

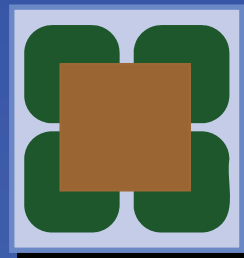
9th Angioplasty Summit 2004, Seoul, Korea, April 2004.

Contemporary Antithrombotic Therapy in PCI

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Associate Professor of Medicine
Department of Cardiovascular Medicine

THE CLEVELAND CLINIC FOUNDATION
Cleveland, Ohio

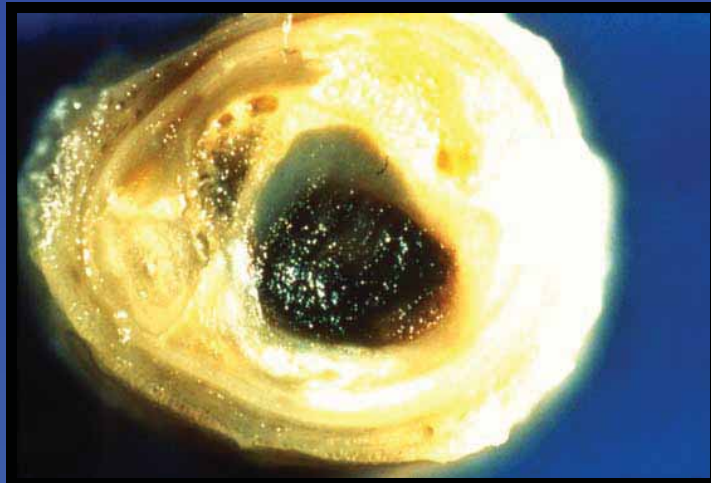


ACS and PCI

Plaque Rupture



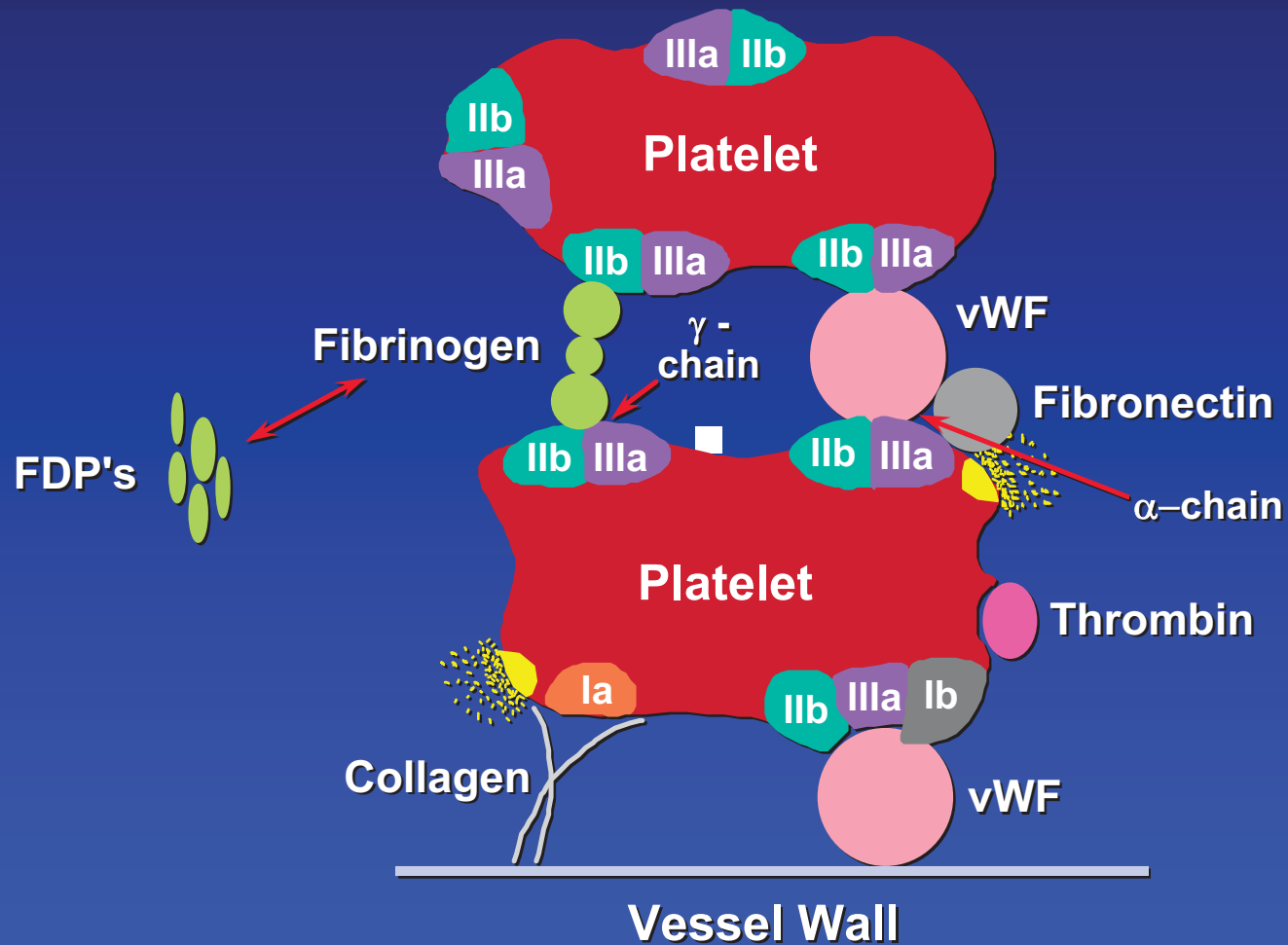
Thrombosis



Embolization



Platelets

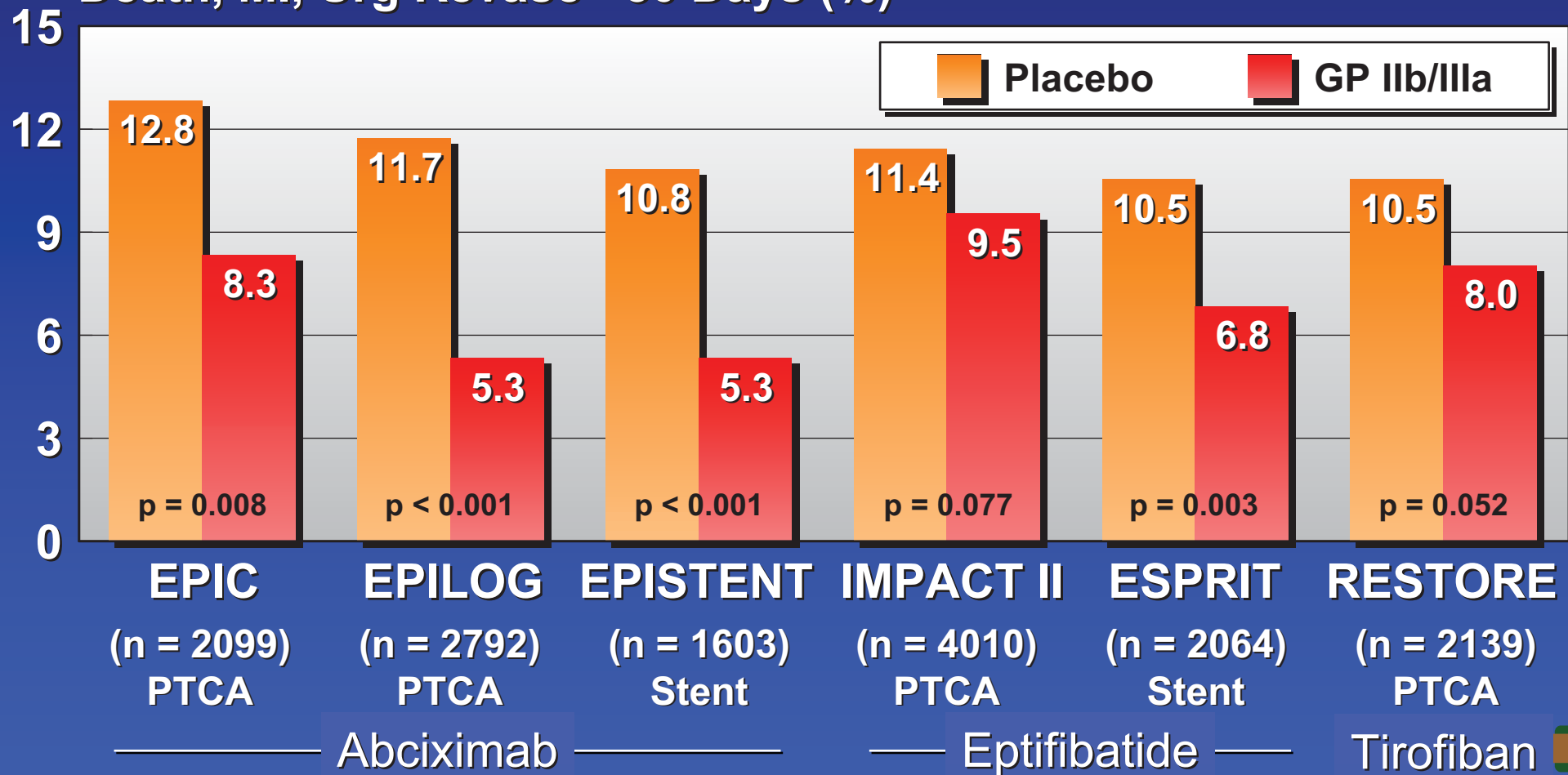


Modified from Fuster et al. Circ 1990;82:II-47

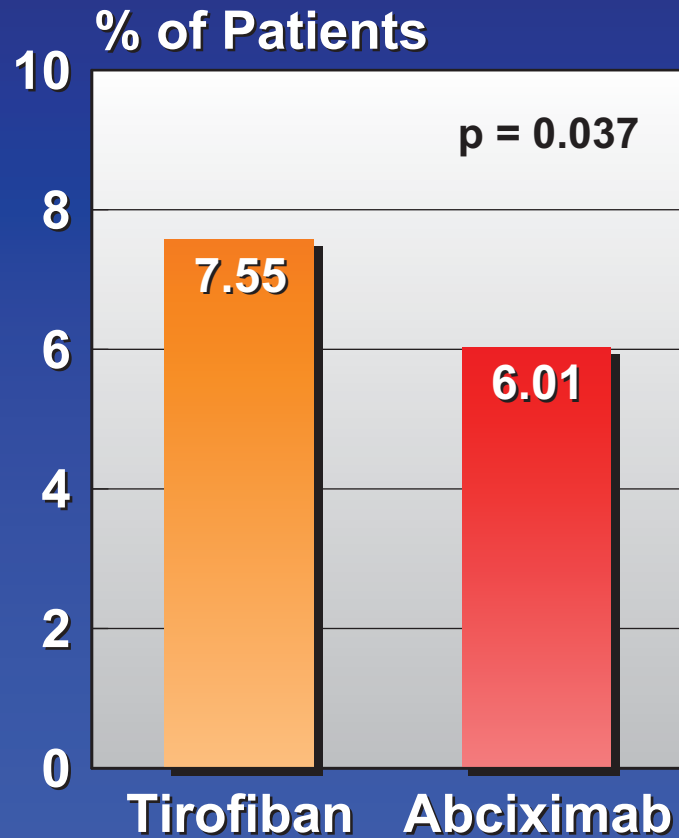
GP IIb/IIIa Interventional Trials

Primary Composite Endpoint at 30 Days

Death, MI, Urg Revasc - 30 Days (%)

