Unprotected Left Main Stenting with DES

Where we are, Where we are going …

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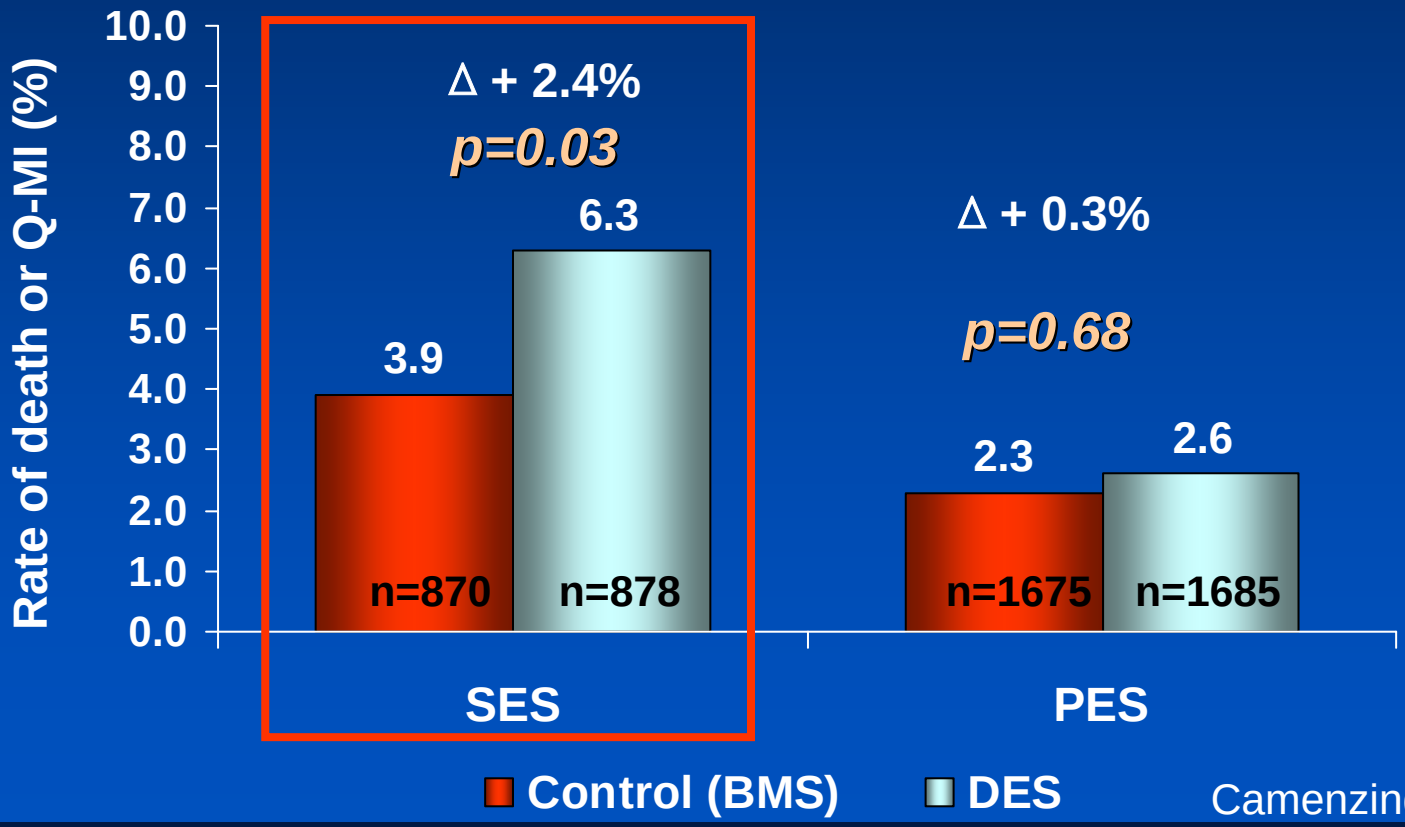
Safety Issue...

Incidence of All Death or MI in Pooled DES Data

All randomized studies up to latest available follow-up



Camenzind E, ESC 2006

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

Five publications in NEJM 2007;356:989-1039

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

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.

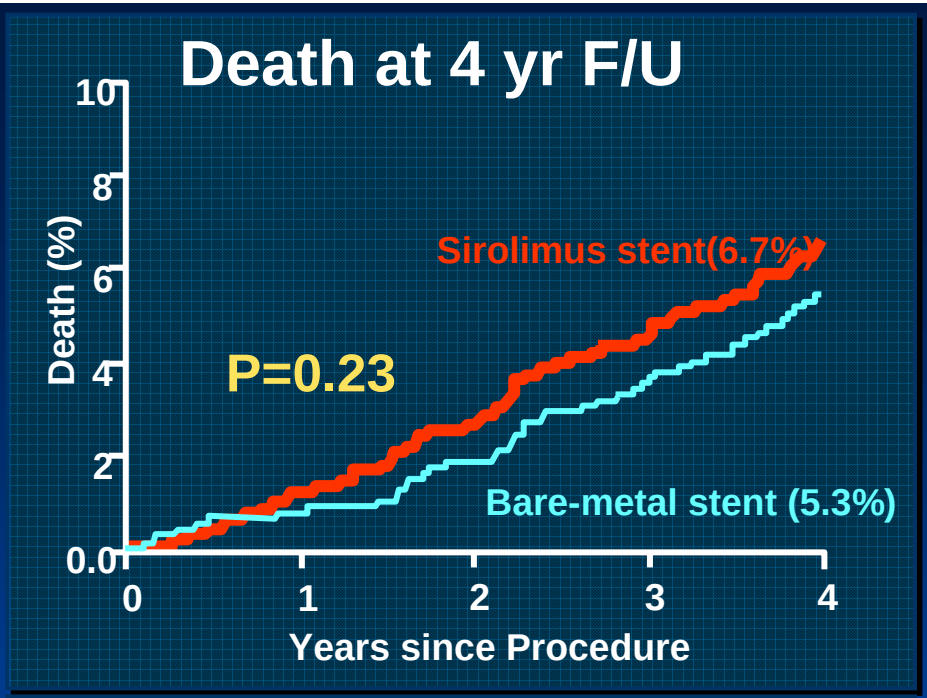
Pooled analysis of 1748 patients in 4 RCTs between SES or BMS

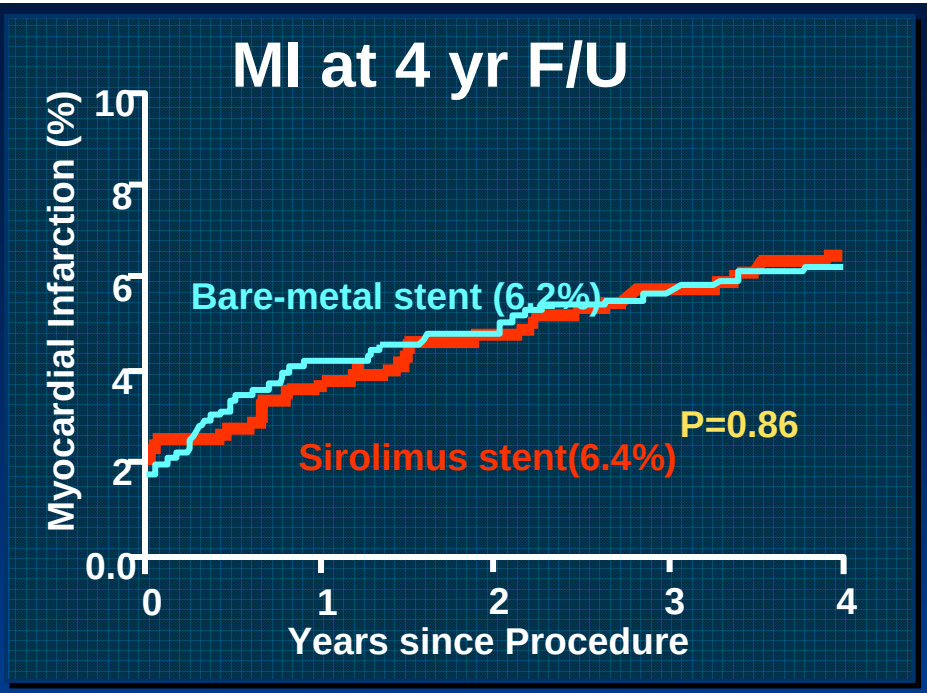
3513 patients in 5 RCTs between PES or BMS

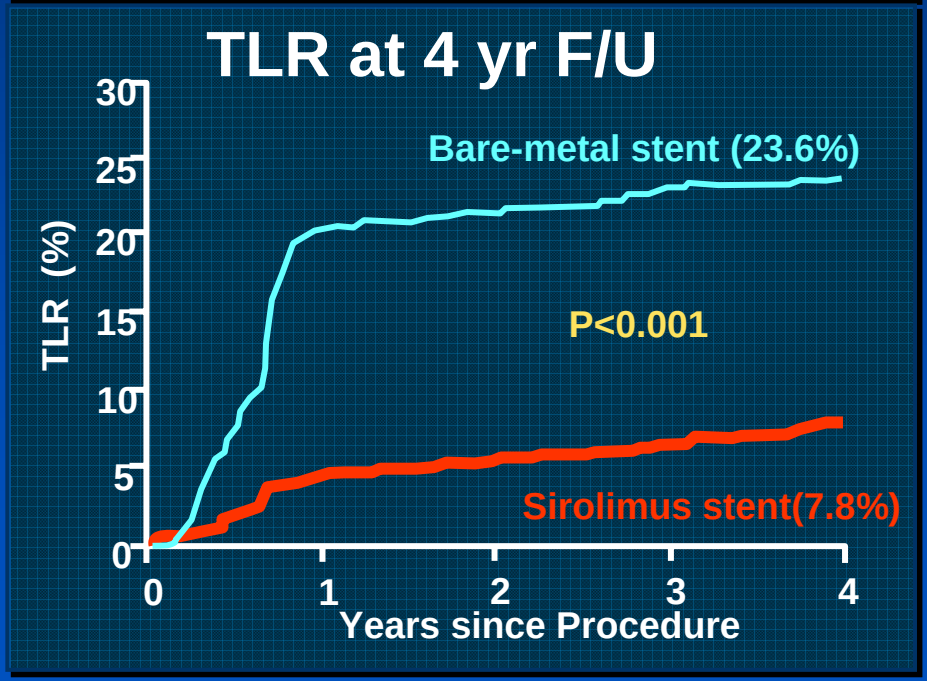
(SES Trials: RAVEL, SIRIUS, E-SIRIUS, C-SIRIUS)

(PES Trials: TAXUS-I, TAXUS-II, TAXUS-IV, TAXUS-V, TAXUS VI)

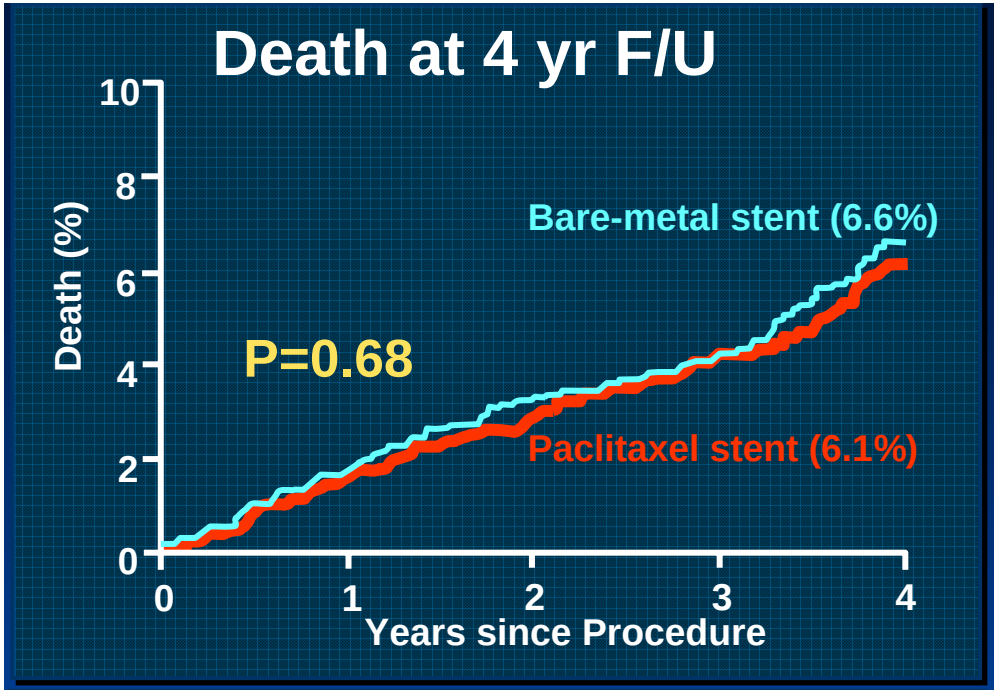
NEJM 2007;356:998-1008

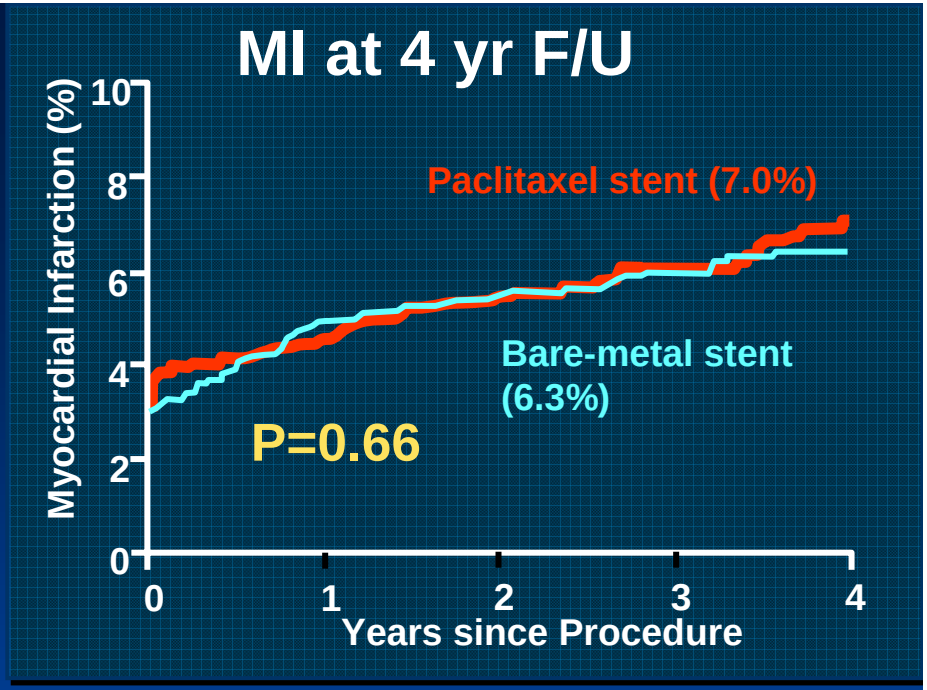


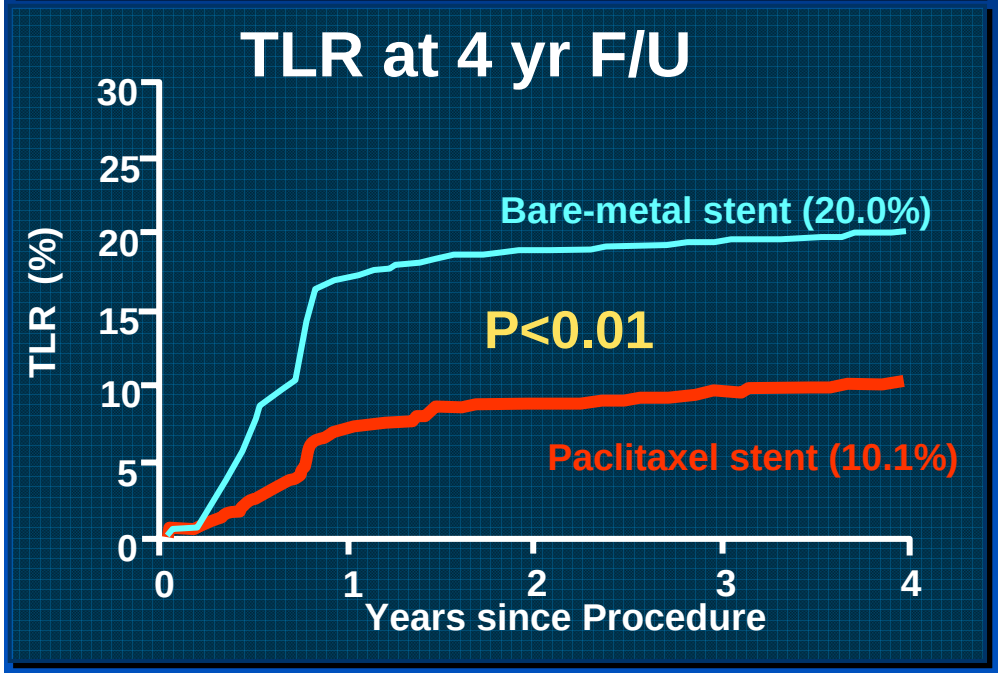




No difference in rates of death and MI. However, significant difference in TLR after SES

