Optimizing Outcomes of Primary PCI: From CADILLAC to HORIZONS

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CADILLAC: Enrollment

AMI <12 hours, any age, cardiogenic shock excluded
n=2,681 at 76 centers in N.A., S.A. and Europe

Angiography

? met angiographic criteria

No

Registry (n=599)
PTCA - 127 (5%)
Stent - 142 (5%)
CABG - 140 (5%)
Med Rx - 190 (7%)
Randomized:
89% of all PCI
94% of all stent

Yes

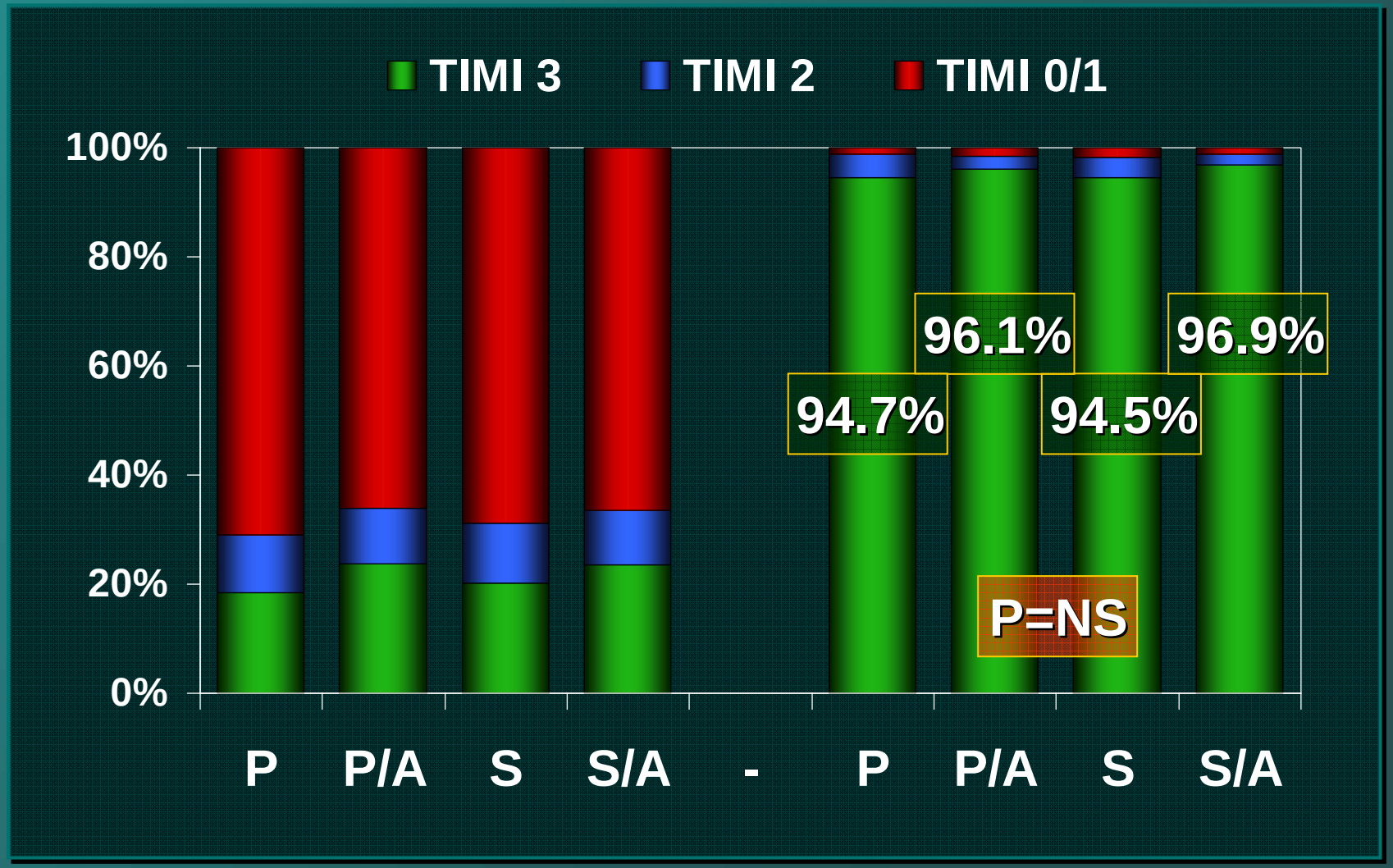
n=2,082 (78%)

Randomize

- Primary PTCA (n=518)
- Primary PTCA + Abciximab (n=528)
- MultiLink stent (n=512)
- MultiLink stent + Abciximab (n=524)

