PCI in Coronary Heart Disease Update – Qeasaria 2008

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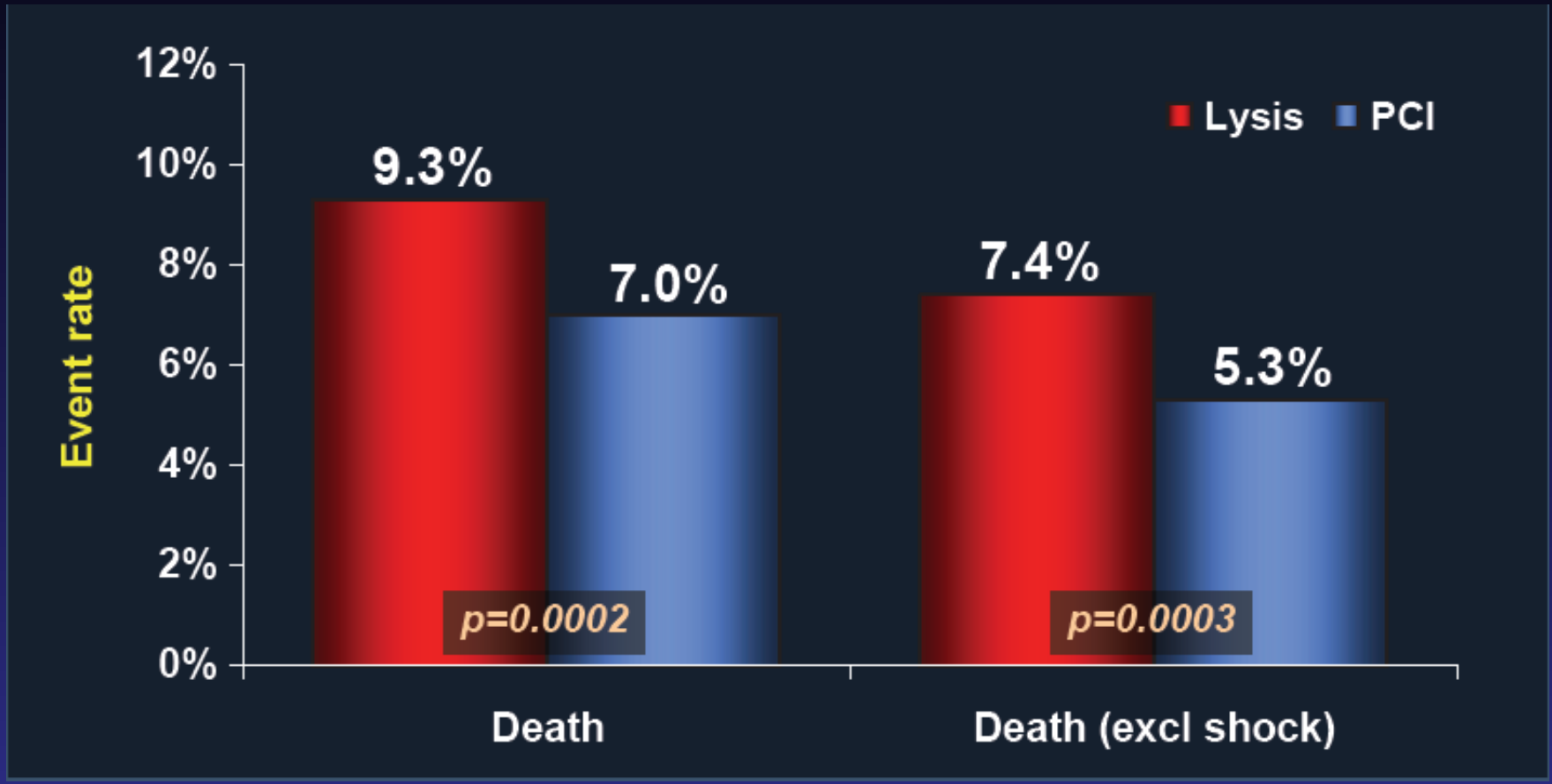
Outline

- Primary PCI
- Non-ST elevation ACS
- Stable Angina

23 Randomized Studies of Primary PCI vs. Lysis

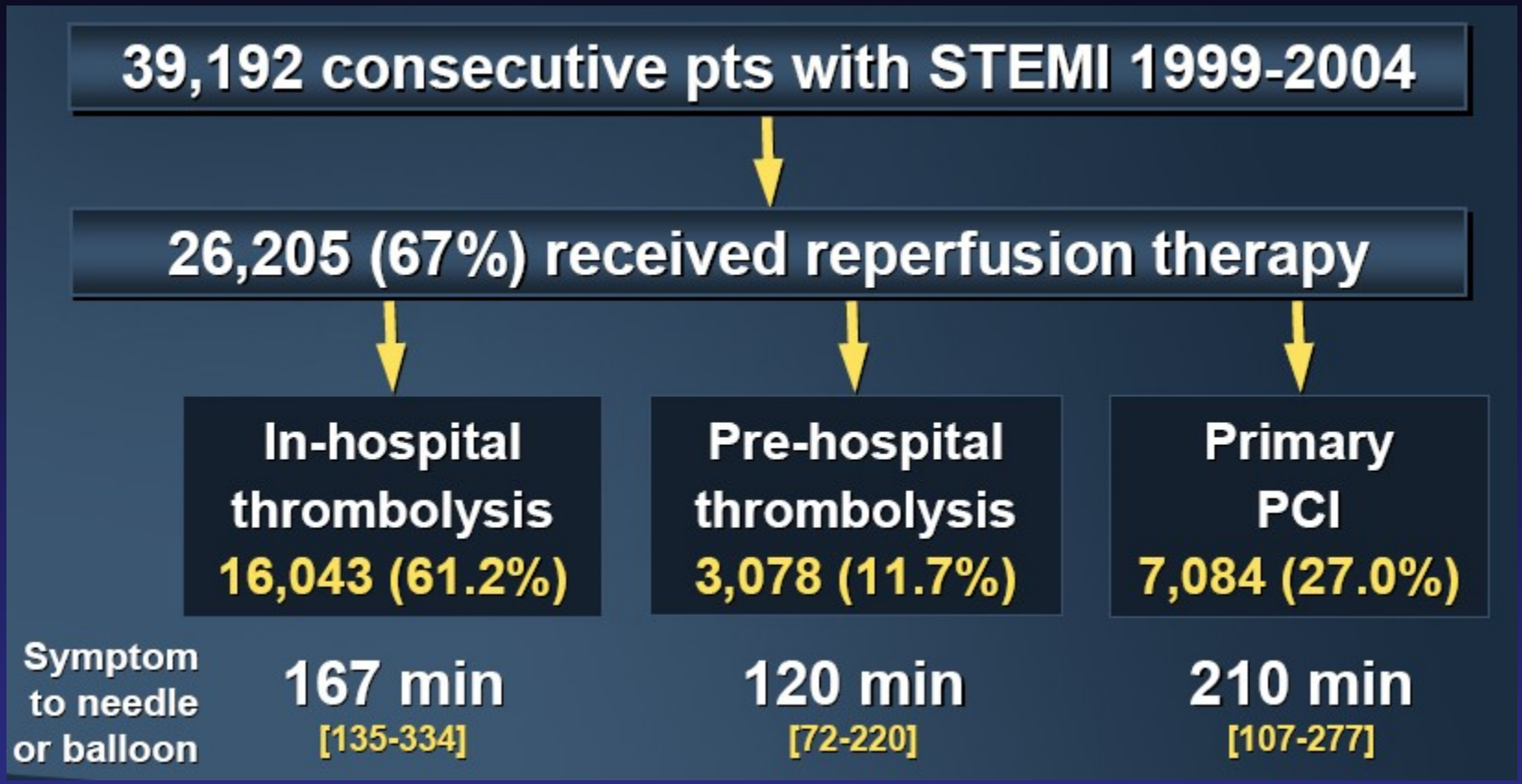
n=7739



Keeley et at, Lancet 2003

The RIKS-HIA Registry

Consecutive pts admitted in 75 of 78 hospitals with CCUs in Sweden



Stenestrand U et al. *JAMA 2006*

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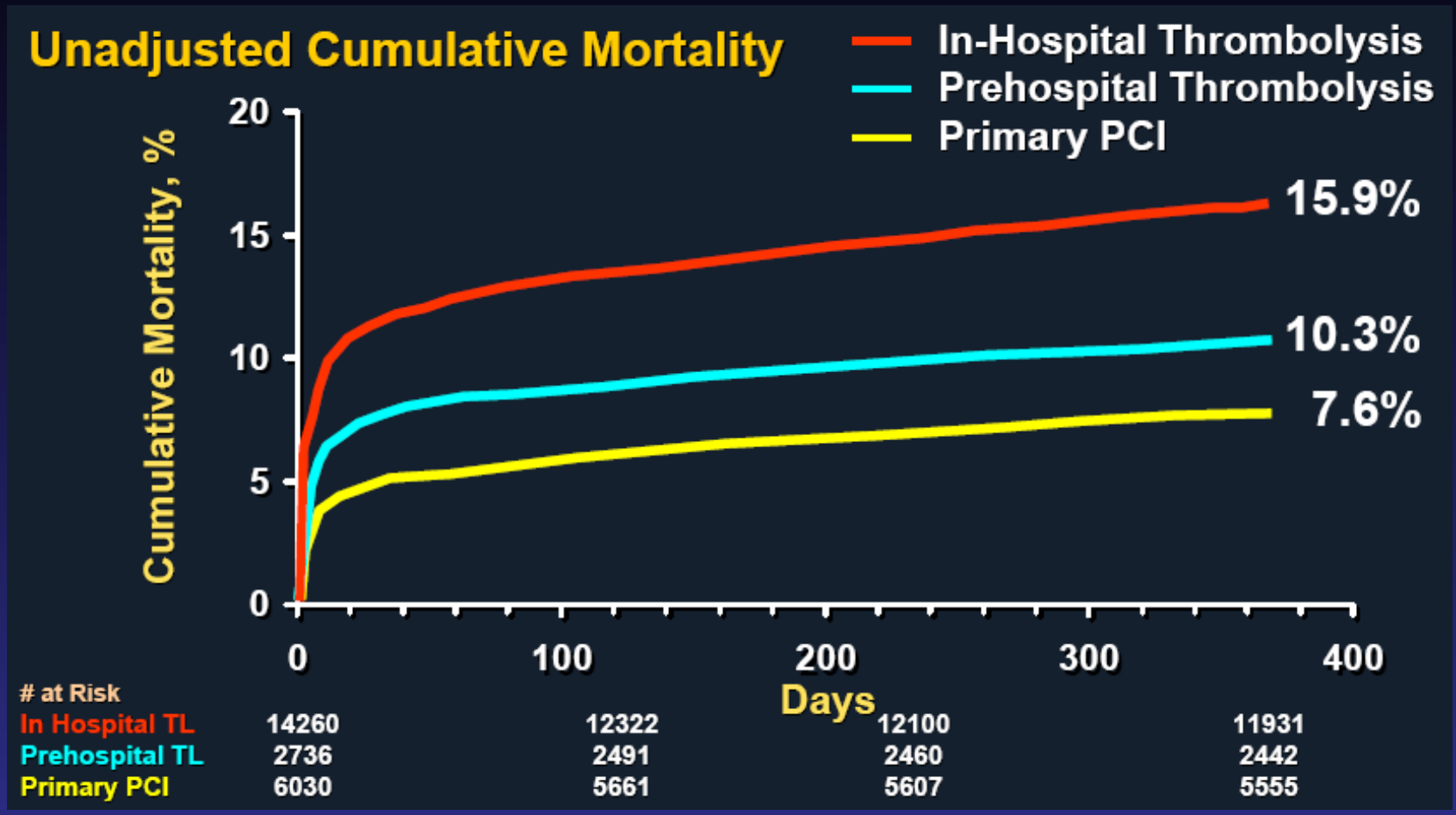

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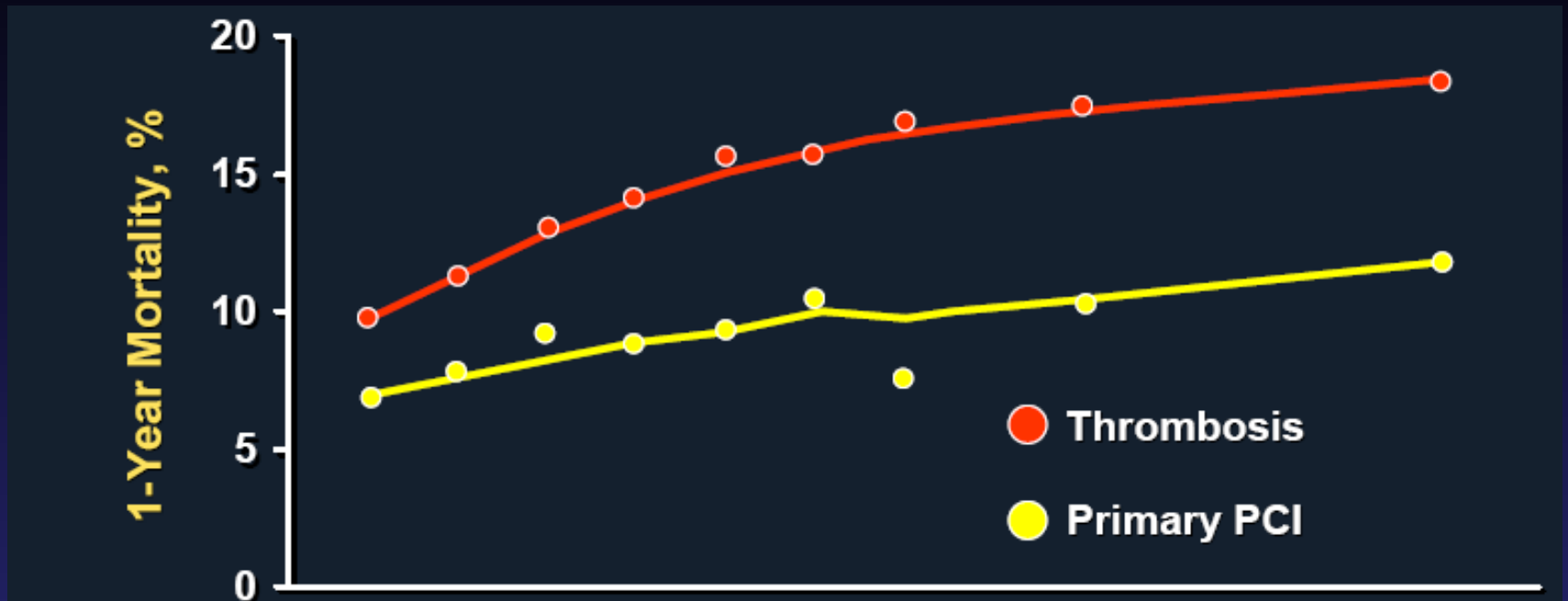
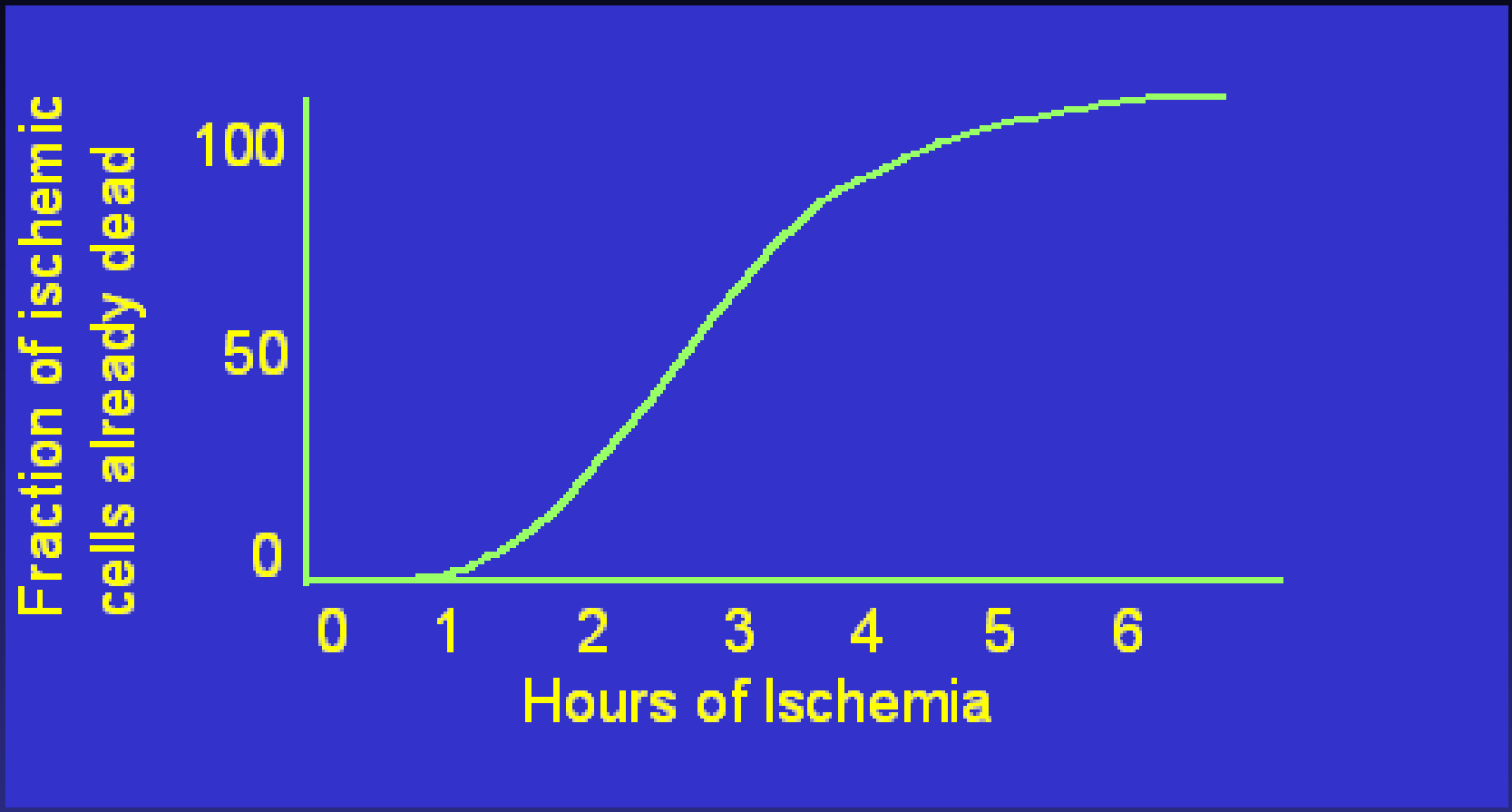


Thrombolysis									
No. of Deaths	122	503	503	332	239	159	121	196	139
Total No. of Pts	1248	4375	3659	2199	1438	946	658	1061	703
Primary PCI									
No. of Deaths	7	61	81	50	43	37	17	41	31
Total No. of Pts	125	895	1126	776	567	453	282	458	332

Stenestrand U et al. *JAMA 2006*

How Late After Symptom Onset Does Opening the Infarct Related Artery Still Provide Benefit?

