STEMI – Antithrombotic Therapy and Interventional Techniques in the Catheterization Laboratory

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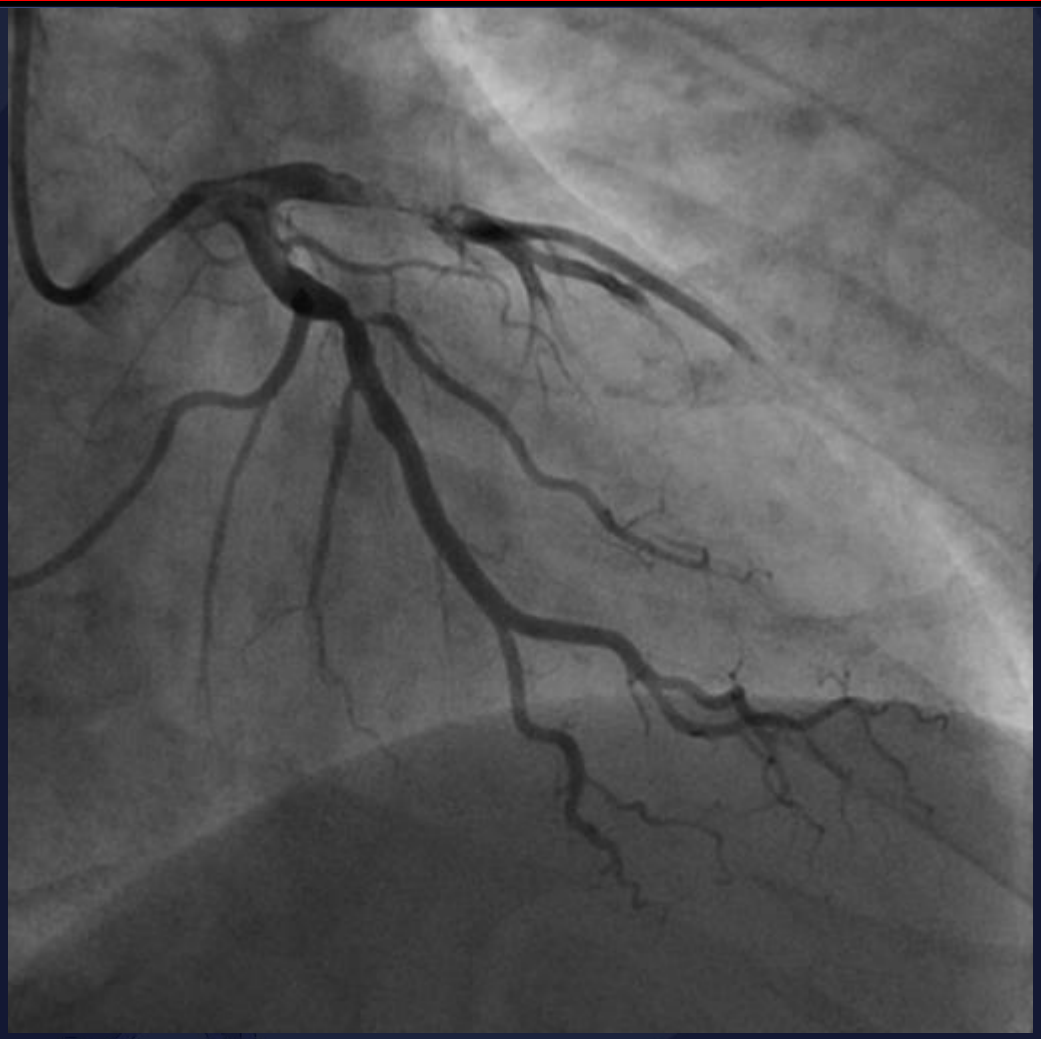
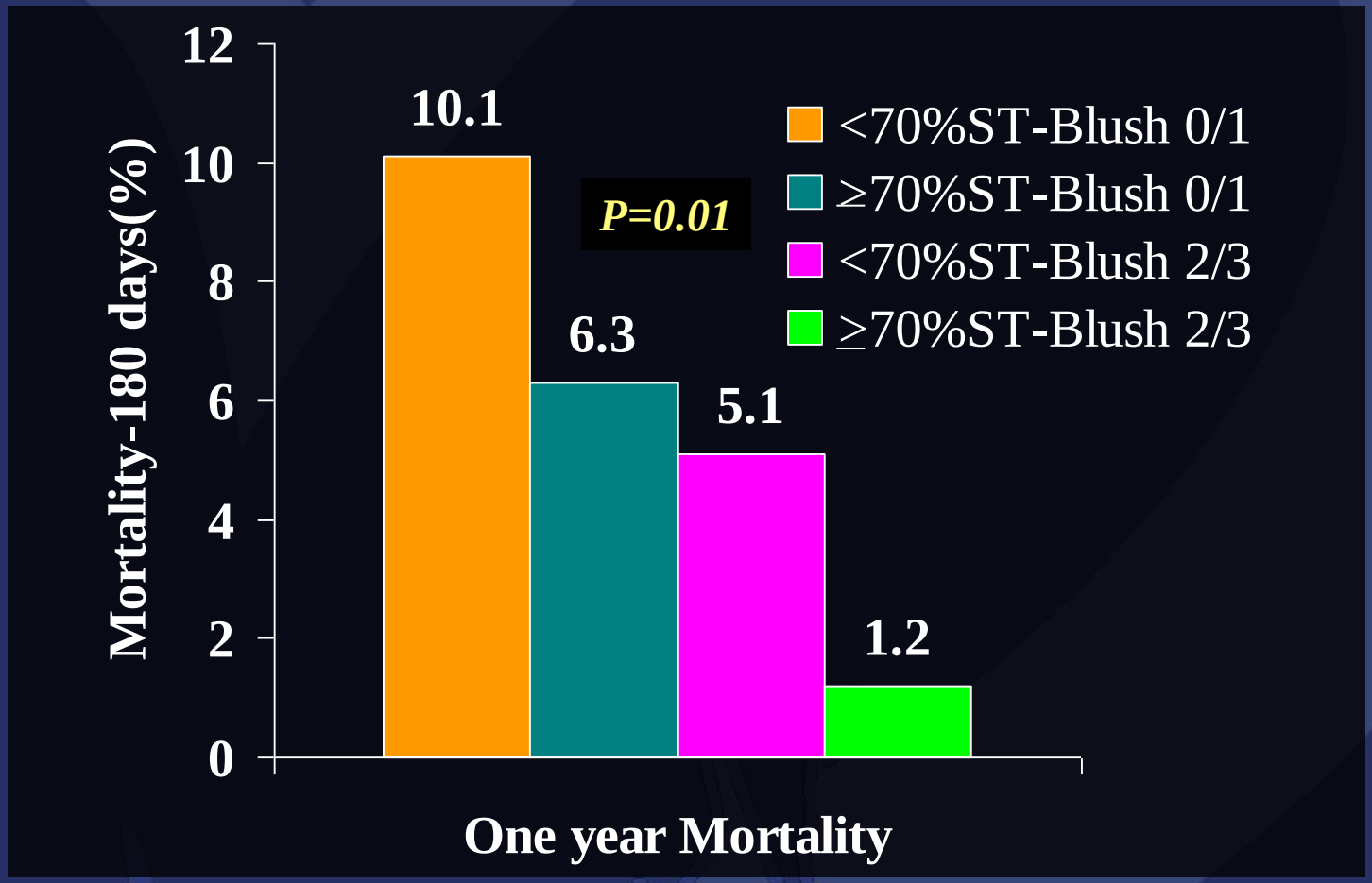
The Goal of Primary PCI in STEMI

- Restore flow in the culprit artery and optimize myocardial perfusion (by angio and EKG criteria)
- Preserve LV function.
- Reduce MI complications
- Reduce mortality.



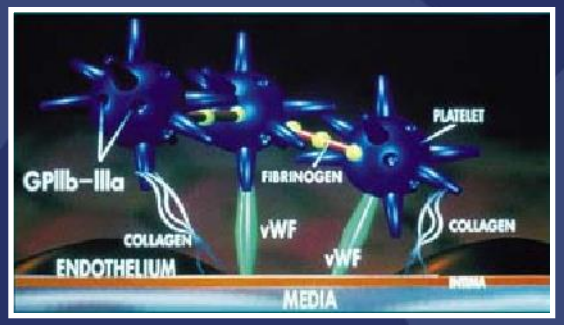
Markers of myocardial perfusion - ST Resolution and Myocardial Blush in STEMI

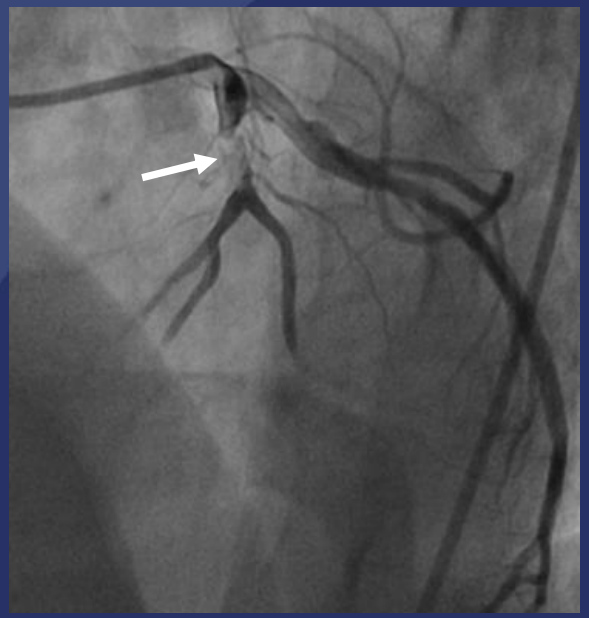
Sub-Analysis of the CADILLAC Trial (N=456)

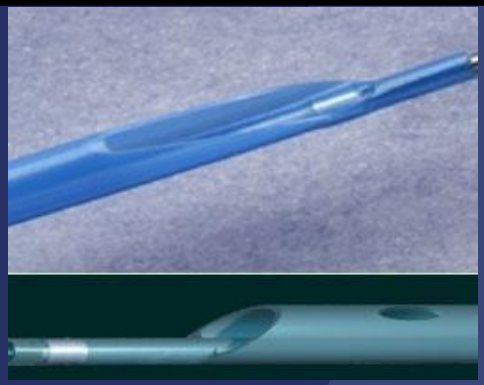


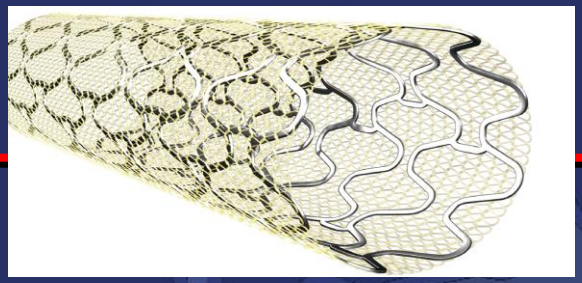
Sorajja P. et al Eur Heart J 2005

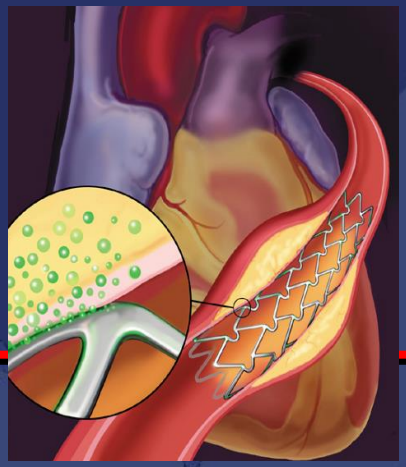
Attempts to Optimize STEMI PCI



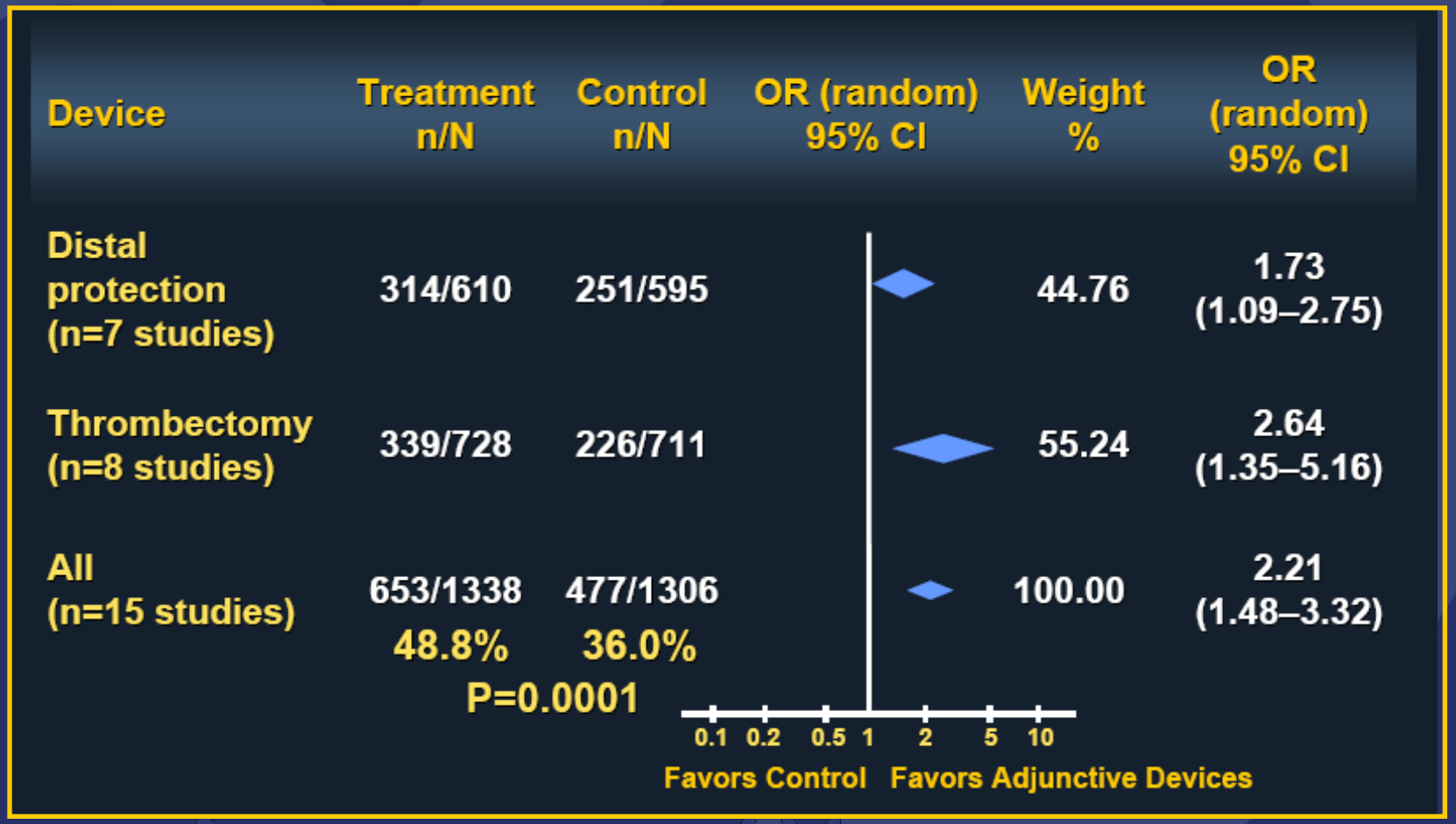








Manual thrombectomy and distal embolic protection devices : Myocardial Blush



Meta-analysis of 15 STEMI studies

De Luca G. et al Am Heart J 2007

Manual thrombectomy and distal embolic protection devices : 30 day mortality

Device	Treatment n/N	Control n/N	OR (random) 95% CI	RR (95% CI)	P Value
Distal protection (n=6 studies)	16/672 2.4%	24/659 3.6%		0.65 [0.35, 1.21]	0.18
Thrombectomy (n=12 studies)	28/1076 2.6%	21/1065 2.0%		1.32 [0.76, 2.29]	0.33
All (n=18 studies)	44/1748 2.5%	45/1724 2.6%		0.96 [0.64, 1.45]	0.86

P=0.88

Meta-analysis of 18 STEMI studies

De Luca G. et al Am Heart J 2007

THROMBUS ASPIRATION

TAPAS Study overview

Randomized, Open Label, Single Center Trial

Patients presenting with Acute Myocardial Infarction within 12 hours after onset of symptoms

