DES for Everybody ?
(First Generation DES).
The Washington Hospital Center Experience

A. Pichard,

L. Satler, K. Kent, R. Waksman,

W. Suddath, N. Bernardo, H. Sievert,

S. Epstein, N. Weissman,

A. Fuisz, G. Weigold, J. Lindsay, L Miller.

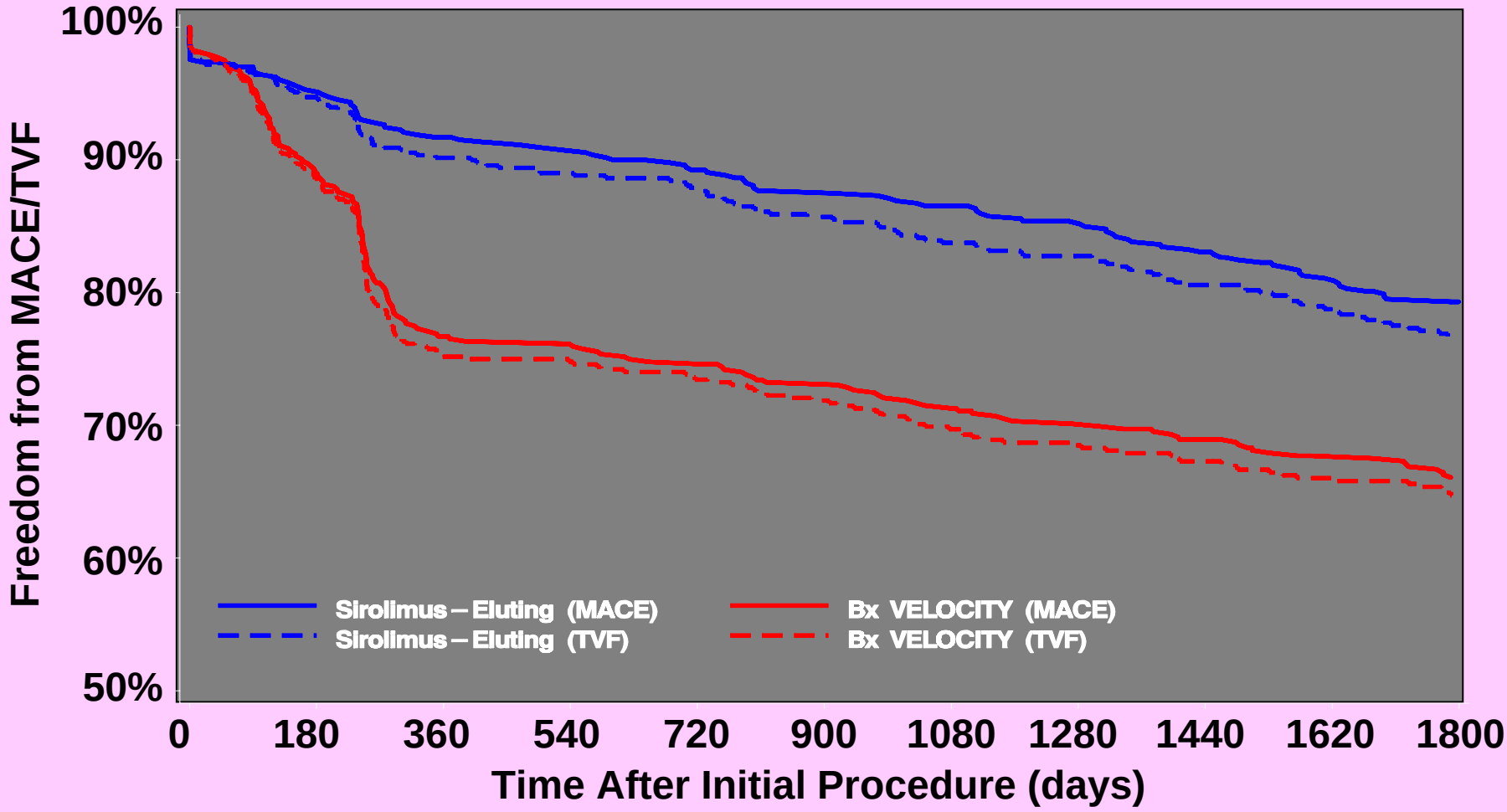
Washington Hospital Center (WHC) Cardiac Cath Labs 2006

- 12,300 diagnostic catheterizations
- 5,600 coronary angioplasties
- 2,500 peripheral cases
- 1,500 cardiac MR
- 1200 Cardiac CT
- 3,600 IVUS

