

Angioplasty Summit: April 26, 2007

AMI Intervention in DES Era and Beyond

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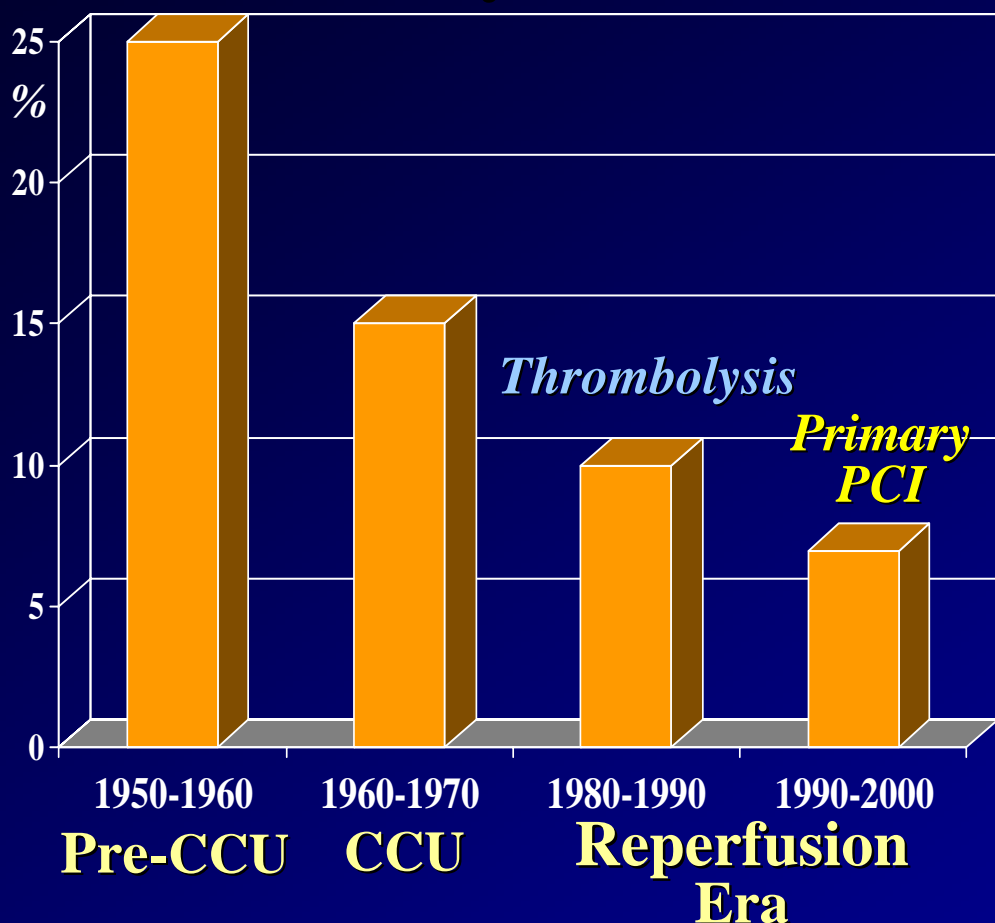


