Old issue, unsolved Fibrinolysis

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Goals of Reperfusion therapies in Acute ST-segment elevation MI

Prompt restoration of coronary artery blood flow

Restoration of myocardial tissue perfusion

Minimization of reperfusion injury

Primary PCI

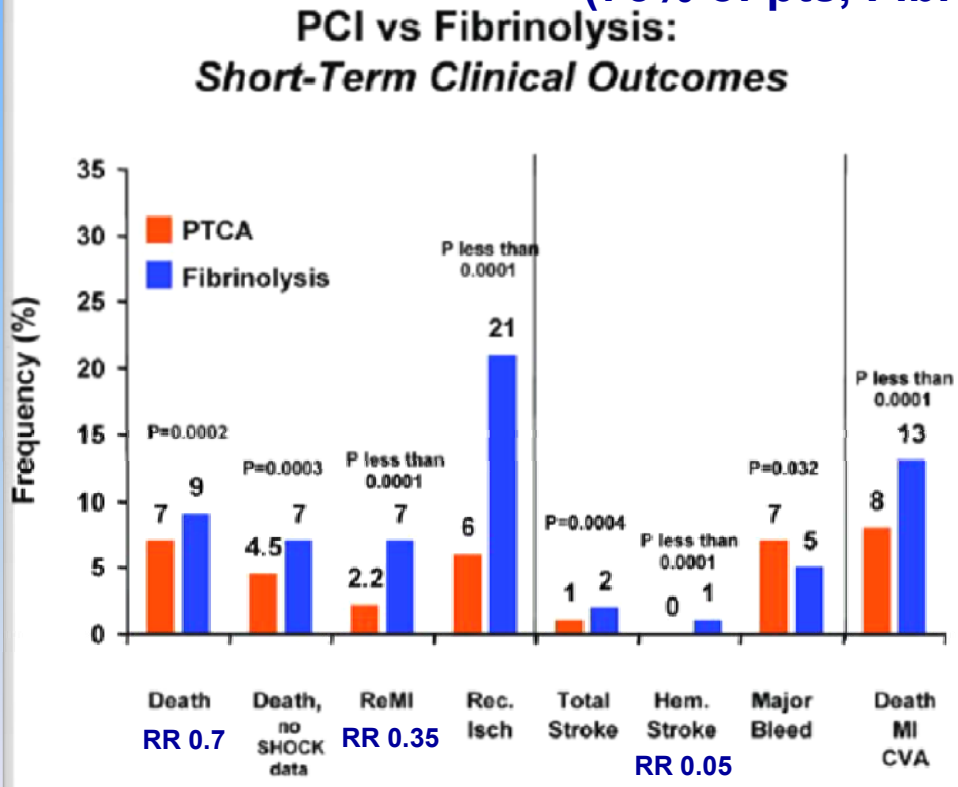
Fibrinolysis

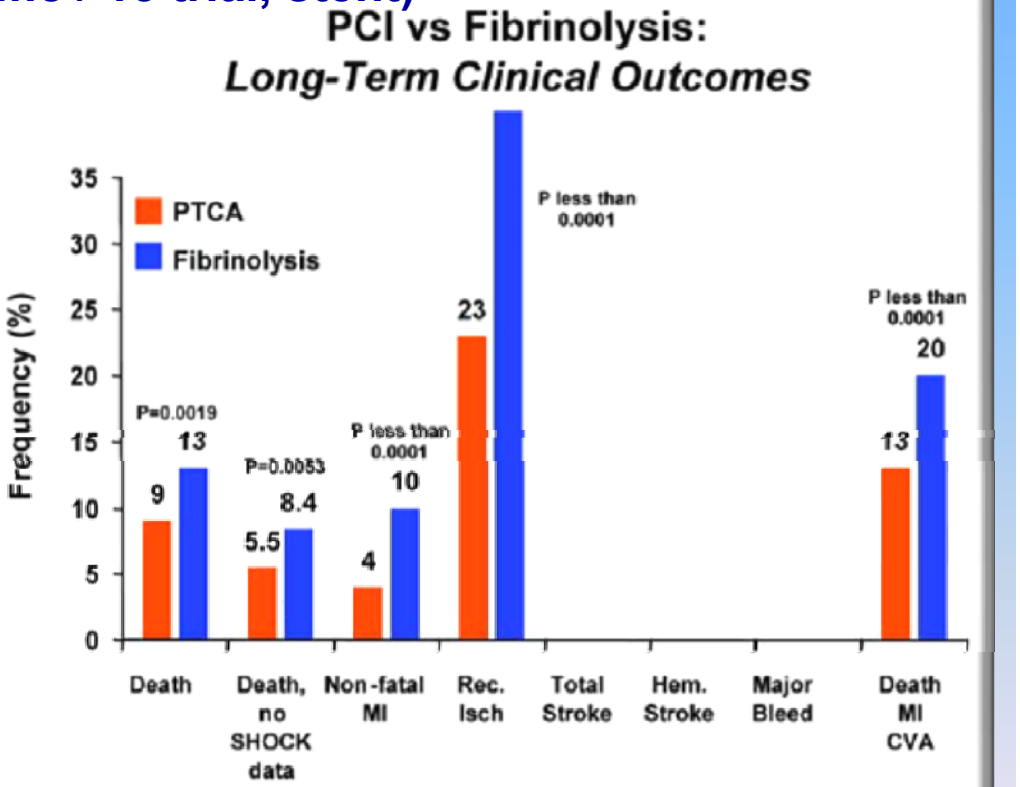
Minimizes LV dysfunction

Prevention of pump failure or ventricular arrhythmia

Efficacy and safety of PCI vs fibrinolysis In Acute STEMI

23 trial, 7739pts meta-analysis
(75% of pts, Fibrin specific / 15 trial, stent)





Lancet 2003;361:13-20

Primary PCI
2004 ACC/AHA guidelines

Class I

1.If immediately available, primary PCI should be performed in patients with STEMI (including true posterior MI) or MI with new or presumably new LBBB who can undergo PCI of the infarct artery within 12 hours of symptom onset, If performed in a timely fashion (balloon inflation within 90 minutes of presentation) by persons skilled in the procedure (individuals who perform more than 75 PCI/yr) The procedure should be supported by experienced personnel in an appropriate laboratory environment (a laboratory that performs more than 200 PCI procedures/yr, of which at least 36 are primary PCI for STEMI, and has cardiac surgery capability).
(Level of Evidence: A)

Feasibility of primary PCI

-The Proportion of Acute care center having a PCI center(<25% in US)

-Staffing availability for 24 hour and 7 days

-The volume of primary PCI (>36 primary PCI cases per year)

On-site fibrinolysis **vs**

Transfer for primary PCI

서부경남 지역 primary PCI center

종합병원 24개, PCI 가능병원 4개(15%)

Check points, when selecting reperfusion strategy

1) to determine time from onset of symptoms

2) high-risk attributes

3) relative bleeding risks associated with fibrinolysis

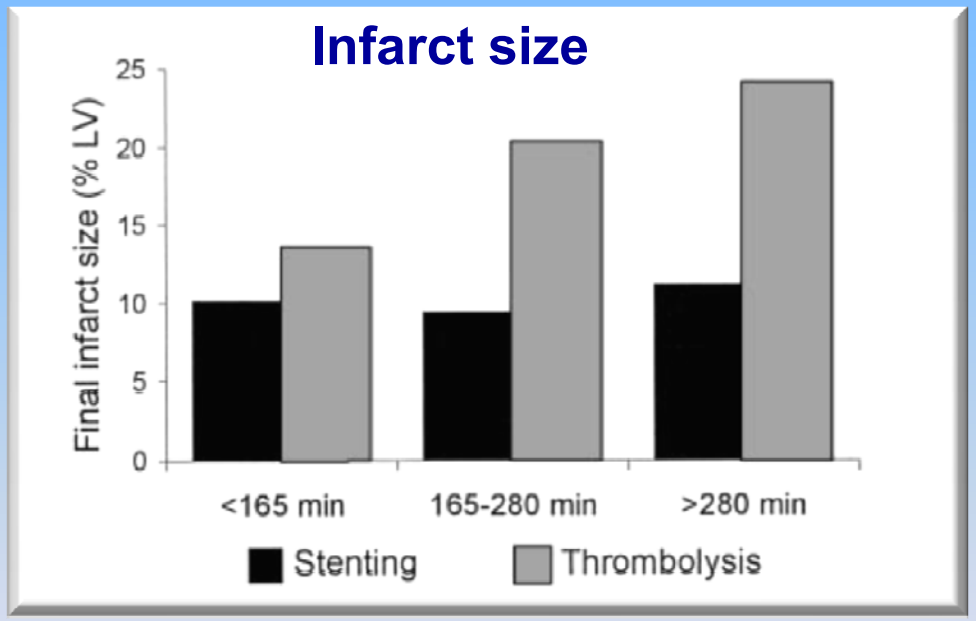
4) total time required for achieving balloon inflation

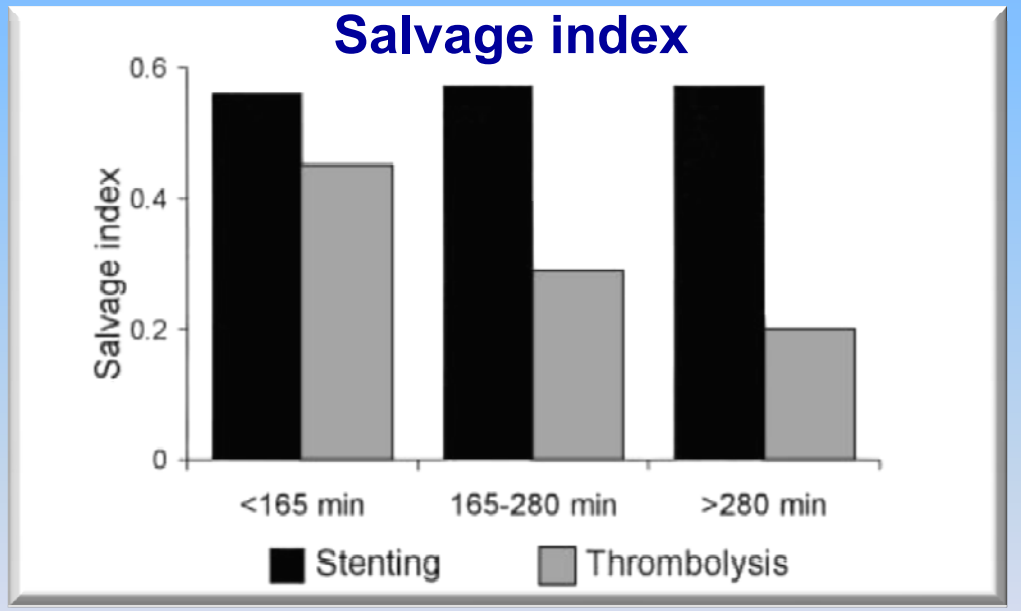
Time from symptom onset

Time dependency of reperfusion therapy

Restoration of full antegrade flow in PCI

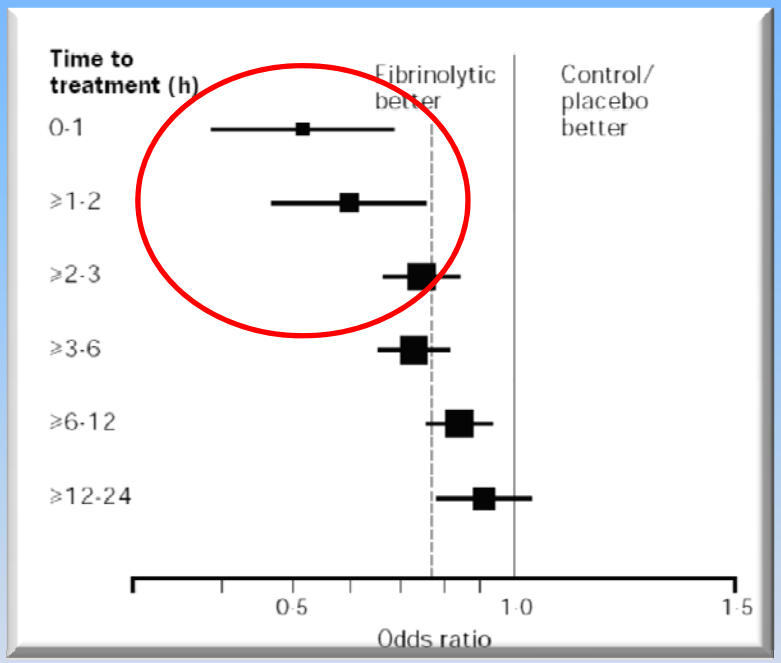
Maturation of thrombi with passage of time

