Treatment of STEMI in 2010: Management of Patients Presenting to Non-PCI Centers

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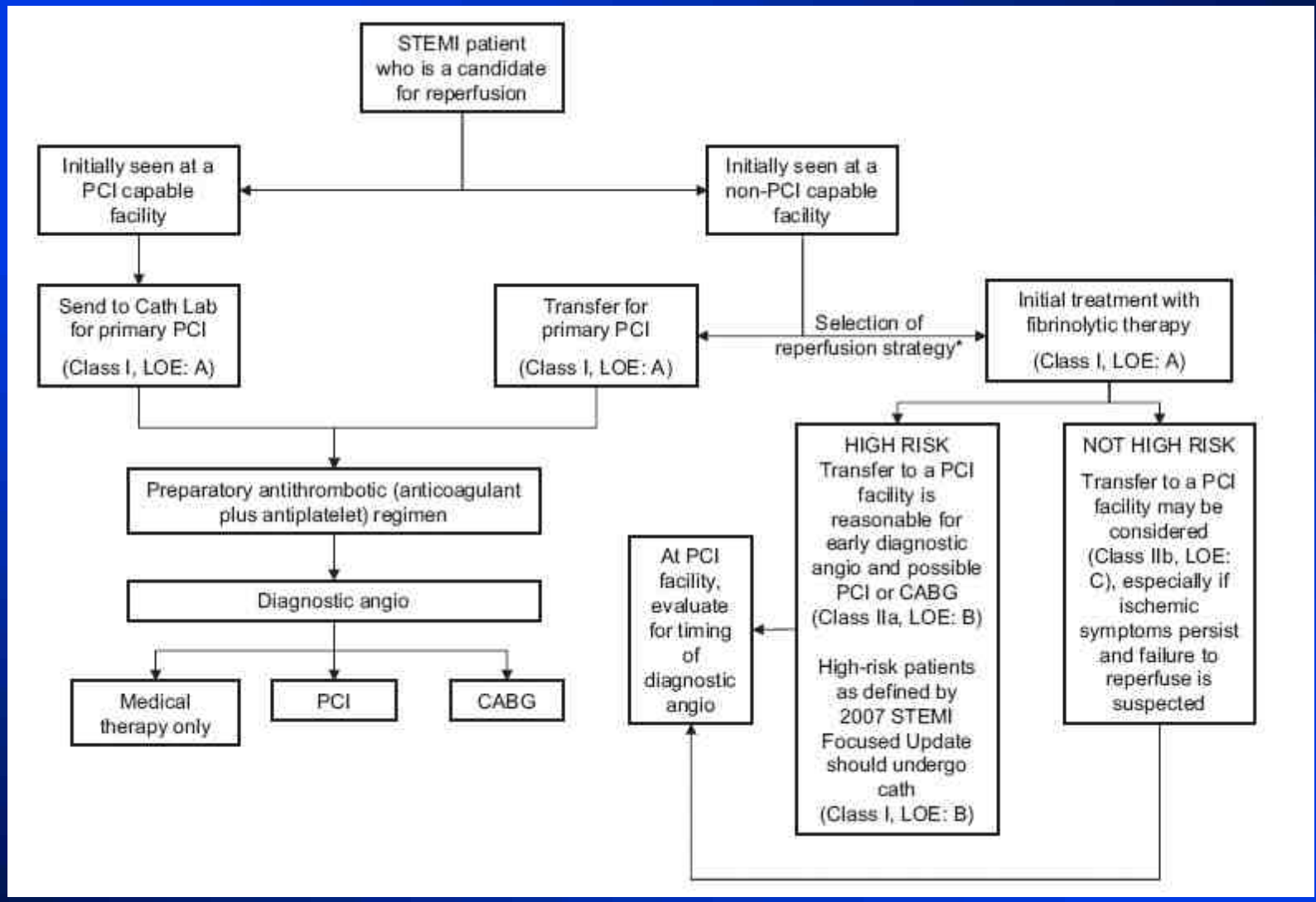
AMI Rx

Pathophysiology: The Basic Lessons of First Two Decades of Reperfusion Therapy (2004)

- Five "drivers" of mortality (age, sBP, Killip class, HR, MI location) establish baseline risk
- "Time is muscle"
  - Especially 1st 2-3 hrs
  - Maximum clinical impact is for high risk
  - Late reperfusion may still ↓infarct size, remodeling, VT/VF
- TIMI 3 flow is good
- TIMI 3 flow with microvascular perfusion is better
- Bleeding adversely impacts long term mortality
- Reinfarction is bad

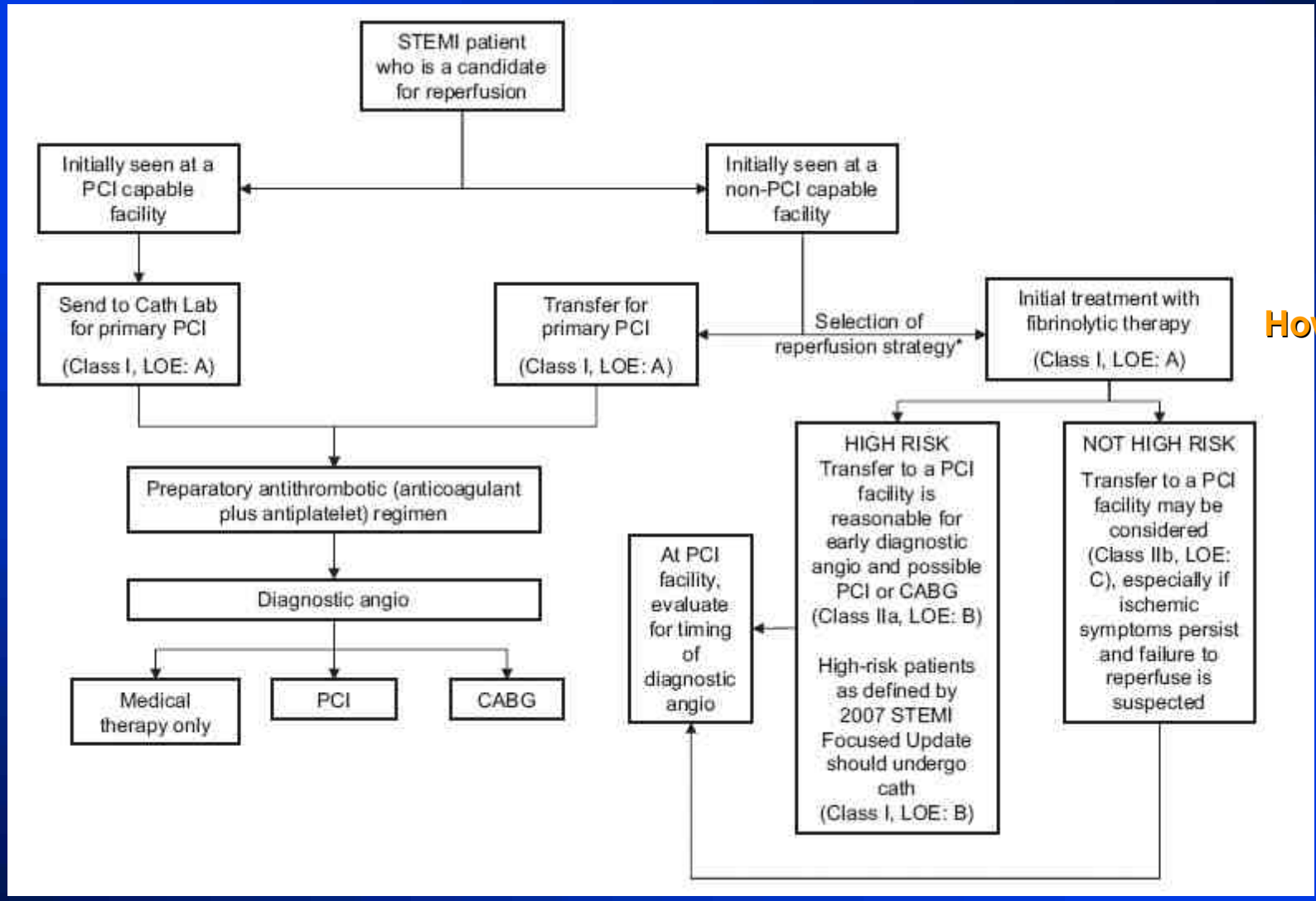
2009 ACC Guidelines: Triage and Transfer for PCI



FJ Kushner et al., 2009 STEMI Guideline Updates

SGE; 0410-1, 48

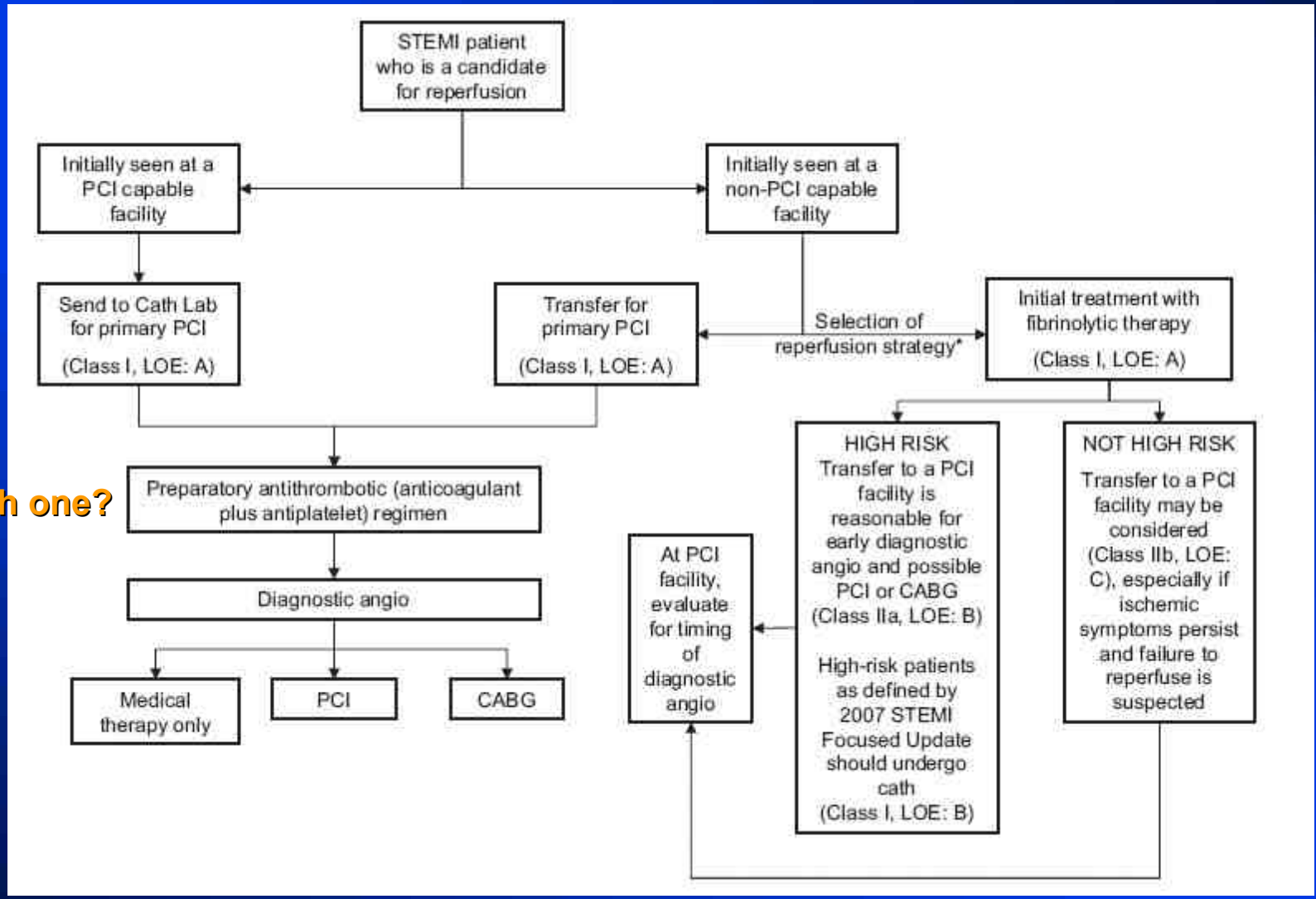
2009 ACC Guidelines: Triage and Transfer for PCI



How do you tell?

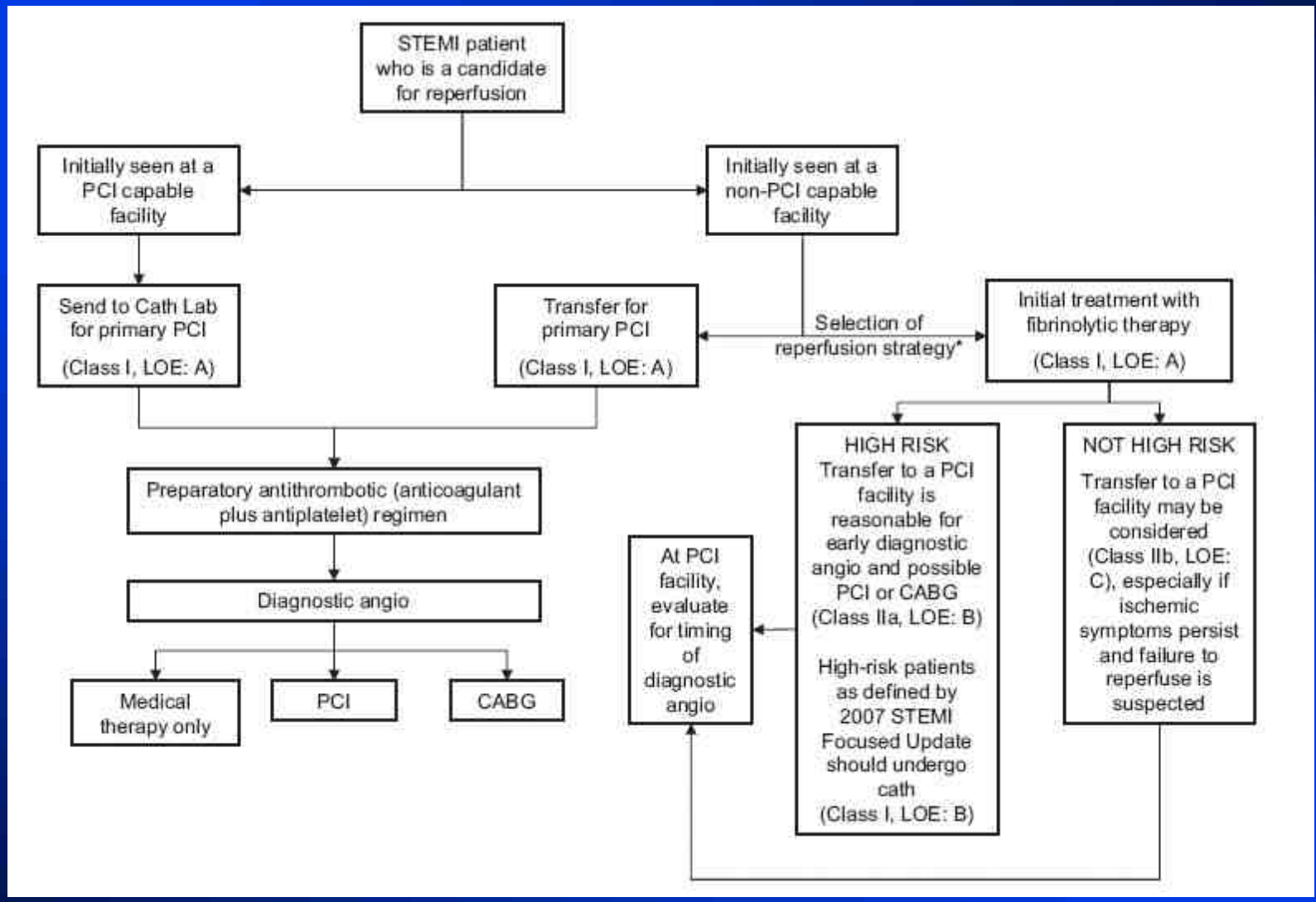
FJ Kushner et al., 2009 STEMI Guideline Updates

