



Updated and Guideline Based Treatment of Patients with STEMI

Eli I. Lev, MD

Director, Cardiac Catheterization Laboratory

Hasharon Hospital, Rabin Medical Center

Associate Professor of Cardiology

Tel-Aviv University, Israel

Treatment goals:

1. Achieve early and effective reperfusion
2. Reduce MI complications and mortality, and preserve LV function

Methodology:

1. Primary PCI – restore flow in the culprit artery
2. Reduce thrombus load
3. Early and effective anti-platelet therapy

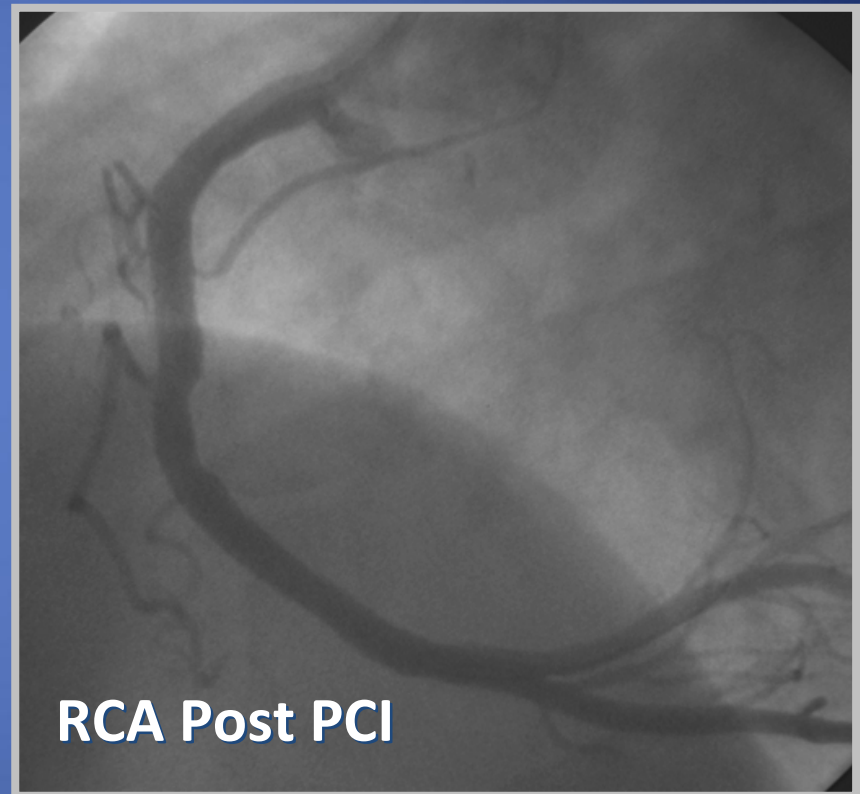
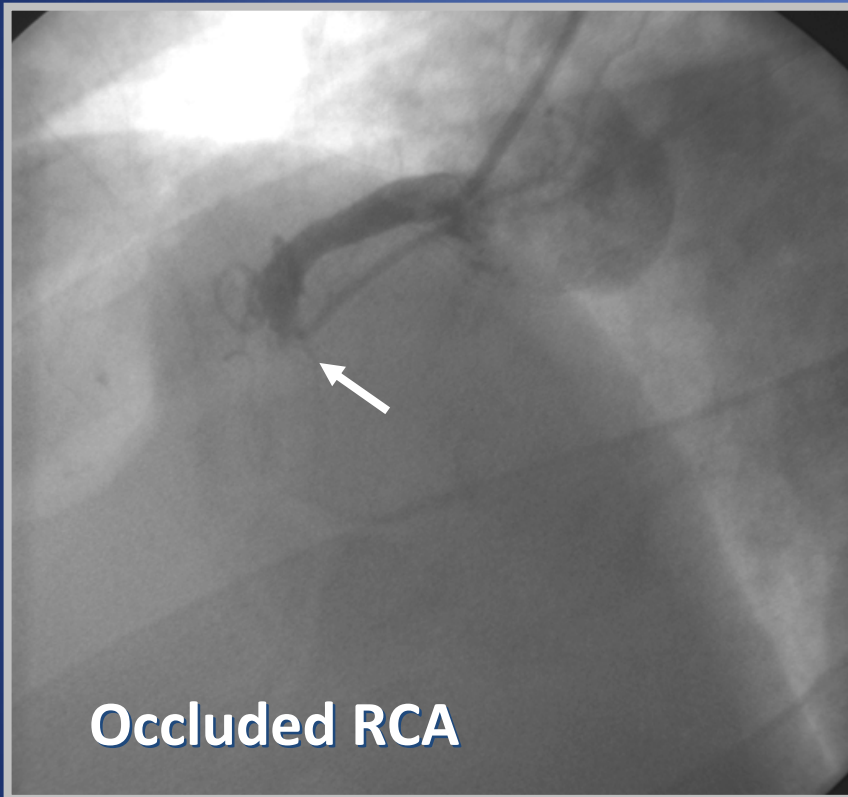
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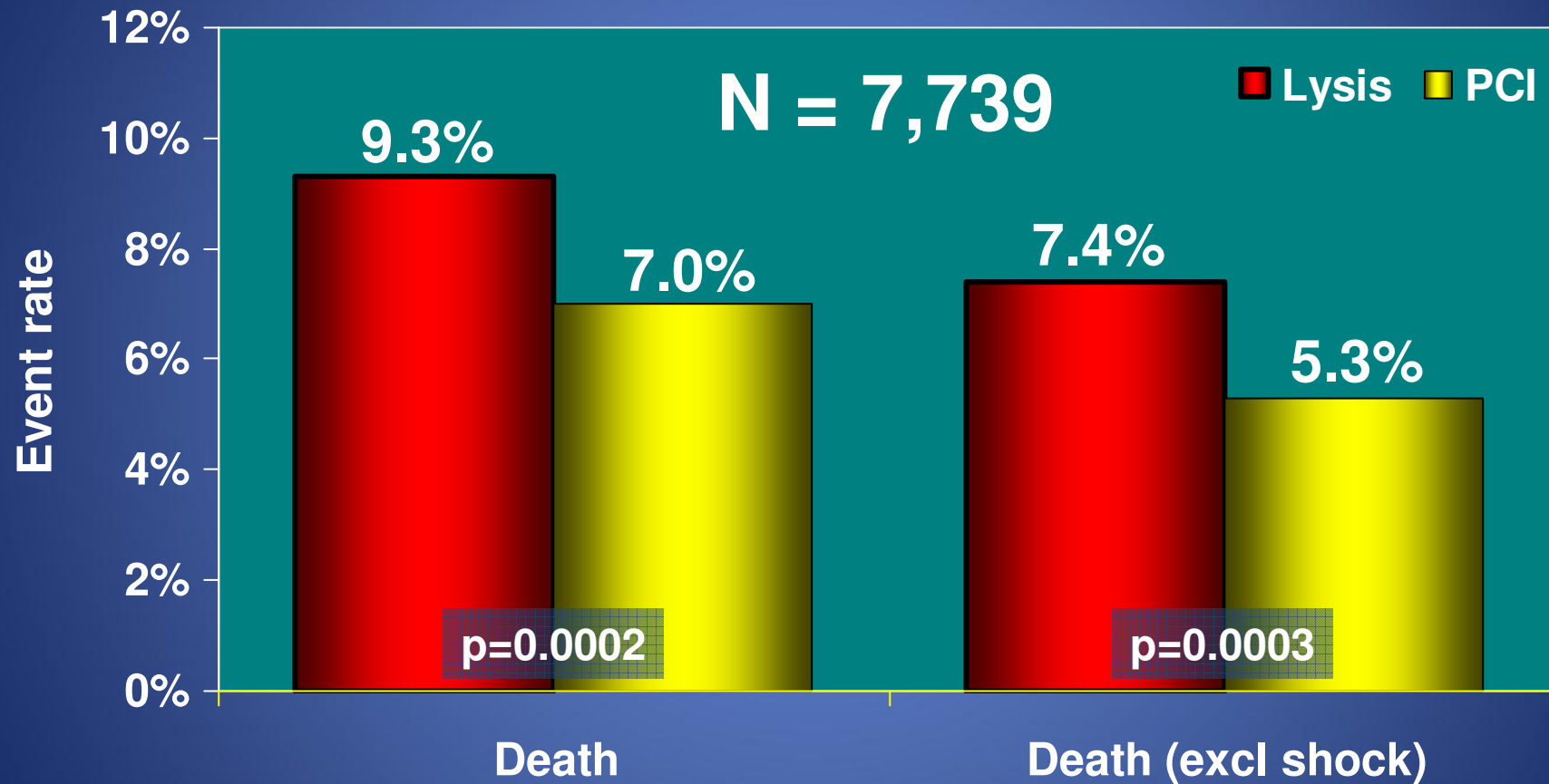
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Primary PCI in STEMI

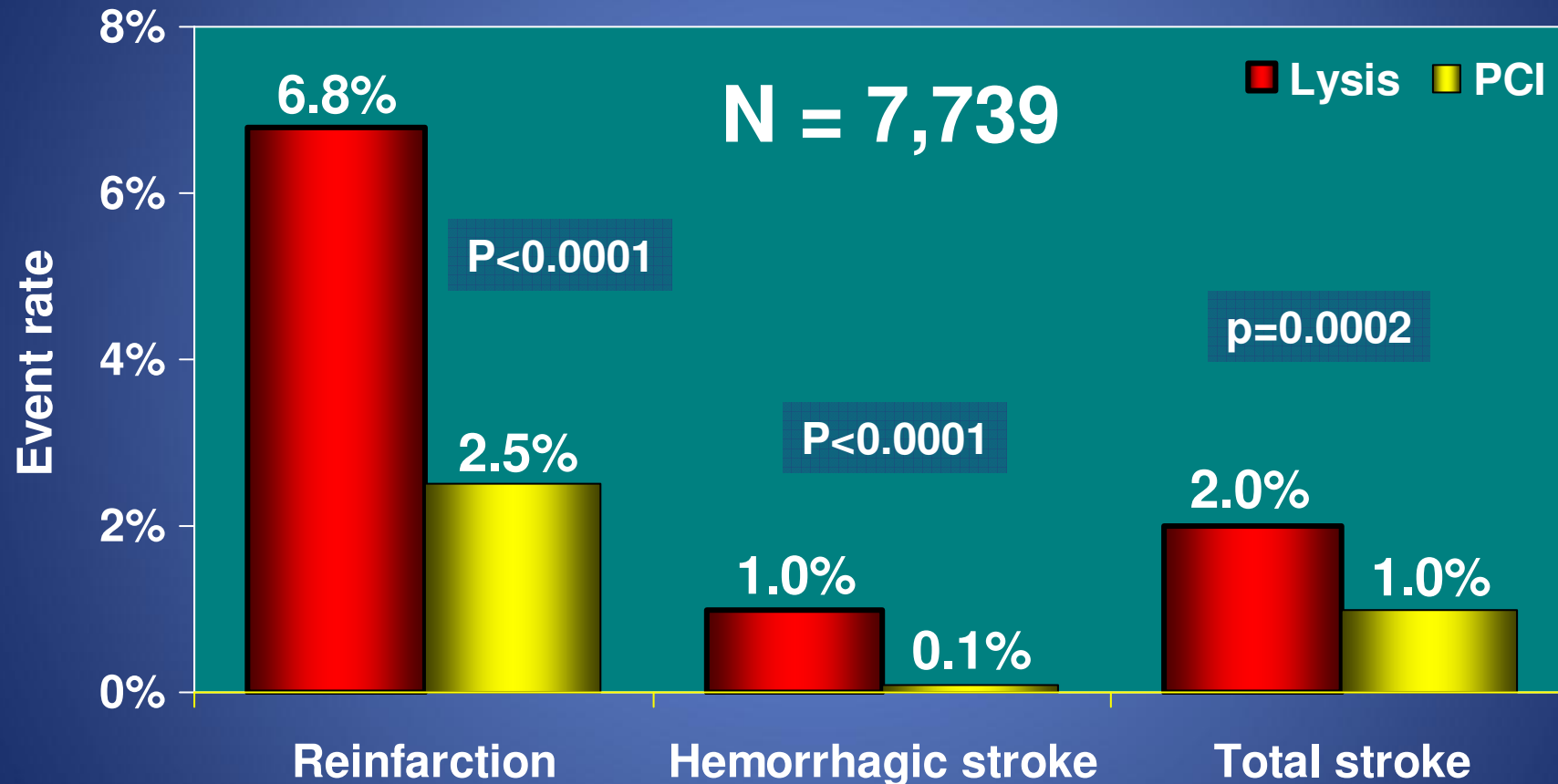


23 Randomized Trials of PCI vs. Lysis



Keeley, Grines. *Lancet* 2003;361:13-20

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Keeley, Grines. *Lancet* 2003;361:13-20

AHA/ACC , ESC Guidelines



STEMI patients presenting to a hospital with PCI capability should be treated with primary PCI within 90 min of first medical contact as a systems goal.

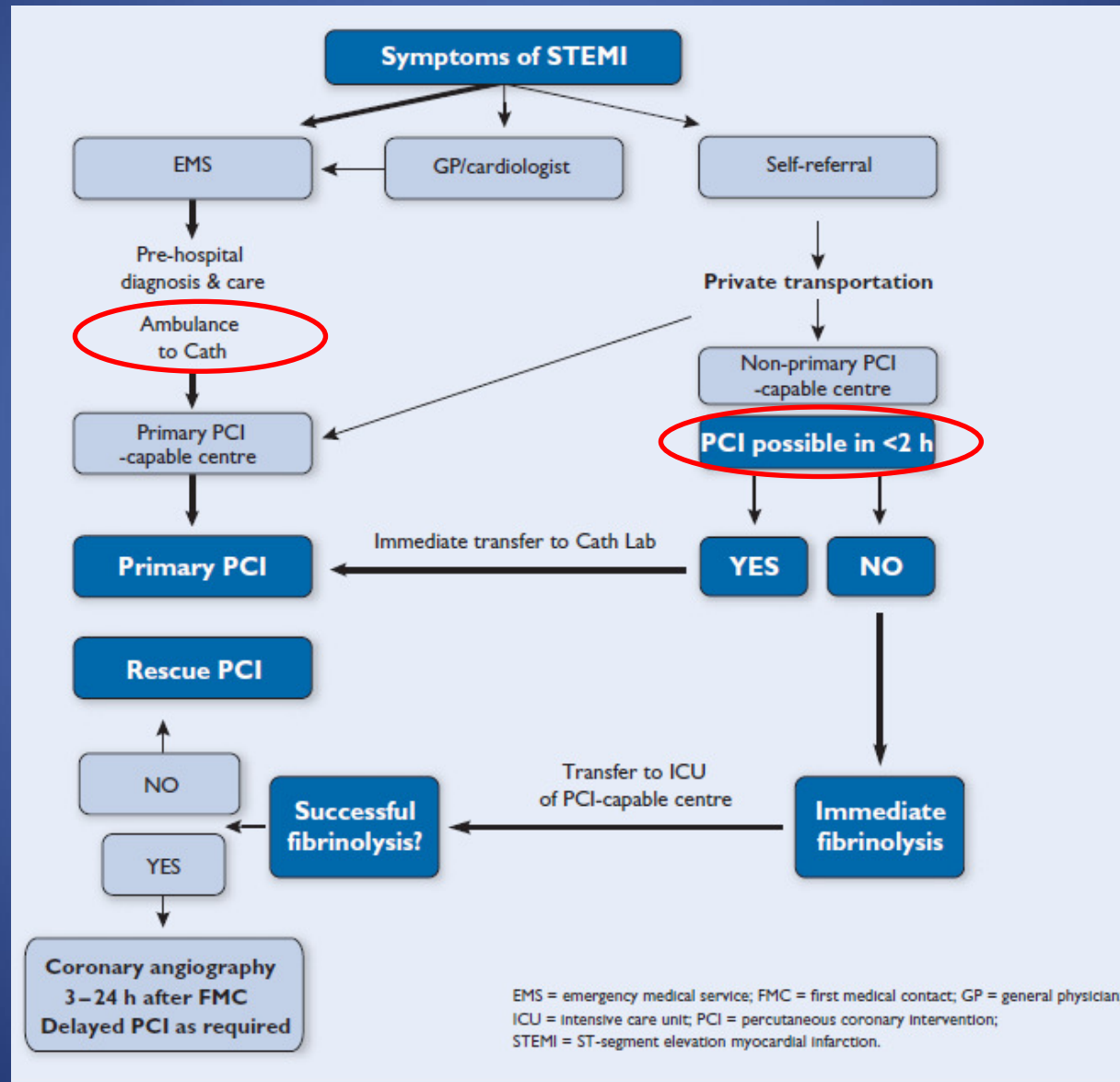
Class ^a	Level ^b
I	A

ESC 2010

Primary PCI is recommended in patients with chest pain <12 hrs + persistent ST-seg. elevation or previously undocumented LBBB, ASAP and at any rate <2 hrs from FMC (> 12 hrs from chest pain – class IIa recom.)