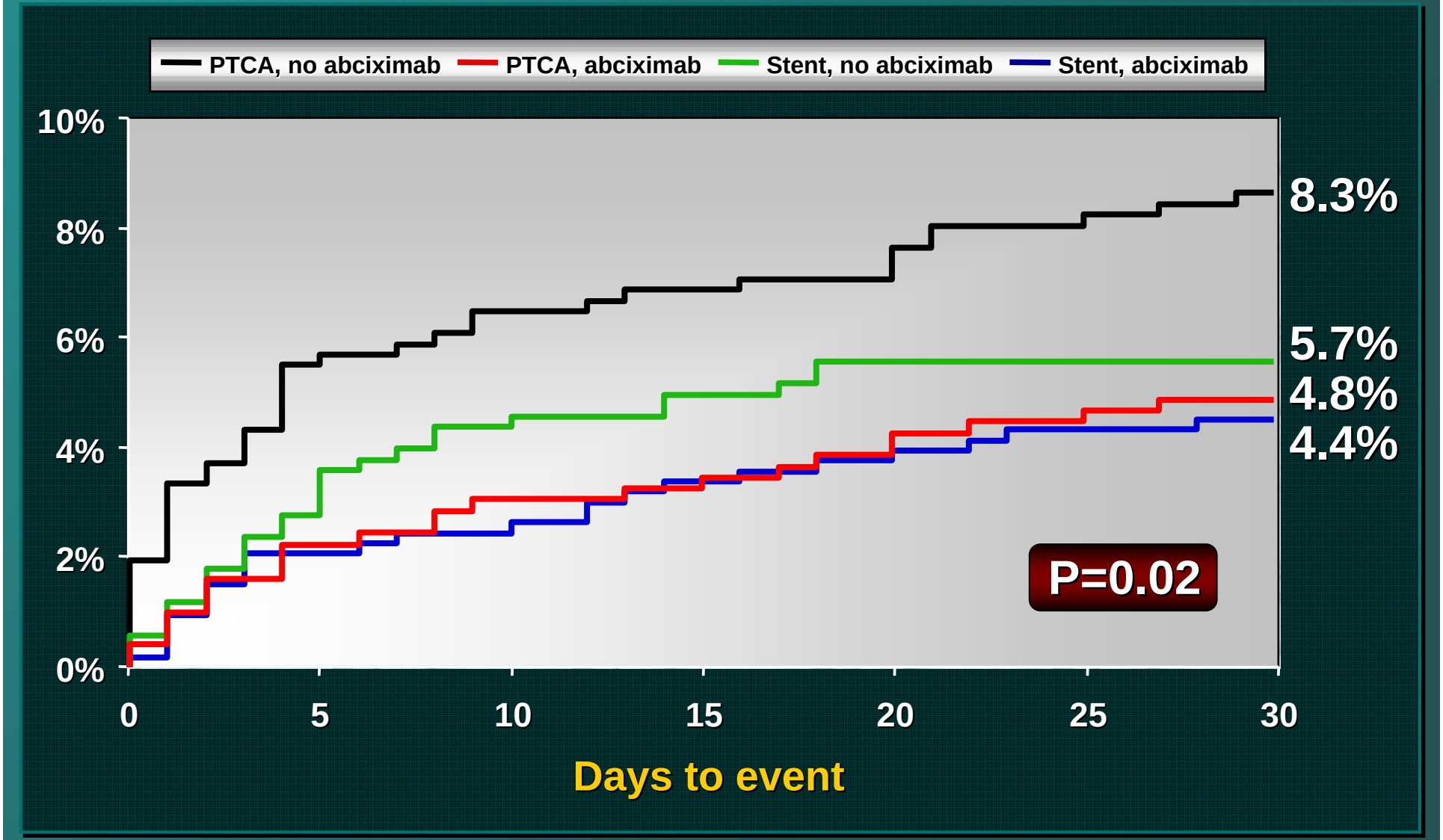
Stone GW et al. NEJM 2002;346:957-66

CADILLAC: TIMI Flows



Stone GW et al. NEJM 2002;346:957-66

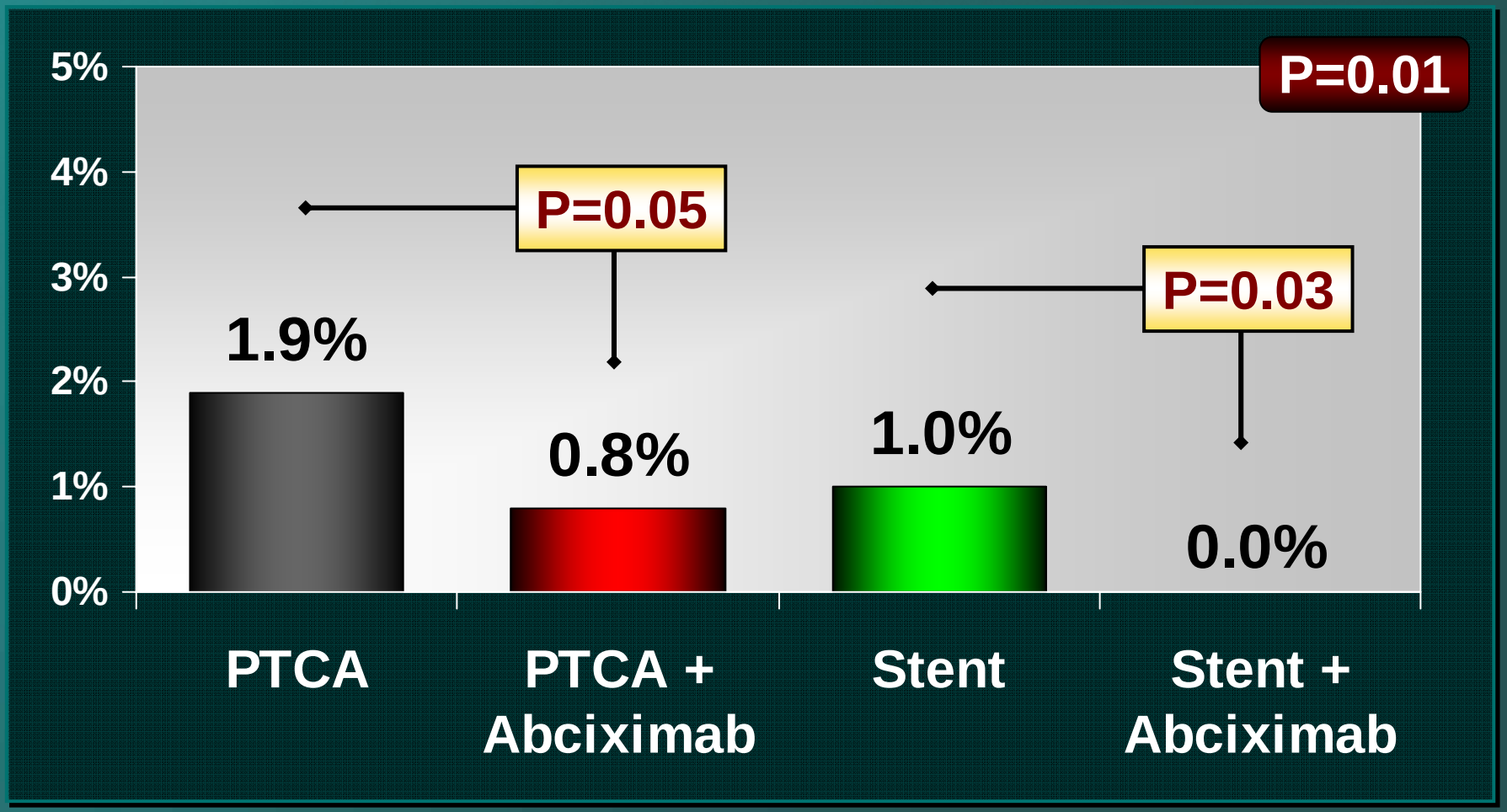
CADILLAC: 30-Day MACE



Stone GW et al. NEJM 2002;346:957-66

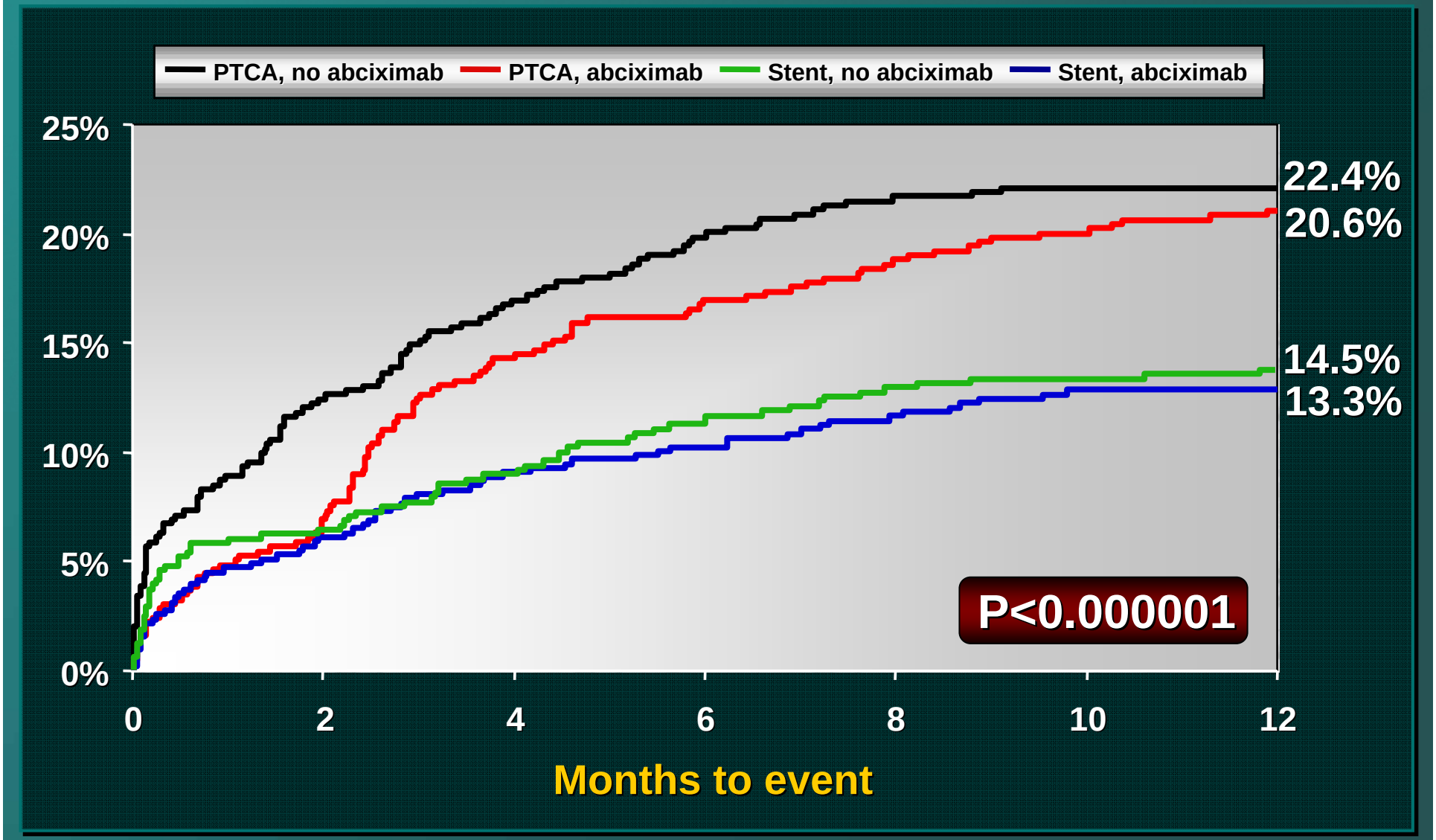
CADILLAC: Subacute Thrombosis

- 30 days -



Stone GW et al. NEJM 2002;346:957-66

CADILLAC: 12 Month MACE



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Primary PCI After CADILLAC

What problems are left?

