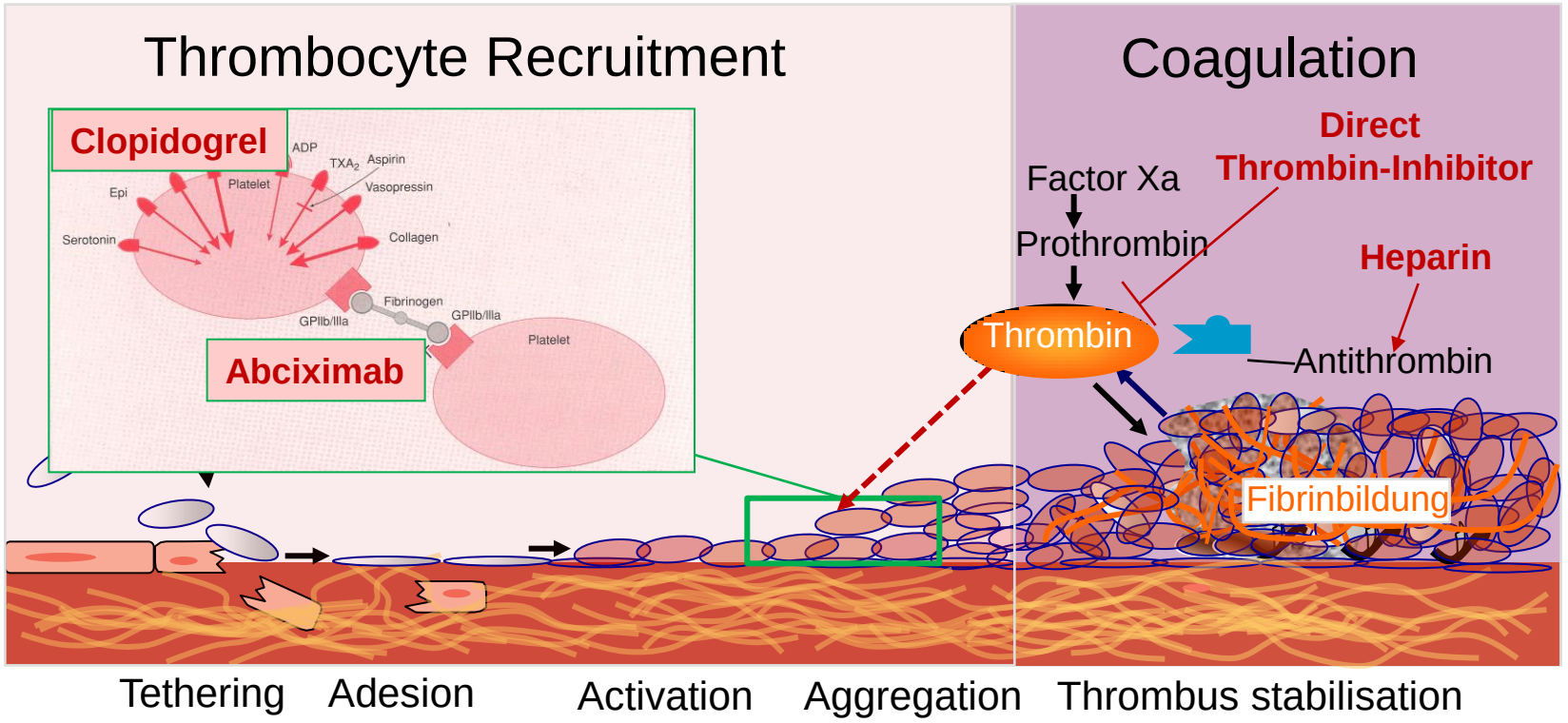
Do We Need Individualized Anticoagulation during Percutaneous Coronary Interventions?

Julinda Mehilli, MD, FESC

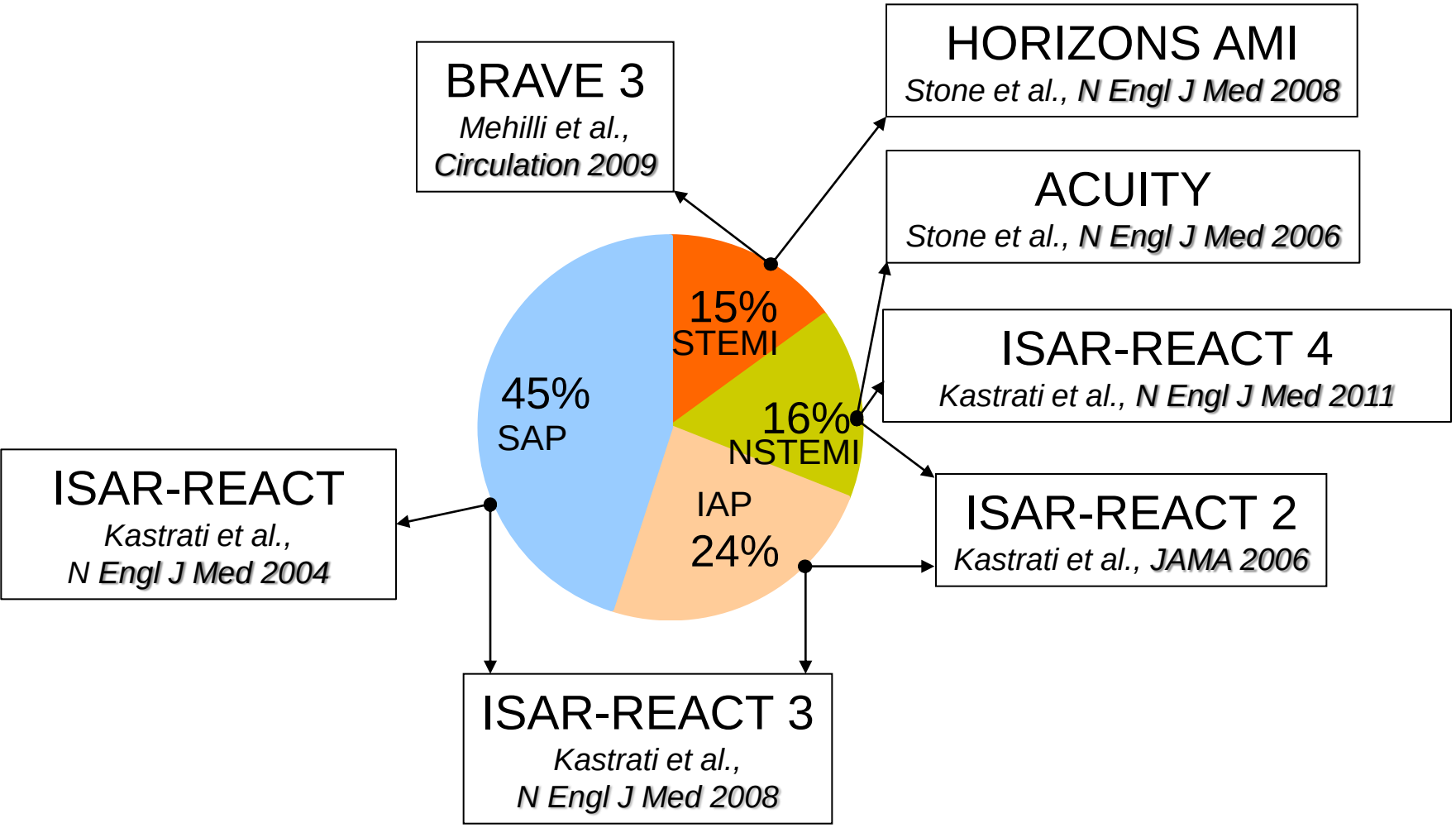
Deutsches Herzzentrum,
Technische Universität, München