Based on the 2007 Focused Update of the ACC/AHA Guidelines for Management of Patients With STEMI (Circulation and JACC 2007), and the ESC guidelines for myocardial revascularization (Eur Heart J 2010)

ESC 2010 myocardial revascularization guidelines





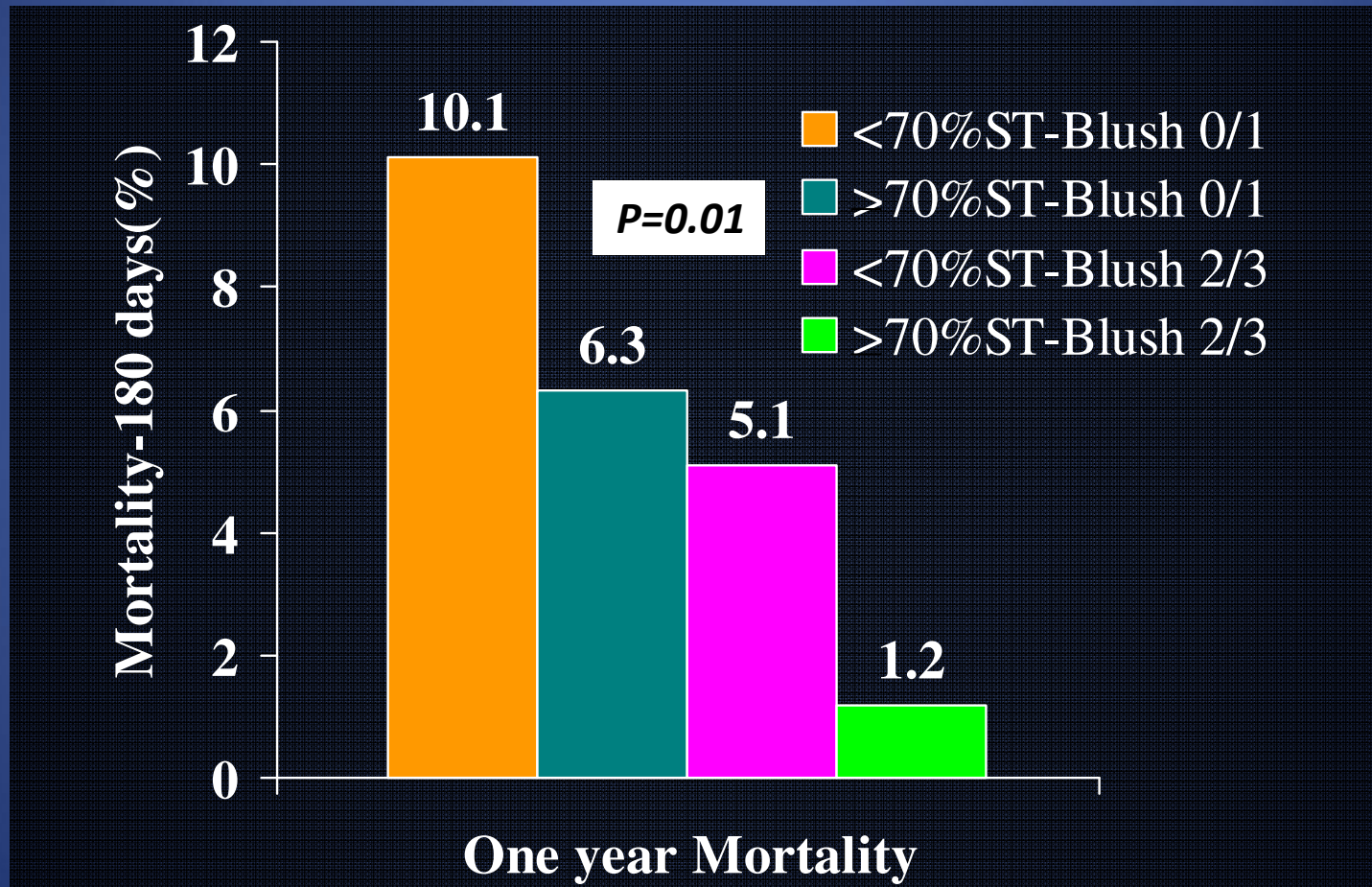
Primary PCI in 1336 consecutive STEMI patients: Rabin Medical Center Experience

1336 pts (2001-2009) with STEMI (about 170 per year) mean age 61 ± 13 years [range 24-101]. PCI successful in 94% of non-shock pts and 84% of shock pts.

Mortality	30 day	6 months	12 months
Non shock pts [n=1224]	3.5%	5.9%	7.7%
Age ≥ 75 yrs [n=207]	8.2%	16.2%	19.4%
Age < 75 yrs [n=1017]	2.3%	3.8%	8.8%
Male [n=982]	2.9%	4.9%	6.2%
Female [n=242]	6.2%	10%	13.2%
Cardiogenic shock [n=112]	55%	60%	64%

Markers of myocardial perfusion - ST Resolution and Myocardial Blush in STEMI

Sub-Analysis of the CADILLAC Trial (N=456)



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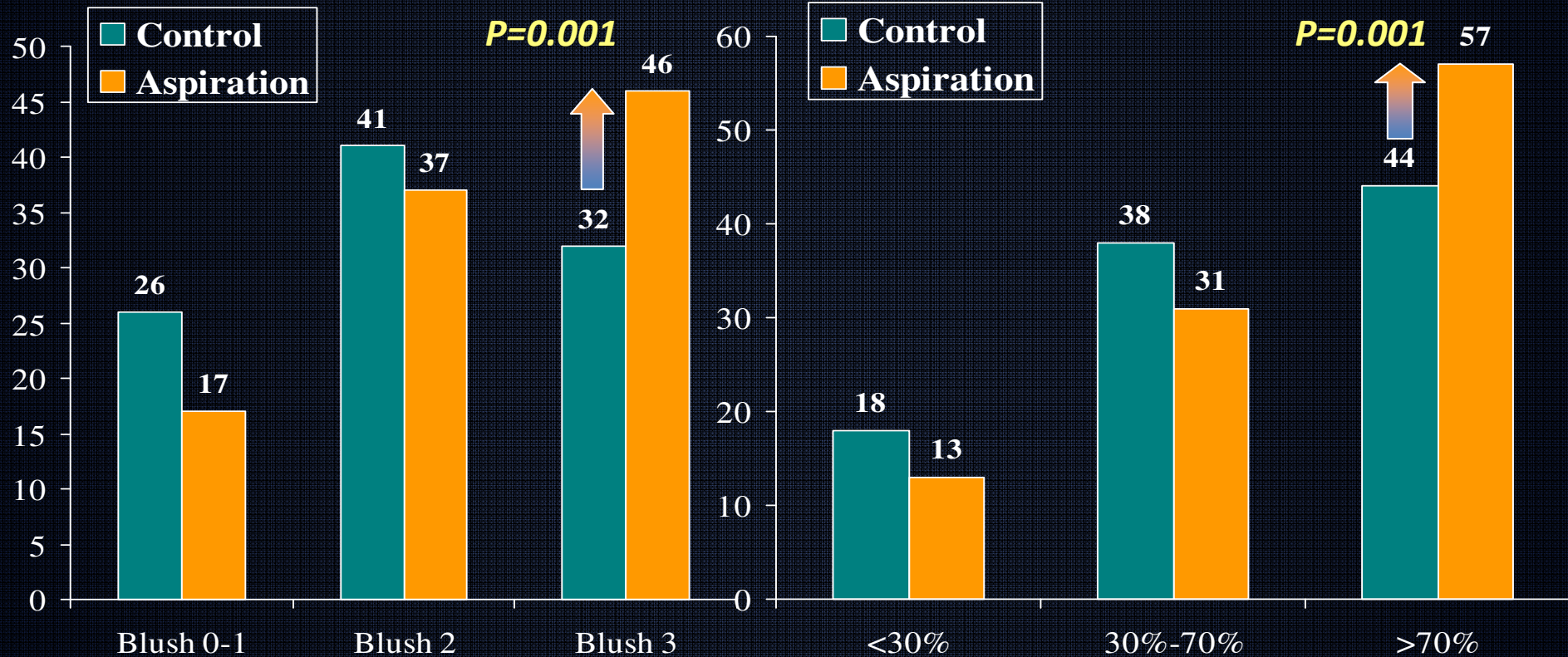
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TAPAS: Thrombus Aspiration with aspiration catheter. 1,071 patients with STEMI randomized

