

Current Advances and Best Practices in Acute STEMI Management

A pharmacoinvasive approach



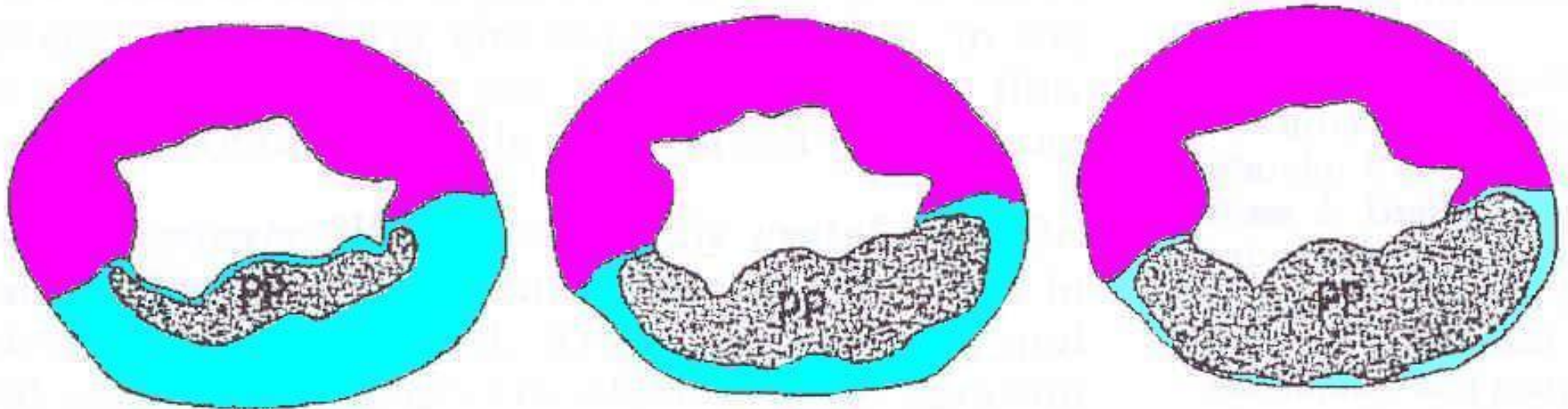
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Frans Van de Werf: Disclosures

- **Research grants for conducting trials on reperfusion therapy:
Boehringer Ingelheim, Genentech, SanofiAventis,
Proctor&Gamble, Wyeth**
- **Speaker's bureau:
Boehringer Ingelheim, Genentech, SanofiAventis, Merck, AZ**
- **Advisory board:
Boehringer Ingelheim, Menarini, GSK, Merck, AZ, The
Medicines Company**

- **The Benefit of Reperfusion therapy for STEMI is very much time dependent !**

Progression of Cell Death versus Time after Coronary Occlusion in Dogs



40 minutes

3 hours

96 hours



= Nonischemic

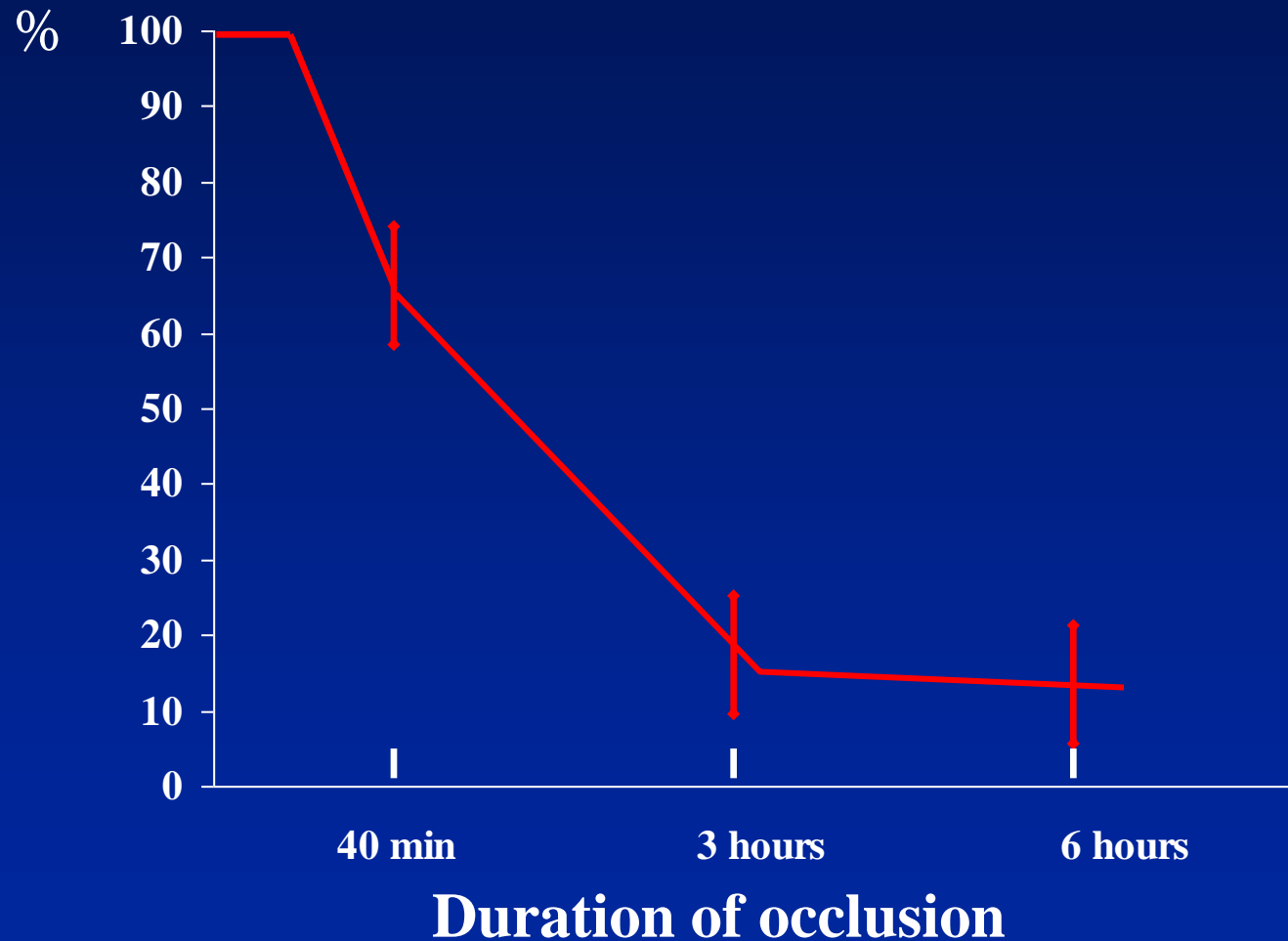


= Ischemic
(Viable)