Survival and left ventricular function

- Reperfuse faster
- Approaches to limit myocardial and/or reperfusion injury
- Cell Rx

Bleeding and thrombocytopenia

Caused by invasive procedures + ASA, Plavix, UFH and GP IIb/IIIa inhibitors

Restenosis and IA reocclusion

From BMS

⇓

⇑ Recurrent ischemia

⇑ Rehosp

⇑ TVR

⇓ QOL

⇑ costs

HORIZONS

HORIZONS AMI Trial

3400 randomized pts undergoing primary PCI

Anti-thrombotic therapy
Randomize 1:1

- UFH + IIb/IIIa inhibitor
- Bivalirudin + bail-out IIb/IIIa

Hypothesis: Bivalirudin compared to UFH + routine IIb/IIIa will reduce the composite rate of death, reinfarction, TVR, stroke and major bleeding at 30-days

Target vessel stenting
Randomize 3:1

- TAXUS stent
- Bare metal Express stent

Hypothesis: Use of the polymer-based slow-release paclitaxel-eluting TAXUS stent will safely reduce the 1-year rate of ischemia-driven TVR

Sponsor: The Cardiovascular Research Foundation (PI: Gregg W. Stone), with unrestricted grant support from: Boston Scientific & The Medicine's Co.

Why is bleeding important?

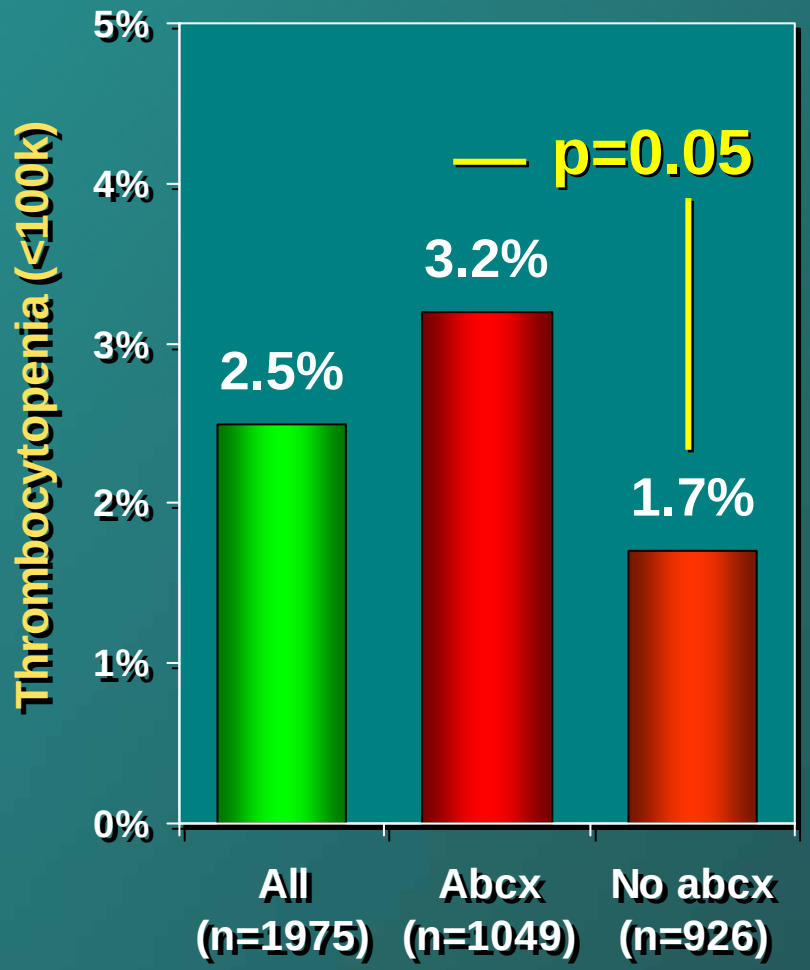
CADILLAC: Impact of Bleeding

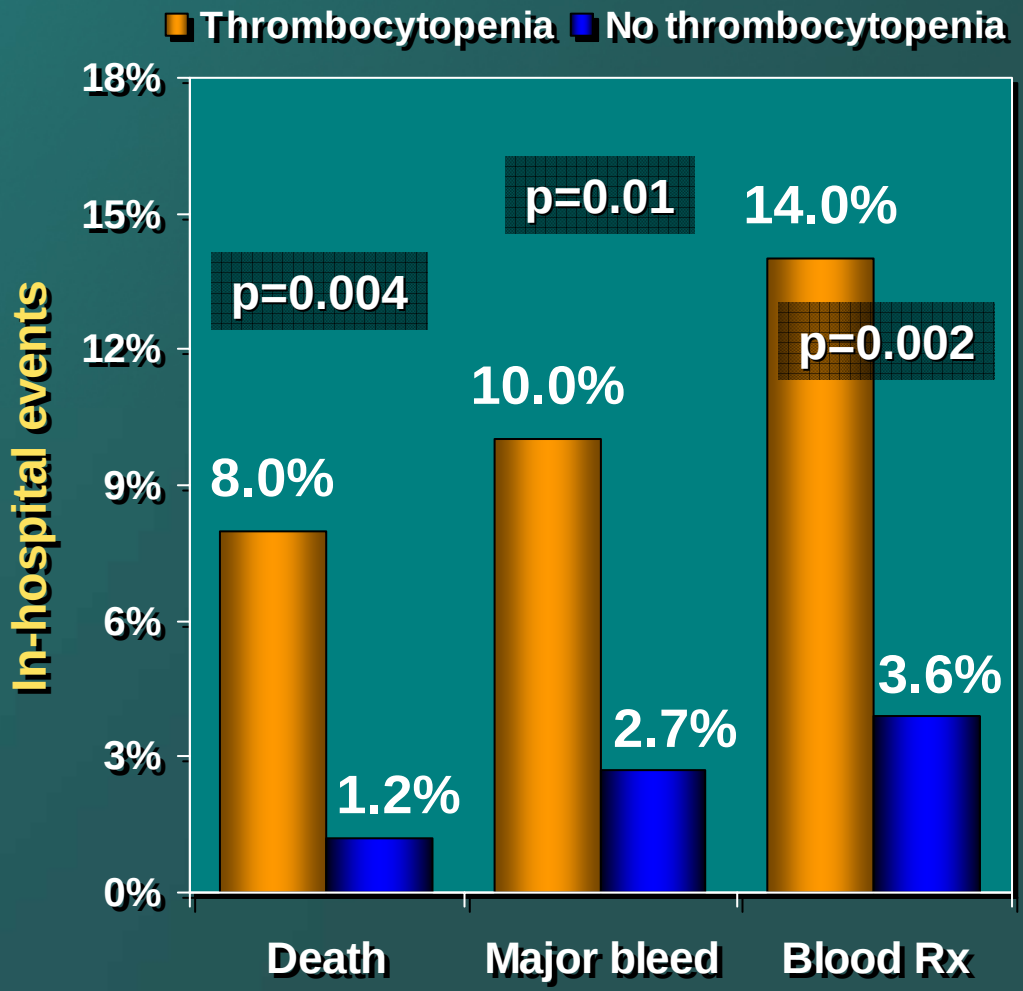
Any bleeding occurred in 446/2082 pts = 21.4%

Moderate or severe bleeding occurred in 60 pts = 2.9%

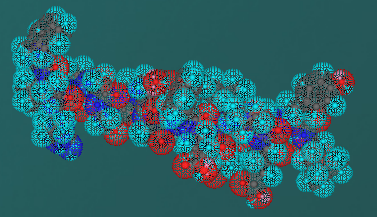
In-hospital outcomes	Major bleed	No major bleed	P-value
Death	5.0%	1.5%	0.07
Stroke	3.3%	0.4%	0.03
Subacute thrombosis	3.3%	0.6%	0.06
Ischemic TVR	11.7%	2.1%	0.0004
LOS (days)	5.9	3.5	<0.0001
Cost ($)	18,684	11,561	<0.0001

CADILLAC: Impact of Acquired Thrombocytopenia (<100,000)





Bleeding Complications



	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
Large hematoma	0.8	2.5	<0.001
Retroperitoneal hemorrhage	0.2	0.5	0.06
Major organ bleeding	0.5	1.5	<0.001
Intracranial hemorrhage	0	0.1	1.00
Thrombocytopenia (<100K)	0.7	1.7	<0.001
Transfusion	1.7	2.5	0.02