The Promise of DES

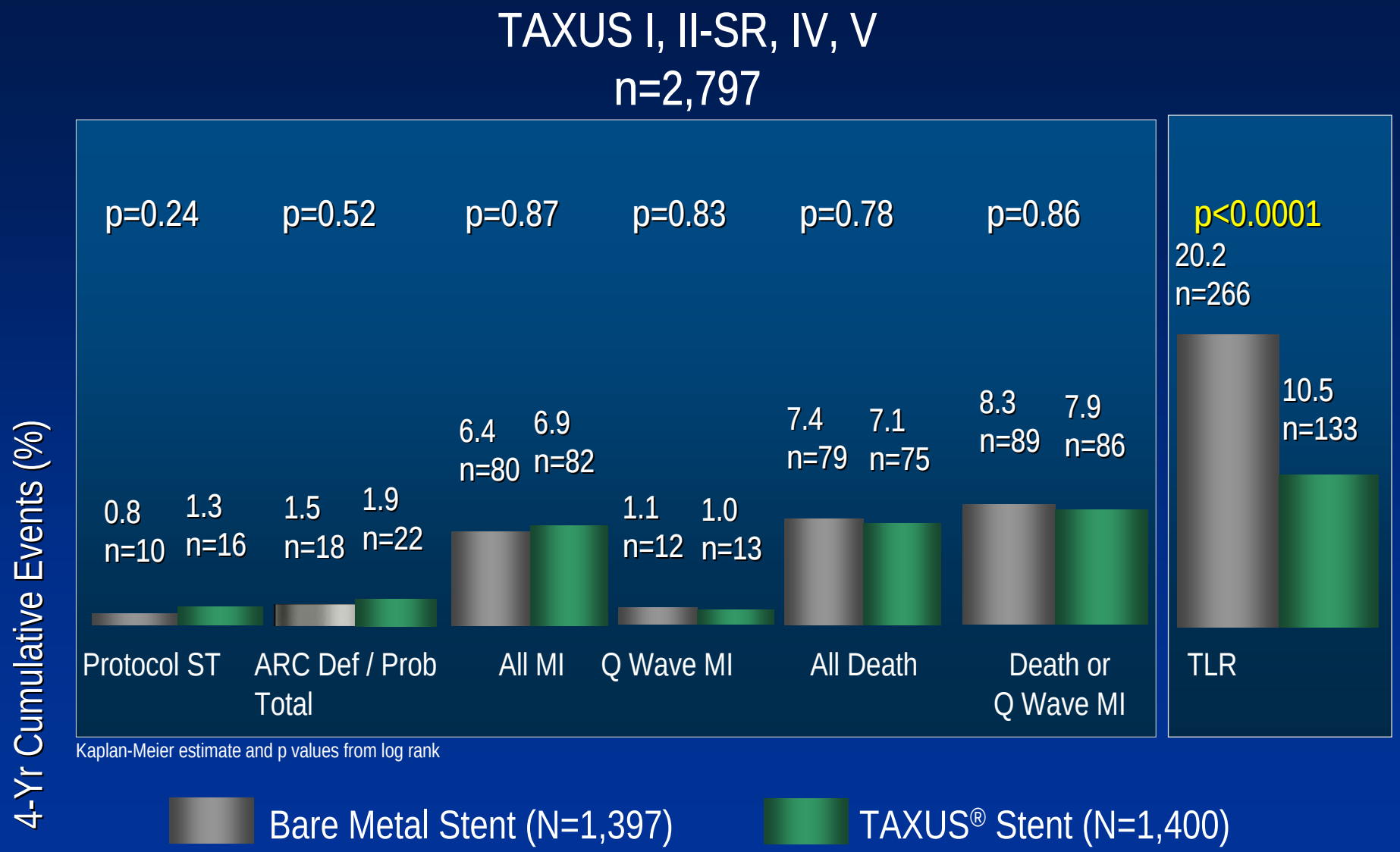
- **Minimal or no Restenosis**
  - **All lesions benefit from DES:**
    - **Simple and complex**
    - **Single and multiple**
    - **Acute and chronic lesions**
    - **Native vessels and grafts**
    - **Chronic Total Occlusions.**
- **No side effects**

SIRIUS 5 year ("On Label"). Survival Free From MACE / TVF



Leon, M., et al., ACC 2007 Poster Presentation March 26, 2007

TAXUS® Stent 4-Year Meta-Analysis ("On Label")



TAXUS Stent 4-year meta-analysis includes TAXUS I (5 yr), II-SR cohort I (4 yr), IV (4 yr), V (2 yr) (N=2,797). The safety and effectiveness of the TAXUS® Stent have not been established in patients for longer than 12 months.