2009 ACC Guidelines: Triage and Transfer for PCI



FJ Kushner et al., 2009 STEMI Guideline Updates

2009 ACC Guidelines: Triage and Transfer for PCI

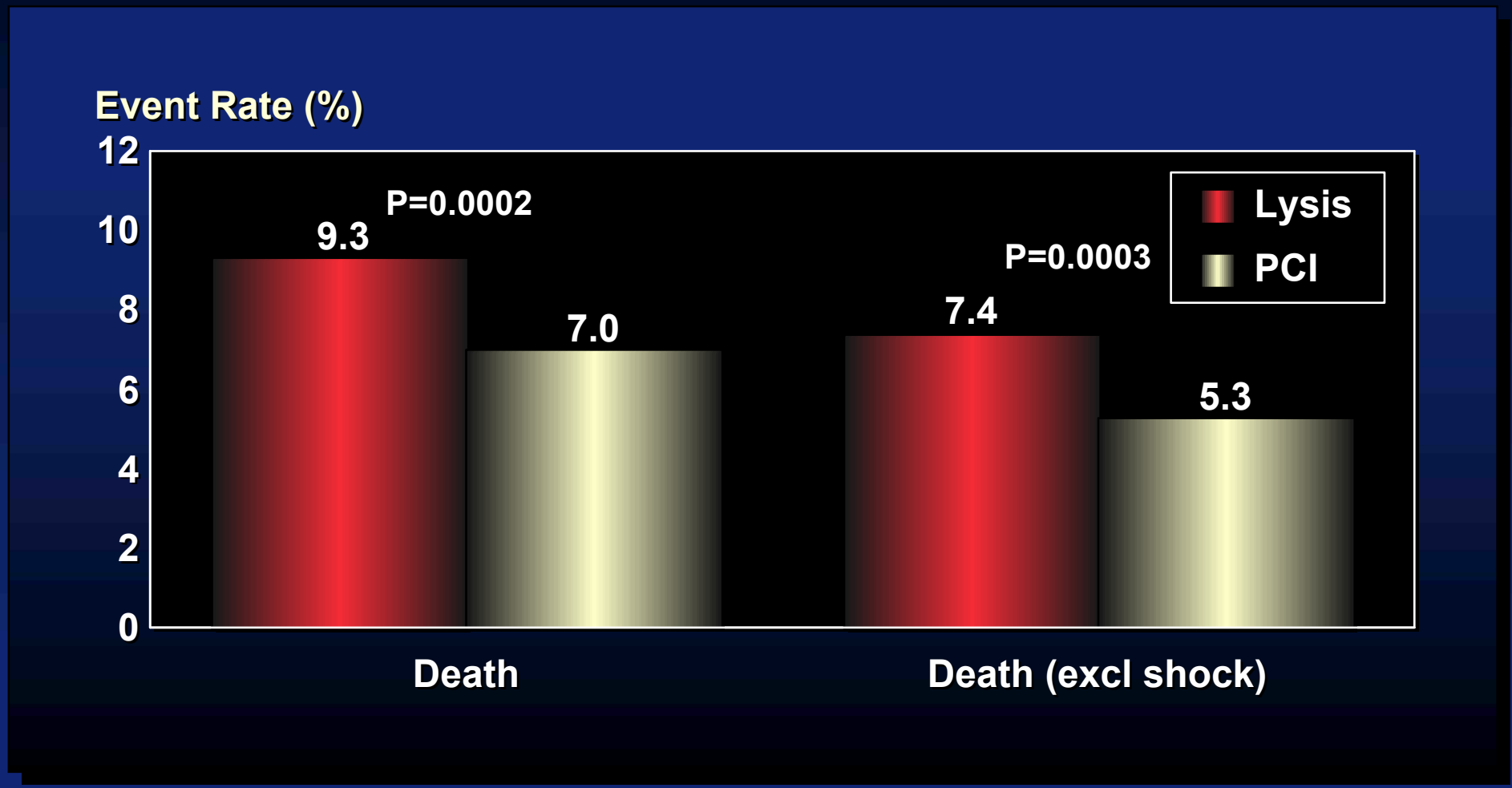


How high risk?

FJ Kushner et al., 2009 STEMI Guideline Updates

SGE; 0410-1, 48

23 Randomized Trials of PCI vs. Lysis N=7,739



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

SGE; 1006-8, 11

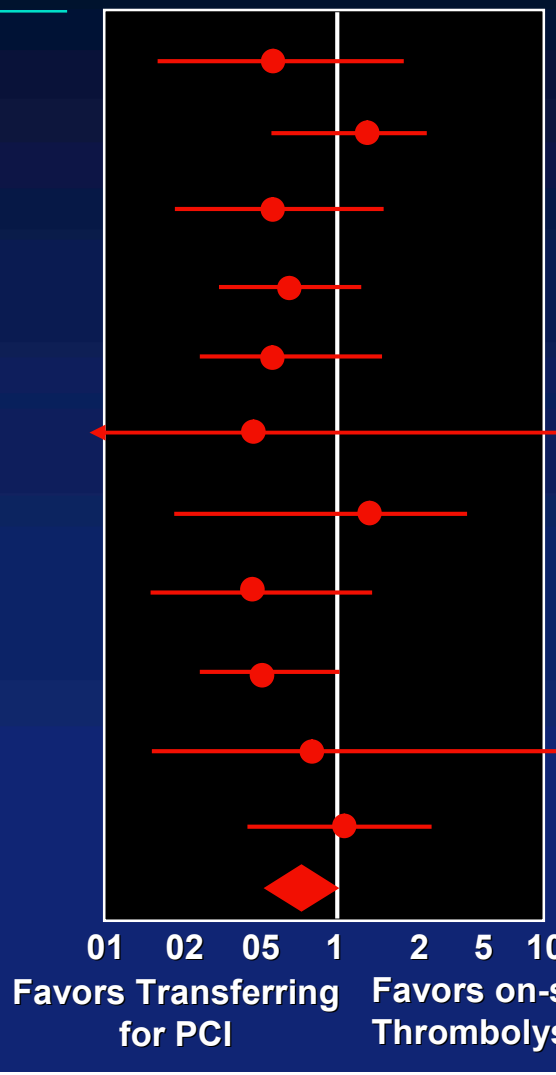
Primary PCI: Access

- 42.0% PCI hospital is closest facility
- 79.0% within 60 minute prehospital time

Nallamothu et al. Circulation 2006;113:1189

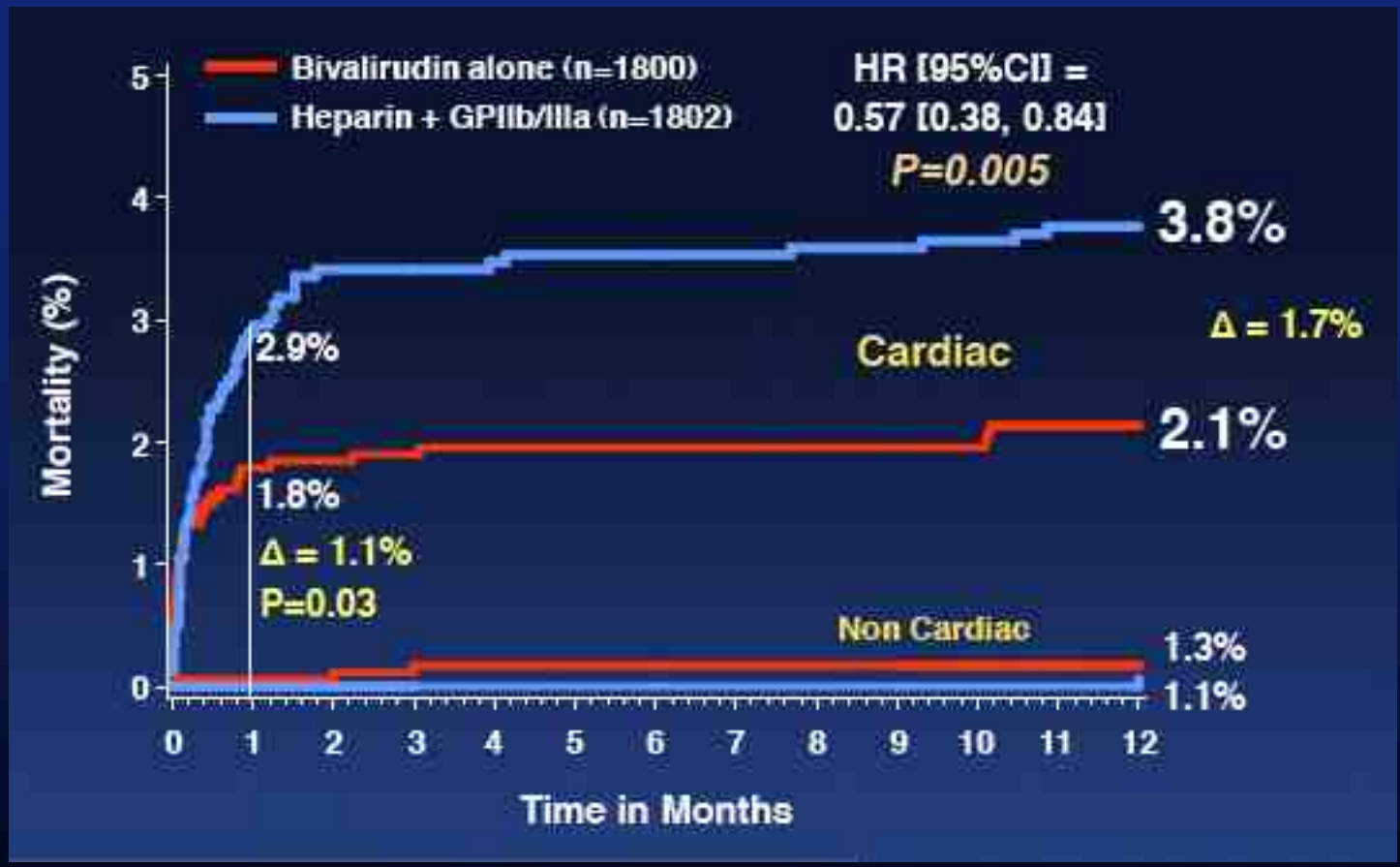
Transfer for Primary Angioplasty Versus Thrombolysis in STEMI

Study	Transferring for PCI	On Site Thrombolysis	OR (95% CI)
AIR-PAMI	6/71	8/66	0.67 (0.22,2.04)
CAPTIM	20/421	16/419	1.26 (0.64,2.46)
Caress	9/267	14/300	0.64 (0.27,1.50)
DANAMI-2	37/567	48/562	0.75 (0.48,1.17)
Dobrzycki et al	12/201	18/200	0.64 (0.30, 1.37)
HIS	1/25	2/23	0.44 (0.30,5.18)
Massirichi	11/149	5/75	1.12 (0.37,3.34)
PRAGUE	19/201	14/99	0.63 (0.30,1.32)
PRAGUE 2	29/429	42/421	0.65 (0.40,1.07)
SWEDES	3/101	4/104	0.77 (0.17,3.51)
TRANSFER-AMI	19/512	18/498	1.03 (0.53,1.98)
Total (95% CI)	166/29	189/2767	0.77 (0.62, 0.96)



Ann Emerg Med 2008:52:665

HORIZONS Trial



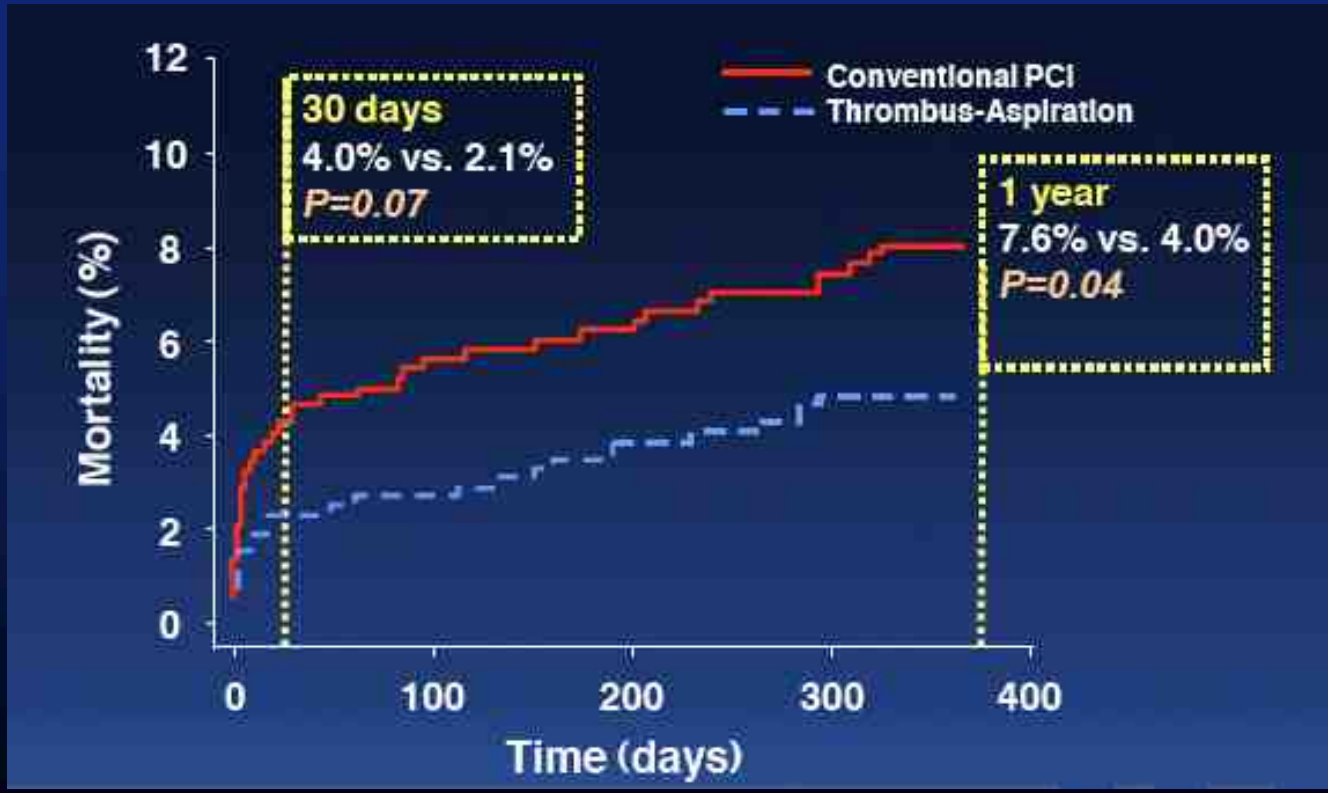
Number at risk					
Bivalirudin alone	1800	1705	1684	1669	1520
Heparin + GPIIb/IIIa	1802	1678	1663	1646	1486

