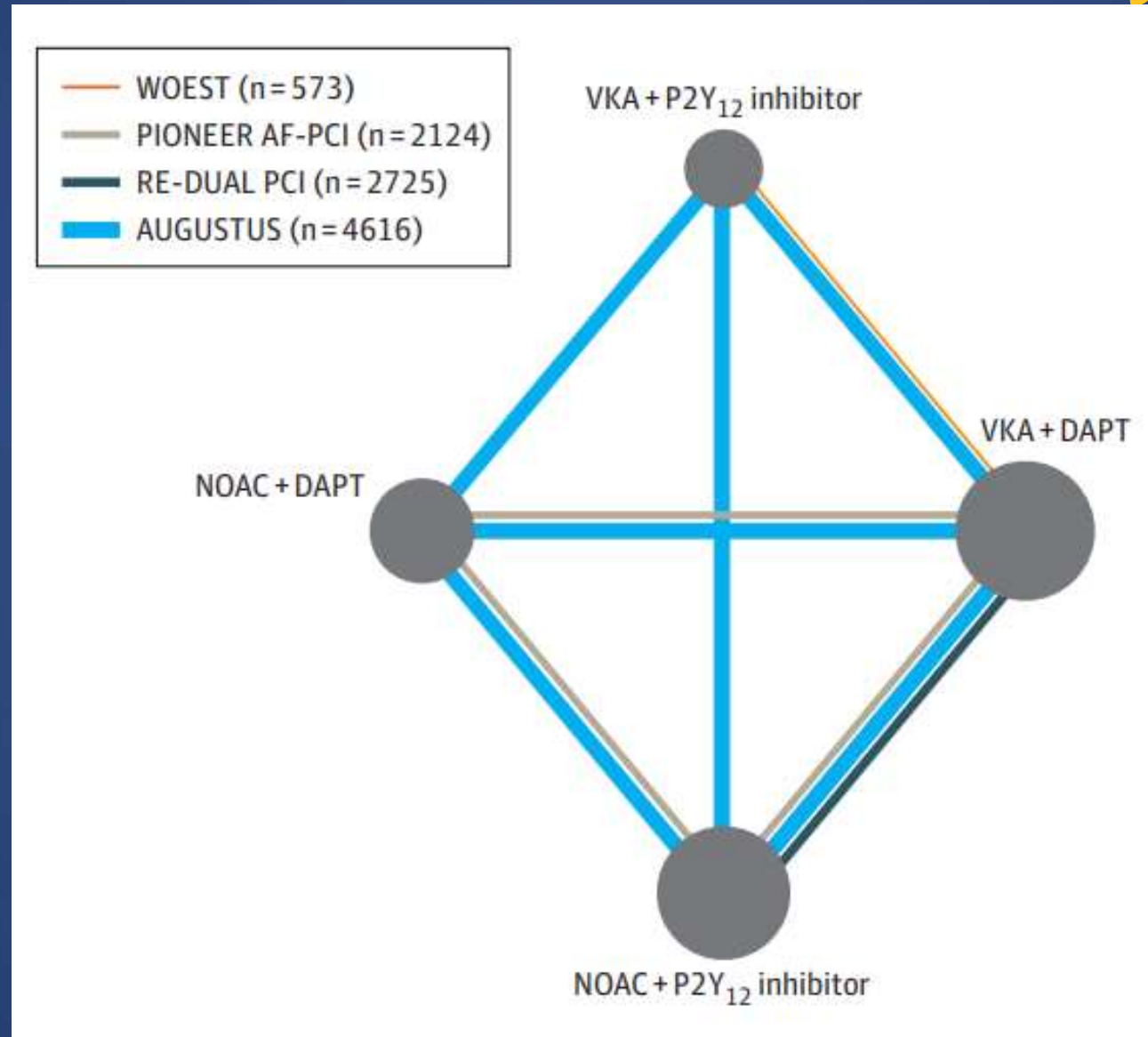
### C Death or Hospitalization, According to Intervention Combination



#### No. at Risk

Vitamin K antagonist and aspirin	1154	1016	939	899	864	836	492
Apixaban and aspirin	1153	1026	970	923	888	863	459
Vitamin K antagonist and placebo	1154	1019	946	906	868	837	509
Apixaban and placebo	1153	1064	995	958	933	909	488

# Safety and Efficacy of Antithrombotic Strategies in Patients with AF after PCI: Meta-analysis of RCTs



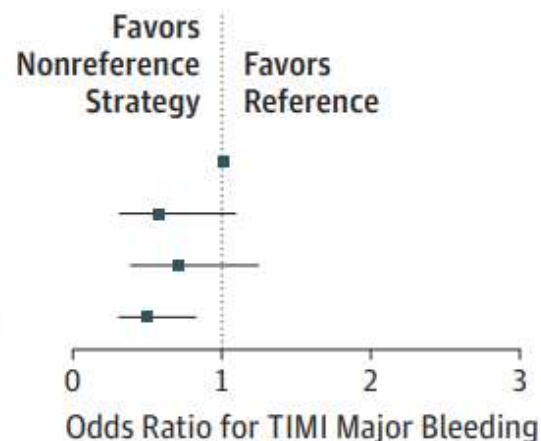


# Safety and Efficacy of Antithrombotic Strategies in Patients with AF after PCI: Meta-analysis of RCTs

**A** TIMI major bleeding

Odds ratio (95% CI)

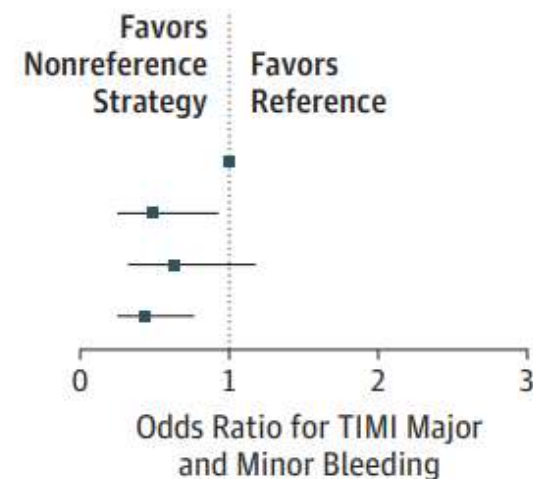
VKA + DAPT (reference)	
VKA + P2Y <sub>12</sub> inhibitor	0.58 (0.31-1.08)
NOAC + DAPT	0.70 (0.38-1.23)
NOAC + P2Y <sub>12</sub> inhibitor	0.49 (0.30-0.82)



**B** TIMI major and minor bleeding

Odds ratio (95% CI)

