

Corso residenziale di aggiornamento a cura della sezione regionale SIFC Campania

SINDROMI CORONARICHE ACUTE, DIABETE ED APPROPRIATEZZA PRESCRITTIVA: ESPERIENZE INTEGRATE

NAPOLI
Palazzo Caracciolo

23
ottobre
2013

Algoritmo decisionale nel trattamento del paziente STEMI

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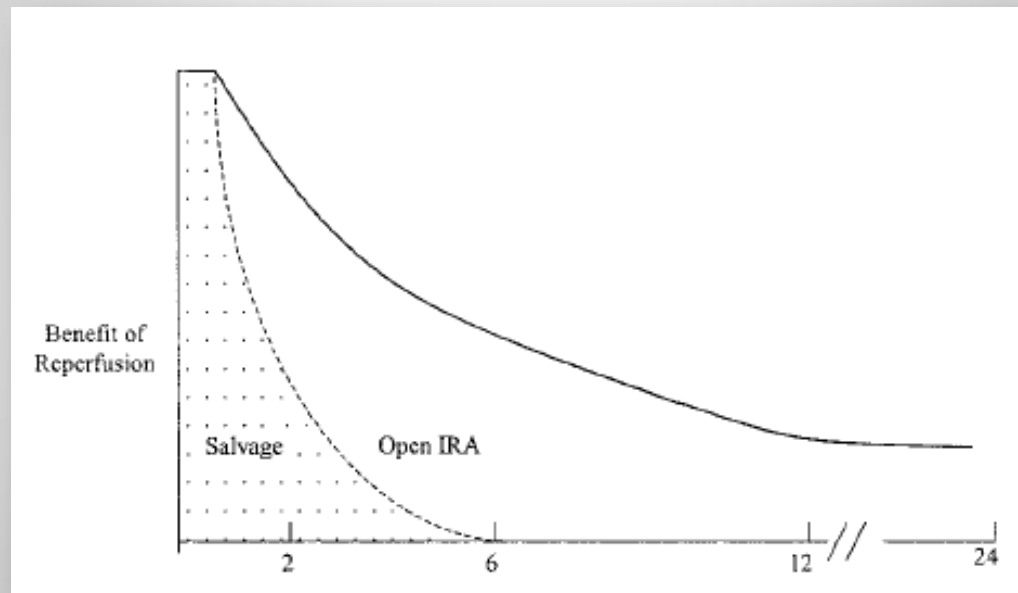


Epidemiology and patterns of care of patients admitted to Italian intensive cardiac care units: the BLITZ-3 registry N (6986)

	Blitz-1 2001	In-ACS Outcome 2006	Blitz-3 2008
PCI Primaria	15%	48%	45%
Trombolisi	50%	28%	15%
2b/3a	18%	42%	39%
ASA	93%	96%	94%
ASA/Clopidogrel	34%	70%	77%

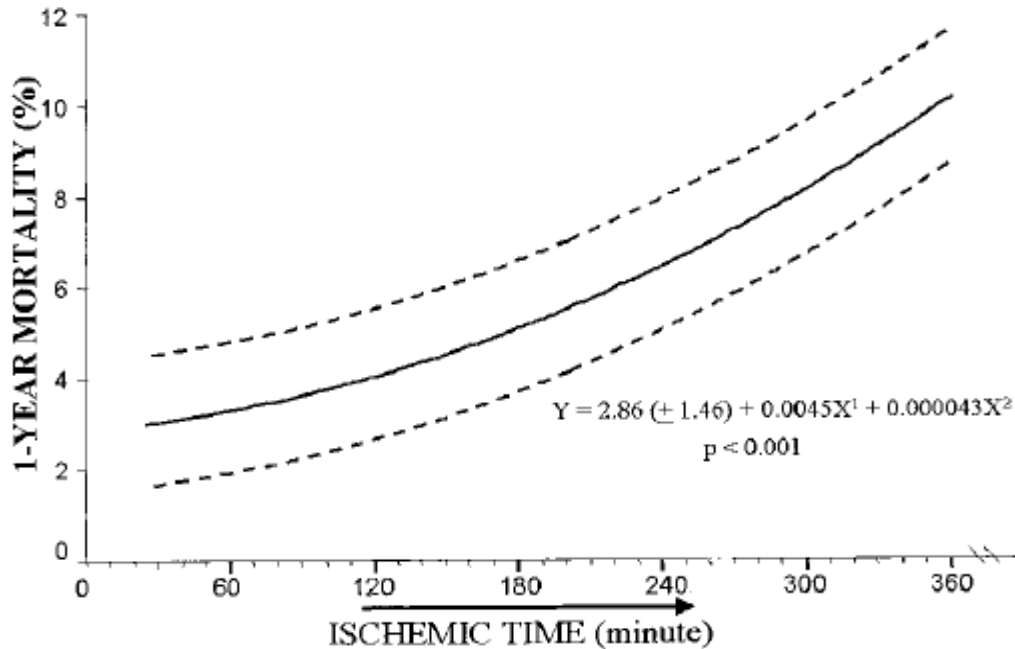
Time is muscle

Primary goal of treatment of acute coronary occlusion:
early, complete, and sustained
myocardial reperfusion



- 0 - 0.5 hrs Prevent infarction
- 0.5 - 2 hrs Substantial salvage + benefit of open IRA
- 2 - 6 hrs Diminishing salvage, benefit of open IRA
- > 6 hrs Little no salvage, benefit of open IRA

Every minute counts...

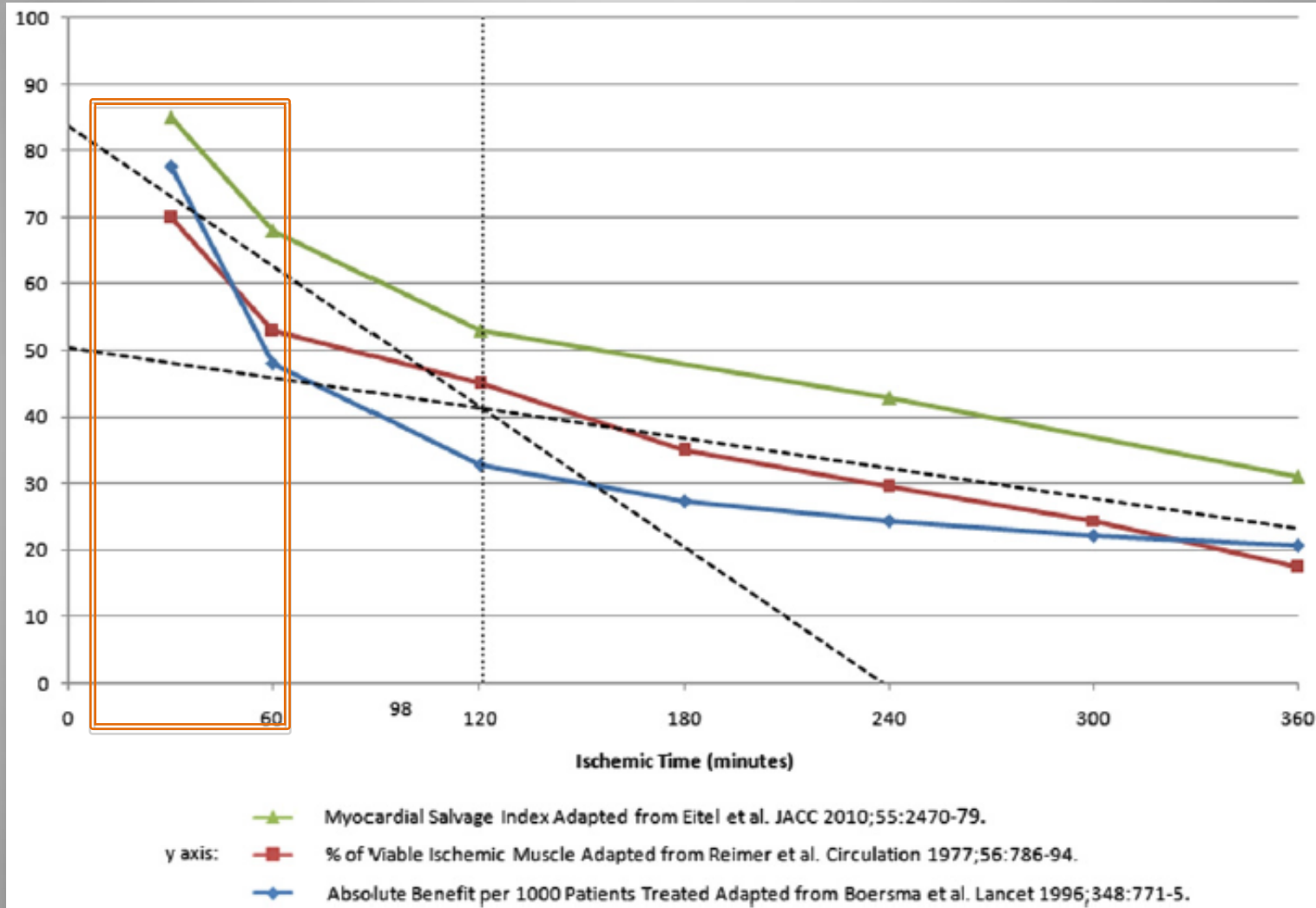


The risk of 1-year mortality is increased by 7.5% for each 30-minute delay!

De Luca G. et al, Circulation 2004;109:1223-1225

Early reperfusion: myocardial salvage and reduction in mortality and morbidity long-term.

Total Ischaemic Time, Infarct Size and Outcome



To treat the culprit lesion **as soon as possible...**

...Which reperfusion strategy?

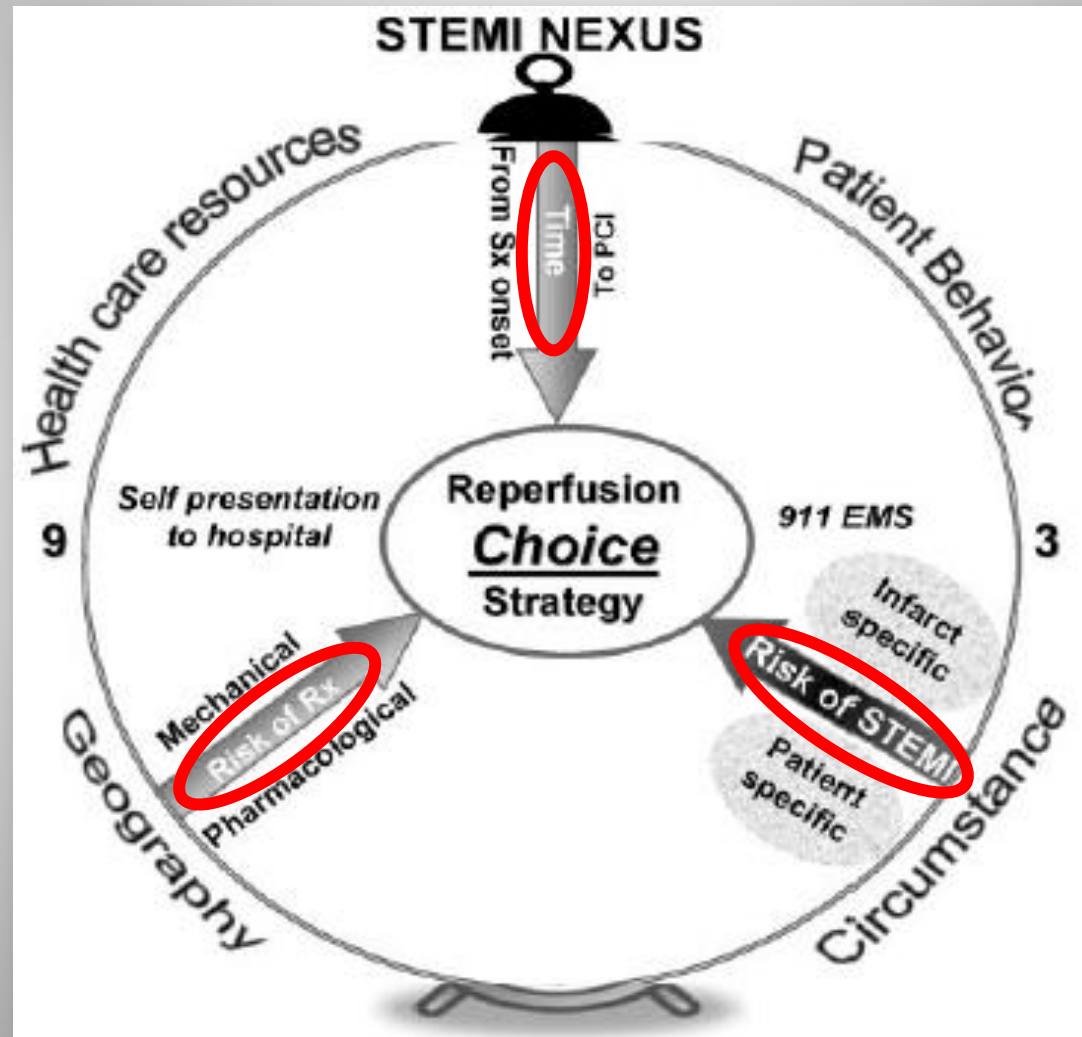
Pharmacological reperfusion-
Thrombolysis

Mechanical reperfusion-
Percutaneous coronary intervention (PCI)