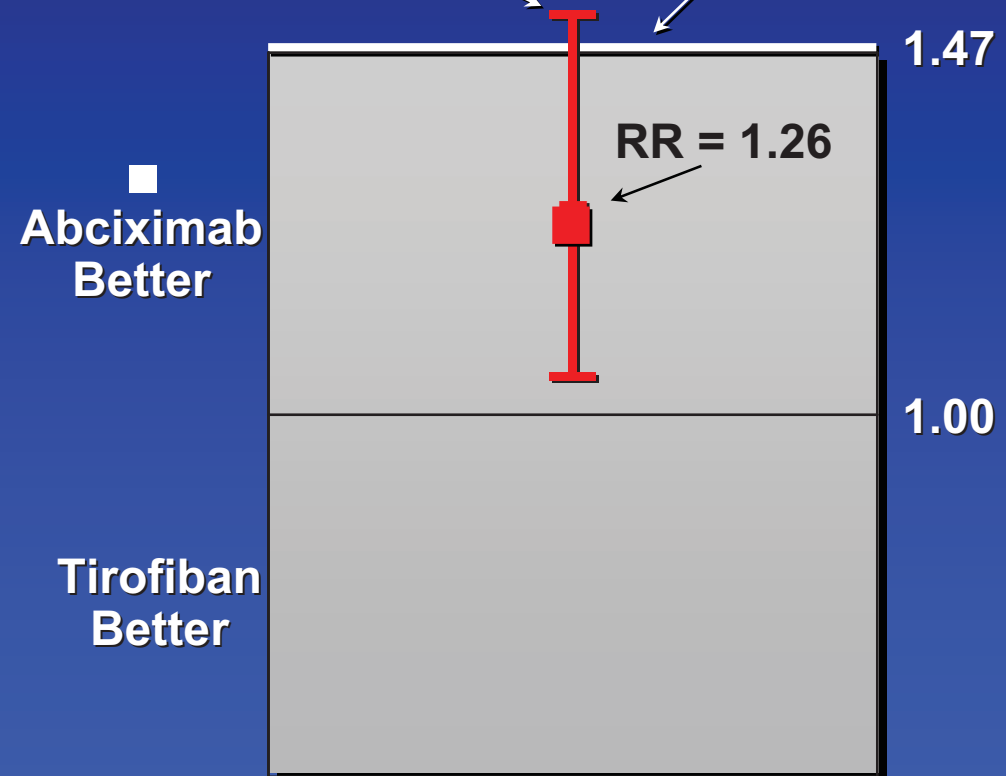


Death, MI, Urg TVR
at 30 Days

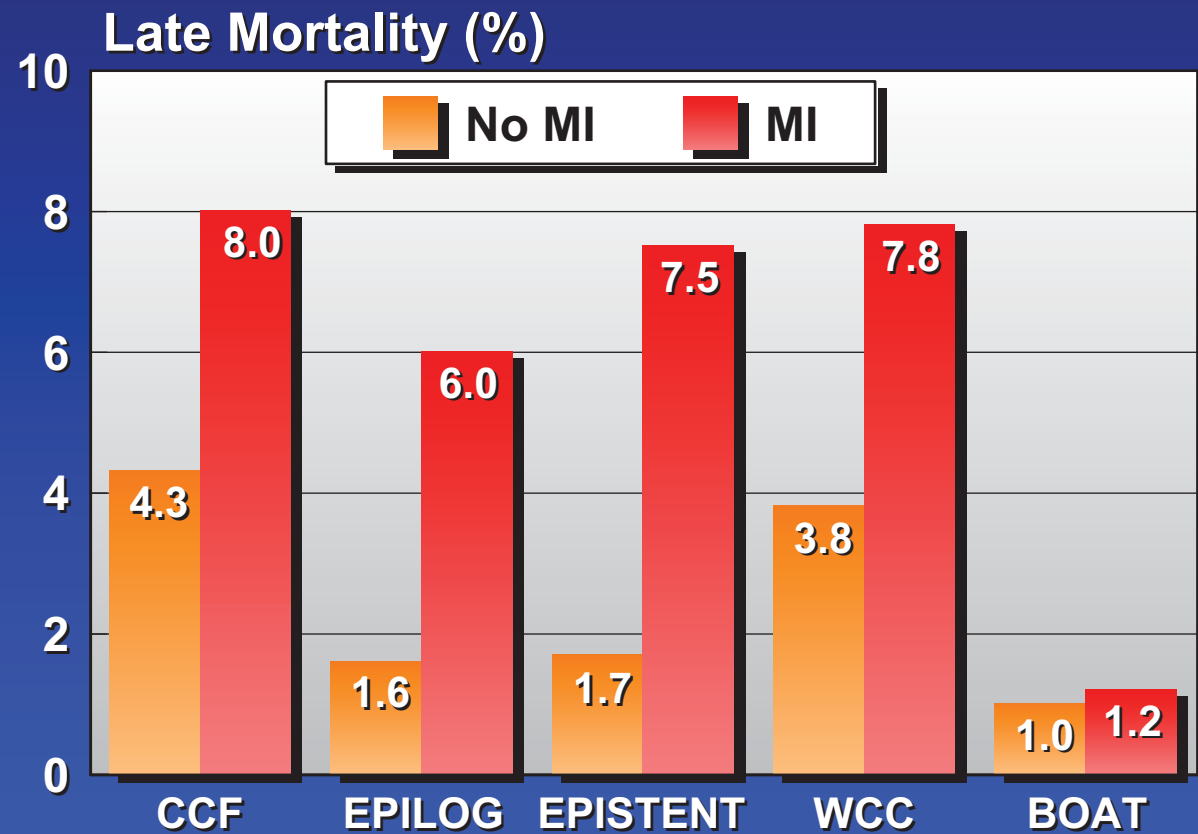
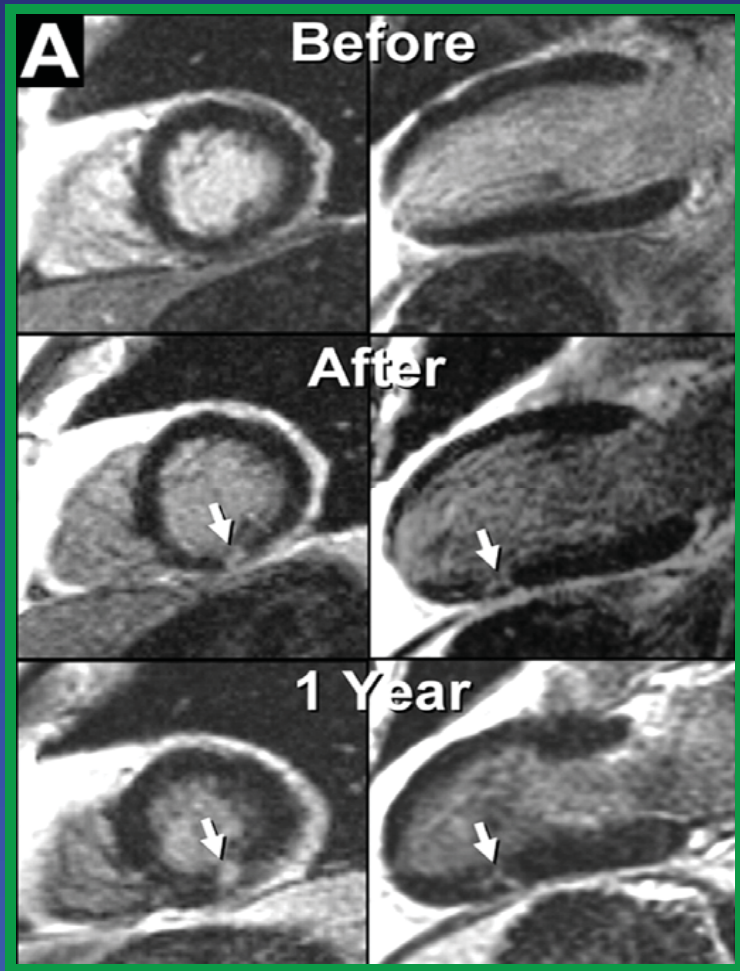


Upper bound of 95%
confidence interval = 1.52

Non-inferiority boundary



Periprocedural CK-MB Elevation

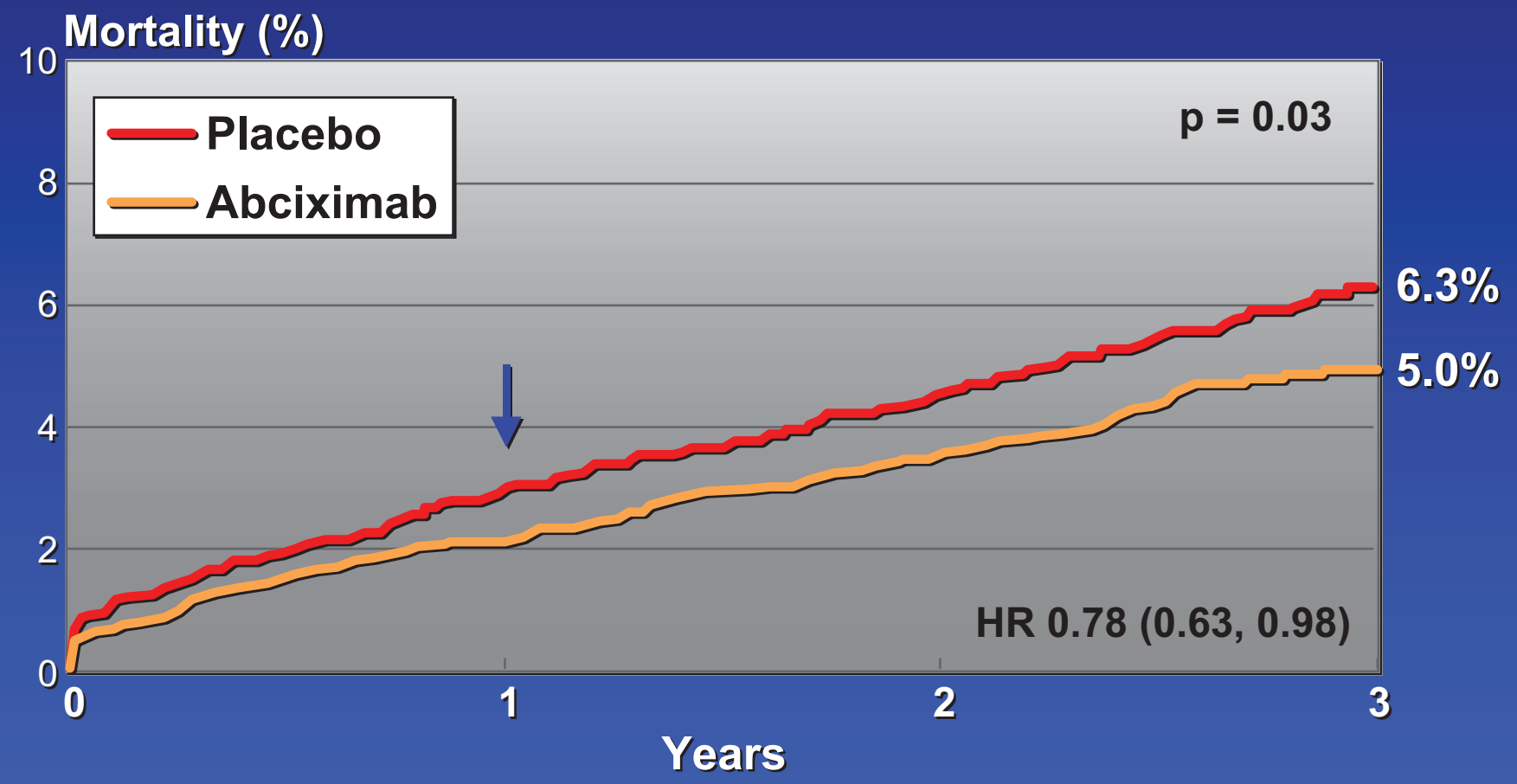


Ricciardi et al. Circulation 2001;103:2780



3-Year Follow Up

EPIC, EPILOG, EPISTENT Trials N = 5799 Patients

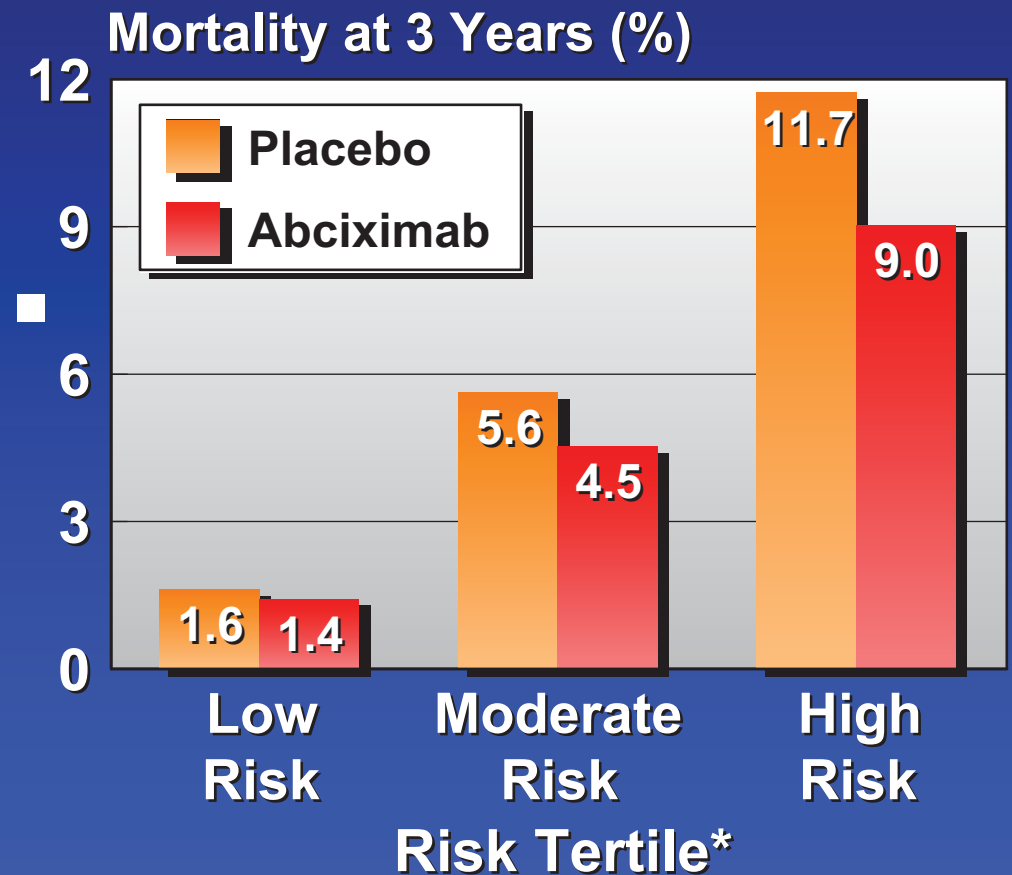




Mortality Risk Score

EPIC, EPILOG, EPISTENT Trials

Risk Factor	Point Score
Age	years - 18
Hx CHF	18
Prior CABG	12
Diabetes	9
Smoked prior yr	9
PVOD	6
HTN	5
Prior MI	4
Creatinine	1 per 0.2 mg/dl