ZWOLLE

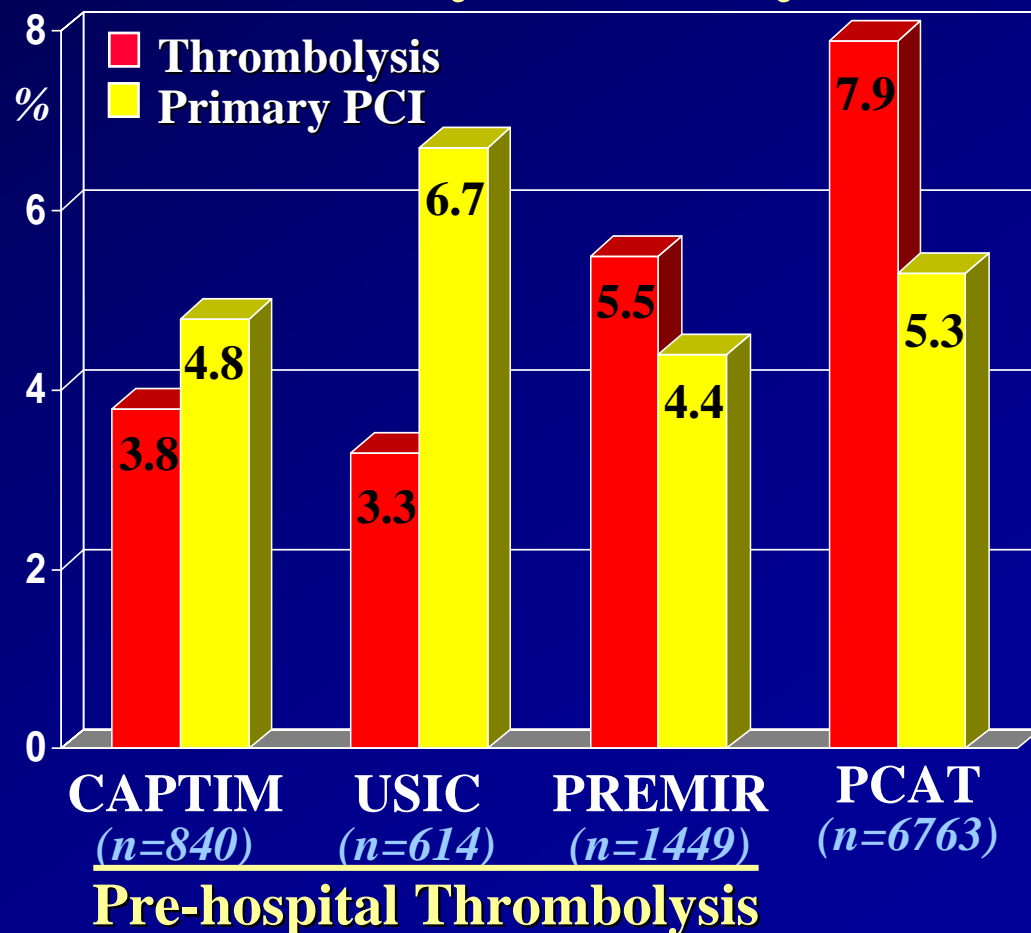


Reperfusion Therapy for STEMI

AMI Mortality in Netherlands



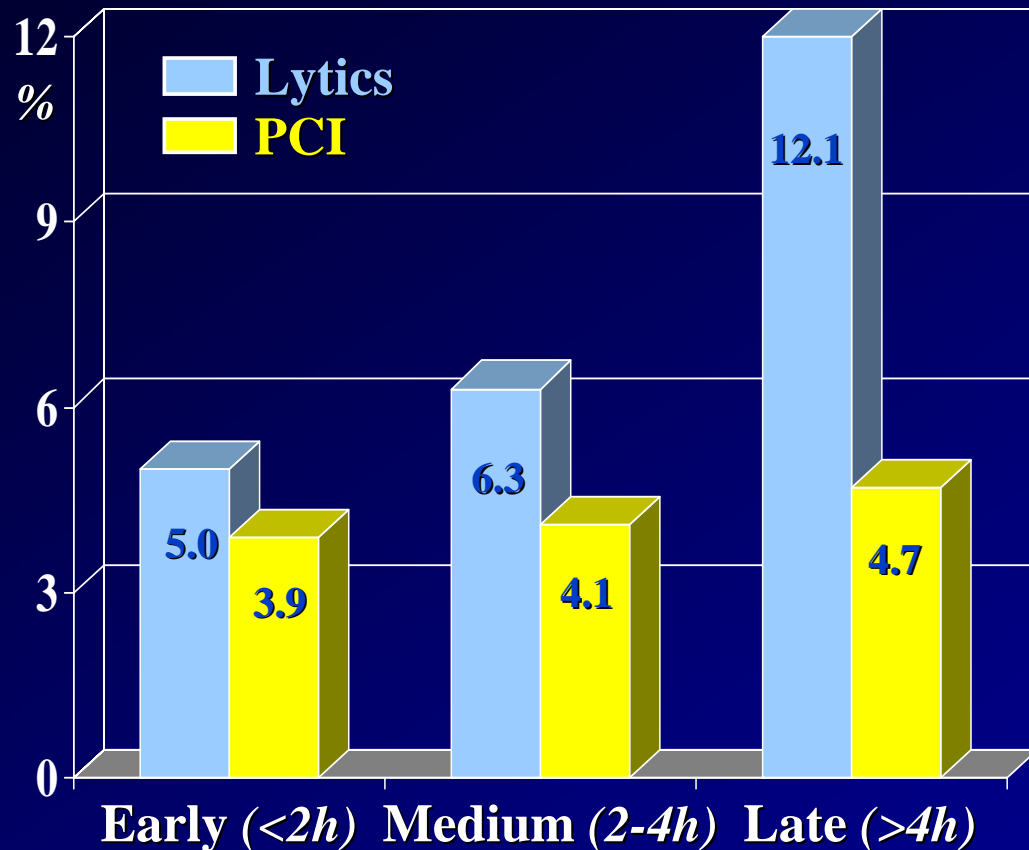
30-Day Mortality



PCI has never been shown to reduce mortality, except in subsets of pts with AMI

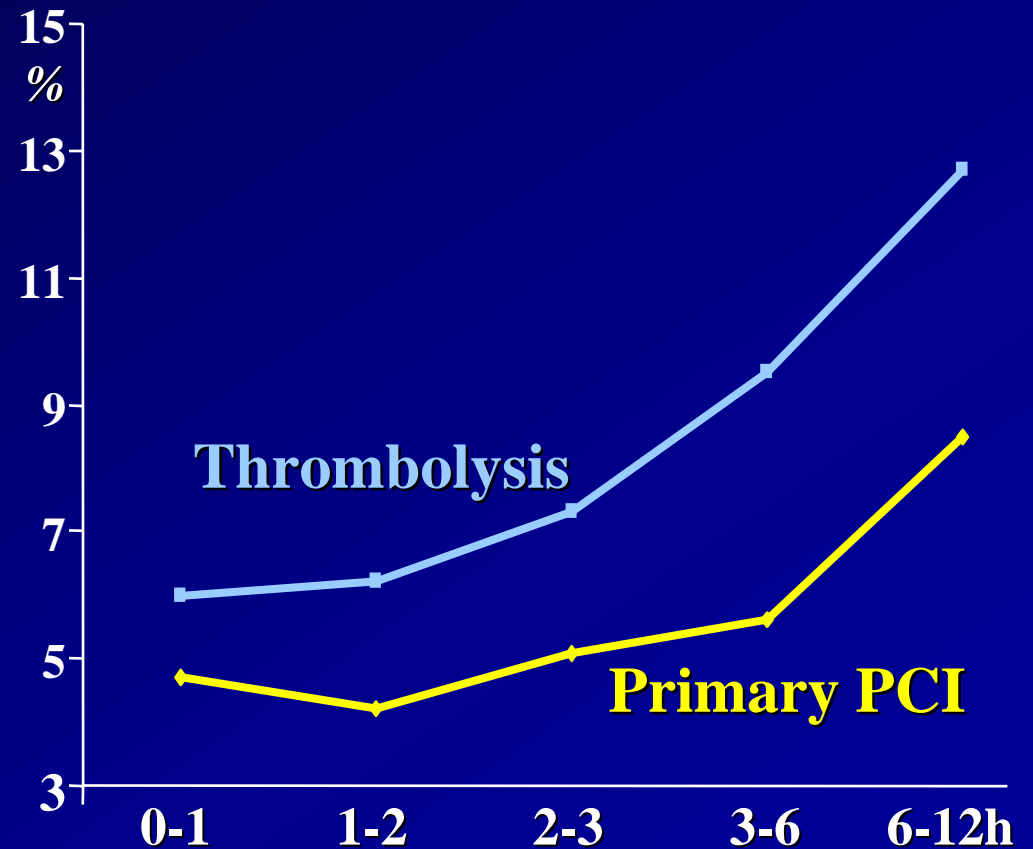
Primary PCI vs Thrombolysis for STEMI

Pooled Analysis: PCI vs Lytics Mortality at 30 days



Zijlstra et al. Eur Heart J 2002

PCAT Meta-Analysis (n=6763) Time-delay & 30-d Mortality

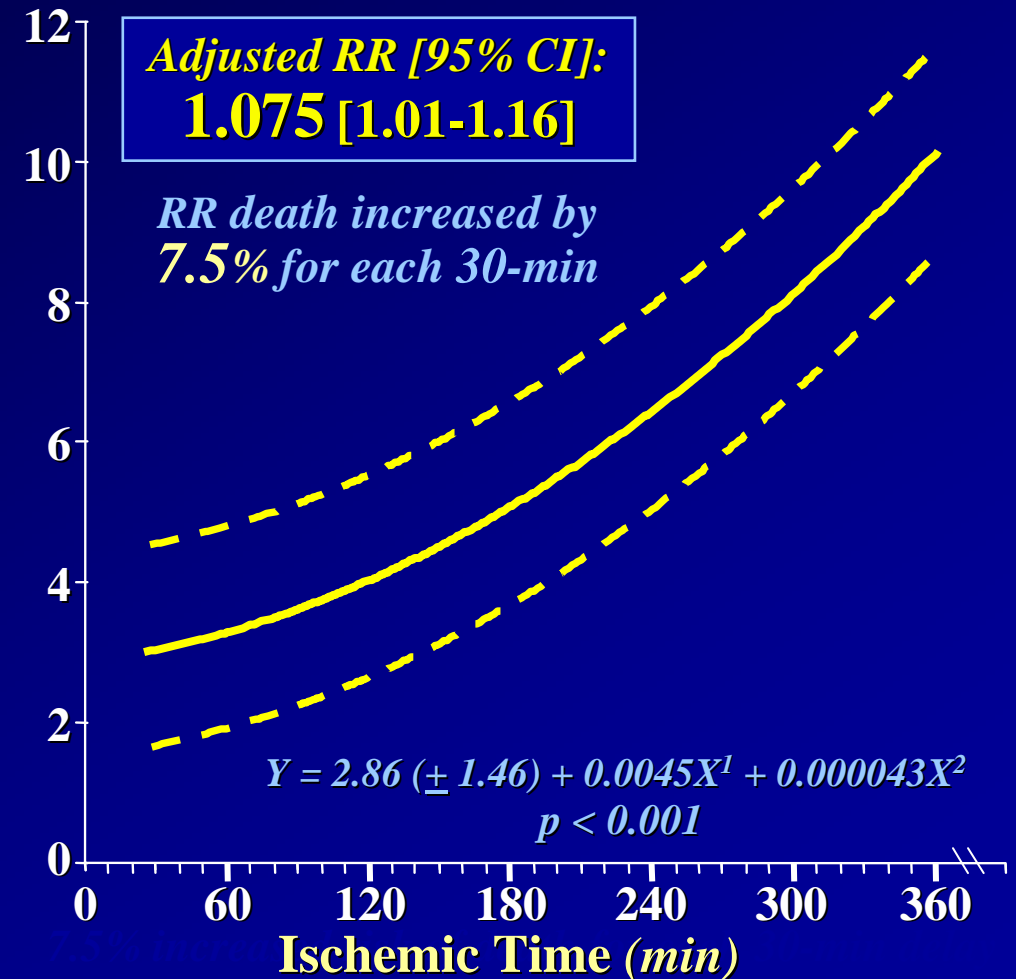
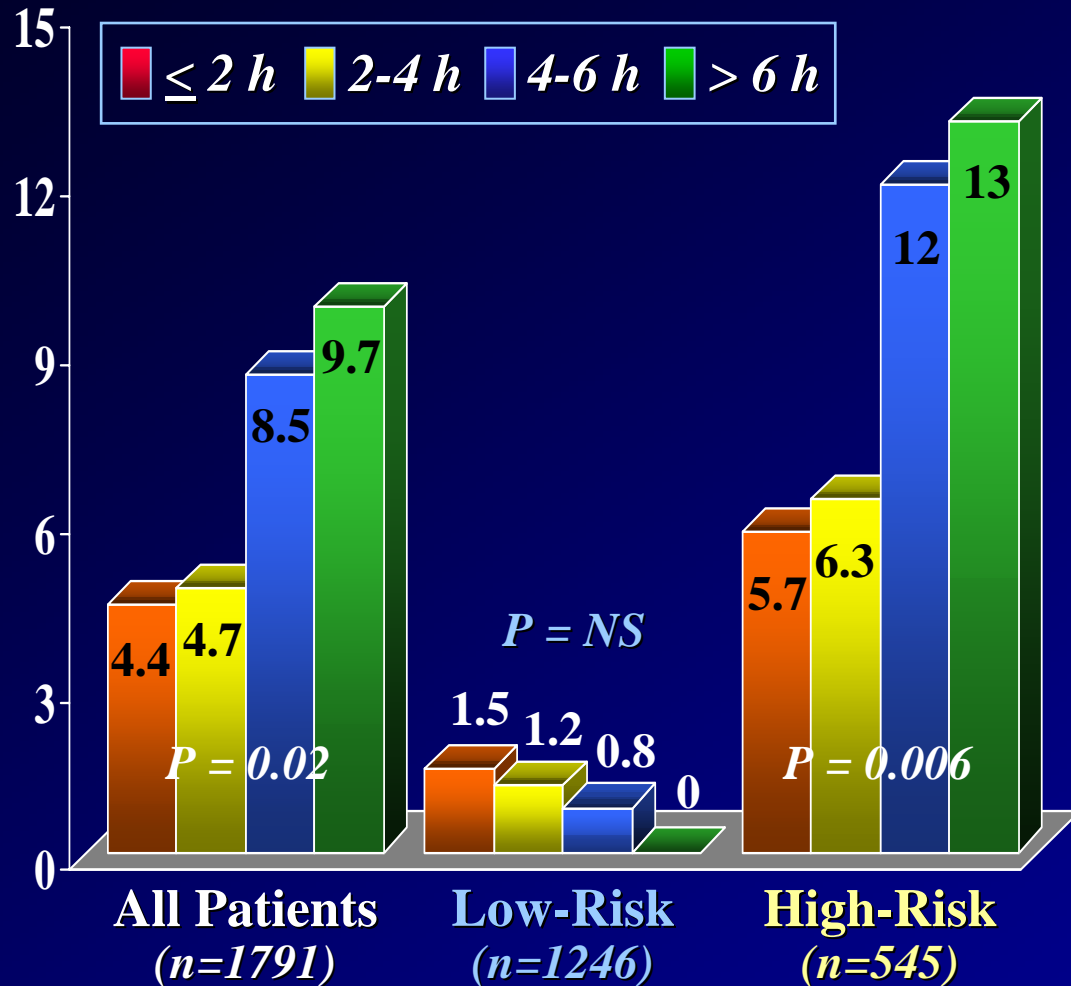


Boersma et al. EHJ 2006

Are time-delays to P-PCI really **NOT** that important?

Zwolle Randomized Trial

Symptom-to-Balloon and One-year Mortality (%)



