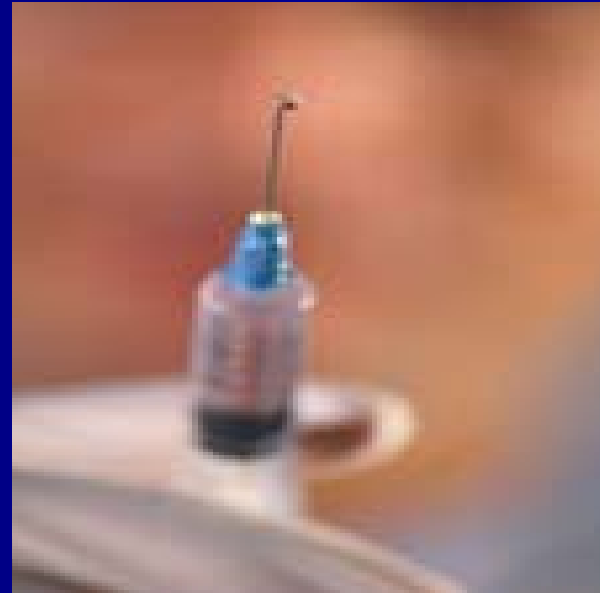


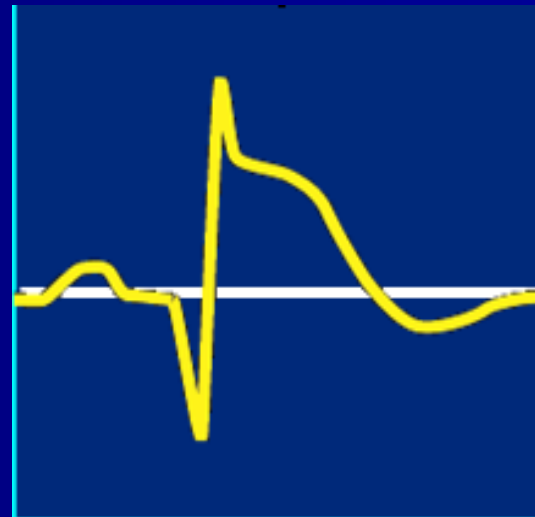
# STRATEGIES OF REPERFUSION

## FACILITATED PCI VS THROMBOLYSIS



**MOHAMMED R ARAFAH**  
**MB BS FACP FRCPC FACC**

# ST elevation myocardial infarction



# Objectives of Reperfusion

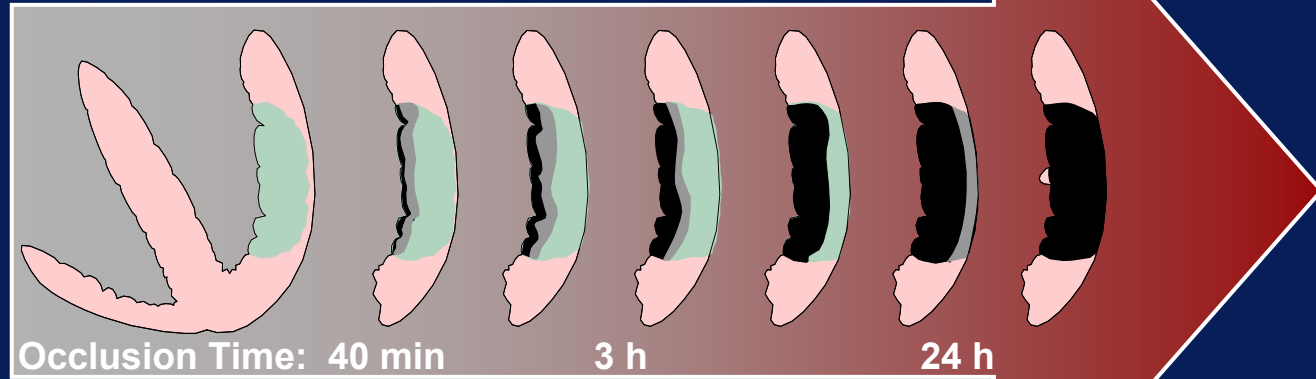
- Effective restoration of coronary patency .
- Less recurrent myocardial ischemia .
- Less coronary reocclusion .
- Less recurrent MI .
- Less Mortality .
- Improved residual left Ventricular Function
- Better clinical outcome including stroke .



