

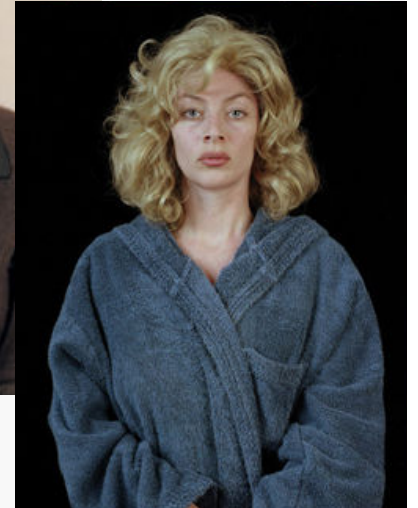
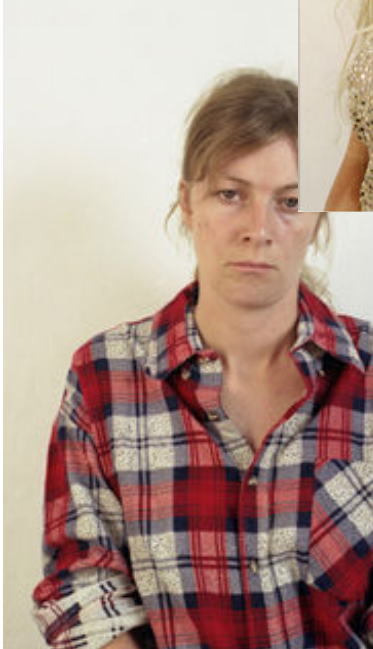
GOOD  
NEWS,  
BAD  
NEWS

About  
**DES**

Moderator : 박승정

Panels : 권현철, 김두일, 김효수, 승기배, 윤정한, 장양수, 정명호, 홍명기

# DES



# What is Good ?

## Efficacy Concerns :

Compare to BMS ?

Compare to Surgery ?



# Expanded Indication of PCI

**Long Lesions**

**Bifurcation Lesions**

**Diabetic Patients**

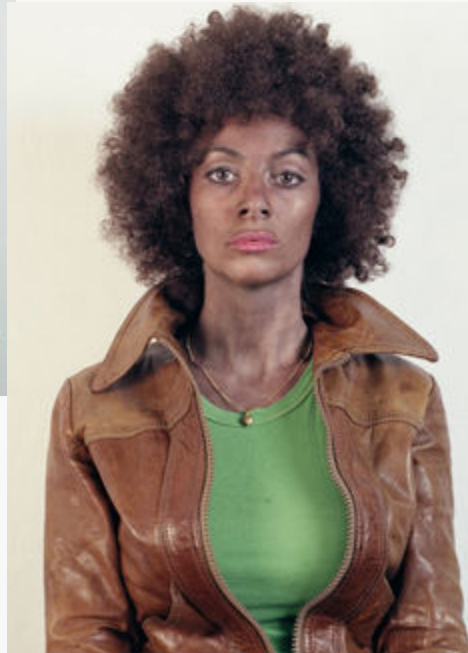
**Left Main Lesions**

# What is Bad ?

## Safety Concerns :

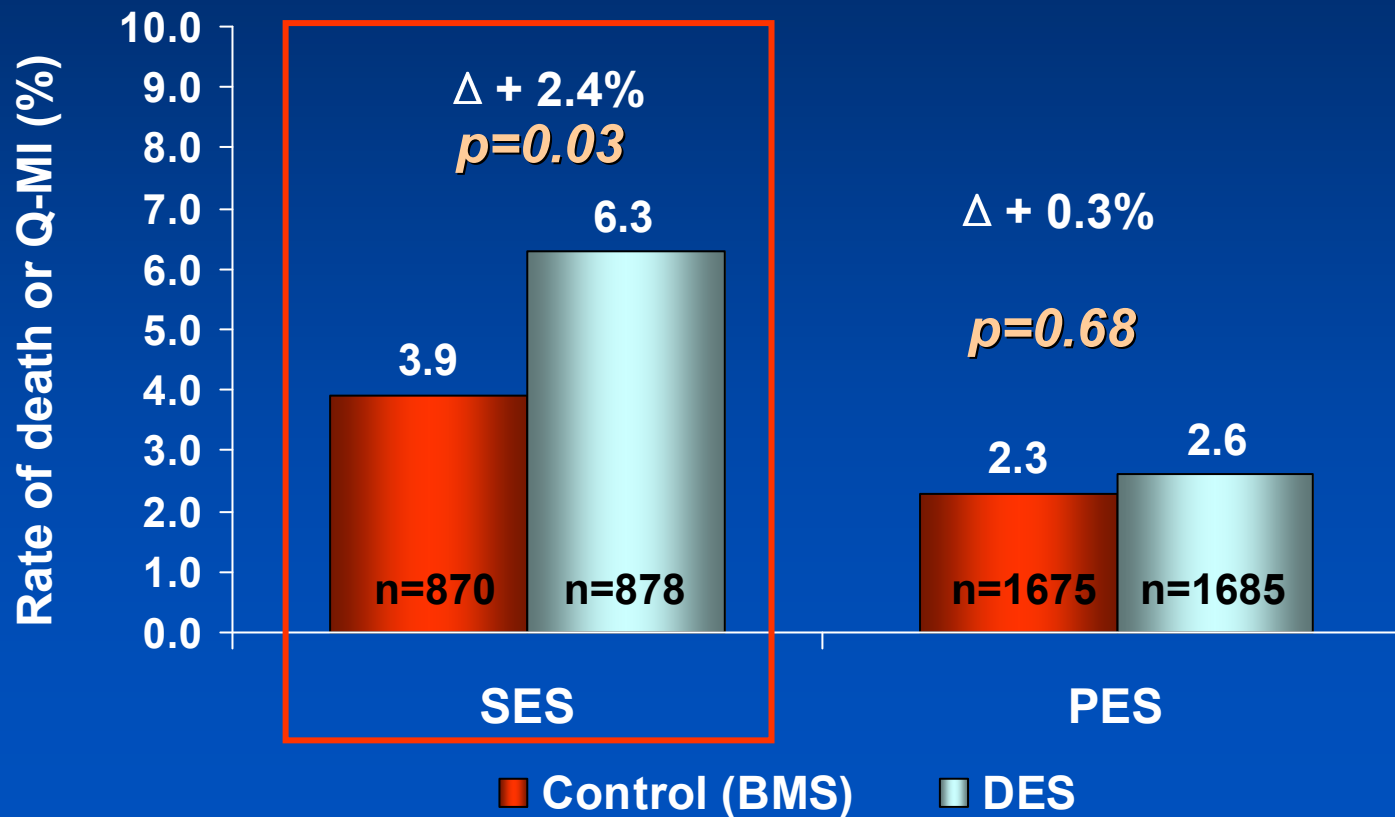
Late Stent Thrombosis

Is it Truth or Myth ?



# First Issue about DES safety

Increased Incidence of All Death or MI  
All randomized studies up to latest available follow-up



Camenzind E, ESC 2006

# FDA Advisory

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Dec 8, 2006

- **No increase of death or MI when DES are used on-label.**
- **Off-label use is associated with increased risk of stent thrombosis**



However,

There have been no prospective, randomized clinical trials involving long-term follow-up of the “off-label” use of DES

# Late Stent Thrombosis

## Is it Truth or Myth ?

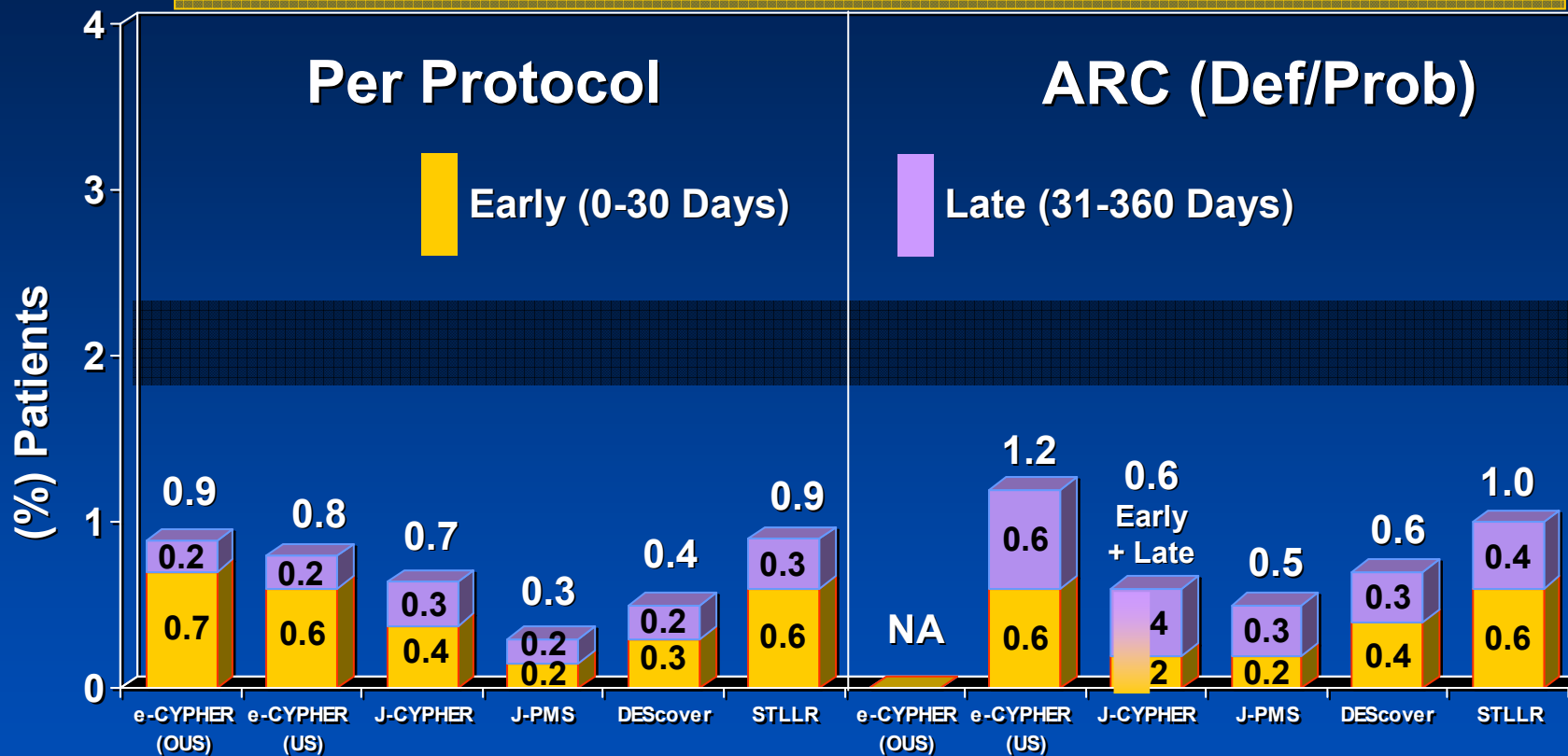


권현철 교수님  
어떻게 생각하세요 ?



# Stent Thrombosis Rates Across 6 Registry

1-year F/U in 25,156 Patients - All Events CEC Adjudicated

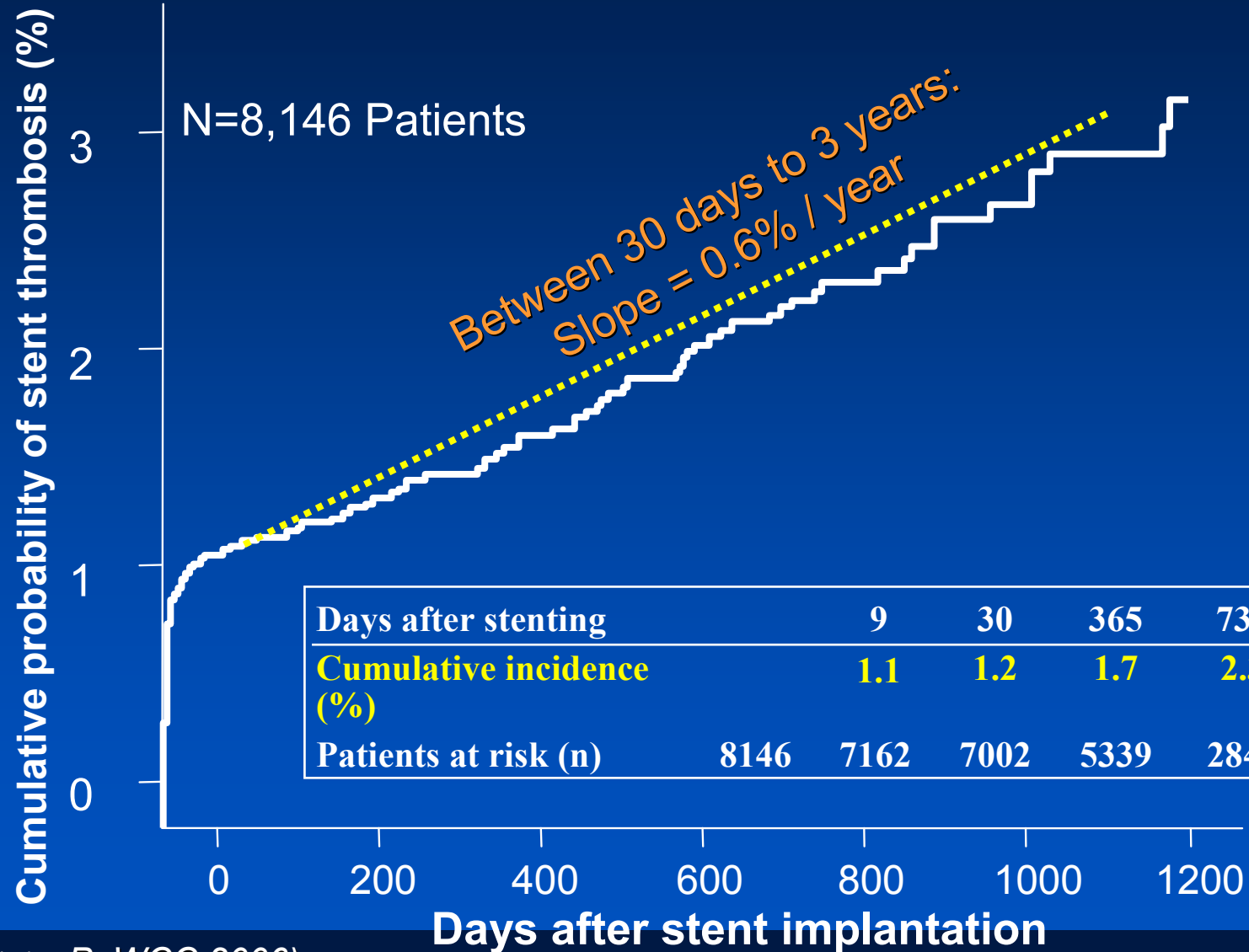


e-CYPHER (OUS)		e-CYPHER (US PMS)		Interim Data		DEScover	STLLR
1 yr F/U	88%	1 yr F/U	98%	J-CYPHER	J-PMS	1 yr F/U	1 yr F/U
n=15,157	n=2,067	n=8,349	n=2,032	89.6%	93.6%	n=4,235	n=1,554