SGE; 1109-9, 2

STEMI

TAPAS

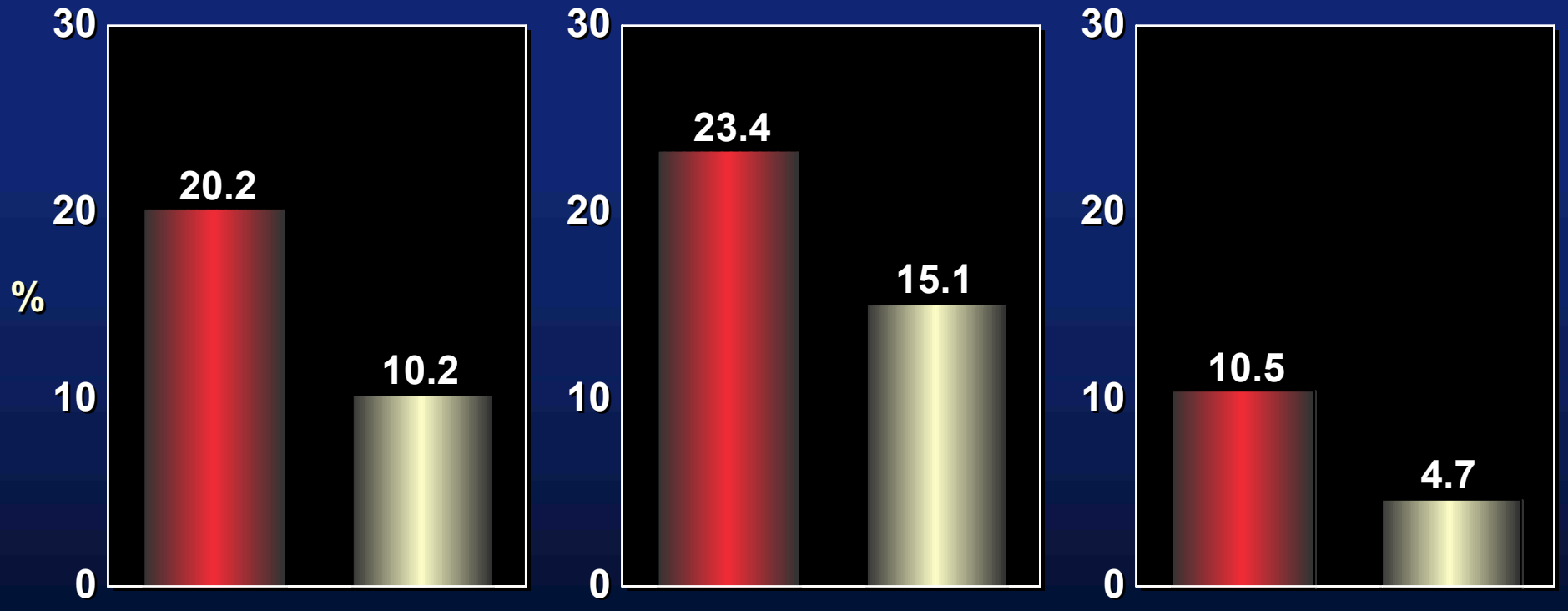
1071 pats with STEMI undergoing primary PCI randomized in the ER to manual aspiration (Export) vs Control



Vlaar et al. Lancet 2008;371:1915-920

ACS - STEMI

IC vs IV Abciximab



Wohrl. Circ '07;1084

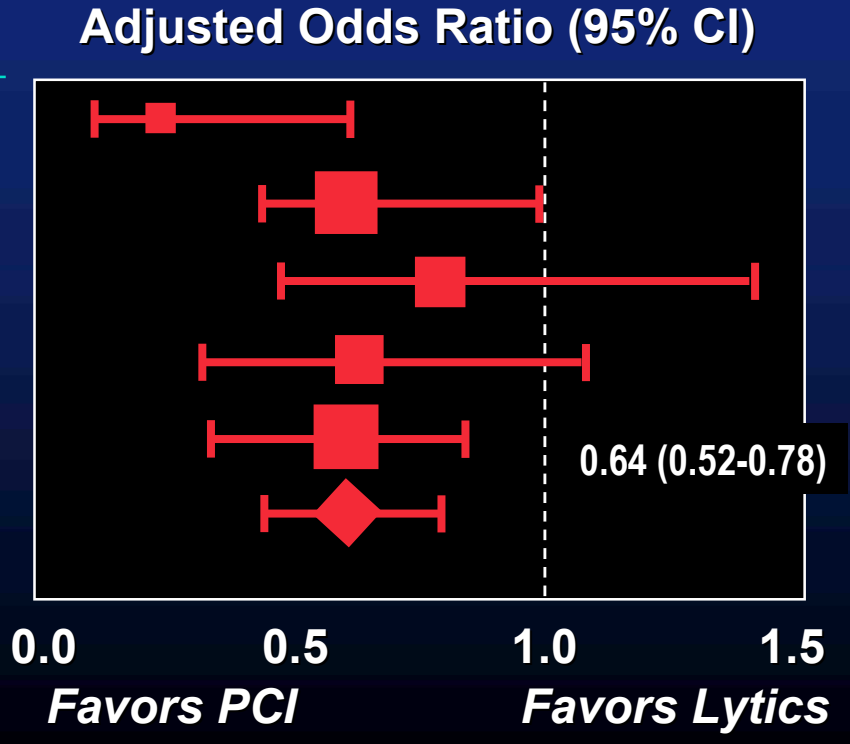
Schuler. TCT '08

Iverson, AHA '09
Circ 126:5999

SGE; 1109-9, 33

PCAT 2: PCI Delay and Baseline-Adjusted Risk of 30-day Mortality

PCI Related Delay	n	30d death		Absolute difference (%)
		Lytic	PCI	
0-30’	669	9.3	3.3	6.0
>30-45’	2,173	7.0	4.7	2.3
>45-60’	1,254	5.7	5.0	0.7
>60-75’	1,197	9.0	6.7	2.3
>75’	1,610	9.5	6.4	3.1
All Pts	6,903	7.9	5.4	2.5