De Luca et al. JACC 2003

De Luca, Suryapranata Circulation 2004

Every minute delay does count: not only for Lytics, but also for P-PCI

Zwolle Pre-hospital Triage in Transferring patients for PCI

Zwolle **PHIAT** protocol (1998 -)
Pre-Hospital Infarct Angioplasty Triage

35 Ambulances + computer-assisted
12-lead tele-ECG, using algorithm

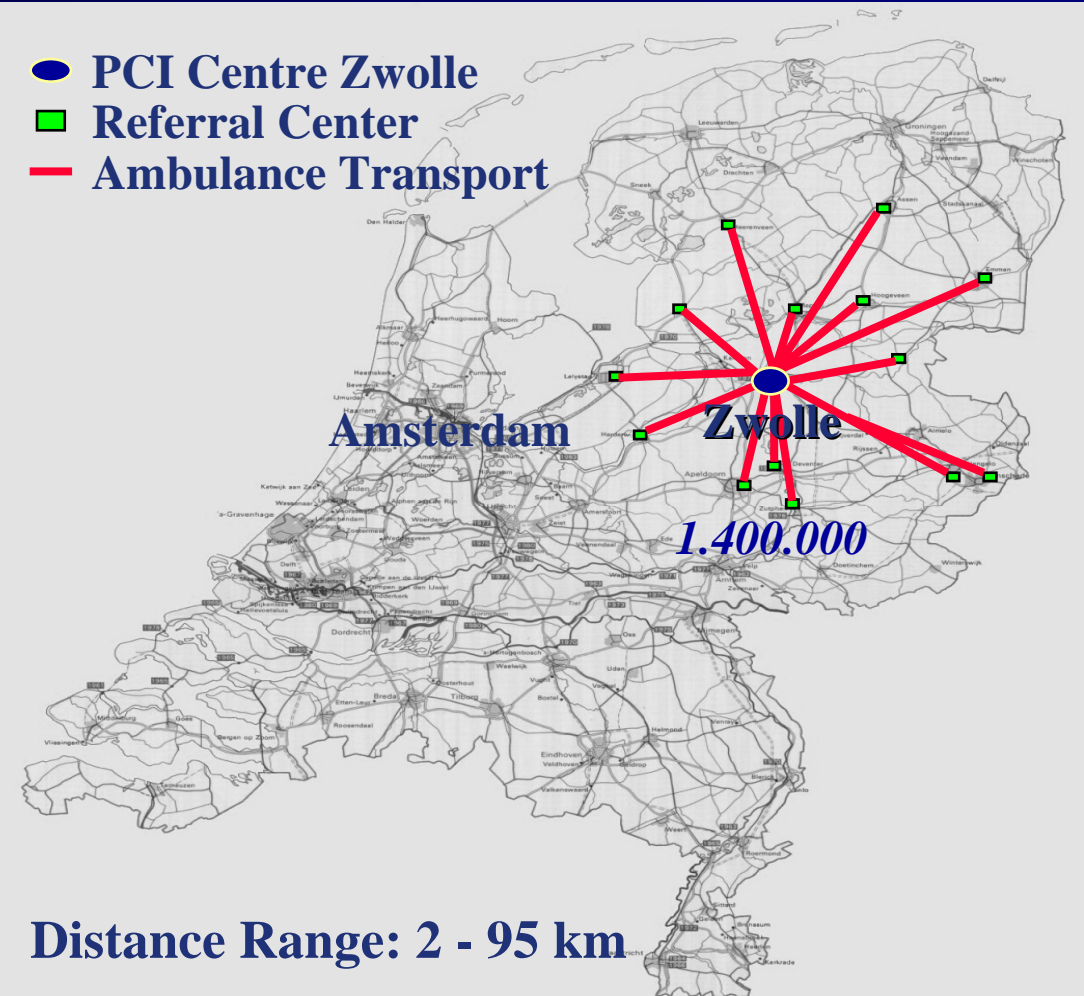


Identification of a large AMI
Ambulance nurse only, no physician



Immediate transfer to Cathlab
Rather than to nearest Hosp/CCU/ER

- PCI Centre Zwolle
- Referral Center
- Ambulance Transport



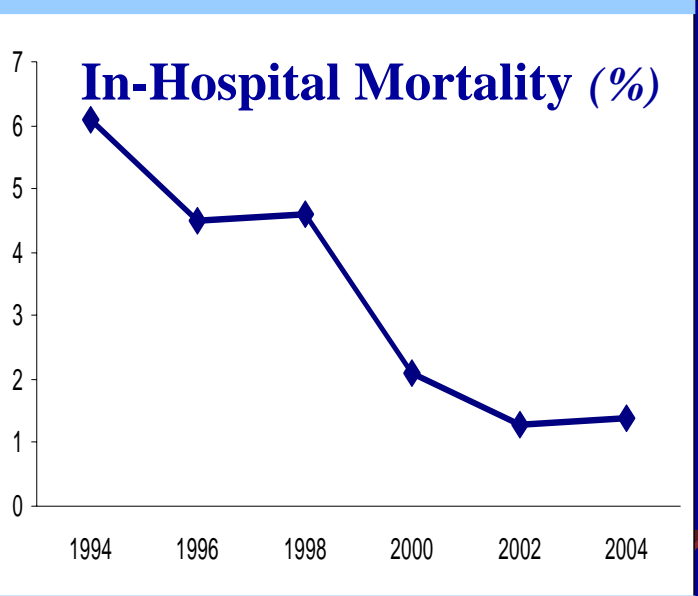
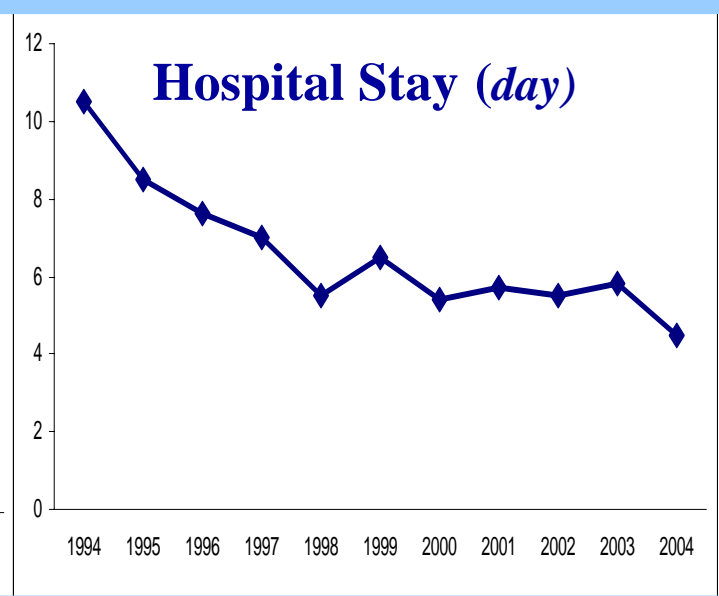
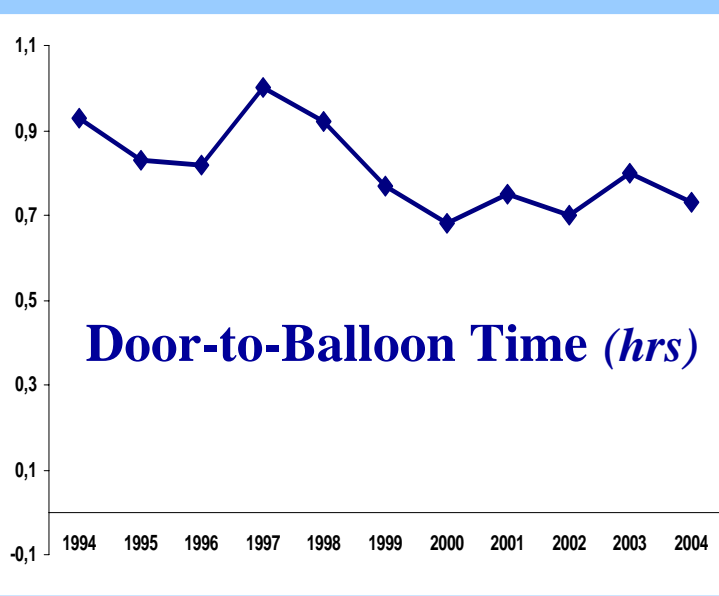
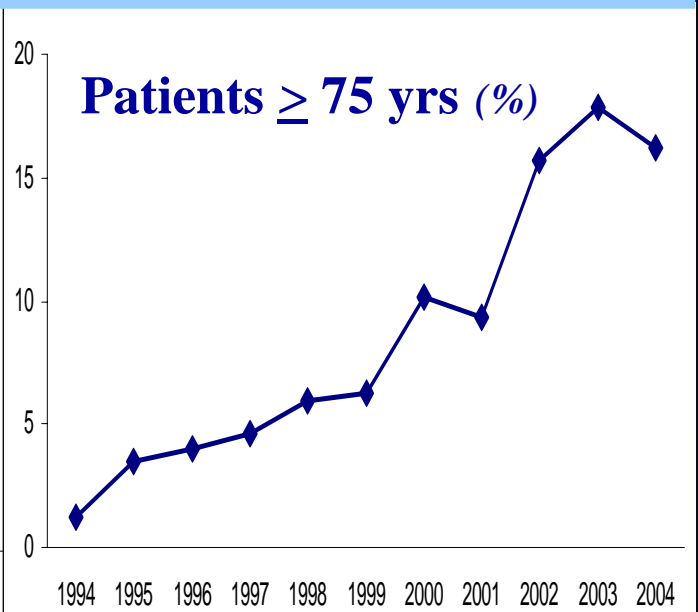
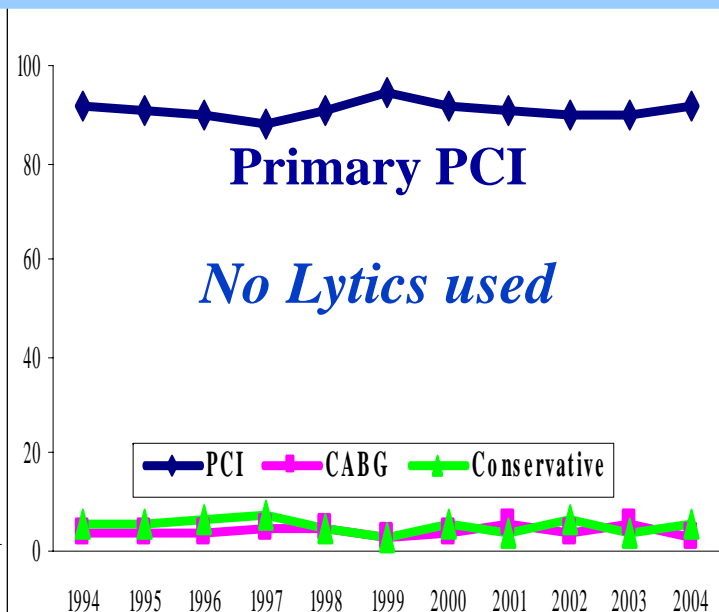
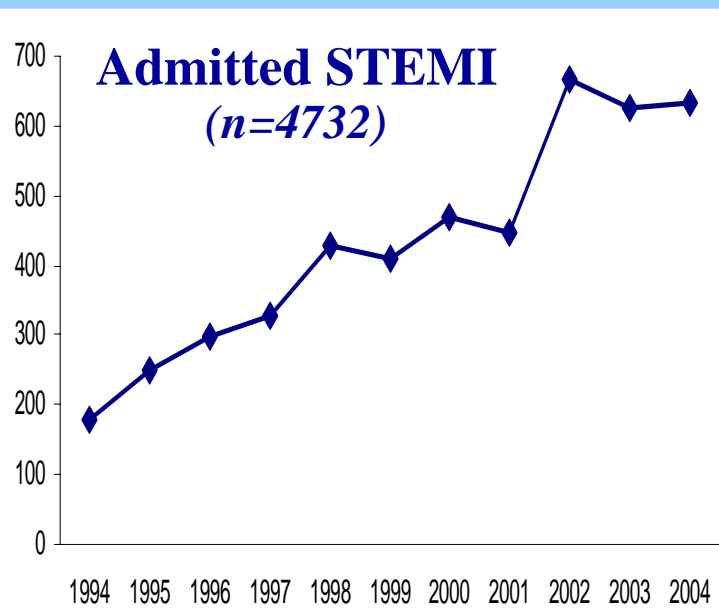
Symptom-Ambulance
91 min

Ambulance-Admission
49 min

Door-Balloon
38 min

Total
178'

Primary PCI for STEMI: Zwolle Experience (1994-2004)