Survival of Myocardium



BRAVE II : Efficacy of Late Primary PCI

365 patients with MI presenting >12 - <48 hours after symptom onset (mean 22.5 hours)
Without ongoing chest pain or Killip class 3/4

Invasive
Angiography, then PCI if necessary
Median randomization time to PCI: 1.7 hrs

Conservative
Conventional medical therapy

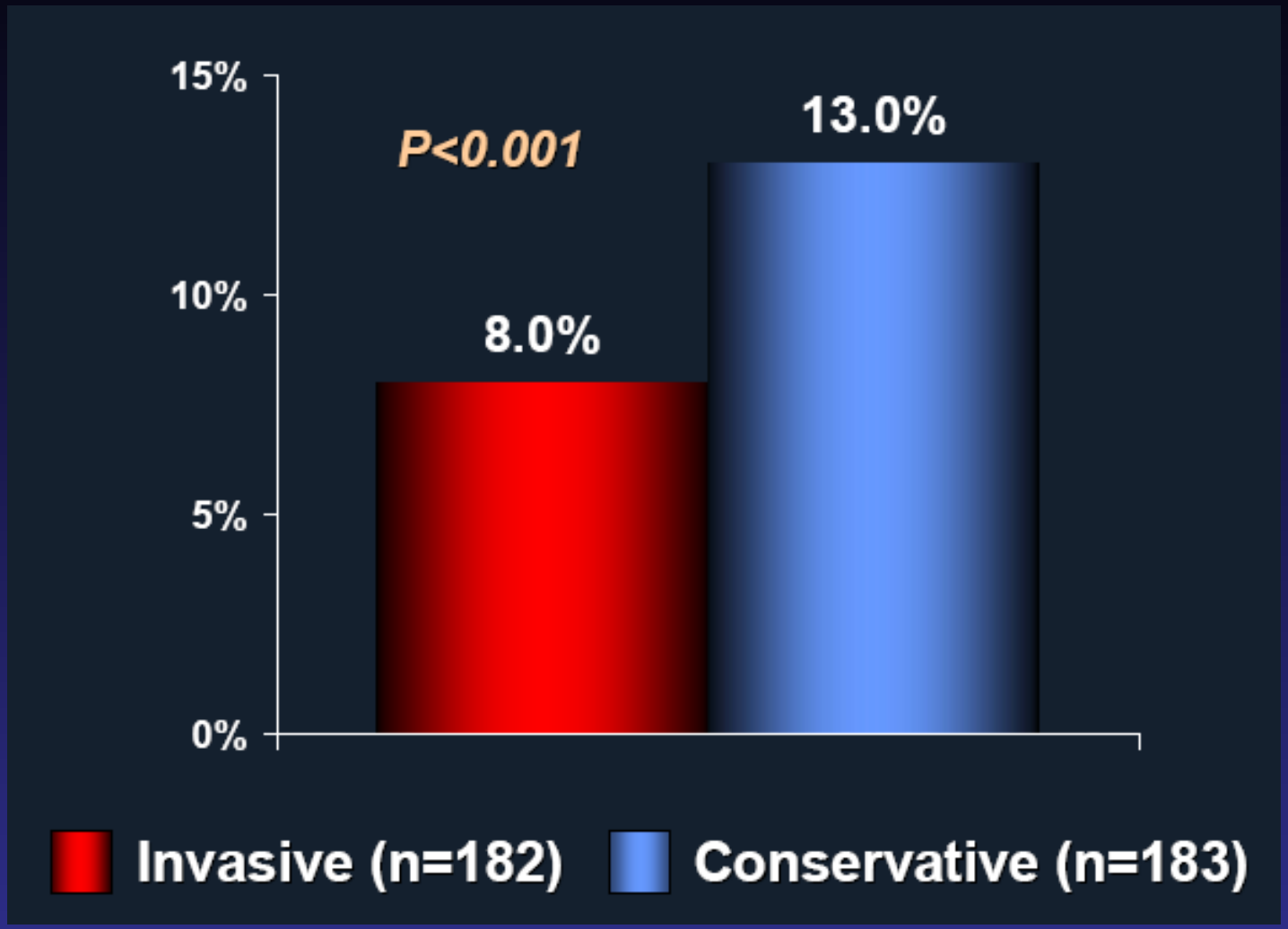
PCI 94.6%, CABG 3.8%, Med Rx 1.6%

Endpoints:

- Primary – Infarct size determined by SPECT at 5-10 days
- Secondary – Death, MI, stroke, at 30 days

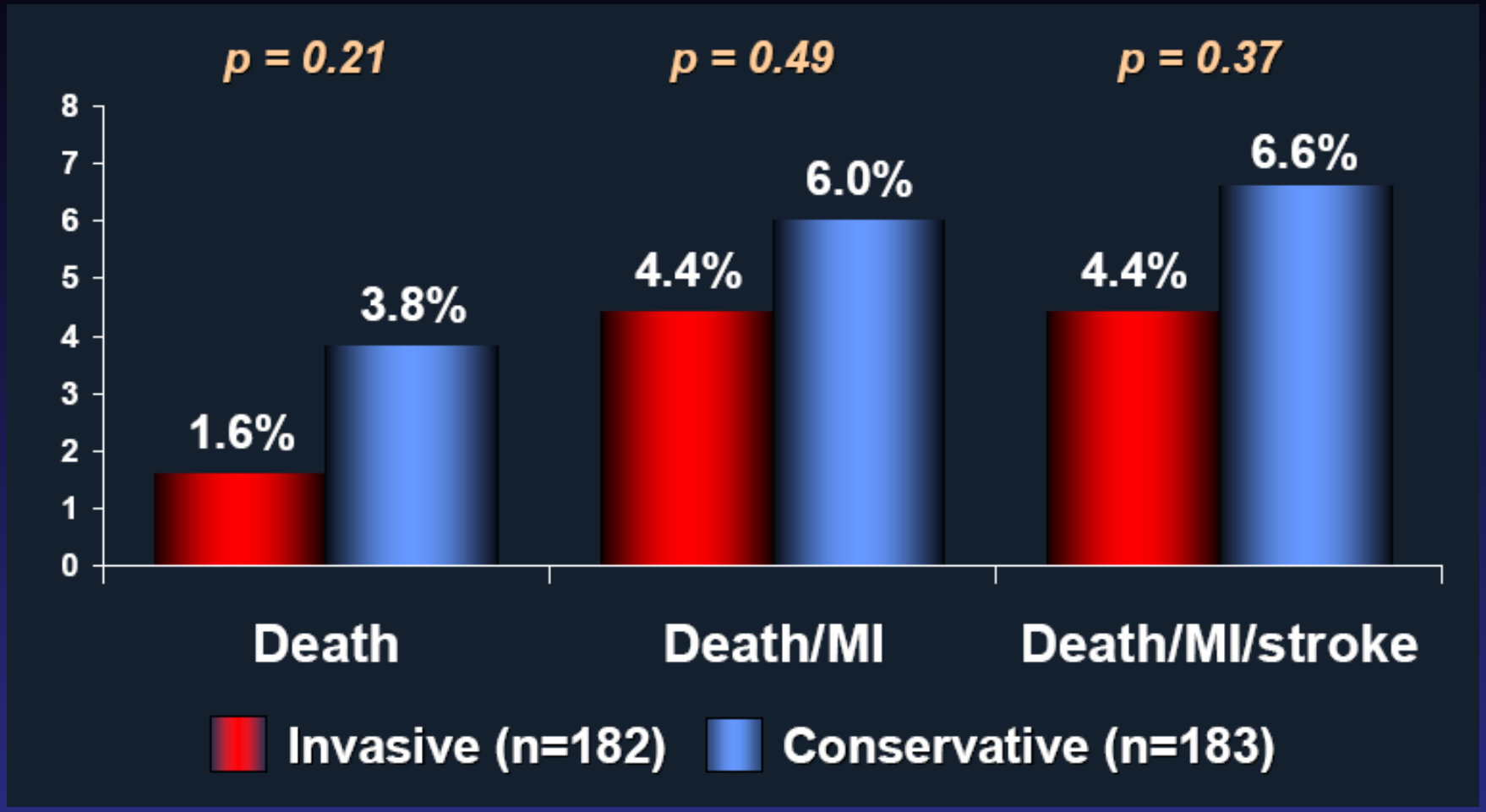
Schomig A et al. *JAMA 2005*

BRAVE 2 – Infarct Size at 7 days



Schomig A et al. *JAMA 2005*

BRAVE 2 – 30 day End-points



Schomig A et al. *JAMA 2005*

OAT Trial

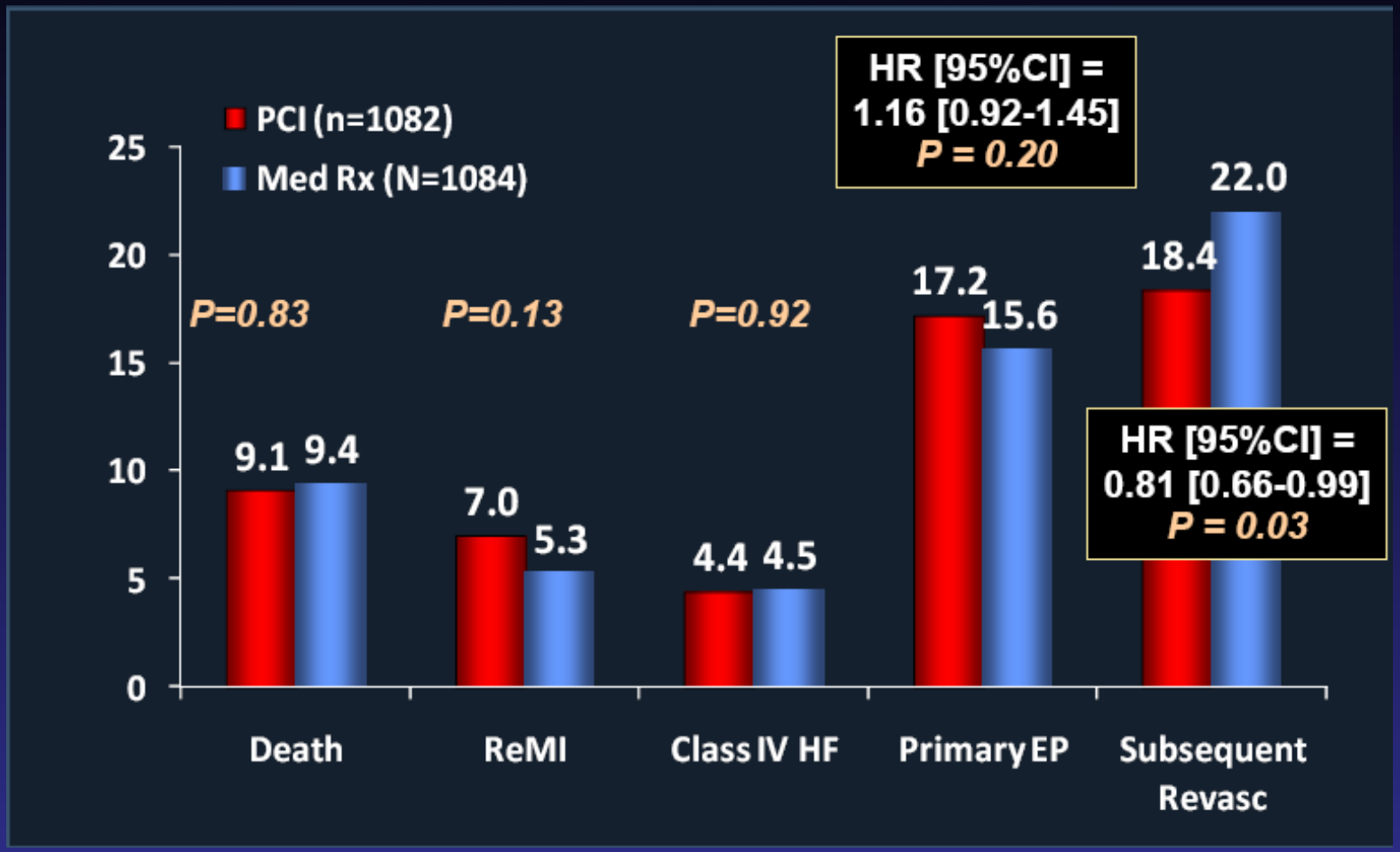
2166 stable pts with occluded IRA 3-28 days after MI with either LVEF <50% or proximal occlusion randomized to PCI with BMS vs. med Rx.

Primary endpoint = death, reMI, or NYHA class IV HF

	PCI N=1082	Med N=1084	P
Lytic Rx	21%	18%	0.10
Q-waves	67%	67%	0.80
MI – rand (days)	8 [5,16]	8 [5, 17]	0.68
ETT performed	27%	28%	0.68
- No ischemia	57%	62%	0.22
- Mild ischemia	34%	27%	0.22