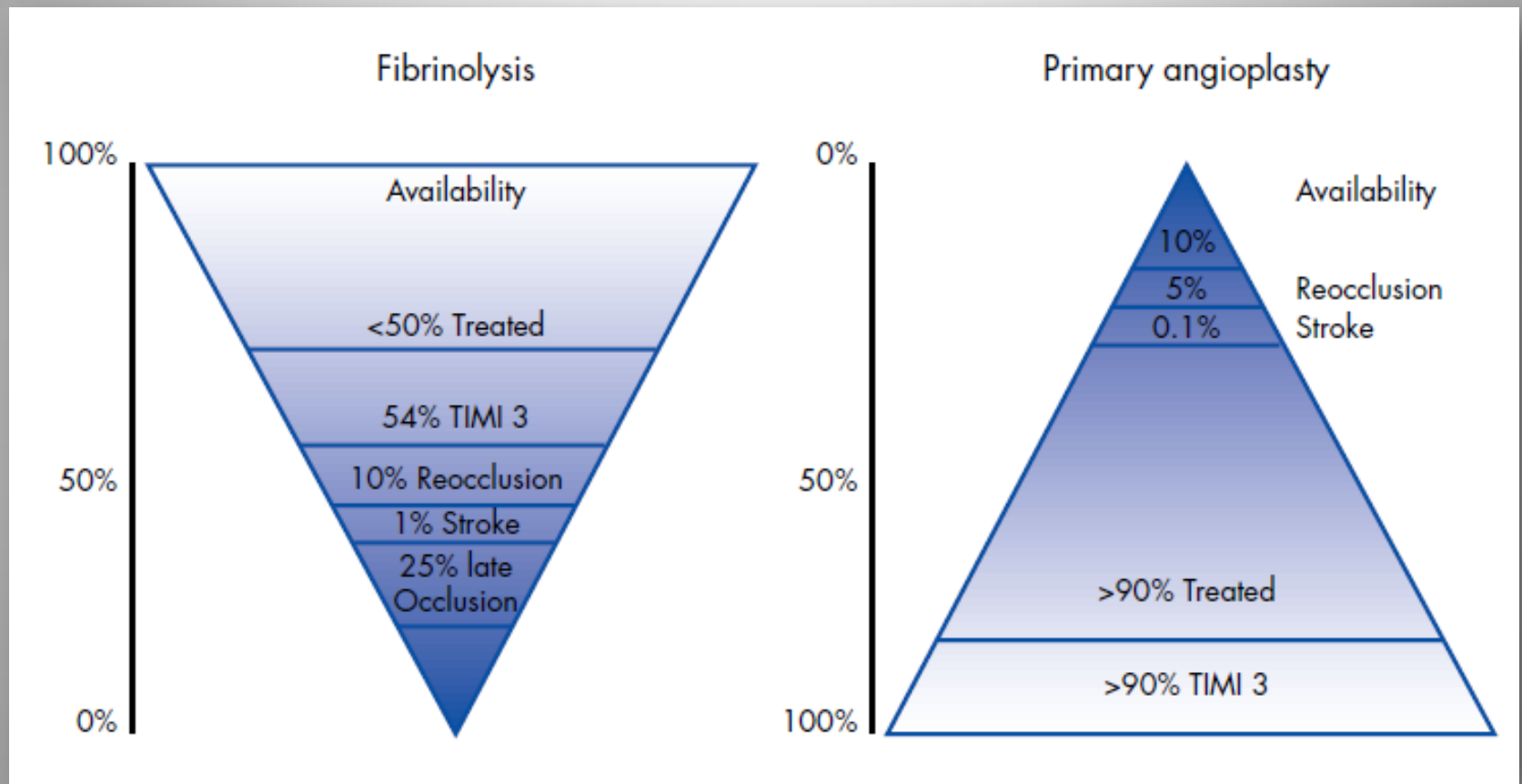
Surgical reperfusion-
Coronary Artery Bypass Graft (CABG)



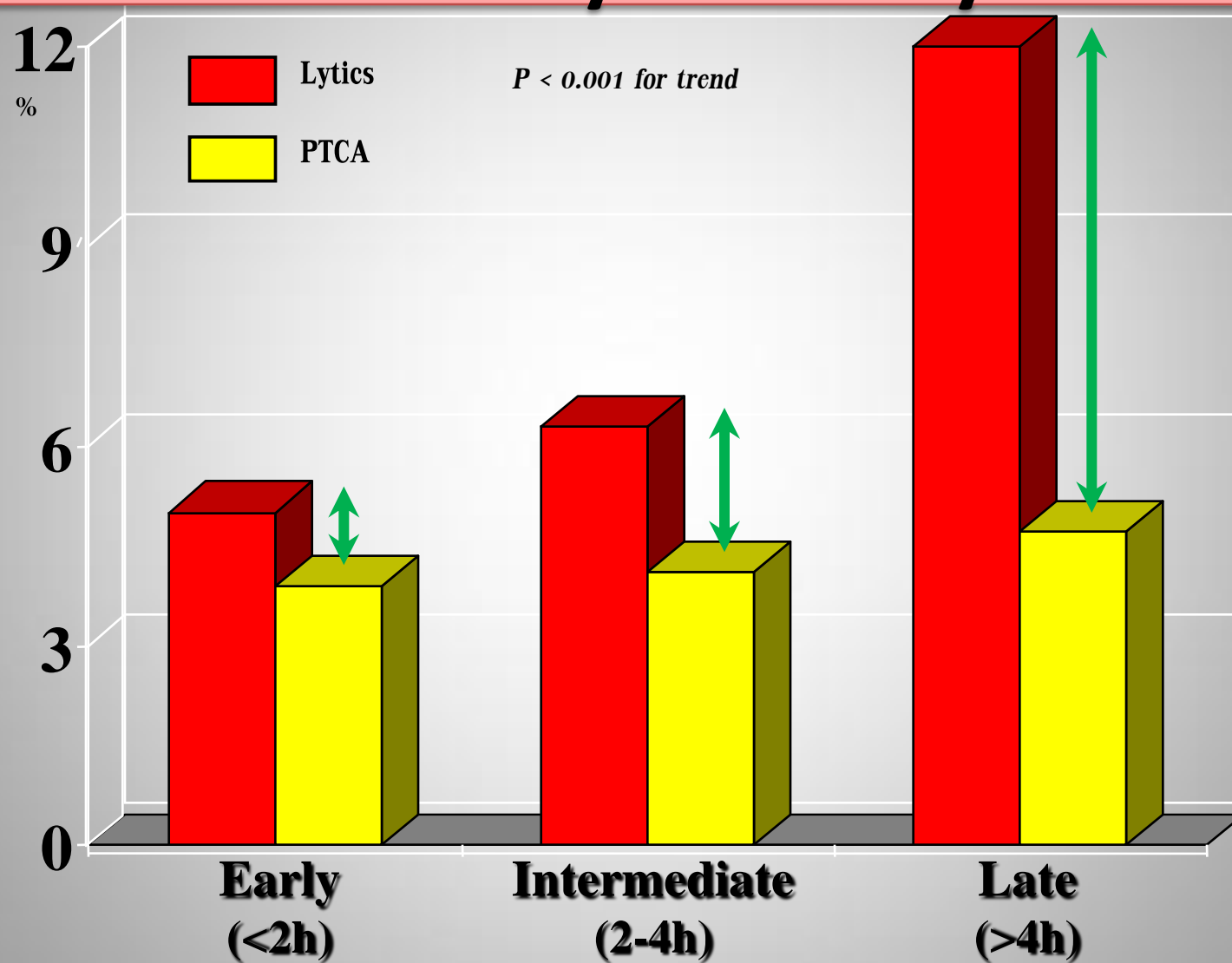
Is duration of symptoms the key modulator of the choice of reperfusion for ST-elevation myocardial infarction?



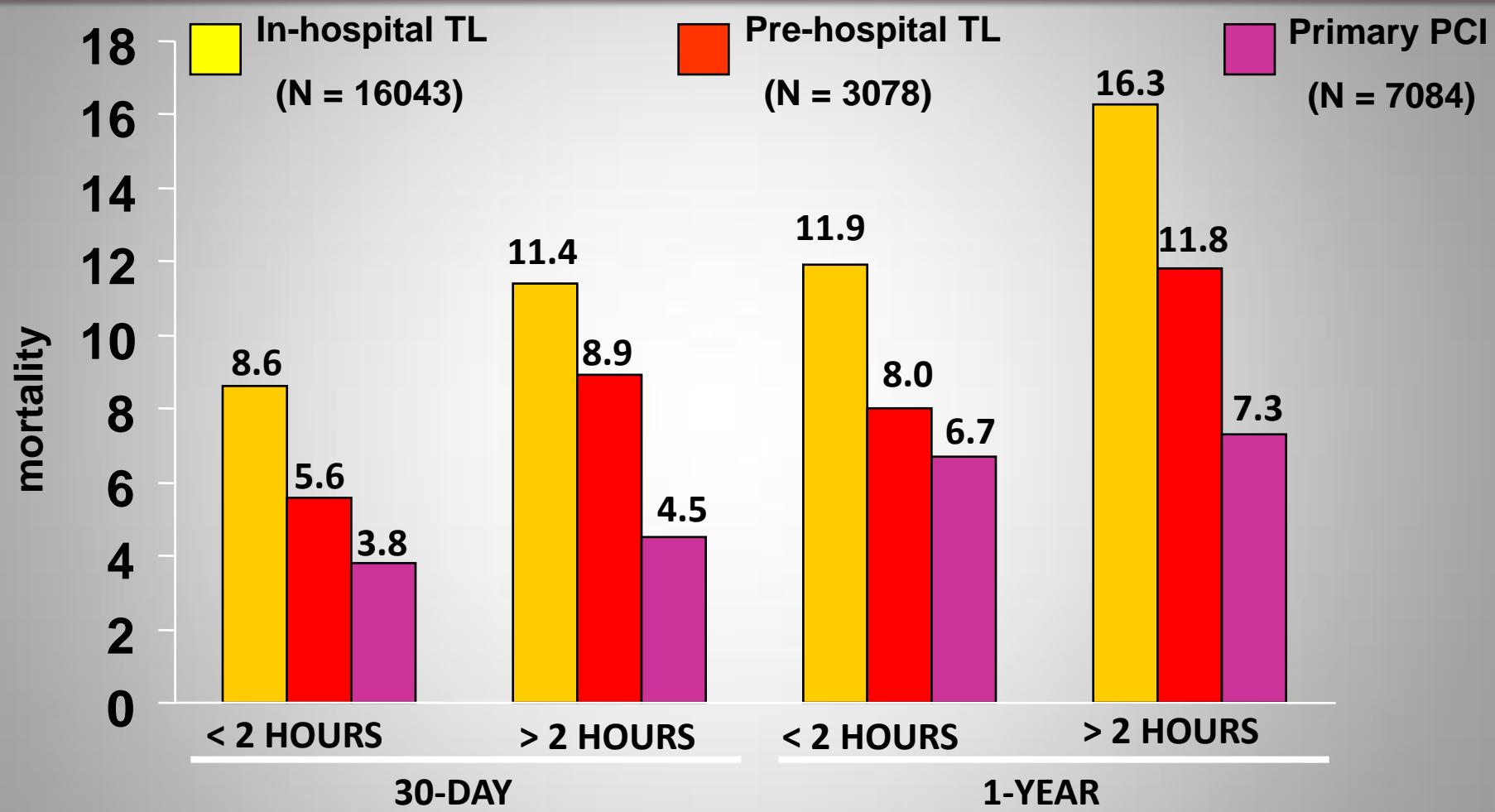
FIBRINOLYSIS vs PCI



Pooled Analysis: Time delay & Mortality at 30 days



Long-term outcome of primary percutaneous coronary intervention vs prehospital and in-hospital thrombolysis for patients with ST-elevation myocardial infarction.

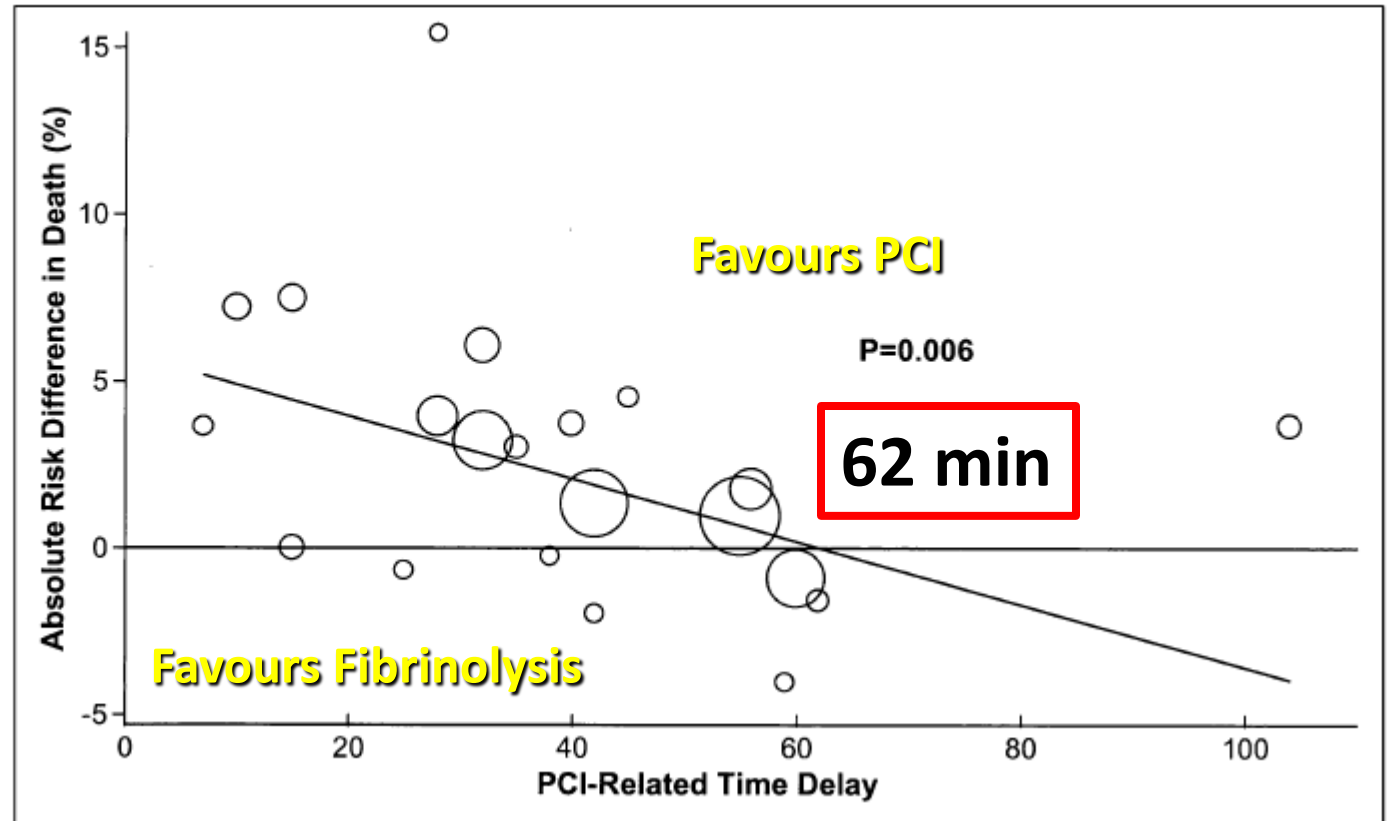


	In-Hospital Thrombolysis (n = 16 043)	Prehospital Thrombolysis (n = 3078)	Primary PCI (n = 7084)
Delay symptom to reperfusion start, median (ICR), h:min			
All	2:47 (1:47-4:37)	2:00 (1:12-3:40)	3:30 (2:15-5:34)
≤2 h	1:30 (1:10-1:45)	1:13 (0:55-1:35)	1:35 (1:15-1:50)
>2 h	3:45 (2:45-5:45)	3:40 (2:40-5:42)	4:14 (2:57-6:15)