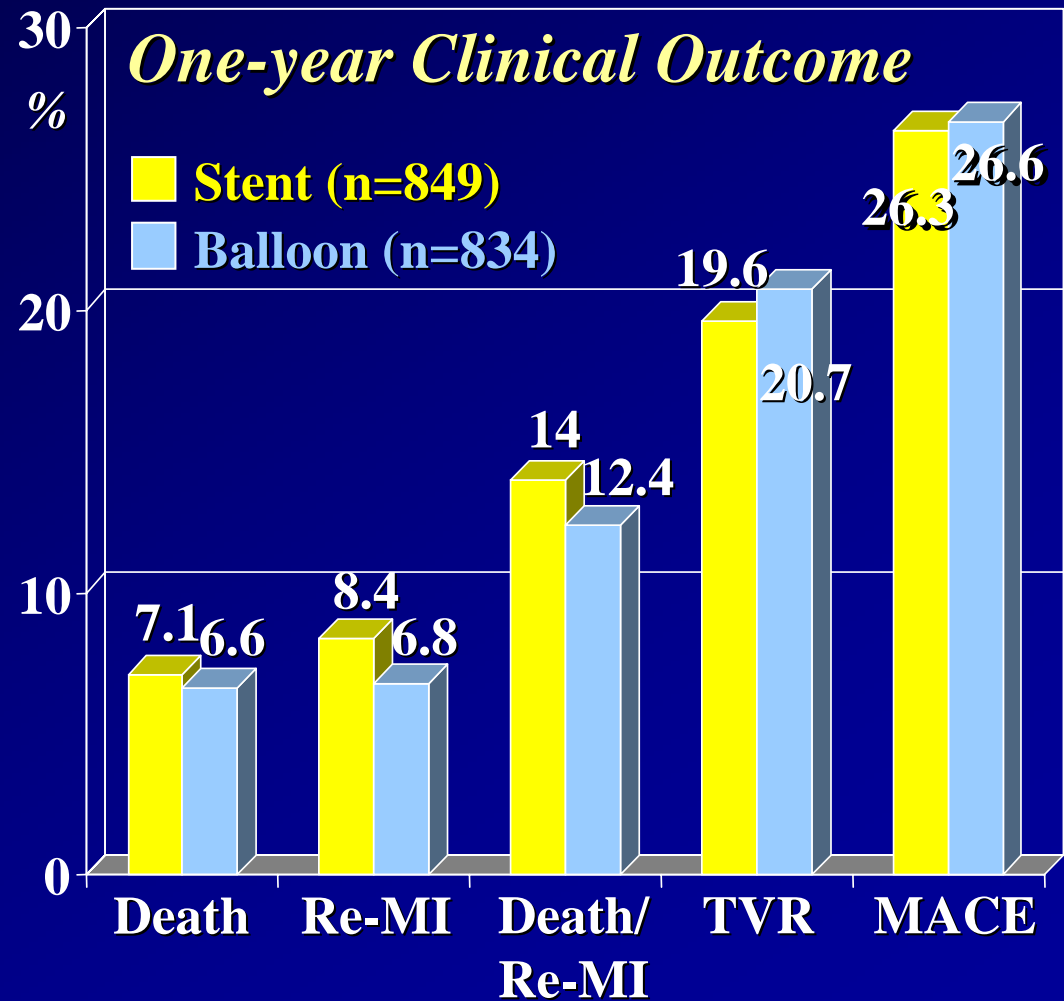


Routine Stent vs Balloon in a consecutive series of unselected pts

Zwolle-6 “Real World” Randomized Trial

<i>Post-PCI Results</i>	Stent (n=849)	Balloon (n=834)
TIMI-3 Post (%)	88	88
MBG II-III (%)	81	80
Distal emboli (%)	14	18
Compl ST-res (%)	56	54
LVEF (%)	44	45
LDH Q48h (U/L)	1227	1286

Suryapranata et al. Heart 2005



- *Stent doesn't improve epi-/myo-cardial reperfusion, unlike to reduce mortality*
- *Stent has never been shown to reduce mortality, as compared to balloon*

Meta-Analysis: Stenting vs Balloon for STEMI (13 RCT's; n=6921)

12-month MORTALITY

STUDY	STENTING n/N (%)	BALLOON n/N (%)	OR (fixed) 95% CI	Weight %	OR 95% CI	P value
WITHOUT ABCIXIMAB						
CADILLAC	17/512 (3.3%)	28/518 (5.4%)		16.47	0.60 [0.32, 1.11]	1.0
FRESCO	1/75 (1.3%)	4/75 (5.3%)		2.42	0.24 [0.03, 2.20]	0.36
Jacksch et al	5/231 (2.2%)	7/231 (3.0%)		4.19	0.71 [0.22, 2.26]	0.56
PAMI	26/452 (5.8%)	14/448 (3.1%)		8.11	1.89 [0.97, 3.67]	0.056
PASTA	3/67 (4.5%)	6/69 (8.7%)		3.46	0.49 [0.12, 2.05]	0.49
PSAAMI	4/44 (9.1%)	8/44 (18.2%)		4.45	0.45 [0.12, 1.62]	0.35
STENTIM-2	3/101 (3.0%)	2/110 (1.8%)		1.14	1.65 [0.27, 10.1]	0.58
ZWOLLE-5	3/112 (2.7%)	4/115 (3.5%)		2.35	0.76 [0.17, 3.49]	1.0
ZWOLLE-6	47/785 (6.0%)	45/763 (5.9%)		26.26	1.02 [0.67, 1.55]	0.94
WITH ABCIXIMAB						
STOPAMI-3	25/305 (8.2%)	28/306 (9.2%)		15.71	0.89 [0.50, 1.56]	0.67
STOPAMI-4	7/90 (7.8%)	11/91 (12.1%)		6.21	0.61 [0.23, 1.66]	0.33
CADILLAC	28/524 (5.3%)	16/528 (3.0%)		9.23	1.81 [0.97, 3.38]	0.061
ABCIXIMAB	60/919 (6.5%)	55/925 (5.9%)		31.25	1.10 [0.76, 1.61]	0.6
CONTROL	109/2379 (4.6%)	118/2373 (5.0%)		68.75	0.92 [0.70, 1.20]	0.5
TOTAL (95% CI)	169/3298 (5.1%)	173/3298 (5.2%)		100.00	0.97 [0.78, 1.21]	0.81

De Luca, Suryapranata et al. JACC 2006

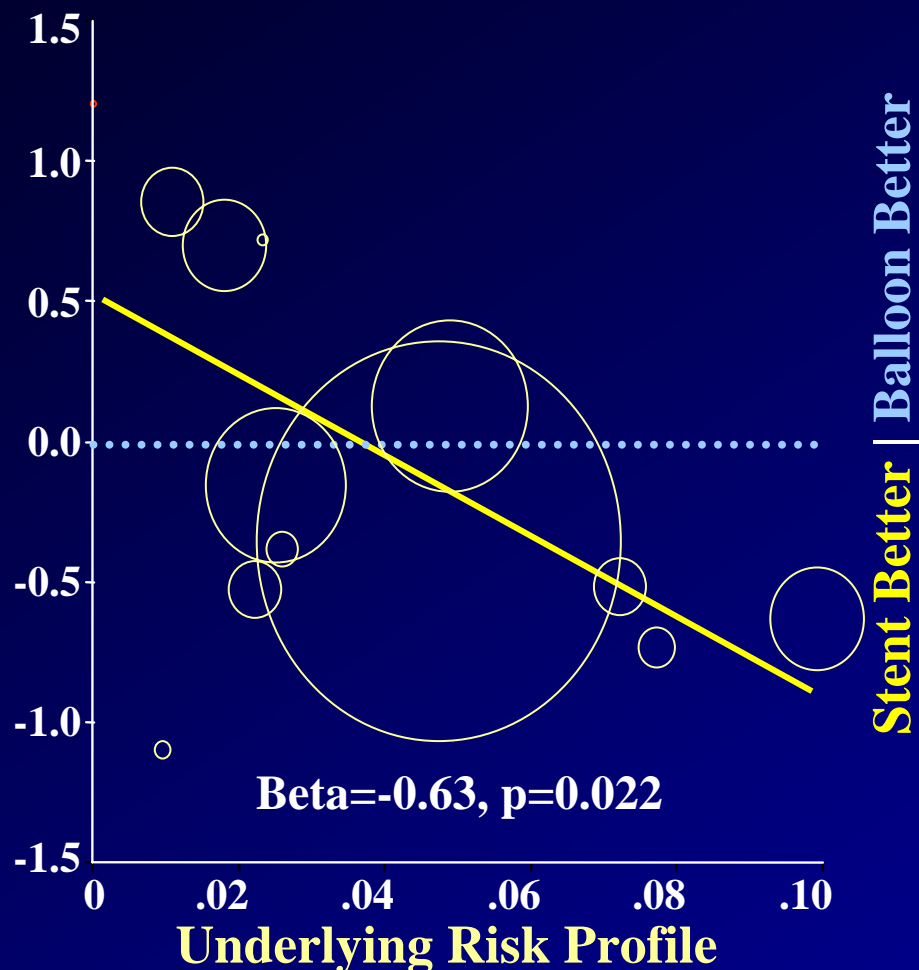
0.1 0.2 0.5 1 2 5 10

STENT BETTER

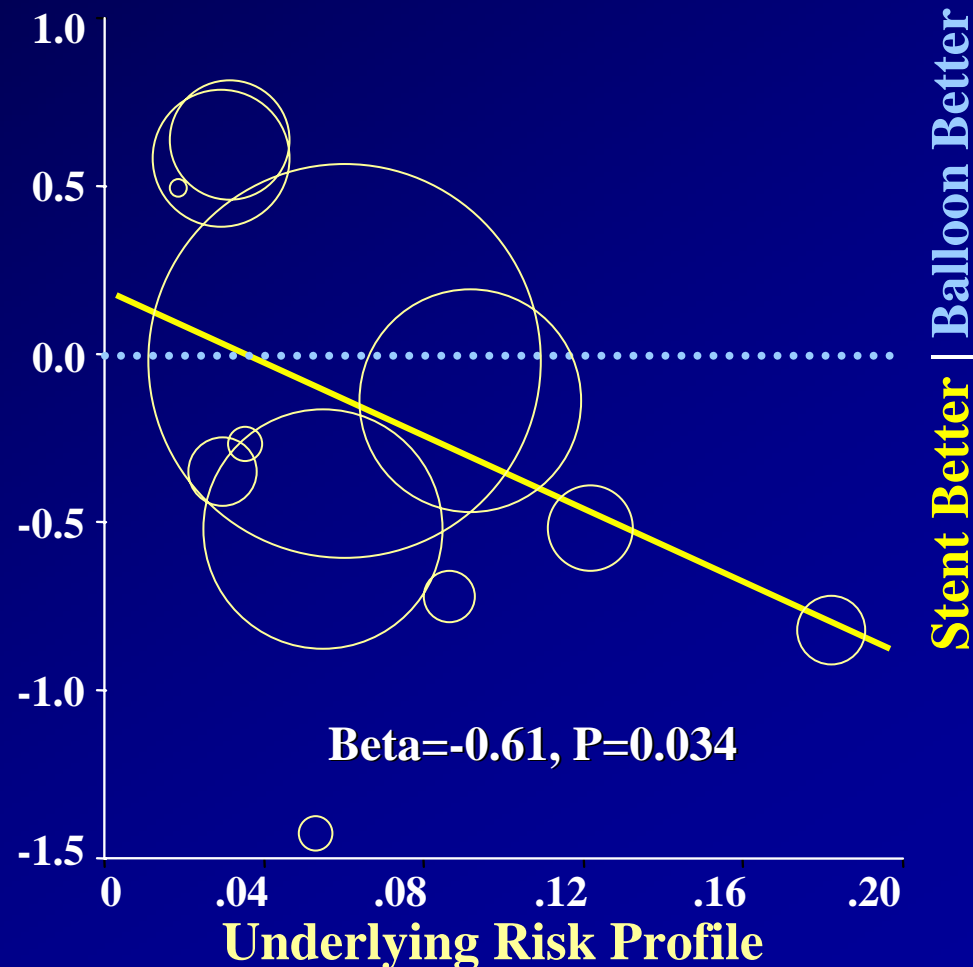
BALLOON BETTER

Meta-Regression Analysis: *Stenting vs Balloon* for AMI (n=6921)