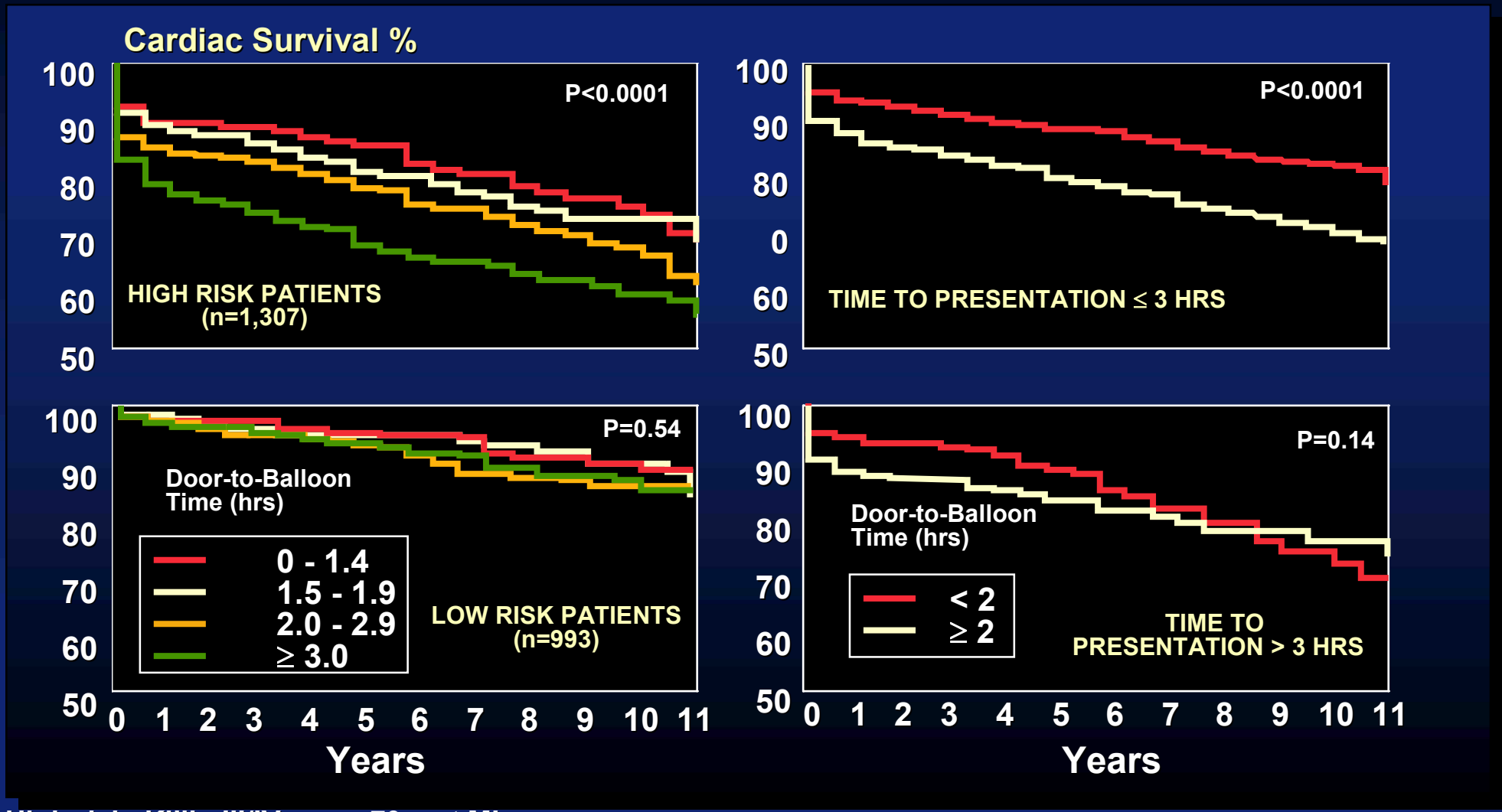


Boersma E et al. TCT 2005

SGE; 1006-8, 14

Primary PCI

Door → Balloon Time - Importance of Risk & Time to Presentation

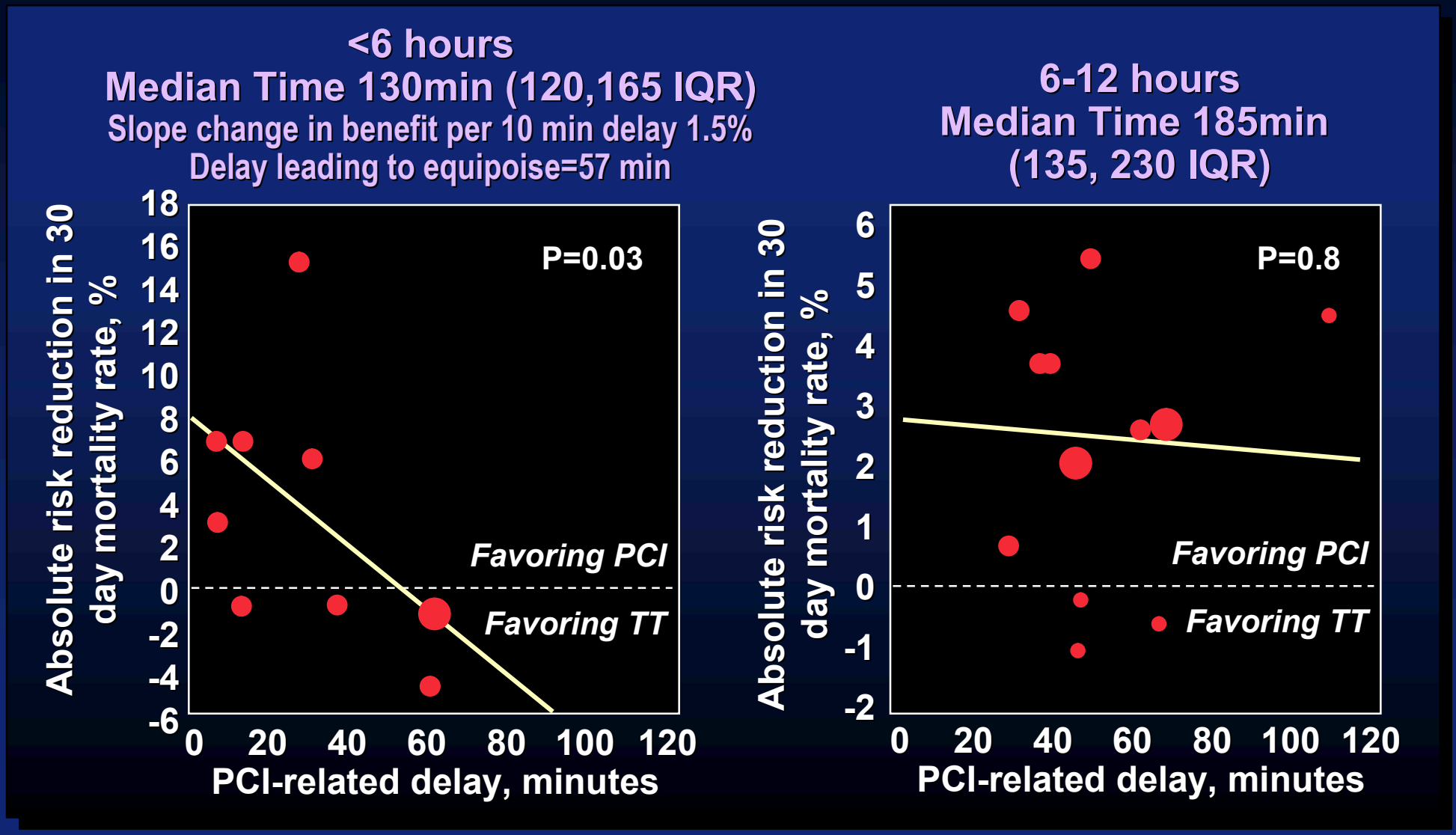


High risk: Killip III/IV, age >70, ant MI

Brodie JACC 2006;47:289

SGE; 0106-4, 5

Symptom Onset

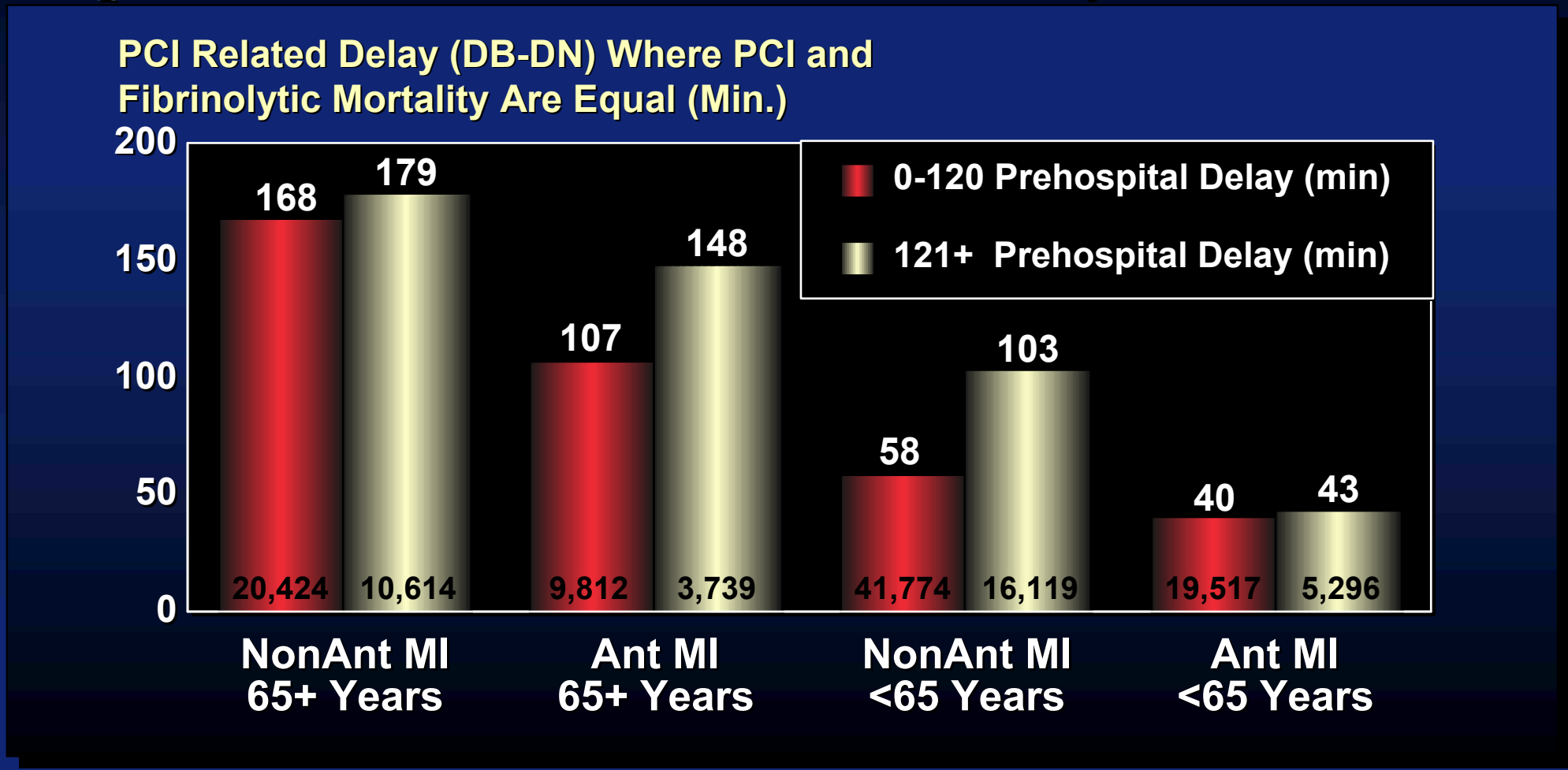


Tarantini et al Circulation 2004;110:III-539

SGE; 1006-8, 10

Primary PCI

Impact of Door to Balloon Time Delays

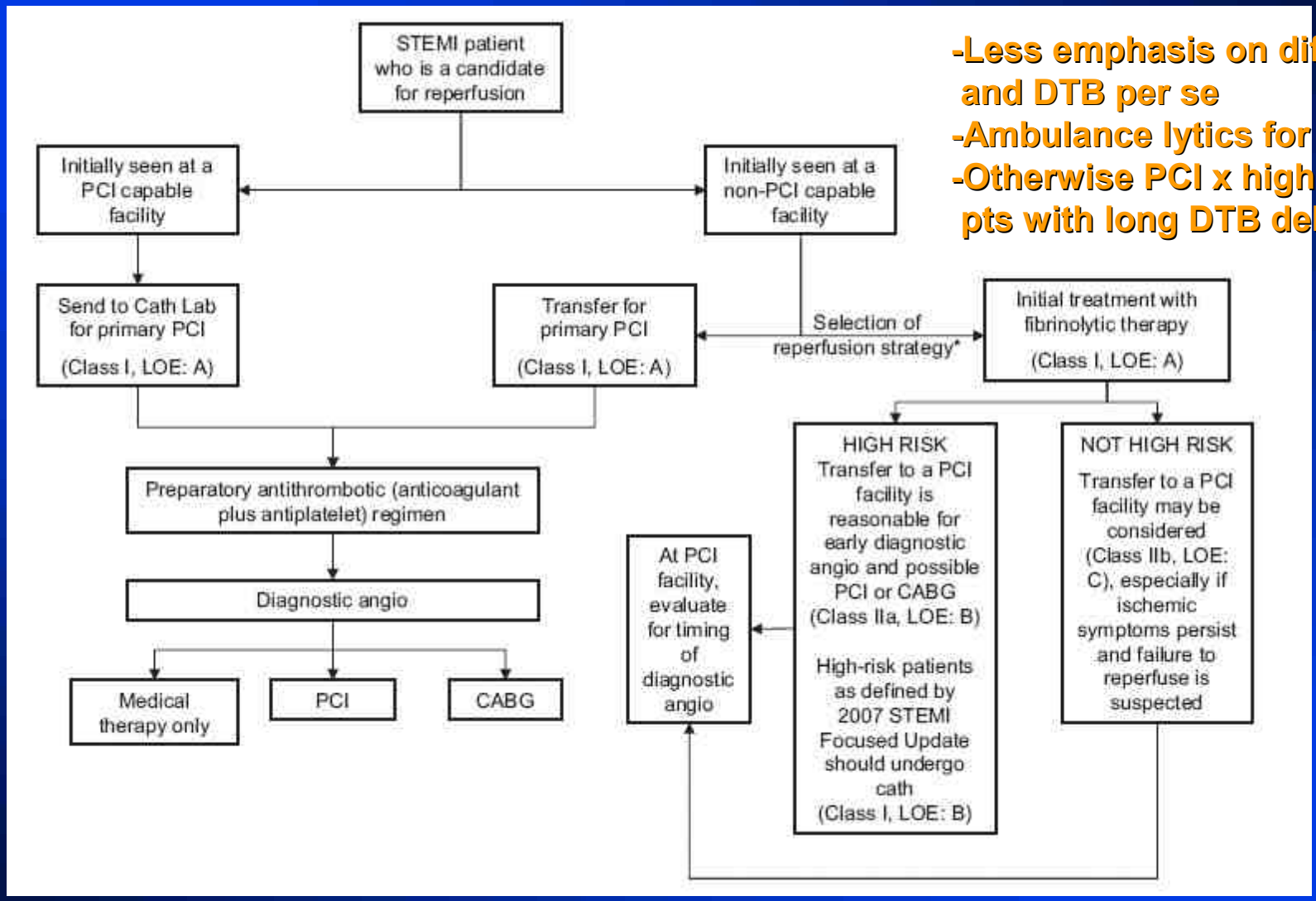


NRMI 2-4:192,509 patients

Pinto, Circ 114:2019 '06

SGE; 1007-6, 1

2009 ACC Guidelines: Triage and Transfer for PCI



-Less emphasis on difference between DTN and DTB per se
-Ambulance lytics for presenting w/i< 1-2 hrs
-Otherwise PCI x high risk, early presenting pts with long DTB delay

FJ Kushner et al., 2009 STEMI Guideline Updates

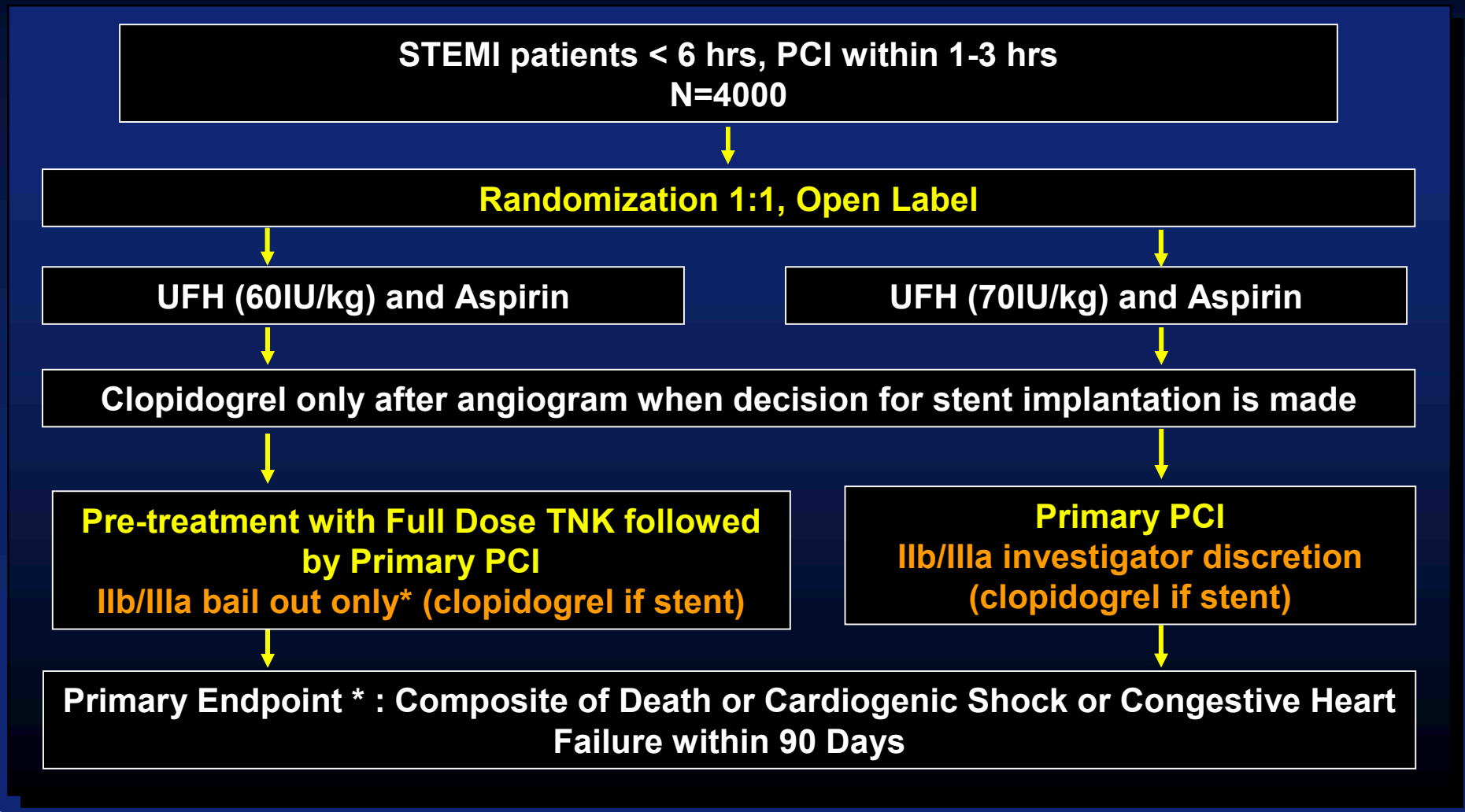
PCI After Lytics

Facilitated PCI/Rationale

- Early reperfusion salvages myocardium
- In many areas, door to balloon times exceed ACC recommended <90 min
- Some combination of antiplatelet + lytic treatment can open IRA before PCI in many cases

ASSENT IV - Trial Design

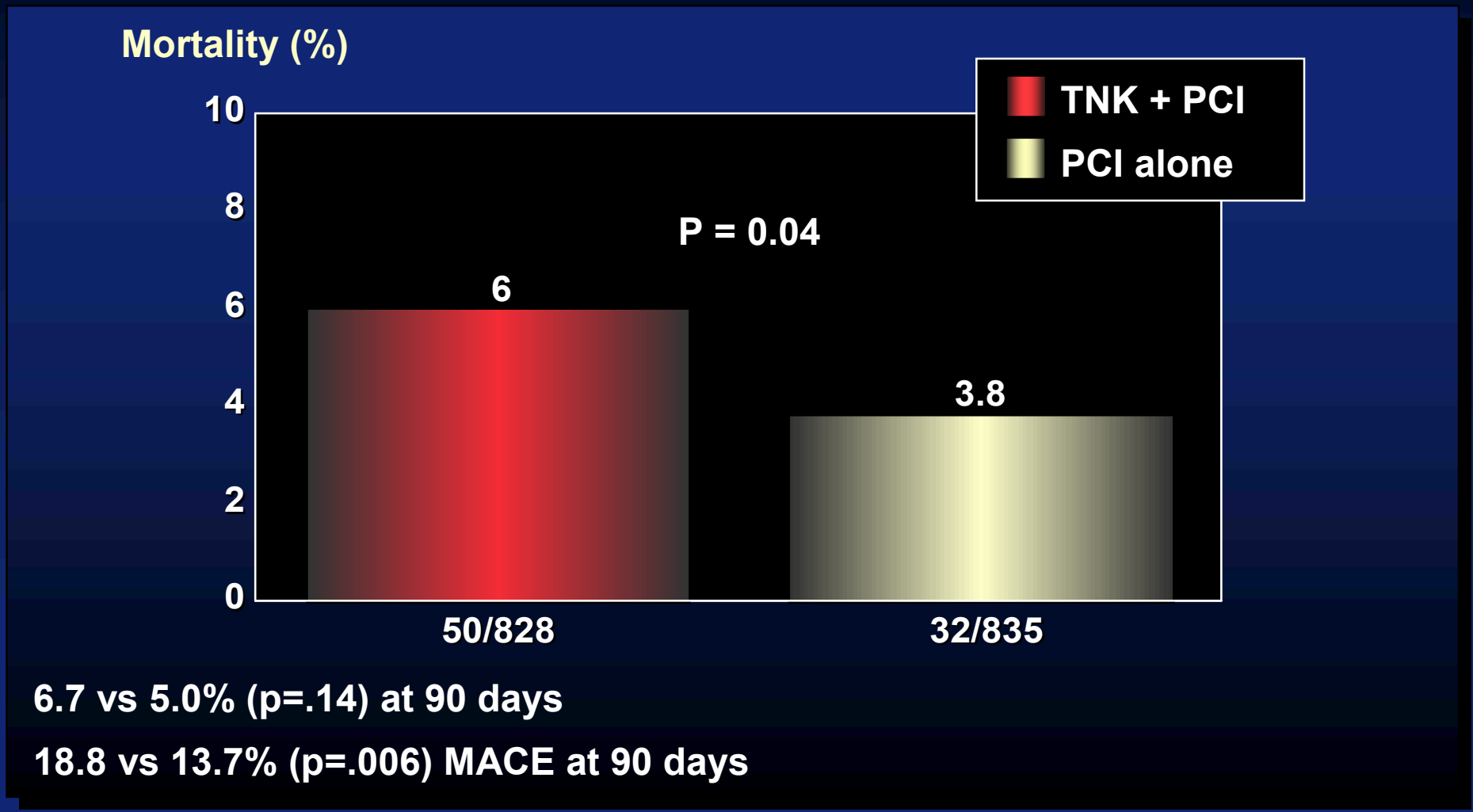
ASSENT IV Study Design



**Used in only 9.6%*

Stopped on Basis of Mortality at 30 Days

ASSENT IV Preliminary Data



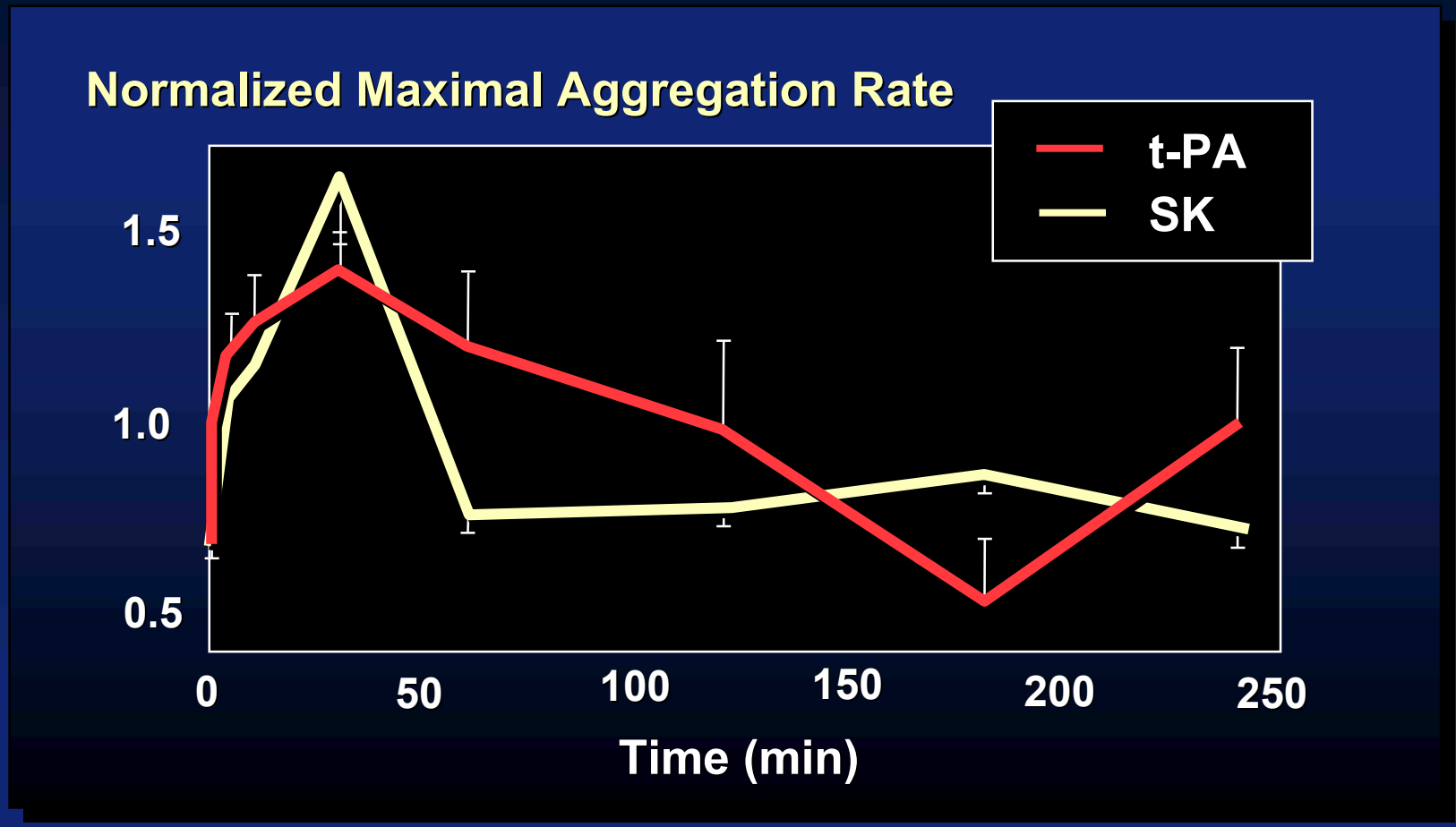
6.7 vs 5.0% (p=.14) at 90 days

18.8 vs 13.7% (p=.006) MACE at 90 days

Van de Werf ESC 2005

Acute MI

Platelet Activation by Fibrinolytics



Rabbit model, .05mM ADP as agonist

Rudd and Loscalzo, CircRes '90

FINESSE: Study Design

Acute ST Elevation MI (or New LBBB*) within 6h pain onset
Presenting at Hub or Spoke with estimated time to PCI between 1 and 4 hours