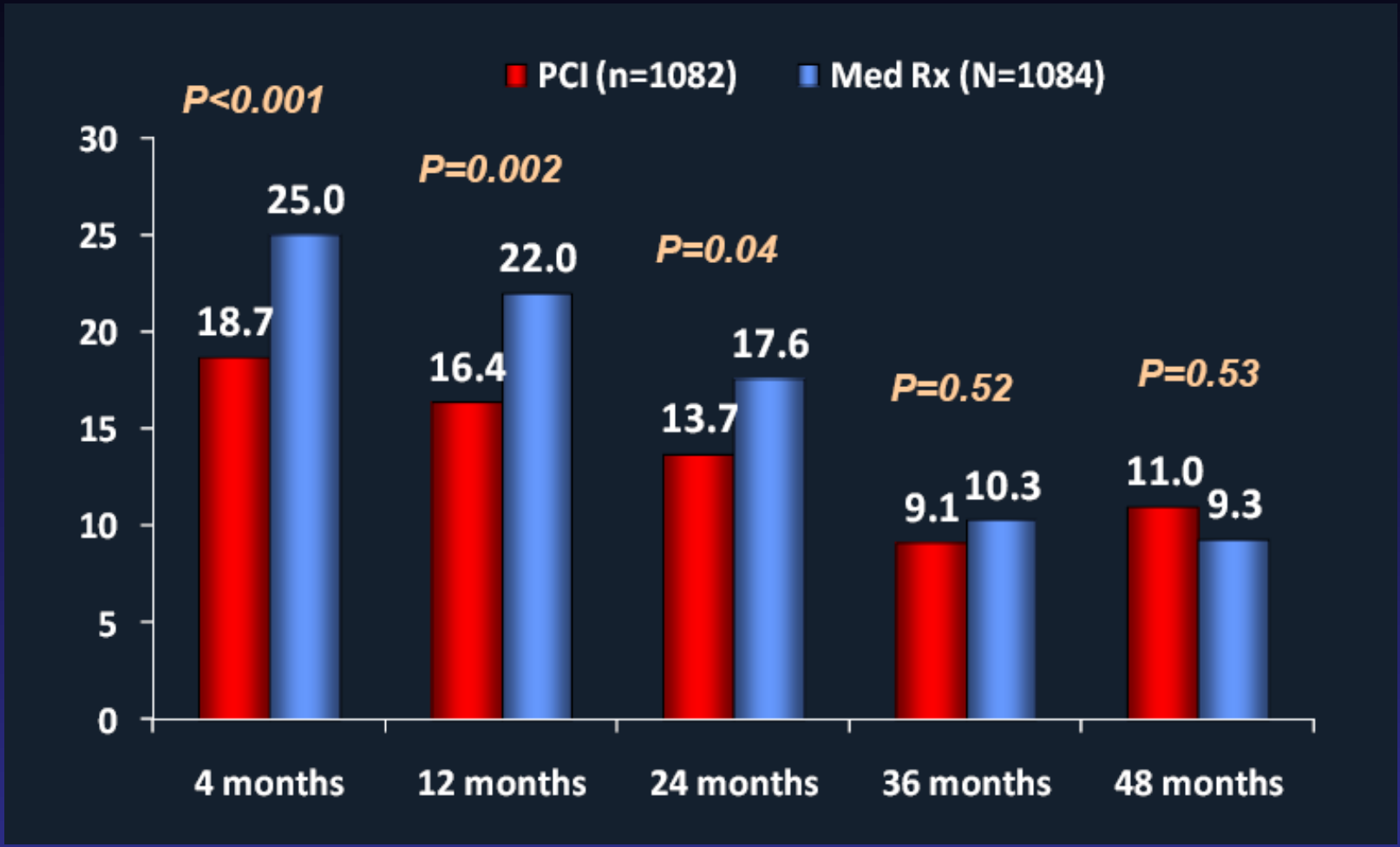
Hochman JS et al. N Engl J Med 2006

OAT Trial
Adverse Events at 4 years



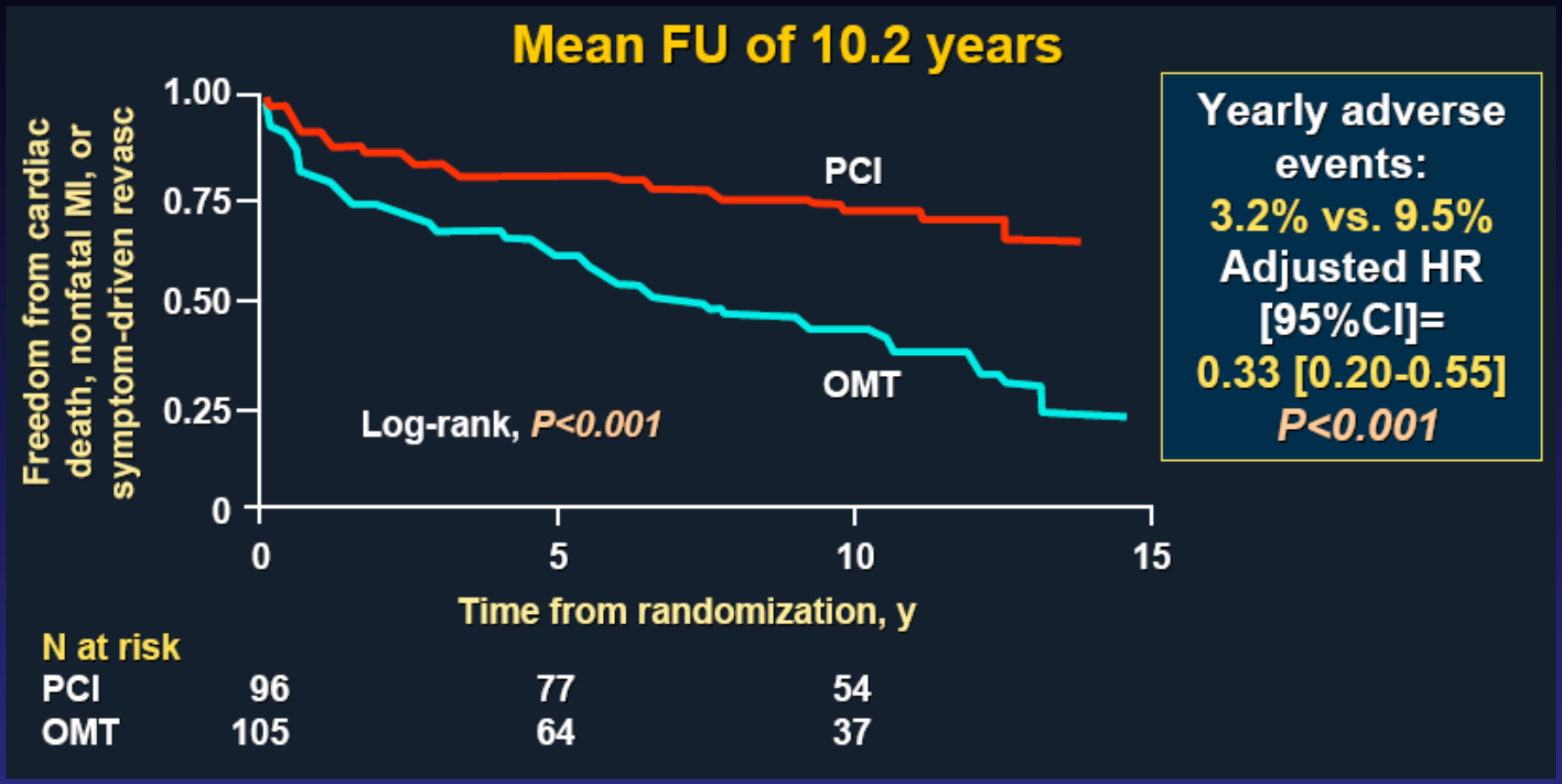
Hochman JS et al. N Engl J Med 2006

OAT Trial
Angina during follow-Up



Hochman JS et al. N Engl J Med 2006

SWISSI II: 201 pts with MI within 3 months + silent ischemia and 1-2 vessel CAD randomized to PCI with intended complete revasc vs. optimal medical therapy at 3 SWISS hospitals

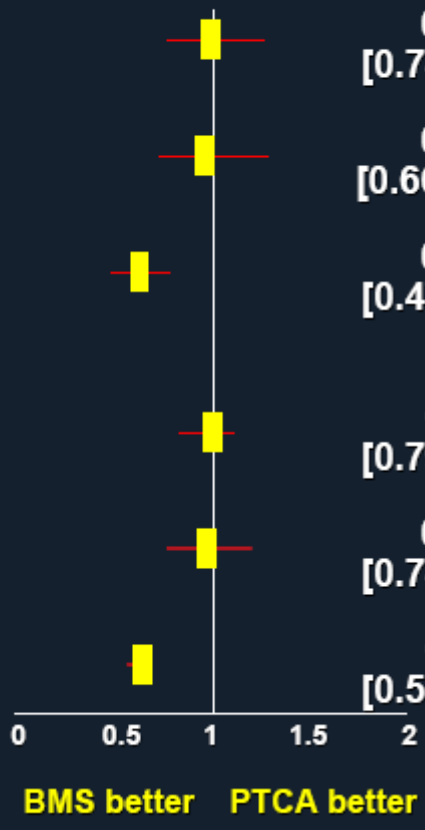


Erne P et al. JAMA 2007

What is the optimal device for primary PCI: balloon angioplasty, bare metal stents or drug-eluting stents, and what is the role of GP IIb/IIIa inhibitors?

13 RCTs of BMS vs. Balloon PTCA in AMI N=6922

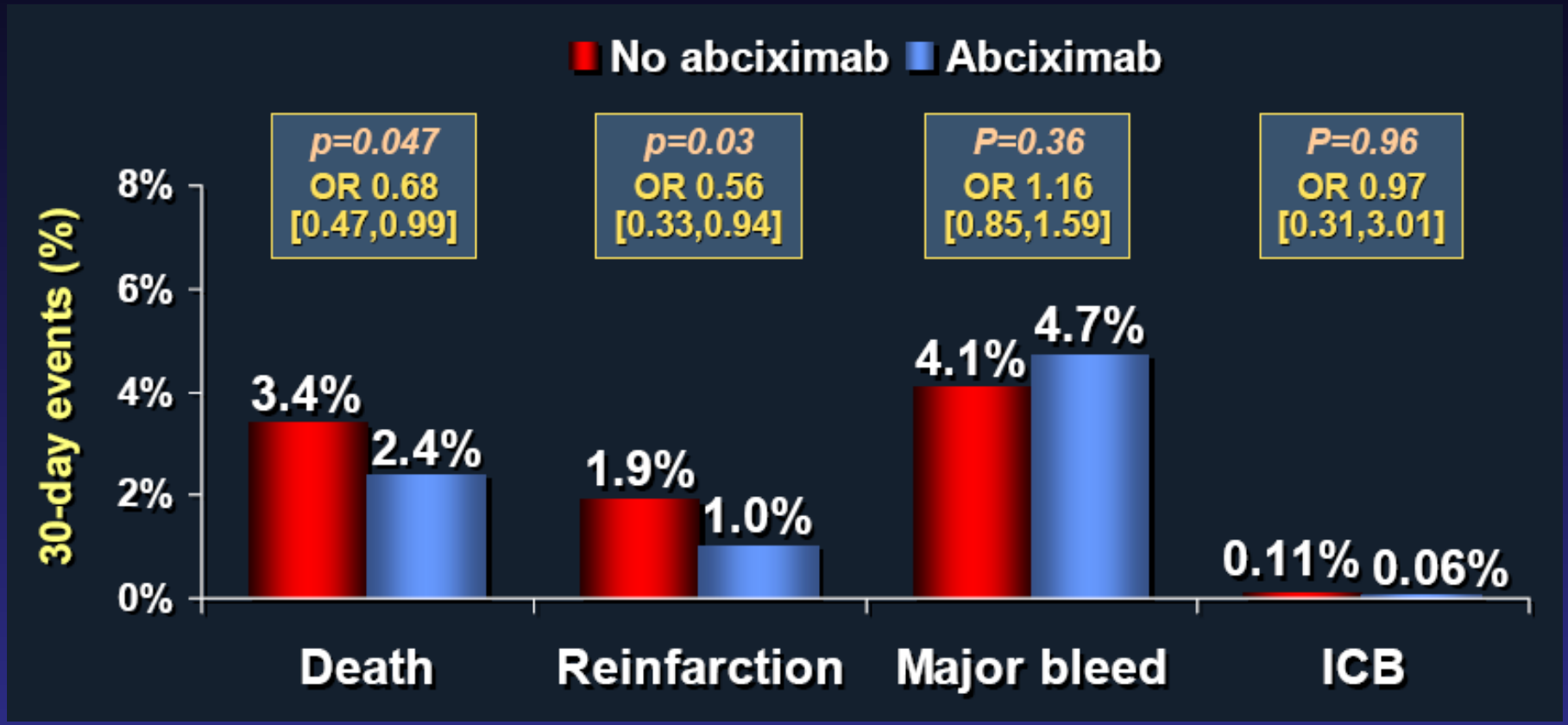
30 day events	Bare metal stents	Balloon angioplasty	RR [95% CI]	RR [95% CI]	P Value
Mortality	2.9%	3.0%		0.97 [0.74, 1.27]	0.83
Reinfarction	2.0%	2.2%		0.92 [0.66, 1.27]	0.61
TVR	3.1%	5.1%		0.60 [0.47, 0.77]	0.0001
6-12 month events					
Mortality	5.1%	5.2%		0.98 [0.79, 1.10]	0.82
Reinfarction	3.7%	3.9%		0.94 [0.74, 1.20]	0.61
TVR	11.3%	18.4%		0.62 [0.55, 0.69]	<0.0001



De Luca G et al. Int J Cardiol 2007

Abciximab in Primary PCI Meta-analysis

8 RCTs 3,949 pts with AMI w/i 12°° undergoing primary (7) or rescue (1) PCI rand to abciximab vs. placebo



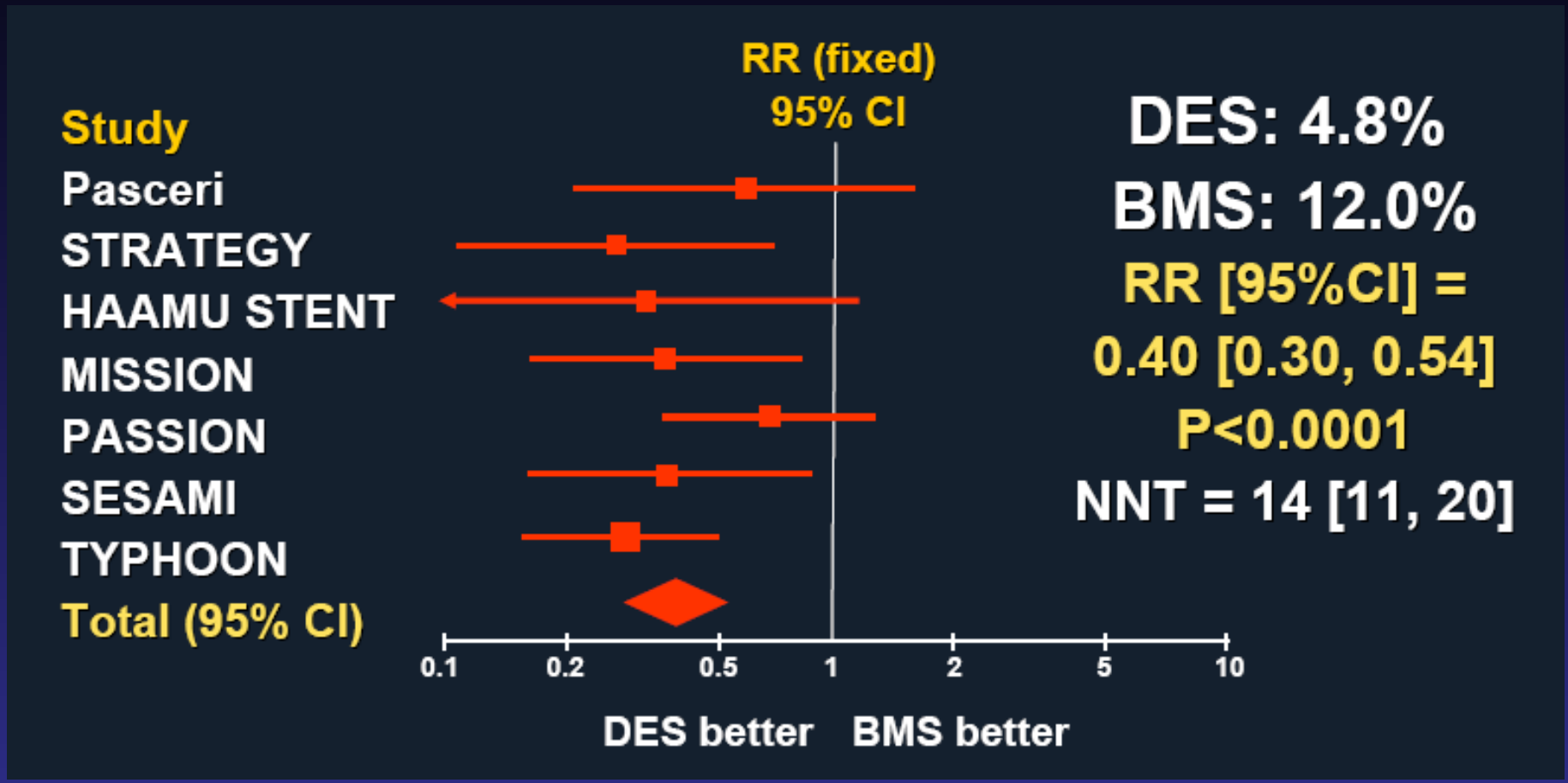
De Luca G et al. JAMA 2005

9 DES vs. BMS RCTs in AMI *(N=3,728 patients)*

Trial	DES	N	Rescue PCI	Angio FU	Clinical FU
Pasceri	Cypher	65	18%	100%	12 mo
STRATEGY	Cypher	175	0%	90%	8 mo
PASSION	Taxus	605	0%	0%	12 mo
TYPHOON	Cypher	712	0%	26%	12 mo
SESAMI	Cypher	320	18%	52%	12 mo
Haamu-Stent	Taxus	164	45%	88%	12 mo
MISSION!	Cypher	316	0%	82%	12 mo
MultiStrategy	Cypher	745	0%	0%	8 mo
DEDICATION	Mixed	626	0%	87%	8 mo