Log (OR) for 30-day Mortality



Log (OR) for 12-month Mortality

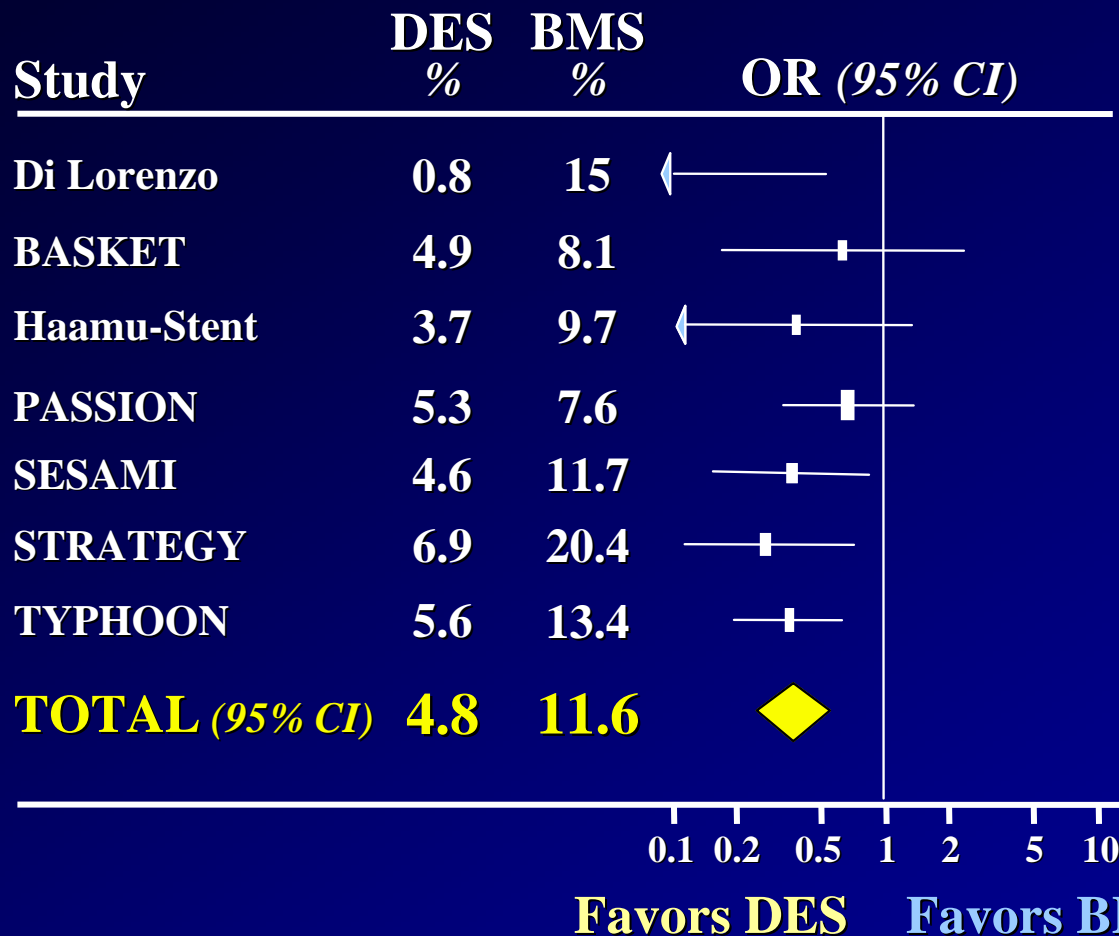


De Luca, Suryapranata et al. JACC 2006

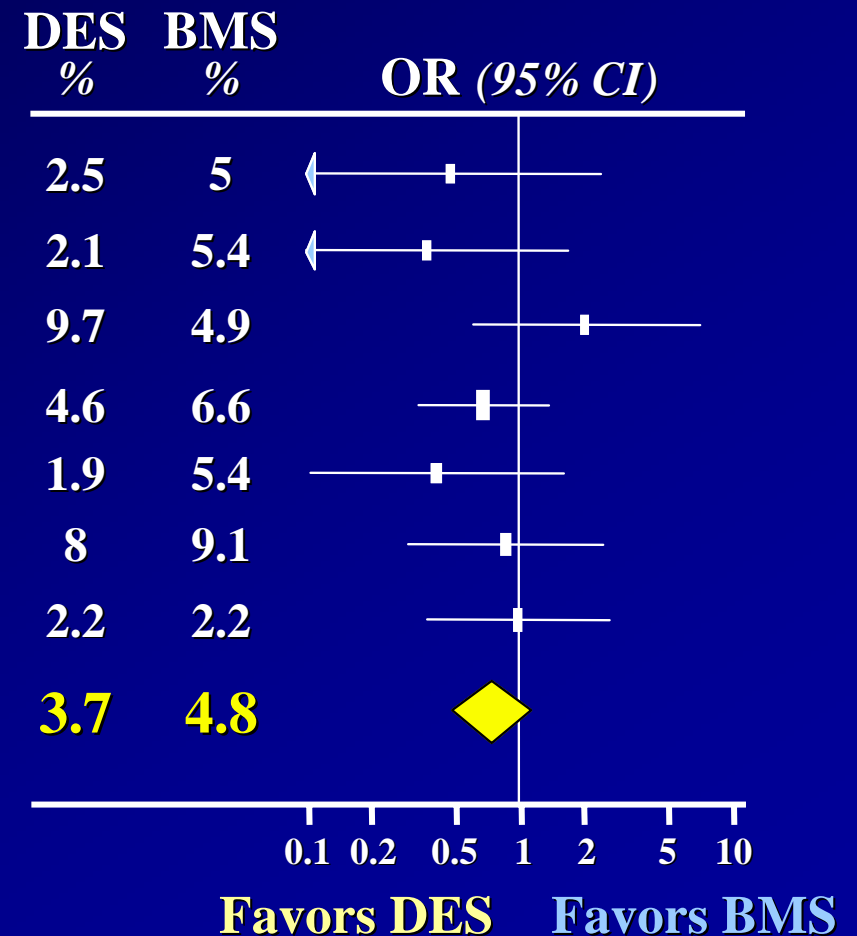
The higher the risk profile, the greater the benefits from Stenting

Meta-Analysis: DES vs BMS for STEMI (n=2360)

TVR @ 6-12 Months



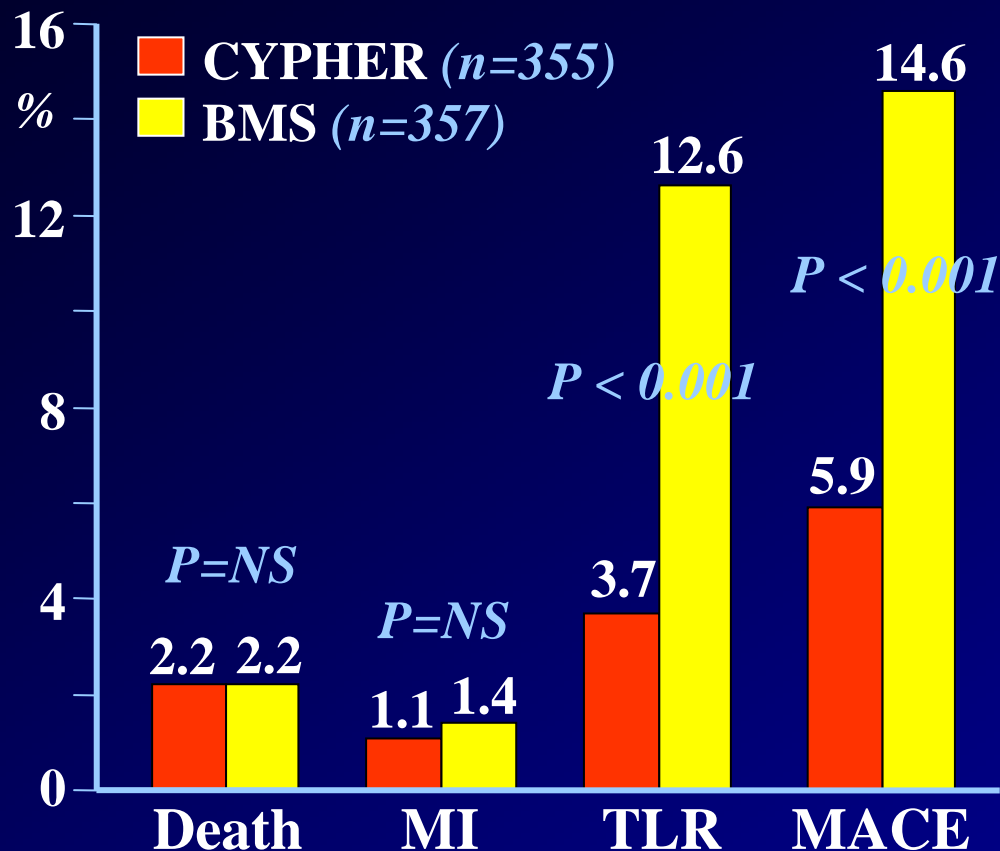
Mortality @ 6-12 Months



No difference in Stent Thrombosis (1.2 vs 1.9%) or re-MI (2.3 vs 2.7%)