Pathophysiology of Arteriel Thrombosis



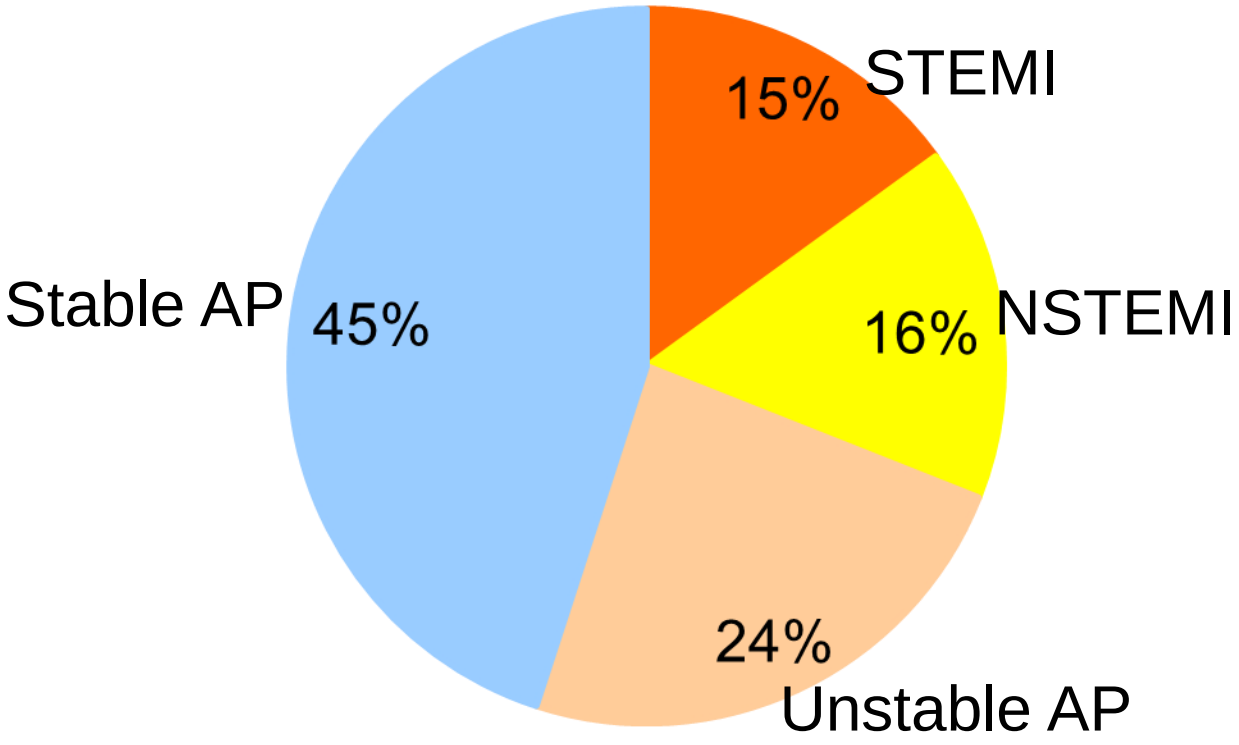
Modified from Kulkarni et al., JCI 2000

Adjunct Antithrombotic Therapy

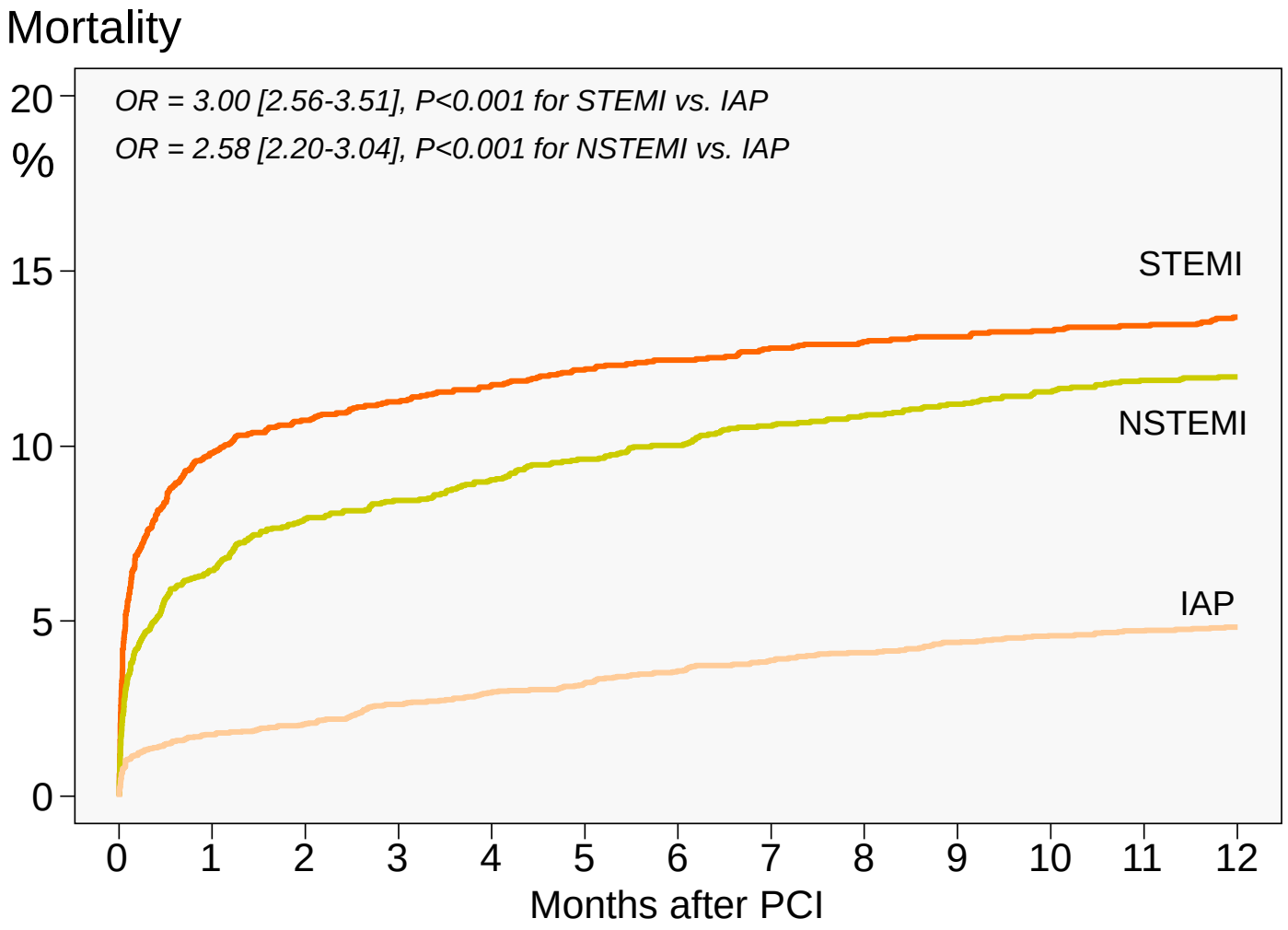


Spectrum of Clinical Presentation at Cath Lab of Patients with CAD

10-Year Experience in Deutsches Herzzentrum and Rdl
- ~20,000 patients with CAD and PCI -

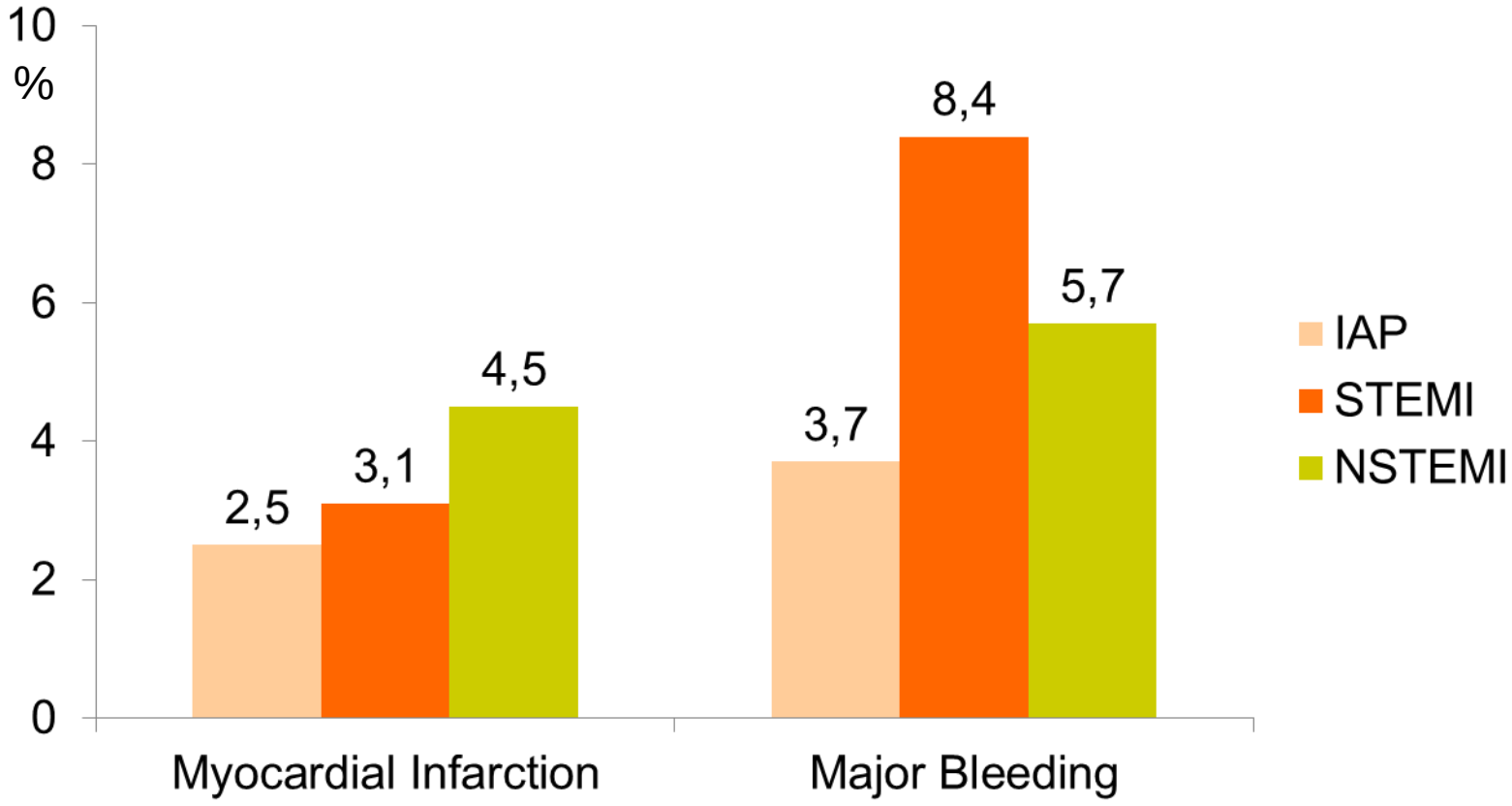


Clinical Presentation and Mortality after PCI



Ndrepepa et al.,Cardiology 2009

Clinical Presentation and Peri-PCI Events



Ndrepepa et al.,Cardiology 2009

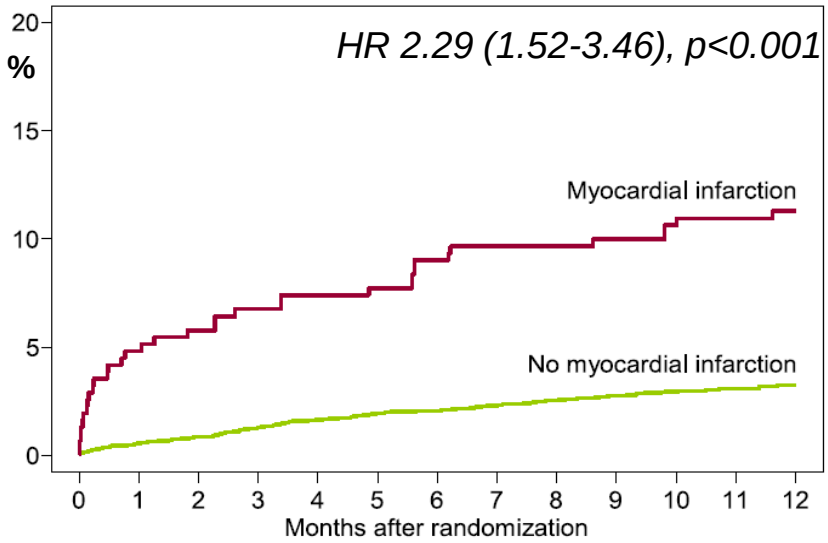
REACT 3A EHJ 2009
ACUITY NEJM 2006
HORIZONS AMI NEJM 2008

Balance Between Antiischemic and Pro-bleeding Effects

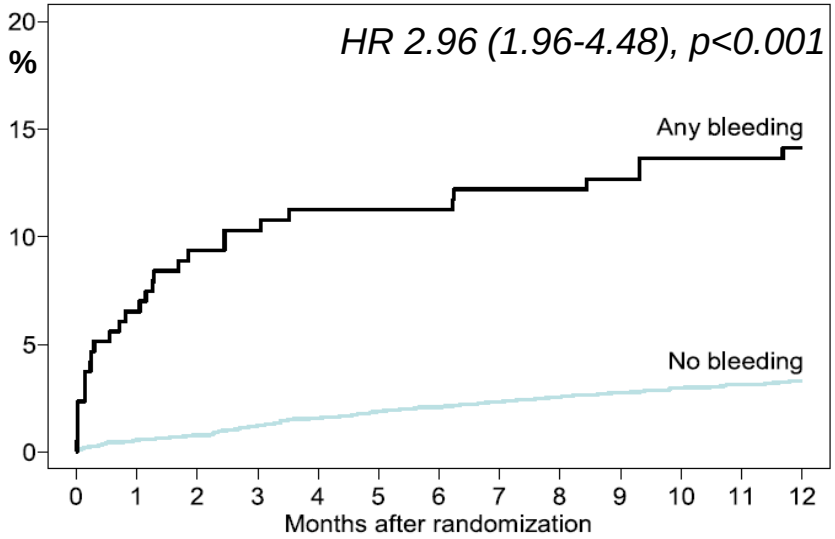
ISAR-REACT, ISAR-SWEET, ISAR-SMART-2 und ISAR-REACT-2 Trials