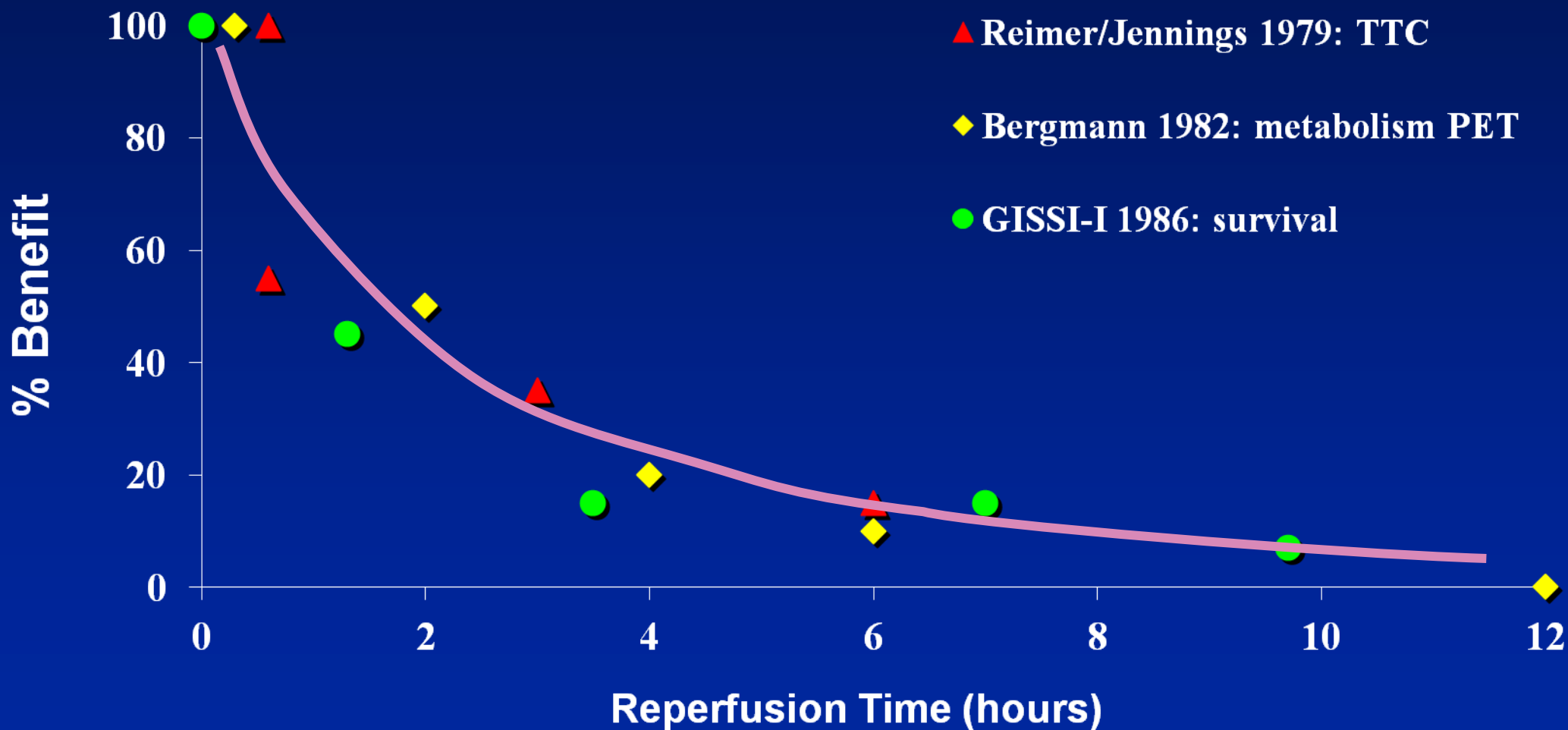


= Necrotic

Salvageable Ischemic Myocardium with Respect to the Duration of Ischemia



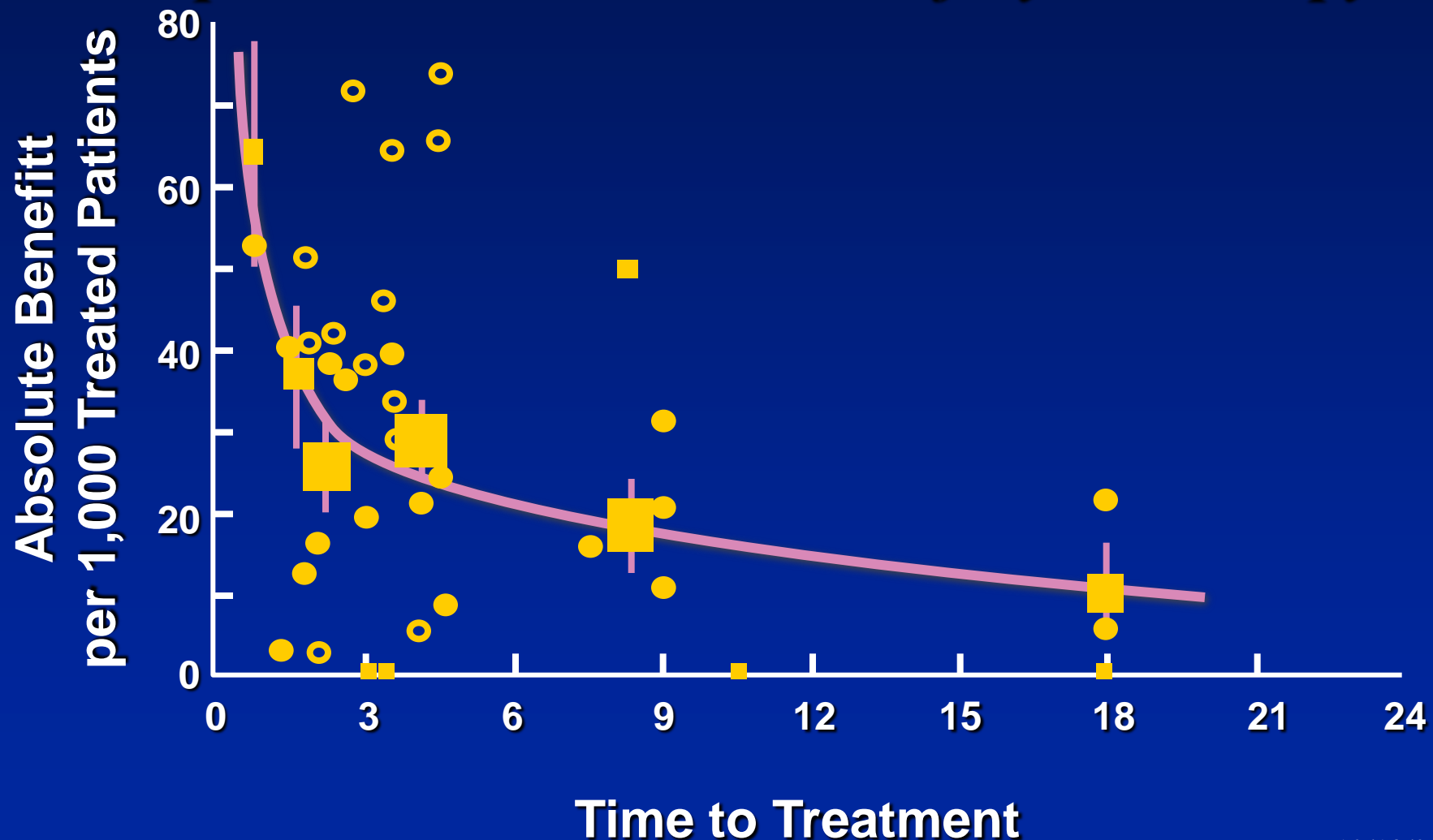
The Importance of Time to Reperfusion



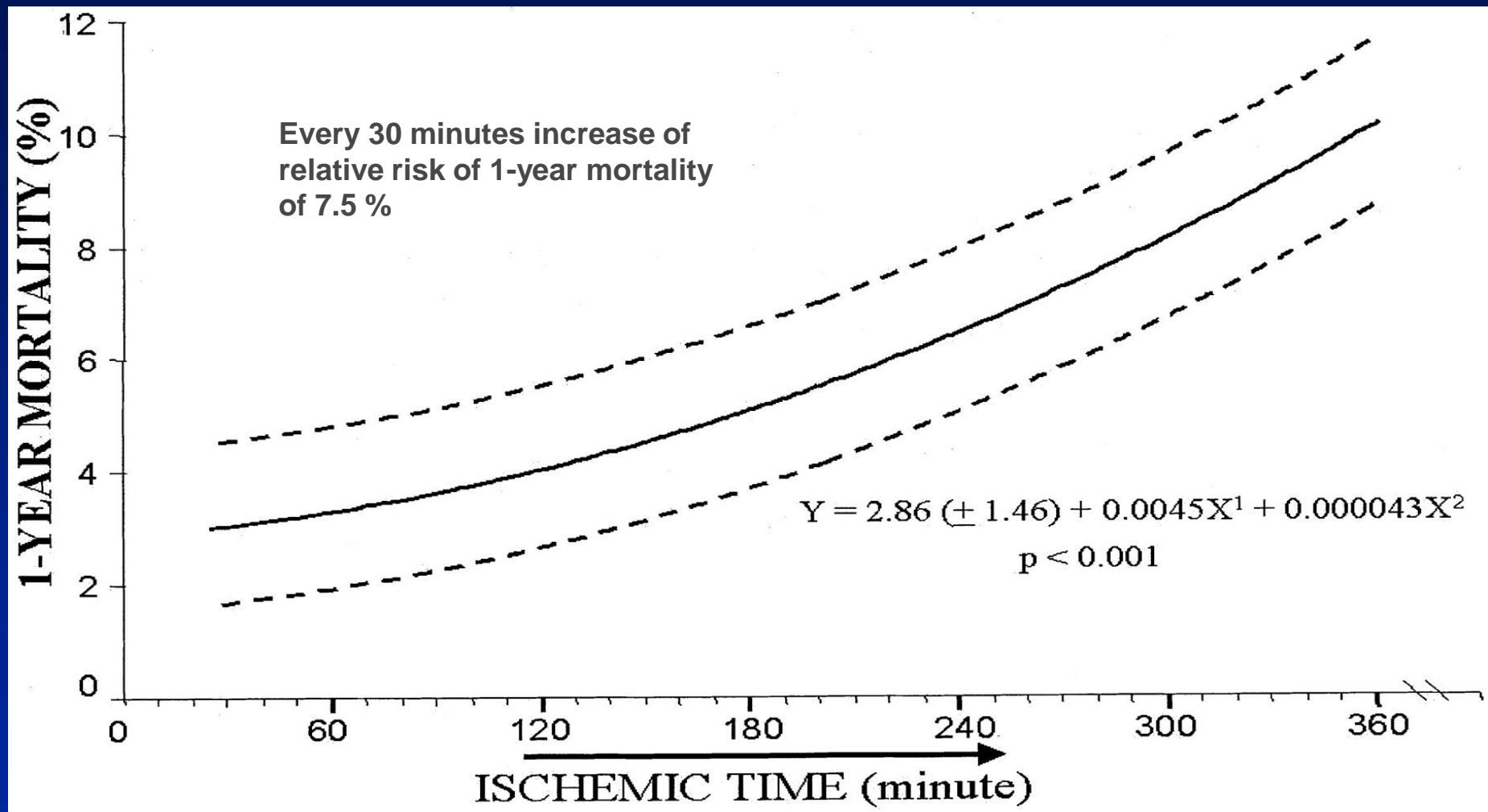
The Importance of Time to Reperfusion

A Meta-analysis of 50,246 Pts

in placebo controlled trials of Lytic Therapy



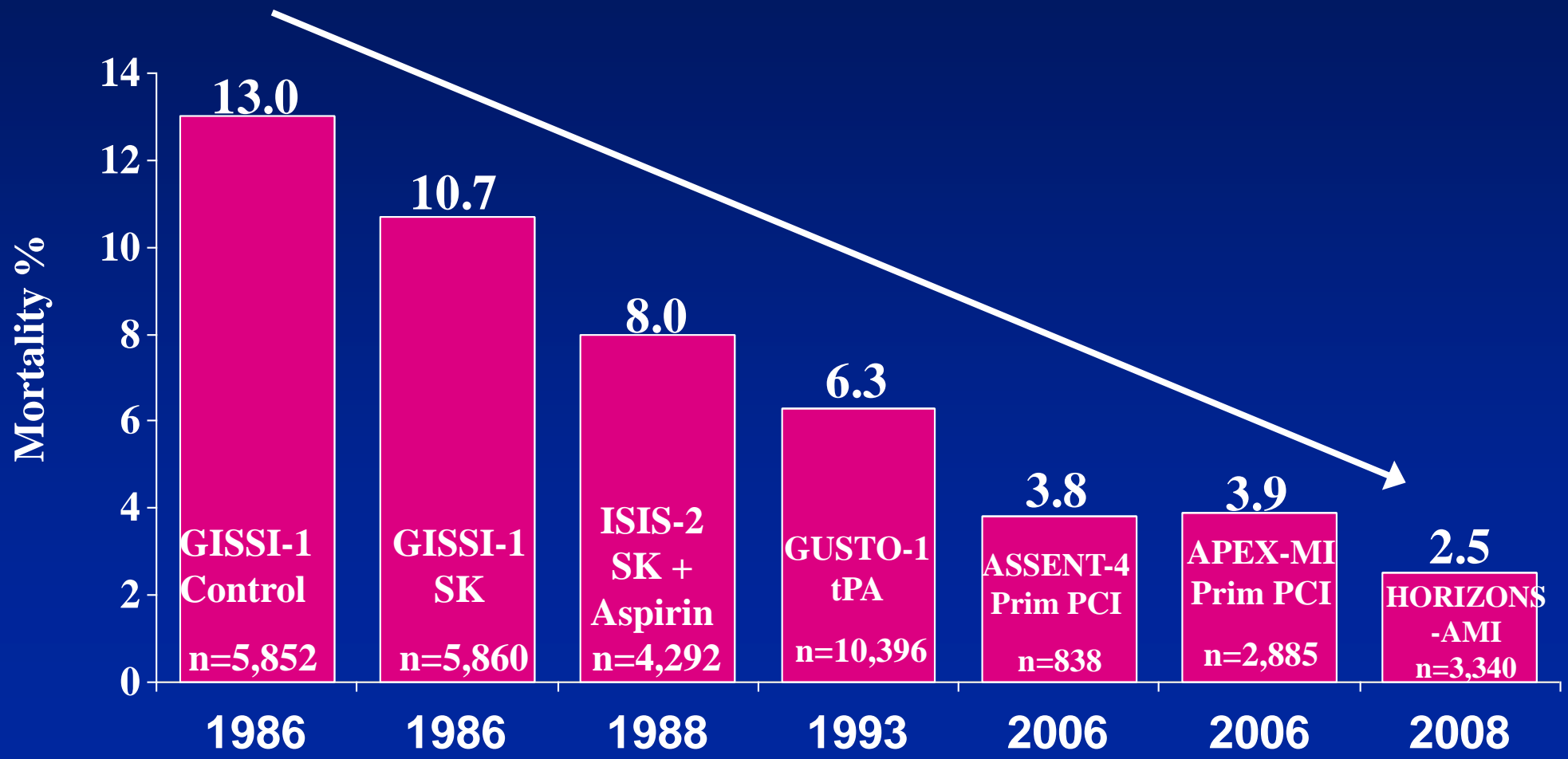
Primary PCI : Time to treatment and 1-year