# Acute MI



IS

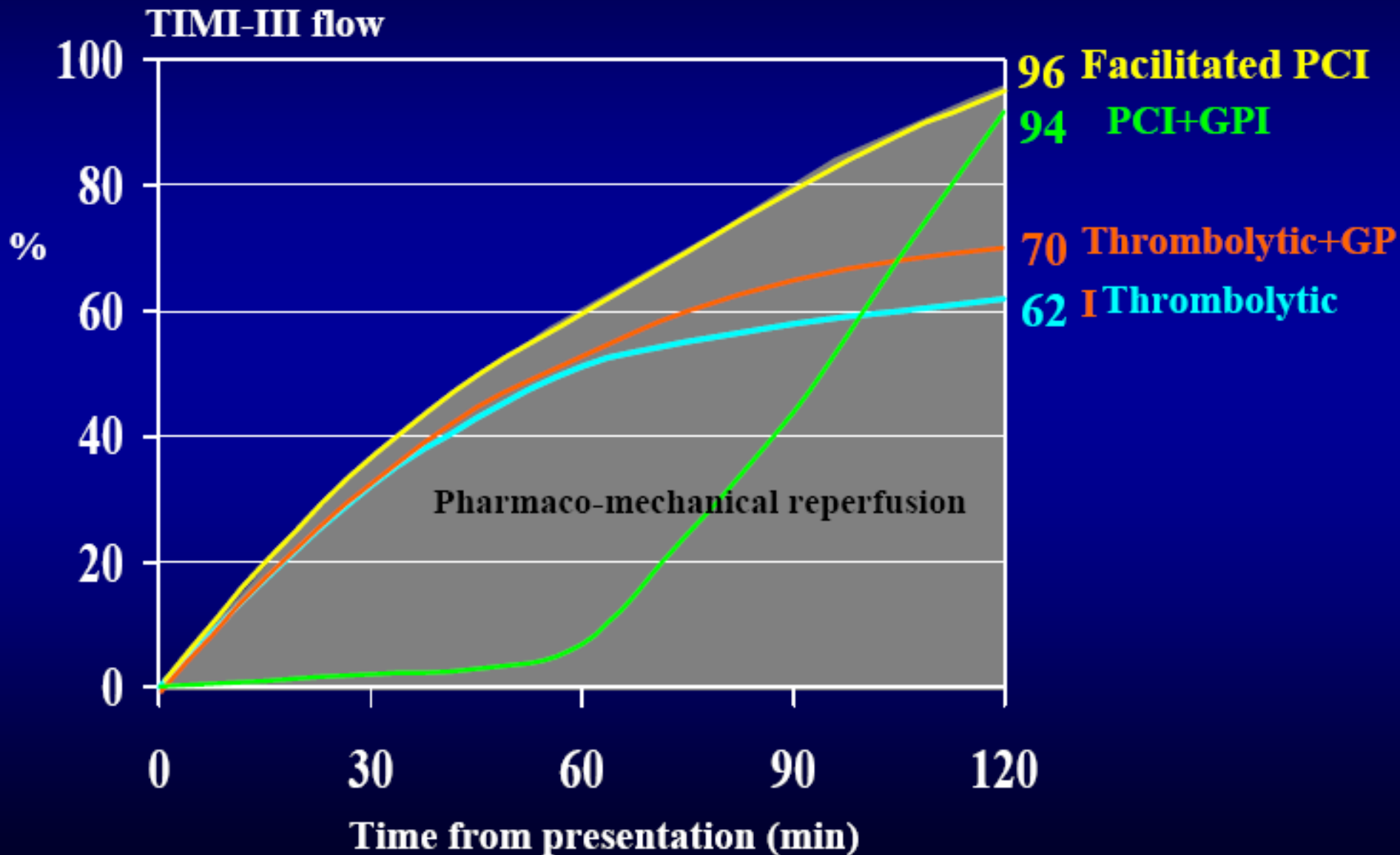


IS



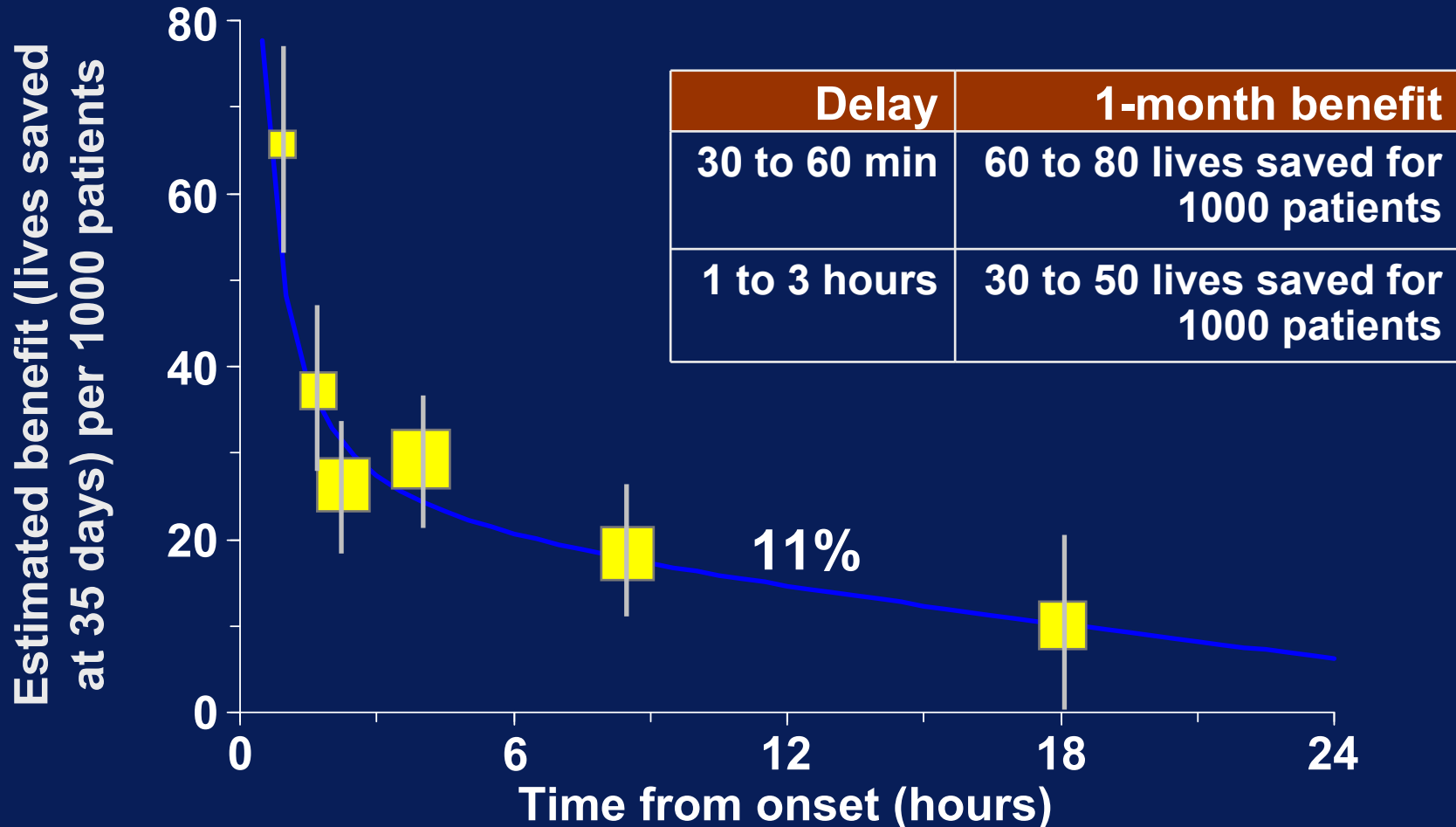
# Evolving Patterns in Treatment of Acute

## MI Improving the TIMI Flow



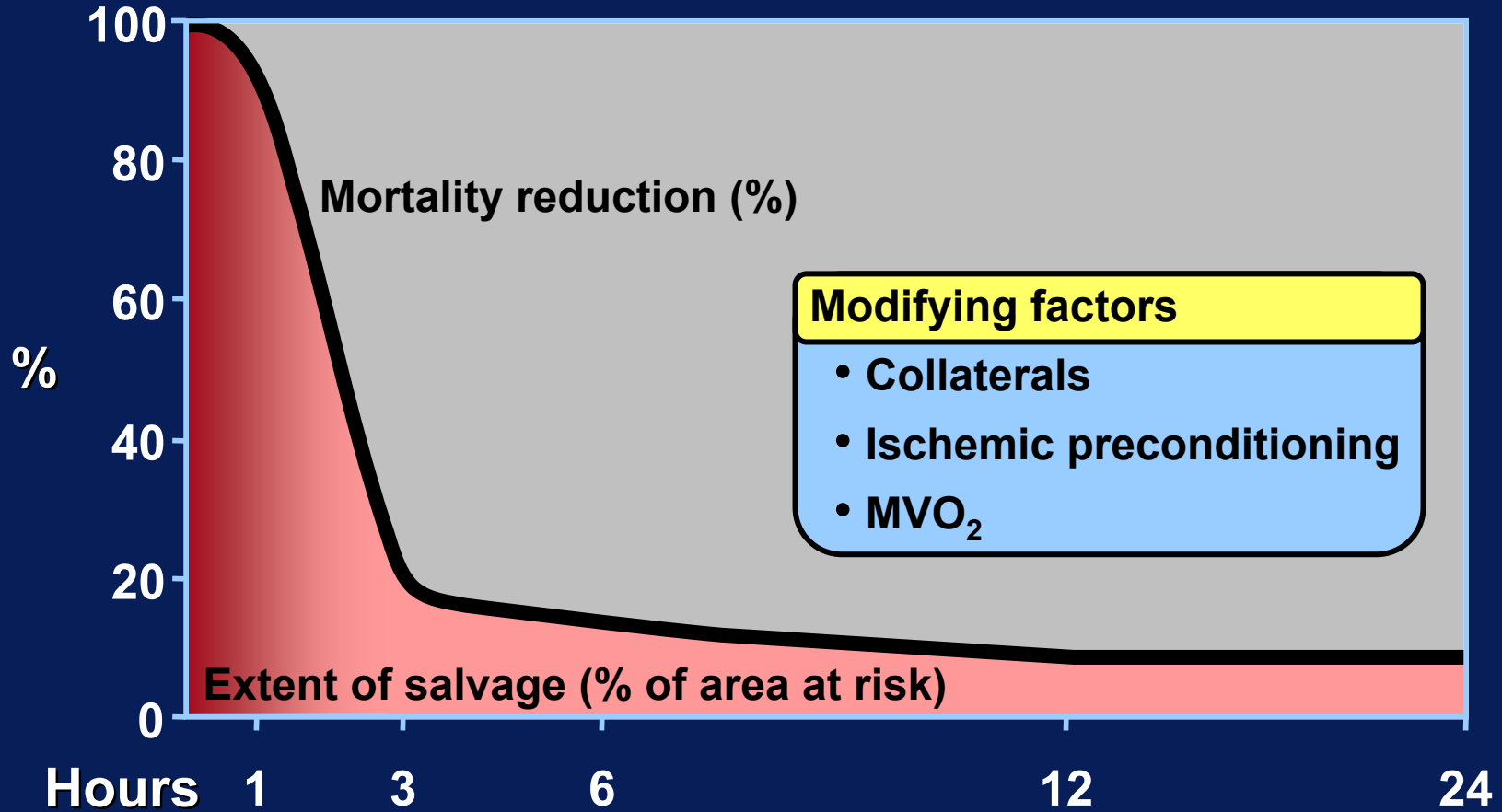
# Mortality Reduction Depends on the Delay “Onset of Pain - Thrombolytic Treatment”

Eric Boersma's meta-analysis (22 trials from 83 to 93 - 50246 patients)

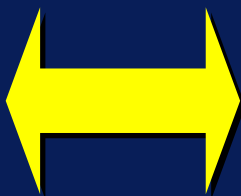


BOERSMA, E. et al Early thrombolytic in acute myocardial treatment infarction : reappraisal of the golden hour - Lancet 1996 ; 771 - 775

# Relationship Between Mortality Reduction and Extent of Salvage

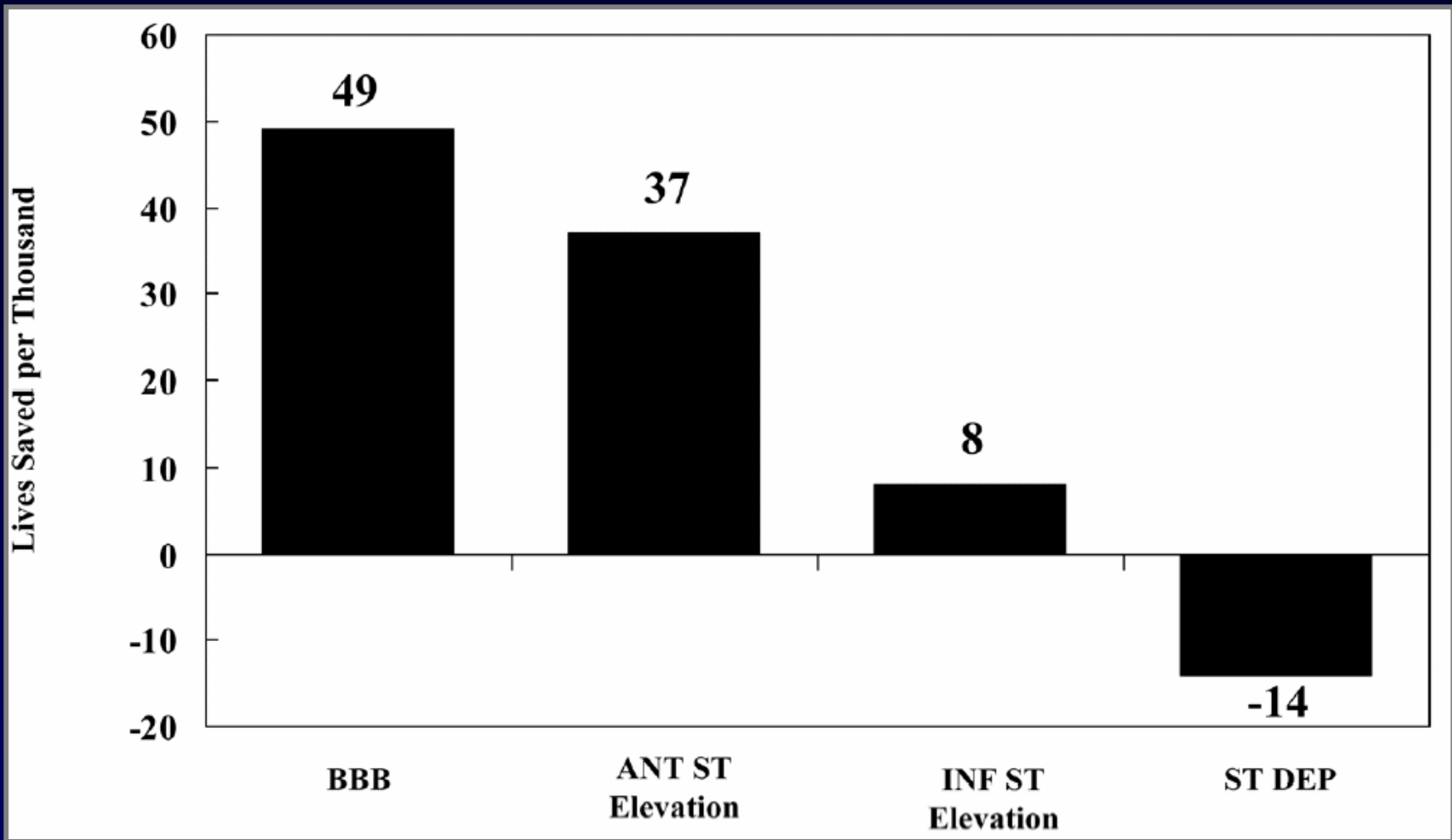


**Treatment objectives**



**Time to treatment is critical**

**Opening the IRA (PCI > lysis)**



Effect of fibrinolytic therapy on mortality according to admission electrocardiogram. Patients with bundle-branch block (BBB) and anterior ST-segment elevation (ANT ST Elevation) derive the most benefit from fibrinolytic therapy. Effects in patients with inferior ST-segment elevation (INF ST Elevation) are much less, while patients with ST-segment depression (ST DEP) do not benefit.