n=5.384

Mortality

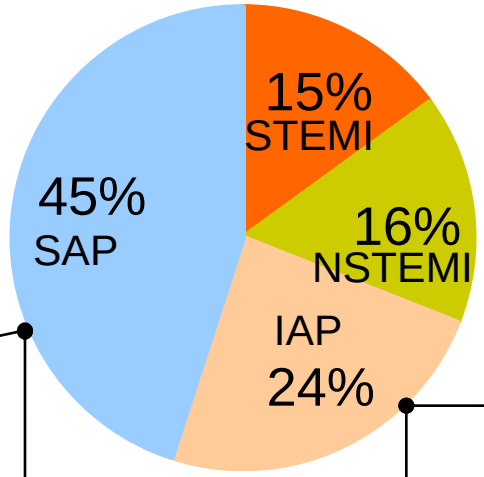


Mortality



Ndrepepa et al.,JACC 2008

Adjunct Antithrombotic Therapy



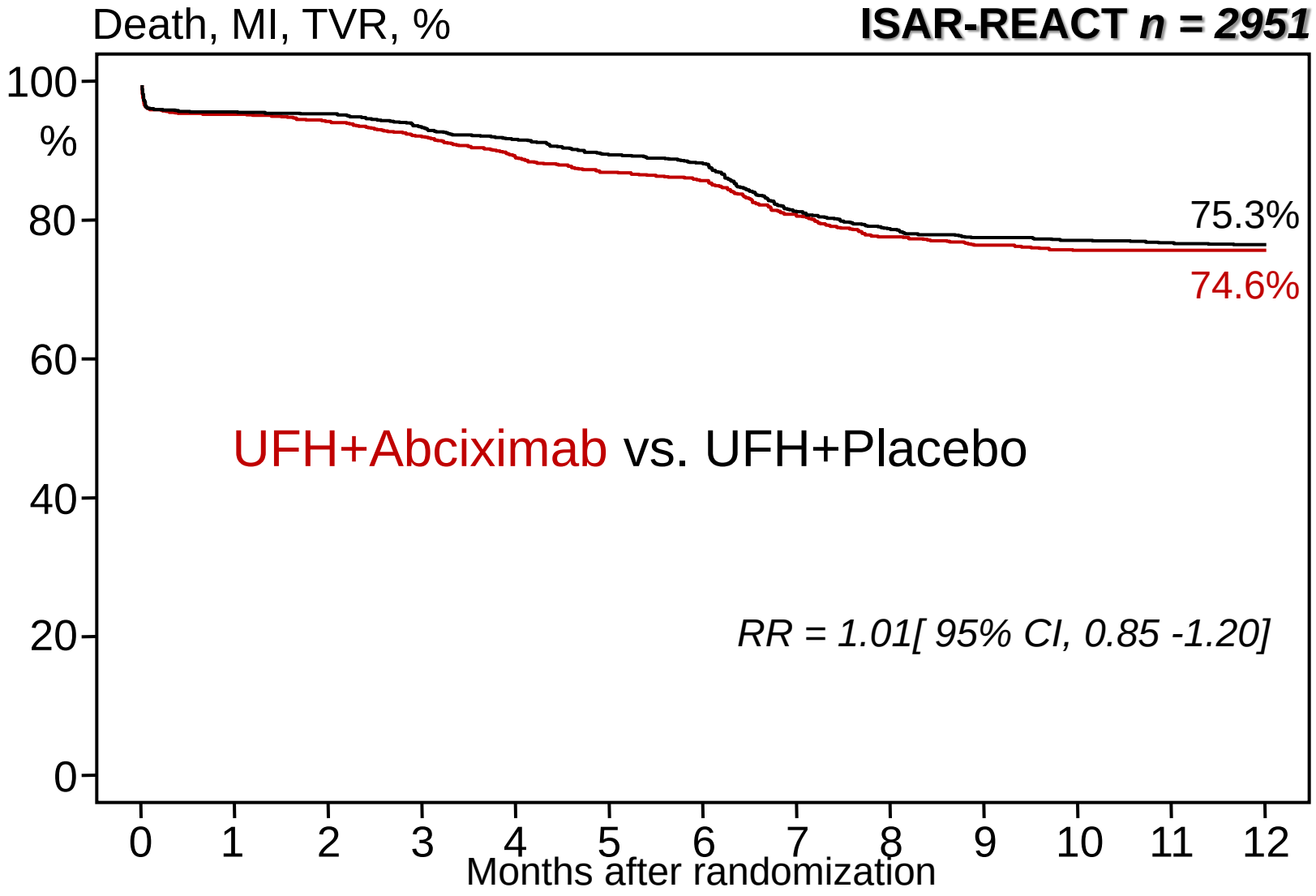
ISAR-REACT
Kastrati et al.,
N Engl J Med 2004

ISAR-REACT 2
Kastrati et al., JAMA 2006

ISAR-REACT 3
Kastrati et al.,
N Engl J Med 2008

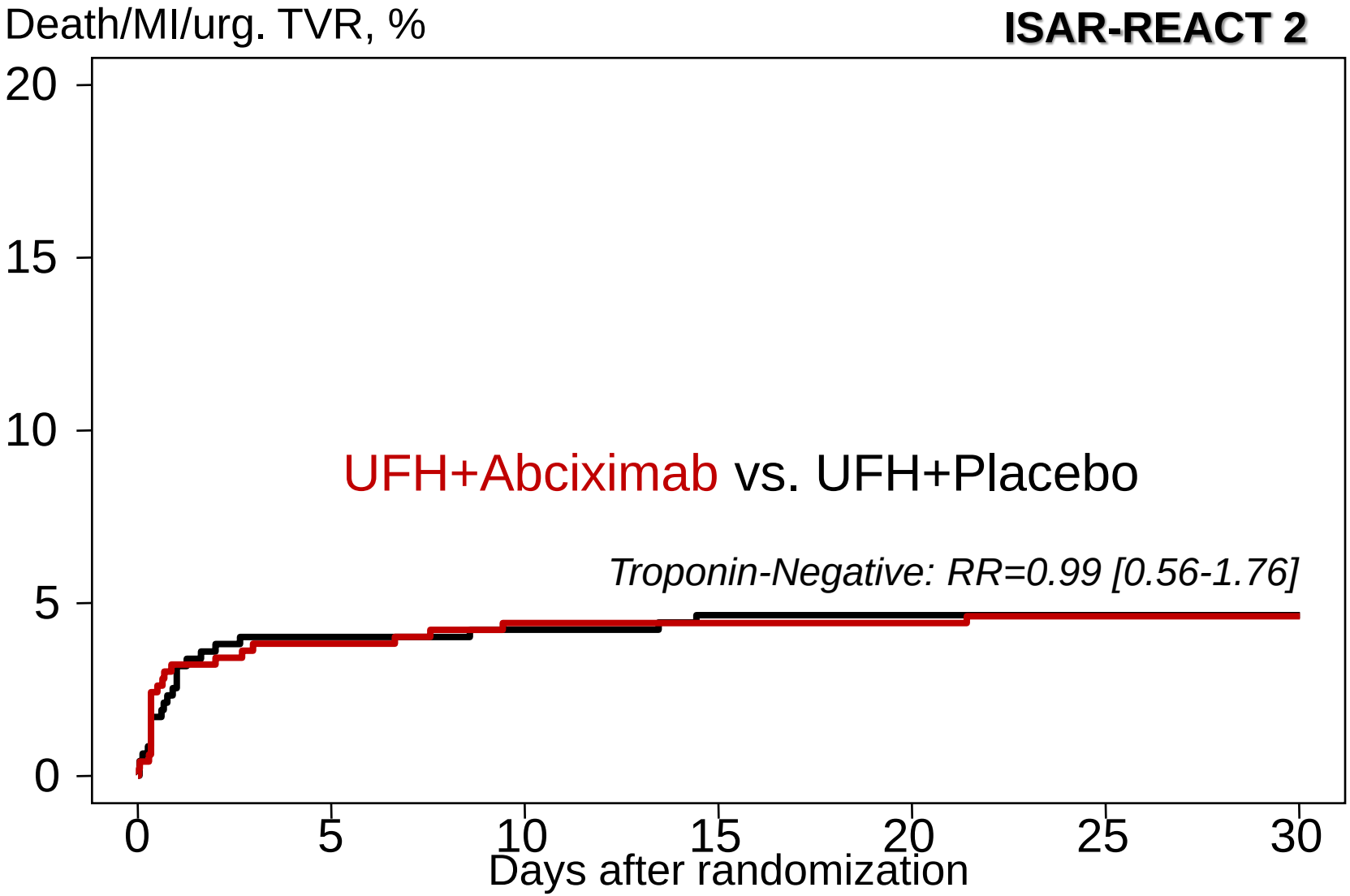
ISAR-REACT 3A
Schulz et al.,
Eur Heart J 2010