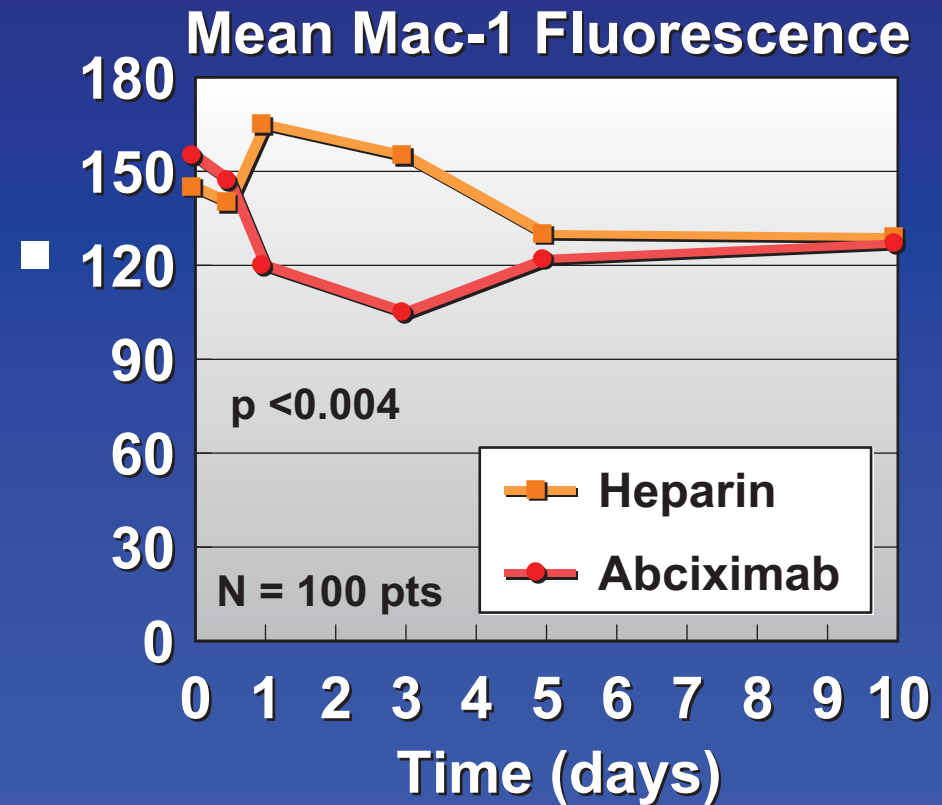
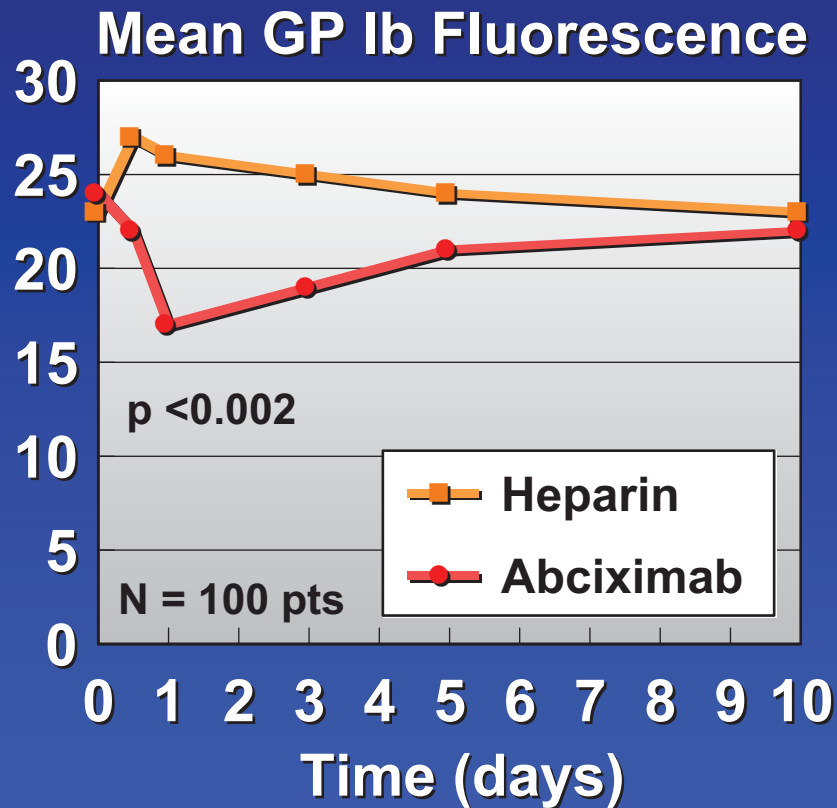


Kereiakes et al. AJC 2002;90:628.



Abciximab and Inflammation

Reduced Monocyte Platelet Interaction and Mac-1 Expression During Stenting for Acute MI

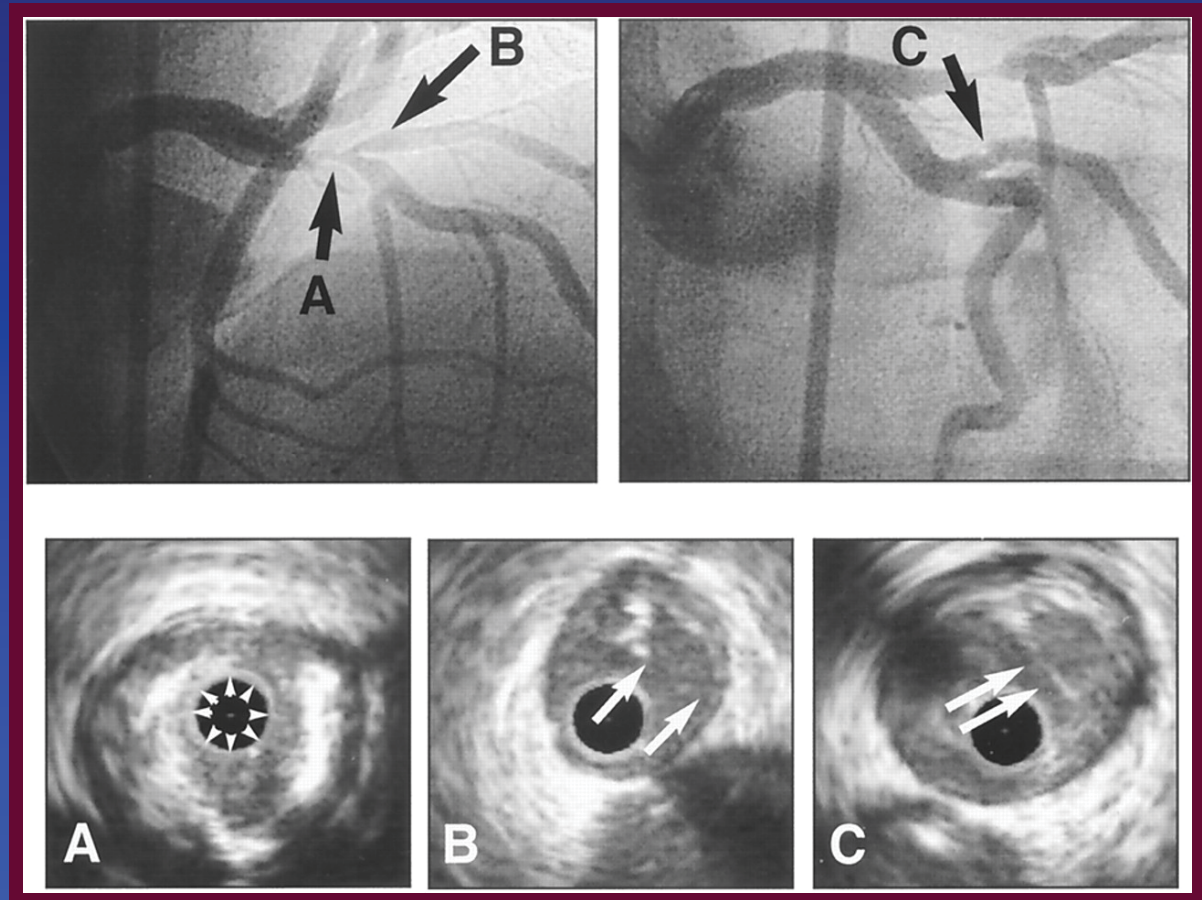
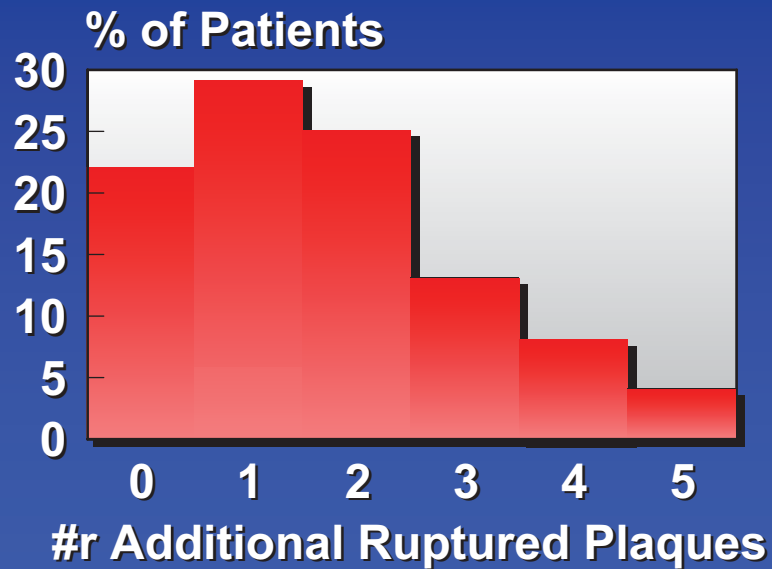


Neumann et al. JACC 1999;34:1420.