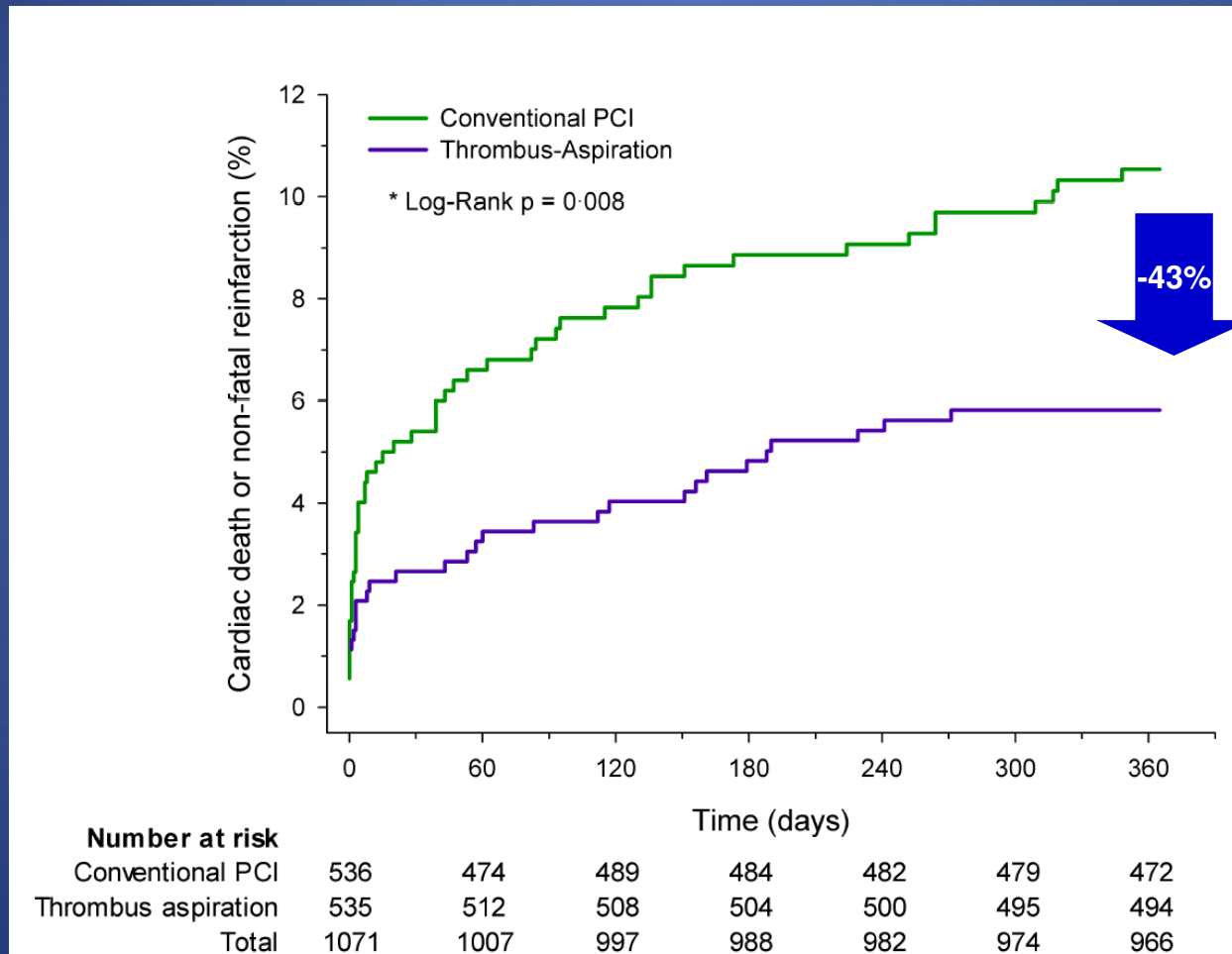
Blush score

ST Resolution @60 min



TAPAS Study: Clinical Events

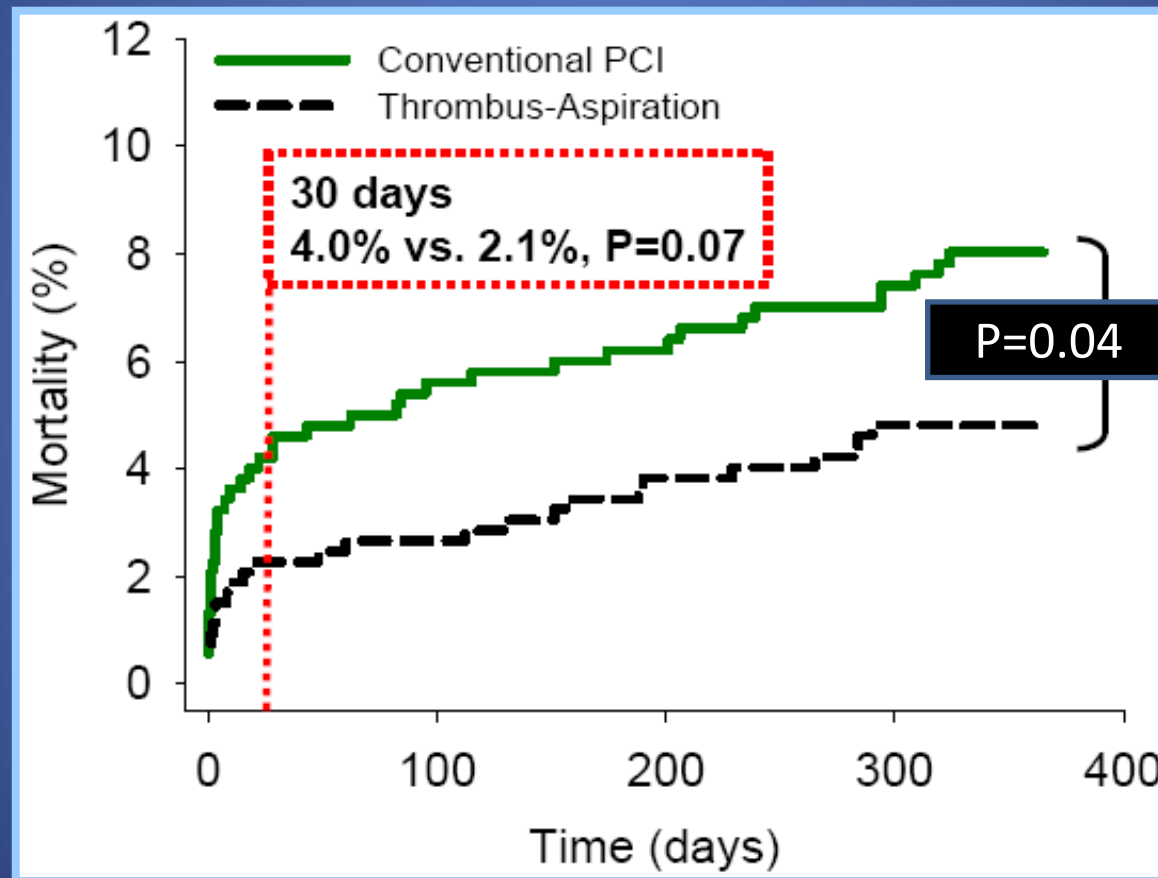
Sig. reduction of cardiac death or non-fatal MI in Aspiration Group at 1 year



Vlaar et al (TAPAS): a 1-year follow-up study, Lancet 2008; 371: 2008; 1915-20

TAPAS Study: Clinical Events

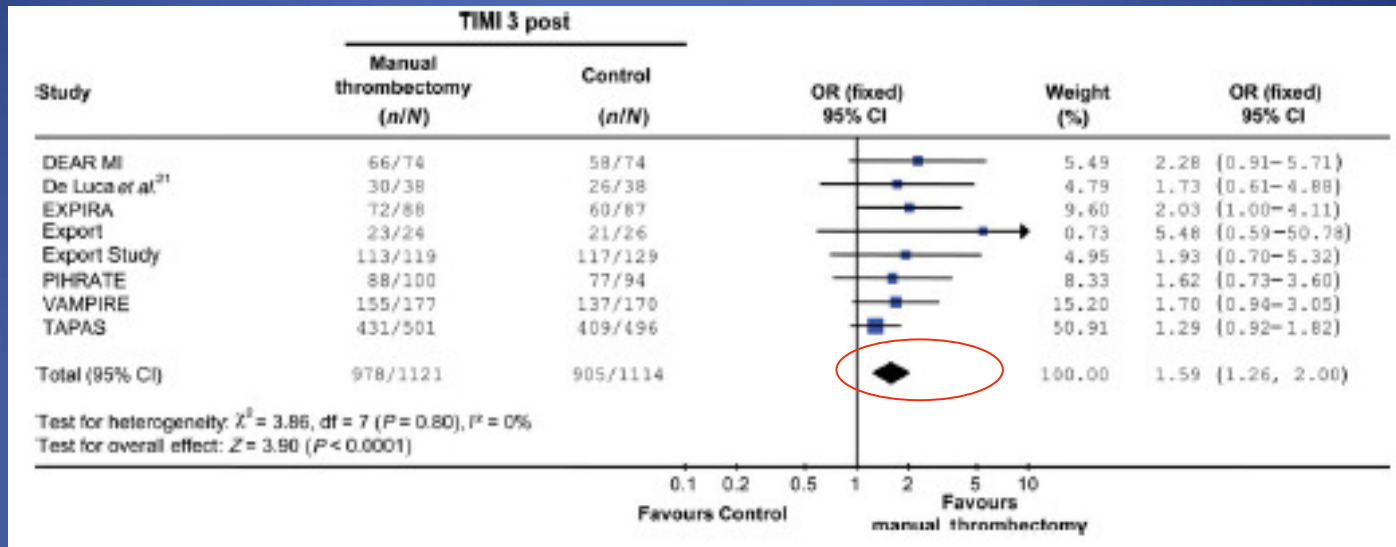
Mortality



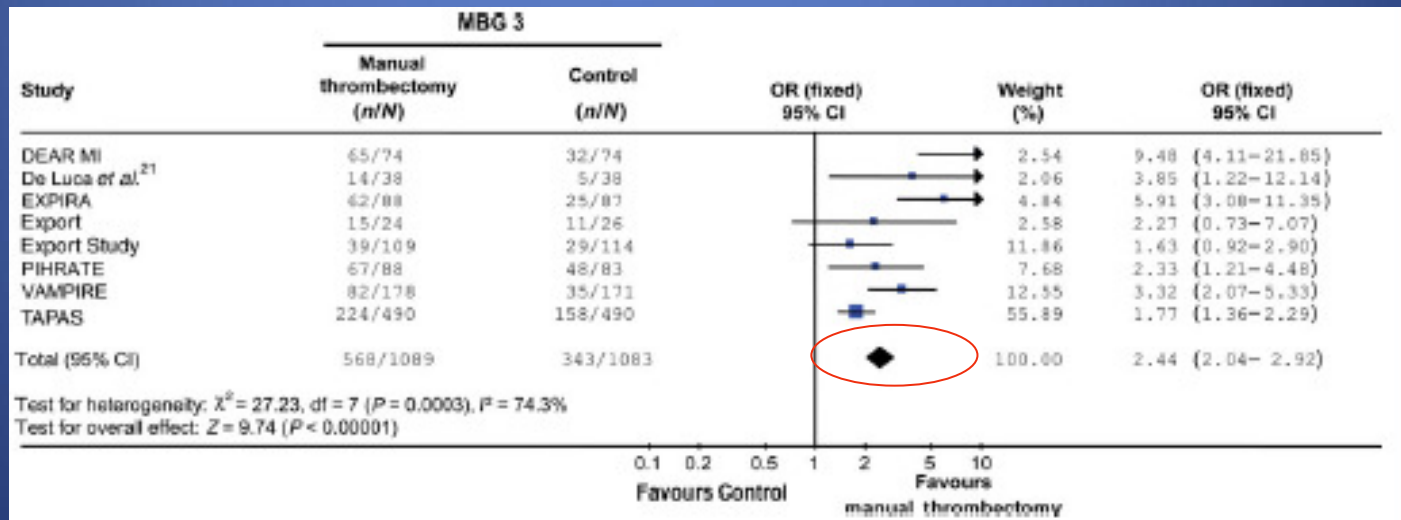
Svilaas T et al. N Engl J Med 2008
Vlaar PG et al. Lancet 2008

Aspiration Meta-analysis

TIMI 3 post



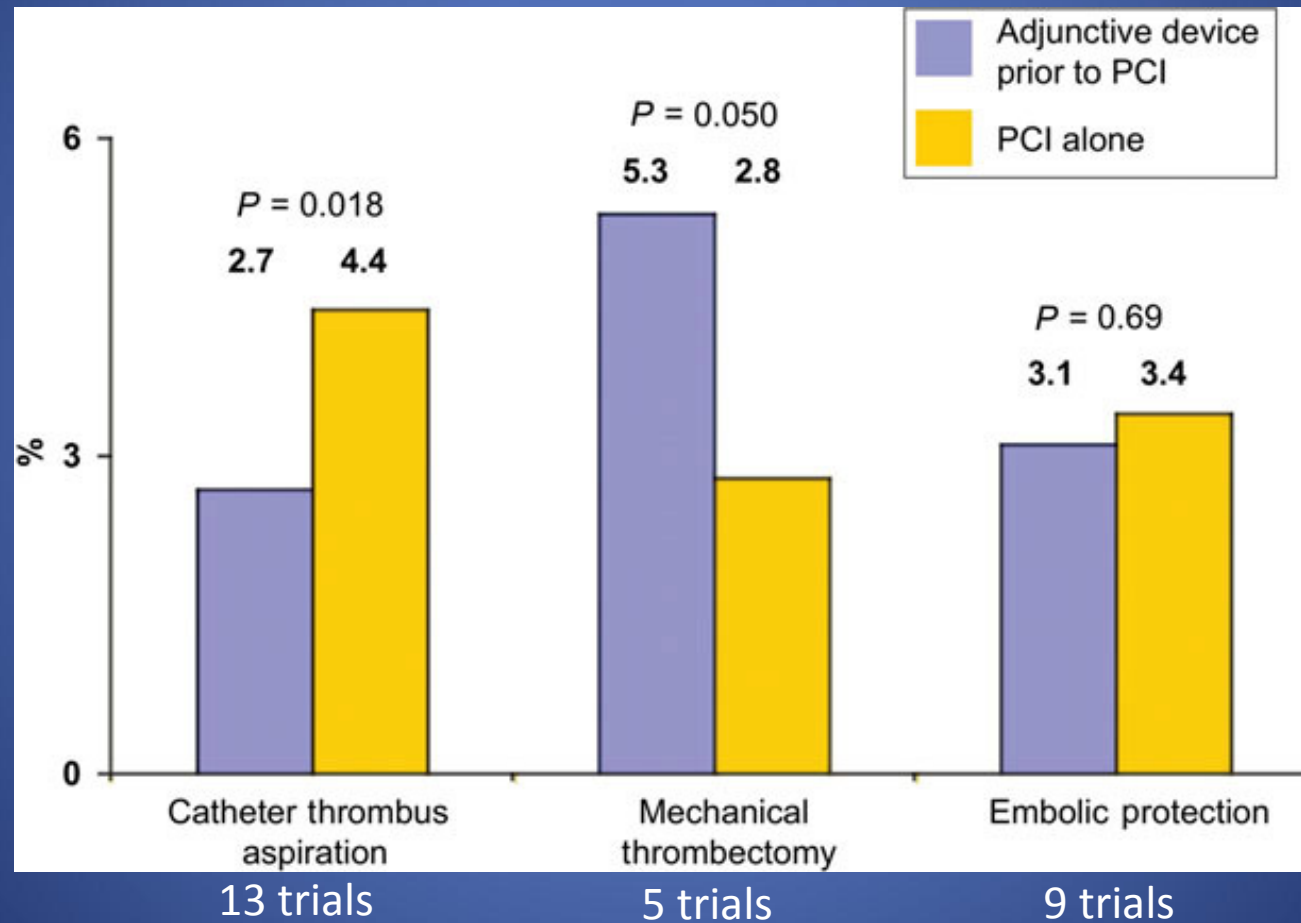
MBG 3



8 STEMI studies, 2417 patients in aspiration group, *De Luca et al, EHJ 2008*

Aspiration Meta-analysis

6 month mortality



Guidelines

- **ESC 2010 myocardial revascularization guidelines:** “Manual catheter thrombus aspiration should be considered during PCI of the culprit lesion in STEMI”. Class IIa recommendation, level of evidence A.
- **ACC/AHA 2009 focused update:** “Aspiration thrombectomy is reasonable for patients undergoing primary PCI . Class IIa recommendation, level of evidence B.

Based on the 2009 Focused Update of the ACC/AHA Guidelines for Management of Patients With STEMI (Circulation and JACC 2009), and the ESC guidelines for myocardial revascularization (Eur Heart J 2010)

Treatment goals:

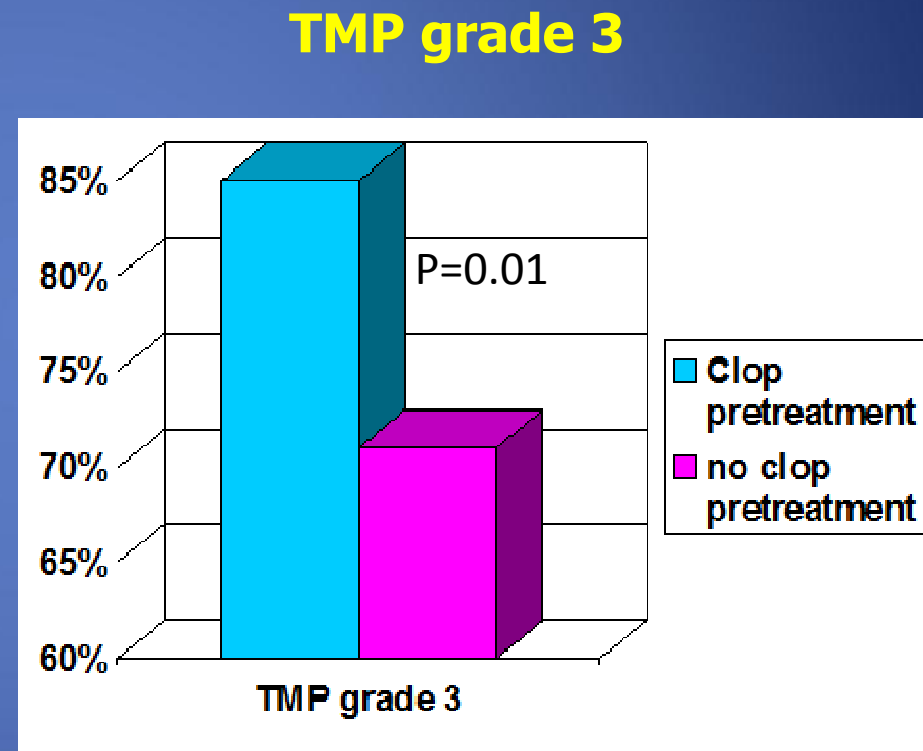
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Effect of Clopidogrel Pretreatment on TIMI Perfusion Grade and Clinical Outcomes in Patients Undergoing Primary PCI for AMI

- 292 pts with STEMI treated with primary PCI allocated into 2 groups:
 1. those who received clopidogrel loading before the PCI (n=165)
 2. those who received clopidogrel loading immediately after PCI (n=127)
- No differences in baseline clinical characteristics.