Patients with Stable Angina
Heparin alone or with GPI



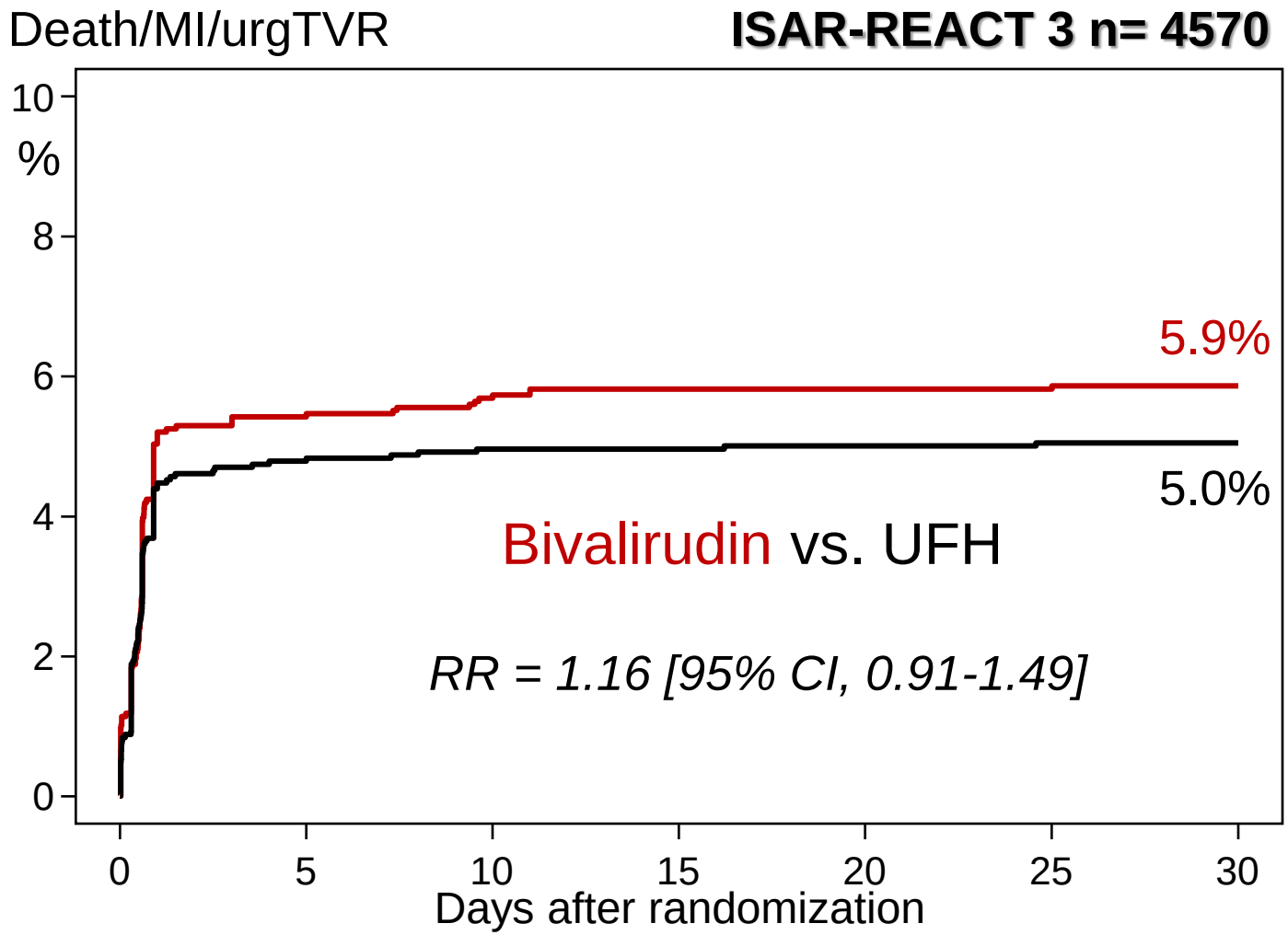
ISAR-REACT, NEJM 2004

Patients with Unstable Angina
Heparin alone or with GPI



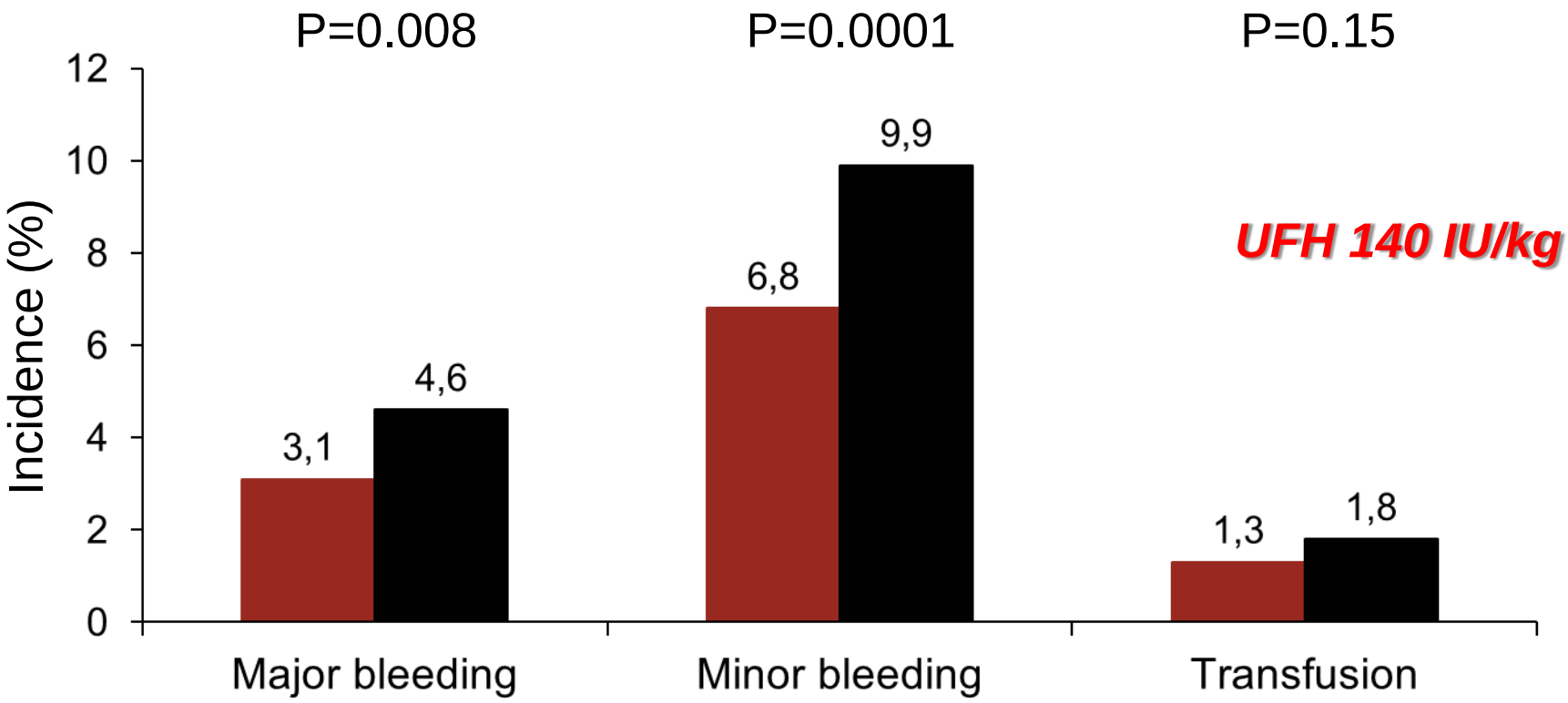
ISAR-REACT 2, JAMA 2006

Patients with Stable/Unstable Angina
Heparin alone or Bivalirudin



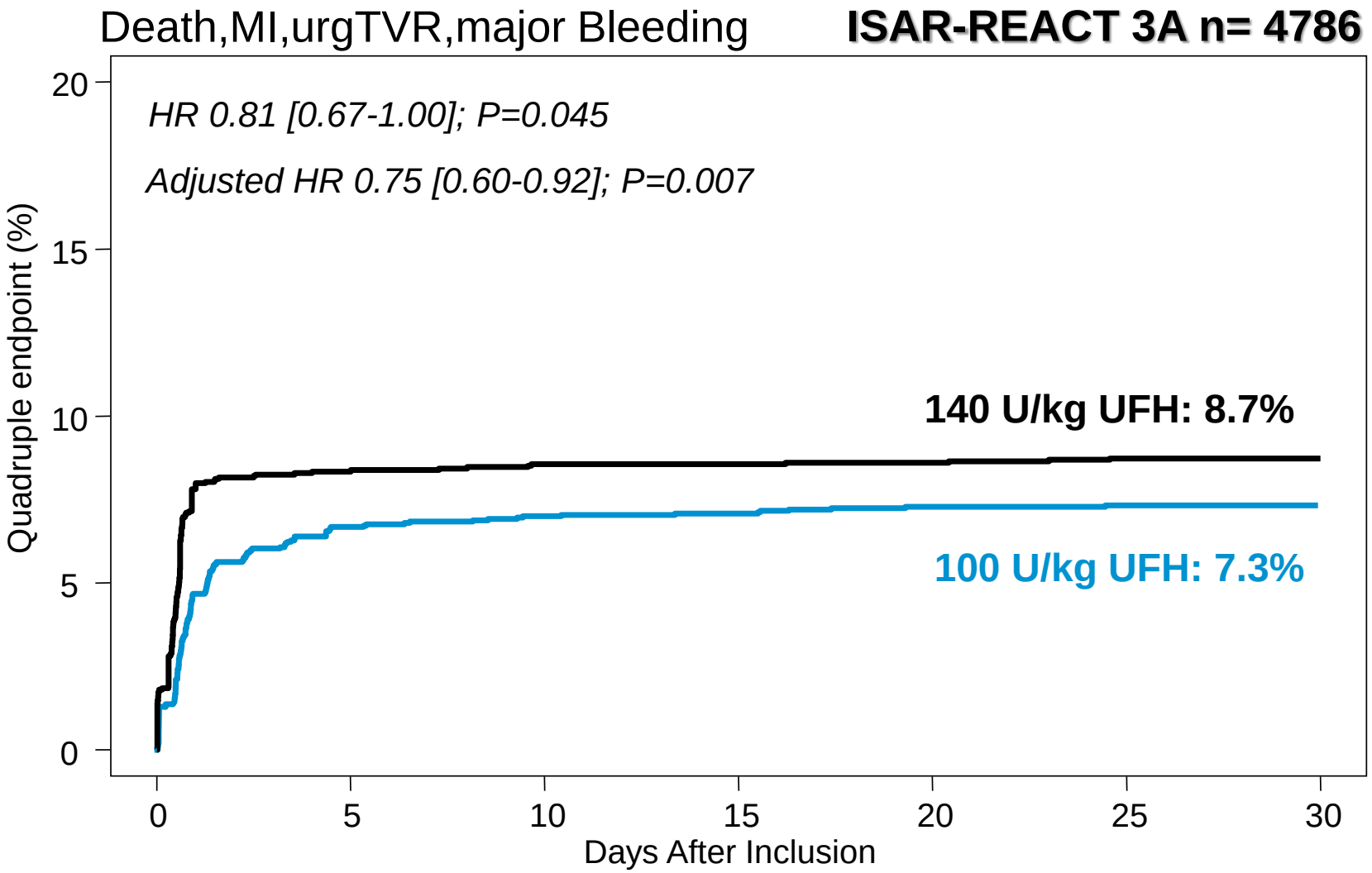
ISAR-REACT 3, NEJM 2008

Patients with Stable/Unstable Angina
Heparin alone or Bivalirudin



ISAR-REACT 3, NEJM 2008

Patients with Stable/Unstable Angina
High or Low Dose Heparin

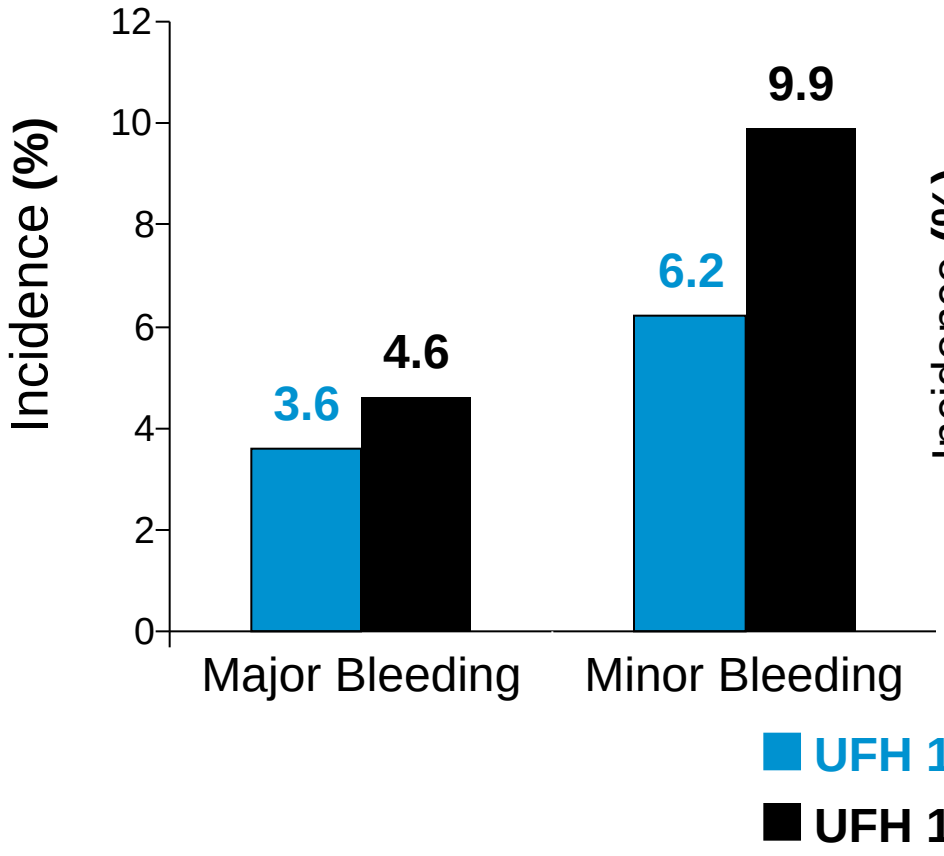


ISAR-REACT 3A, Eur Heart J 2009

Patients with Stable/Unstable Angina
High or Low Dose Heparin

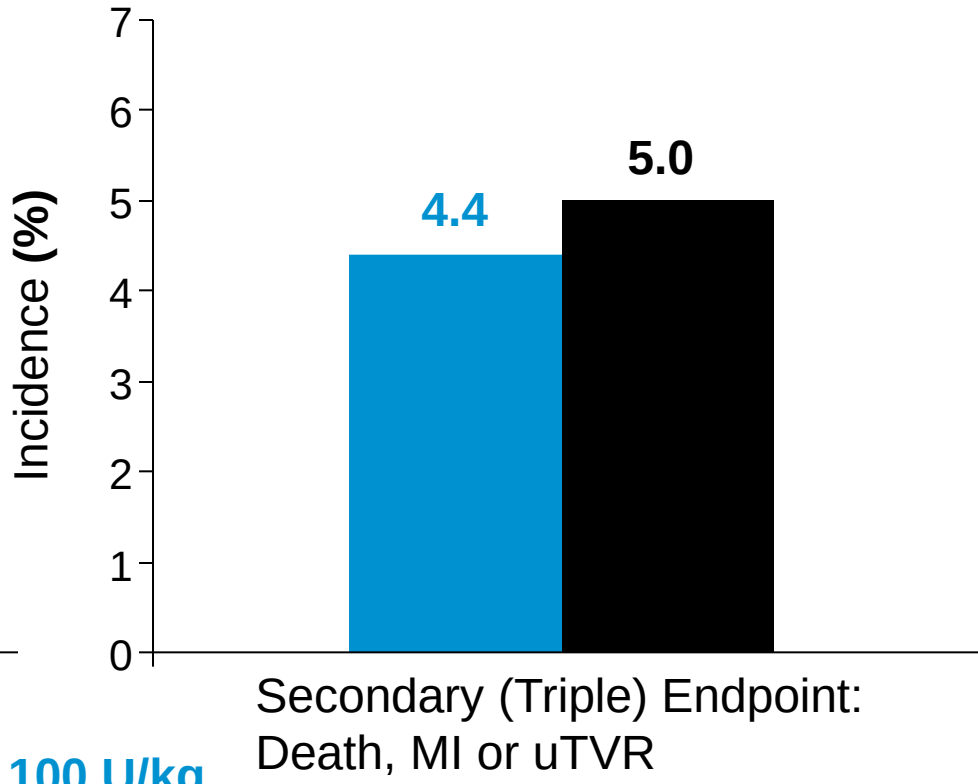