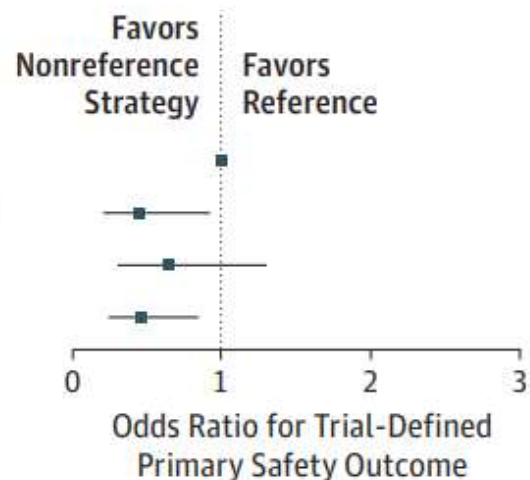
VKA + DAPT (reference)	
VKA + P2Y <sub>12</sub> inhibitor	0.49 (0.26-0.92)
NOAC + DAPT	0.63 (0.33-1.17)
NOAC + P2Y <sub>12</sub> inhibitor	0.43 (0.25-0.76)



**C** Trial-defined primary safety outcome

Odds ratio (95% CI)

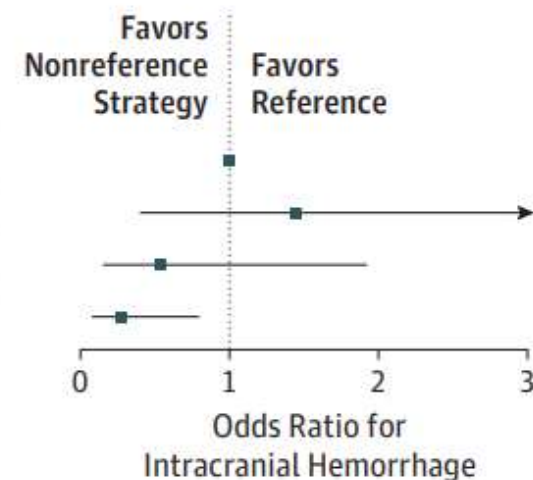
VKA + DAPT (reference)	
VKA + P2Y <sub>12</sub> inhibitor	0.45 (0.21-0.92)
NOAC + DAPT	0.64 (0.31-1.31)
NOAC + P2Y <sub>12</sub> inhibitor	0.47 (0.25-0.85)



**D** Intracranial hemorrhage

Odds ratio (95% CI)

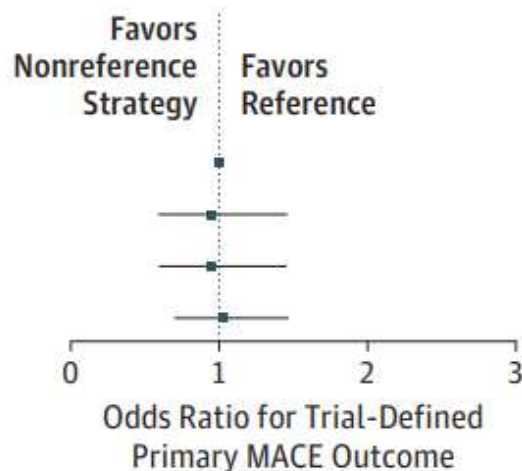
VKA + DAPT (reference)	
VKA + P2Y <sub>12</sub> inhibitor	1.44 (0.40-5.22)
NOAC + DAPT	0.54 (0.15-1.92)
NOAC + P2Y <sub>12</sub> inhibitor	0.26 (0.08-0.79)



# Safety and Efficacy of Antithrombotic Strategies in Patients with AF after PCI: Meta-analysis of RCTs

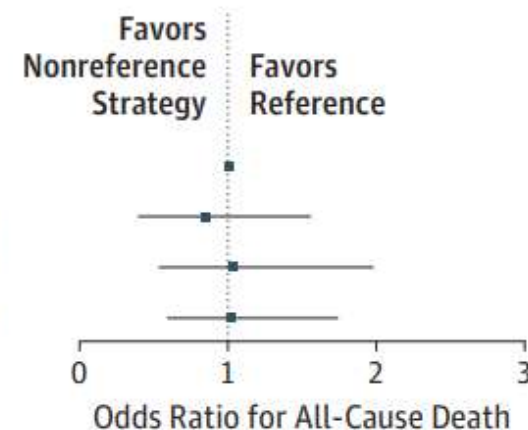
**A** Trial-defined primary MACE

Odds ratio (95% CI)	
VKA + DAPT (reference)	
VKA + P2Y <sub>12</sub> inhibitor	0.96 (0.60-1.46)
NOAC + DAPT	0.94 (0.60-1.15)
NOAC + P2Y <sub>12</sub> inhibitor	1.02 (0.71-1.97)



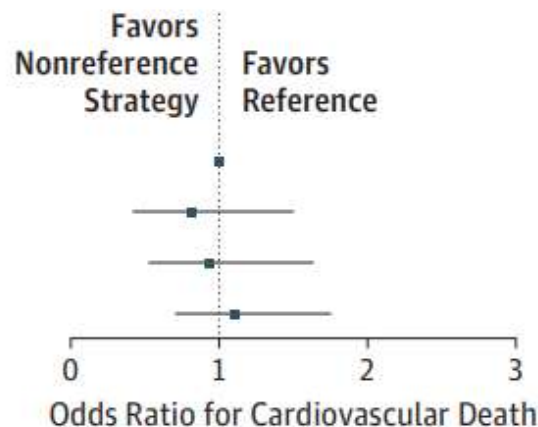
**B** All-cause death

Odds ratio (95% CI)	
VKA + DAPT (reference)	
VKA + P2Y <sub>12</sub> inhibitor	0.84 (0.40-1.56)
NOAC + DAPT	1.04 (0.54-1.98)
NOAC + P2Y <sub>12</sub> inhibitor	1.02 (0.59-1.74)



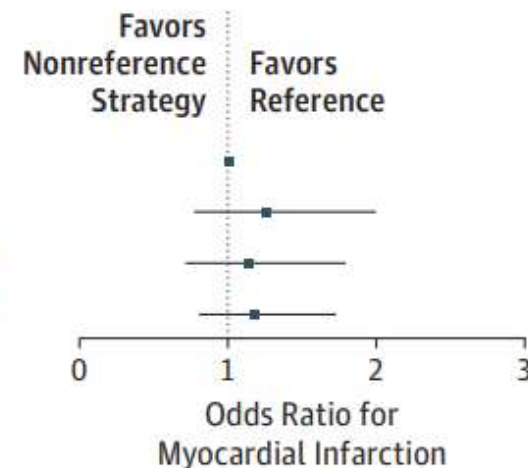
**C** Cardiovascular death

Odds ratio (95% CI)	
VKA + DAPT (reference)	
VKA + P2Y <sub>12</sub> inhibitor	0.82 (0.42-1.49)
NOAC + DAPT	0.94 (0.53-1.63)
NOAC + P2Y <sub>12</sub> inhibitor	1.11 (0.70-1.75)