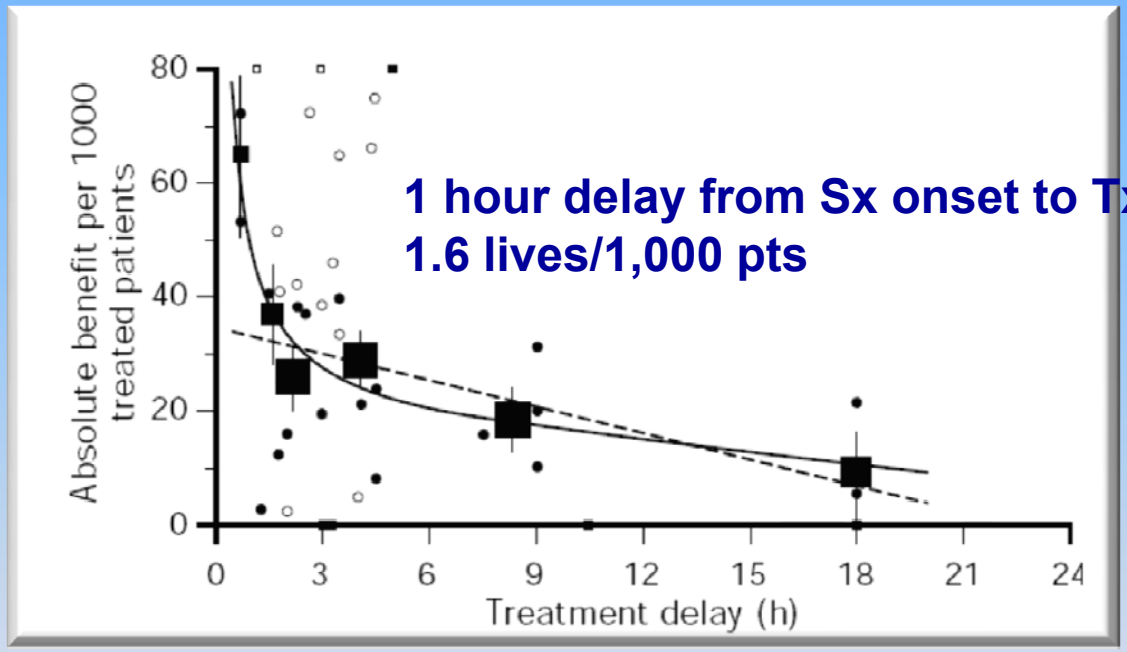




Circulation. 2003;108:1084-1088

Relation between delay and mortality In thrombolysis: *not linear*

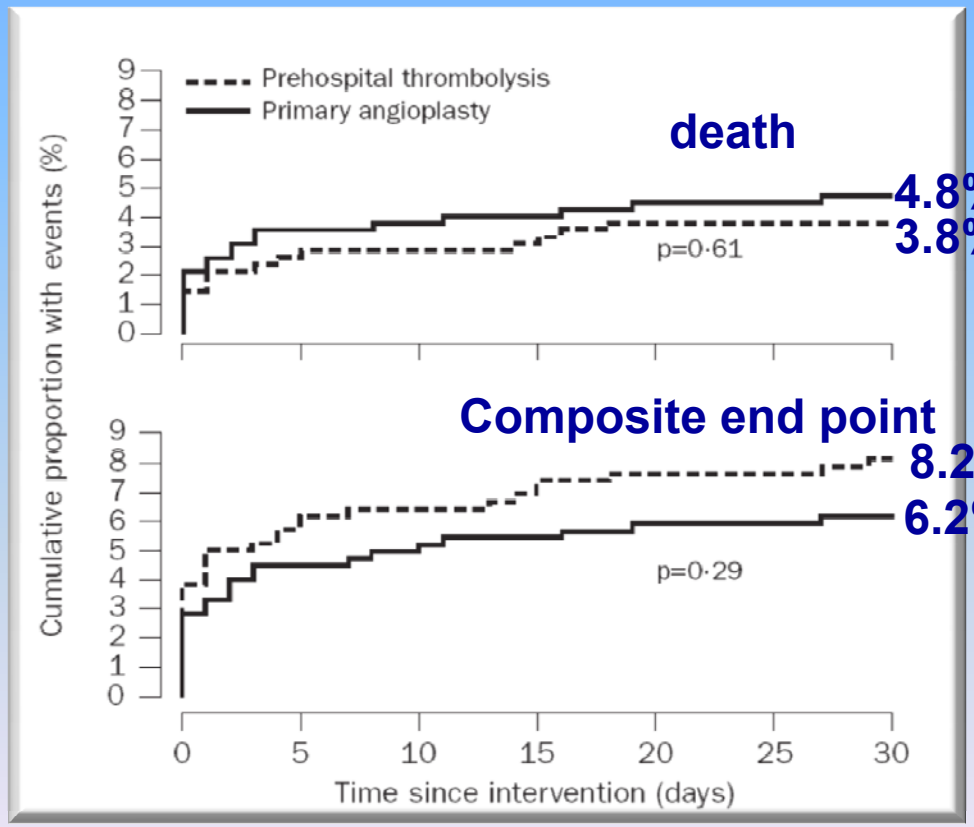




Lancet 1996; 348: 771–75

PCI vs thrombolysis in early hours

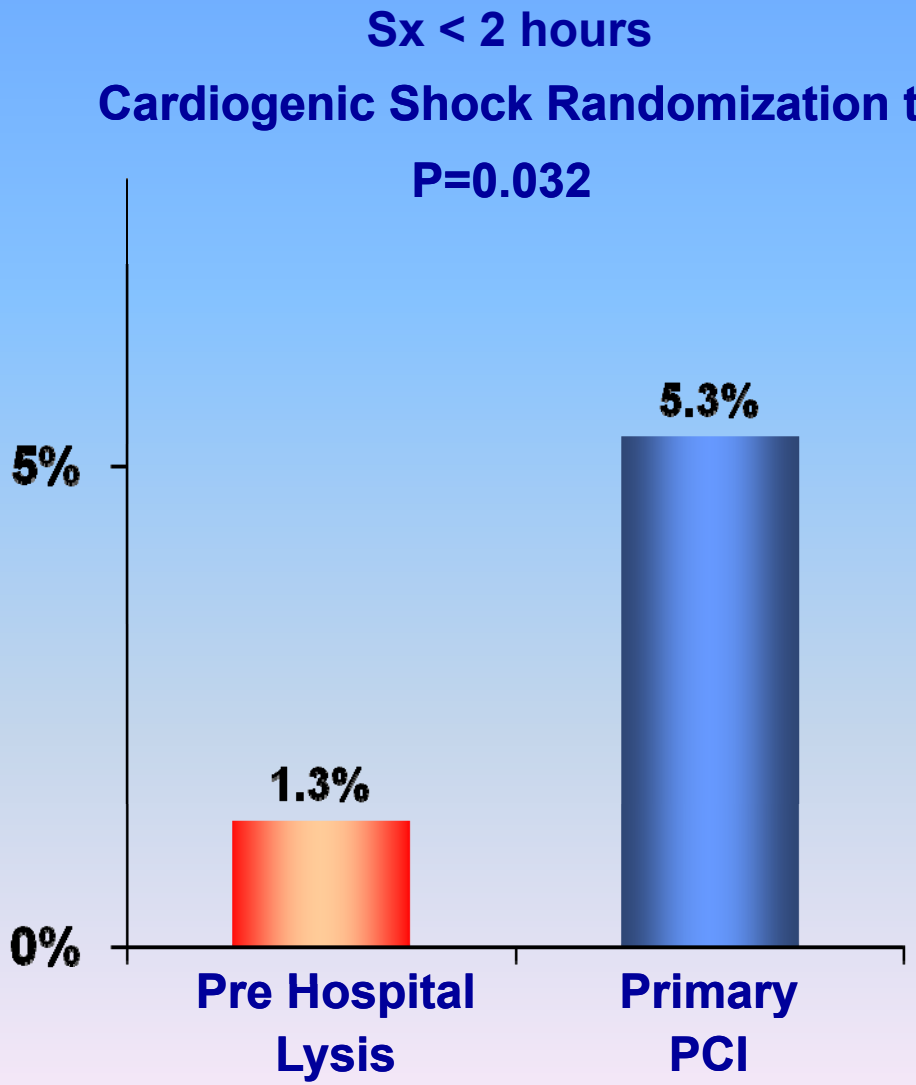
CAPTIM trial

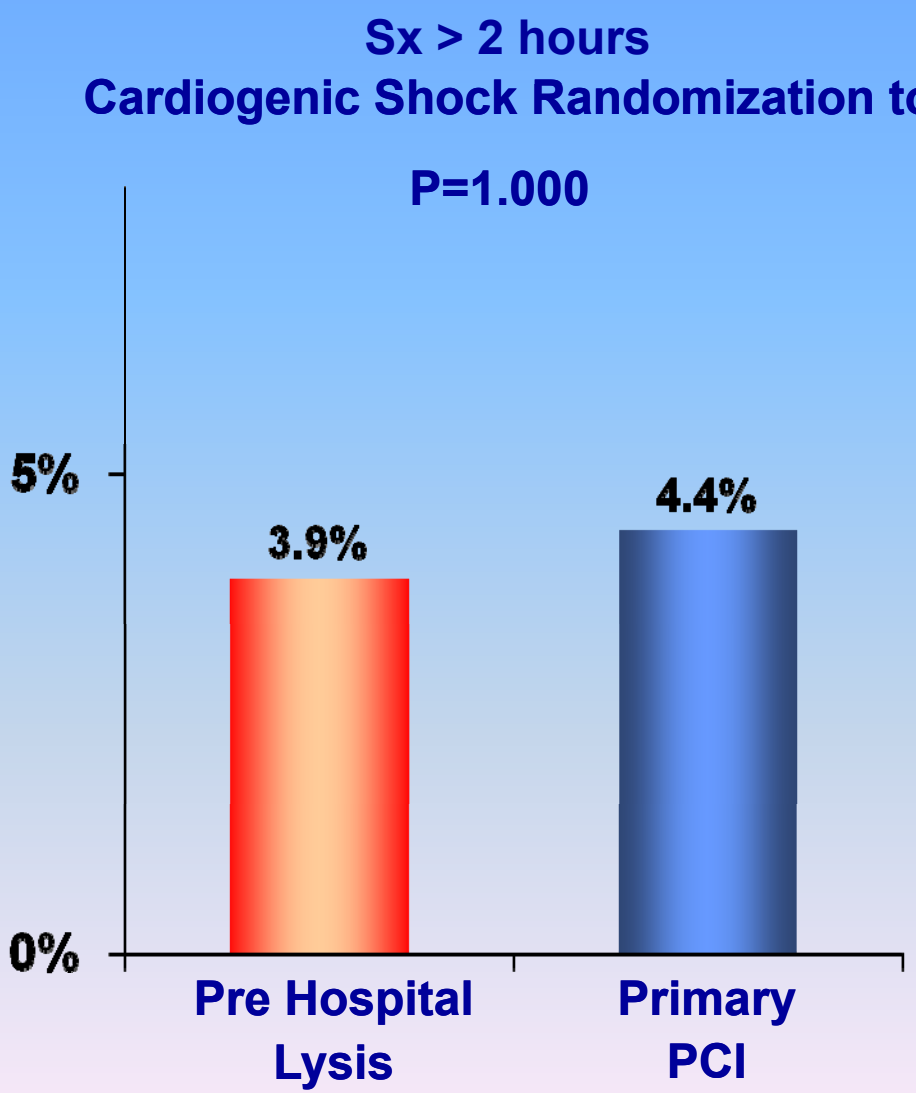


Lancet 2002; 360: 825–29

STEMI within 6 hours
Mobile emergence care units
Prehospital thrombolysis vs transfer for PCI
(n=419, 130min) (n=421, 190min)
From symptom onset

CAPTIM 1 Year Results

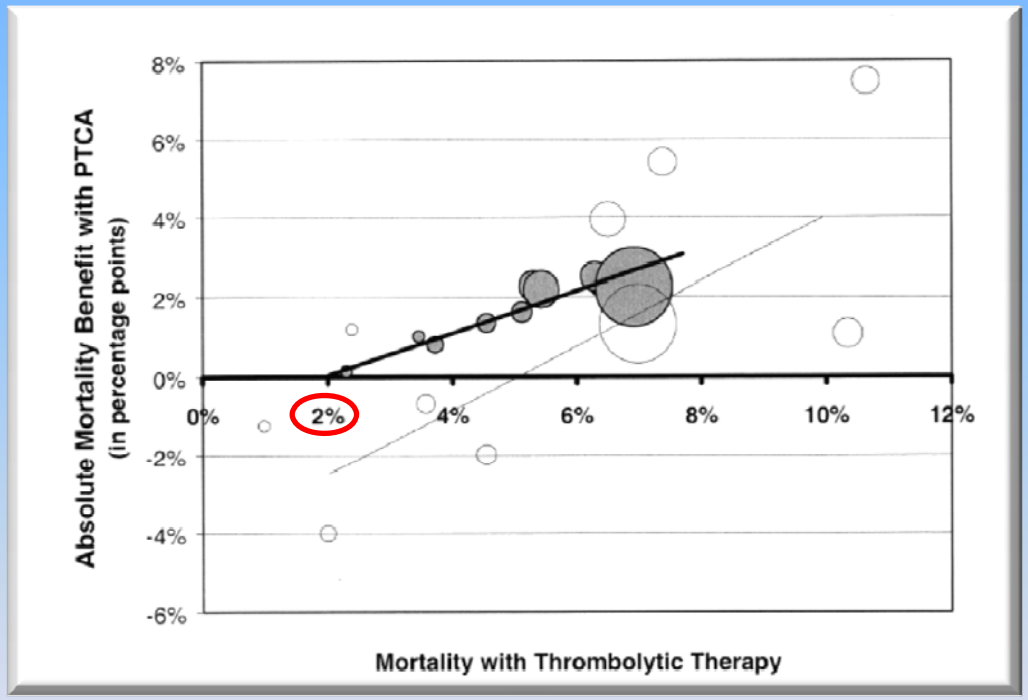




GW Symposium, AHA 2002

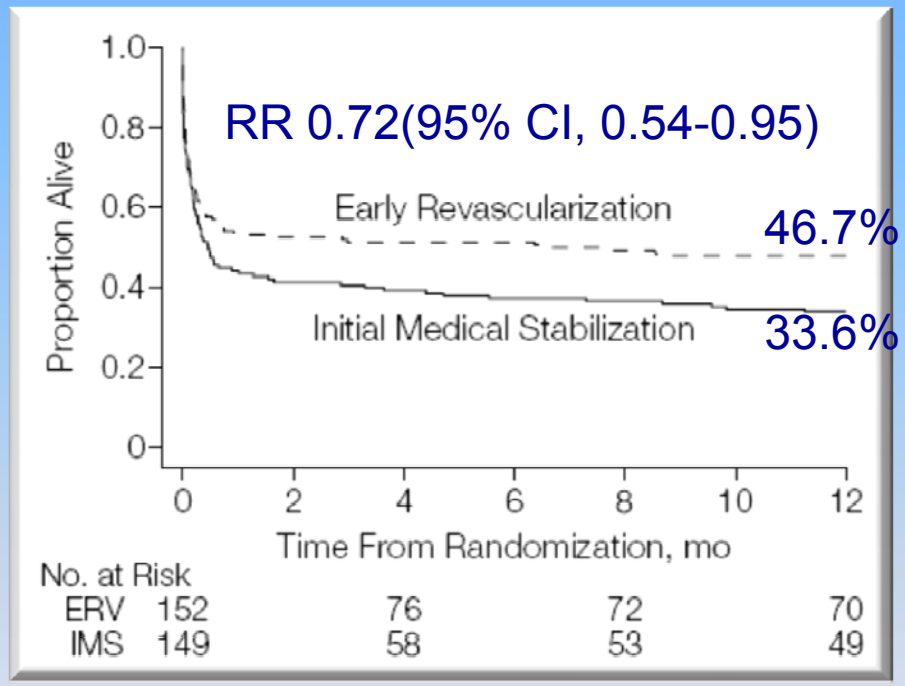
High risk features

Estimated risk of mortality And benefits of PCI in STEMI



J Gen Intern Med 2002;17;887-894

1 yr outcome in SHOCK trial



JAMA. 2001;285:190-192

Cardiogenic shock, Heart failure, anterior wall MI

Predictors of Hospital Death
In patients with CHF complicating AMI

Variables	Adjusted OR	95% CI
Anterior MI	1.85	1.78, 1.92
CHF on admission	**1.68**	**1.62, 1.75**
Age (decade)	1.58	1.55, 1.61
Posterior MI	1.57	1.46, 1.68
Transferred in	1.40	1.34, 1.47
History of stroke	1.36	1.29, 1.44
History of CABG	1.25	1.18, 1.32
Diabetes	1.21	1.17, 1.26
History of angina	1.06	1.01, 1.11
Previous MI	1.04	1.00, 1.09
History of CHF	0.92	0.88, 0.97
IV fibrinolytics	**0.91**	**0.87, 0.95**
Male	0.84	0.81, 0.87
History of PTCA	0.82	0.76, 0.88
Current smoking	0.80	0.77, 0.84
SQ heparin	0.75	0.67, 0.83
IV heparin	0.73	0.69, 0.76
Primary PTCA	**0.67**	**0.63, 0.72**
Chest pain at presentation	0.53	0.50, 0.55
ACE inhibitor	0.51	0.48, 0.53
Aspirin	0.42	0.41, 0.44
PO beta blocker	0.42	0.41, 0.44