Landmark Clinical Studies

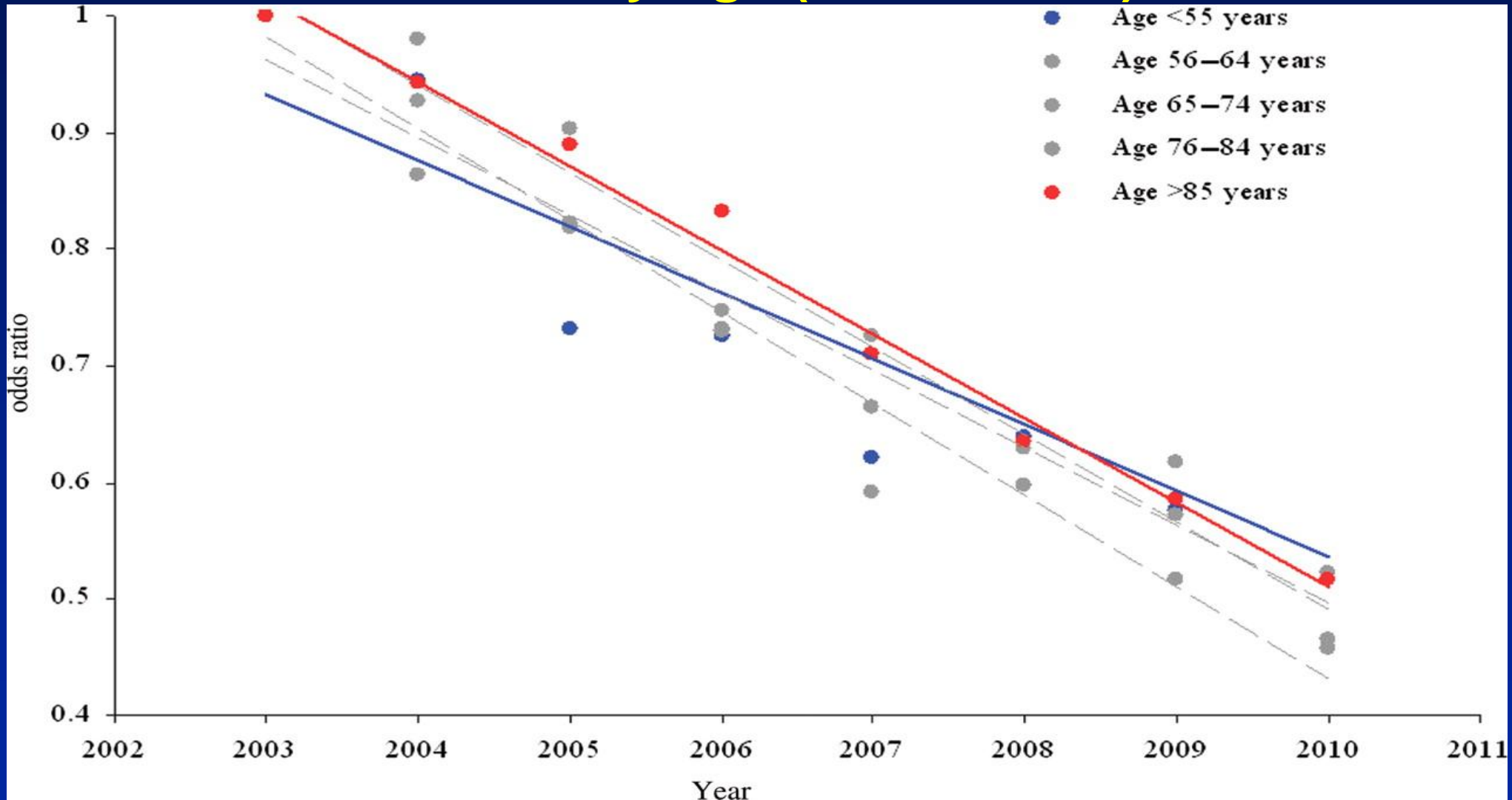
- The efficacy of **intravenous streptokinase**. **GISSI-1**, *Lancet* 1986
- The additional survival benefit with **upfront aspirin** in combination with streptokinase. **ISIS-2**, *Lancet* 1988
- The greater survival benefit with a **fibrin-specific agent (tPA)** as compared with streptokinase. **GUSTO-I**, *New Engl J Med* 1993
- The superiority of **primary PCI** over in-hospital fibrinolytic therapy, **Meta-analysis**, *Lancet* 2003

Early Mortality Rates (21-35 days) in Major Randomized STEMI trials: 1986 - 2006



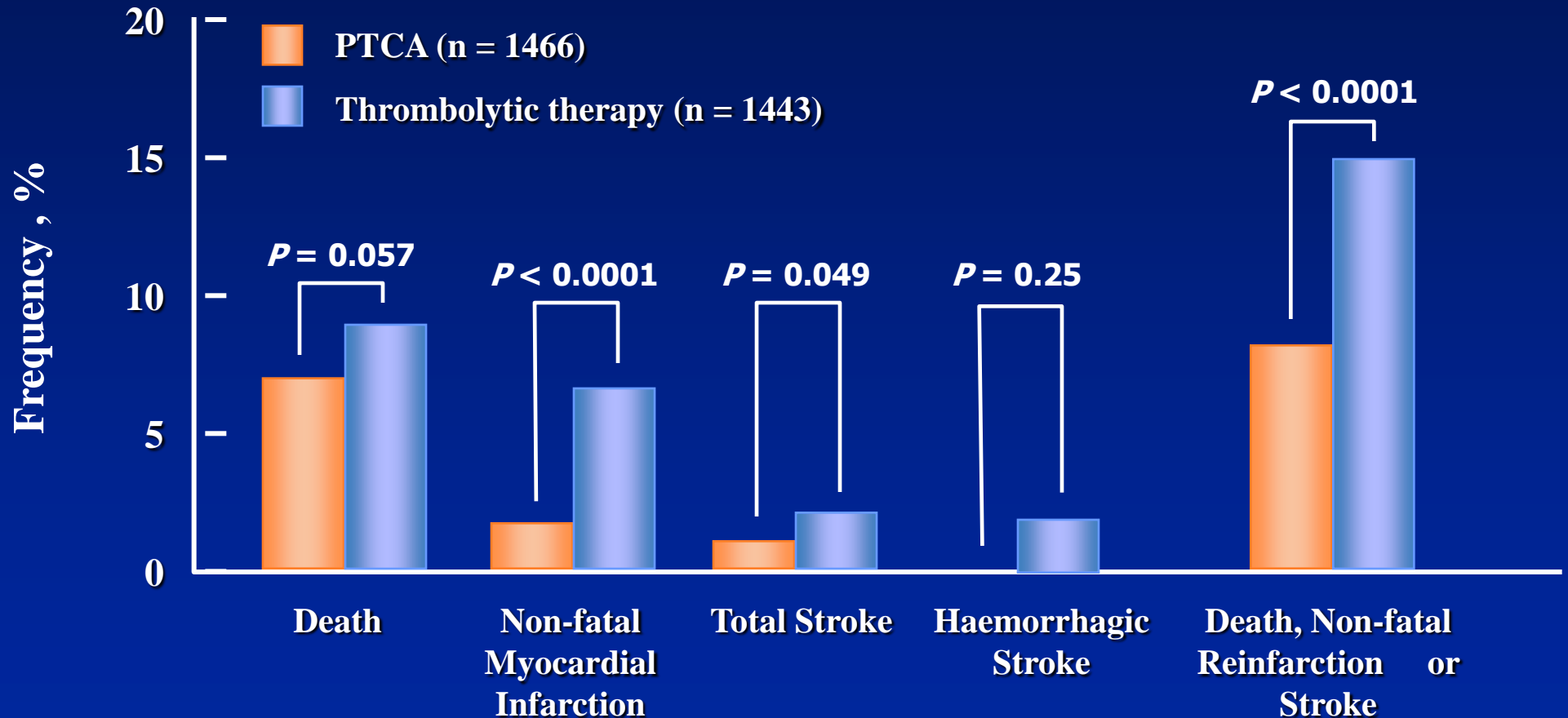
The Benefit of Reperfusion

ORs by Year for In-Hospital All-Cause Mortality, Stratified by Age (2003 = base)