Bivalirudin During Primary PCI

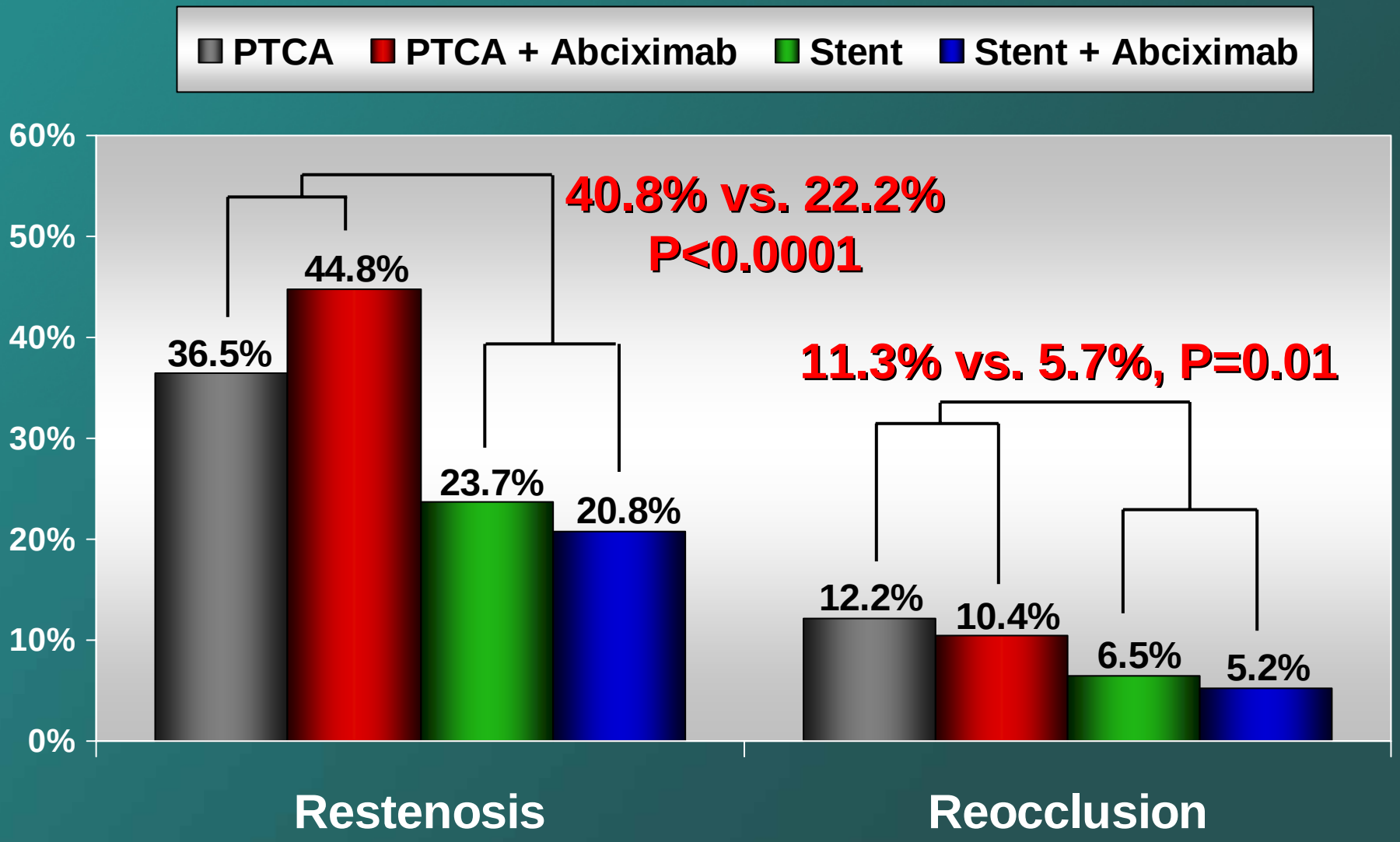
Illinois Heart experience (n=91)

"Real world", including 17.6% cardiogenic shock

GP IIb/IIIa inhibitor used	2	(2.2%)
TIMI-3 flow established	89	(97.8%)
30 day events		
Death	3	(3.3%)
Reinfarction	0	
Ischemic TVR	0	
Recurrent ischemia	0	
Stroke	0	
Major bleeding	0	
Transfusion	0	
Pseudoaneurysm	1	(1.1%)

Stella JF
J Inv Cardiol
2004;16:451-4

CADILLAC: Angiographic Restenosis



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Playing Devil's Advocate

Why is a Trial of Drug-eluting Stents in Primary Angioplasty Necessary?

- **Drug-eluting stents in AMI…**
  - **May not be necessary**
  - **May not be cost-effective**
  - **Need to be proven safe**

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Why is a Trial of Drug-eluting Stents in Primary Angioplasty Necessary?

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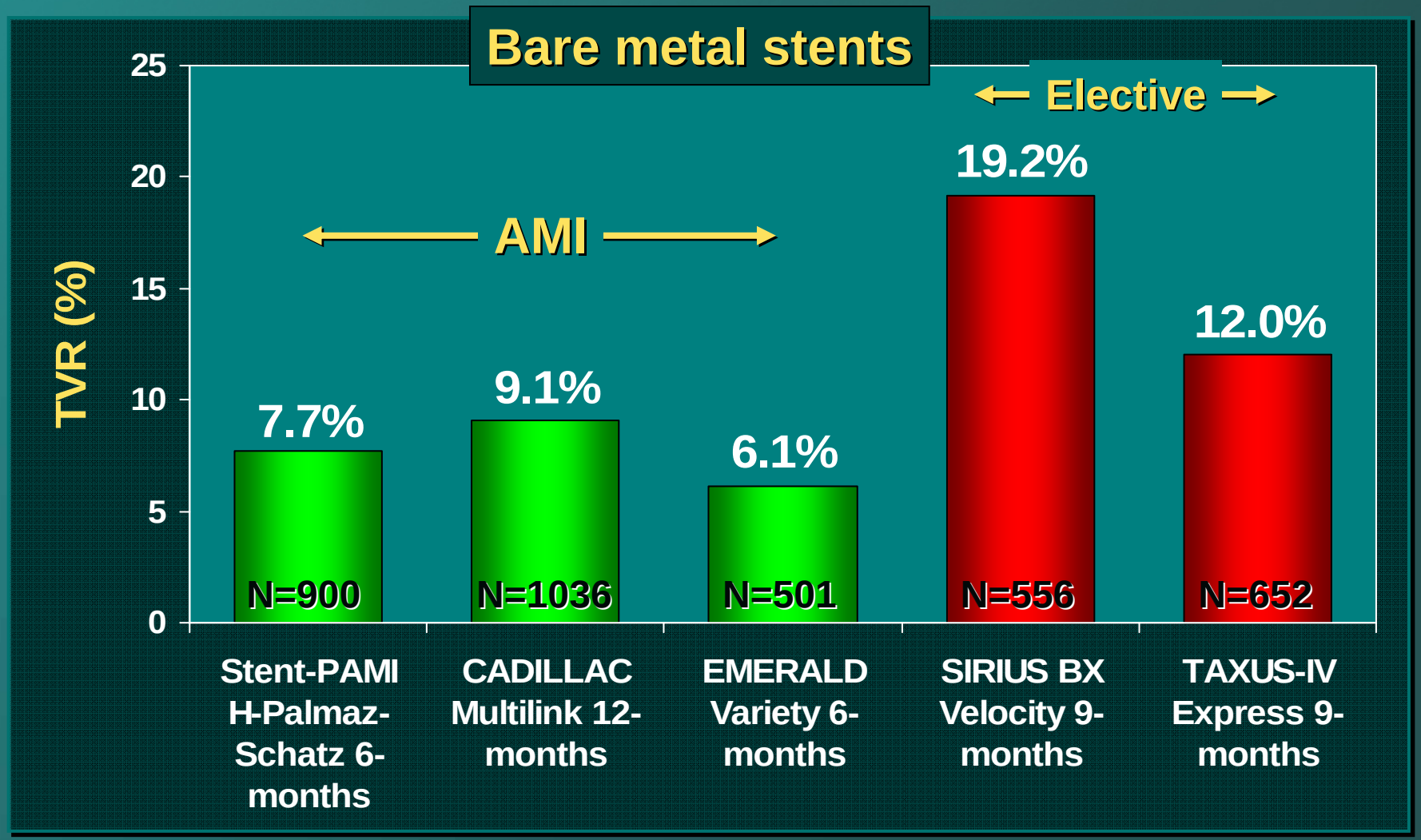
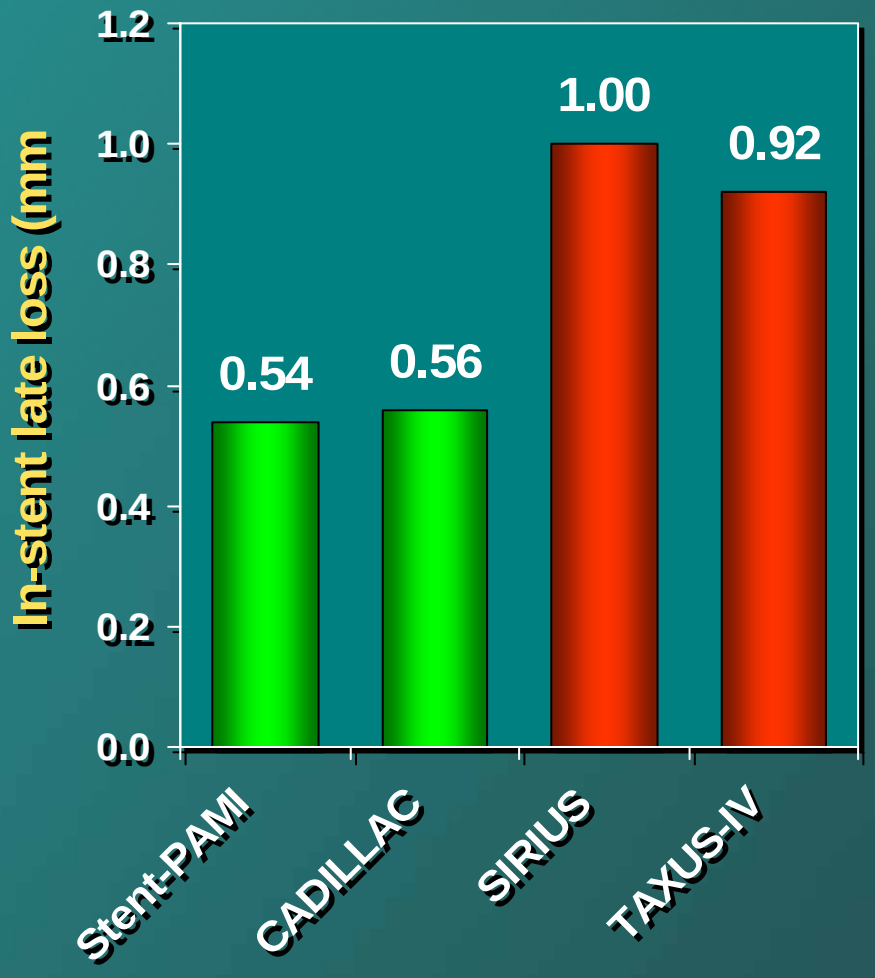
    - **Bare metal stents work pretty well for primary PCI in AMI!**

