

Novel Biomarkers in Acute Coronary Syndromes

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SOUTHWESTERN

The Problem

- ACS is heterogeneous with respect to:
 - Pathophysiology
 - Presentation
 - Prognosis
 - Response to therapy

...yet, we use a similar treatment approach
for most patients

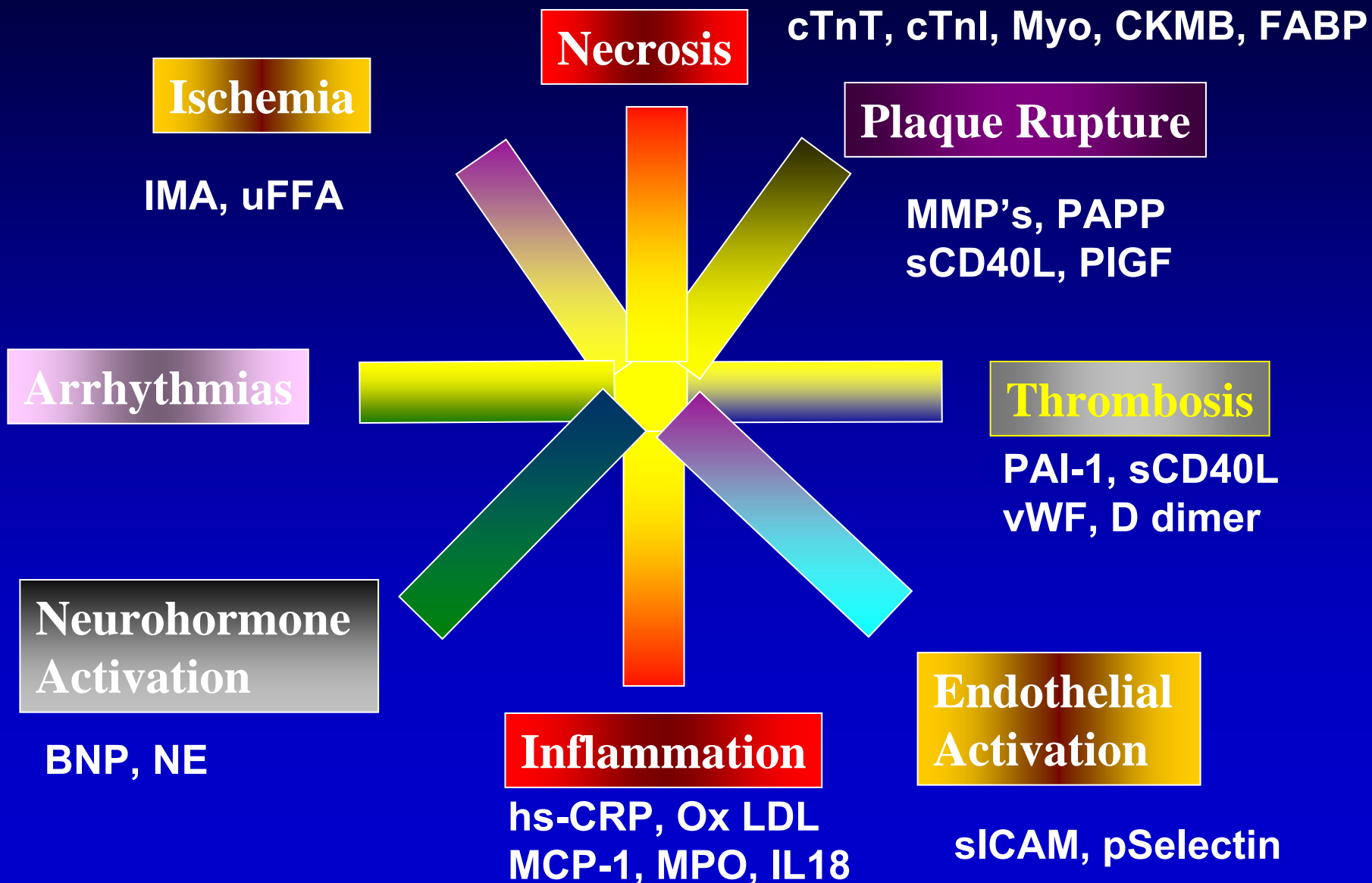
The Biologic Hard Drive



Potential roles

- Diagnosis/differential diagnosis
- Risk stratification
- Therapeutic decision-making
- Disease monitoring
- Identification of drug targets
- Better understanding of pathophysiology

Potential Biomarker Targets in ACS

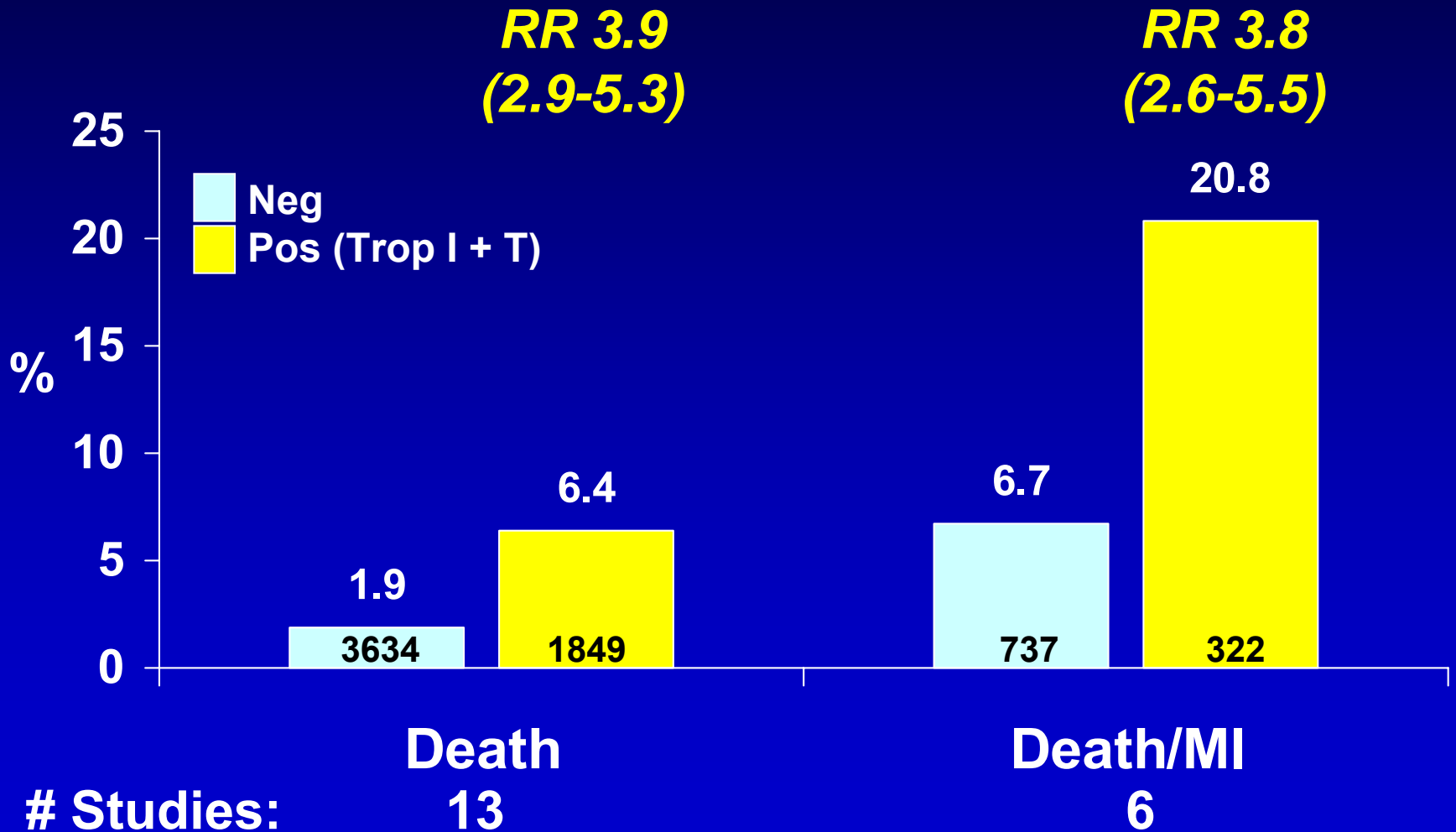


Characteristic of an “Ideal” Cardiac Biomarker

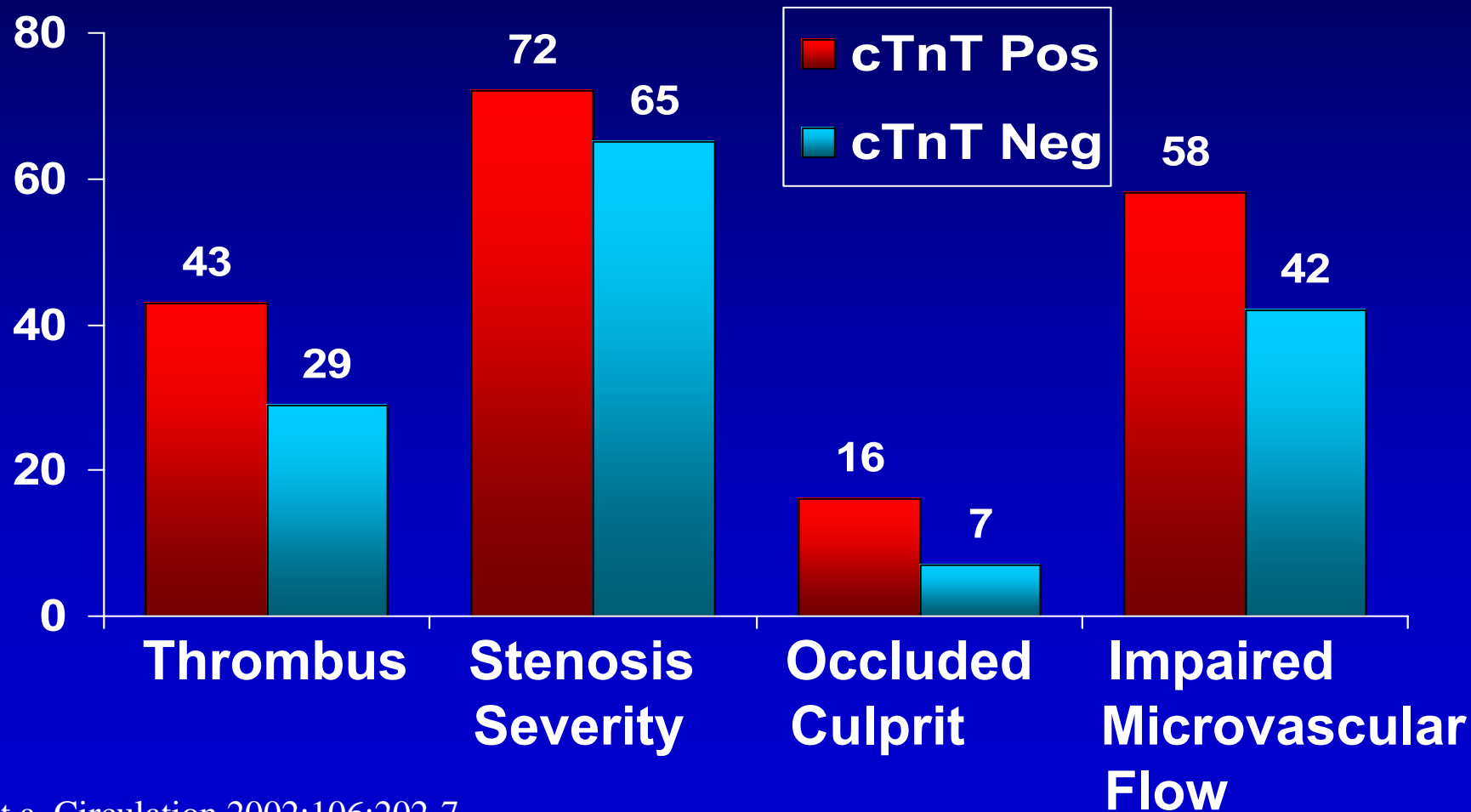
- Easy and reliable measurement
- High PPV/NPV for diagnosis/prognostic assessment
- **INCREMENTAL** diagnostic/prognostic value
- Guides clinical decision-making
- Cost-effective
- Examples
 - 12 lead ECG
 - Troponin?