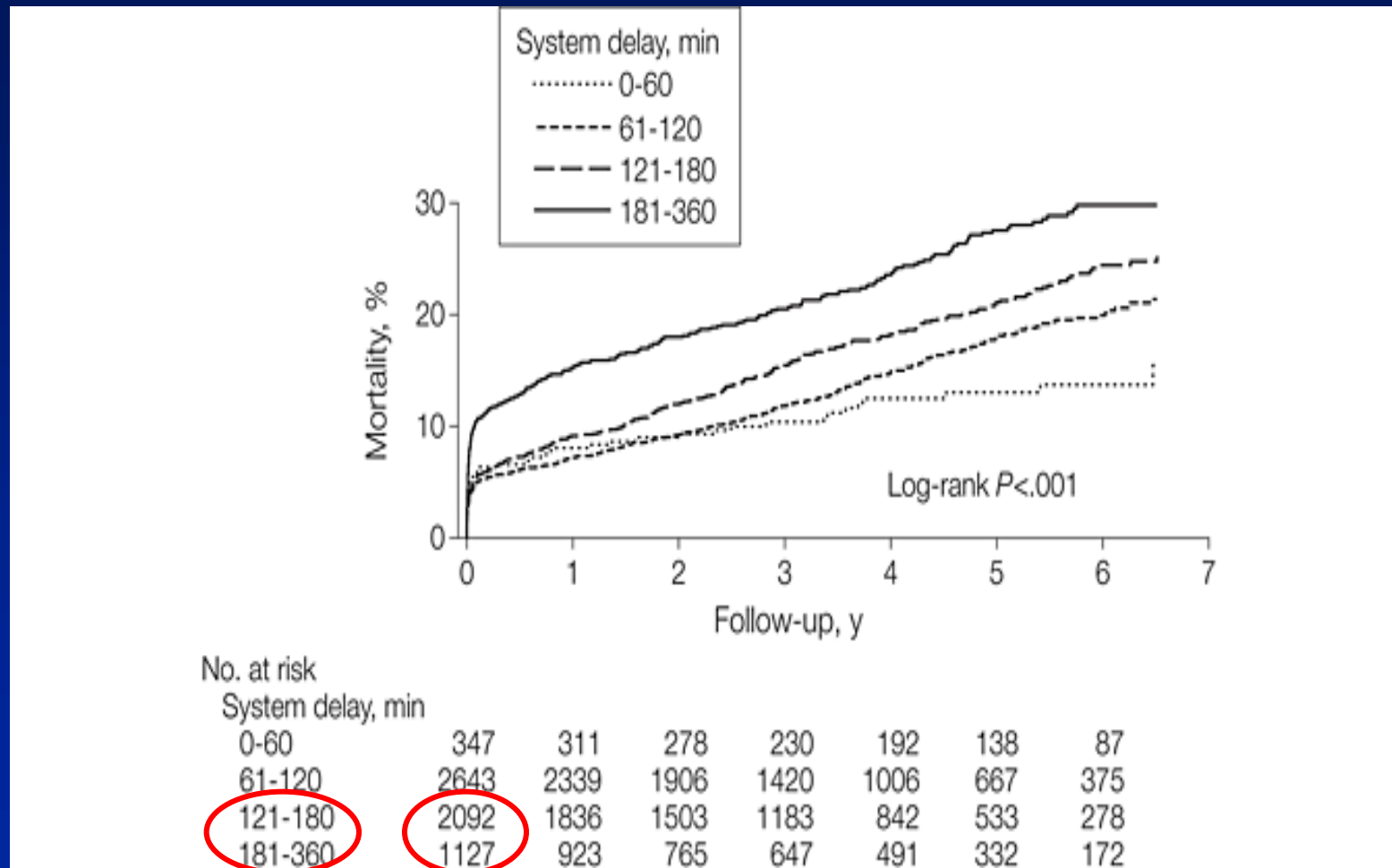


- **Time delays remain a major problem !**

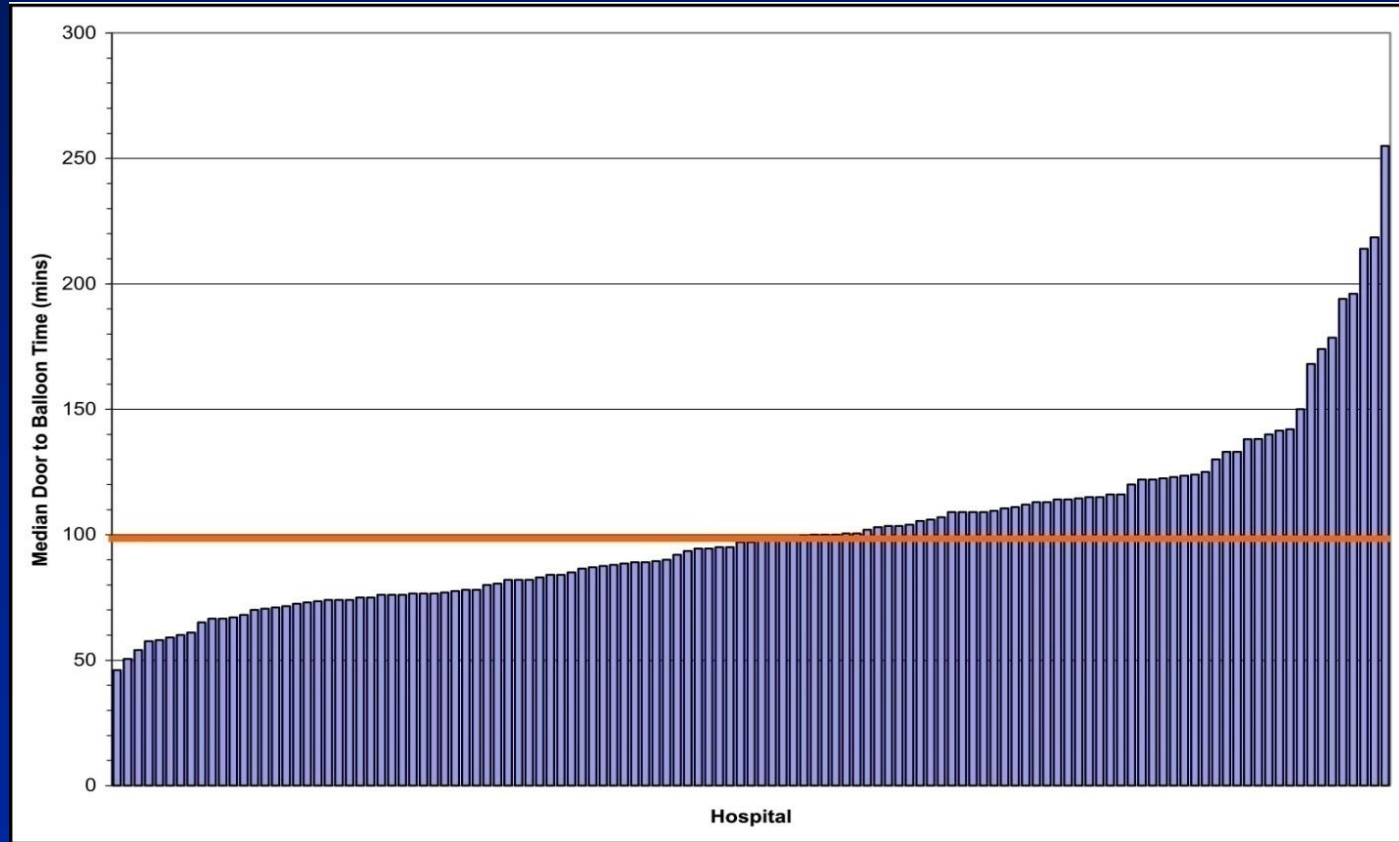
On-Site Thrombolysis vs Transfer for PCI



Mortality in 6209 Danish Patients With STEMI Treated With Primary PCI



HORIZONS-AMI: Median Door-to-Balloon Times



Multivariate predictors of longer door-to-balloon time in 2 298 pts from HORIZONS -AMI

Variable	Estimate	SE	p Value
• Presentation to non-angioplasty hospital	53.94	2.18	<0.001
• Respiratory failure	41.55	13.79	0.003
• Previous congestive heart failure	15.17	6.57	0.02
• Presentation during daytime weekday hours	-10.52	1.99	<0.001
• Diabetes mellitus	9.30	2.75	<0.001
• Previous angina	8.02	2.44	0.001
• Men	-7.08	2.36	0.003
• Infarct-related artery: circumflex	6.26	2.02	0.002
• Left ventricular ejection fraction	-0.25	0.09	0.003