Off Label use of DES

Washington Hospital Center. 12 months Outcome

Presented at FDA Dec 06 and ACC 07

3138 pts with DES, 4476 lesions

On Label n=2228 lesions

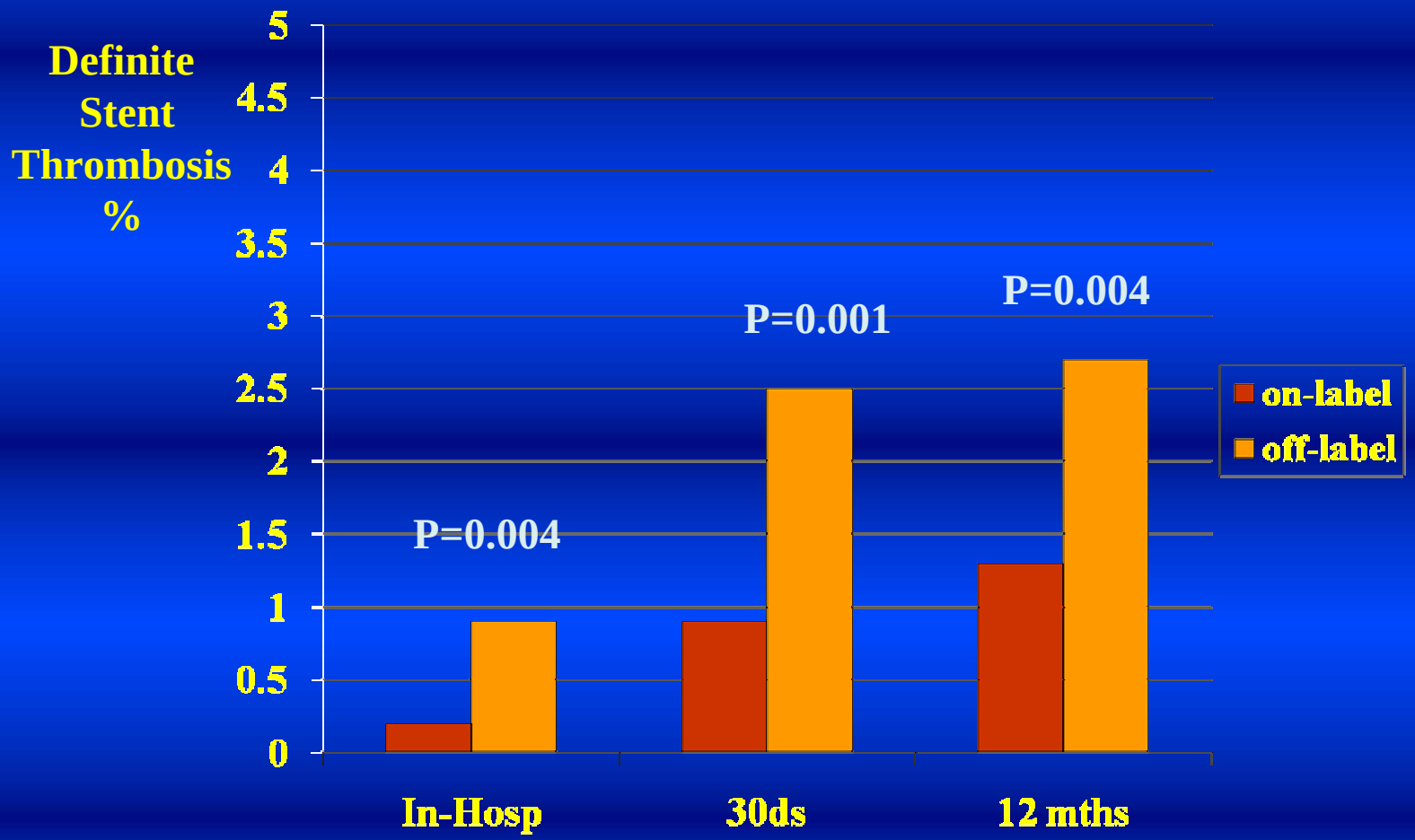
Off Label n=2248 lesions

Off label use:: AMI 22%, SVG 10%, ISRS 17%, CTO 5%, LMCA 3.6%, MVD and complex lesions 42%.