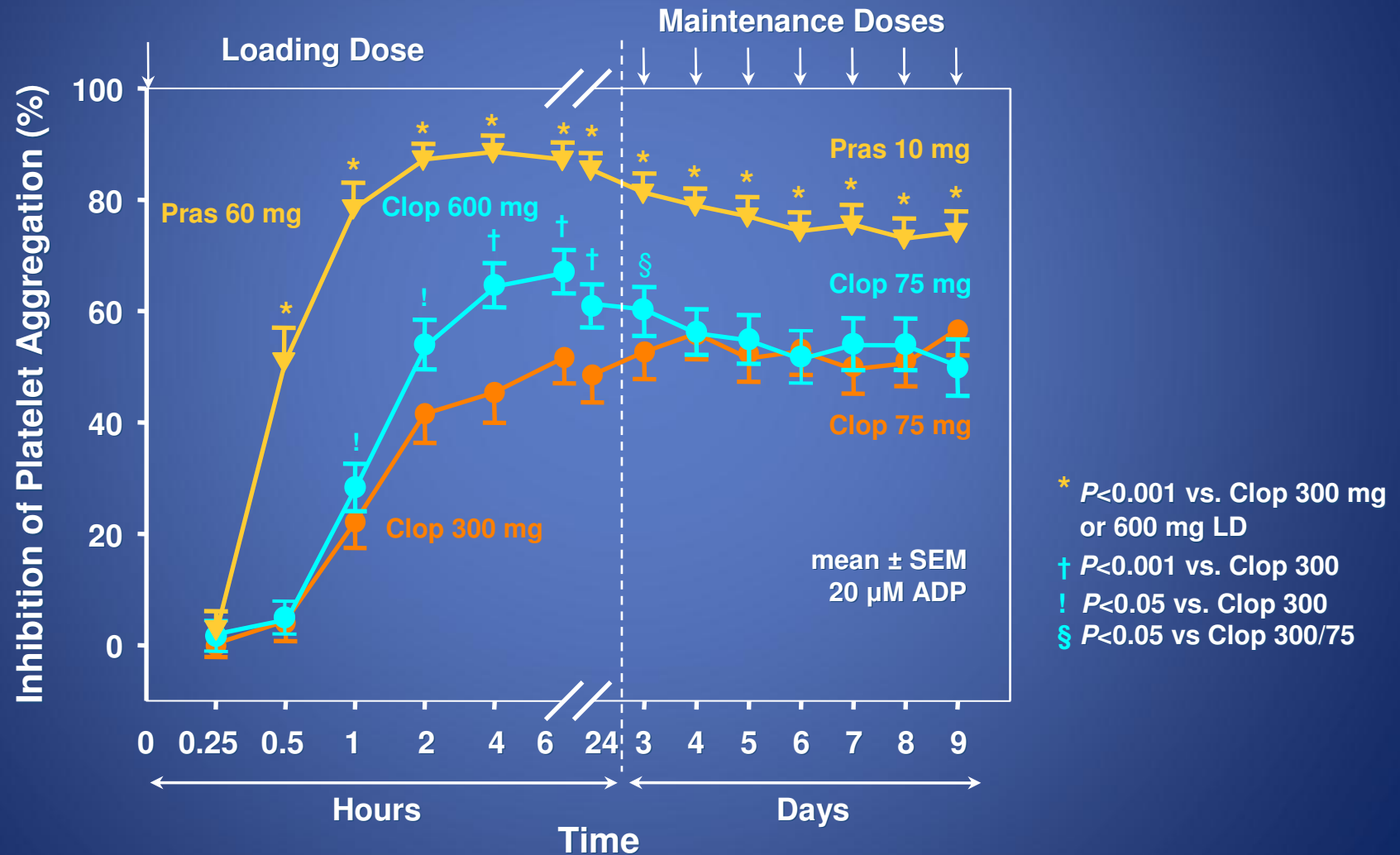


SCARR REGISTRY

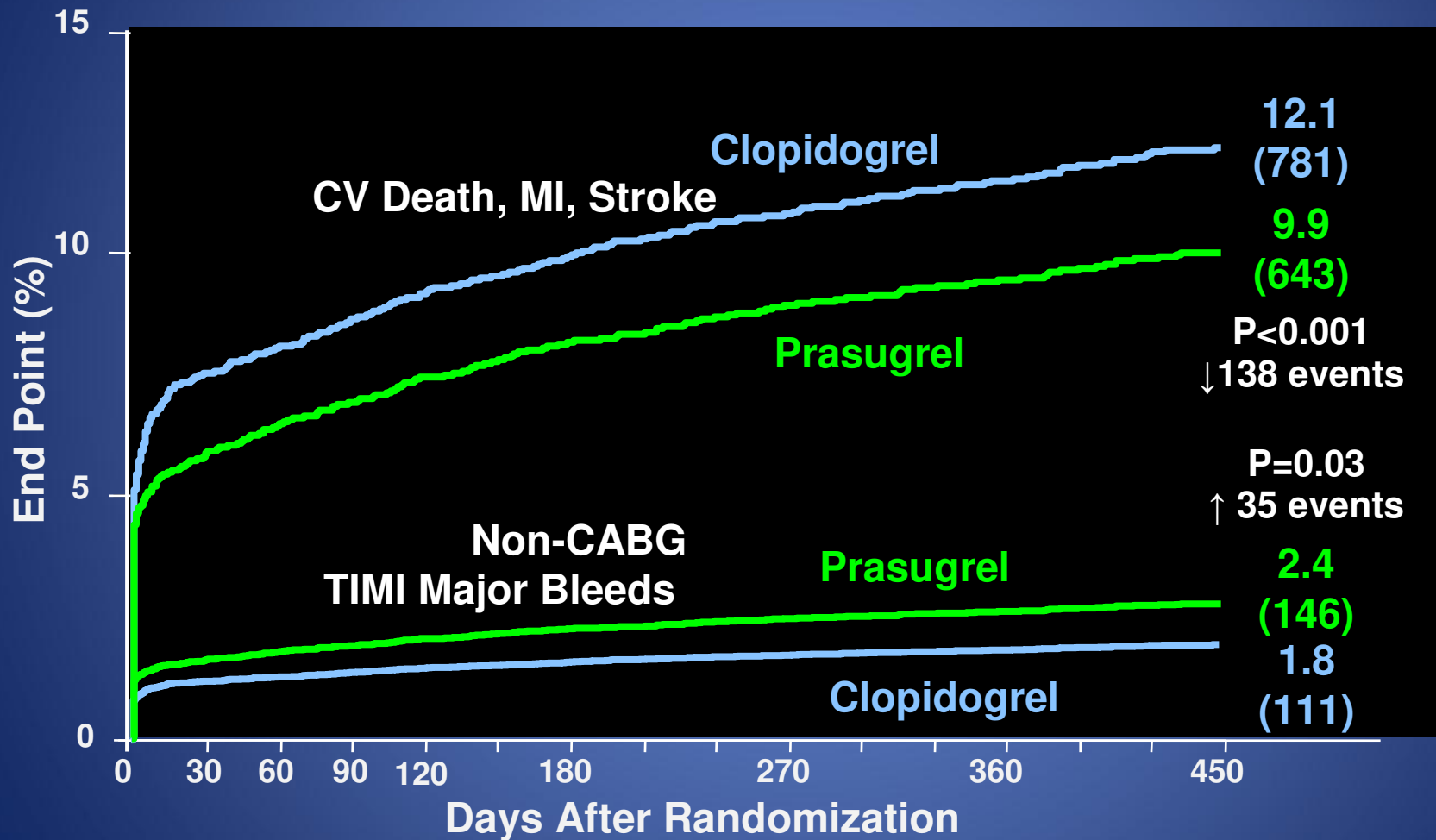
- **Effect of upstream clopidogrel treatment in patients with STEMI undergoing PCI.**
- 13847 patients who underwent PCI for STEMI (2003- 08)
- 71% received upstream clopidogrel Rx, 29% did not
- After propensity score adjustment, a significant relative risk reduction (HR 0.82, 95% CI 0.73-0.93) in death/MI at 1 year was observed.
- The secondary endpoint of total 1-year death was significantly reduced (HR 0.76, 95% CI: 0.64-0.90).

New Antiplatelet Medications

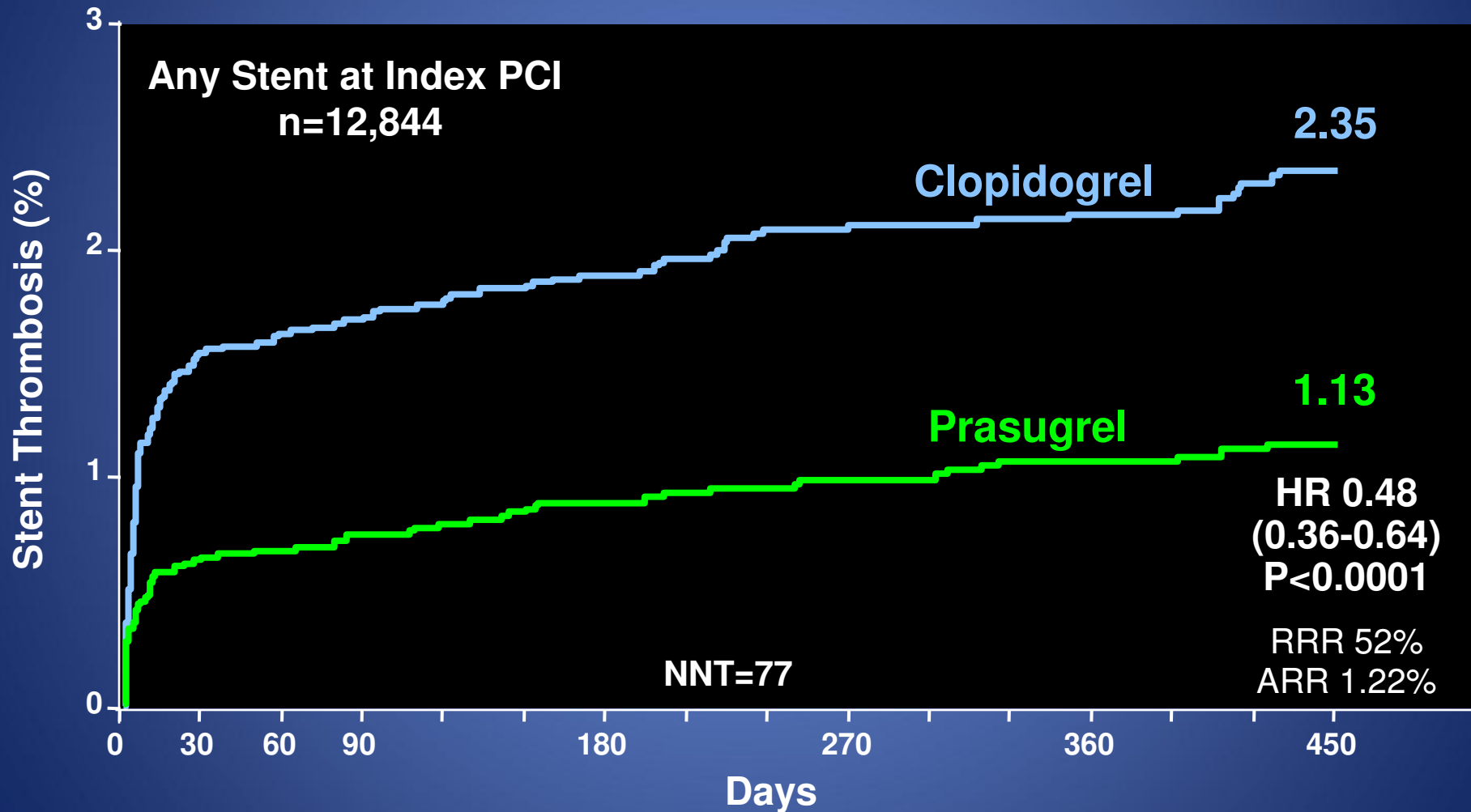
Prasugrel vs. Clopidogrel : Higher IPA During Loading and Maintenance Phases



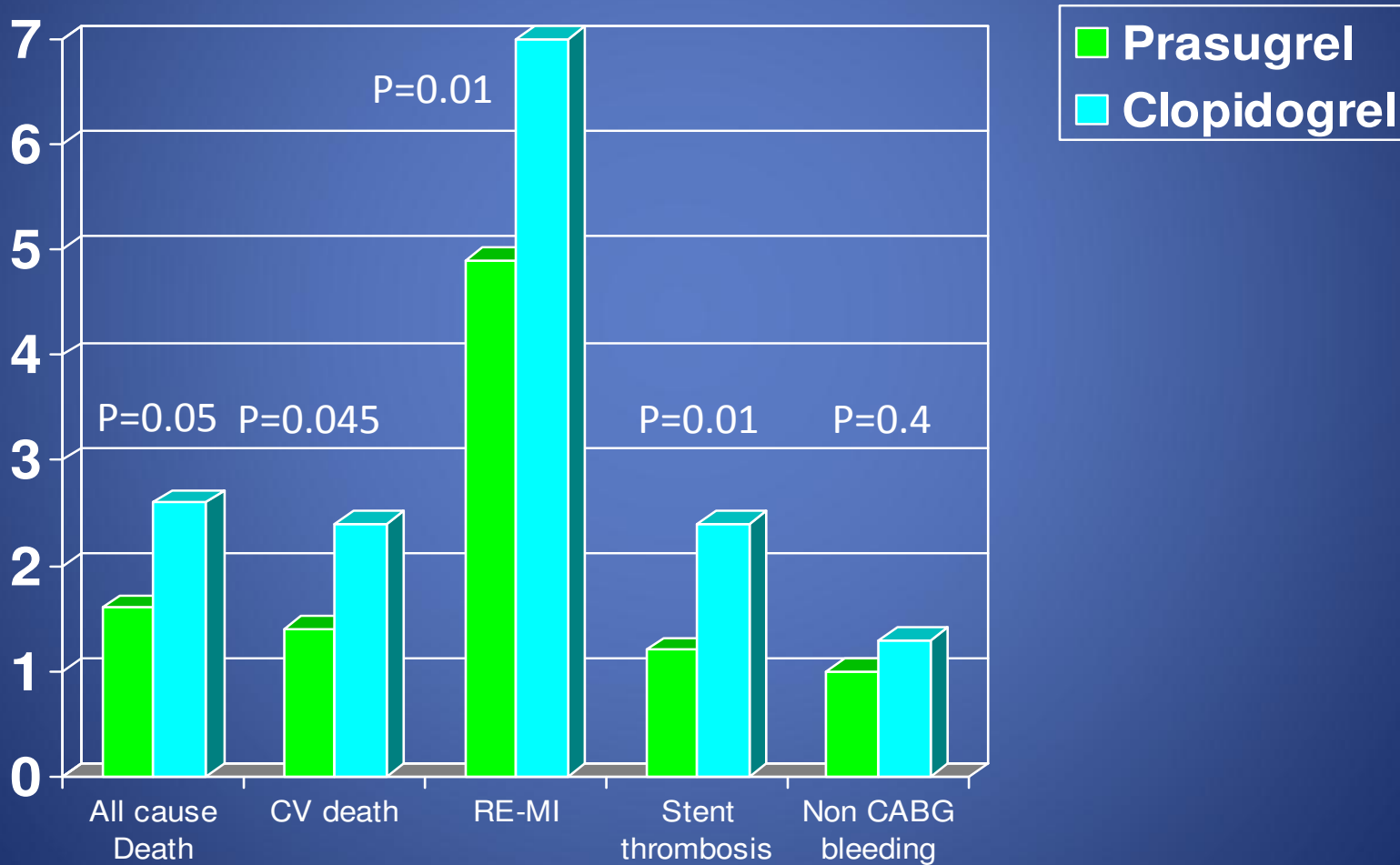
TRITON-TIMI 38: Rates of Key Study End Points (All ACS, n=13,500)