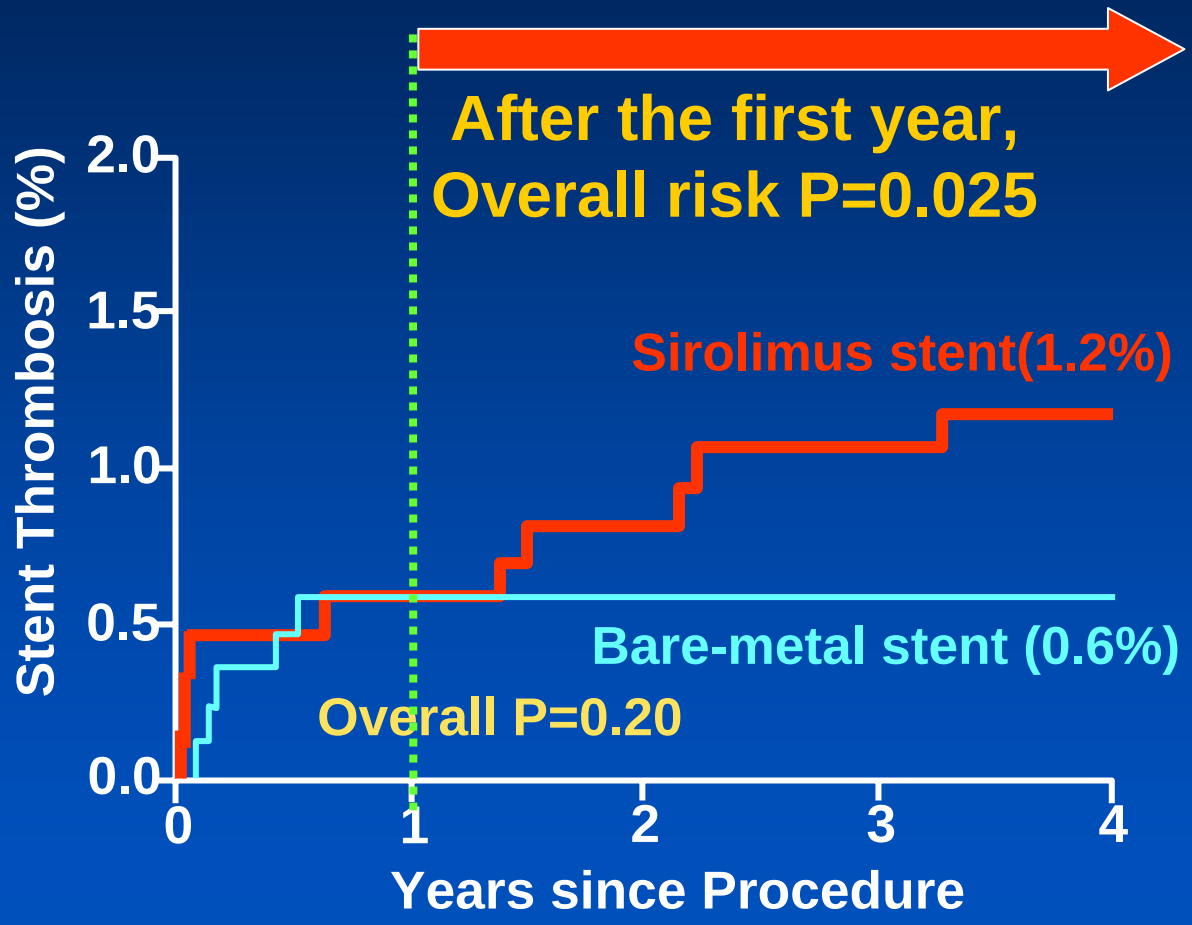




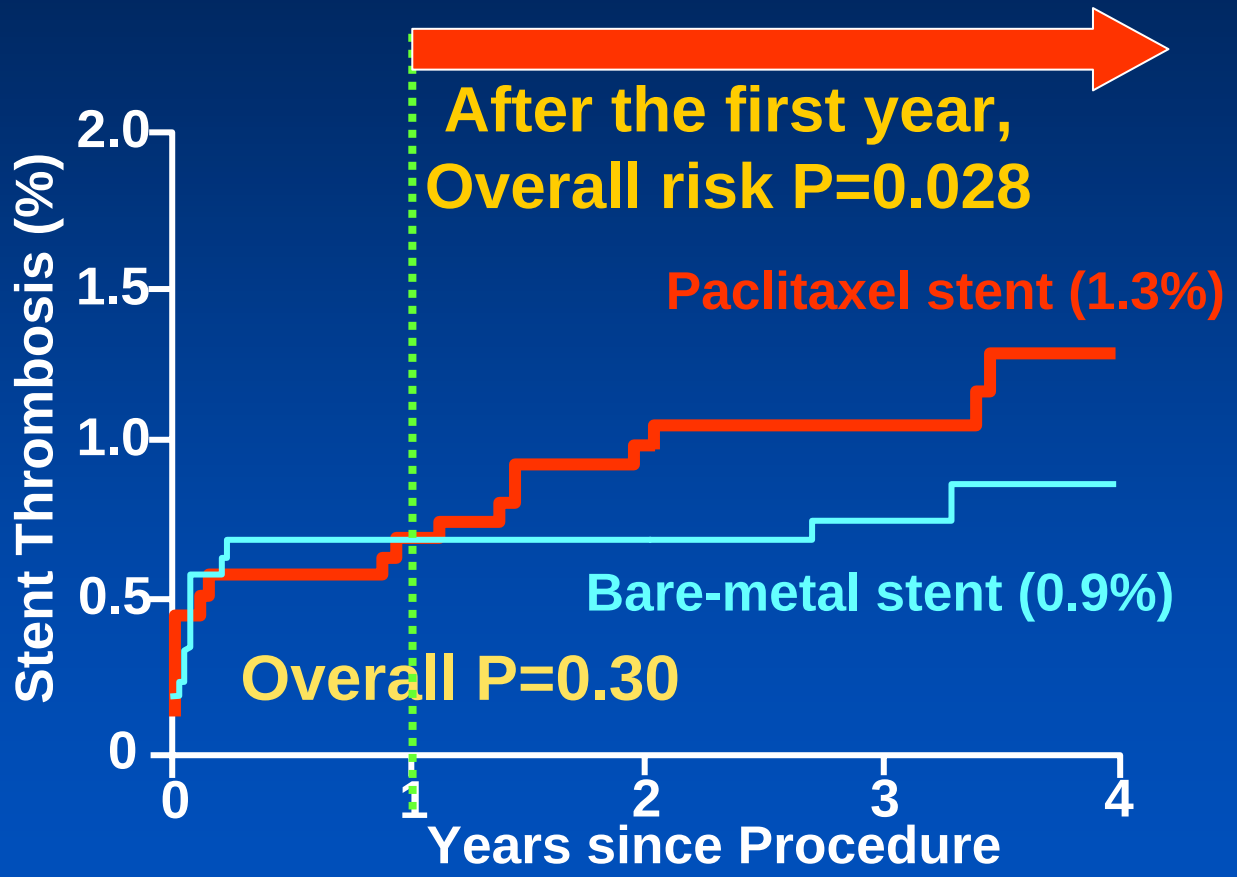


No difference in rates of death and MI. However, significant difference in TLR after PES

Stent Thrombosis After SES
(Protocol Definition)



Stent Thrombosis After PES
(Protocol Definition)



Conclusions

Pooled Data Analysis from RCTs

- Stent thrombosis after 1 year was more common with both SES and PES than with BMS.
- 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.

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*

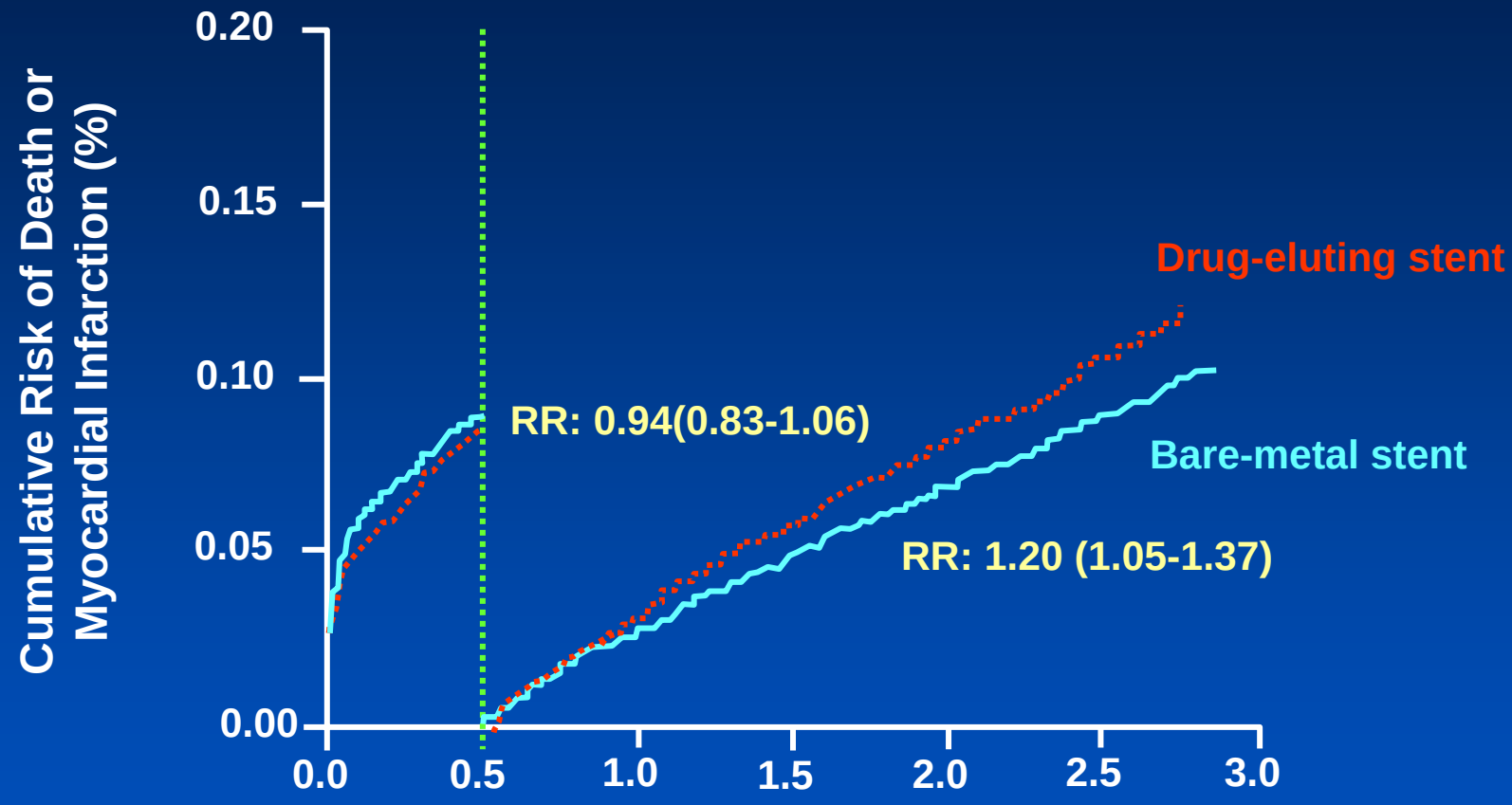
Pooled analysis of 6033 patients treated with DES and
13,738 patients treated with BMS
Data from Swedish Coronary Angiography and Angioplasty Registry

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

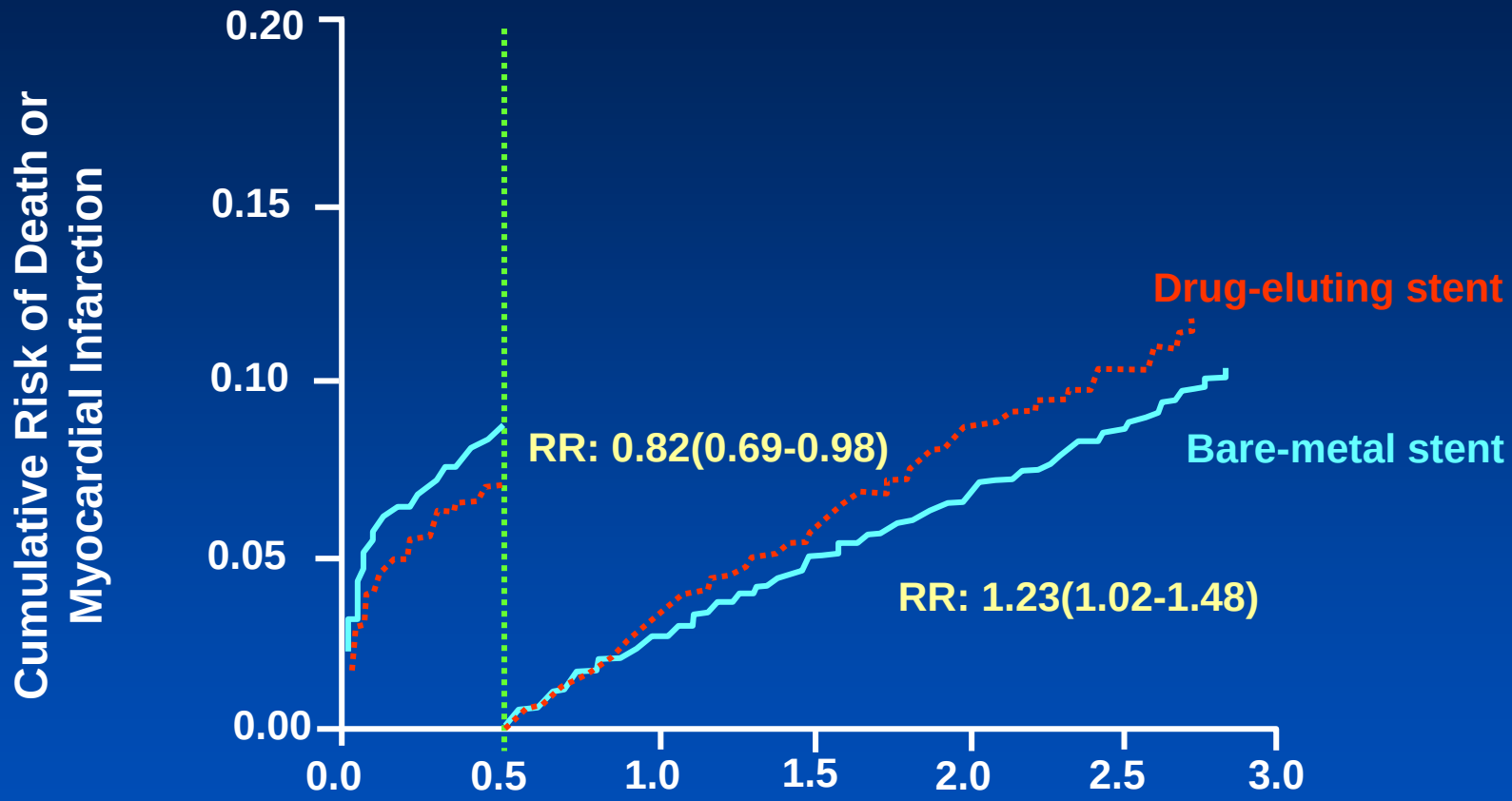
Composite Event: death or MI



No. at Risk							
Bare-metal stent	12,880	12,473	12,146	9158	5810	3104	8
Drug-eluting stent	5,770	5,604	5,426	3378	1704	611	0

Landmark Analysis of the One-Stent Subgroup

Composite Event: death or MI



No. at Risk							
Bare-metal stent	9556	9292	9053	6827	4360	2328	7
Drug-eluting stent	3432	3341	3238	1981	982	369	0

Conclusions

Pooled Analysis from Registry Data

- DESs were associated with an increased rate of death, as compared with BMSs.
- 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

One-Stent Subgroup

Stent length — no. (%)		
<10 mm	64 (8.4)	182 (5.0)
10–14 mm	74 (29.9)	792 (21.8)
15–16 mm	67 (26.9)	796 (21.9)
17–19 mm	13 (12.8)	341 (9.4)
20–23 mm	92 (10.6)	675 (18.6)
24–25 mm	16 (7.0)	382 (10.5)
26–30 mm	04 (3.0)	187 (5.2)
≥31 mm	53 (1.5)	272 (7.5)