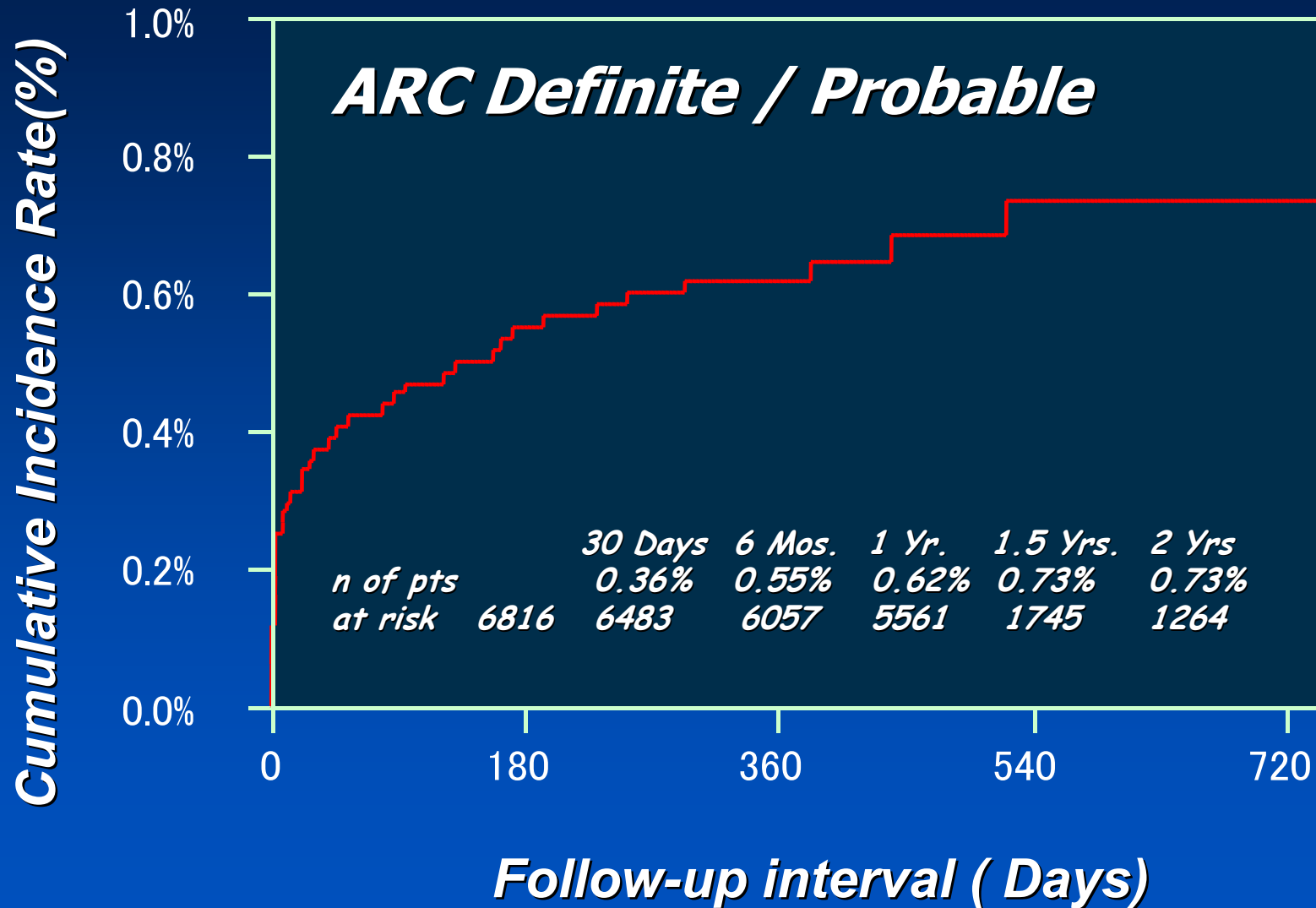


# Incidence of DES Stent Thrombosis

Bern - Rotterdam Cohort Study



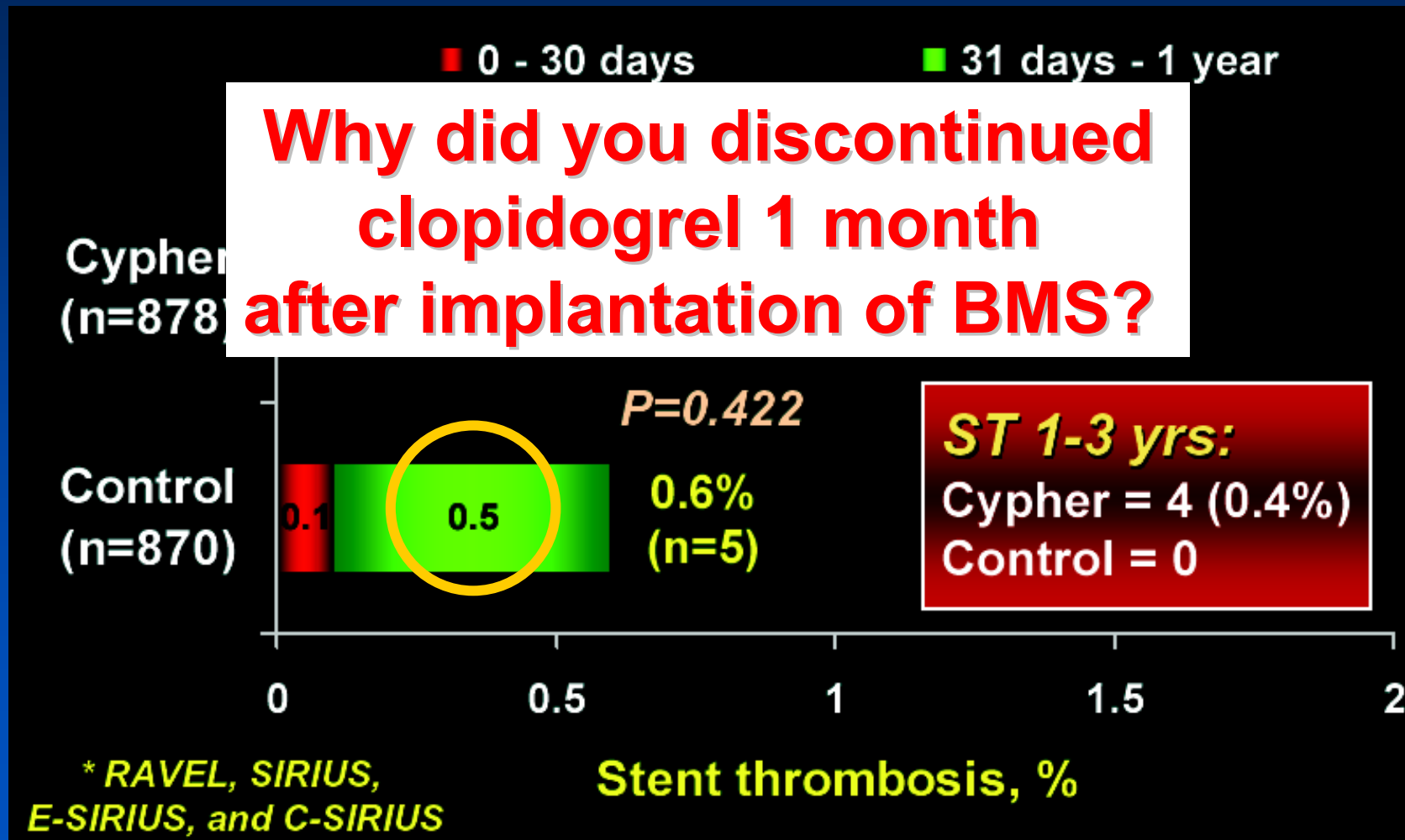
# Stent Thrombosis in the J-CYPHER Registry



Slide used with permission from Dr. Takeshi Kimura

# 4-study Cypher Meta-Analysis

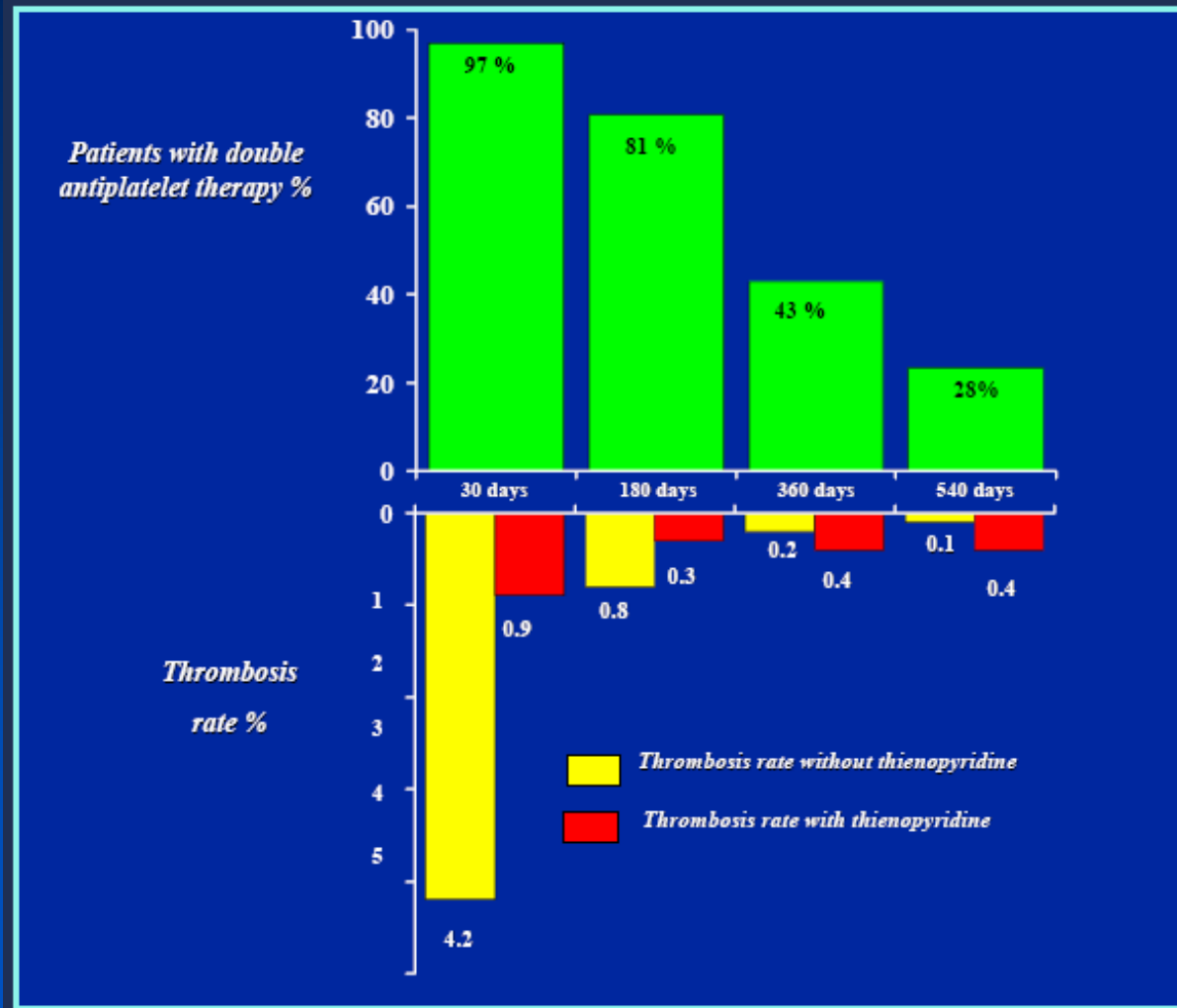
## Definite Stent Thrombosis



# Milan, Siegburg, Naple Experience

N=3021

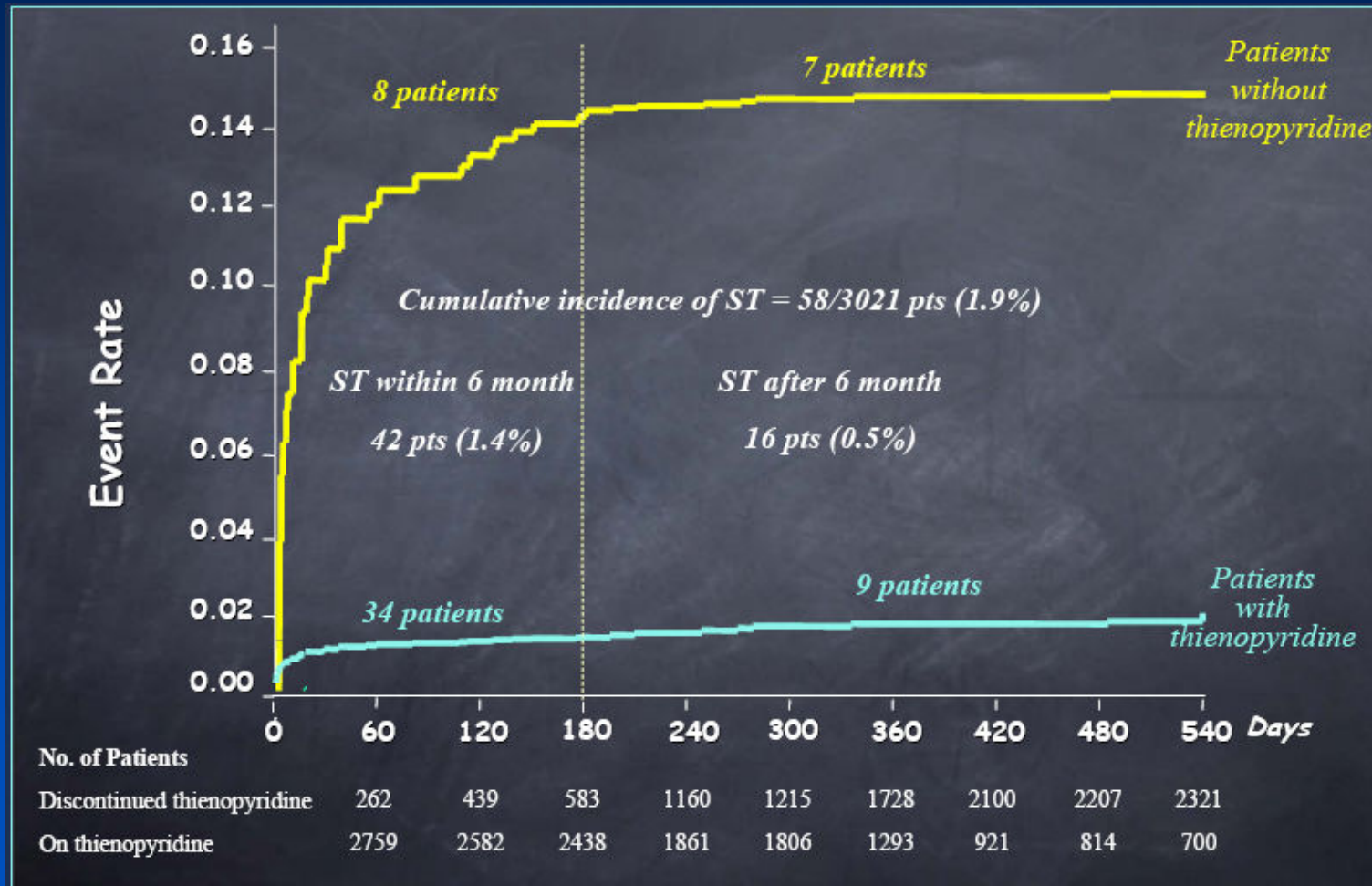
After 6 month,  
the relationship  
between  
antiplatelet  
discontinuation  
and stent  
thrombosis is not  
evident.