**D** Myocardial infarction

Odds ratio (95% CI)	
VKA + DAPT (reference)	
VKA + P2Y <sub>12</sub> inhibitor	1.25 (0.77-1.99)
NOAC + DAPT	1.13 (0.72-1.78)
NOAC + P2Y <sub>12</sub> inhibitor	1.18 (0.81-1.72)

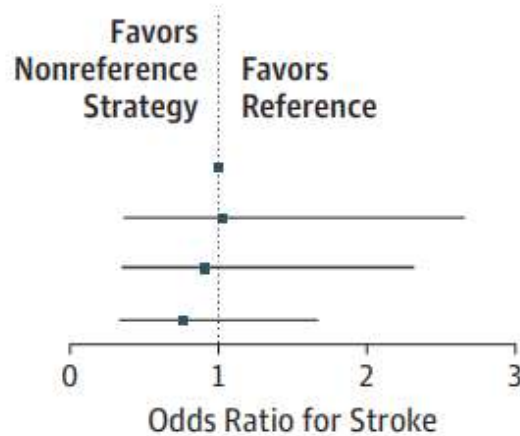


# Safety and Efficacy of Antithrombotic Strategies in Patients with AF after PCI: Meta-analysis of RCTs

## E Stroke

### Odds ratio (95% CI)

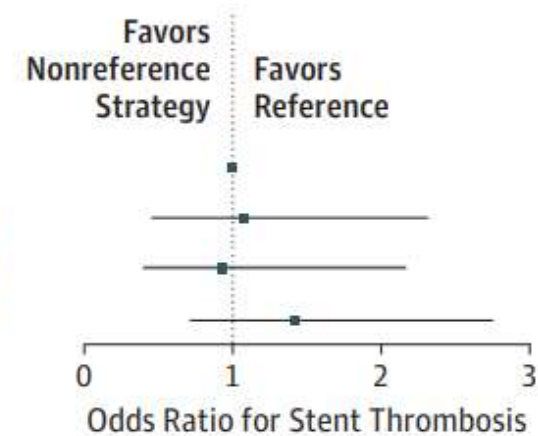
VKA + DAPT (reference)	
VKA + P2Y <sub>12</sub> inhibitor	1.02 (0.36-2.65)
NOAC + DAPT	0.91 (0.35-2.32)
NOAC + P2Y <sub>12</sub> inhibitor	0.77 (0.34-1.67)



## F Stent thrombosis

### Odds ratio (95% CI)

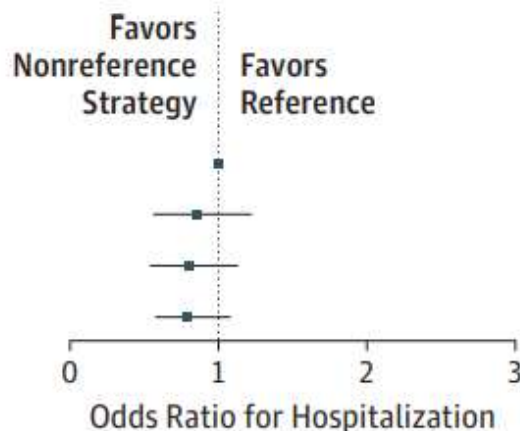
VKA + DAPT (reference)	
VKA + P2Y <sub>12</sub> inhibitor	1.08 (0.46-2.31)
NOAC + DAPT	0.93 (0.40-2.17)
NOAC + P2Y <sub>12</sub> inhibitor	1.41 (0.71-2.76)



## G Hospitalization

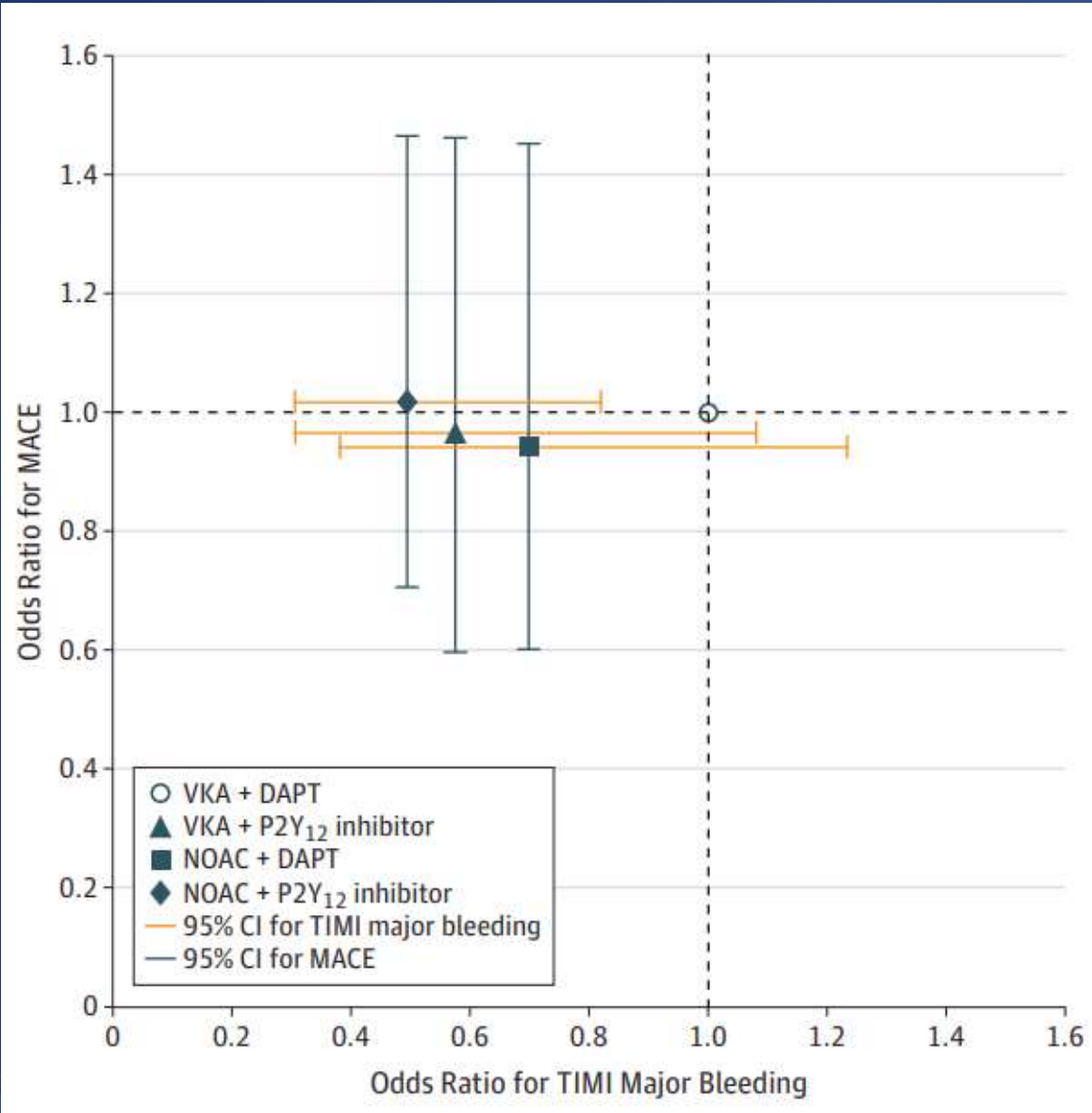
### Odds ratio (95% CI)