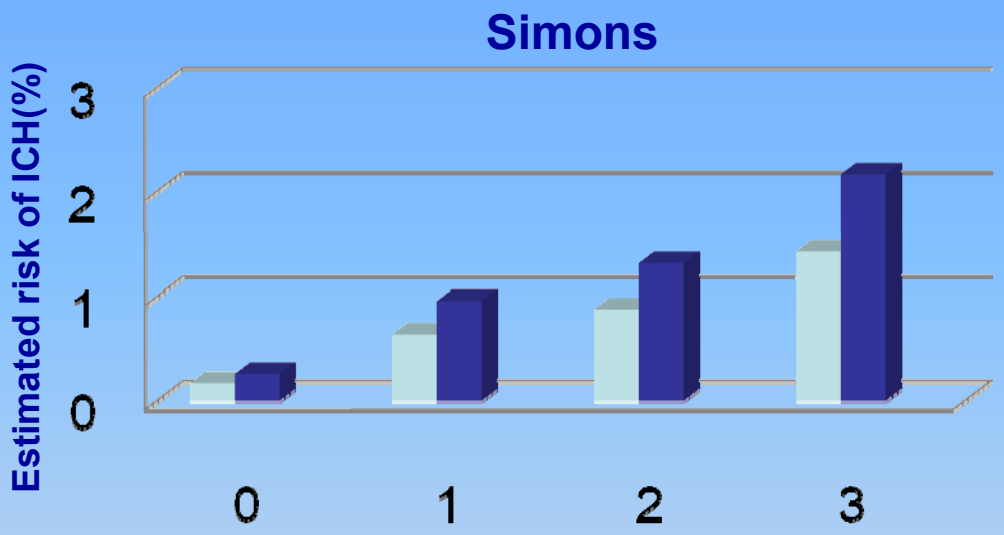
J Am Coll Cardiol 2002;40:1389 –94

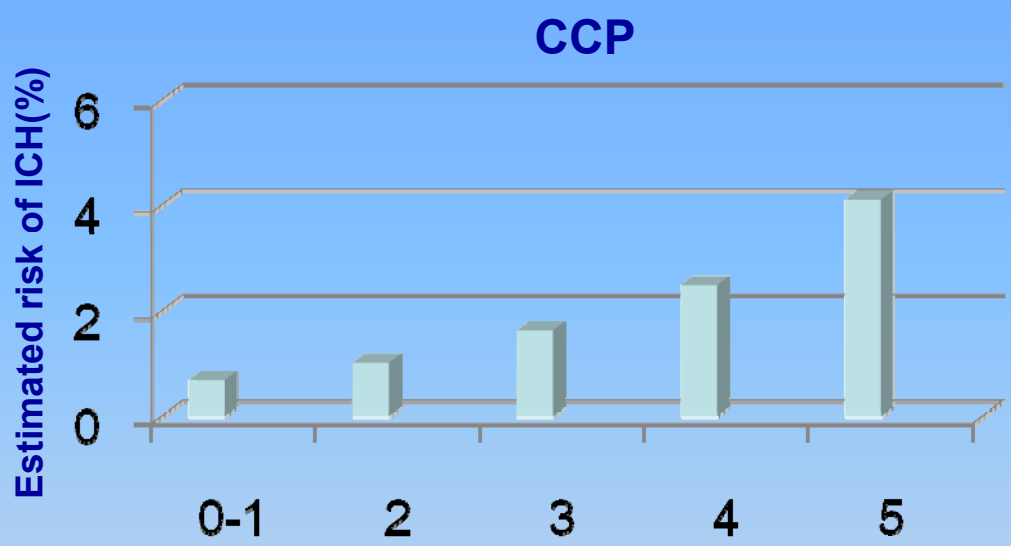
Risk of bleeding

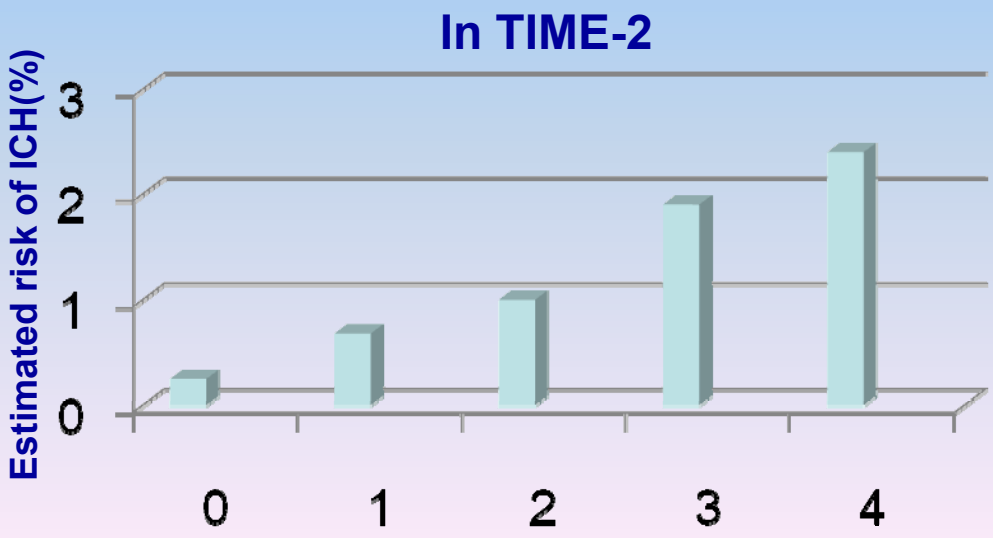
Models for estimating risk of ICH

Risk Factor* Model	Simoons et al	CCP	InTIME-2
Age, y	Greater than 65 = 1 point Weight 70 kg or less = 1 point	75 or greater = 1 point 65 kg or less (women) = 1 point 80 kg or less (men) = 1 point	75 or greater = 1 point 67 kg or less = 1 point
Hypertension on admission	SBP: 170 mmHg or greater = 1 point DBP: 95 mmHg or greater = 1 point Both SBP and DBP above limits = 1 point	SBP: 160 mmHg or greater = 1 point 170 mmHg or greater = 1 point	SBP: 160 mmHg or greater = 1 point 170 mmHg or greater = 1 point
Treatment assignment			
rtPA	1 point	1 point	–
nPA	–	–	1 point
Female	–	1 point	–
Black race	–	1 point	1 point
Prior stroke	–	1 point	1 point
Prior nifedipine use	–	–	1 point
Excessive anticoagulation	–	1 point	–

Estimation of risk ICH with fibrinolysis







Contraindication / Caution 2004 ACC / AHA guidelines

Class I

1. Healthcare providers should ascertain whether the patient has neurological contraindications to fibrinolytic therapy, including
   : any history of intracranial hemorrhage or significant closed head or facial trauma within the past 3 months, uncontrolled hypertension, or ischemic stroke within the past 3 months. *(Level of Evidence: A)*

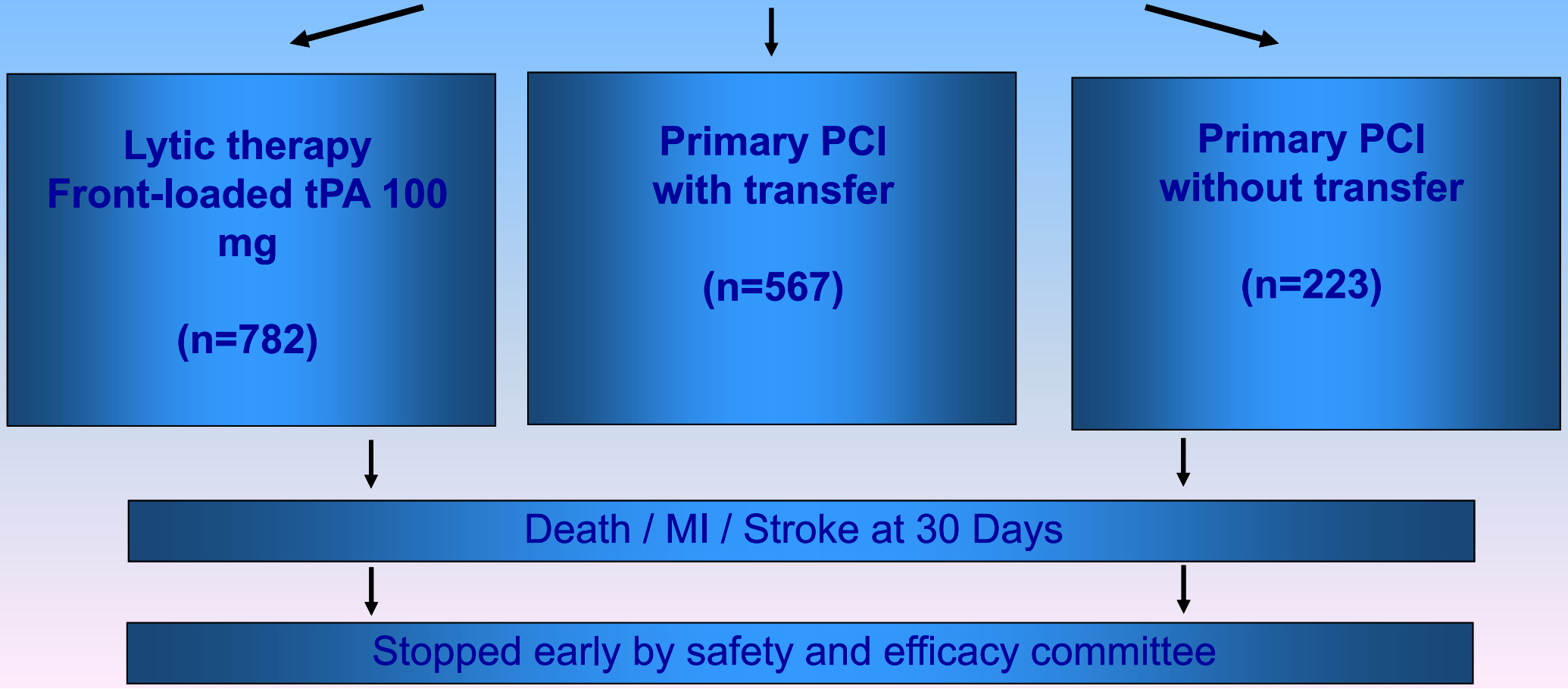
2. STEMI patients at substantial (greater than or equal to 4%) risk of ICH should be treated with PCI rather than with fibrinolytic therapy. *(Level of Evidence: A)*

Time required for transport to skilled PCI lab

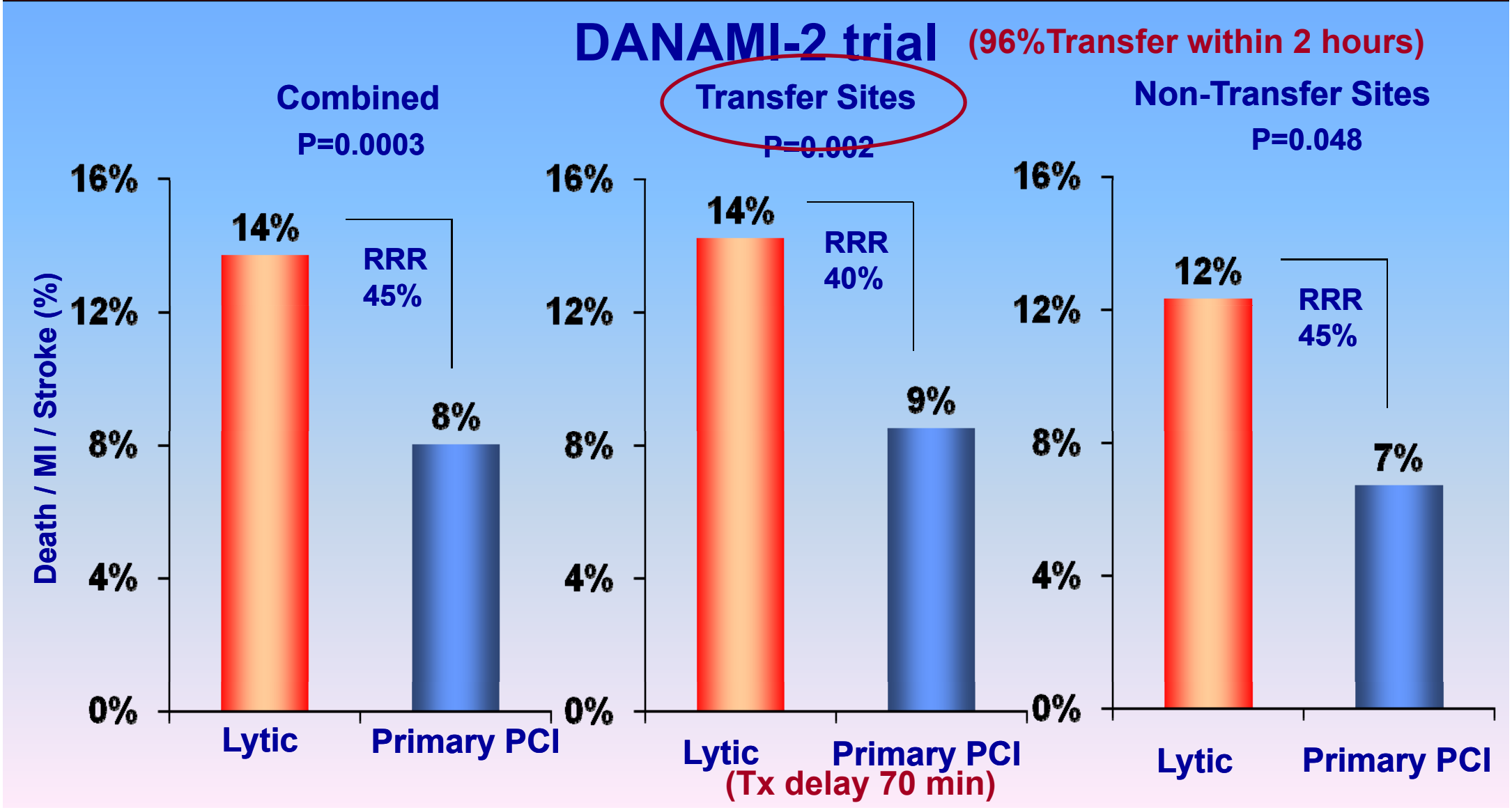
Transfer for PCI vs immediate fibrinolysis In centers without cath LAB

DANAMI-2: Study Design

High-risk ST elevation MI patients (≥4 mm elevation), Sx < 12 hrs
5 PCI centers (n=443) and 22 referring hospitals (n=1,129), transfer in ≤ 3 hrs



Transfer for PCI vs immediate fibrinolysis In centers without cath LAB



Transfer time in real world

Door to Balloon Times Among Patients Transferred in NRMI 4

Door to Data:
50th: 8 Min.
25th: 4 Min.
75th: 16 Min.