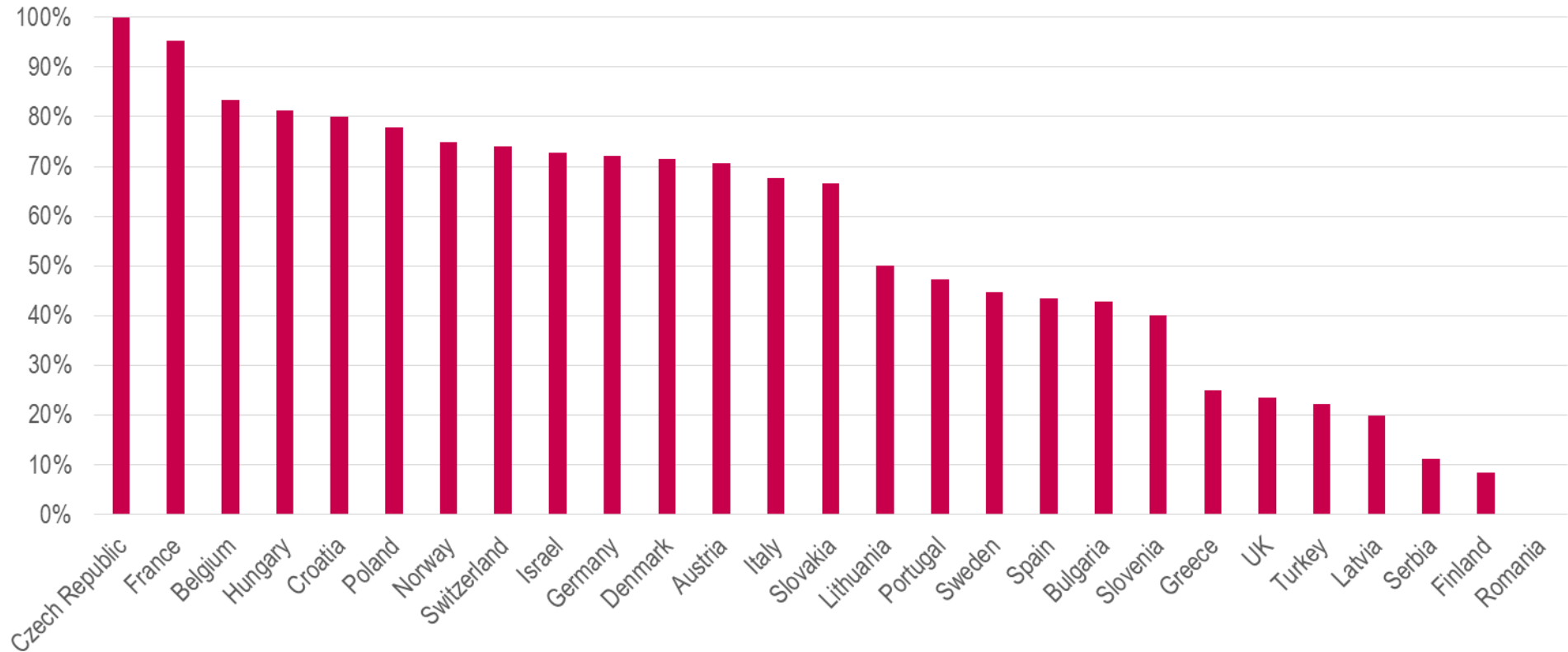
Hospitals with cath labs



✓ UNITED STATES	18.0%
✓ EUROPE	10.0%
✓ BRAZIL	5.5%

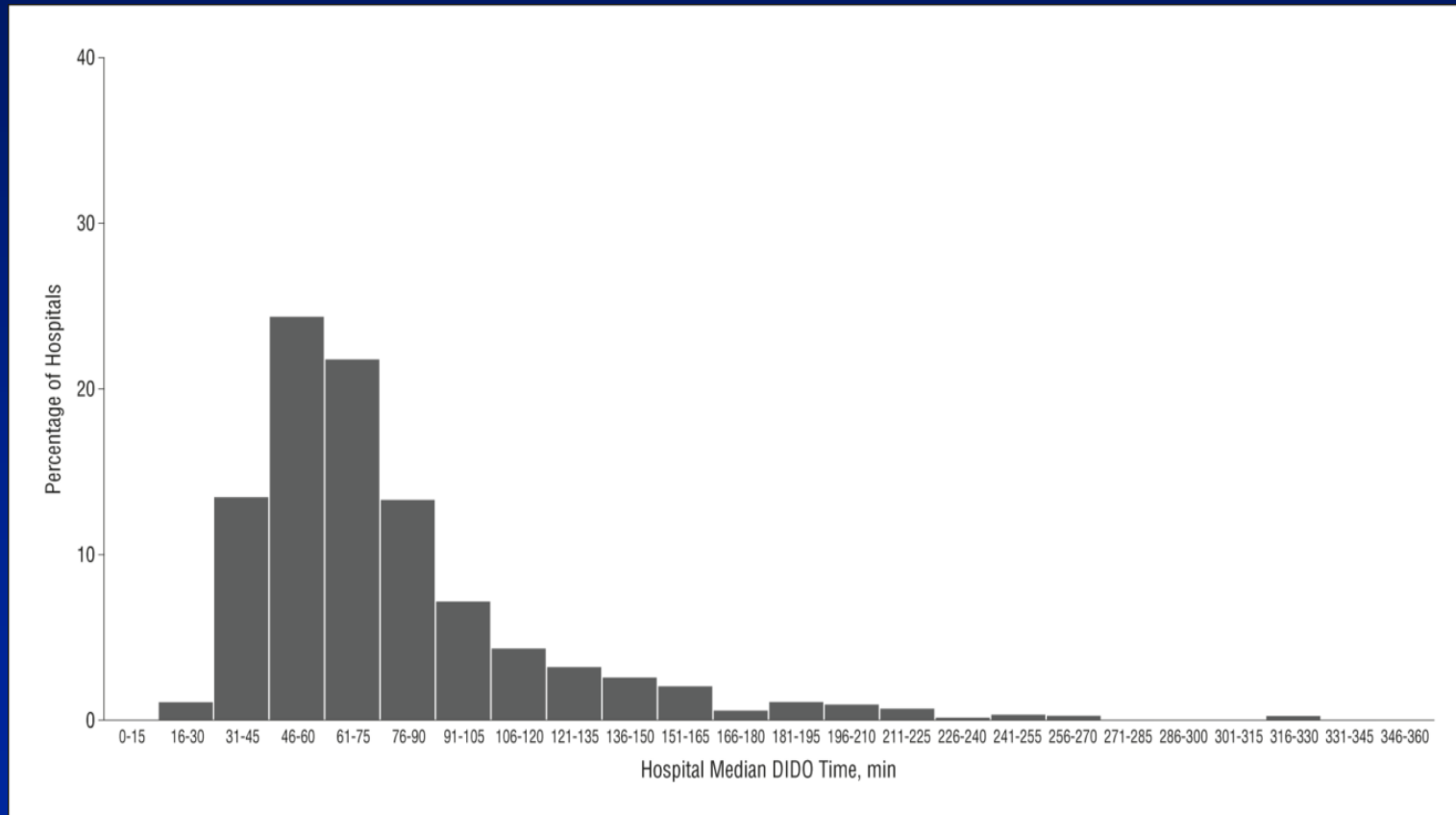
Only 55% of all PCI centres offer 24/7 PPCI service

% of PCI centres which are 24/7



Door-In to Door-Out Time Among Patients Transferred for Primary PCI in the USA

Distribution of median door-in to door-out (DIDO) times for 1034 hospitals reporting at least 5 patients in 2009



Problems and challenges in cardiovascular emergencies



STUDY AIM

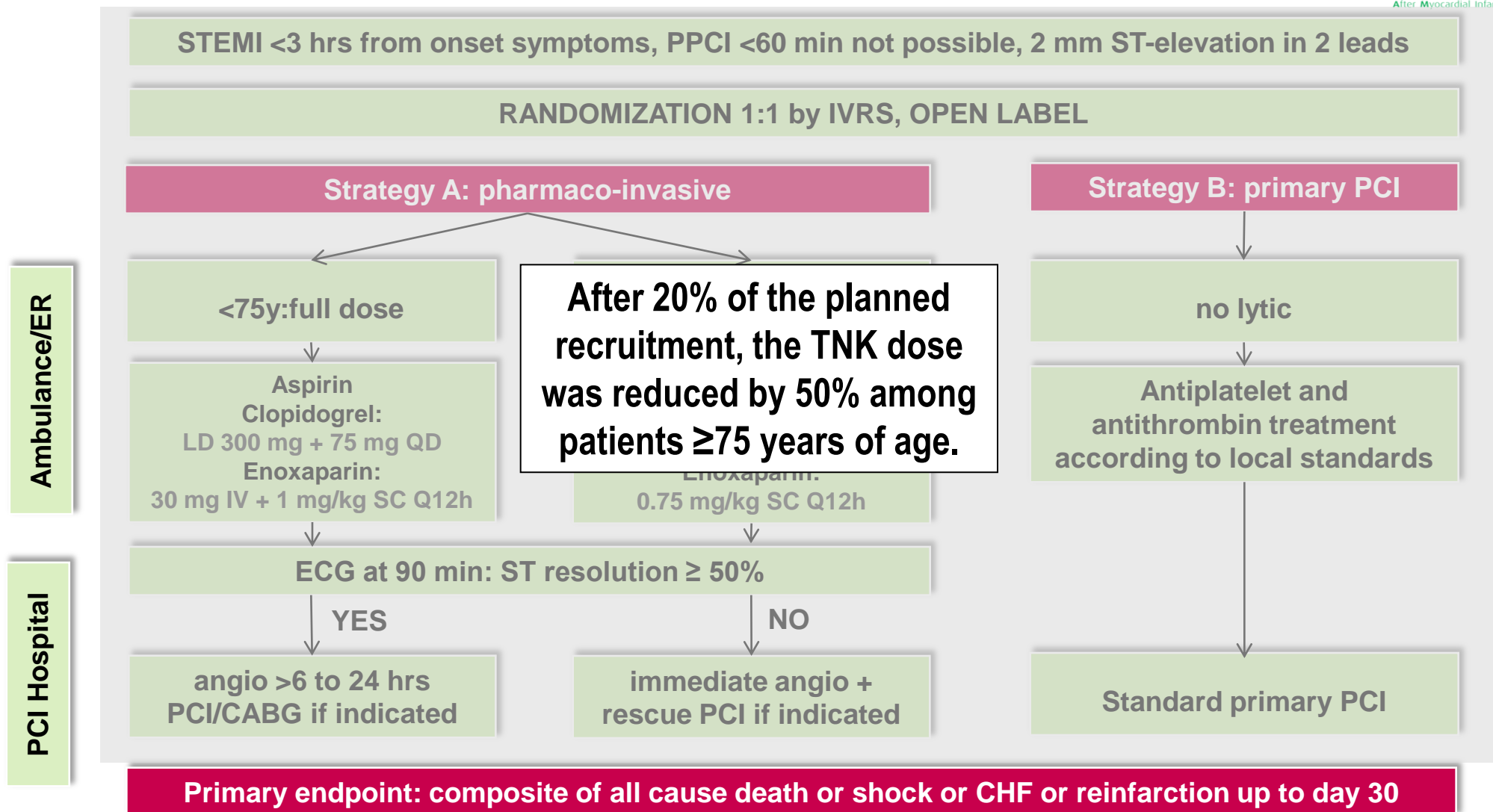


A strategy of early fibrinolysis followed by coronary angiography within 6-24 hours or rescue PCI if needed was compared with standard primary PCI

