

# ***Bivalirudin: Is It Standard of Care in the Cath Lab? No, Heparin with GPI is Still a Viable Option***

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# Disclosure Statement of Financial Interest

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

## Affiliation/Financial Relationship

- **Grant/Research Support to Institution**
- **Consulting Fees/Honoraria**

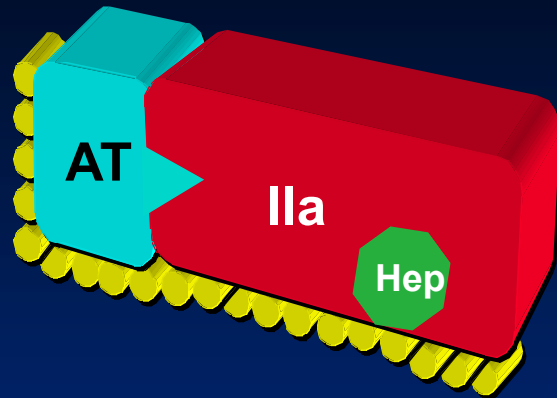
## Company

- Sanofi/BMS- Significant
- The Medicines Company
- Astra Zeneca, Abbott Vascular, Regado Biosciences, Janssen

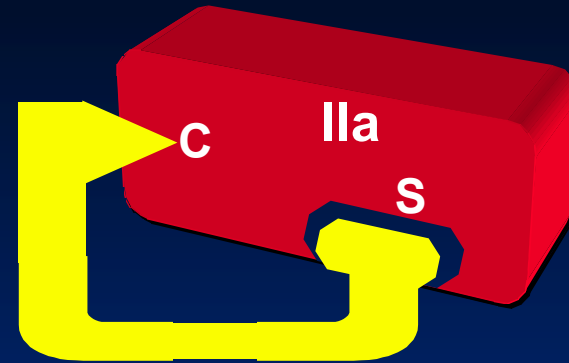
# Disclosure Statement

I have led the Clinical Coordinating Center for the HORIZONS AMI study and a *strong believer* for the use of Bivalirudin in all cases!!!

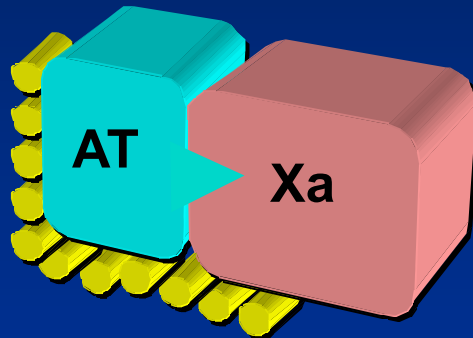
# Four Anticoagulant Choices



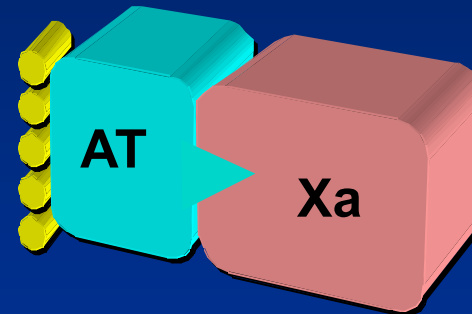
UFH



Direct antithrombin



LMWH



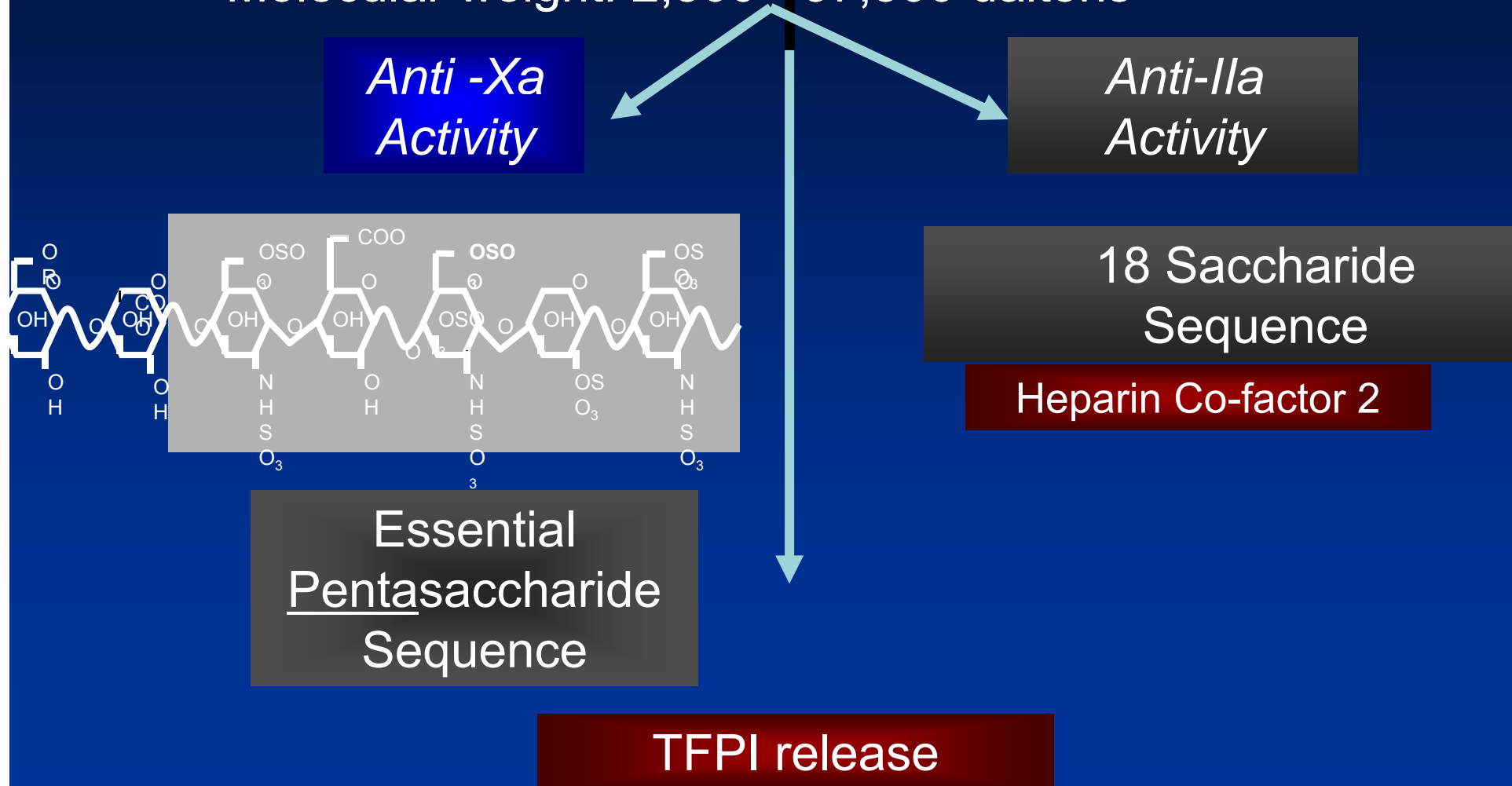
Pentasaccharide

Konkle BA, Schafer AI. In: Zipes DP, Libby P, Bonow RO, Braunwald E, eds. *Braunwald's Heart Disease*. Vol 2. 7th ed. Philadelphia: Elsevier Saunders; 2005:2067-2092.