Reprinted with permission from Elsevier (Fibrinolytic Therapy Trialists' Collaborative Group. The Lancet 1994;343:311-22)



# Time of REPERFUSION

- Door to needle time ----- 30 minutes
- Door to balloon time ---- 90 minutes

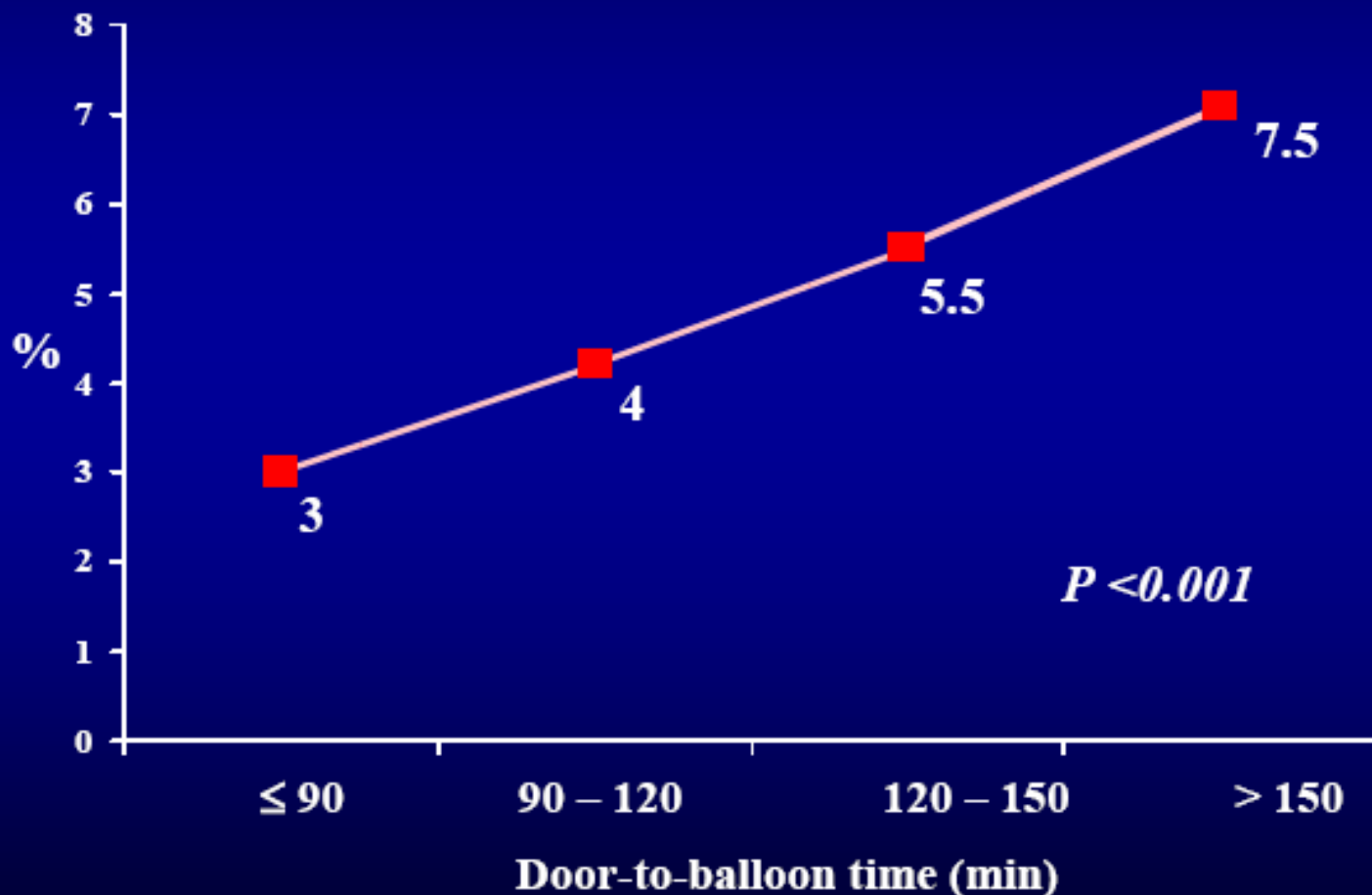
# The expected benefit of fibrinolytic therapy<sup>1-2</sup>.

<b>Door-to-needle</b>	<b>Absolute mortality reduction per 1000</b> (The relative benefit, however, appeared to vary by age, with a smaller relative reduction in risk for the Oldest Pts)
<b>0 to 6 h</b>	<b>30</b>
<b>7 to 12 h</b>	<b>20</b>
<b>13 to 18 h</b>	<b>~ 10</b> <b>(a statistically uncertain benefit, more randomized evidence needed<sup>1</sup> )</b>

1. Fibrinolytic Therapy Trialists' (FTT) Collaborative Group. Indications for fibrinolytic therapy in suspected acute myocardial infarction: collaborative overview of early mortality and major morbidity results from all randomised trials of more than 1000 patients. *Lancet* 1994;343:311-22.
2. Weaver WD, Simes RJ, Betriu A, et al. Comparison of primary coronary angioplasty and intravenous thrombolytic therapy for acute myocardial infarction: a quantitative review. *JAMA* 1997; 278:2093-8.

# National Registry of Myocardial Infarction (NRFMI) 3 & 4: STEMI Patients

## *Relation of Door-to-Balloon Time with In-Hospital Mortality*



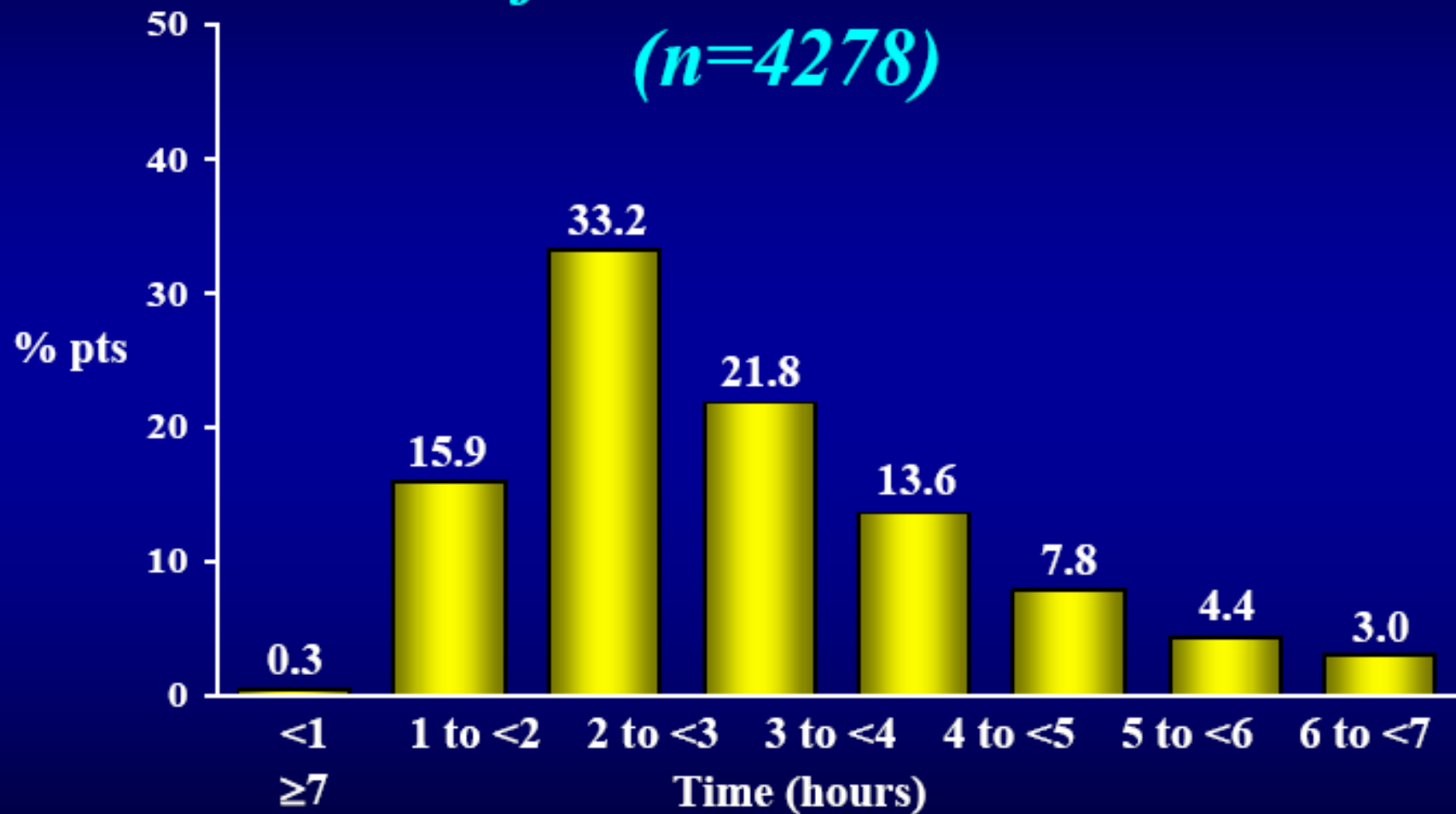
# NRMI 3/4 – Primary PCI in Transfer



## Patients

### *Distribution of Total Door-to-Balloon Time*

*(n=4278)*



*\* Only 4.2% of patients were treated within 90 minutes (the benchmark recommended by national quality guidelines).*