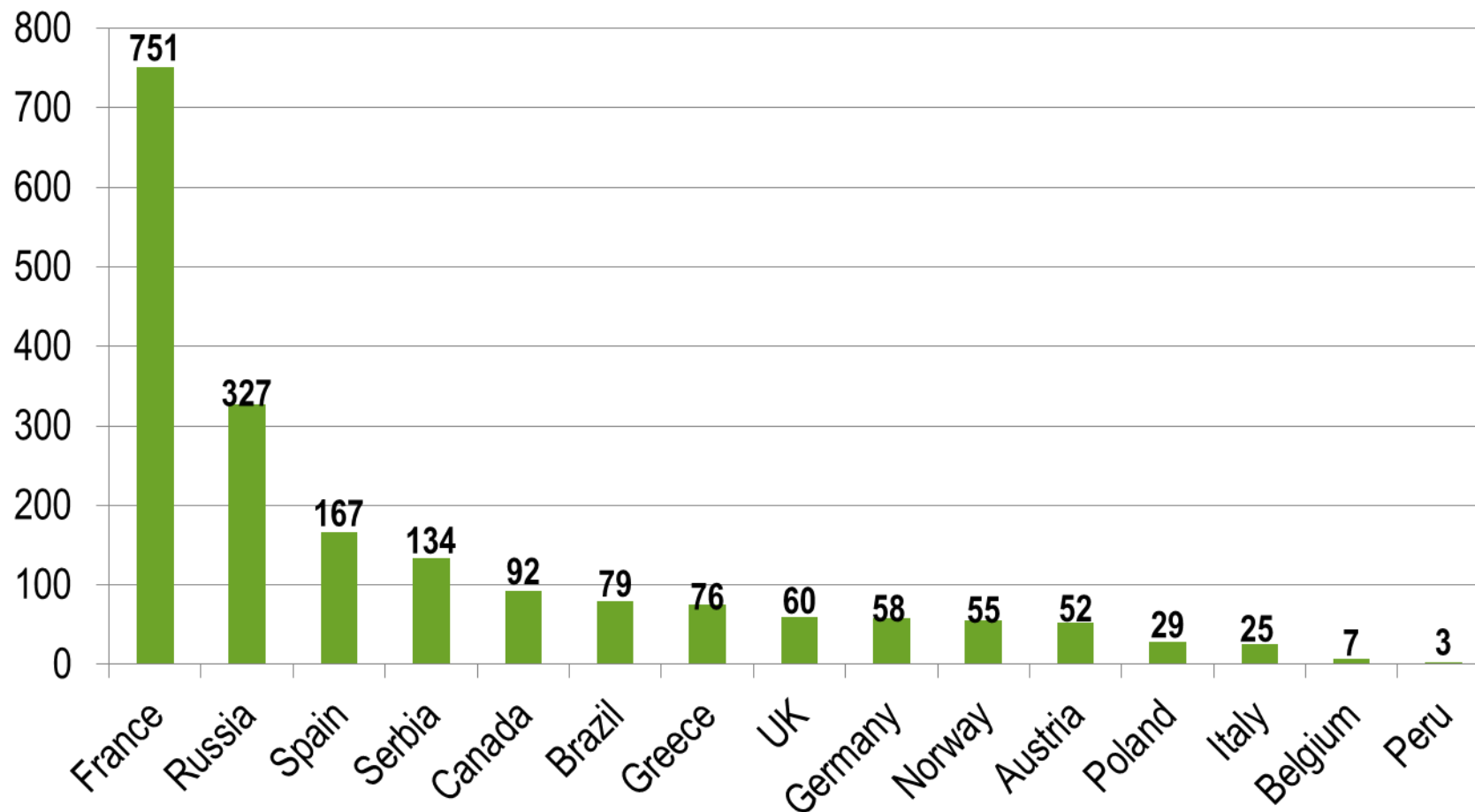
in

STEMI patients with at least 2 mm ST-elevation in 2 contiguous leads presenting within 3 hours of symptom onset and unable to undergo primary PCI within 1 hour.