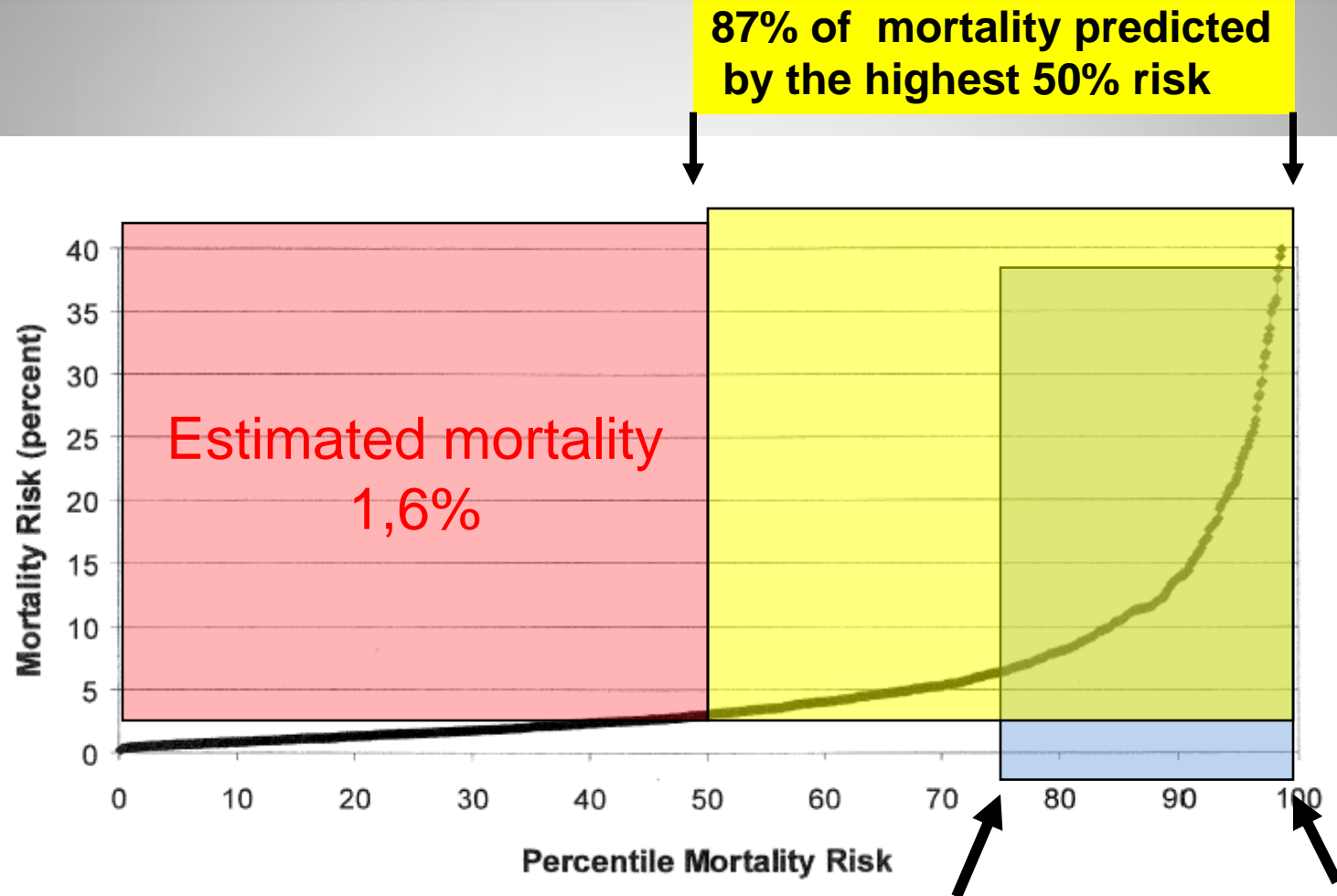
Stenestrand et al. JAMA 2006; 296: 1749-56

IS TIME (ALMOST) EVERYTHING?

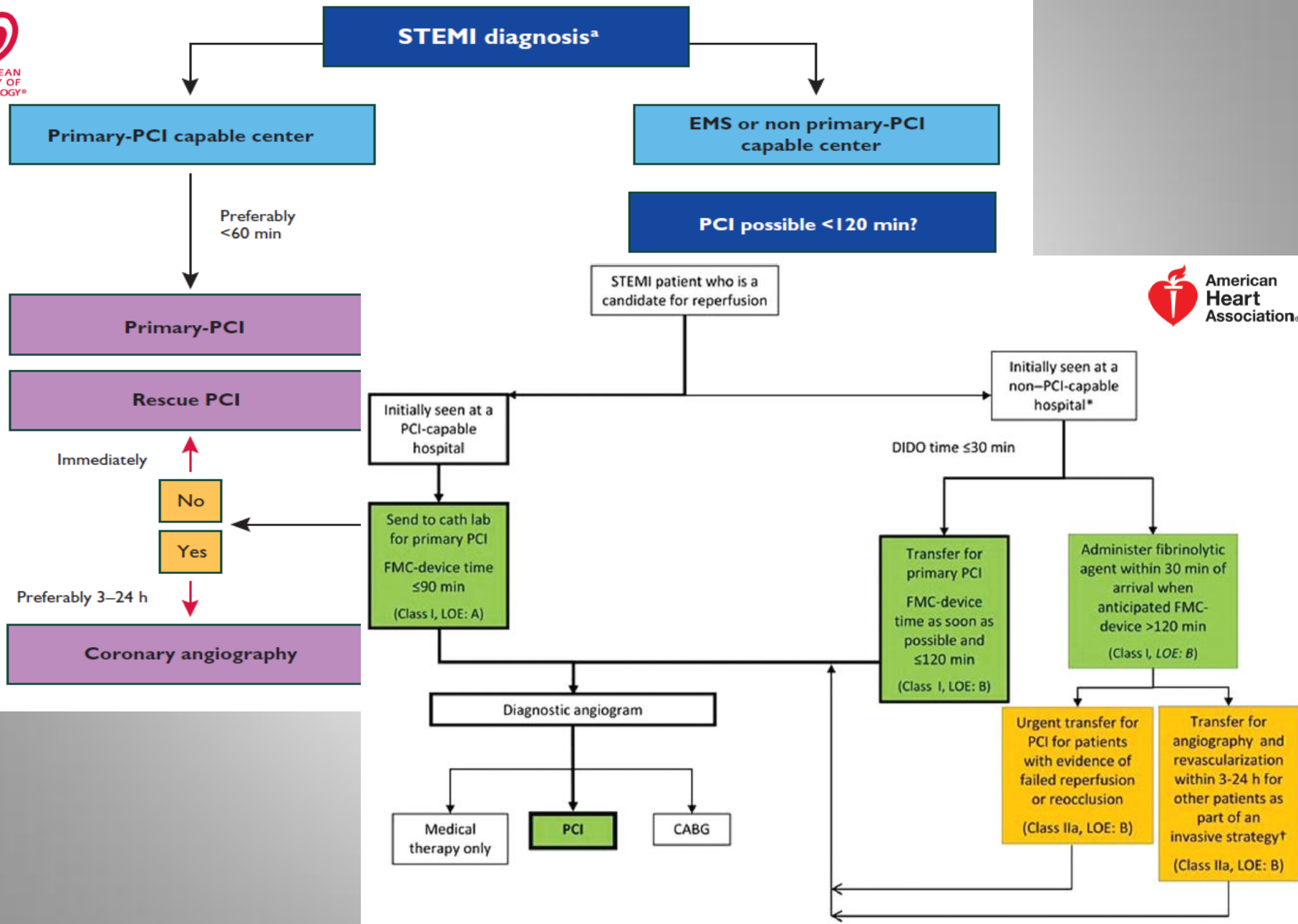
FIGURE 1. Absolute risk reduction in 4- to 6-week mortality rates with primary PCI as a function of PCI-related time delay. Circle sizes reflect the sample size of the individual study. Values >0 represent benefit and values <0 represent harm. Solid line, weighted meta-regression.



Is Primary angioplasty for some as Good as Primary Angioplasty for All?



Guidelines



Maximal PCI-related delay= 120 min

Target for quality assessment= 60- 120 min



- Se i pazienti si presentano a un centro capace di fare PCI primaria

tempo da FMC ≤ **60 minuti**

- Se i pazienti vengono trasferiti a un centro capace di fare PCI primaria

tempo da FMC ≤ **90 minuti**

(≤ 60 minuti se arrivano precocemente soggetti con ampiezza a rischio)



- Se i pazienti si presentano a un centro capace di fare PCI primaria

tempo da FMC ≤ **90 minuti**

- Se i pazienti vengono trasferiti a un centro capace di fare PCI primaria

tempo da FMC ≤ **120 minuti**

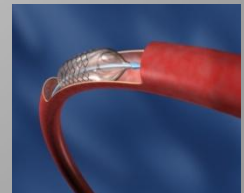
Fibrinolisi preferita

- Presentazione precoce (≤ 3 ore dall'esordio dei sintomi e latenza della strategia invasiva)
- Strategia invasiva non possibile
 - Laboratorio di emodinamica occupato/non disponibile
 - Accesso vascolare difficile
- Latenza della strategia invasiva
 - Durata del trasporto prolungata
 - Door-to-balloon > 90 minuti
 - > 1 ora di ritardo rispetto alla fibrinolisi immediata



Strategia invasiva preferita

- Disponibilità di laboratorio di emodinamica
- Door-to-balloon < 90 minuti
- STEMI ad alto rischio
 - Shock cardiogeno
 - Classe Killip ≥ 3
- Controindicazioni alla fibrinolisi
- Presentazione tardiva (> 3 hr)
- Diagnosi dubbia di STEMI



So...Primary PCI in STEMI

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

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



EUROPEAN
SOCIETY OF
CARDIOLOGY®

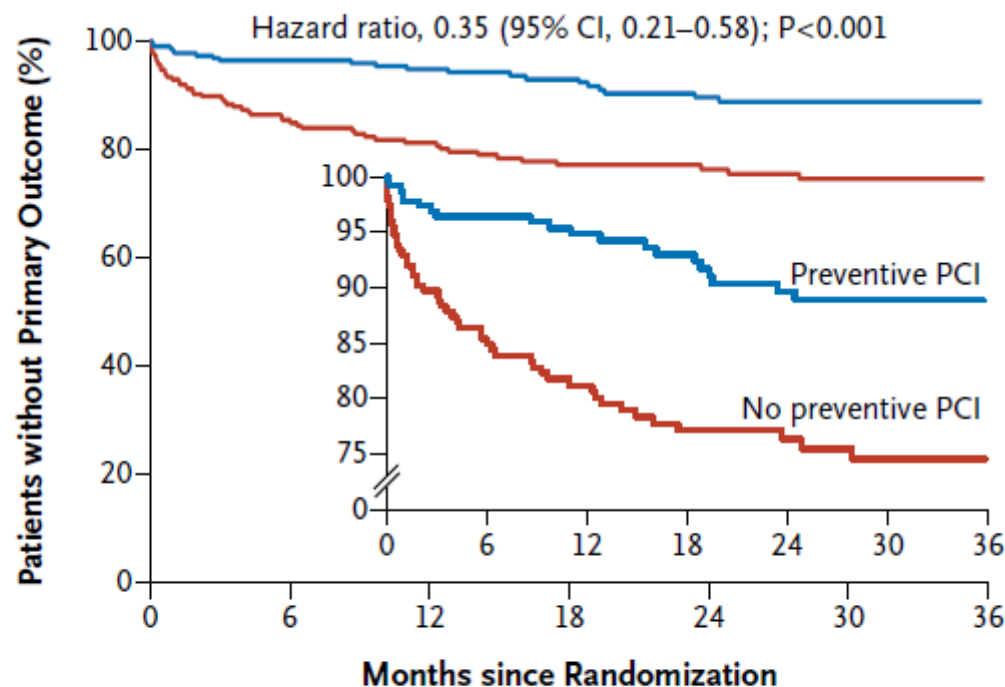


American
Heart
Association®

	COR	LOE
<u>Ischemic symptoms <12 h</u>	I	A
<u>Ischemic symptoms <12 h and contraindications to fibrinolytic therapy</u> irrespective of time delay from FMC	I	B
<u>Cardiogenic shock or acute severe HF</u> irrespective of time delay from MI onset	I	B
Evidence of ongoing ischemia 12 to 24 h after symptom onset	IIa	B
PCI of a noninfarct artery at the time of primary PCI in patients without hemodynamic compromise	III: Harm	B

Only culprit lesion?

Primary PCI should be performed in patients with ST-elevation myocardial infarction and multivessel coronary artery disease. Preventive PCI in noninfarct coronary arteries with major stenoses significantly reduced the risk of adverse cardiovascular events, as compared with PCI limited to the infarct artery.



No. at Risk

Preventive PCI	234	196	166	146	118	89	67
No preventive PCI	231	168	144	122	96	74	50

CONCLUSIONS

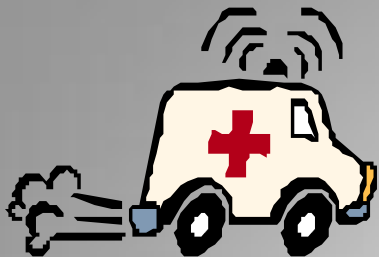
In patients with STEMI and multivessel coronary artery disease undergoing infarct-artery PCI, preventive PCI in noninfarct coronary arteries with major stenoses significantly reduced the risk of adverse cardiovascular events, as compared with PCI limited to the infarct artery. (Funded by Barts and the London Charity; PRAMI Current Controlled Trials number, ISRCTN73028481.)