Data to Cath Lab Arrival:
50th: 137 Min.
25th: 87 Min.
75th: 220 Min.

Cath Lab to Balloon:
50th: 39 Min.
25th: 29 Min
75th: 53 Min.

Total Door to Balloon Time: 198 minutes (25th: 137; 75th: 281)
Percent of Patients with Door to Balloon Time < 90 Min.: 4.8%

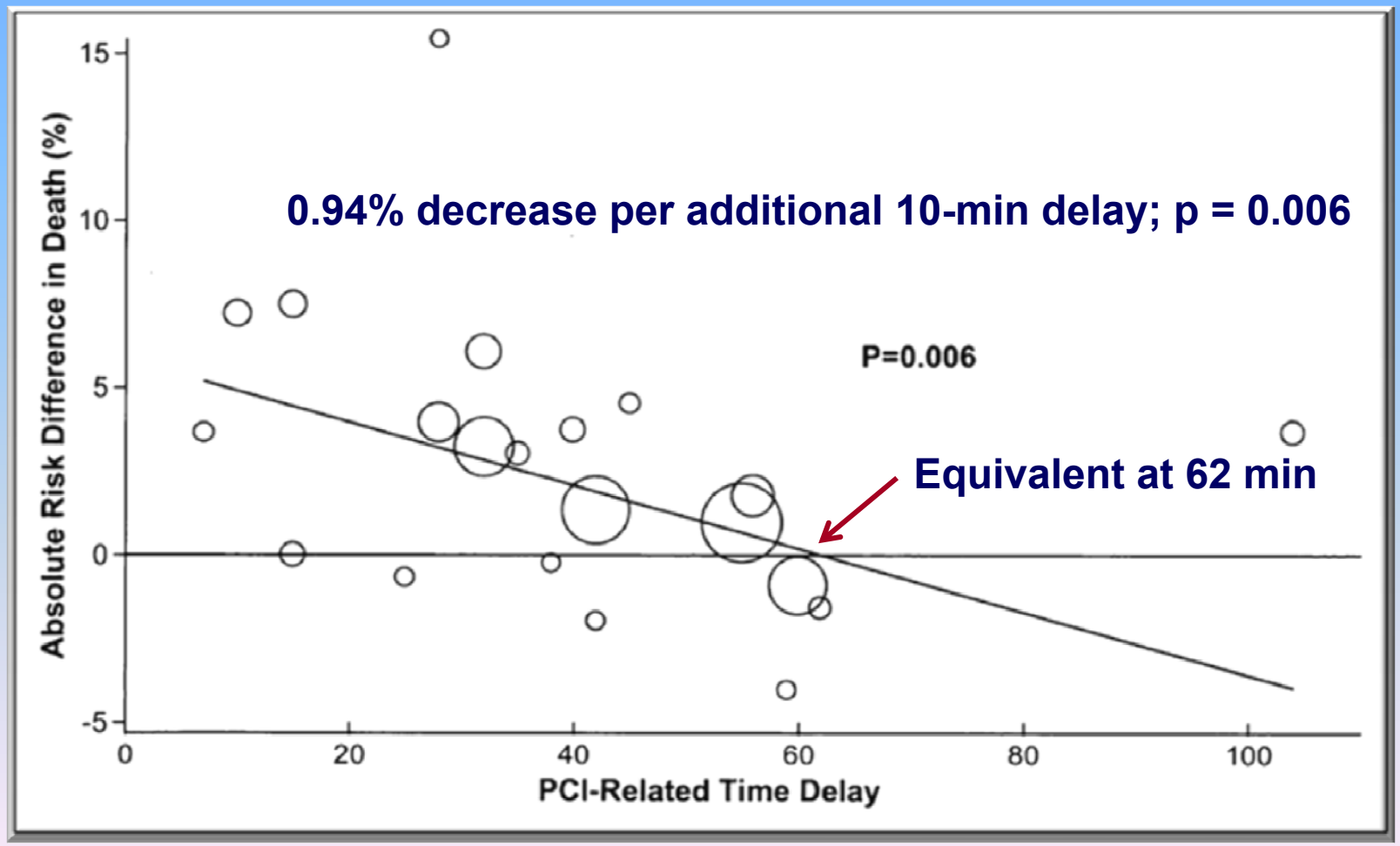
Sample Size: 1,292; Time Period: October 2000 – September 2001

Gibson CM, 2002

NRMI 4 Transfer-In Annual Data Report 2002

Relation between transfer delay for PCI And mortality reduction

Analysis of 21 studies



Am J Cardiol 2003;92:824–826

Selection of reperfusion strategy ACC/AHA guidelines

STEP 1: Assess time and risk

- Time since onset of symptoms
- Risk of STEMI
- Risk of fibrinolysis
- Time required for transport to a skilled PCI lab

STEP 2: Determine if fibrinolysis or invasive srtategy is preferered

If presentation is less than 3 hours and there is no delay to an invasive strategy, there is no preference for either strategy

Fibrinolysis is generally preferred if:

- *Early presentation (3 hours from symptom onset and delay to invasive strategy) (see below)*
- *Invasive strategy is not an option*
  Catheterization lab occupied/not available
  Vascular access difficulties
  Lack of access to a skilled PCI lab†‡
- *Delay to invasive strategy*
  Prolonged transport
  (Door-to- balloon) – (door-to-needle) is >1 hour*§
  Medical contact-to-balloon or door-to-balloon is >90 minutes

An invasive strategy is generally preferred if:

- *Skilled PCI lab available with surgical backup*†‡
  Medical contact-to-balloon or-door-to-balloon is <90 minutes
  (Door-to-balloon) – (door-to-needle) is <1 hour*
- *High risk from STEMI*
  Cardiogenic shock
  Killip class is ≥3
- *Contraindications to fibrinolysis including increased risk of bleeding and ICH*
- *Late presentation*
  Symptom onset was >3 hours ago
- *Diagnosis of STEMI is in doubt*

Comparison of fibrinolytic agents

	Streptokinase	Alteplase	Reteplase	Tenecteplase-tPA
Dose	1.5 MU over 30-60 min	Up to 100 mg in 90 min (based on weight)*	10 U IV over 2 min	30-50 mg based on weight
Bolus administration	No	No	Yes	Yes
Antigenic	Yes	No	No	No
Allergic reactions (hypotension most common)	Yes	No	No	No
Systemic fibrinogen depletion	Marked	Mild	Moderate	Minimal
90-min patency rates, approximate %	50	75	60-70	75
TIMI grade 3 flow, %	32	54	60	63
ICH, %	0.34	0.69	0.76	0.69
Cost per dose	$613	$2974	$2750	$2833 for 50 mg

Choice of fibrinolytic agents

STEMI within 4 hours of symptom onset

Greater area at risk (anterior wall MI)

Lower bleeding risk

: high intensity fibrinolytic regimen

(Fibrin-specific agent: Alteplase < Reteplase and Tenecteplase-tPA)

STEMI within 4 ~ 12 hours of symptom onset

Smaller area at risk (inferior wall MI)

Greater bleeding risk

: low intensity fibrinolytic regimen

(Fibrin-nonspecific agent: Streptokinase or Urokinase)

Ancillary therapy to fibrinolysis Anticoagulants

Plasmin-mediated thrombin activation

2007 STEMI Focused Update Recommendation

Class I

Patients undergoing reperfusion with **fibrinolytics** should receive **anticoagulant** therapy for a minimum of **48 hours**(*Level of Evidence: C)*
*and preferably for the duration of the **index hospitalization**, up to 8 days*
*(regimens **other than** **UFH*** are recommended
if anticoagulant therapy is given for more than 48 hours
because of the risk of heparin induced thrombocytopenia with prolonged UFH treatment).
(*Level of Evidence: A)*

Anticoagulant regimens with established efficacy include:

-UFH

-Enoxaparin- ExTRACT TIMI 25

-Fondaparinux- OASIS 6

Anticoagulants to fibrinolysis
Enoxaparin-ExTRACT TIMI 25

STEMI < 6 h
Lytic eligible

ASA

Lytic choice by MD
(TNK, tPA, rPA, SK)

Double-blind, double-dummy

ENOX

< 75 y: 30 mg IV bolus
SC 1.0 mg / kg q 12 h (Hosp DC)

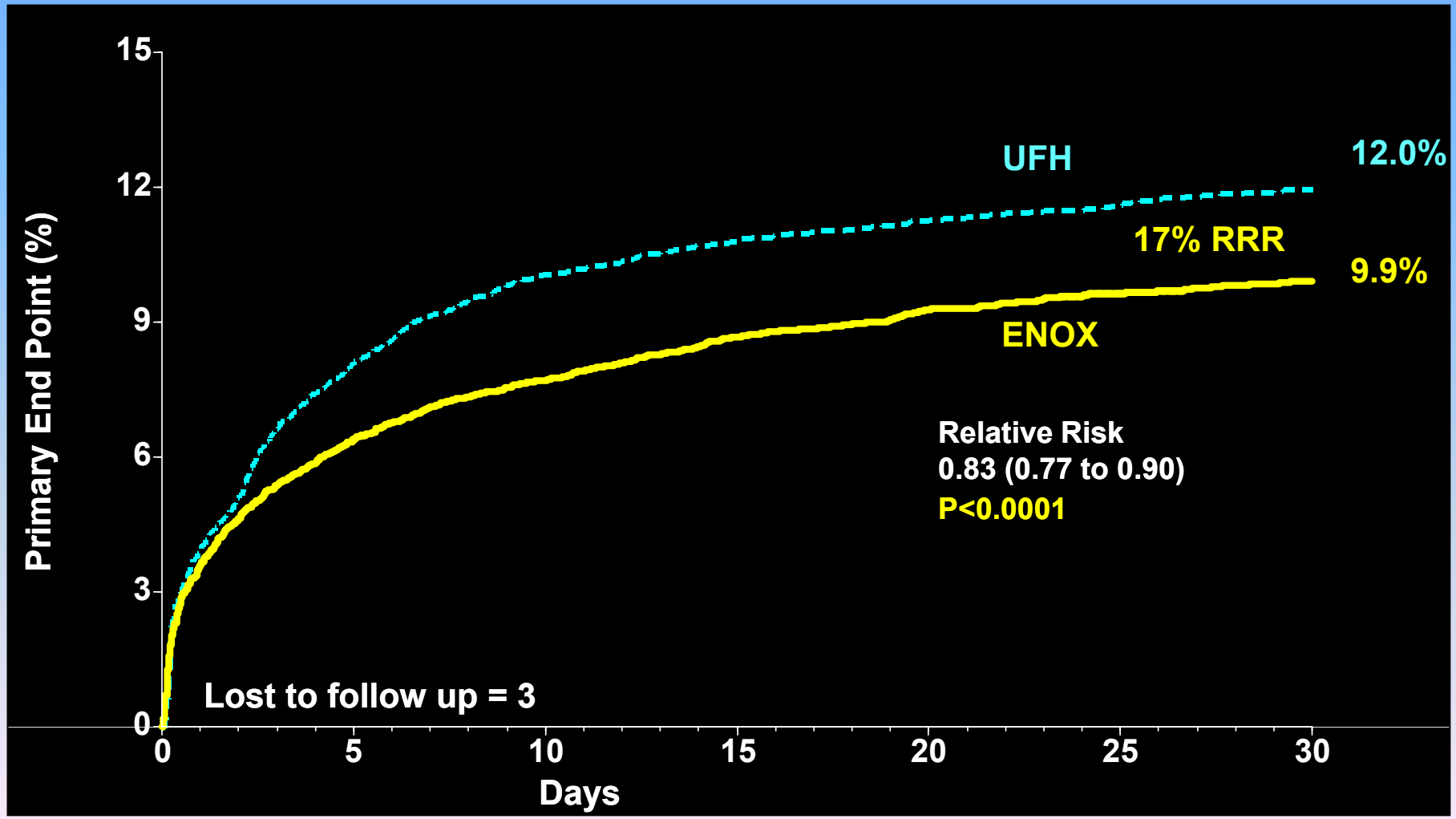
≥ 75 y: No bolus
SC 0.75 mg / kg q 12 h (Hosp DC)

CrCl ≤ 30: 1.0 mg / kg q 24 h

UFH
60 U / kg bolus (4000 U)
Inf 12 U / kg / h (1000 U / h)
Duration: at least 48 h
Cont'd at MD discretion