HR 0.79 [0.59-1.05]; P=0.11

Adjusted HR 0.71 [0.53-0.97]; P=0.03



HR 0.87 [0.67-1.13]; P=0.29

Adjusted HR 0.82 [0.62-1.08]; P=0.15

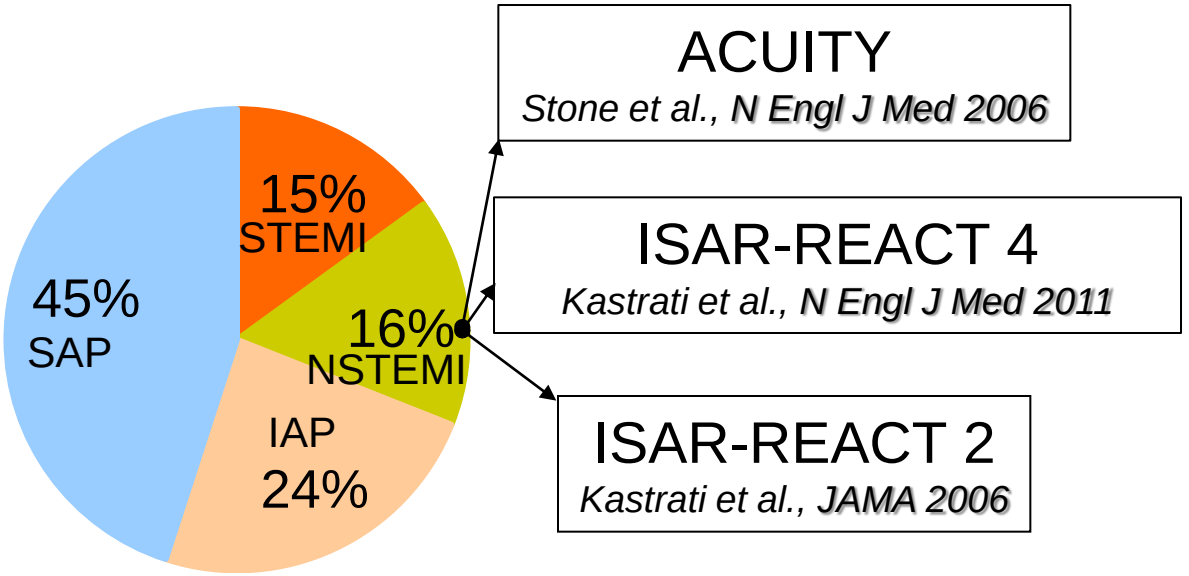


UFH 100 U/kg

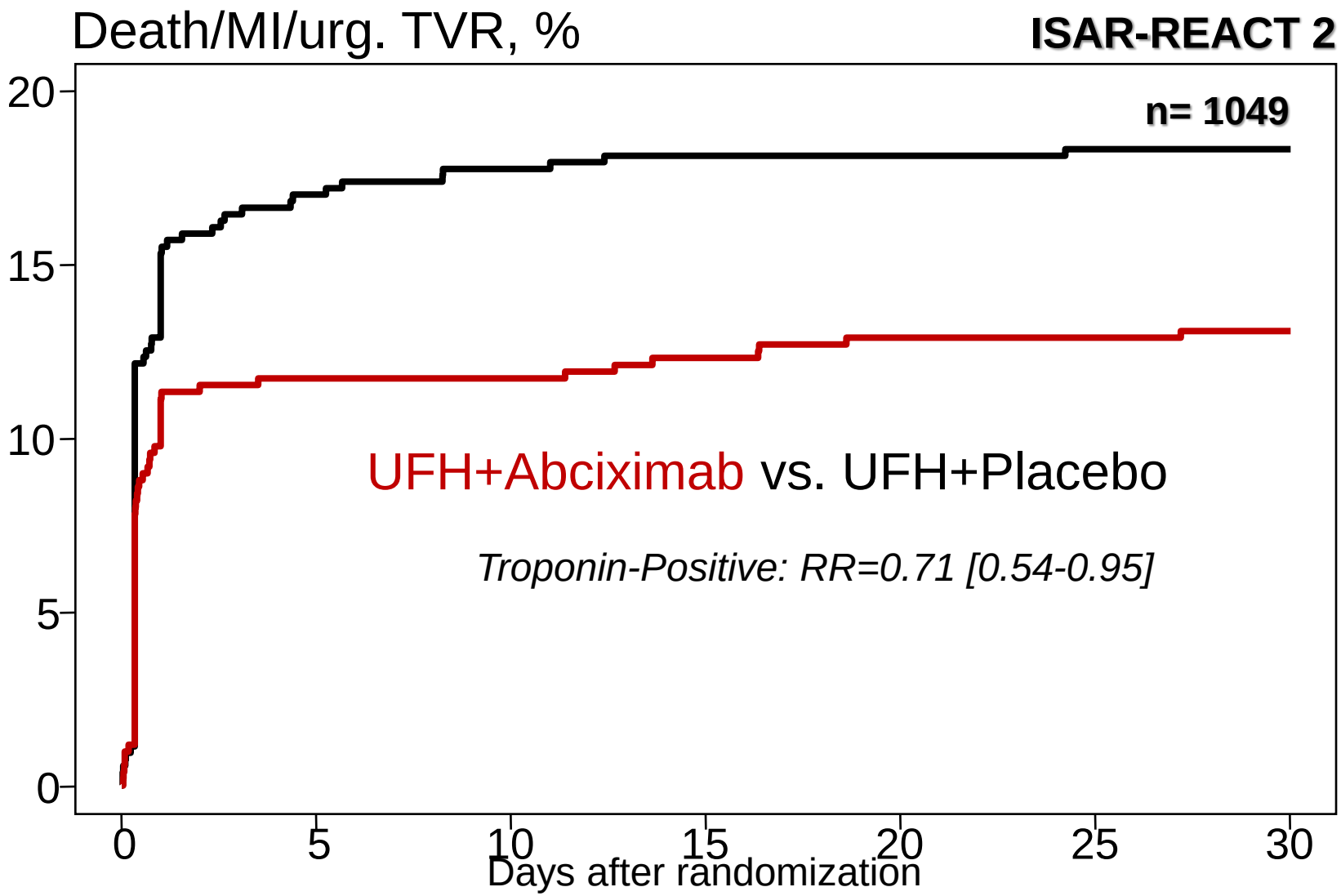
UFH 140 U/kg

ISAR-REACT 3A, Eur Heart J 2009

Adjunct Antithrombotic Therapy

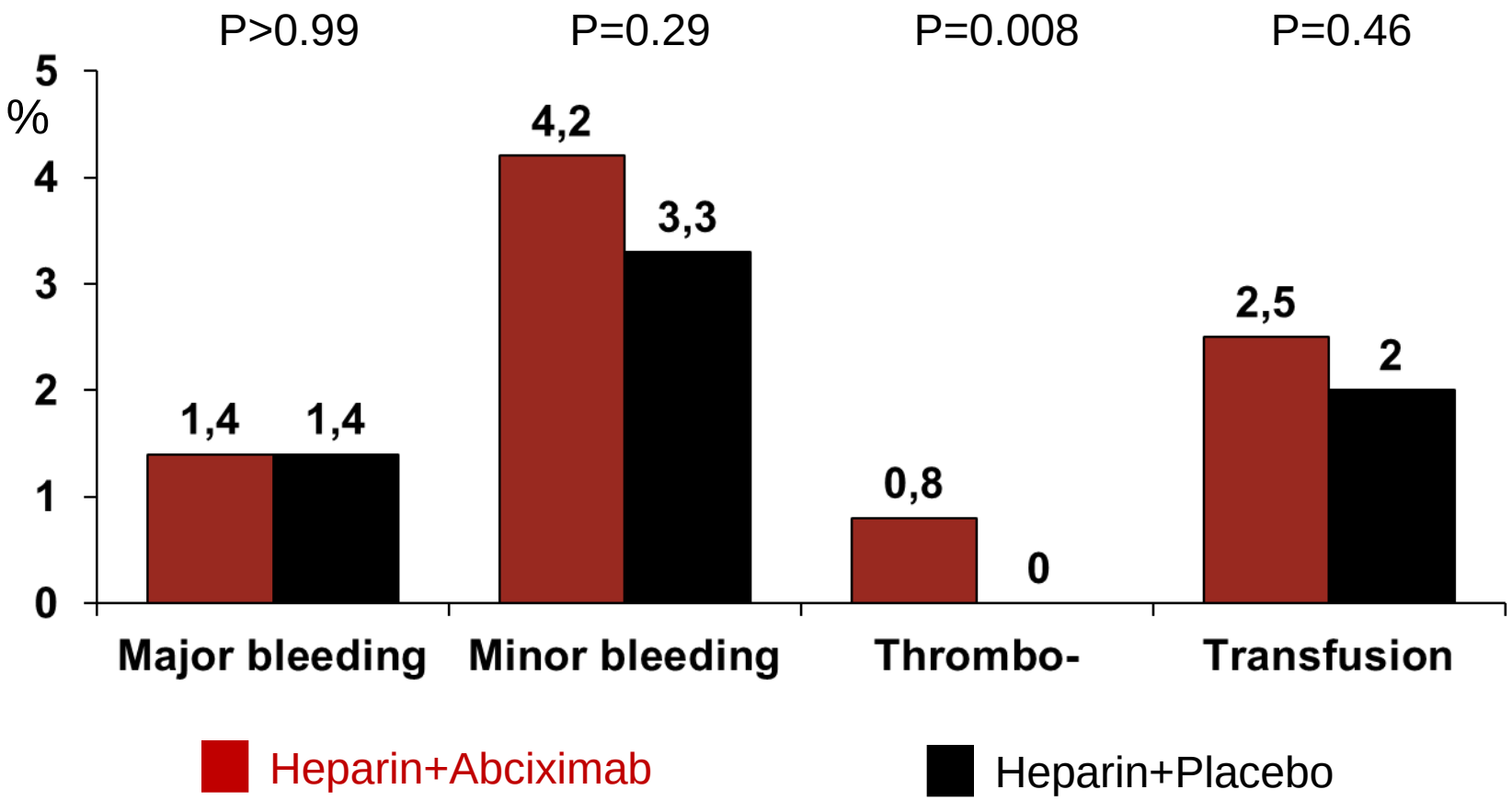


Patients with NSTEMI
Heparin alone or with GPI

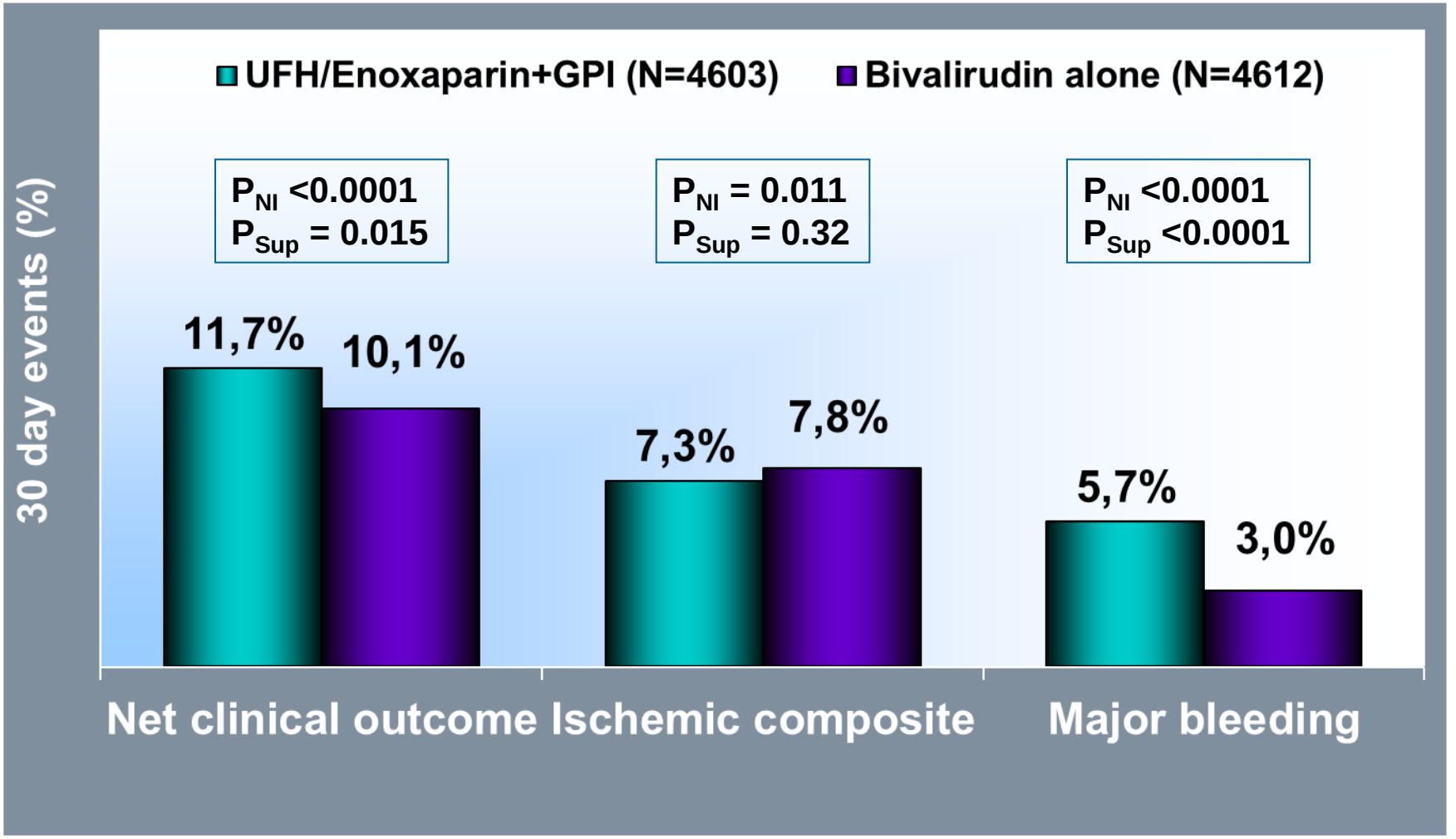


ISAR-REACT 2, JAMA 2006

Patients with NSTEMI
Heparin alone or with GPI



Patients with NSTEMI
Heparin with GPI or Bivalirudin?



ACUITY, NEJM 2006

ISAR-REACT 4 Trial flow-chart

1,721 Pts with NSTEMI

Pre-treated with 600 mg of clopidogrel

Double-blind
(double-dummy drug)