Prognostic Value of Pos. Troponin Test in ACS

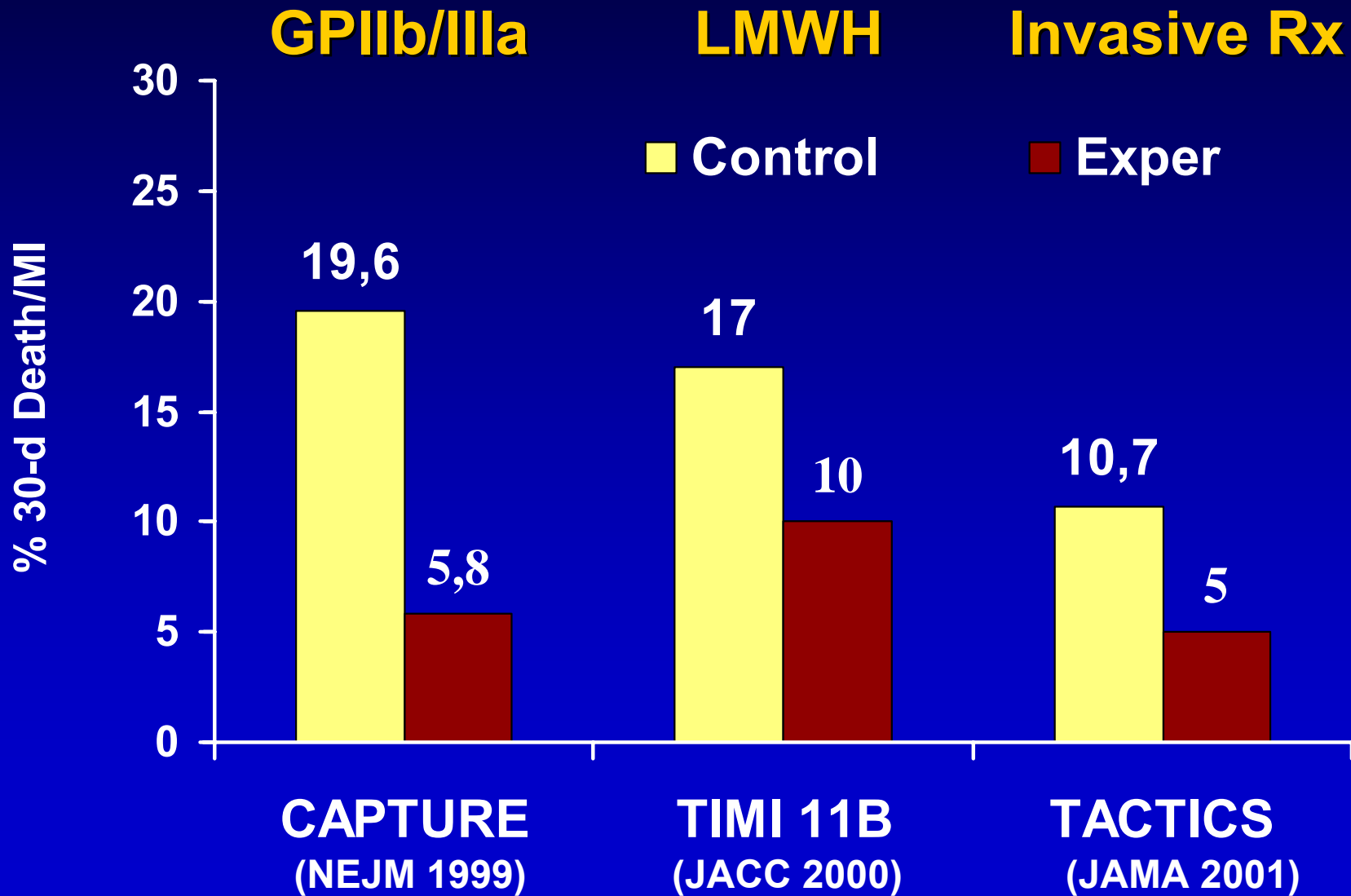
ACC/AHA Guidelines for UA/NSTEMI JACC 36:970,2000



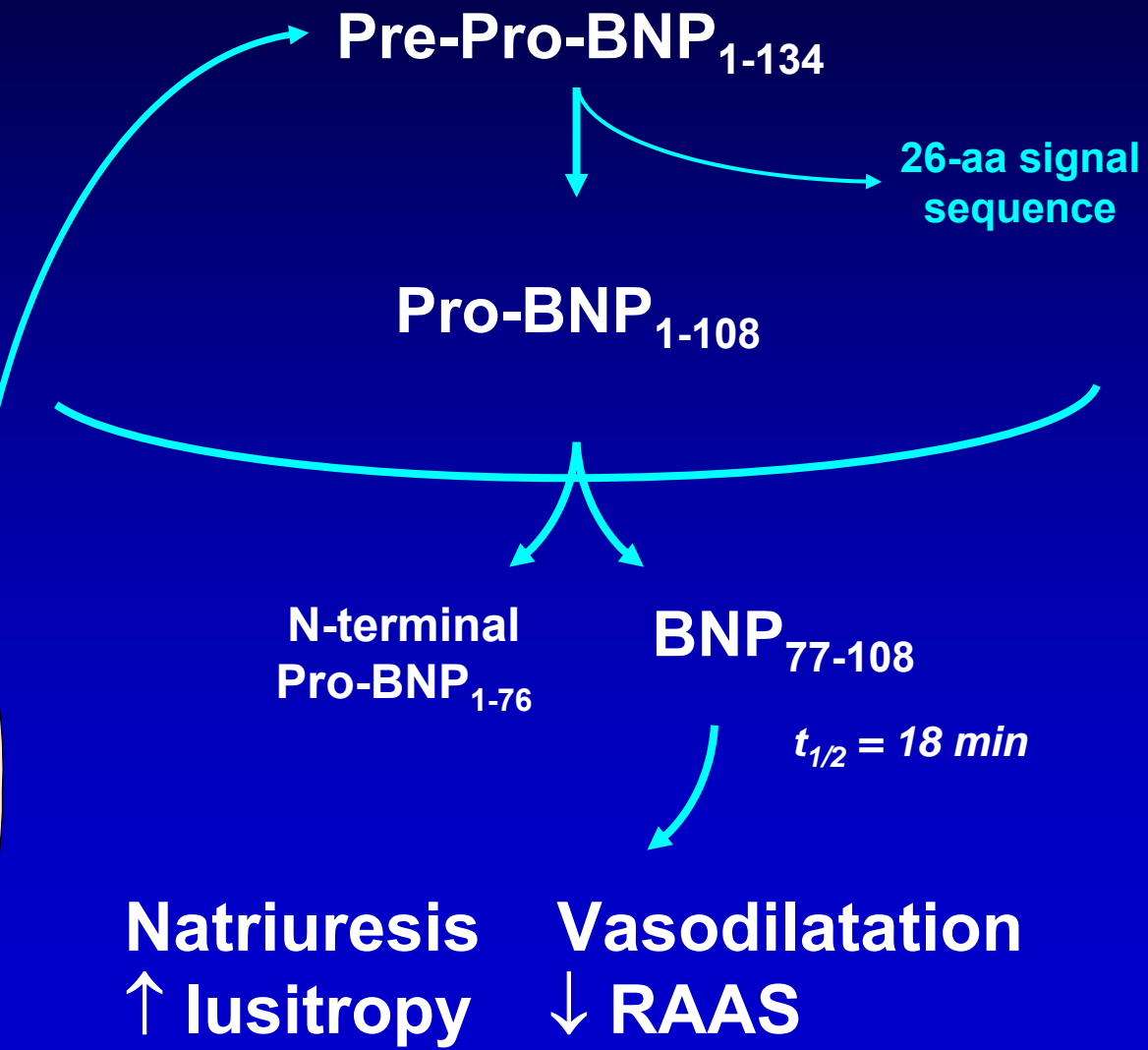
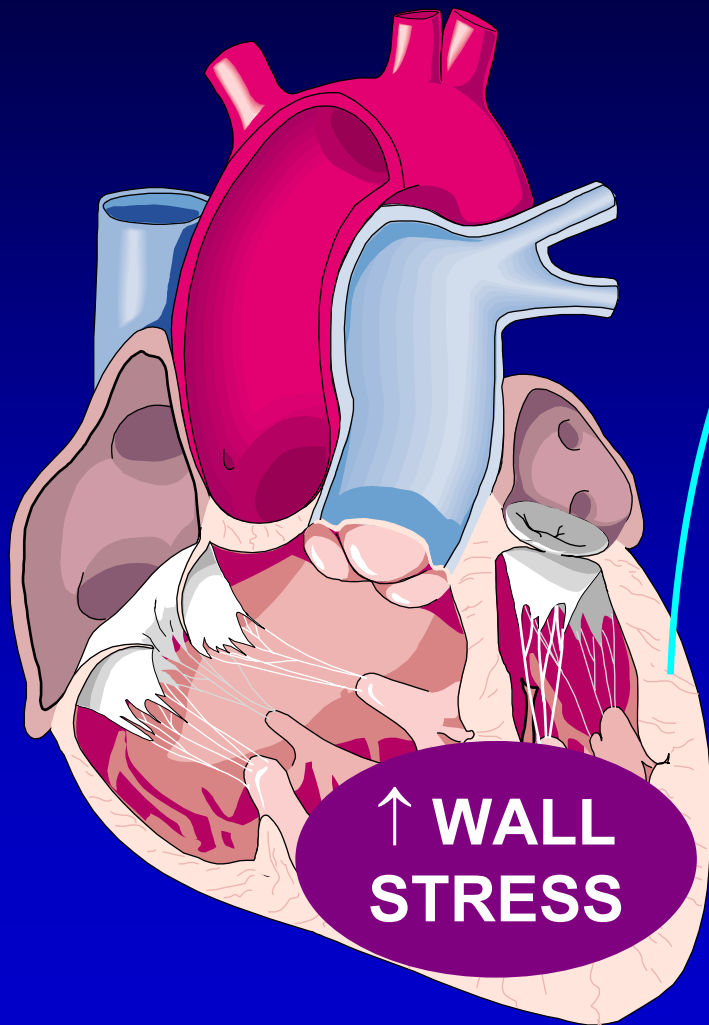
Relation of cTnT to Epicardial and Microvasculature Perfusion in TACTICS