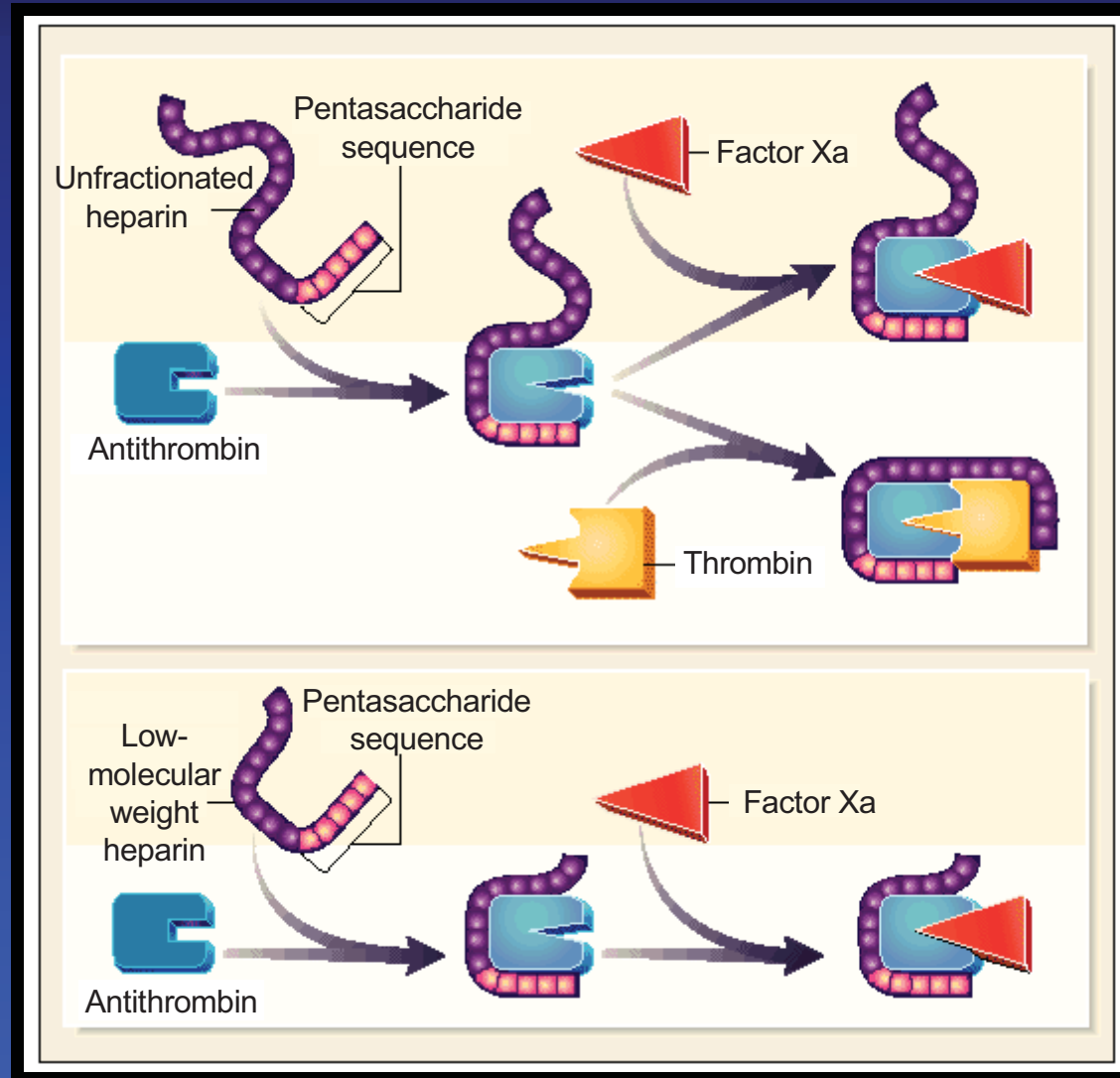
Acute Coronary Syndromes

Multiple Plaque Rupture - IVUS Study

- 24 pts within 2.3 ± 1.5 wks of ACS onset
- 3-vessel IVUS



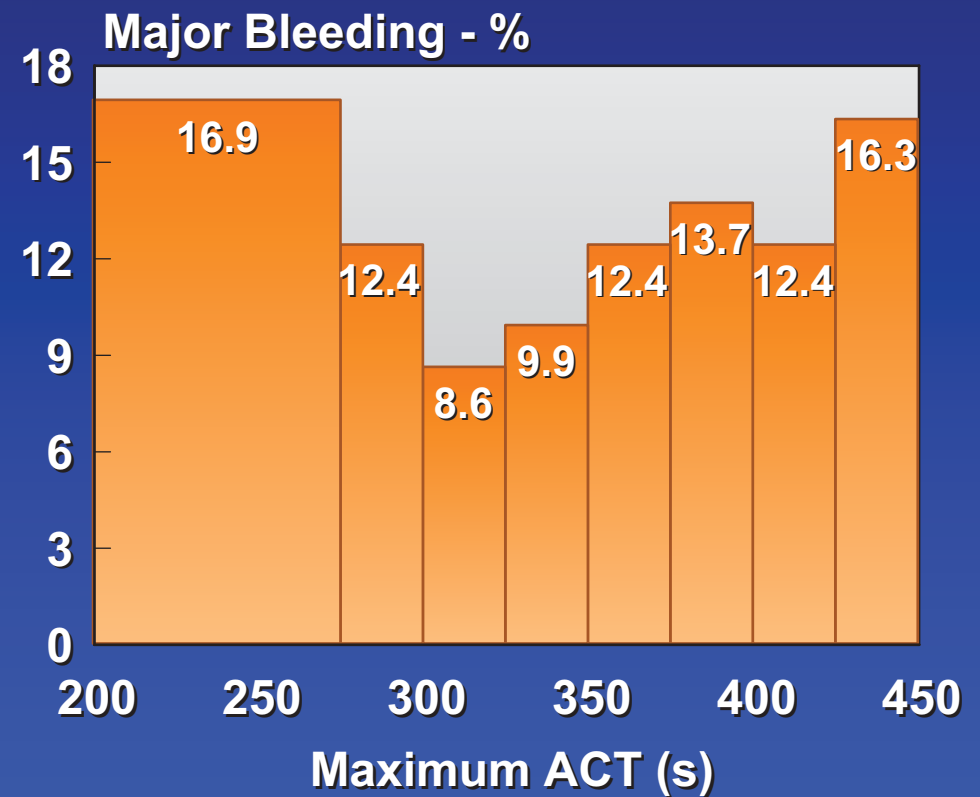
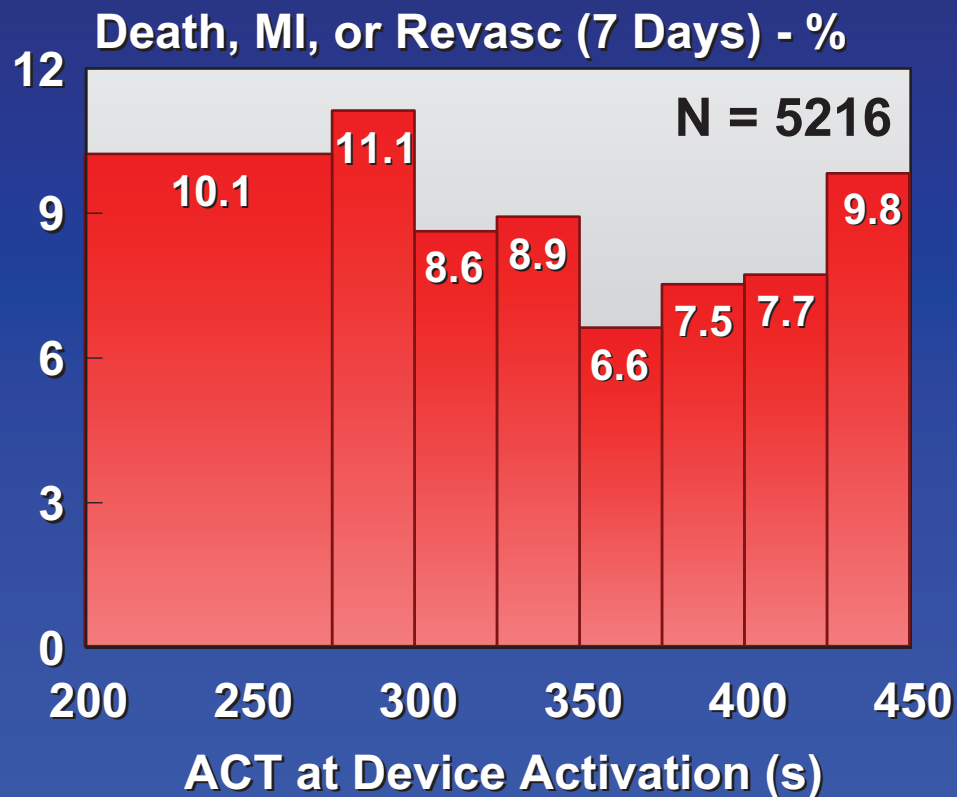
Heparins



Weitz JI. NEJM 1997;337:689.

Heparin During PCI

ACT and Clinical Outcome

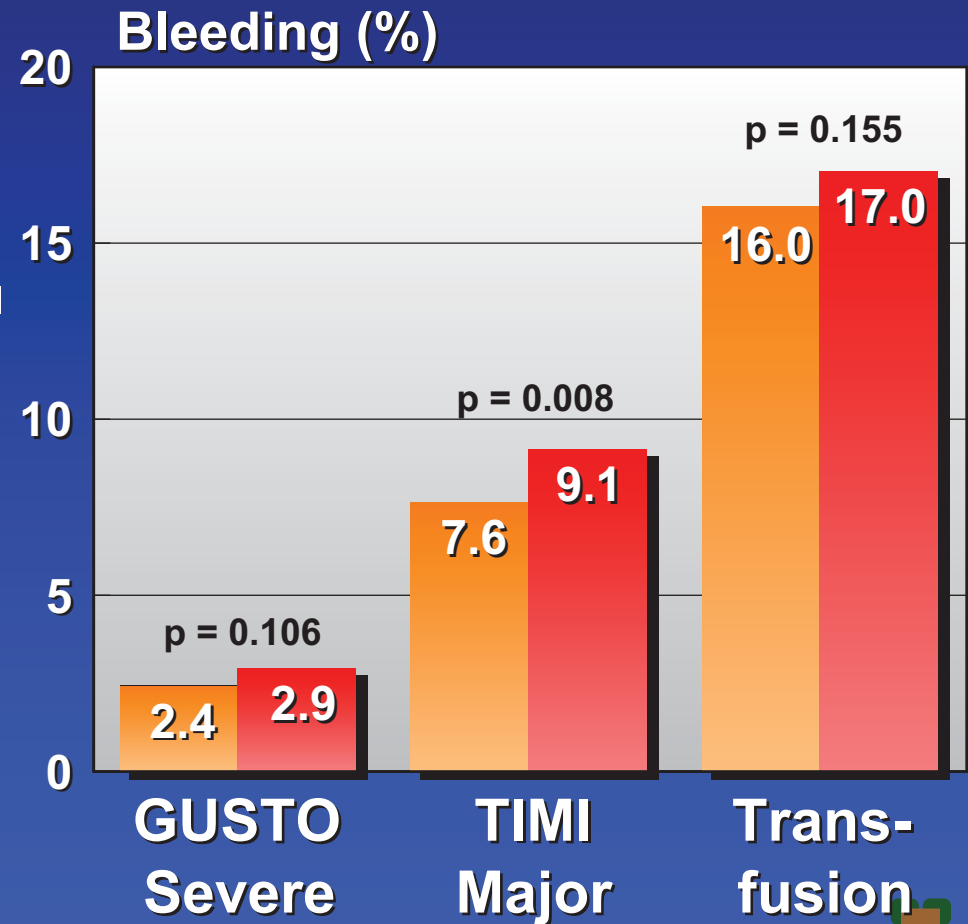
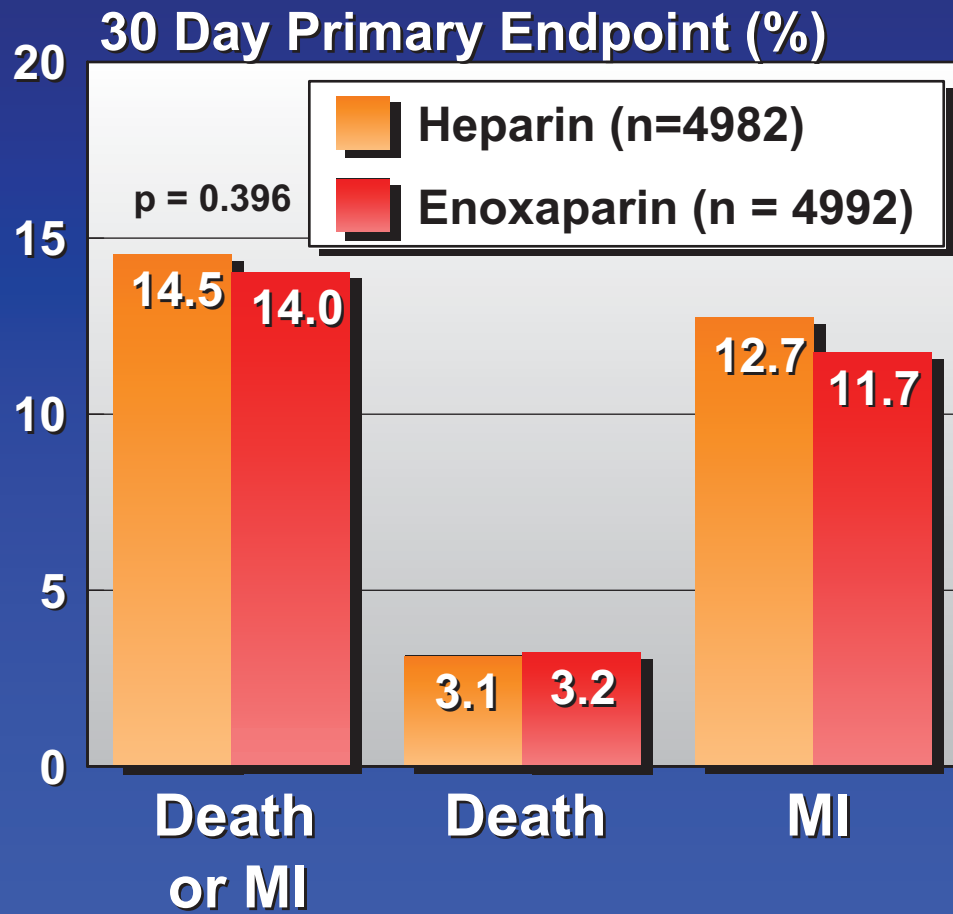


Chew DP. Circulation 2001;103:961.