861 pts

Abciximab

Bolus of 0.25 mg/kg
Infusion of 0.125 µg/kg/min for 12h

Unfractionated heparin

Bolus of 70 U/kg

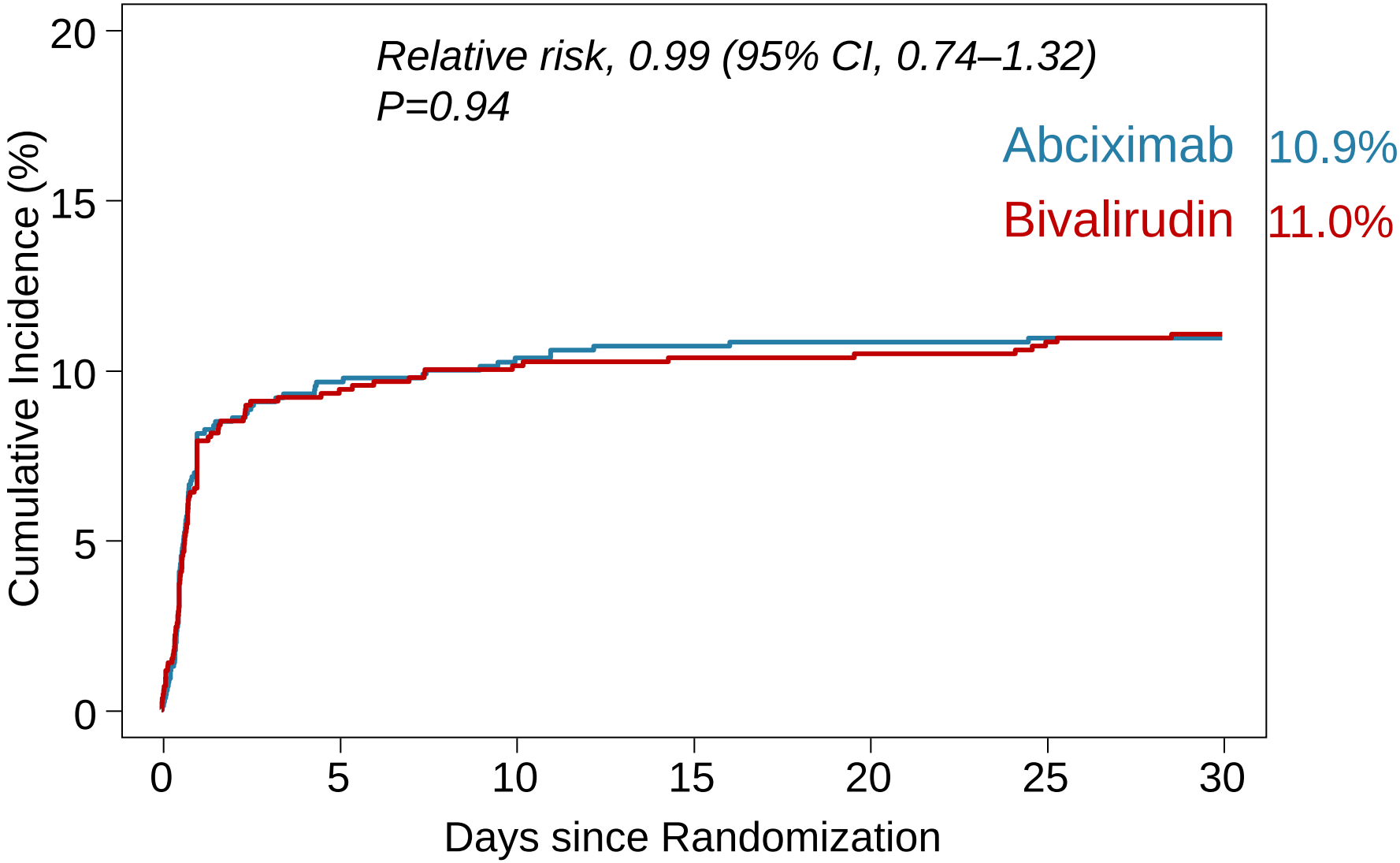
860 pts

Bivalirudin

Bolus of 0.75 mg/kg
Infusion of 1.75 mg/kg/hr
for duration of PCI

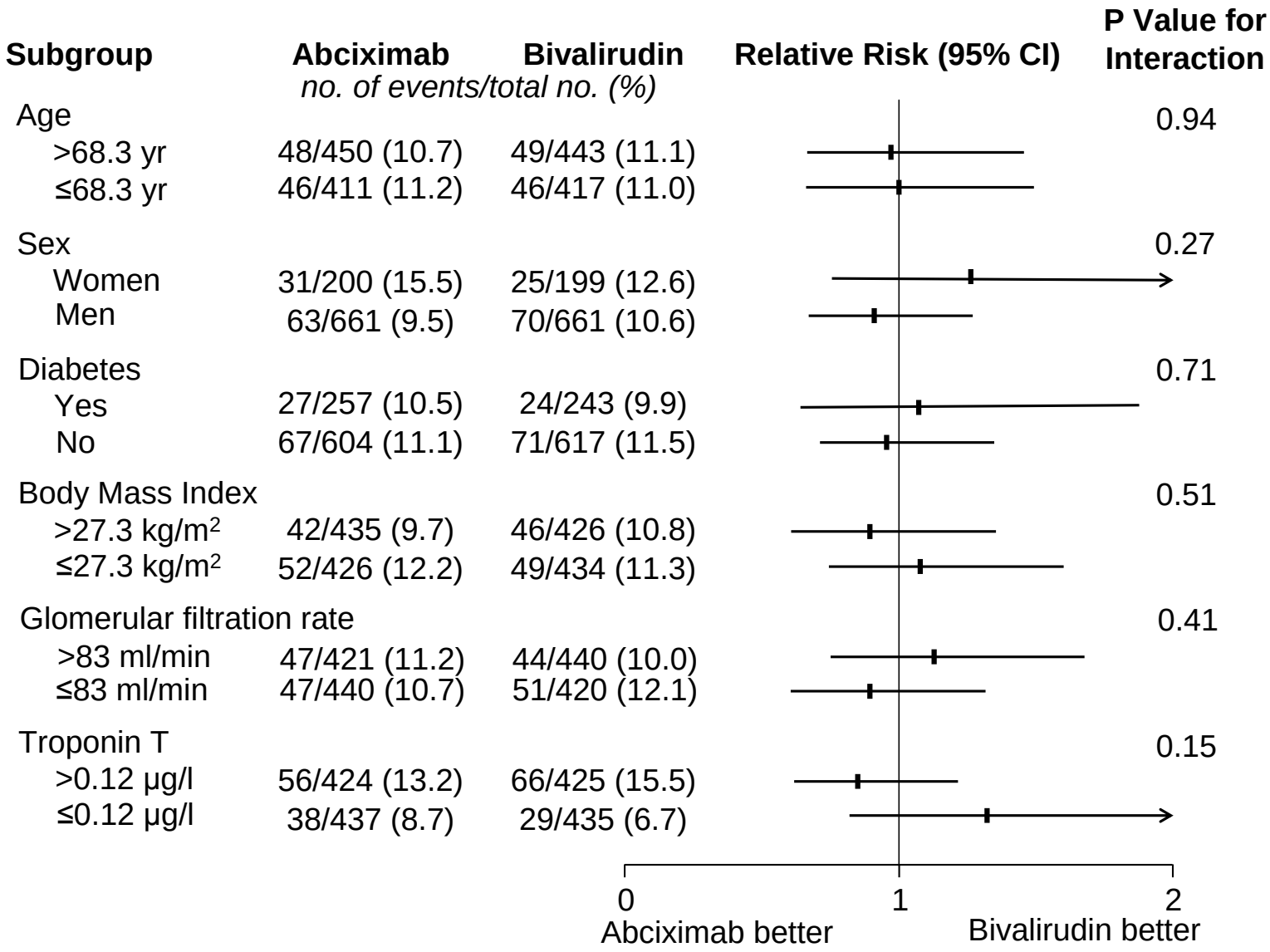
No PCI:	2 patients	2 patients

Primary endpoint
Death, large MI, uTVR, major bleeding

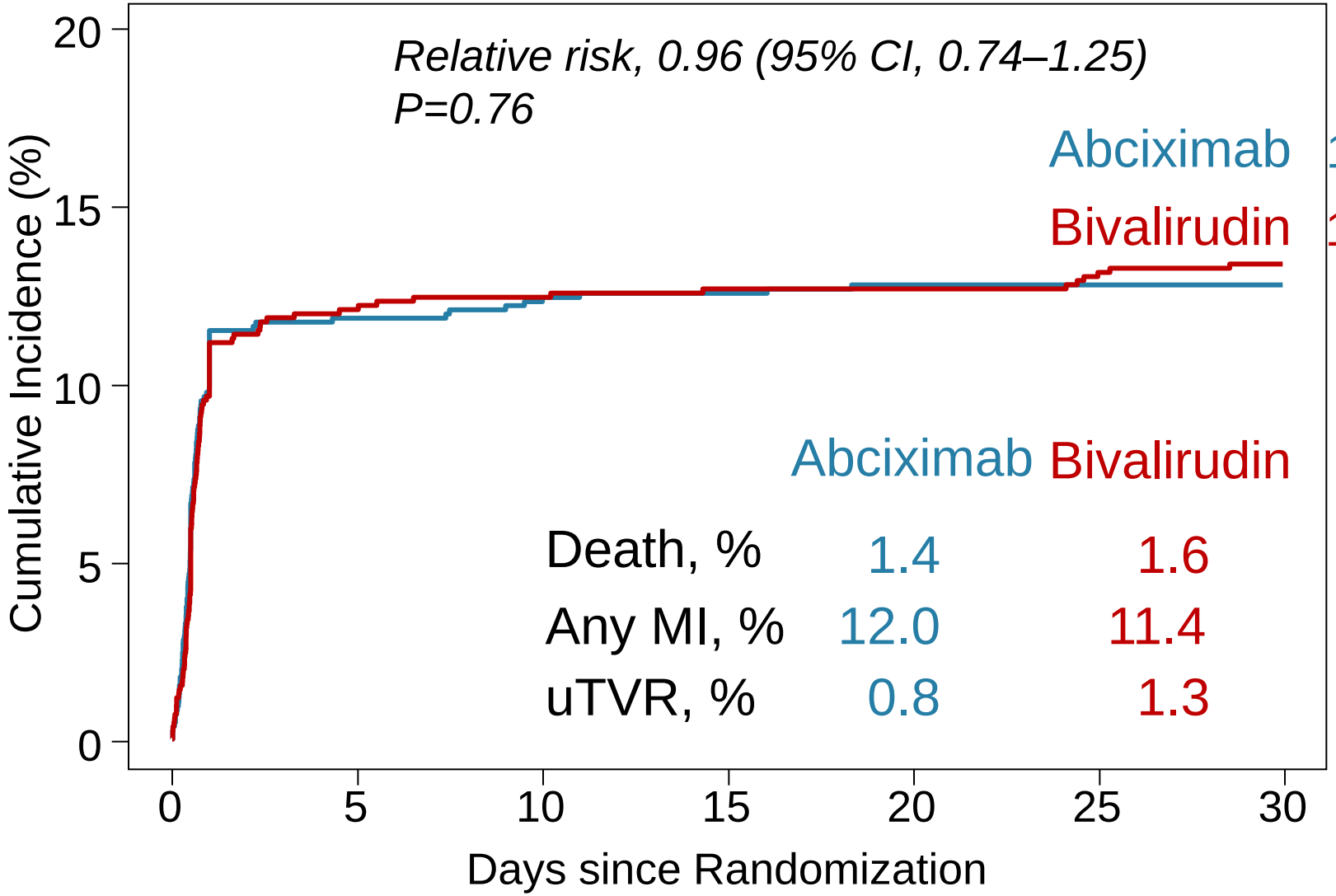


ISAR-REACT 4, N Engl J Med 2011

Primary endpoint analysis in various subsets
Death, large MI, uTVR, major bleeding