Randomized Trial: DES vs BMS for STEMI @ 1-year F/U

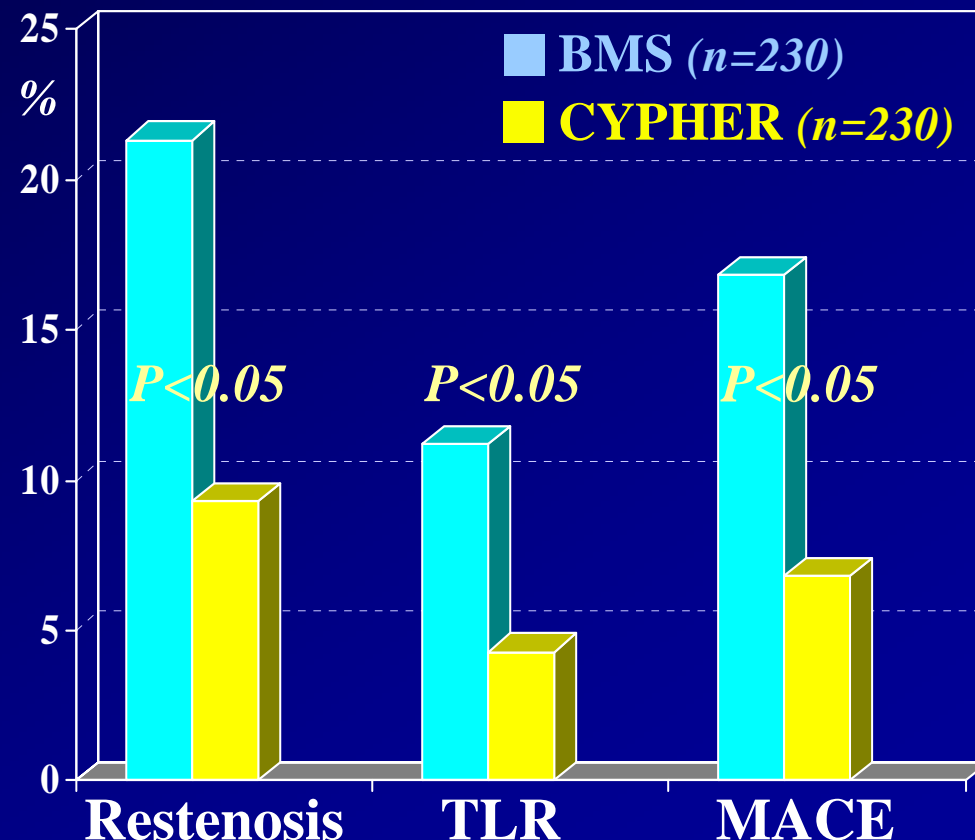
TYPHOON



Stent Thrombosis: 3.4 vs 3.6%

Spaulding et al. NEJM 2006

SESAMI

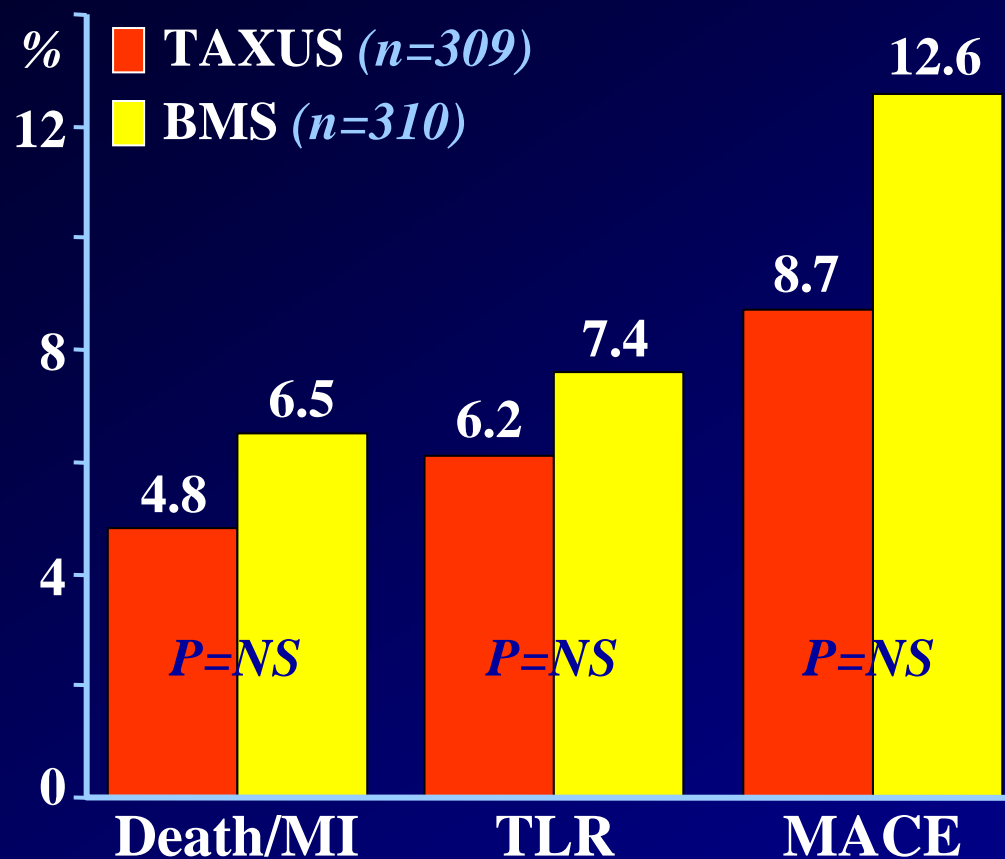


Menichelli et al. EuroPCR 2006

No difference in Mortality or re-MI @ 1-year F/U

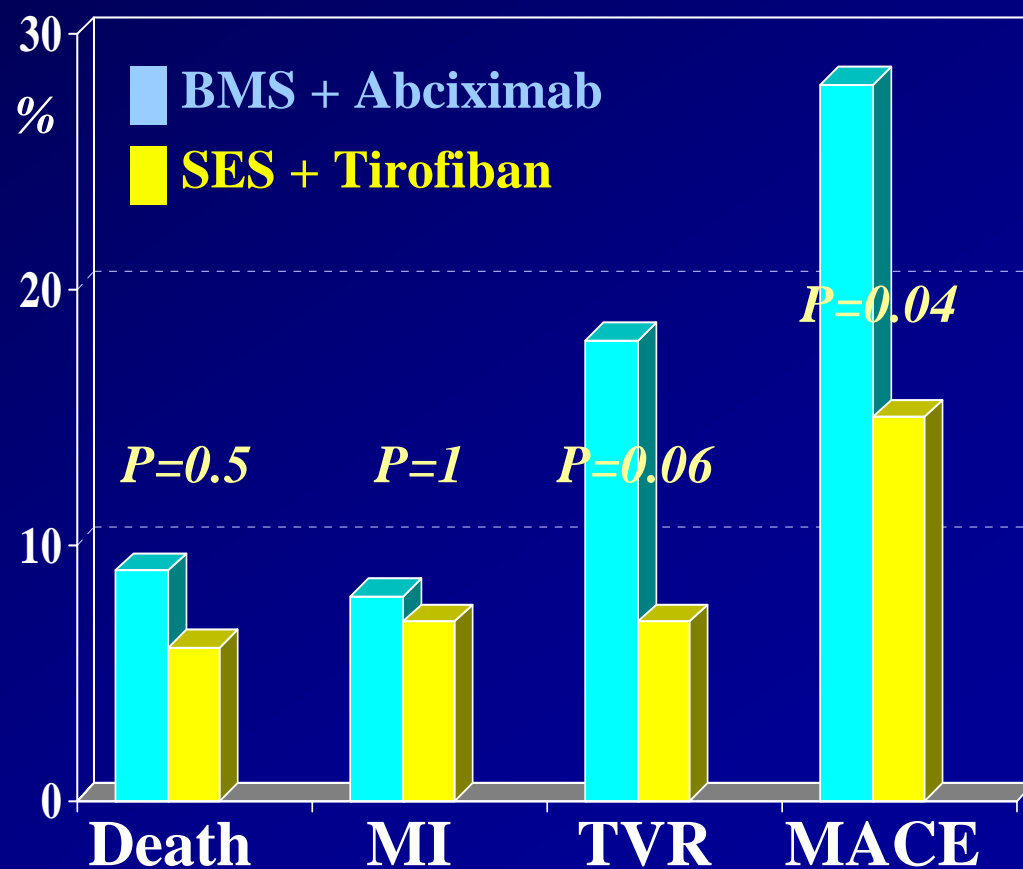
Randomized Trial: DES vs BMS for STEMI @ 1-year F/U