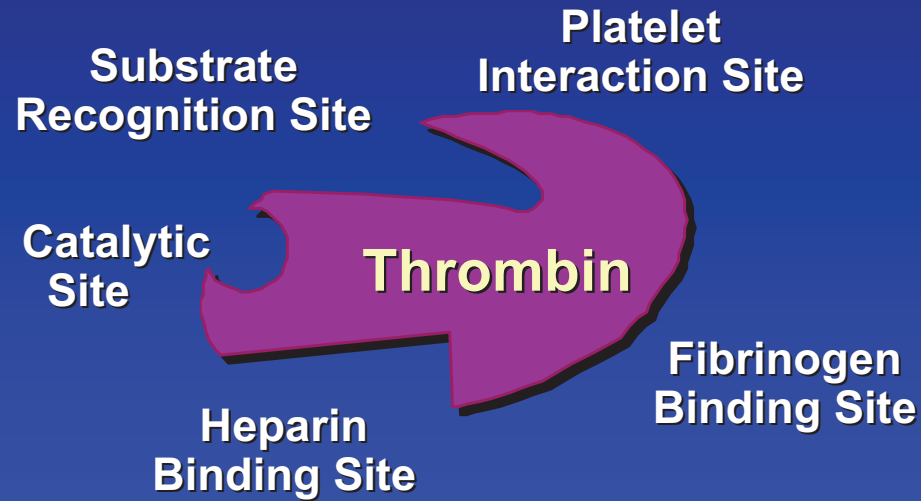


SYNERGY Trial

Ischemic and Hemorrhagic Endpoints

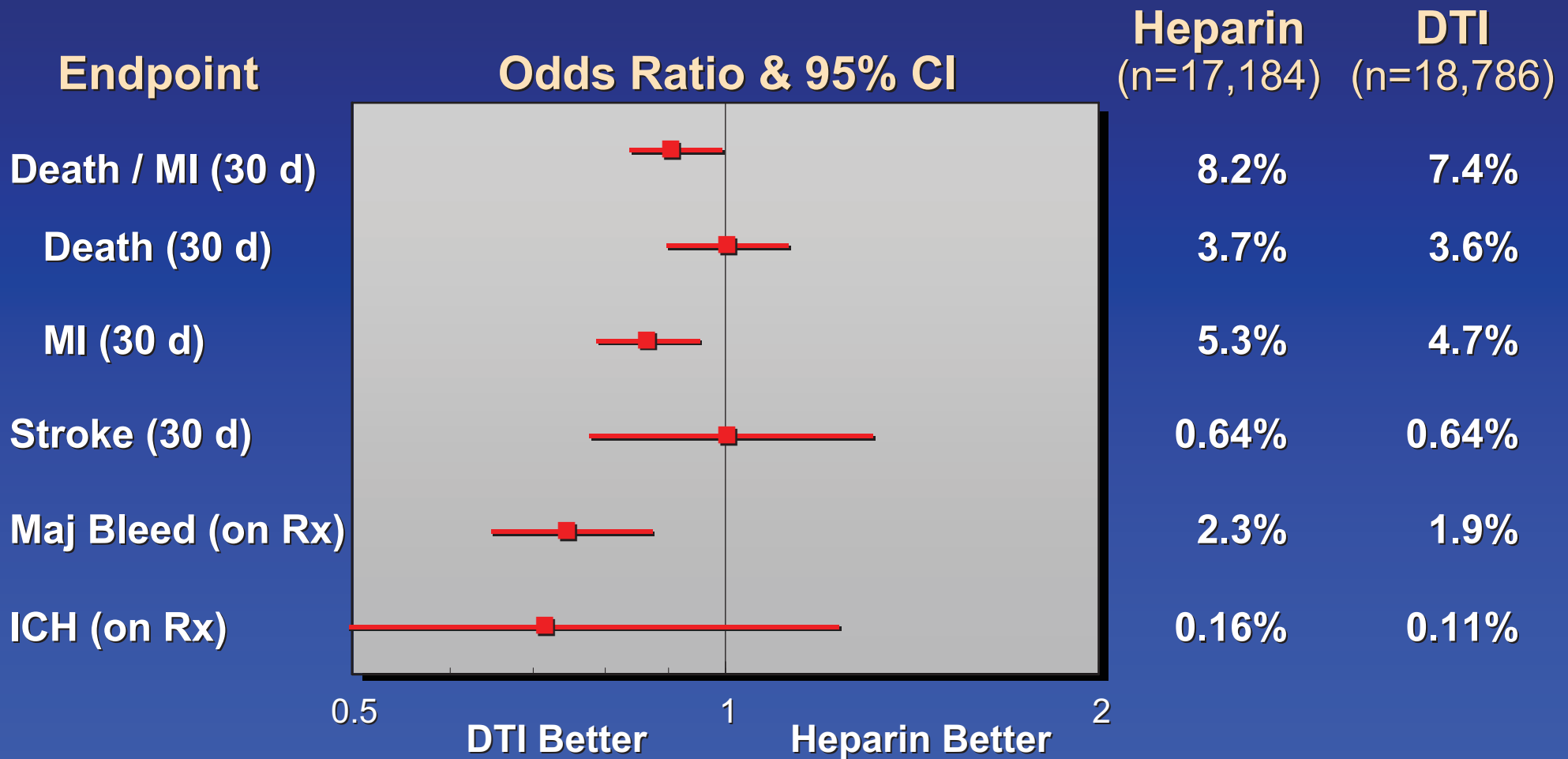


Direct Thrombin Inhibitors



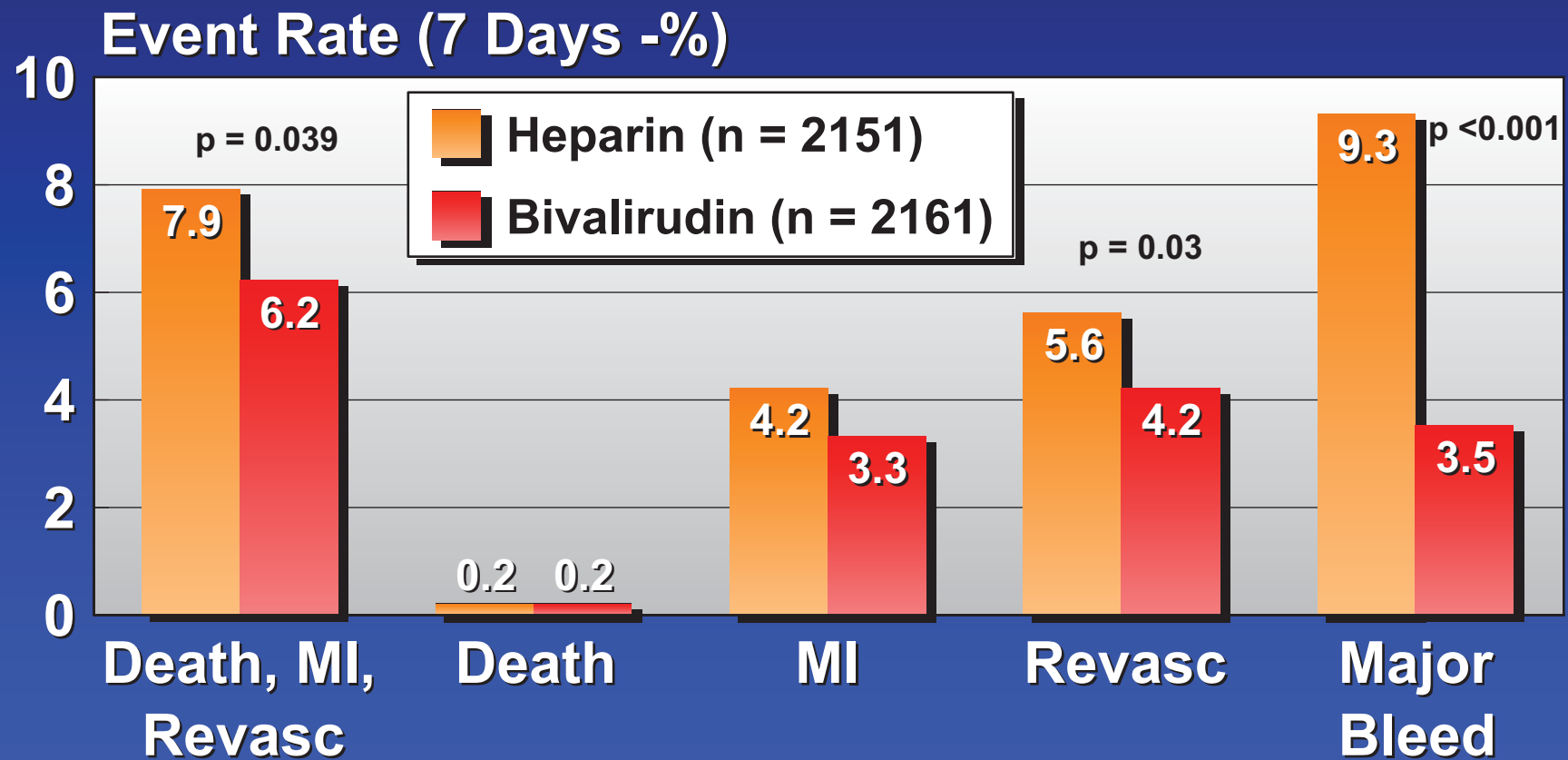
Direct Thrombin Inhibitors in ACS

Meta-Analysis vs Heparin



Bivalirudin Angioplasty Trial

Bivalirudin vs Heparin During PTCA for ACS

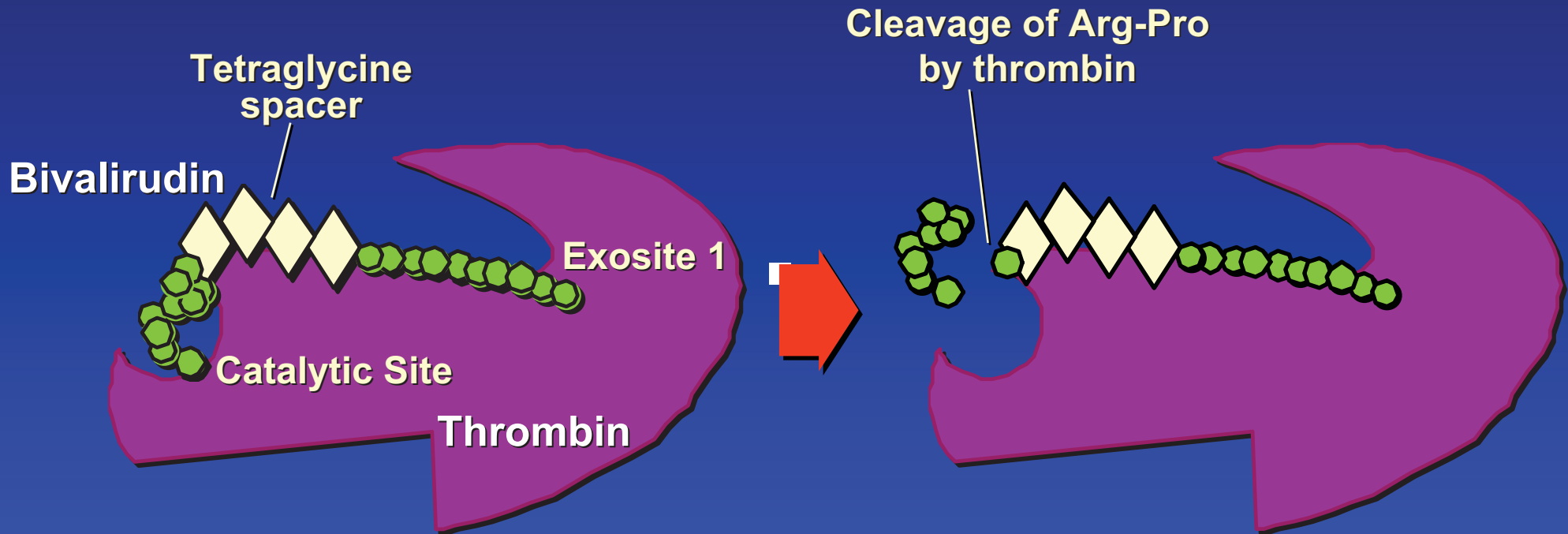


Bittl JA et al. Am Heart J 2001;142:952.3



Bivalirudin

Reversible Thrombin Inhibition



Catalytic Site - active fibrin cleavage site
Exosite 1 - substrate (fibrin) binding site

Once bound to thrombin, bivalirudin converted from non-competitive inhibitor of both catalytic site and exosite 1 to competitive inhibitor of exosite 1 only

Bates and Weitz. *AJC* 1998;82:12P.