1:1 randomization
N = 1071 patients
1 site
Netherlands

Primary Aspiration with Export Catheter n = 535

Conventional Stenting n = 536

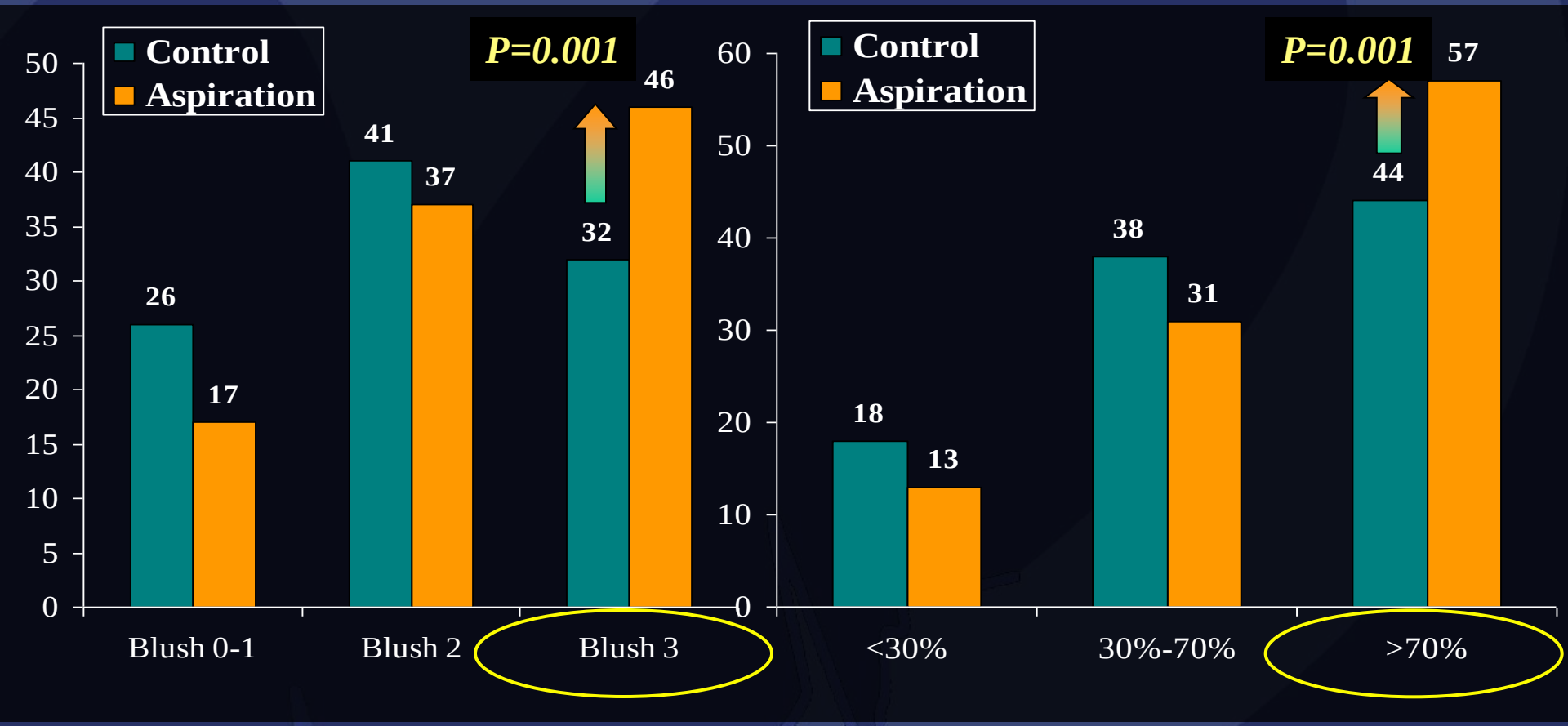
Procedure **30d** **1yr**

Primary Endpoint:
- **Myocardial Blush Grade of 0 or 1**

Secondary Endpoints:
- **TIMI 3 flow**
- **Complete resolution of ST-segment elevation**
- **Absence of persistent ST-segment deviation,**
- **Reinfarction, death, and MACE at 30 days.**

Svilaas T et al. N Engl J Med 2008

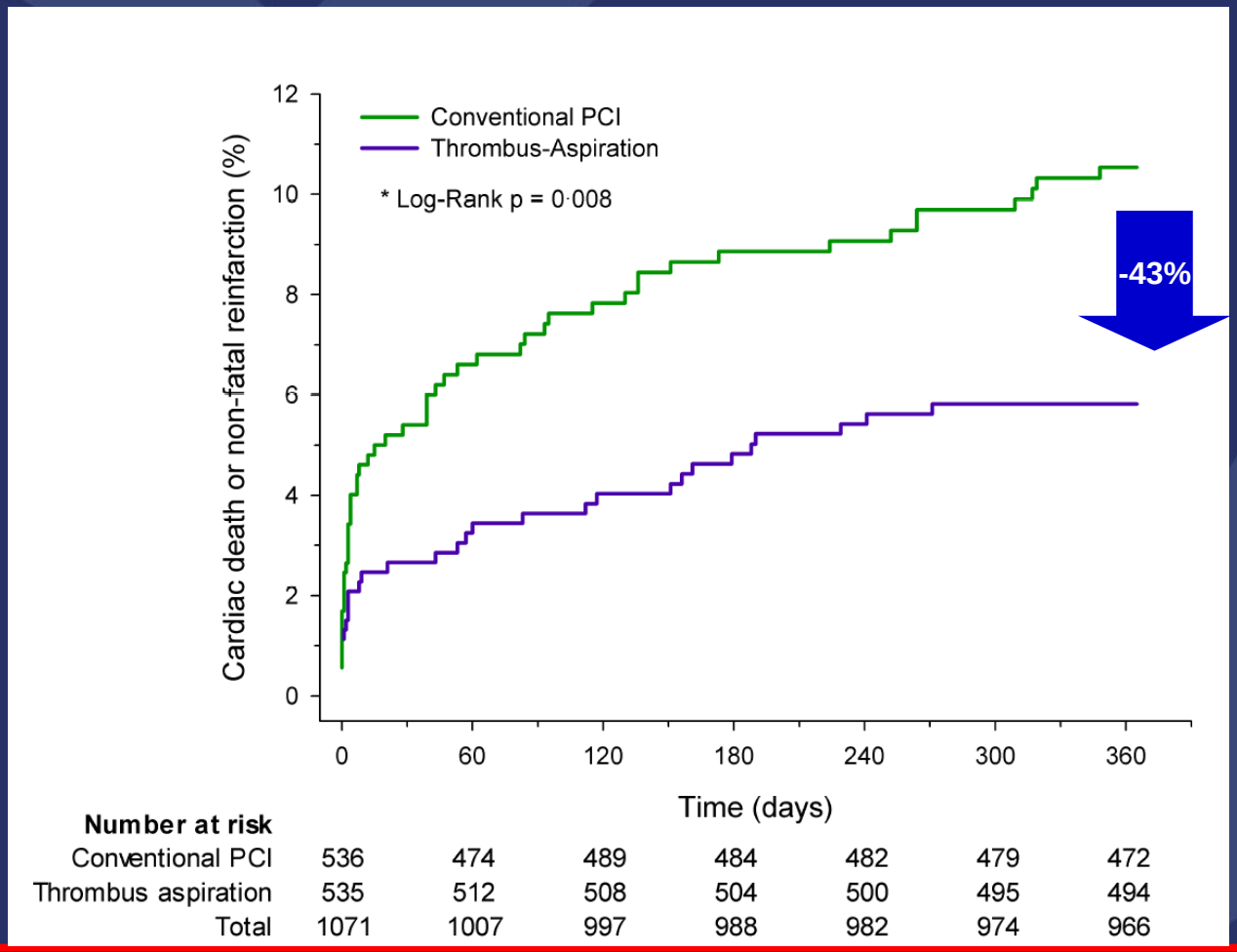
TAPAS study



Svilaas T et al. N Engl J Med 2008

TAPAS Study: Clinical Events

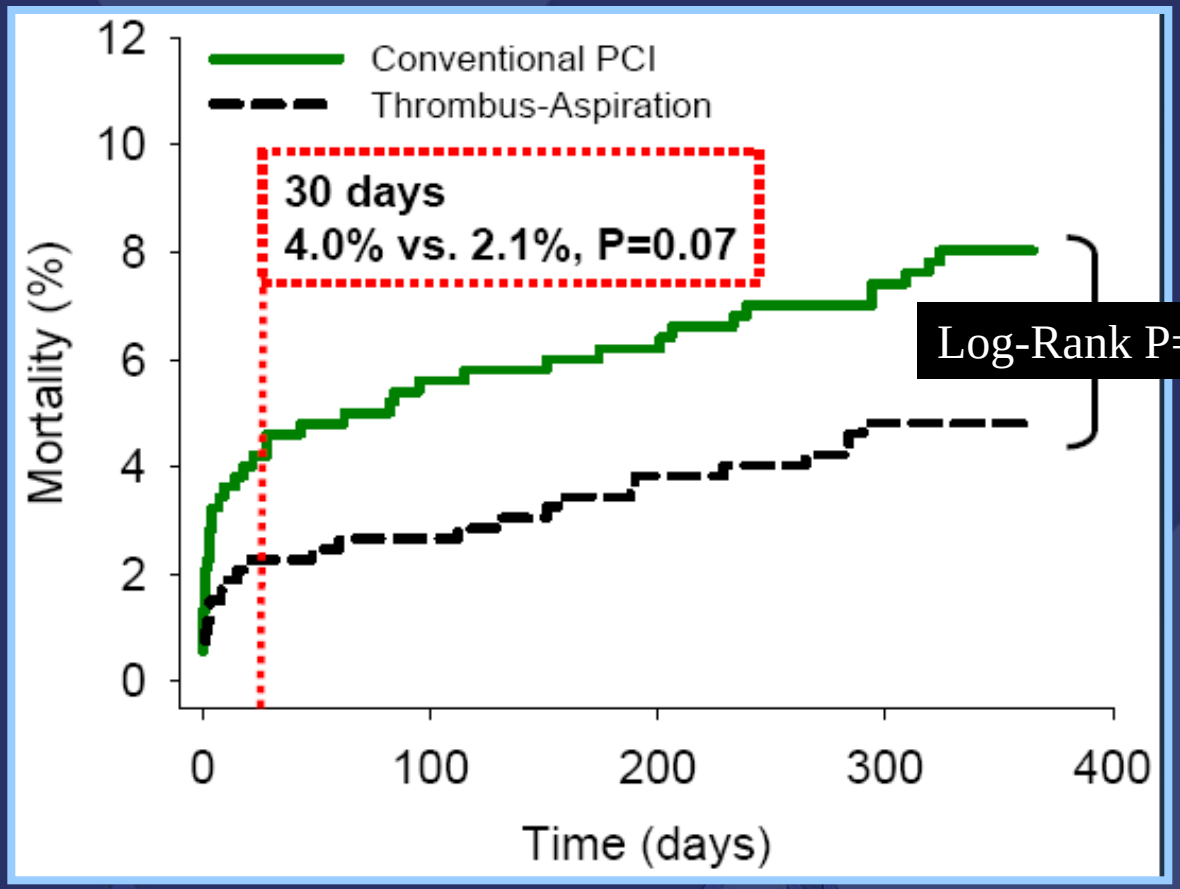
*Sig. reduction of **cardiac death or non-fatal MI** in Aspiration Group at 1 year*