Chieffo A, TCT 2006

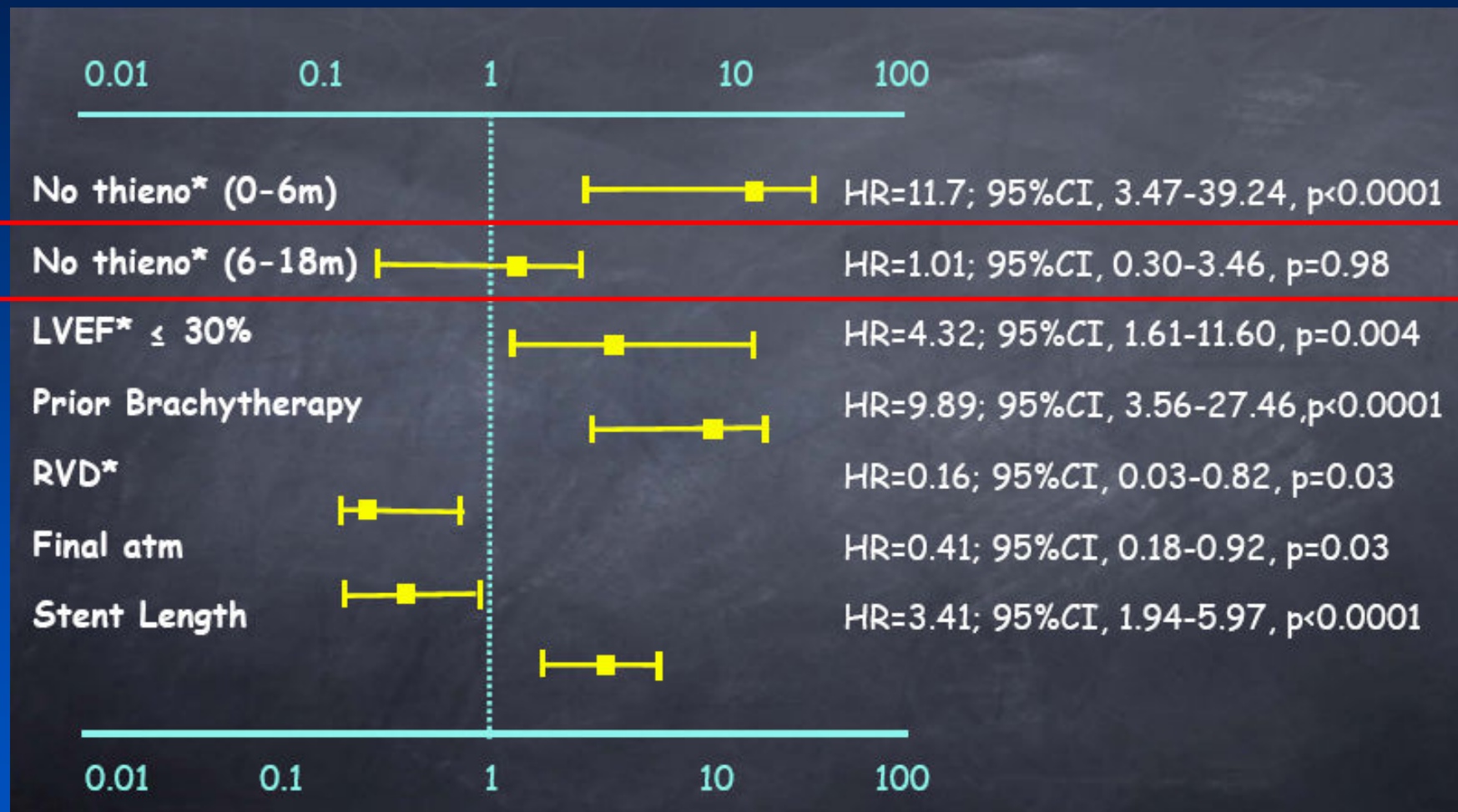
# Milan, Siegburg, Naple Experience

## Cumulative Hazard Function



Chieffo A, TCT 2006

# Milan, Siegburg, Naple Experience



Chieffo A, TCT 2006

# Discussion Discussion

# And Data



# Late Stent Thrombosis

## Is it Truth or Myth ?



홍명기 교수님은  
어떻게 생각하세요 ?

# Academic Research Consortium (ARC) Proposed Standard Definitions

- **Definite/Confirmed**

- Acute coronary syndrome AND
- [Angiographic confirmation of thrombus or occlusion  
OR
- Pathologic confirmation of acute thrombosis]

- **Probable**

- Unexplained death within 30 days
- Target vessel MI without angiographic confirmation of thrombosis or other identified culprit lesion

- **Possible**

- Unexplained death after 30 days

# Meta analysis of RCTs and Registry Data

Series	Analysis	No. of patients	Comparison	F/U period	Death or MI difference
Spaulding et al	4 RCTs	878 / 870	SES / BMS	4	No
Kastrati et al	14 RCTs	2486 / 2472	SES / BMS	4	No
Mauri et al	8 RCTs	878 / 1400 / 2267	SES / PES / BMS	4	No
Stone et al	9 RCTs	878 / 1755 / 3513	SES / PES / BMS	4	No
Lagerqvist et al	Registry	6033 / 13738	DES / BMS	3	Yes

Five consecutive publications in NEJM 2007;356:989-1039

ORIGINAL ARTICLE

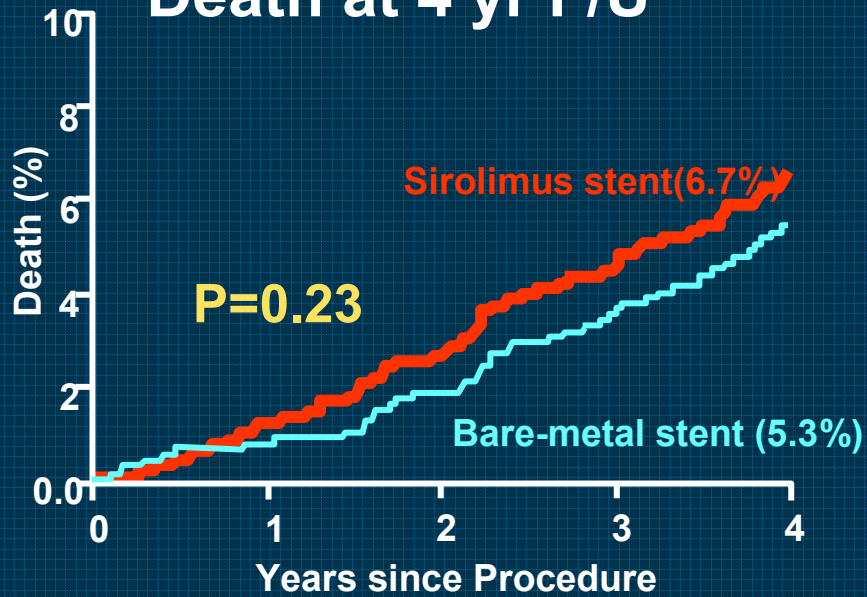
## Safety and Efficacy of Sirolimus- and Paclitaxel-Eluting Coronary Stents

Gregg W. Stone, M.D., Jeffrey W. Moses, M.D., Stephen G. Ellis, M.D.,  
Joachim Schofer, M.D., Keith D. Dawkins, M.D., Marie-Claude Morice, M.D.,  
Antonio Colombo, M.D., Erick Schampaert, M.D., Eberhard Grube, M.D.,  
Ajay J. Kirtane, M.D., Donald E. Cutlip, M.D., Martin Fahy, M.Sc.,  
Stuart J. Pocock, Ph.D., Roxana Mehran, M.D., and Martin B. Leon, M.D.

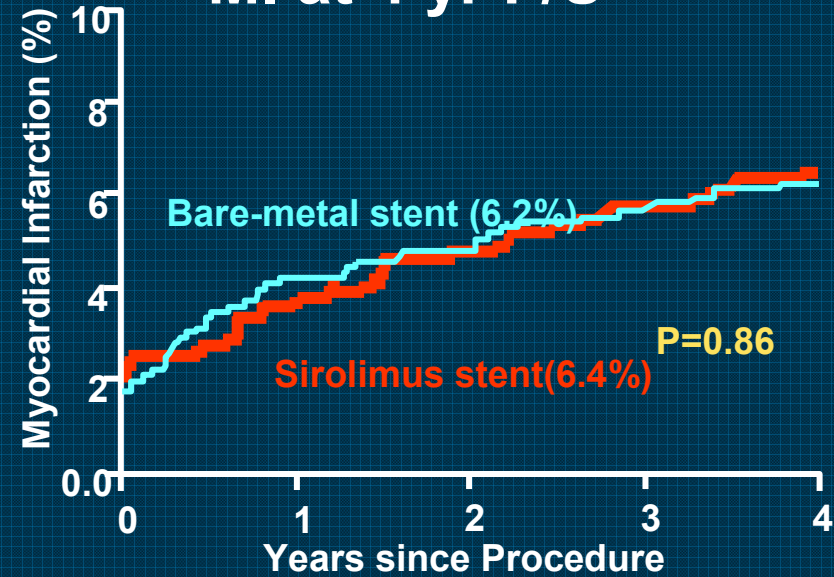
Pooled analysis of 1748 patients in 4 RCTs between SES or BMS  
3513 patients in 5 RCTs between PES or BMS  
**(SES Trials: RAVEL, SIRIUS, E-SIRIUS, C-SIRIUS)**  
**(PES Trials: TAXUS-I, TAXUS-II, TAXUS-IV, TAXUS-V, TAXUS VI)**

NEJM 2007;356:998-1008

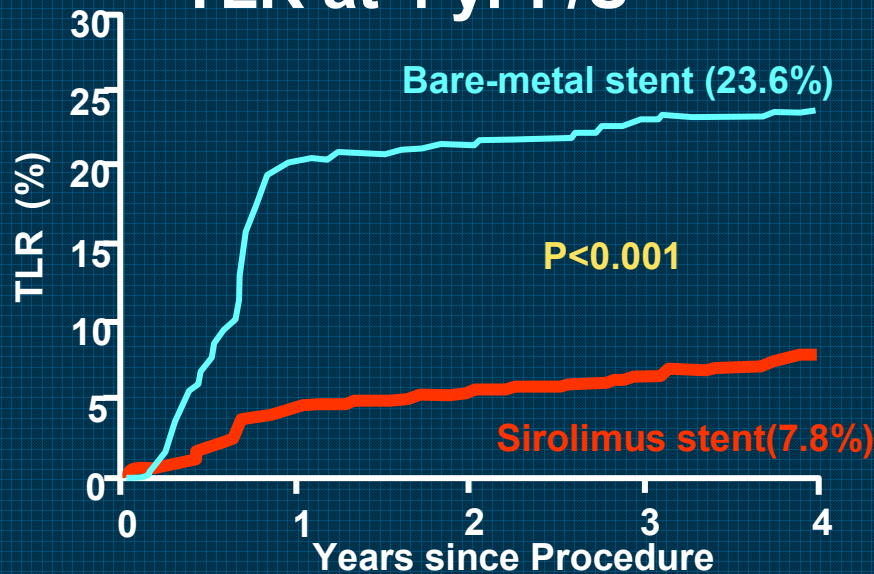
## Death at 4 yr F/U



## MI at 4 yr F/U

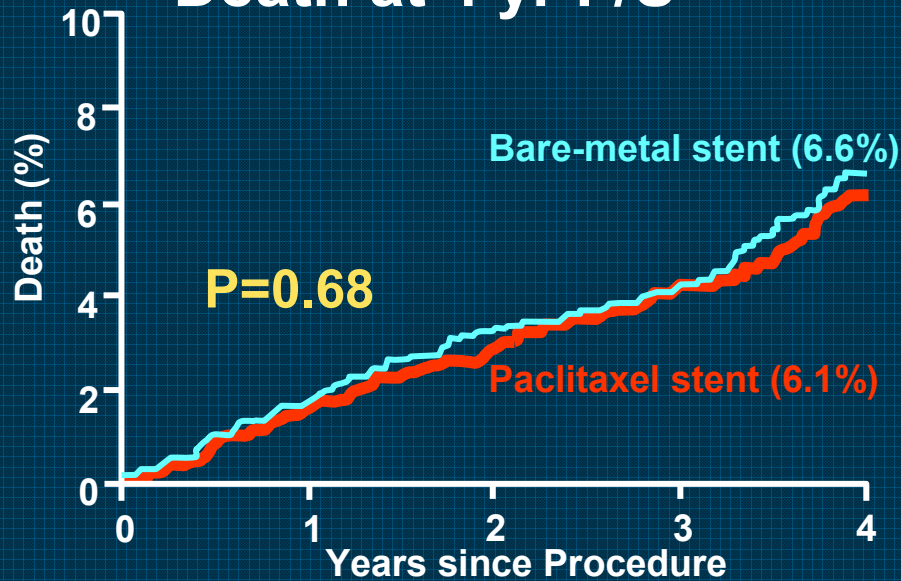


## TLR at 4 yr F/U

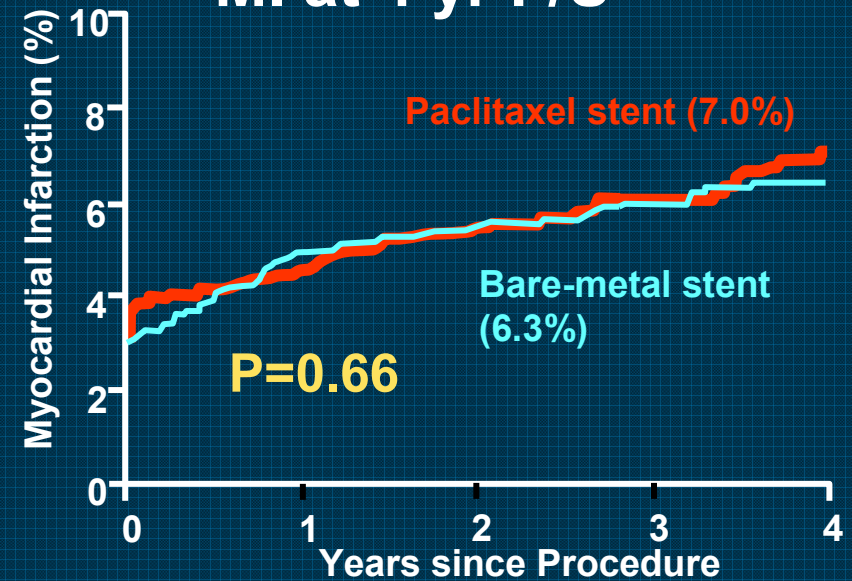


No difference in rates of death and MI. However, significant difference in TLR after **SES**