TRITON-TIMI 38: ARC Definite/Probable Stent Thrombosis:

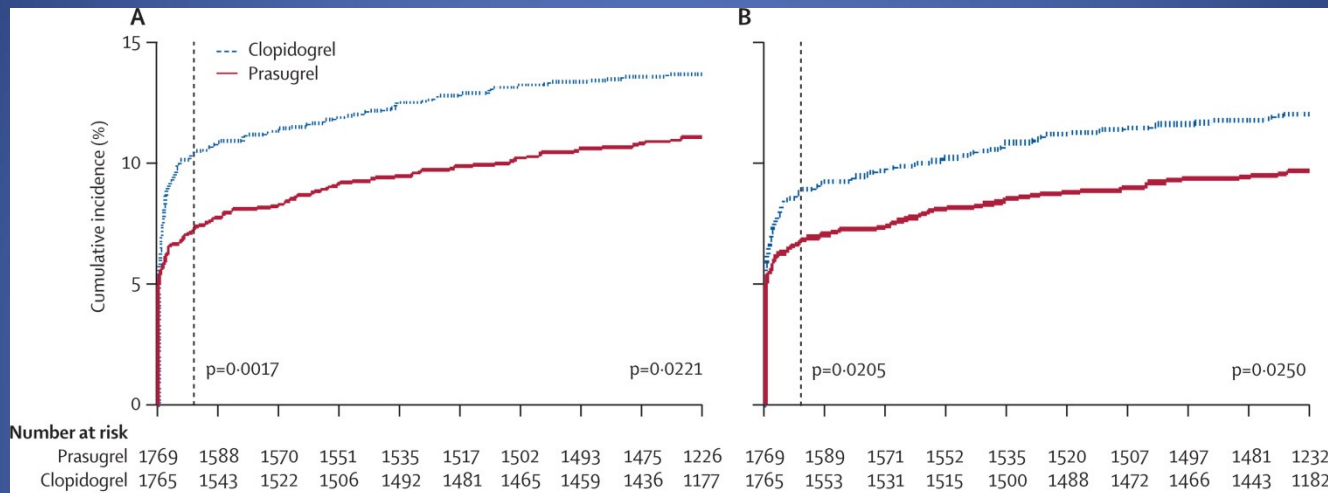


TRITON-TIMI 38: STEMI Subgroup (n=3,534)



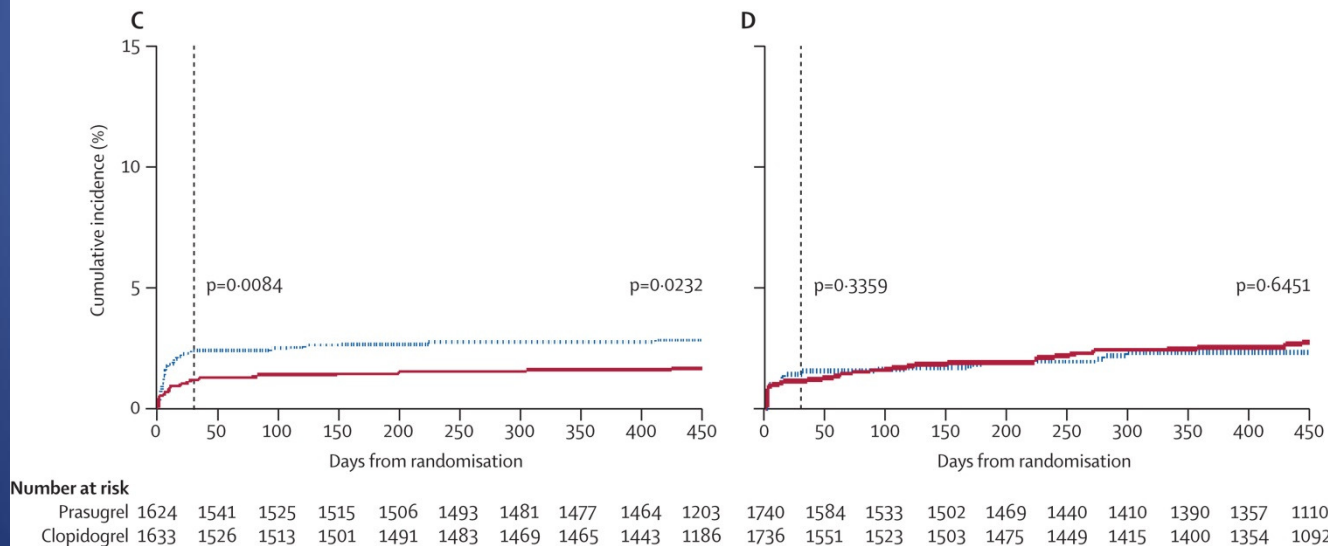
TRITON-TIMI 38: STEMI Subgroup (n=3,534)

Death
MI
Stroke



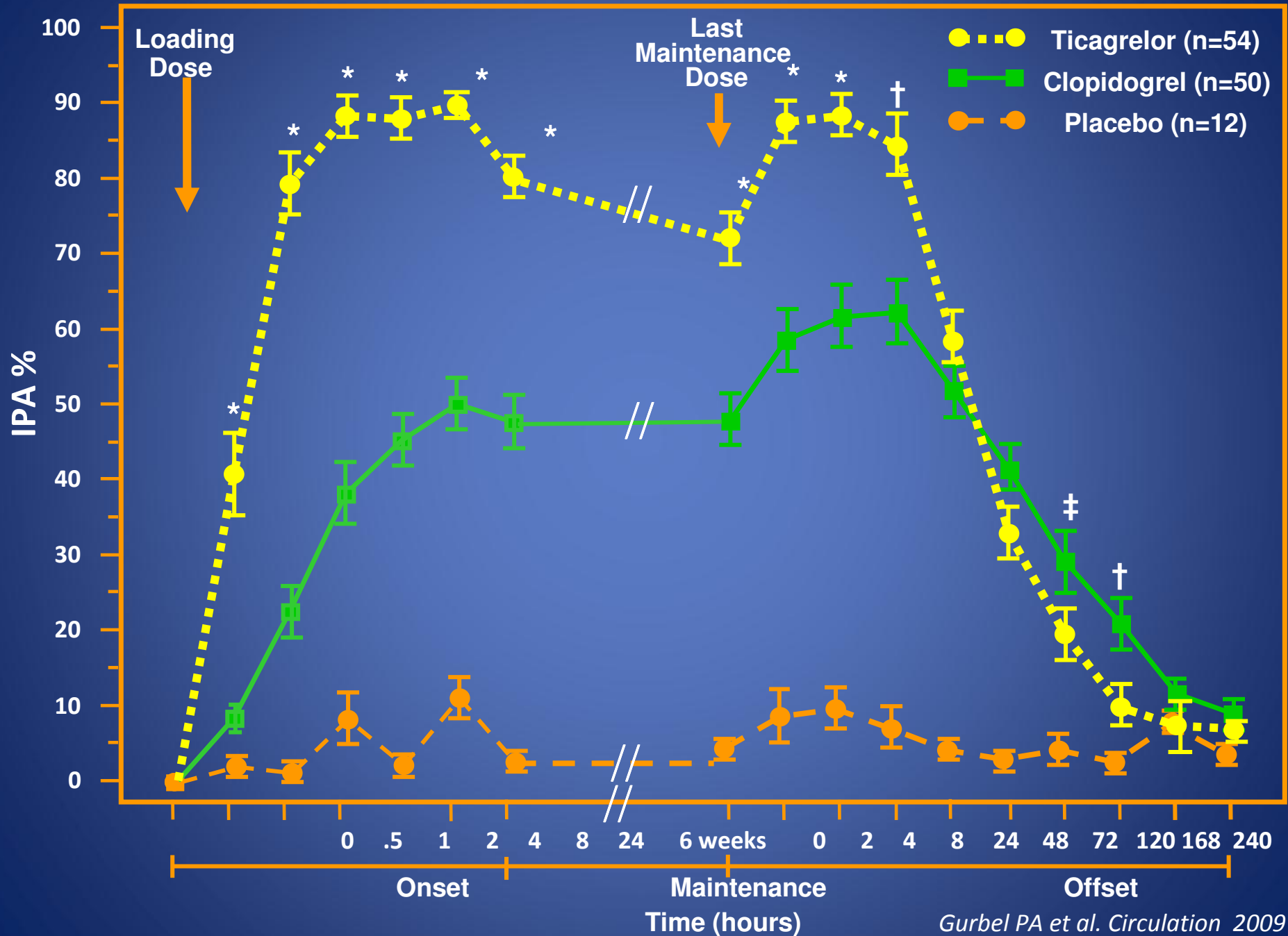
Death
MI
UTVR

Stent
Thrombosis

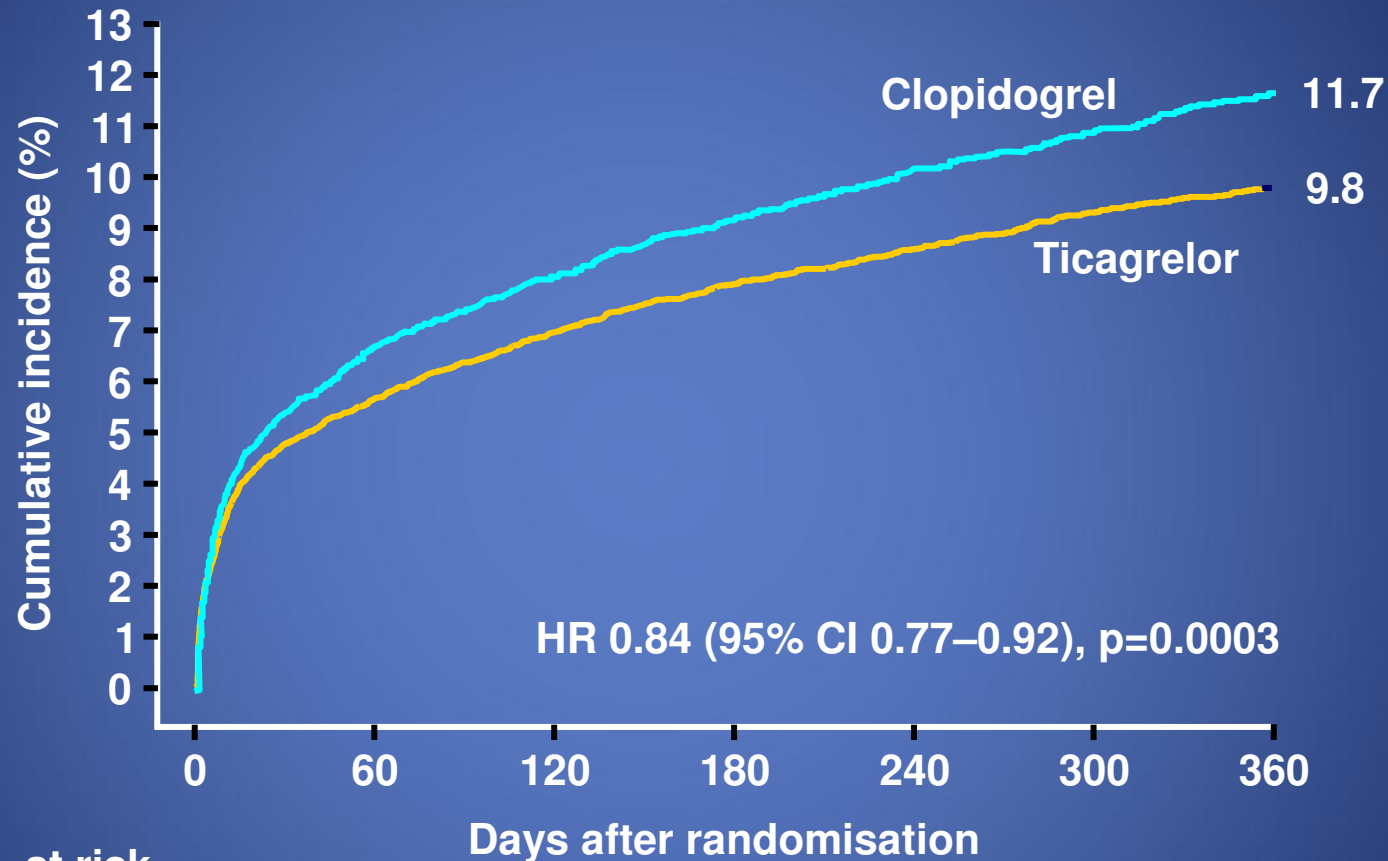


Non-CABG
Related
TIMI
Major
Bleeding

Ticagrelor (180 / 90 mg) vs. Clopidogrel (600 / 75 mg) IPA

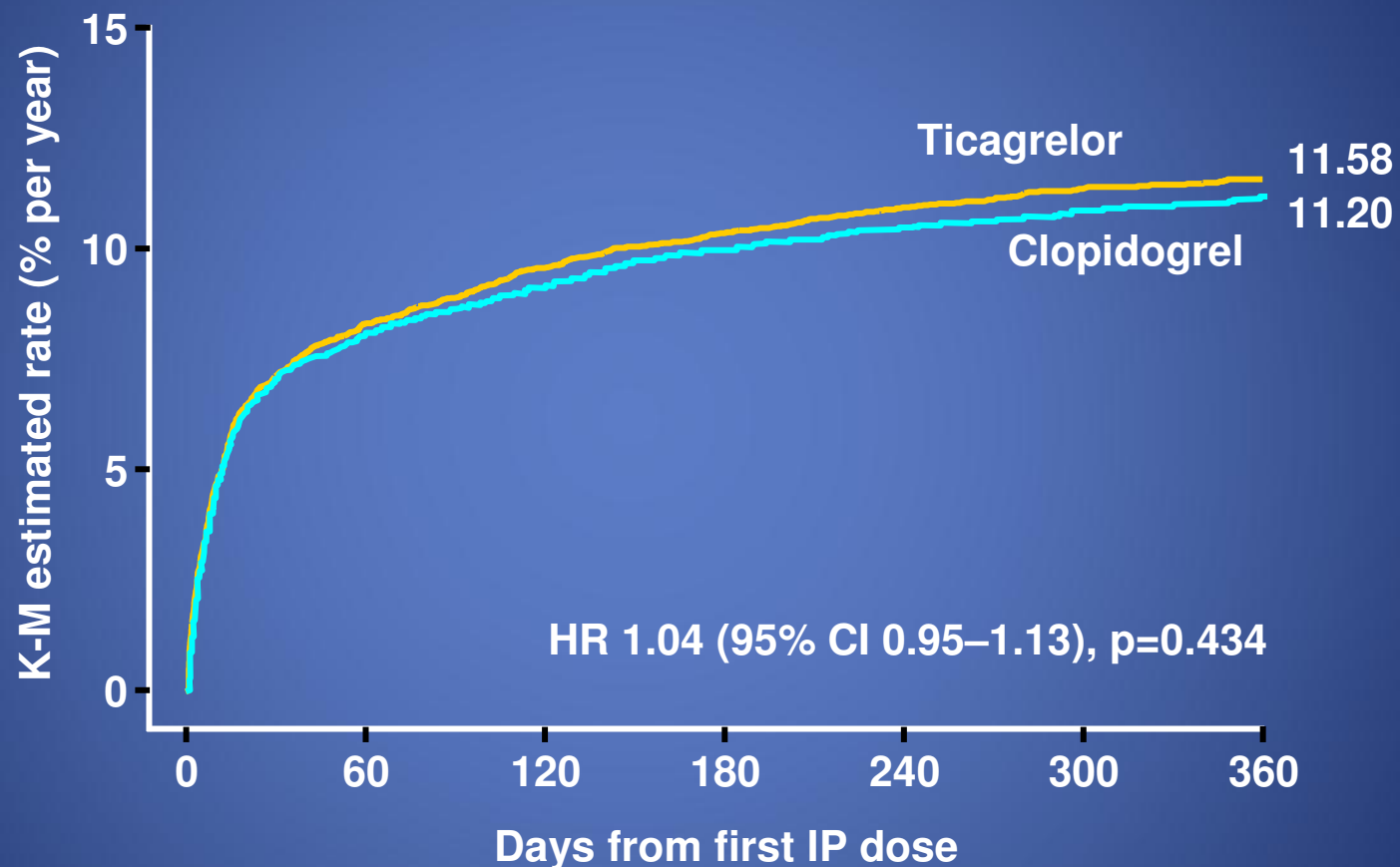


PLATO - Primary efficacy endpoint (composite of CV death, MI or stroke), n=18,624 ACS patients