B



arm

B



'3 MUST' For Pre-hospital Care

Recommendations	Class ^a	Level ^b
Ambulance teams <u>must be trained and equipped to identify STEMI</u> (with use of ECG recorders and telemetry as necessary) and administer initial therapy, including thrombolysis where applicable.	I	B
The prehospital management of STEMI patients <u>must be based on regional networks</u> designed to deliver reperfusion therapy expeditiously and effectively, with efforts made to make primary PCI available to as many patients as possible.	I	B
Primary PCI-capable centres must deliver a <u>24/7 service and be able to start primary PCI as soon as possible</u> but always within 60 min from the initial call.	I	B

Targets:

- < 10 min ECG transmission
- < 5 min tele-consultation
- < 120 min to first balloon inflation
- < 30 min start fibrinolytic therapy

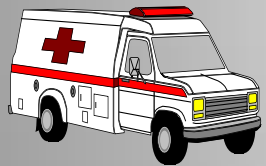
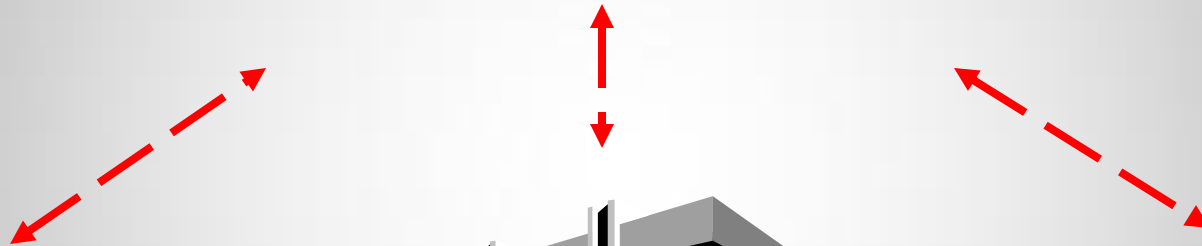
STEMI CHAIN



Early Recognition Early Transmission Early Activation Early Reperfusion

Inter-hospital network: Hub & Spoke

Centrale Operativa 118



118-Spoke

Ospedale Hub

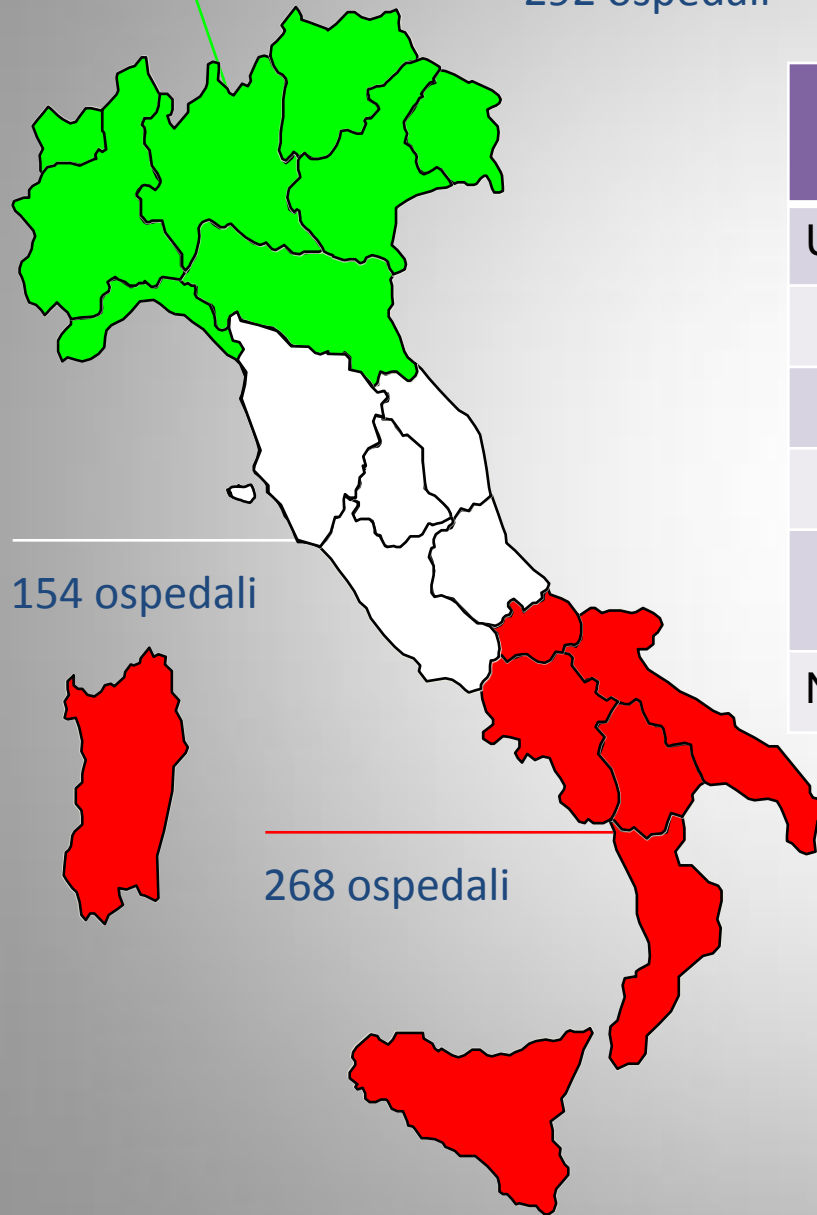
Ospedale Spoke

... la migliore terapia riperfusiva nel contesto temporale, clinico ed organizzativo....

STEMI network in Italy

292 ospedali

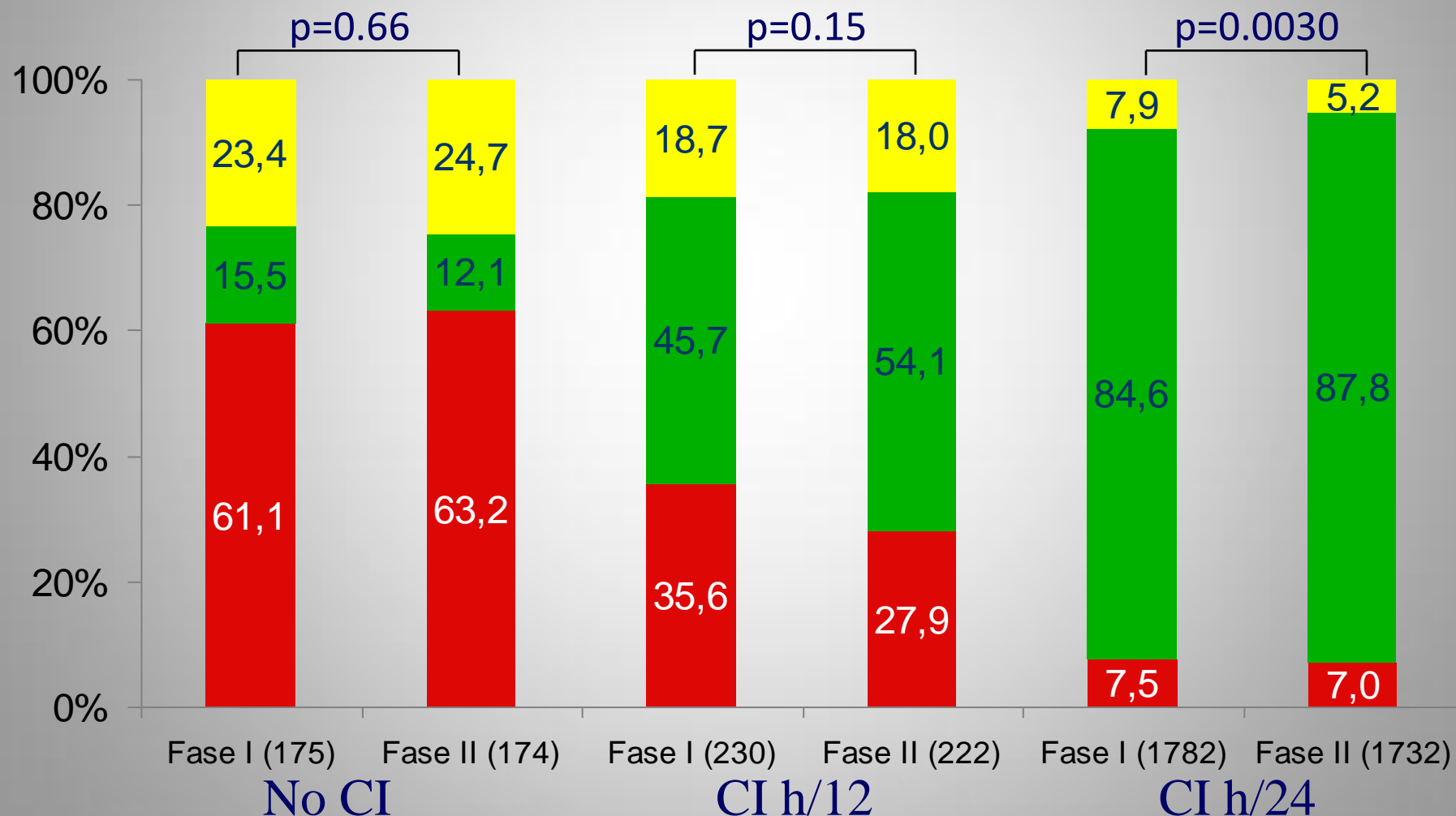
714 ospedali dotati di cardiologia



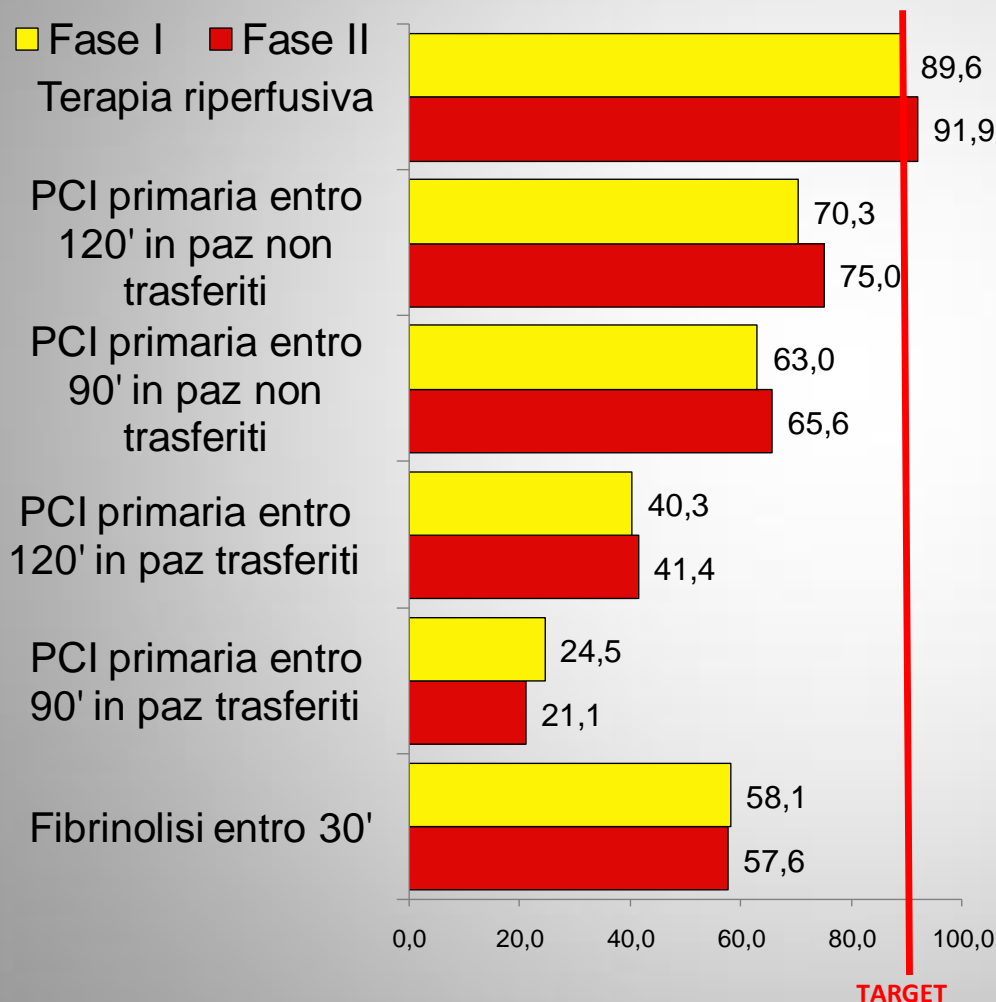
	Nord (n.292)	Centro (n. 154)	Sud (n. 268)
UTIC	168 (58%)	92 (60%)	146 (54%)
Rete STEMI	161 (56%)	78 (51%)	97 (36%)
Hub	95 (33%)	35 (23%)	37 (14%)
Spoke	66 (23%)	43 (28%)	60 (22%)
No Rete STEMI	7 (2%)	14 (9%)	49 (18%)
No UTIC	124 (42%)	62 (40%)	122 (46%)

Trattamenti Riperfusivi in Pazienti con STEMI nelle due Fasi e Divisi per Tipologia Centri

■ Fibrinolisi ■ PCI primaria ■ Nessuna TR



Livelli di Adesione agli Indicatori di Processo nelle Fasi I e II in Pazienti Idonei (STEMI)

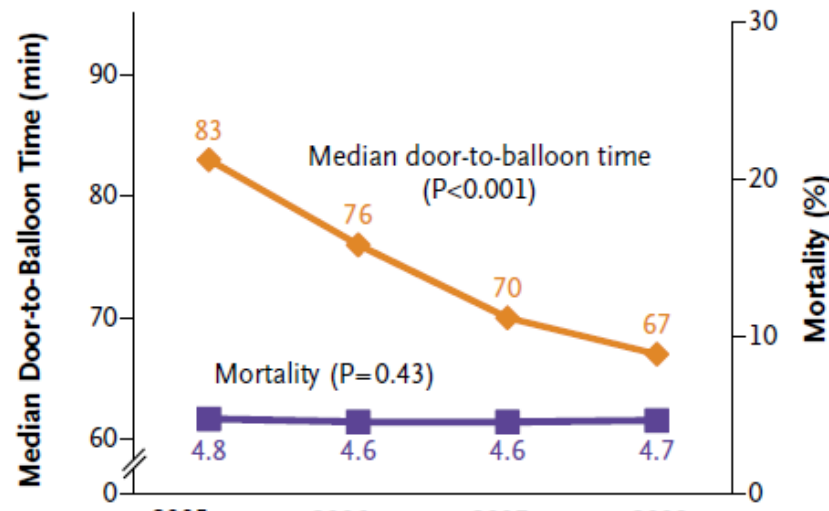


**Insufficiente rispetto
dei tempi raccomandati
per l'erogazione della
terapia riperfusiva!**

Door-to-Balloon Time and Mortality among Patients Undergoing Primary PCI

Daniel S. Menees, M.D., Eric D. Peterson, M.D., Yongfei Wang, M.S., Jephtha P. Curtis, M.D., John C. Messenger, M.D., John S. Rumsfeld, M.D., Ph.D., and Hitinder S. Gurm, M.B., B.S.