*Brahmajee et al, Circulation*

*2005;111:761*



# The NEW ENGLAND JOURNAL of MEDICINE

SPECIAL ARTICLE

Volume 355:2308-2320    November 30, 2006    Number 22

## Strategies for Reducing the Door-to-Balloon Time in Acute Myocardial Infarction

*Elizabeth H. Bradley, Ph.D., Jeph Herrin, Ph.D., Yongfei Wang, M.S., Barbara A. Barton, R.N.,  
Tashonna R. Webster, M.P.H., Jennifer A. Mattera, M.P.H., Sarah A. Roumanis, R.N., Jephtha P.  
Curtis, M.D., Brahmajee K. Nallamothu, M.D., David J. Magid, M.D., M.P.H., Robert L. McNamara  
M.D., M.H.S., Janet Parkosewich, R.N., M.S.N., Jerod M. Loeb, Ph.D., and Harlan M. Krumholz,  
M.D.*

# *Results*

**In multivariate analysis, six strategies were significantly associated with a faster door-to-balloon time.**

**1 - Emergency medicine physicians activate the catheterization laboratory (mean reduction in door-to-balloon time, 8.2 minutes),**

**2 - Having a single call to a central page operator activate the laboratory (13.8 minutes),**

**3 - The emergency department activate the catheterization laboratory while the patient is en route to the hospital (15.4 minutes),**

# *Results*

**4 - Expecting staff to arrive in the catheterization laboratory within 20 minutes after being paged (vs. >30 minutes) (19.3 minutes),**

**5 - An attending cardiologist always on site (14.6 minutes),**

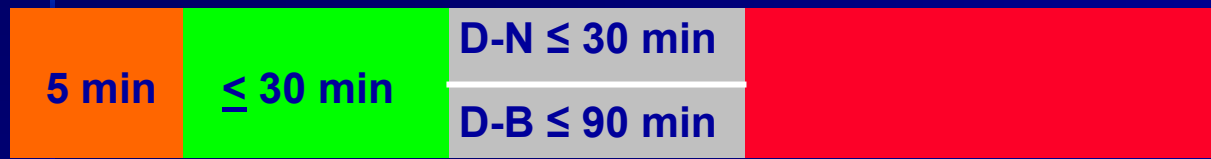
**6 - Staff in the emergency department and the catheterization laboratory use real-time data feedback (8.6 minutes).**

Despite the effectiveness of these strategies, only a minority of hospitals surveyed were using them.

# Reperfusion

■ Patient ■ Transport ■ Inhospital ■ Reperfusion

## Goals



↑  
Media campaign  
Patient education

↑  
Greater use of  
9-9-7  
Prehospital Rx

↑  
Prehospital  
ECG

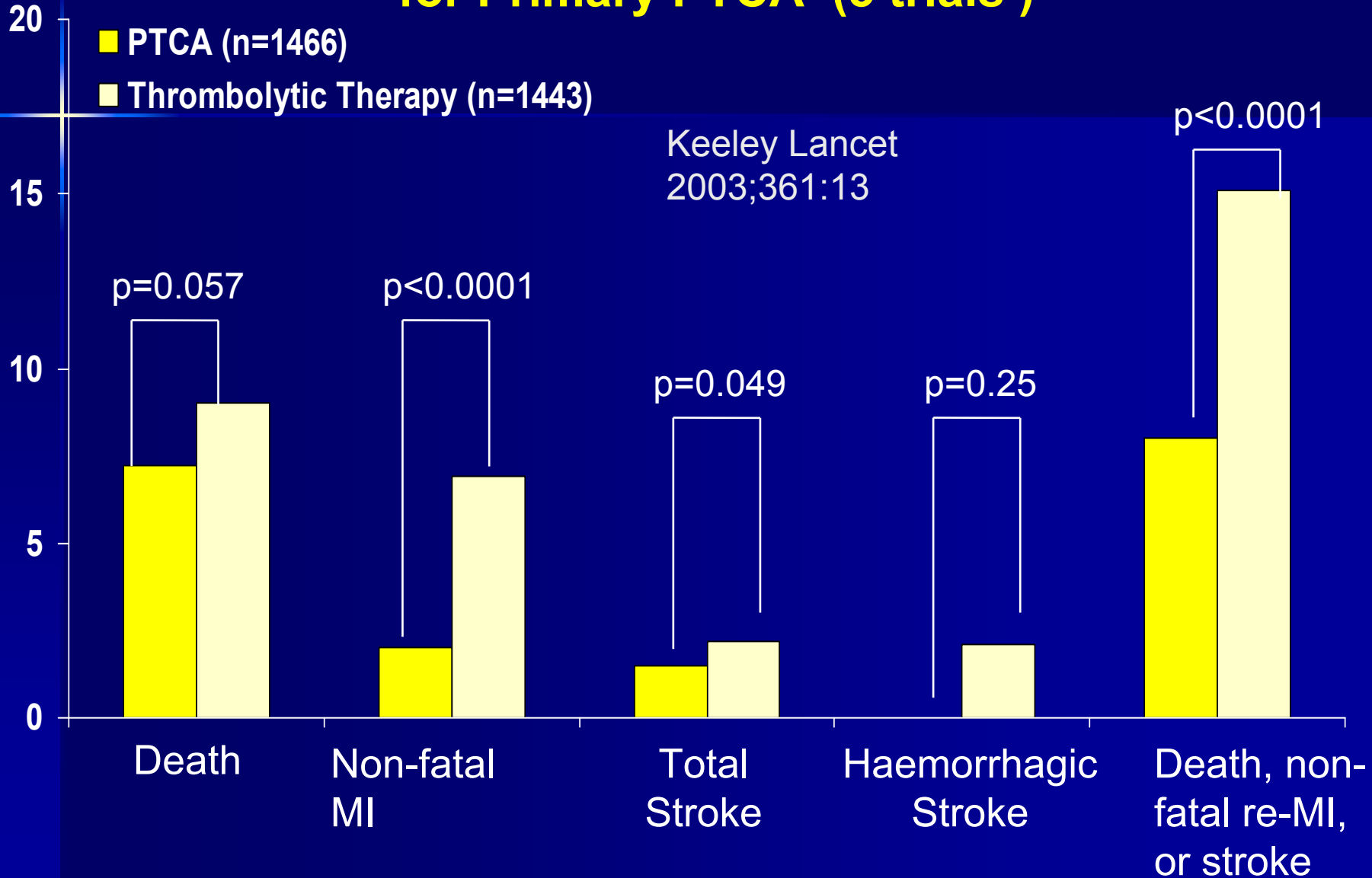
↑  
MI protocol  
Critical pathway  
Quality  
improvement  
program