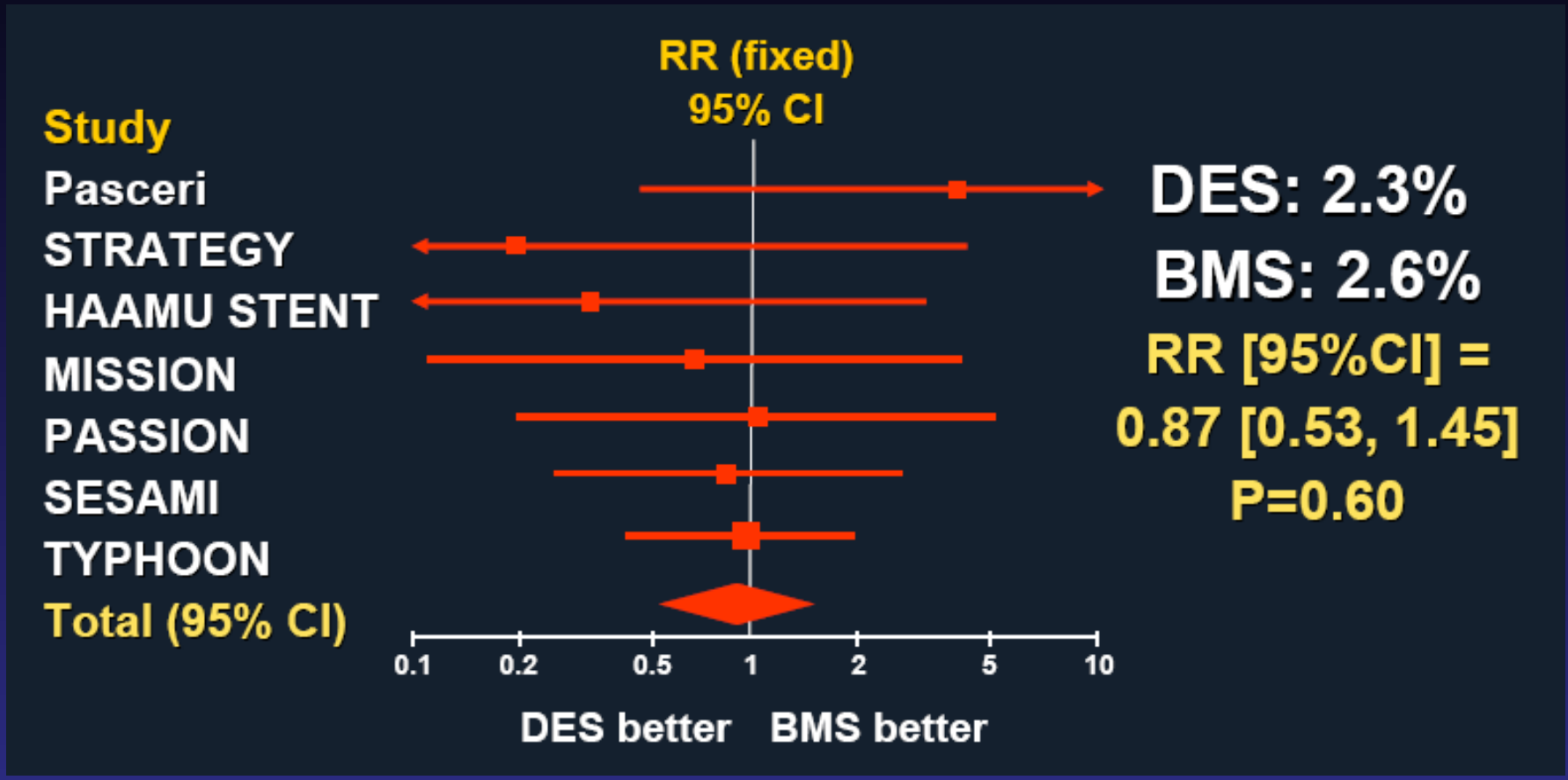
Stone G. Fellows Course 2008

7 DES vs. BMS RCTs in AMI (n=2,357)
TLR at 8–12 Months



Pasceri V et al. AHJ 2007

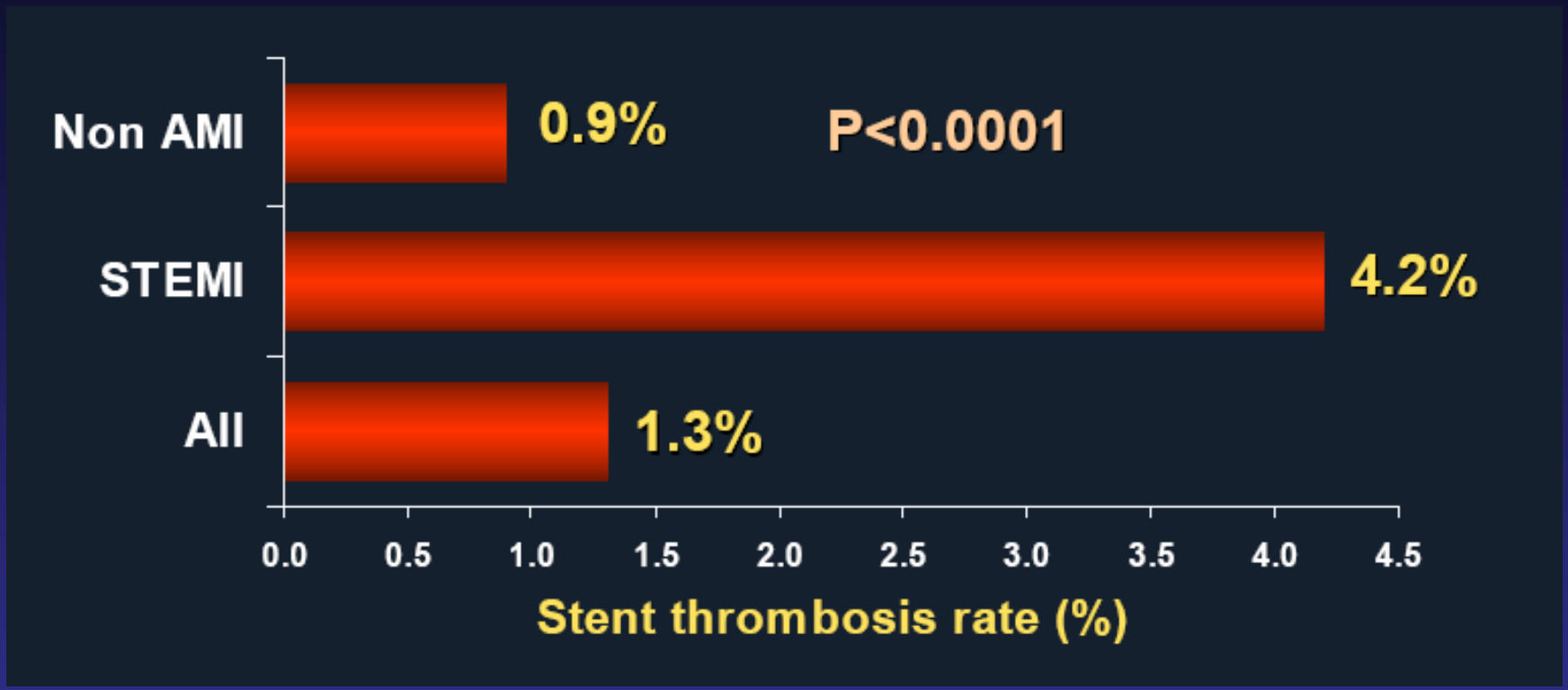
7 DES vs. BMS RCTs in AMI (n=2,357) Stent Thrombosis at 8–12 Months



Pasceri V et al. AHJ 2007

The Spanish ESTROFA Registry

23,500 pts treated w/DES at 20 Spanish hospitals from 2002–06;
63% PES, 37% SES. Dual antiplatelet Rx for 8±3 months.
1.3% ST rate at median FU 22 (11, 32) mos ; 2.0% ST at 3 yrs



De la Torre Hernandez J et al. JACC 2008

The Spanish ESTROFA Registry
Multivariate Predictors of Stent Thrombosis (n=14,120)

Early (≤30 days)	HR (95% CI)	P value
STEMI	6.9 (4.0-12.0)	<.0001
Stent length (per mm↑)	1.08 (1.06–1.10)	0.0001
Diabetes	1.8 (1.0–3.0)	0.04
Renal insufficiency	3.1 (1.1–9.2)	0.04
ACS	2.6 (1.3–4.9)	0.003
LAD	2.2 (1.4–3.7)	0.001

De la Torre Hernandez J et al. JACC 2008

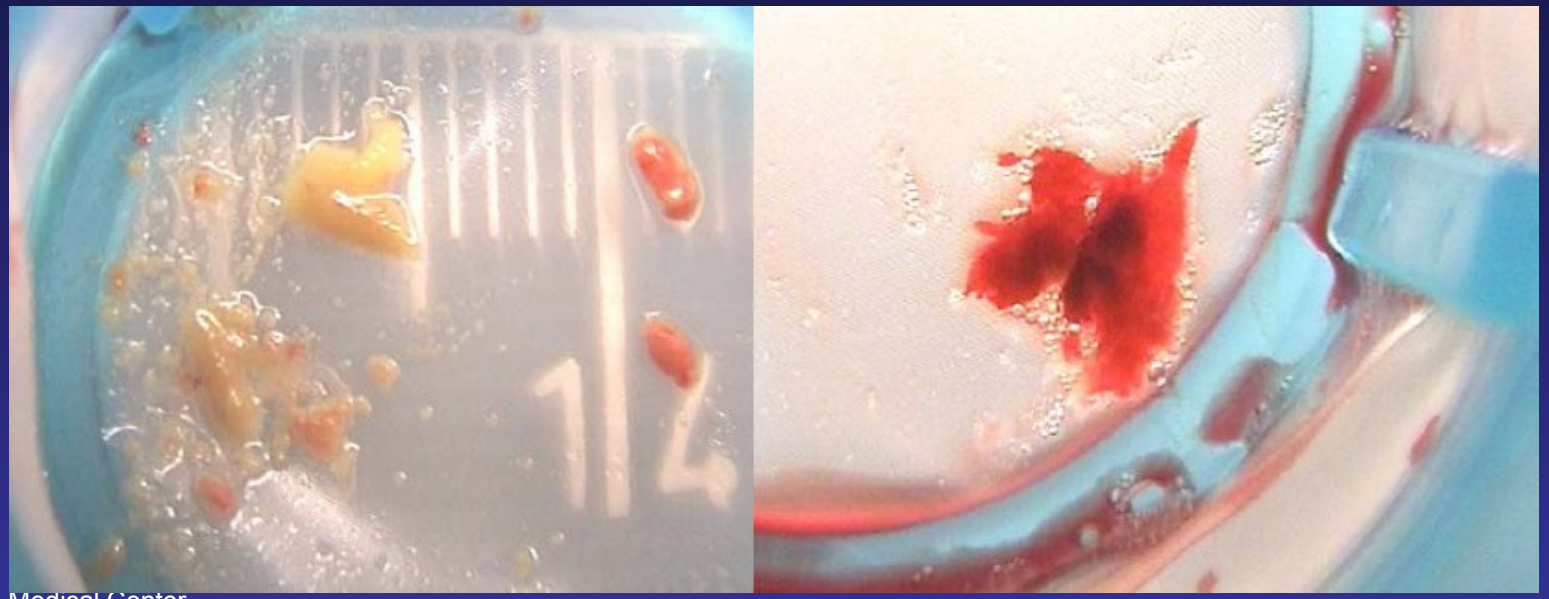
The Spanish ESTROFA Registry
Multivariate Predictors of Stent Thrombosis (n=14,120)

	HR (95% CI)	P value
Late		
STEMI	5.5 (3.5–7.6)	<0.0001
LAD	3.0 (2.0–4.4)	<0.0001
Stent length (per mm↑)	1.07 (1.05–1.09)	<0.0001

De la Torre Hernandez J et al. JACC 2008

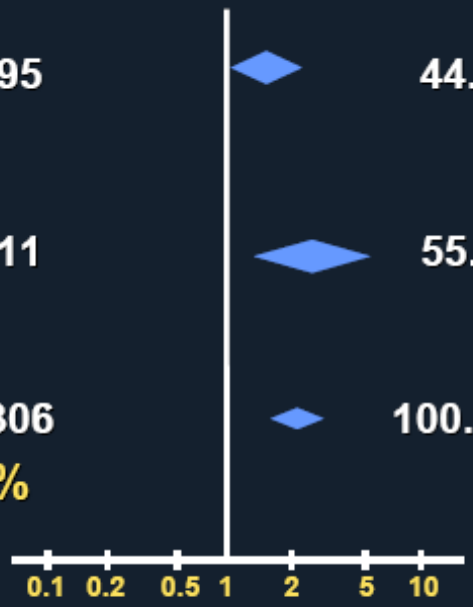
Is thrombus retrieval useful during primary PCI?

Distal Protection and Thrombectomy in AMI - Macroscopic embolic debris can be retrieved from >75% of cases



Myocardial Blush-3 Flow: *15 RCTs*

Device	Treatment n/N	Control n/N	OR (random) 95% CI	Weight %	OR (random) 95% CI
Distal protection (n=7 studies)	314/610	251/595		44.76	1.73 (1.09–2.75)
Thrombectomy (n=8 studies)	339/728	226/711		55.24	2.64 (1.35–5.16)
All (n=15 studies)	653/1338	477/1306		100.00	2.21 (1.48–3.32)
	48.8%	36.0%			
	P=0.0001				



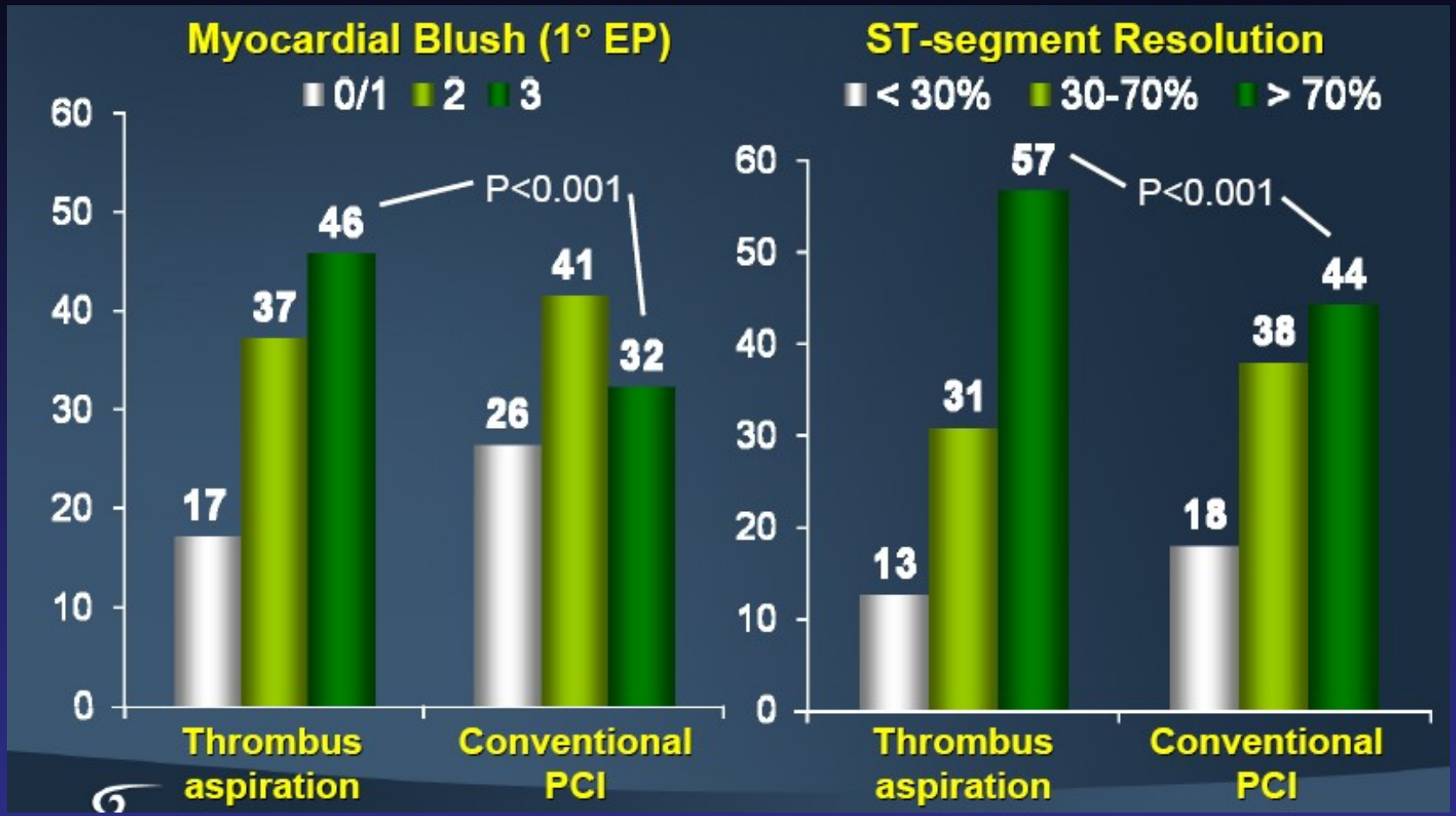
De Luca G et al. AHJ 2007

Mortality at 30 Days: *18 RCTs*

Device	Treatment n/N	Control n/N	OR (random) 95% CI	RR (95% CI)	P Value
Distal protection (n=6 studies)	16/672 2.4%	24/659 3.6%		0.65 [0.35, 1.21]	0.18
Thrombectomy (n=12 studies)	28/1076 2.6%	21/1065 2.0%		1.32 [0.76, 2.29]	0.33
All (n=18 studies)	44/1748 2.5%	45/1724 2.6%		0.96 [0.64, 1.45]	0.86
	P=0.88				

De Luca G et al. AHJ 2007

TAPAS: 1,071 pts with STEMI undergoing primary PCI at a single center were randomized in the ER to manual aspiration (Export) vs. control