VKA + DAPT (reference)	
VKA + P2Y <sub>12</sub> inhibitor	0.86 (0.57-1.23)
NOAC + DAPT	0.80 (0.55-1.13)
NOAC + P2Y <sub>12</sub> inhibitor	0.80 (0.59-1.08)





# Safety and Efficacy of Antithrombotic Strategies in Patients with AF after PCI: Meta-analysis of RCTs



- A regimen of NOACs plus P2Y<sub>12</sub> inhibitor was associated with less bleeding compared with VKAs plus DAPT.
- Strategies omitting aspirin caused less bleeding, including intracranial bleeding, without significant difference in MACE, compared with strategies including aspirin.
- Our results support the use of NOAC plus P2Y<sub>12</sub> inhibitor as the preferred regimen post-percutaneous coronary intervention for these high-risk patients with AF.
- A regimen of VKA plus DAPT should generally be avoided.

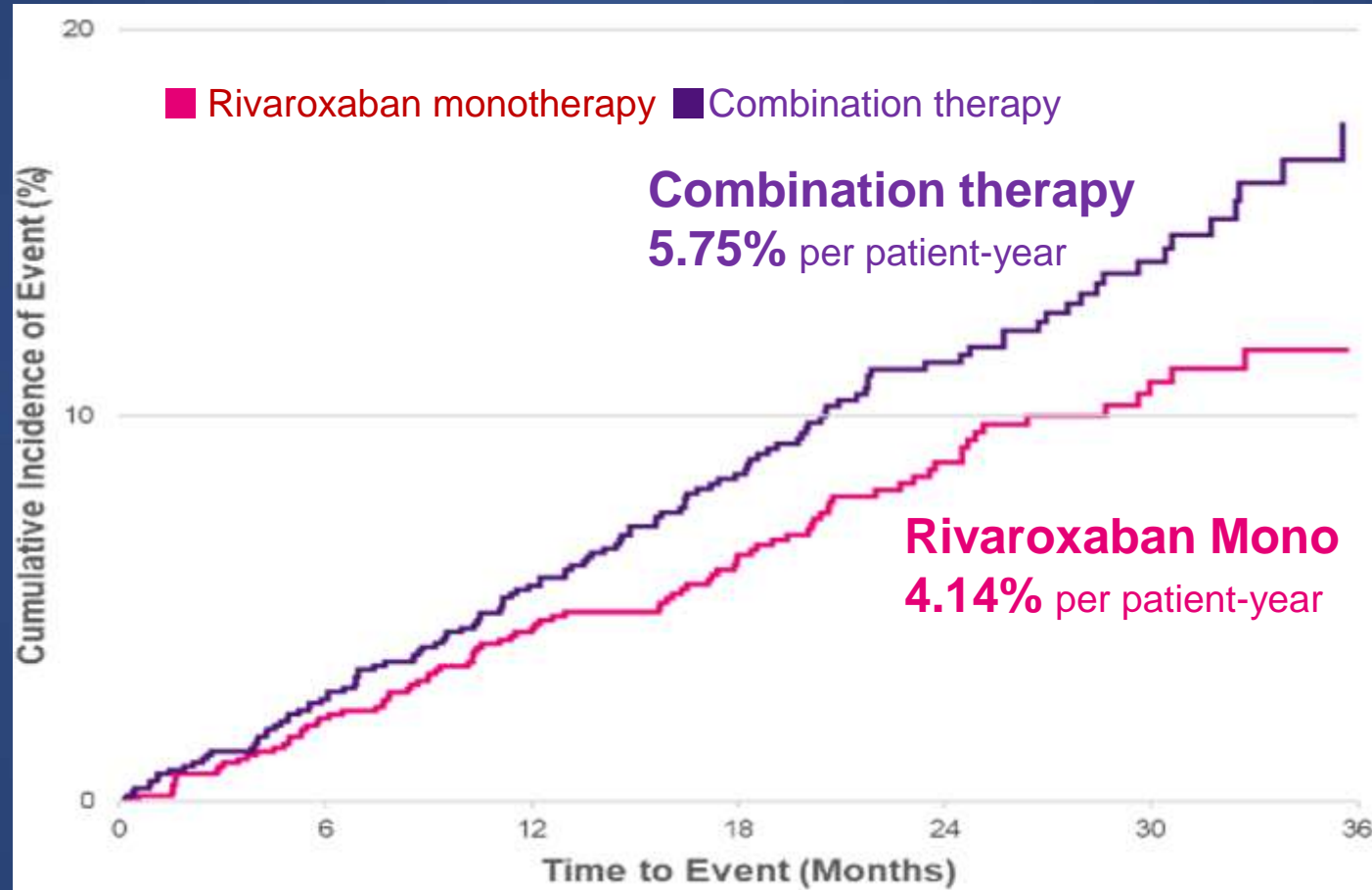


# AFIRE

## Early Termination of the Trial

- The evaluation of the patients was planned to continue until September 2018.
- Because of a **higher risk of death from any cause in the combination-therapy group**, the independent data and safety monitoring committee recommended early termination of the trial in July 2018.
- The median treatment duration was 23.0 months (interquartile range, 15.8 to 31.0)
- The median follow-up period was 24.1 months ( interquartile range, 17.3 to 31.5)