↑  
Bolus lytics  
Dedicated  
PCI team

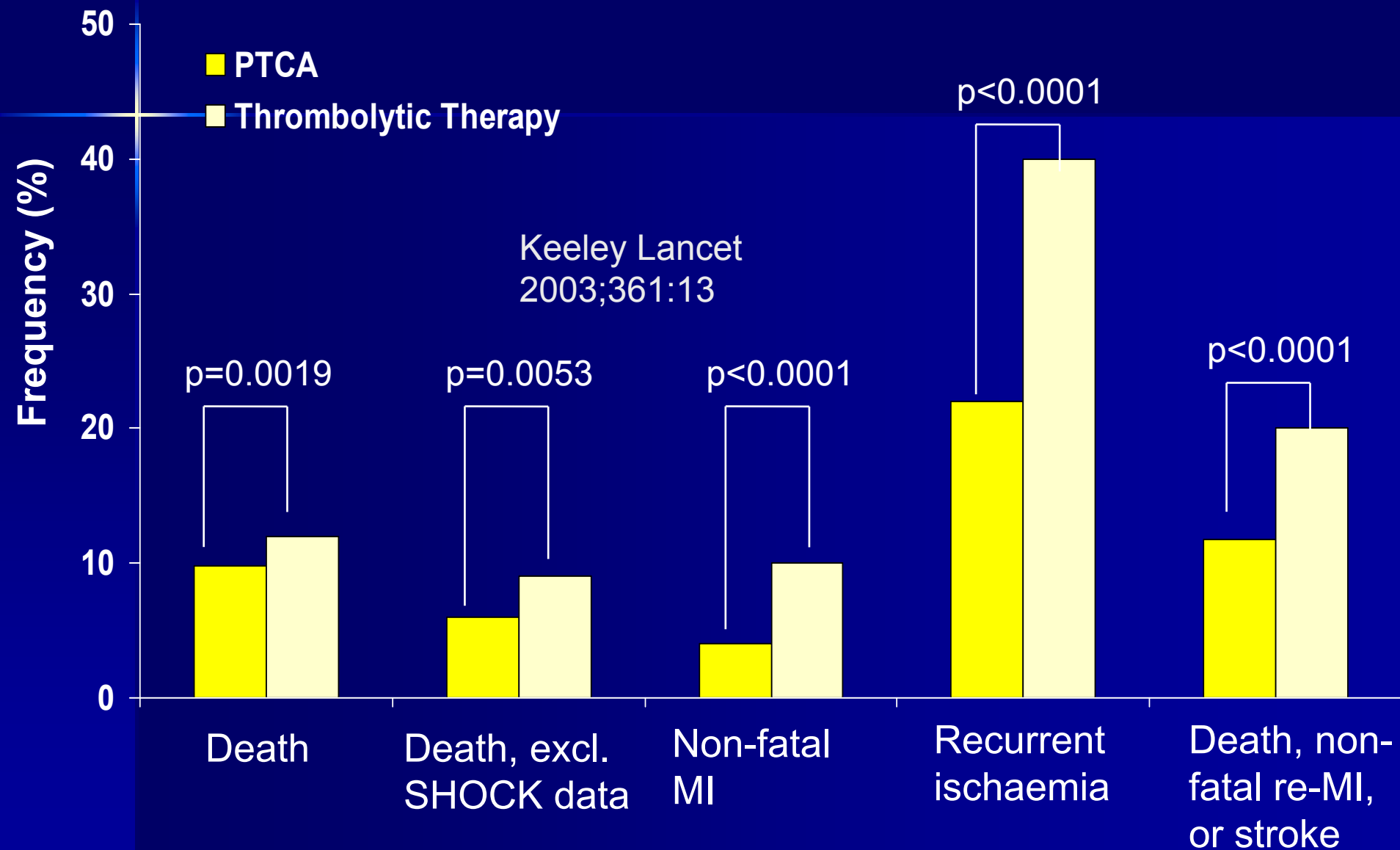
Methods of  
Speeding  
Time to  
Reperfusion



# Short-term Outcomes in Individuals Treated with On-Site Thrombolytic Therapy or After Emergent Transfer for Primary PTCA (5 trials)



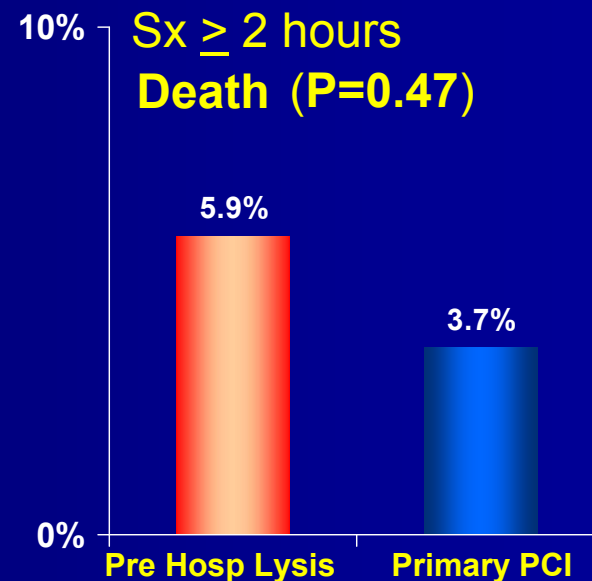
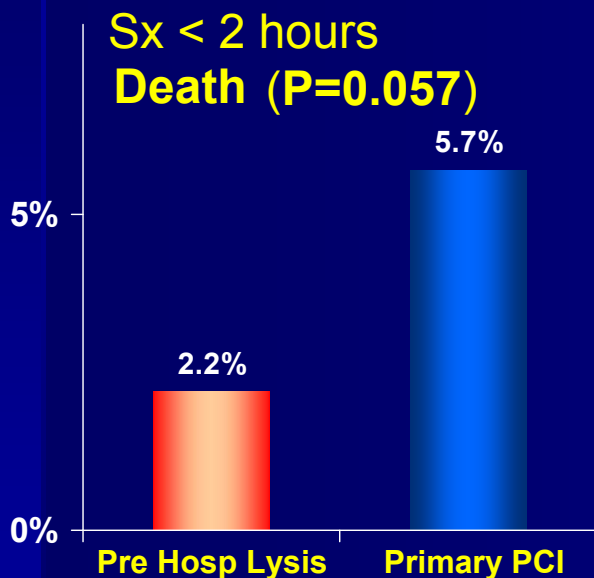
# Long Term Outcomes in Individuals Treated with Primary PTCA or Thrombolytic Therapy



# Prehospital Fibrinolysis

## CAPTIM trial:

Patients (n=840) randomized < 2 h after symptom onset had a strong trend toward lower 30-day mortality with prehospital fibrinolysis than did those randomized to primary PCI.



Bonnefoy E, Lapostolle F, Leizorovicz A, et al for the Comparison of Angioplasty and Prehospital Thrombolysis in Acute Myocardial Infarction Study Group. Primary angioplasty versus prehospital fibrinolysis in acute myocardial infarction: a randomised study. *Lancet* 2002;360:825-9.

# Euro Heart II 2005

# PCR

6356 Patient with ACS

3039 (48%) ST Elevation MI

1847 (61%) Primary Reperfusion

Excluding patient :

- 27% Late presentation .
- 15% Uncertain diagnosis .
- 11% Early ST elevation resolution .

# Euro Heart II

- Reperfusion :
  - 59% PCI
  - 41% Thrombolysis
- 30 Days MORTALITY 6.8%

# Combination Therapy

**Fibrinolytics or other pharmacologics 'facilitate' PCI**

## **Pharmacoinvasive Recanalization:**

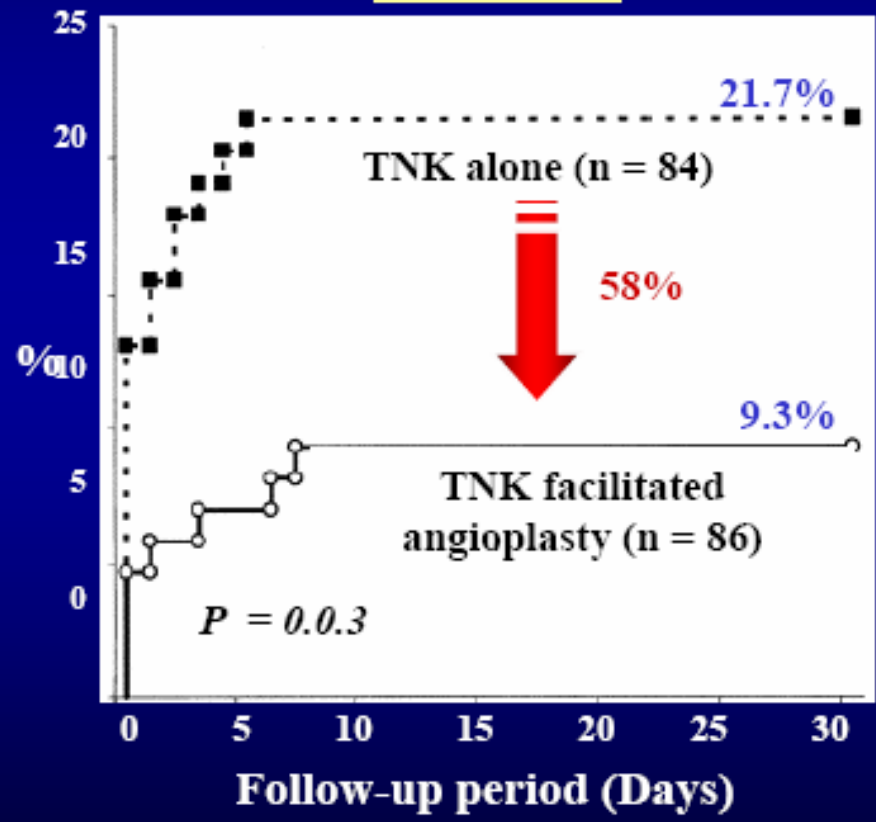
**Capitalizes on the rapidity of initiation & widespread feasibility of pharmacologic thrombolysis to promptly restore 'some' myocardial blood flow, coupled with the more complete restoration achievable with subsequent PCI**

**Dauerman & Sobel, *JACC* 2003;42:646-51**

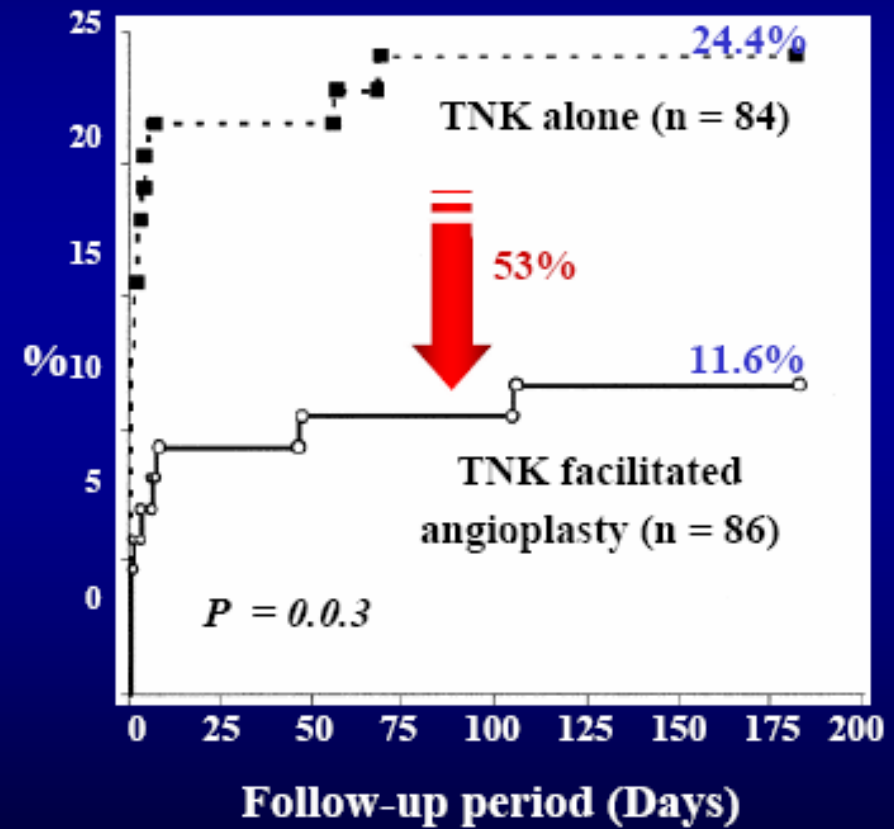
# CAPITAL AMI Study: Combined Angioplasty and Pharmacological Intervention vs. Thrombolysis Alone in AMI