Svilaas T et al. N Engl J Med 2008

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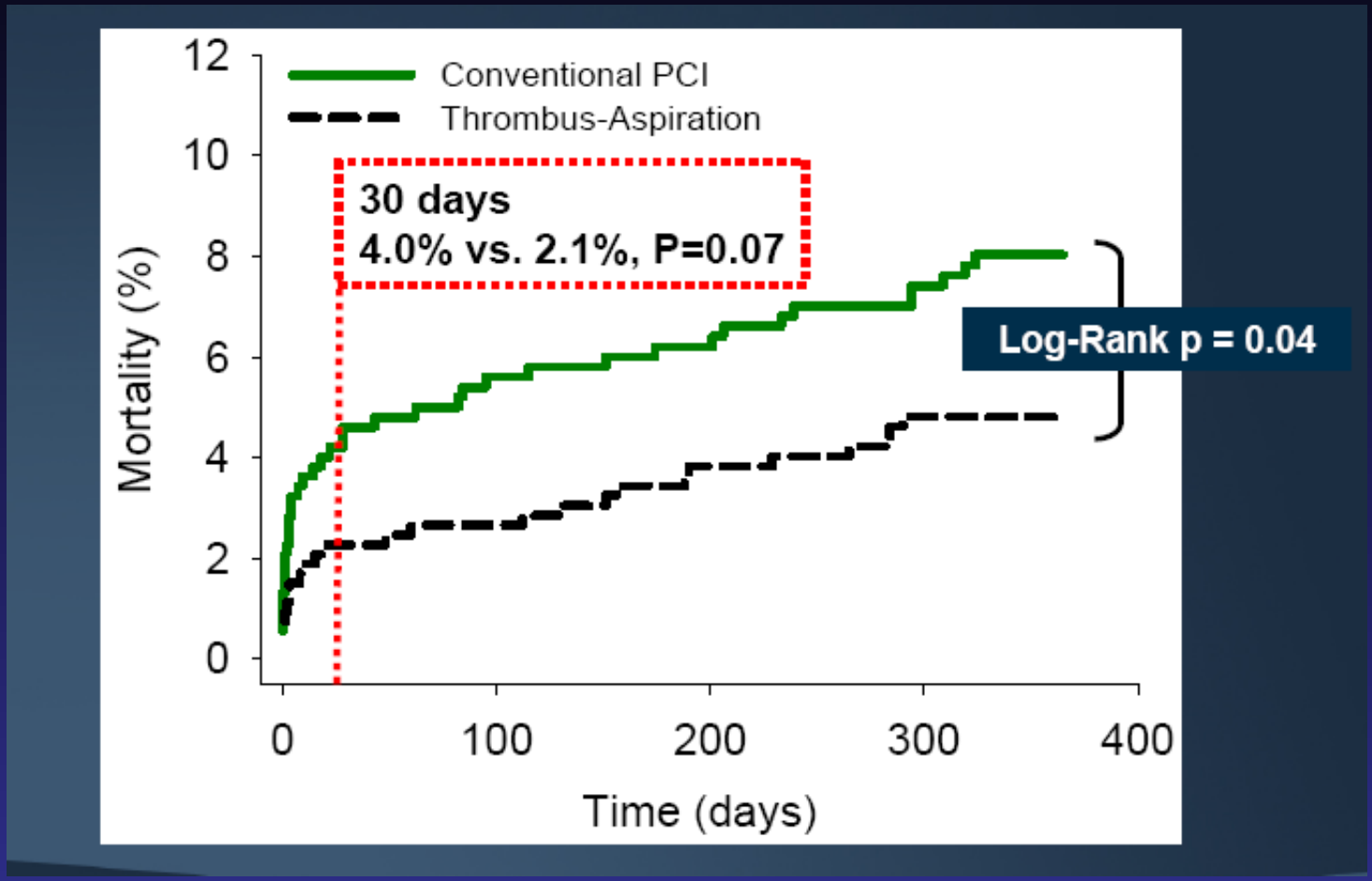
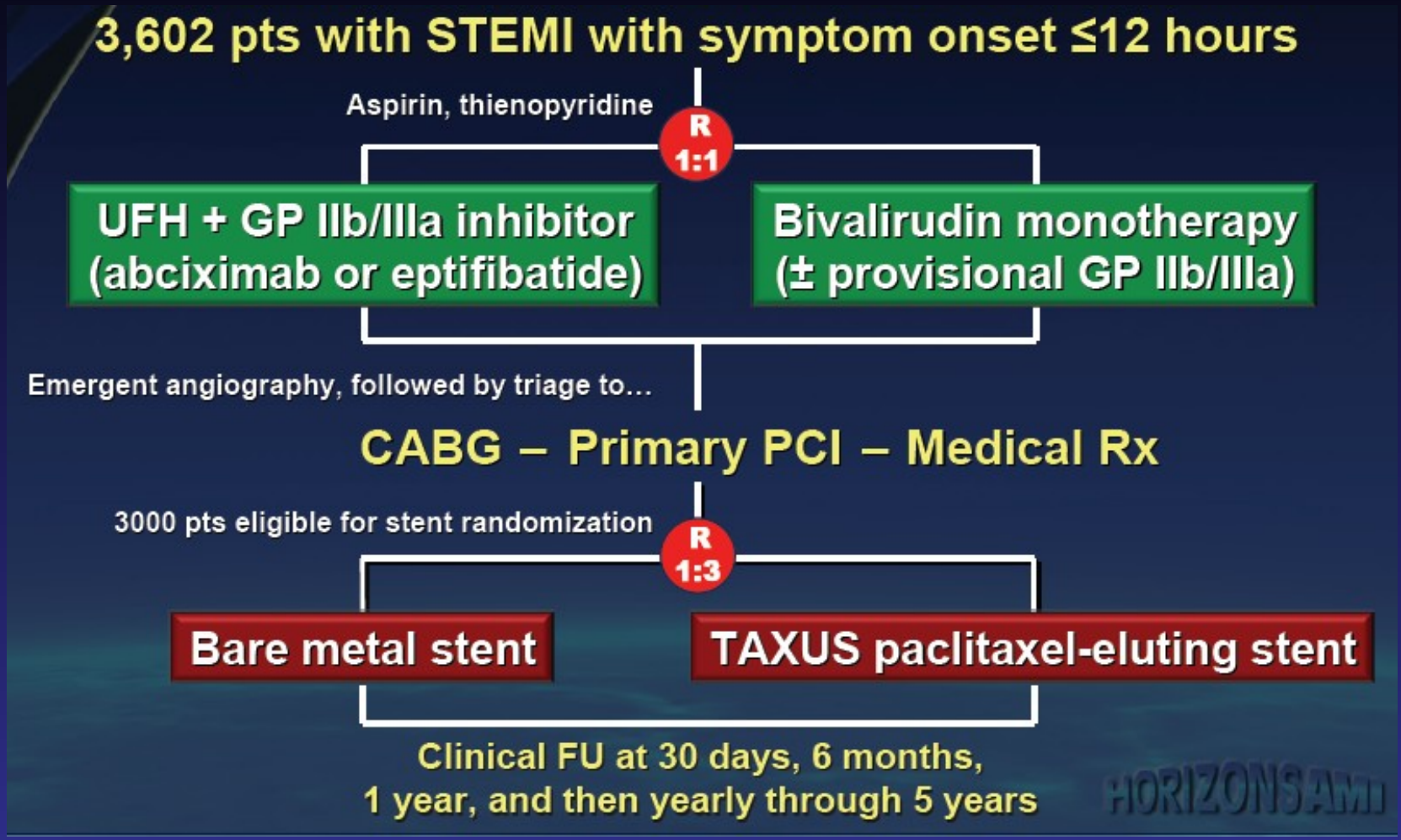


Svilaas T et al. N Engl J Med 2008

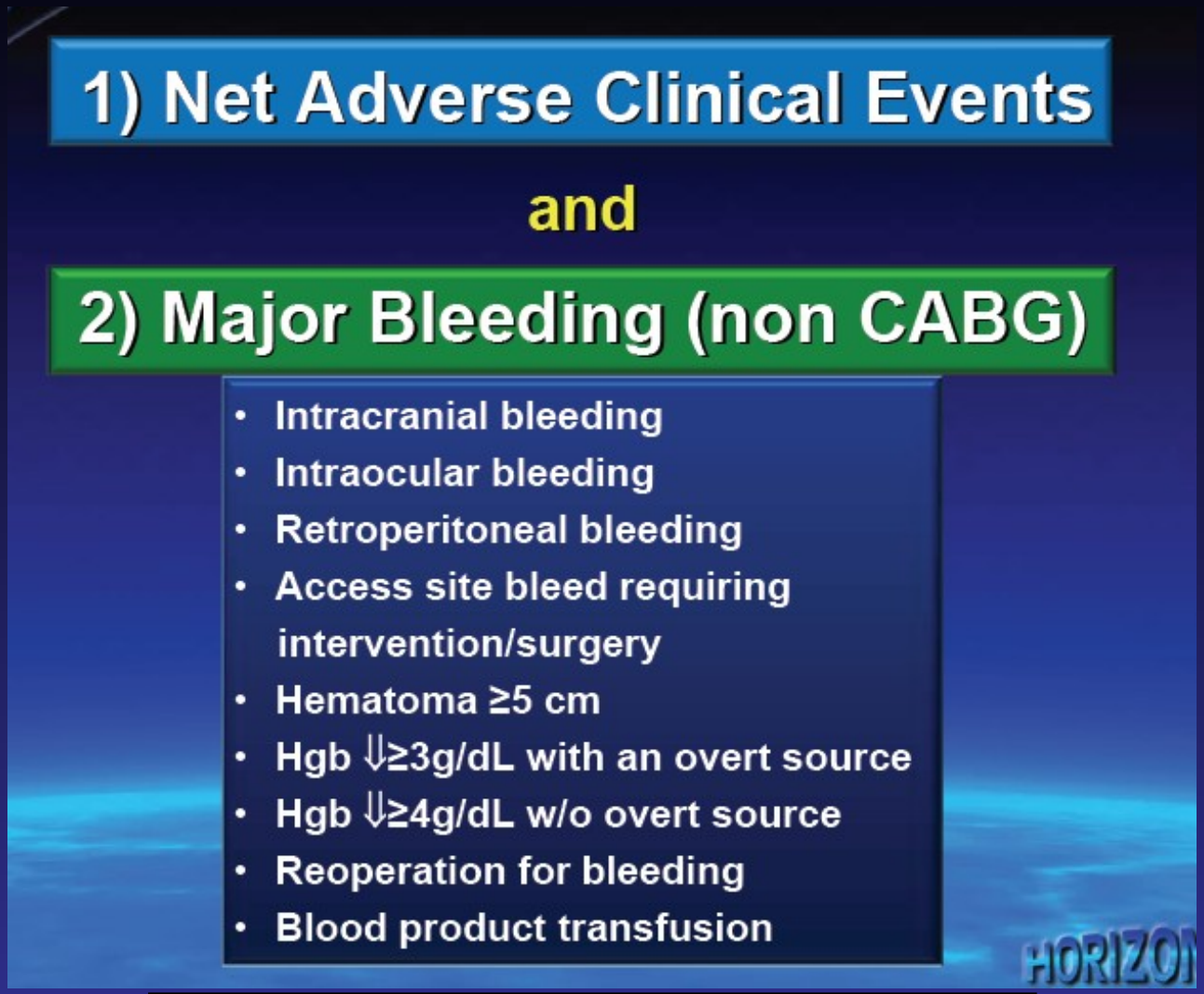
What is the Optimal anti-Thrombotic Regimen in Primary PCI?

HORIZONS-AMI



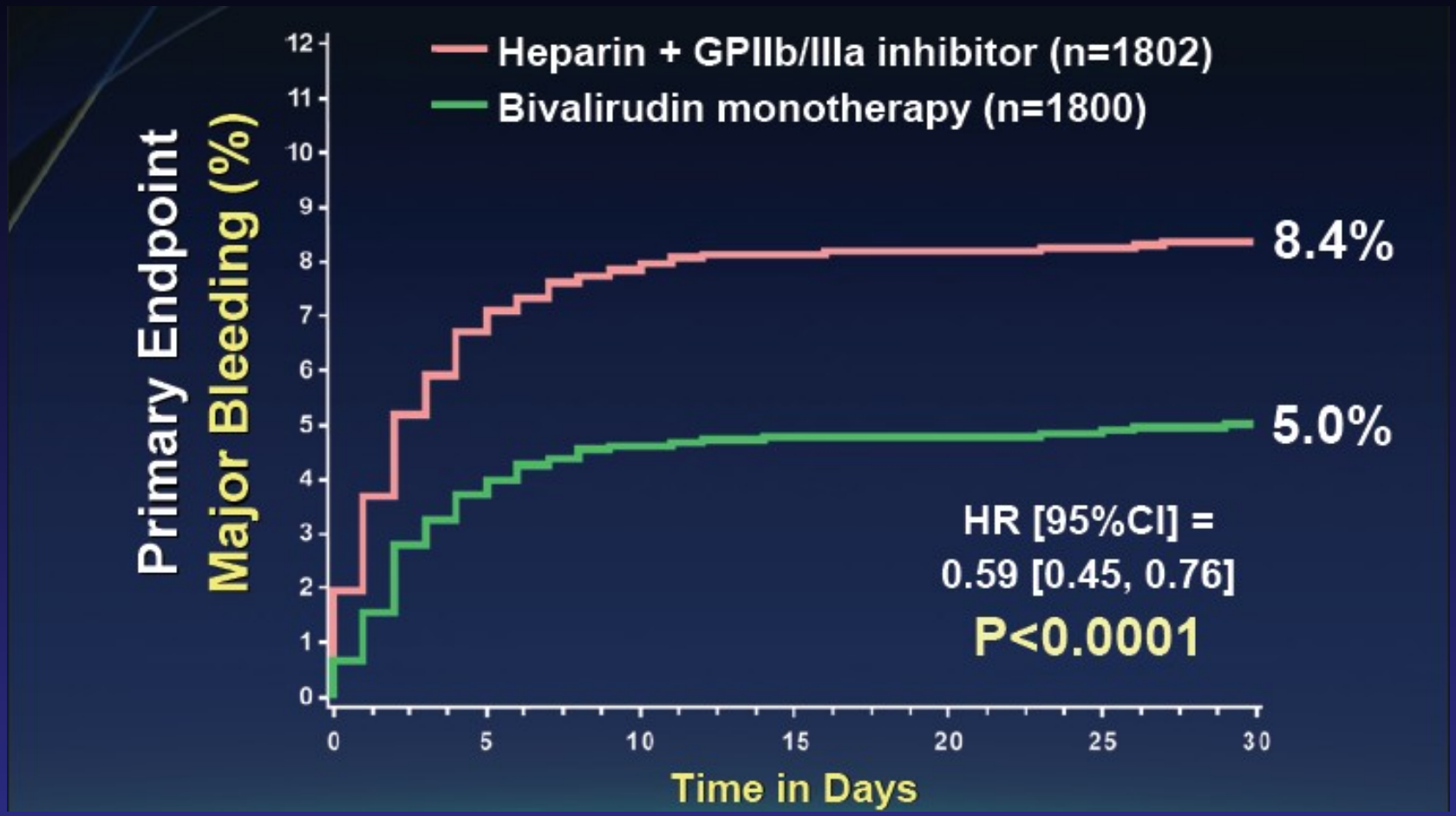
Stone G et al. N Engl J Med 2008

HORIZONS-AMI – Primary End-points



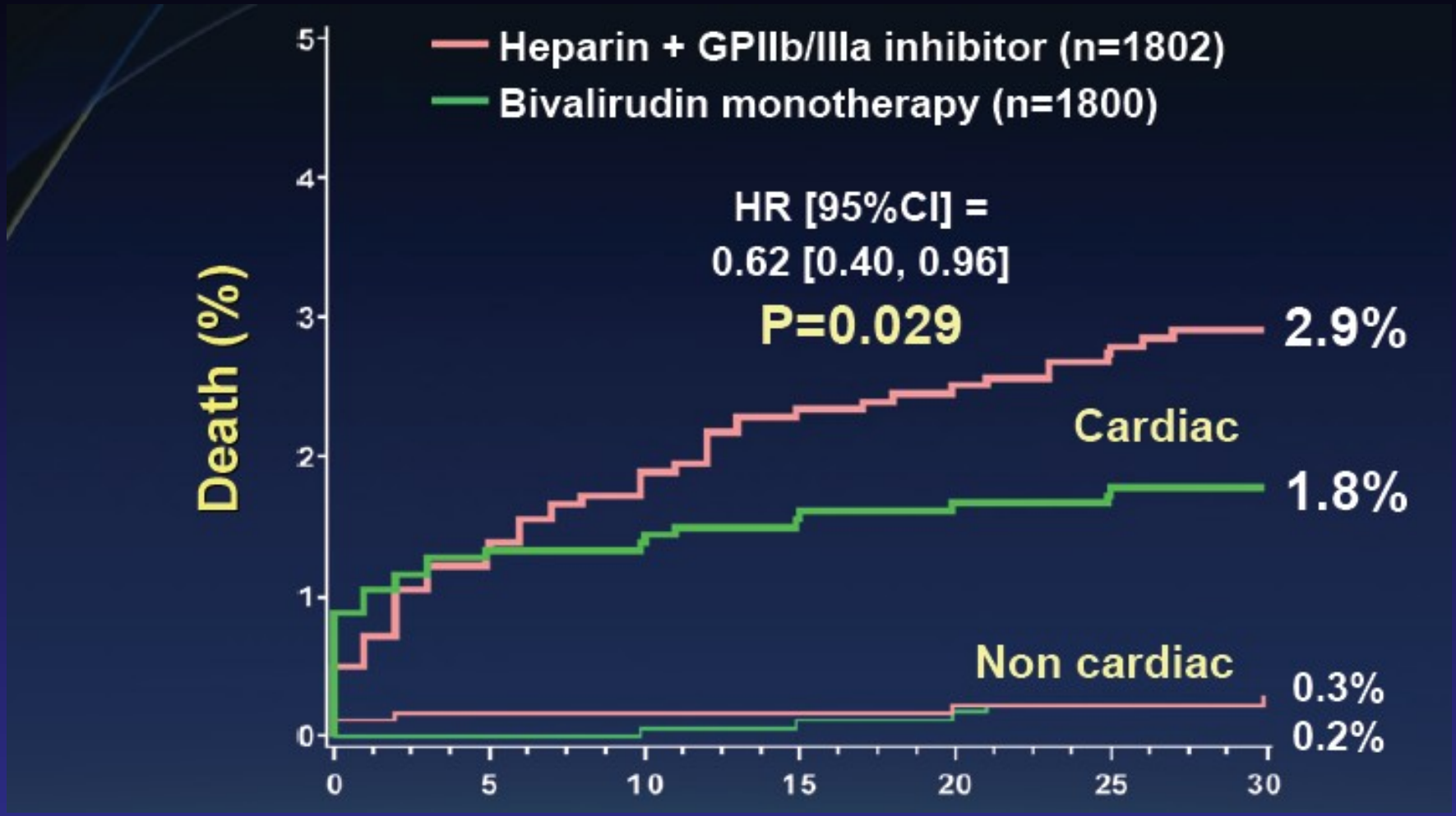
Stone G et al. N Engl J Med 2008

HORIZONS-AMI – Major bleeding (non-CABG)



Stone G et al. N Engl J Med 2008

HORIZONS-AMI – Mortality



Stone G et al. N Engl J Med 2008

HORIZONS-AMI – Stent Thrombosis

	UFH + GP IIb/IIIa (N=1553)	Bivalirudin (N=1571)	P Value
ARC 30d definite or probable stent thrombosis*	1.9%	2.5%	0.30
- definite	1.4%	2.2%	0.09
- probable	0.5%	0.3%	0.24
- acute (≤24 hrs)	0.3%	1.3%	0.0007
- subacute (>24 hrs – 30d)	1.7%	1.2%	0.28