# Primary Efficacy Endpoint\* (CV Events or Death)



**HR, 0.72 (0.55 - 0.95)**  
**P<0.001 (noninferiority)**

## Number of patients at risk

Rivaroxaban monotherapy

1107      1071      984      774      518      309      89

Combination therapy

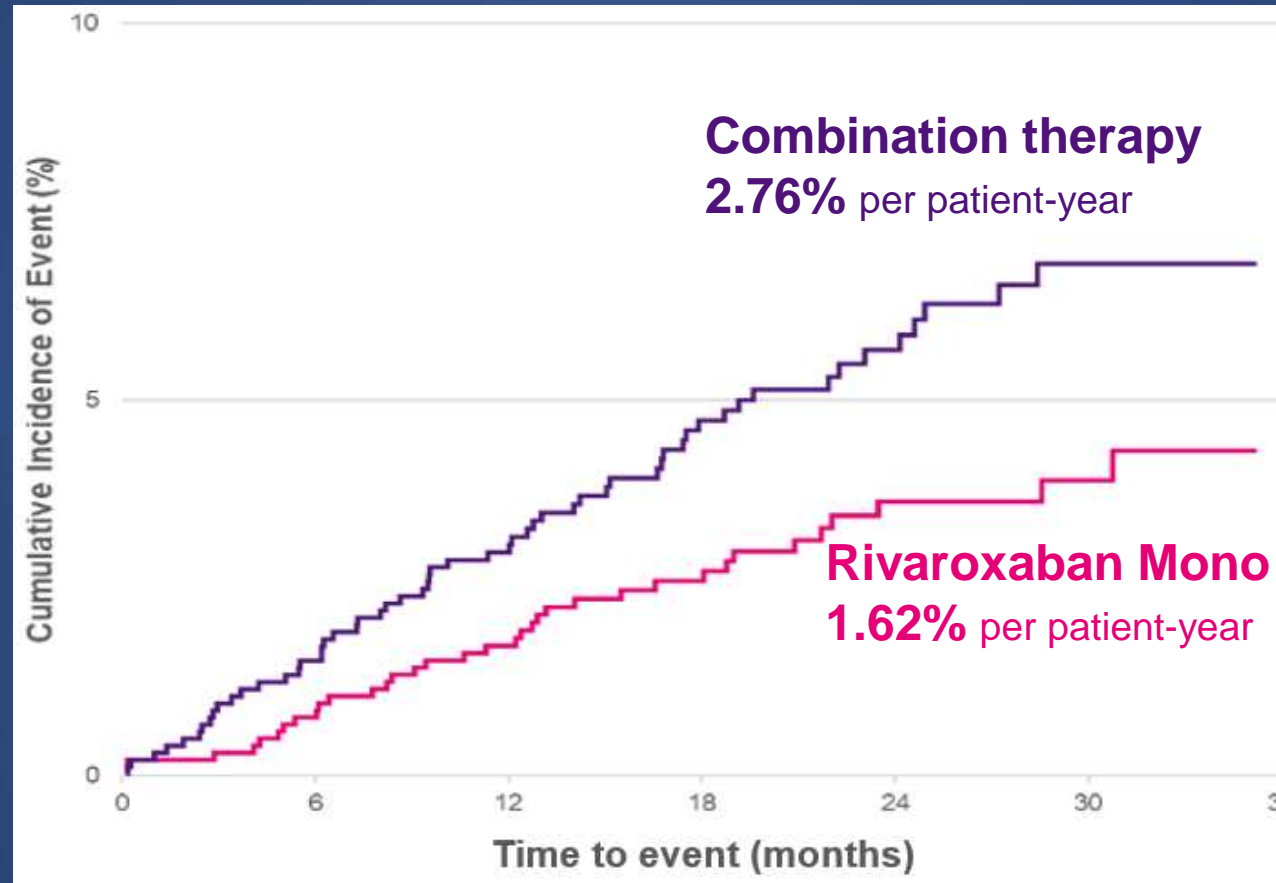
1108      1057      962      754      499      292      80

Bayer does not recommend off-label use of products. Before prescribing any products, please consult the relevant local prescribing information.

\*The composite endpoint included stroke, systemic embolism, myocardial infarction, unstable angina requiring revascularization and all-cause mortality

Yasuda S et al, *N Engl J Med* 2019;381:1103–1113

# Primary Safety Endpoint (Major Bleeding)\*



## Number of patients at risk

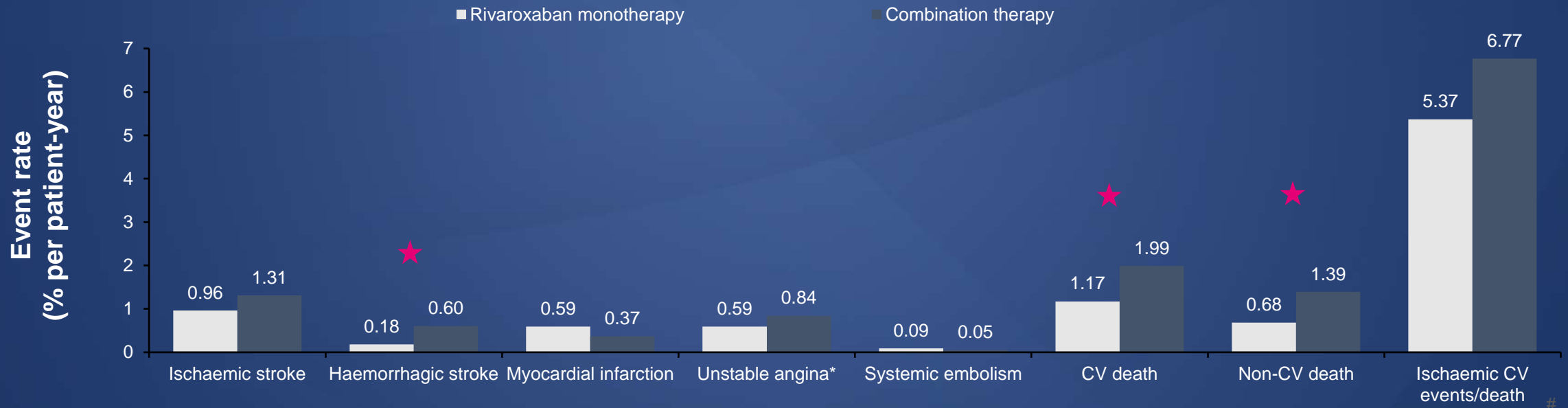
Rivaroxaban monotherapy	1099	1074	994	786	526	312	89
Combination therapy	1099	1055	962	750	506	294	80

Bayer does not recommend off-label use of products. Before prescribing any products, please consult the relevant local prescribing information.

\*As defined according to the criteria of the International Society on Thrombosis and Haemostasis

# Secondary Efficacy Endpoints

Lower rate of all-cause mortality for rivaroxaban monotherapy versus combination therapy (HR=0.55; 95% CI 0.38–0.81), due to lower incidences of both CV and non-CV death  
Trial terminated early because of higher risk of death in the combination therapy group  
The most common causes of death were heart failure, stroke and cancer



Bayer does not recommend off-label use of products. Before prescribing any products, please consult the relevant local prescribing information.