	Bare-Metal Stent (N = 10,319)	Drug-Eluting Stent (N = 3638)
Restenotic lesion — no. (%)	121 (1.2)	243 (6.7)
Treated vessel — no. (%)		
Right coronary artery	3,463 (33.6)	557 (15.3)
Left main coronary artery	99 (1.0)	82 (2.3)
Left anterior descending artery	3,969 (38.5)	2260 (62.1)
Left circumflex artery	2,386 (23.1)	619 (17.0)
CABG graft	397 (3.8)	119 (3.3)

One-Stent Subgroup

They treated longer lesions, more LAD and more Diabetics. (more complex lesion and patients subsets)

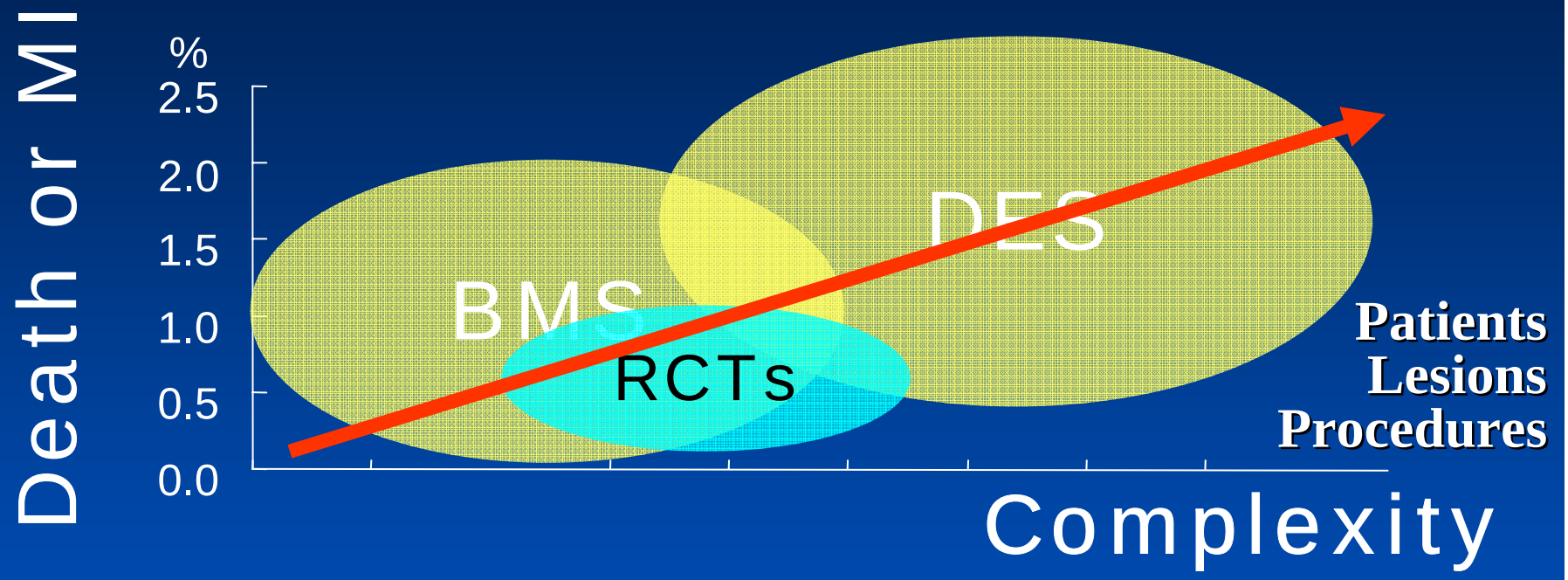
One-Stent Subgroup	Bare-Metal Stent (N = 10,319)	Drug-Eluting Stent (N = 3638)
Diabetes — no. (%)	1,618 (15.7)	855 (23.5)
Hypertension — no. (%)	4,368 (42.6)	1614 (44.7)
Previous PCI — no. (%)	1,068 (10.6)	606 (16.9)
Previous CABG — no. (%)	948 (9.5)	384 (10.7)
Previous myocardial infarction — no. (%)	3,693 (35.8)	1338 (36.8)
Aspirin before procedure — no. (%)	8,542 (82.8)	3161 (86.9)
Clopidogrel — no. (%)	5,248 (51.0)	2085 (57.4)

Despite
appropriate statistical adjustment,

- 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.

Bo Largerqvist NEJM 2007;356:1009-19

We Have to Realize Paradigm Shift in Real World 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 in BMS.

Perspective

Stent Thrombosis Redux — The FDA Perspective

Andrew Farb, M.D., and Ashley B. Boam, M.S.

As compared with on-label use,
off-label use is associated with increased risks of stent thrombosis and death or myocardial infarction

NEJM 2007;356:10

Off-label Use
Unprotected
Left Main Stenting with DES

More Prone to Stent Thrombosis ?

Unprotected Left Main Stenting

More Prone to Stent Thrombosis ?

Yes,

Off label -
Complex
Procedure

Previous pilot
data suggested
high risk SAT

Catastrophic
manifestation

No,

Big Vessel
Large Stent
High flow area

Stent Thrombosis in AMC

1191 Patients with DES
Median 19.4 months F/U

Stent thrombosis	15 /1911 (0.8%)	
Case-fatality rate	6 (40%)	
Angiographic-confirmed	9 (0.47%)	
SES	11 (0.7%)	**P = 0.45**
PES	4 (1.1%)	

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

Independent Predictors of ST
Multivariate Analysis

Variables	(95% CI)	P
Acute / subacute stent thrombosis		
Primary stenting in acute MI	74.22 (5.89-861.45)	0.001

We didn't find any lesion specific variables such as bifurcation and left main stenting as an independent predictor of stent thrombosis except total stent length in the era of DES

• 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

Unprotected LM stenting at 3 Year Follow-up

Comparison Data of DES and BMS

AMC Pooled Data Analysis of
570 patients with Unprotected LM stenting, 2007

570 Patients with Unprotected LM stenting

Primary End point: Death from any cause at 3 years F/U

Other outcomes: Stent thrombosis,
Composite of death, MI and reintervention

Baseline Characteristics

	DES (N=315)	BMS (N=255)	p
Age (years)	59.8 ± 11.4	56.3 ± 11.7	<0.001
Men	71.1 %	66.7 %	0.253
Risk factors			
Smoker	21.6 %	34.1 %	0.001
Cholesterol > 200mg/dL	20.6 %	23.9 %	0.347
Diabetes mellitus	29.9 %	18.8 %	0.003
Hypertension	46.8 %	31.8 %	<0.001
Previous PCI	22.9 %	2.3 %	<0.001

Baseline Characteristics

	DES (N=315)	BMS (N=255)	p
Clinical manifestation			<0.001
Stable angina	54.8%	32.3%	
Unstable angina	39.8%	62.6%	
Myocardial infarction within 2 weeks	5.4%	5.1%	
LV ejection fraction (%)	60.0 ± 8.2	61.2 ± 8.0	0.003

Angiographic Findings

	DES (N=315)	BMS (N=255)	p
Angiographic diagnosis			<0.001
LM + 1 vessel	20.6 %	28.0 %	
LM + 2 vessel	26.3 %	15.4 %	
LM + 3 vessel	31.4 %	8.3 %	
LM only	21.6 %	48.4 %	
RCA involvement	40.0 %	15.3 %	<0.001
LM site			<0.001
Ostium	22.5 %	47.6 %	
Shaft	5.1 %	14.6 %	
Bifurcation	72.4 %	37.8 %	

QCA findings

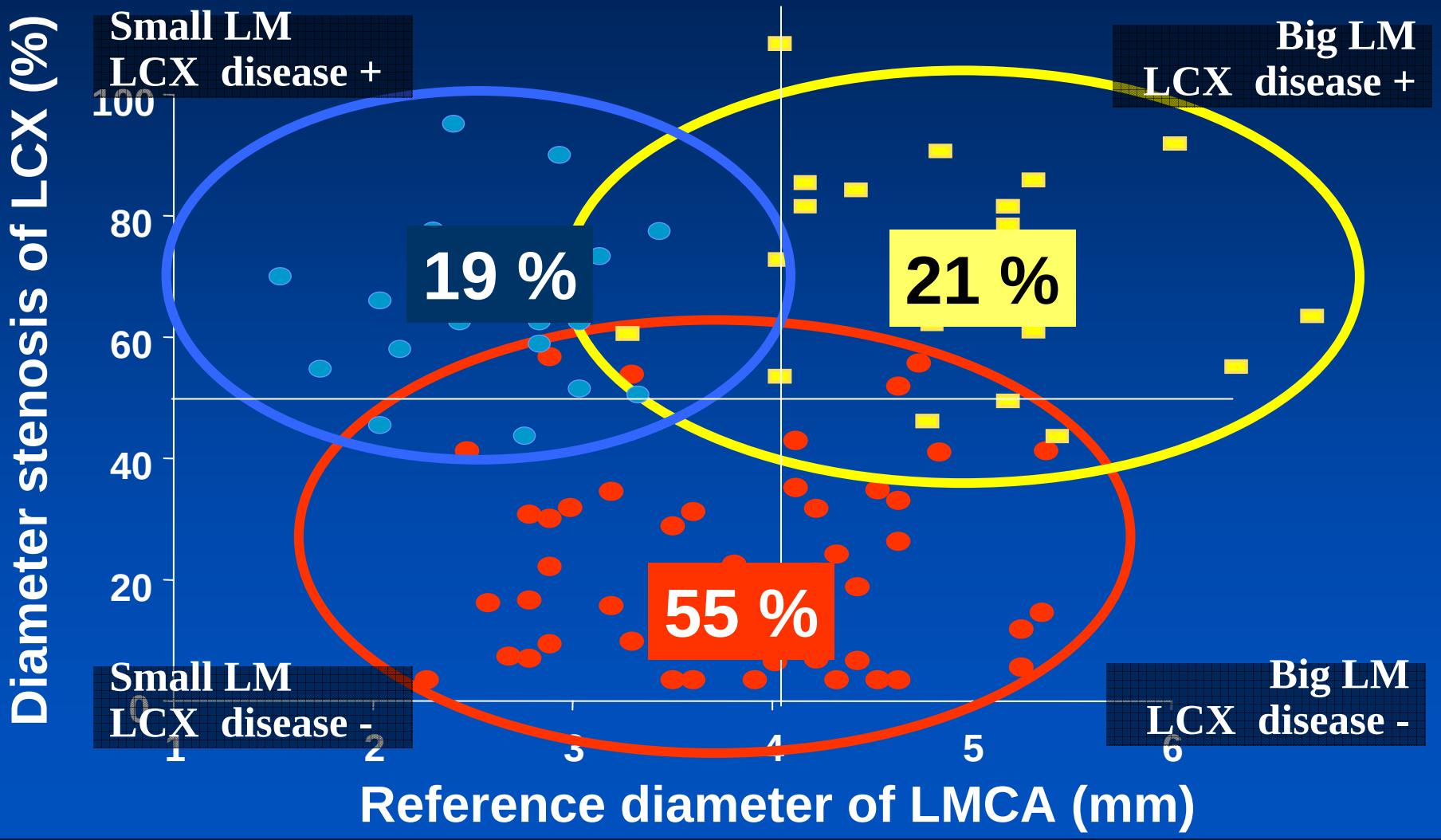
	DES (N=315)	BMS (N=255)	p
Reference vessel size, mm	3.39 ± 0.63	3.99 ± 0.70	<0.001
Lesion length, mm	22.5 ± 15.8	11.6 ± 5.3	<0.001
MLD, mm			
Pre-intervention	1.20 ± 0.81	1.25 ± 0.55	0.267
Post-intervention	3.33 ± 0.53	4.10 ± 0.60	<0.001
Diameter stenosis, %			
Pre-intervention	64.0 ± 21.4	68.5 ± 13.8	0.150
Post-intervention	0.43 ± 15.5	-0.40 ± 12.4	0.001
Acute gain, mm	2.13 ± 0.69	2.85 ± 0.75	<0.001

Procedural Characteristics

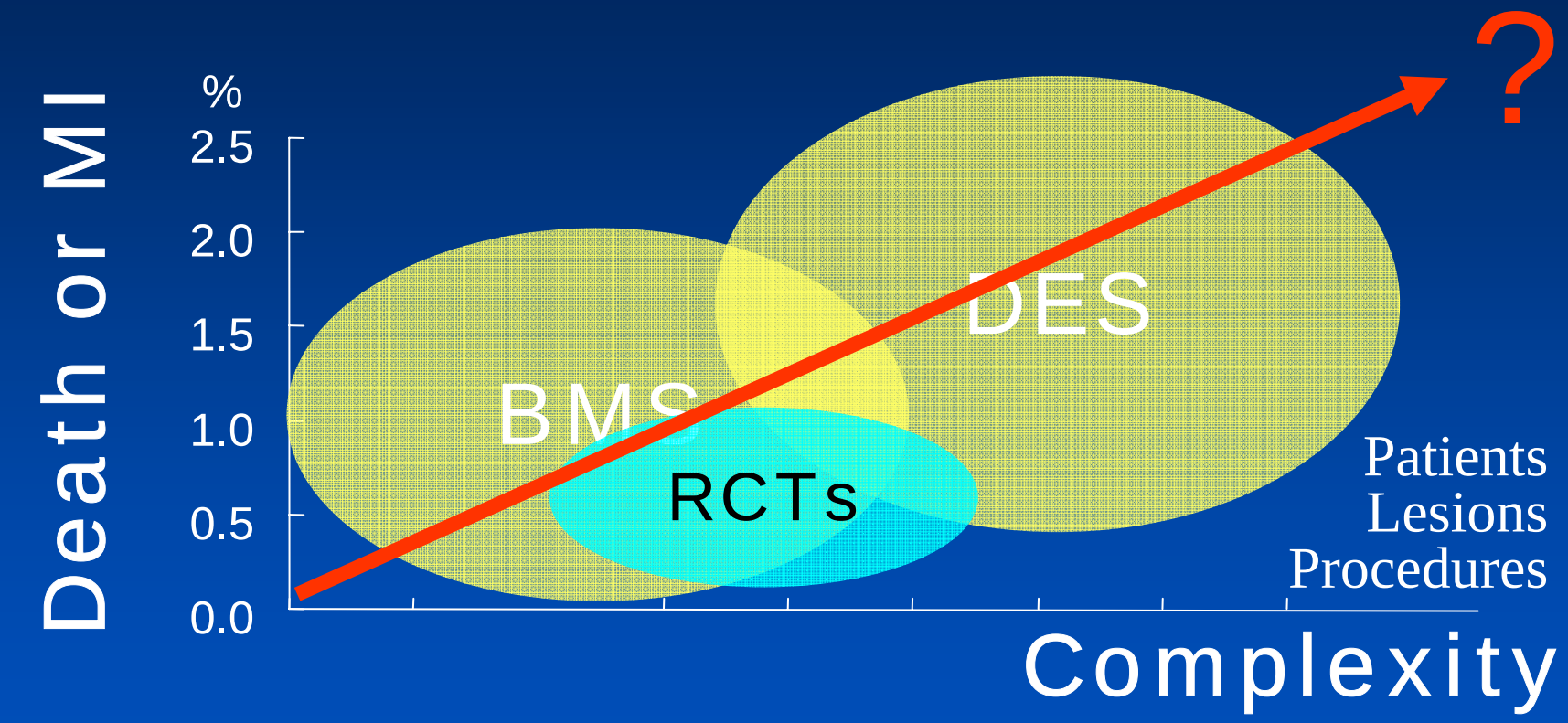
	DES (N=315)	BMS (N=255)	p
SES / PES	301 / 14		
GP IIb/IIIa inhibitor	6.7 %	2.0 %	0.008
Use of IABP	8.1 %	2.4 %	0.005
Total stent length, mm	30.1±13.3	13.3±5.3	<0.001
Total number of stents	2.5 ± 1.3	1.6±0.7	<0.001
Use of IVUS	85.3 %	84.6%	0.457
Bifurcation PCI technique			<0.001
Simple (provisional T)	54.8 %	72.5%	
Kissing	20.6 %	10.1%	
Crush	19.2 %	0	
Others (culotte, Y, etc)	6.9 %	17.4%	