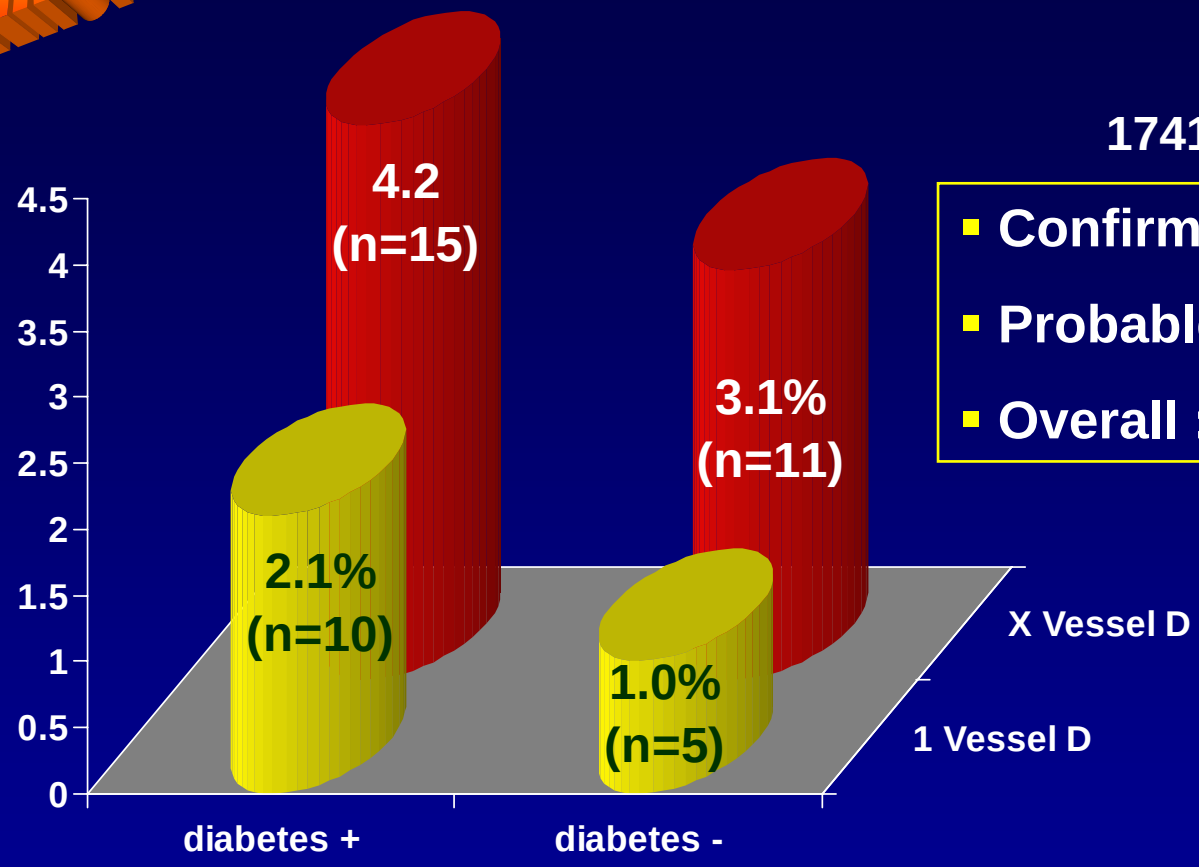
Off Label use of DES. Stent Thrombosis.