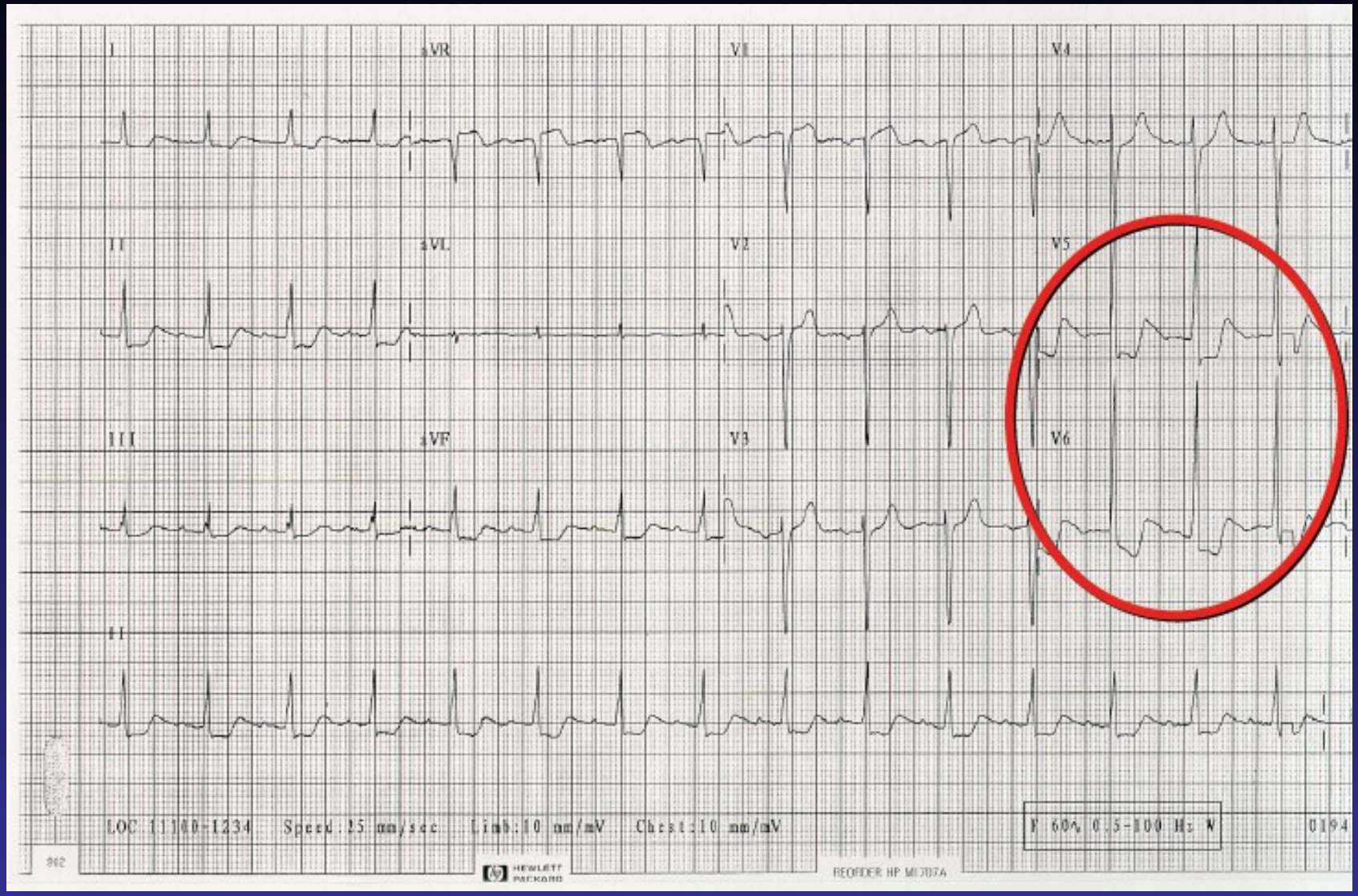
Stone G et al. N Engl J Med 2008

NSTE-ACS

A case of ACS

- 76 year old woman presents to ER with shoulder discomfort
- Chronic risk factors: hyperlipidemia, type II diabetes, HTN, chronic renal insufficiency
- Left shoulder pain improved with movement, massage therapy. Similar symptoms on exercise bike, resolves after 10 minutes
- Exam: HR 90, BP 118/70; crackles at both lung bases
- Labs: creatinine 1.7 mg/dL, Troponin T 0.32

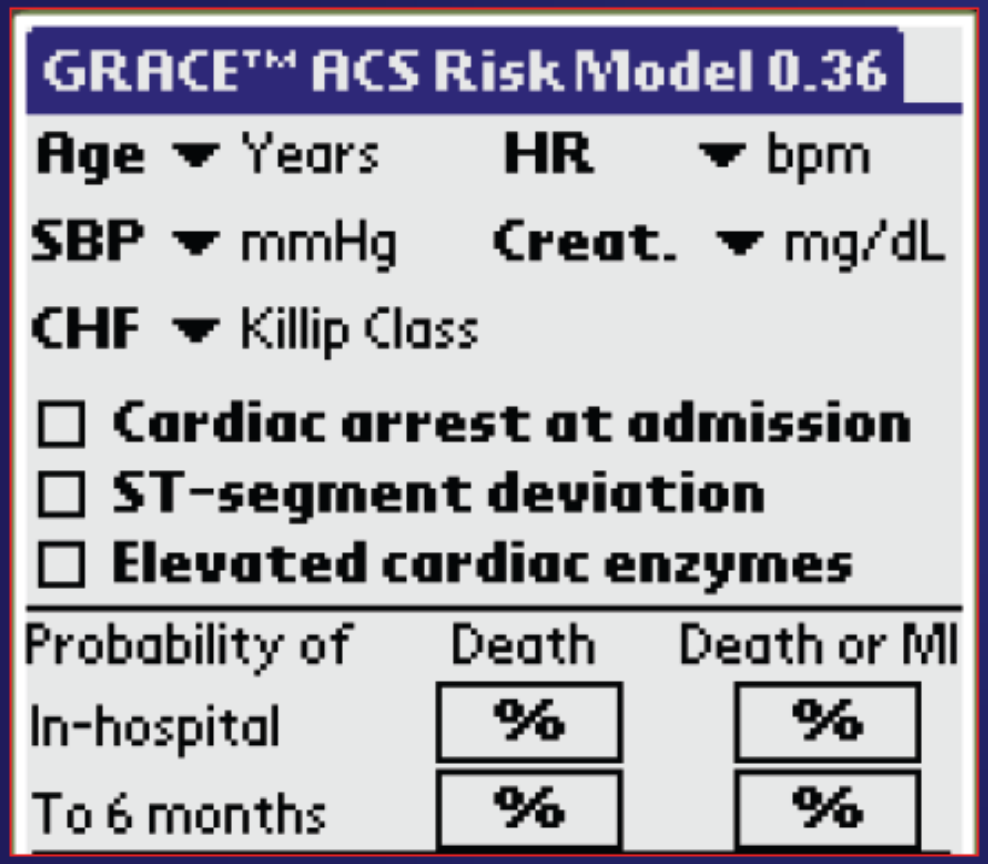
A case of ACS


I
aVR
V1
V4
II
aVL
V2
V5
III
aVF
V3
V6
II
LOC 11100-1234 Speed:25 mm/sec Limb:10 mm/mV Chest:10 mm/mV
F 60~ 0.5-100 Hz N
0194
HEWLETT PACKARD
RECORDER HP M1707A

According to GRACE score, what is her in-hospital and 6-month mortality rate?

- 2-3% and 5%
- 5% and 9%
- 10% and 15%
- 20% and 30%

GRACE Score



Variables

- Age (continuous)
- Killip class
- Blood pressure
- ST deviation
- Cardiac arrest
- Creatinine
- Elevated CK-MB or Tn
- Heart rate

GRACE Score

Variables

Age (continuous)	76
Killip class	II
Blood pressure	118/70
ST deviation	yes
Cardiac arrest	no
Creatinine	1.7
Elevated CK-MB/Tn	yes
Heart rate	90

	In-hosp	6 mo
Death	20%	30%
Death/MI	30%	50%

Selection of Initial Treatment Strategy: Invasive Versus Conservative Strategy

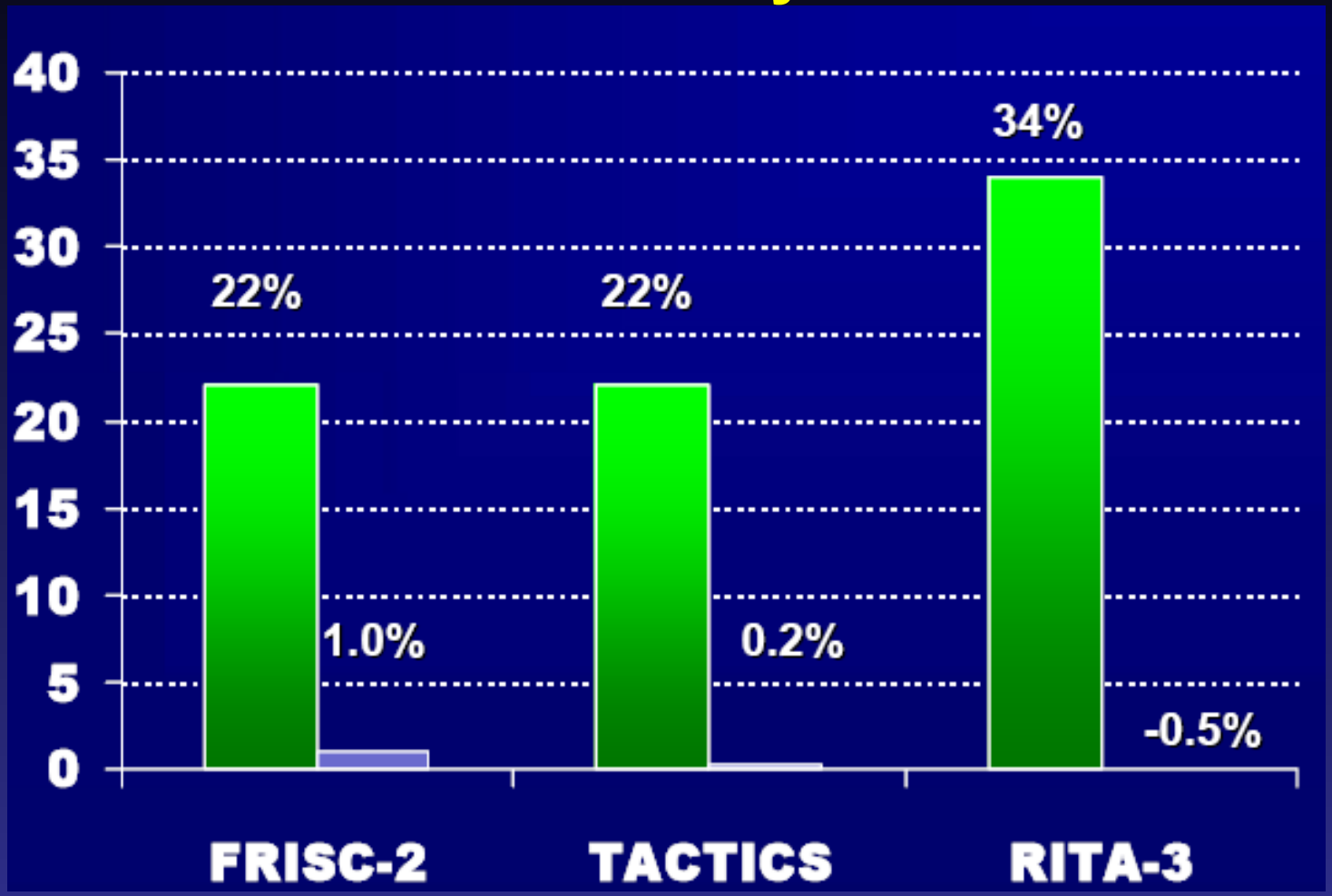
Preferred Strategy	Patient Characteristics
Invasive	Recurrent angina or ischemia at rest or with low-level activities despite intensive medical therapy
	Elevated cardiac biomarkers (TnT or TnI)
	New or presumably new ST-segment depression
	Signs or symptoms of HF or new or worsening mitral regurgitation
	High-risk findings from noninvasive testing
	Hemodynamic instability
	Sustained ventricular tachycardia
	PCI within 6 months
	Prior CABG
	High risk score (e.g., TIMI, GRACE)
	Reduced left ventricular function (LVEF less than 40%)
Conservative	Low risk score (e.g., TIMI, GRACE)
	Patient or physician preference in the absence of high-risk features

UA/NSTEMI ACC/AHA guidelines. Circulation 2007

Non STE ACS

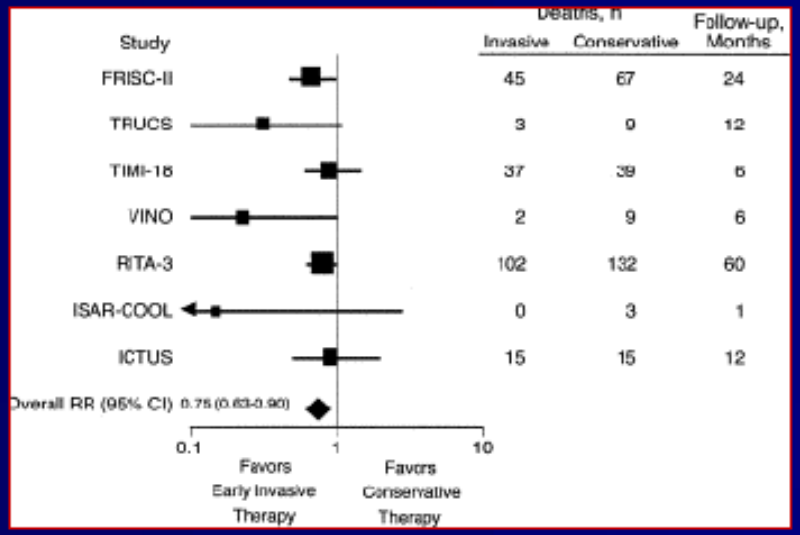
Early Versus Invasive
What's new?

Randomized Trials in NonSTMI: Relative reduction in composite outcome and absolute difference in mortality

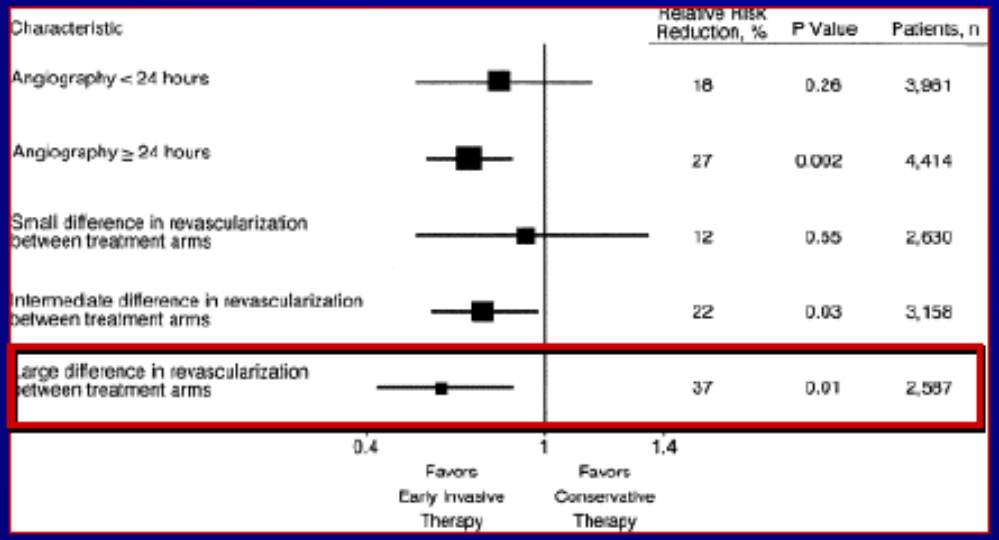


Bogarty et al. Lancet 2003

Early Invasive vs Selective Invasive Meta-analysis, average 2 year follow-up



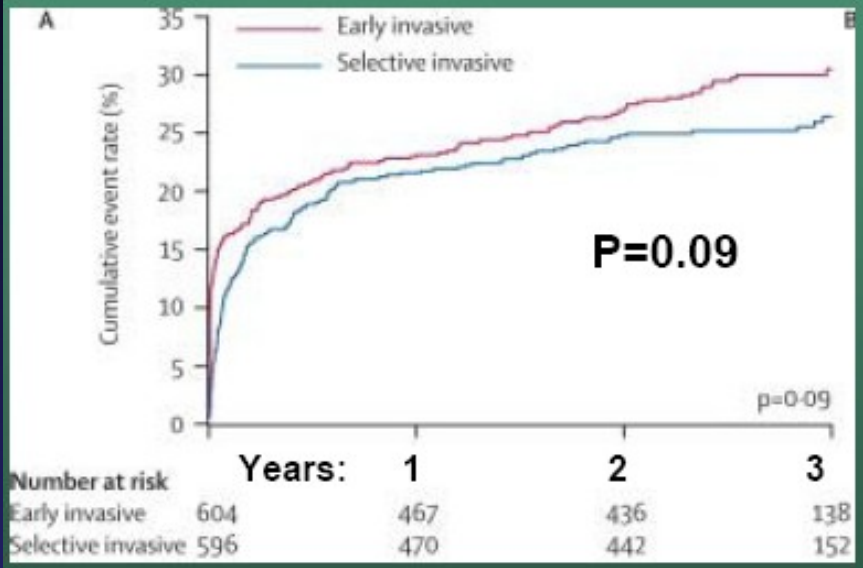
Death
(25% RRR, p=0.001)