Bivalirudin vs Heparin + GP IIb/IIIa During PCI

N ~ 6000 Patients: Urgent or Elective PCI

Randomization - double blind, triple dummy

Heparin

65 U/kg initial bolus

Planned GP IIb/IIIa
(abciximab or eptifibatide)

target ACT
≥ 225 sec

Bivalirudin

0.75 mg/kg initial bolus,
1.75 mg/kg-hr during PCI

Provisional GP IIb/IIIa
(abciximab or eptifibatide)

abciximab: 0.25 mg/kg bolus, 0.125 µg/kg-min (max 10 µg/min) x 12 hrs

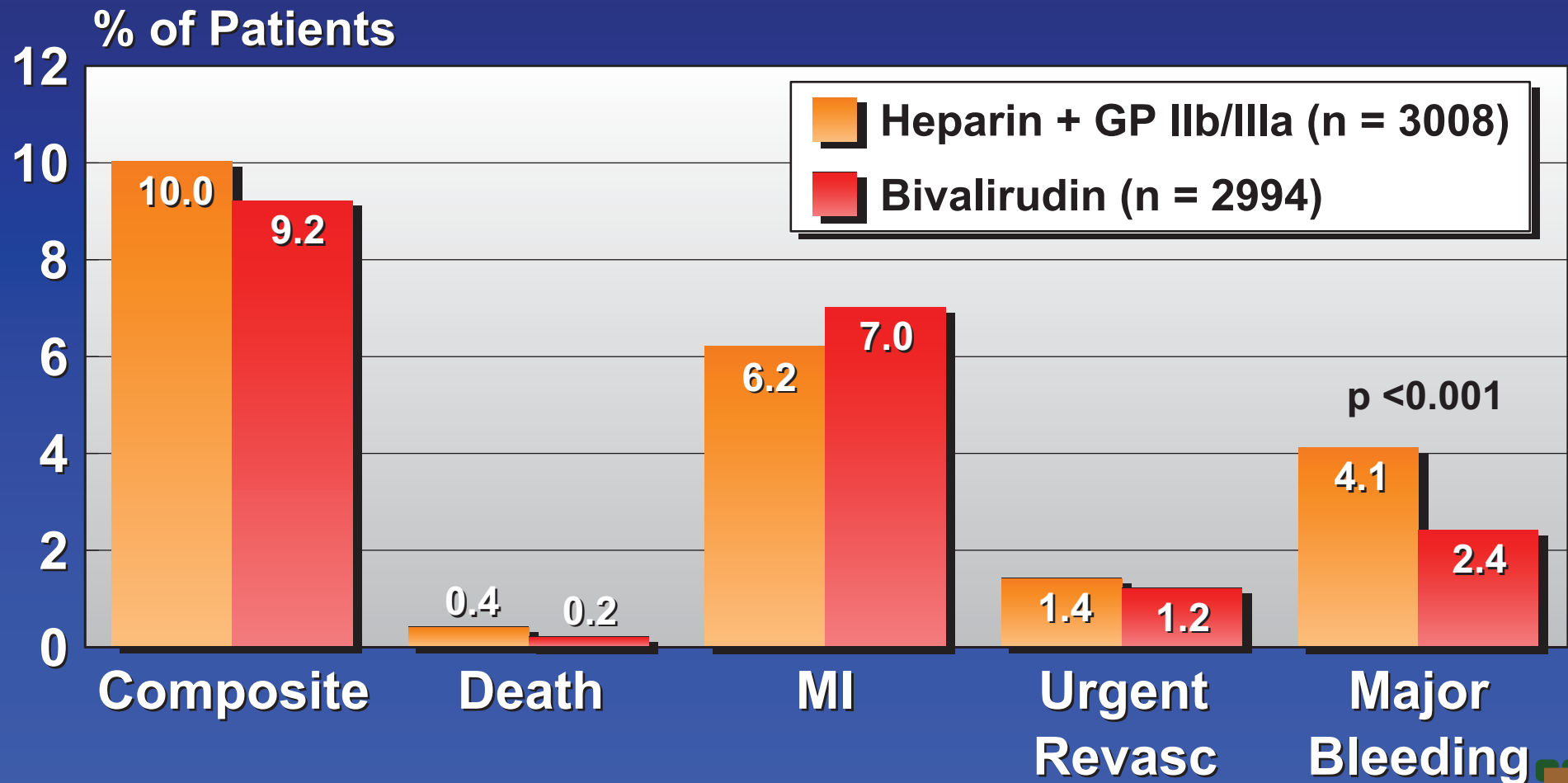
eptifibatide: 180 µg/kg double bolus, 2.0 µg/kg-min x 18-24 hrs

• “Quadruple Endpoint” at 30 Days •



Quadruple Endpoint

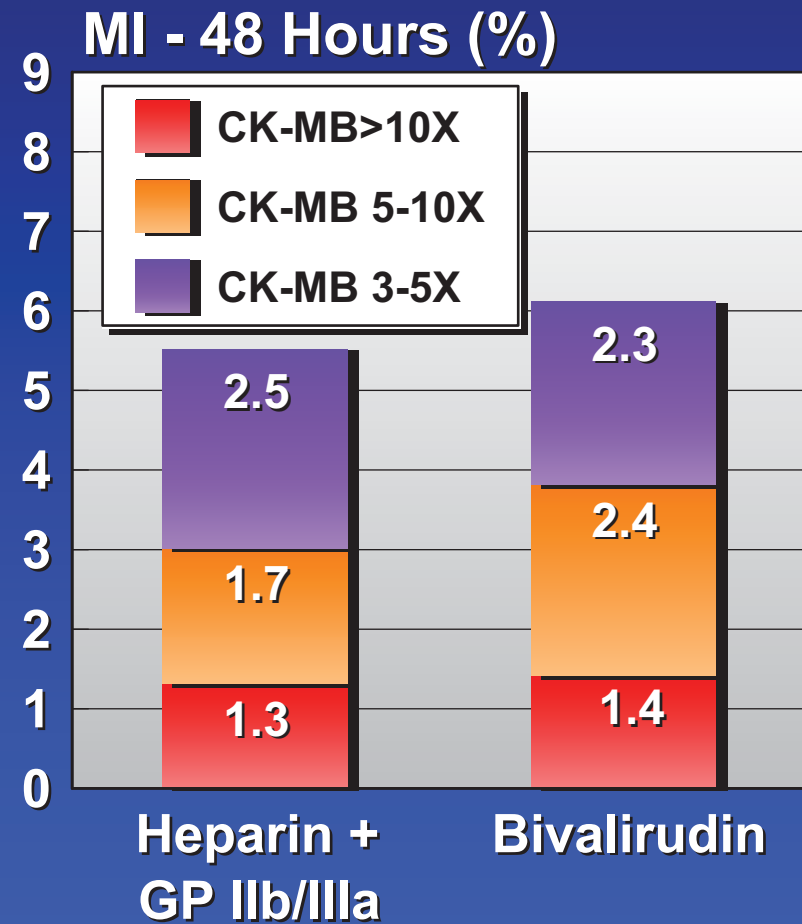
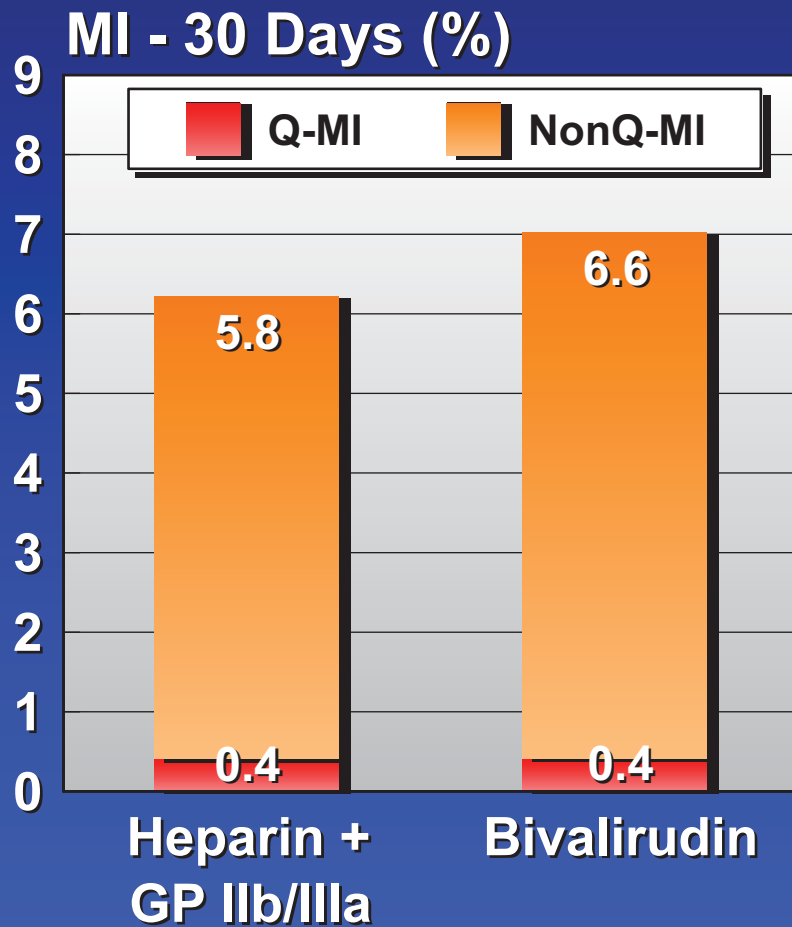
30 Day Primary Endpoint Components





Myocardial Infarction

Types of MI





Bleeding Complications

(% of Patients)	Bivalirudin N = 2994	Heparin + GP IIb/IIIa N = 3008	P-value
Major bleeding	2.4	4.1	< 0.001
Minor bleeding	13.4	25.7	<0.001
TIMI Major	0.6	0.9	0.30
TIMI Minor	1.3	3.0	<0.001
Thrombocytopenia (<100K)	0.7	1.7	<0.001
Transfusions	1.7	2.5	0.021
PRBC	1.4	1.9	0.166
Platelets	0.3	0.6	0.133
Retroperitoneal hemorrhage	0.2	0.5	0.062
Sheath site hemorrhage	0.8	2.5	<0.001





Advantages of Bivalirudin

Duration of Study Drug Infusions

Abciximab	12 hrs
Eptifibatide	18 hrs
Bivalirudin	0.73 hrs

Wholesale Acquisition Costs

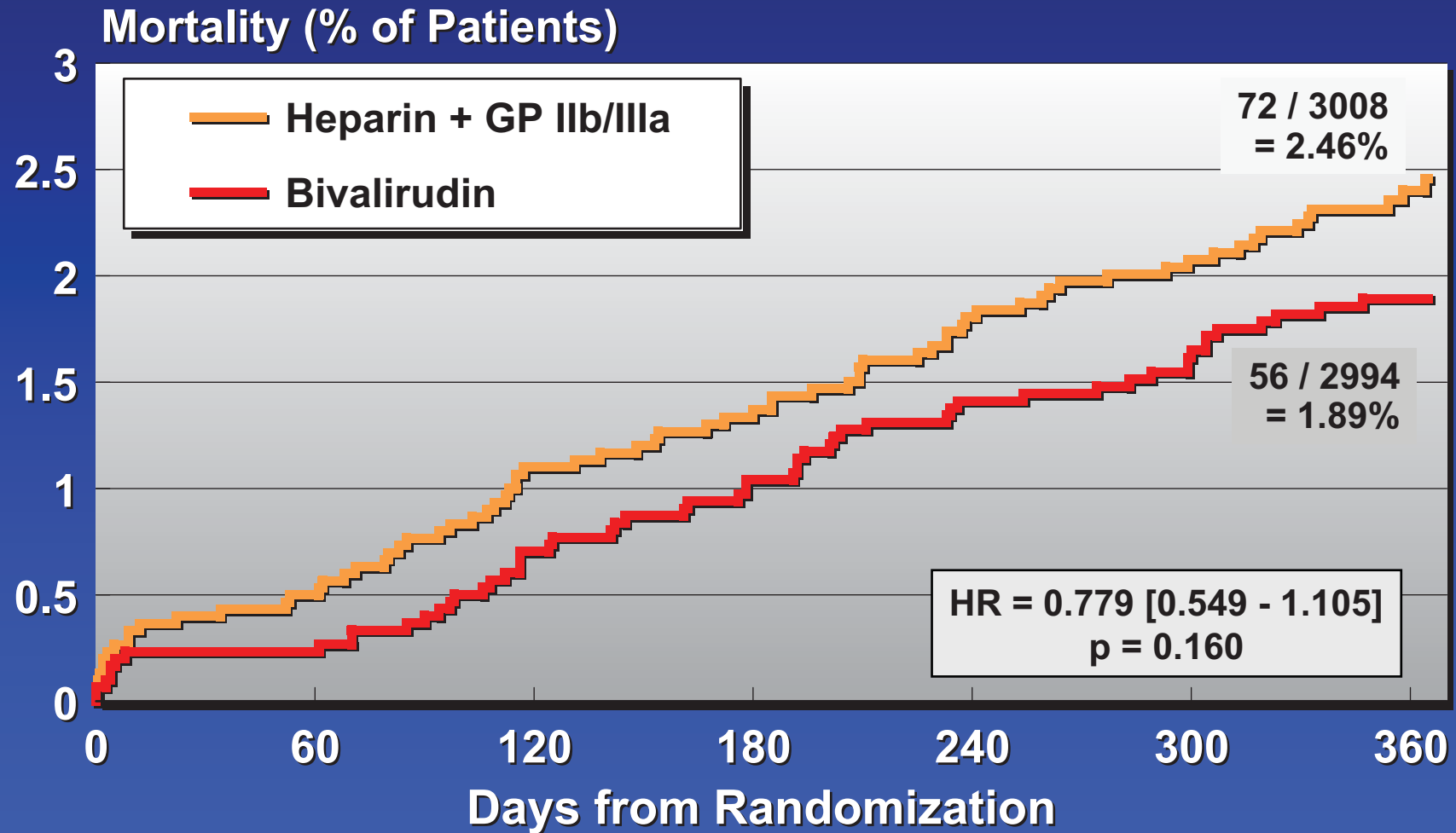
Abciximab	\$1300
Eptifibatide	\$615
Bivalirudin	\$470