Washington Hospital Center. 12 months Outcome

Presented at FDA Dec 06



Stent thrombosis



1741 pts with Cypher

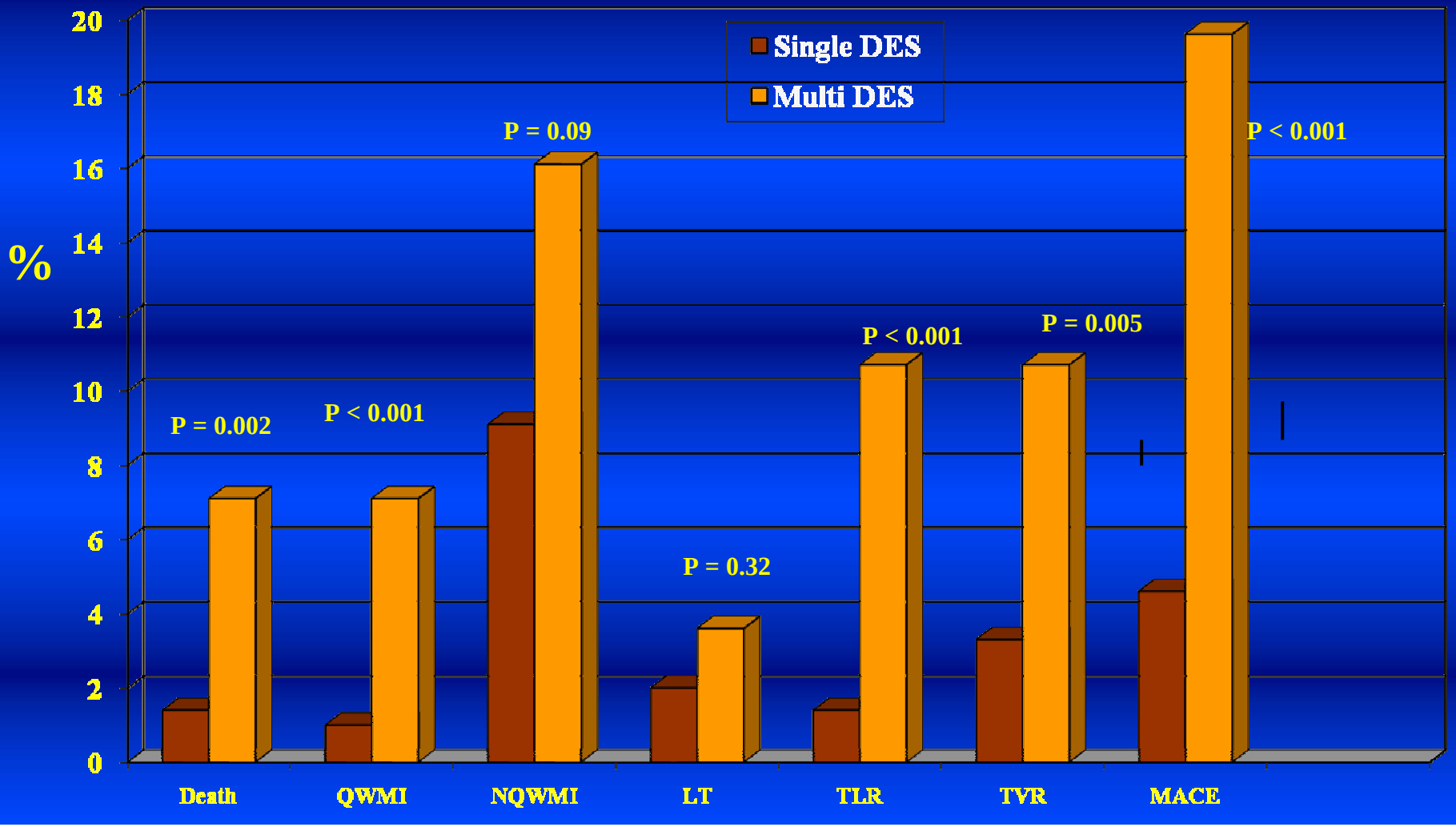
- Confirmed : 1.6% (27 pts)
- Probable : 0.8% (14 pts)
- Overall : 2.4% (41 pts)

db+ 3% vs. db- 1.7%	p=.07
Ins+ DM 3.7% vs. db- 1.7%	p=.001
XVD 3.7% vs. 1VD 1.5%	p<004

3 versus 1 Sirolimus Eluting Stents.