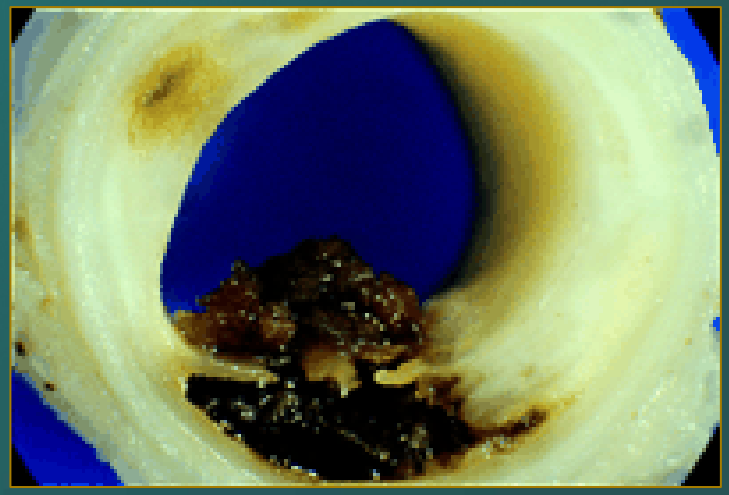
Clinical Restenosis (TVR) after Primary Stenting in AMI



Late Loss After Bare Metal Stenting

in Acute Myocardial Infarction



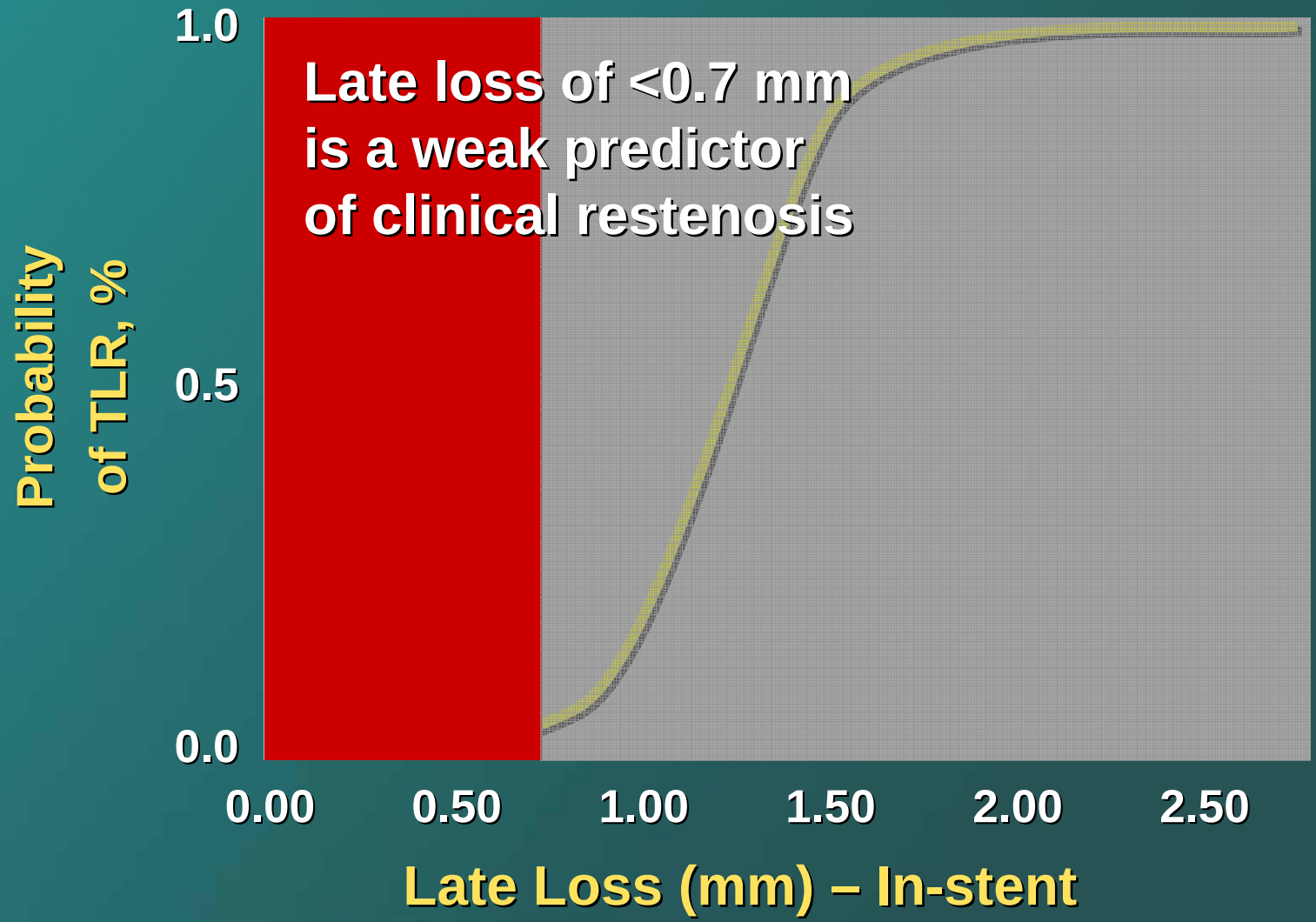


Plaque rupture

The culprit plaque in AMI has relatively low plaque mass and a potentially lower restenosis rate