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

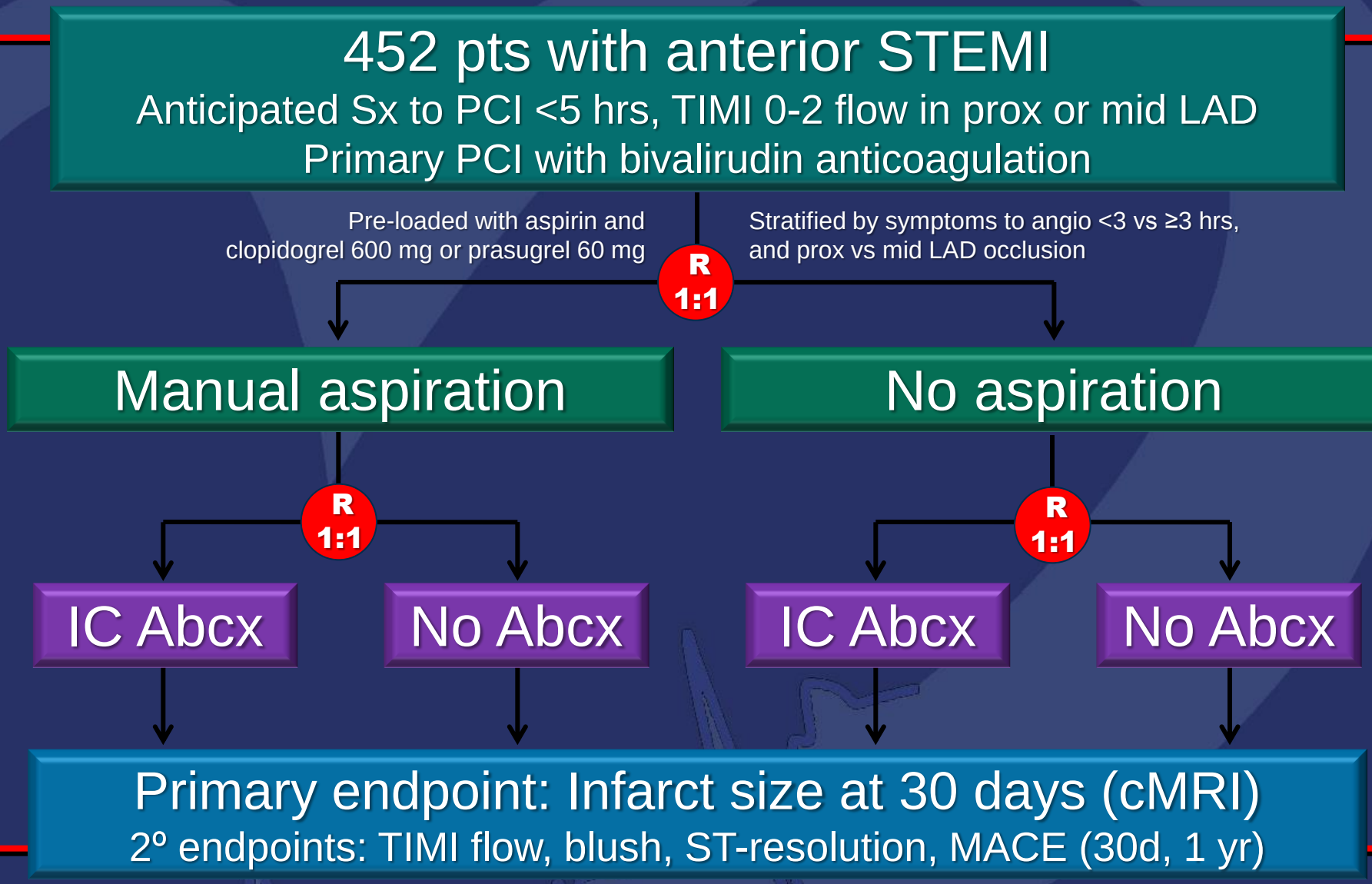
TAPAS Study: Clinical Events

Mortality



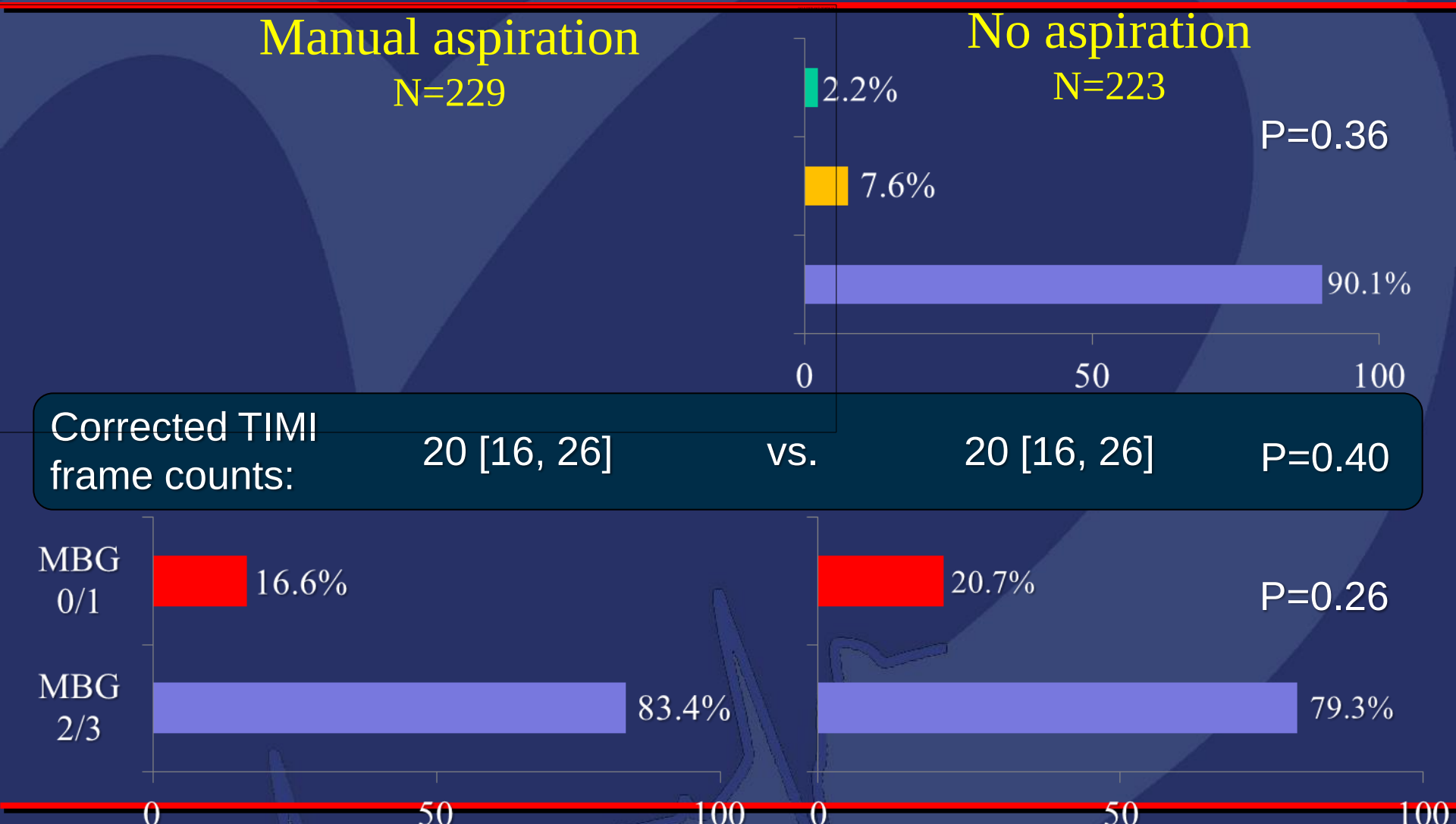
Svilaas T et al. N Engl J Med 2008
Vlaar PG et al. Lancet 2008

INFUSE-AMI Trial



Infuse-AMI, Stone G et al, JAMA 2012

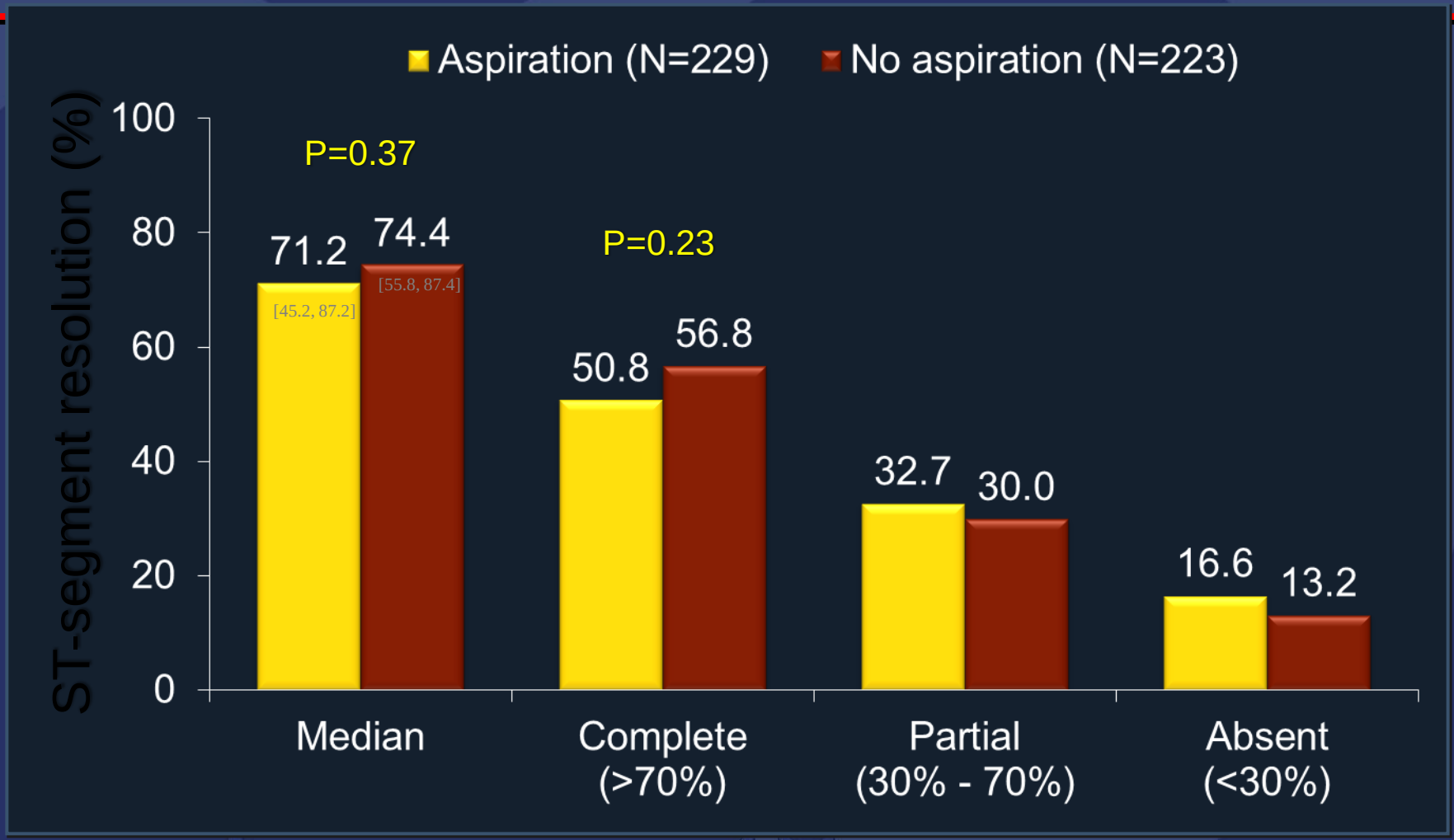
INFUSE-AMI: Reperfusion post-PCI*



*Core laboratory assessed

Infuse-AMI, Stone G et al, JAMA 2012

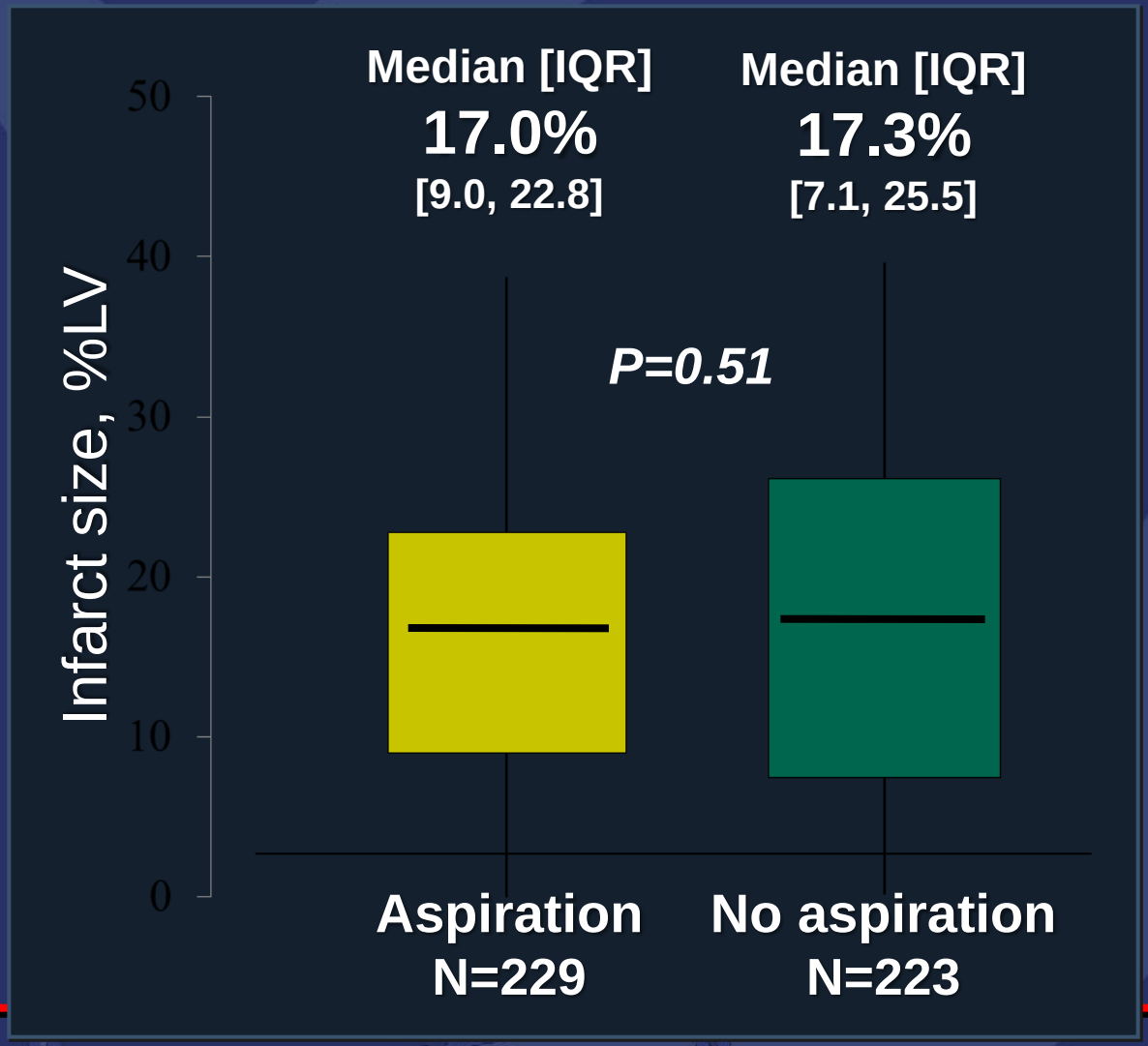
INFUSE-AMI: STR 60 minutes post-PCI*



*Core laboratory assessed

Infuse-AMI, Stone G et al, JAMA 2012

INFUSE-AMI: Infarct size at 30 days*
- Major secondary endpoint -



*Core laboratory assessed. No interaction was present between the 2 randomization groups for the primary 30-day infarct size endpoint (p=0.46)

Updated aspiration meta-analysis

- **Aspiration thrombectomy vs. conventional PPCI (18 trials, n=3,936):**
- **ST-segment resolution at 60 minutes (RR=1.31; 95% CI 1.16-1.48; p<0.0001) and TIMI blush grade 3 post-PCI (RR=1.37; 95% CI 1.19-1.59; p<0.0001) were both improved by aspiration**
- **MACE: RR = 0.76; 95% CI 0.63-0.92; p=0.006 with aspiration**
- **All-cause mortality (RR=0.71, 95% CI 0.51-0.99; p=0.049) - significantly reduced with aspiration**
- **Trend or reductions in re-MI (p=0.11) and TVR (p=0.06).**
- **Final infarct size (p=0.64) and ejection fraction (p=0.32) at 1 month were similar.**

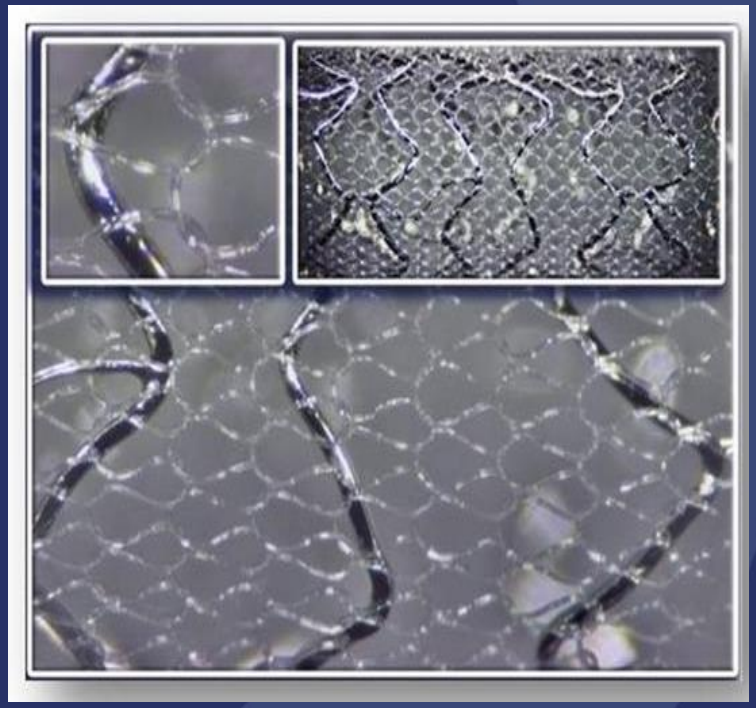
Kumbhani DJ, et al JACC 2013

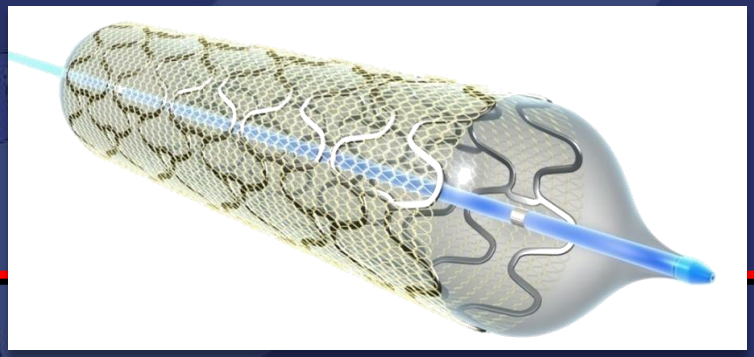
2012 STEMI ESC Guidelines

Recommendations	Class [a]	Level [b]	Ref [c]
Indications for primary PCI			
Primary PCI is the recommended reperfusion therapy over fibrinolysis if performed by an experienced team within 120 min of FMC.	I	A	69, 99
Primary PCI is indicated for patients with severe acute heart failure or cardiogenic shock, unless the expected PCI related delay is excessive and the patient presents early after symptom onset.	I	B	100
Procedural aspects of primary PCI			
Stenting is recommended (over balloon angioplasty alone) for primary PCI.	I	A	101, 102
Primary PCI should be limited to the culprit vessel with the exception of cardiogenic shock and persistent ischaemia after PCI of the supposed culprit lesion.	IIa	B	75, 103–105
If performed by an experienced radial operator, radial access should be preferred over femoral access.	IIa	B	78, 79
If the patient has no contraindications to prolonged DAPT (indication for oral anticoagulation, or estimated high long-term bleeding risk) and is likely to be compliant, DES should be preferred over BMS.	IIa	A	80, 82, 106, 107
Routine thrombus aspiration should be considered.	IIa	B	83–85
Routine use of distal protection devices is not recommended.	III	C	86, 108
Routine use of IABP (in patients without shock) is not recommended.	III	A	97, 98