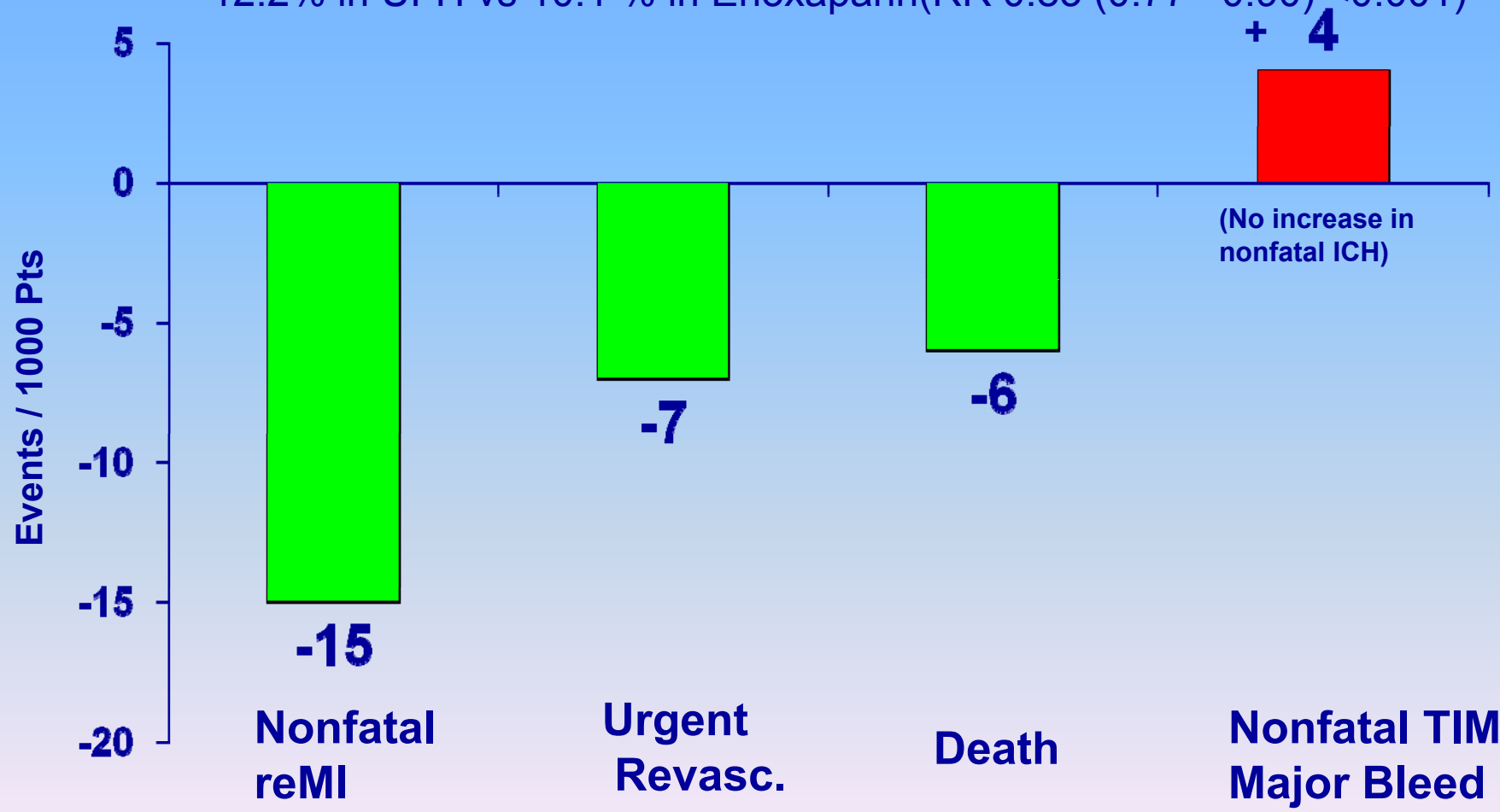
Day 30
1° Efficacy Endpoint: Death or Nonfatal MI
1° Safety Endpoint: TIMI Major Hemorrhage

Anticoagulants to fibrinolysis
Enoxaparin-ExTRACT TIMI 25

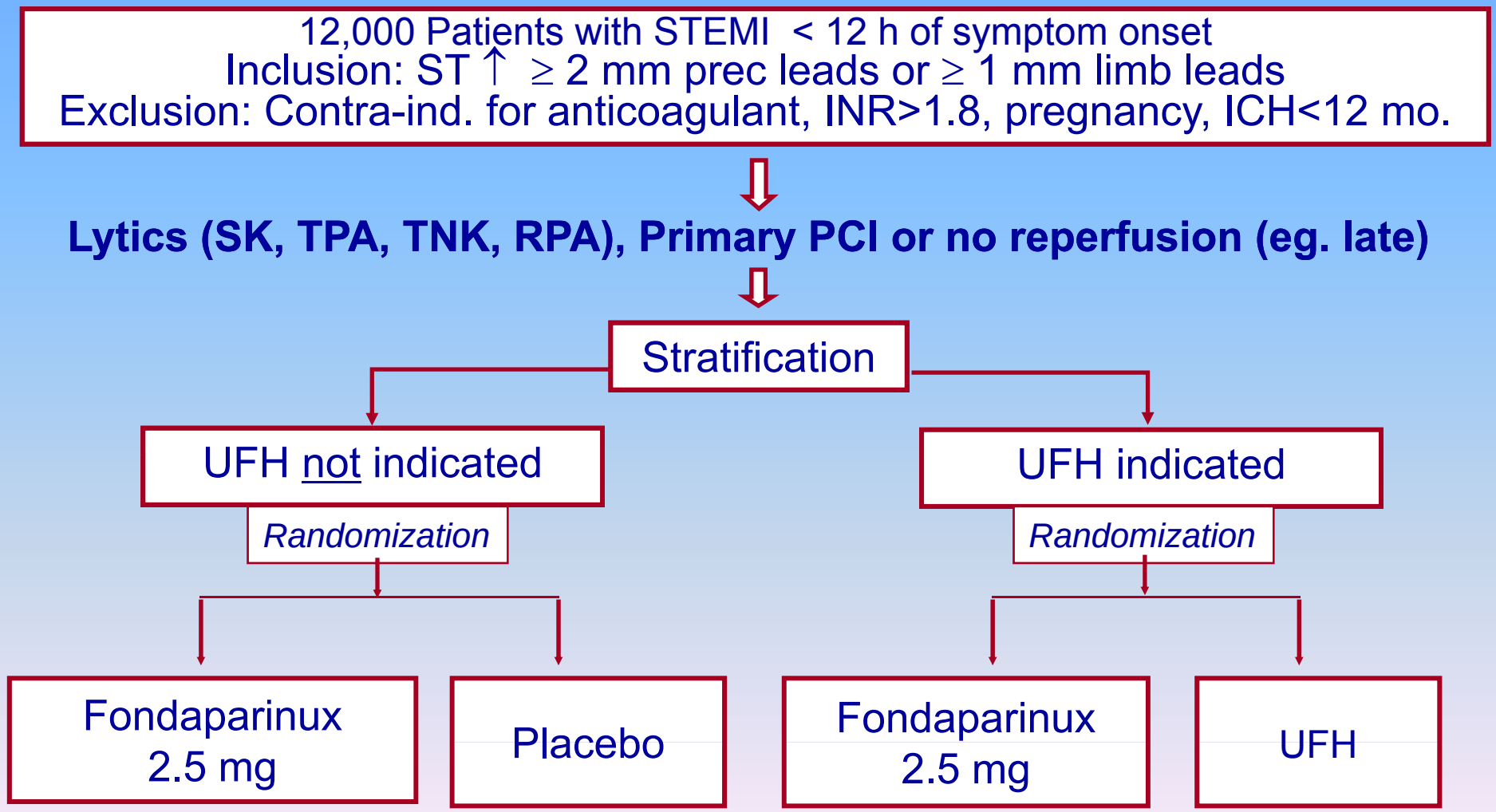


Anticoagulants to fibrinolysis
Enoxaparin-ExTRACT TIMI 25

Net clinical benefit(death, MI, ICH)
12.2% in UFH vs 10.1 % in Enoxaparin(RR 0.83 (0.77– 0.90) <0.001)



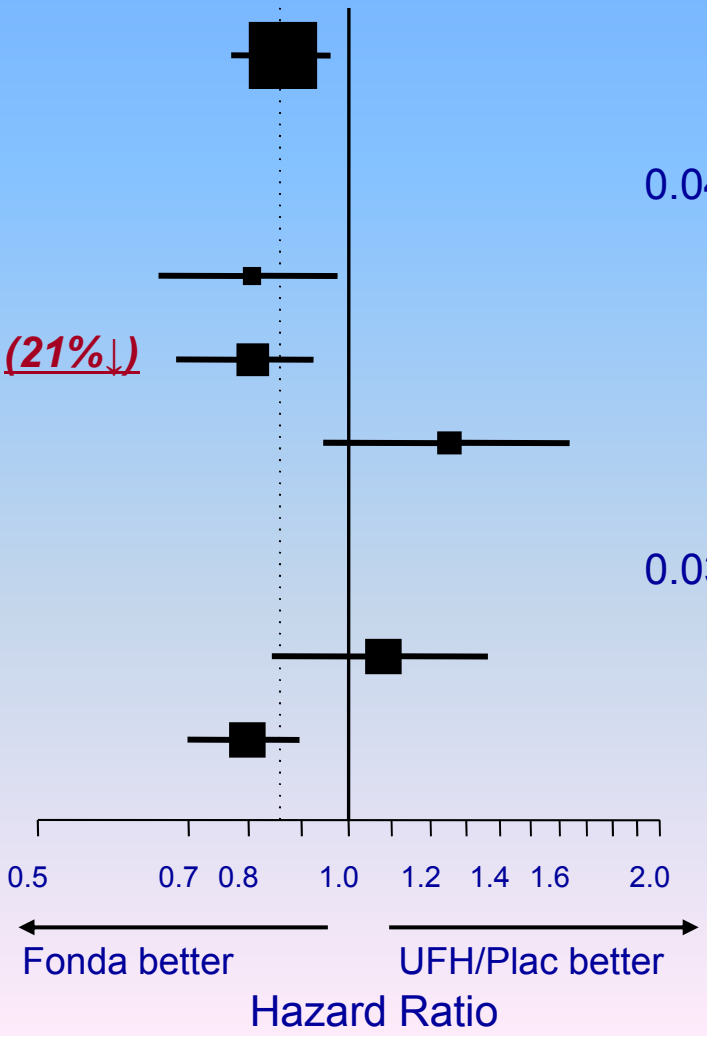
Anticoagulants to fibrinolysis
Fondaparinux-OASIS 6



Anticoagulants to fibrinolysis
Fondaparinux-OASIS 6

Death or MI at 30 days

	N	UFH/Placebo	Fonda	Interaction P value
Overall	12092	11.2%	9.7%	
Initial Reperfusion Rx				0.04
None	2867	15.1	12.2	
Thrombolytic	5436	13.6	10.9 ***(21%↓)***	
Primary PCI	3789	4.9	6.0	
GRACE Risk Score				0.03
< 112	5958	4.3	4.6	
>=112	6134	18.0	14.5	



Anticoagulants to fibrinolysis Thienopyridine

2009 STEMI Focused Update Recommendation

Class I

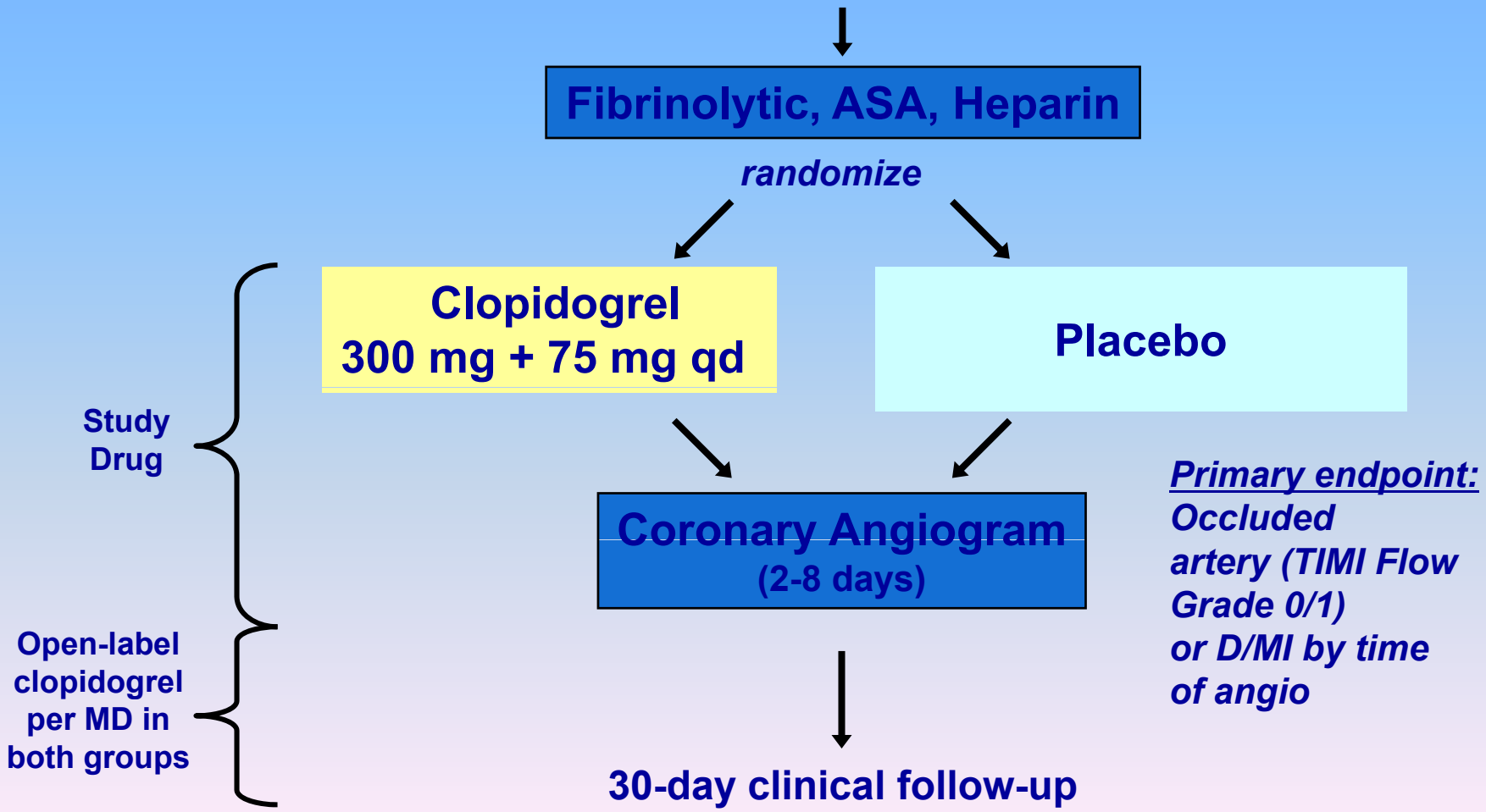
1.Clopidogrel 75 mg per day orally should be added to aspirin in patients with STEMI regardless of whether they undergo reperfusion with **fibrinolytic therapy or** do **not** receive **reperfusion therapy**. (*Level of Evidence: A)*
*Treatment with clopidogrel should continue for at least **14** **days**. (Level of Evidence: B)*