*Localized IMI excluded

Randomize 1:1:1
N=3000

*Only 5U if ≥75

Placebo Placebo	Placebo Abciximab	Reteplase (5U+5U)* Abciximab

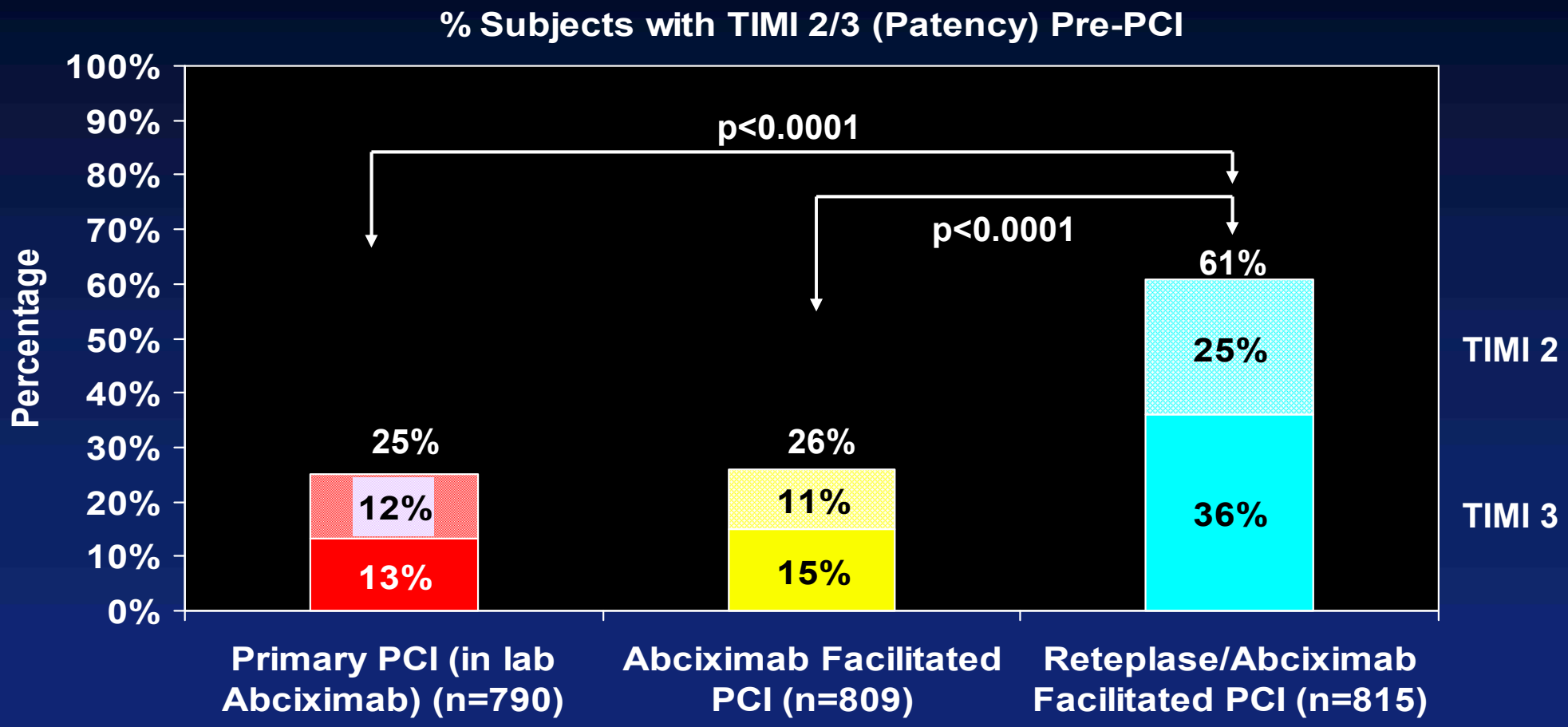
Transfer To Cath Lab
ASA, unfractionated heparin 40U/kg (max 3000u)
or enoxaparin (0.5 mg/kg IV + 0.3 mg/kg SC) – substudy only

Abciximab	Placebo	Placebo

Primary PCI with Abciximab Infusion (12 h)

Primary endpoint at 90 days: All-cause mortality, resuscitated VF occurring > 48H, cardiogenic shock, or readmission/ED visit for CHF

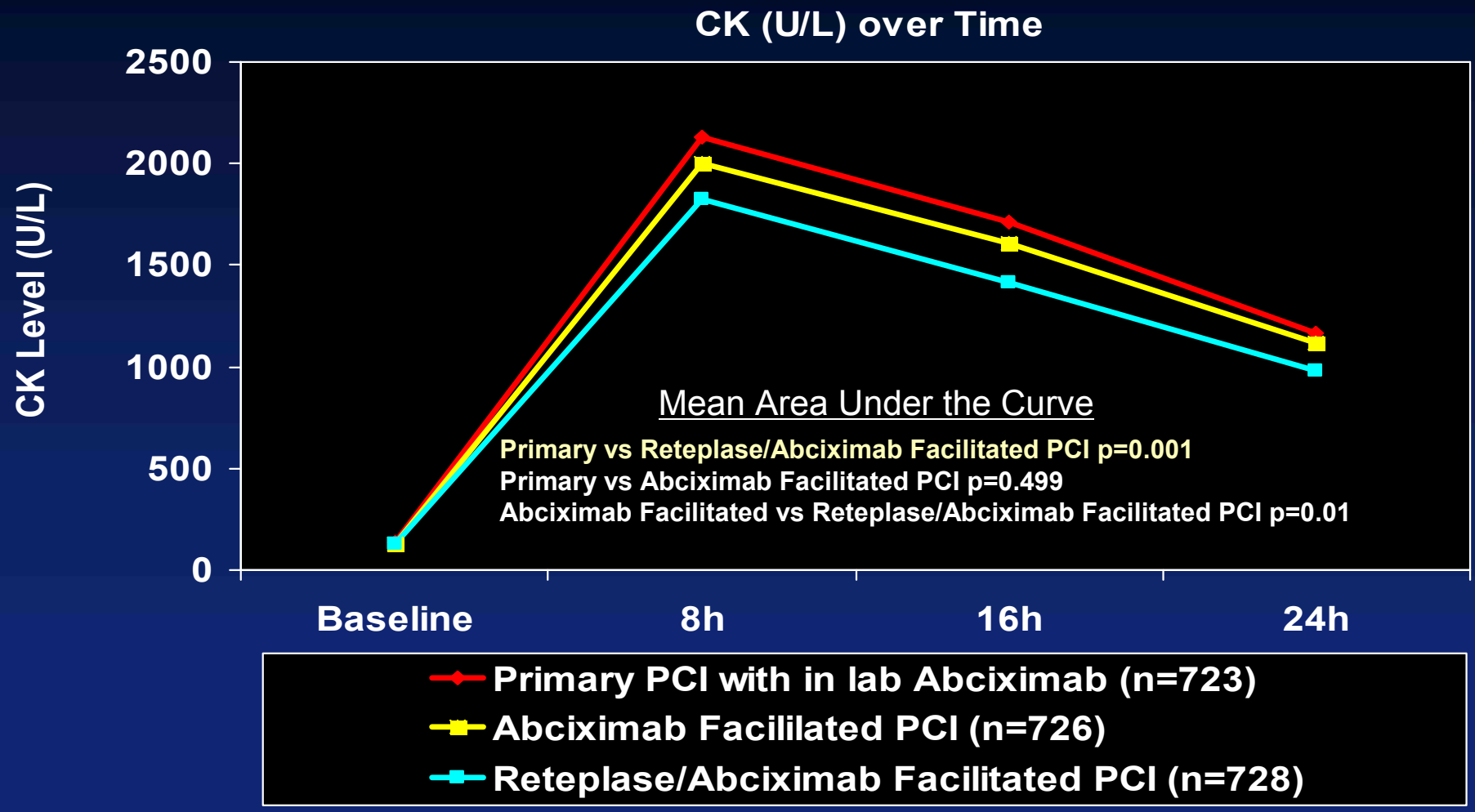
TIMI Flow in IRA Pre-PCI



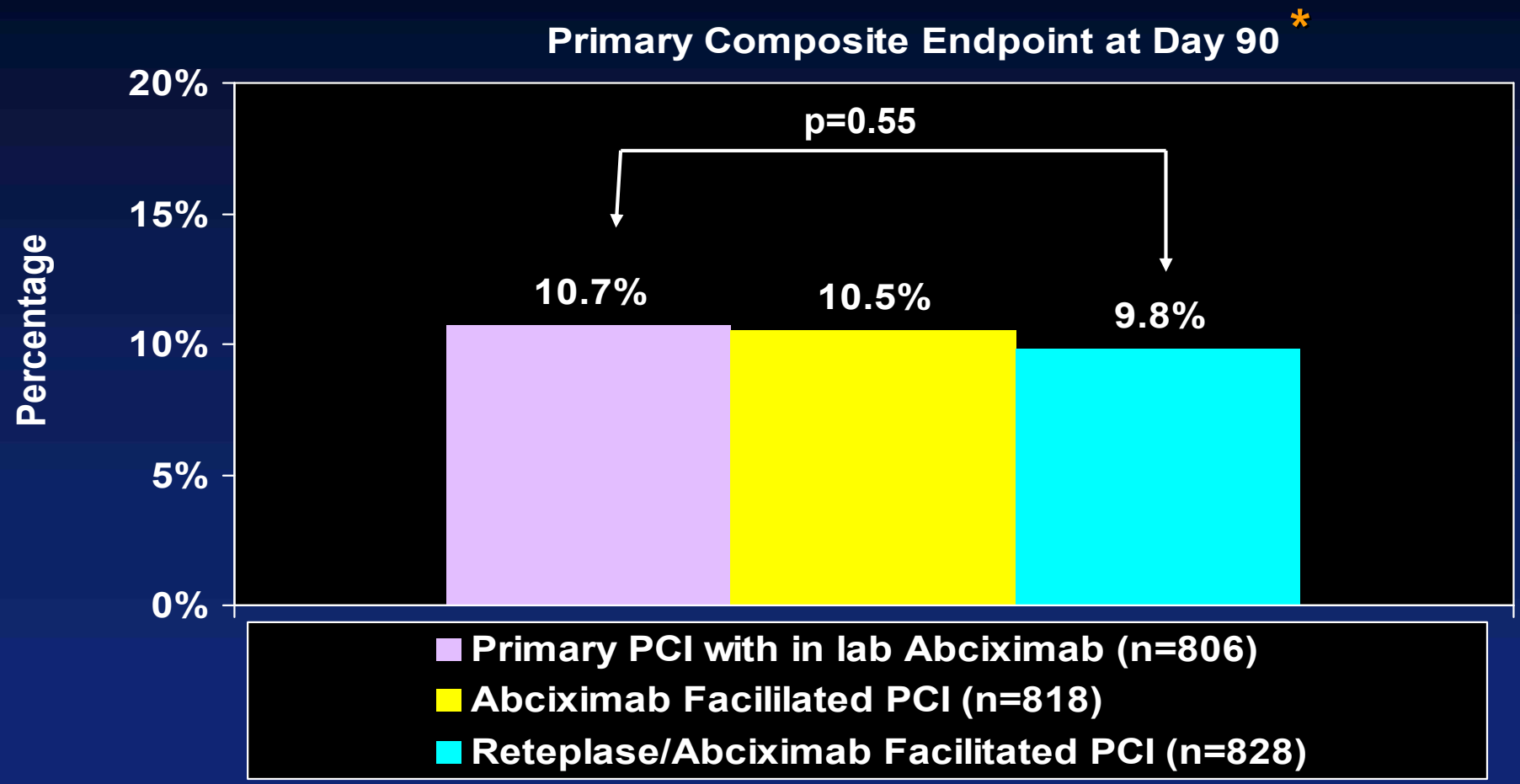
Ave Time from First Abciximab Bolus to Angiogram In Facilitated Groups:	74min	76min

Modified ITT Population with Index PCI: ITT, PCI and any dose of study drug (active or placebo); Investigator assessment

Time Course of CK (Median)