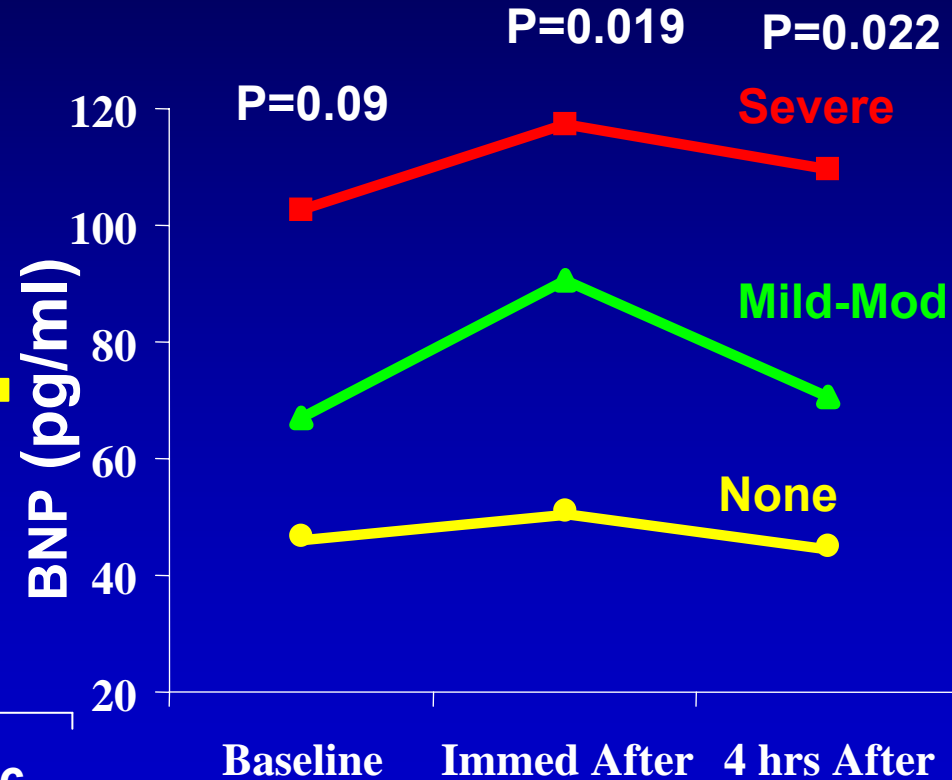
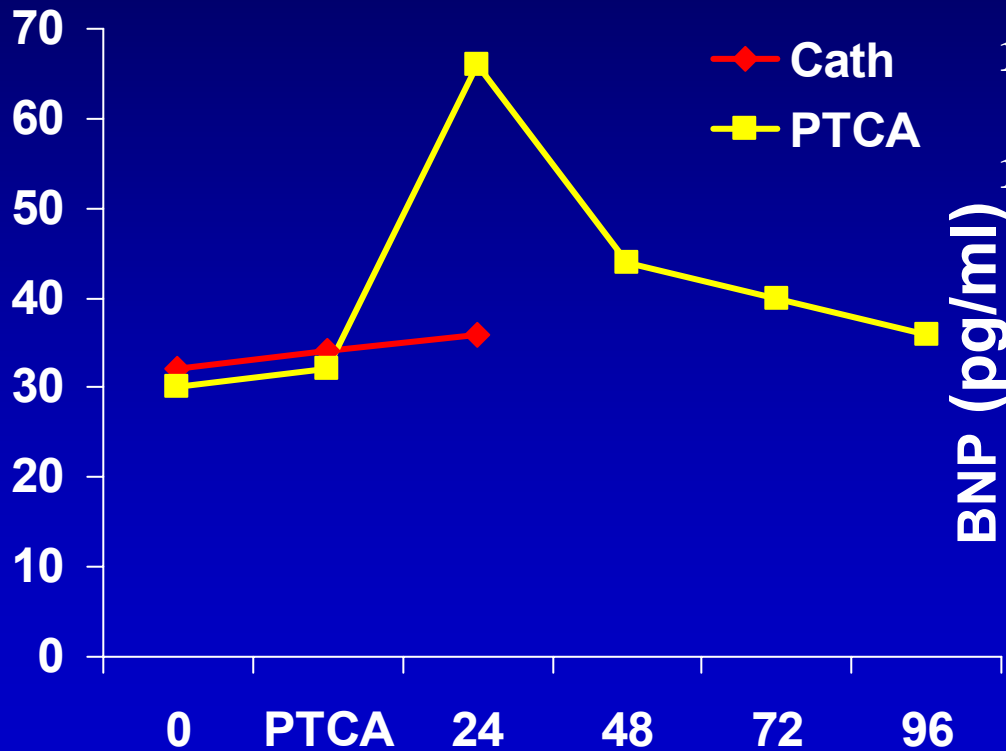
Troponins in Clinical Decision-Making



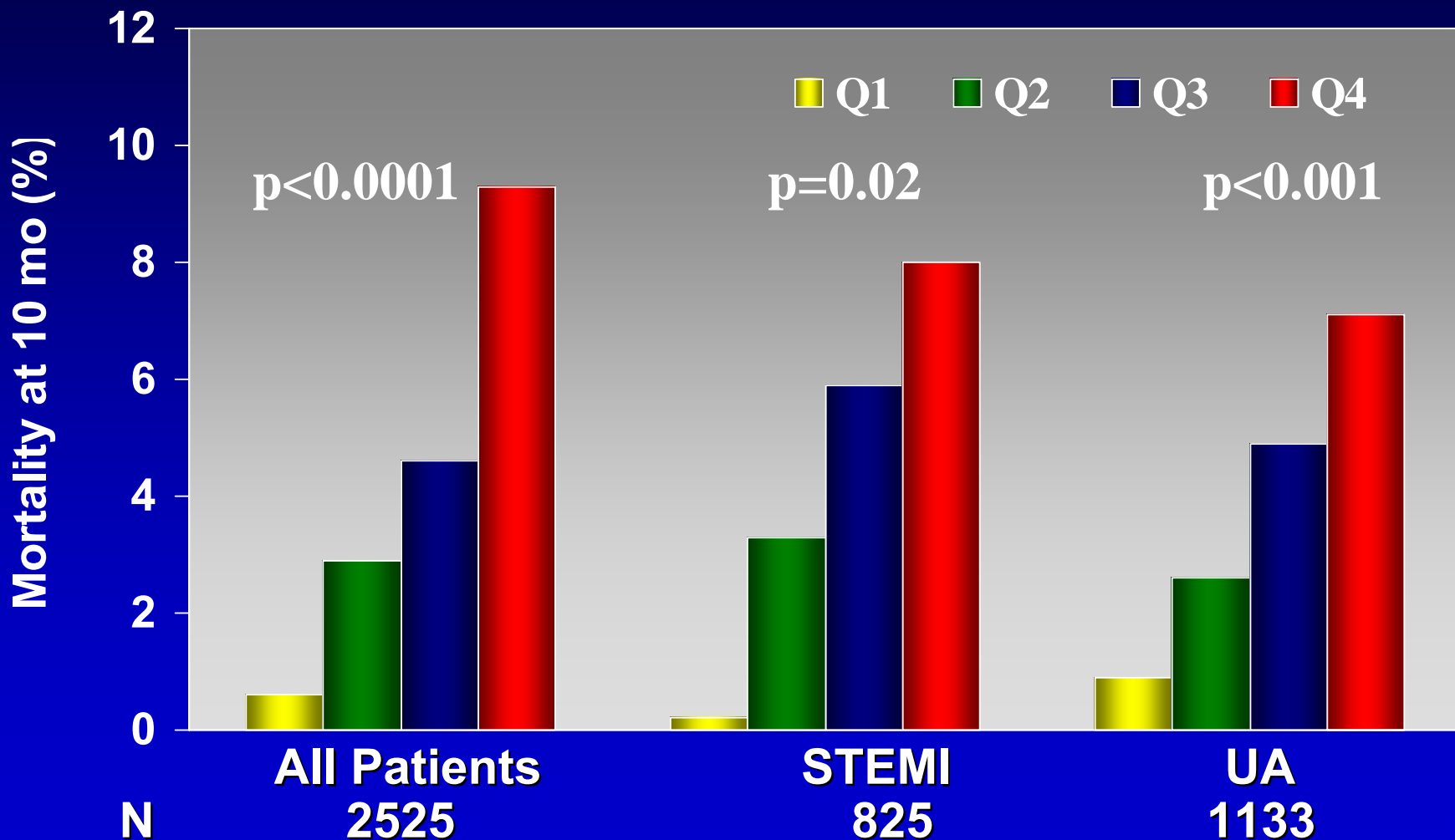
B-type Natriuretic Peptide (BNP)