Class II

1. In patients **less than 75 years** of age who receive fibrinolytic therapy or who do not receive reperfusion therapy, it is reasonable to administer an oral **loading dose of clopidogrel 300mg**. (Level of Evidence: C)
2. **Long-term maintenance therapy** (e.g., 1 year) with clopidogrel (75 mg per day orally) is reasonable in STEMI patients regardless of whether they undergo reperfusion with fibrinolytic therapy or do not receive reperfusion therapy. (Level of Evidence: C)

Anticoagulants to fibrinolysis Thienopyridine-CLARITY TIMI 28

Double-blind, randomized, placebo-controlled trial in 3491 patients, age 18-75 yrs with STEMI < 12 hours

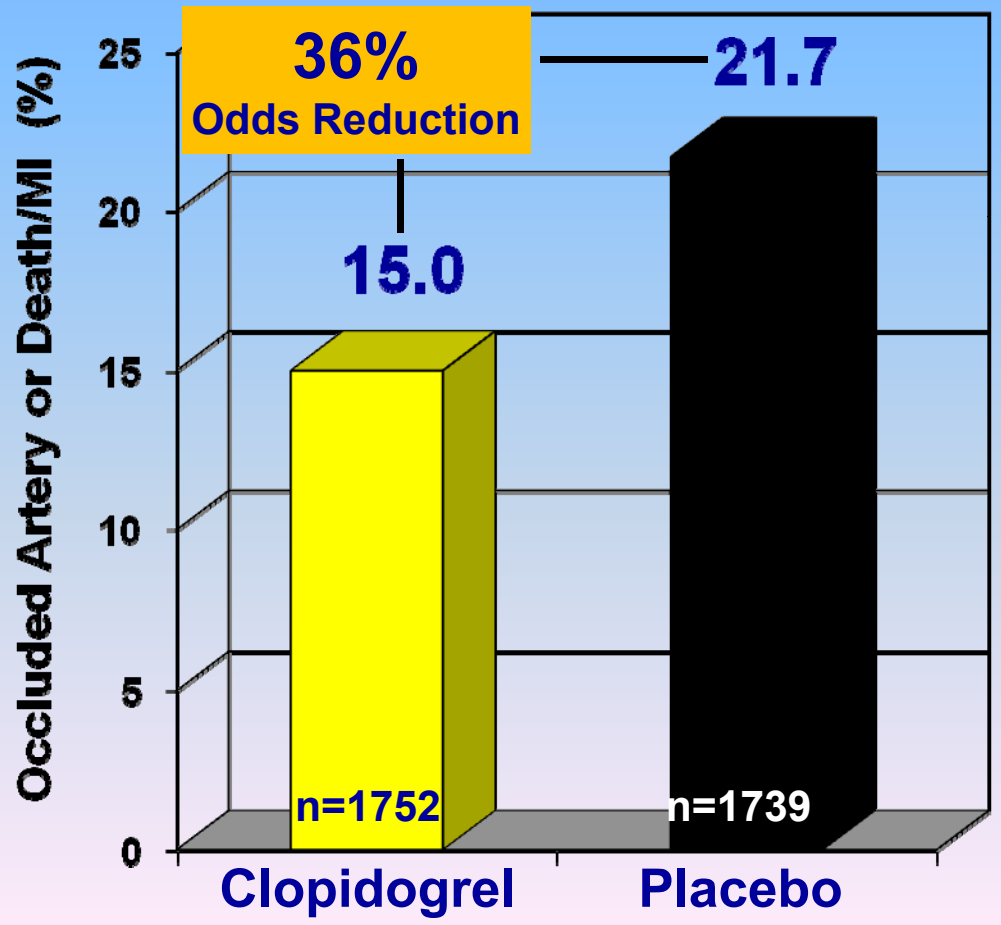


Primary endpoint:
Occluded artery (TIMI Flow Grade 0/1) or D/MI by time of angio

Anticoagulants to fibrinolysis Thienopyridine-CLARITY TIMI 28

Primary Endpoint:

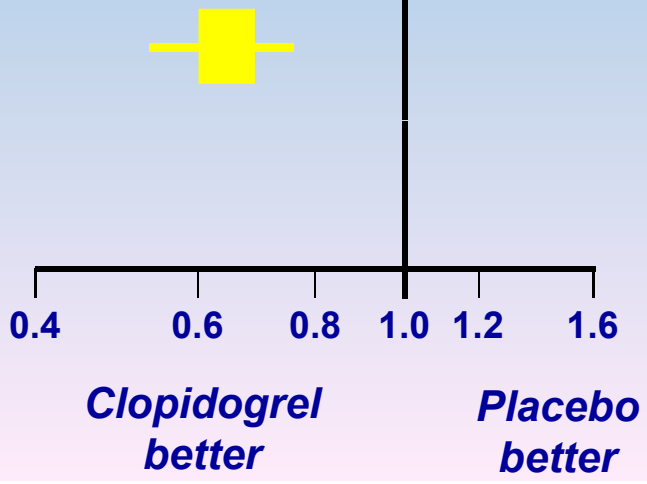
Occluded Artery (or Death/MI thru Angio/HD)



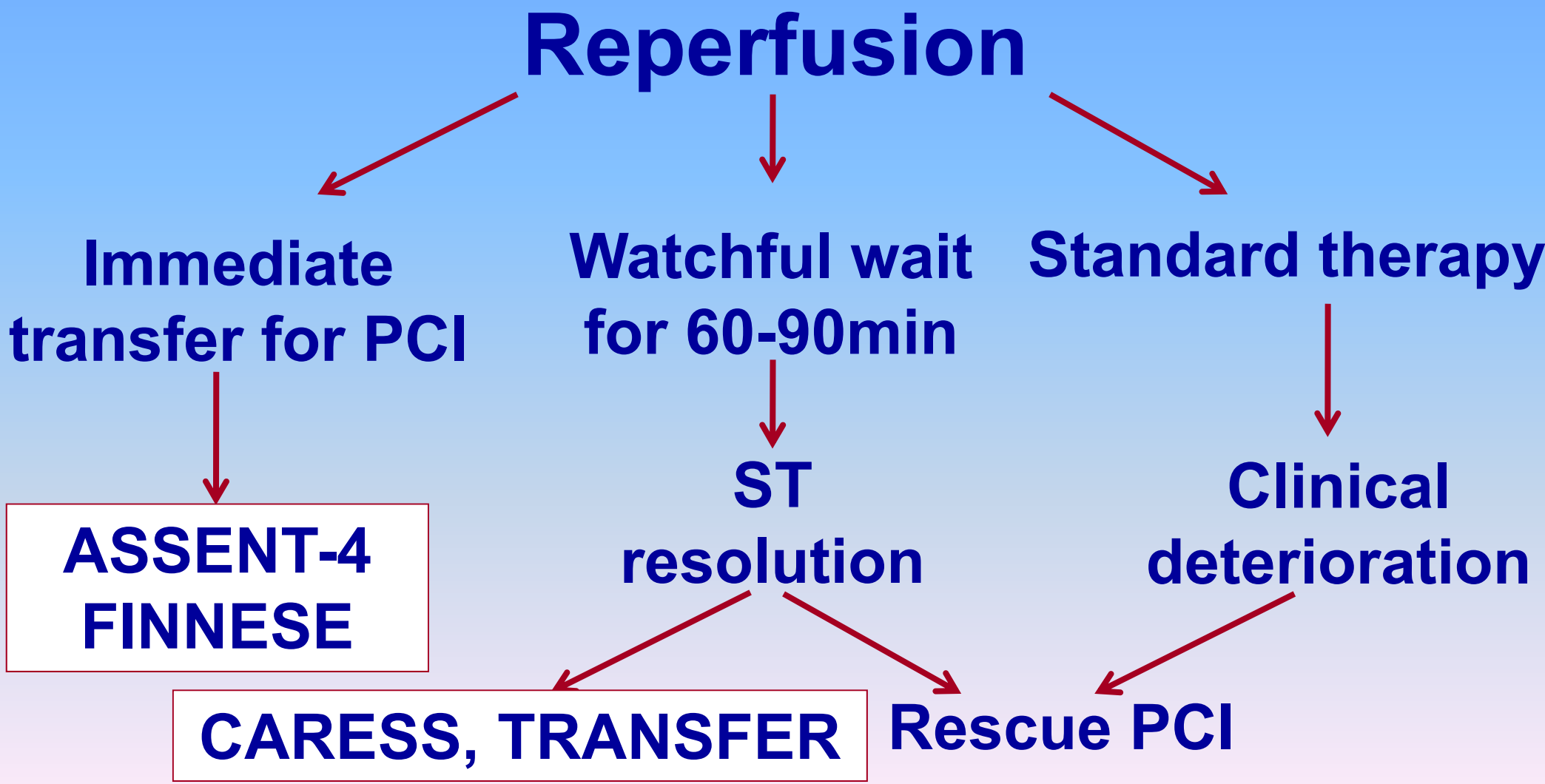
Odds Ratio 0.64

(95% CI 0.53-0.76)

P=0.00000036



After assessment of reperfusion



Facilitated PCI vs Primary PCI

Facilitated PCI

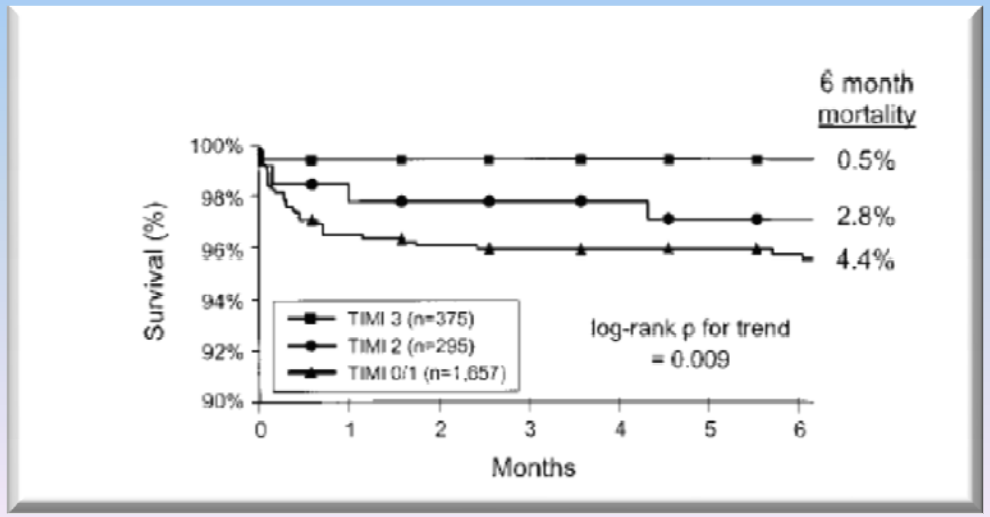
Definition

Facilitated PCI refers to a strategy of planned immediate PCI after an initial pharmacological regimen such as Full dose fibrinolysis, half-dose fibrinolysis, a GP IIb/IIIa inhibitor, or a combination of reduced-dose fibrinolytic therapy and a platelet GP IIb/IIIa inhibitor

Advantages

- -Earlier time to reperfusion
- -Improved patient stability
- -Higher TIMI flow rates
- -Greater procedural success rates
- -Improved survival rates

Impact of initial TIMI flow grade on Cumulative survival



Circulation. 2001;104:636-641

Facilitated PCI vs Primary PCI
ASSENT-4 trial

1667 patients age ≥ 18 years with ST elevation myocardial infarction (summed ST deviation ≥ 6 mm); time from symptom onset within 6 hrs; intent to perform primary PCI

Randomized
Mean follow-up: 6 mos (30 days reported to date)
63% of patients received clopidogrel/ticlopidine *during* PCI
Additional UFH was given to 67.4% in the TNK + PCI group and 70.1% in the PCI alone group

Full-dose TNK + Primary PCI
60 IU/kg, maximum 4000 IU
n=829
GP IIb/IIIa inhibitors allowed only for bail out use

Primary PCI
70 IU/kg, no maximum dose
n=838
GP IIb/IIIa inhibitors allowed at physician discretion

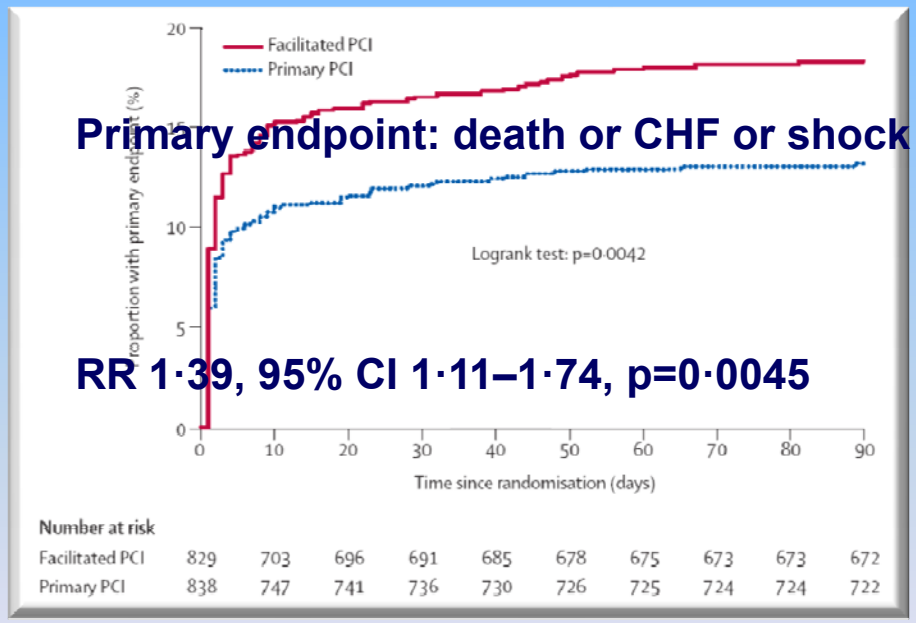
- Primary Endpoint: Composite of death, shock, or congestive heart failure at 90 days.
- Secondary Endpoint: Composite of death, shock, or congestive heart failure at 30 days; shock or CHF at 90 days; single components of the composite endpoint.