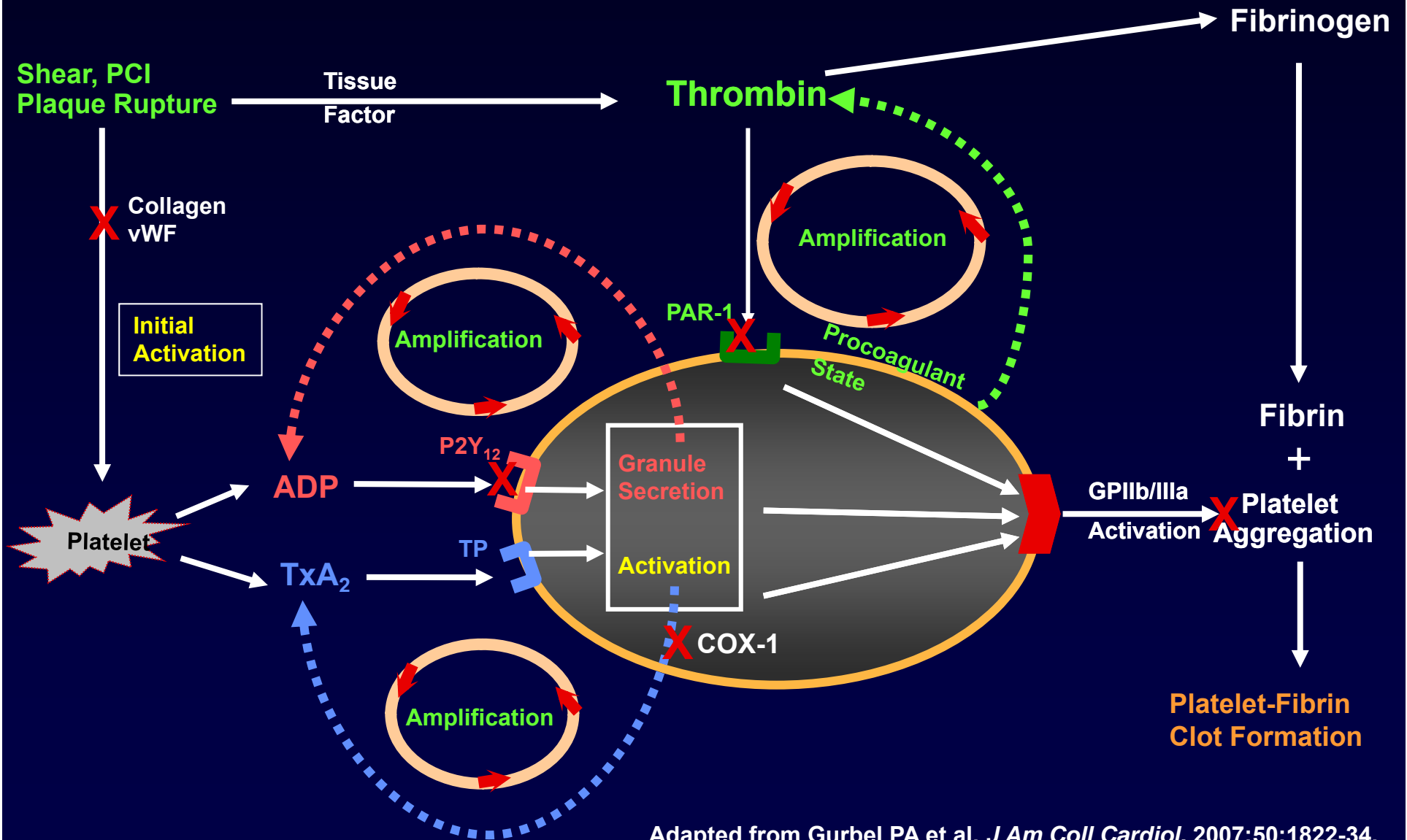
 = saccharide unit.

# Unfractionated Heparin

- Complete structure remains unknown
  - Unbranched heteropolysaccharide chain
- Molecular weight: 2,500 - 57,500 daltons



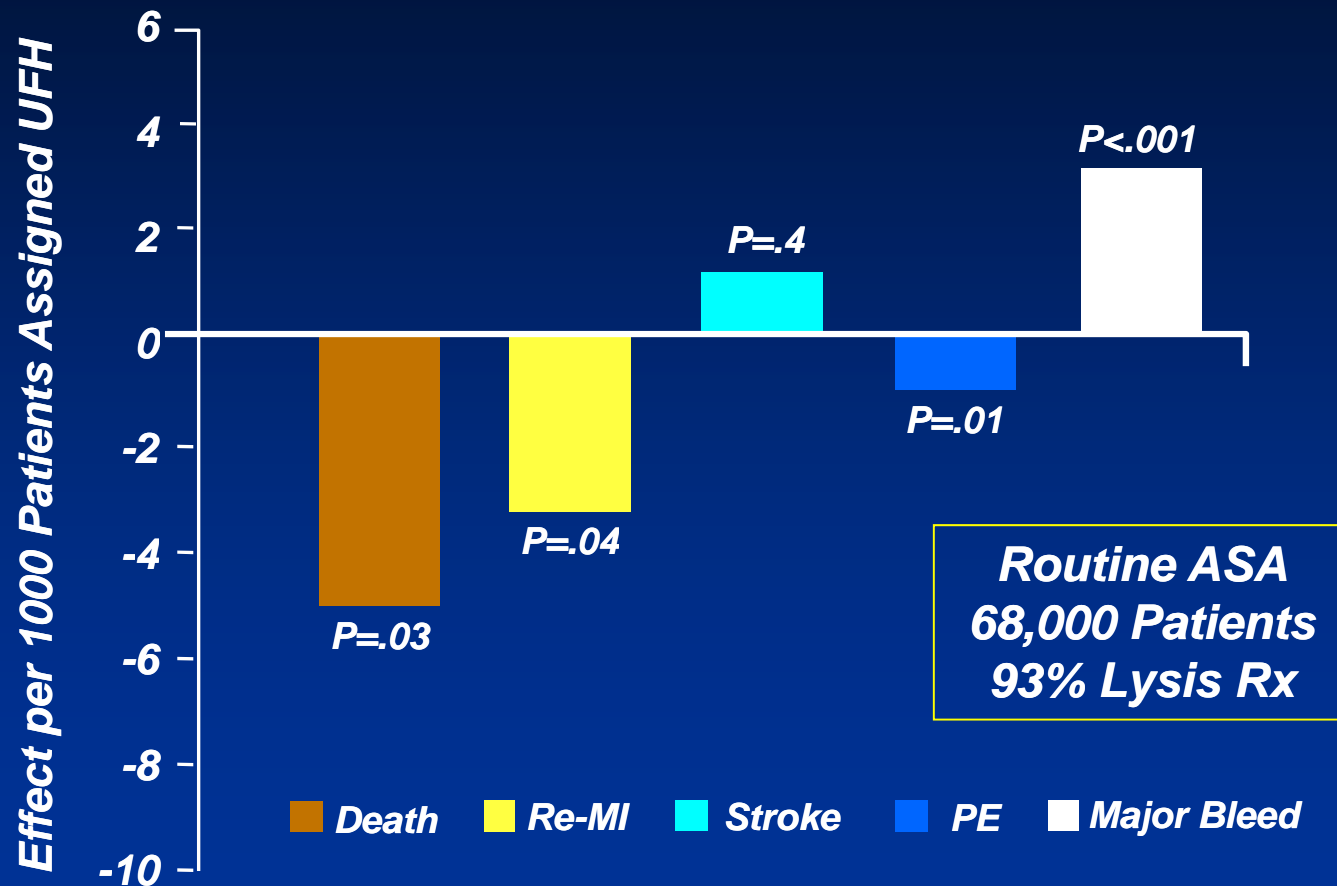
# Central Role of Platelets and Interaction with Coagulation in the Genesis of Thrombosis



Adapted from Gurbel PA et al. *J Am Coll Cardiol.* 2007;50:1822-34.