Ischemia as a Stimulus for BNP release



BNP & Risk of Death



Adjusted Risk of 10-month Mortality

Age > 75

Killip Class II-IV

ST Deviation \geq 1 mm

New LBBB

Diabetes

cTnl > 1.5 ng/mL

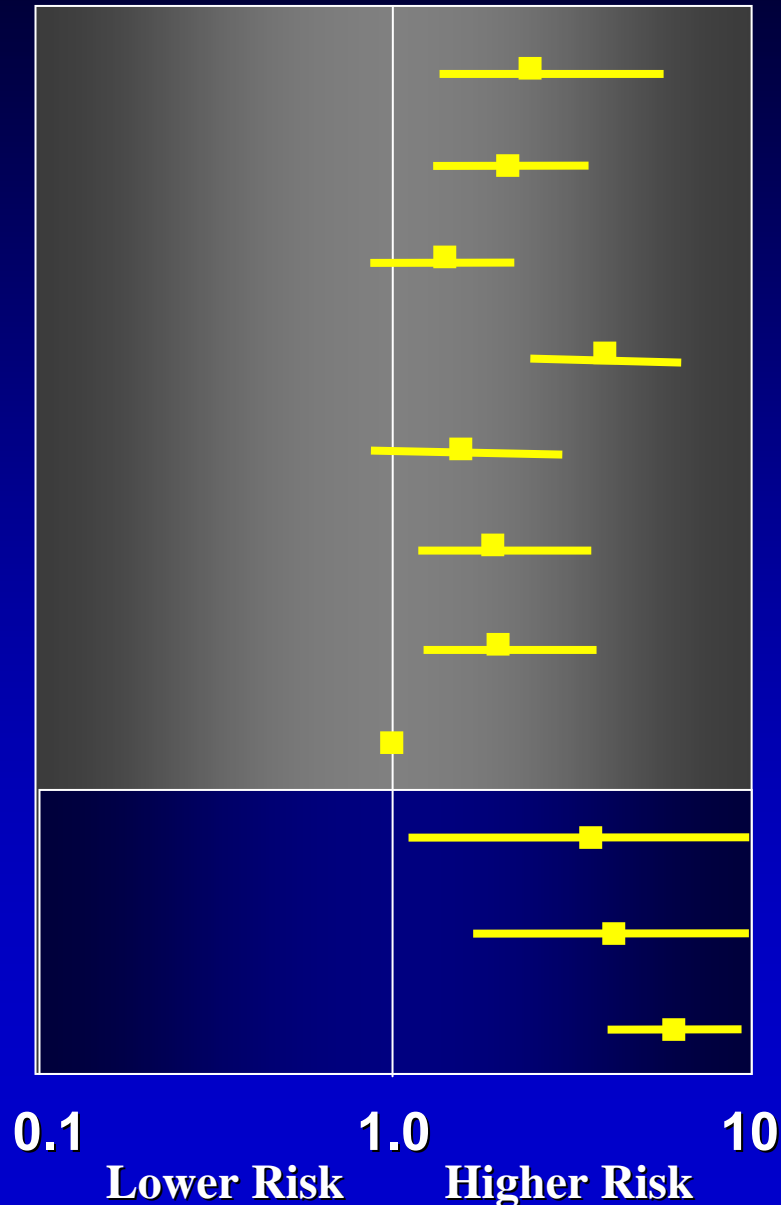
CRP > 1.5 ng/mL

BNP, quartile 1 (reference)