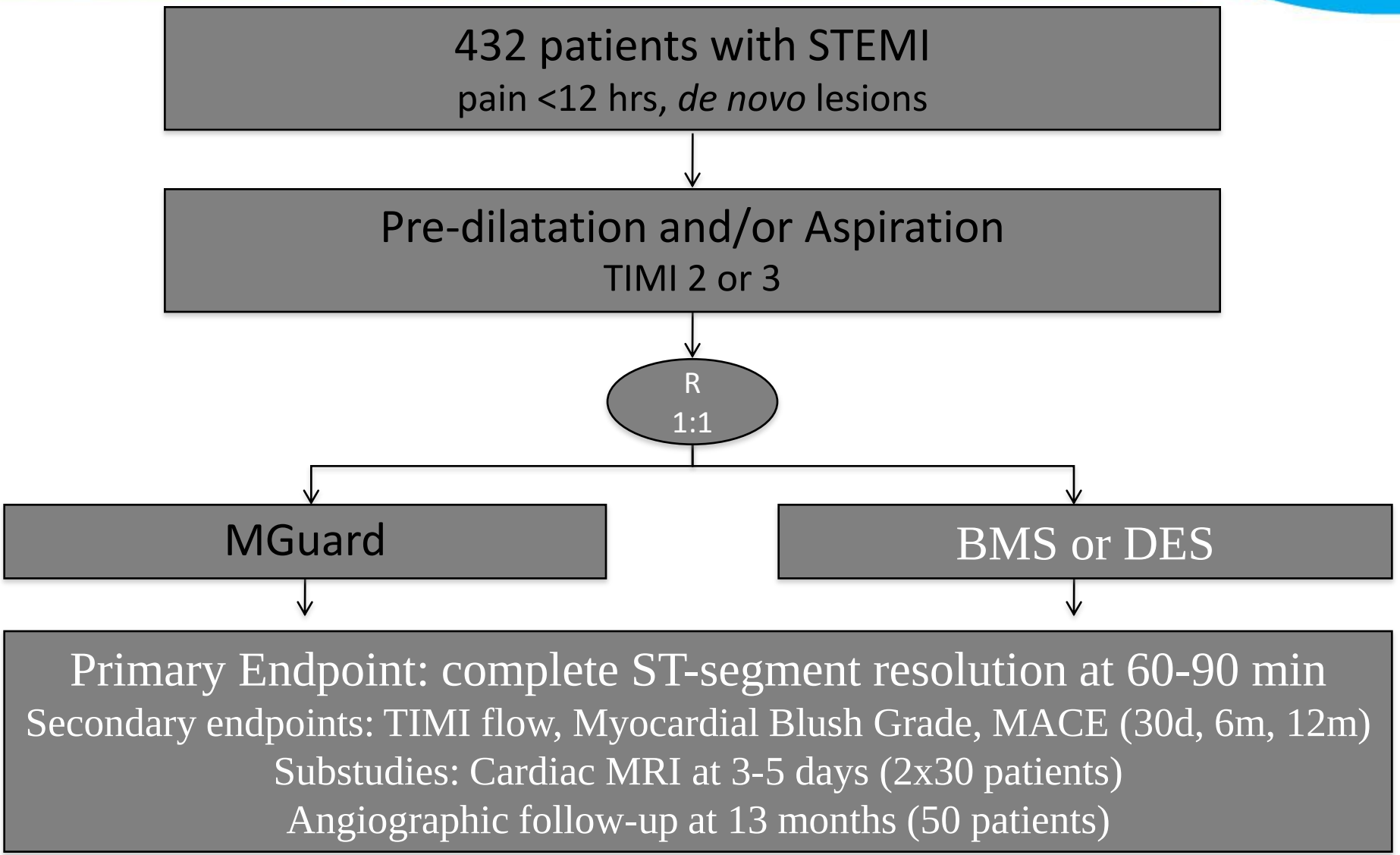
The MGuard Coronary Stent System

- A stent wrapped with ultra-thin (20μm) polymer mesh sleeve.
- The mesh is designed for plaque sealing during stent expansion in order to prevent embolization of athero-thrombotic debris.
- The sleeve expands seamlessly when the stent is deployed, without affecting the structural integrity of the stent.



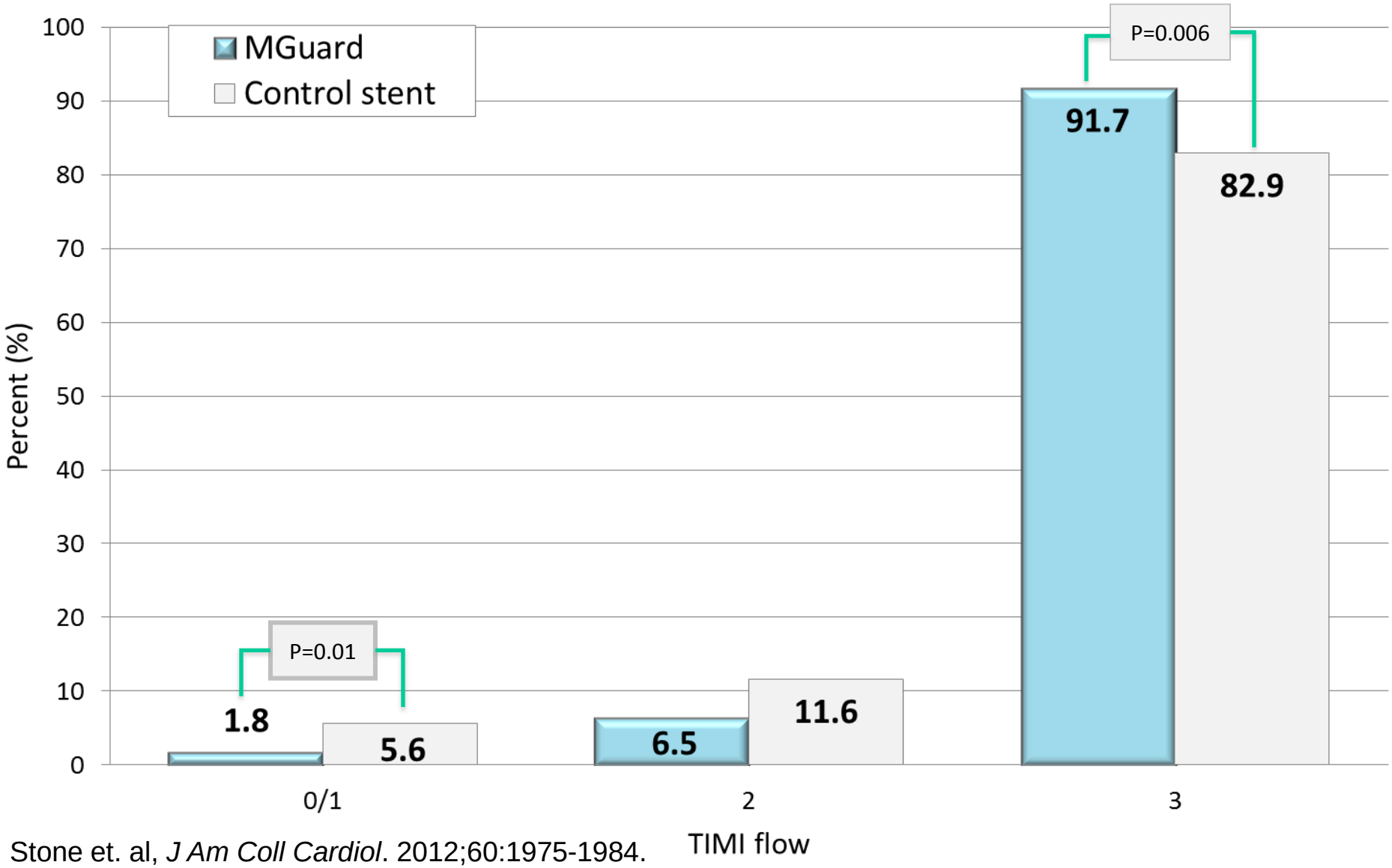


MASTER TRIAL DESIGN



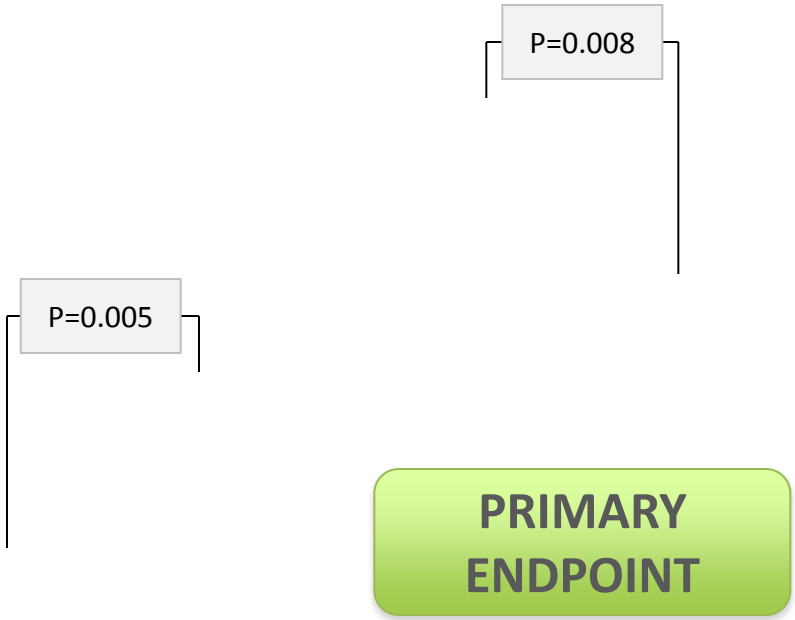
Stone G et al, JACC 2012

TIMI FLOW



Stone et. al, *J Am Coll Cardiol*. 2012;60:1975-1984.

ST SEGMENT RESOLUTION



Stone et. al, *J Am Coll Cardiol*. 2012;60:1975-1984.

30 DAYS CLINICAL RESULTS*

	MGUARD (N=217)	CONTROL BMS / DES (N=216)	P
MACE	4 (1.8%)	5 (2.3%)	0.75
All cause mortality	0 (0.0%)	4 (1.9%)	0.06
Cardiac death	0 (0.0%)	4 (1.9%)	0.06
Reinfarction	3 (1.4%)	2 (0.9%)	1.00
TLR, ischemia-driven	4 (1.8%)	1 (0.5%)	0.37
TVR, ischemia-driven	5 (2.3%)	1 (0.5%)	0.10
Stent Thrombosis			
Definite or Probable	3 (1.4%)	2 (0.9%)	0.67
Definite	3 (1.4%)	1 (0.5%)	0.62
Stroke	1 (0.5%)	0 (0.0%)	1.00
TIMI Bleeding			
Major or Minor	4 (1.9%)	4 (1.9%)	0.75
Major	3 (1.4%)	2 (0.9%)	1.00

* Secondary endpoints

Stone et. al, *J Am Coll Cardiol*. 2012;60:1975-1984.

Anti-thrombotic Therapy

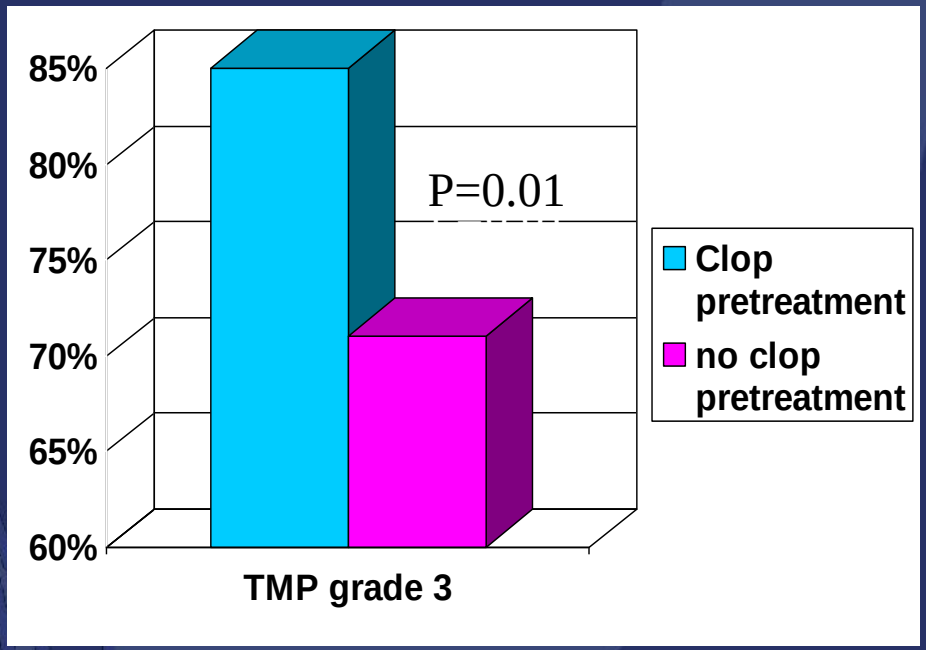
Effect of Clopidogrel Pretreatment on TIMI Perfusion Grade and Clinical Outcomes in Patients Undergoing Primary PCI for AMI

- 292 pts with STEMI treated with primary PCI allocated into 2 groups:

  1. those who received clopidogrel loading before the PCI (in the ER or CCU) (n=165)

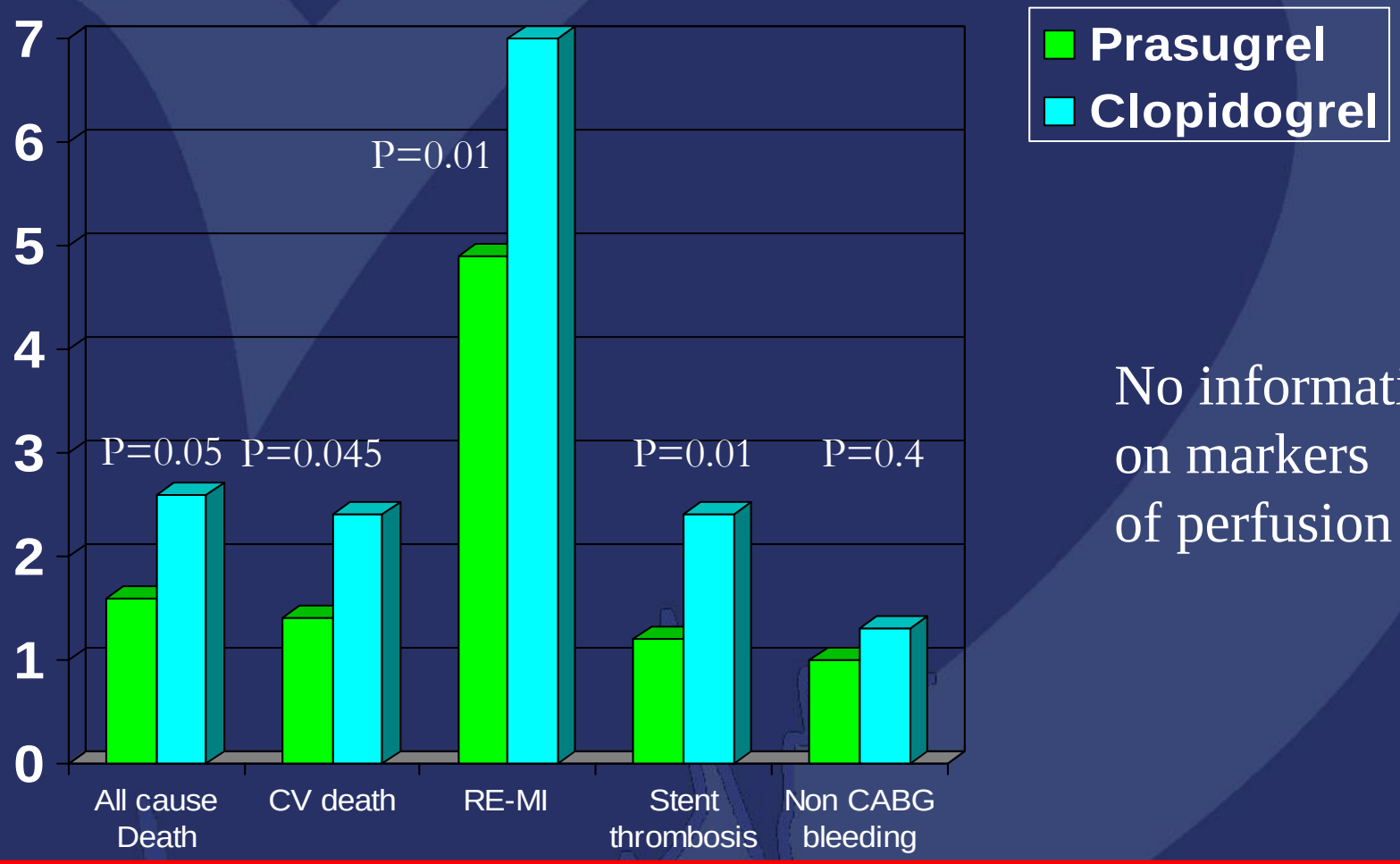
  2. those who received clopidogrel loading immediately after PCI (n=127)

- No differences in baseline clinical characteristics.