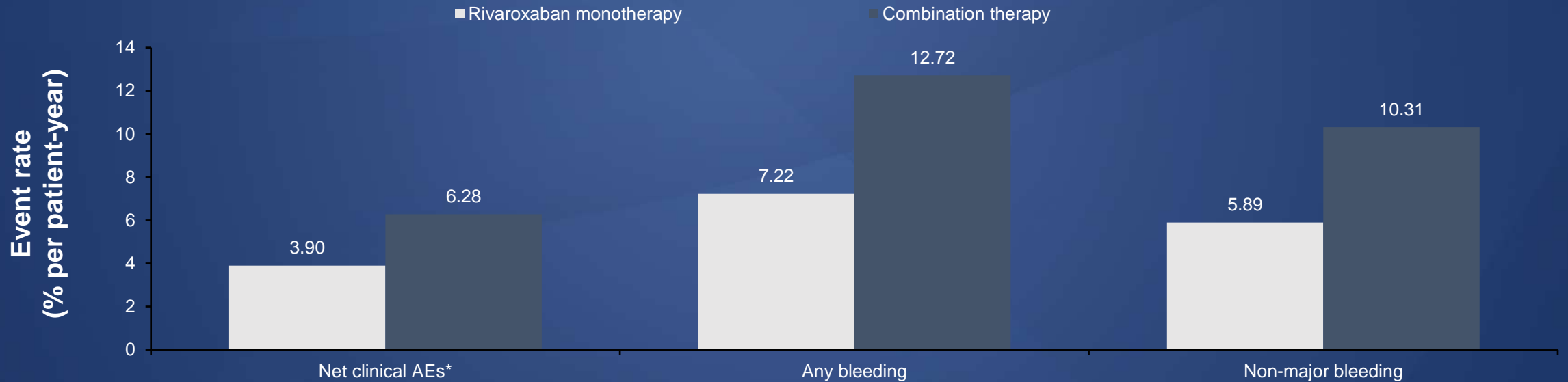
\*Unstable angina requiring revascularization; #composite of death from any cause, myocardial infarction, unstable angina requiring revascularization, stroke, transient ischaemic attack, systemic arterial embolism, venous thromboembolism, revascularization or stent thrombosis



# Other Secondary Endpoints

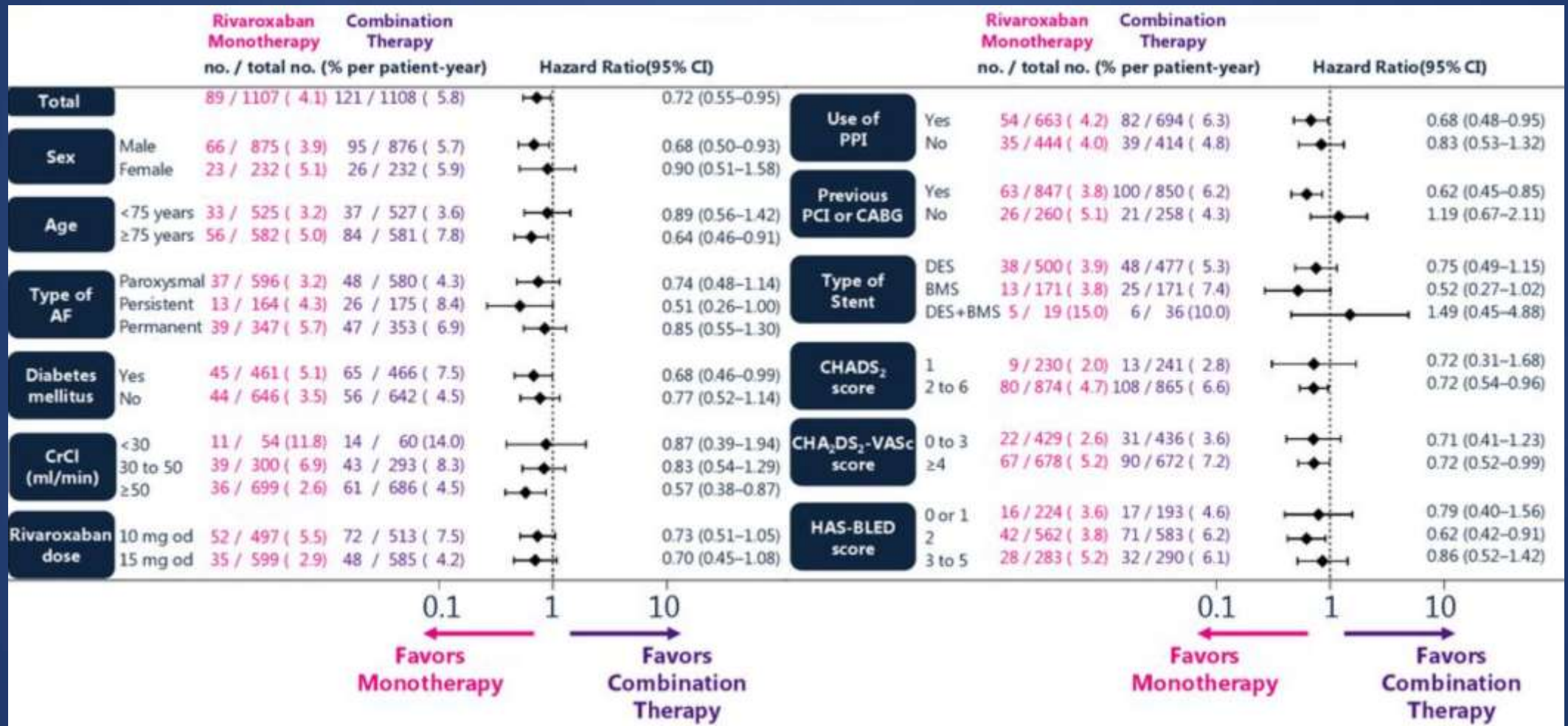
Lower rate of net clinical AEs\* for rivaroxaban monotherapy versus combination therapy (HR=0.62; 95% CI 0.47–0.82)

Lower rate of non-major bleeding events for rivaroxaban monotherapy versus combination therapy (HR=0.58; 95% CI 0.46–0.72)