## Kaplan-Meier Curves of Death, re-MI, UA or Stroke

### 30 Days



### 6 Months



**ASSENT-4**

**Tenecteplase prior to PCI**



# Study Endpoints



## Primary Endpoint:

- composite of 90-day mortality or cardiogenic shock\* or congestive heart failure\*

## Secondary and Tertiary Endpoints:

- composite triple endpoint within 30 days
- cardiogenic shock or CHF within 90 days
- single components of composite endpoint at different time points, re-MI, TVR, rehospitalization, NT-proBNP, TIMI flow before and after PCI

\* adjudicated by CEC

# AMI <6 hours

Cath likely in 1-3 hours

Total ST elev  $\geq 6$  mm (anterior), or  $\geq 6$  mm ST deviation including  $\geq 4$  mm ST elev (inferior), or LBBB presumed new

**N=4,000**

**open label**

**ASA**  
**UFH (bolus)**  
**TNK**

**ASA**  
**UFH (bolus)**  
**No lytic**

**Cath lab**

**Angiography / PCI**  
**(immediate)**

**Angiography / PCI**  
**(immediate)**

**UFH/Stent/clopidogrel**

**UFH/Stent/clopidogrel**

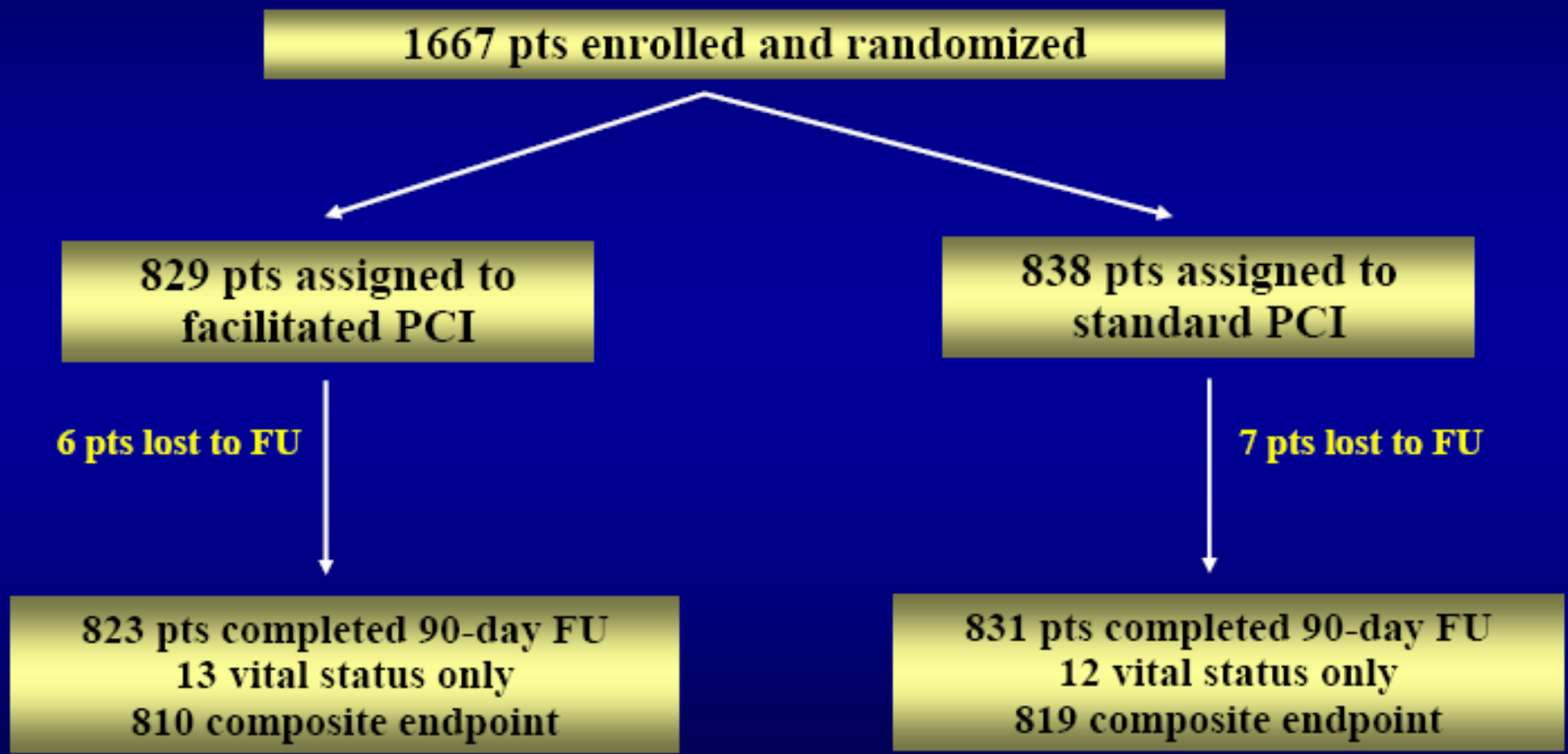
**NO GP IIb/IIIa inhibitors**

**$\pm$  GP IIb/IIIa at investigator discretion**

**90 day death, cardiogenic shock or CHF**

# Primary vs. Tenecteplase-Facilitated PCI in Patients with STEMI AMI: ASSENT – 4 PCI

## Trial Design

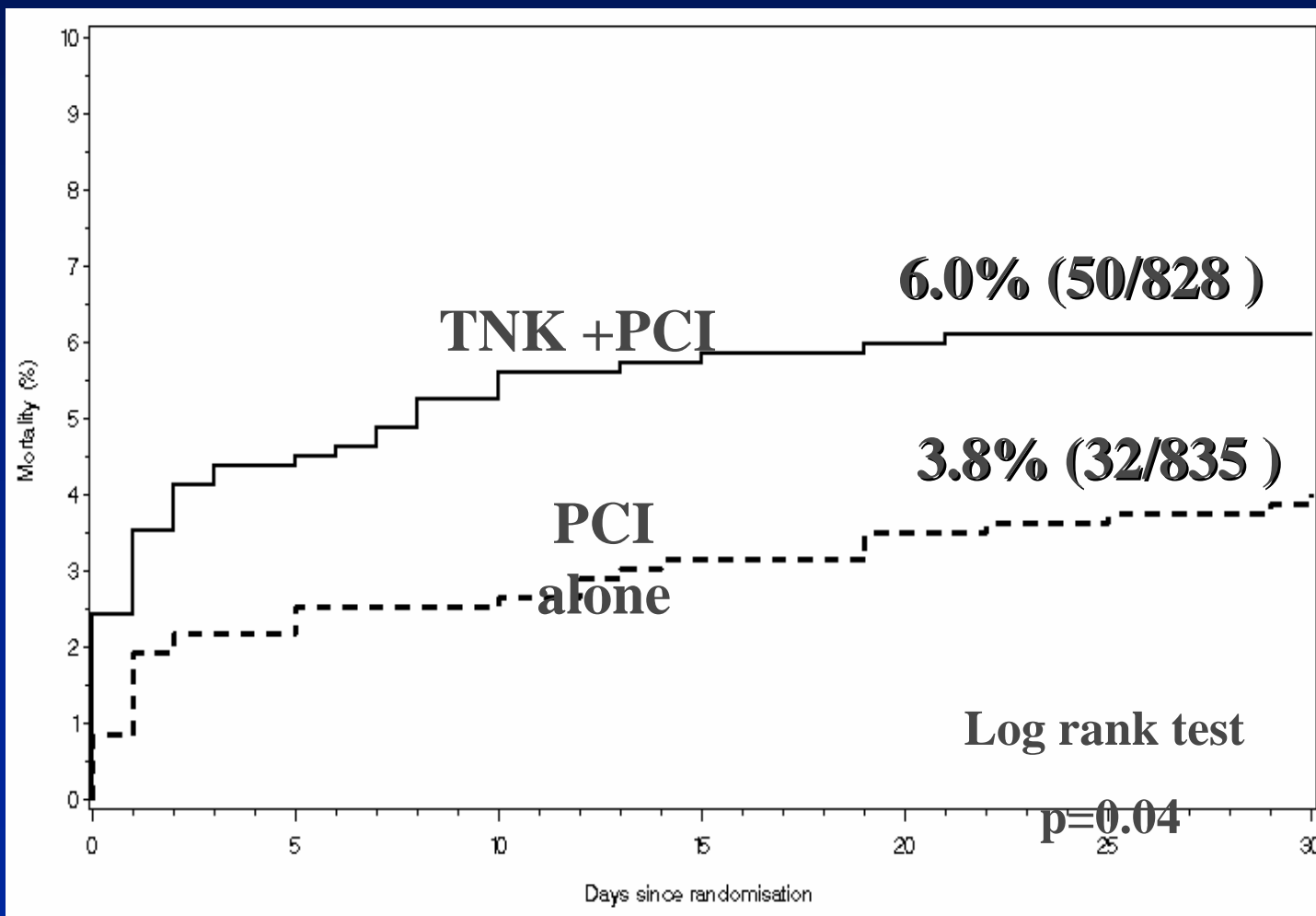