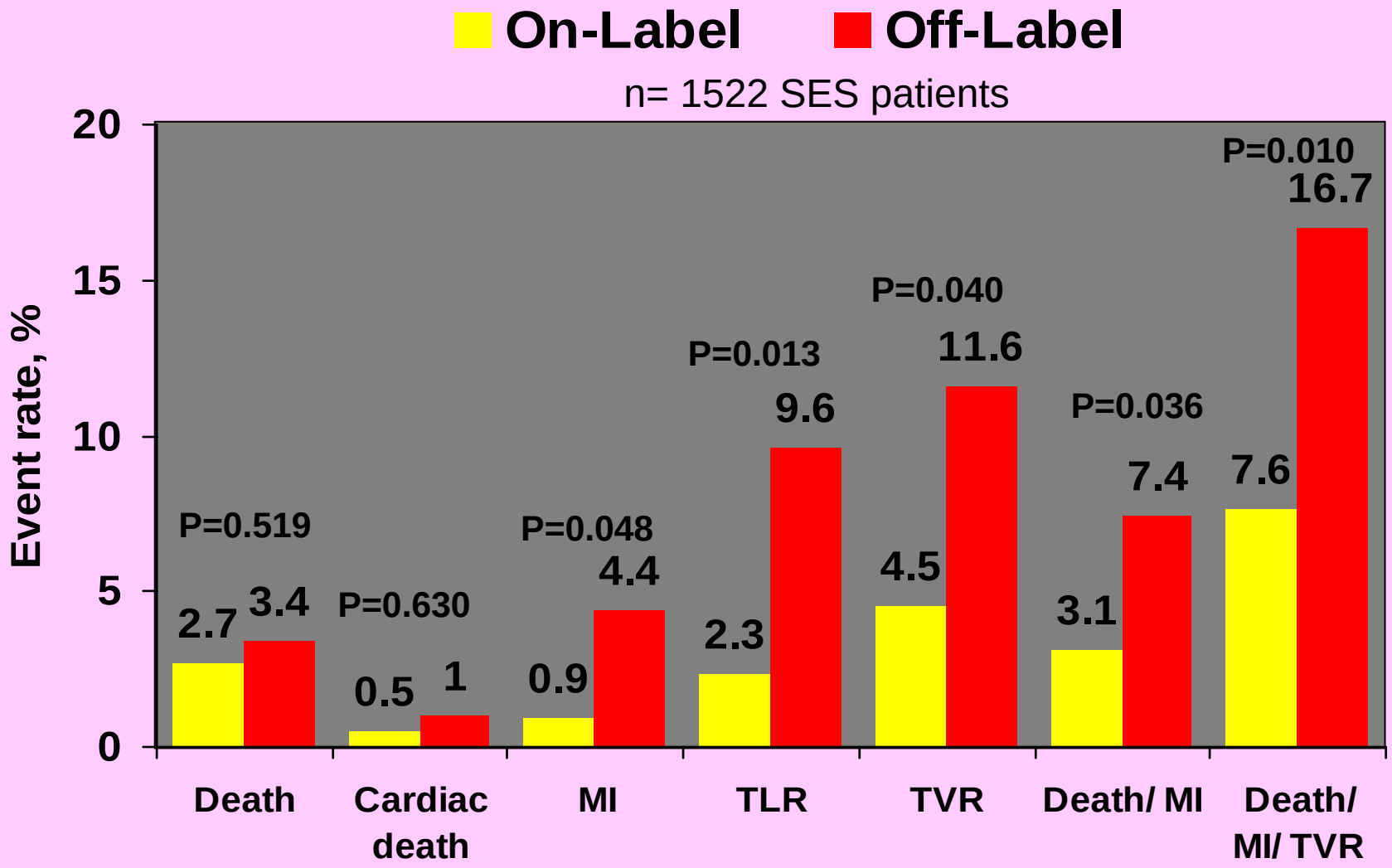
6-Month Clinical Outcomes.

WHC: Chu et al. CCI 2006, 68:62-66



MATRIX Registry. 2 year outcome

Dangas et al., ACC 2007



Unexpected Scientific Publications

- Basket Late
- European Congress Sept 06
- TCT 06
- FDA Panel Dec 06

Internal Medicine World Report January 2007

FDA Panel Discourages Off-Label Use of Drug-Eluting Stents

Continuing Antiplatelet Therapy Emphasized

BY WAYNE KUZNAR

GAITHERSBURG, Md—After 2 days of testimony, a uncertainty hung over advisory panel hearing to examine the safety eluting stents (DESs). I DESs were deemed to additional risk to pati used for simple sten called on-label use, with bare-metal stents

But when used off-l as for bifurcation lesio tiple stenoses, the ben ratio of DESs was not a at least 60% of DESs are used off-label, and some estimate this