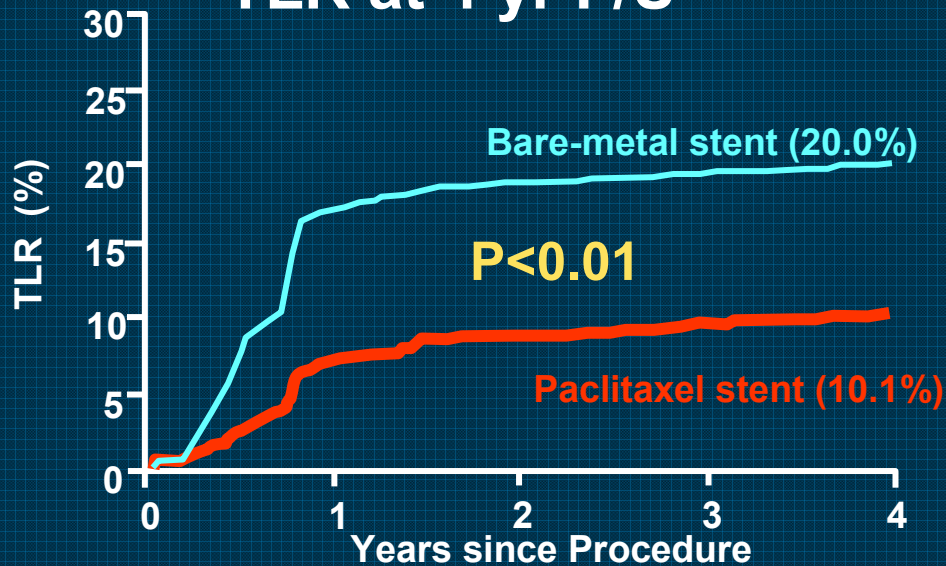
## Death at 4 yr F/U



## MI at 4 yr F/U



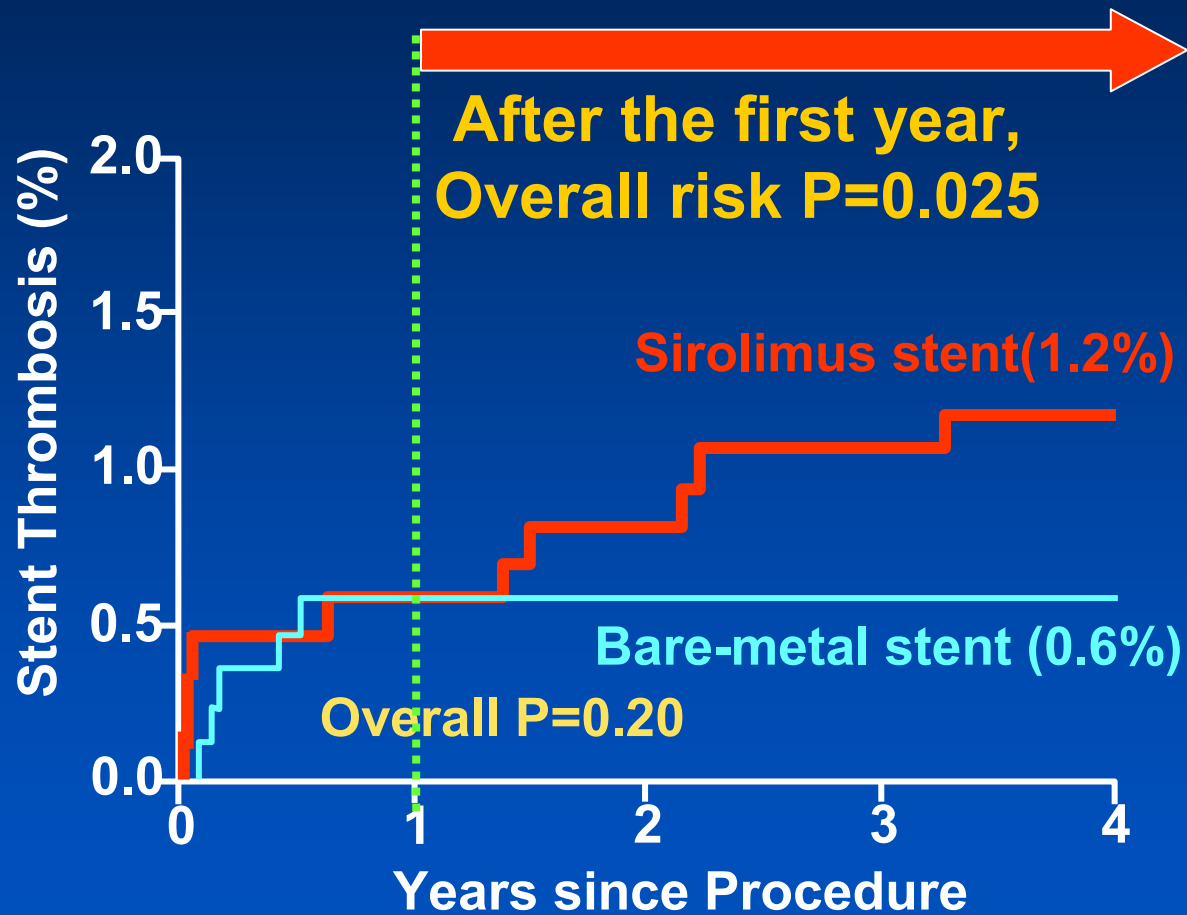
## TLR at 4 yr F/U



No difference in rates of death and MI. However, significant difference in TLR after **PES**

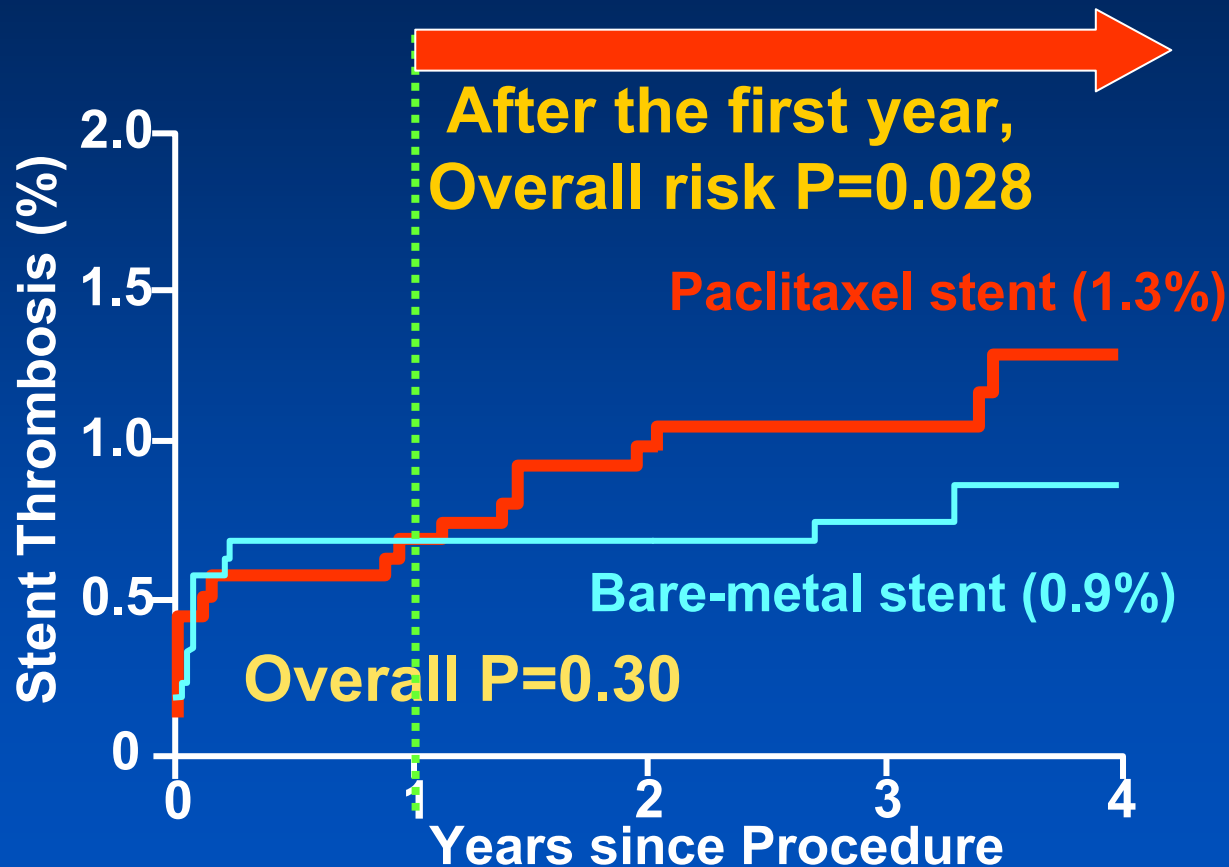
# Stent Thrombosis After SES

## (Protocol Definition)



# Stent Thrombosis After PES

## (Protocol Definition)





# Conclusions

## Pooled Data Analysis from RCTs

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- There were no significant differences in the cumulative rates of death or myocardial infarction at 4 years
- Both DESs (SES, PES) were associated with a marked reduction in TLR.
- Stent thrombosis after 1 year was more common with both SES and PES than with BMS.

# Discussion Discussion

And  
Data

ORIGINAL ARTICLE

# Long-Term Outcomes with Drug-Eluting Stents versus Bare-Metal Stents in Sweden

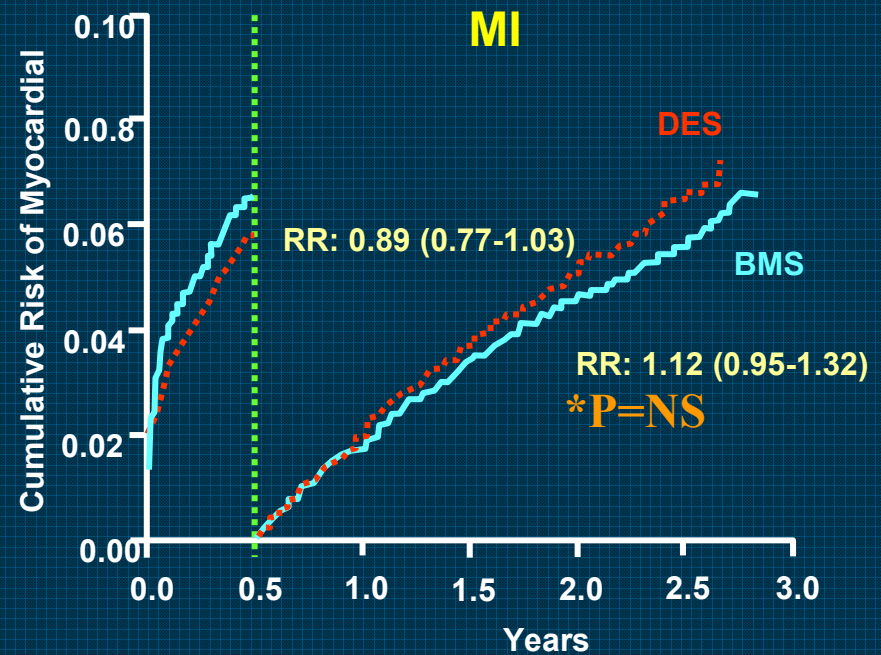
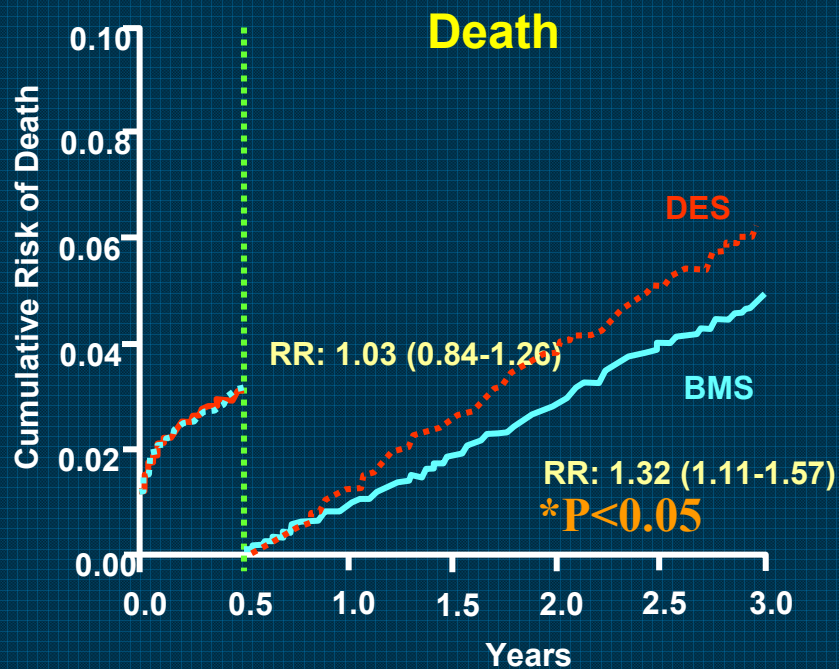
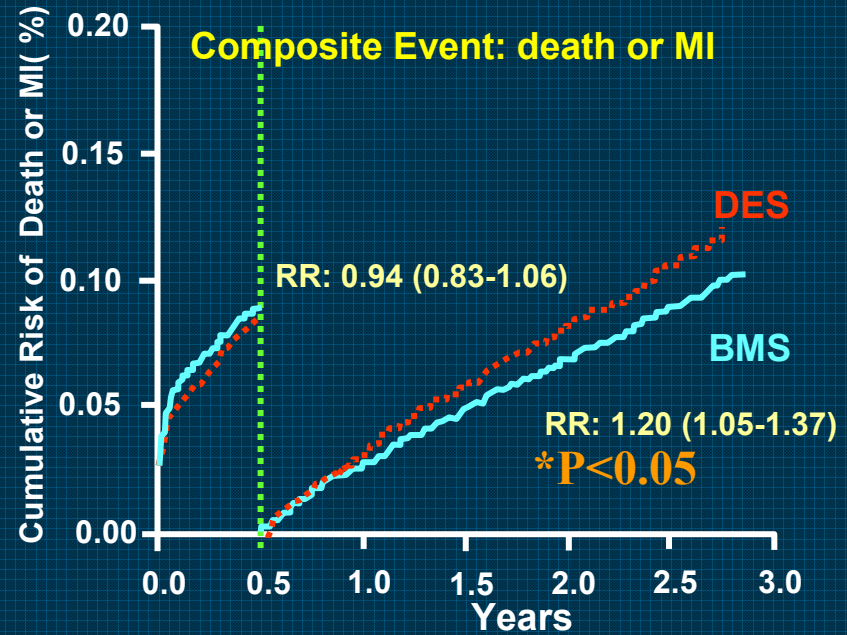
Bo Lagerqvist, M.D., Ph.D., Stefan K. James, M.D., Ph.D.,  
Ulf Stenestrand, M.D., Ph.D., Johan Lindbäck, M.Sc., Tage Nilsson, M.D., Ph.D.,  
and Lars Wallentin, M.D., Ph.D., for the SCAAR Study Group\*