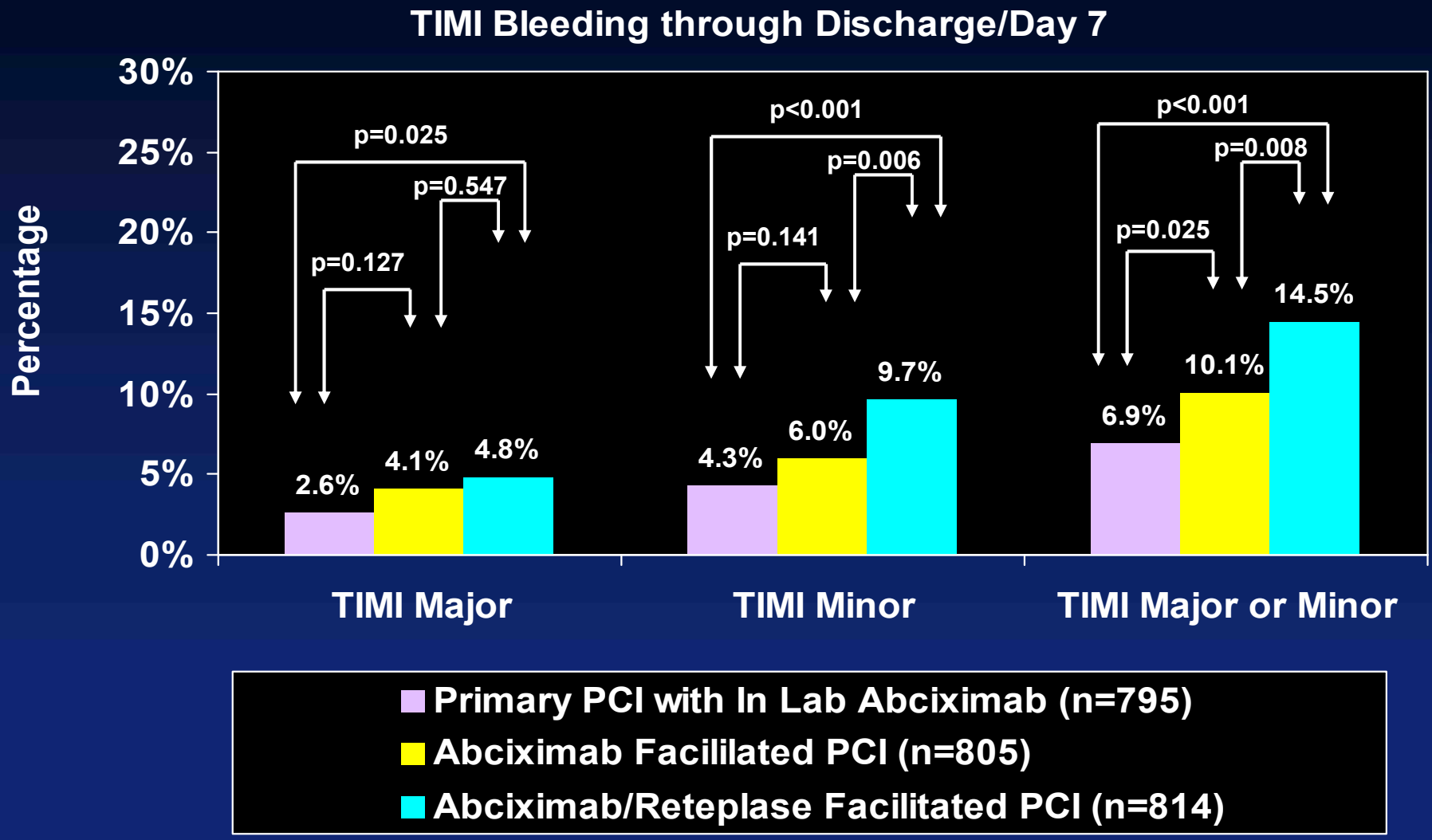


Primary Endpoint

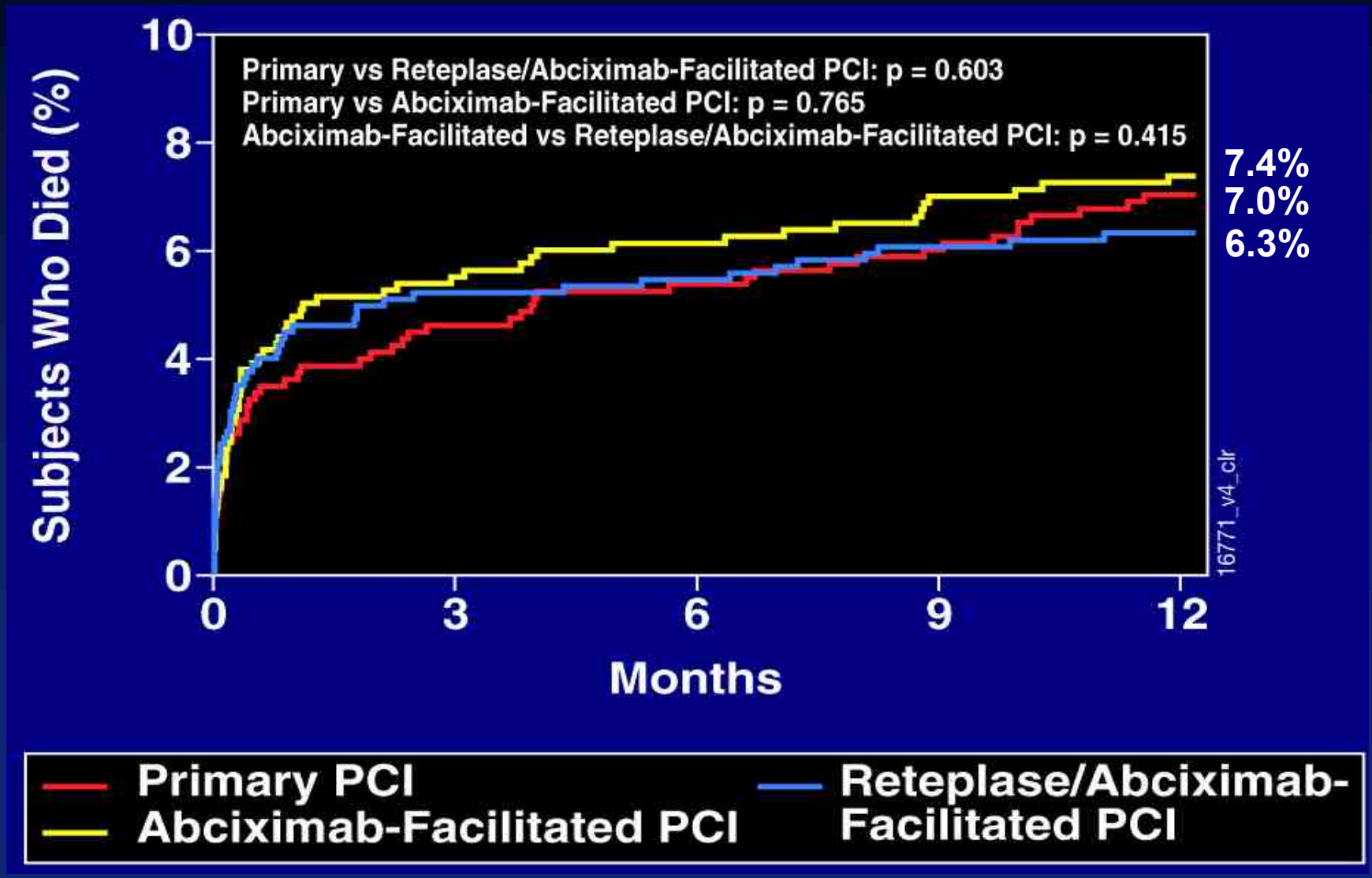


* Death< HF, shock or VT/VF > 48 hrs

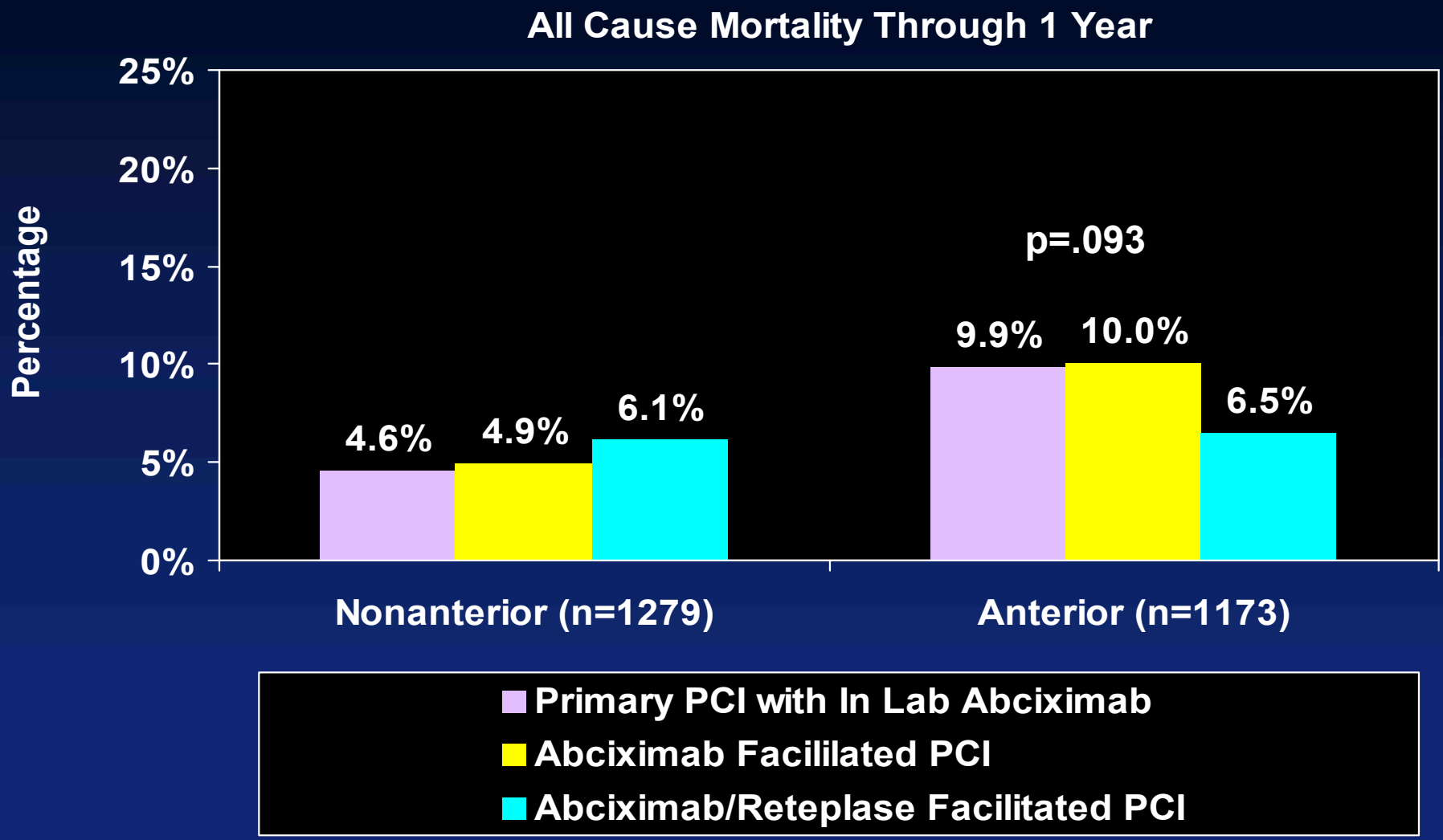
TIMI Major or Minor Bleeding (nonintracranial) through Discharge/Day7



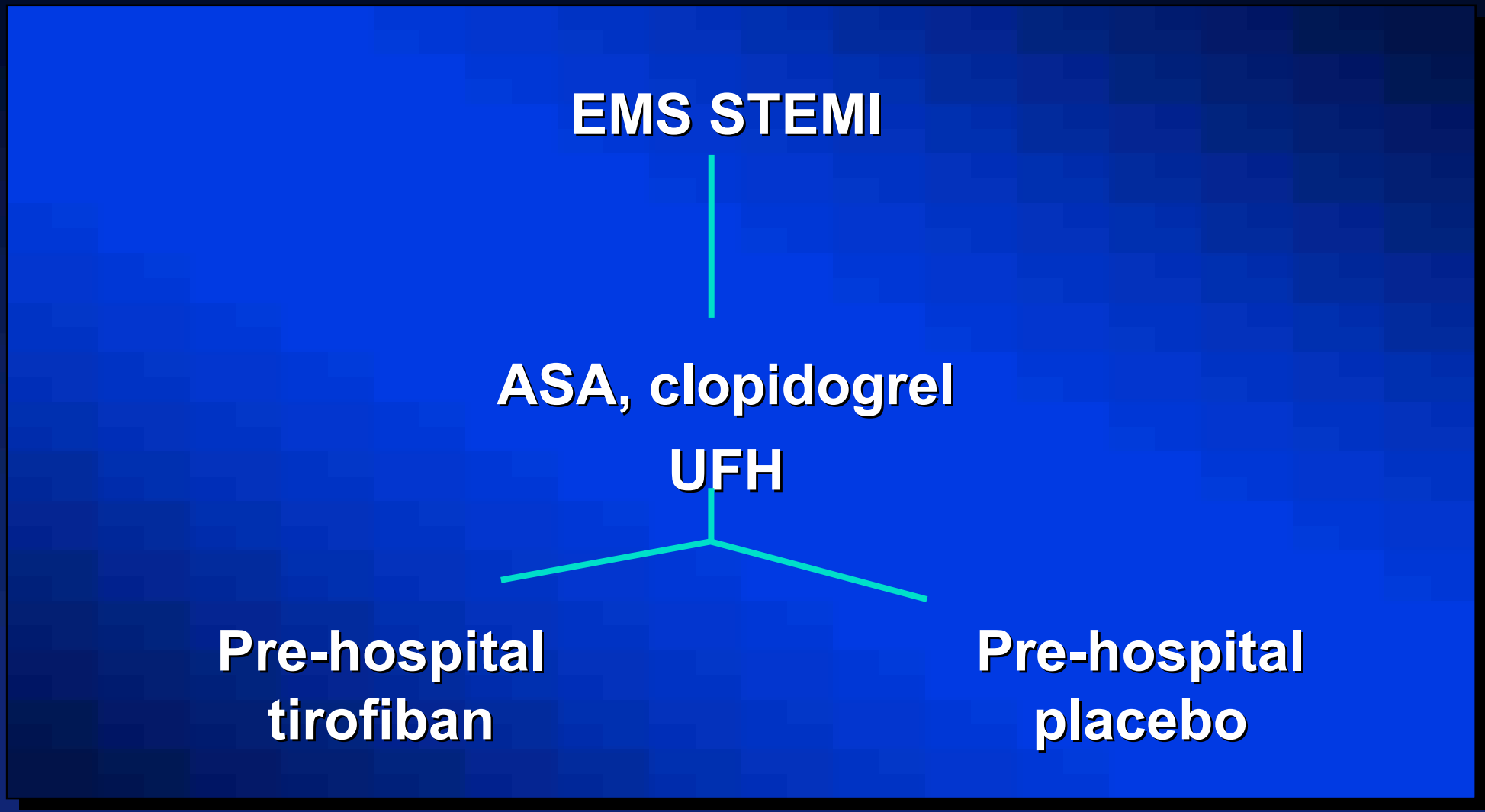
All Cause Mortality Through 1 Year



1 Year Mortality by Infarct Location



On-TIME 2: Study Design

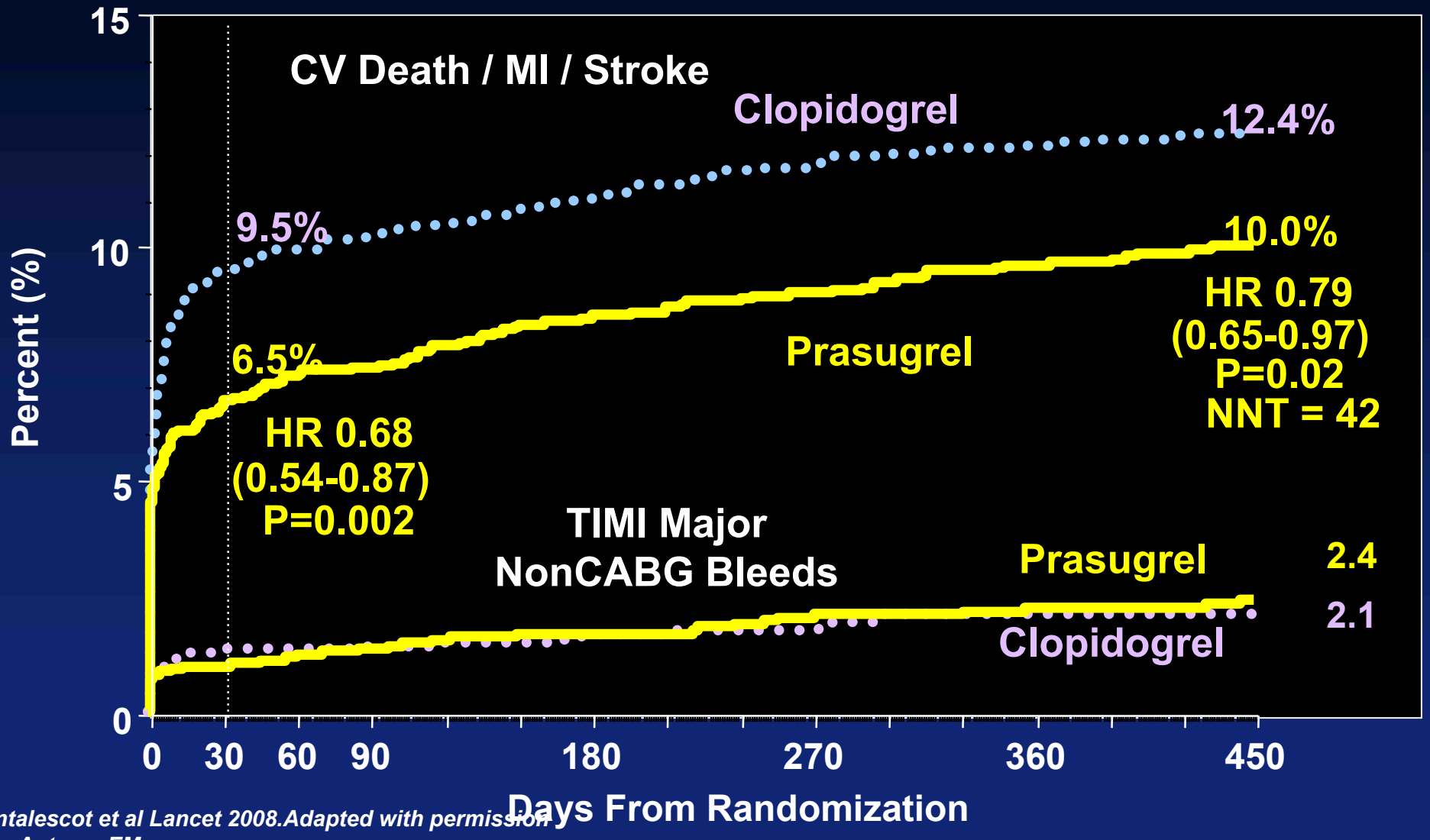


On-TIME 2: Clinical Events

	Placebo (n=477)	Tirofiban (n=473)	p value
Clinical outcome			
Death/recurrent MI/urgent TVR or thrombotic bail-out	157/477 (32·9%)	123/473 (26·0%)	0·020
Death/recurrent MI or urgent TVR	39/477 (8·2%)	33/473 (7·0%)	0·485
Death	19/477 (4·0%)	11/473 (2·3%)	0·144
Recurrent MI	14/477 (2·9%)	13/473 (2·7%)	0·863
Urgent TVR	20/477 (4·2%)	18/473 (3·8%)	0·761
Urgent PCI	19/477 (4·0%)	11/473 (2·3%)	0·144
Urgent CABG	1/477 (0·2%)	7/473 (1·5%)	0·038
Thrombotic bail-out	140/492 (28·5%)	97/488 (19·9%)	0·002
TIMI flow grade 0–2 or slow reflow	45/492 (9·1%)	29/488 (5·9%)	0·058
Dissection	6/492 (1·2%)	5/488 (1·0%)	0·722
Distal embolisation	58/492 (11·8%)	44/488 (9·0%)	0·155
Side-branch closure	4/492 (0·8%)	3/488 (0·6%)	1·000
Abrupt closure of culprit vessel	11/492 (2·2%)	1/488 (0·2%)	0·004
Clinical instability	15/492 (3·0%)	13/488 (2·7%)	0·718
Prolonged ischaemia	4/492 (0·8%)	4/488 (0·8%)	1·000