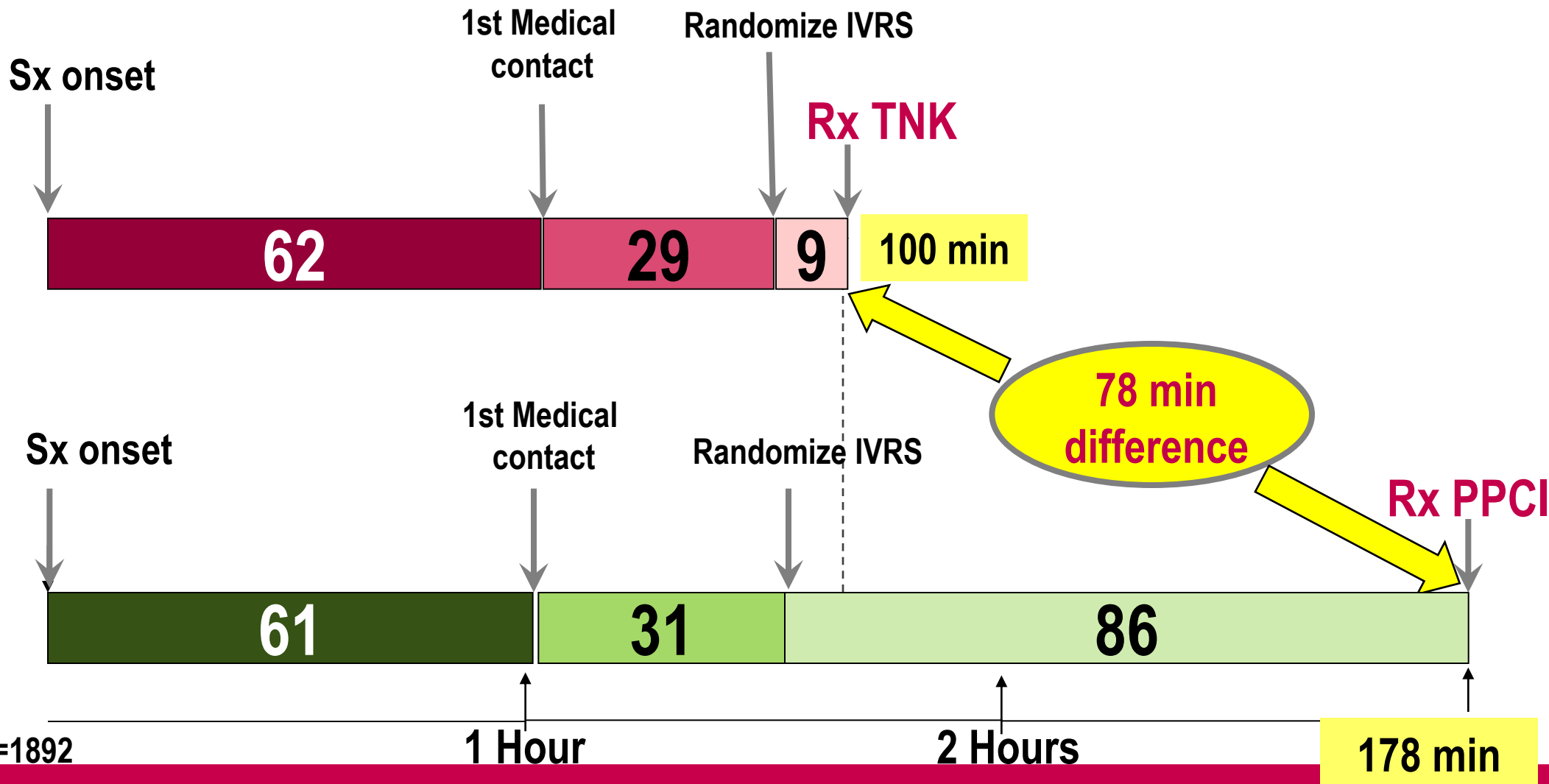
STUDY PROTOCOL



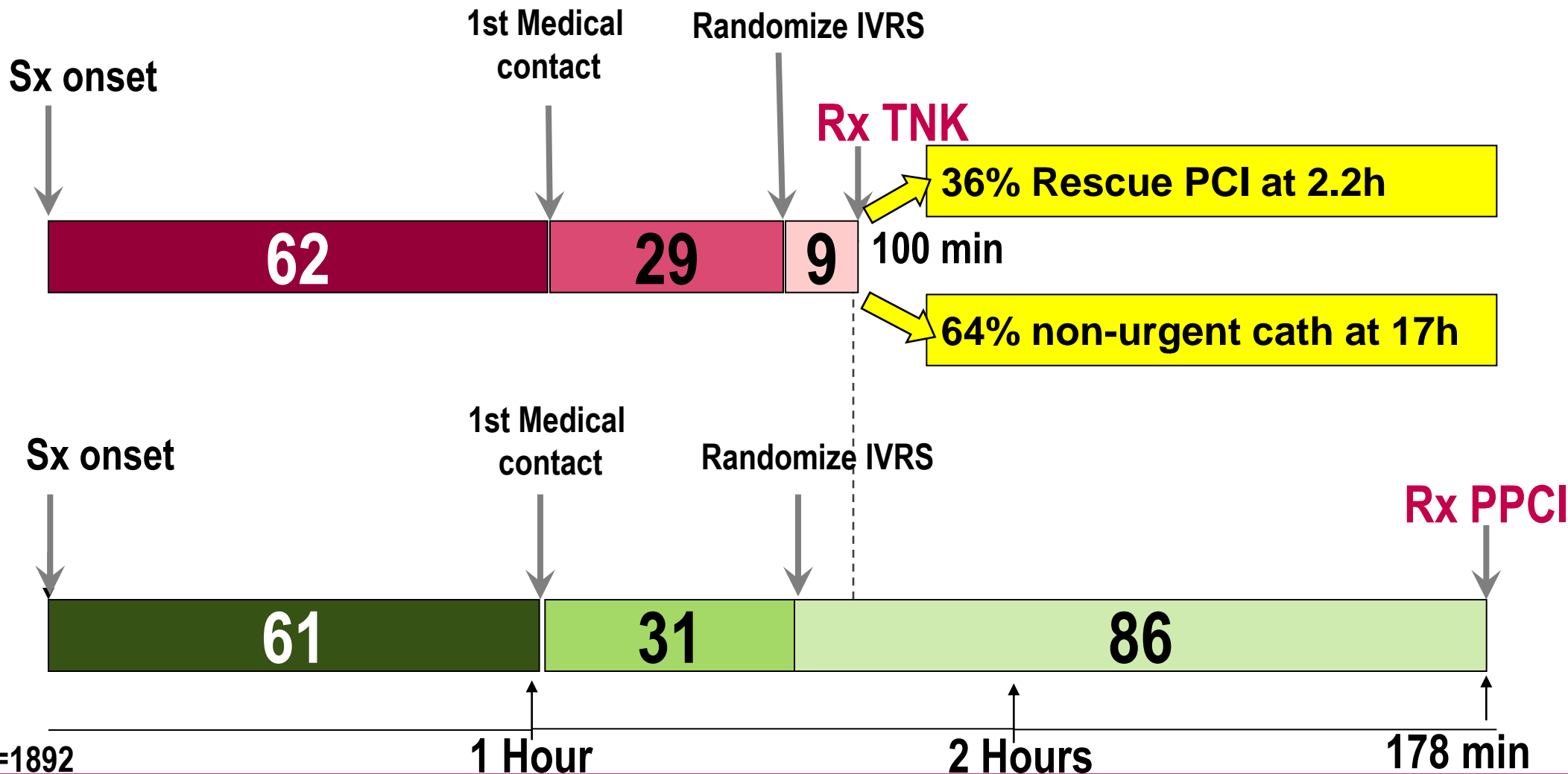
PATIENTS PER COUNTRY



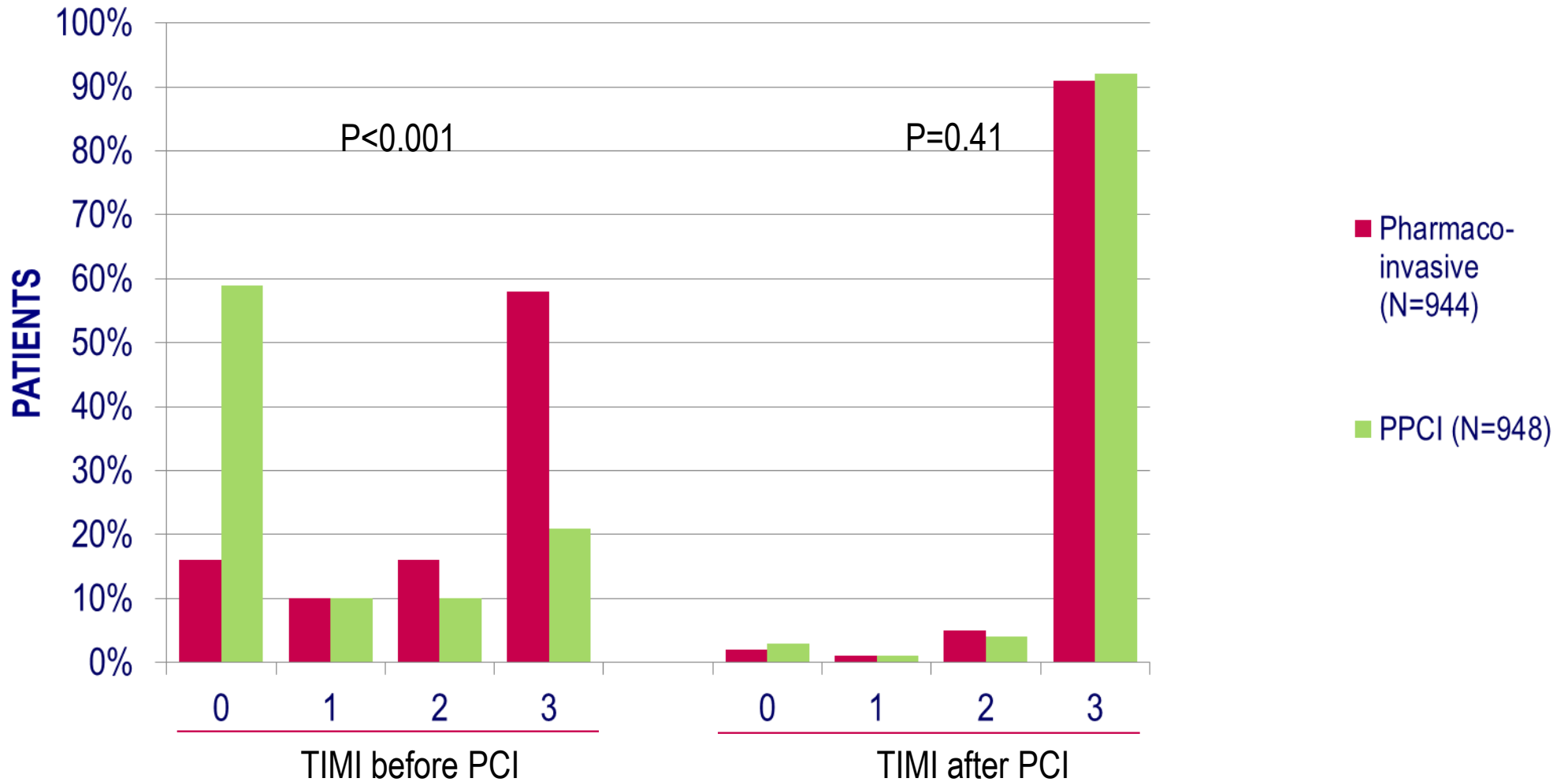
MEDIAN TIMES TO TREATMENT (min)



MEDIAN TIMES TO TREATMENT (min)



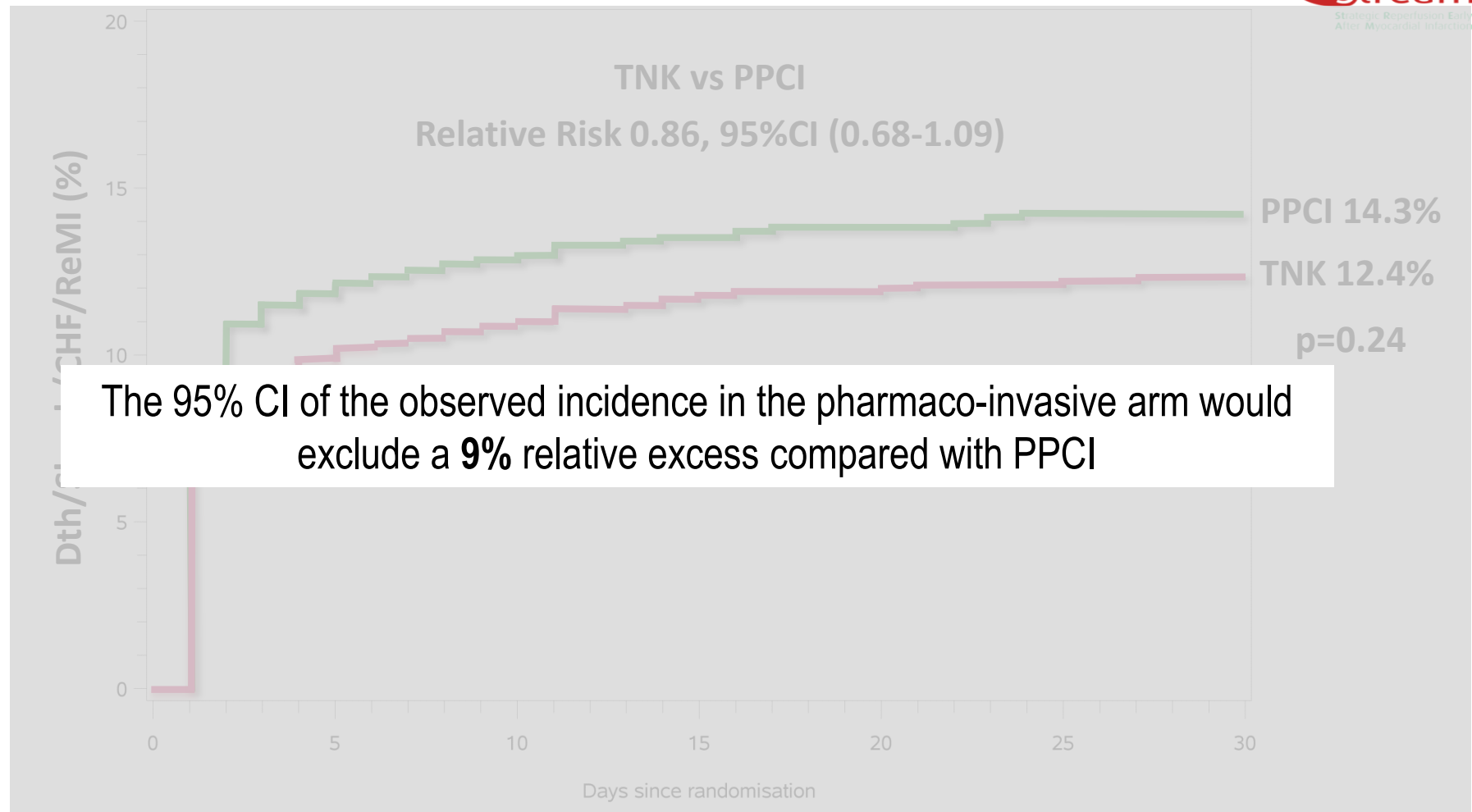
TIMI FLOW RATES



INVASIVE PROCEDURES

	Pharmaco-invasive (N=944)	PPCI (N=948)	P-value
PCI performed	80%	90%	<0.001
Stents deployed	96%	96%	0.95
CABG performed	4.7%	2.1%	0.002