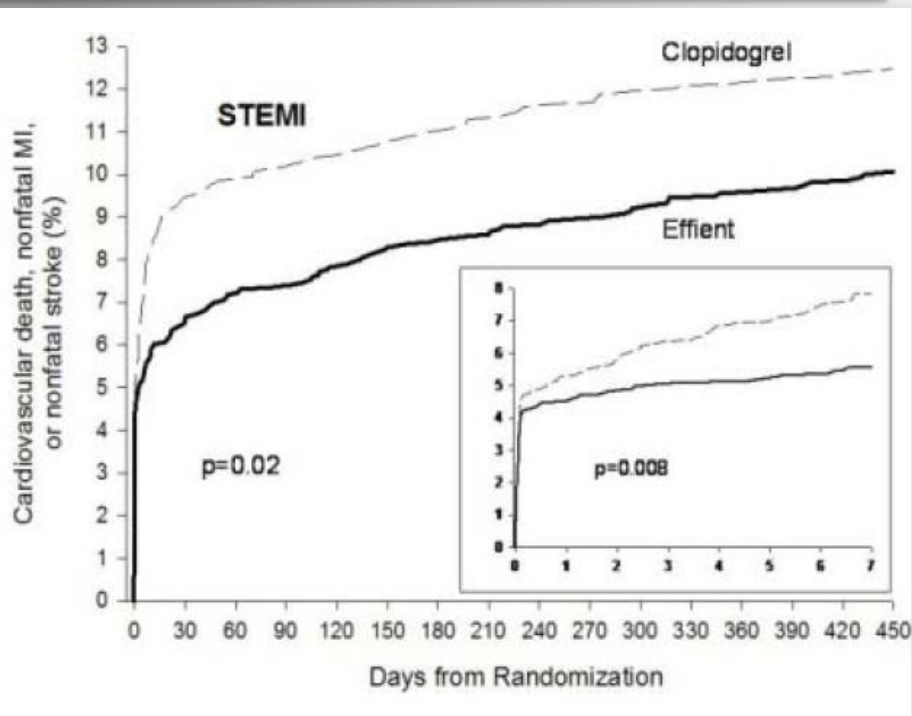
A Overall (N=96,739)



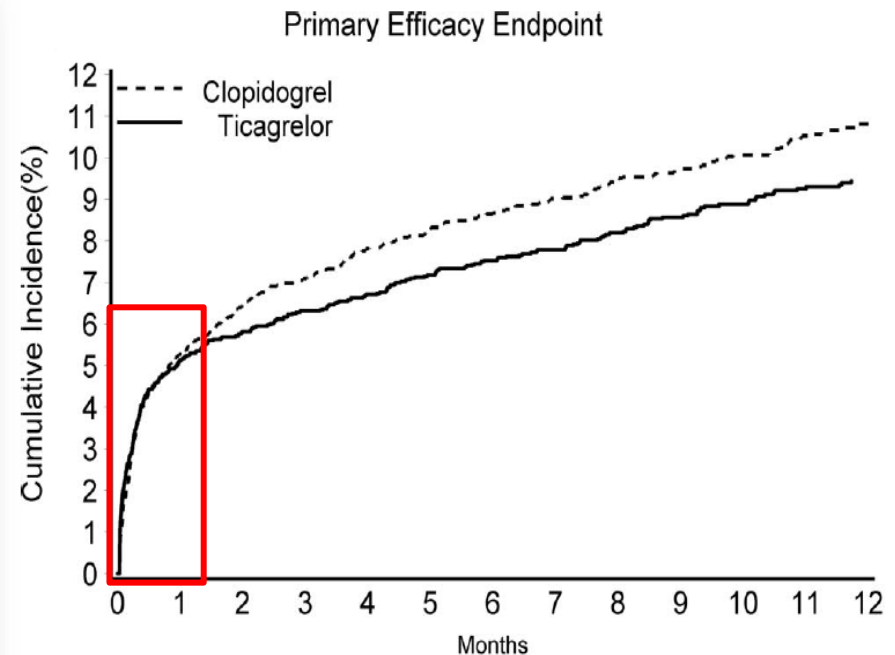
CONCLUSIONS

Although national door-to-balloon times have improved significantly for patients undergoing primary PCI for ST-segment elevation myocardial infarction, in-hospital mortality has remained virtually unchanged. These data suggest that additional strategies are needed to reduce in-hospital mortality in this population. (Funded by the National Cardiovascular Data Registry of the American College of Cardiology Foundation.)

TRITON-TIMI 38: Primary Efficacy Endpoint



PLATO: Primary Efficacy Endpoint



Novel P2Y₁₂ receptor antagonists:

When “*NOT to Use*” or “*Use with Caution*”?

– Prasugrel.

Contraindicated: high-risk bleeding; prior TIA/stroke; hypersensitivity

Precautions: elderly, low-weight; CABG/surgery (7days).

– Ticagrelor.

Contraindicated: high-risk bleeding; prior hemorrhagic stroke; severe hepatic dysfunction

Precautions: COPD/asthma, bradyarrhythmia without pacemaker, compliance (b.i.d. administration), drug interactions (CYP 3A4 interfering agents); aspirin dose (<100mg), CABG/surgery (5-7days).

Anti Gp IIb-IIIa



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.	Ila	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
Upstream use of a GP IIb/IIIa inhibitor (vs. in-lab use) may be considered in high-risk patients undergoing transfer for primary PCI.	IIb	B
Options for GP IIb/IIIa inhibitors are (with LoE for each agent):		
• Abciximab		A
• Eptifibatide (with double bolus)		B
• Tirofiban (with a high bolus dose)		B



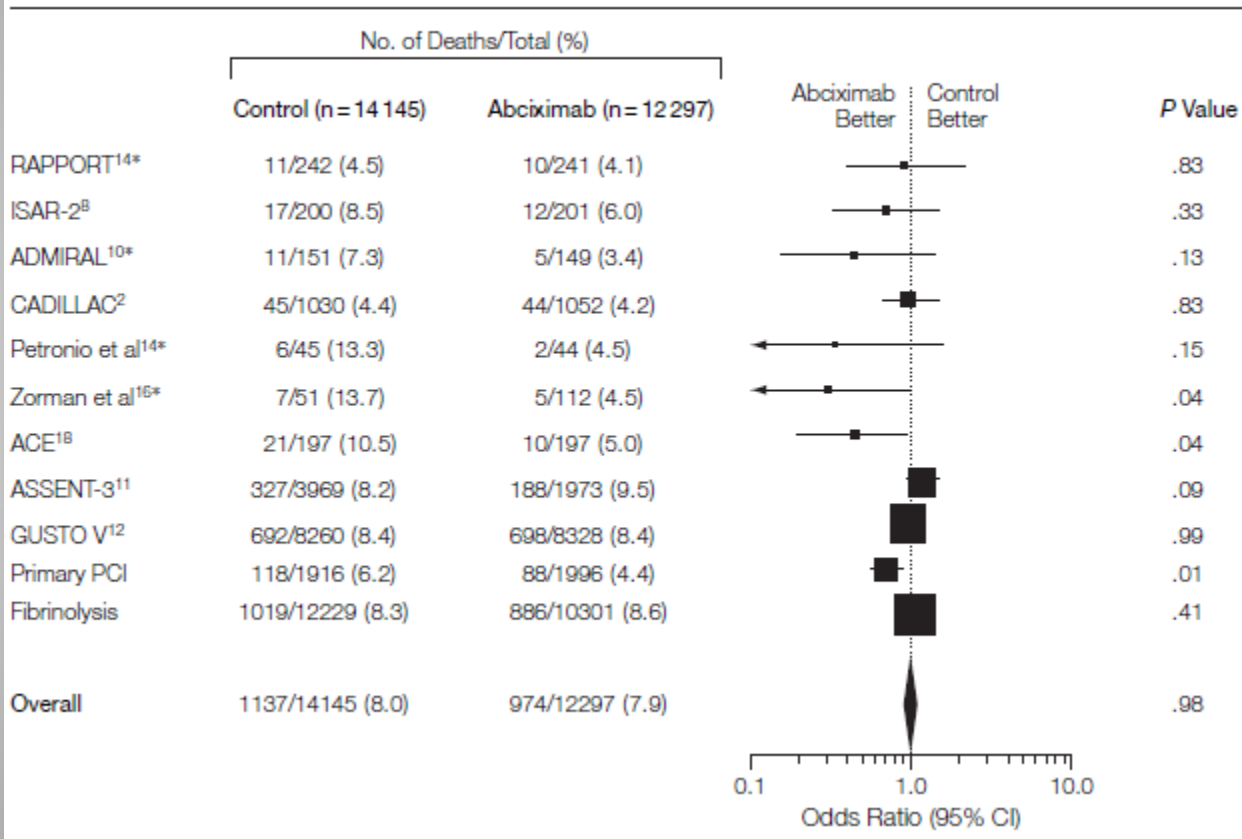
IV GP IIb/IIIa receptor antagonists in conjunction with UFH or bivalirudin in selected patients

- Abciximab: 0.25-mg/kg IV bolus, then 0.125 mcg/kg/min (maximum 10 mcg/min)
- Tirofiban: (high-bolus dose): 25-mcg/kg IV bolus, then 0.15 mcg/kg/min
 - In patients with CrCl <30 mL/min, reduce infusion by 50%
- Eptifibatide: (double bolus): 180-mcg/kg IV bolus, then 2 mcg/kg/min; a second 180-mcg/kg bolus is administered 10 min after the first bolus
 - In patients with CrCl <50 mL/min, reduce infusion by 50%
 - Avoid in patients on hemodialysis
- Pre-catheterization laboratory administration of IV GP IIb/IIIa receptor antagonist
- Intracoronary abciximab 0.25-mg/kg bolus

Ila	A
Ila	B
Ila	B
IIb	B
IIb	B

IIb or Not IIb...

Figure 2. Abciximab and Long-Term (6- and 12-Month) Mortality From Fixed-Effects Model



Anticoagulant therapy



Recommendations	Class	Level
Anticoagulants		
An injectable anticoagulant must be used in primary PCI.	I	C
Bivalirudin (with use of GP IIb/IIIa blocker restricted to bailout) is recommended over unfractionated heparin and a GP IIb/IIIa blocker.	I	B
Enoxaparin (with or without routine GP IIb/IIIa blocker) may be preferred over unfractionated heparin.	IIb	B
Unfractionated heparin with or without routine GP IIb/IIIa blocker must be used in patients not receiving bivalirudin or enoxaparin.	I	C
Fondaparinux is not recommended for primary PCI.	III	B
The use of fibrinolysis before planned primary PCI is not recommended.	III	A



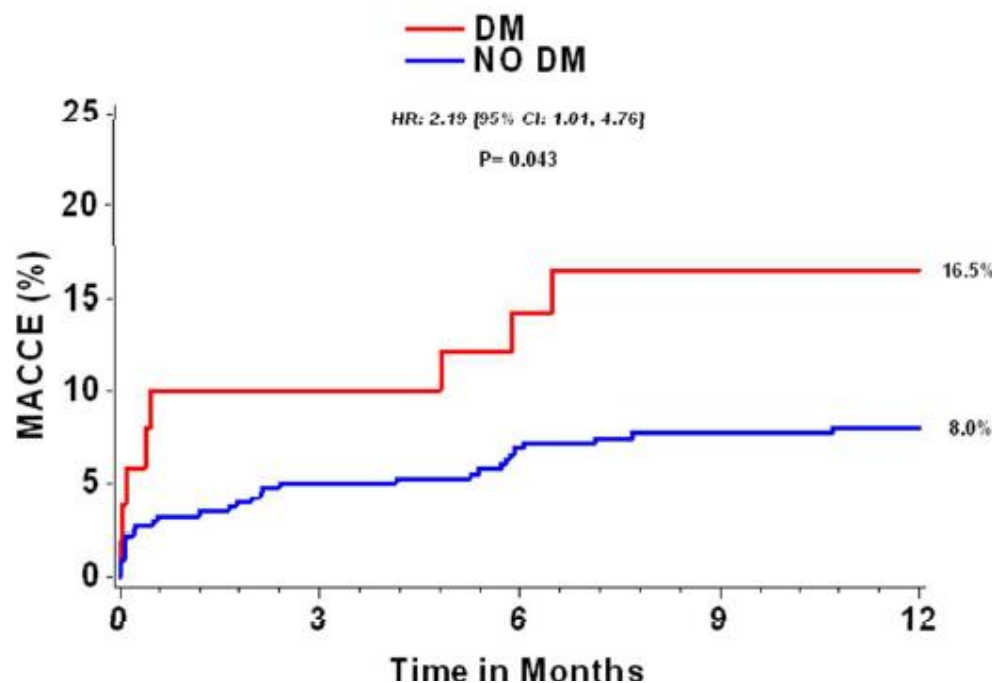
Anticoagulant therapy

- UFH:
 - With GP IIb/IIIa receptor antagonist planned: 50- to 70-U/kg IV bolus to achieve therapeutic ACT \ddagger
 - With no GP IIb/IIIa receptor antagonist planned: 70- to 100-U/kg bolus to achieve therapeutic ACT \S
- Bivalirudin: 0.75-mg/kg IV bolus, then 1.75-mg/kg/h infusion with or without prior treatment with UFH. An additional bolus of 0.3 mg/kg may be given if needed.
 - Reduce infusion to 1 mg/kg/h with estimated CrCl <30 mL/min
 - Preferred over UFH with GP IIb/IIIa receptor antagonist in patients at high risk of bleeding
- Fondaparinux: not recommended as sole anticoagulant for primary PCI

I	C
I	C
I	B
IIa	B
III: Harm	B

Diabetic patient with STEMI

Outcomes in Diabetic Patients Undergoing Primary Percutaneous Coronary Intervention for Acute Anterior Myocardial Infarction: Results from the INFUSE-AMI Study



Conclusions: Patients with DM presenting with STEMI had a higher baseline risk profile than those without DM. Although reperfusion success and infarct size were similar, diabetic patients experienced more death, reinfarction, stent thrombosis and revascularization than non-diabetics.

TRITON-TIMI 38: Diabetic Subgroup (N=3146)

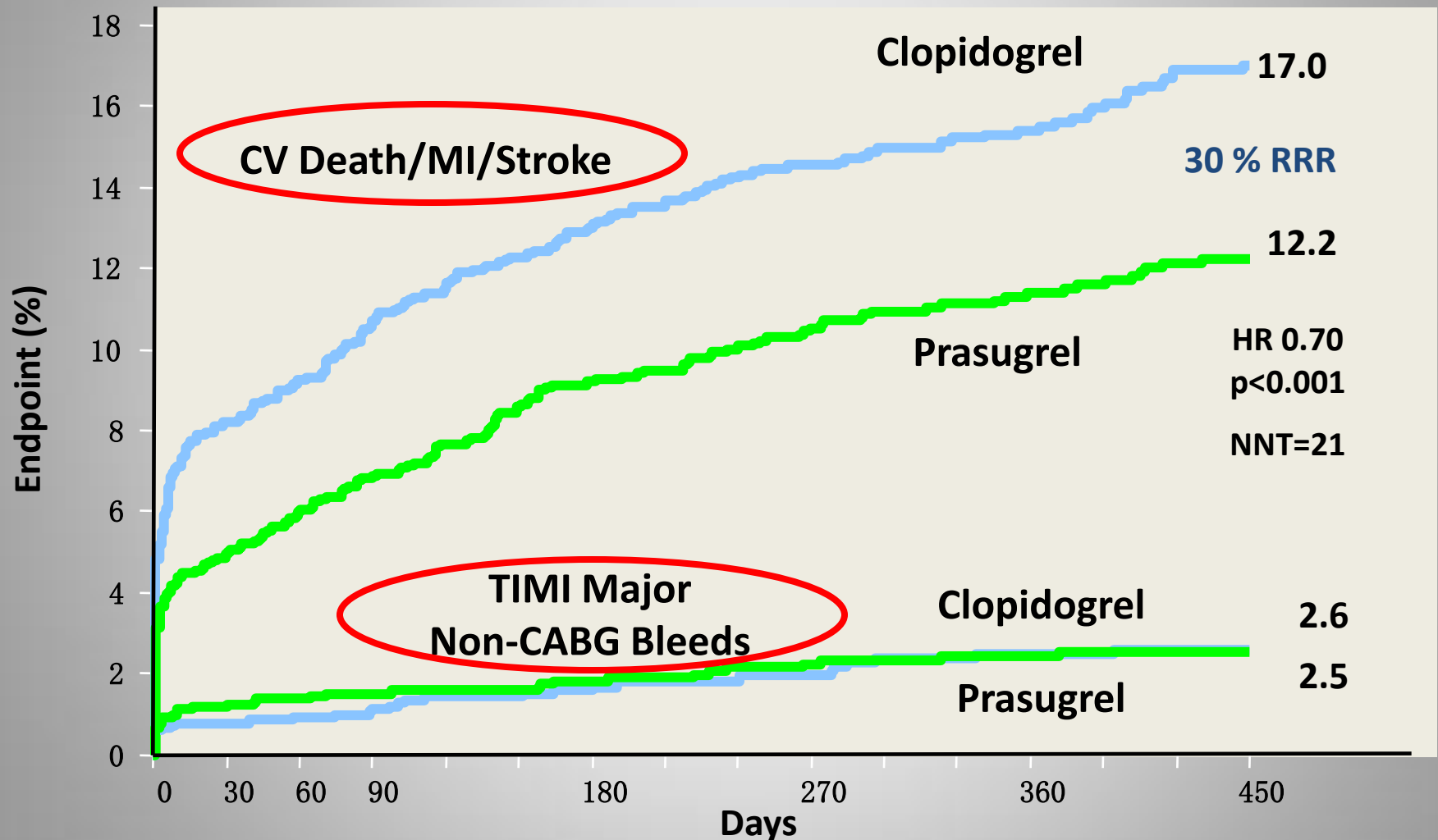
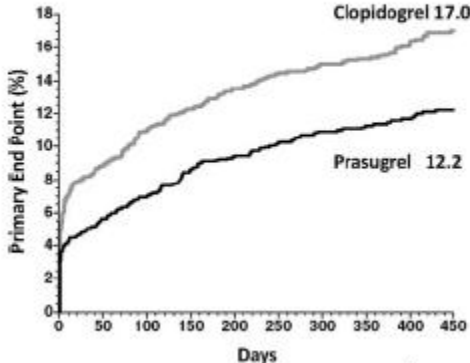
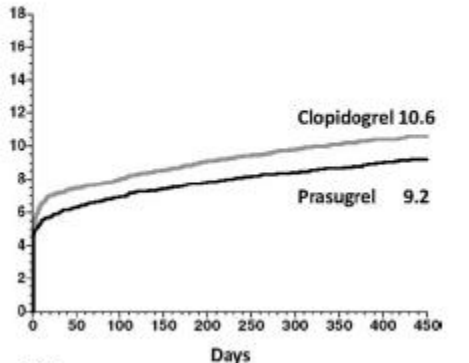