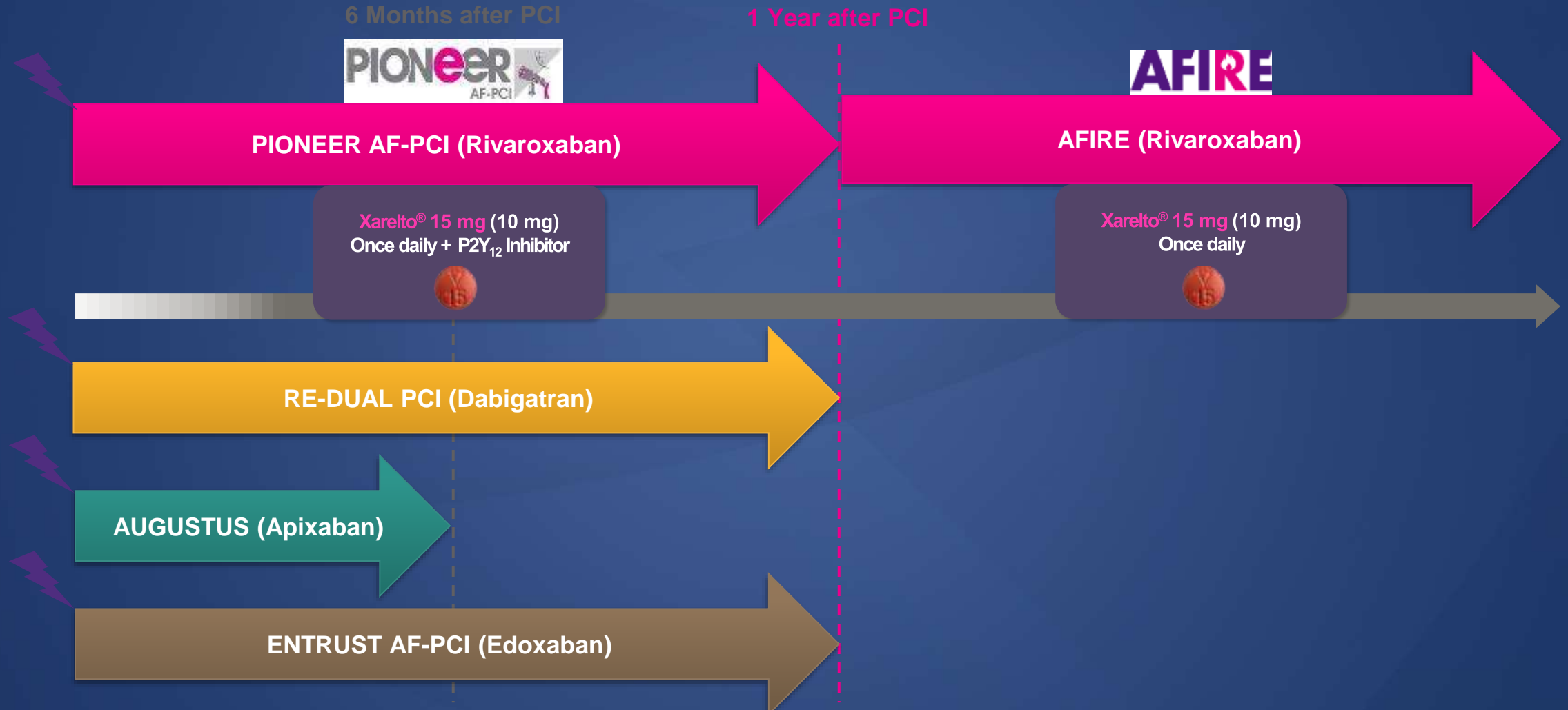


\*Composite of death from any cause, myocardial infarction, stroke or major bleeding, transient ischaemic attack, systemic arterial embolism, venous thromboembolism, revascularization or stent thrombosis

# Subgroup Analysis for Primary Efficacy Endpoint



# AF-PCI Trials among NOACs



Please note this information is from separate, independent studies and the studies are not directly comparable owing to different study design. Therefore it should be carefully interpreted.

1. Gibson CM et al, New Engl J Med 2016; doi: 10.1056/NEJMoa1611594
2. Christopher PC et al, New Engl J Med 2017; 377:1513-1524
3. Lopes RD et al, New Engl J Med 2019; DOI: 10.1056/NEJMoa1817083
4. Vranckx P et al, American Heart Journal. 2018;196:105-112

# EPIC-CAD Trial

## Edoxaban-based long-term antithrombotic therapy with AF and CAD

(Edoxaban versus Edoxaban with antiPlatelet agent In patients with atrial fibrillation and Chronic stable Coronary Artery Disease)

### EPIC-CAD trial

Patients with high-risk atrial fibrillation (CHA<sub>2</sub>DS<sub>2</sub>-VASc score  $\geq 2$ ) and stable coronary artery disease\* (Approximately N=1,038)

Randomization

Edoxaban monotherapy (Approximately N=519)

Edoxaban plus single antiplatelet therapy (Approximately N=519)

Primary endpoint – net clinical outcomes (a composite of all-cause death, stroke, systemic embolic event, myocardial infarction, unplanned revascularization, and major bleeding or clinically relevant non-major bleeding) at 1 year after randomization

\***Stable coronary artery disease** was defined as (1) prior coronary revascularization (either PCI or CABG,  $\geq 6$  months for stable angina or  $\geq 12$  months for acute coronary syndrome, or (2) Anatomically confirmed obstructive CAD ( $\geq 50\%$  stenosis on coronary angiography or CT angiography) on medical therapy not requiring revascularization.



# EPIC-CAD Trial

## *Edoxaban-based long-term antithrombotic therapy with AF and CAD*

### Inclusion criteria

- 1. Patients aged  $\geq 18$  y
- 2. Patients with AF with high embolic risk (CHA<sub>2</sub>DS<sub>2</sub>-VASc score  $\geq 2$ )
- 3. Patients with stable CAD
  - Coronary revascularization (either PCI or CABG) at least 6 mo for stable angina or at least 1 y for ACS before study enrollment
  - Anatomically confirmed (with  $\geq 50\%$  stenosis of major coronary artery by CAG or coronary CTA on optimal medical therapy not requiring revascularization

# EPIC-CAD Trial

## *Edoxaban-based long-term antithrombotic therapy with AF and CAD*

### Exclusion criteria

- 1. Patients with thrombocytopenia (<50,000/uL)
- 2. High risk of bleeding prohibiting anticoagulant use according to the attending physician's discretion (ie, baseline comorbidities, hyper- or hypocoagulable state, increased prothrombin time, or activated partial thromboplastin time)
- 3. Prior history of intracranial hemorrhage
- 4. Mechanical prosthetic valve or moderate-to-severe mitral stenosis
- 5. Patients contraindicated for edoxaban or antiplatelets
- 6. Planned PCI or CABG within 1 y after randomization
- 7. Liver cirrhosis or liver dysfunction (AST or ALT >  $\times 3$  of normal range or coagulation abnormality)
- 8. Creatinine clearance <30 mL/min
- 9. Life expectancy <12 mo
- 10. Patients unable to provide written informed consent or participate in long-term follow-up
- 11. Pregnant or lactating women
- 12. Patients actively participating in another drug or device investigational study