# UFH Is Superior to Placebo for Reducing Mortality and Reinfarction in STEMI

Meta-Analysis of 26 Randomized Trials

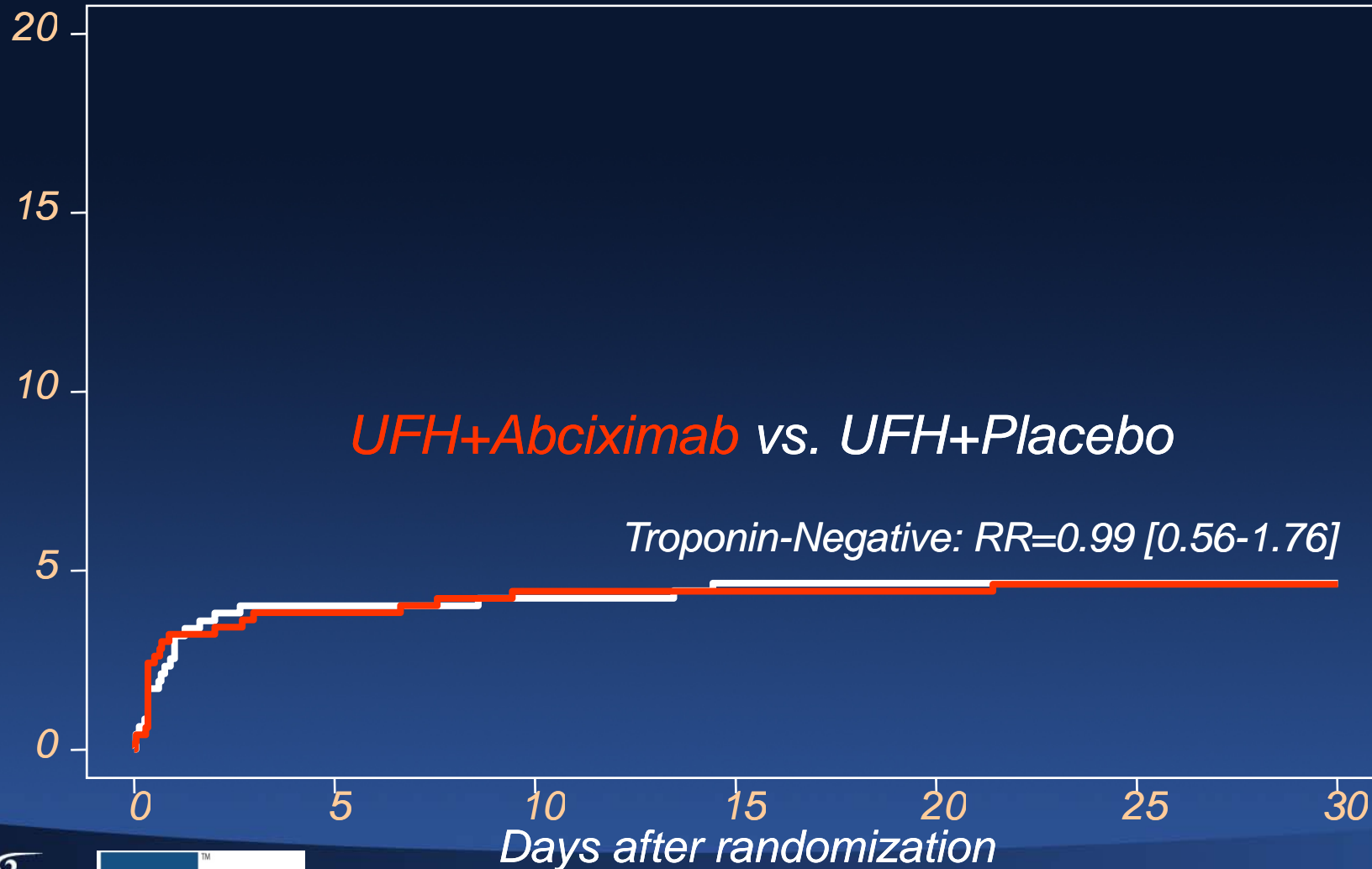


Collins R, et al. N Engl J Med. 1997;336:847-860.

# Patients with Unstable Angina Heparin alone or with GPI

Death/MI/urg. TVR, %

ISAR-REACT 2

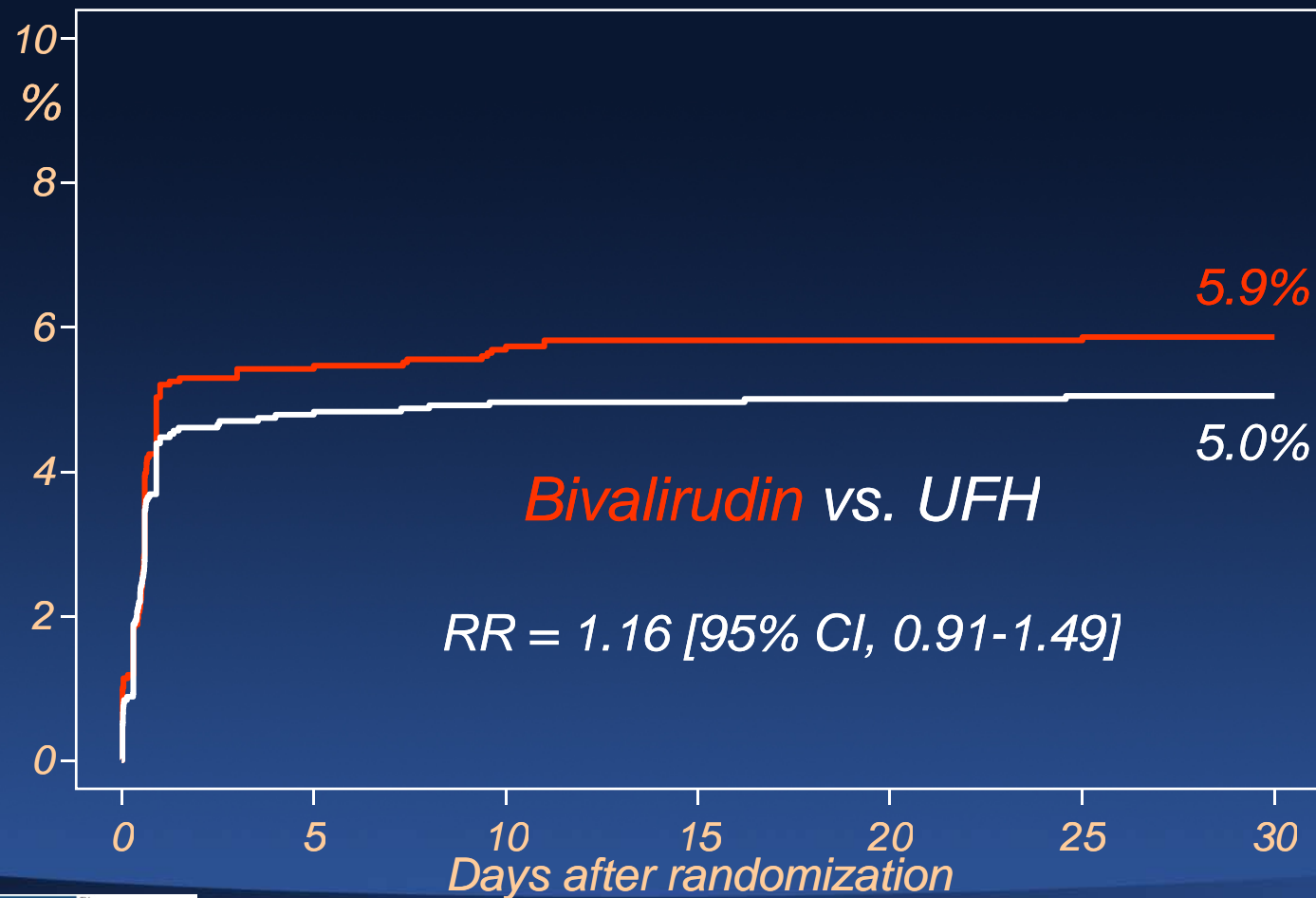




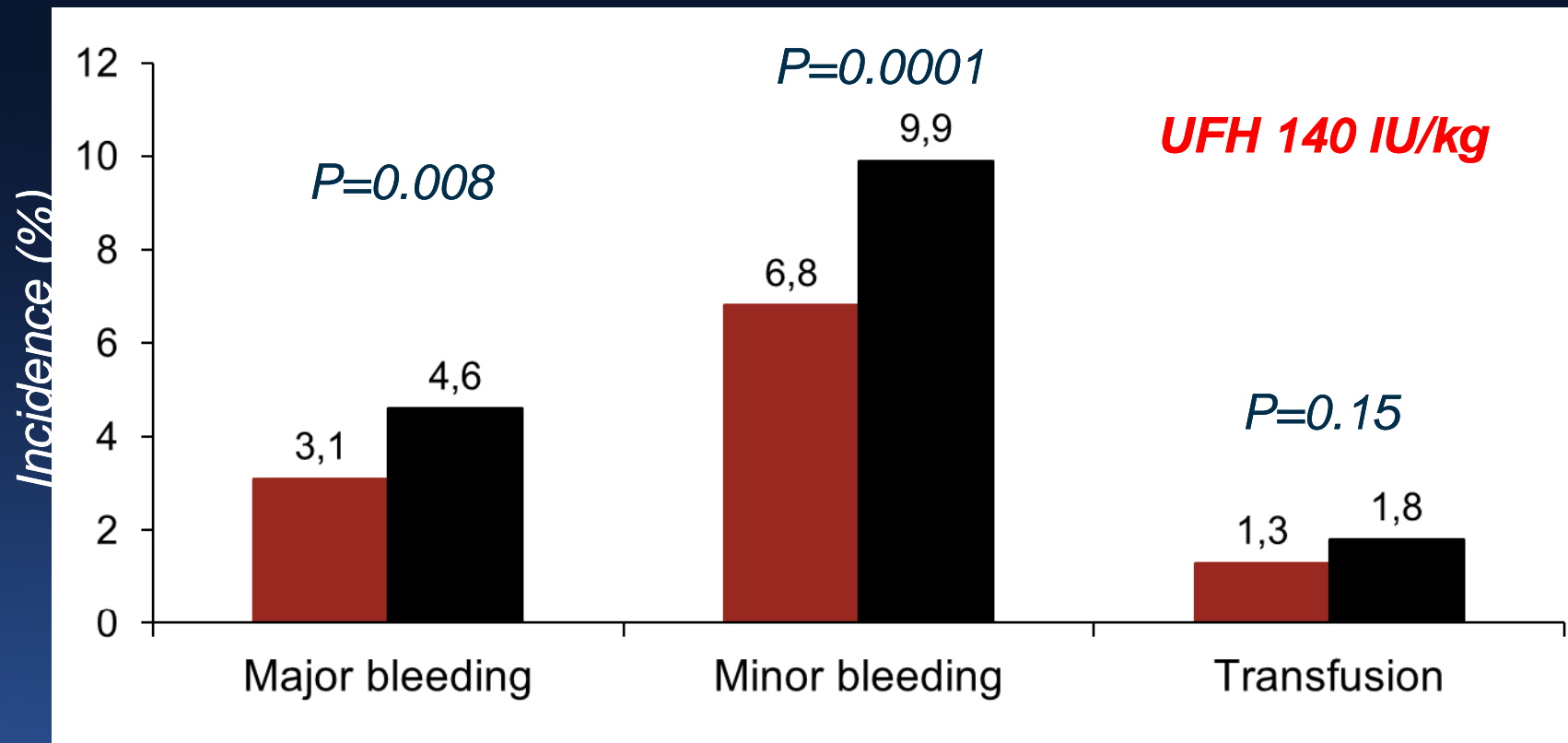
# Patients with Stable/Unstable Angina Heparin alone or Bivalirudin