TAXUS IV

TLR as a Function of Late Loss



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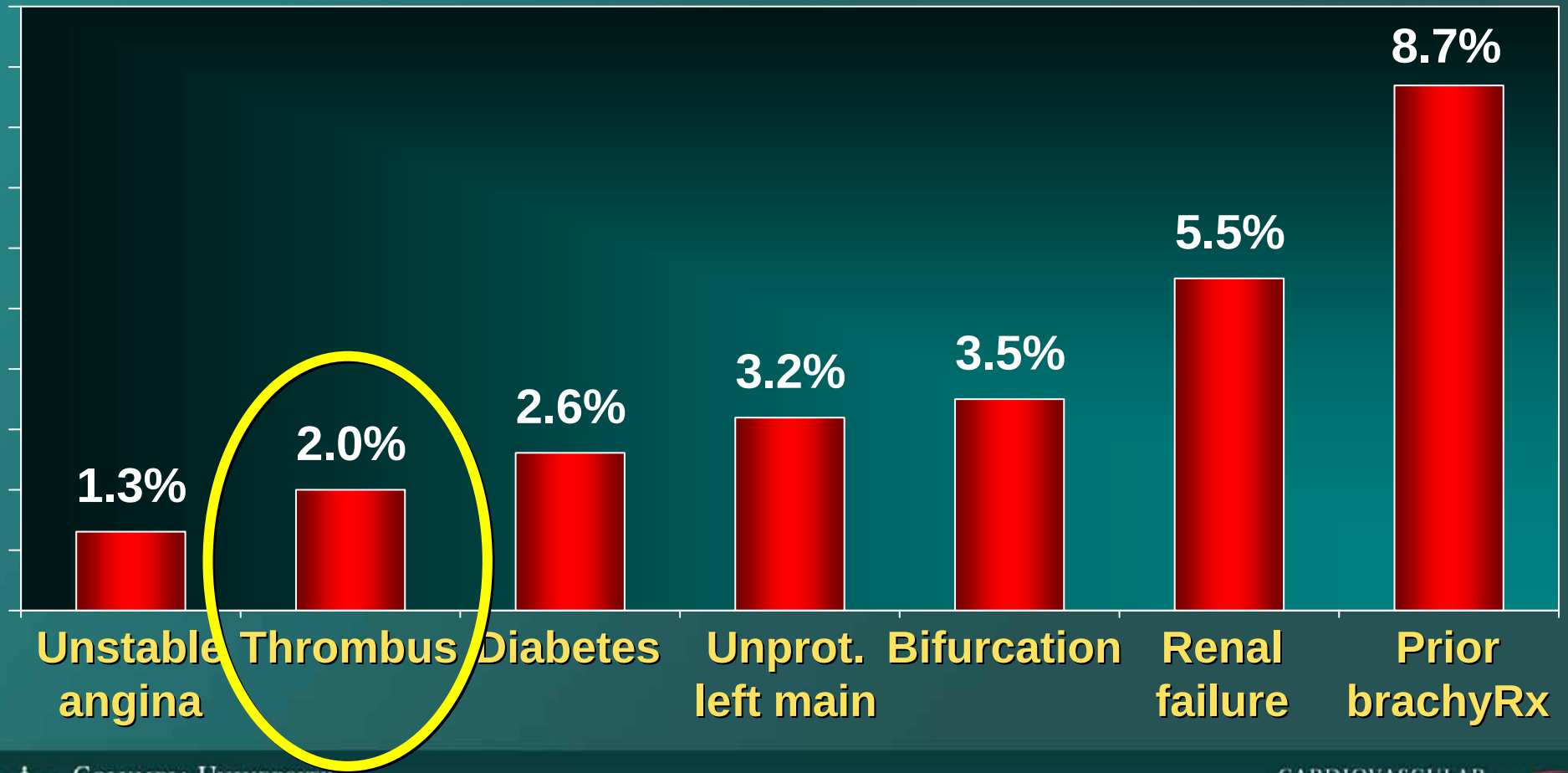
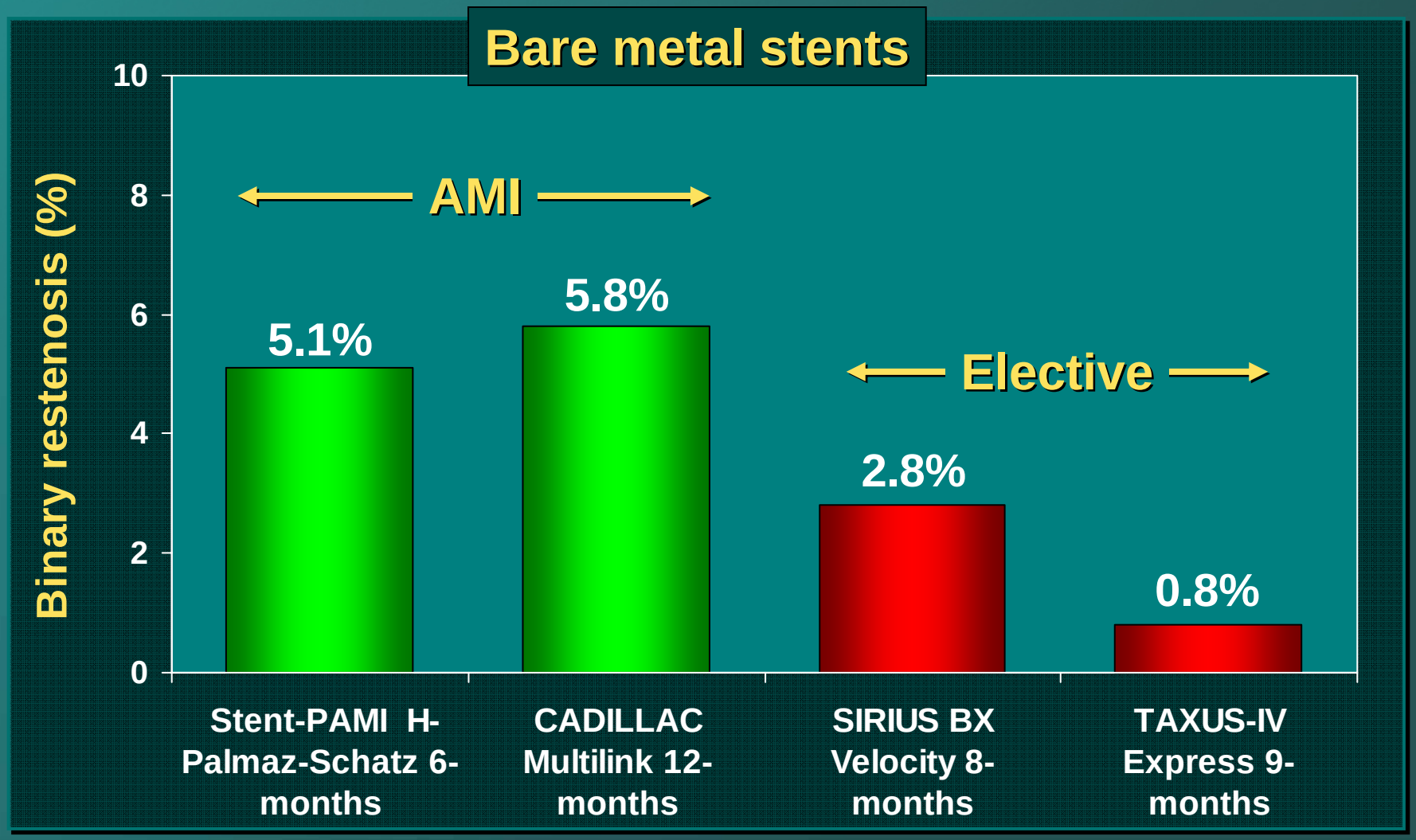
Centro Cuore Columbus

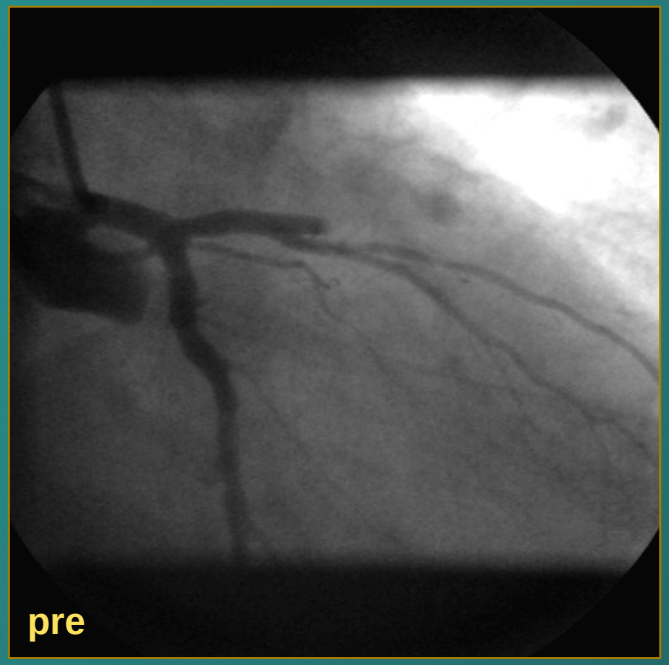
Stent Thrombosis in High Risk Groups

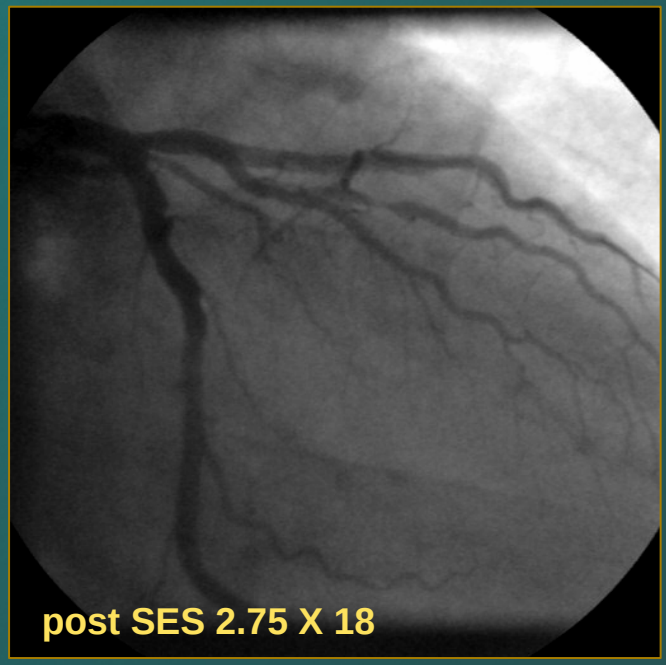
Stent thrombosis occurred in 27/2229 pts (1.2%) treated with DES (SES or PES)