# EPIC-CAD Trial

## *Edoxaban-based long-term antithrombotic therapy with AF and CAD*

### Primary endpoint

- Net clinical outcomes – composites of all-cause death, stroke, systemic embolic event, myocardial infarction, unplanned revascularization of the major coronary artery, and major bleeding or clinically relevant nonmajor bleeding event

### Secondary endpoints

- Efficacy outcomes
  - 1) All-cause death
  - 2) Cardiovascular death
  - 3) Myocardial infarction
  - 4) Ischemic stroke
  - 5) Systemic embolism
  - 6) Unplanned revascularization
  - 7) Composite of hard clinical endpoints (all-cause death, myocardial infarction, ischemic stroke, and systemic embolism)
  - 8) Stent thrombosis (in patients who underwent coronary stenting)

# EPIC-CAD Trial

## *Edoxaban-based long-term antithrombotic therapy with AF and CAD*

### Secondary endpoints

- Safety outcomes

- 1) Composite of major or clinically relevant nonmajor bleeding during follow-up as defined by the International Society on Thrombosis and Hemostasis (ISTH)
- 2) Fatal bleeding (ISTH, BARC 5)
- 3) Major bleeding (ISTH, BARC 3, TIMI major bleeding)
- 4) Clinically relevant nonmajor bleeding (ISTH, BARC, and TIMI criteria)
- 5) Any bleeding (ISTH, BARC, and TIMI criteria)
- 6) Intracranial hemorrhage
- 7) Gastrointestinal hemorrhage



# ADORE Trial

## Evaluation of Routine Functional Testing after PCI

**TABLE 2** Functional Test Results of Patients Who Underwent Routine Functional Testing

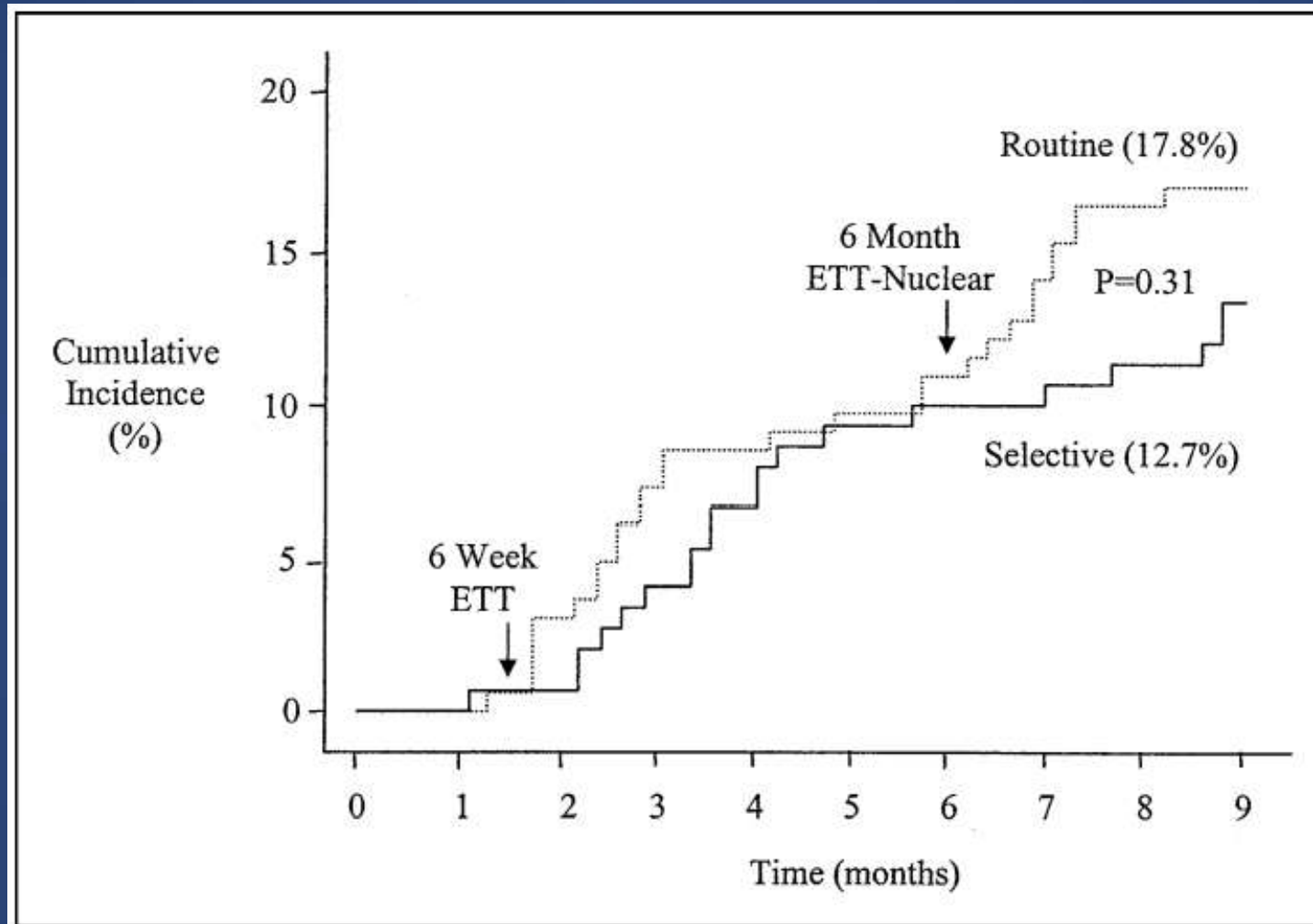
Test Result	Timing of Functional Test	
	6 Wks	6 Mon*
No. of METs achieved (mean $\pm$ SD)	9 $\pm$ 3%	9 $\pm$ 3%
Mean maximum predicted heart rate achieved	91 $\pm$ 19%	89 $\pm$ 18%
Maximum predicted heart rate $\geq$ 85%	66%	65%
Electrically or clinically positive	23%	30%
Electrically, clinically, or imaging positive <sup>†</sup>	–	38%
Electrically and clinically negative	60%	57%

**TABLE 3** Functional Test Results at Nine Months\*

Test Result	Functional Testing Strategy		
	Routine	Selective	p Value
No. of METs achieved (mean $\pm$ SD)	10 $\pm$ 3%	9 $\pm$ 3%	0.09
Mean maximum predicted heart rate achieved	90 $\pm$ 21%	91 $\pm$ 16%	0.87
Maximum predicted heart rate $\geq$ 85%	68%	69%	0.89
Electrically or clinically positive	20%	22%	0.76
Electrically and clinically negative	69%	70%	0.89

# ADORE Trial

## Evaluation of Routine Functional Testing after PCI



**FIGURE 1.** Cardiac procedure use during the 9-month follow-up period. ETT = exercise treadmill test.