Table 4. Clinical Events for Prasugrel Versus Clopidogrel by Diabetes Status

	Clopidogrel	A				No Diabetes	
		DM	No DM				
		HR 0.70 (0.58-0.85), P<0.001	HR 0.86 (0.76-0.98), P = 0.02				
Subjects without DM (n=10 462), n	5225						
CVD/MI/CVA*	10						
CVD/MI*	10	P interaction = 0.09					
MI†	8						
CV death	1						
Stent thrombosis	2						
Major hemorrhage‡	1						
Major or minor‡	3						
D/MI/CVA*/major bleed‡	12						
All diabetes (n=3146), n	1570	1576					
CVD/MI/CVA*	17.0	12.2	0.70 (0.58–0.85)	<0.001	0.09		
CVD/MI*	15.4	10.8	0.68 (0.56–0.84)	<0.001	0.08		
MI†	13.2	8.2	0.60 (0.48–0.76)	<0.001	0.02		
CV death	4.2	3.4	0.85 (0.58–1.24)	0.40	0.78		
Stent thrombosis	3.6	2.0	0.52 (0.33–0.84)	0.007	0.63		
Major hemorrhage‡	2.6	2.5	1.06 (0.66–1.69)	0.81	0.29		
Major or minor‡	4.3	5.3	1.30 (0.92–1.82)	0.13	0.93		
D/MI/CVA*/major bleed‡	19.2	14.6	0.74 (0.62–0.89)	0.001	0.05		

Abbreviations as in Table 2.

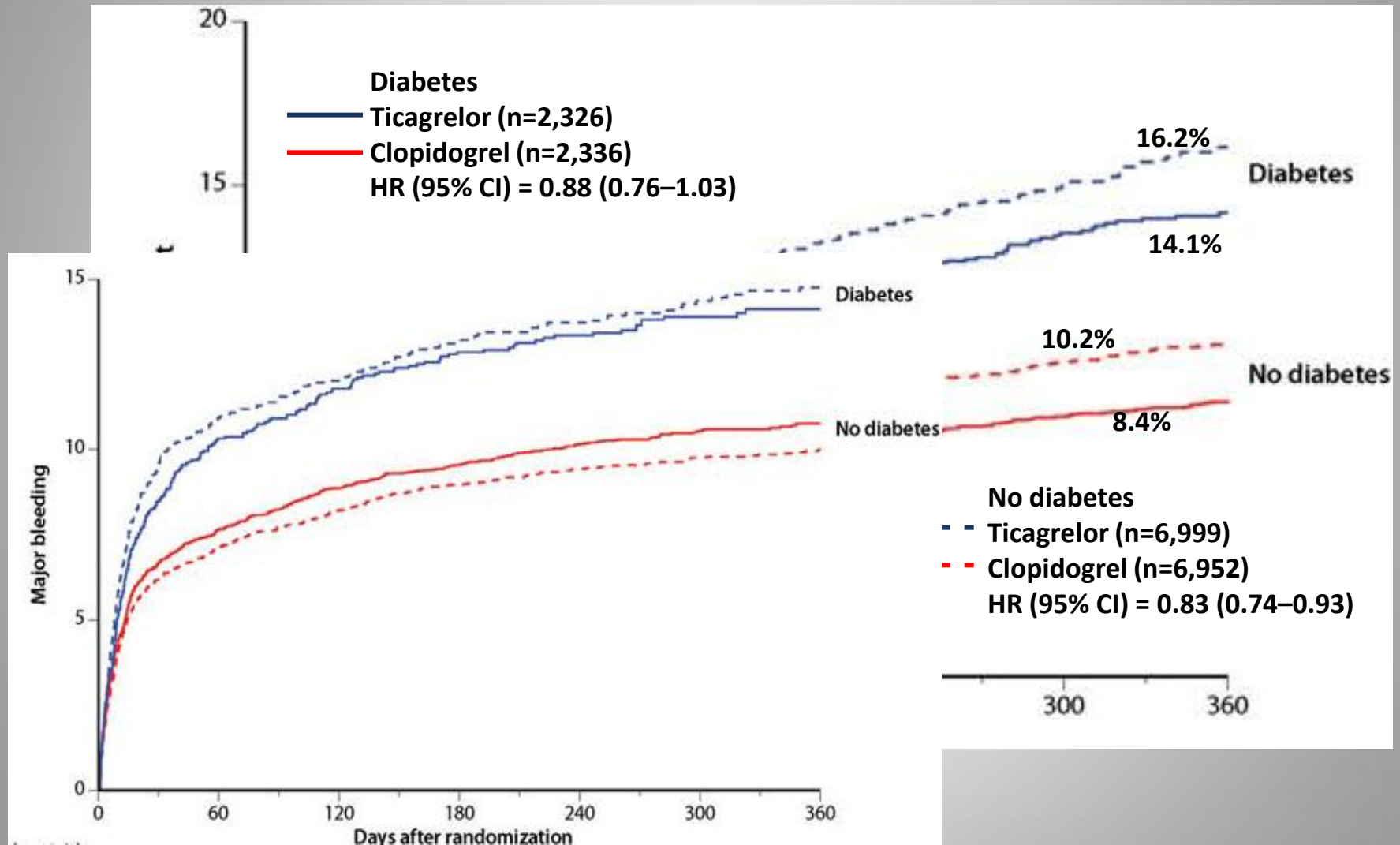
*The composite of cardiovascular death and nonfatal end points (MI alone or MI/stroke).

†Any MI (fatal or nonfatal).

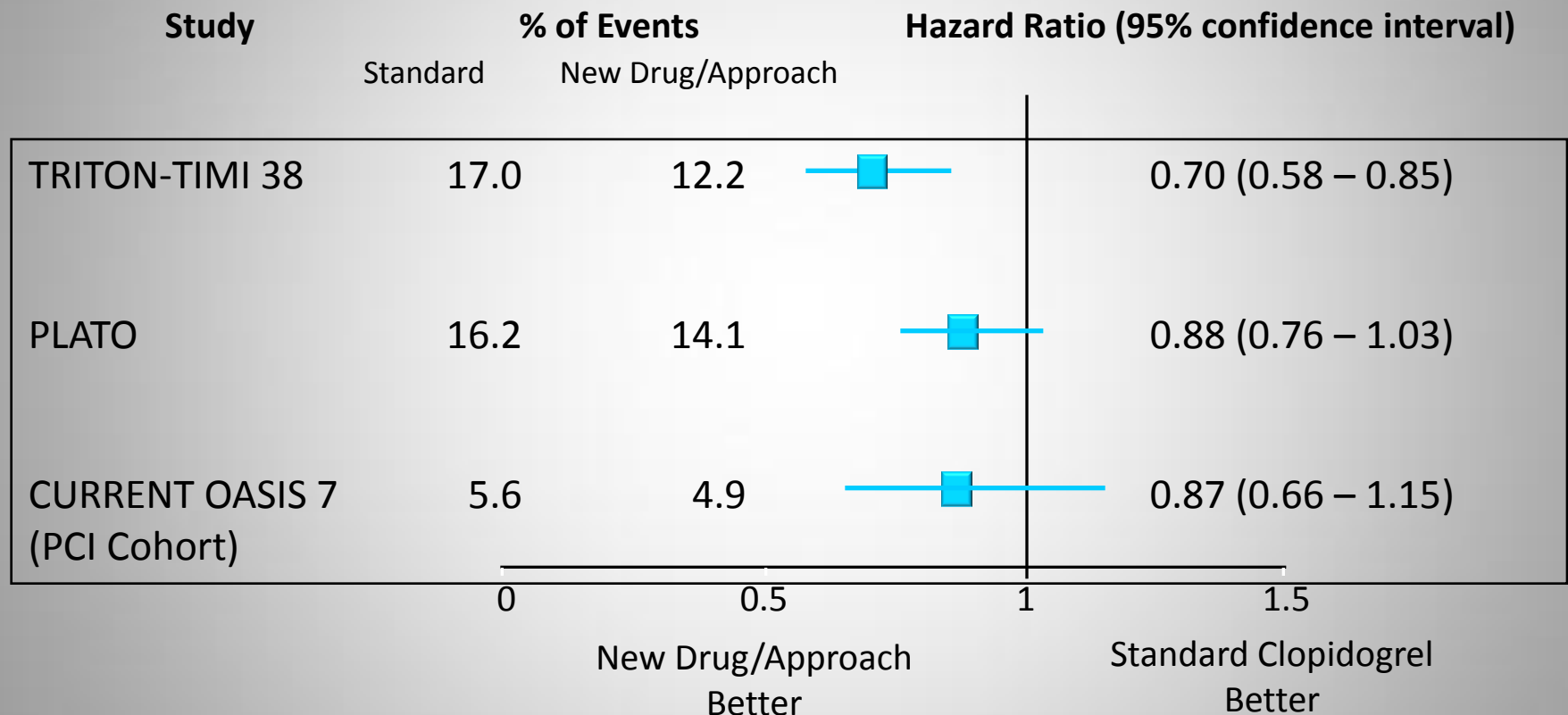
‡Not related to CABG.

PLATO: Diabetic Subgroup (N=4662)

Primary composite endpoint – Major bleeding



Efficacy of New Drugs/Approaches in Reducing Adverse Outcomes in Diabetes Mellitus From Large-Scale Clinical Trials



CURRENT-OASIS= Clopidogrel Optimal Loading Dose Usage to Reduce Recurrent Events Optimal Antiplatelet Strategy for Interventions; PCI=percutaneous intervention; PLATO= A Study of Platelet Inhibition and Patient Outcomes; TRITON-TIMI= Trial To Assess Improvement in Therapeutic Outcomes by Optimizing Platelet Inhibition With Prasugrel Thrombolysis in Myocardial Infarction. Reprinted with permission from Ferreiro JL, Angiolillo DJ. *Circulation* 2011; 123: 798-813.

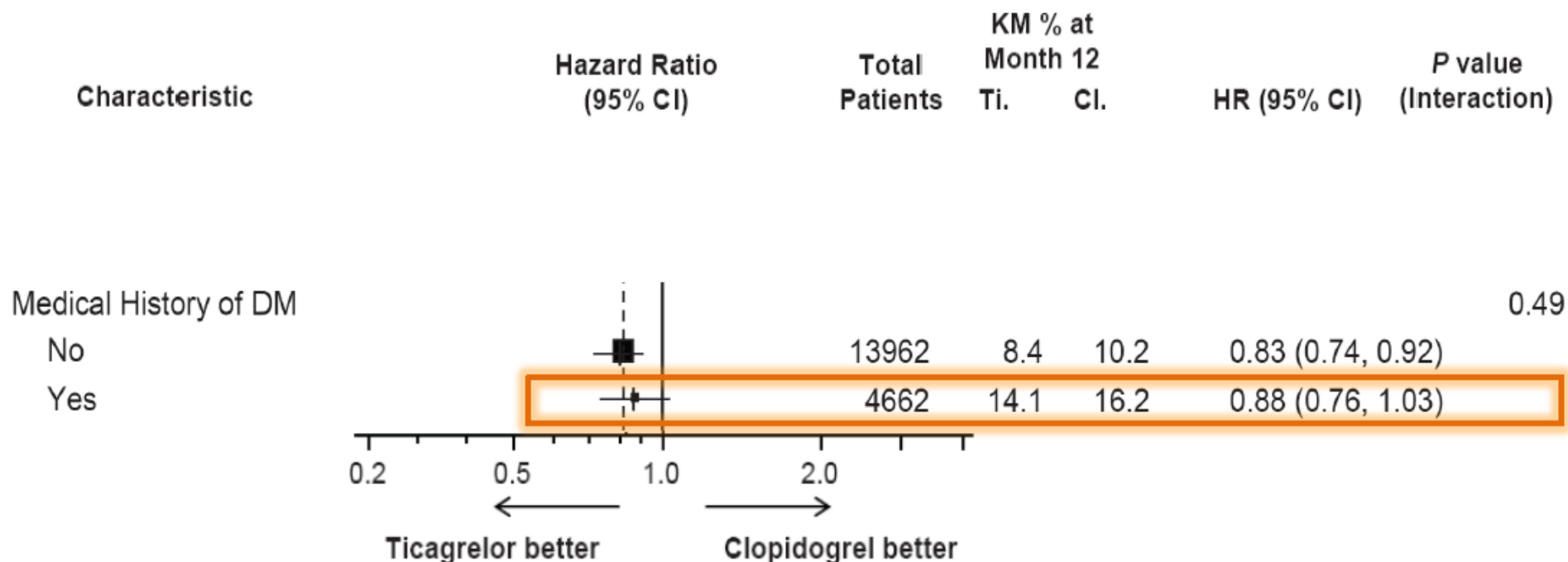
Conclusions

- The best reperfusion treatment is one that bring to early, complete and sustained myocardial reperfusion in the largest number of patients, but with the lowest rate of undesirable effects.
- A tailored reperfusion strategy based on the risk profile of patient and considering delay at presentation may prove more rational.
- All patients should have access to all resources, in order to choose the most appropriate.
- A well structured regional system of STEMI care helps to select the appropriate reperfusion strategy and guarantee timely restoration of coronary blood flow.