Death/MI/urgTVR

ISAR-REACT 3 n= 4570



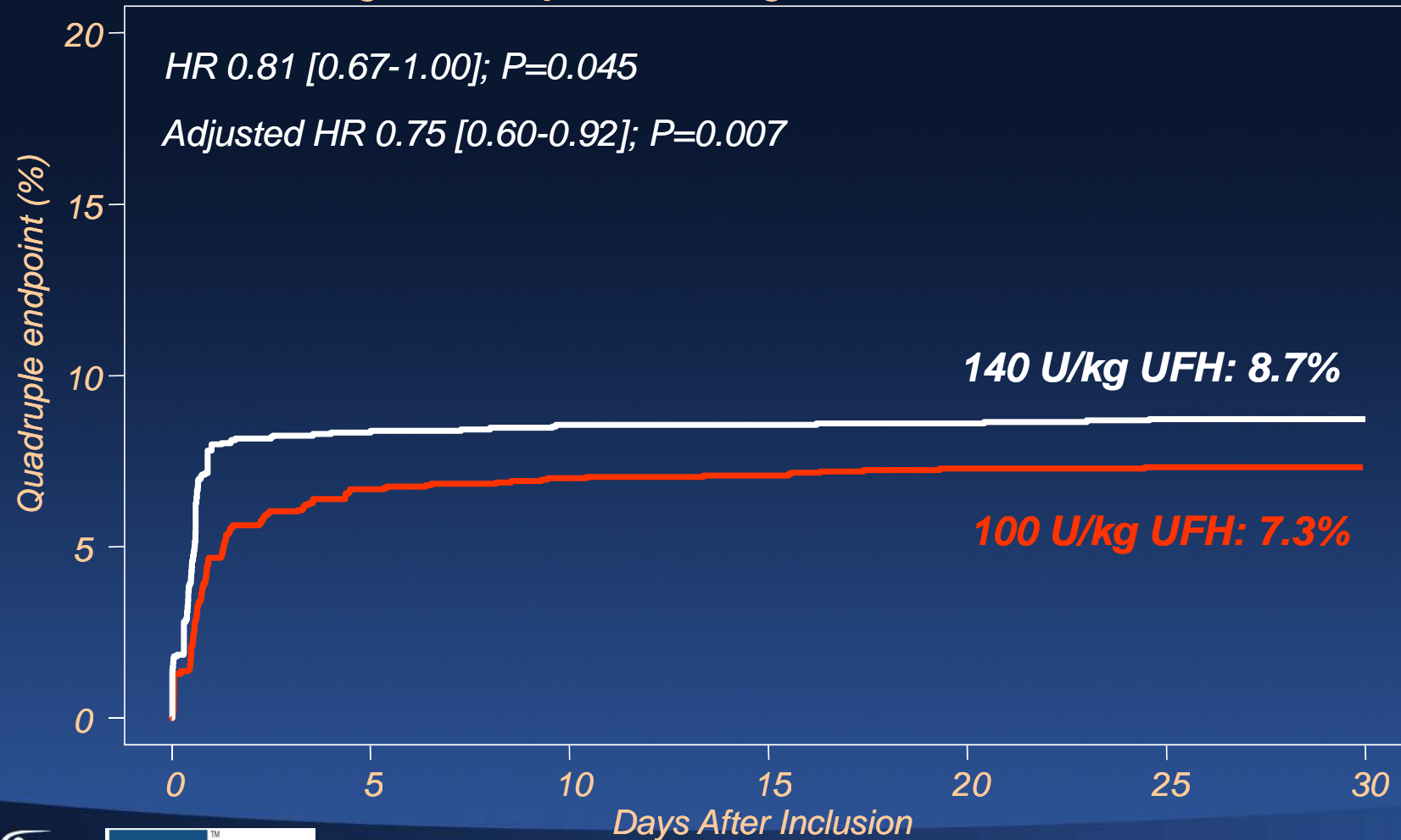
# Patients with Stable/Unstable Angina Heparin alone or Bivalirudin



# Patients with Stable/Unstable Angina High or Low Dose Heparin

Death,MI,urgTVR,major Bleeding

ISAR-REACT 3A n= 4786



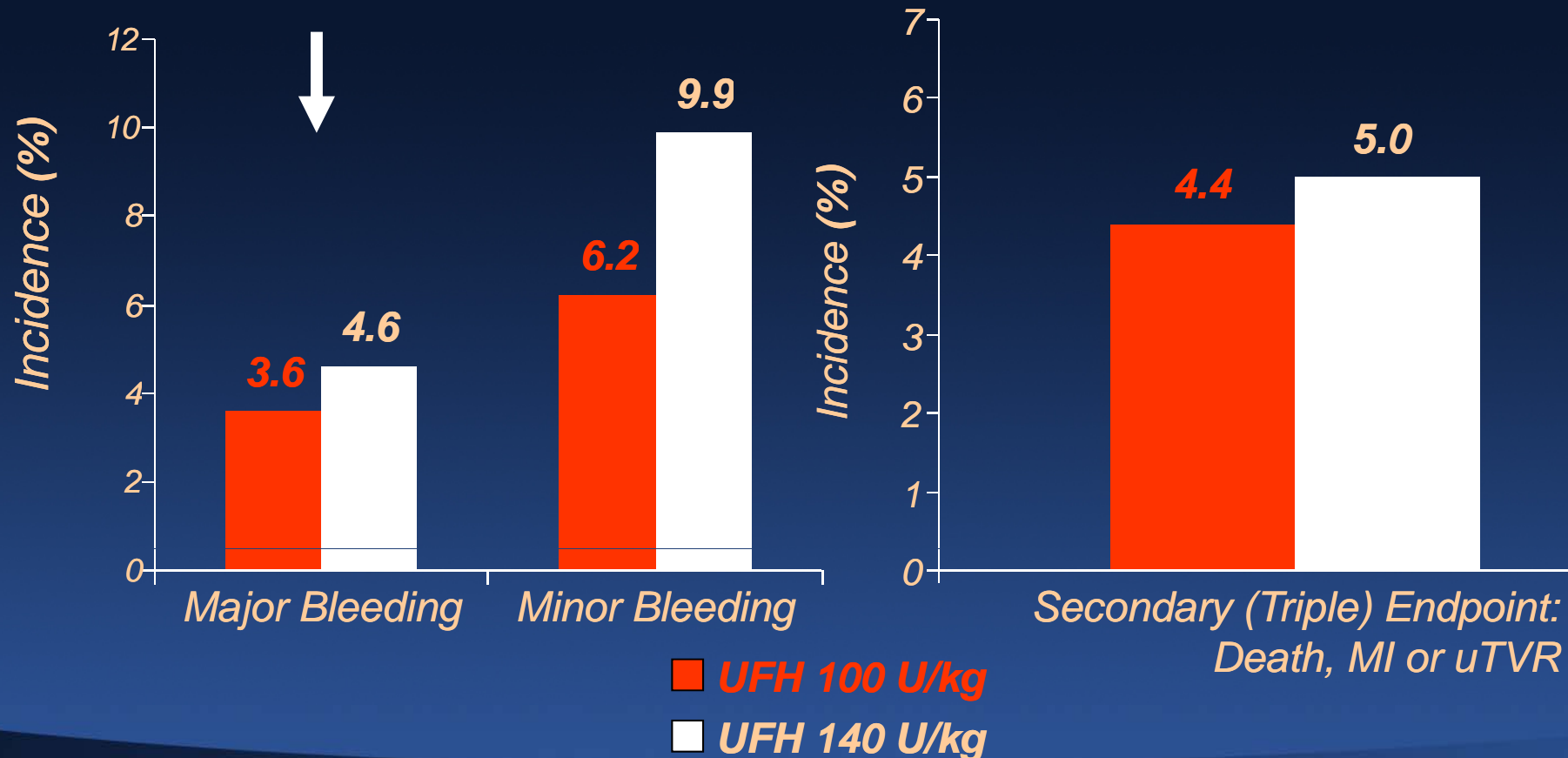
# Patients with Stable/Unstable Angina High or Low Dose Heparin