■ approximate costs based upon average 87 kg patient in REPLACE-2



1-Year Results

Mortality

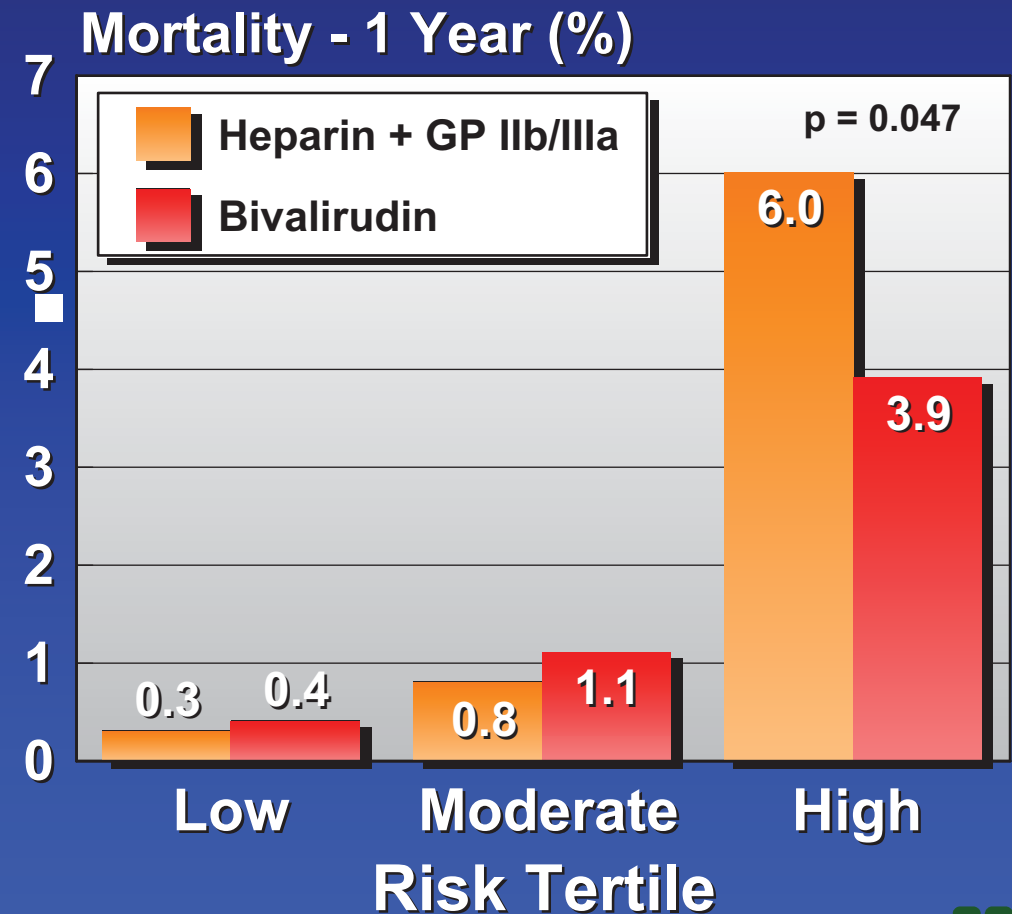




1 Year Mortality

Mortality by Risk Tertile

Risk Factor	Hazard Ratio
Age	1.05 /yr
Tobacco	1.85
Hx angina	2.02
CHF	3.10
Diabetes	1.50
Creatinine	1.66 /mg/dl
BMI \leq 28	0.90
BMI $>$ 28	1.14
USA - NE	0.41
USA - SE	0.57

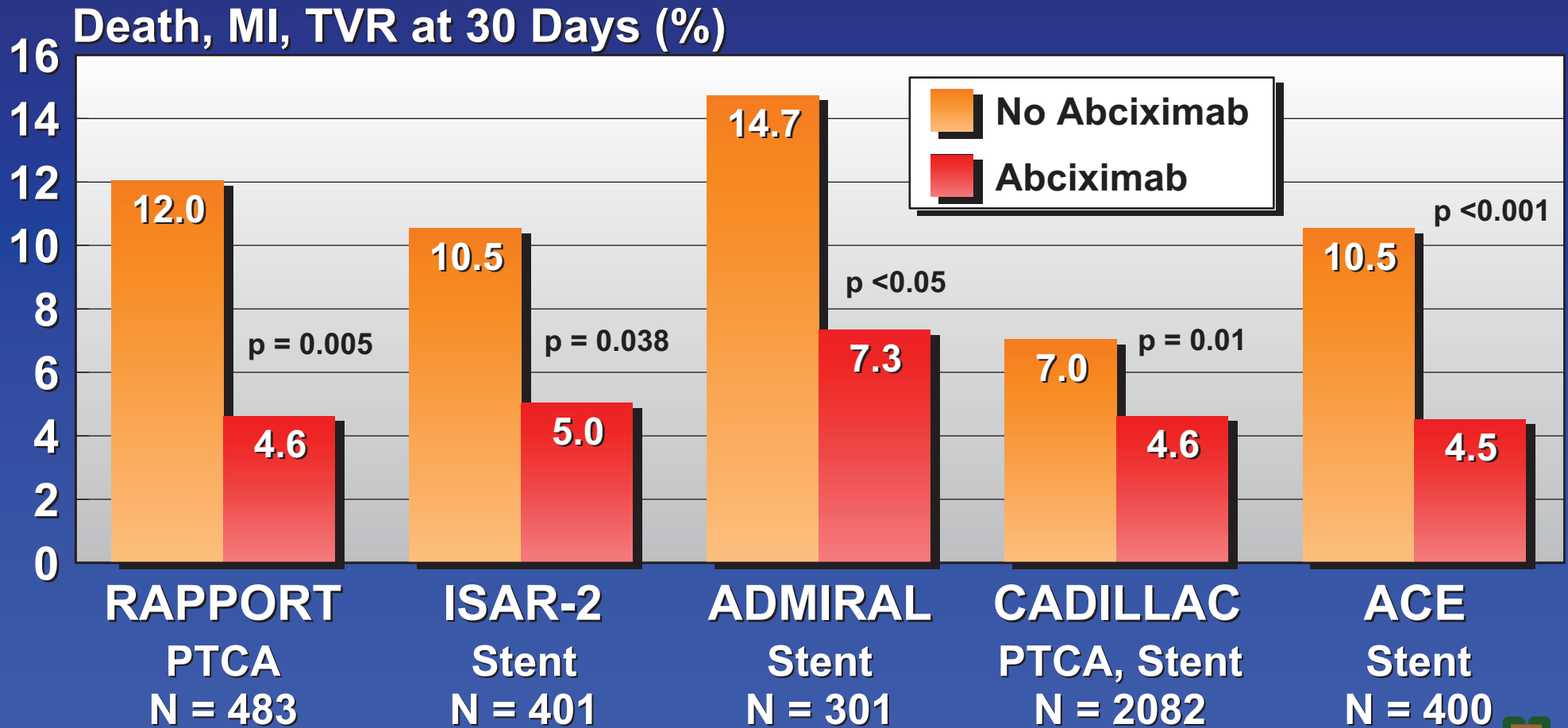


Acute MI or Ongoing Anticoagulant Therapy

- v primary or rescue PCI for acute MI
- v UFH within prior 6 hr unless aPTT \leq 50 s or ACT \leq 175 s
- v LMWH within prior 8 hr ■
- v bivalirudin within prior 24 hr
- v abciximab within prior 7 days
- v eptifibatide or tirofiban within prior 12 hr
- v warfarin Rx