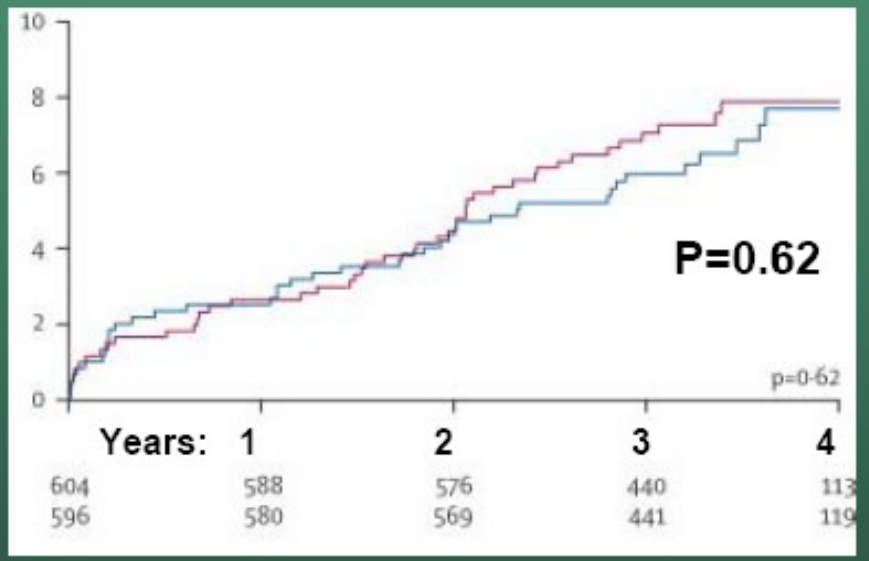
Death, according to time to cath and Δ revasc rates

Bavry et al. JACC 2006

ICTUS – 4 year follow-up



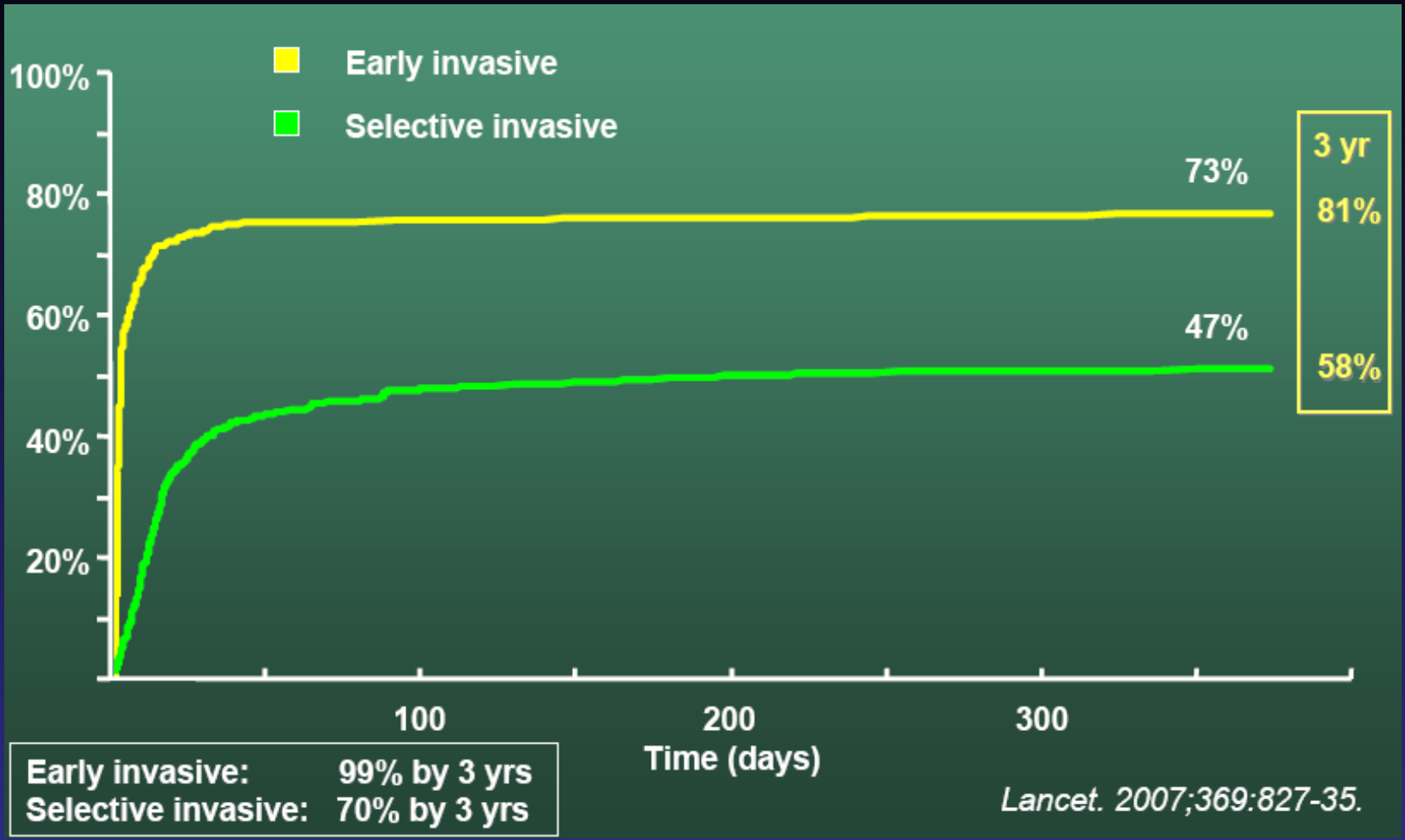
Death, MI, Rehosp for angina



Death

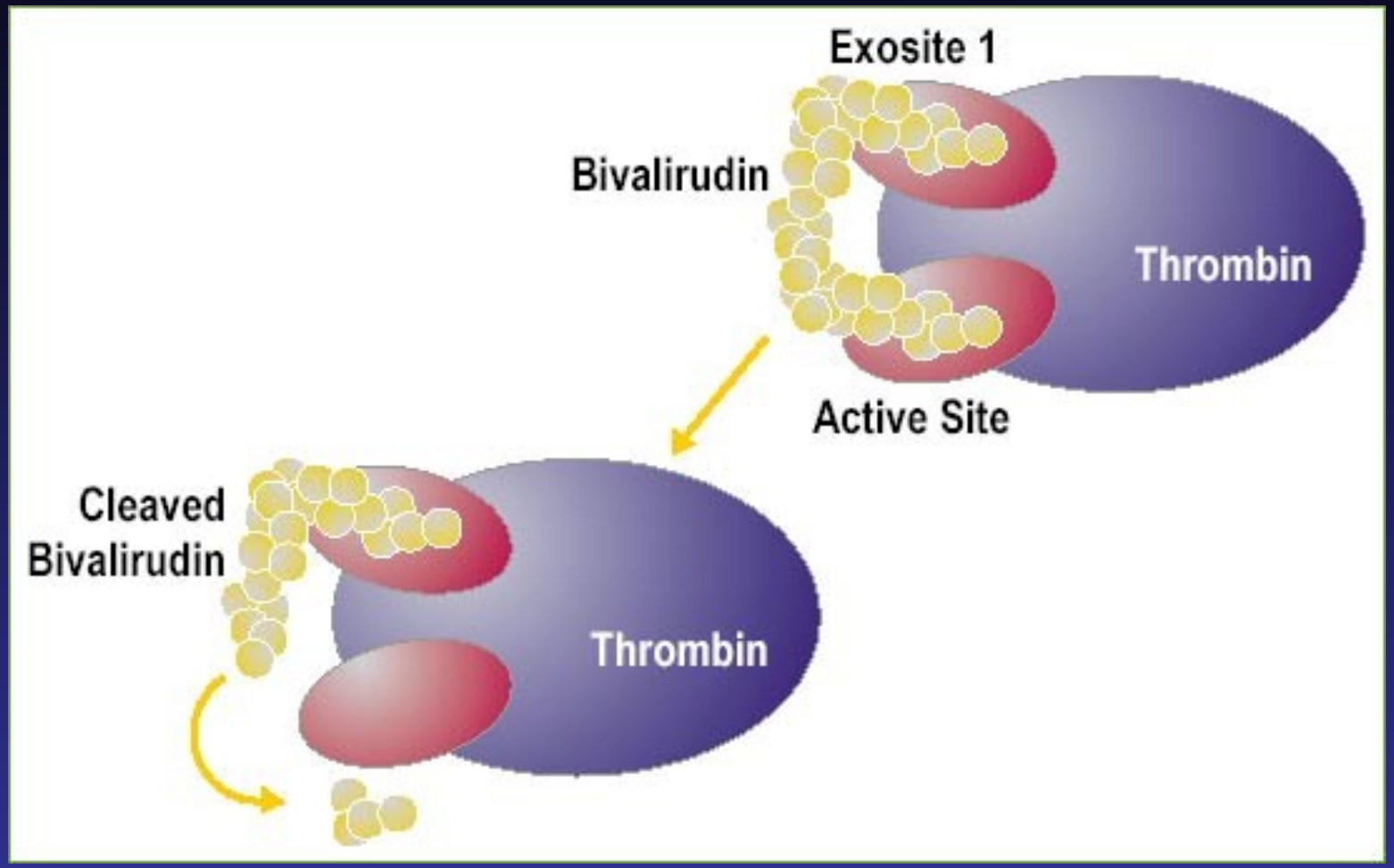
Lancet 2007

ICTUS – 4 year follow-up



Lancet 2007

Bivalirudin



ACUITY Study

13,809 pts with mod-high risk ACS undergoing early invasive therapy

- Heparin + GPIIb/IIIa
- Bivalirudin + GPIIb/IIIa
- Bivalirudin alone

Stone G et al. N Engl J Med 2006

ACUITY: 30 day outcome

Outcome	Unfractionated Heparin or Enoxaparin plus Glycoprotein IIb/IIIa Inhibitors (N=4603)	Bivalirudin plus Glycoprotein IIb/IIIa Inhibitors (N=4604)	Risk Ratio (95% CI)	P Value	Bivalirudin Alone (N=4612)	Risk Ratio (95% CI)††	P Value†
Net clinical outcome — no. (%)	538 (11.7)	541 (11.8)	1.01 (0.90–1.12)	<0.001‡ 0.93	466 (10.1)	0.86 (0.77–0.97)	<0.001‡ 0.015
Composite ischemia — no. (%)	334 (7.3)	356 (7.7)	1.07 (0.92–1.23)	0.007‡ 0.39	360 (7.8)	1.08 (0.93–1.24)	0.01‡ 0.32
Death from any cause	62 (1.3)	70 (1.5)		0.48	74 (1.6)		0.31
Myocardial infarction	227 (4.9)	229 (5.0)		0.93	248 (5.4)		0.33
Q wave	50 (1.1)	44 (1.0)		0.53	50 (1.1)		0.99
Non–Q wave	177 (3.8)	187 (4.1)		0.59	199 (4.3)		0.25
Unplanned revascularization for ischemia	105 (2.3)	123 (2.7)		0.23	110 (2.4)		0.74
Major bleeding (not related to CABG) — no. (%)	262 (5.7)	243 (5.3)	0.93 (0.78–1.10)	<0.001‡ 0.38	139 (3.0)	0.53 (0.43–0.65)	<0.001‡ <0.001
Intracranial	3 (<0.1)	3 (<0.1)		1.00	3 (<0.1)		1.00
Retroperitoneal	24 (0.5)	26 (0.6)		0.78	7 (0.2)		0.002
Access-site hemorrhage	117 (2.5)	117 (2.5)		1.00	38 (0.8)		<0.001
Requiring intervention or surgery	24 (0.5)	28 (0.6)		0.58	14 (0.3)		0.10
Hematoma ≥5 cm	102 (2.2)	101 (2.2)		0.94	32 (0.7)		<0.001
Hemoglobin decrease ≥3 g/dl with overt source	102 (2.2)	83 (1.8)		0.16	45 (1.0)		<0.001
Hemoglobin decrease ≥4 g/dl with no overt source	39 (0.8)	33 (0.7)		0.48	33 (0.7)		0.47
Blood transfusion	125 (2.7)	119 (2.6)		0.70	75 (1.6)		<0.001
Reoperation for bleeding	2 (<0.1)	5 (0.1)		0.45	4 (0.1)		0.69
All major bleeding — no. (%)	543 (11.8)	512 (11.1)		0.31	421 (9.1)		<0.001
Minor bleeding (not related to CABG) — no. (%)§	993 (21.6)	1001 (21.7)		0.84	592 (12.8)		<0.001
Bleeding according to the TIMI scale — no. (%)	306 (6.6)	297 (6.5)		0.70	183 (4.0)		<0.001
Major	86 (1.9)	76 (1.7)		0.43	43 (0.9)		<0.001
Minor	295 (6.4)	281 (6.1)		0.54	170 (3.7)		<0.001
Acquired thrombocytopenia — no. (%)¶	511 (11.1)	497 (10.8)		0.64	457 (9.9)		0.06

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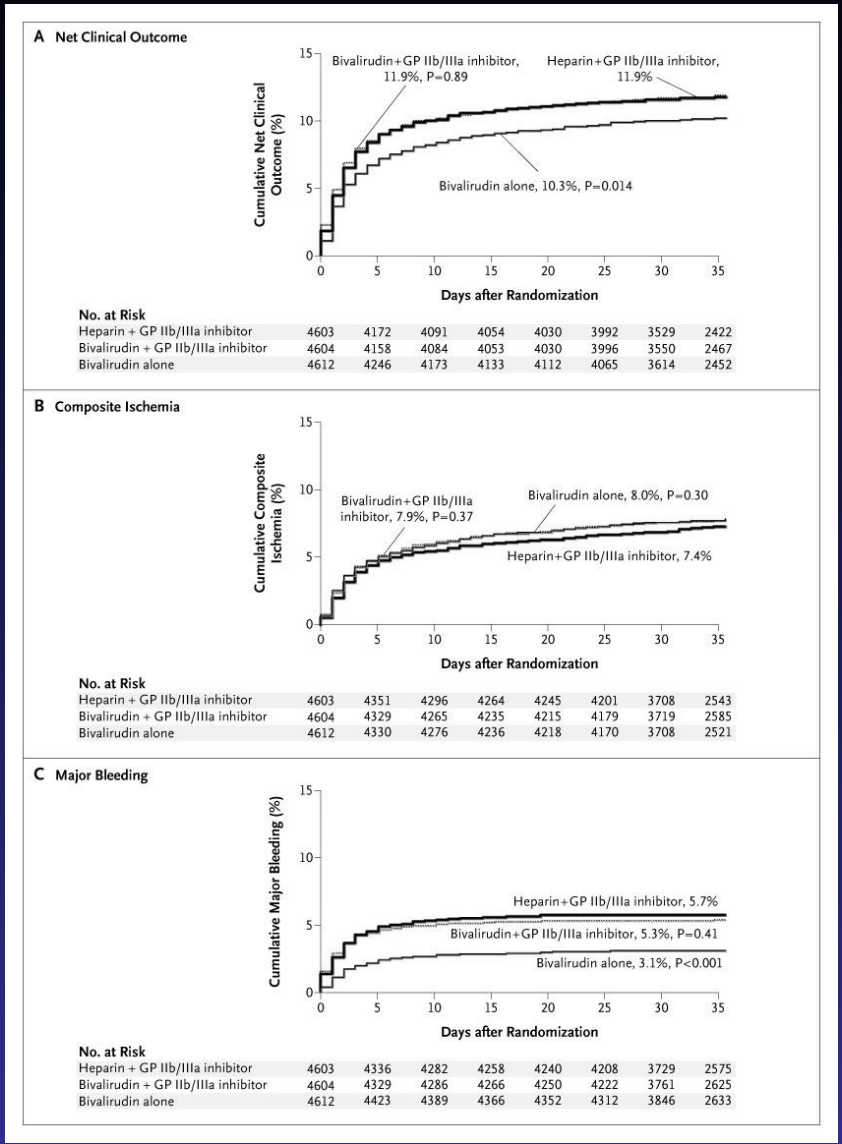
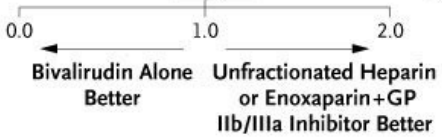
ACUITY - 30 day outcome



Acuity - Subgroup analysis

A Composite Ischemia

Variable	No. of Patients	Percentage of Patients: Bivalirudin alone	Percentage of Patients: Heparin+GP IIb/IIIa inhibitor	Relative Risk (95% CI)	P Value for Interaction
CK MB/troponin					0.65
Elevated	5073	9.4	8.4	1.12 (0.94–1.34)	
Normal	3403	5.7	5.4	1.04 (0.79–1.38)	
ST-segment deviation					0.96
Yes	3197	10.1	9.3	1.09 (0.88–1.34)	
No	6008	6.6	6.1	1.08 (0.89–1.31)	
TIMI risk score					0.16
0–2	1291	4.2	5.8	0.73 (0.45–1.18)	
3–4	4407	7.4	6.1	1.21 (0.97–1.51)	
5–7	2449	11.0	10.6	1.04 (0.83–1.31)	
Thienopyridine before angiography or PCI					0.054
Yes	5753	7.0	7.3	0.97 (0.80–1.17)	
No	3304	9.1	7.1	1.29 (1.03–1.63)	
Treatment strategy					0.82
PCI	5180	8.8	8.2	1.07 (0.90–1.28)	
CABG	1040	16.1	15.1	1.06 (0.80–1.41)	
Medical therapy	2995	3.4	2.7	1.24 (0.83–1.85)	
GP IIb/IIIa inhibitor					NA
Upstream	6906	7.8	6.9	1.13 (0.95–1.36)	
Deferred	6921	7.8	7.6	1.02 (0.86–1.22)	
Randomization to angiography or intervention, thirds					0.46
Early (<3.0 hr)	2918	6.0	5.8	1.04 (0.78–1.39)	
Intermediate (3.0–19.7 hr)	2925	7.0	5.5	1.26 (0.95–1.67)	
Late (>19.7 hr)	2981	10.0	9.9	1.01 (0.81–1.25)	