PRIMARY ENDPOINT

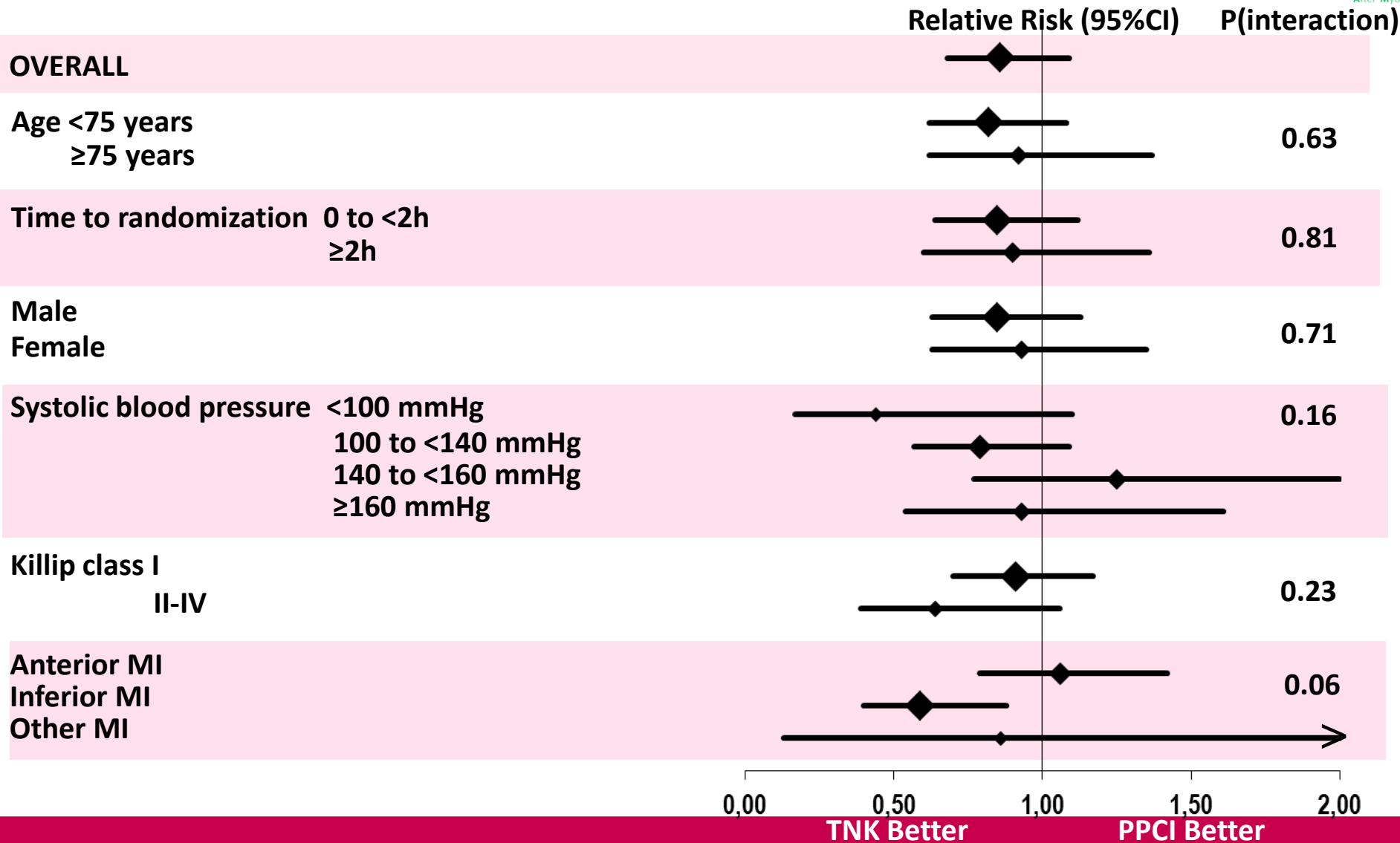


Number at risk							
Tenecteplase	943	848	837	829	827	825	823
Primary PCI	948	836	824	818	815	811	811

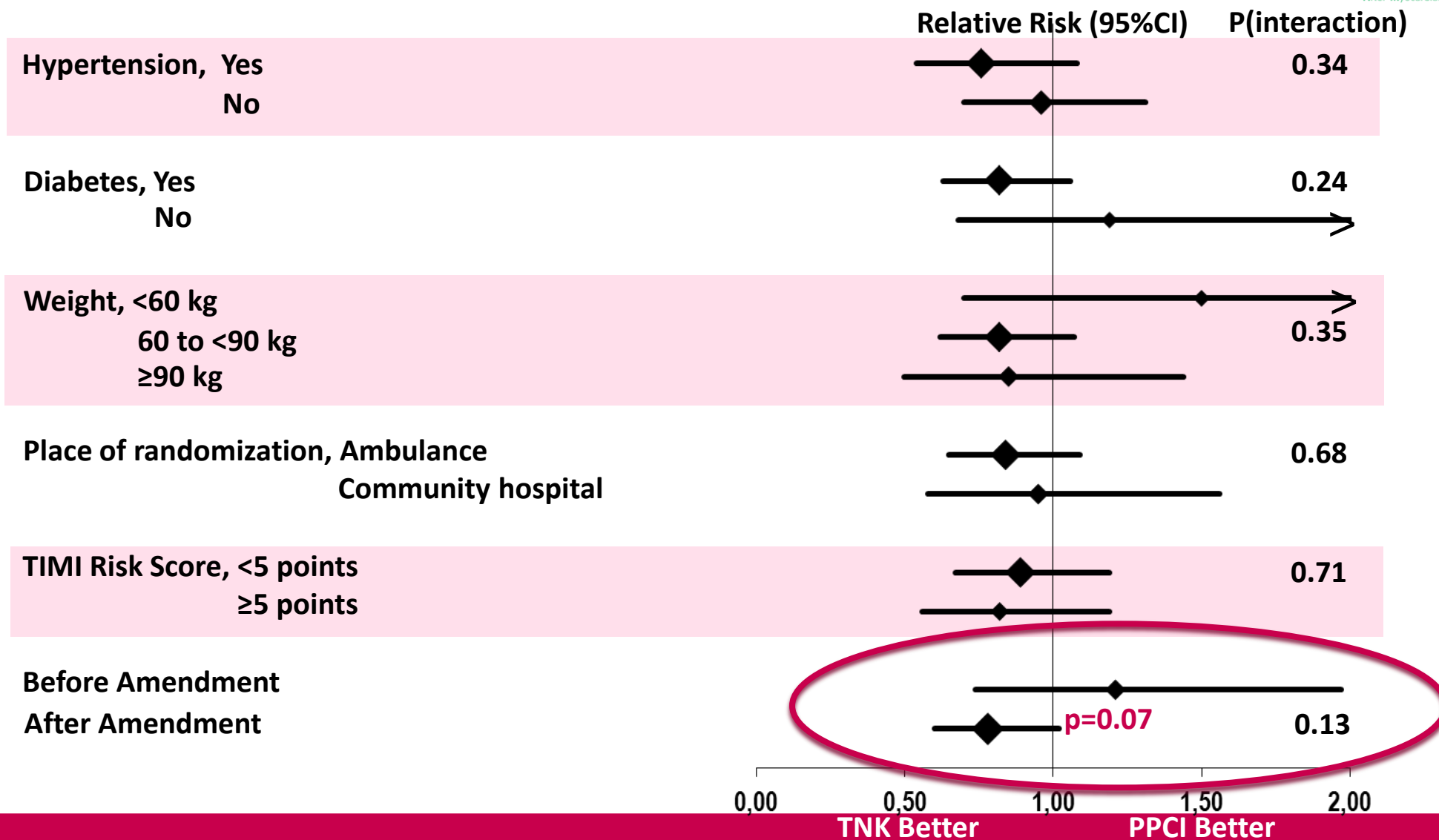
SINGLE ENDPOINTS UP TO 30 DAYS

	Pharmaco-invasive (N=944)	PPCI (N=948)	P-value
All cause death	(43/939) 4.6%	(42/946) 4.4%	0.88
Cardiac death	(31/939) 3.3%	(32/946) 3.4%	0.92
Congestive heart failure	(57/939) 6.1%	(72/943) 7.6%	0.18
Cardiogenic shock	(41/939) 4.4%	(56/944) 5.9%	0.13
Reinfarction	(23/938) 2.5%	(21/944) 2.2%	0.74

Subgroup analyses for primary endpoint within 30 days



Subgroup analyses for primary endpoint within 30 days



STROKE RATES

	Pharmaco-invasive	PPCI	P-value
TOTAL POPULATION (N=1892)			
Total stroke	15/939 (1.60%)	5/946 (0.53%)	0.03
fatal stroke	7/939 (0.75%)	4/946 (0.42%)	0.39
Haemorrhagic stroke	9/939 (0.96%)	2/946 (0.21%)	0.04
fatal haemorrhagic stroke	6/939 (0.64%)	2/946 (0.21%)	0.18
POST AMENDMENT POPULATION (N=1503)			
Total stroke	9/747 (1.20%)	5/756 (0.66%)	0.30
fatal stroke	3/747 (0.40%)	4/756 (0.53%)	>0.999
Haemorrhagic stroke	4/747 (0.54%)	2/756 (0.26%)	0.45
fatal haemorrhagic stroke	2/747 (0.27%)	2/756 (0.26%)	>0.999

IN-HOSPITAL BLEEDING COMPLICATIONS

	Pharmaco-invasive (N=944)	PPCI (N=948)	P-value
Major non-ICH bleeding	6.5%	4.8%	0.11
Minor non-ICH bleeding	21.8%	20.2%	0.40
Blood transfusions	2.9%	2.3%	0.47

CONCLUSIONS

A strategy of fibrinolysis with bolus tenecteplase and contemporary antithrombotic therapy given before transport to a PCI-capable hospital coupled with timely coronary angiography :

- **circumvents the need for an urgent procedure in about two thirds of fibrinolytic treated STEMI patients.**
- **is associated with a small increased risk of intracranial bleeding.**
- **is as effective as primary PCI in STEMI patients presenting within 3 hours of symptom onset who cannot undergo primary PCI within one hour of first medical contact.**

ORIGINAL ARTICLE

Fibrinolysis or Primary PCI in ST-Segment Elevation Myocardial Infarction

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Hans-Richard Arntz, M.D., Ph.D., Sigrun Halvorsen, M.D., Ph.D.,
Kurt Huber, M.D., Stefan Grajek, M.D., Ph.D., Claudio Fresco, M.D.,
Erich Bluhmki, M.D., Ph.D., Anne Regelin, Ph.D., Katleen Vandenberghe, Ph.D.,
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for the STREAM Investigative Team*

Reperfusion: Conclusions Anno 2013

- **Reperfusion therapy is the most effective treatment to offer to STEMI patients and its broad application has significantly reduced case fatality rates both in studies and in the real world over the last 20 years**
- **Major efforts are still needed to shorten delay times especially in patients presenting first to facilities without a cath lab**
- **Distances, weather and traffic conditions are a frequent reason why patients can't get timely PCI**
- **Especially in patients presenting early to an ambulance system or hospital without a cath lab fibrinolytic therapy should be considered when there is any doubt about timely PCI**

STE ACS Primary PCI vs In-Hospital Thrombolysis : Clinical Outcomes