HR 0.79 [0.59-1.05]; P=0.11

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

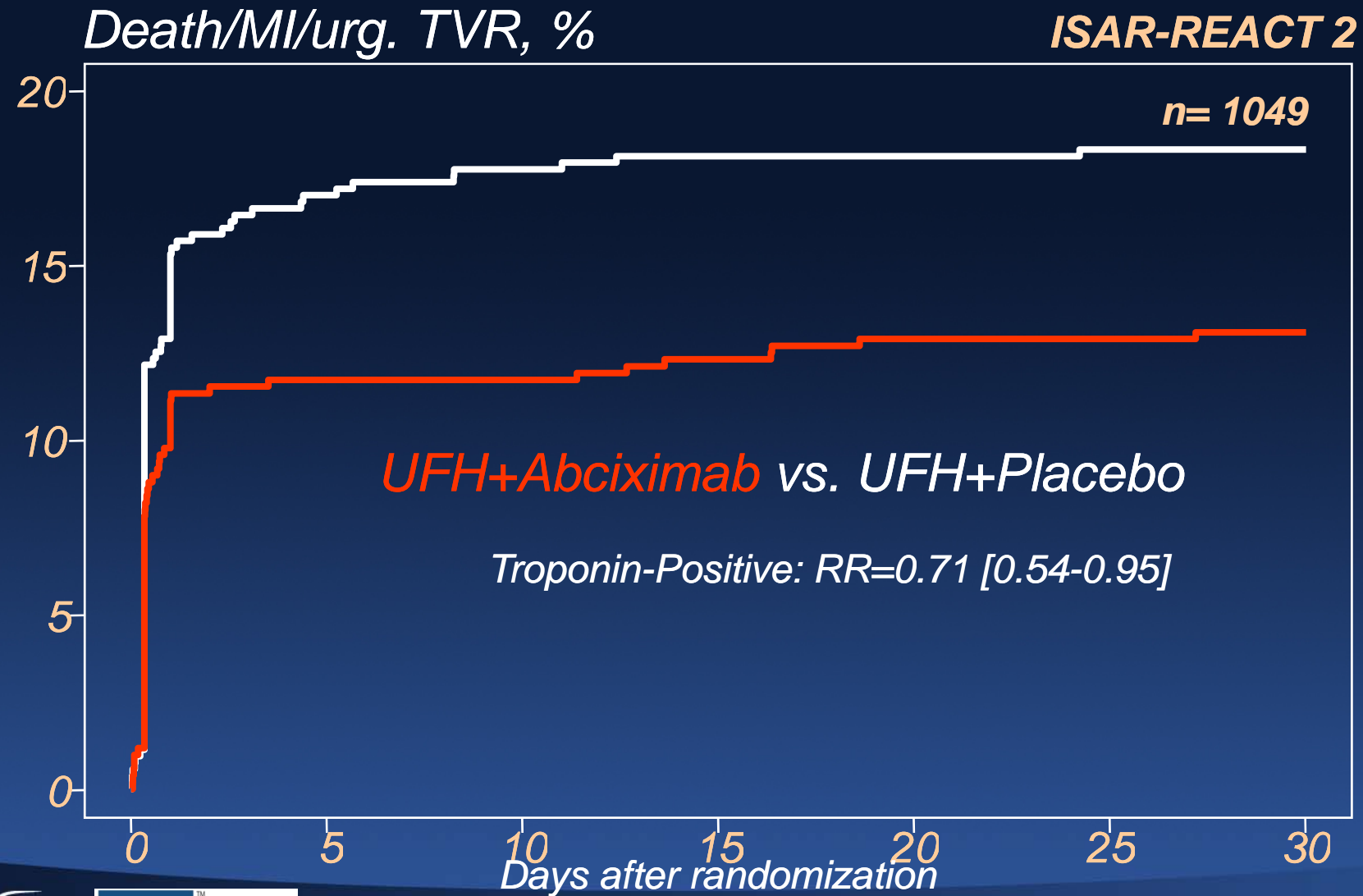
HR 0.87 [0.67-1.13]; P=0.29

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



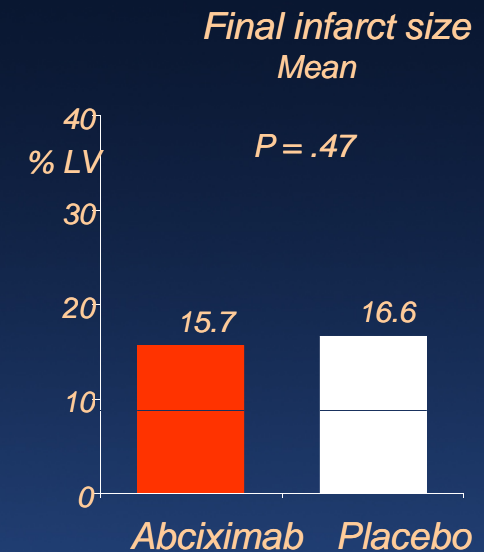
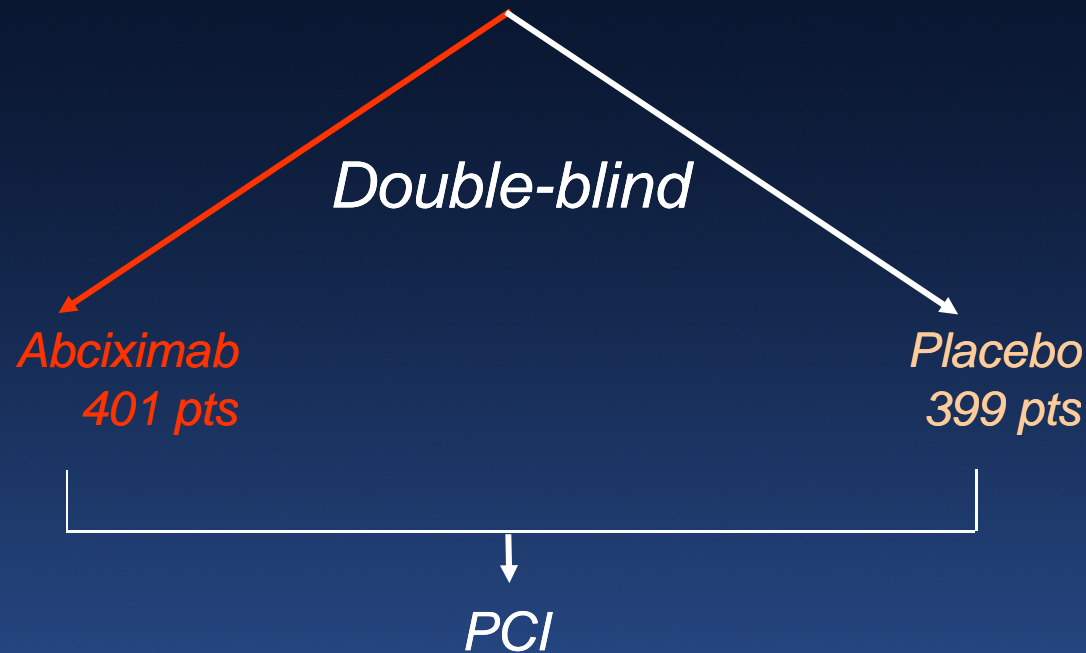
# Patients with NSTEMI