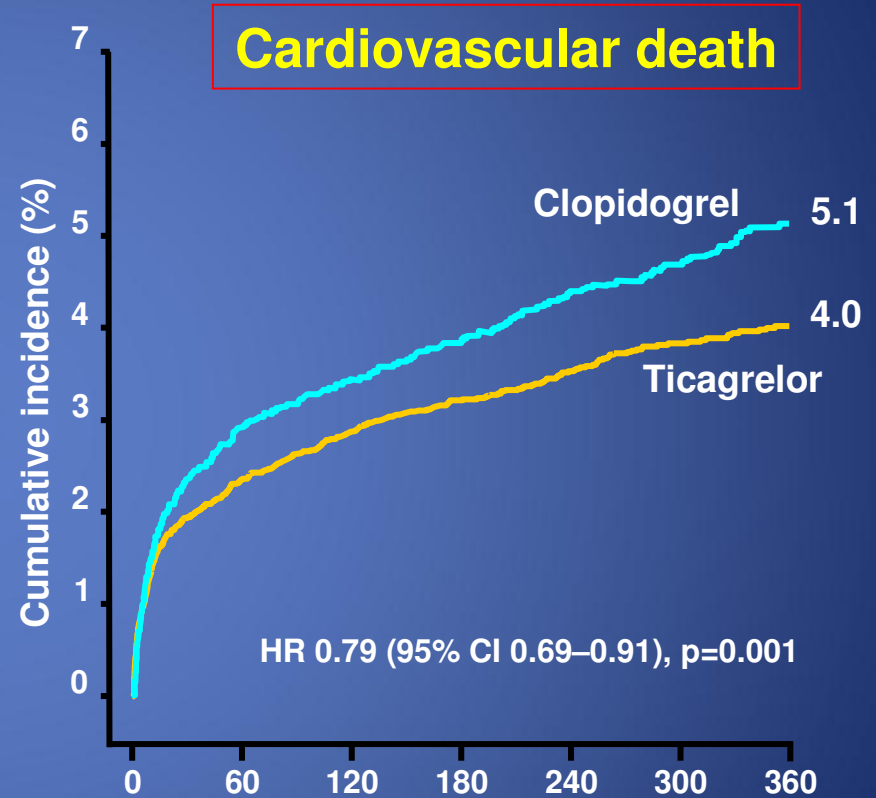
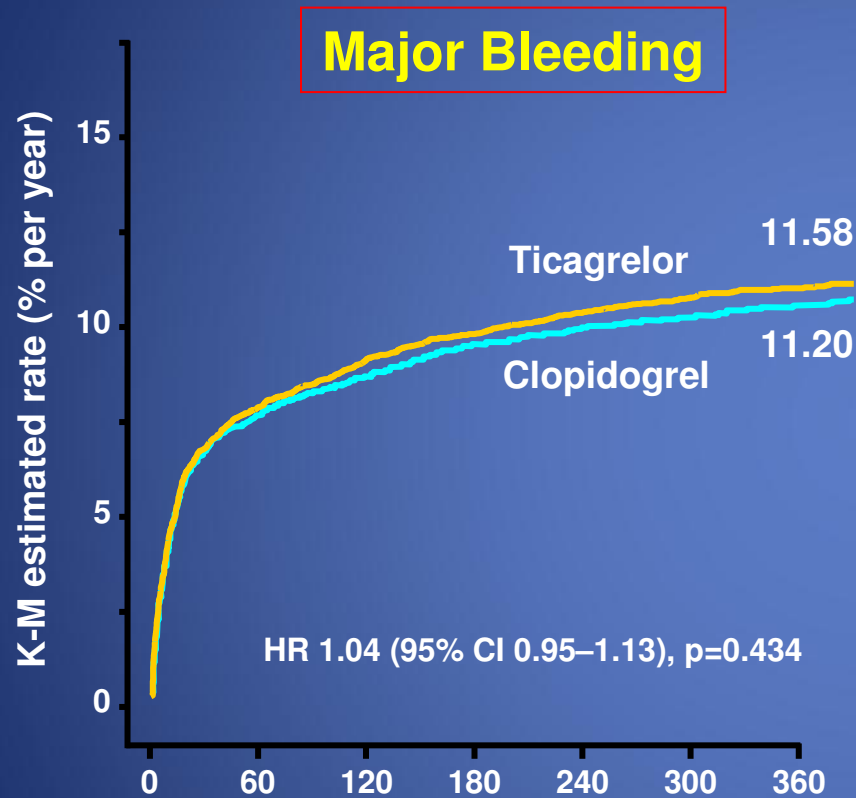
No. at risk	Days after randomisation						
	0	60	120	180	240	300	360
Ticagrelor	9,333	8,628	8,460	8,219	6,743	5,161	4,147
Clopidogrel	9,291	8,521	8,362	8,124	6,743	5,096	4,047

PLATO - Primary safety event - Major bleeding



No. at risk	0	60	120	180	240	300	360
Ticagrelor	9,235	7,246	6,826	6,545	5,129	3,783	3,433
Clopidogrel	9,186	7,305	6,930	6,670	5,209	3,841	3,479

Primary safety event – Major bleeding and secondary efficacy endpoint – CV death

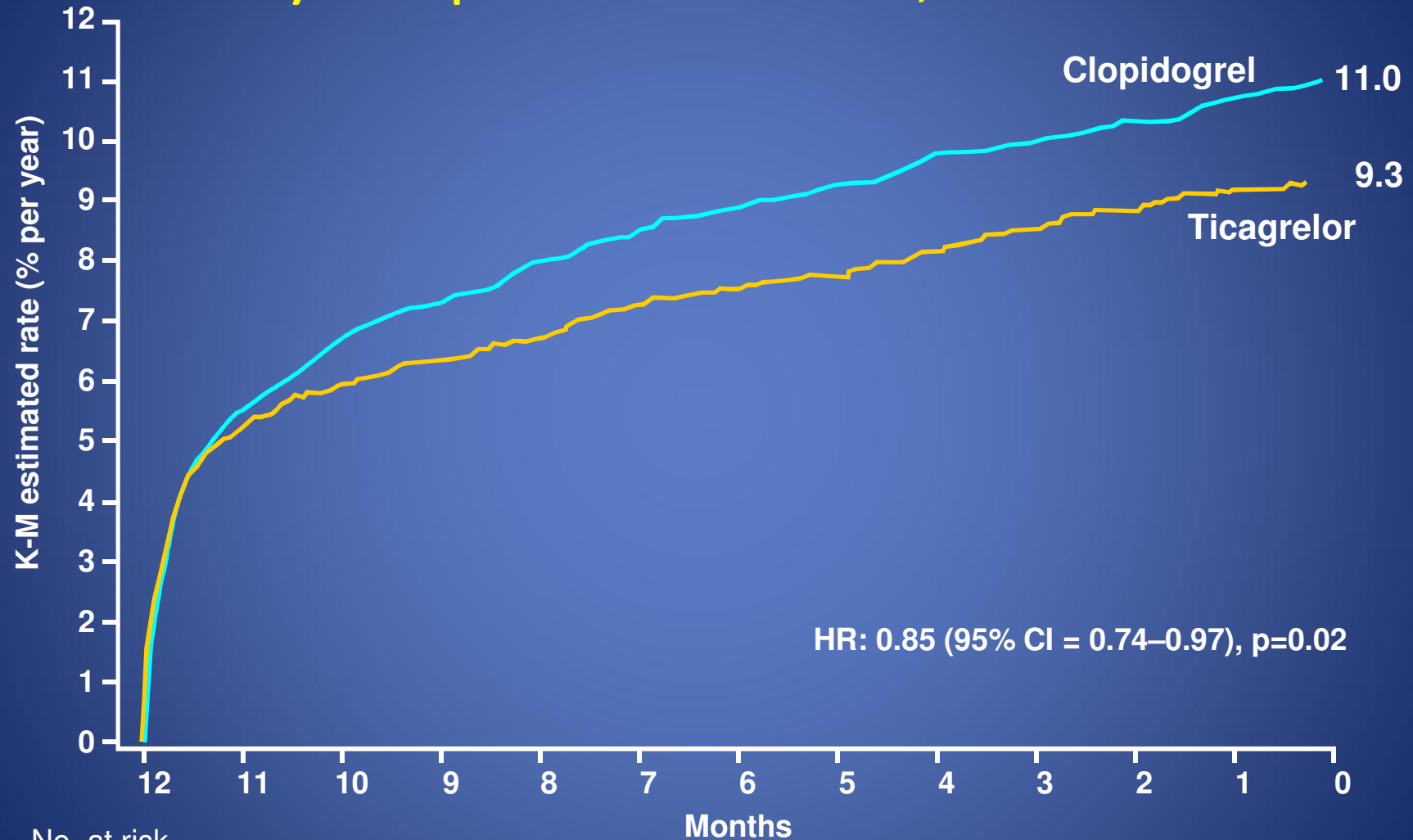


No. at risk	Days after randomisation						
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No. at risk	Days after randomisation						
	0	60	120	180	240	300	360
Clopidogrel	9,333	8,294	8,822	8,626	7,119	5,482	4,419
Ticagrelor	9,291	8,865	8,780	8,589	7,079	5,441	4,364