# Angiographic Data (2) As Reported By Investigators



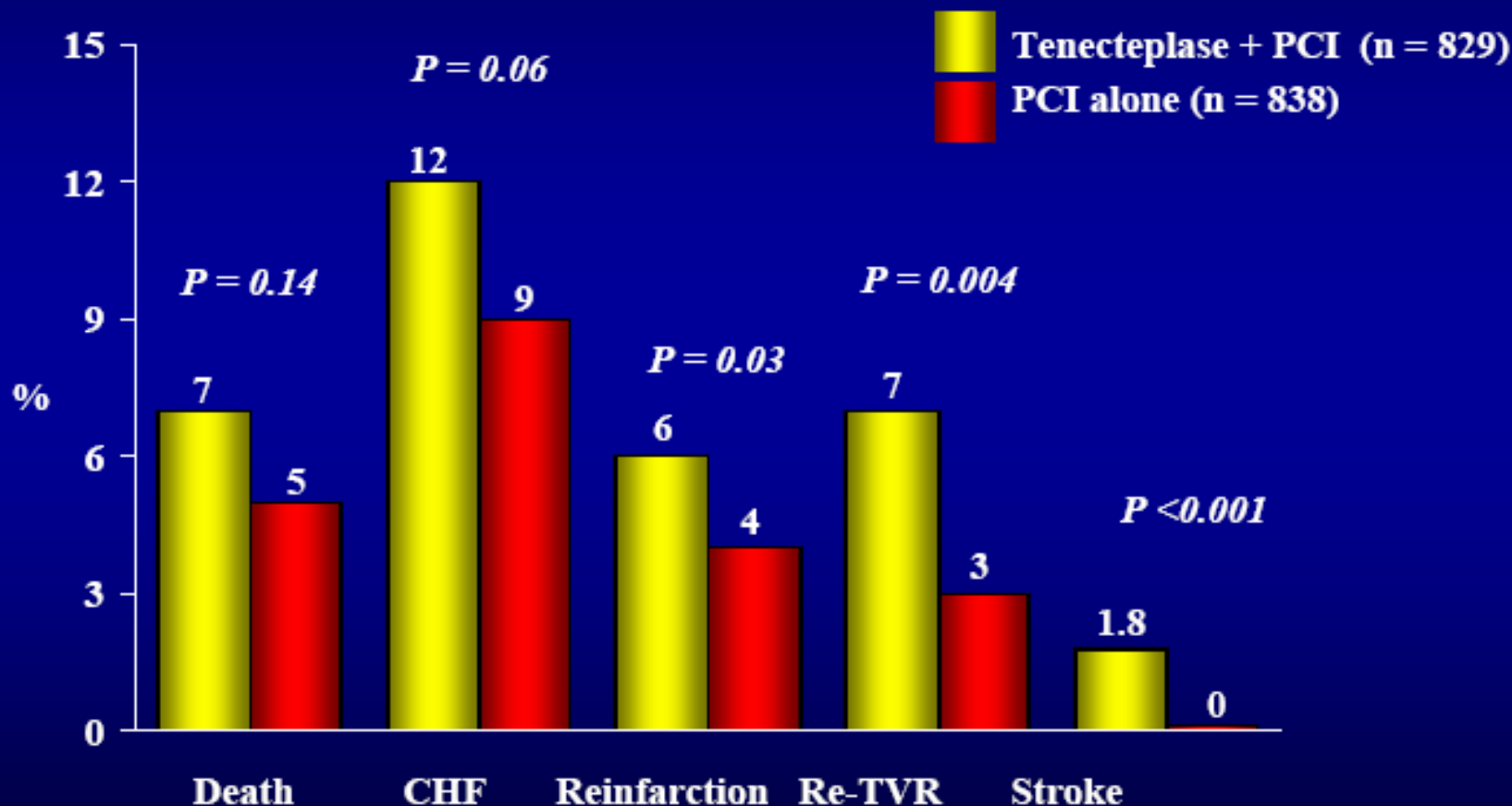
	%	TNK + PCI	PCI alone	p-value
PCI performed		87.1	91.1	0.01
with stent		81.3	85.7	0.02
(DES)		19.1	19.7	0.97
 TIMI flow after PCI				 0.03
TIMI 0		2.1	1.7	
TIMI 1		2.1	0.5	
TIMI 2		7.7	8.9	
<b>TIMI 3</b>		<b>87.6</b>	<b>88.7</b>	
Cannot be assessed		0.6	0.1	

# Kaplan-Meier Curves for 30 DAY MORTALITY



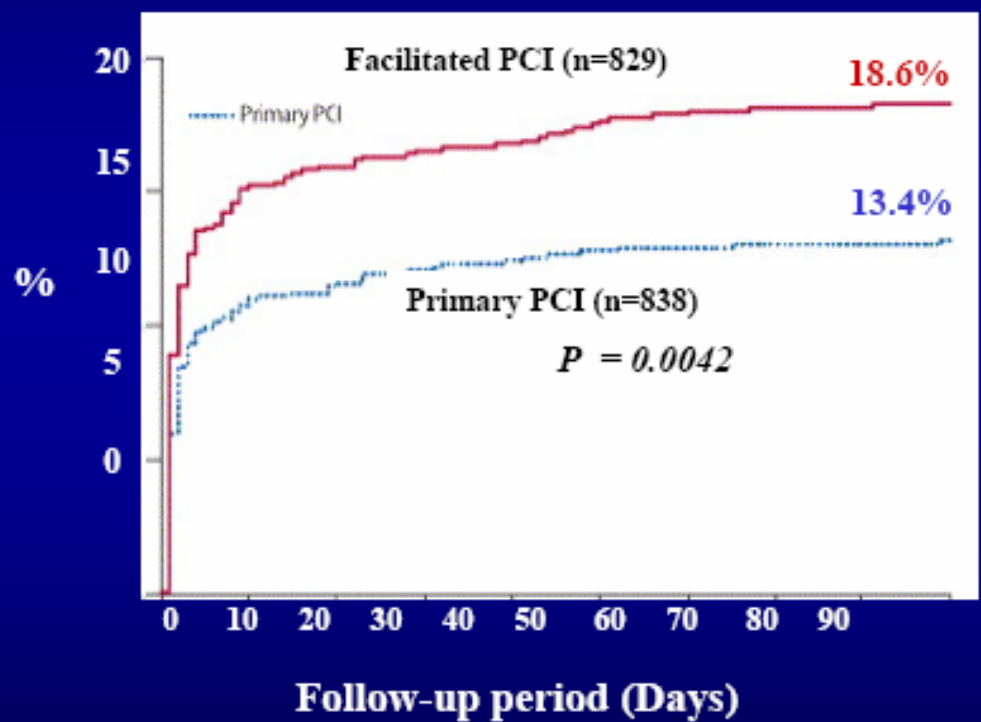
# Primary vs. Tenecteplase-Facilitated PCI in Patients with STEMI AMI: ASSENT – 4 PCI

*Clinical Endpoints at 90-Days of Randomization*



# Primary vs. Tenecteplase-Facilitated PCI in Patients with STEMI AMI: ASSENT – 4 PCI

*Kaplan-Meyer Curves for Primary Endpoint: Death, CHF or Shock in 90 Days*



No. at risk										
Facilitated PCI	829	703	696	691	685	678	675	673	373	672
Primary PCI	838	747	741	736	730	726	725	724	724	722

*Van de Werf et al, ESC 2005  
Lancet 2006;367:569*

# 30 Day Mortality: Subgroups



%	TNK +PCI	PCI alone
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Treatment started  
in PCI hosp  
n=754