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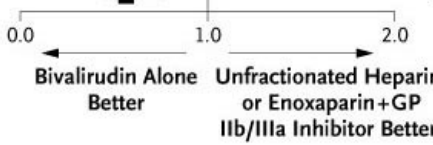
ACUITY - Subgroup analysis

B Major Bleeding

Variable	No. of Patients	Percentage of Patients: Bivalirudin alone	Percentage of Patients: Heparin+GP IIb/IIIa inhibitor	Relative Risk (95% CI)	P Value for Interaction
CK MB/troponin					0.09
Elevated	5073	3.8	6.4	0.59 (0.46–0.75)	
Normal	3403	1.8	4.8	0.38 (0.25–0.57)	
ST-segment deviation					0.46
Yes	3197	3.9	6.7	0.58 (0.43–0.79)	
No	6008	2.5	5.1	0.50 (0.38–0.65)	
TIMI risk score					0.91
0–2	1291	2.5	5.4	0.47 (0.26–0.84)	
3–4	4407	2.6	4.8	0.54 (0.39–0.74)	
5–7	2449	4.1	7.5	0.54 (0.39–0.76)	
Thienopyridine before angiography or PCI					0.53
Yes	5753	3.1	5.9	0.53 (0.41–0.68)	
No	3304	2.9	4.8	0.60 (0.42–0.86)	
Treatment strategy					0.90
PCI	5180	3.5	6.8	0.52 (0.40–0.66)	
CABG	1040	2.0	4.2	0.49 (0.23–1.01)	
Medical therapy	2995	2.5	4.4	0.57 (0.38–0.84)	
GP IIb/IIIa inhibitor					NA
Upstream	6906	3.0	6.1	0.50 (0.40–0.63)	
Deferred	6921	3.0	5.3	0.57 (0.45–0.72)	
Randomization to angiography or intervention, thirds					0.92
Early (<3.0 hr)	2918	2.9	5.4	0.54 (0.38–0.78)	
Intermediate (3.0–19.7 hr)	2925	2.9	4.9	0.60 (0.42–0.87)	
Late (>19.7 hr)	2981	3.4	6.0	0.57 (0.40–0.79)	



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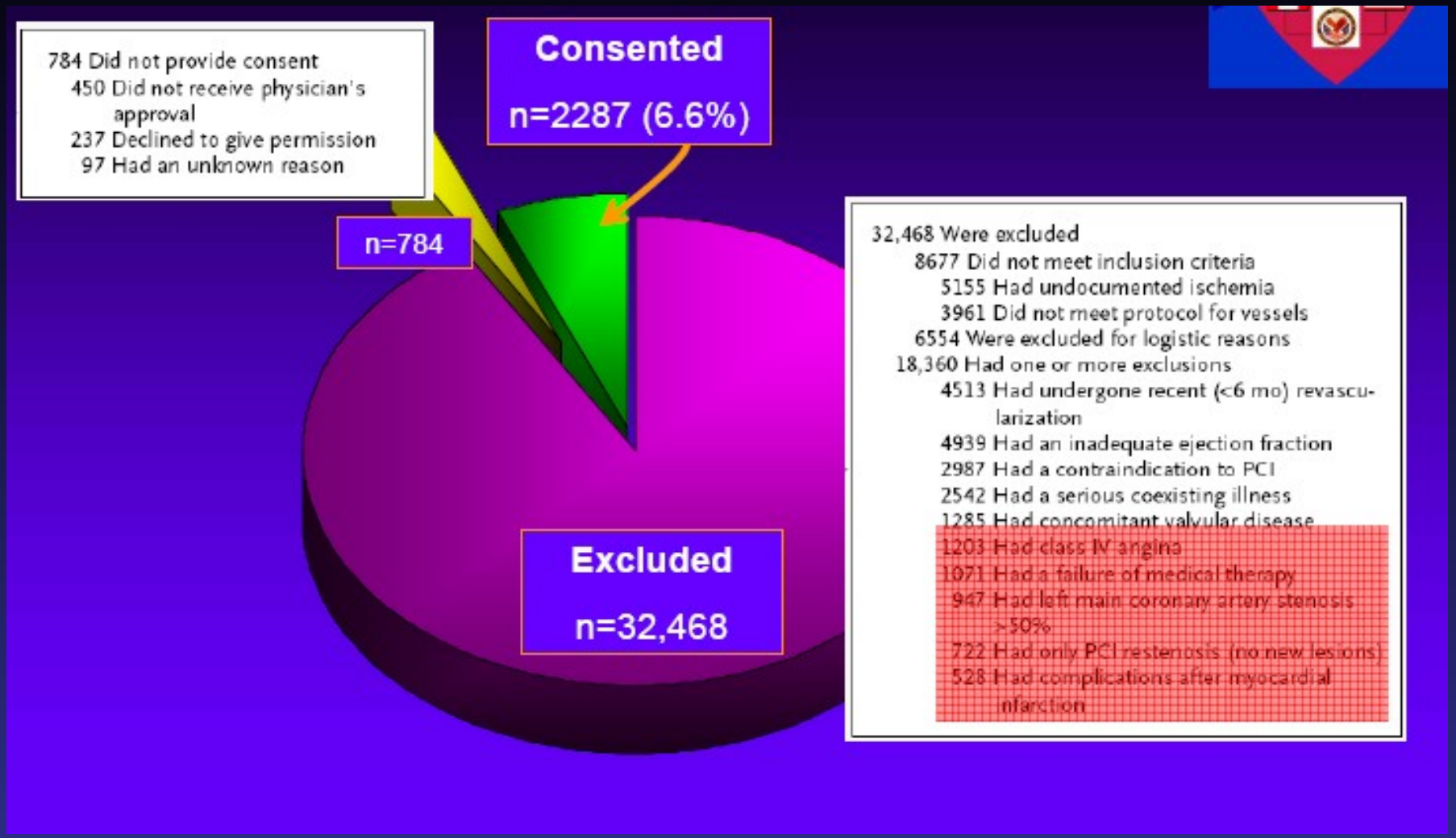
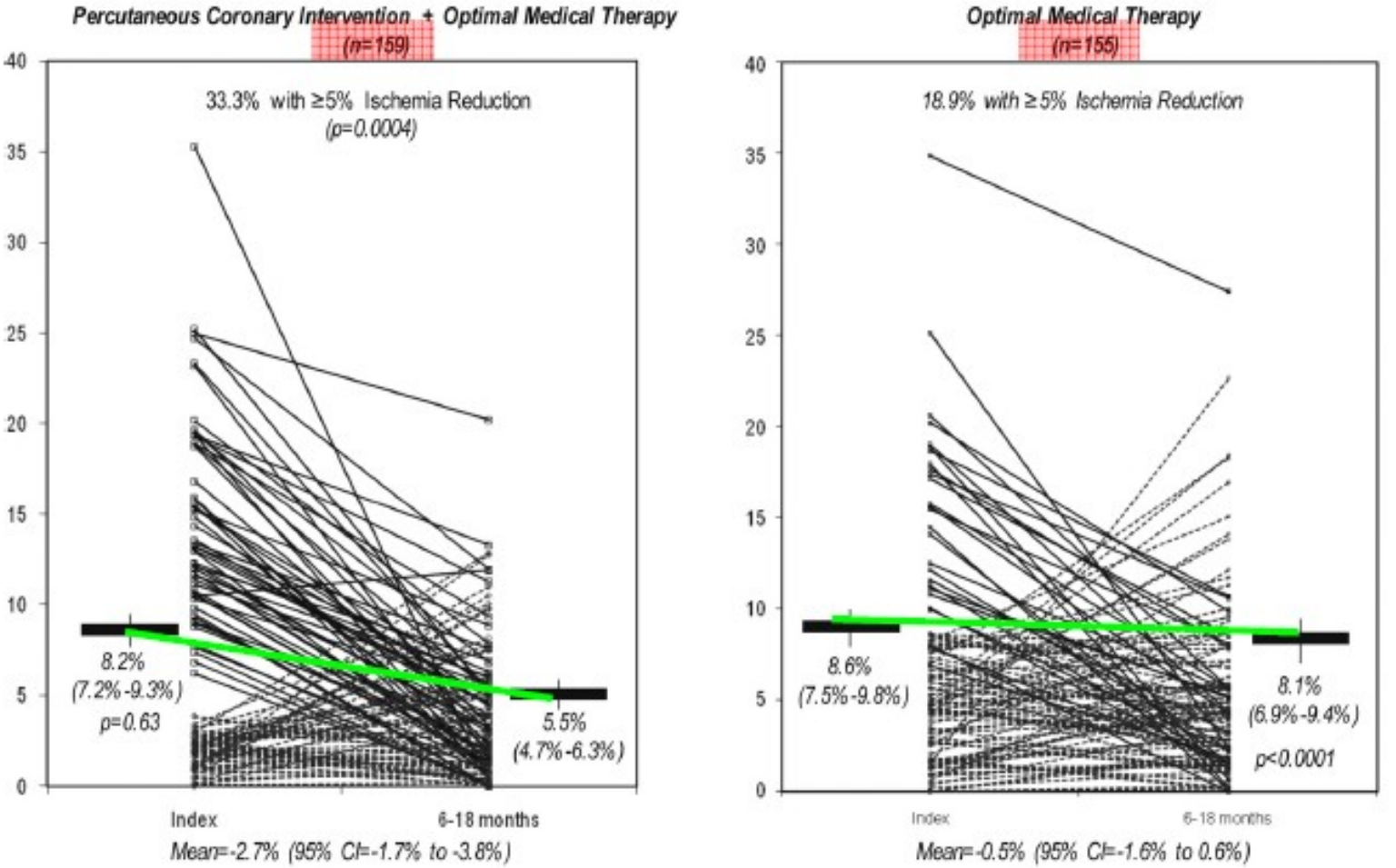
PCI in Stable Angina

COURAGE – Patients Screening



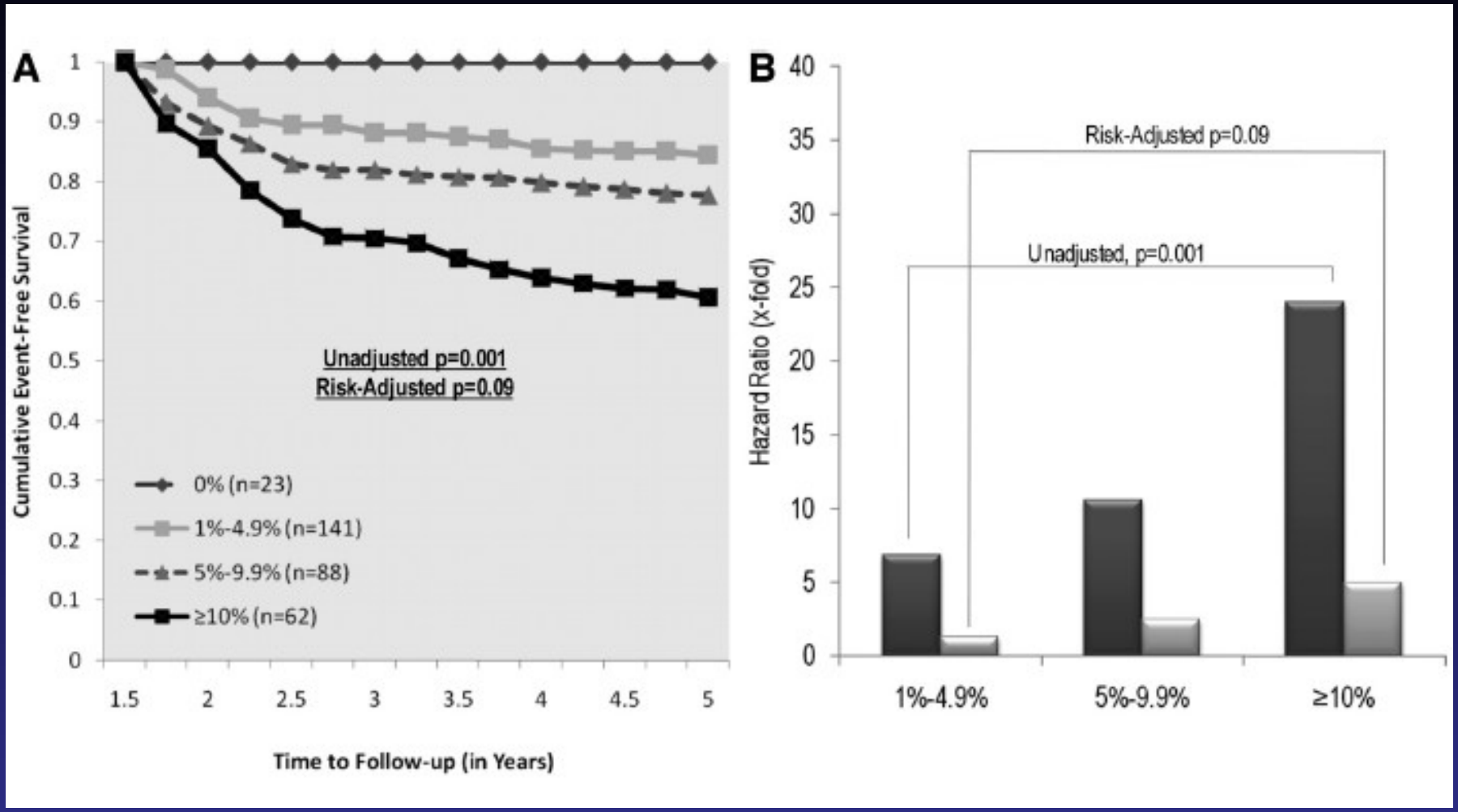
COURAGE Trial. N Engl J Med 2007

COURAGE – Nuclear Substudy



COURAGE Trial. Circulation 2008

COURAGE – Outcome by residual ischemia



COURAGE Trial. Circulation 2008

ACC/AHA Guidelines for PCI in Stable AP (2005)

- Class IIa
  - PCI is reasonable in patients with symptomatic ischemia or CCS I or II AP and with 1 or more significant lesions in 1 or 2 coronaries suitable for PCI with a likelihood of success and low risk… The vessels to be dilated must subtend a moderate to large area of viable myocardium or be associated with moderate to severe degree of ischemia in noninvasive testing (level of evidence B)

ACC/AHA Guidelines for PCI in Stable AP (2005)

- Class IIb
  - The effectiveness of PCI for patients with asymptomatic ischemia or CCS I or II who have 2 or 3 VD with significant proximal LAD who are eligible for CABG with 1 arterial conduit and who have treated diabetes or abnormal LV function is not well established (Level B)
  - PCI might be considered for patients with asymptomatic ischemia or CCS I or II with non-proximal LAD that subtends a moderate area of viable myocardium and demonstrates ischemia in noninvasive testing (level C)

ESC Guidelines for PCI in Stable AP (2005)

Table 1 Recommendations of PCI indications in stable CAD

Indication	Classes of recommendations and levels of evidence	Randomized studies for levels A or B
Objective large ischaemia	I A	ACME[a] ACIP[b]
Chronic total occlusion	IIa C	—
High surgical risk, including LV-EF < 35%	IIa B	AWESOME
Multi-vessel disease/diabetics	IIb C	—
Unprotected LM in the absence of other revascularization options	IIb C	—
Routine stenting of *de novo* lesions in native coronary arteries	I A	BENESTENT-I STRESS
Routine stenting of *de novo* lesions in venous bypass grafts	I A	SAVED VENESTENT

Assuming that the lesions considered most significant are technically suited for dilatation and stenting, the levels of recommendation refer to the use of stainless steel stents.

[a]The benefit was limited to symptom improvement and exercise capacity.

[b]ACIP is not a pure trial of PCI vs. medical treatment as half of the revascularization patients were treated with bypass graft surgery. Drug-eluting stents are discussed subsequently.

תודה ובהצלחה!

ע"פ הנחיות ACC/AHA מ 2007 לטיפול בחולים עם NSTEMI מה אינו מהווה קריטריון לטיפול פולשני מוקדם?

- חולה עבר PCI לעורק עוקף לפני 3 חודשים
- חולה 5 שנים לאחר ניתוח מעקפים
- ניקוד GRACE גבוה
- אירועי NSVT
- מקטע פליטה של 38%

מתן ביוואלירודין לעומת אינטגרילין + הפארין בחולים עם STEMI העוברים PCI ראשוני כרוך בכל הנ"ל פרט ל:

- ירידה משמעותית של 41% בשיעור דימומים מאג'וריים במעקב ל 30 יום
- ירידה משמעותית של 38% בשיעור תמותה מסיבה קרדיאלית במעקב ל 30 יום
- עליה משמעותית בשיעור של סטנט טרומבוזיס אקוטי (מתחת ל 24 שעות)
- ירידה משמעותית בשיעור של סטנט טרומבוזיס סובאקוטי (מעל 24 שעות)

ע"פ ה ESTROFA REGISTRY שפורסם ב JACC ב 2008 מה מהנ"ל אינו מהווה גורם חיזוי לסטנט טרומבוזיס מוקדם (מתחת ל 30 יום)?

- השתלת תומך בחולה עם STEMI
- אורך התומך
- אי ספיקת כליות
- סוכרת
- אי ספיקת לב

מה מהנ"ל נכון לגבי PCI ראשוני בחולה עם STEMI?

- שימוש בקטטר המבצע אספירציה של הקריש טרם השתלת תומך משפר הישרדות ב 30 יום.
- אין כל הוכחה כי מתן ABCIXIMAB משפר תוחלת חיים.
- מחקר BRAVE -2הוכיח כי PCI לאחר 12 שעות מתחילת כאבים משפר הישרדות אך אינו משפיע על גודל האוטם.
- השימוש בתומך משחרר תרופה אינו יעיל מבחינת הורדת שכיחות TLR