## Heparin alone or with GPI

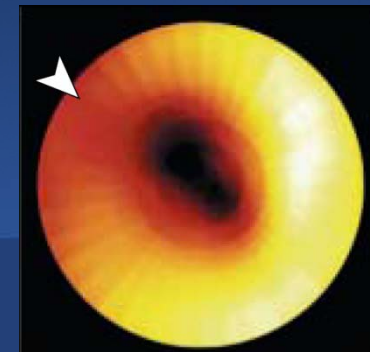


# Patients with STEMI Heparin alone or with GPI

800 Patients with STEMI  
Pretreatment with 600 mg of clopidogrel

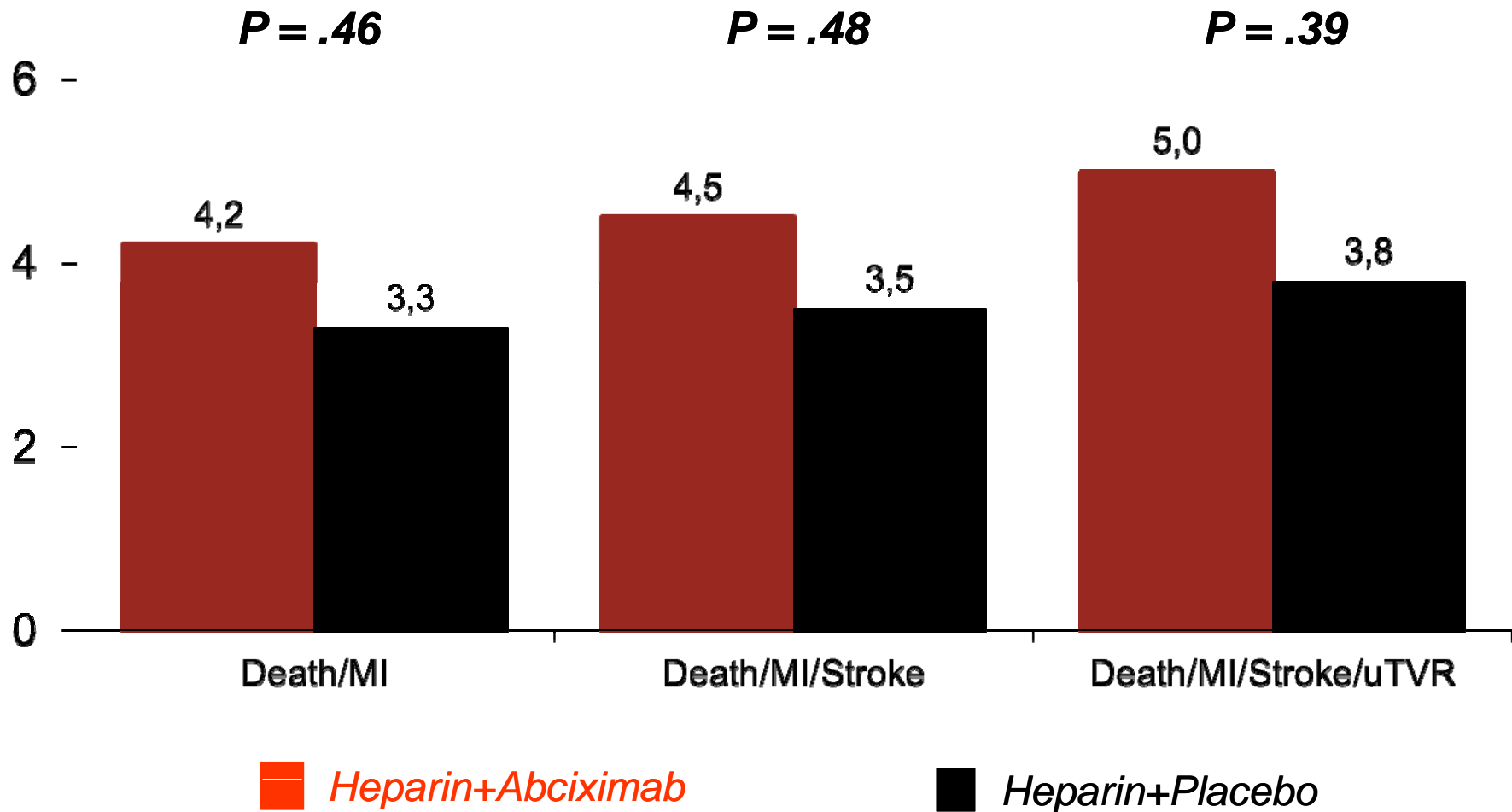


Primary endpoint: Scintigraphic final infarct size



# Patients with STEMI

## Heparin alone or with GPI



# For primary PCI



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# IIb/IIIa antagonists

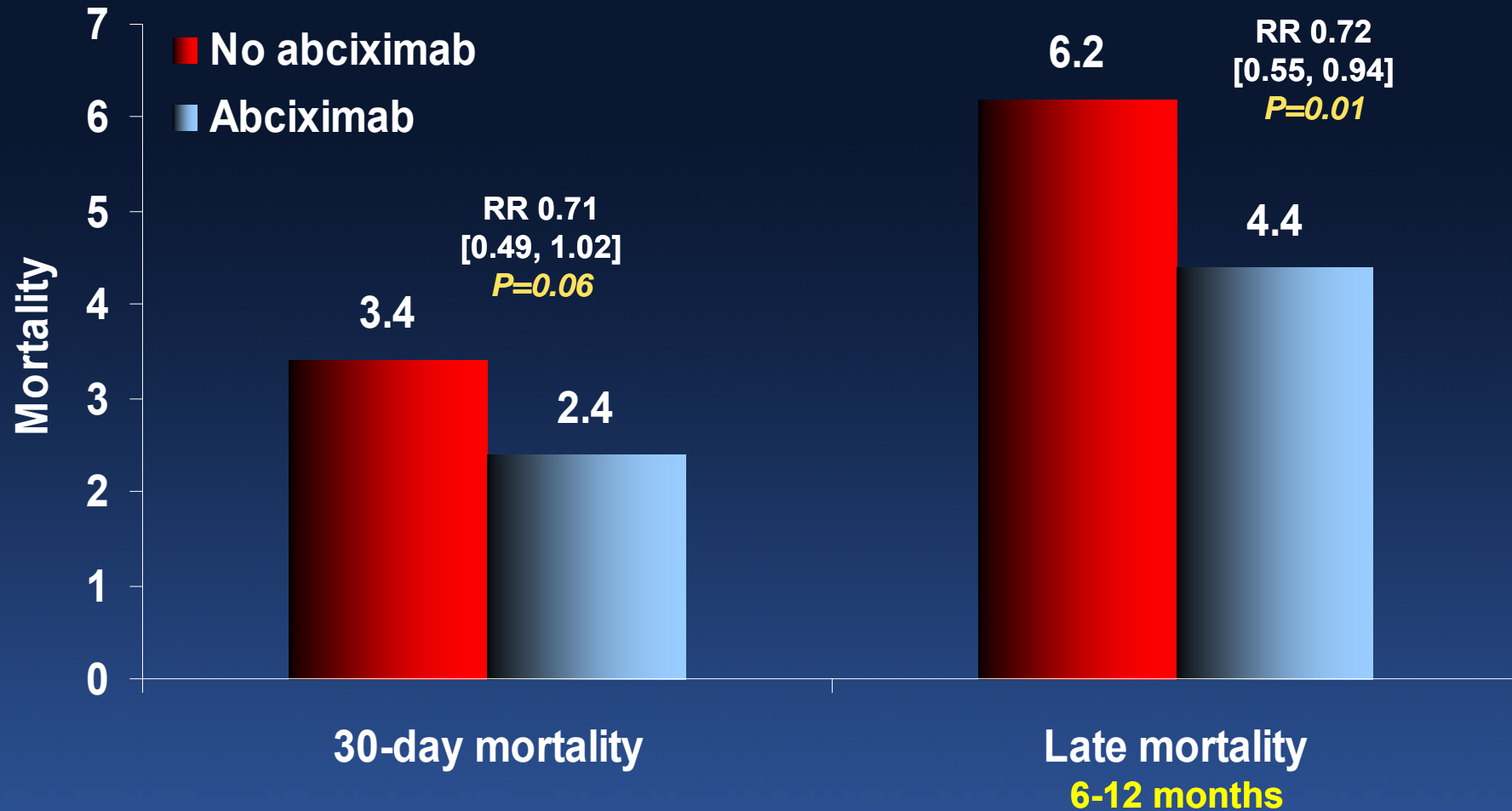


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# Abciximab in primary PCI meta-analysis

8 RCTs – 3,949 patients with AMI w/ 12° undergoing primary (7) or rescue (1) PCI randomized to abciximab vs. placebo or control