Lancet 2006; 367: 569–78

Facilitated PCI vs Primary PCI ASSENT-4 trial

In hospital death, TNK 6%(43 of 664) vs PCI 3%(22 of 656), p=0·0105

TIMI 3 flow before PCI, TNK 353/812(43%) PCI 124/821(15%)
TIMI 3 flow after PCI, TNK 631/719(88%) PCI 677/763(89%)



Lancet 2006; 367: 569–78

Facilitated PCI vs Primary PCI ASSENT-4 trial

Clinical end points

	Tenecteplas and PCI (n=829/117min, RTB)	PCI alone (n=838/107min, RTB)	p
Death	55/823 (7%)	41/831 (5%)	0·1412
CHF	97/807 (12%)	75/818 (9%)	0·0640
Shock	51/807 (6%)	39/817 (5%)	0·1933
Reinfarction	49/805 (6%)	30/820 (4%)	0·0279
Repeat target vessel revascularisation	53/805 (7%)	28/818 (3%)	0·0041
Rehospitalisation for congestive heart failure	15/807(2%)	11/818 (1%)	0·4356
Rehospitalisation for shock	0/807	1/817 (1%)	0·9999
Rehospitalisation for other cardiac reason	6 (10%)	90/819 (11%)	0·6878

Suboptimum antithrombotic co-therapy

(no infusion of heparin after bolus, no up-front loading of clopidogrel, prohibition of glycoprotein IIb/IIIa inhibitors)

Lancet 2006; 367: 569–78

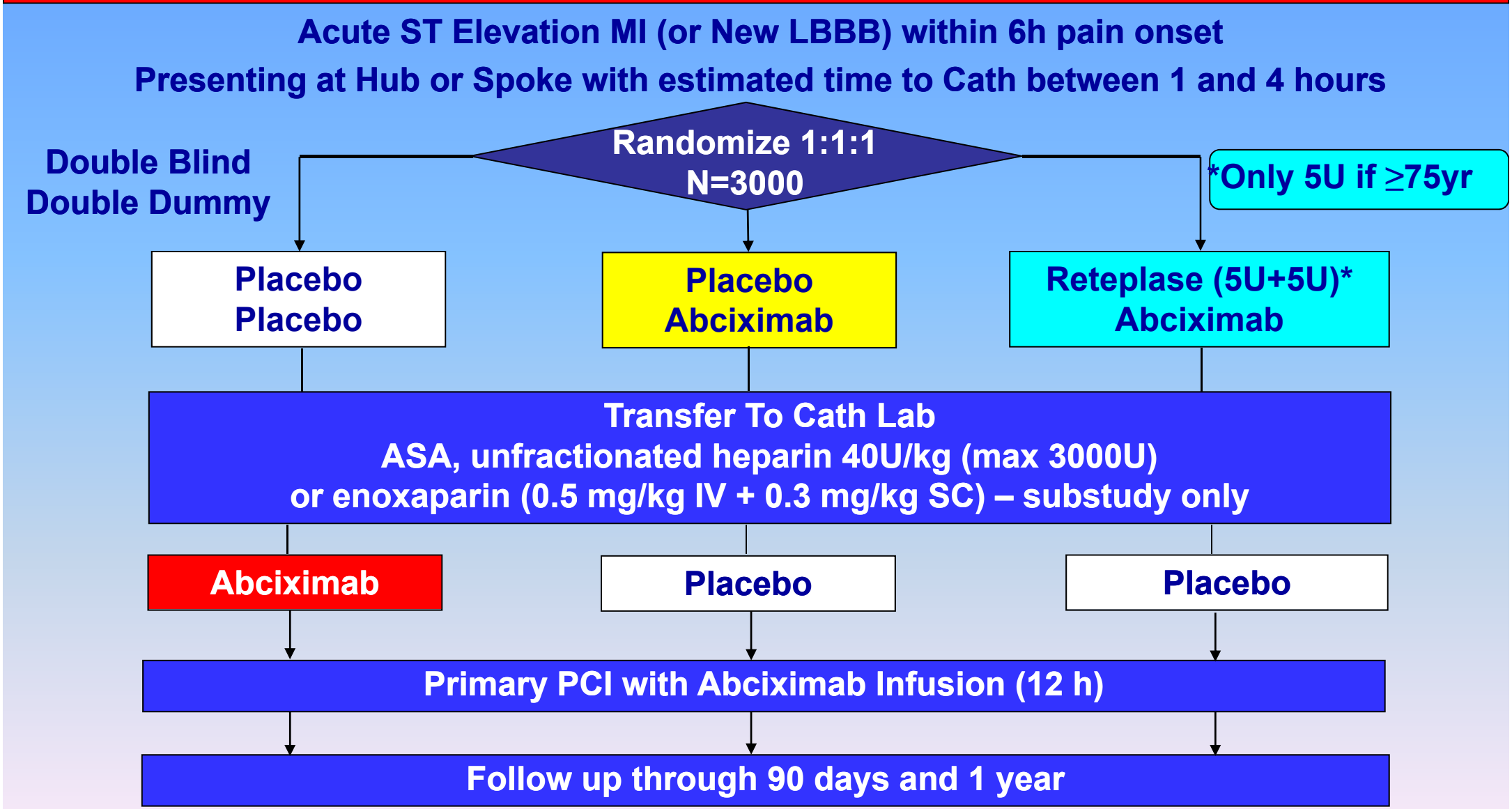
Facilitated PCI vs Primary PCI
ASSENT-4 trial

Strokes and non-cerebral bleeding complications within 90 days

	Tenecteplase and PCI (n=829)	PCI alone (n=838)	p
In-hospital stroke			
Intracranial haemorrhage	8 (1·0%)	0	0·0037
Primary ischaemic stroke	5 (0·6%)	0	0·0302
Unclassified stroke	2 (0·2%)	0	0·2472
Total	15(1·8%)	0	0·0001
Stroke after discharge (up to day 90)			
Intracranial haemorrhage	1(0·1%)	1(0·1%)	>0·999
Primary ischaemic stroke	4(0·5%)	0	0·0602
Unclassified stroke	2(0·2%)	0	0·2466
In-hospital bleeding complications			
Major	46(5·6%)	37(4·4%)	0·3118
Minor	210(25·3%)	159(19·0%)	0·0021
Blood transfusions	48(6·2%)	33(4·2%)	0·0873

Lancet 2006; 367: 569–78

FINESSE: Study Design



FINESSE: early reperfusion markers

Efficacy parameter	Primary PCI	Abciximab-facilitated	Combination (abciximab/ reteplase)-facilitated	Combination - facilitated vs primary PCI (P)	Combination-facilitated vs abciximab-facilitated (P)
ST resolution (70% in 60-90min)	31.0 %	33.1 %	43.9 %	0.003	0.01
Initial TIMI 3 flow	12.0 %	14.1 %	32.8 %	0.001	0.001
AUC for CK	1860 IU/l/hr	1782 IU/l/hr	1625 IU/l/hr	0.001	0.01

N Engl J Med 2008;358:2205-17.

FINESSE Results:

Endpoint	Primary PCI (%)	Abciximab-facilitated (%)	Combination (abciximab/ reteplase)-facilitated (%)	Combination-facilitated vs primary PCI (P)	Combination-facilitated vs abciximab-facilitated (P)
Primary end point *	10.7	10.5	9.8	NS	NS
All-cause mortality	4.5	5.5	5.2	NS	NS
TIMI major bleeding	2.6	4.1	4.8	0.025	NS
TIMI minor bleeding	4.3	6.0	9.7	<0.001	0.006

* All cause mortality; rehospitalization or ED treatment for CHF; resuscitated ventricular fibrillation occurring > 48 hours after randomization; cardiogenic shock

*Median door to balloon time for all pts: 2.2 hrs (1.8-2.8) (120min in Hub / 155 min in Spoke)

Facilitated PCI
2007 STEMI ACC/AHA guidelines

Class IIb

1. Facilitated PCI using regimens other than full-dose fibrinolytic therapy might be considered as a reperfusion strategy when all of the following are present: a. Patients are at high risk, b. PCI is not immediately available within 90 minutes, and c. Bleeding risk is low (younger age, absence of poorly controlled hypertension, normal body weight). *(Level of Evidence: C)*

Class III

1. A planned reperfusion strategy using full-dose fibrinolytic therapy followed by immediate PCI may be harmful. *(Level of Evidence: B)*

Routine early PCI vs rescue PCI after fibrinolysis

Routine PCI vs rescue PCI after fibrinolysis
TRANSFER-AMI trial

Community Hospital Emergency Department

High Risk ST Elevation MI within 12 hours of symptom onset

↓

TNK + ASA + Heparin or Enoxaparin + Clopidogrel

↓

Randomization

Pharmacoinvasive Strategy
Urgent Transfer to PCI Centre

Standard Treatment

↓

Assess chest pain, ST↑ resolution at 60-90 minutes after randomization

↓

Failed Reperfusion**

Successful Reperfusion

PCI Centre Cath Lab

Cath / PCI within 6 hrs regardless of reperfusion status

Cath and Rescue PCI ± GP IIb/IIIa Inhibitor

Elective Cath ± PCI > 24 hrs later

Repatriation of stable patients within 24 hrs of PCI

** ST segment resolution < 50% & persistent chest pain, or hemodynamic instability

Routine PCI vs rescue PCI after fibrinolysis TRANSFER-AMI trial

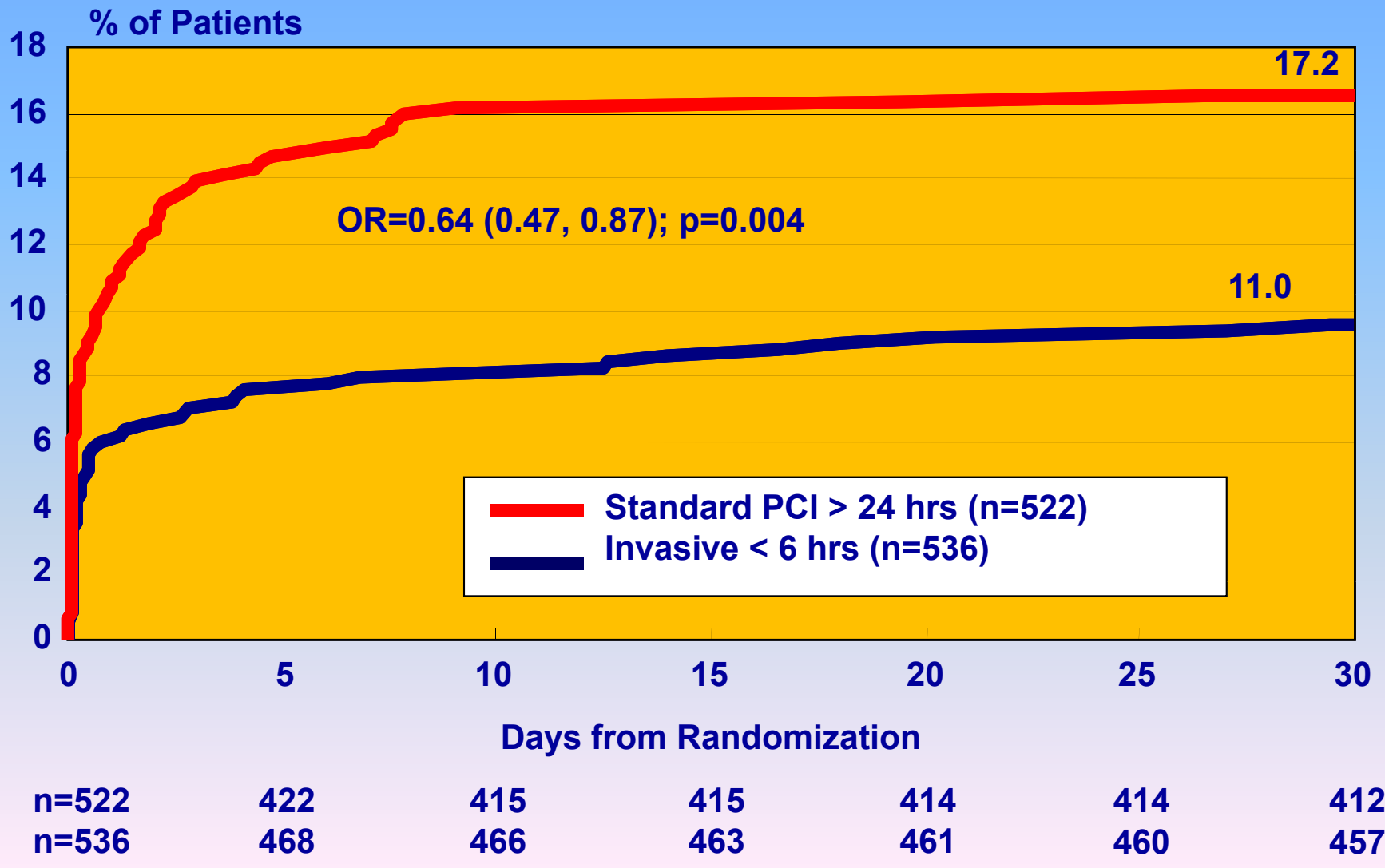
Inclusion Criteria

- Within 12 hrs of symptom onset
- ≥ 2 mm ST-segment elevation in 2 anterior leads

OR

- ≥ 1 mm ST-segment elevation in 2 inferior leads and at least one of the following high-risk criteria:
  - SBP < 100
  - HR > 100
  - Killip Class II-III
  - ≥ 2mm ST-segment depression in anterior leads
  - ≥ 1 mm ST-segment elevation in V_4R

Primary Endpoint: 30-Day Death, re-MI, CHF, Severe Recurrent Ischemia, Shock



Routine PCI vs rescue PCI after fibrinolysis TRANSFER-AMI trial

Efficacy end points

End Point	Standard Treatment (N=522) (PCI, 67.4% / 32.5hrs)	Routine Early PCI (N=536) (PCI, 84.9% / 2.8hrs)	Relative Risk with Routine Early PCI (95% CI)	P Value
Efficacy end points at 30 days — no. (%)				
Primary end point	90 (17.2)	59 (11.0)	0.64 (0.47–0.87)	0.004
Death	8 (3.4)	24 (4.5)	1.30 (0.71–2.36)	0.39
Reinfarction	30 (5.7)	18 (3.4)	0.57(0.33–1.04)	0.06
Death or reinfarction	47 (9.0)	38 (7.1)	0.79 (0.52–1.19)	0.25
Recurrent ischemia	11 (2.1)	1 (0.2)	0.09 (0.01–0.68)	0.003
Death, reinfarction, or recurrent ischemia	58 (11.1)	39 (7.3)	0.65 (0.44–0.96)	0.03
New or worsening congestive heart failure	29 (5.6)	16 (3.0)	0.54 (0.30–0.98)	0.04
Cardiogenic shock	16 (3.1)	24 (4.5)	1.46 (0.79–2.72)	0.23
Efficacy end points at 6 mo — no./total no. (%)				
Death	23/511 (4.5)	30/528 (5.7)	1.27 (0.77–2.23)	0.39
Reinfarction	33/511 (6.5)	21/528 (4.0)	0.60 (0.34–1.05)	0.07
Death or reinfarction	54/511 (10.6)	47/528 (8.9)	0.83 (0.55–1.25)	0.36

N Engl J Med 2009;360:2705-18.