Continued on page 10

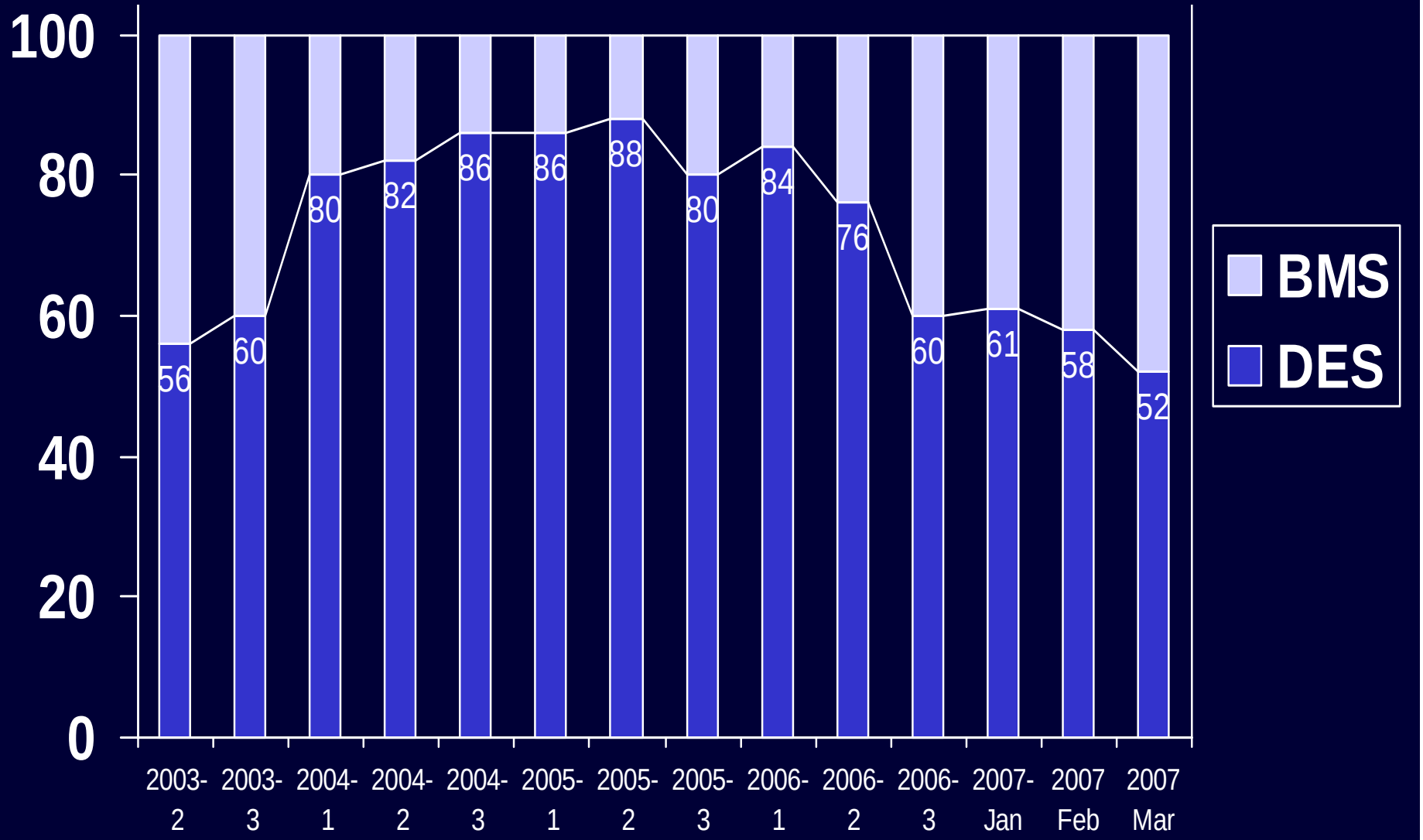
When DES are used Off-label, they are associated with increased risk of stent thrombosis, myocardial infarction and death, compared with on-label use.

However:

It is in complex lesions (off label) that DES should have the most benefit.