GP IIb/IIIa in Acute MI

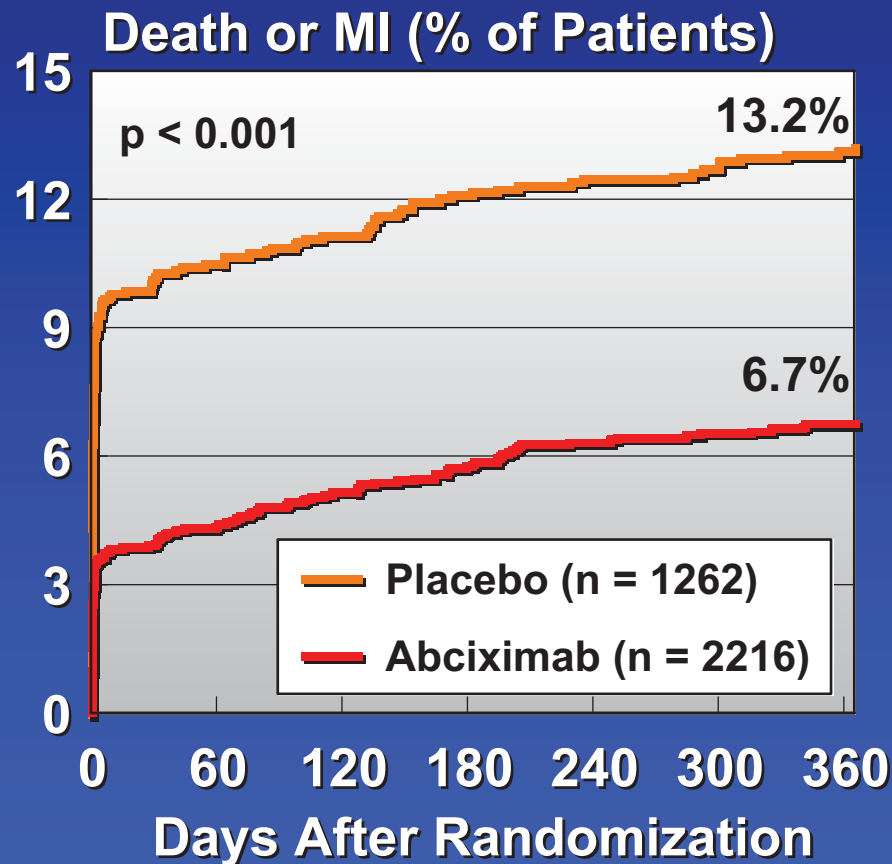
Abciximab and PCI - 30 Day Endpoint



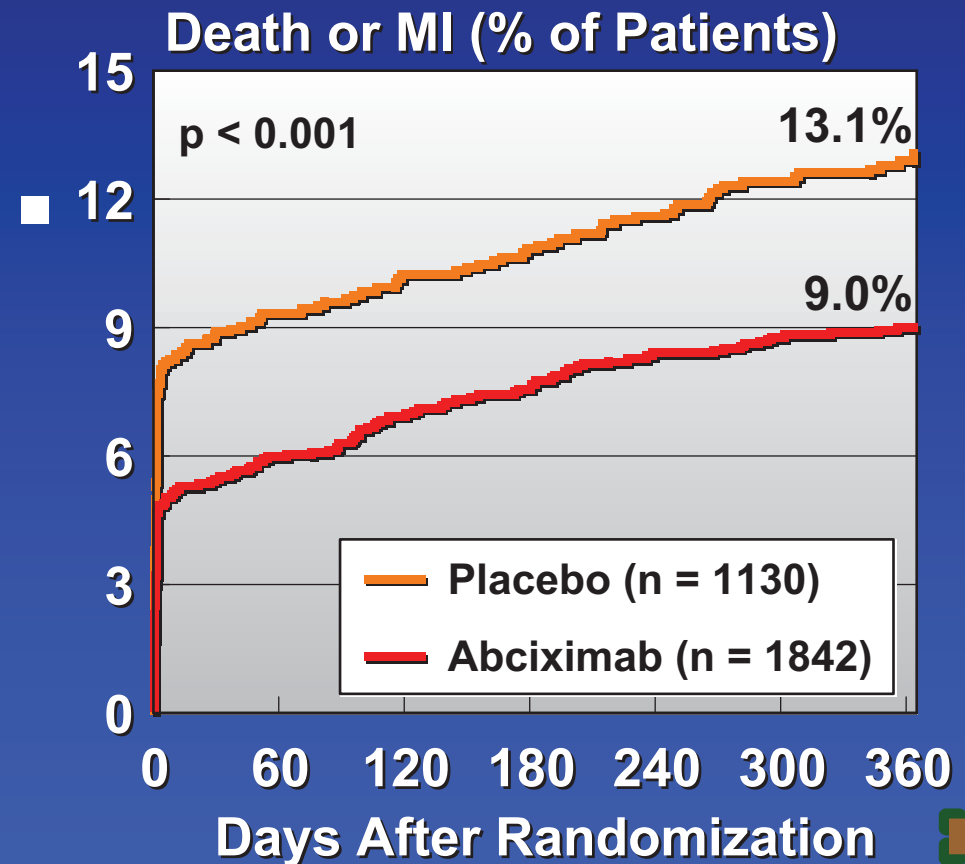
GP IIb/IIIa in PCI for USA

EPIC, EPILOG, EPISTENT Trials

Unstable Angina



Stable Angina

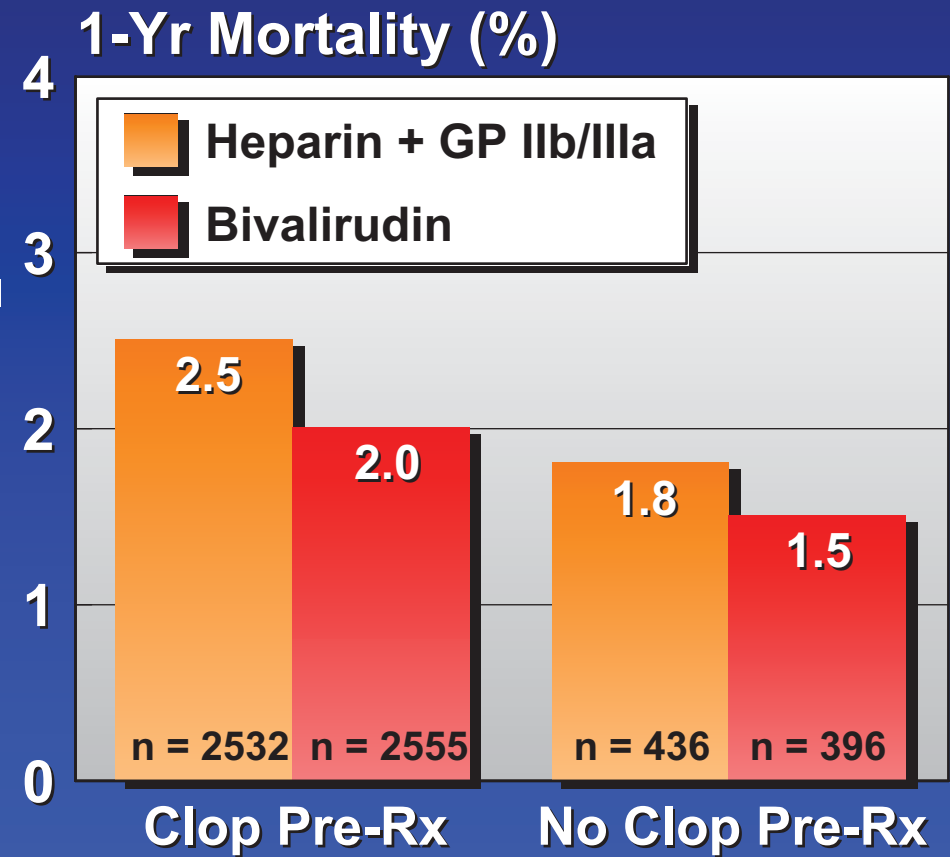
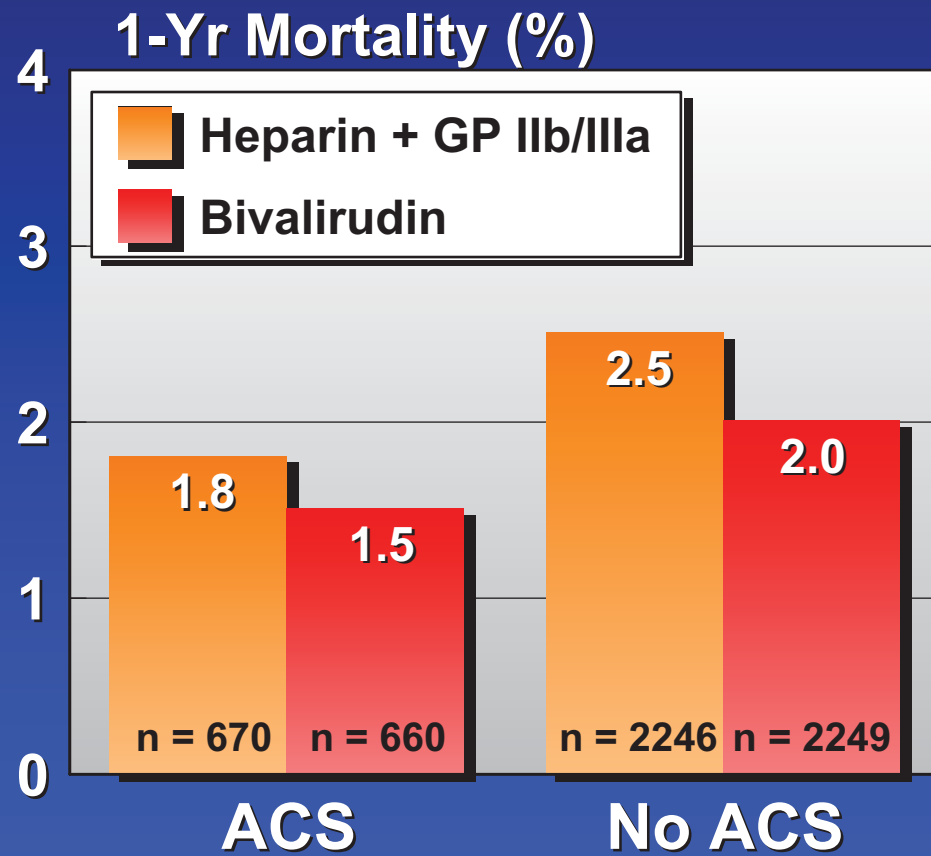




1-Year Results

ACS

Clopidogrel Pre-Rx

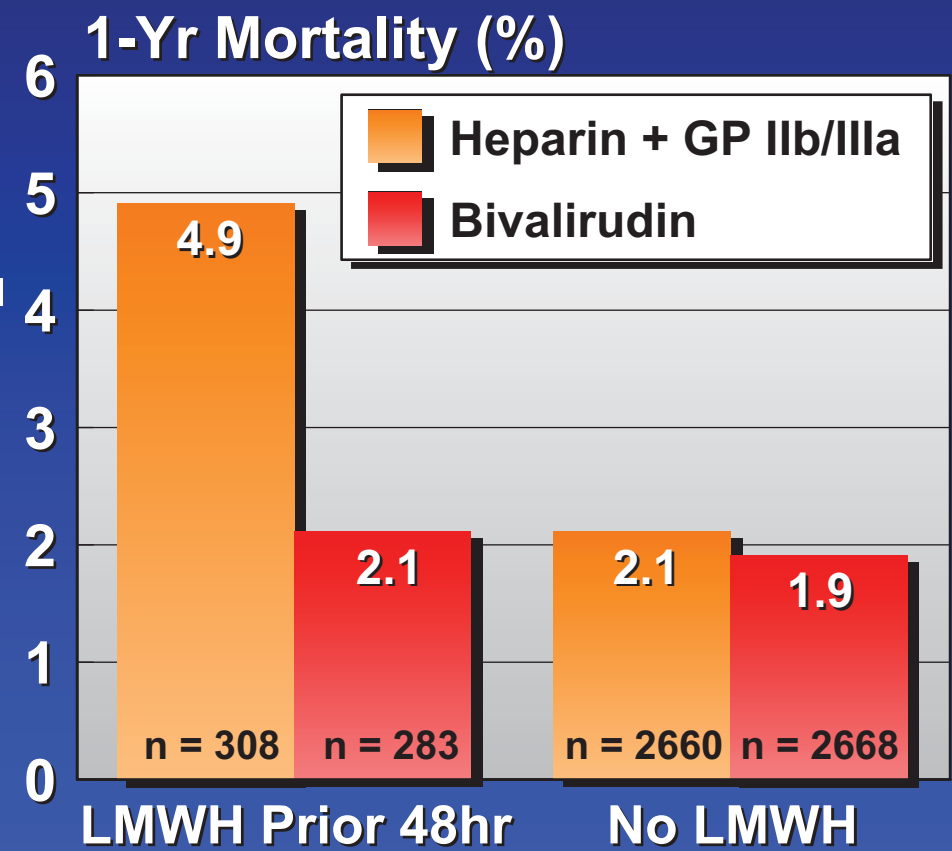
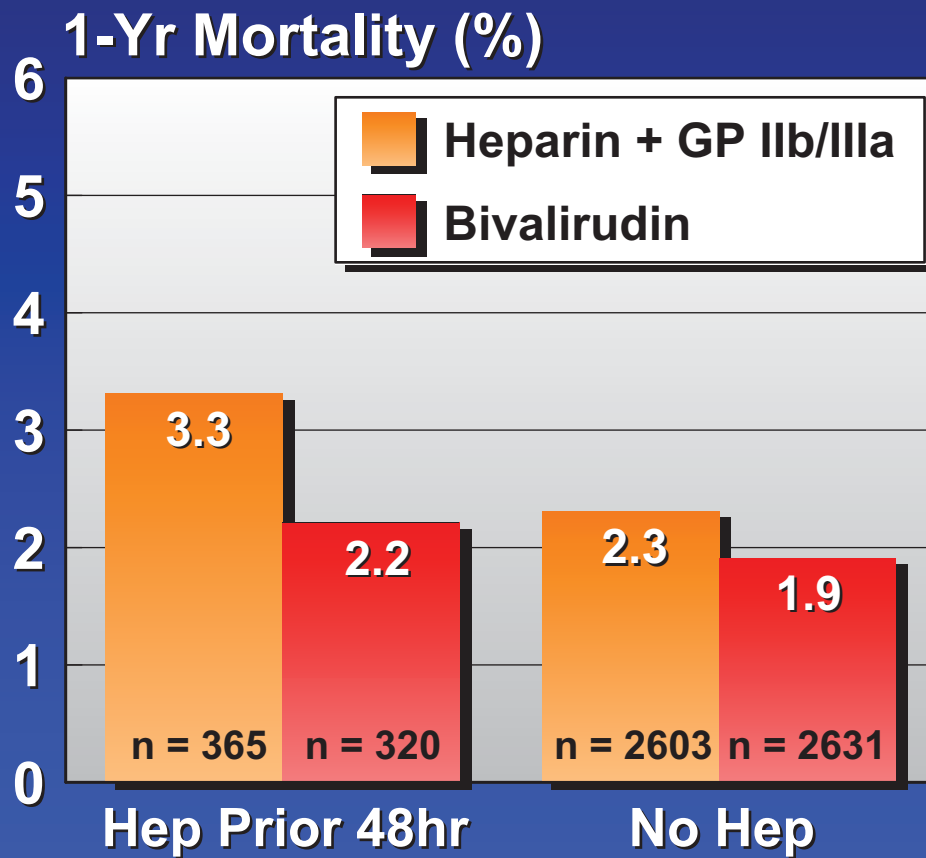




1-Year Results

Heparin Pre-Rx

LMWH Pre-Rx



Antithrombotic Rx in PCI

A Stratified Approach

Low / Moderate-Risk PCI

Aspirin

Clopidogrel
for 1 year
Consider Pre-Rx

Bivalirudin

High-Risk PCI w/o Pre-Rx

Aspirin

Clopidogrel
for 1 year
Consider Pre-Rx

Heparin

Abciximab

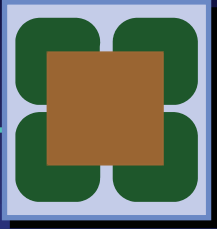
High-Risk ACS/ PCI w/ Pre-Rx

Aspirin

Clopidogrel
for 1 year
Consider Pre-Rx

**Heparin or
Enoxaparin**

**Eptifibatide
or Tirofiban**

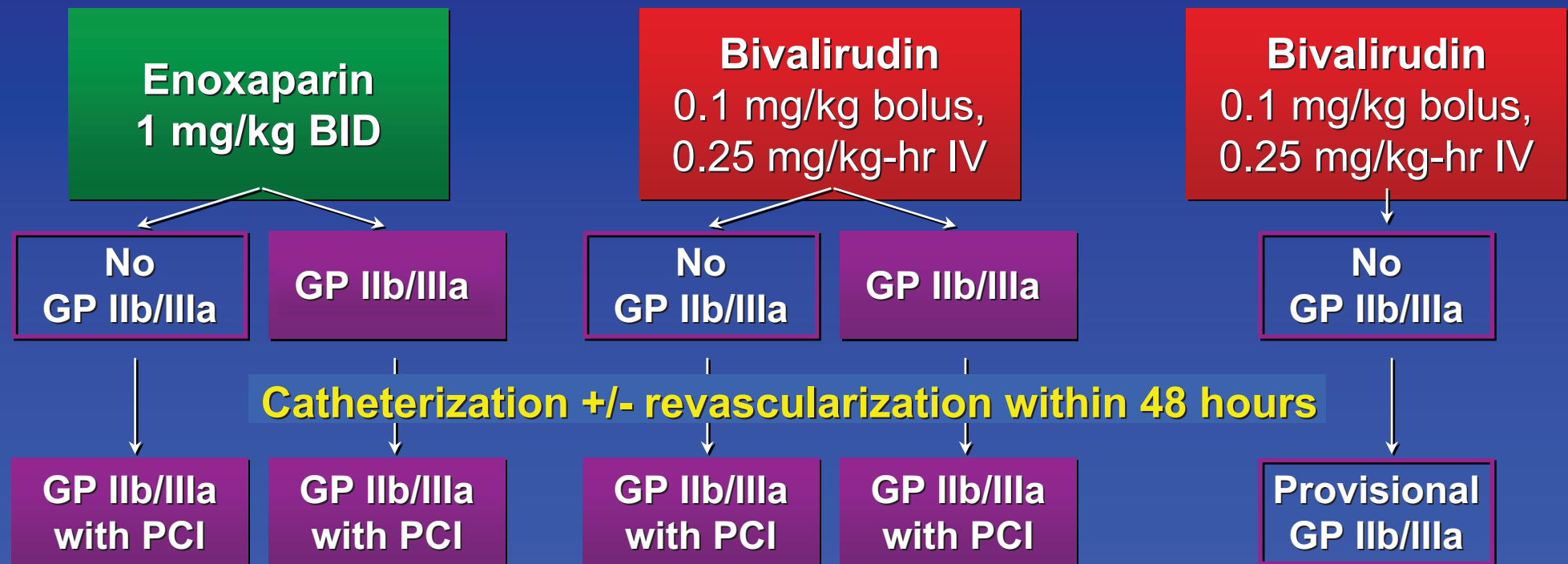


ACUITY Trial

Bivalirudin in ACS

UA or NSTEMI, TIMI Risk Score 3-7, new ST Δ 's, or Troponin or CK elevation
(N = 13,800 patients, 600 sites in NA, Europe, Australasia)

Aspirin + clopidogrel per local practice



1° Endpoint: Death, MI, TVR, Bleeding - 30 Days