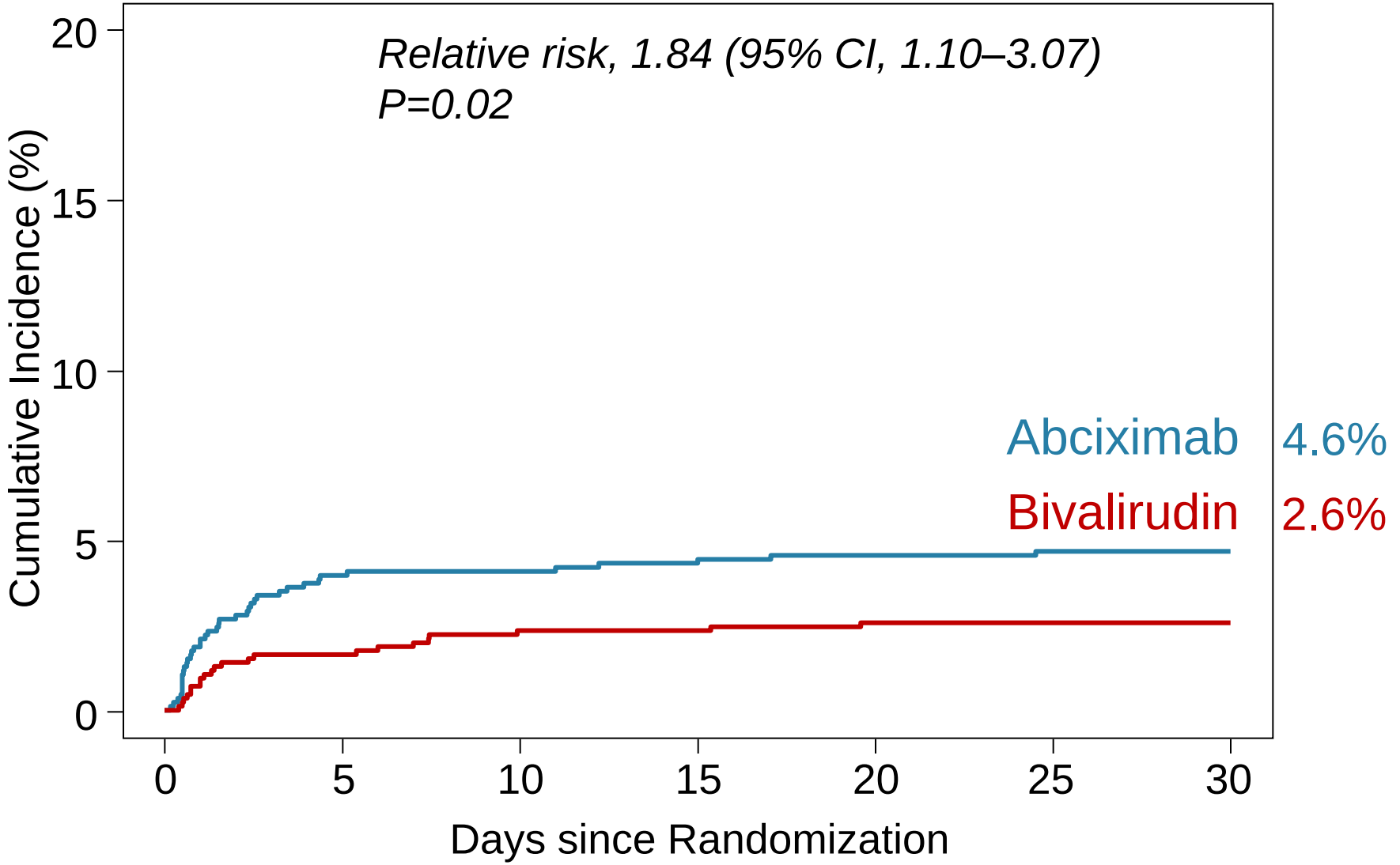


Secondary efficacy endpoint - Death, any MI, uTVR



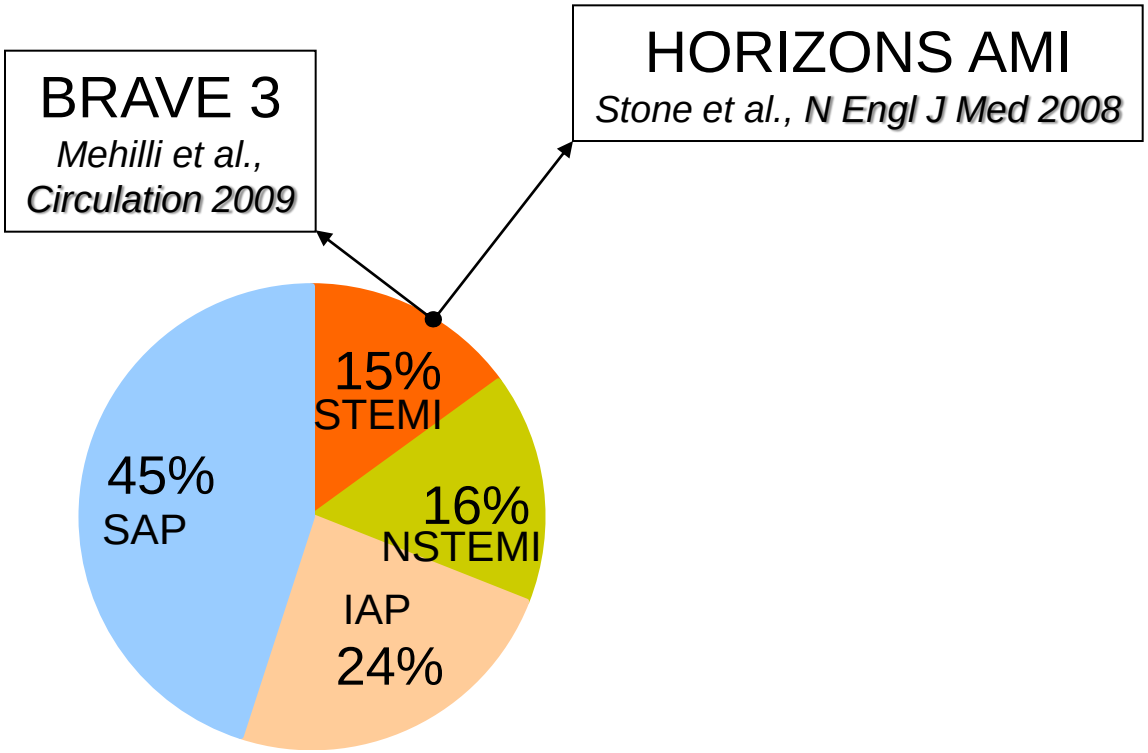
ISAR-REACT 4, N Engl J Med 2011

Secondary safety endpoint - Major bleeding



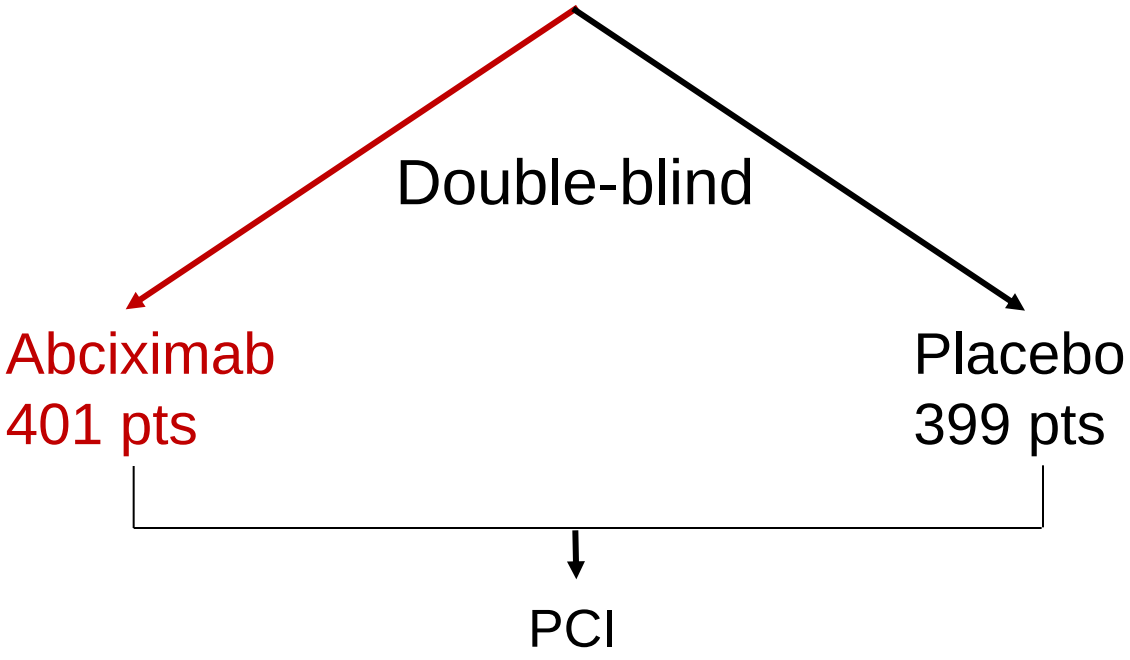
ISAR-REACT 4, N Engl J Med 2011

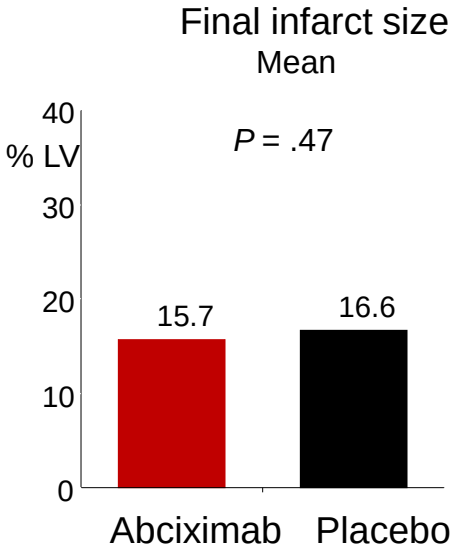
Adjunct Antithrombotic Therapy

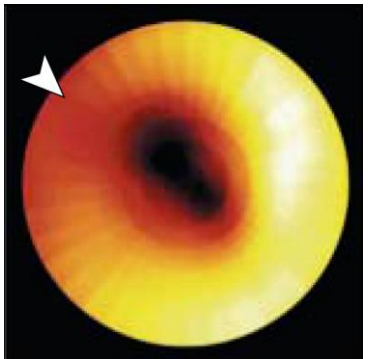


Patients with STEMI
Heparin alone or with GPI

800 Patients with STEMI
Pretreatment with 600 mg of clopidogrel



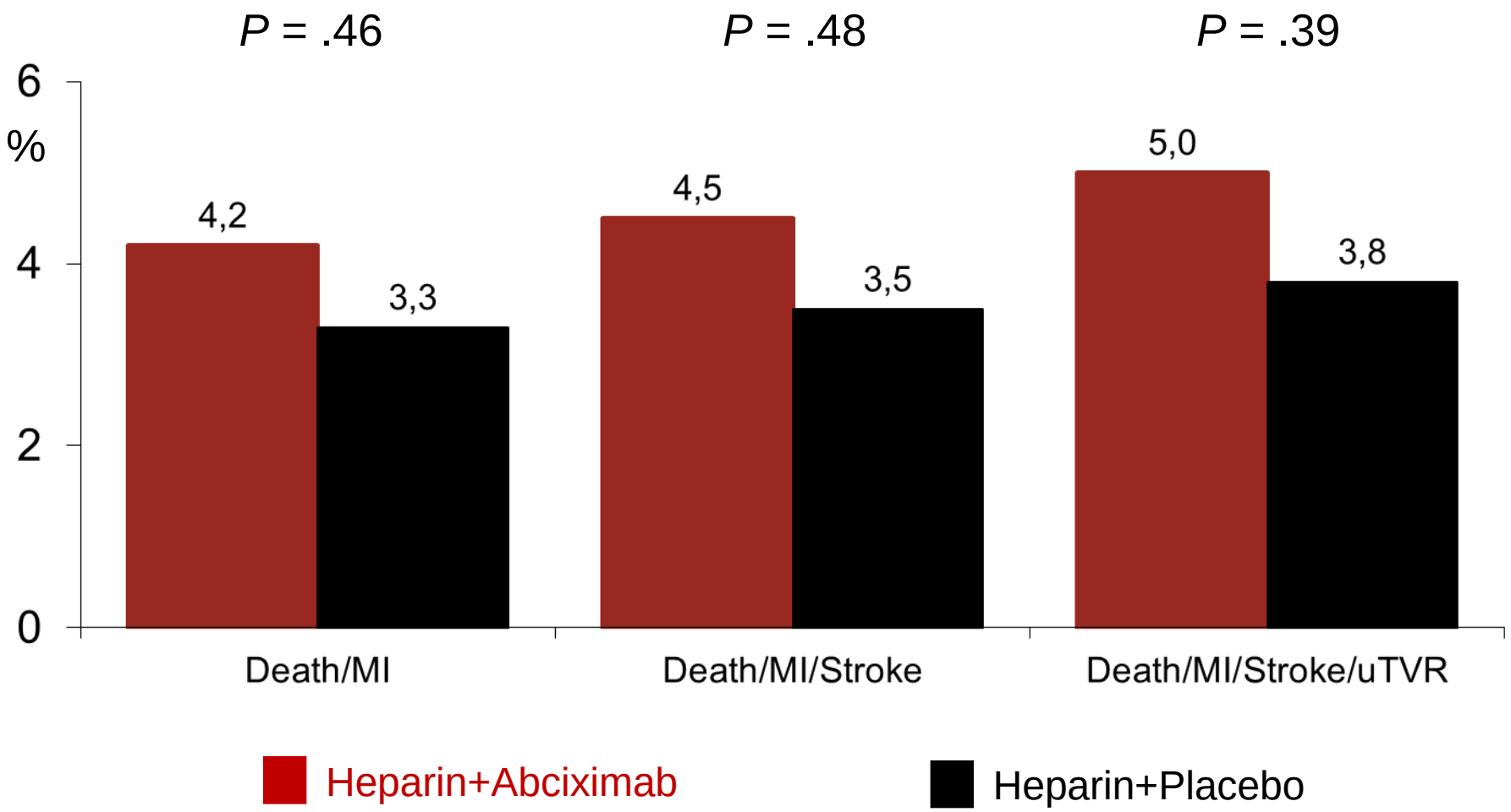




<u>Primary endpoint:</u> Scintigraphic final infarct size

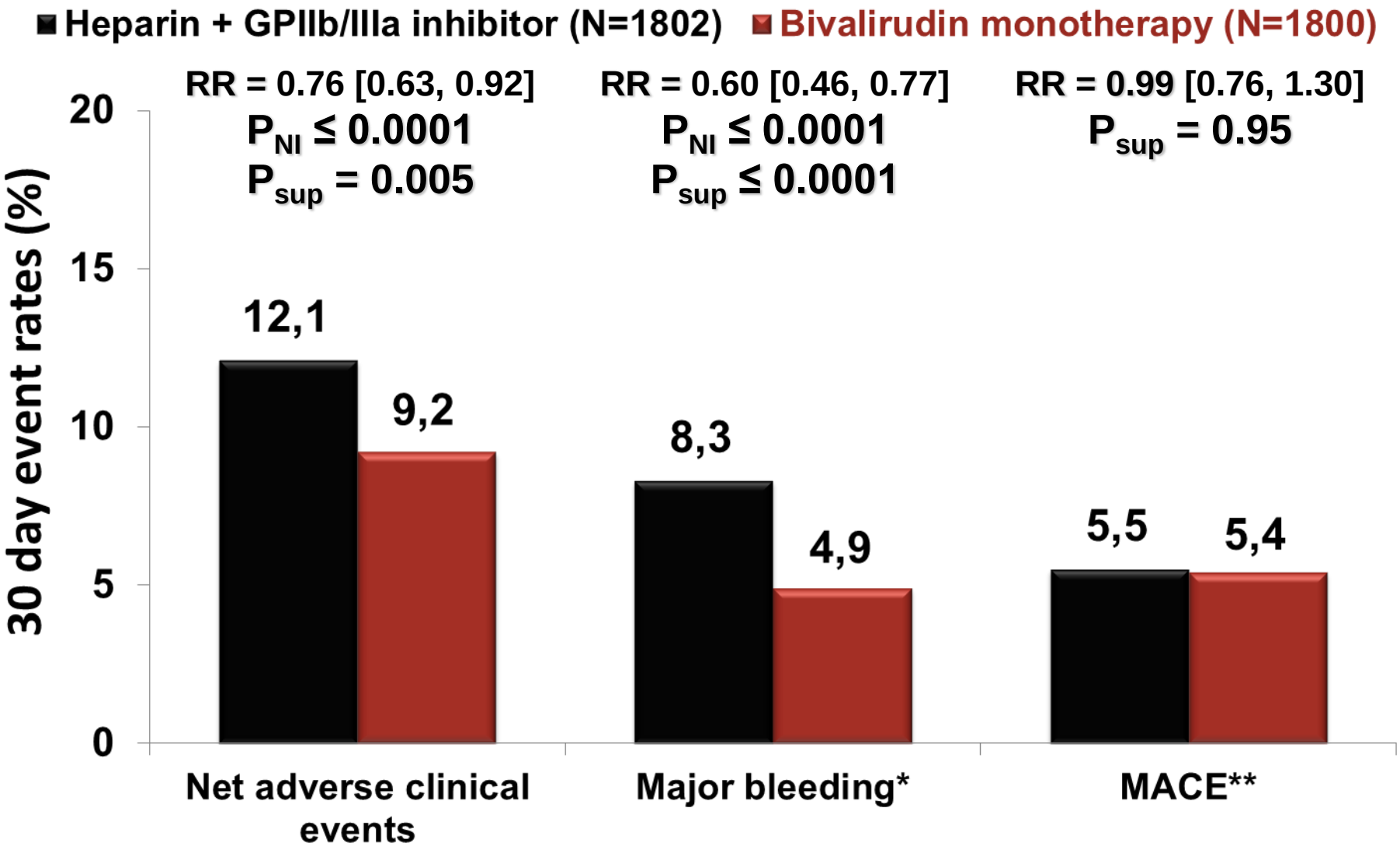
BRAVE 3, Circulation 2009

Patients with STEMI
Heparin alone or with GPI



BRAVE 3, Circulation 2009

Patients with STEMI
Heparin and GPI or Bivalirudin