TRITON TIMI-38

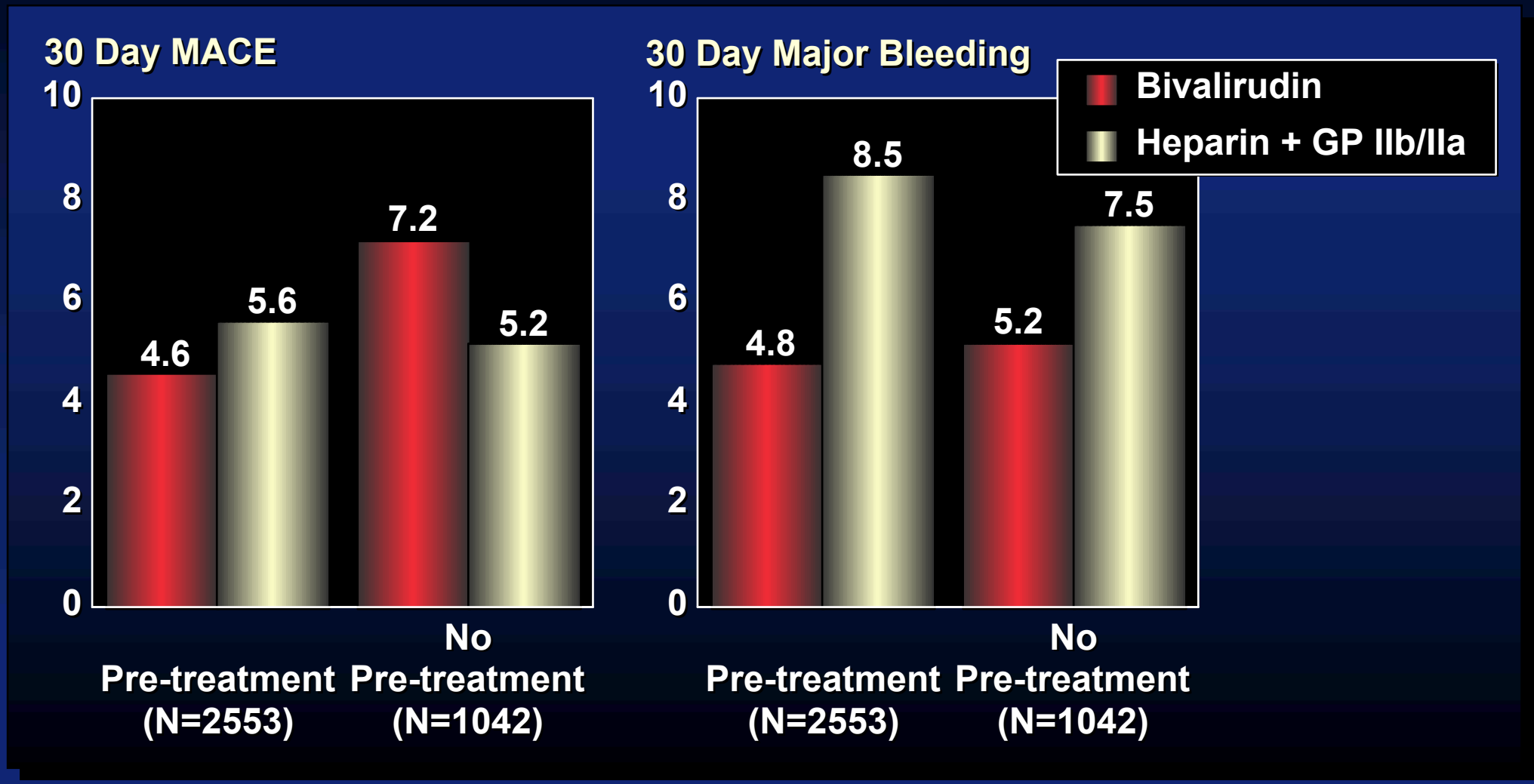
STEMI Cohort N=3534



Montalescot et al Lancet 2008.Adapted with permission from Antman EM.

SGE; 0410-8, 31

Impact of Pre-randomization Heparin in the HORIZONS-AMI Trial

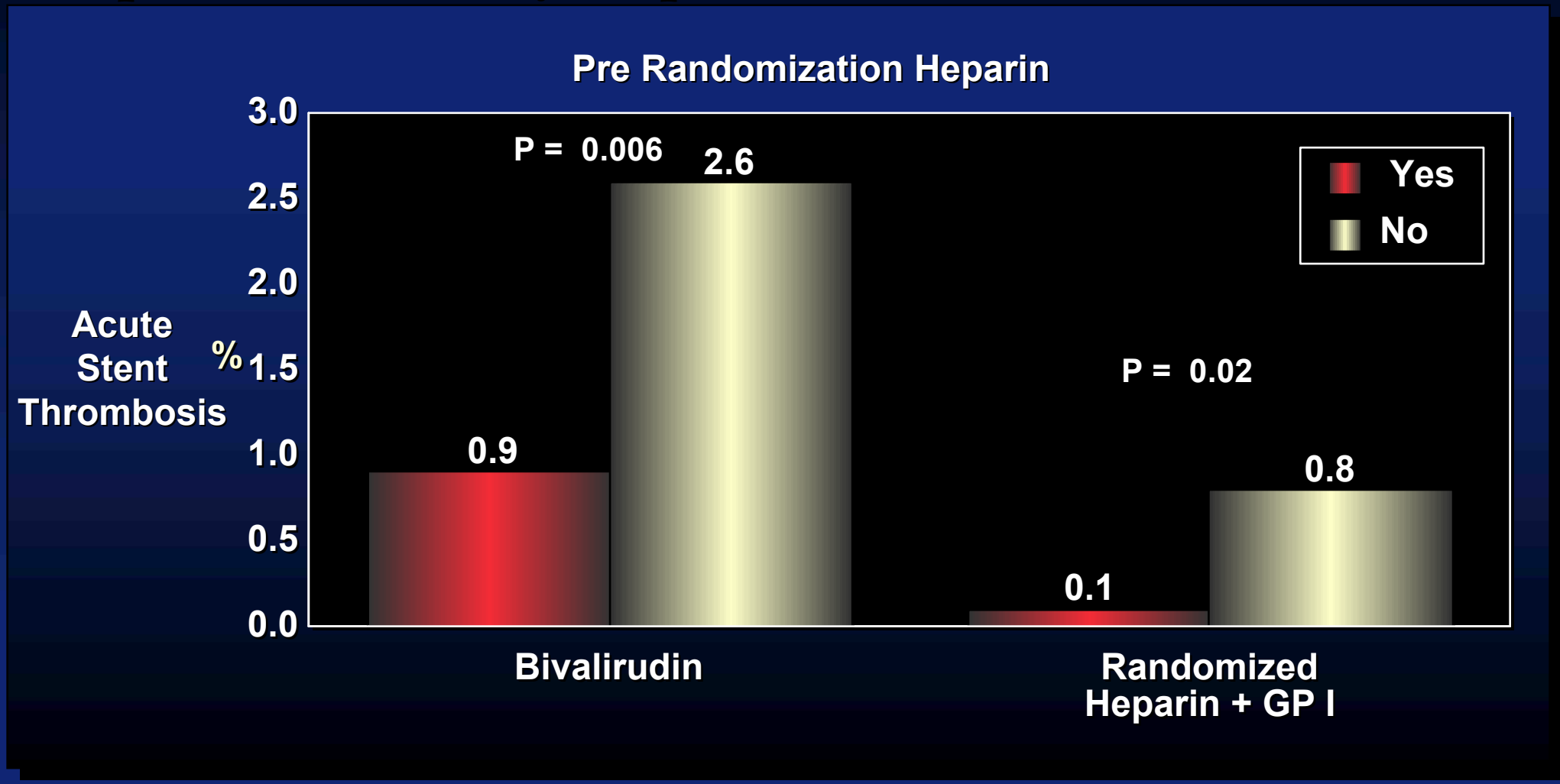


Astroulakis Z, Hill JM, Eur Heart J Suppl 2009;11:C13-C18

SGE; 0310-3, 71

STEMI

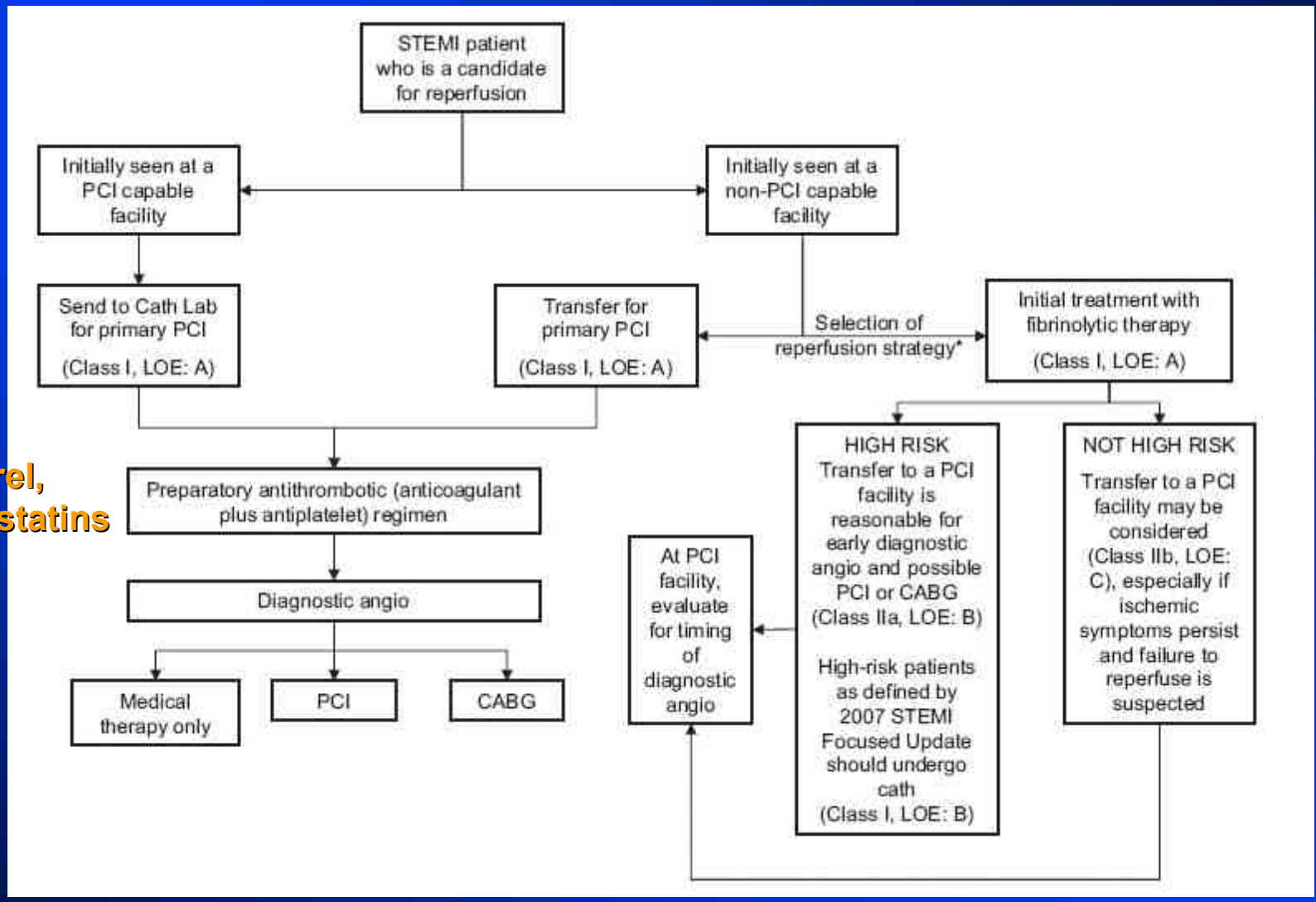
Importance of Early Heparin Administrative/Horizons