Pooled analysis of 6033 patients treated with DES and  
13,738 patients treated with BMS  
Data from Swedish Coronary Angiography and Angioplasty Registry

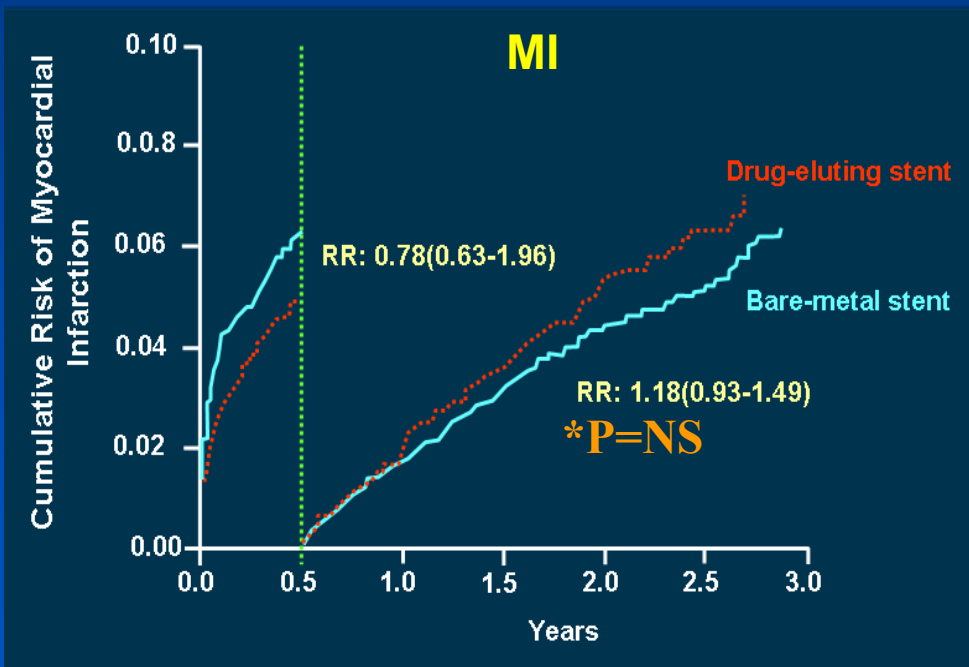
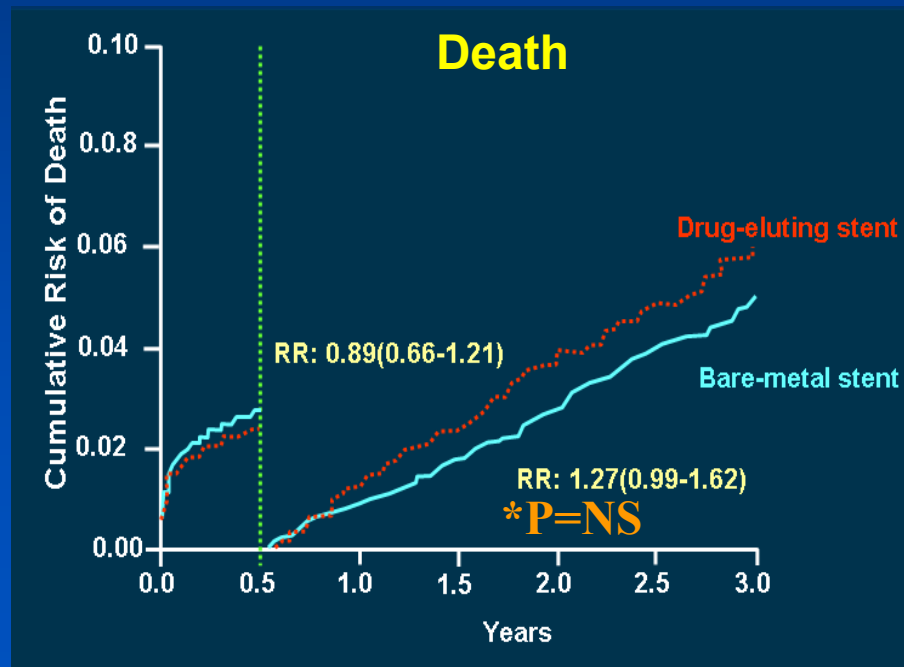
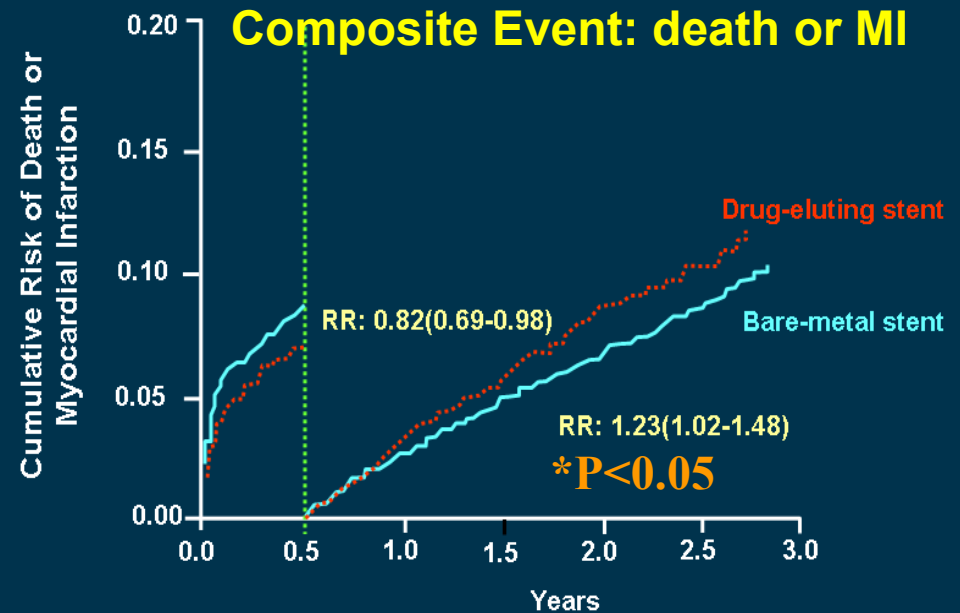
Outcome analysis was based on 1424 deaths and 2463 myocardial  
infarction during 3 years follow-up period and was adjusted for  
differences in baseline characteristics.

NEJM 2007;356:1009-19

# Landmark Analysis of the All Study Group



# Landmark Analysis of the One-Stent Subgroup



# Conclusions

## Pooled Analysis from Registry Data (Sweden)

---

- DESs were associated with an increased rate of death, as compared with BMSs after 6 months.
- The trend were appeared after 6 months, when the risk of death was 0.5 percentage point higher and a composite of death or myocardial infarction was 0.5 to 1.0 percentage point higher per year.
- The long-term outcome safety of DES needs to be ascertained in large, randomized trials

# Discussion Discussion

# And Data

# Despite appropriate statistical adjustment,

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- Higher late-event rates in patients with DESs may be related with a higher proportion of high-risk patients.
- Another limitation is the lack of information about the duration of clopidogrel treatment in individual patients
- Also, changes in event rates over the time might have been influenced by the small number of patients with DESs early in the study period.



# Early and late coronary stent thrombosis of sirolimus-eluting and paclitaxel-eluting stents in routine clinical practice: data from a large two-institutional cohort study

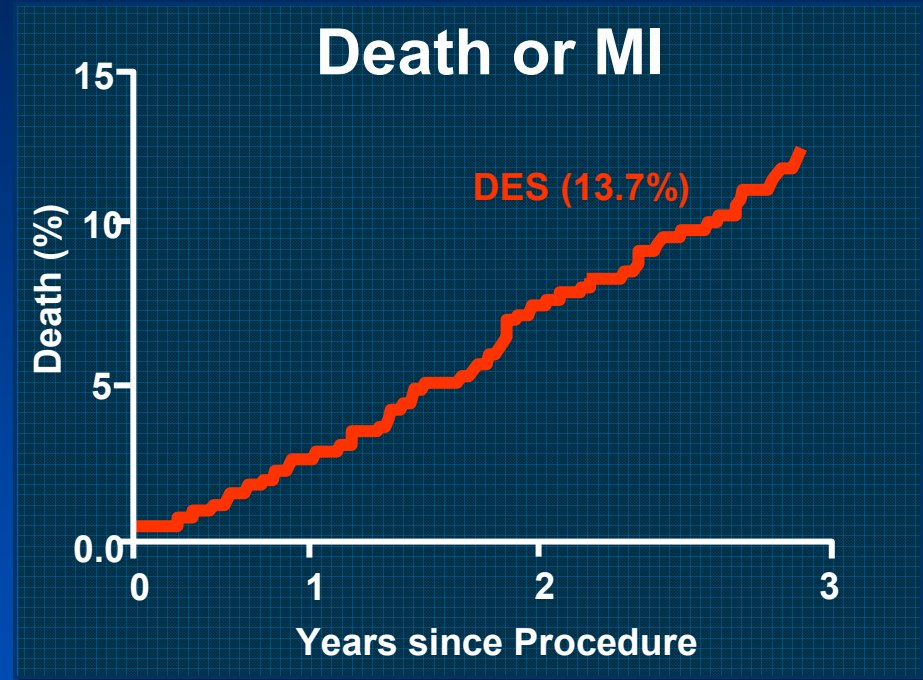
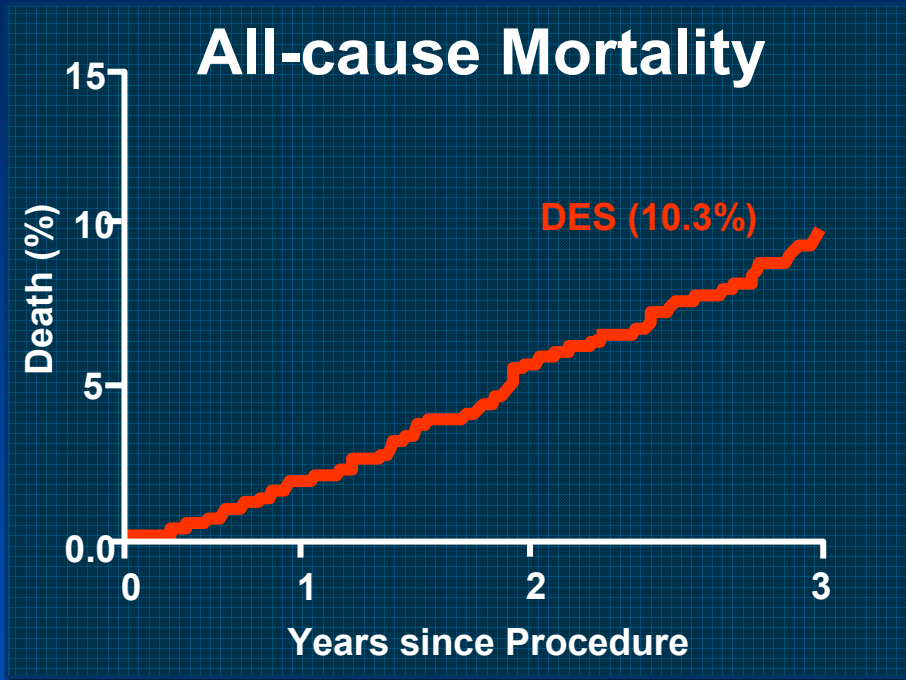
*Joost Daemen, Peter Wenaweser, Keiichi Tsuchida, Linda Abrecht, Sophia Vaina, Cyrill Morger, Neville Kukreja, Peter Juni, Georgios Sianos, Gerrit Hellige, Ron T van Domburg, Otto M Hess, Eric Boersma, Bernhard Meier, Stephan Windecker, Patrick W Serruys*

Pooled analysis of 8146 patients treated with SES (n=3823) or PES (n=4323): Data from University Hospital Bern, Switzerland and Erasmus Medical Center, Netherlands