# Bivalirudin

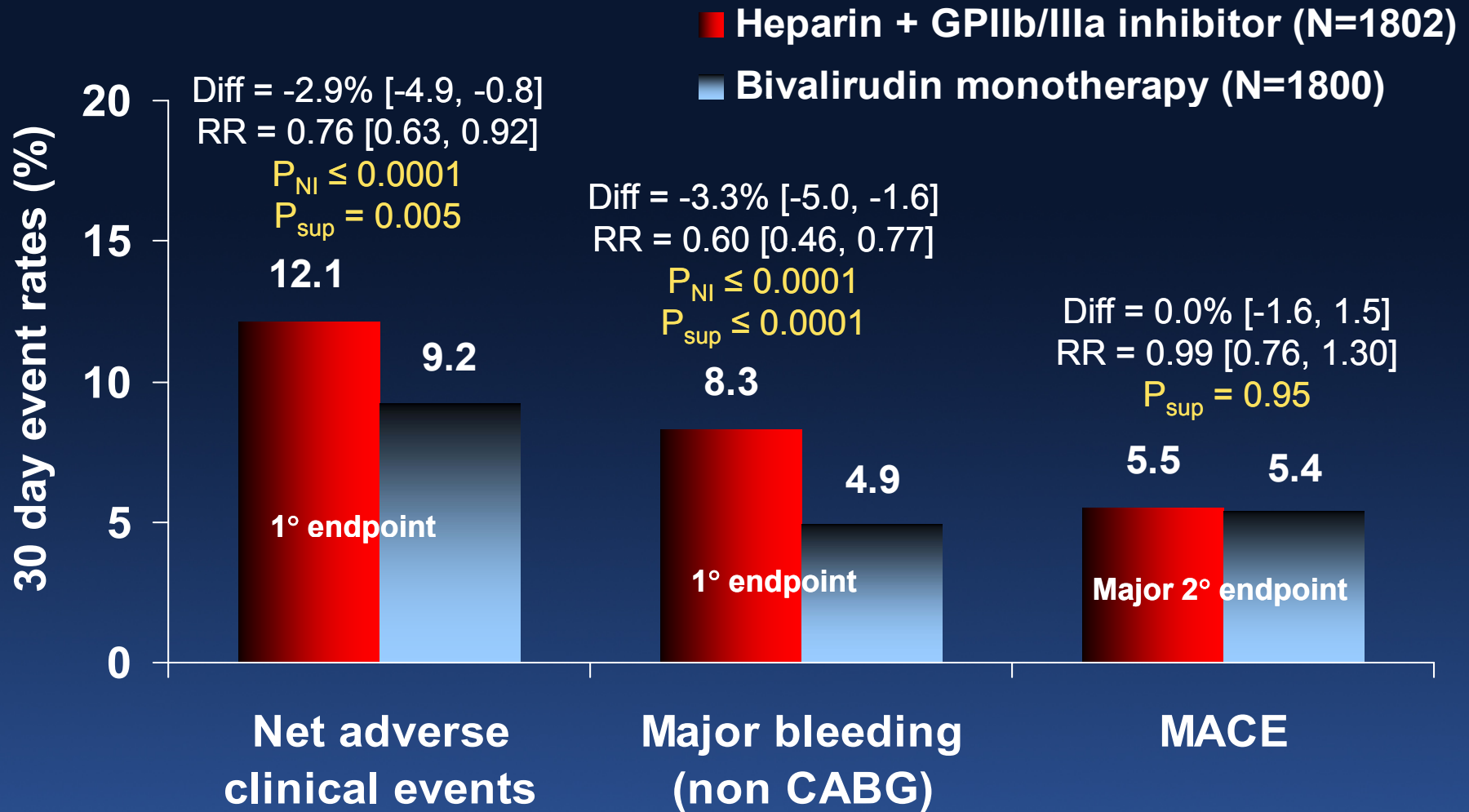


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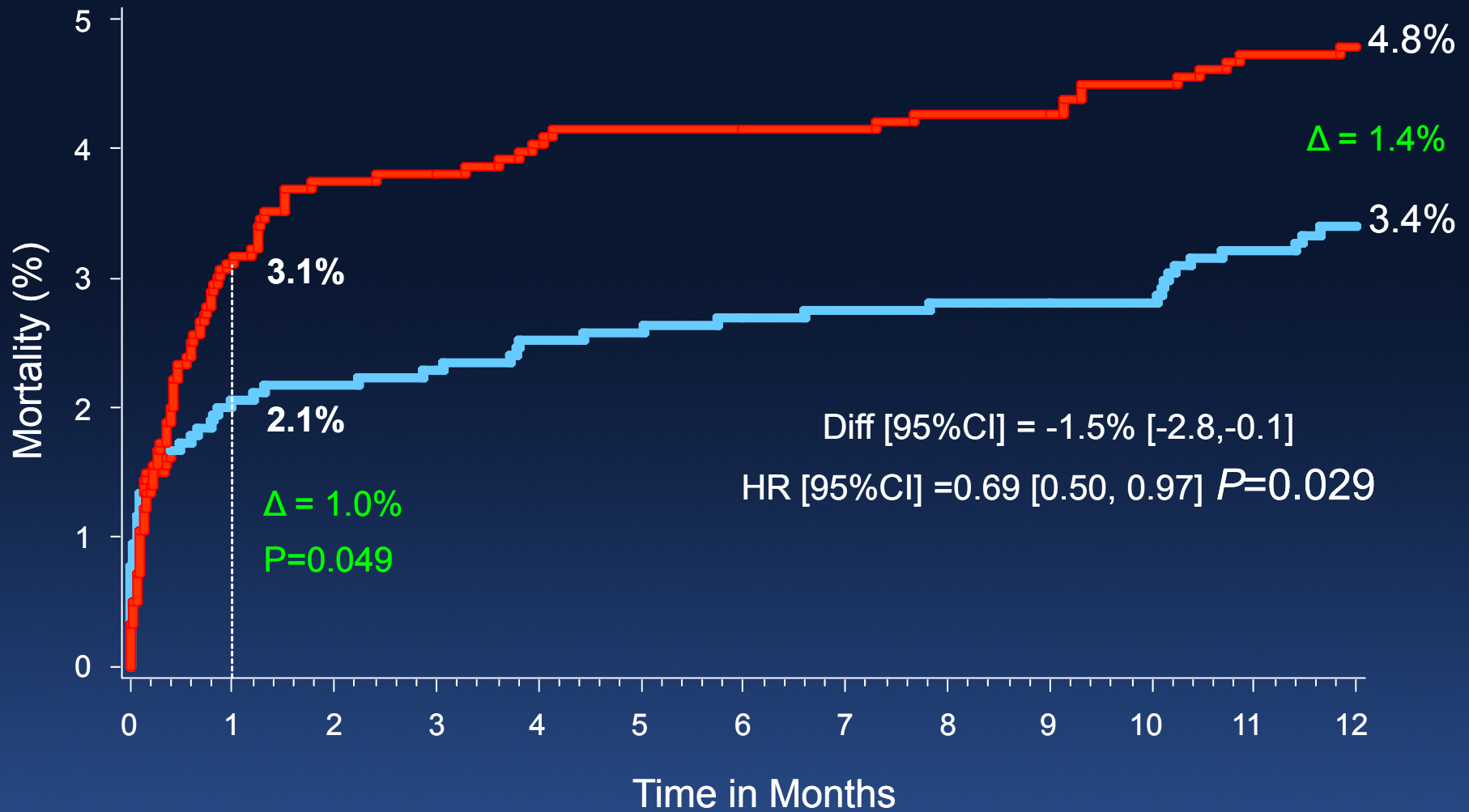
  
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# Primary endpoints at 30-days



# 1-year All-cause mortality



Number at risk

Bivalirudin alone	1800	1705	1684	1669	1520
Heparin + IIb/IIIa	1802	1678	1663	1646	1486

# 30 Day Stent Thrombosis

	UFH + GP IIb/IIIa (1553)	Bivalirudin (1571)	P
<b>ARC 30d definite or probable stent thrombosis*</b>	<b>1.9%</b>	<b>2.5%</b>	<b>0.30</b>
- definite	1.4%	2.2%	0.09
- probable	0.5%	0.3%	0.24
- acute (≤24 hrs)	0.3%	1.3%	<b>0.0007</b>

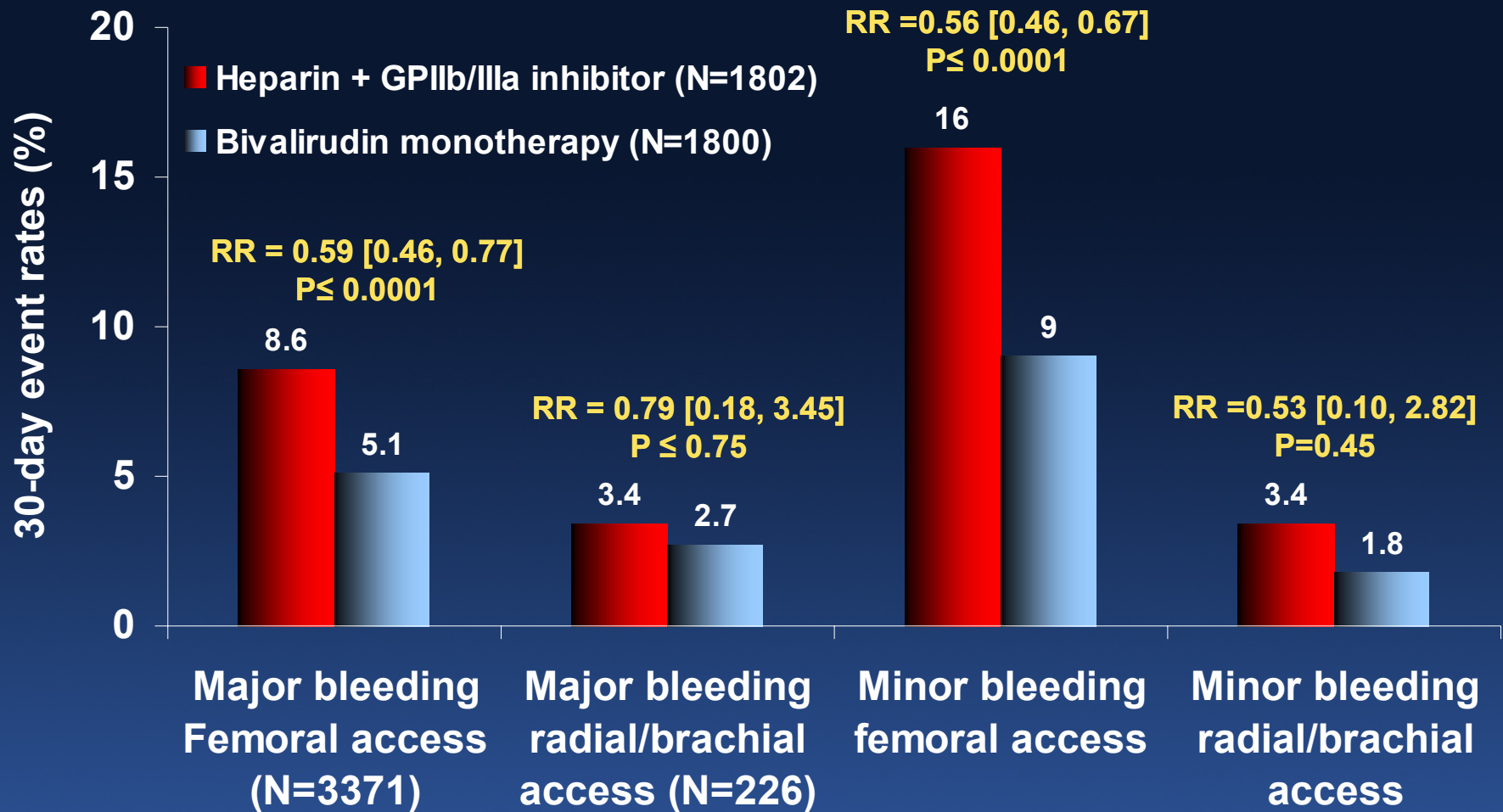
\*Protocol definition of stent thrombosis, CEC adjudicated