Different Treatment Strategy

● Single stent Cross-over ● Crush ■ Kissing



Paradigm Shift in Real World Practice of LM PCI



Unprotected LM stenting

Comparison Data of DES and BMS

Safety Issue

AMC Data 2007

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

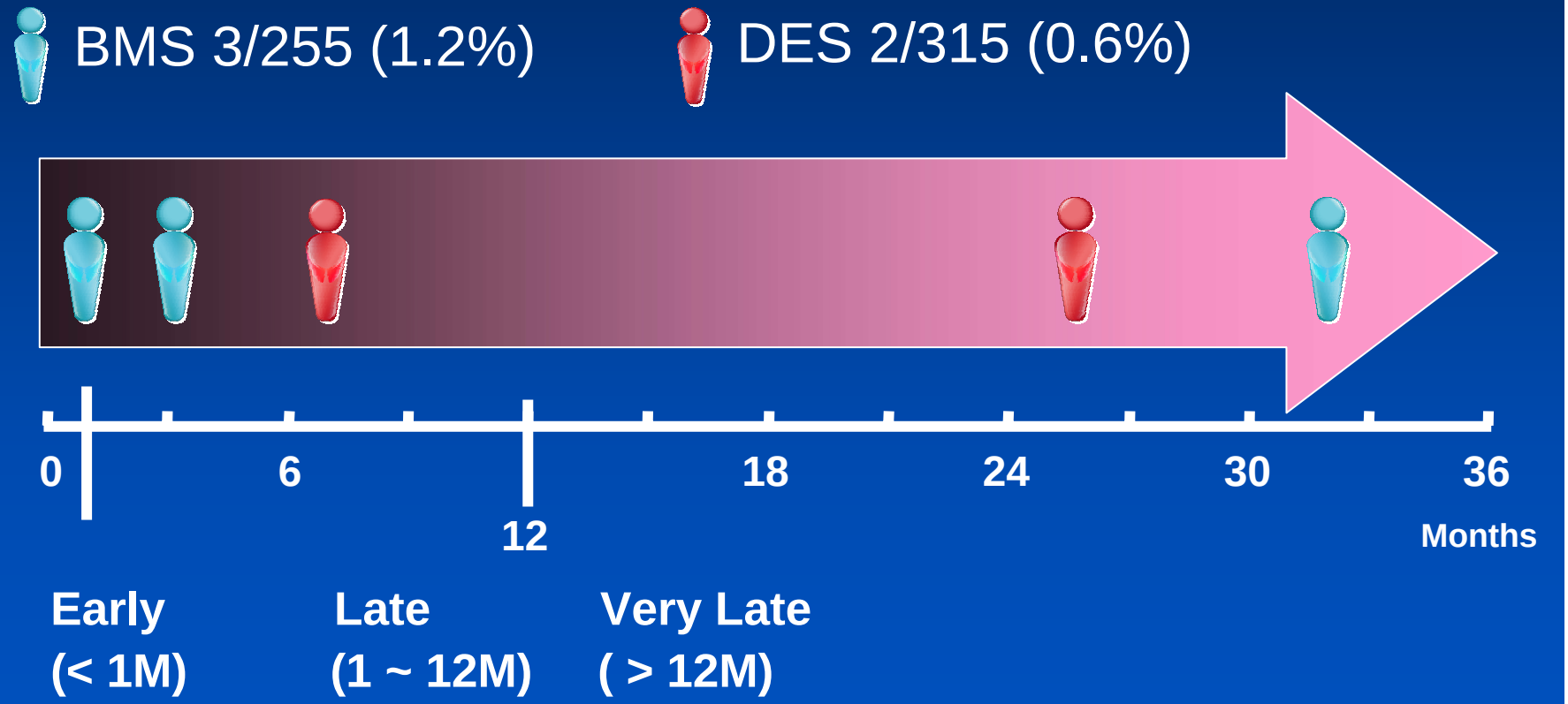
Total Stent Thrombosis Rate at 3 Year Follow-up

0.9 % (5 / 570 Patients)

1.2 % (3/255) **0.6 % (2/315)**

Pooled Data Analysis 2007
Under ARC Definition of Stent Thrombosis

No Definite Stent Thrombosis, Probable 1 patient (0.2%) Possible 4 patients (0.7%)



Early Clinical Outcomes at 30 Days

	DES (N=315)	BMS (N=255)	p
• Death	0	0.4% (1)	0.45
Cardiac	0	0.4% (1)	0.45
Non-cardiac	0	0	NA
• MI	0	0	NA
Q MI	0	0	NA
Non-Q MI	0	0	NA
• TLR	0	0.4% (1)	0.45
TVR	0.3% (1)	0.4% (1)	0.99
Death/ MI/ TVR	0.3% (1)	0.4% (1)	0.99
• Stent thrombosis	0	0.4% (1)*	0.67

*1 death due to severe heart failure and VF in BMS : **Probable**

Late Clinical Outcomes after 30 Days to 1 Year

	DES (N=315)	BMS (N=255)	p
Death	1.6% (5)	1.2% (3)	0.74
Cardiac	1.0% (3)	0.8% (2)	0.99
Non-cardiac	0.6% (2)	0.4% (1)	0.99
MI	0	0	NA
Q MI	0	0	NA
Non-Q MI	0	0	NA
TLR	4.4% (14)	15.7% (40)	<0.001
TVR	4.4% (14)	16.9% (43)	<0.001
Death/ MI/ TVR	6.0% (19)	17.3% (44)	<0.001
Stent thrombosis	0.3% (1) *	0.4% (1)	0.99

*1 death due to unexplained SCD at 3.6 months after discontinued aspirin + plavix antiplatelet therapy in DES : **Possible**

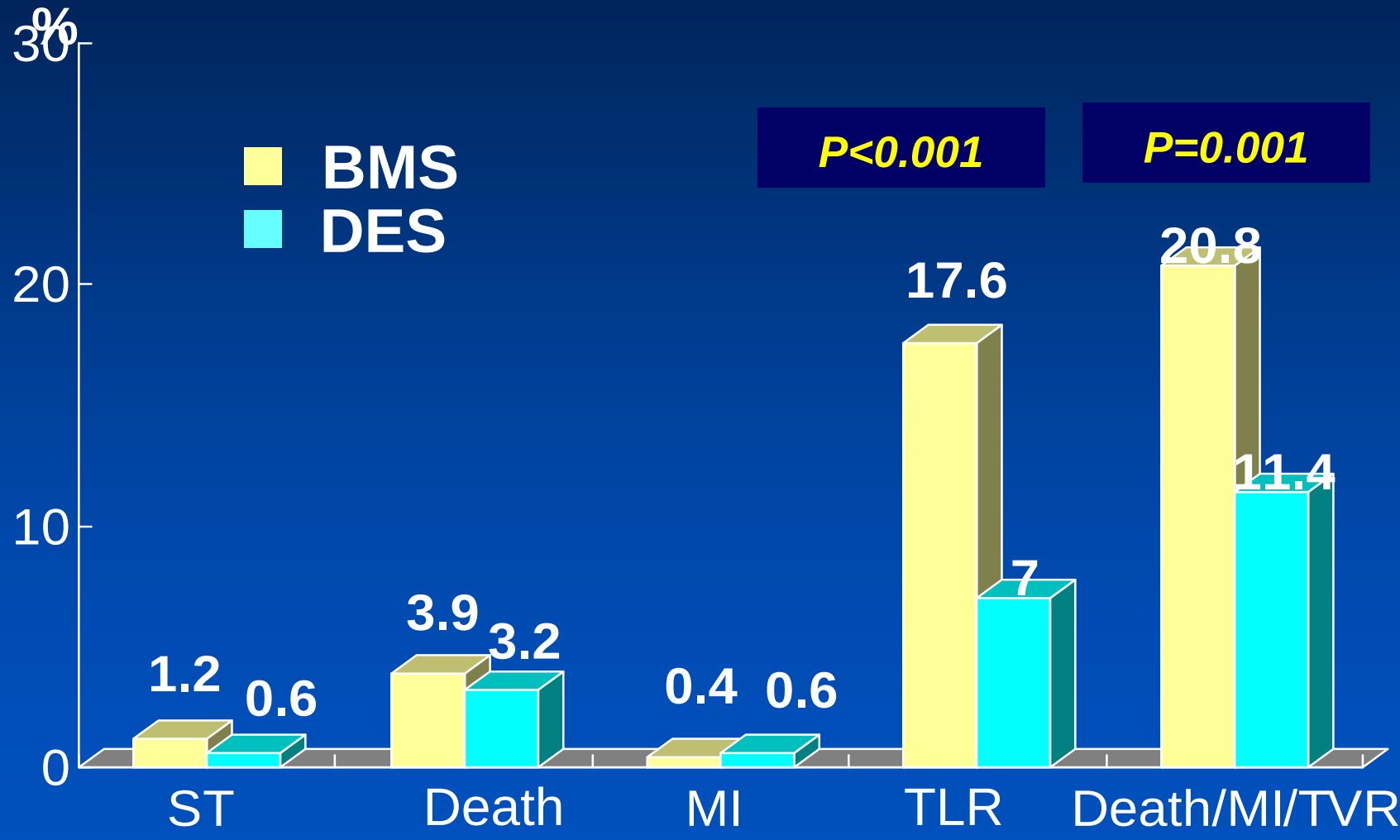
Very Late Clinical Outcomes after 1 Year to 3 Year

	DES (N=315)	BMS (N=255)	p
Death	1.6% (5)	2.4% (6)	0.55
Cardiac	0.3% (1)	2.0% (5)	0.09
Non-cardiac	1.3% (4)	0.4% (1)	0.39
MI	0.6% (2)	0.4% (1)	0.99
Q MI	0.6% (2)	0.4% (1)	0.99
Non-Q MI	0	0	NA
TLR	2.5% (8)	1.6% (4)	0.56
TVR	2.9% (9)	1.6% (4)	0.40
Death/ MI/ TVR	5.1% (16)	3.1% (8)	0.30
Stent thrombosis	0.3% (1)	0.4% (1)	0.99

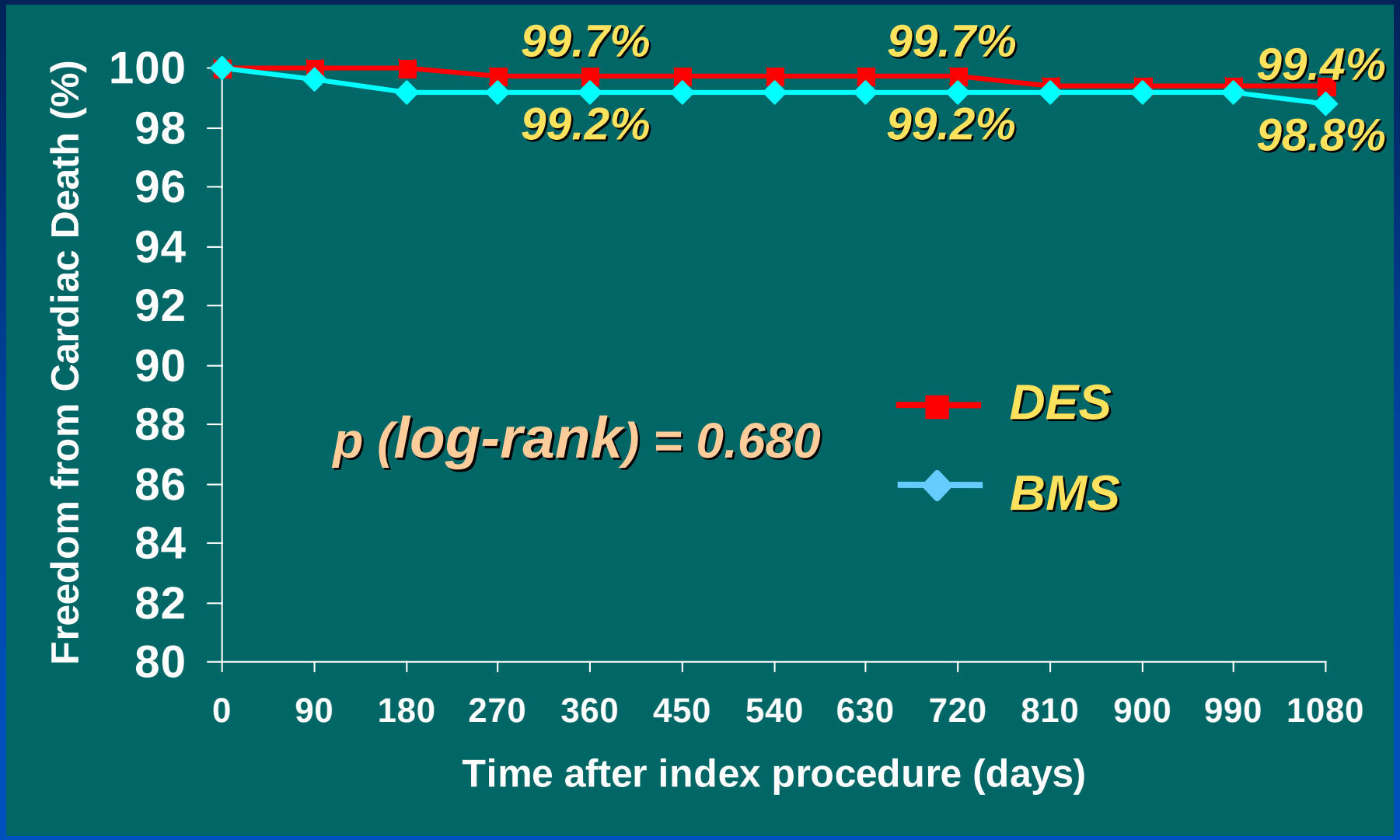
Clinical Outcomes at 3 Year Follow-up

	DES (N=315)	BMS (N=255)	p
• Death	3.2% (10)	3.9% (10)	0.99
Cardiac	1.3% (4)	3.1% (8)	0.37
Non-cardiac	1.9% (6)	0.8% (2)	0.28
• MI	0.6% (2)	0.4% (1)	0.52
Q MI	0.6% (2)	0.4% (1)	0.52
Non-Q MI	0	0	NA
• TLR	7.0% (22)	17.6% (45)	<0.001
TVR	7.6% (24)	18.8% (48)	<0.001
Death/ MI/ TVR	11.4% (36)	20.8% (53)	0.002
• Stent thrombosis	0.6% (2)	1.2% (3)	0.68