Grazie

PLATO: Hazard Ratios and Rates of Primary End Point in Predefined Subgroups of Study Patients



Sottogruppo diabetici del PLATO - Sicurezza

	n	Overall	Ticagrelor	Clopidogrel	HR (95% CI)	P-value (interaction)
Non-CABG-related major bleeding, PLATO defined						
No diabetes	13 798	3.8 (461)	4.1 (253)	3.4 (208)	1.22 (1.01–1.46)	0.69
Diabetes	4621	5.2 (207)	5.5 (109)	4.9 (98)	1.13 (0.86–1.49)	

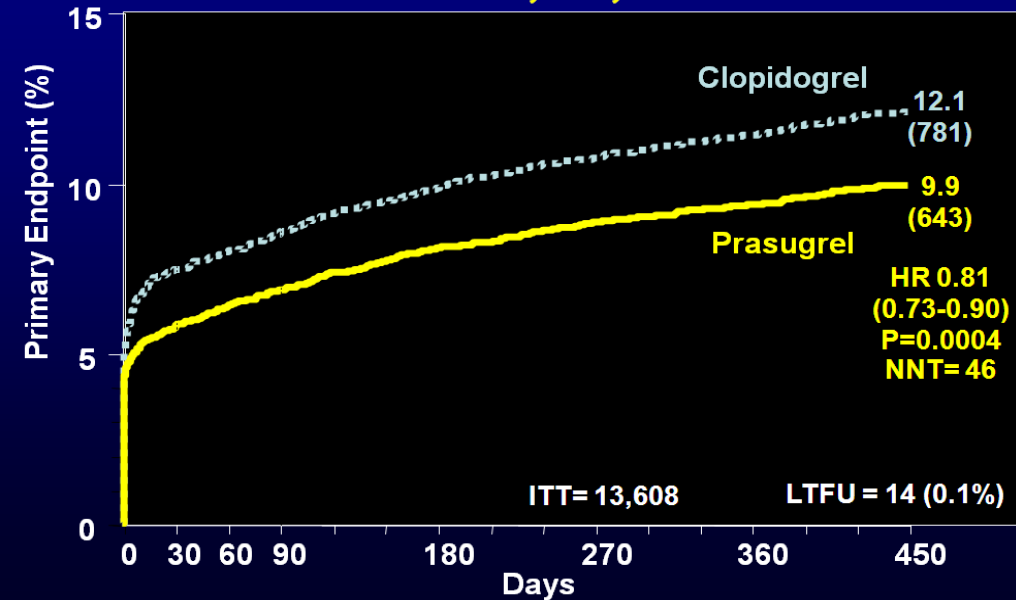
Bleeding occurred with similar frequency in the ticagrelor and clopidogrel groups independent of DM status (Figure 1C). Interaction tests were not significant irrespective of bleeding type and definition (i.e. PLATO major, fatal or life threatening, or TIMI major). **PLATO-defined major bleeding events unrelated to CABG were numerically more frequent in the ticagrelor group,** whereas bleeding events related to CABG were numerically

complications. **Non-CABG-related major bleeding events were, however, more frequent than in the clopidogrel group.** These findings were consistent among both diabetic and non-diabetic patients.

I sanguinamenti maggiori non correlati a CABG sono stati numericamente più frequenti con Ticagrelor, sia nei pazienti diabetici che non.

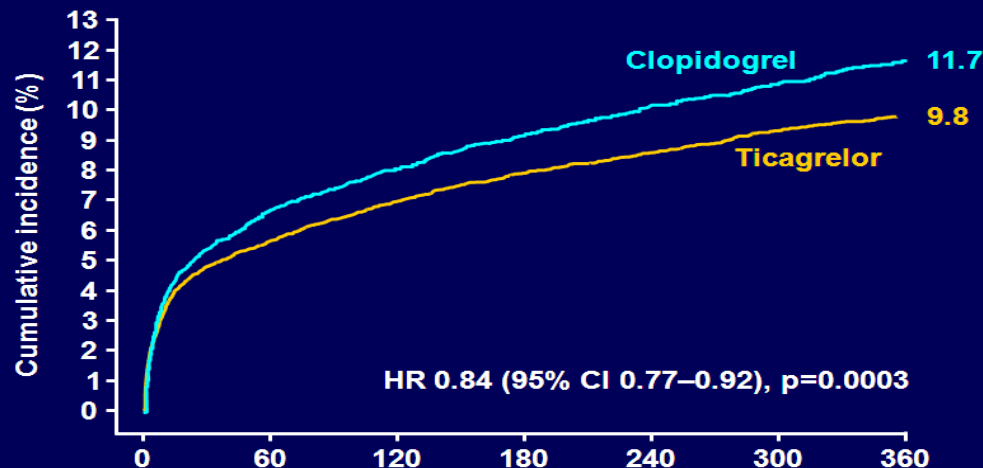
James S,

Primary Endpoint CV Death, MI, Stroke



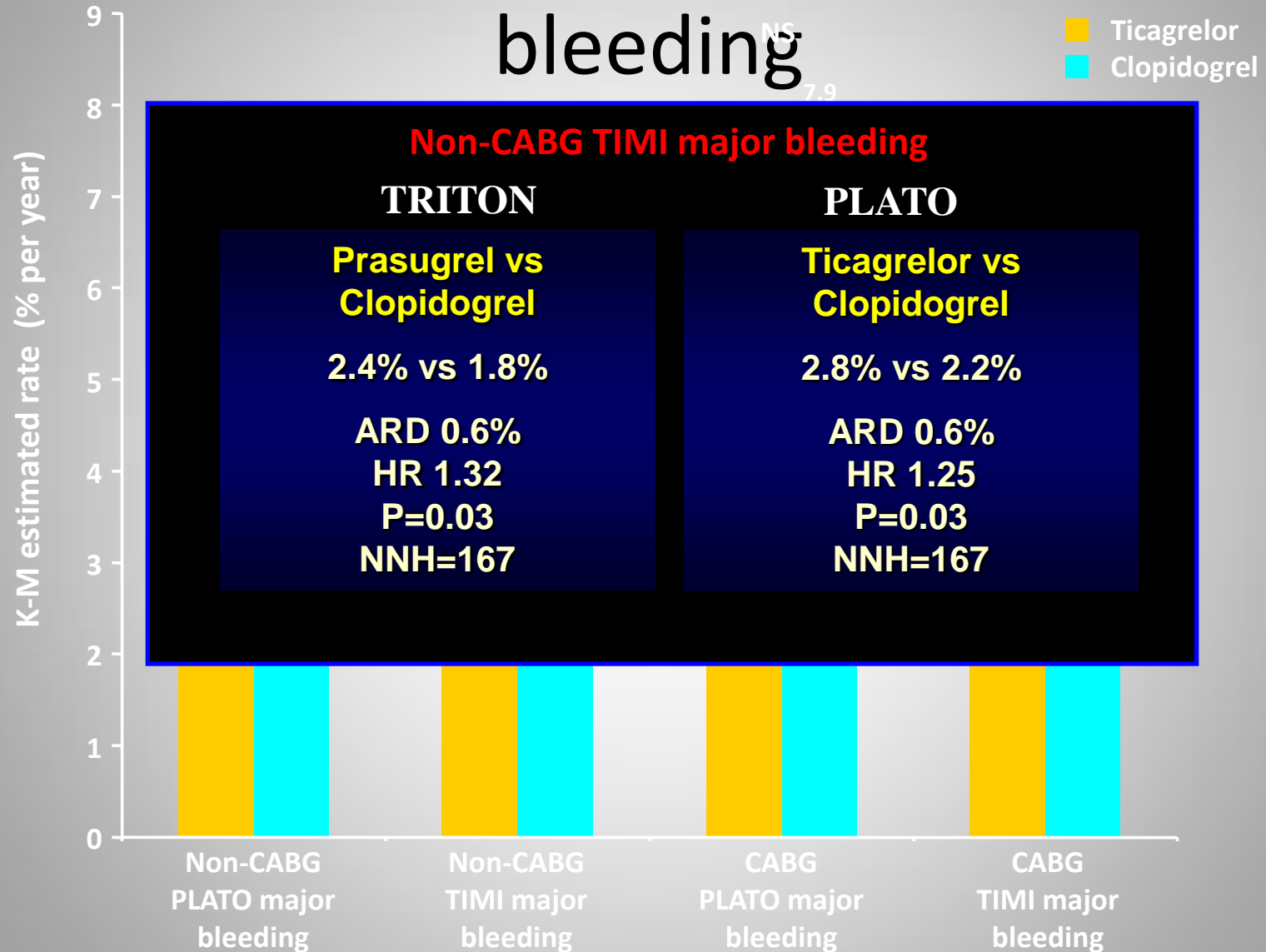
TRITON TIMI 38 (prasugrel vs clopidogrel)

K-M estimate of time to first primary efficacy event (composite of CV death, MI or stroke)



PLATO (ticagrelor vs clopidogrel)

Non-CABG and CABG-related major bleeding



TRITON vs PLATO

Proof of concept: Higher IPA to Support ACS

Differences between trials

1. Patient Population

TRITON: ACS undergoing PCI

PLATO: Full spectrum ACS

2. Pretreatment

TRITON: No pretreatment (except STEMI)

PLATO: Pretreatment

3. Clopidogrel Loading Dose

TRITON: 300mg

PLATO: 300-600mg

4. Duration of trial (median)

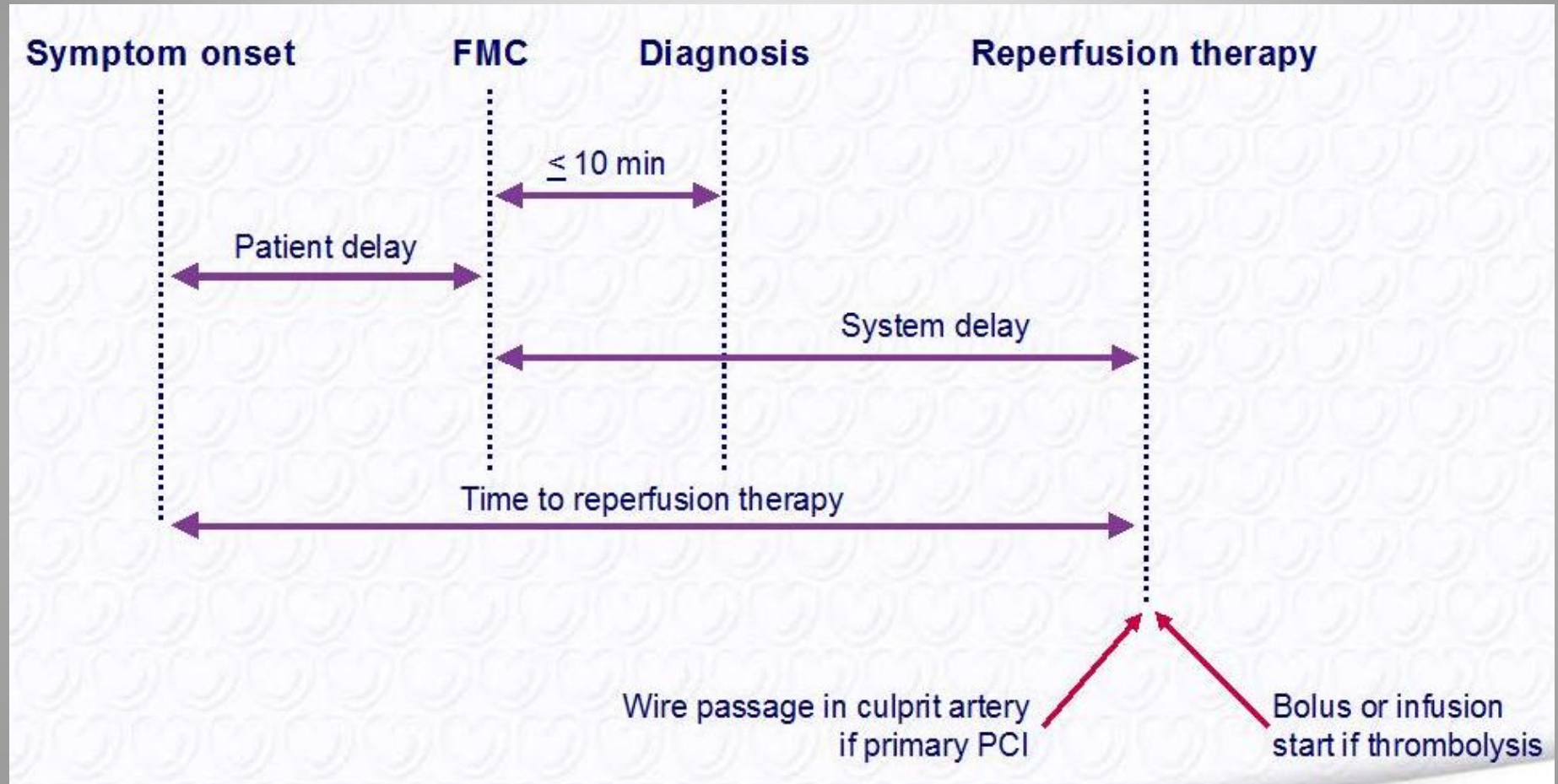
TRITON: 14.5 months

PLATO: 9 months

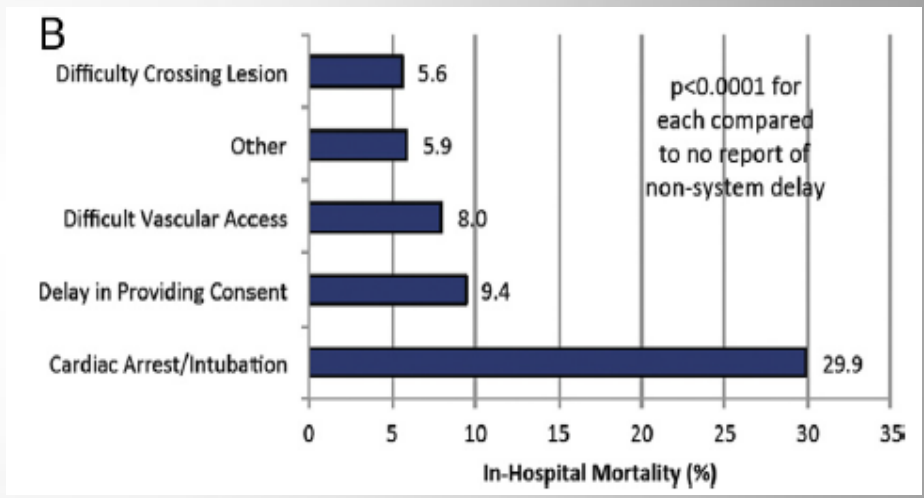
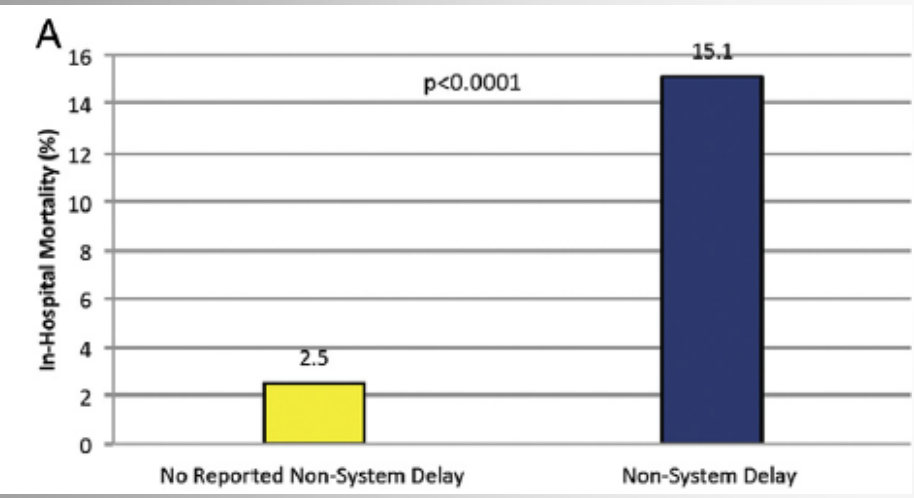
Table 13 Contraindications to fibrinolytic therapy