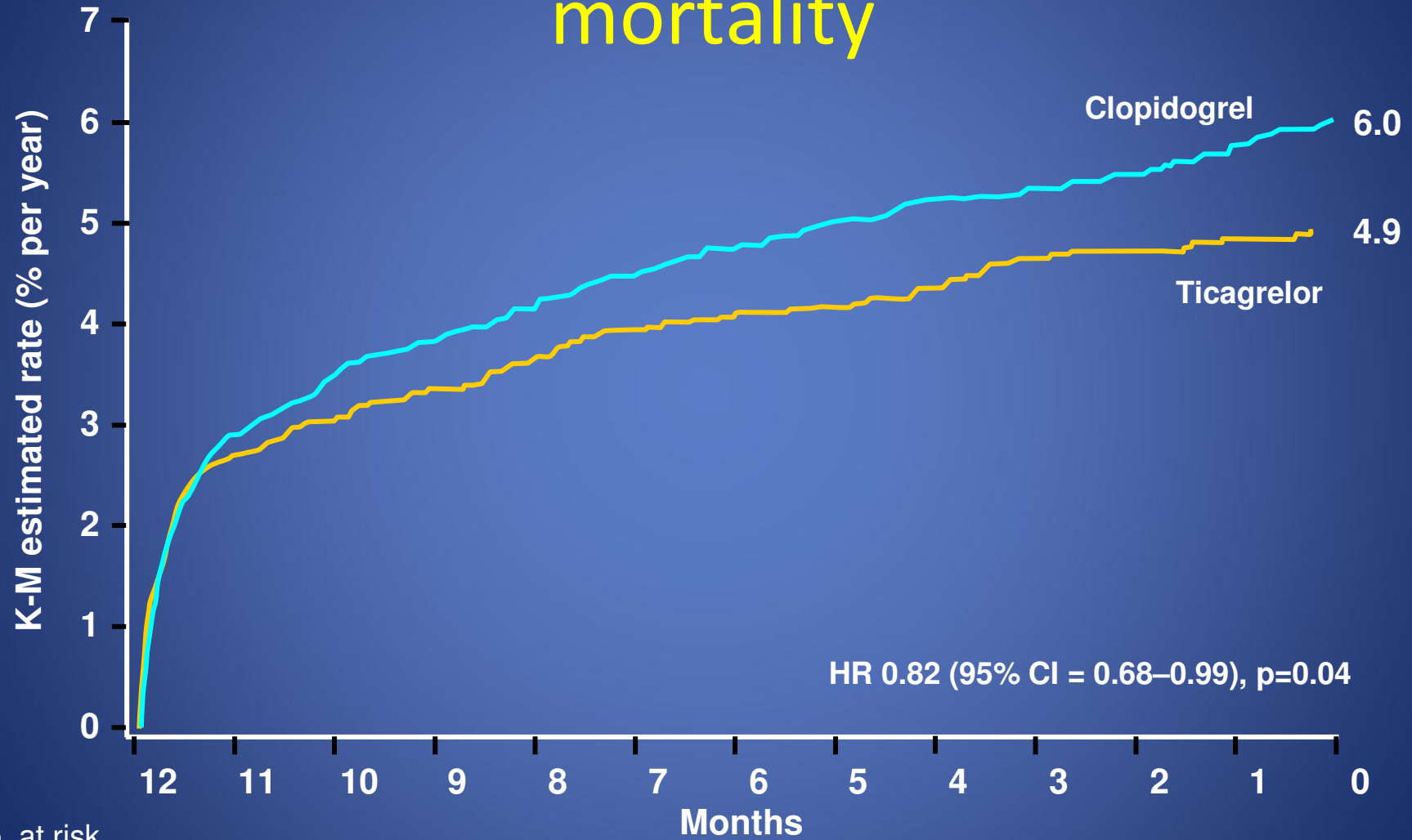
PLATO STEMI substudy – 8,430 patients

Primary endpoint: CV death, MI or stroke



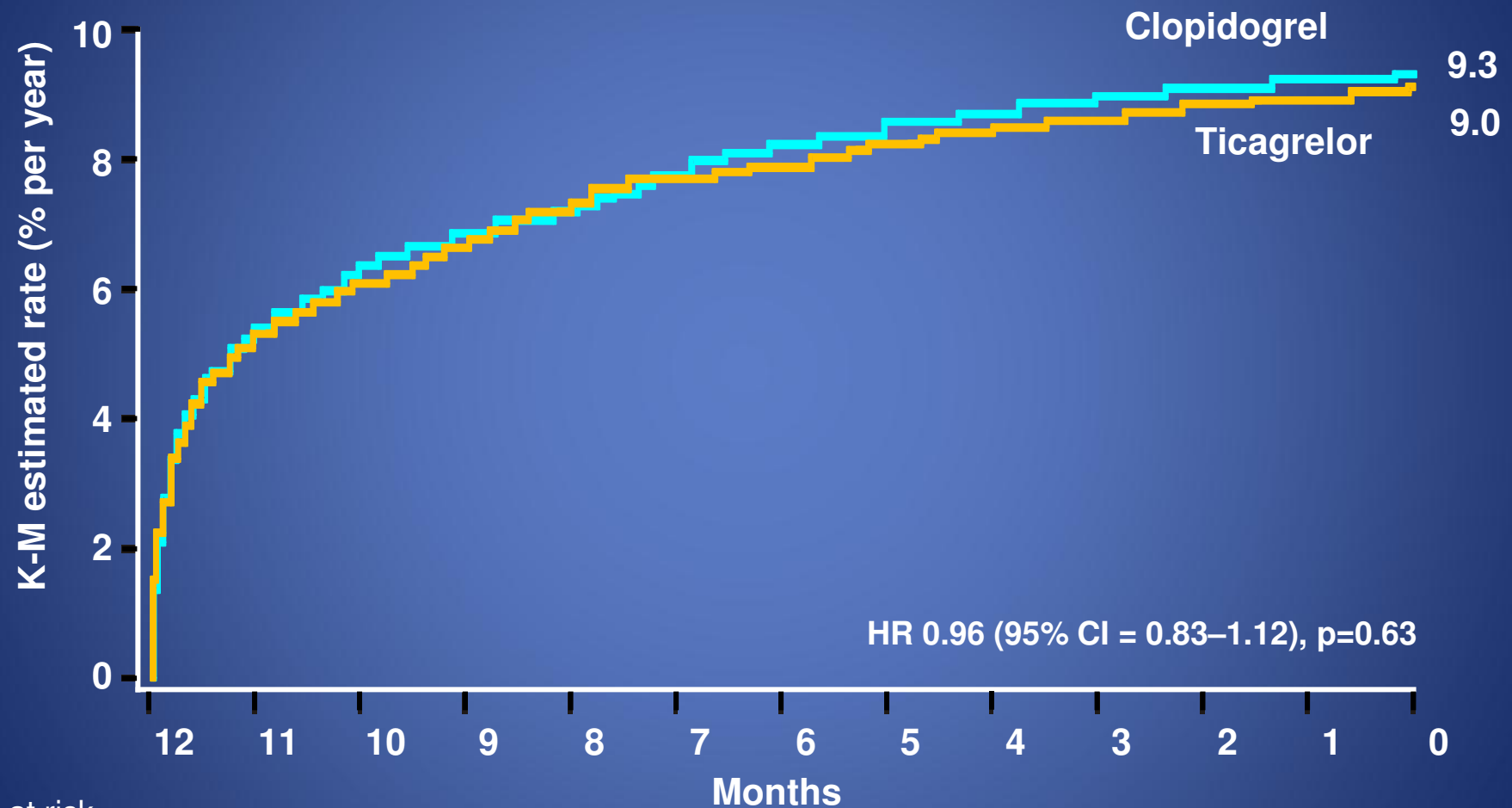
No. at risk	12	11	10	9	8	7	6	5	4	3	2	1	0
Ticagrelor	4,201	3,887	3,834	3,732	3,011	2,297	1,891						
Clopidogrel	4,129	3,892	3,823	3,730	3,022	2,333	1,868						

PLATO STEMI: 8,430 patients - All cause mortality



No. at risk	12	11	10	9	8	7	6	5	4	3	2	1	0
Ticagrelor	1,993	2,413	3,150	3,876	3,962	4,005	4,201						
Clopidogrel	1,980	2,471	3,195	3,912	3,989	4,029	4,229						

PLATO STEMI - 8,430 patients: major bleeding



No. at risk	12	11	10	9	8	7	6	5	4	3	2	1	0
Ticagrelor	1,640	1,786	2,440	3,137	3,254	3,431	4,165						
Clopidogrel	1,635	1,804	2,441	3,159	3,297	3,430	4,181						

ACC/AHA 2009 Focused Update STEMI Guidelines

- **Class I:** A loading dose of thienopyridine is recommended for **STEMI patients for whom PCI is planned**. Regimens should be 1 of the following:
 - a At least 300 to 600 mg of clopidogrel should be given as early as possible before or at the time of primary or nonprimary PCI. (*Level of Evidence: C*)
 - **b Prasugrel 60 mg should be given as soon as possible for primary PCI. (*Level of Evidence: B*)**

ACC/AHA 2009 Focused update STEMI Guidelines

- The duration of thienopyridine therapy should be as follows:
- In patients receiving a stent during PCI, clopidogrel 75 mg daily, or prasugrel 10 mg daily (in pts weighing < 60 kg, consider lowering maintenance to 5 mg) **should be given for ≥ 12 mo.** (unless risk of bleeding is high - earlier d/c should be considered)
- In patients taking a thienopyridine in whom CABG is planned and can be delayed, it is recommended that the drug be discontinued... **withdrawal should be ≥ 5 days in pts receiving clopidogrel and ≥ 7 days in pts receiving prasugrel**
- Prasugrel is not recommended for pts with h/o stroke or TIA

ESC 2010 Myocardial Revascularization STEMI Guidelines

STEMI			
Antiplatelet therapy			
	ASA	I	B
	Clopidogrel ^f (with 600 mg loading dose as soon as possible)	I	C
	Prasugrel ^d	I	B
	Ticagrelor ^d	I	B
	+ GPIIb-IIIa antagonists (in patients with evidence of high intracoronary thrombus burden)		
		Abciximab	IIa A
		Eptifibatide	IIa B
		Tirofiban	IIb B
		Upstream GPIIb-IIIa antagonists	III B

^d Depending on approval and availability

GP IIb/IIIa inhibitors in the updated ACC/AHA 2009 STEMI guidelines

Class IIa

1. It is reasonable to start treatment with glycoprotein IIb/IIIa receptor antagonists (abciximab (9,11) [*Level of Evidence: A*], tirofiban (11,12) [*Level of Evidence: B*] or eptifibatide (6,7,9) [*Level of Evidence: B*]) at the time of primary PCI (with or without stenting) in selected patients with STEMI.

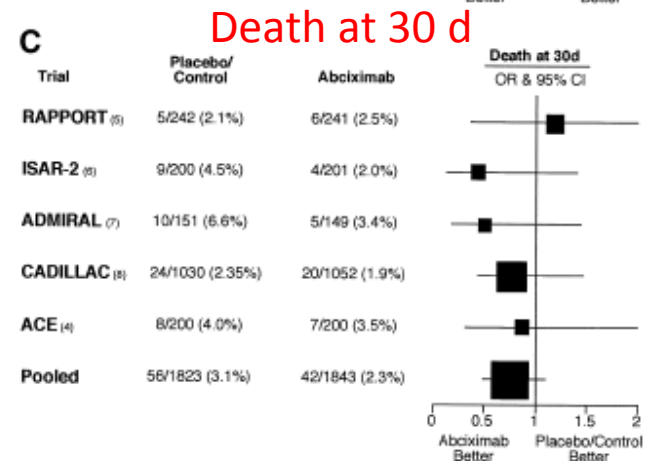
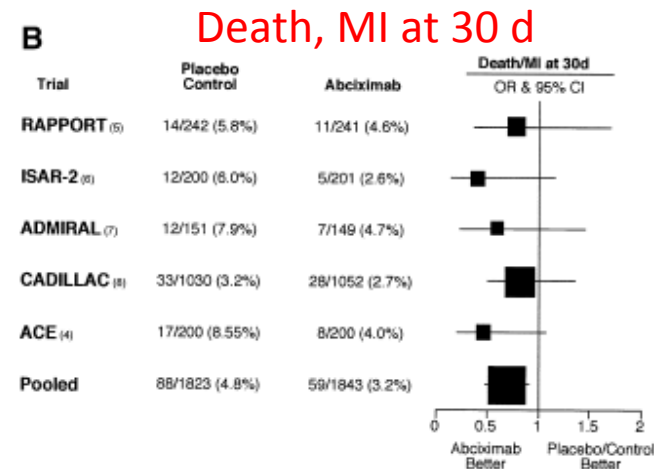
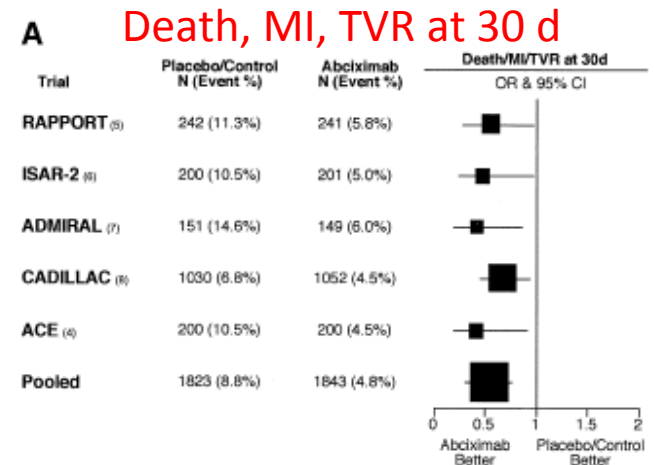
Class IIb

1. The usefulness of glycoprotein IIb/IIIa receptor antagonists (as part of a preparatory pharmacological strategy for patients with STEMI before their arrival in the cardiac catheterization laboratory for angiography and PCI) is uncertain (8,10). (*Level of Evidence: B*)

GP IIb/IIIa Inhibitors in STEMI – abciximab meta-analysis

Overall 46% reduction in death, reinfarction, and TVR; a 34% reduction in death or reinfarction; and 26% reduction in death

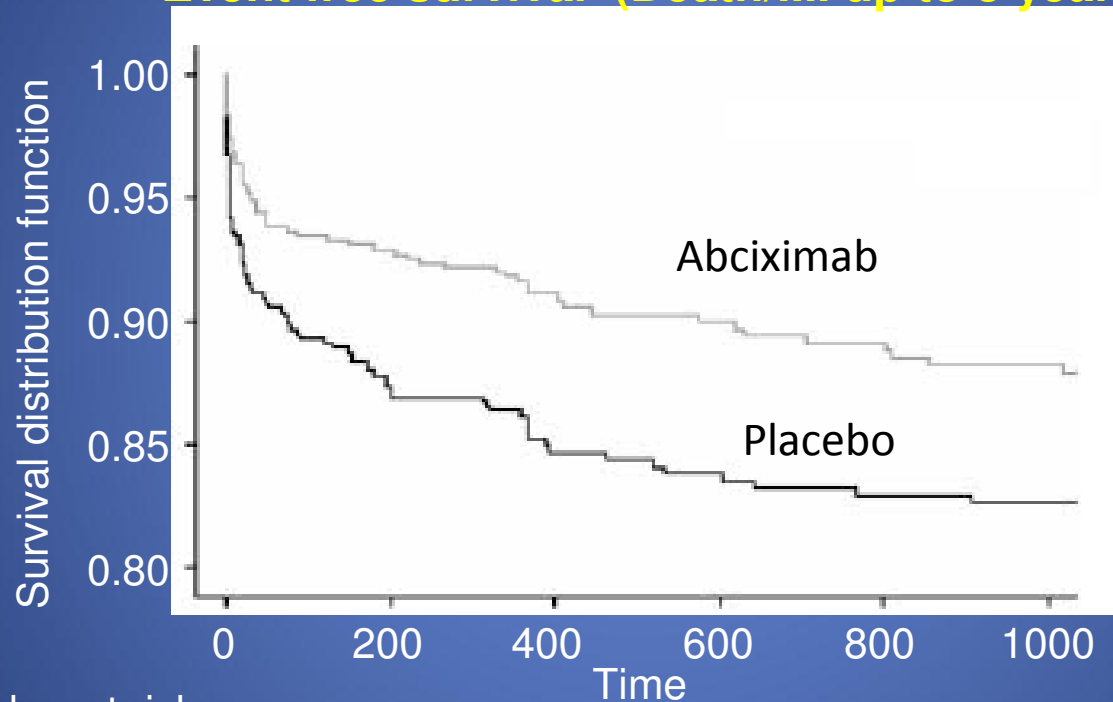
Topol E, Neumann FJ, Montalescot G.
JACC 2003; 42:1886-9



European Meta-analysis on Individual Patient Data (n=1101) with Long-Term Follow-up

ACE, ADMIRAL, ISAR-2 – Primary Endpoint

Event free survival (Death/MI up to 3 years)



↓37% RRR

↓6.1% ARR

NNT=19

Number at risk

Placebo	551	471	297	294	291	290
Abciximab	550	505	311	307	304	301

Value of GPIIb/IIIa Inhibitors in Patients with STEMI receiving prasugrel, ticagrelor or 600 mg clopidogrel

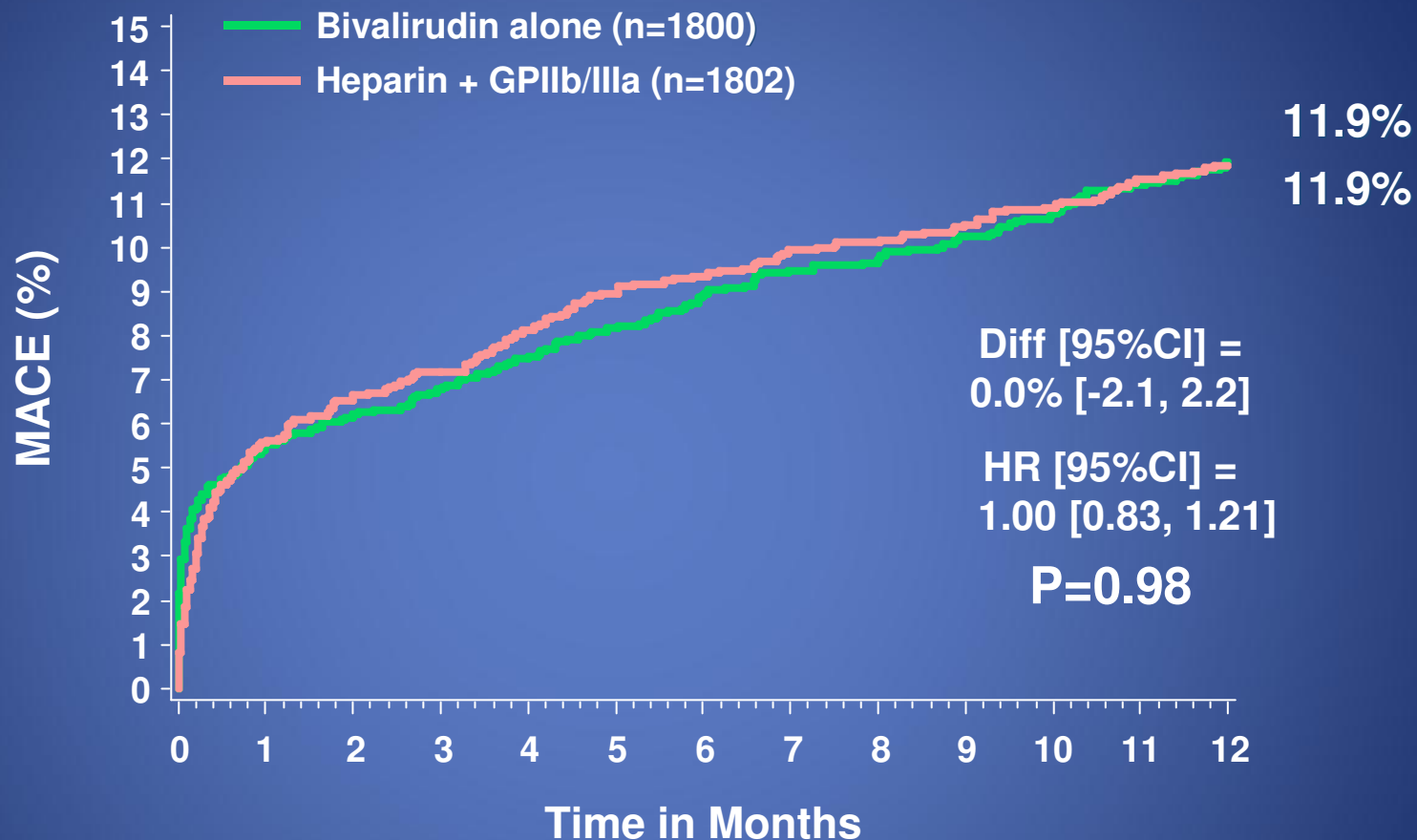
- Clopidogrel – BRAVE-3 trial: 800 patients with STEMI, given 600 mg clopidogrel in ICCU before PCI, randomized to receive abciximab vs. placebo. No effect on infarct size (by SPECT) or on MACE.
- No direct information for prasugrel and ticagrelor from dedicated studies to this question, but in TRITON and PLATO in subgroup analyses no significant differences in outcomes between pts receiving vs. not receiving GP IIb/IIIa inhibitors