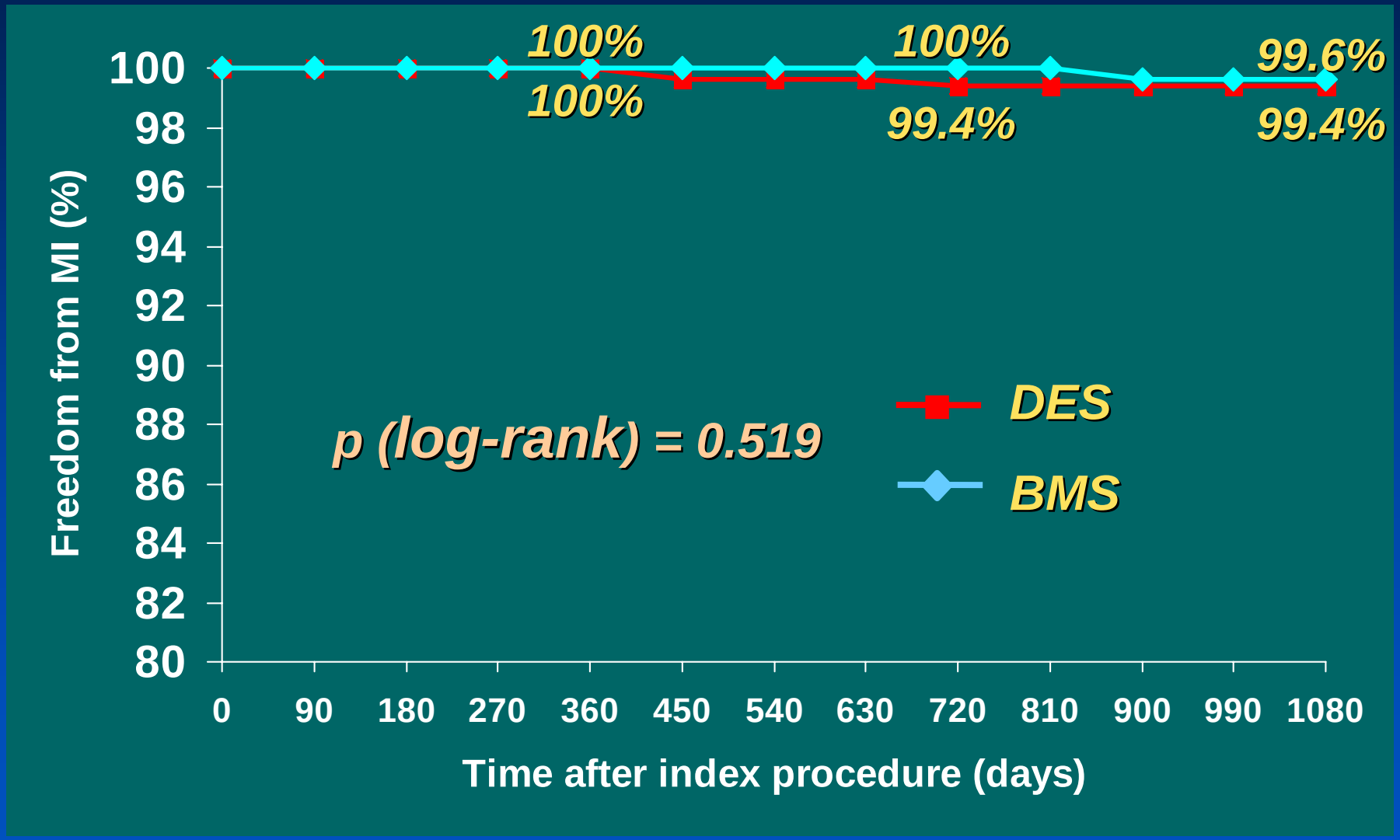
Clinical Outcomes at 3 Year Follow-up



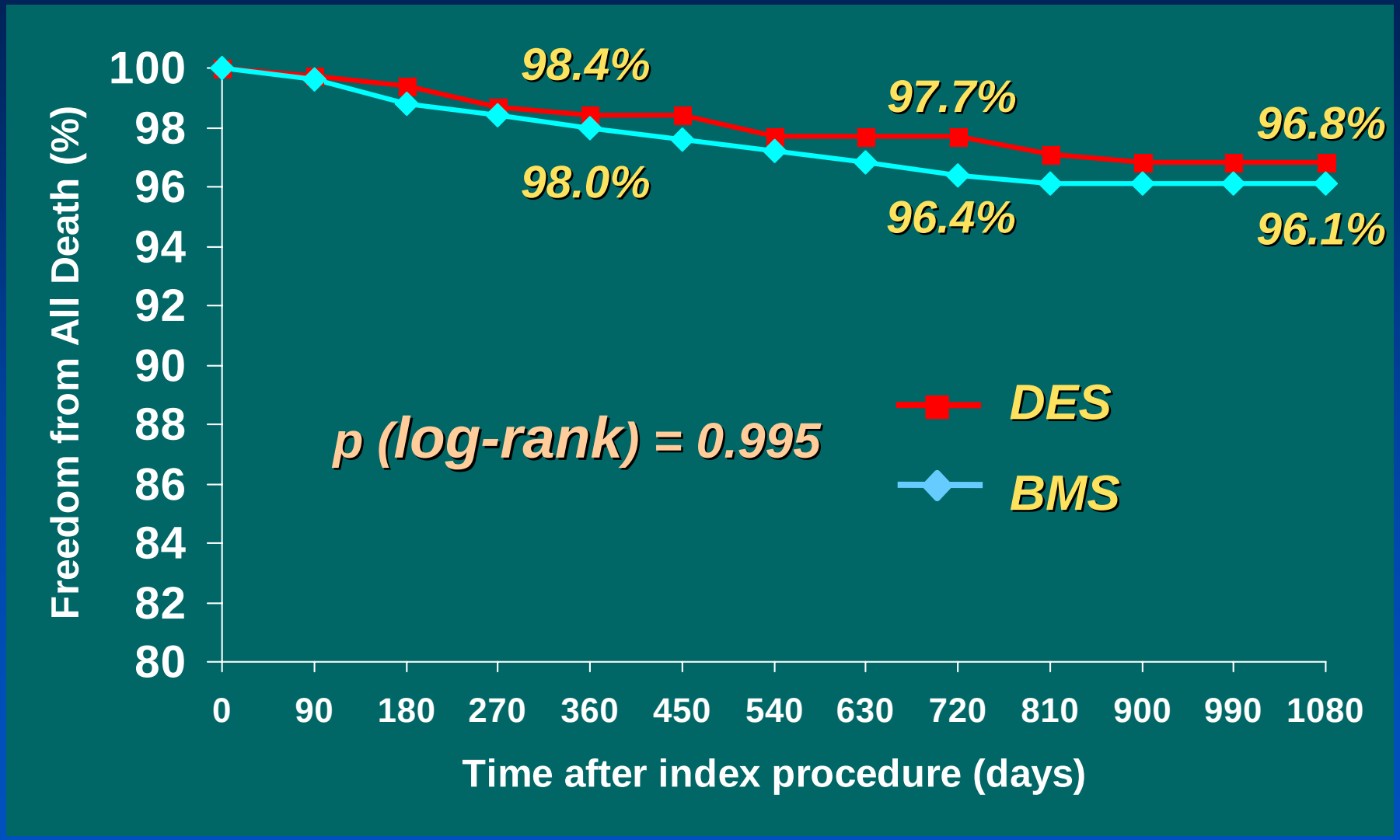
Survival-free from Stent thrombosis at 3 Year Follow-up



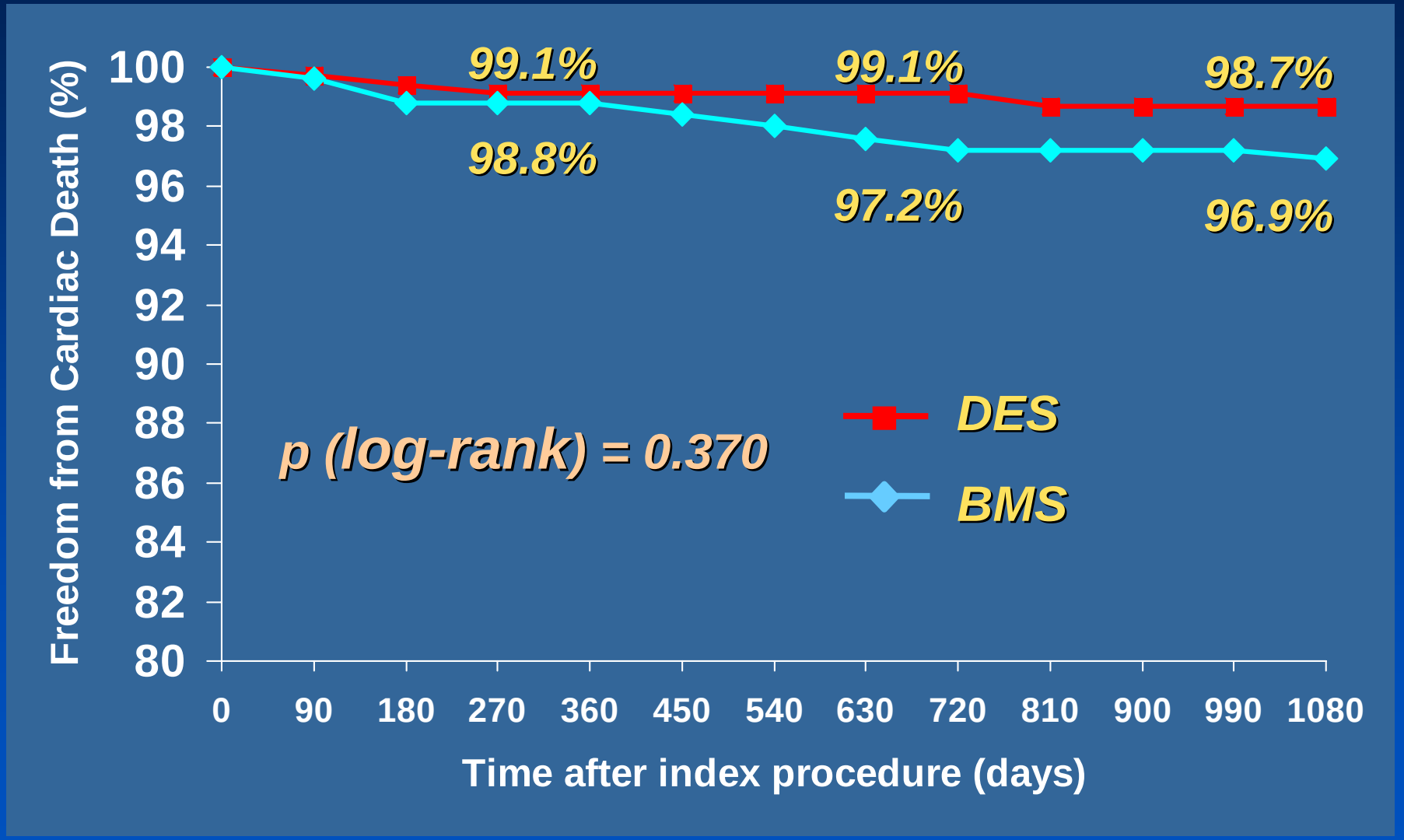
Survival-free from Myocardial Infarction at 3 Year Follow-up



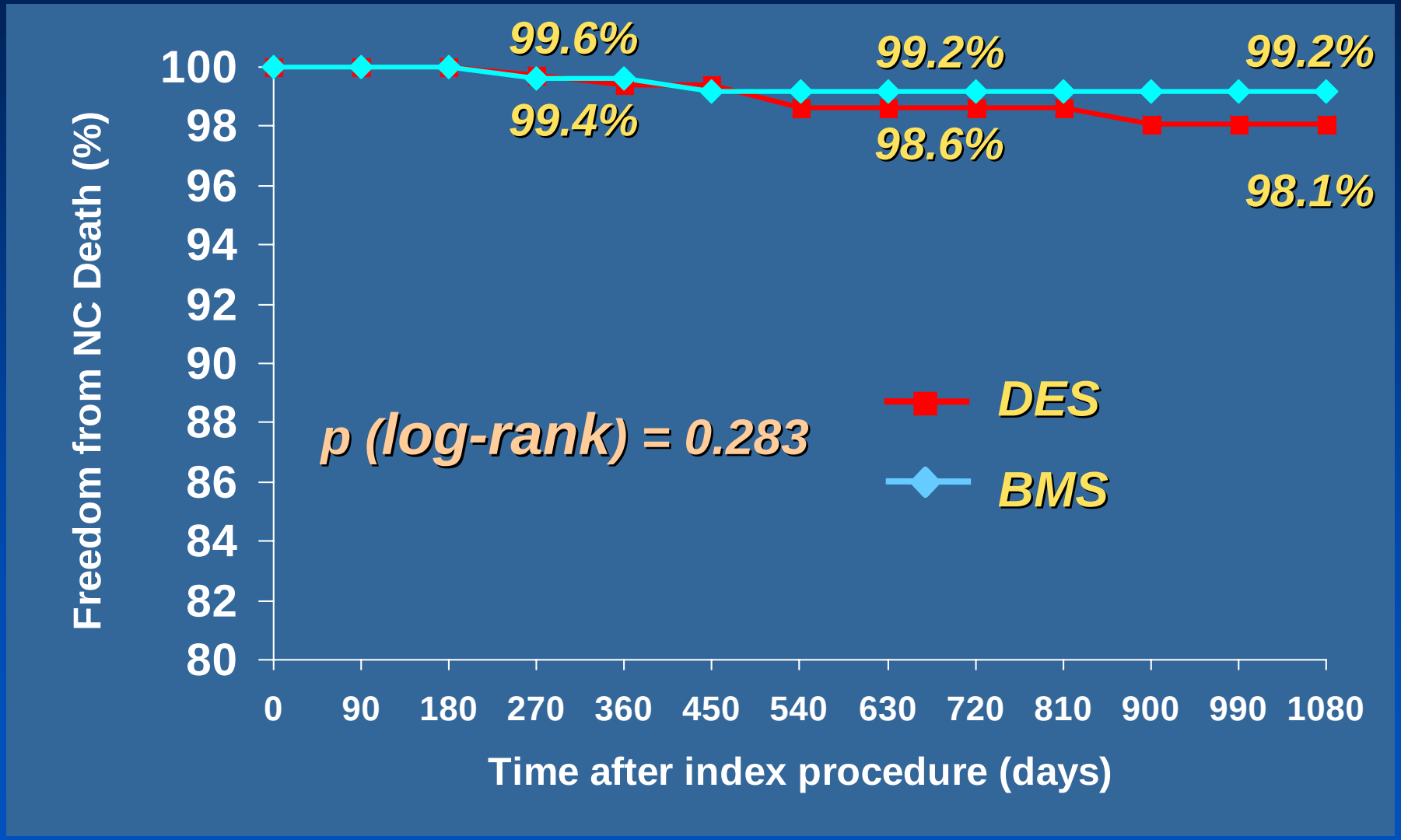
Survival-free from All-Cause Mortality at 3 Year Follow-up



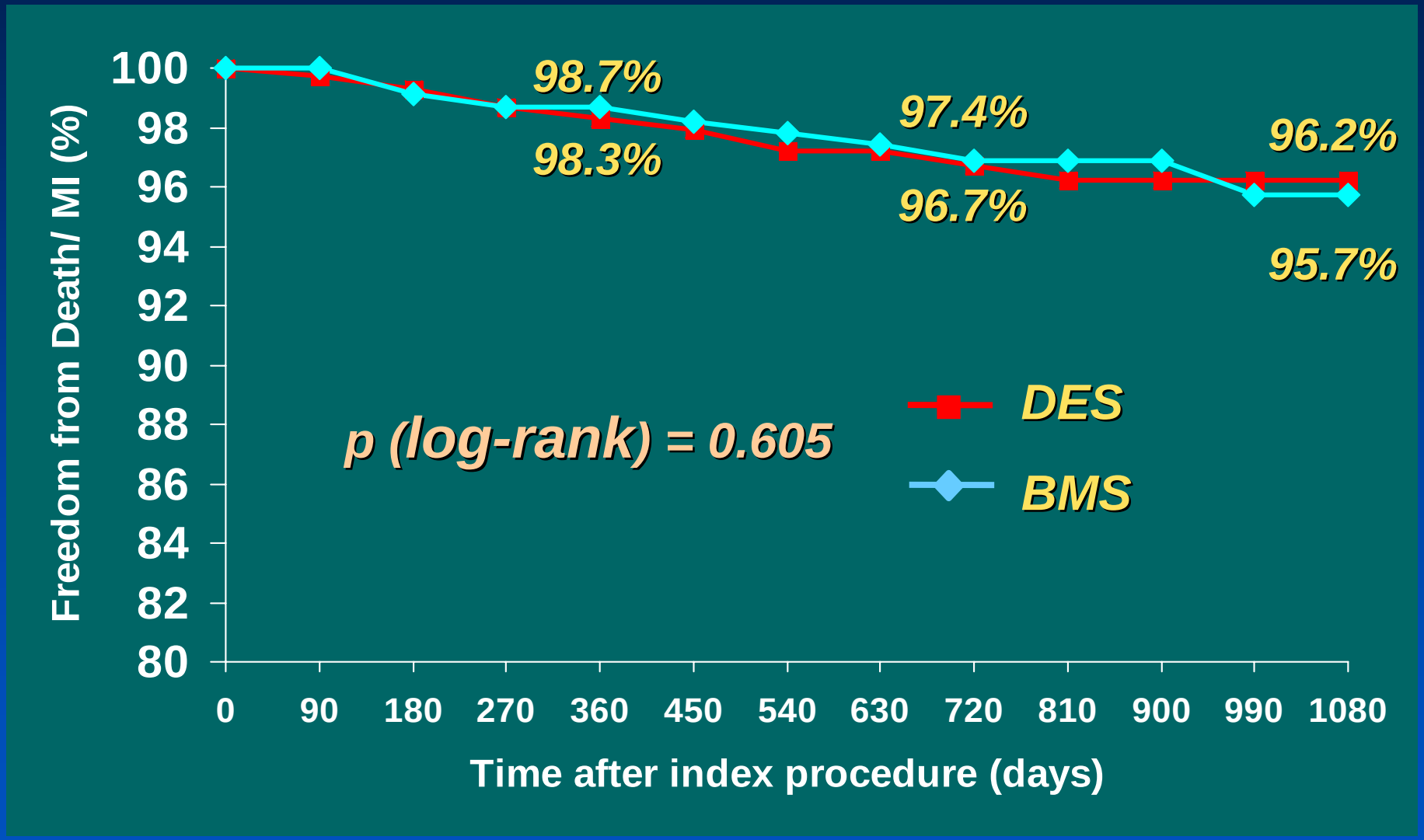
Survival-Free from Cardiac Mortality at 3 Year Follow-up



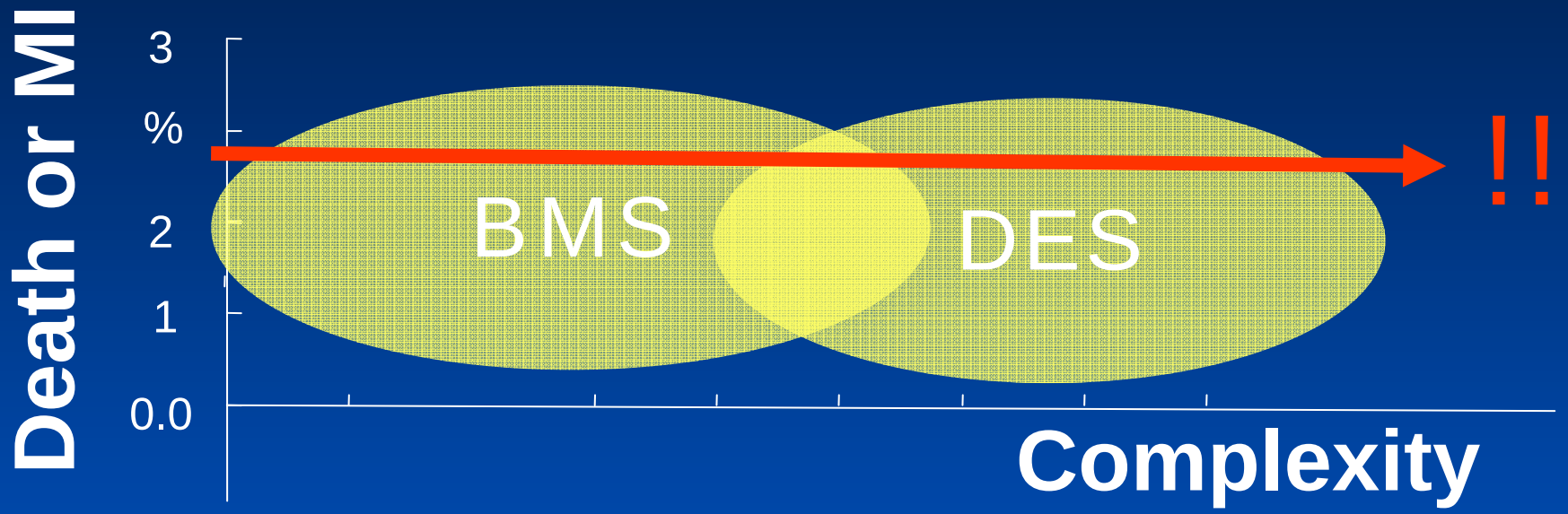
Survival-Free from Non-Cardiac Mortality at 3 Year Follow-up



Survival-free from All Death or MI at 3 Year Follow-up



Death or MI
were comparable in LM stenting with DES



- Although patients treated with DES were more complex lesions and patients subset, there was no differences in the rate of all-cause mortality and MI between the DES and BMS era.