Routine PCI vs rescue PCI after fibrinolysis TRANSFER-AMI trial

Safety end points

End Point	Standard treatment (N=522)	Routine Early PCI (N=536)	Relative Risk with routine early PCI (95% CI)	P Value
Any bleeding	84 (16.1)	110 (20.5)	1.27 (0.98–1.65)	0.06
Intracranial hemorrhage	6 (1.1)	3 (0.6)	0.49 (1.22–1.93)	0.34
Bleeding at access site	18 (3.4)	27 (5.0)	1.46 (0.81–2.61)	0.20
TIMI bleeding				
Minor	17 (3.3)	26 (4.8)	1.49 (0.82–2.71)	0.19
Major	47 (9.0)	40 (7.4)	0.83 (0.55–1.24)	0.36
Major, non–CABG-related	25 (4.8)	18 (3.4)	0.70 (0.39–1.27)	0.24
GUSTO bleeding				
Mild	47 (9.0)	70 (13.0)	1.45 (1.02–2.05)	0.04
Moderate	29 (5.6)	34 (6.3)	1.14 (0.70–1.84)	0.59
Severe	8 (1.5)	6 (1.1)	0.73 (0.25–2.09)	0.55
Severe, non–CABG-related	7 (1.3)	5 (0.9)	0.69 (0.22–2.17)	0.53
Major TIMI or severe GUSTO bleeding	47 (9.0)	40 (7.4)	0.83 (0.55–1.24)	0.36

N Engl J Med 2009;360:2705-18.

Routine PCI vs rescue PCI after fibrinolysis CARESS in AMI trial

Inclusion criteria: STEMI pts(<75 yrs)

-admitted to a centre without PCI facilities

-within 12 h from onset of symptoms

-high risk features(one or more of the following):

cumulative ST-segment elevation of more than 15 mm, new onset LBBB, previous MI, Killip class of 2 or more, or LVEF < 35%

600 STEMI

Aspirin 300–500 mg intravenously

Reteplase 5 U+5 U at 30 min

Unfractionated heparin 40 U/kg (max 3000 per U) →7 U/kg/h

Abciximab 0.25 mg/kg bolus →0.125 µg/kg per min for 12 h to a maximum of 10 µg/min

Immediate PCI(298)

135 (96–175) min

CAG:289(97%)/PCI:255(85.6%)

Standard care/rescue PCI(300)

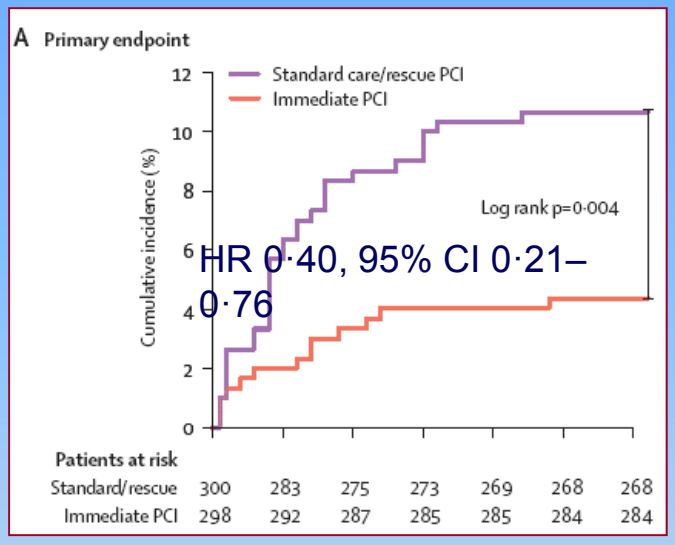
211 (157–290) min

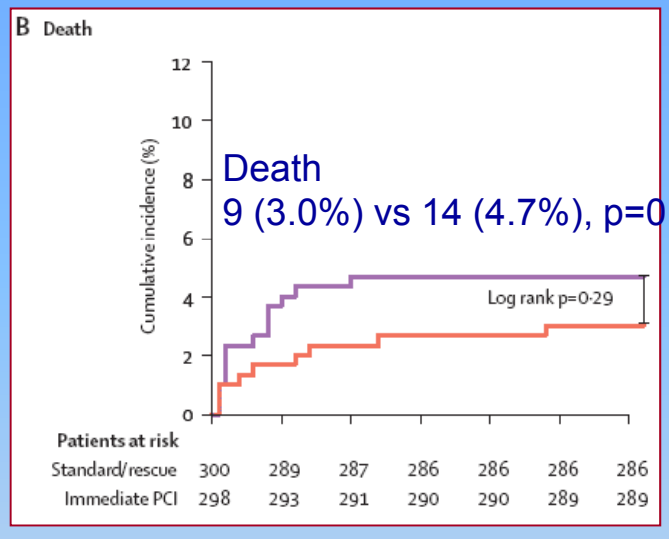
CAG:107(35.7%)/PCI:91(30.3%)

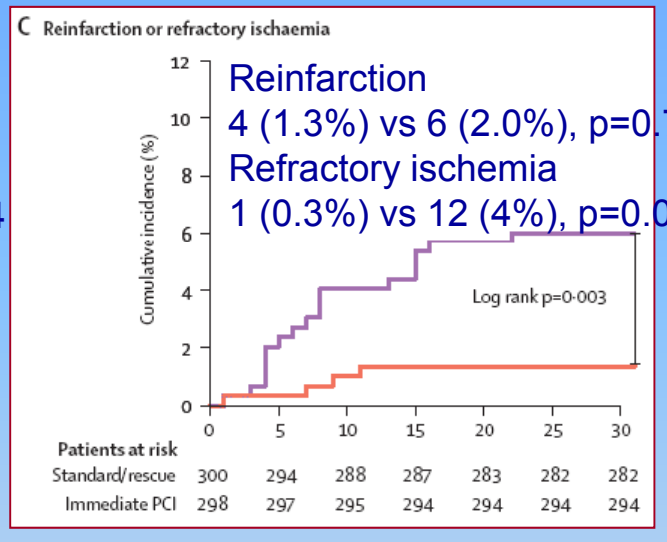
Rescue PCI in Clinical deterioration

(eg, persistent ST-segment elevation at 90 min greater than 50% compared with the baseline ECG, ongoing chest pain, or haemodynamic instability, in the standard care/rescue group)

Routine PCI vs rescue PCI after fibrinolysis CARESS in AMI trial







	Immediate PCI	Standard care/rescue	p*
30-day bleeding events			
Major	10 (3.4)	7 (2.3%)	0.47
Minor	32 (10.8)	12 (4.0%)	0.002
TIMI bleeding classification			
Major	8 (2.7)	7 (2.3%)	0.80
Minor	10 (3.4)	4 (1.3%)	0.11
Minimal	23 (7.7)	7 (2.3%)	0.002
30-day cerebrovascular events	2 (0.7)	4 (1.3%)	0.50
Ischaemic	0 (0.0)	1 (0.3%)	1
Haemorrhagic	2 (0.7)	3 (1.0%)	1

Recommendation for Triage and transfer for PCI

2009 STEMI Focused Update Recommendation

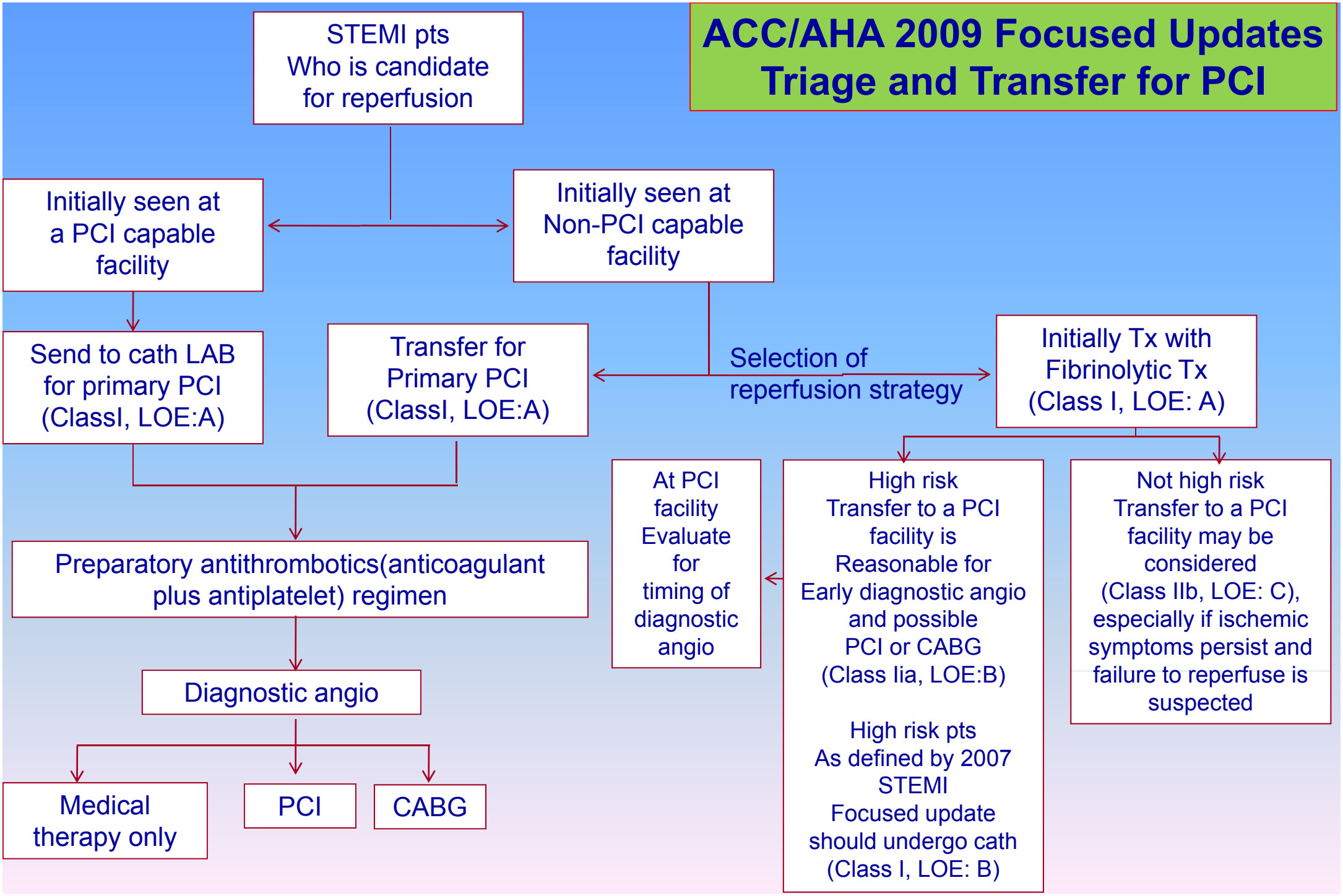
Class IIa

1. It is reasonable for high-risk* patients who receive fibrinolytic therapy as primary reperfusion therapy at a non–PCI-capable facility to be transferred as soon as possible to a PCI-capable facility where PCI can be performed either when needed or as a pharmacoinvasive strategy. Consideration should be given to initiating a preparatory antithrombotic (anticoagulant plus antiplatelet) regimen before and during patient transfer to the catheterization laboratory (*Level of Evidence: B*)

Facilitated PCI
Rescue PCI
Routine early angioplasty

⇢ **Pharmacoinvasive Therapy**

ACC/AHA 2009 Focused Updates Triage and Transfer for PCI



Summary

1. The timely performed Primary PCI is a superior strategy, compared to thrombolysis in STEMI patients. But substantial proportion of STEMI patients present initially to hospitals without ready access to skilled primary PCI.

2. Where PCI cannot be performed within the optimal time frame, fibrinolysis is more preferred reperfusion options, especially in early presentation with low bleeding risk.

3. In patients with low bleeding risk and early presentation, high intensity fibrinolytic regimen is recommended. Patients undergoing fibrinolysis should receive thienopyridine and anticoagulants.

4. High risk patient treated by thrombolytics in non-PCI capable facility should be transferred as soon as possible PCI capable facility with preparatory antithrombotic regimen.

Conclusion

The appropriate and timely use of thrombolysis in non-PCI capable center is likely more important than primary PCI with unacceptable delay in STEMI patients, especially with early presentation.

But High risk patients should be transferred as soon as possible for early PCI irrespective of reperfusion state by thrombolysis.

Thank You for Your Attention