7.3

3.8

Treatment started  
in community hosp  
n=588

6.0

4.0

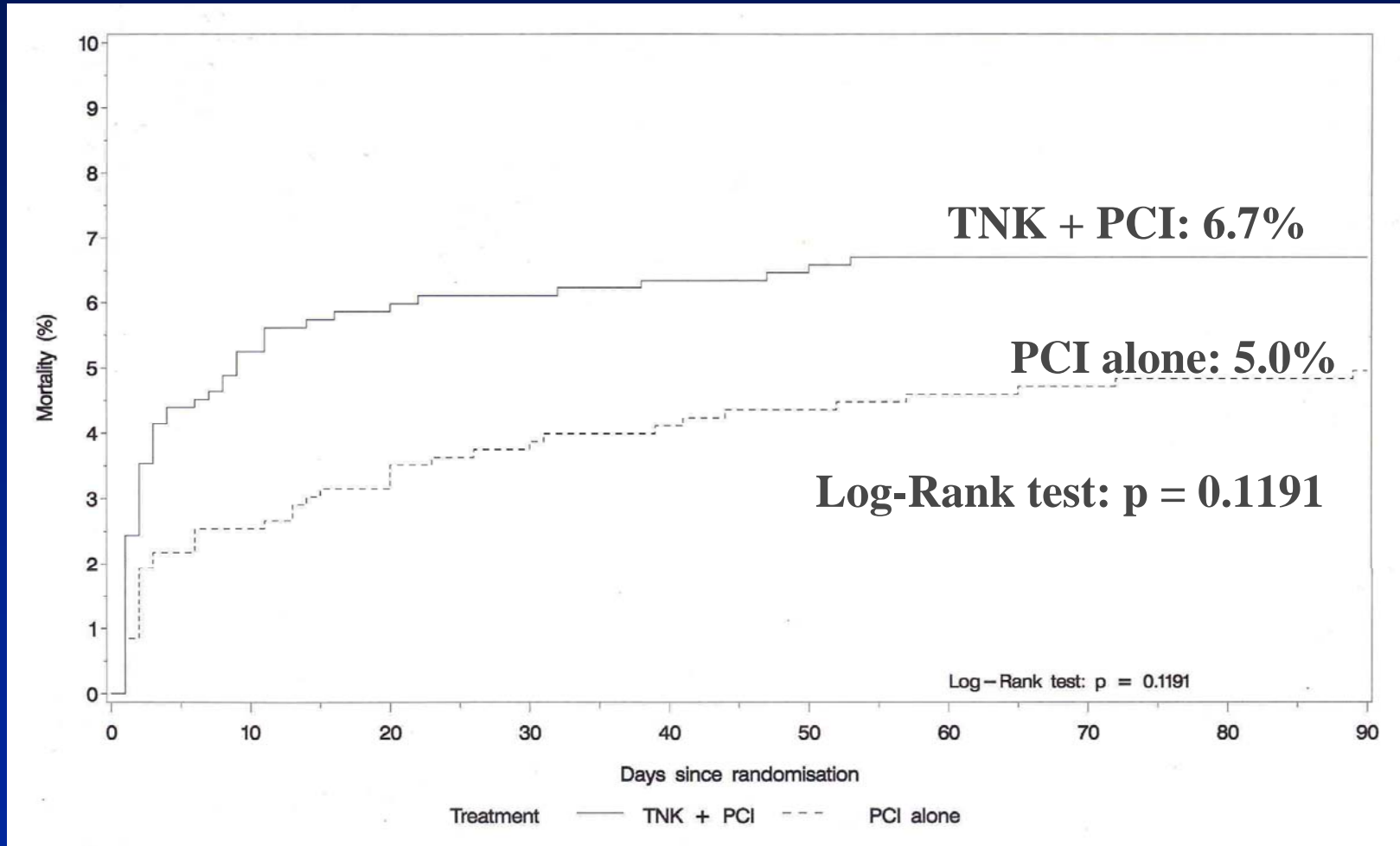
Treatment started  
in ambulance  
n=325

3.1

3.7



# Kaplan-meier Curve For Mortality



# Stroke Rates Up To Day 90



%	TNK + PCI	PCI alone	p-value
<b>IN-HOSPITAL</b>			
Intracranial haemorrhage	8 (0.97)	0	0.004
Primary ischemic stroke	5 (0.60)	0	0.03
Unclassified	2 (0.24)	0	0.25
Total	15 (1.81)	0	<0.001
<b>AFTER DISCHARGE</b>			
Intracranial haemorrhage	1 (0.12)	1 (0.12)	>0.99
Primary ischemic stroke	4 (0.48)	0	0.06
Unclassified	2 (0.24)	0	0.25
<b>TOTAL</b>	<b>22 (2.65)</b>	<b>1 (0.12)</b>	<b>&lt;0.0001</b>

# Conclusions



1. In this prematurely terminated trial the incidence of the combined clinical endpoint of death, congestive heart failure or shock at 90 days was significantly higher in the TNK + PCI arm than in the PCI arm
2. Major bleeding complications and ICH rates were also more frequent in the TNK + PCI arm
3. Therefore, a strategy of routine, immediate PCI following full dose lytic, as used in this trial, cannot be recommended

# Conclusions (2)

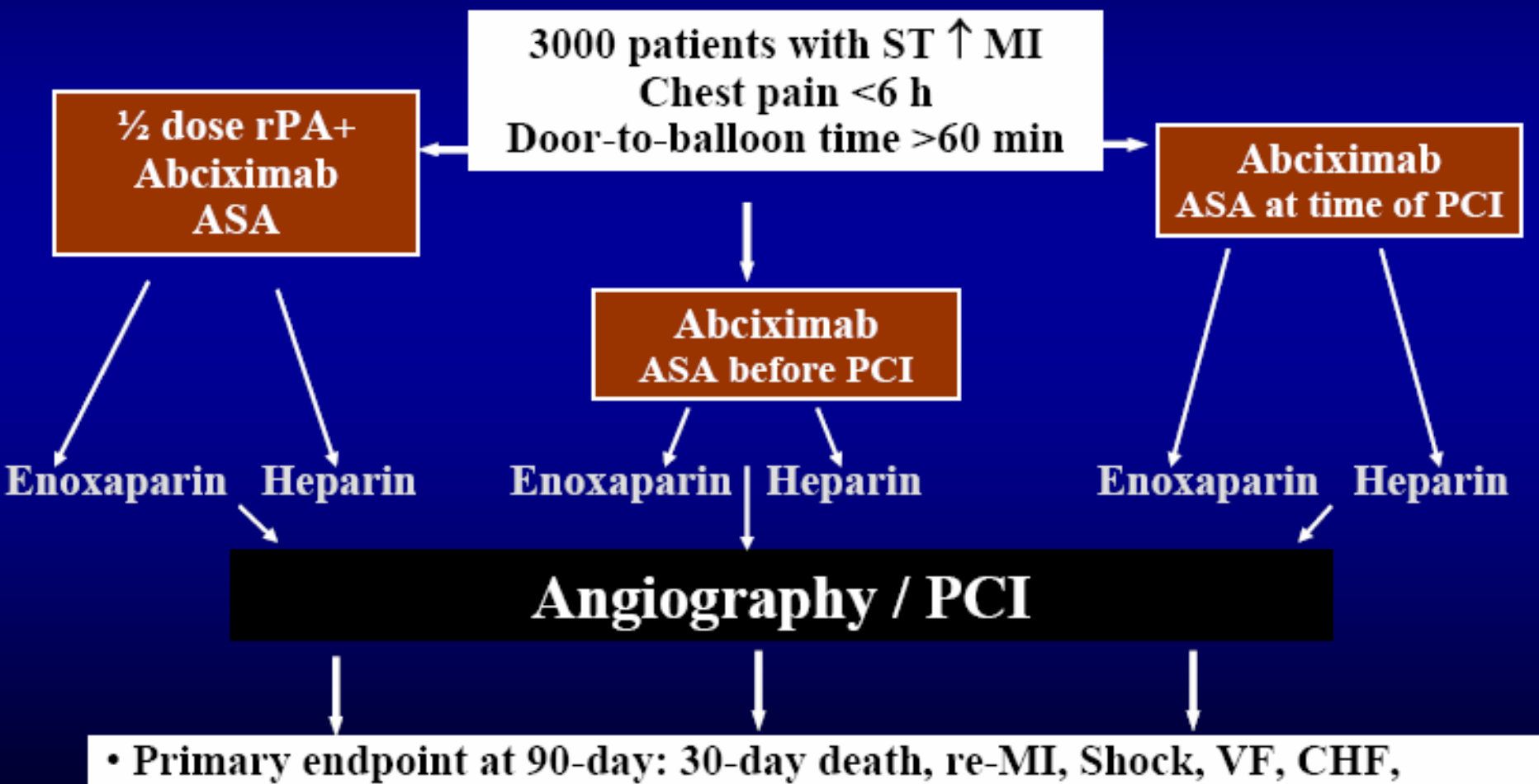


3. Early abrupt vessel closure, repeat TVR and re-MI were reported more by the investigators in the TNK + PCI arm suggesting a pro-thrombotic effect
4. Therefore, a strategy of routine, immediate PCI following full dose lytic, as used in this trial, cannot be recommended

# Facilitated Intervention with Enhanced reperfusion

## Speed to Stop Events: FINESSE Trial

### Study Design



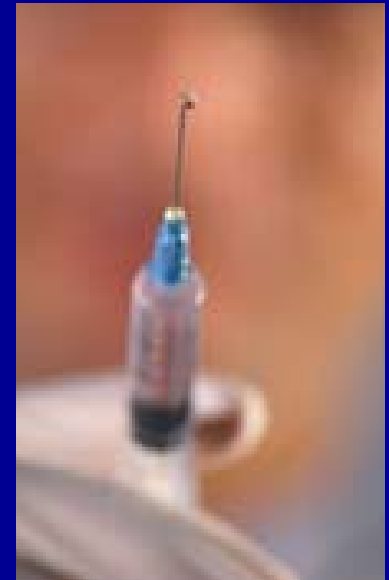
# Reperfusion Options for STEMI Patients

## *Select Reperfusion Treatment.*

*If presentation is < 3 hours and there is no delay to an invasive strategy, there is no preference for either strategy.*

### Fibrinolysis generally preferred

- ♥ ■ *Early presentation ( $\leq 3$  hours from symptom onset and delay to invasive strategy)*
- ♥ ■ *Invasive strategy not an option*
  - Cath lab occupied or not available
  - Vascular access difficulties
  - No access to skilled PCI lab
- ♥ ■ *Delay to invasive strategy*
  - Prolonged transport
  - Door-to-balloon more than 90 minutes
  - > 1 hour vs fibrinolysis (fibrin-specific agent) now



# Reperfusion Options for STEMI Patients

## *Select Reperfusion Treatment.*

*If presentation is < 3 hours and there is no delay to an invasive strategy, there is no preference for either strategy.*

### Invasive strategy generally preferred

- ♥
  - *Skilled PCI lab available with surgical backup*
    - *Door-to-balloon < 90 minutes*
- ♥
  - *High Risk from STEMI*
    - *Cardiogenic shock, Killip class  $\geq 3$*
- ♥
  - *Contraindications to fibrinolysis, including increased risk of bleeding and ICH*
- ♥
  - *Late presentation*
    - *> 3 hours from symptom onset*
- ♥
  - *Diagnosis of STEMI is in doubt*



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Thank you for  
listening