Guidelines – anticoagulant Rx

- ACC/AHA 2009 STEMI guidelines : Class I recommendation for both UFH (LOE C) (target ACT depending on whether GPIIb/IIIa inhibitors have been administered), and for bivalirudin treatment (with or without prior UFH Rx) (LOE B)
- ESC 2010 myocardial revascularization guidelines:

Bivalirudin (monotherapy)	I	B
UFH	I	C

HORIZONS 1-Year Major Adverse CV Events

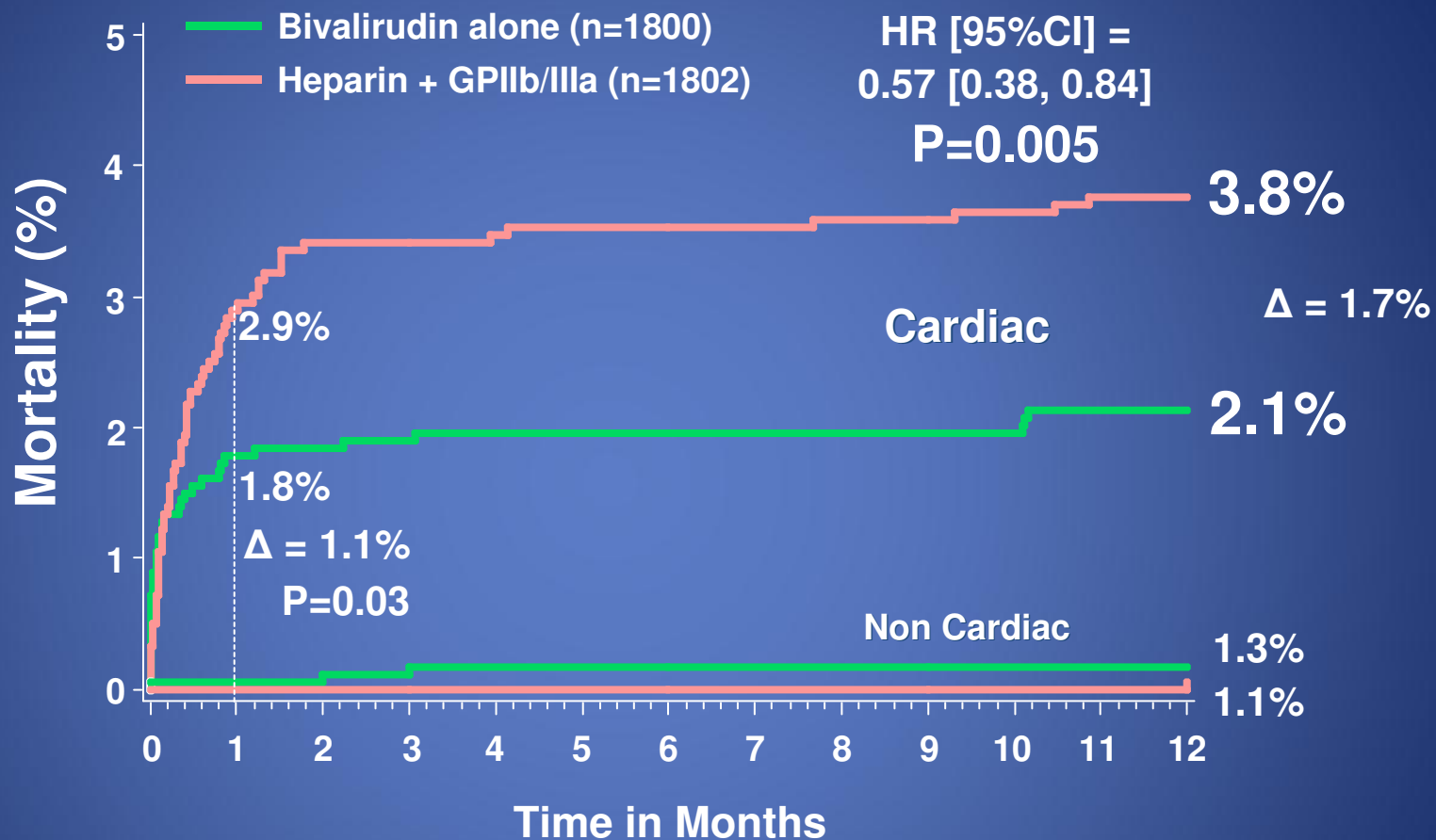


Number at risk

Bivalirudin alone	1800	1627	1579	1544	1394
Heparin+GPIIb/IIIa	1802	1619	1573	1540	1380

*MACE = All cause death, reinfarction, ischemic TVR or stroke

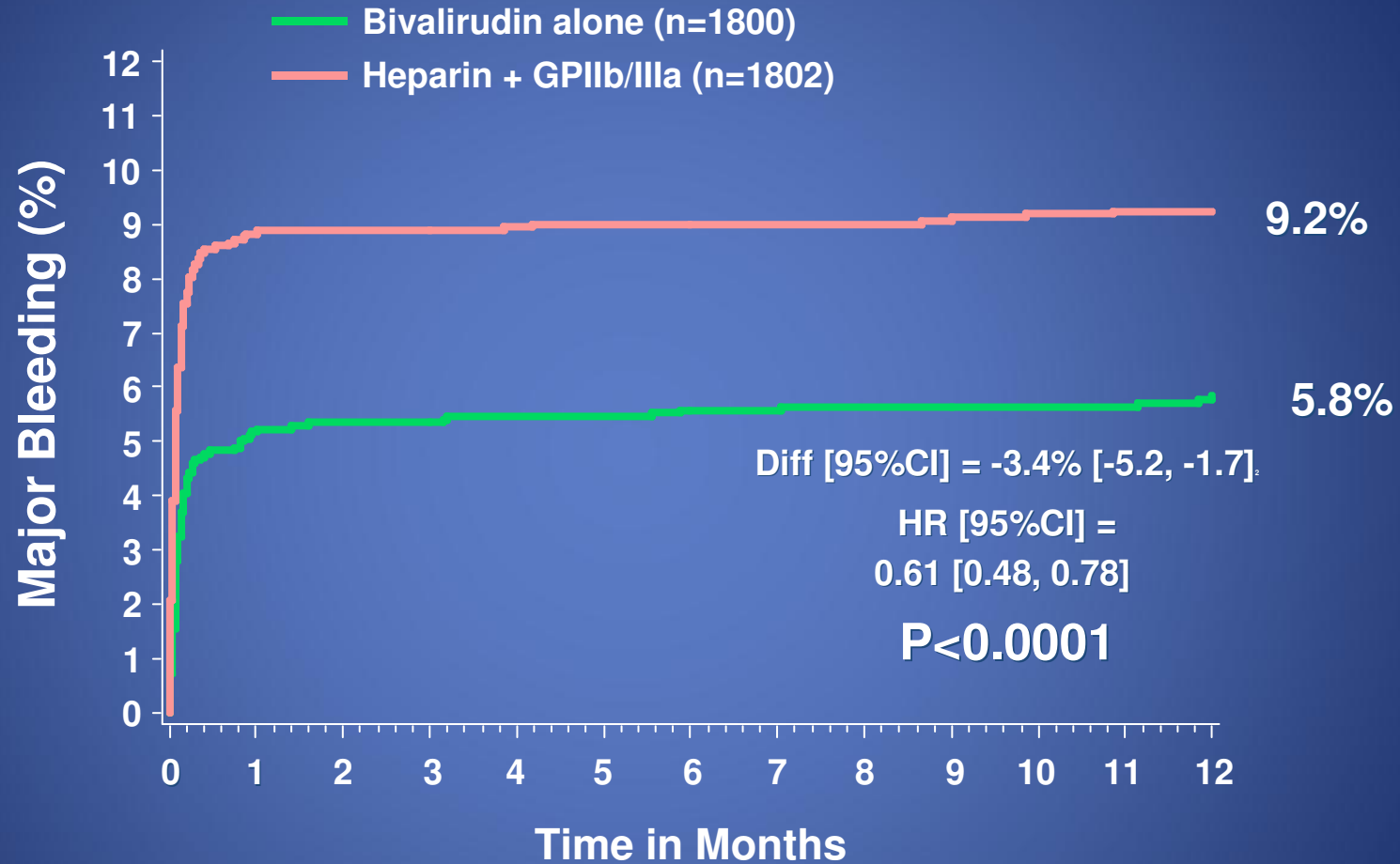
HORIZONS AMI Study 1-Year Mortality: Cardiac and Non Cardiac



Number at risk

Bivalirudin alone	1800	1705	1684	1669	1520
Heparin+GPIIb/IIIa	1802	1678	1663	1646	1486

HORIZONS 1-Year Major Bleeding (non-CABG)



Number at risk

Bivalirudin alone	1800	1621	1601	1586	1448
Heparin+GPIIb/IIIa	1802	1544	1532	1515	1368

Bail-out indications for GP IIb/IIIa inhibitors in HORIZONS:

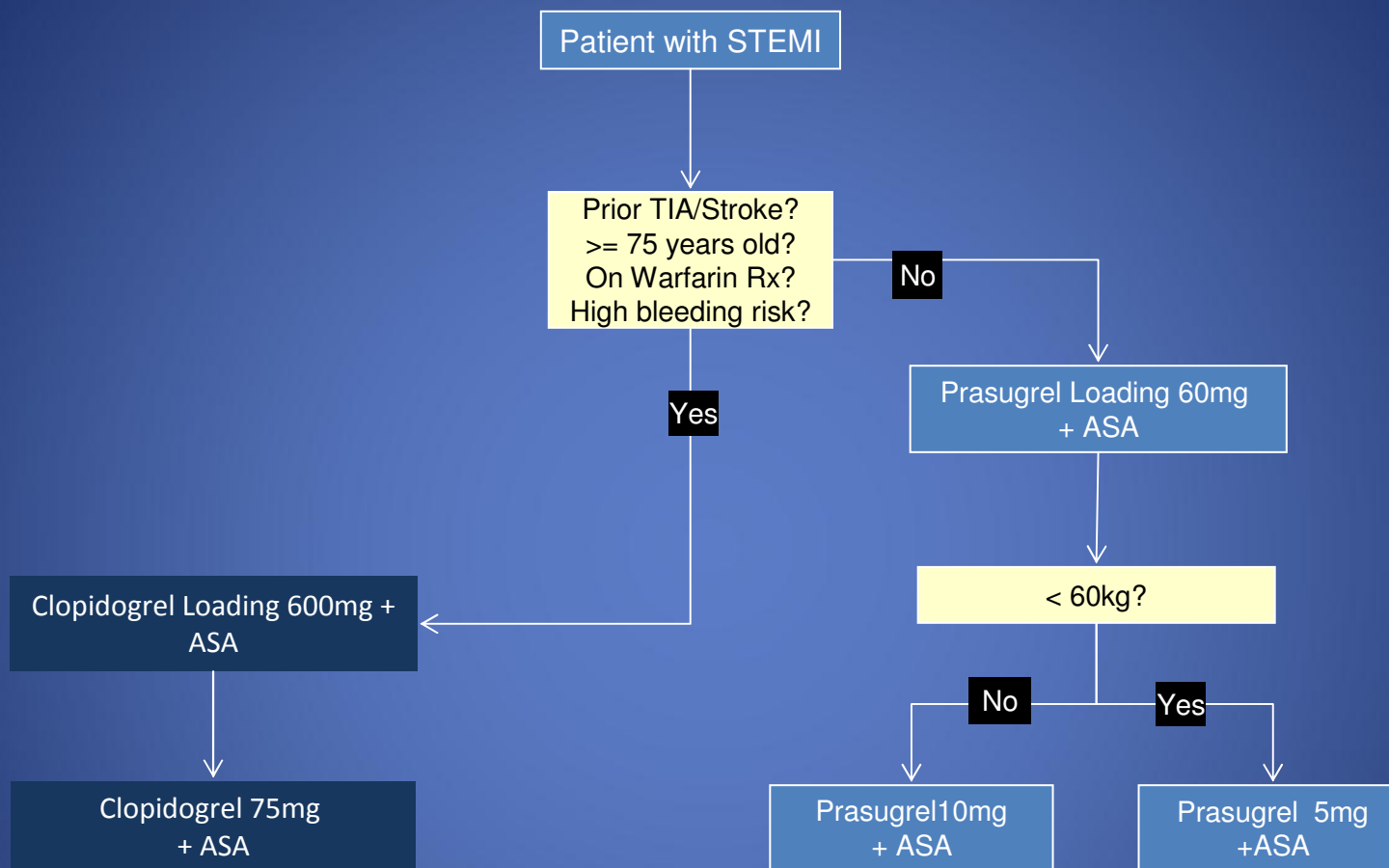
- Hemodynamic instability
- Inadequate reflow / No reflow
- Large thrombus burden

Summary:

Improved outcomes in patients with STEMI can be achieved by:

1. Early and effective primary PCI
2. Reduction of thrombus load - aspiration
3. Early and effective anti-platelet therapy – advantage for the new anti-platelet meds

STEMI Oral Antiplatelet Protocol Example



* Note: Ticagrelor is not yet approved in Israel

THANK YOU