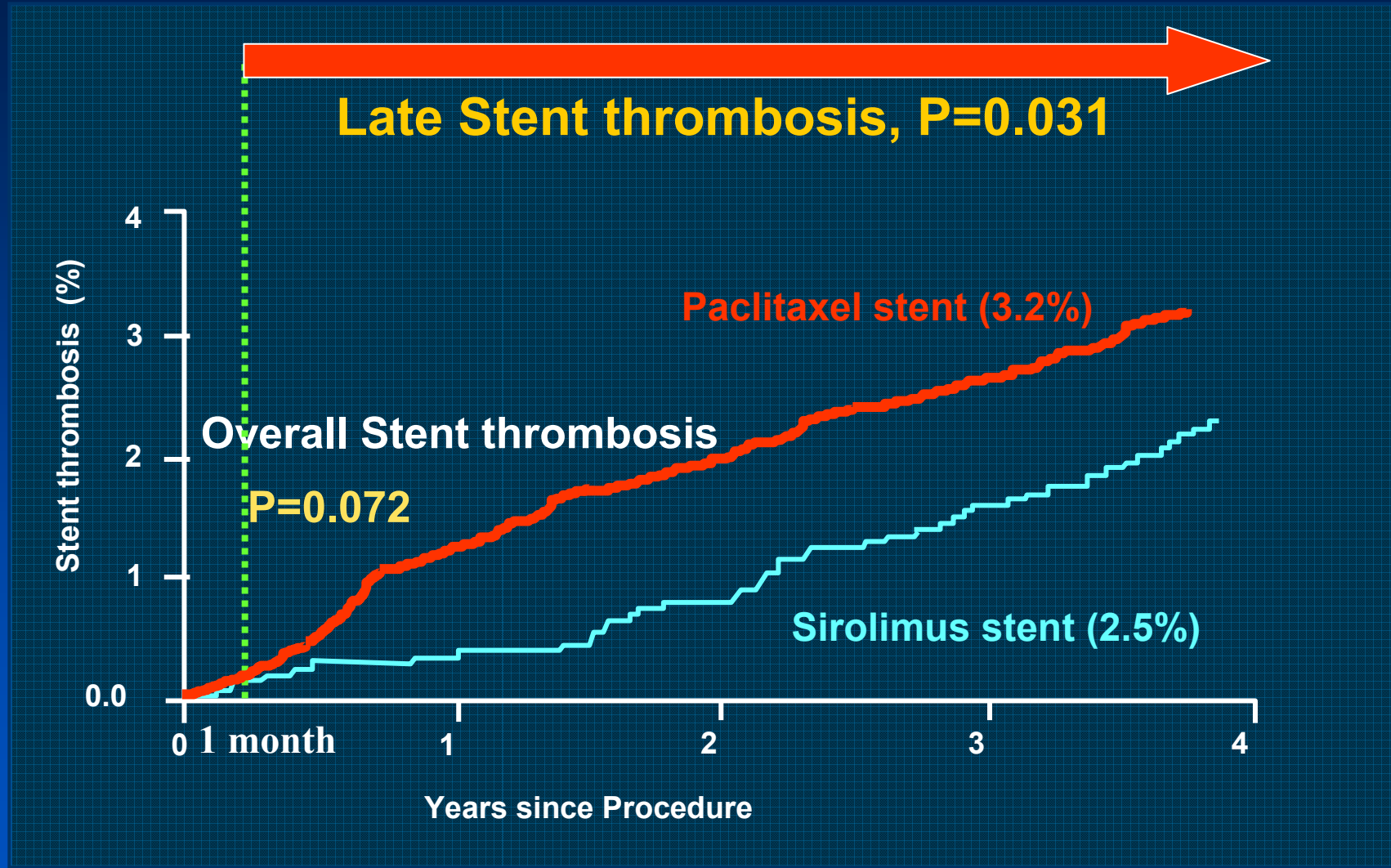
Angiographically documented stent thrombosis was assessed during 3 years follow-up period

Lancet 2007;369:667-678

# All-cause mortality or MI in overall population at 3 year F/U



# Incidence of ST stratified by type of DES



# Discussion Discussion

# And Data

# Clopidogrel Use and Long-term Clinical Outcomes After Drug-Eluting Stent Implantation

Eric L. Eisenstein, DBA

Kevin J. Anstrom, PhD

David F. Kong, MD

Linda K. Shaw, MS

Robert H. Tuttle, MSPH

**Context** Recent studies of drug-eluting intracoronary stents suggest that current antiplatelet regimens may not be sufficient to prevent late stent thrombosis.

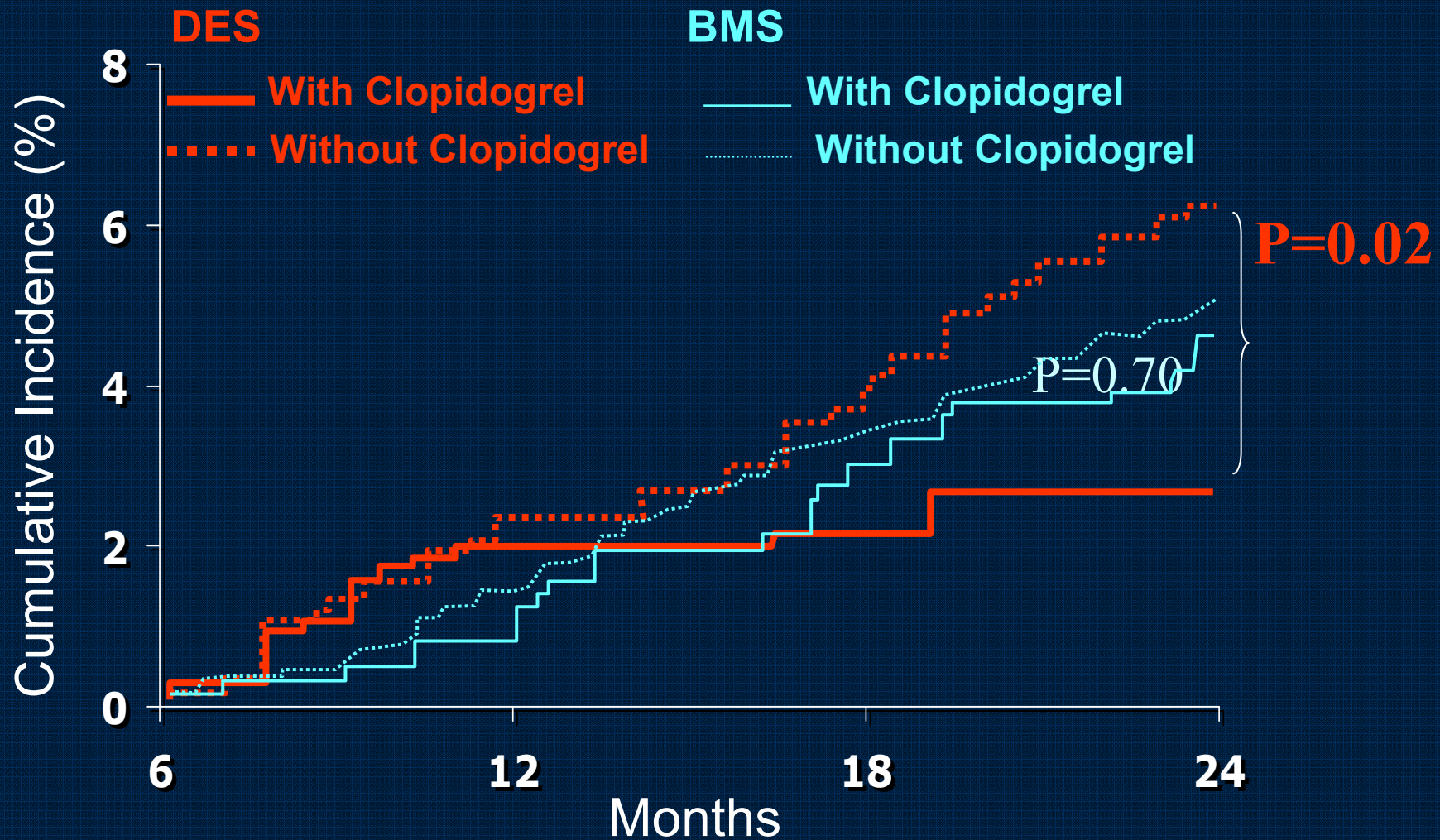
**Objective** To assess the association between clopidogrel use and long-term clinical outcomes of patients receiving drug-eluting stents (DES) and bare-metal stents (BMS) for treatment of coronary artery disease.

Pooled analysis of 4666 patients treated with DES (n=1501) or BMS (n=3165): Data from Duke Heart Center, USA

Landmark Analysis with or without clopidogrel use at 6-month and 12-month

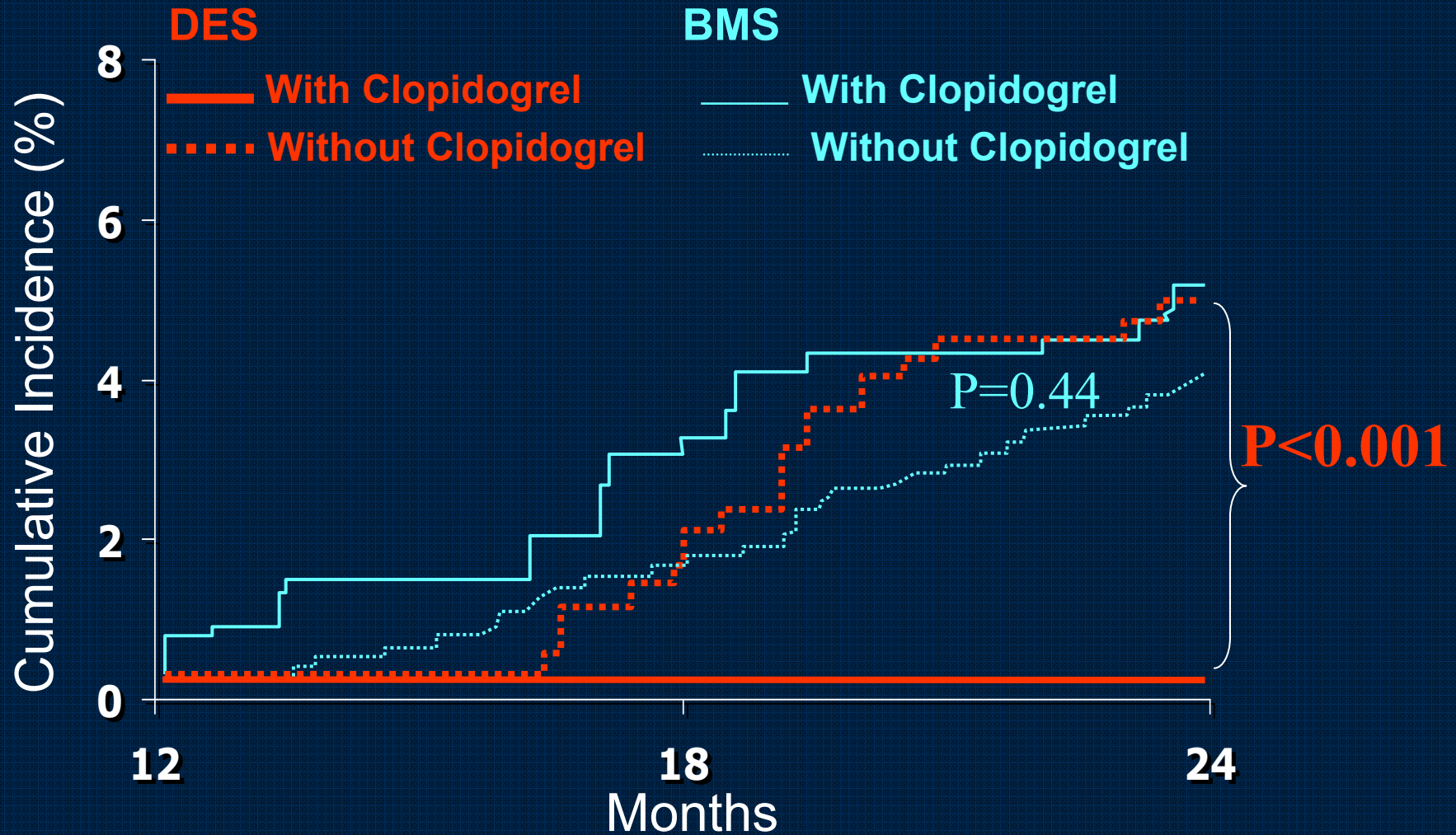
JAMA 2007;297:159-68

# Clopidogrel Use and Composite of Death or MI At 6-month Landmark



Eisenstein et al, JAMA 2007;297

# Clopidogrel Use and Composite of Death or MI At 12-month Landmark



Eisenstein et al, JAMA 2007;297

# Discussion Discussion

# And Data



**Summary ...**

# **Long-Term Incidence of Stent Thrombosis in Real World After DES vs. BMS Implantation**

**10-Year Experience  
from Single Center, AMC 2007**

# Overall 10-yr Study Population

8,152 Patients  
11,138 lesions

Jan,1997

Mar,2003

Feb,2006

**BMS**

**DES**

4,777 patients  
6,478 lesions  
6,667 stents

3,375 patients  
4,660 lesions  
6,411 stents

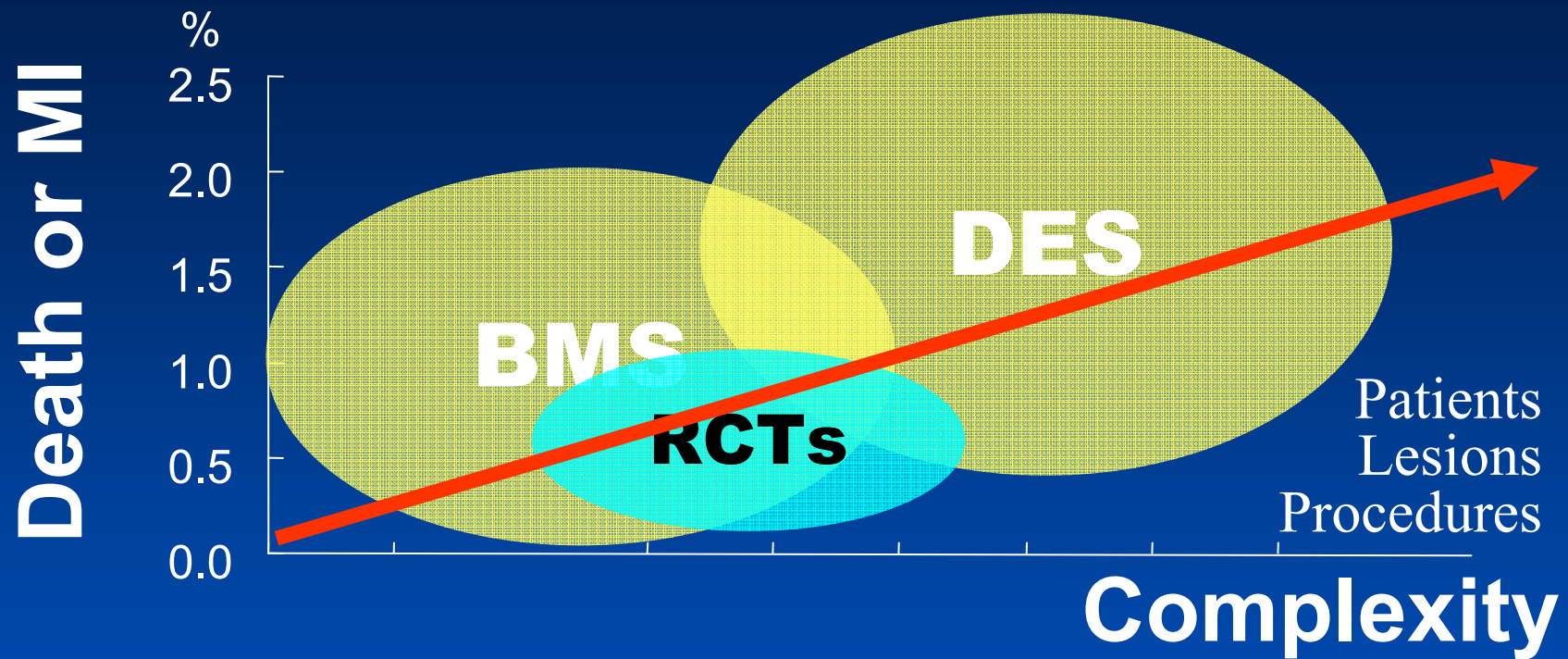
# Paradigm Shift of Patient Characteristics

	BMS (n=4777)	DES (n=3375)	<i>p</i>
Age (yrs)	59±10	61±10	<0.001
Diabetes	1067 (22%)	955 (28%)	<0.001
Hypertension	1973 (41%)	1700 (50%)	<0.001
Previous CABG	32 (1%)	86 (3%)	<0.001
Previous PCI	85 (2%)	715 (21%)	<0.001
LVEF (%)	59±10	58±9	0.026

# Paradigm Shift of Lesion and Procedural Characteristics

	BMS (n=6478)	DES (n=4660)	<i>p</i>
CTO lesion	86 (2.0%)	256 (6%)	<0.001
Bifurcation	667 (10%)	759 (16%)	<0.001
Left main	290 (5%)	325 (7%)	<0.001
Lesion length	18.5±15.0	26.3±14.7	<0.001
Reference diameter	3.2±0.7	2.9±0.5	<0.001
Total No.of stents	1.0±0.2	1.4±0.6	<0.001
Total stent length	19.6±7.7	34.2±18.9	<0.001

# Paradigm Shift of Real Practice



Patients treated with DES had more diabetes mellitus, multi-vessel, multi-lesion PCI, bifurcation location and low LV function, and more complex stenting procedures, which were typical traditional risk factors of unfavorable clinical outcomes.