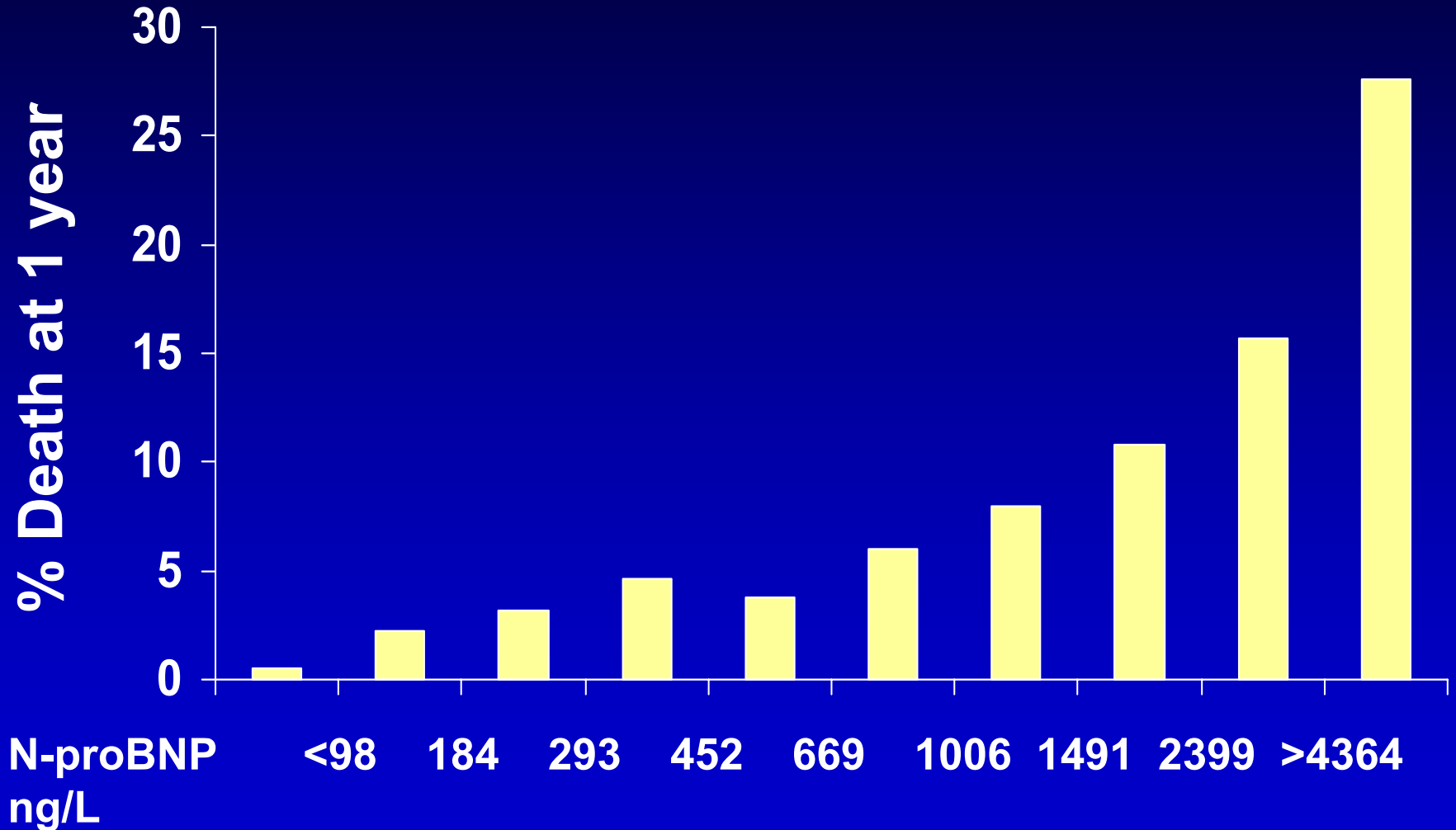
BNP, Quartile 2

BNP, Quartile 3

BNP, Quartile 4

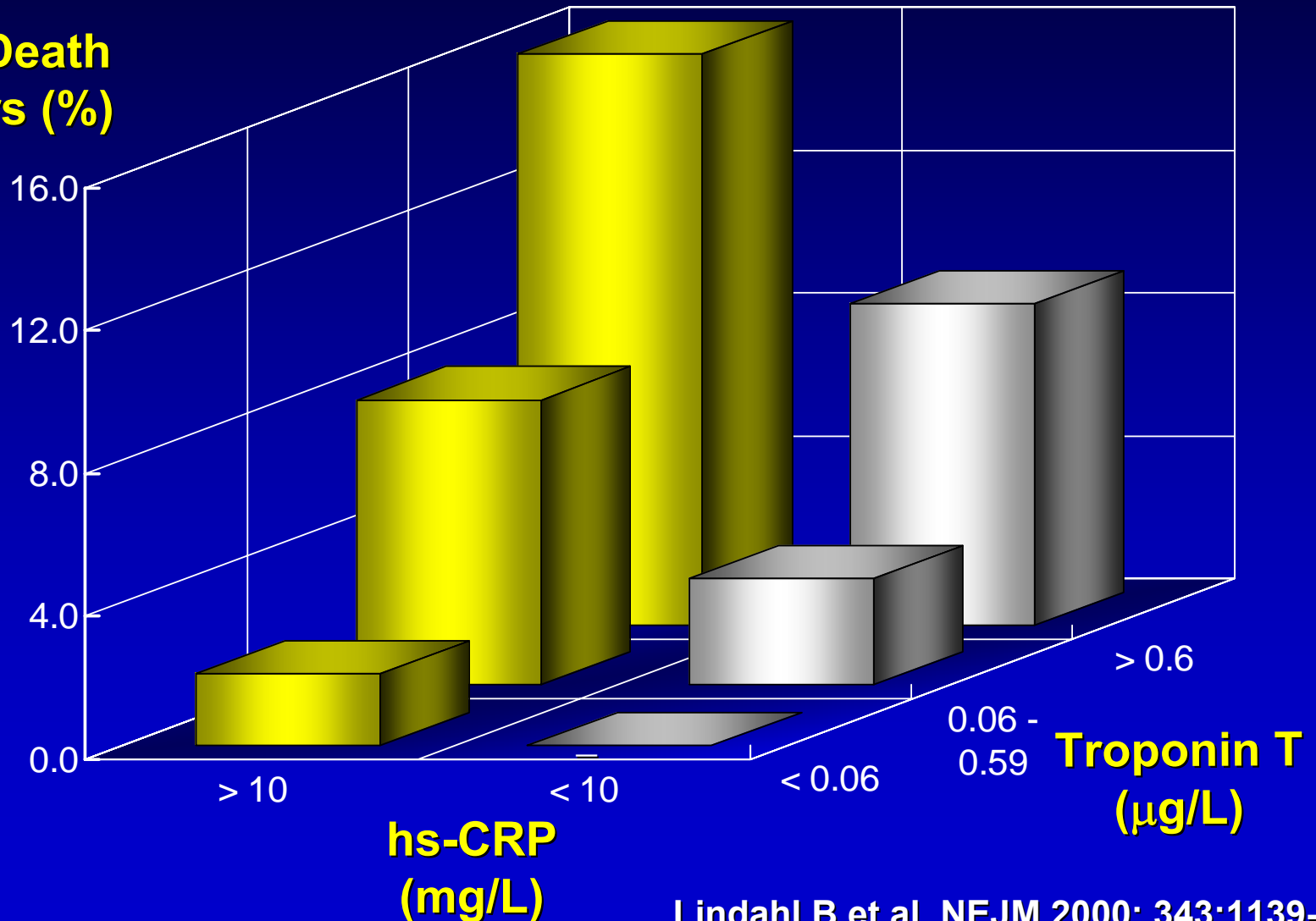


N-proBNP in ACS

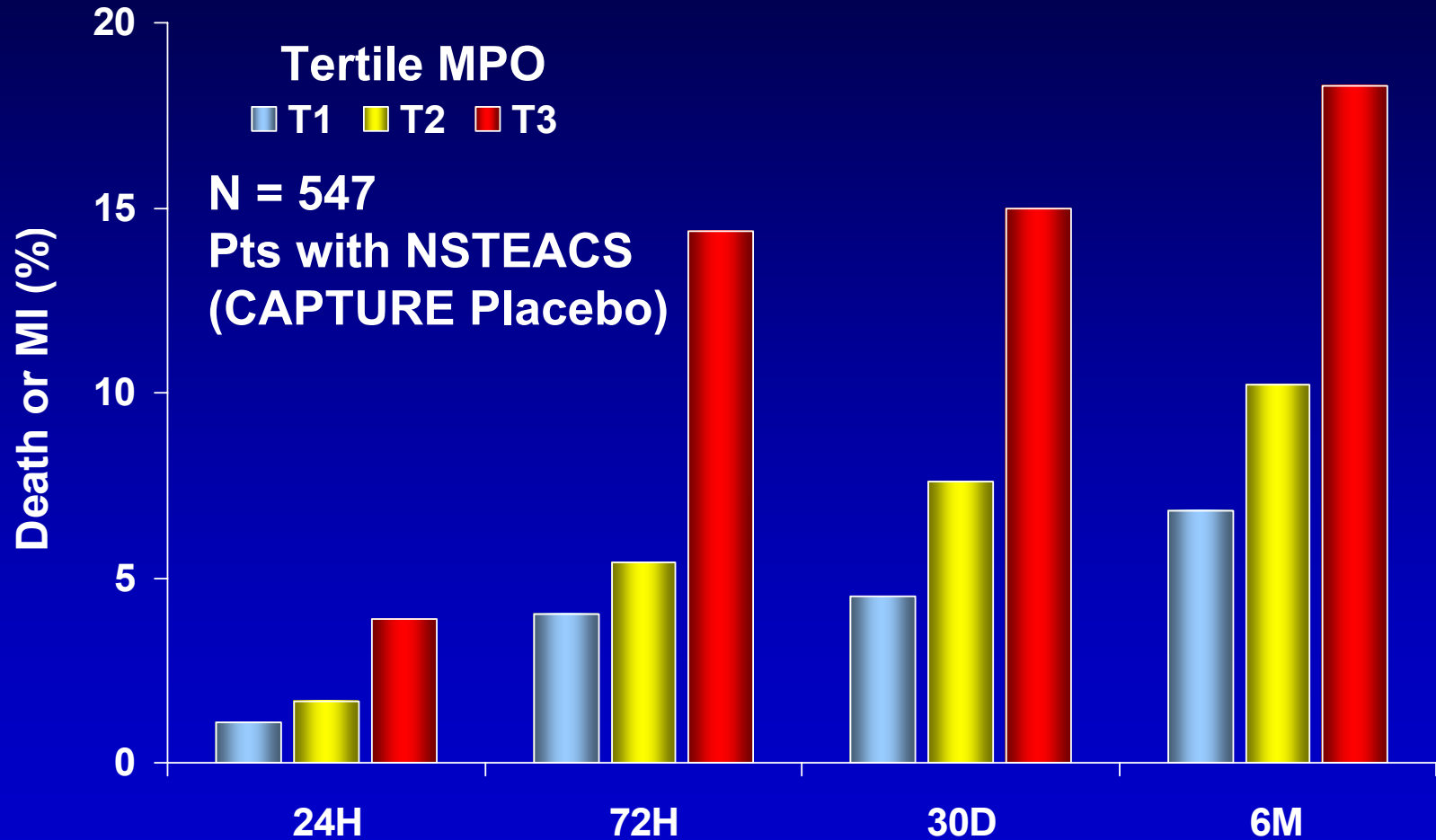


Incidence of Cardiac Death at 2 Years According to hs-CRP and Maximal 24 hour Troponin T Levels

Cardiac Death
at 2 Years (%)

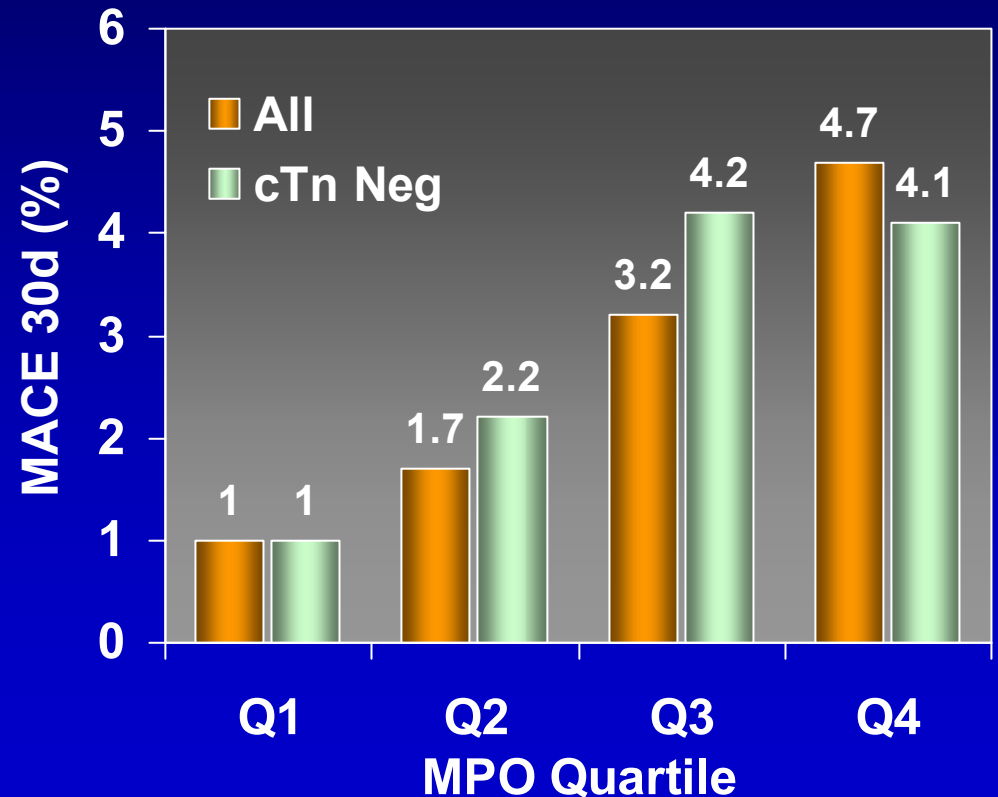
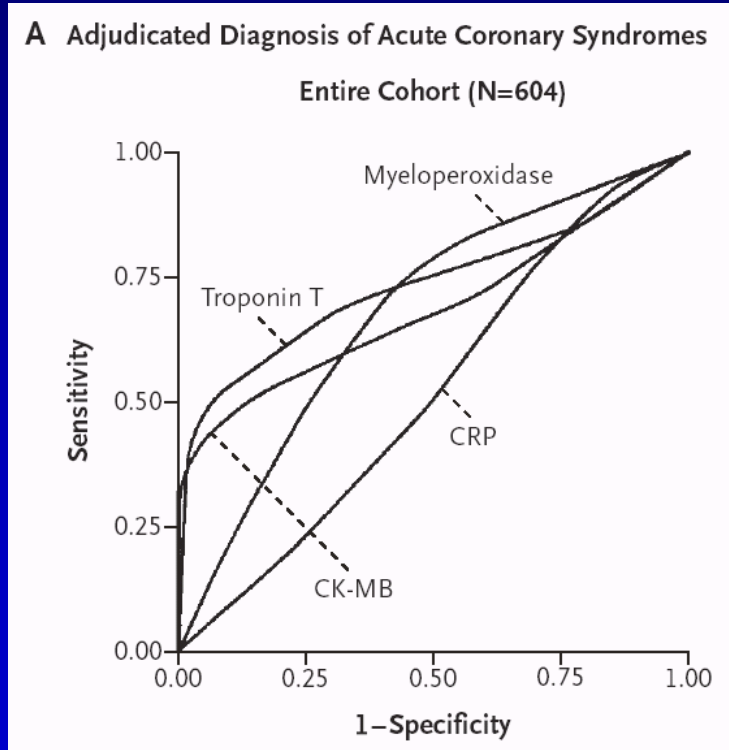


Myeloperoxidase (MPO) in ACS

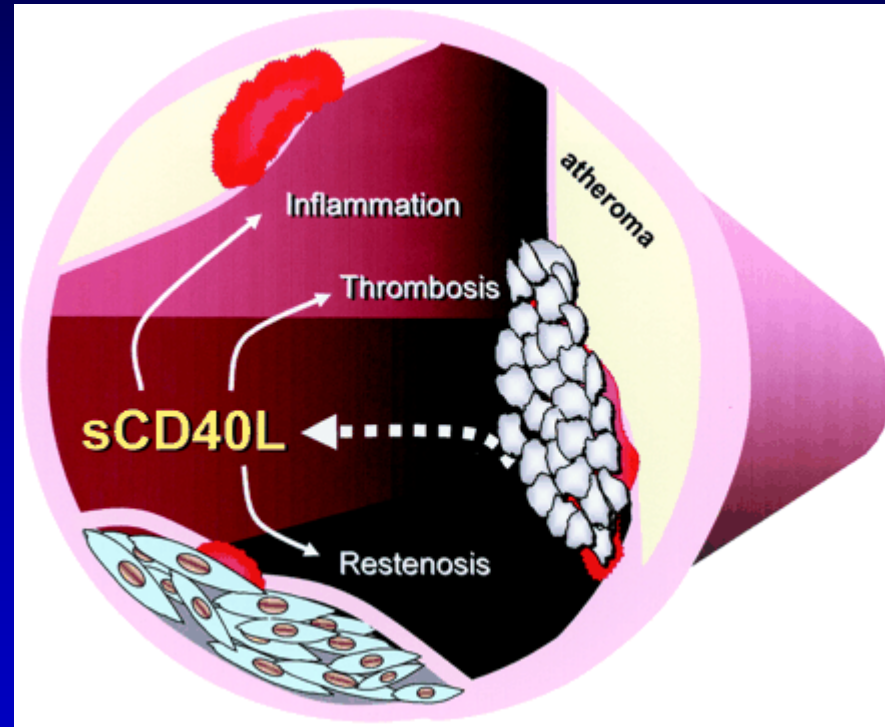
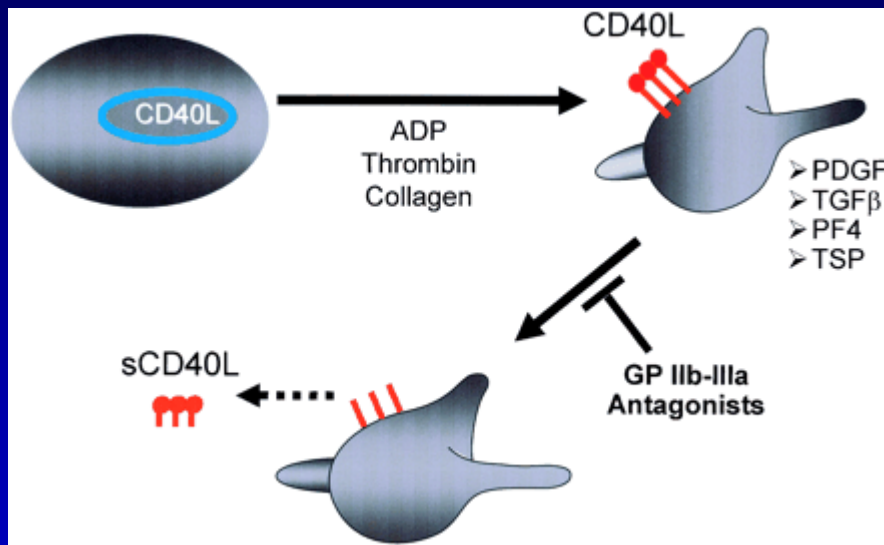