Lev E et al, AJC 2008

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

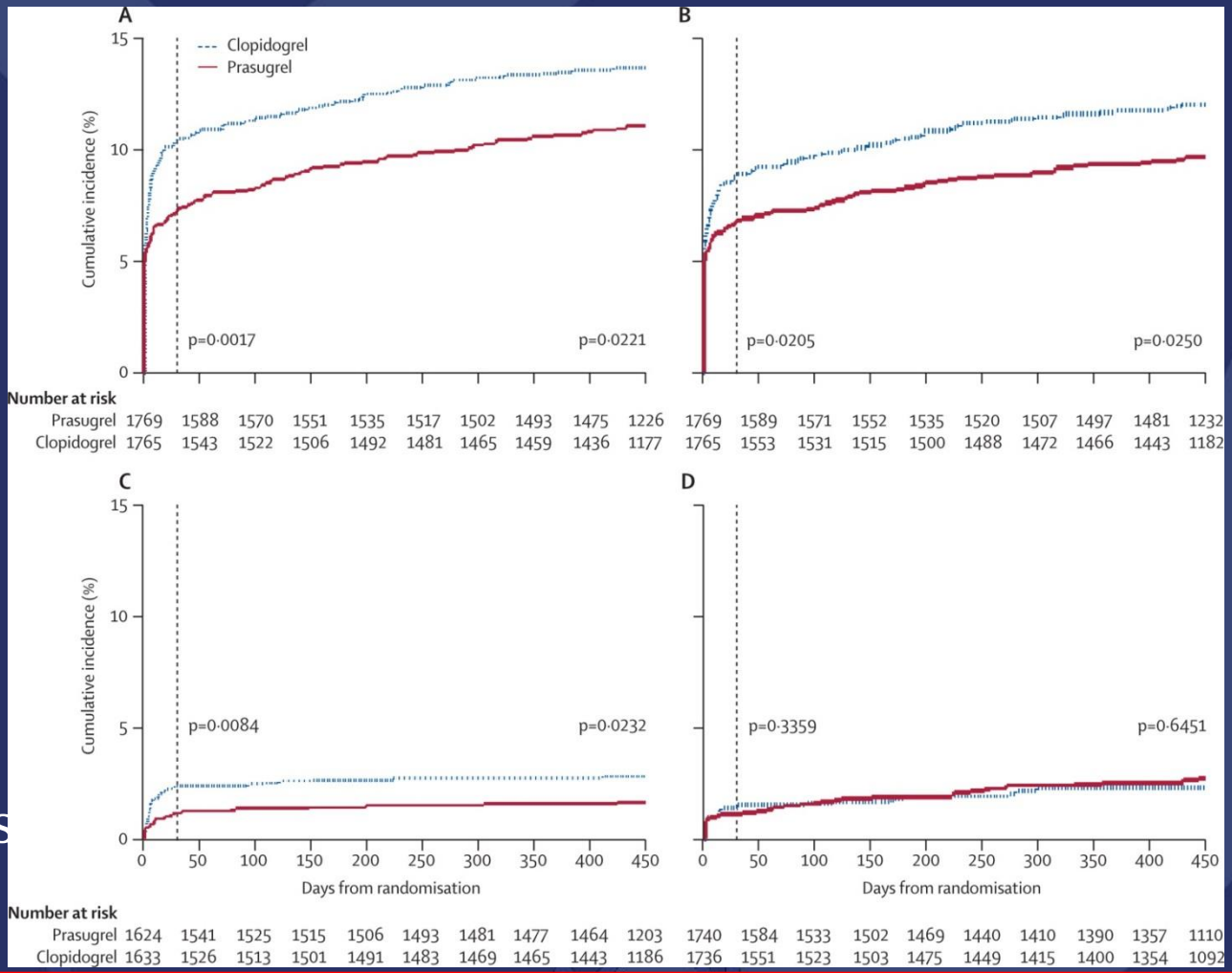


No information on markers of perfusion

Montalescot et al, Lancet 2009

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

Death
MI
Stroke



Death
MI
UTVR

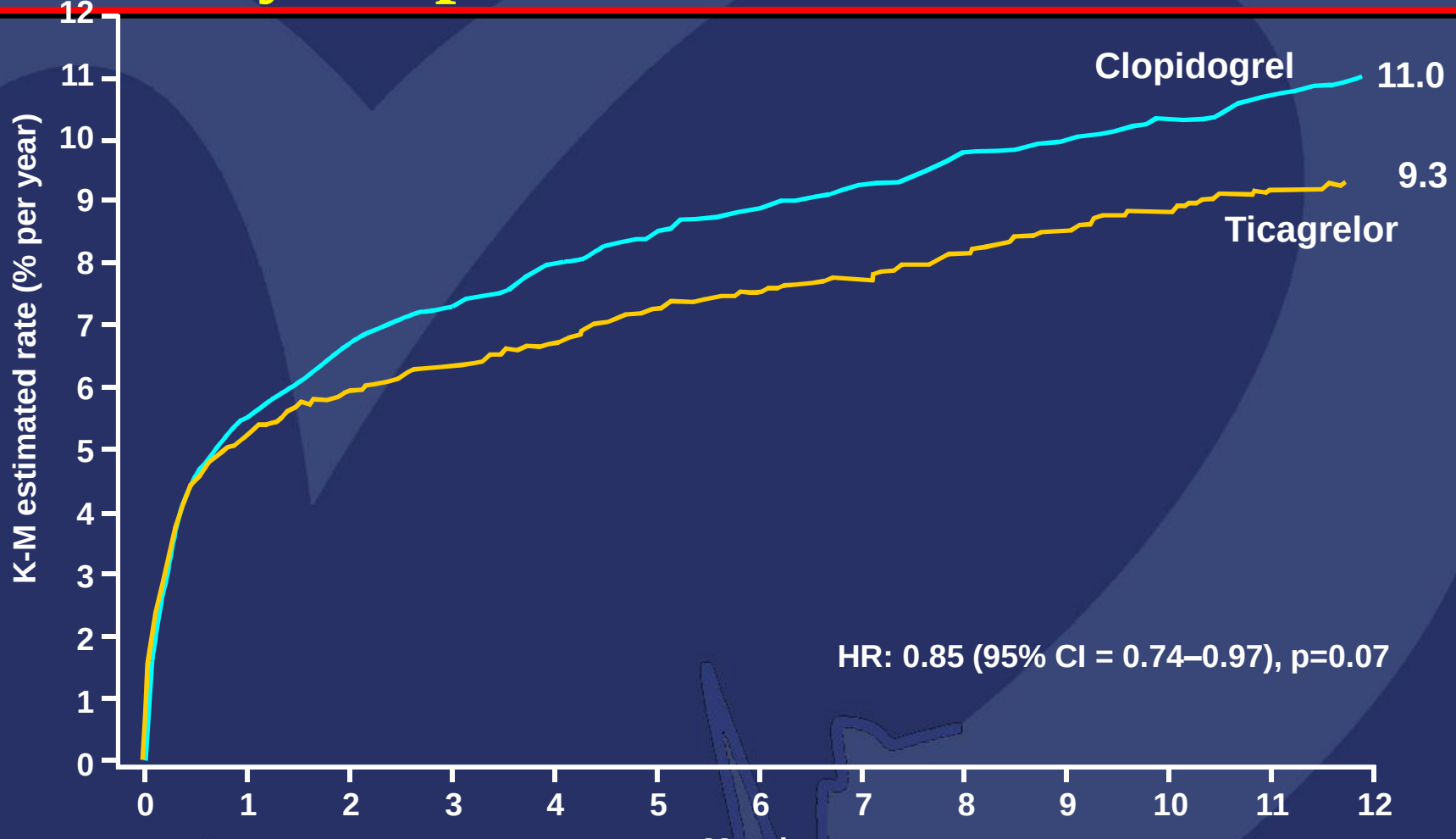
Stent
Thrombosis

Non-CABG
Related
TIMI
Major
Bleeding

Montalescot et al, Lancet 2009

PLATO STEMI – 8,430 patients

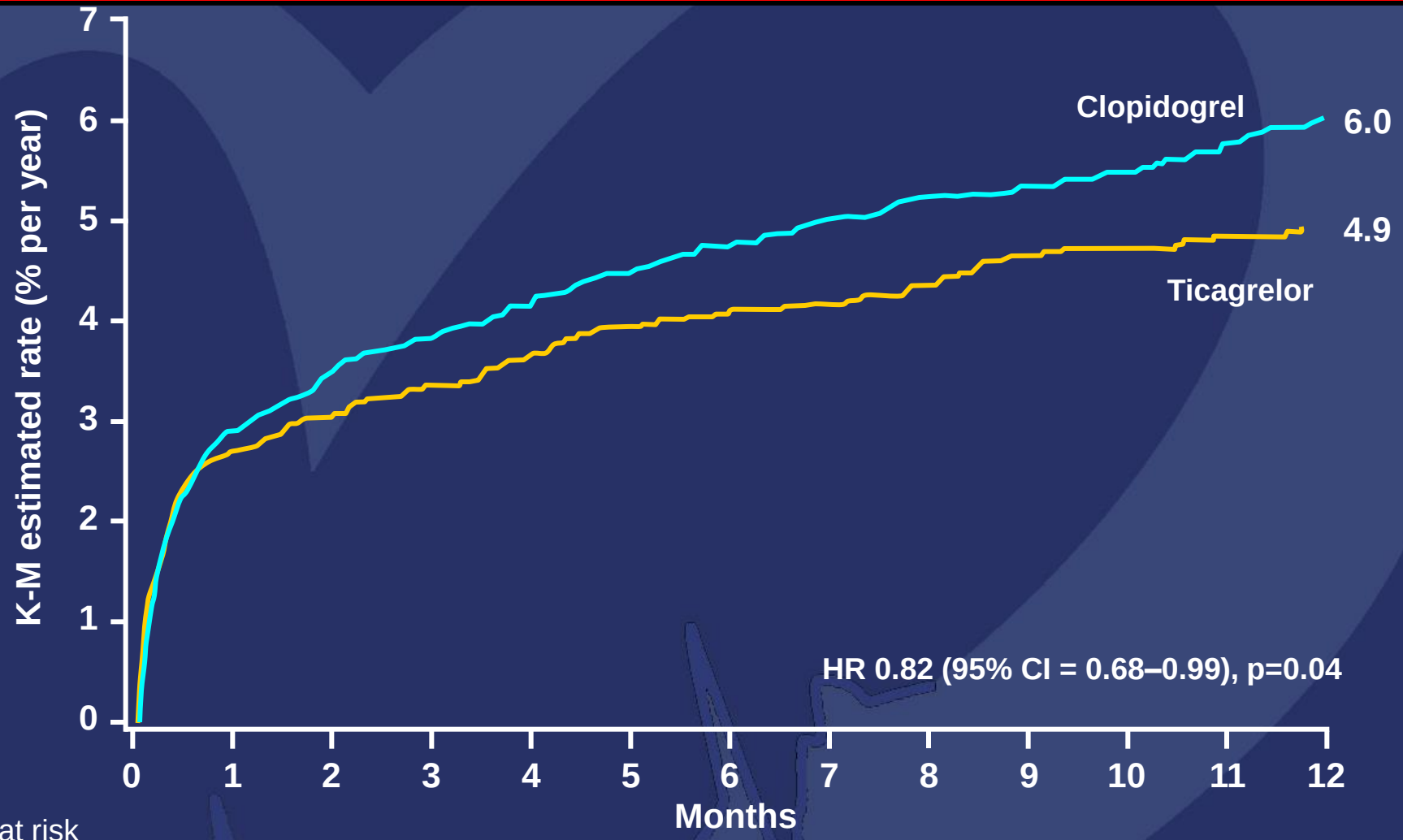
Primary endpoint: CV death, MI or stroke



No. at risk							
Ticagrelor	4,201	3,887	3,834	3,732	3,011	2,297	1,891
Clopidogrel	4,229	3,892	3,823	3,730	3,022	2,333	1,868

Steg G et al, Circulation 2010

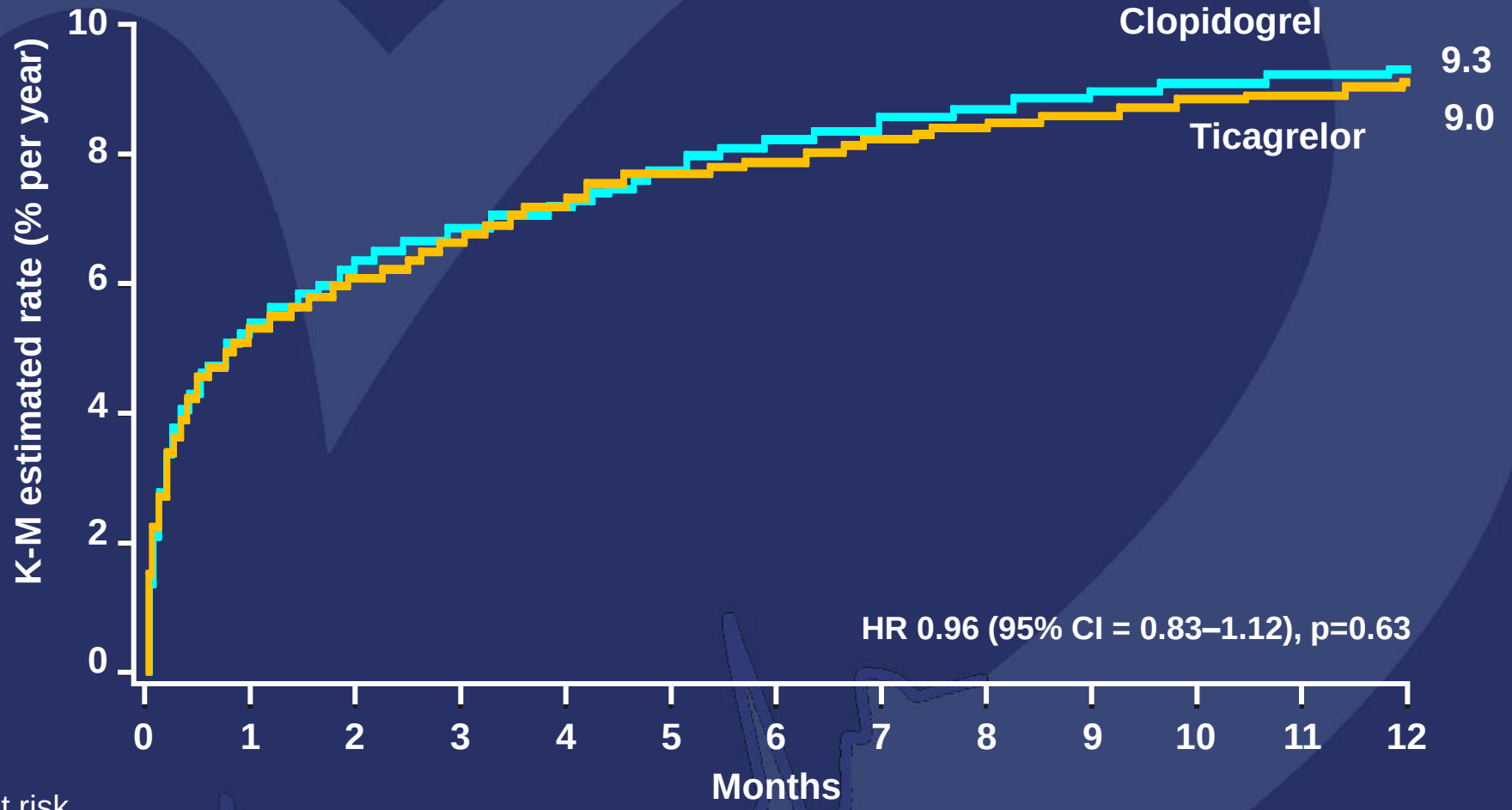
PLATO STEMI - All cause mortality



No. at risk

Ticagrelor	4,201	4,005	3,962	3,876	3,150	2,413	1,993
Clopidogrel	4,229	4,029	3,989	3,912	3,195	2,471	1,980