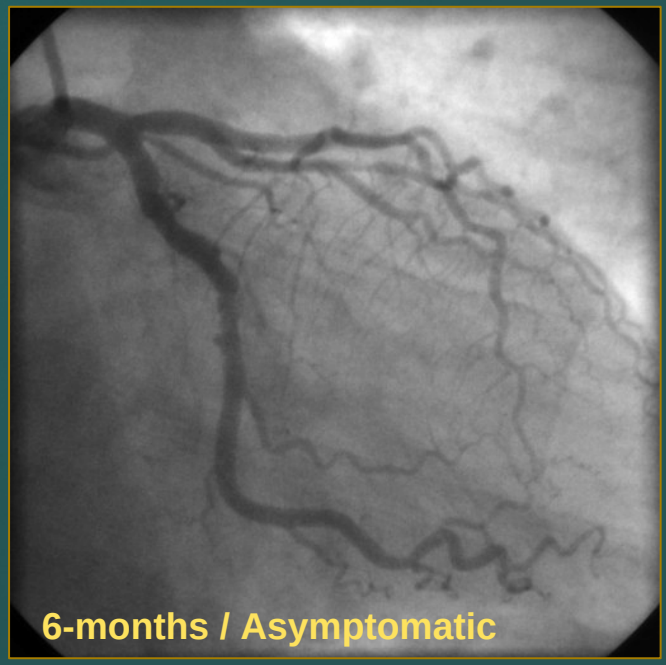
Target Vessel Reocclusion after Primary Stenting in AMI







- 64 year old male
- Ex-smoker, hypertension
- 3.5 hrs chest pain
- Anterior ST elevation



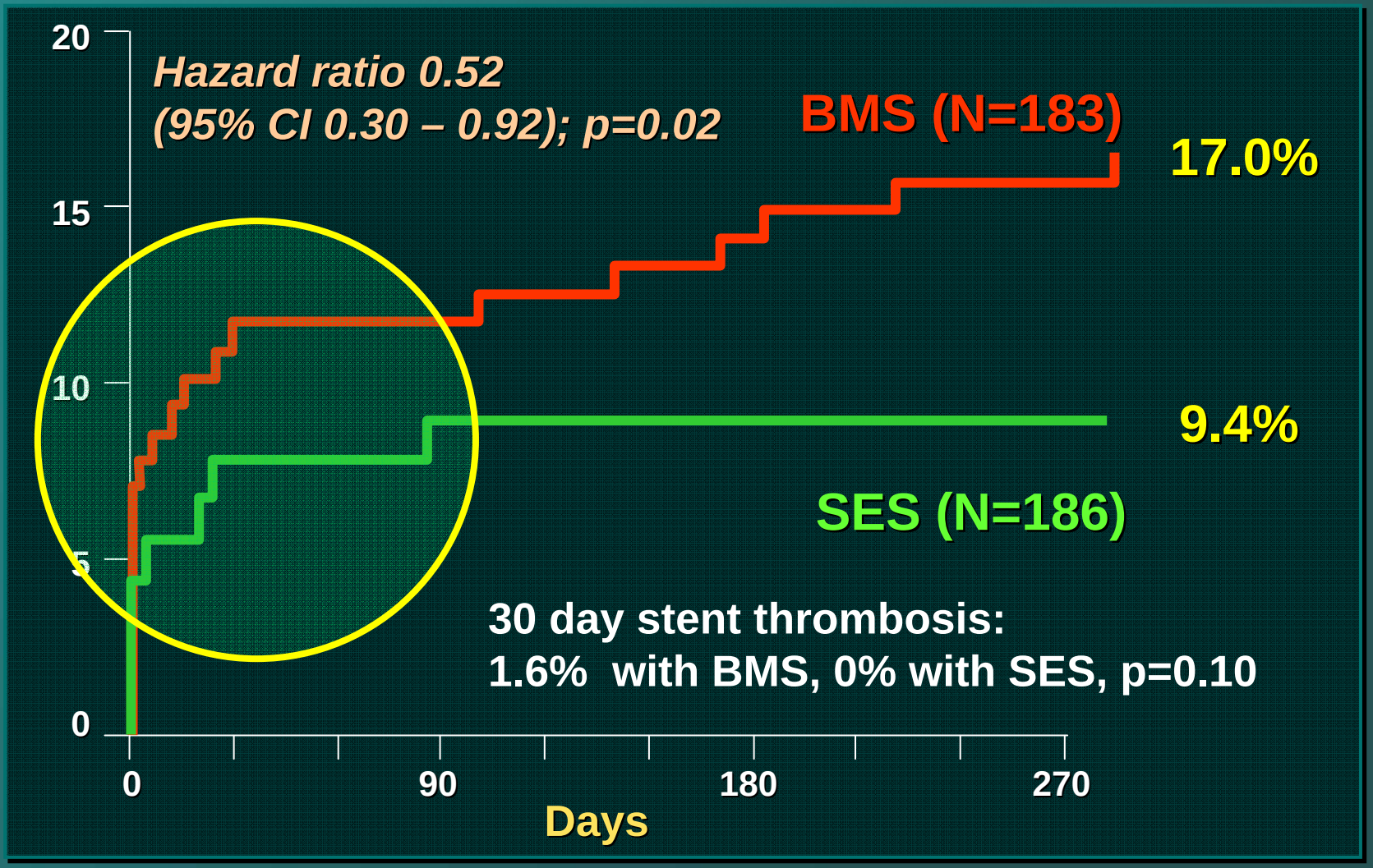
RESEARCH Registry: AMI

6 Month Events

	BMS (N=183)	SES (N=186)	P value
Death	8.2%	8.3%	NS
Death or ReMI	10.4%	8.8%	NS
TVR	8.2%	1.1%	<0.01
MACE	17.0%	9.4%	0.02