MPO for Eval of Pts with Chest Pain

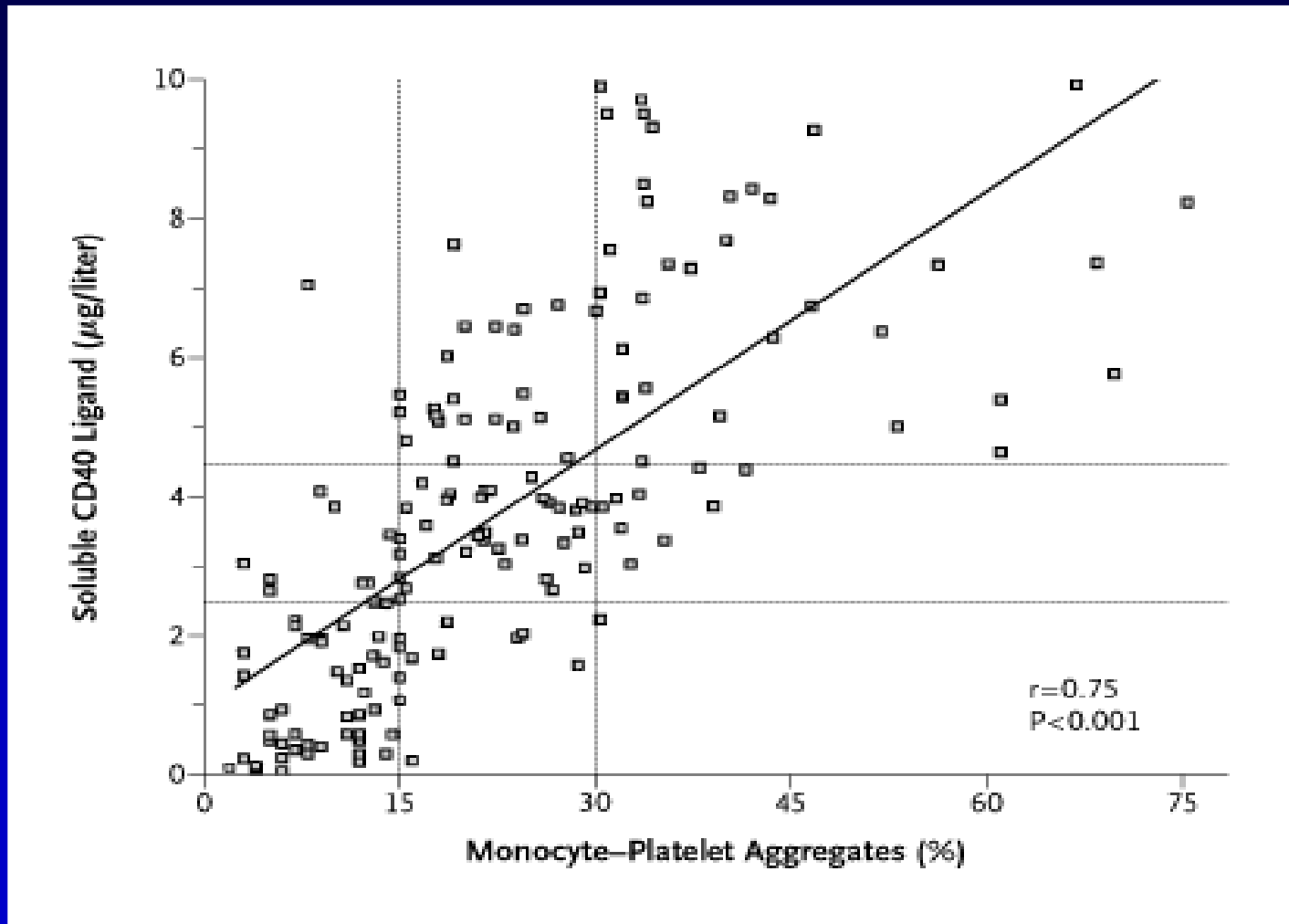
Patients eval in ED within 24h of onset of CP of suspected cardiac origin (N = 640)