PLATO STEMI - Primary safety event: major bleeding



No. at risk							
Ticagrelor	4,165	3,431	3,254	3,137	2,440	1,786	1,640
Clopidogrel	4,181	3,430	3,297	3,159	2,441	1,804	1,635

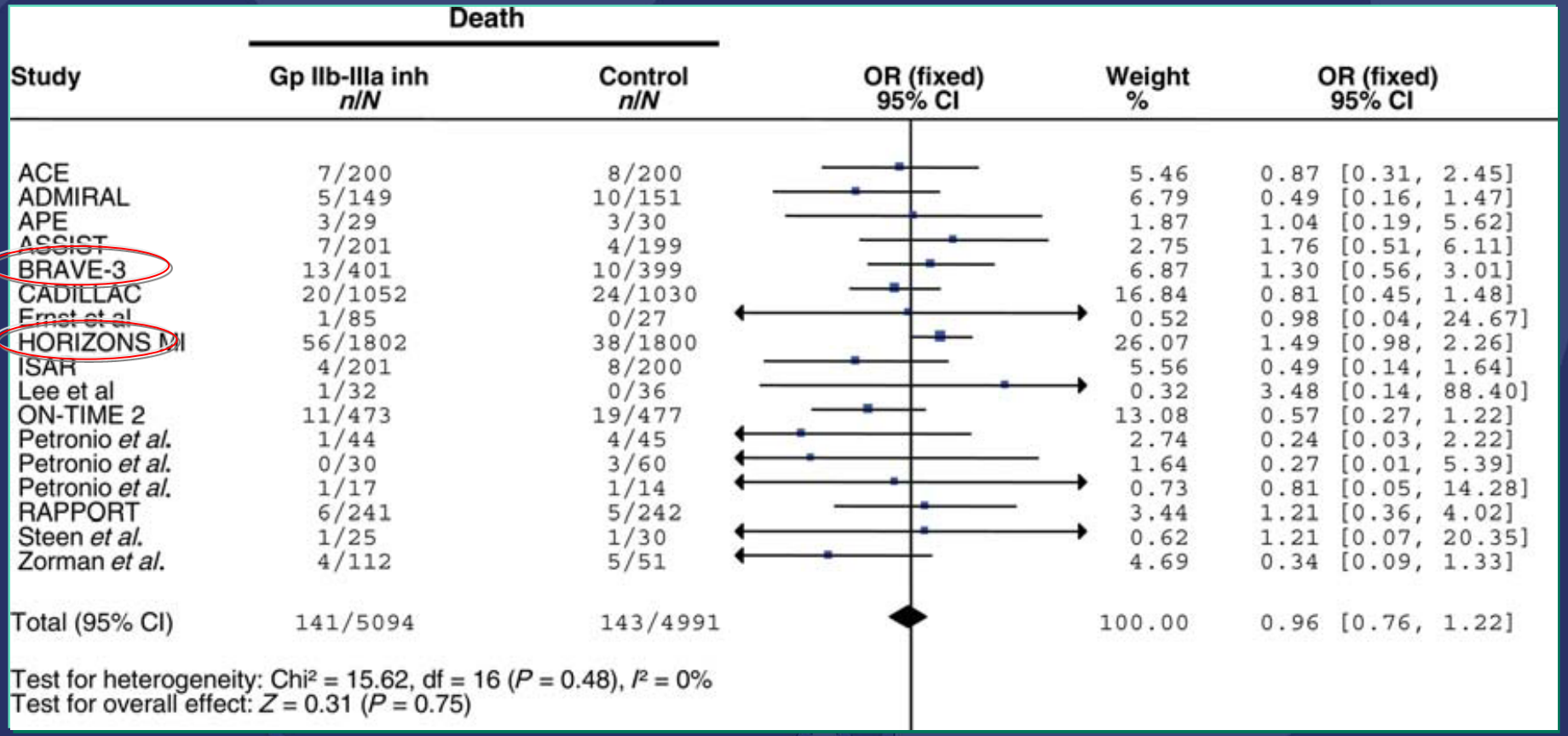
Steg G et al, Circulation 2010

ESC STEMI Guidelines 2012

Antiplatelet therapy		
Aspirin oral or i.v. (if unable to swallow) is recommended	I	B
An ADP-receptor blocker is recommended in addition to aspirin. Options are:	I	A
• Prasugrel in clopidogrel-naive patients, if no history of prior stroke/TIA, age <75 years.	I	B
• Ticagrelor.	I	B
• Clopidogrel, preferably when prasugrel or ticagrelor are either not available or contraindicated.	I	C
GP IIb/IIIa inhibitors should be considered for bailout therapy if there is angiographic evidence of massive thrombus, slow or no-reflow or a thrombotic complication.	IIa	C
Routine use of a GP IIb/IIIa inhibitor as an adjunct to primary PCI performed with unfractionated heparin may be considered in patients without contraindications.	IIb	B

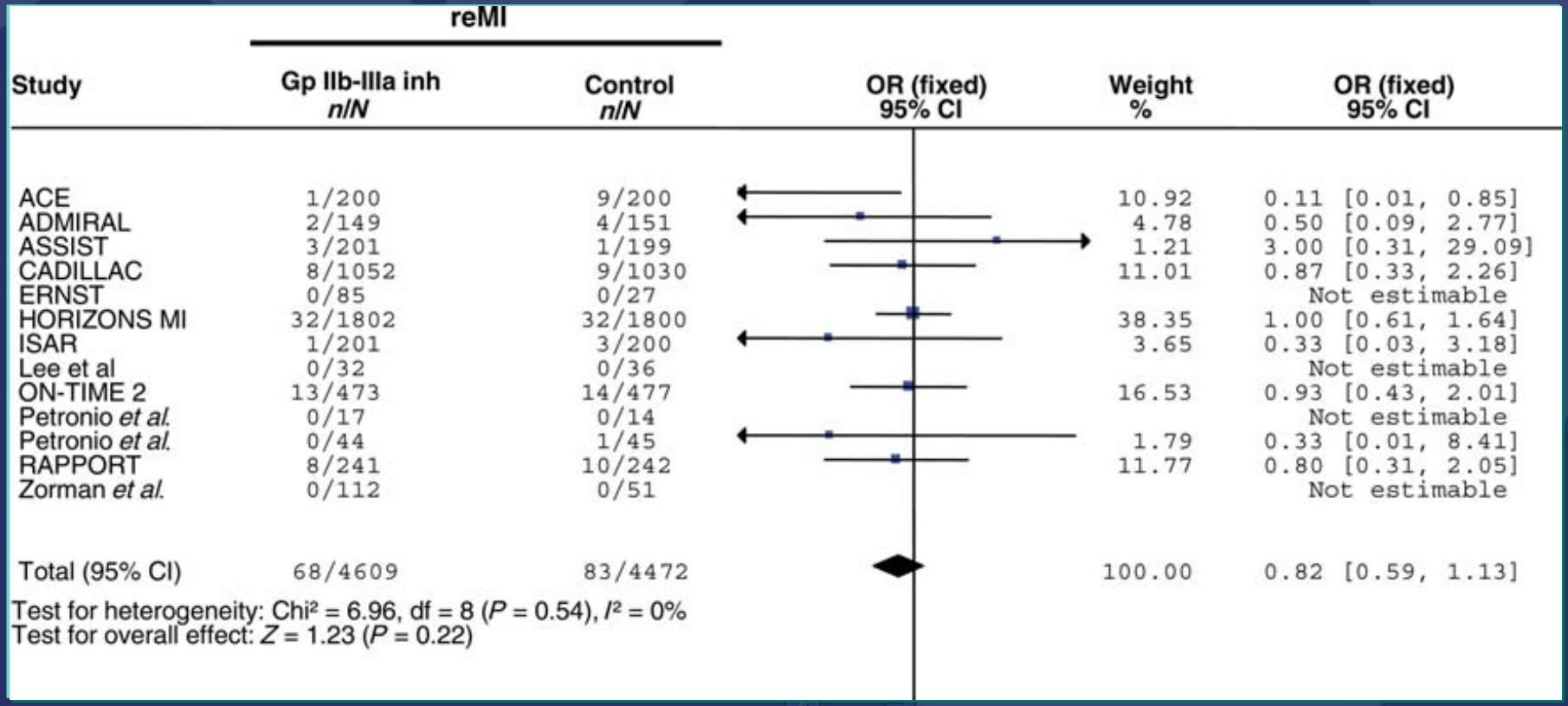
Is there still a role for GP IIb/IIIa inhibitors in the era of the new platelet ADP receptor inhibitors ?