# Independent Predictors of ST

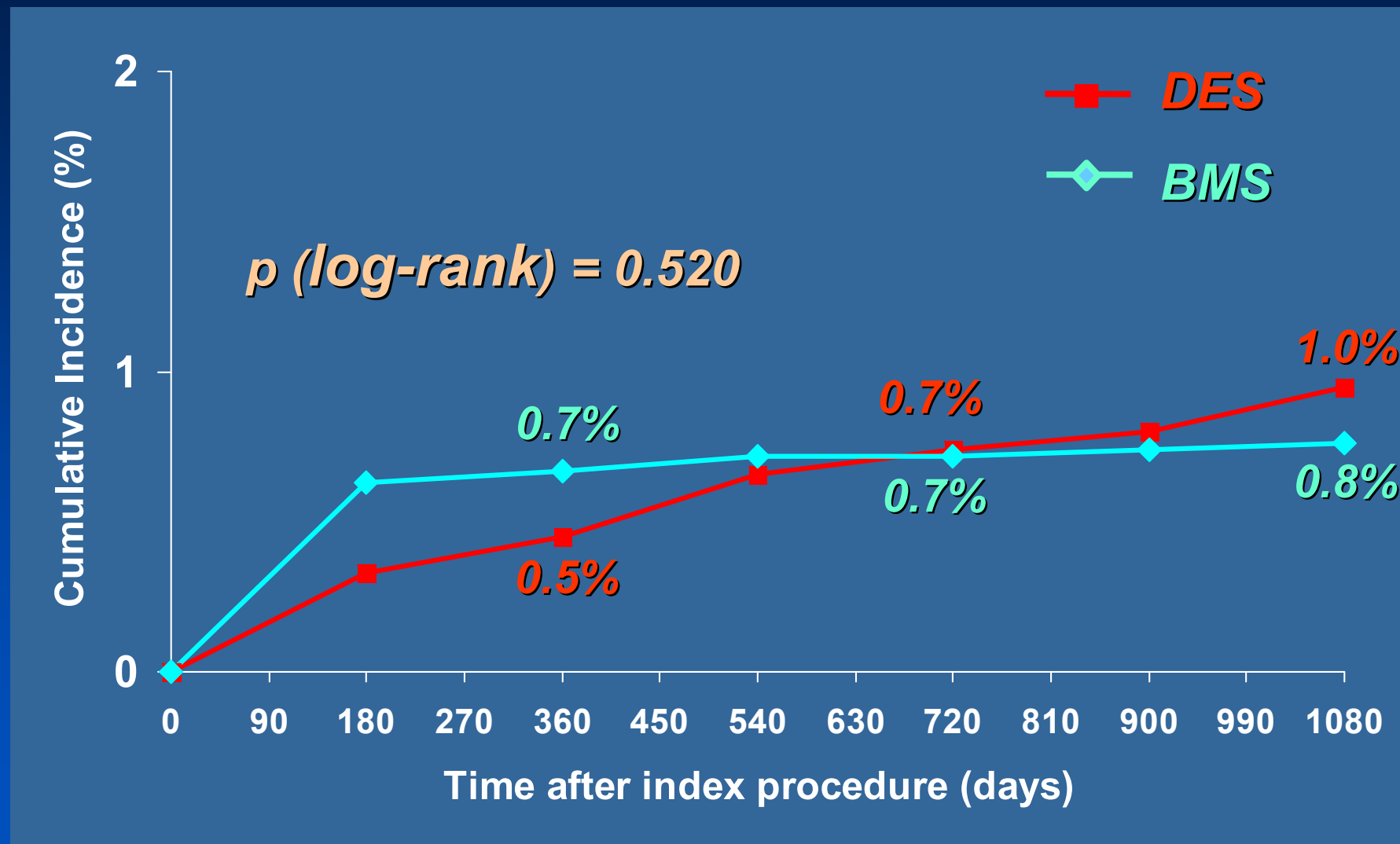
## (2yrs F/U, AMC data )

### *Multivariate Analysis*

Variables	(95% CI)	P
<b>Acute / subacute stent thrombosis</b>		
• Primary stenting in acute MI	74.22 (5.89-861.45)	0.001
• Total stent length	1.04 (1.01-1.08)	0.048
<b>Late stent thrombosis</b>		
• Premature interruption of antiplatelet therapy	24.79 (7.51-81.84)	<0.001
• Renal failure	8.40 (1.81-39.09)	<0.001
<b>Total stent thrombosis</b>		
• Premature interruption of antiplatelet therapy	19.21 (5.63-65.51)	<0.001
• Primary stenting in acute MI	12.24 (1.67-89.71)	0.014
• Total stent length	1.02 (1.001-1.04)	0.037