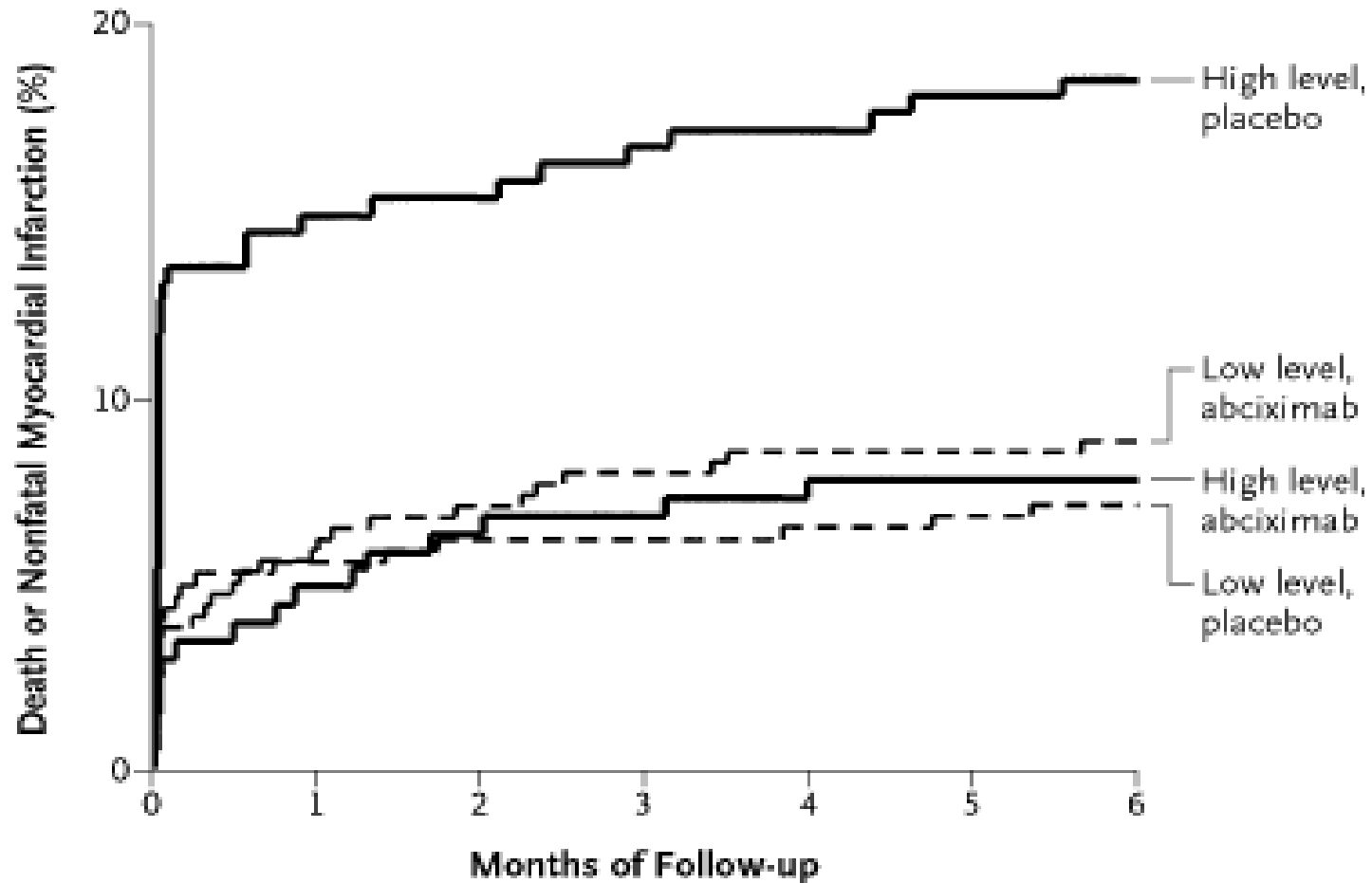
Platelet Derived sCD40L



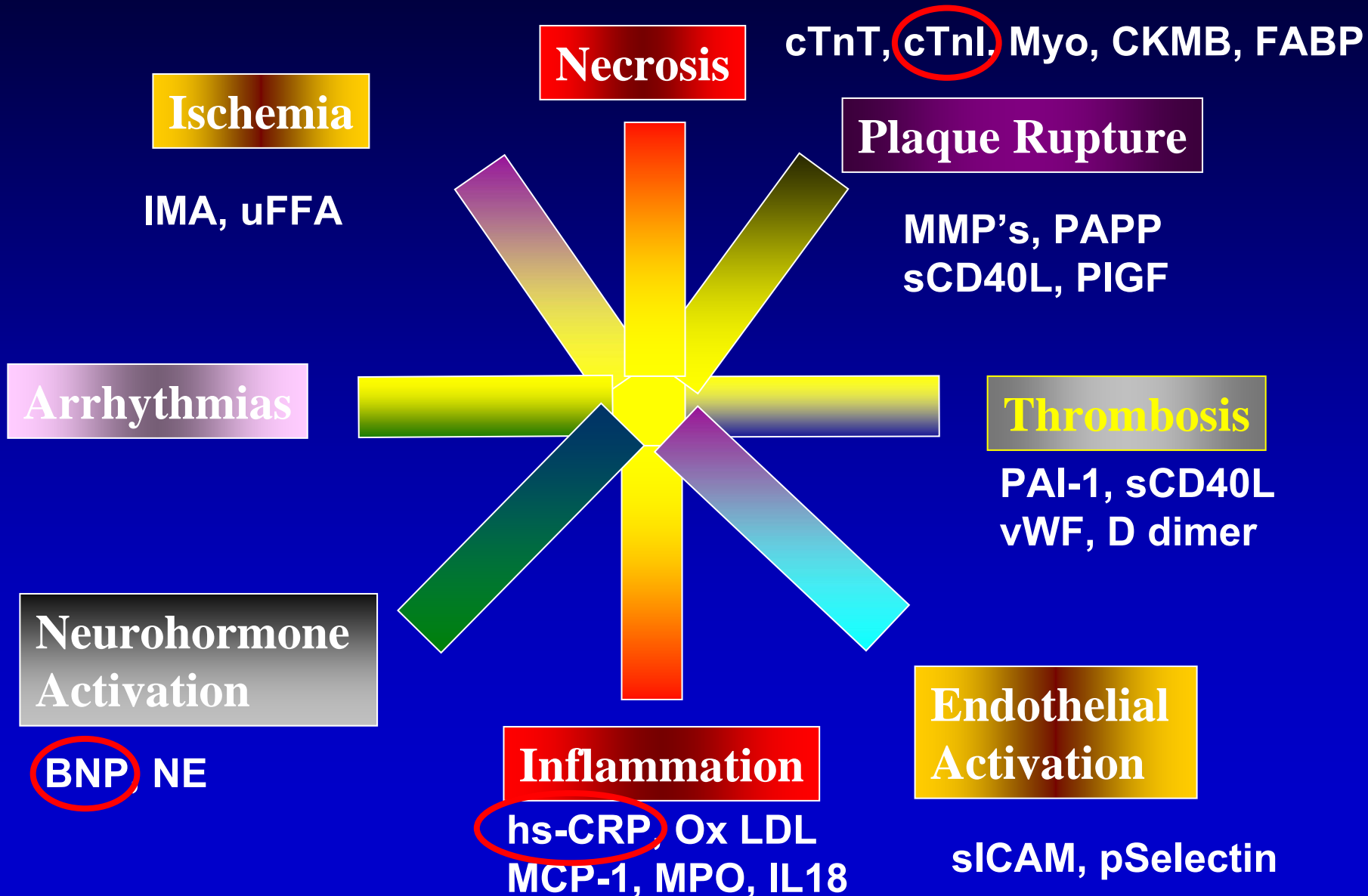
sCD40 Ligand and Platelet Activation



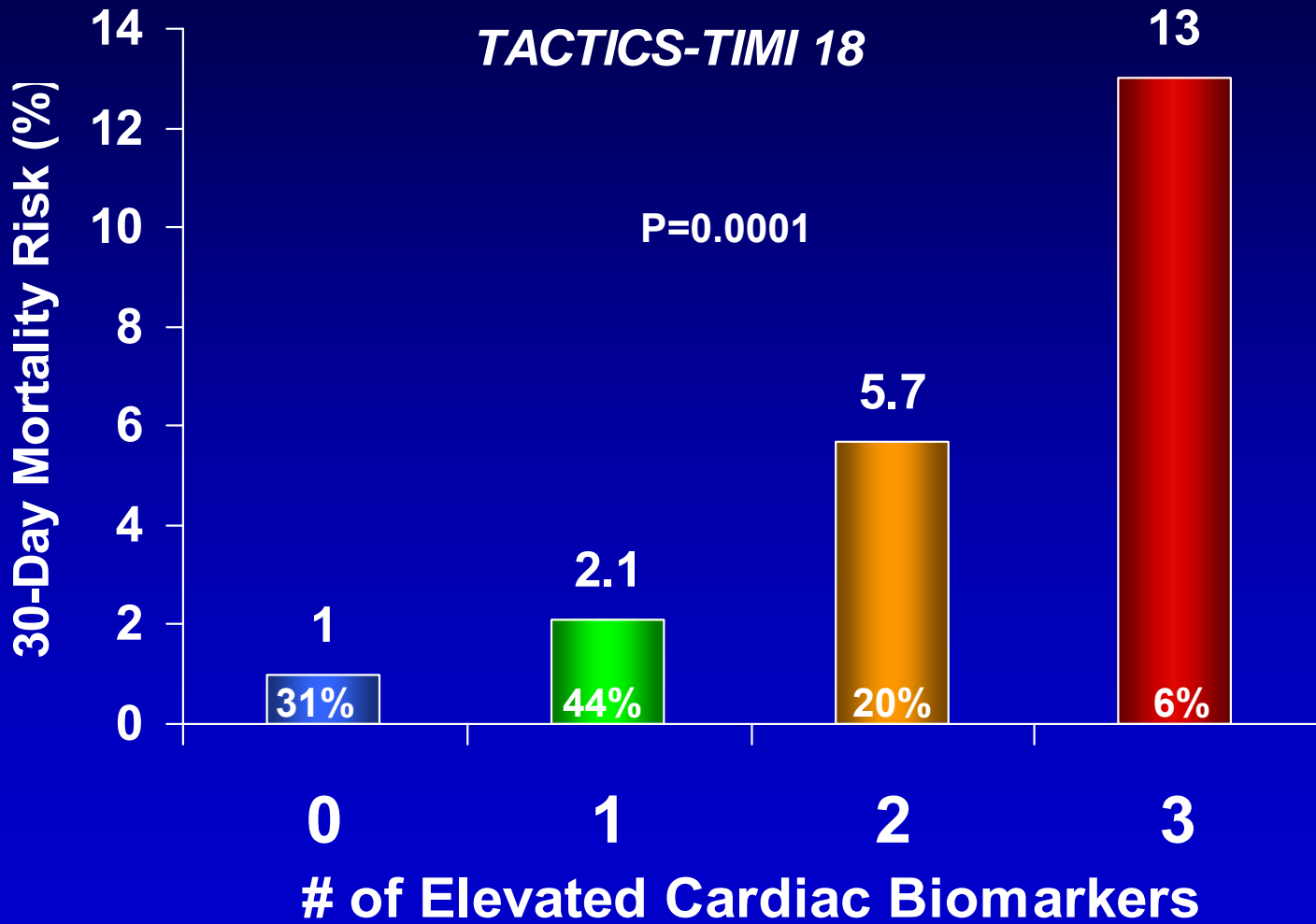
sCD40 L and Abciximab



Multimarker "Profile" in ACS



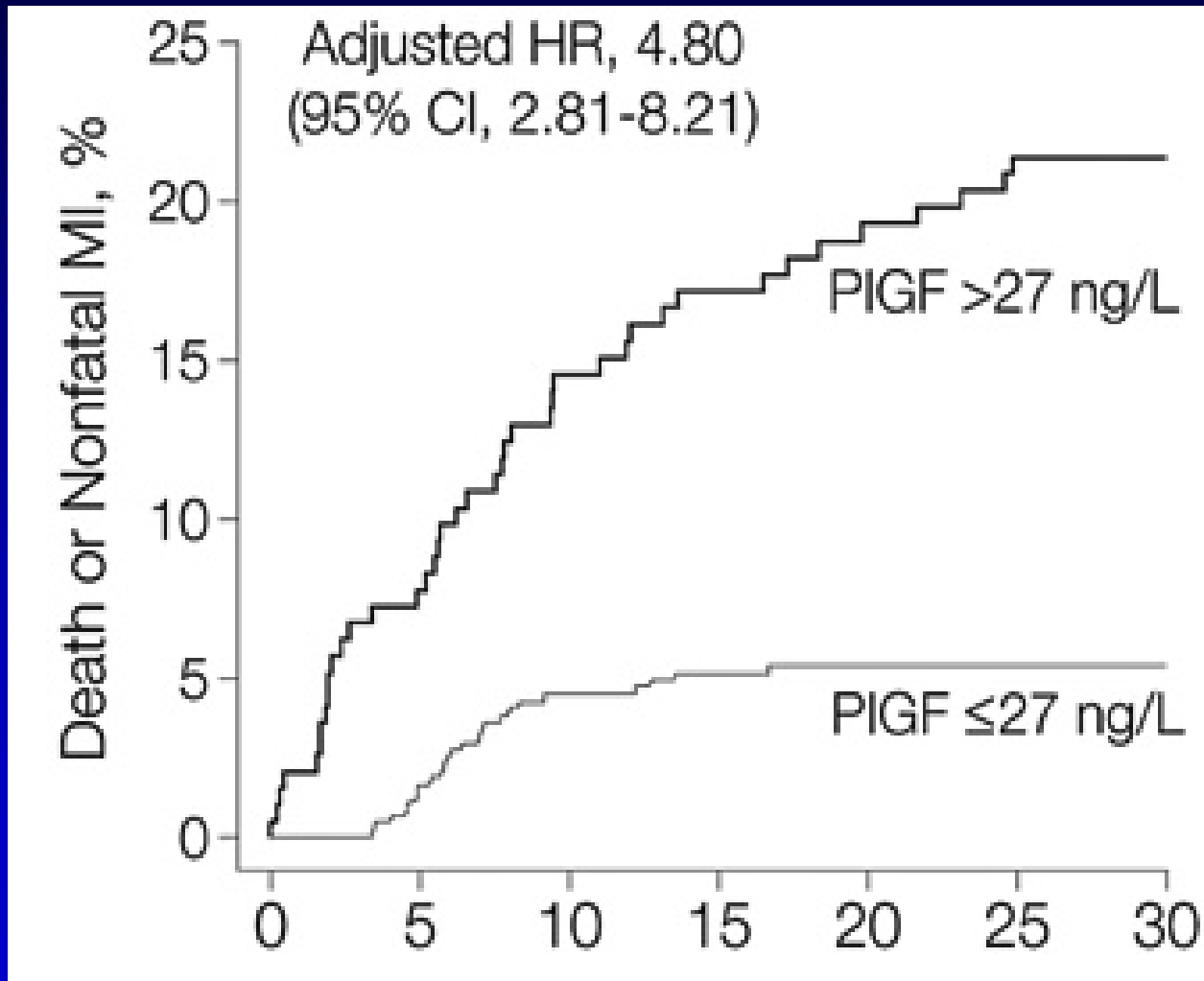
Multimarker Approach: cTnI, CRP, & BNP



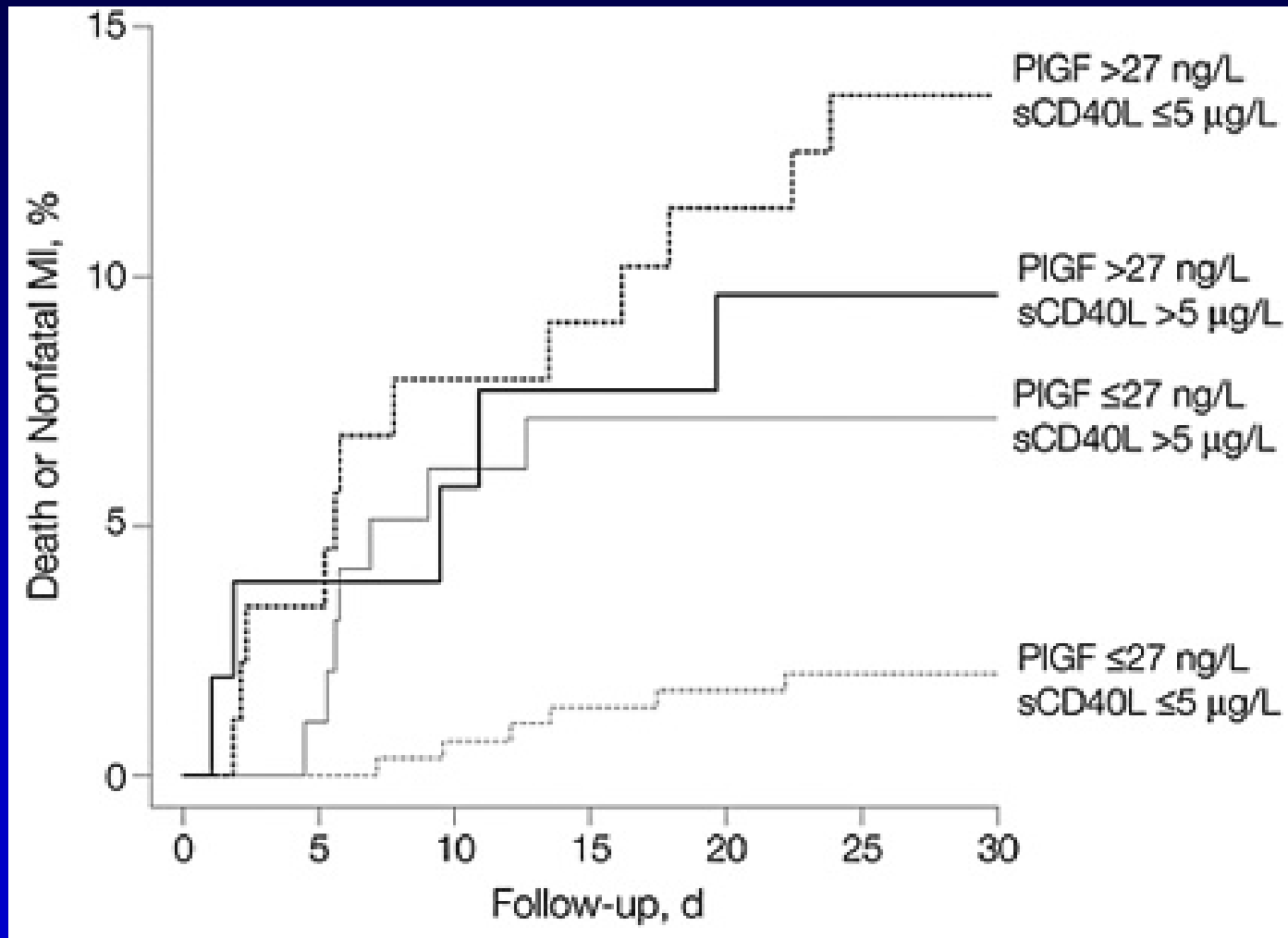
Conclusions

- Hype \neq reality—most reported markers will not be clinically useful
- Troponins and BNP come closest to meeting criteria as ideal biomarkers
- Inflammatory markers show promise, but no clear winner yet
- Multimarker panels will likely emerge as important clinical tools