Absolute
Previous intracranial haemorrhage or stroke of unknown origin at any time
Ischaemic stroke in the preceding 6 months
Central nervous system damage or neoplasms or atrioventricular malformation
Recent major trauma/surgery/head injury (within the preceding 3 weeks)
Gastrointestinal bleeding within the past month
Known bleeding disorder (excluding menses)
Aortic dissection
Non-compressible punctures in the past 24 h (e.g. liver biopsy, lumbar puncture)
Relative
Transient ischaemic attack in the preceding 6 months
Oral anticoagulant therapy
Pregnancy or within 1 week postpartum
Refractory hypertension (systolic blood pressure >180 mmHg and/or diastolic blood pressure >110 mmHg)
Advanced liver disease
Infective endocarditis
Active peptic ulcer
Prolonged or traumatic resuscitation

Components of delay in STEMI and ideal time intervals for intervention



But...
There are also not avoidable “nonsystem delays” : providing consent for the procedure, difficult vascular access, difficulty crossing the culprit lesion during the PCI, and cardiac arrest and/or need for intubation before PCI.



Conclusions Nonsystem reasons for delay in D2BT in ST-segment elevation myocardial infarction patients presenting for primary percutaneous coronary intervention are common and associated with high in-hospital mortality. (J Am Coll Cardiol 2013;61:1688-95) © 2013 by the American College of Cardiology Foundation

Rajesh V. JACC 2013:1688-95

Duration of symptoms – PATIENT DELAY

Recommendations	Class ^a	Level ^b
Reperfusion therapy is indicated in all patients with symptoms of <12 h duration and persistent ST-segment elevation or (presumed) new LBBB.	I	A
Reperfusion therapy (preferably primary PCI) is indicated if there is evidence of ongoing ischaemia, even if symptoms may have started >12 h beforehand or if pain and ECG changes have been stuttering.	I	C
Reperfusion therapy with primary PCI may be considered in stable patients presenting 12–24 h after symptom onset.	IIb	B
Routine PCI of a totally occluded artery >24 h after symptom onset in stable patients without signs of ischaemia (regardless of whether fibrinolysis was given or not) is not recommended.	III	A



Reperfusion therapy should be administered to all eligible patients with STEMI with symptom onset within the prior 12 hours.



Reperfusion therapy is reasonable for patients with STEMI and symptom onset within the prior 12 to 24 hours who have clinical and/or ECG evidence of ongoing ischemia. Primary PCI is the preferred strategy in this population.

Contraindications and Cautions for Fibrinolysis in STEMI

- **Absolute Contraindications:**

- ❖ Previous intracranial hemorrhage
- ❖ Ischaemic stroke in the preceding 6 months
- ❖ Known structural cerebral vascular lesion
- ❖ Known malignant intracranial neoplasm
- ❖ Recent major trauma/surgery/head injury
- ❖ Suspected aortic dissection
- ❖ Known bleeding disorder (excluding menses)
- ❖ Gastrointestinal bleeding within the past months
- ❖ Non-compressible punctures in the past 24 h (e.g. liver biopsy, lumbar puncture..)

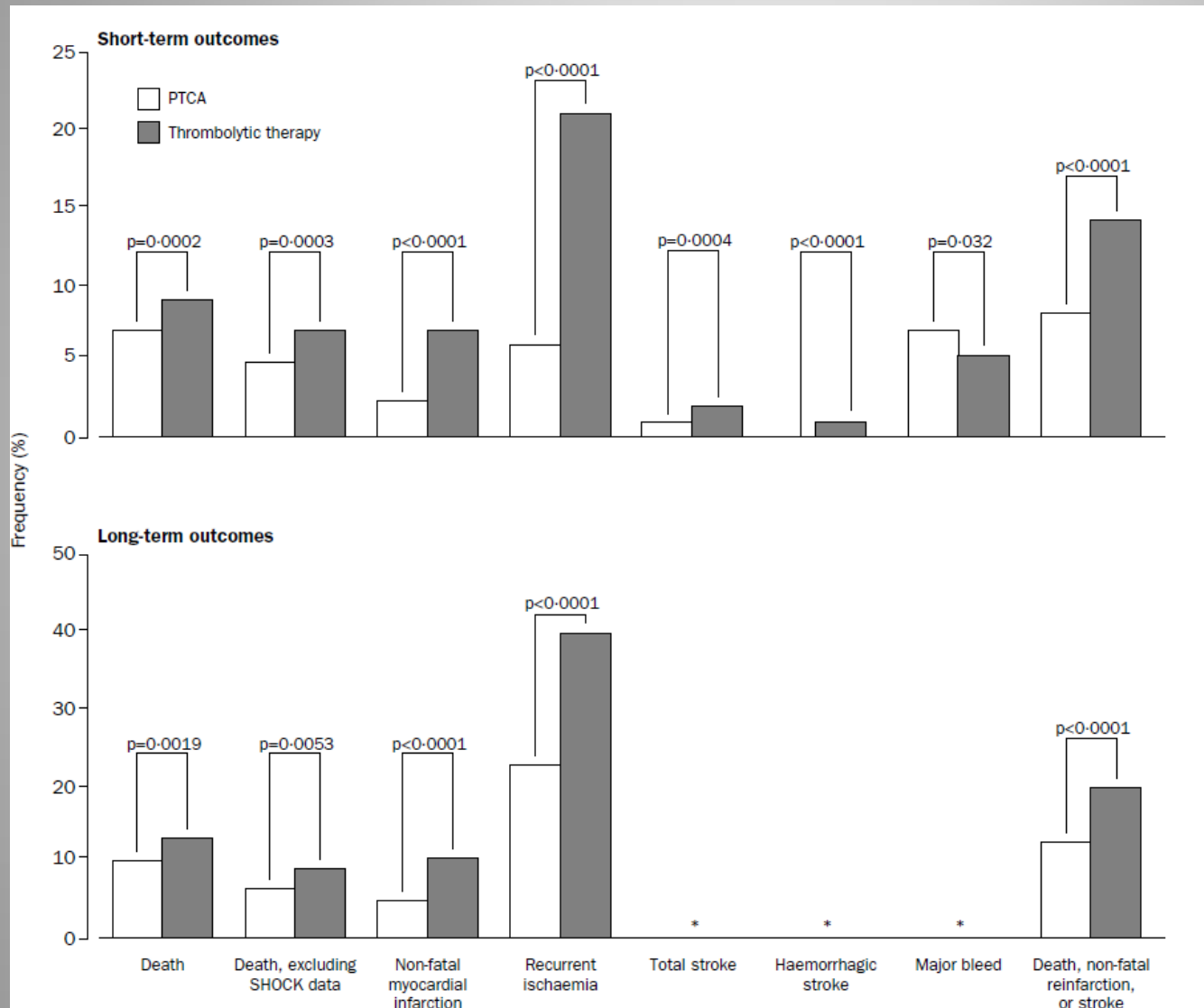
Note: Age restriction for fibrinolysis has been removed compared with prior guidelines.

Contraindications and Cautions for Fibrinolysis in STEMI

- **Relative Contraindications:**

- ❖ Severe uncontrolled hypertension on presentation (SBP > 180 or DBP > 110)
- ❖ Current use of anticoagulants
- ❖ Transient ischaemic attack in the preceding 6 months
- ❖ Traumatic or prolonged (> 10 mt.) resuscitation
- ❖ For streptokinase/anistreplase: prior exposure (> 5 days ago) or prior allergic reaction to these agents
- ❖ Pregnancy
- ❖ Active peptic ulcer

PCI IS BETTER THAN LYSIS!





Fibrinolysis preferred

- Early presentation (≤ 3 hr from symptom onset and delay to invasive strategy)
- Invasive strategy is not an option
 - Catheterization laboratory occupied or not available
 - Vascular access difficulties
 - Lack of access to a skilled PCI laboratory
- Delay to invasive strategy
 - Prolonged transport
 - (Door-to-balloon)–(door-to-needle) more than 1 hr
 - Medical contact-to-balloon or door-to-balloon more than 90 min



Invasive strategy preferred

- Skilled PCI laboratory is available with surgical backup
 - Medical contact-to-balloon or door-to-balloon less than 90 min
- High risk from STEMI
 - Cardiogenic shock
 - Killip class ≥ 3
- Contraindications to fibrinolysis
- Late presentation (> 3 hr)
- Diagnosis of STEMI is in doubt



Riassunto

Le criticità principali relative agli indicatori di processo sono:

- insufficiente utilizzo dell'ecg preH
 - insufficiente rispetto dei tempi raccomandati per la erogazione delle terapie riperfusive (PCI e fibrinolisi), in particolare nei pazienti trasferiti
- insufficiente ricorso al counselling predimissione e invio in riabilitazione

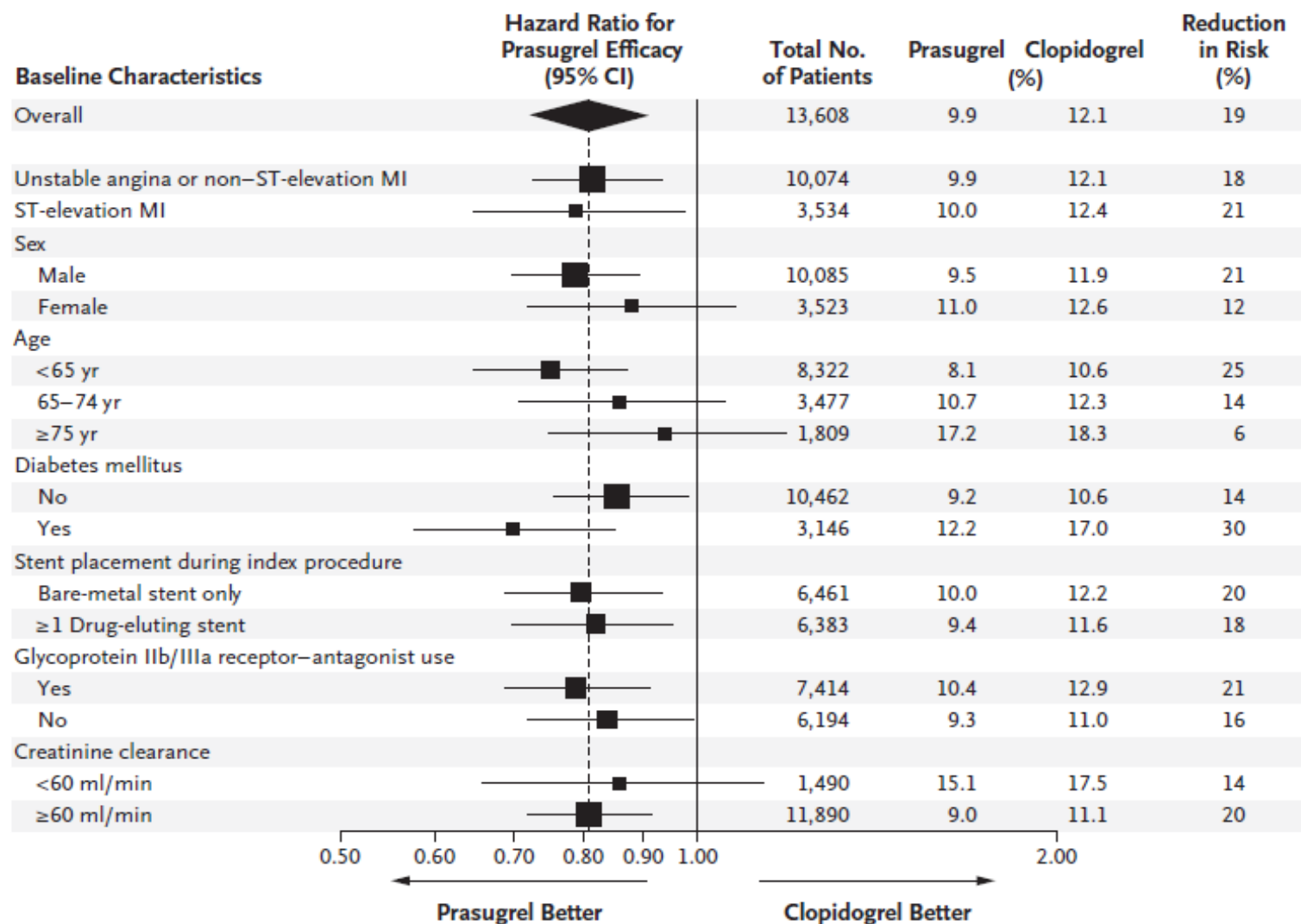


Figure 2. Hazard Ratios and Rates of the Primary End Point, According to Selected Subgroups of Study Patients.

The primary end point was defined as death from cardiovascular causes, nonfatal myocardial infarction (MI), or nonfatal stroke. The percentages are Kaplan–Meier estimates of the rate of the end point at 15 months. For each subgroup, the size of the square is proportional to the number of patients in the subgroups and represents the point estimate of the treatment effect. The overall treatment effect of prasugrel as compared with clopidogrel is represented by the diamond, and the dashed vertical line represents the corresponding overall point estimate. None of the P values for interactions were significant. Glycoprotein IIb/IIIa–receptor antagonist use was that during the index hospitalization.

HORIZONS-AMI

3 years results