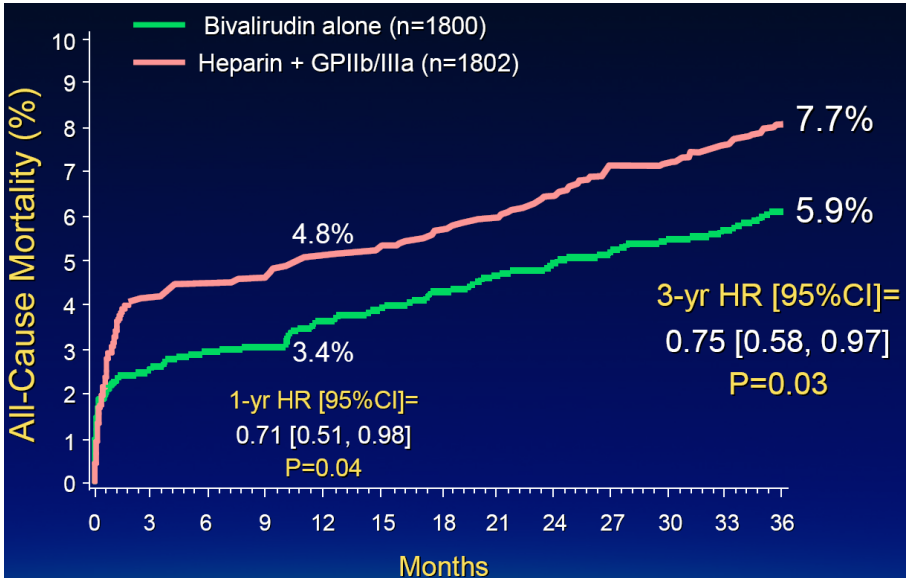
HORIZONS AMI, N Engl J Med 2008

Patients with STEMI
Heparin and GPI or Bivalirudin

Table 3. (Continued.)

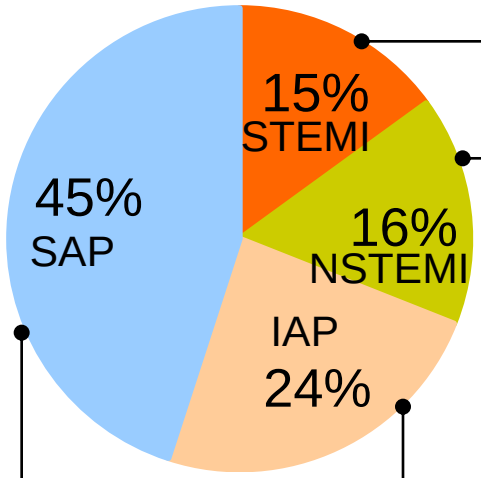
Outcome	Heparin plus a Glycoprotein IIb/IIIa Inhibitor (N=1802)	Bivalirudin Alone (N=1800)	P Value
Patients with stents implanted			
No. of patients	1553	1571	
Stent thrombosis, protocol definition — no. (%)†	30 (1.9)	39 (2.5)	0.30
Definite	22 (1.4)	35 (2.2)	0.09
Probable	8 (0.5)	4 (0.3)	0.24
Acute (≤24 hr)	4 (0.3)	21 (1.3)	<0.001
Subacute (>24 hr–30 days)	26 (1.7)	19 (1.2)	0.28

HORIZONS AMI, NEJM 2008



Stone, Lancet 2010

Adjunct Antithrombotic Therapy



Bivalirudin

as effective as
UFH + Abciximab
regarding ischemic events
superior to
UFH + Abciximab
regarding bleeding events

Heparin bolus 70-100 U/Kg
ACT Monitoring for long procedures