Safety

- In our registry, there was no evidence that DES was associated with high occurrence of death, MI or stent thrombosis compared with BMS.
- Overall incidence of death, MI and stent thrombosis were comparably low in both DES and BMS groups.
- These incidences were not statistically different at each follow-up period of early, late and very late phase.

Unprotected LM stenting

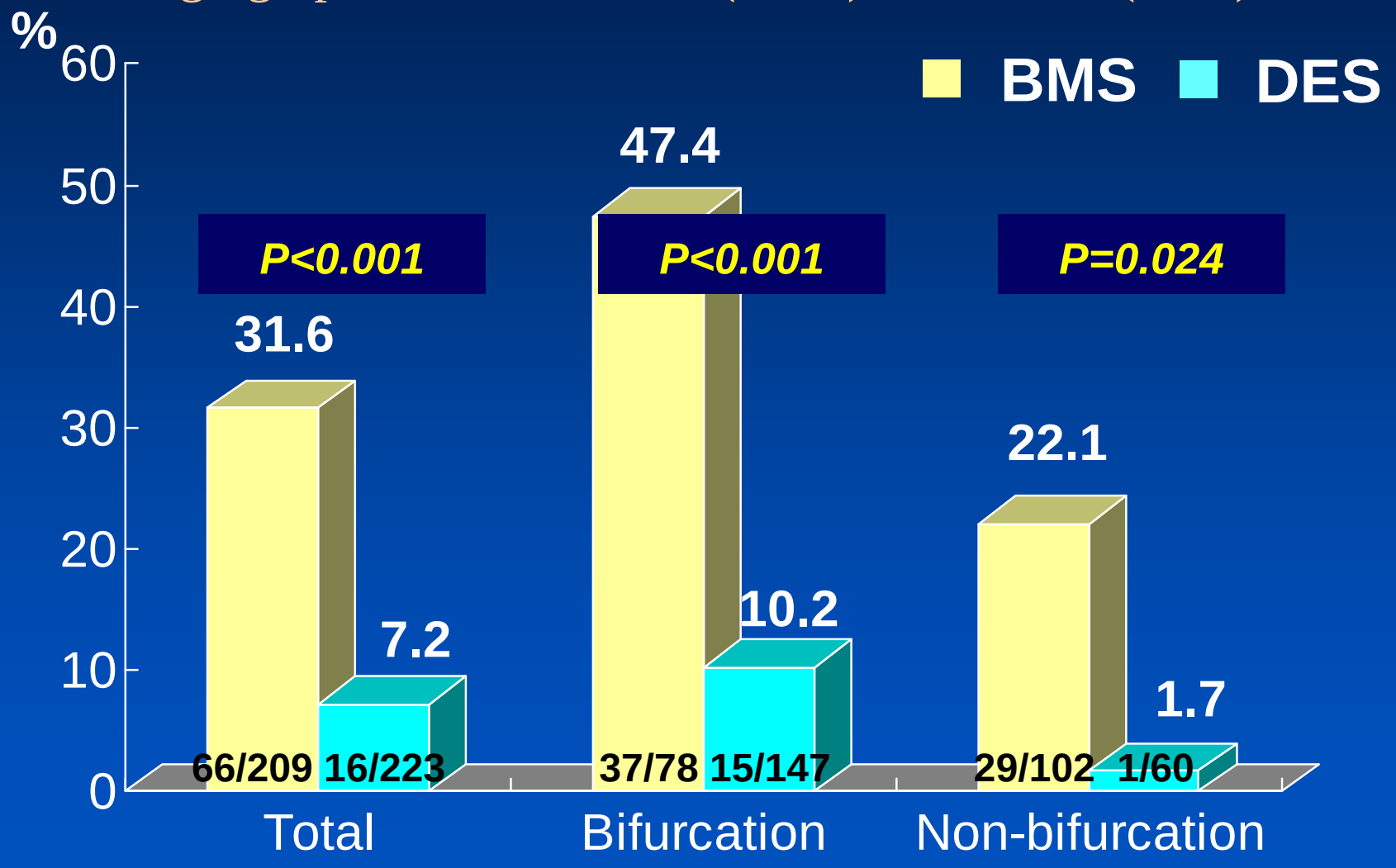
Comparison Data of DES and BMS

Efficacy Issue

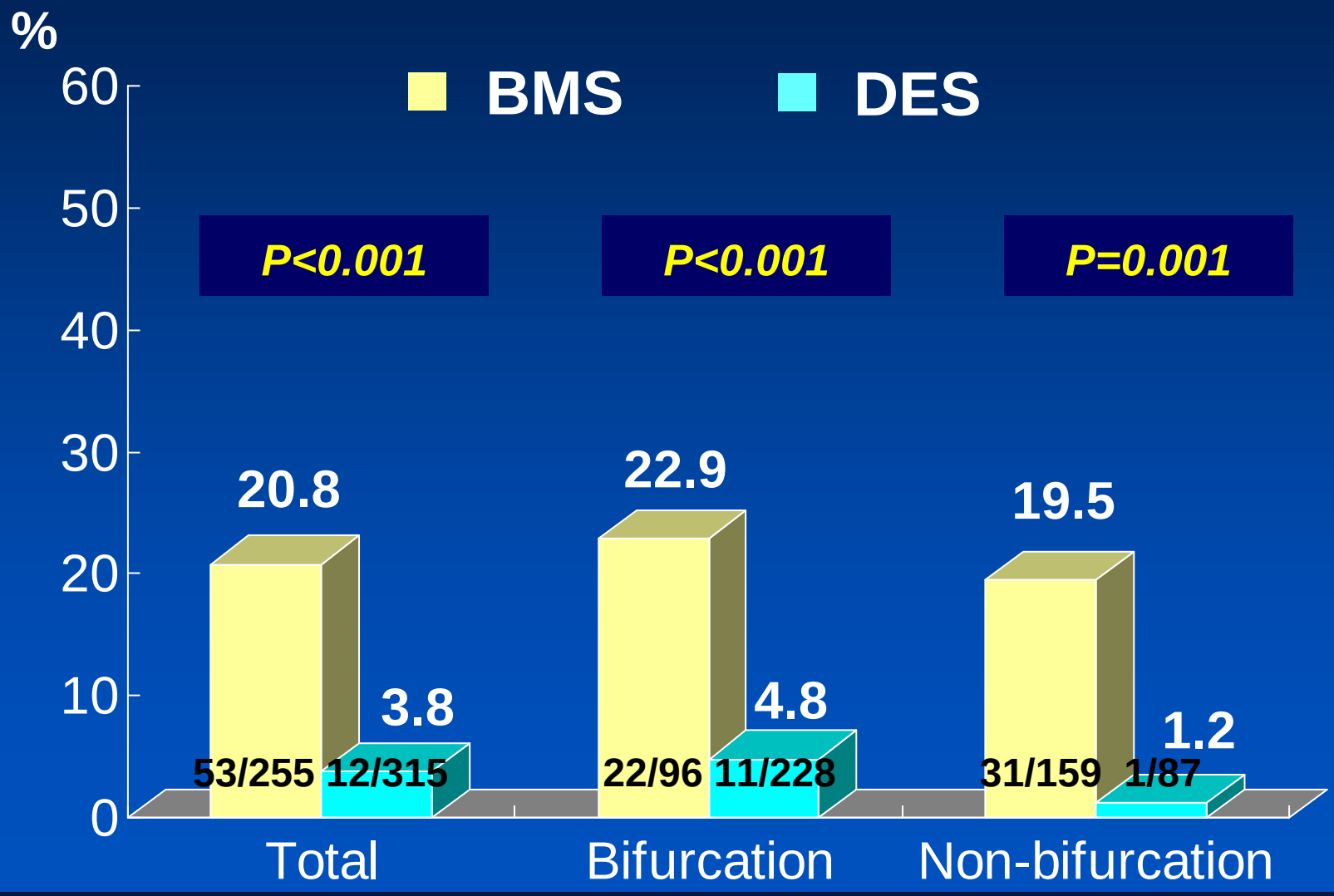
AMC Data 2007

Angiographic Restenosis at 8 Months Follow-up

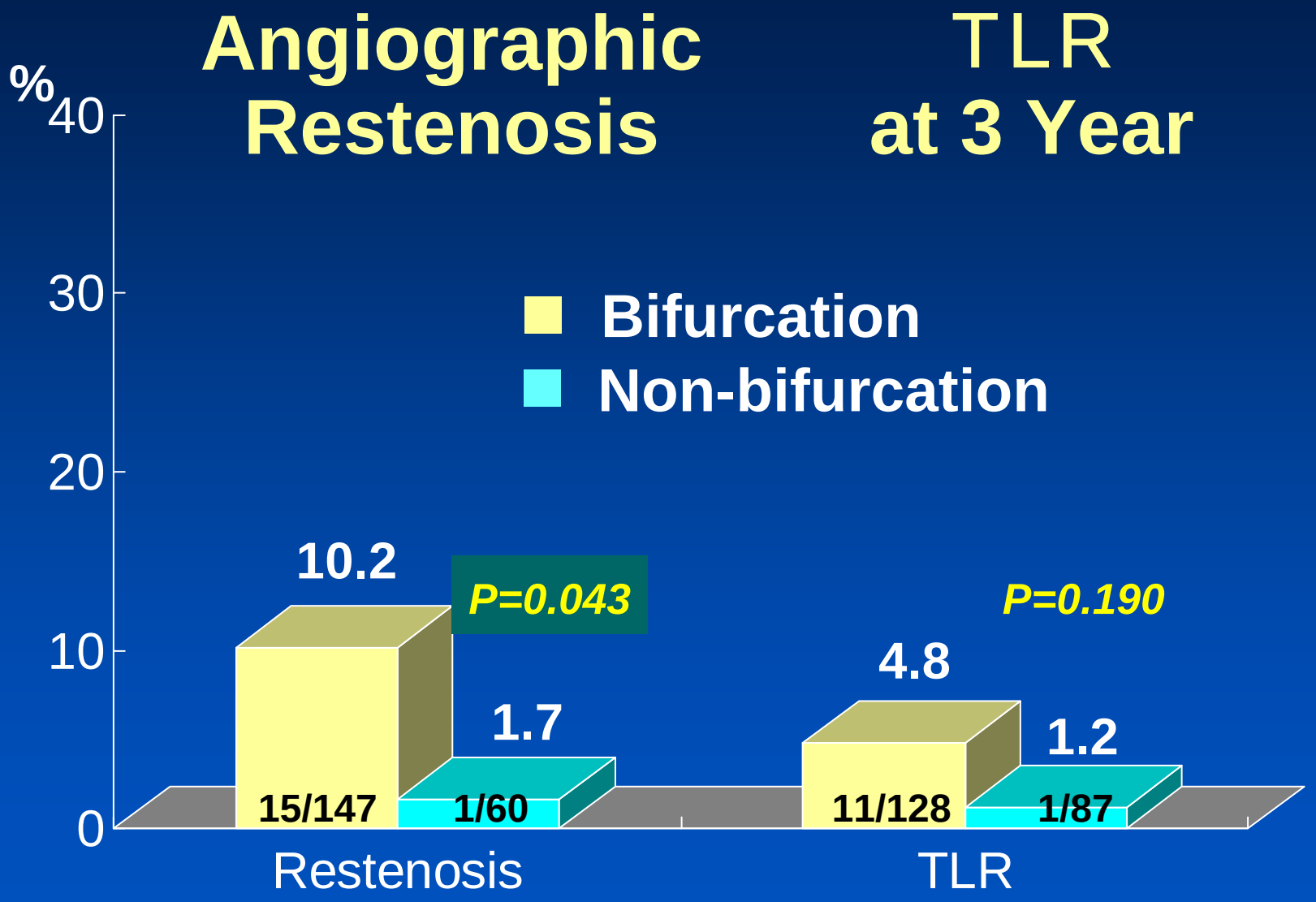
Angiographic F/U in 82.7% (BMS) and 79.5% (DES)