Dangas, ACC 2009

SGE; 0310-3, 72

2009 ACC Guidelines: Triage and Transfer for PCI



ASA, Prasugrel, heparin, BB, statins

FJ Kushner et al., 2009 STEMI Guideline Updates

SGE; 0410-1, 48

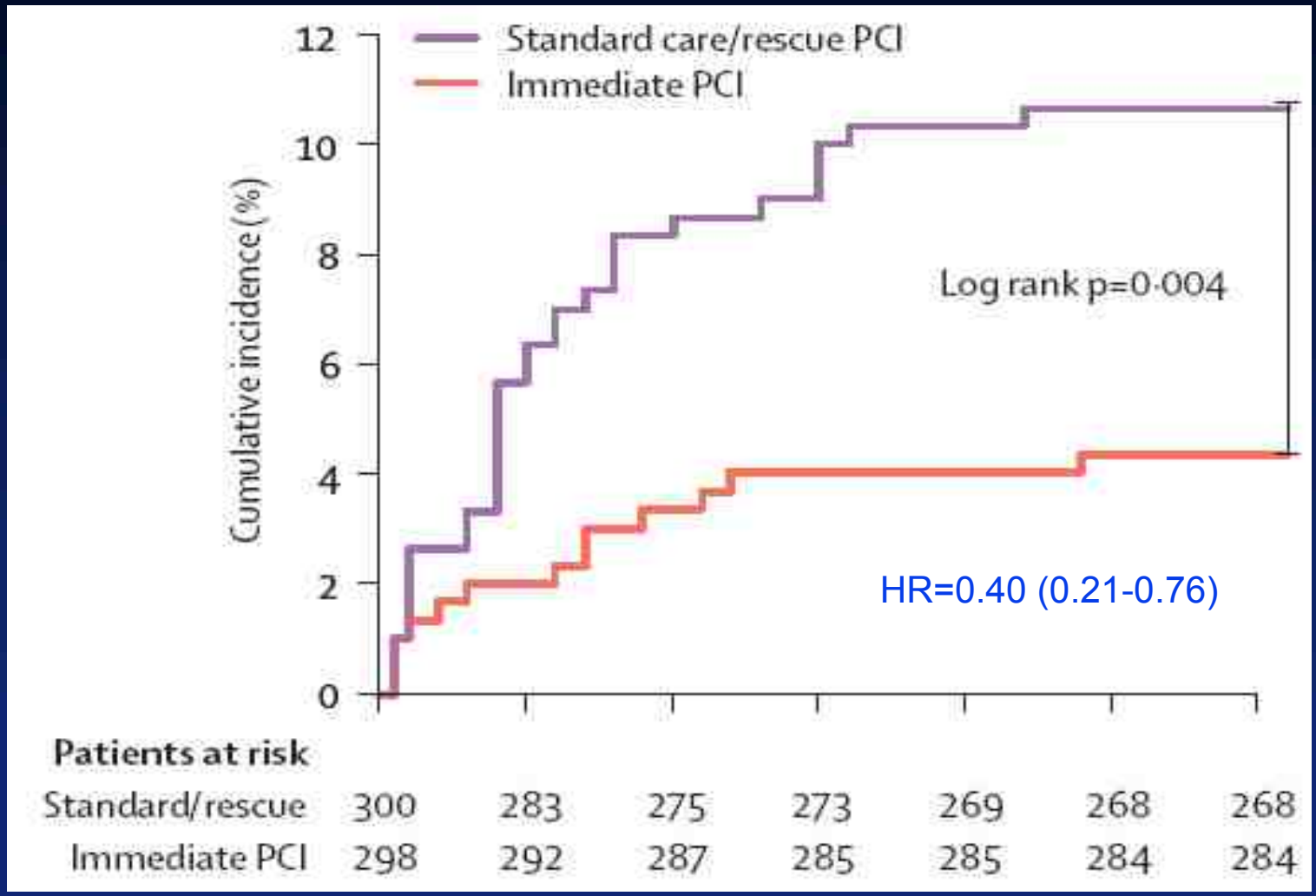
CARESS-IN-AMI: Design

- Designed to address optimum treatment in pts for whom primary PCI not readily available
- Comparison, after half dose reteplase+abciximab, between routine immediate referral for cath/PCI and selective rescue PCI approach in pts who do not qualify for primary angioplasty
- High risk patients only (Killip class > 2, EF ≤35%, ST elevation cumulative > 15 mm)

Di Mario et al. Lancet 2008;371.559

CARESS-IN-AMI: Primary Outcome

primary outcome (composite of all cause mortality, reinfarction, & refractory MI within 30 days) occurred significantly less often in the immediate PCI group vs. standard care/rescue PCI group



Di Mario et al. Lancet 2008;371:559.

Transfer AMI

Cath/PCI After Lysis: Routine or Rescue?

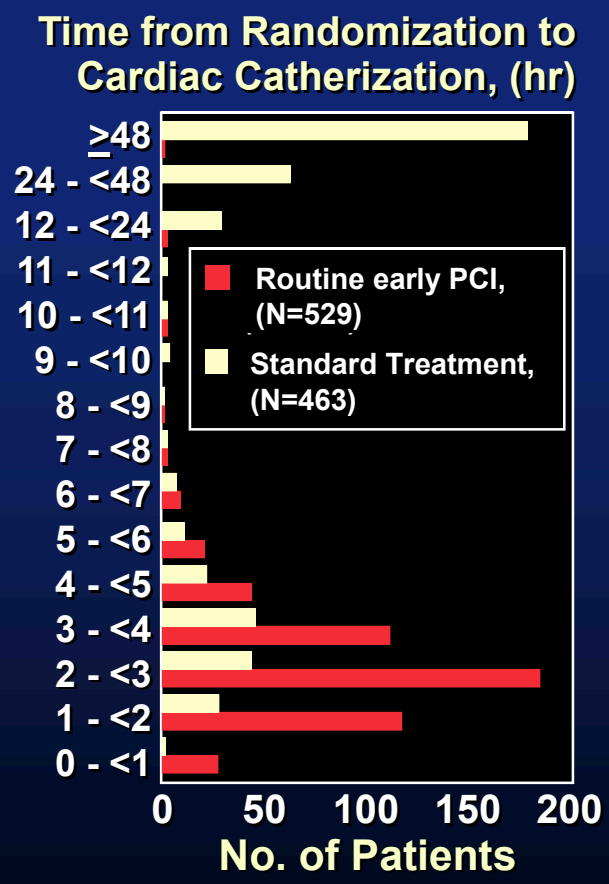
1,059 pts STEMI <12 hrs and any of: SBP <100, HR>100, Killip 2-3 or RVMI rx'd with Tenecteplase

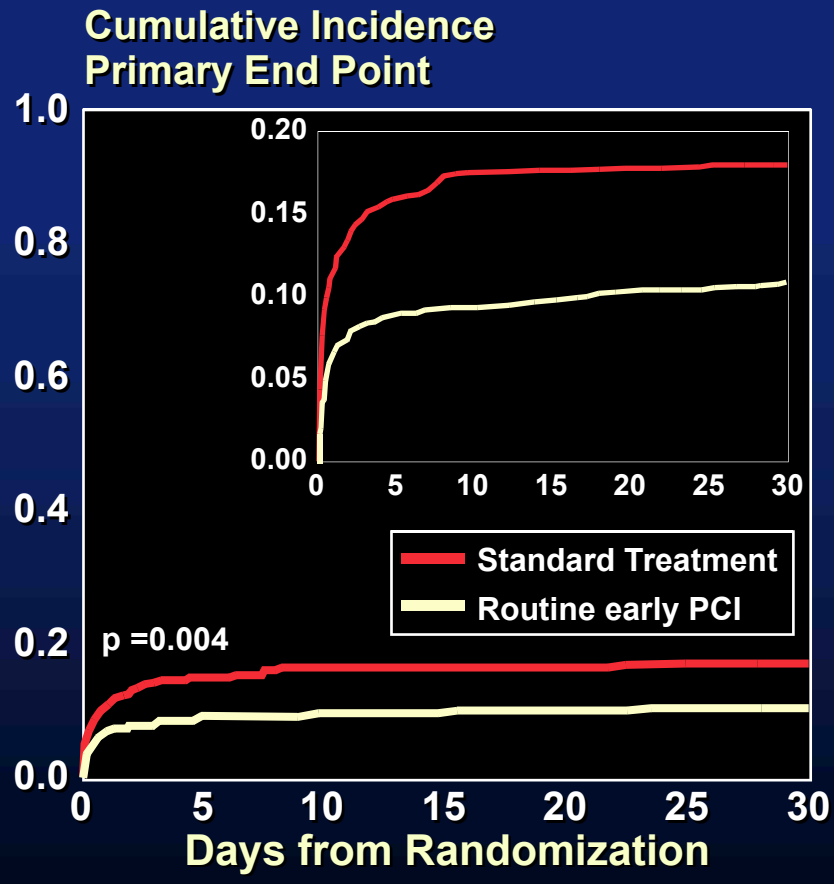
Ⓡ→routine or rescue based angio/PCI

Concomitant rx:
- ASA +/- Clopidogrel;
- UF or LMWH

1° endpoint: death, re-MI, rec ischemia, CHF,

CGS @30 days

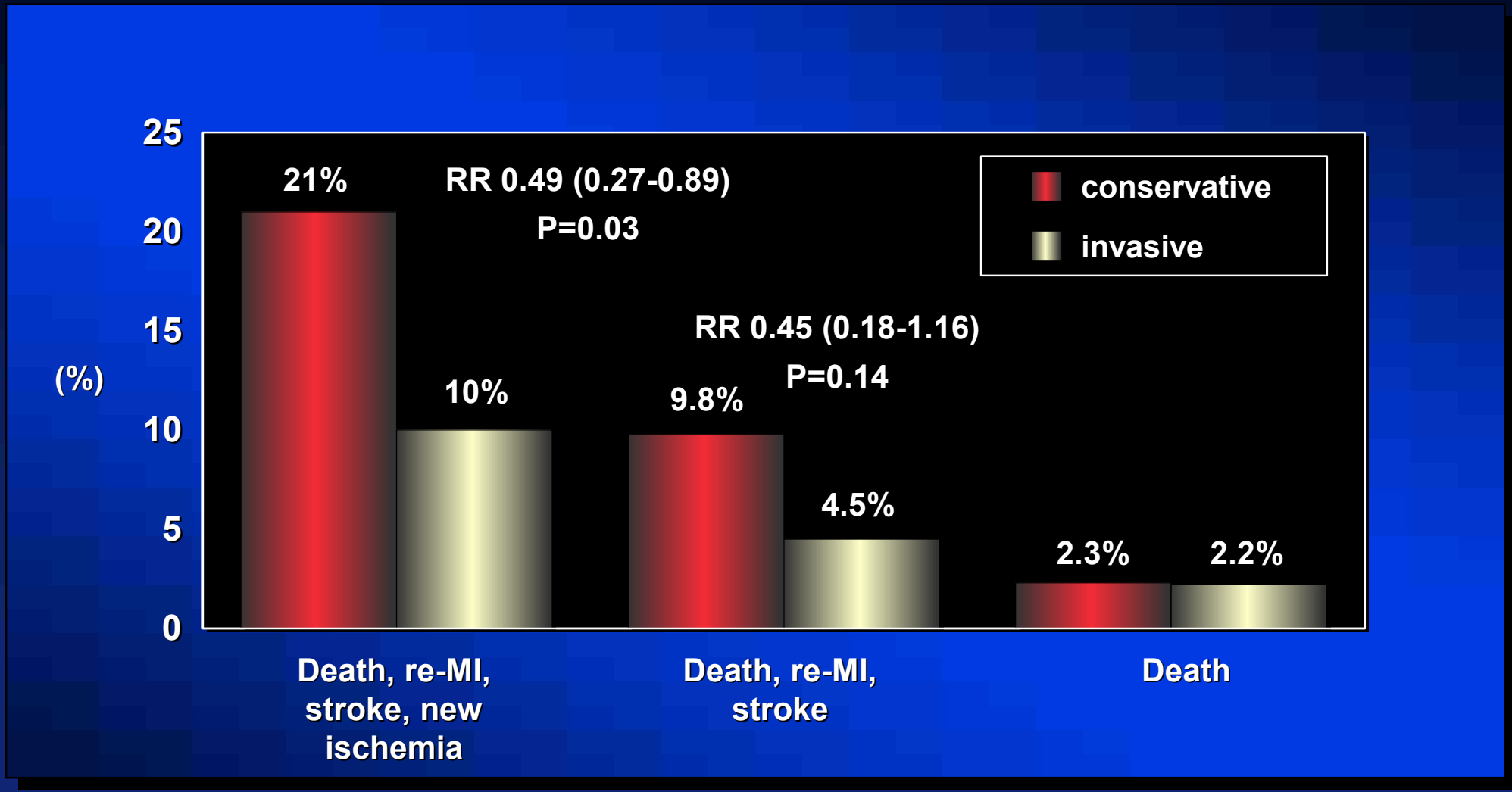




N at risk							
Standard	522	442	434	434	433	433	432
Early PCI	537	488	486	483	481	480	478

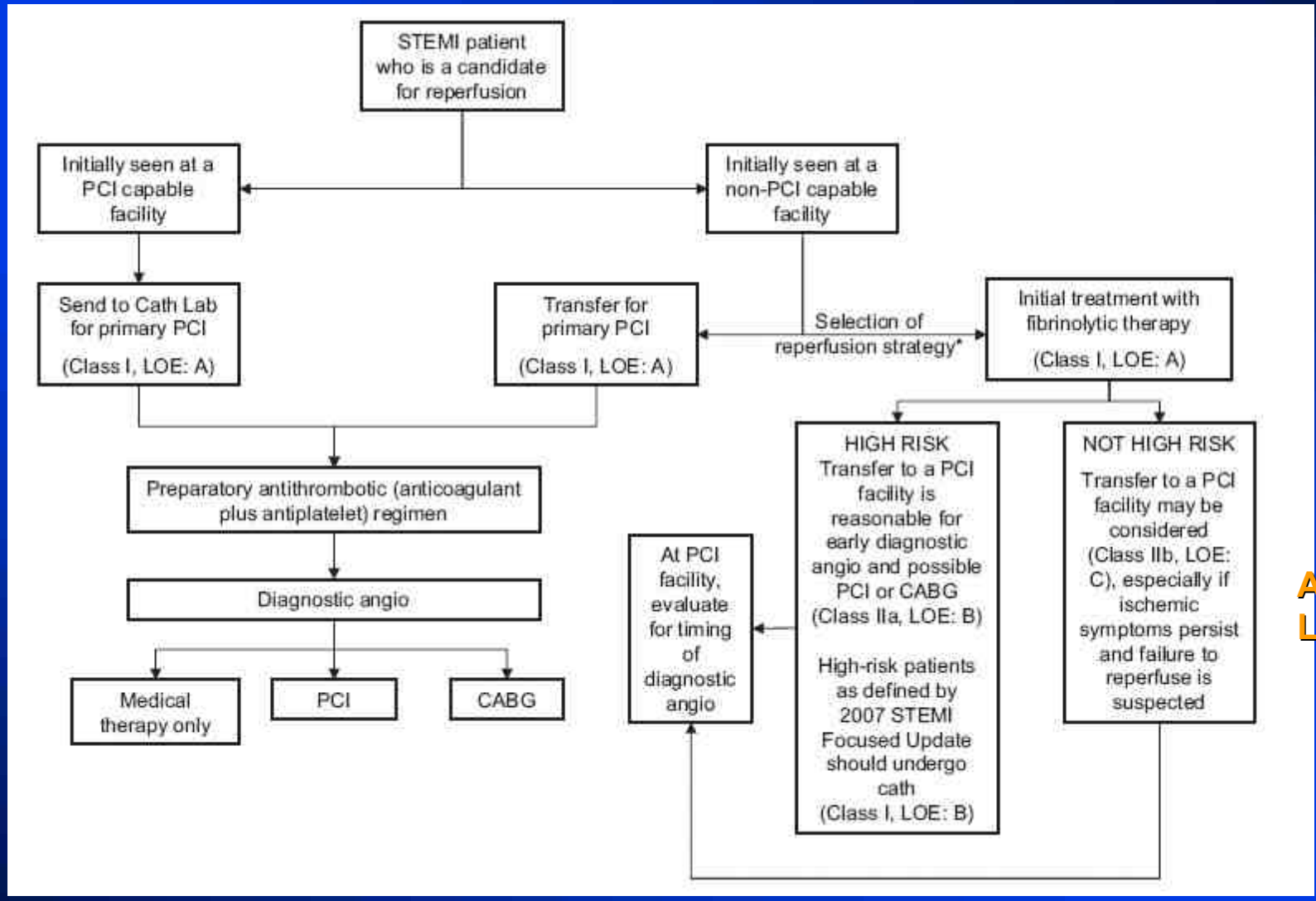
Cantor, NEJM 360:2705, 2009

Clinical Outcome at 30 Days
NORDISTEMI



Bohmer E. JACC 55:102, 2010 n=266 patients > 90 min from FMC->PCI, rx'd with tenecteplase (not selected for high risk)

2009 ACC Guidelines: Triage and Transfer for PCI



All but very Low risk

FJ Kushner et al., 2009 STEMI Guideline Updates

SGE; 0410-1, 48

STEMI: Summary + Conclusions

- PCI trumps primary lytics except
  - sx < 2 hrs if lytics given quickly (ambulance)
  - very long transfer times (time depends on patient risk profile)
- No role for routine facilitated PCI
- If lytics are given, moderate and high risk patients should be transferred for cath/PCI immediately => "pharmaco-invasive strategy"
- Evolution of primary PCI (aspiration thrombectomy, DTI, etc) improves outcomes, makes PPCI "gold standard" a moving target, and should further limit use of other reperfusion strategies
- DAP with prasugrel (except when contraindicated), early BB, ACE-I, statins are also important
- New treatments (eg post-conditioning) need further evaluation