PASSION



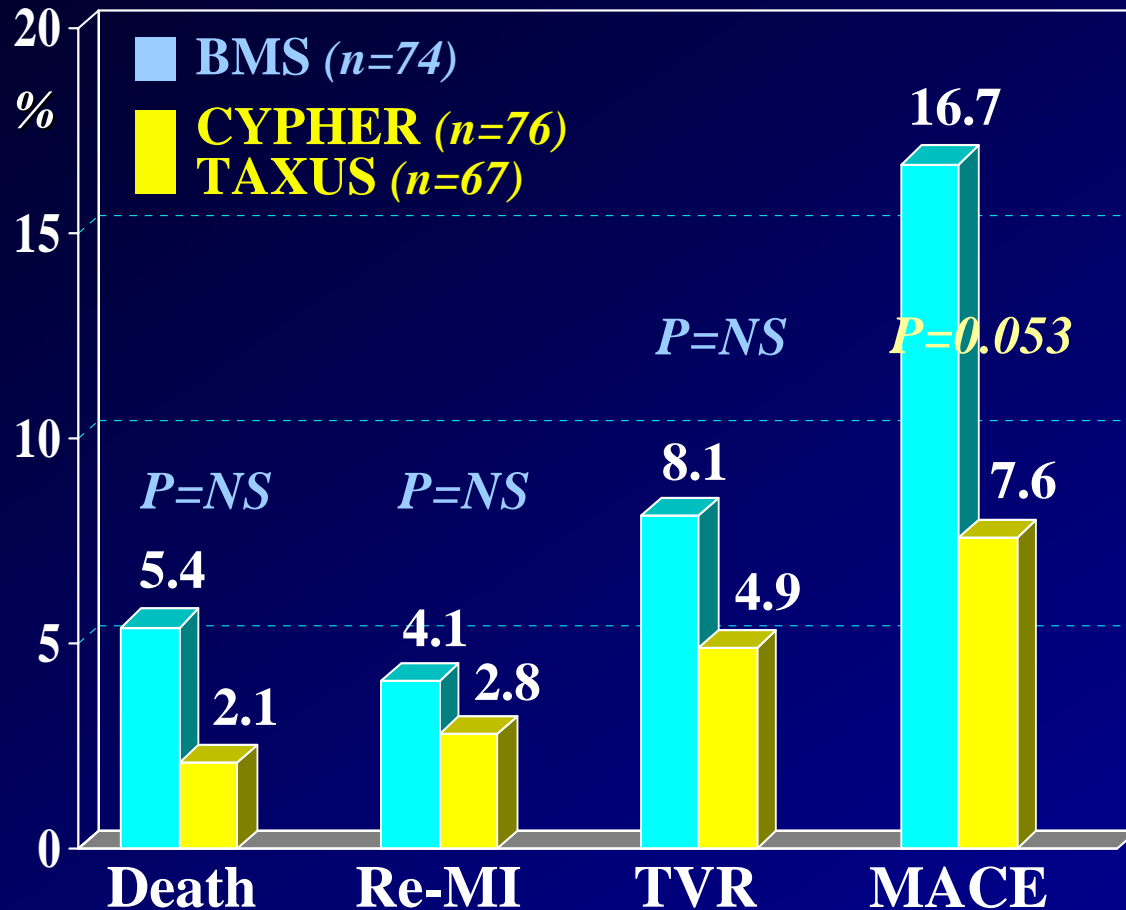
Stent Thrombosis: 1%

STRATEGY



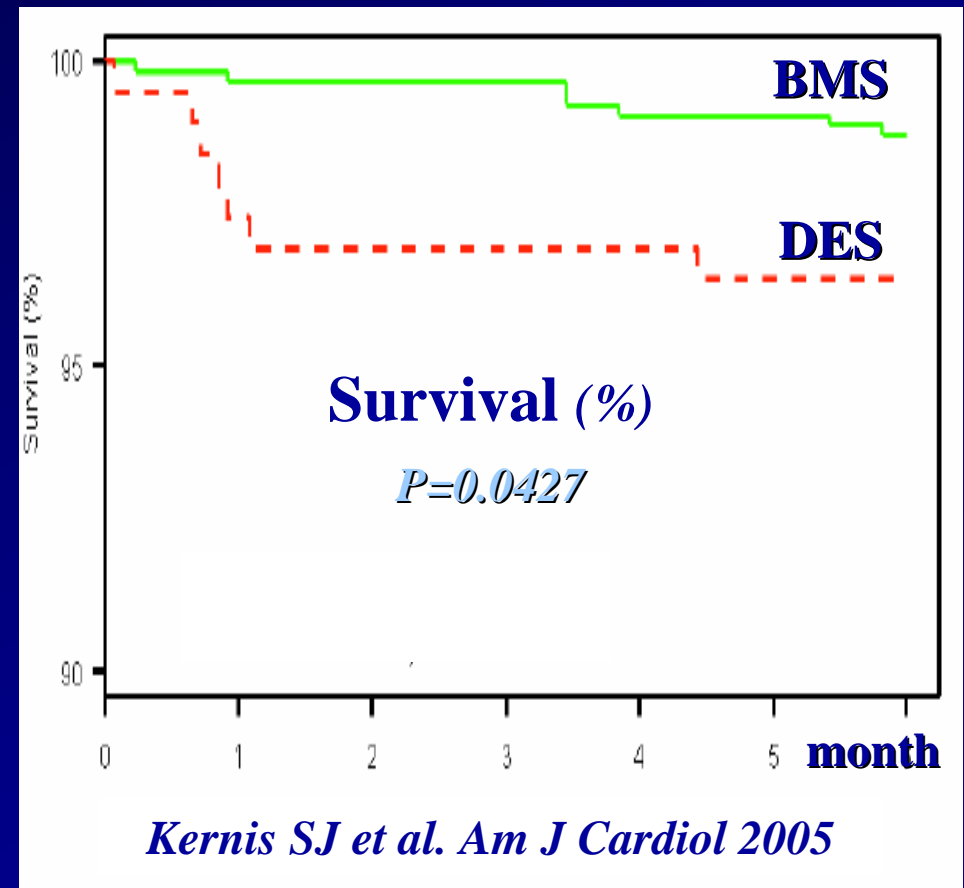
DES vs BMS for STEMI @ 6-month F/U

BASKET Trial



Pittl et al. WCC 2006

PREMIER Registry



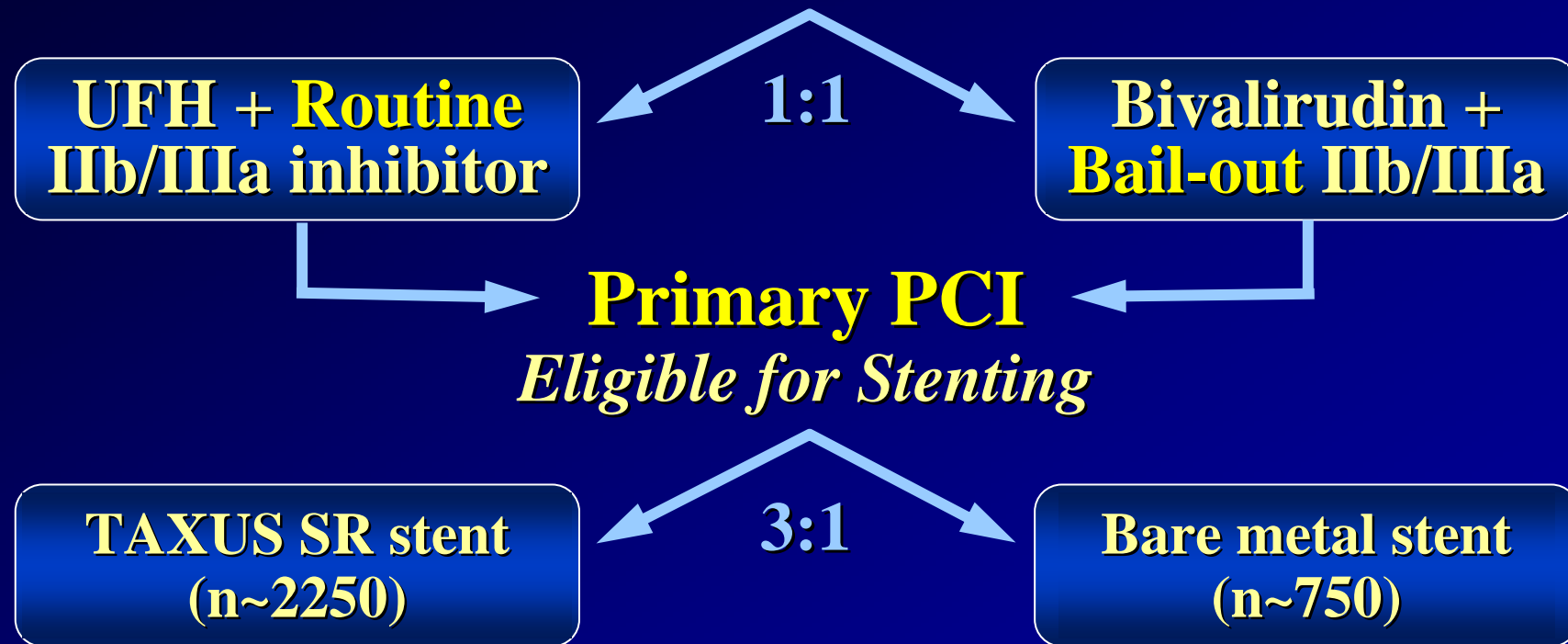
The safety & efficacy of DES for STEMI remain to be established



The **HORIZONS** *Trial*

3400 STEMI patients at 200 International sites

Aspirin 324 mg + Clopidogrel 300 or 600 mg



Clinical F/U at 1, 6, and 12 months, then yearly for 5 years
Angiographic F/U at 13 months: 1500 stent randomized pts

P.I: Gregg W. Stone

The **CEZAR** Trial

Cypher vs Taxus drug-Eluting stent: A Zwolle AMI Randomized trial

Interim Analysis as of August 31, 2006 (n=269)

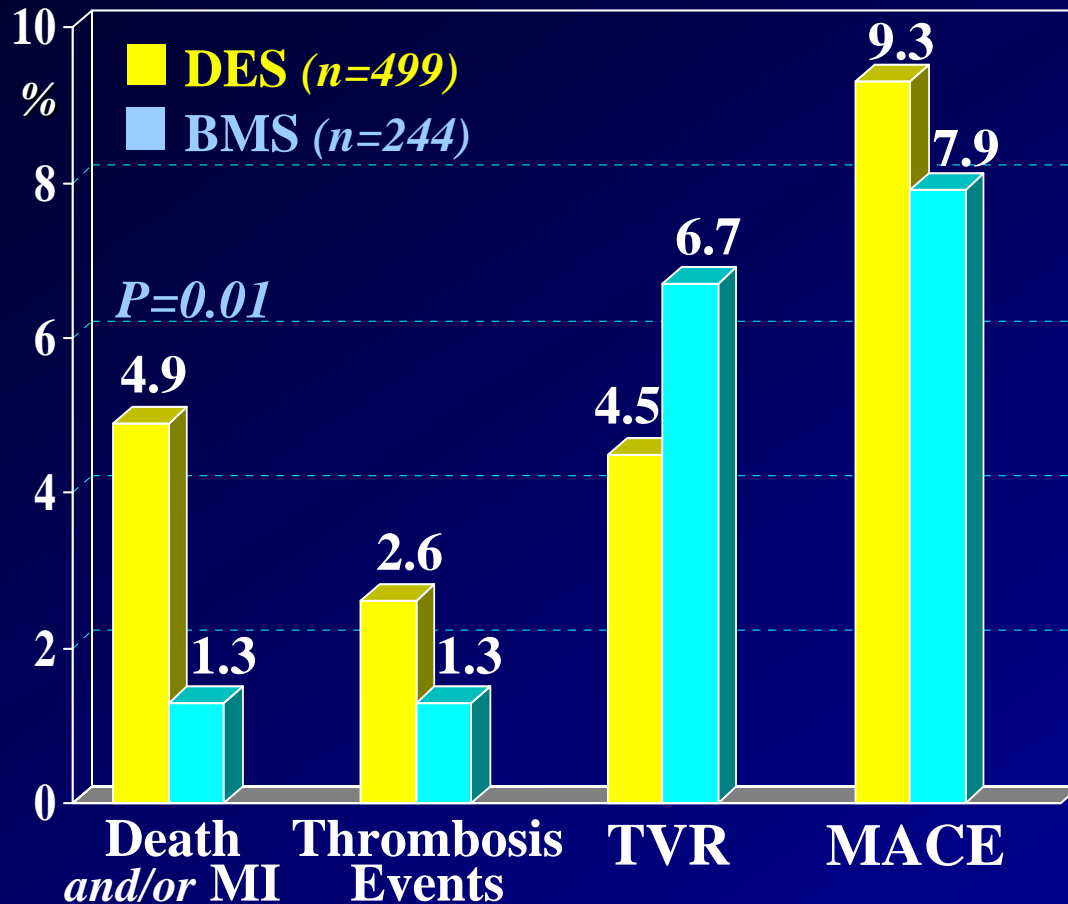
Baseline	TAXUS (n=134)	CYPHER (n=135)	MACE @ 30-day F/U	TAXUS (n=134)	CYPHER (n=135)
Age (mean, yrs)	60	61	Death	2	3
Male (%)	72	70	Re-MI	4	3
Diabetes (%)	12	11	CABG	1	0
Prev MI/PCI (%)	9	6	SAT/TLR	4	5

DES for AMI seems to be feasible and even more effective in reducing TVR
Safety issue of DES on SAT, particularly in AMI's, has yet to be established