Updated meta-analysis of effect of GPIs on 30 day mortality in pts with STEMI



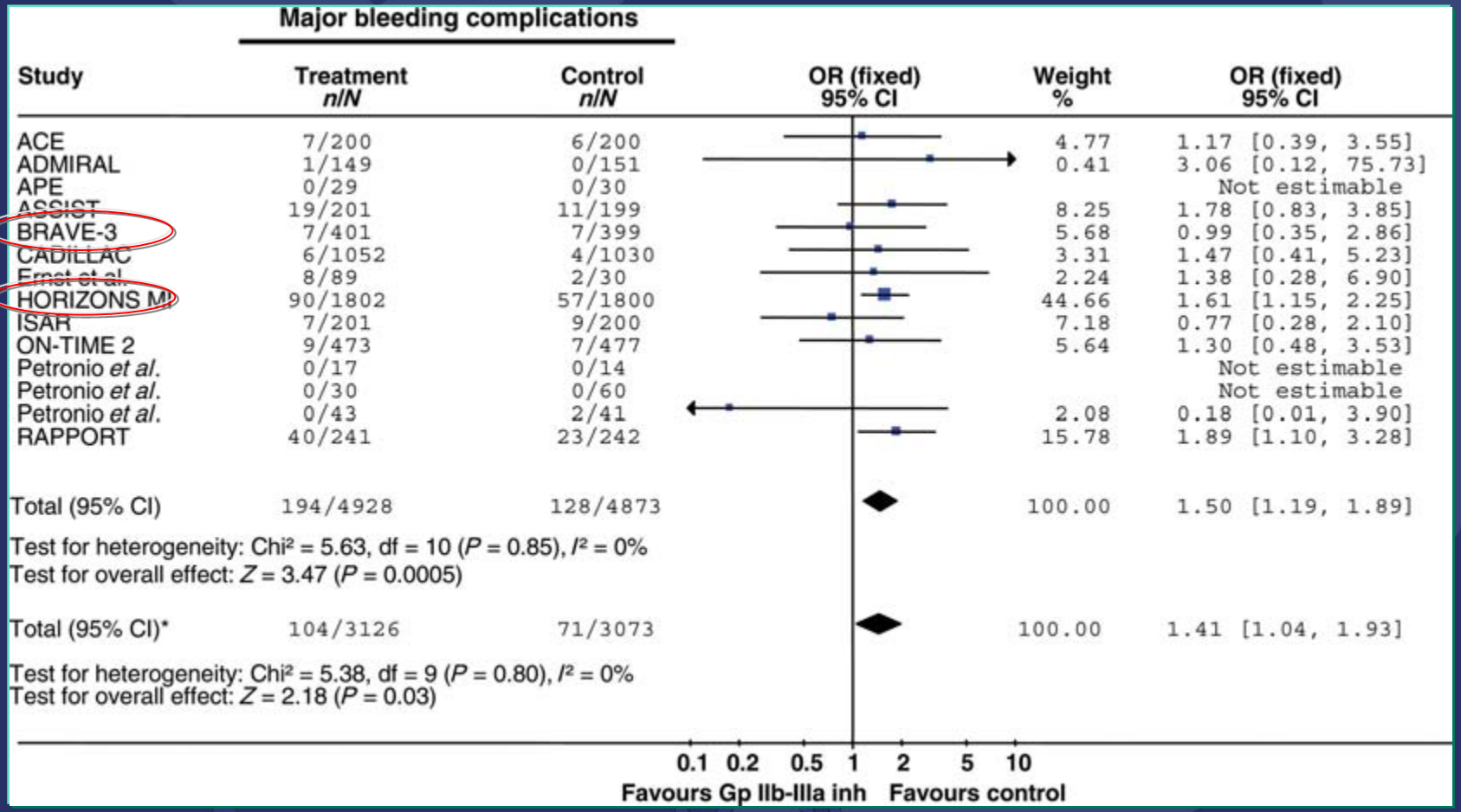
De Luca et al, EHJ 2009

Updated meta-analysis of effect of GP IIb/IIIa inhibitors on 30 day re-MI



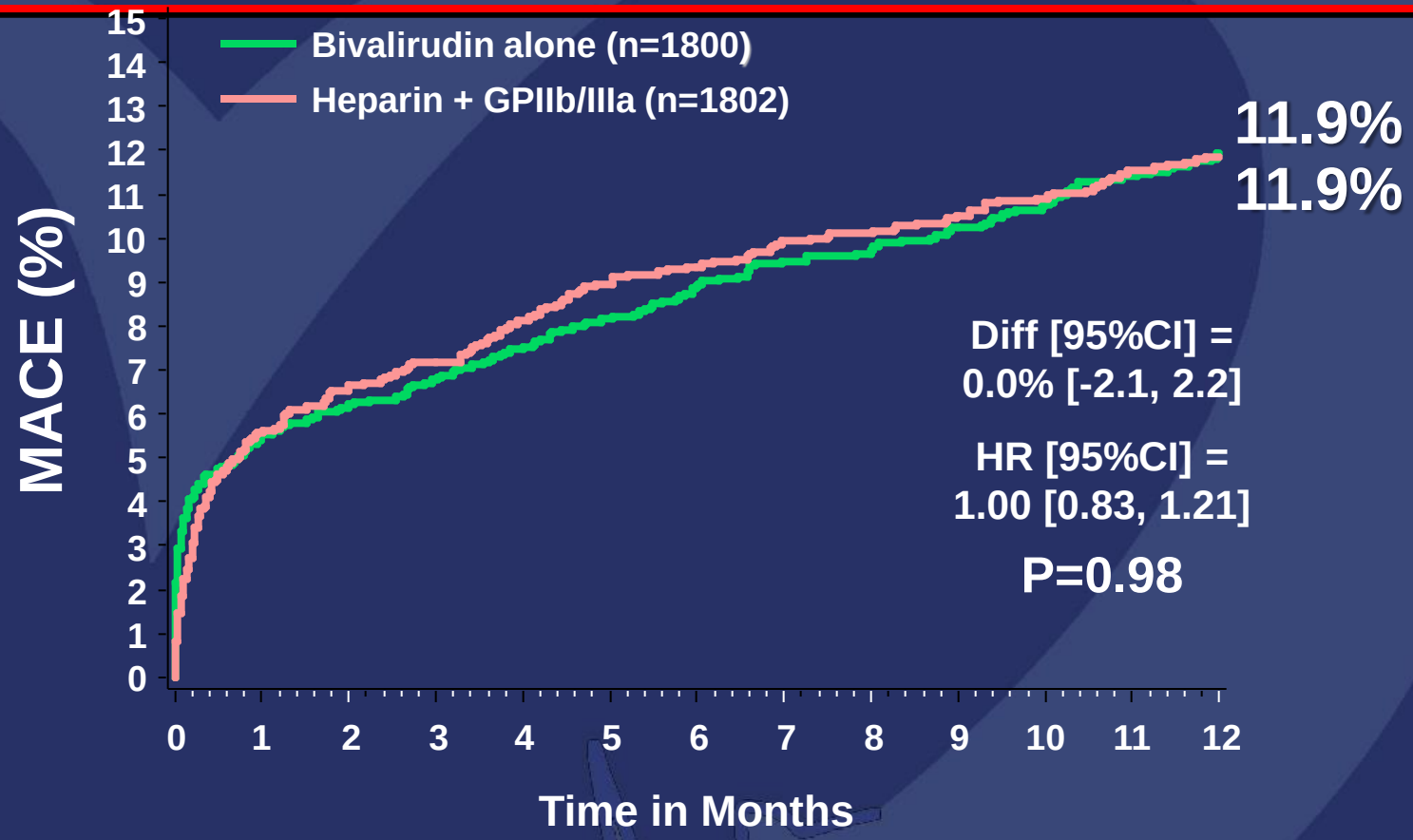
De Luca et al, EHJ 2009

Updated meta-analysis of effect of GP IIb/IIIa inhibitors on major bleeding



De Luca rt al, EHJ 2009

HORIZONS AMI - 1-Year Major Adverse CV Events
3602 patients with STEMI

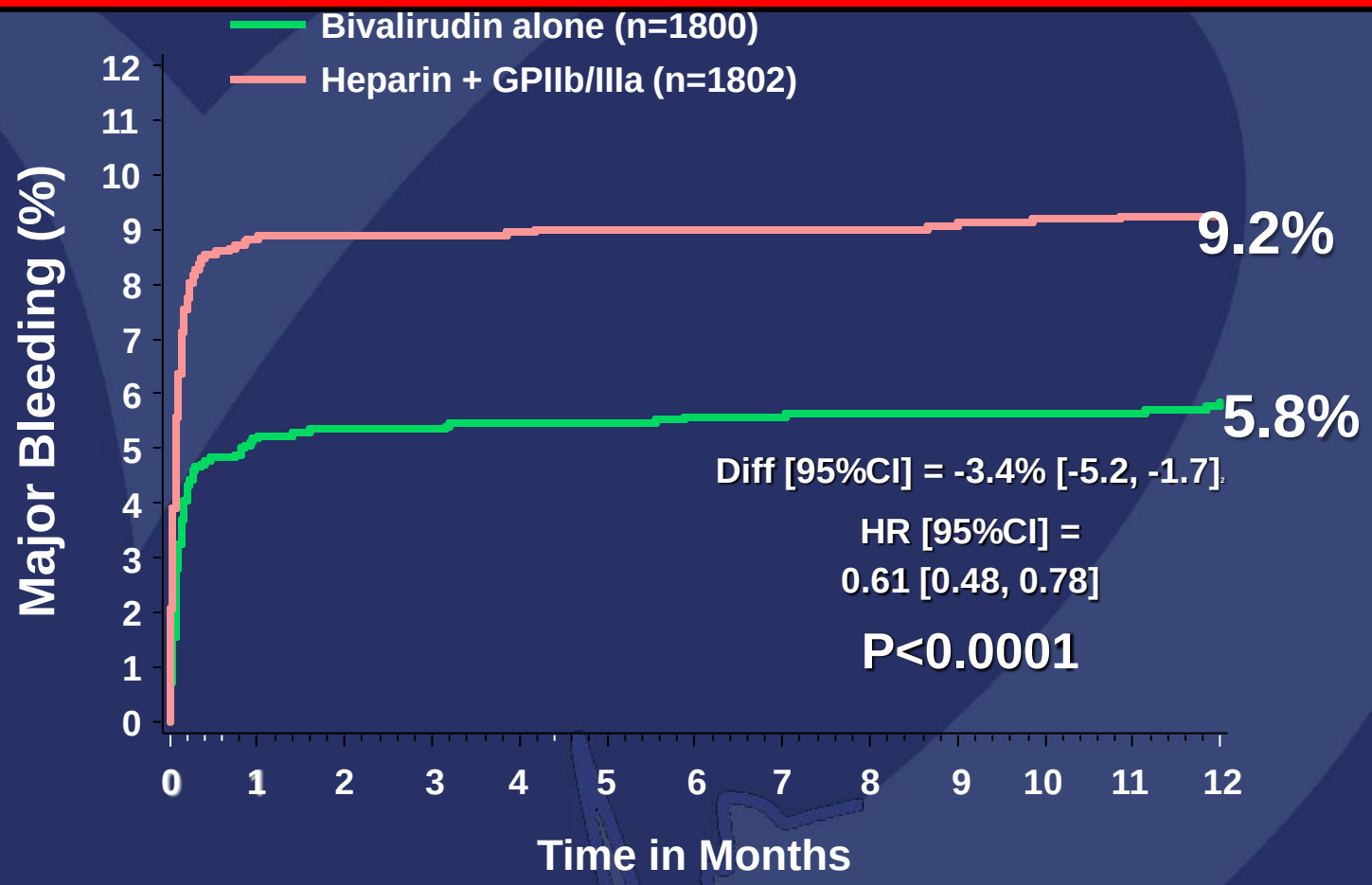


Number at risk					
Bivalirudin alone	1800	1627	1579	1544	1394
Heparin+GPIIb/IIIa	1802	1619	1573	1540	1380

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

Stone G et al, NEJM 2008, Lancet 2009

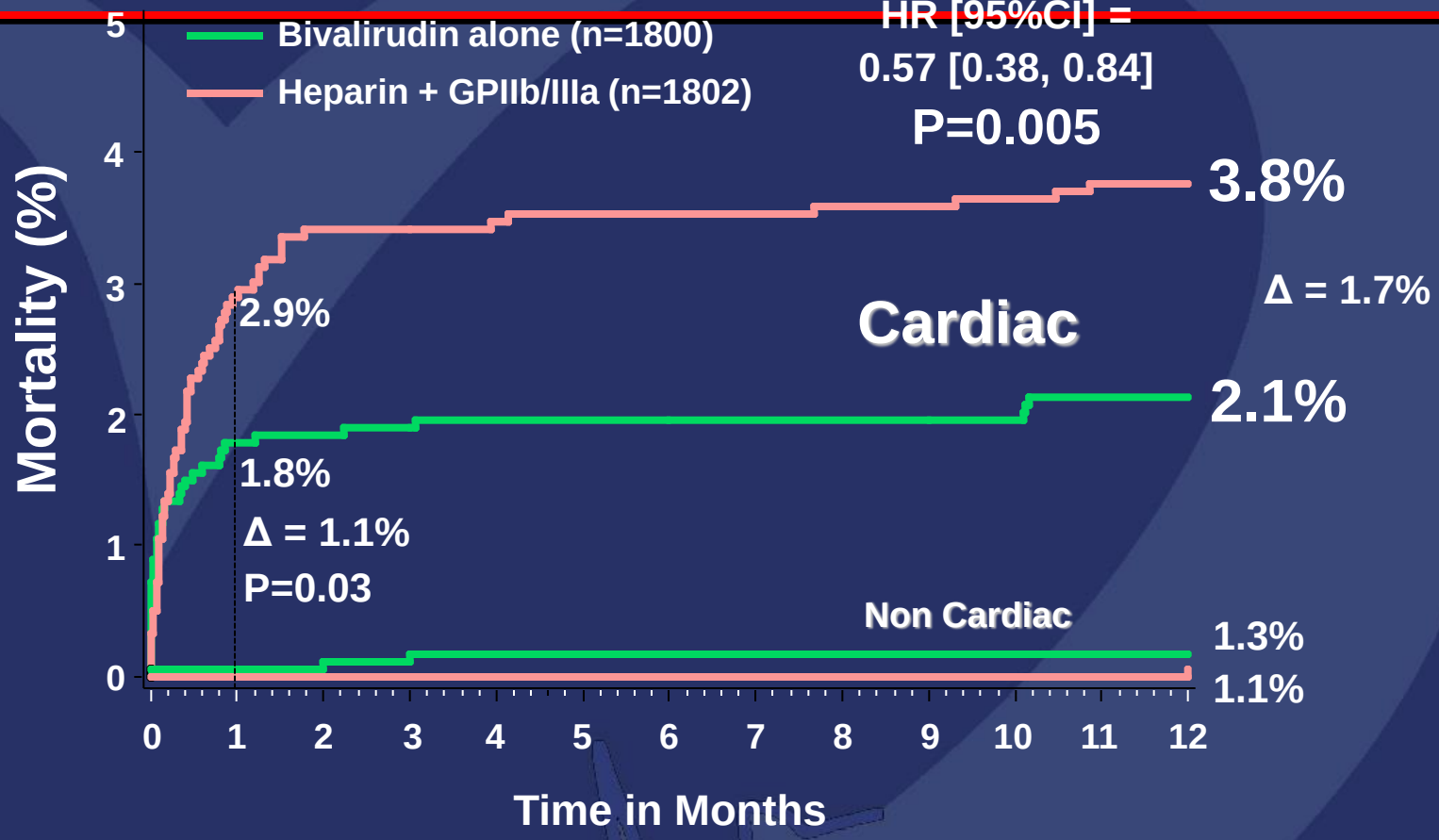
HORIZONS - 1-Year Major Bleeding (non-CABG)



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

Stone G et al, NEJM 2008, Lancet 2009

HORIZONS AMI 1-Year Mortality



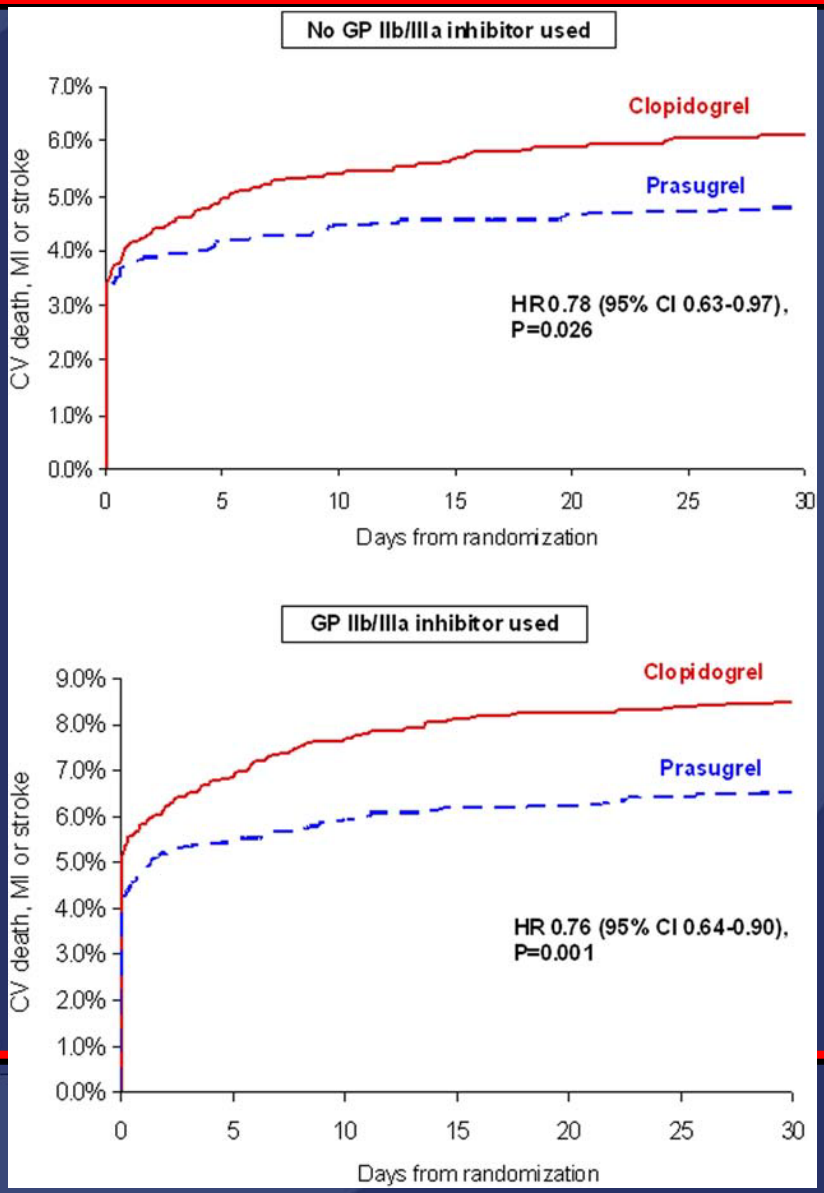
Number at risk

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

Stone G et al, NEJM 2008, Lancet 2009

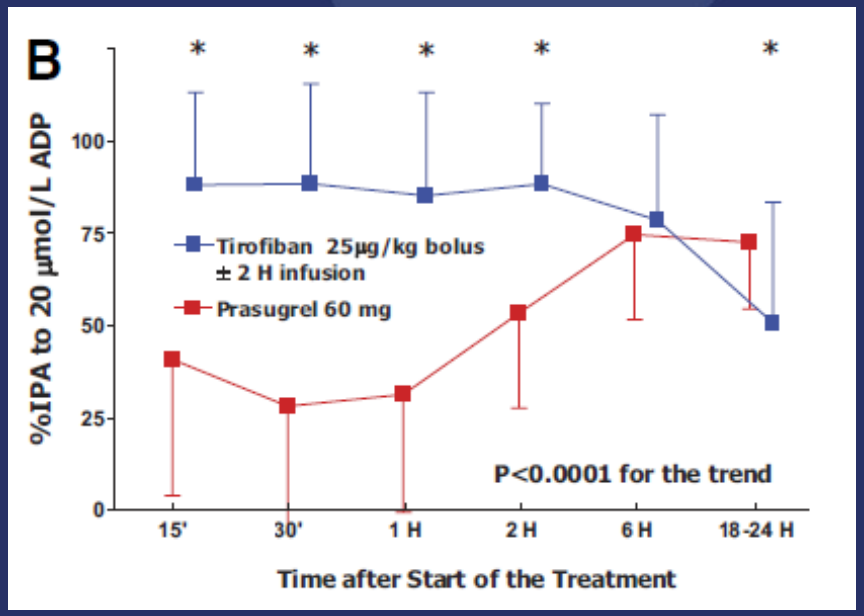
GPIIb/IIIa's and prasugrel in the TRITON

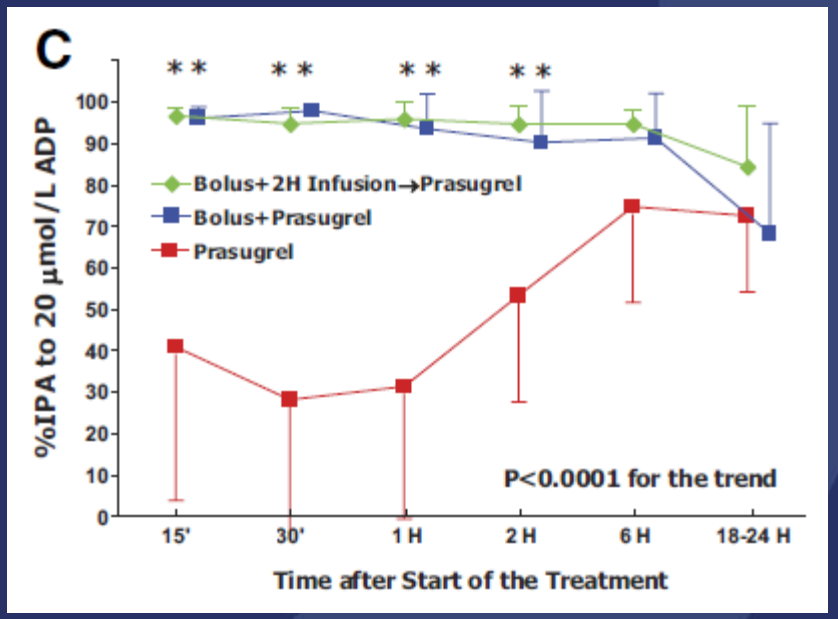
Similar findings for ticagrelor in the PLATO