TLR
at 3 Year Follow-up

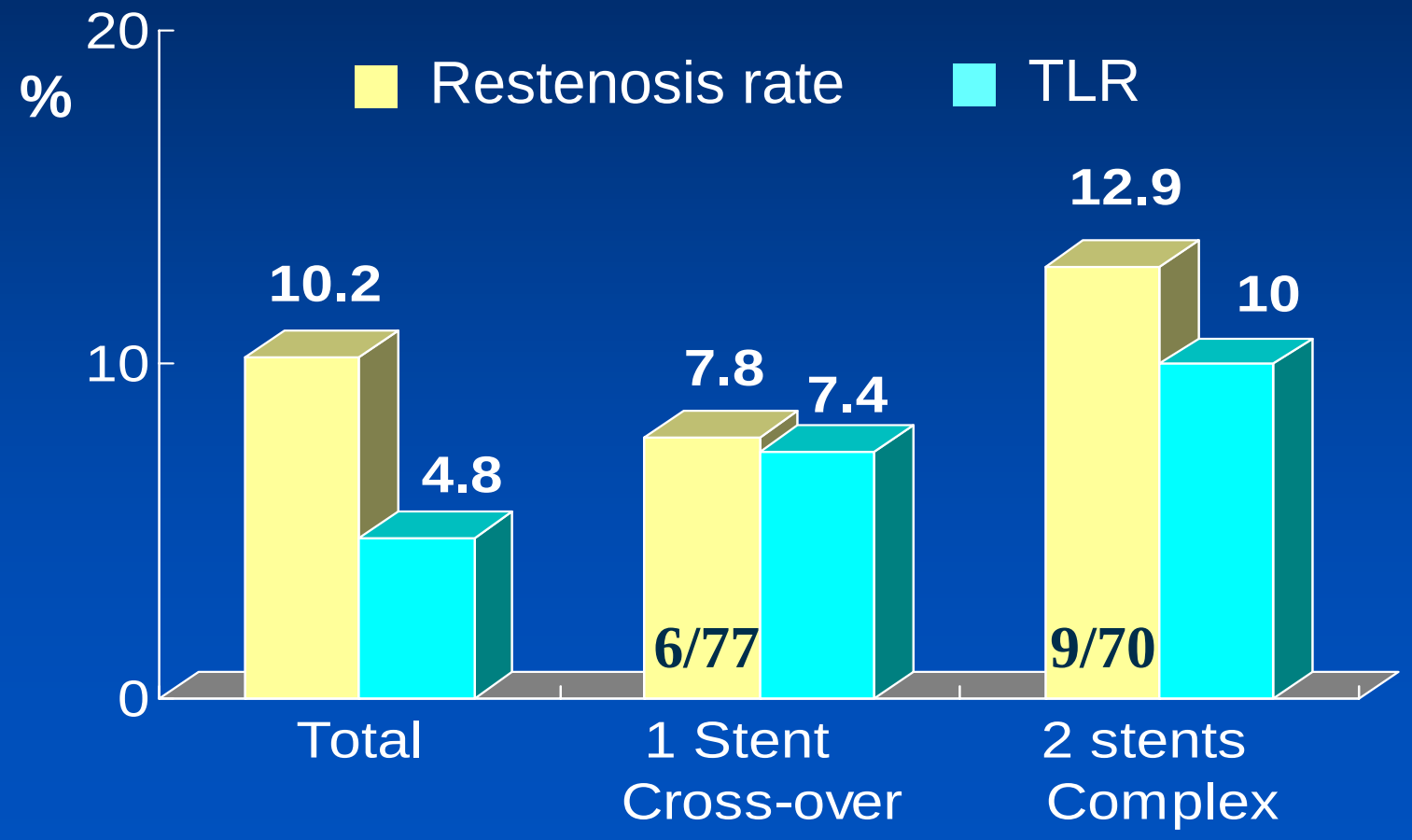


LM PCI with DES



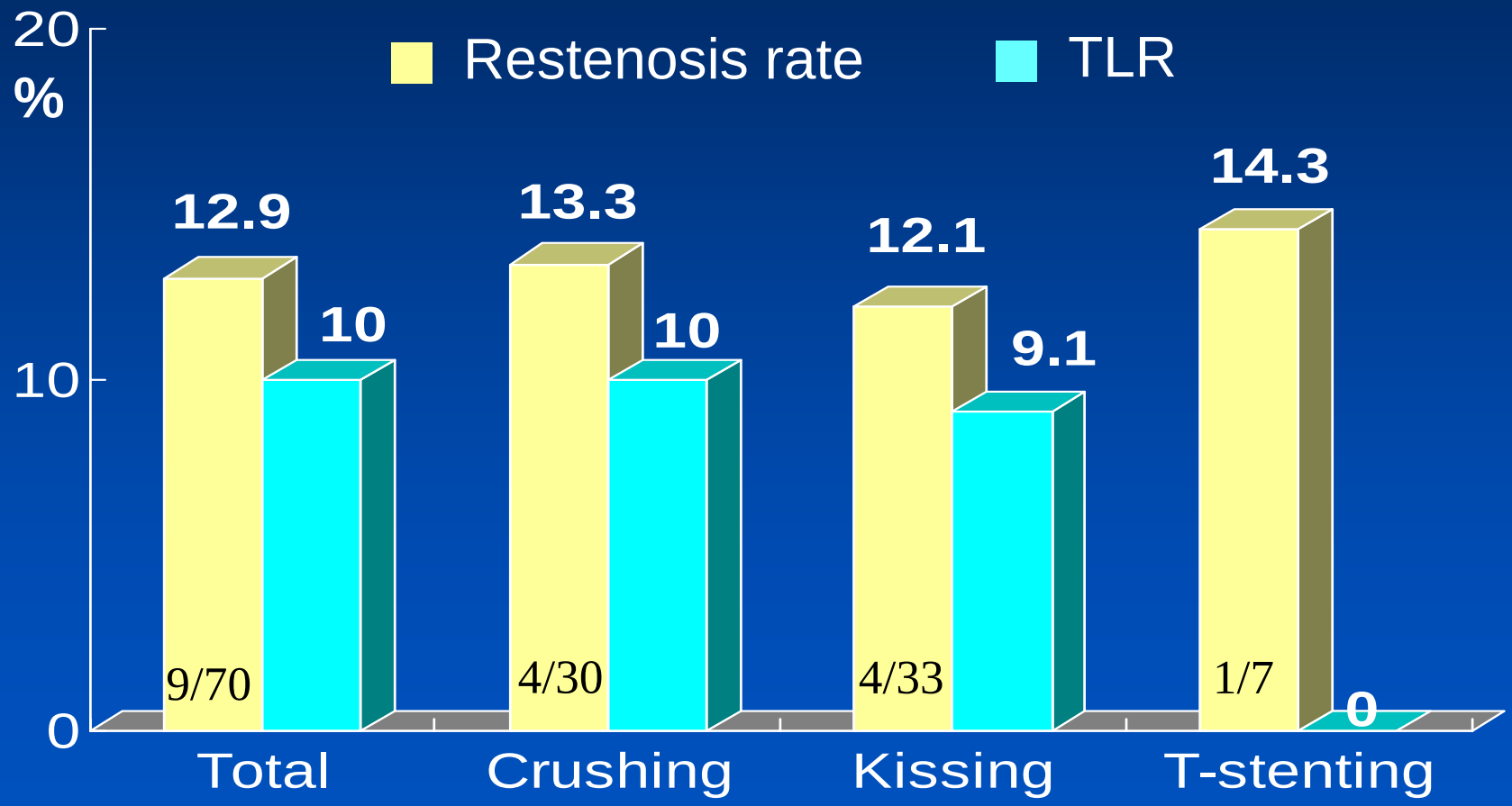
LM PCI with DES

8 Month Restenosis and 3 Year TLR
(Bifurcation PCI 147pts)

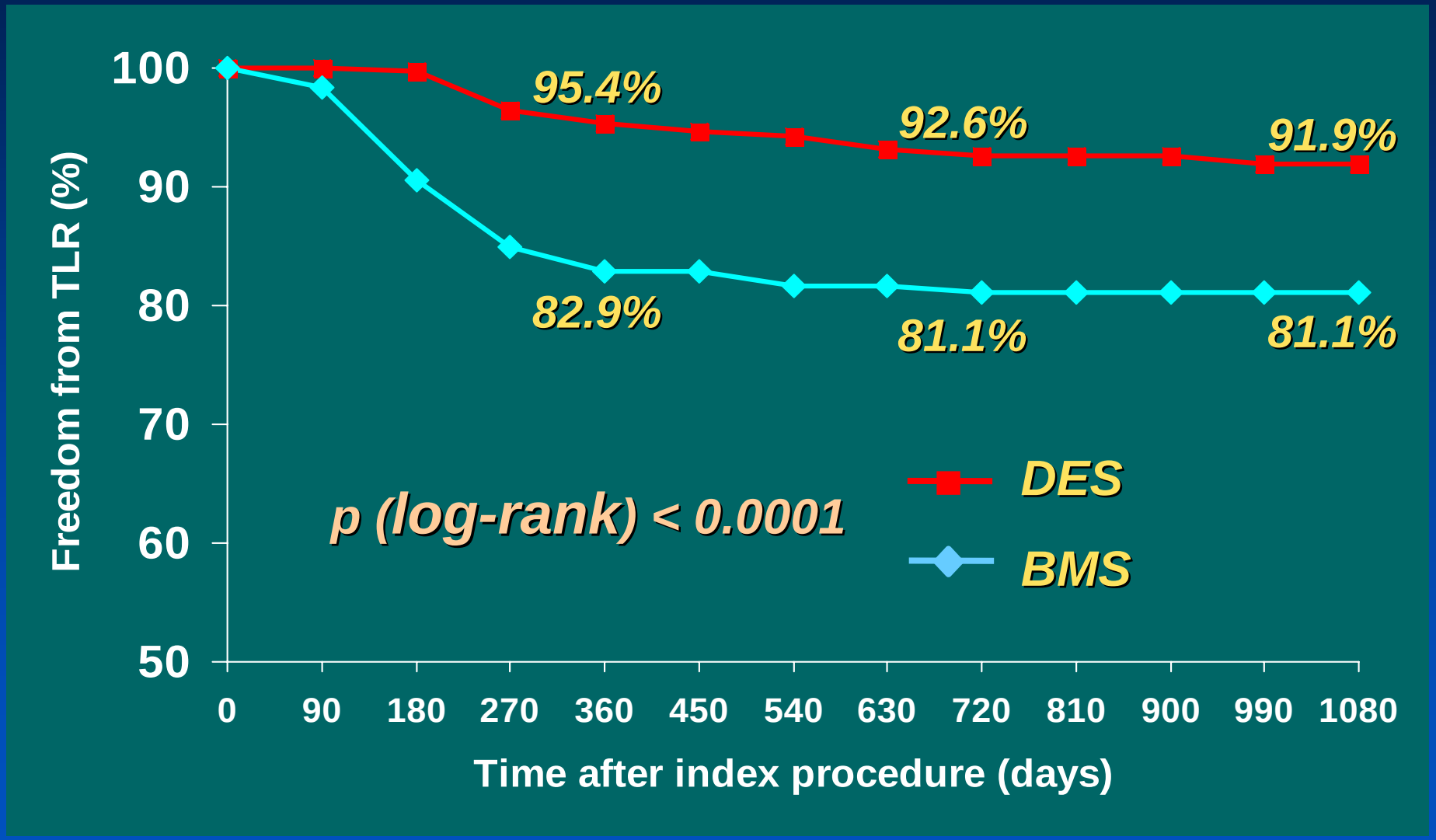


LM Bifurcation PCI with 2 Stents Complex Procedure

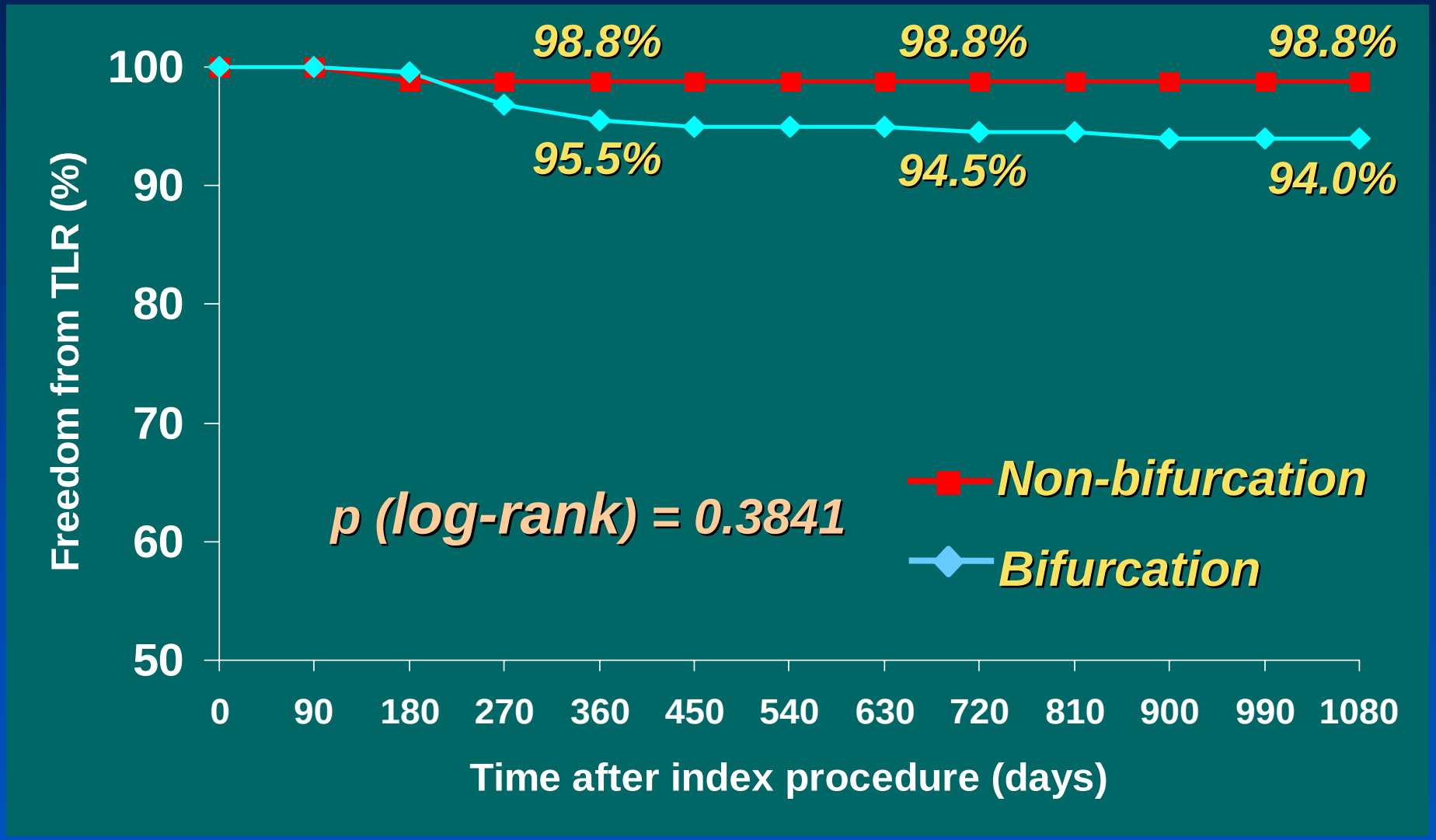
8 Month Restenosis and 3 Year TLR



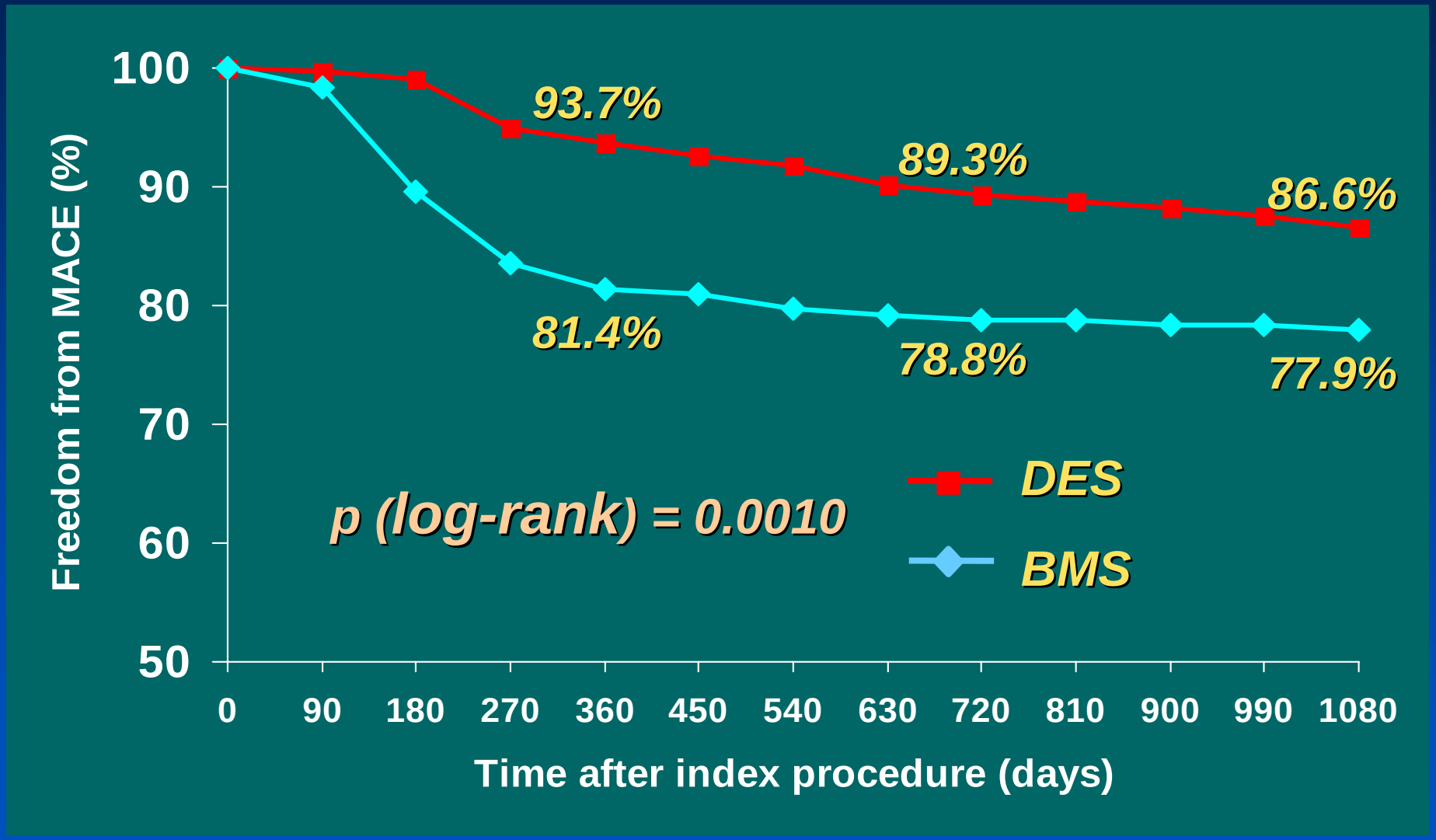
Survival-free from TLR at 3 Year Follow-up