Lemos P. et al. JACC 2004;43:704-8

Cumulative Incidence of Death, MI, or TVR



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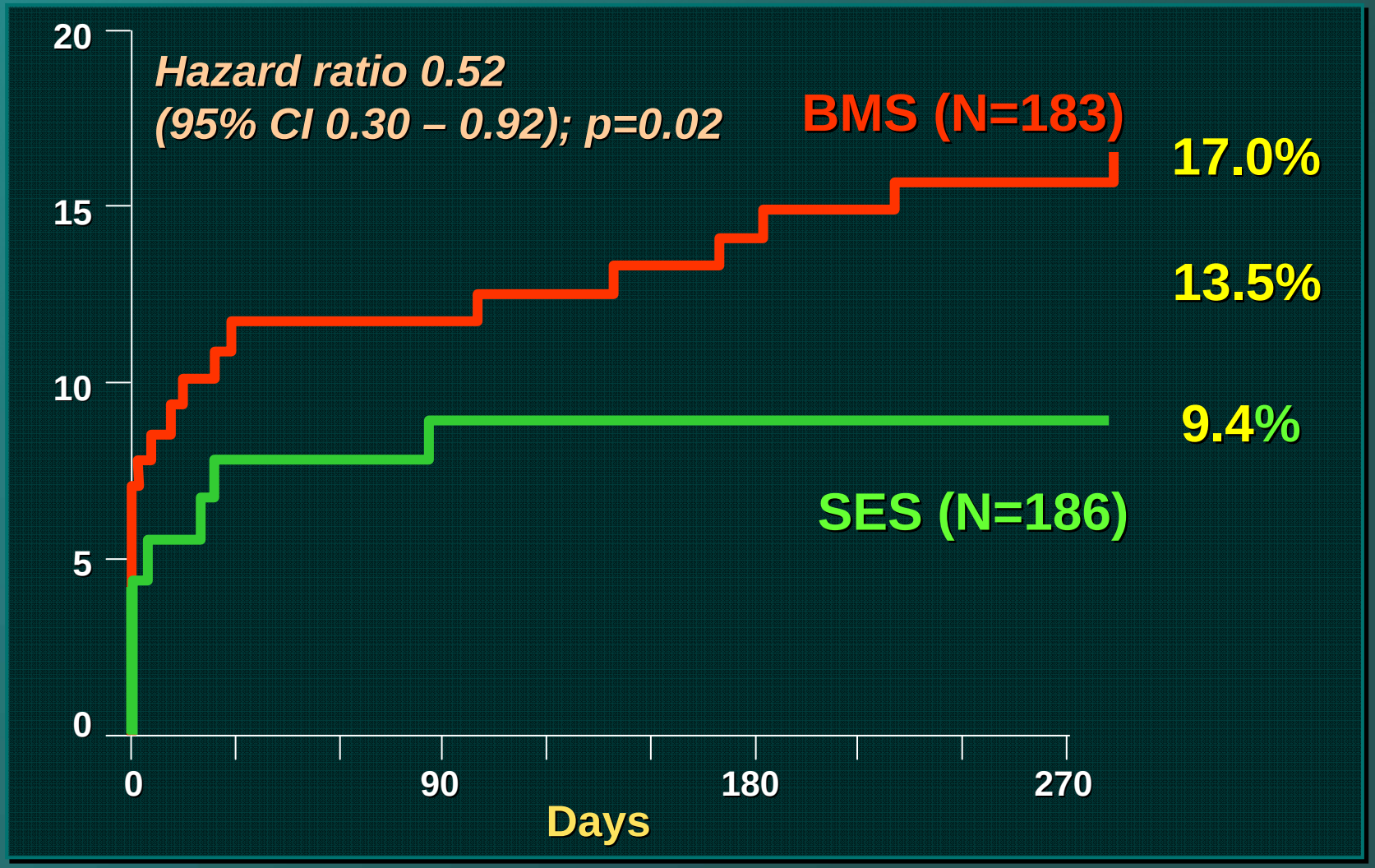


The HORIZONS Trial

3400 patients with STEMI within 12º onset at 200 international sites

Consent

Aspirin 324 mg po chewed

Clopidogrel 300 or 600 mg po load

R

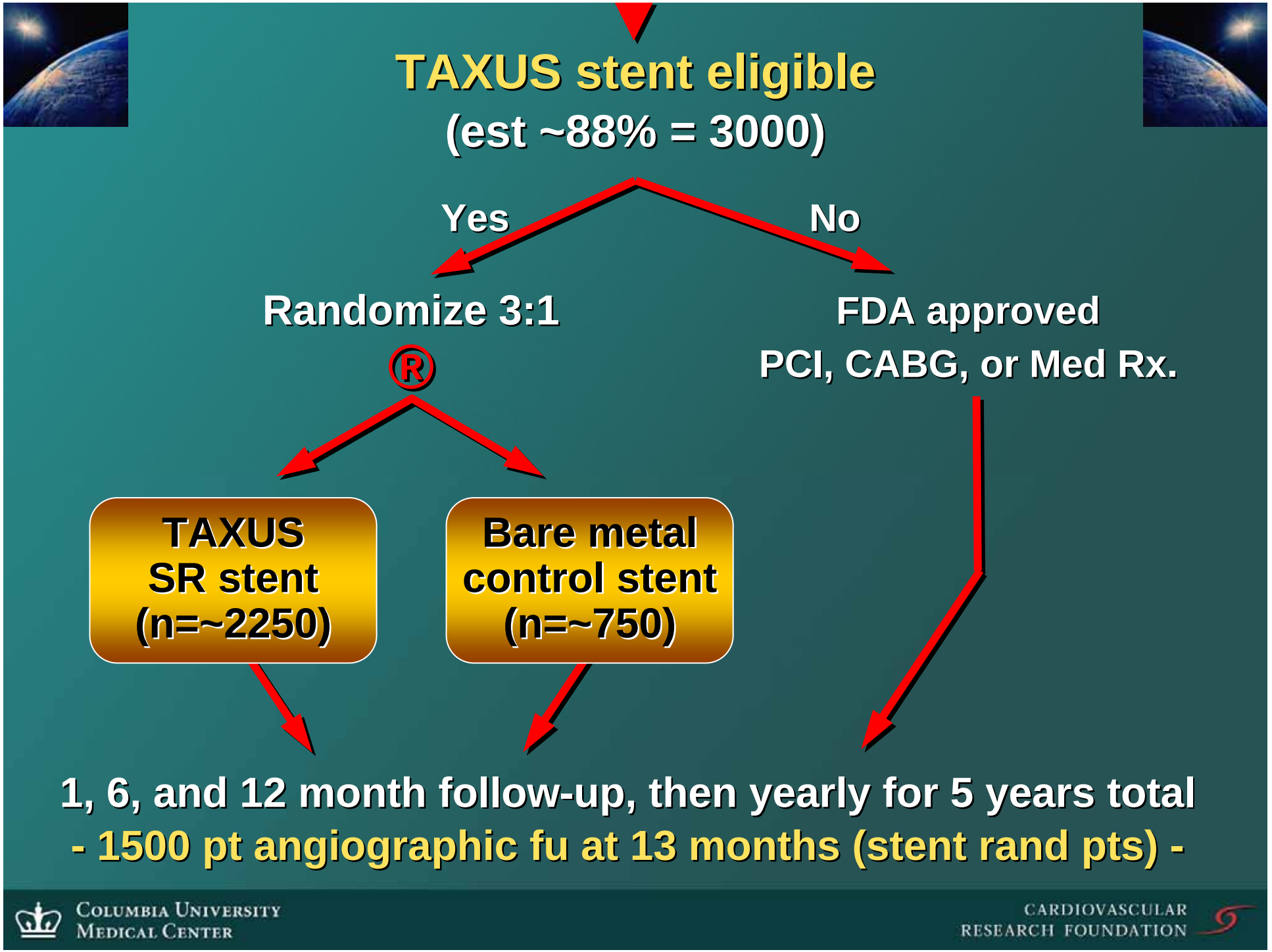
1:1

UFH + IIb/IIIa inhibitor

Bivalirudin + bail-out IIb/IIIa

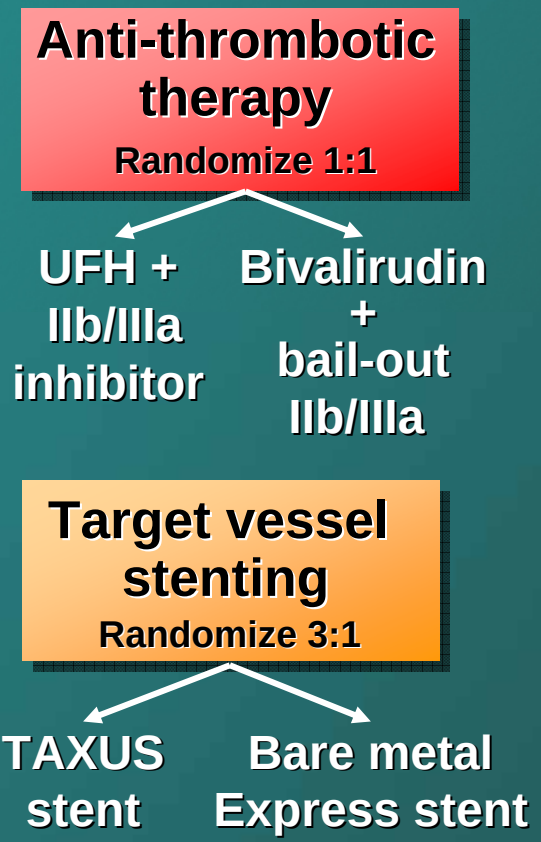
Cath lab

left ventriculography and coronary arteriography


TAXUS stent eligible
(est ~88% = 3000)
Yes
No
Randomize 3:1
R
FDA approved
PCI, CABG, or Med Rx.
TAXUS
SR stent
(n=~2250)
Bare metal
control stent
(n=~750)
1, 6, and 12 month follow-up, then yearly for 5 years total
- 1500 pt angiographic fu at 13 months (stent rand pts) -
Columbia University
Medical Center
CARDIOVASCULAR
RESEARCH FOUNDATION

HORIZONS AMI Trial

3400 randomized pts undergoing primary PCI



Status

Protocol completed

Committees and core labs selected

IDE approved by FDA

200 sites being initiated

8 patients randomized!