## BIV group: 30 Day Stent Thrombosis

	300 mg LD	600 mg LD	P-value
ARC definite or probable*	3.5%	1.7%	0.03
- definite	3.1%	1.5%	0.04
- Probable	0.4%	0.2%	0.61
- acute ( $\leq 24$ hrs)	1.6%	0.9%	0.26
- subacute ( $> 24$ hrs – 30d)	2.1%	0.8%	0.03

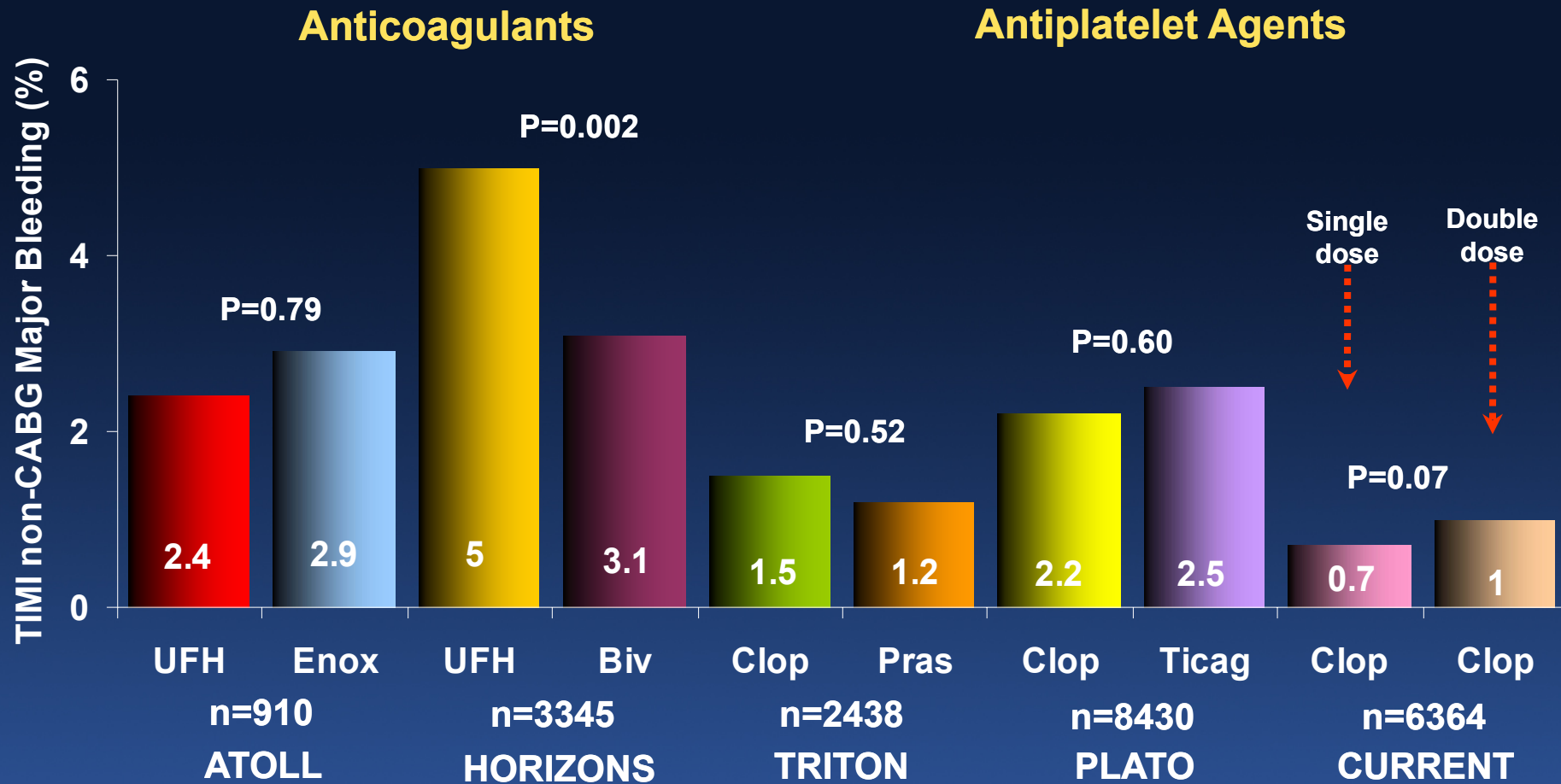
\*Protocol definition of stent thrombosis, CEC adjudicated

# Arterial access site and 30-day non-CABG major or minor bleeding



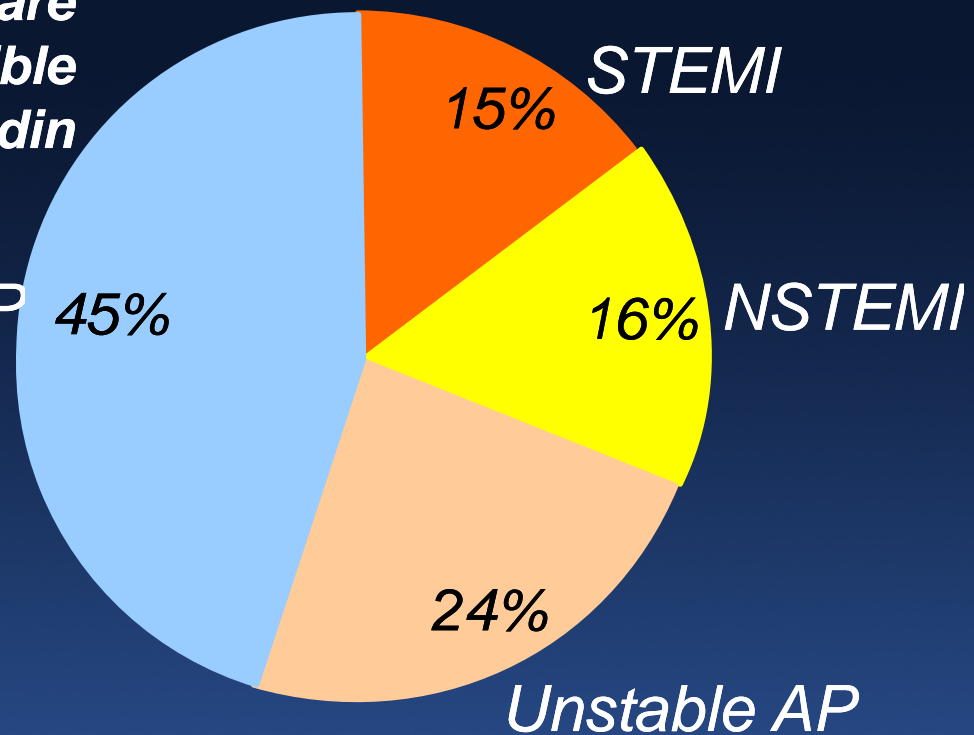
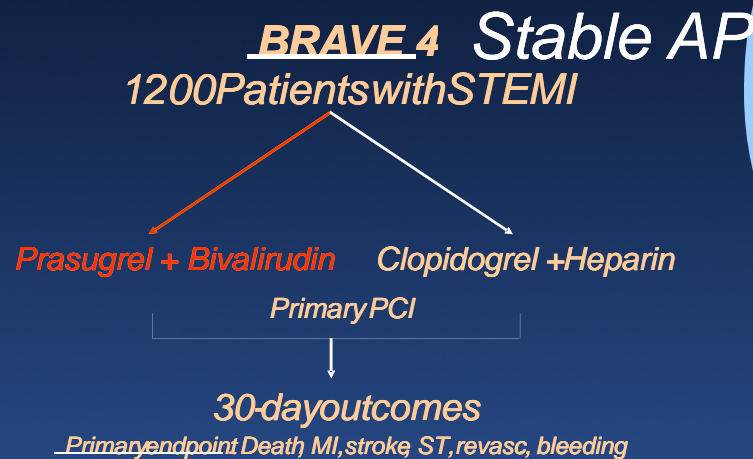


# Bleeding rates with anticoagulants and antiplatelet agents in primary PCI



# Heparin for all?

**Both heparin and bivalirudin are good options, with a possible advantage for bivalirudin**



# Balancing Safety and Efficacy