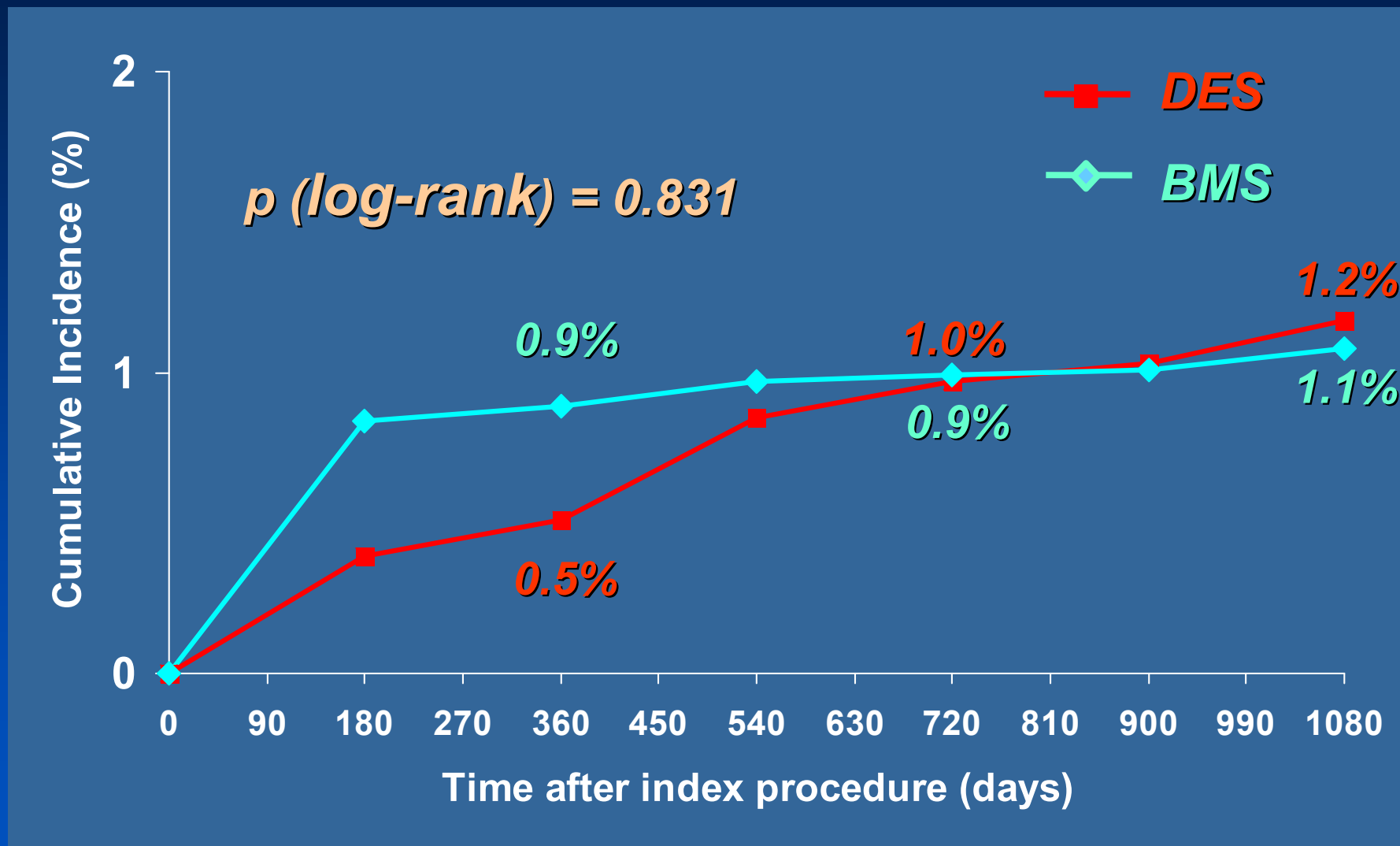
*Park, DW. AJC 2006;98:353-356*

# Incidence of ST (ARC: Definite) upto 3 years

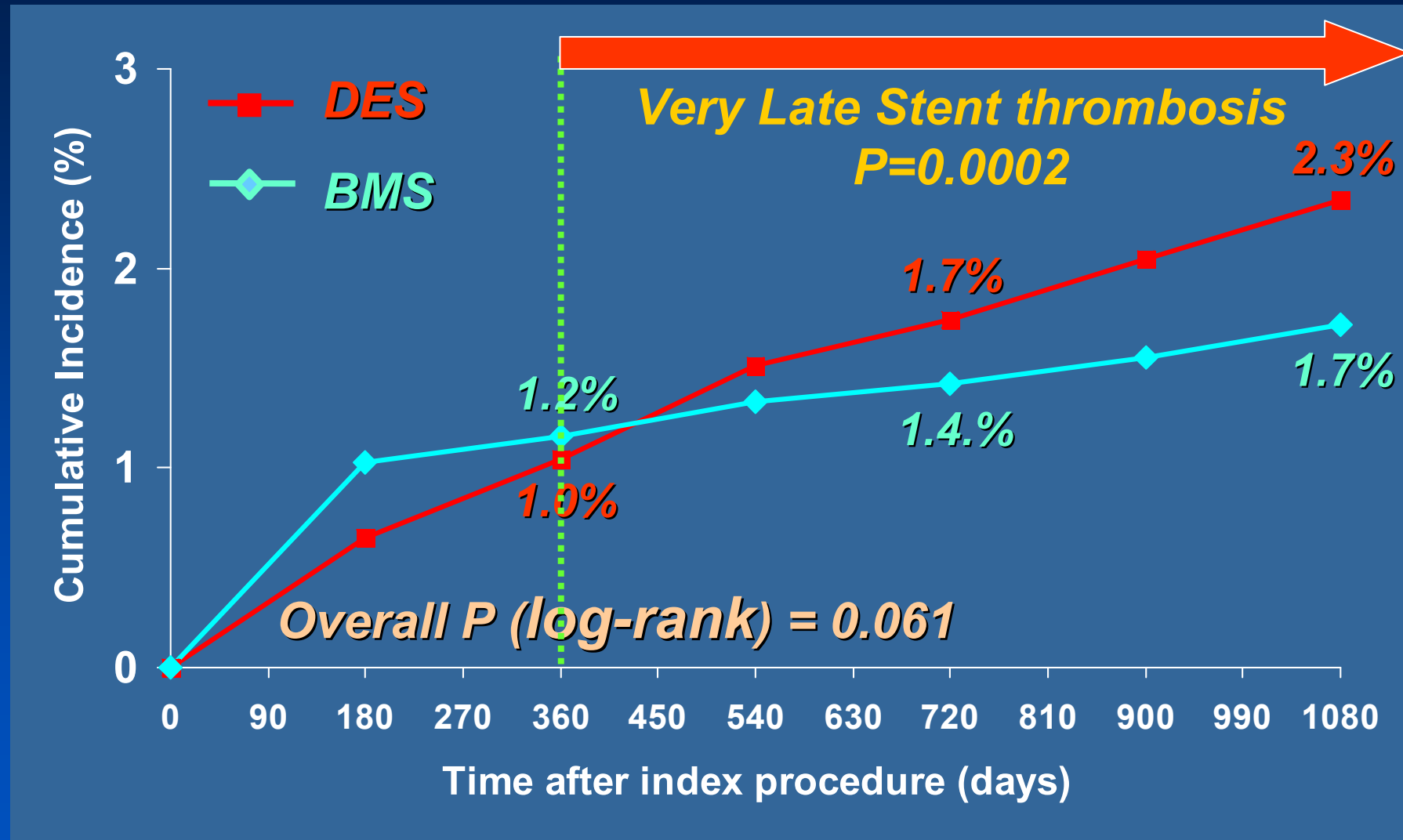




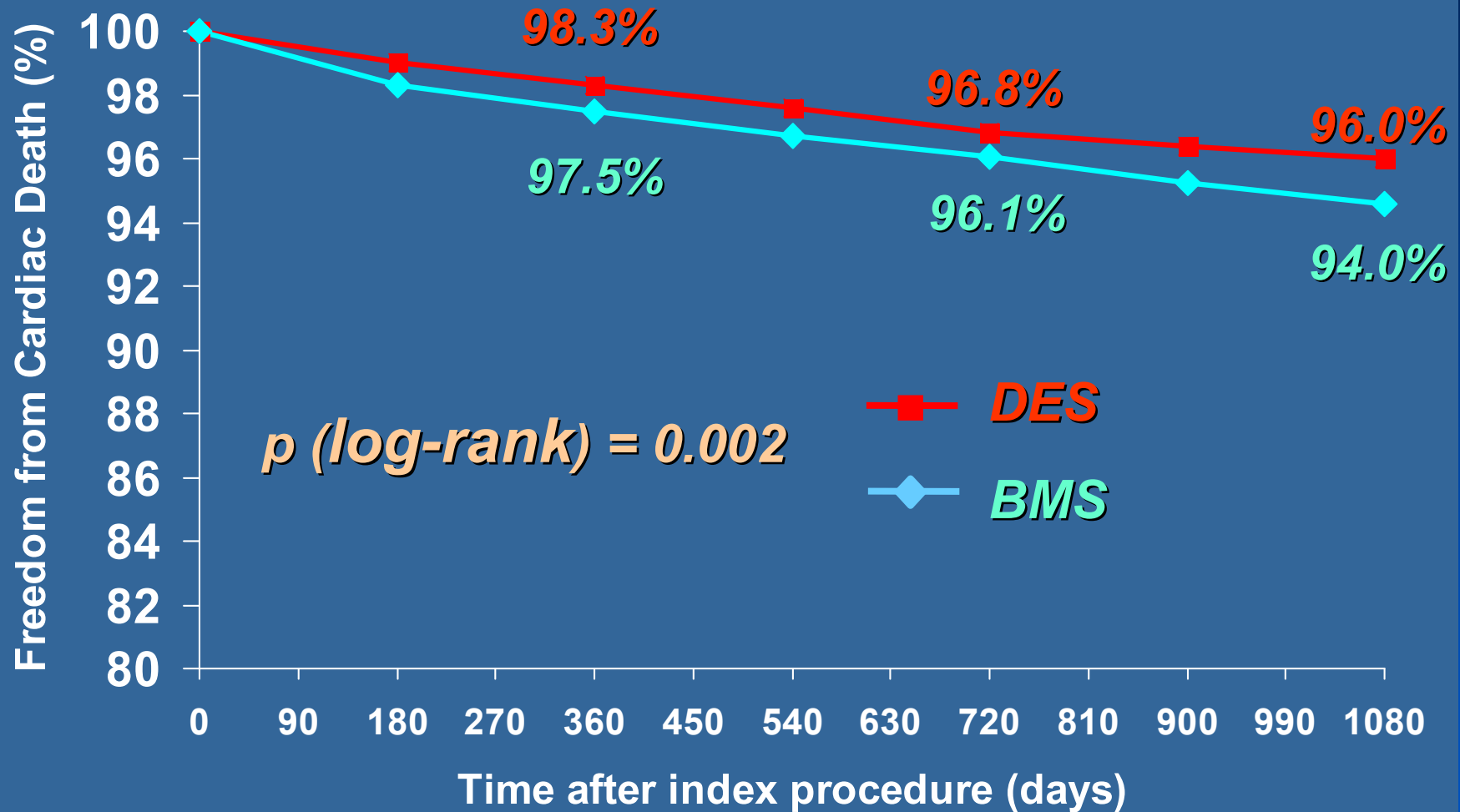
# Incidence of ST (ARC: Definite + Probable) upto 3 years



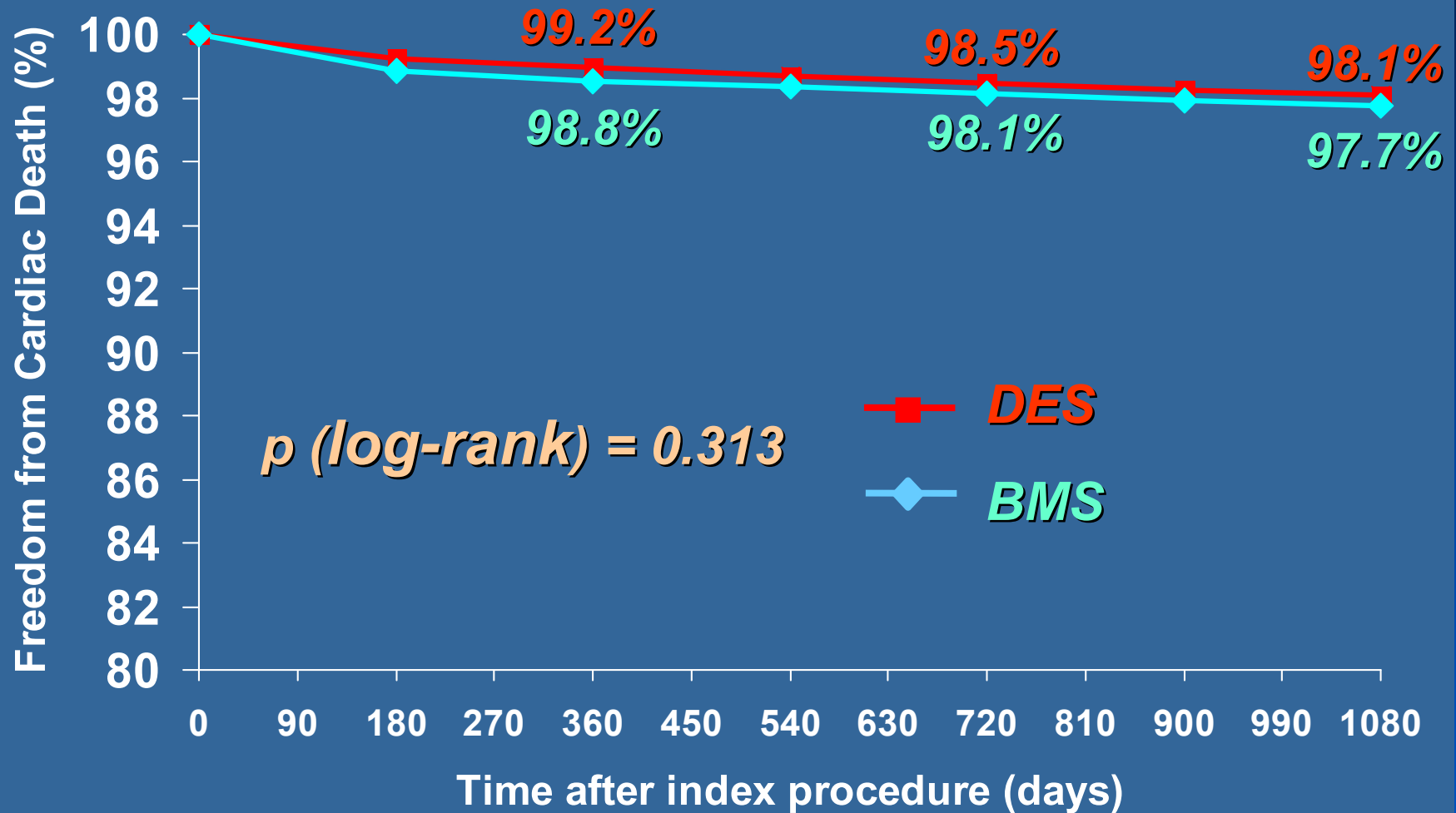
# Incidence of ST (Any ARC Criteria) upto 3 years



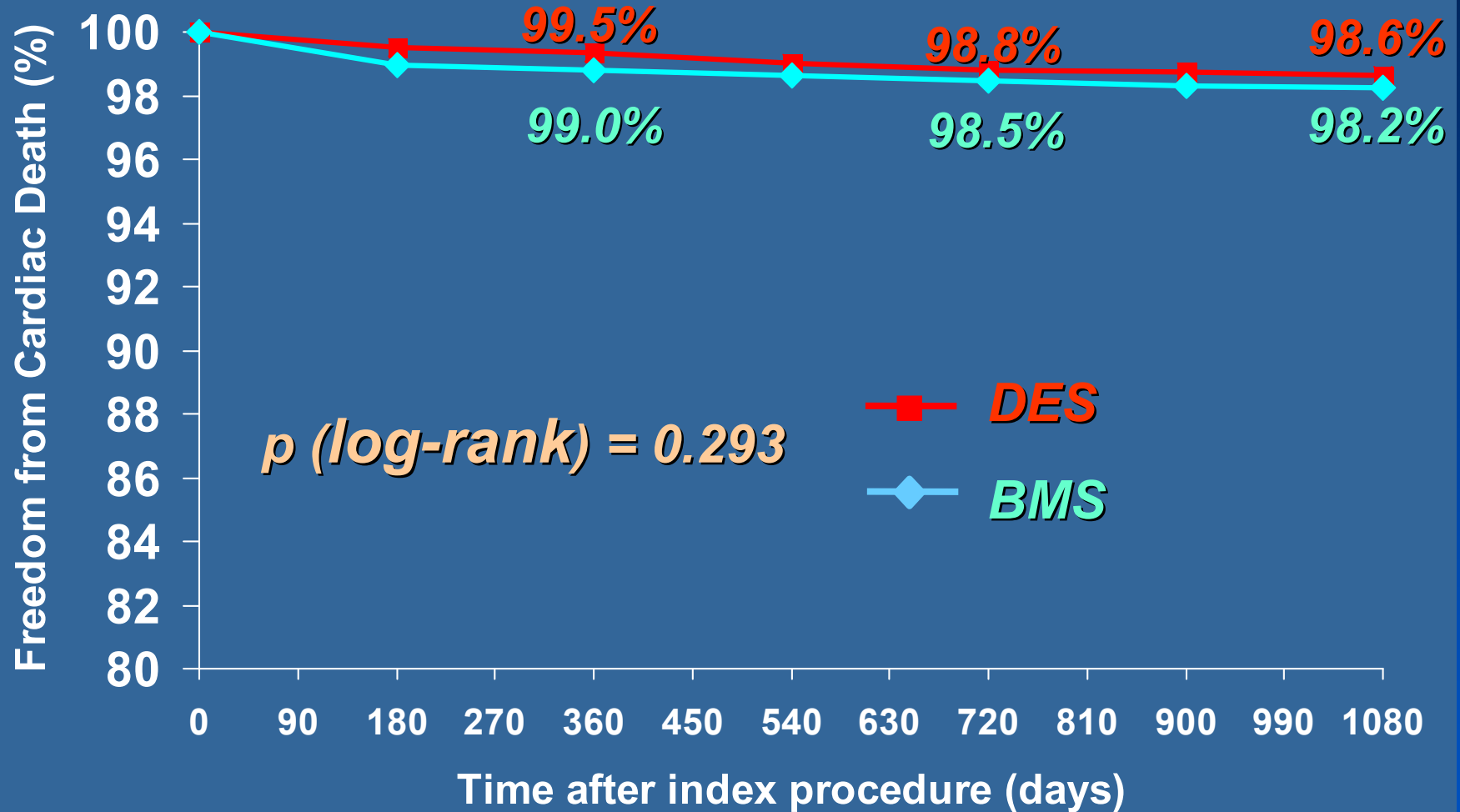
# Survival-Free from All-cause Mortality (up to 3 years)



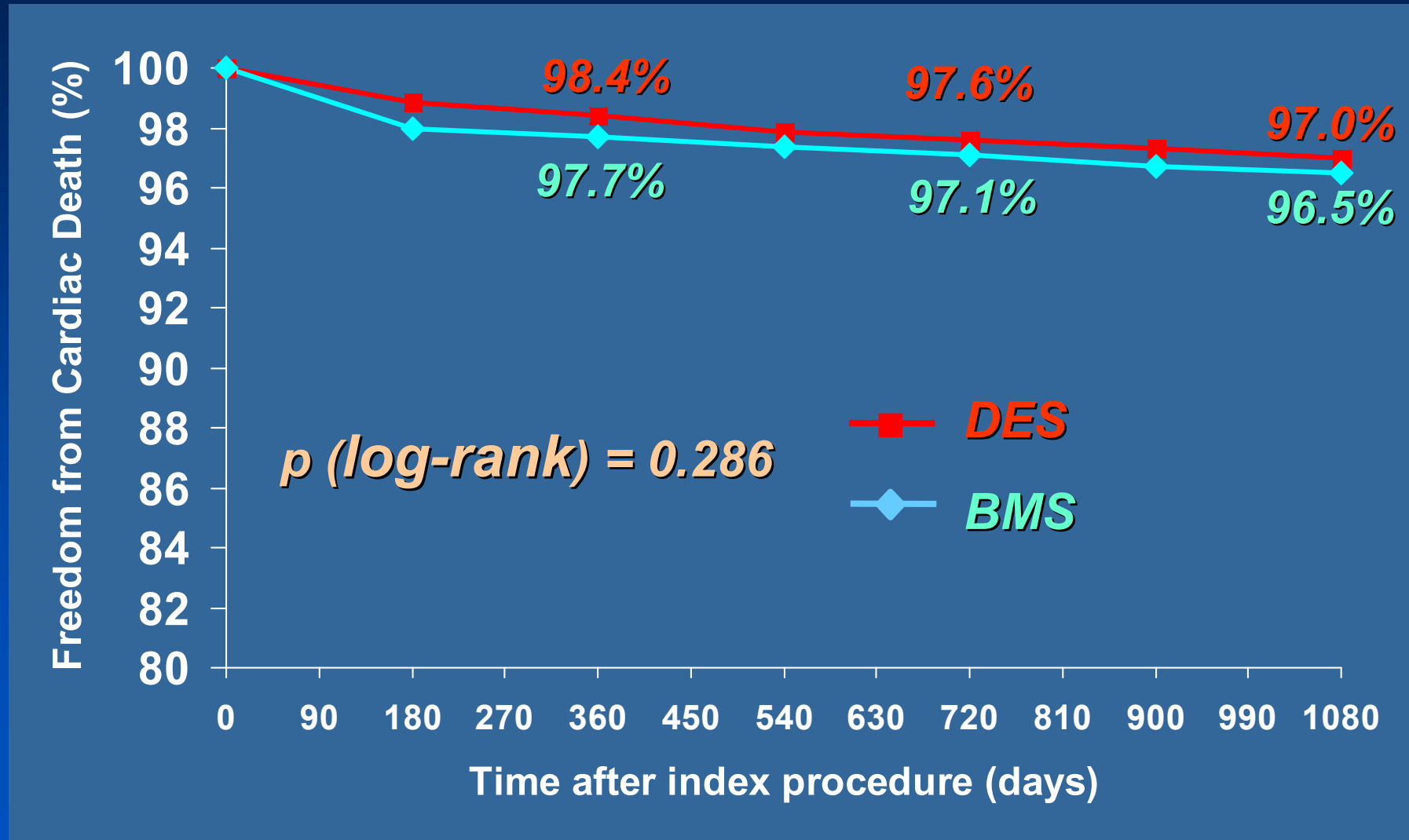
# Survival-Free from Cardiac Death (up to 3 years)



# Survival-Free from MI (up to 3 years)



# Survival-Free from Cardiac Death + MI (up to 3 years)



# Late Stent Thrombosis

## Is it Truth or Myth ?

- Increase late stent thrombosis: Yes / No
- Higher Mortality : No
- Randomized Trial would be almost impossible in the complex patients and lesion subsets ?
- How long should we use antiplatelet therapy ?
- We need a Smart DES.

**Dreams may come true,  
but not always perfect**