Drug-Eluting Stent vs Bare Metal Stent

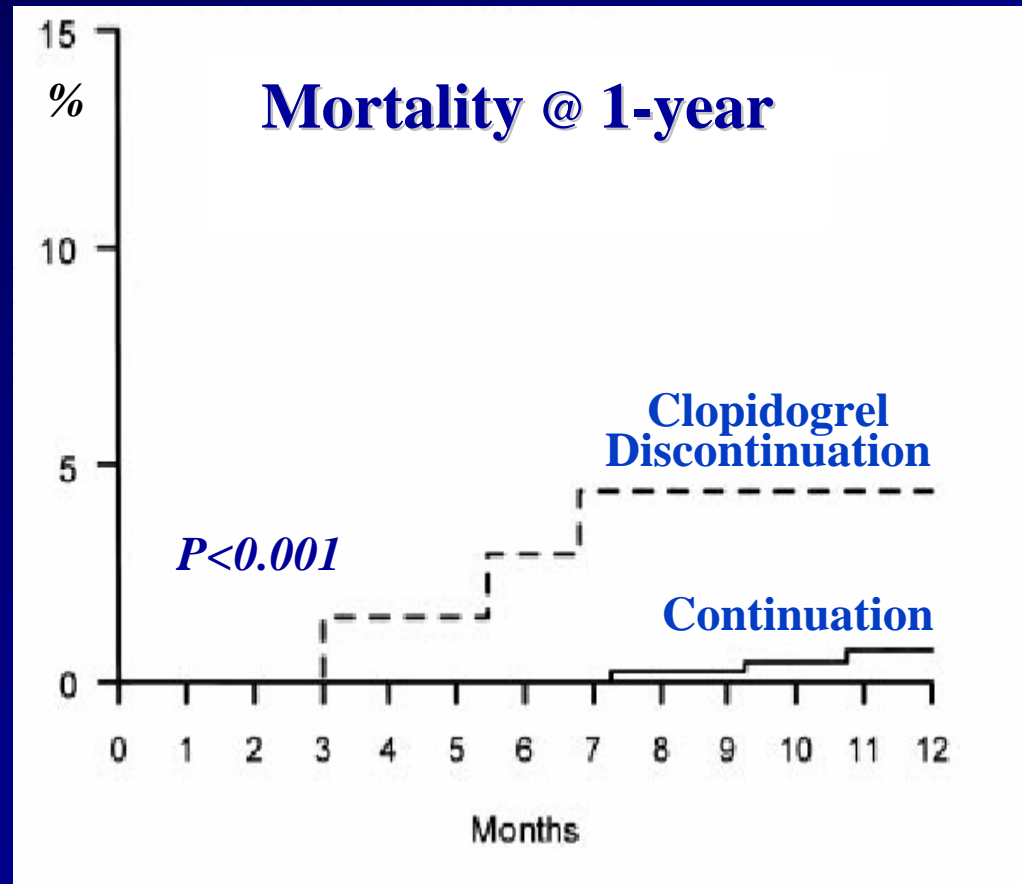
Late Thrombotic Events @ 1-yr after Clopidogrel Discontinuation

BASKET LATE



Pfisterer et al. JACC 2006

PREMIER Registry



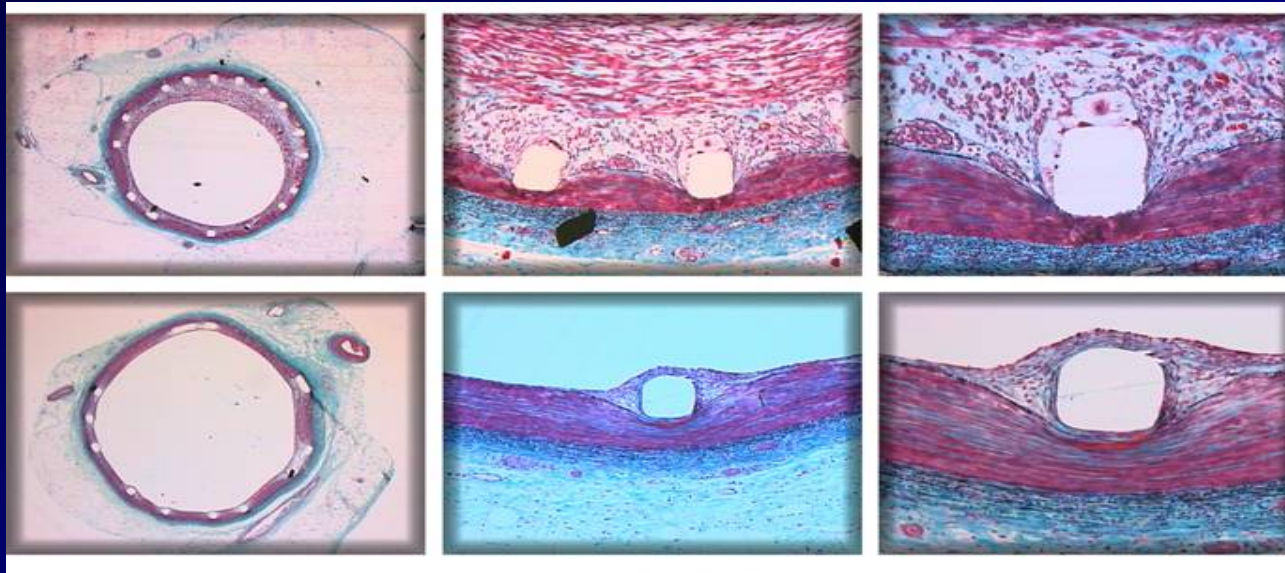
Spertus et al. Circulation 2006

DES issue on Late Thrombosis: Due to Impaired Re-endothelialization?

GENOUS *Endothelial Progenitor Cells* Capture Technology

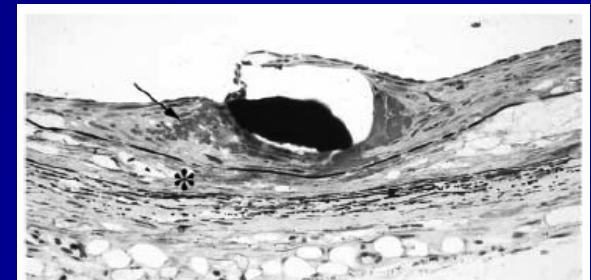
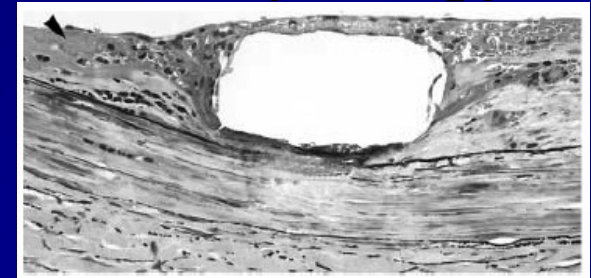
- EPCs are bone marrow derived, present in the circulating blood, (*First described by Asahara in 1996*)
- They have the ability to differentiate into mature endothelial cells, which may accelerate Healing process, protect against thrombus, and minimize restenosis, with safety profile over current *DES*

BMS: *Typical neo-intimal response to stent injury*



Genous: *Complete healing with mature neo-intima*

Brachytherapy



Drug-Eluting Stent

Zwolle **HEALING-AMI** Study

*A pilot trial on safety & feasibility of Genous R-Stent for AMI
Pre-treated with statin, aspirin, and clopidogrel (for only 30-d)*

Preliminary Results

Baseline Characteristics

• Age (yrs)	57	(35-81)
• Male	37	74%
• Diabetes	7	14%
• Hyperchol	13	26%
• Hypertension	17	34%

Clinical Outcome @ 30-d

• Cardiac Death	1
• Re-MI	1*
• SAT + Re-PCI	1*
• CABG	3*
• MACE	4

** Same patient due to edge dissections*

As of March 31, 2007 (n=50)

AMI Intervention in DES Era

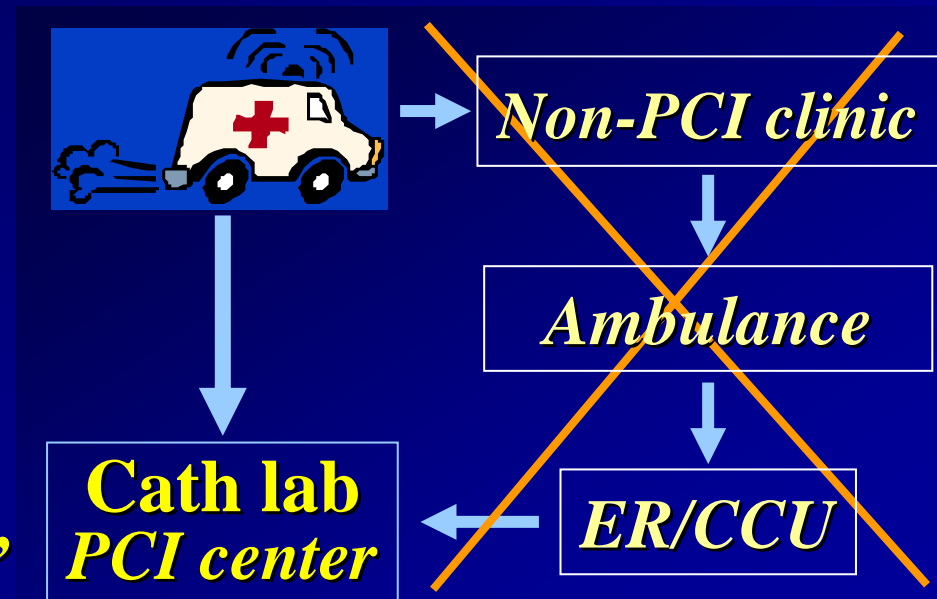
CONCLUSION

- Routine stenting in **unselected** STEMI pts does not seem to improve clinical outcome, when compared to balloon
- Stenting has never been shown to reduce mortality rate, but it is only associated with a reduction in TVR/TLR
- Although DES for AMI seems to be feasible & effective in reducing TVR, safety issue remains to be established
- The potential role of **Genous** stent for *STEMI*, to further reduce SAT and ISR, is currently being investigated



Reperfusion Therapy for STEMI in the Real World How to Extend the Benefits of Early PCI?

- ✓ **Reduction in total Ischemic Time: Pre-hospital triage (*home/ambulance*) for early identification of a large MI**
- ✓ **Immediate transfer of all **high-risk** pts for *primary* PCI**
- ✓ **Improve *regional logistics***
- ✓ **Fast track in PCI centers**
- ✓ ***“The Early The Better”***
***“The Higher The Risk,
The Greater The Benefit”***



The Golden Hour in Casualties of War



1797 Italian Campaign:

- Heaviest wounded First
- Treatment < 15 minutes
- On the spot at front line

Dominique-Jean Larrey
1766 - 1842



MASH

(Mobile Army Surgical Hospital)

Korea 1951-1953

Lt. R. Adams Cowley