O'Donoghue, et al, JACC 2009

FABOLUS-PRO study

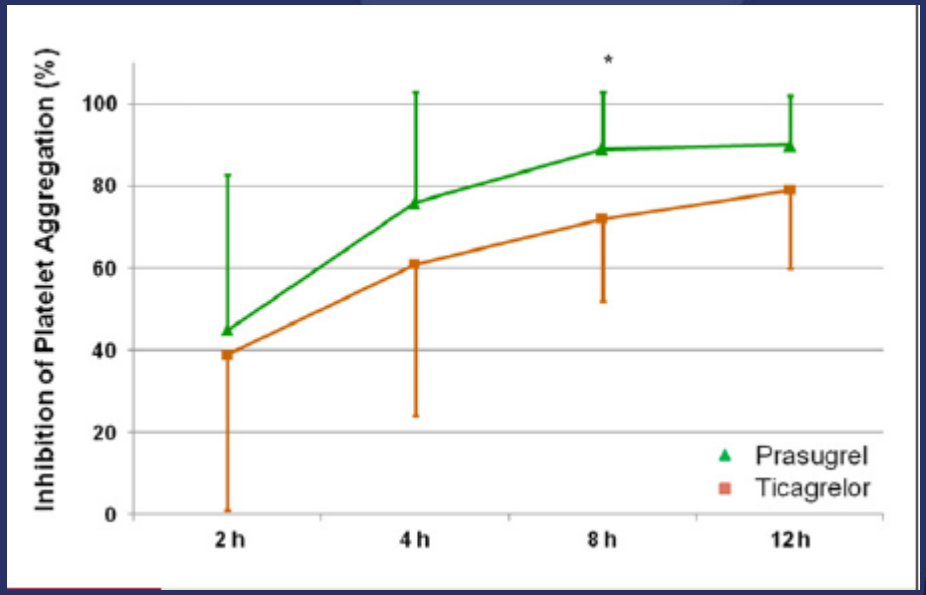


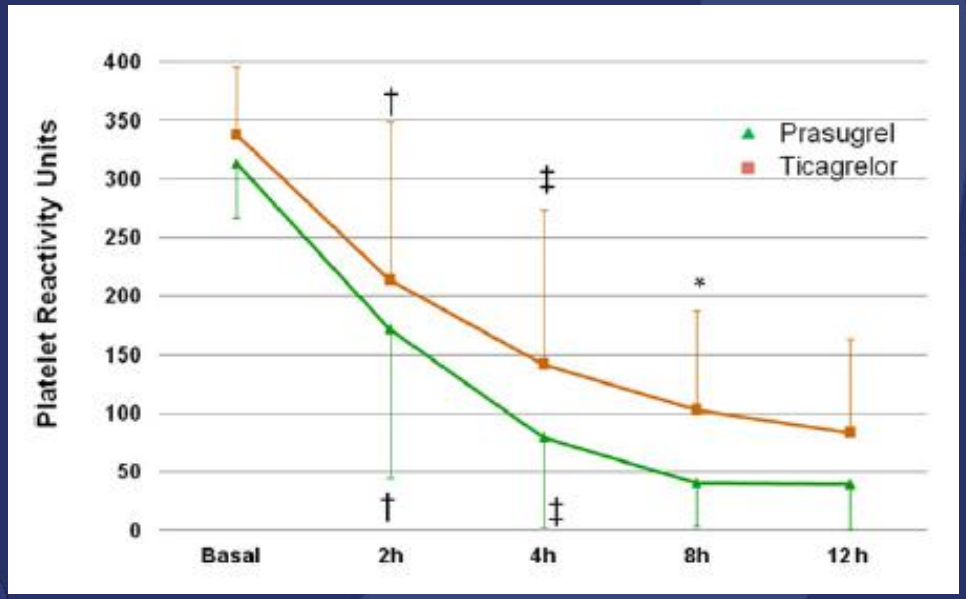


100 pts with STEMI randomized to prasugrel or tirofiban bolus ± maint. or ± prasugrel

Valgimigli et al, JACC Interv 2012

RAPID Study





50 paients with STEMI undergoing primary PCI

Parodi et al, JACC 2013

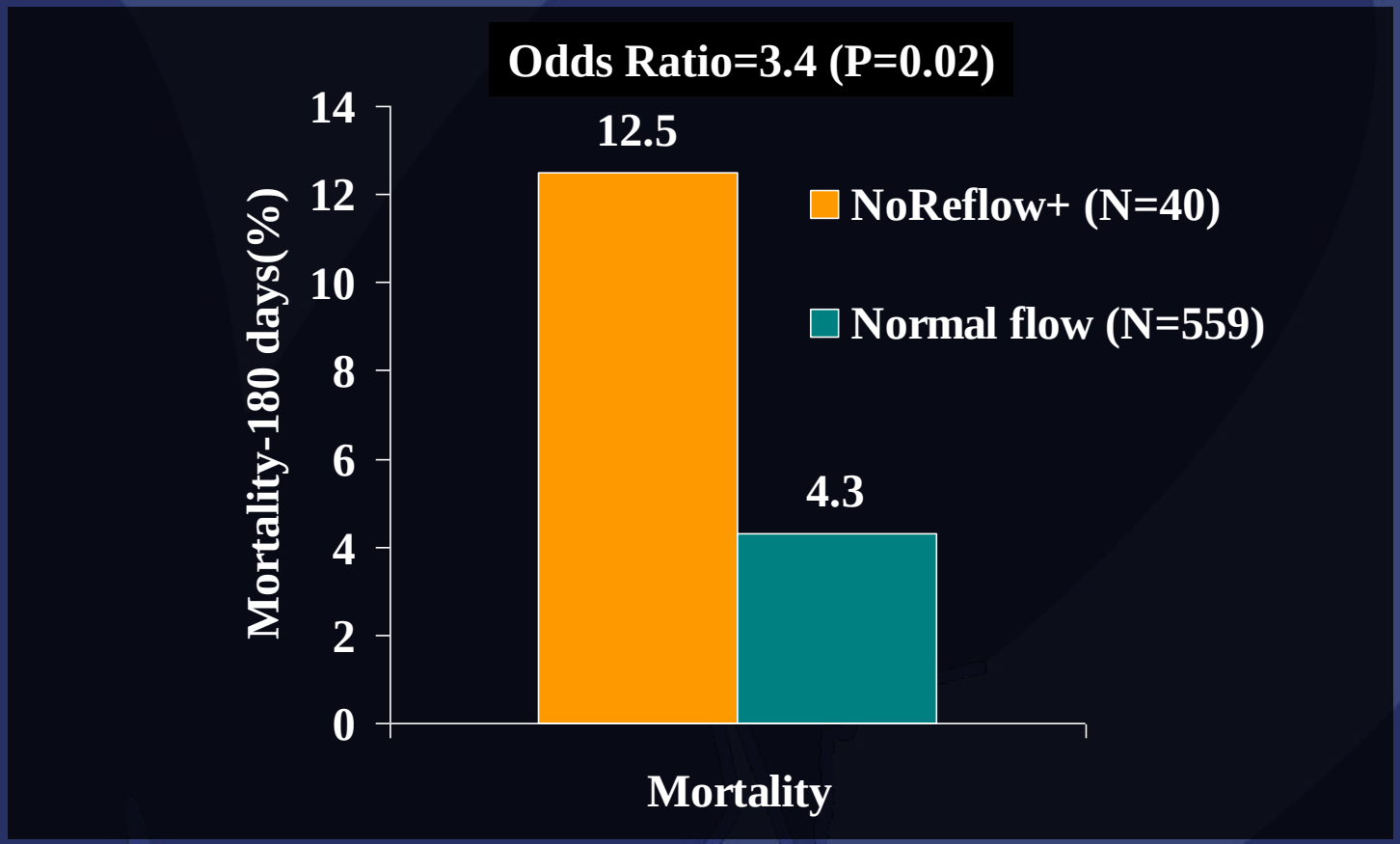
Summary

- Optimizing myocardial perfusion during STEMI is challenging.
- Manual thrombus aspiration appears promising especially from initial studies (TAPAS), but recent studies (INFUSE-MI) and registries failed to duplicate the favorable effect
- Embolic protection devices are of doubtful benefit for STEMI PCI
- Stents such as the MGuard stent may be beneficial in this setting but need to be tested in further clinically powered trials.
- Pharmacotherapy: the new anti-platelet agents clearly have an advantage of clopidogrel in the setting of STEMI primary PCI, should be given ASAP
- GP IIb/IIIa inhibitors should mainly be given in “bailout” situations, but early administrartion as “bridge” should be studied

Thank you !

Effect of 'No Reflow' on STEMI Outcome

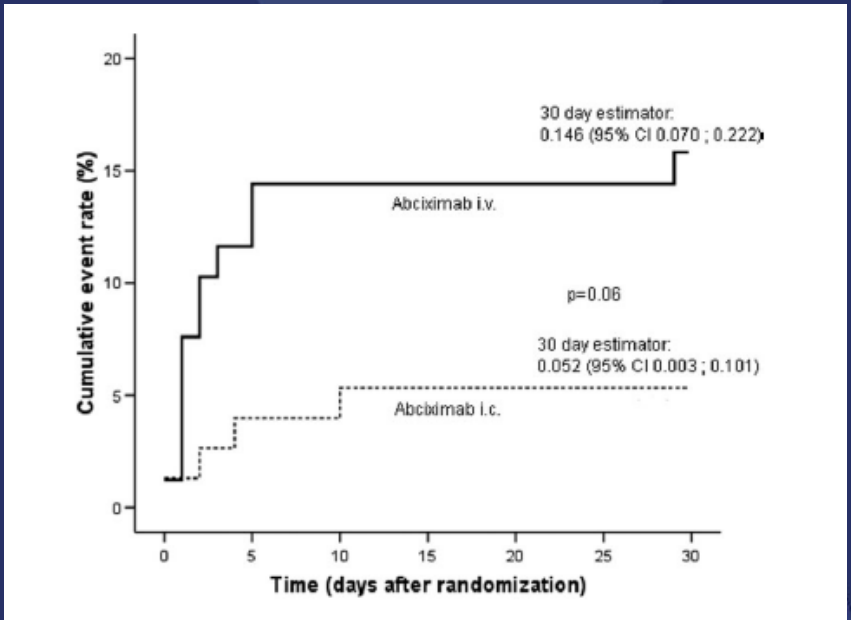
'No Reflow' was associated with ↑ severe LV dysfunction



Brosh D. et al Am J Cardiol 2007

IC GP IIb/IIIa Inhibitors During STEMI

IC vs. IV Abciximab in STEMI

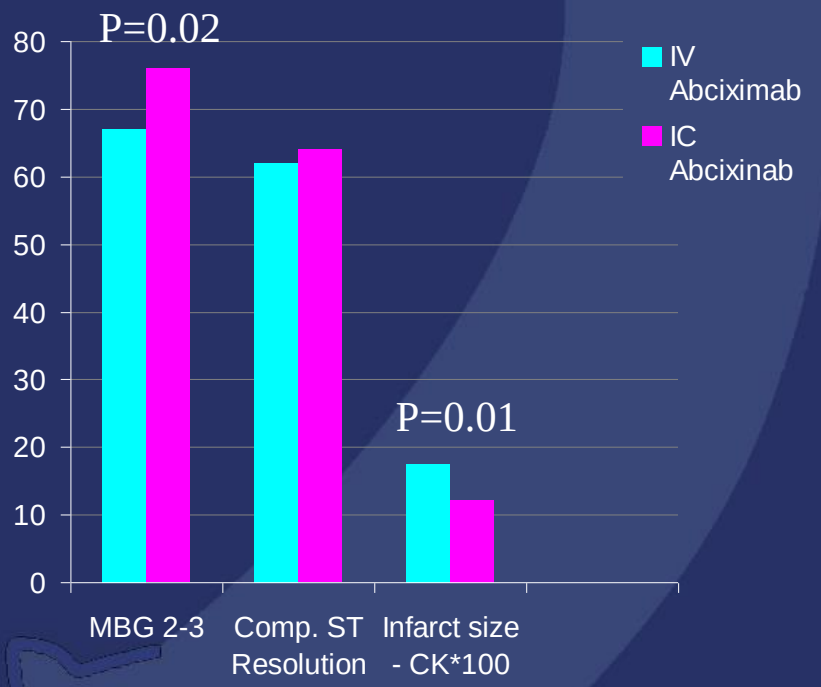


Death, re-infarction, CHF, TVR

Thiele et al, Circulation 2008

CICERO trial

IC vs. IV Abciximab in STEMI

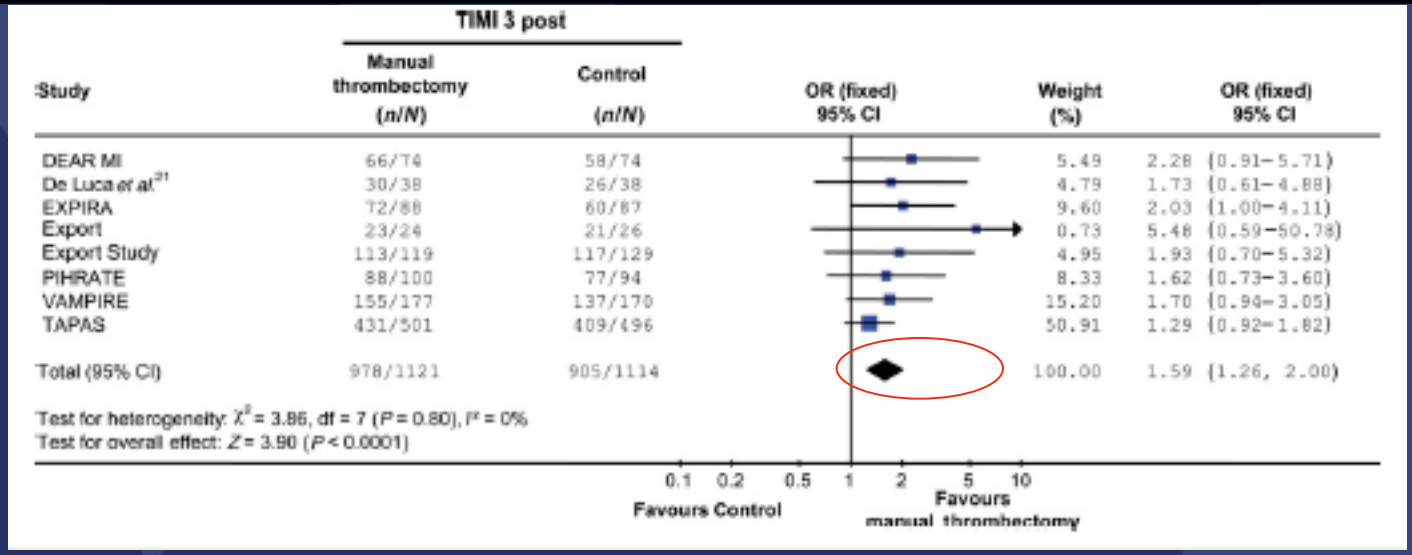


534 STEMI patients,
all underwent thrombus aspiration

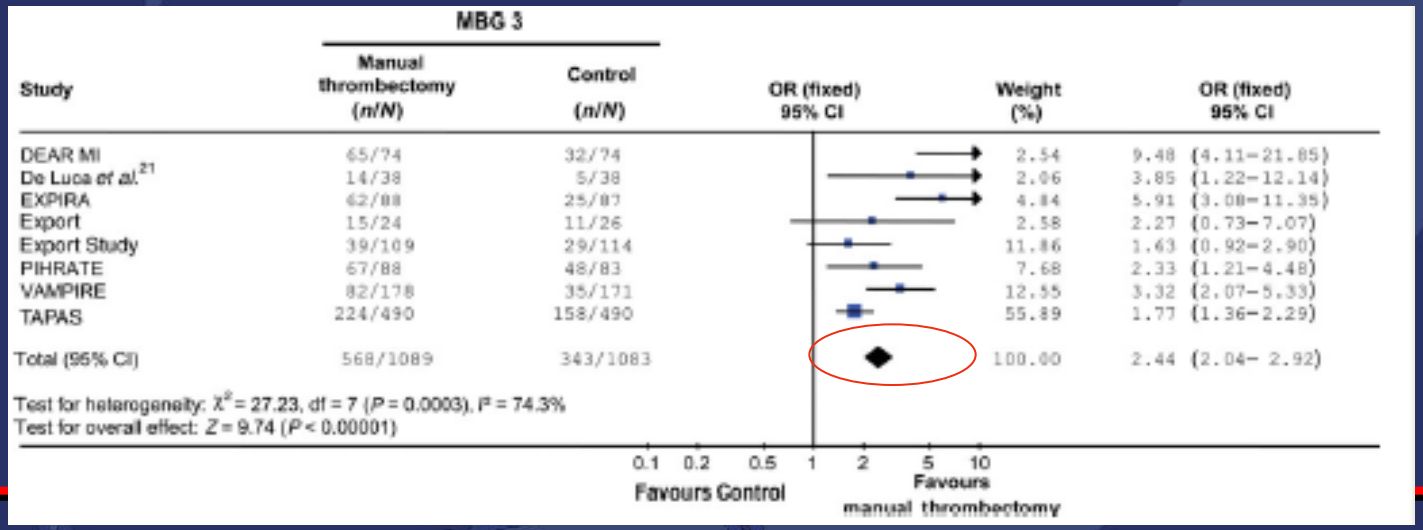
Gu et al, Circulation 2010

Aspiration Updated Meta-analysis

TIMI 3 post



MBG 3



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