Survival-free from TLR in the DES group at 3 Year Follow-up



Survival-free from Death / MI / TLR at 3 Year Follow-up

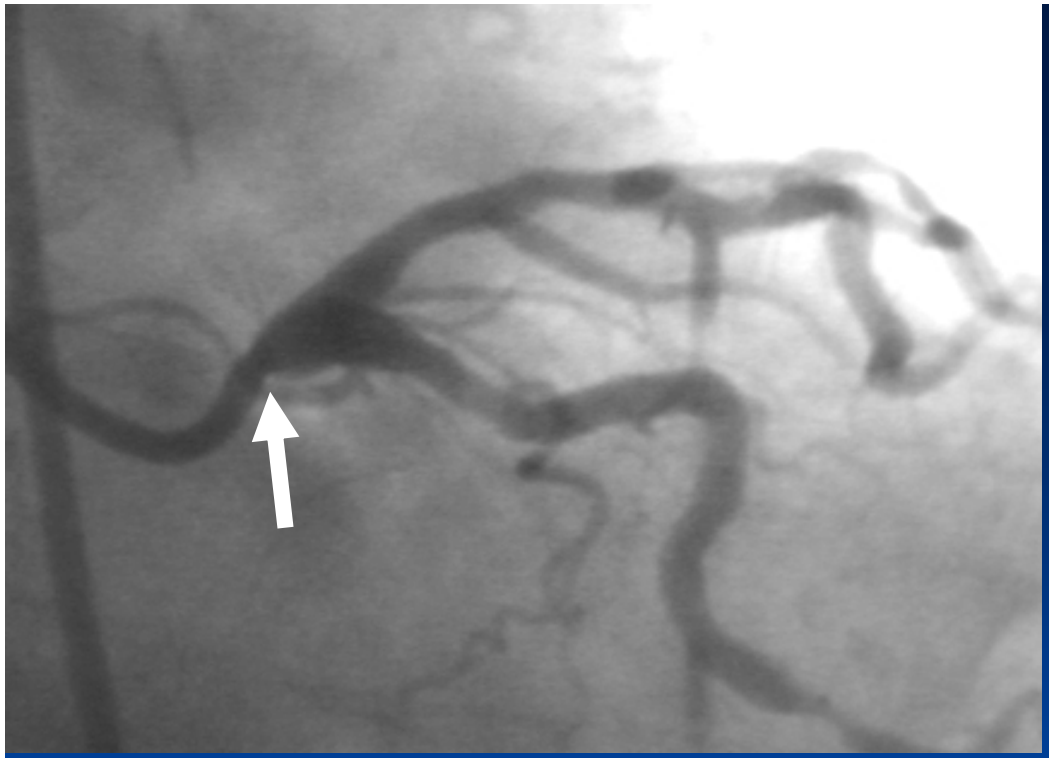


Efficacy

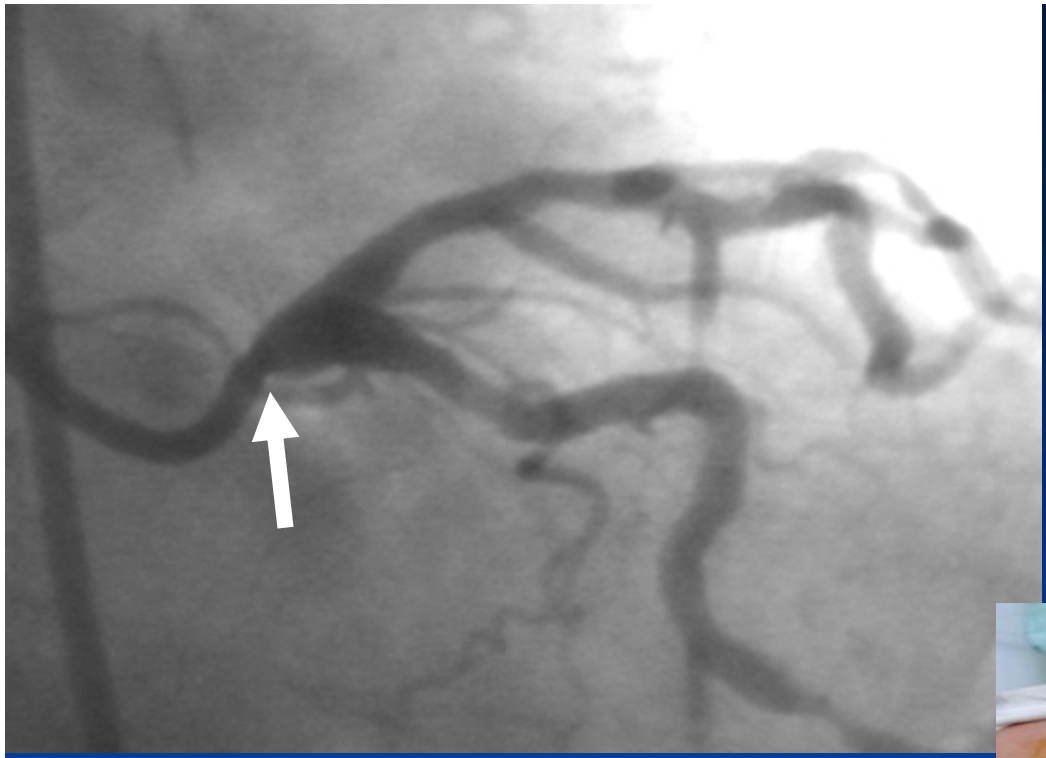
- Efficacy of DES showing low incidence of repeat revascularization remained to 3-years follow-up.
- A significant phenomenon of “late catch-up” (late clinical restenosis, late stent thrombosis) of DES was not observed as compared to BMS.

Conclusion

- Despite a serious concern of long-term safety of DES, our data show that DES appear to be the preferred treatment option in PCI for the selected patients with unprotected LMCA stenosis.

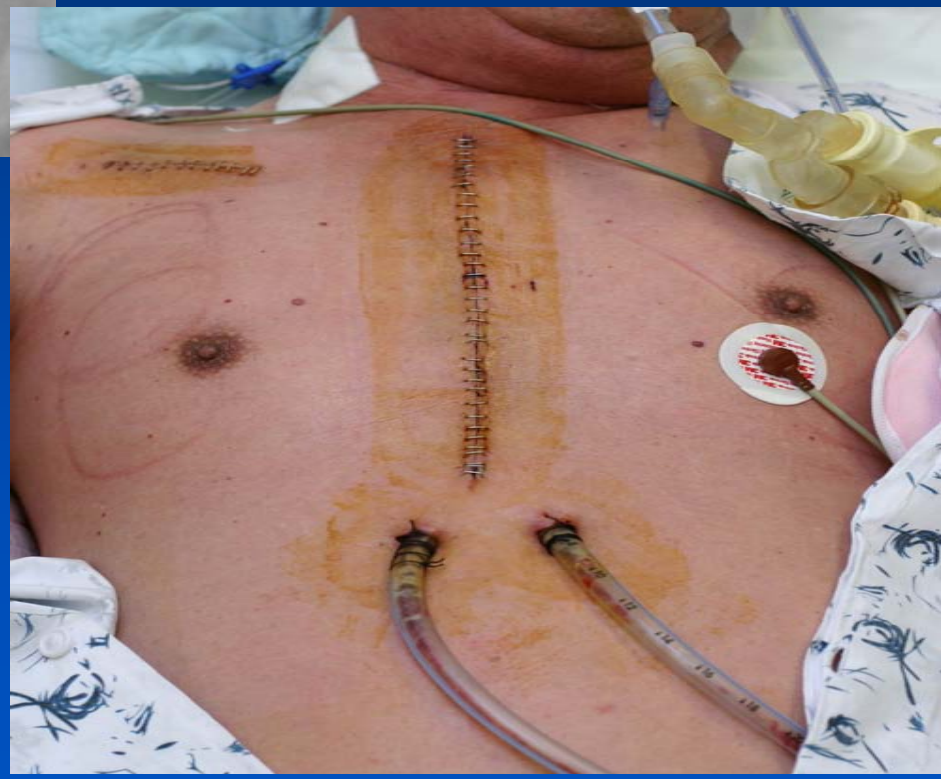


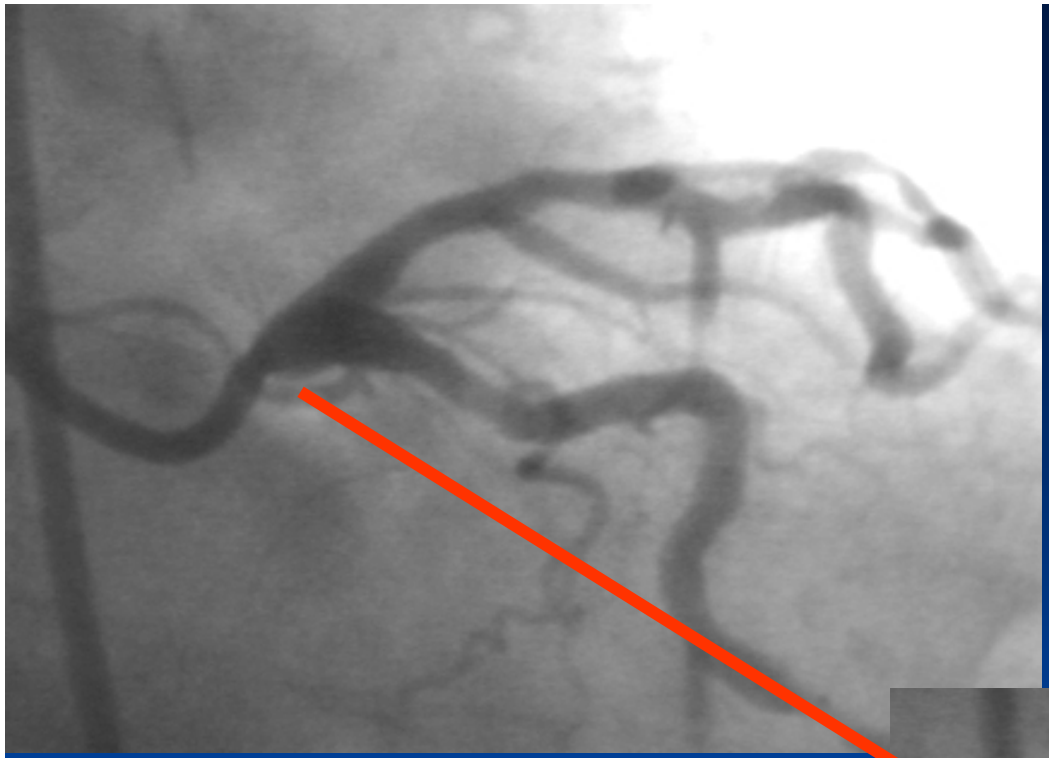
If You Have a
Left Main
Ostial disease…



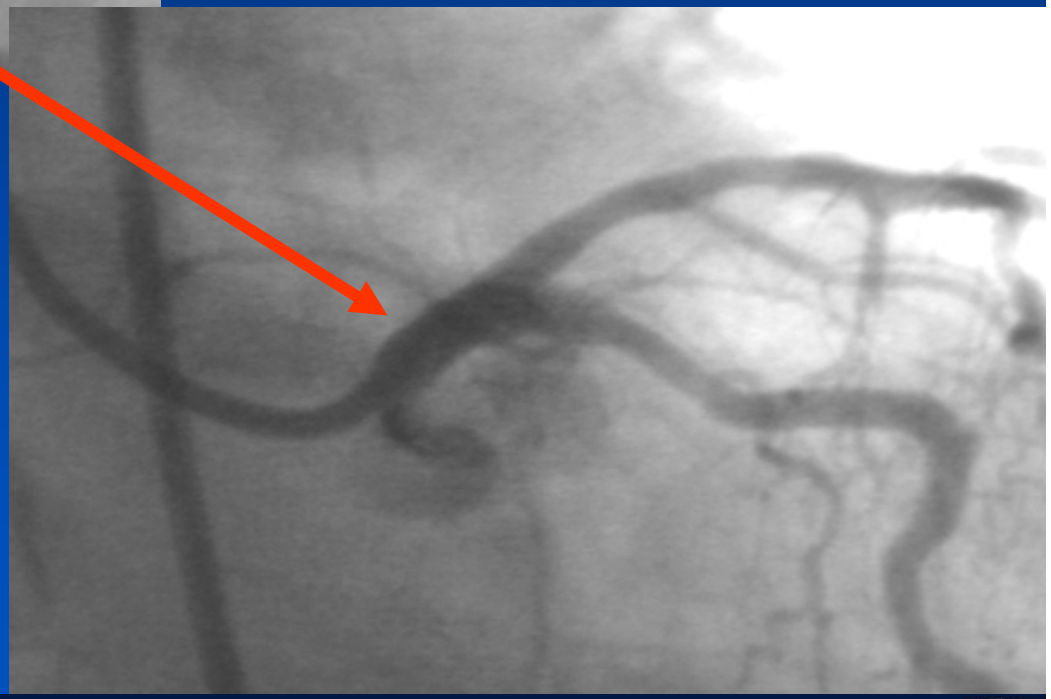
If You Have
Left Main
Ostial disease…

Do you still prefer surgery ?





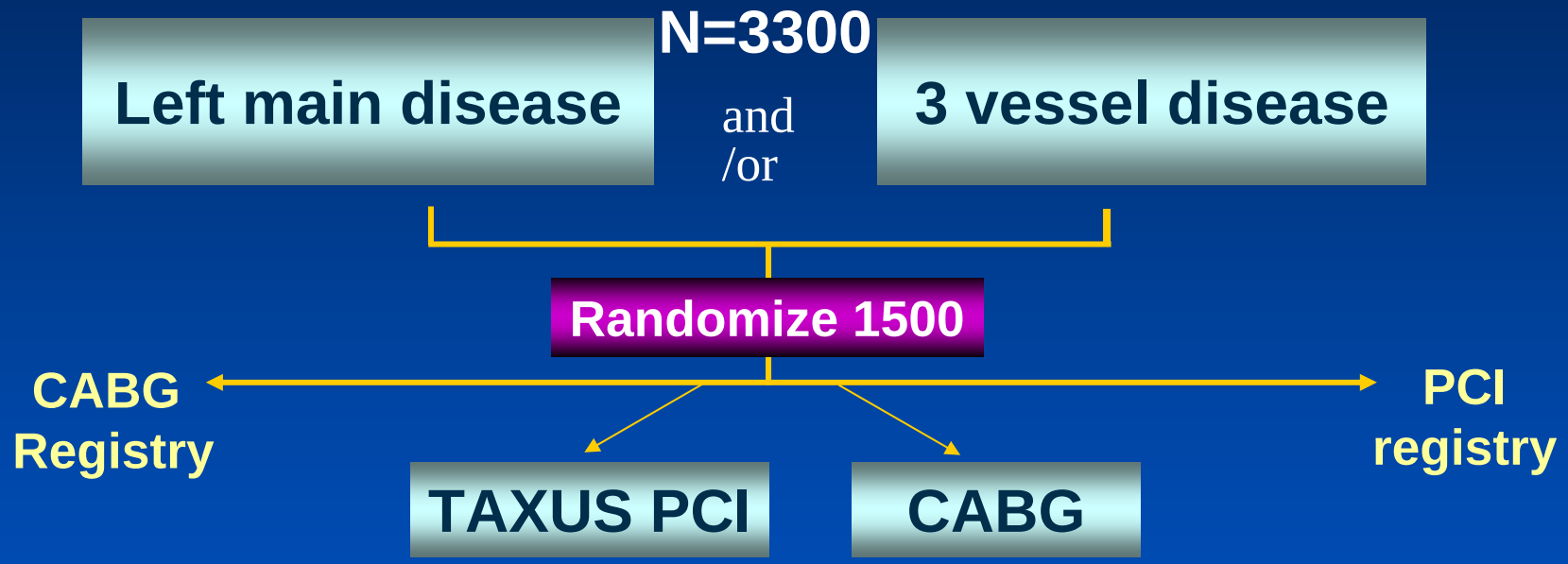
If You Have
Left Main
Ostial disease…



Just Stenting !
It’s only
One-minute work
with 1.6 % TLR

SYNTAX
Randomized Trial

De novo disease acceptable for revascularization



Primary endpiont – 1 year MACCE
All cause death, MI, cerebrovascular
Event, repeat revascularization

Led by Patrick Serruys
And Frederick Mohr

PRE-COMBAT

*PRE*miere of Randomized *COM*parison of *B*ypass Surgery versus *A*ngioplas*T*y using Sirolimus-Eluting Stent in Patients with Left Main Coronary Artery Disease

Left main disease with or without multivessel disease (n=1,600)

Randomization 600 (1:1)

PCI with Cypher (n=300)

CABG (n=300)

Non-randomization

Registry Screening log failure

Primary Endpoint: 1-year major cardiac and cerebrovascular event (MACCE) - death, MI, stroke and TVR

PI: Seung-Jung Park
8 major centers in Korea