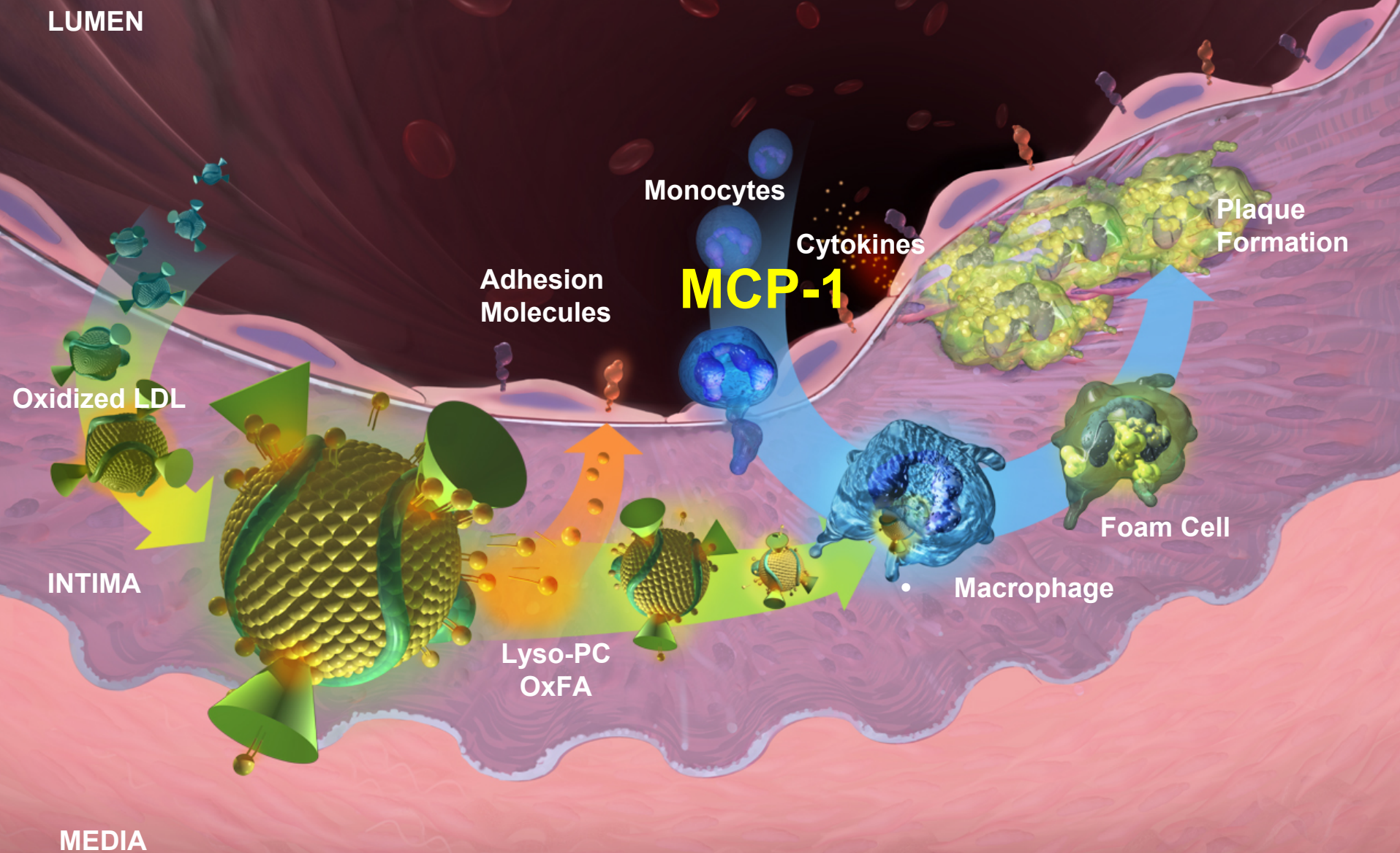
Placental Growth Factor



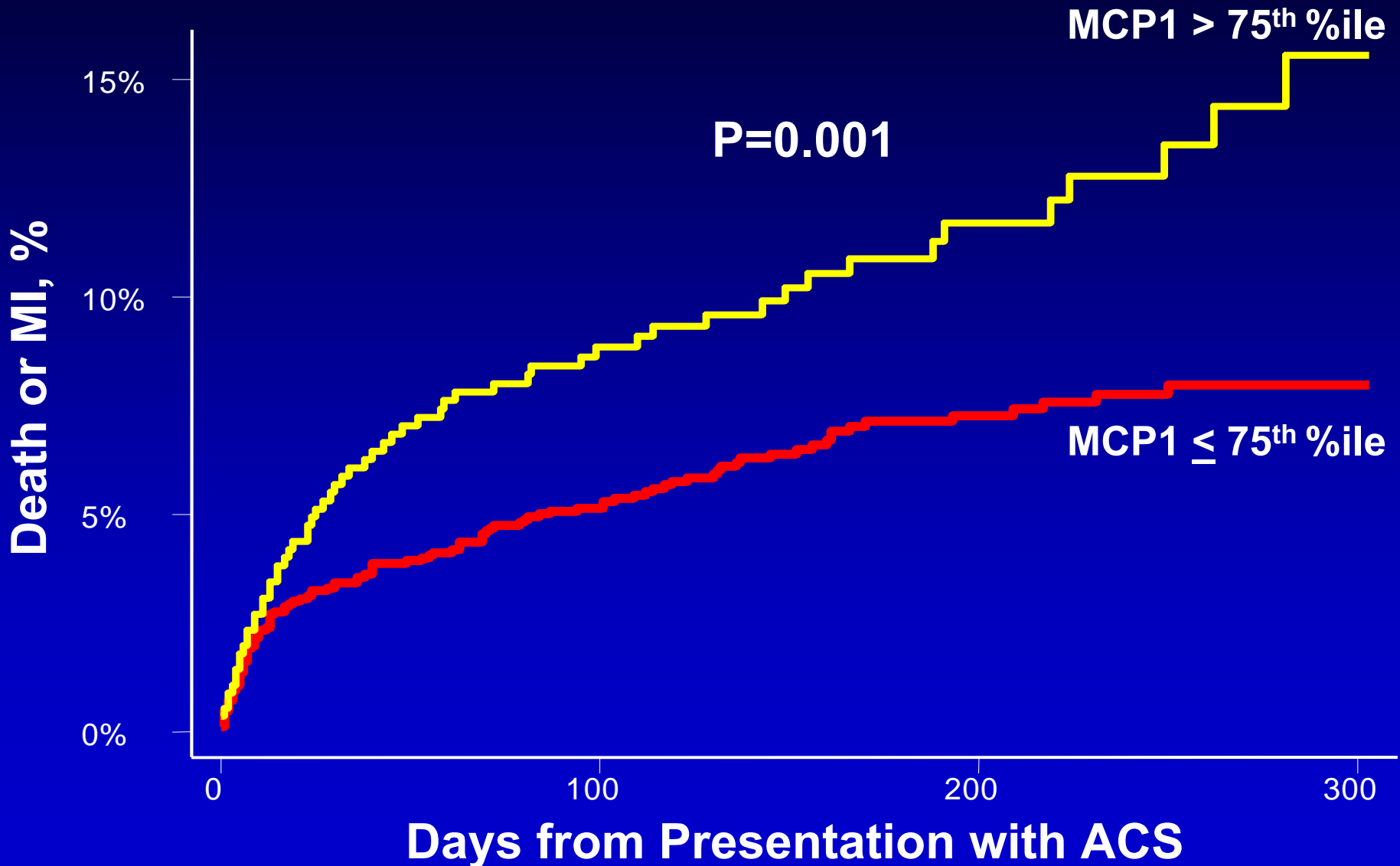
Placental Growth Factor



MCP-1 in Atherosclerosis



MCP-1 in ACS





Association between MCP-1 and CV Risk Factors



Variable	MCP-1 Quartiles (n=3499)				
	Quartile 1	Quartile 2	Quartile 3	Quartile 4	P value
Age (median)	40 [34, 48]	43 [36, 51]	44 [36, 52]	47 [39, 54]	<0.001
White race (%)	22	30	31	34	<0.001
HTN (%)	28	31	35	42	<0.001
DM (%)	8	11	12	14	0.001
Smoking (%)	25	26	32	32	<0.001
Fam Hx CAD (%)	29	32	33	36	0.02
↑ LDL (%)	11	11	14	16	<0.001
Hs-CRP (median)	2.4 [1, 6.1]	2.7 [1.3, 6.5]	3.0 [1.4, 8.7]	3.6 [1.4, 8.7]	<0.001



MCP-1 and Subclinical Atherosclerosis