DES and BMS at WHC

2003-2007

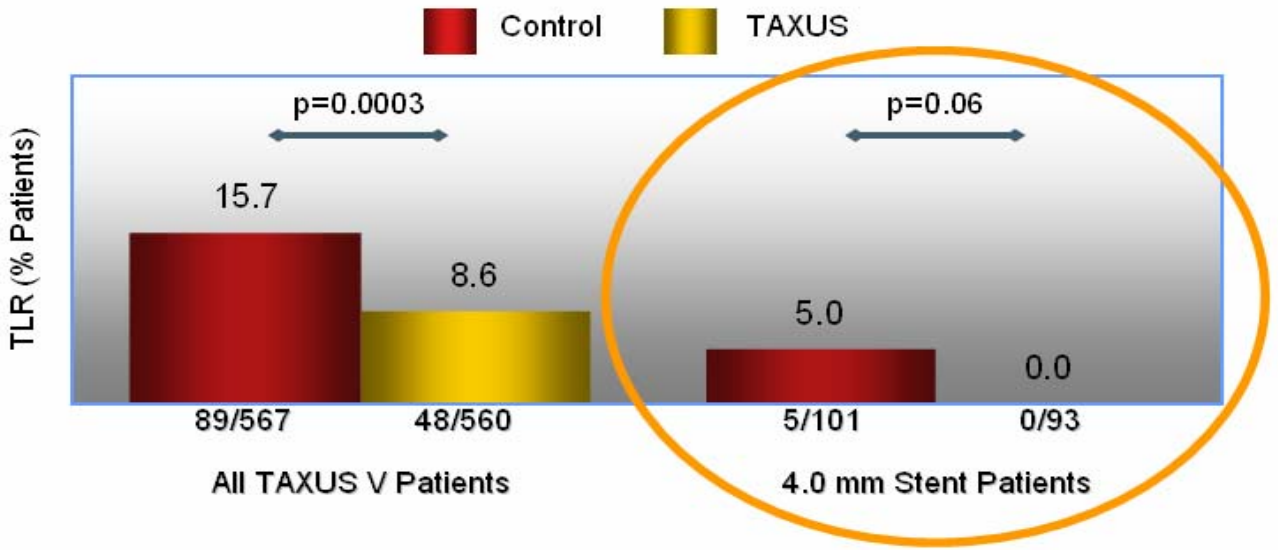


Dual Antiplatelet Mandatory after DES

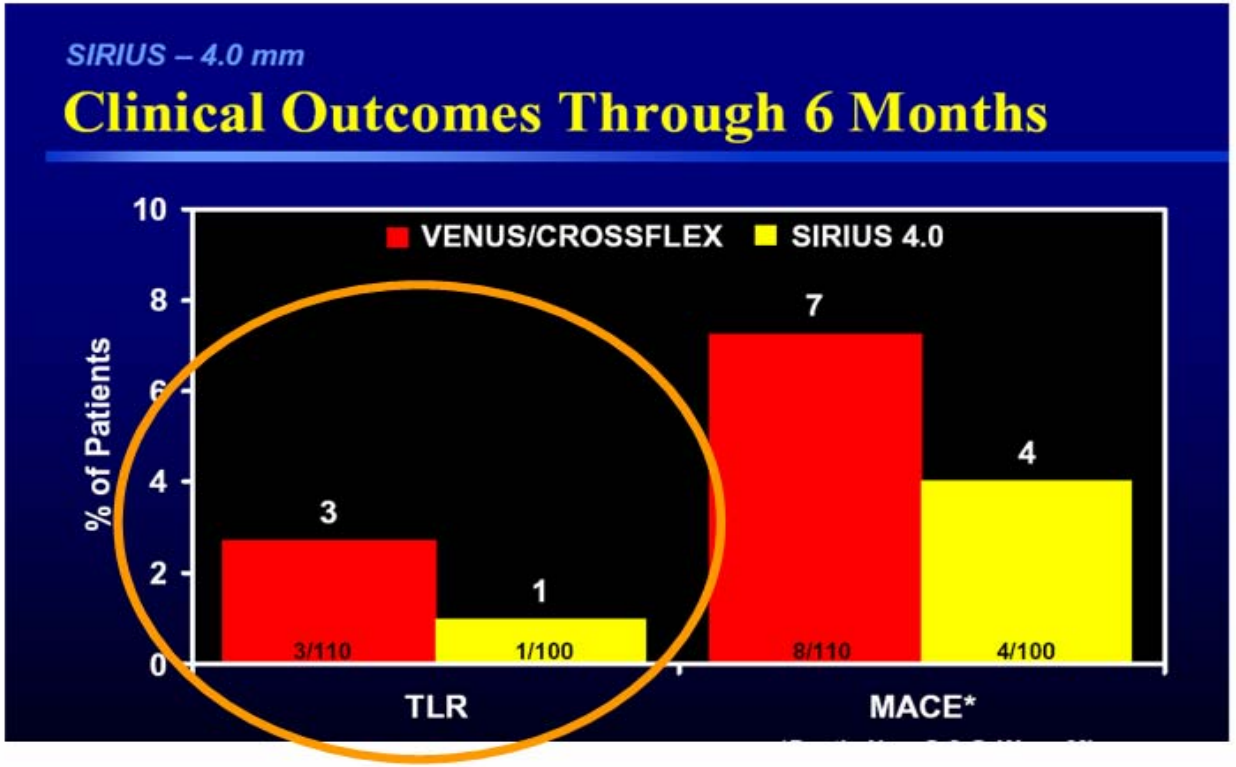
- **We do not use DES in:**
  - **Patients on chronic Coumadin**
  - **Unable, unwilling to take medications as directed (old age, uneducated, irresponsible).**
  - **Unable to pay for medications (Plavix $ 3-4 per day).**
  - **Emergency cases (without detailed discussion about DES prior to PCI).**

Large vessels

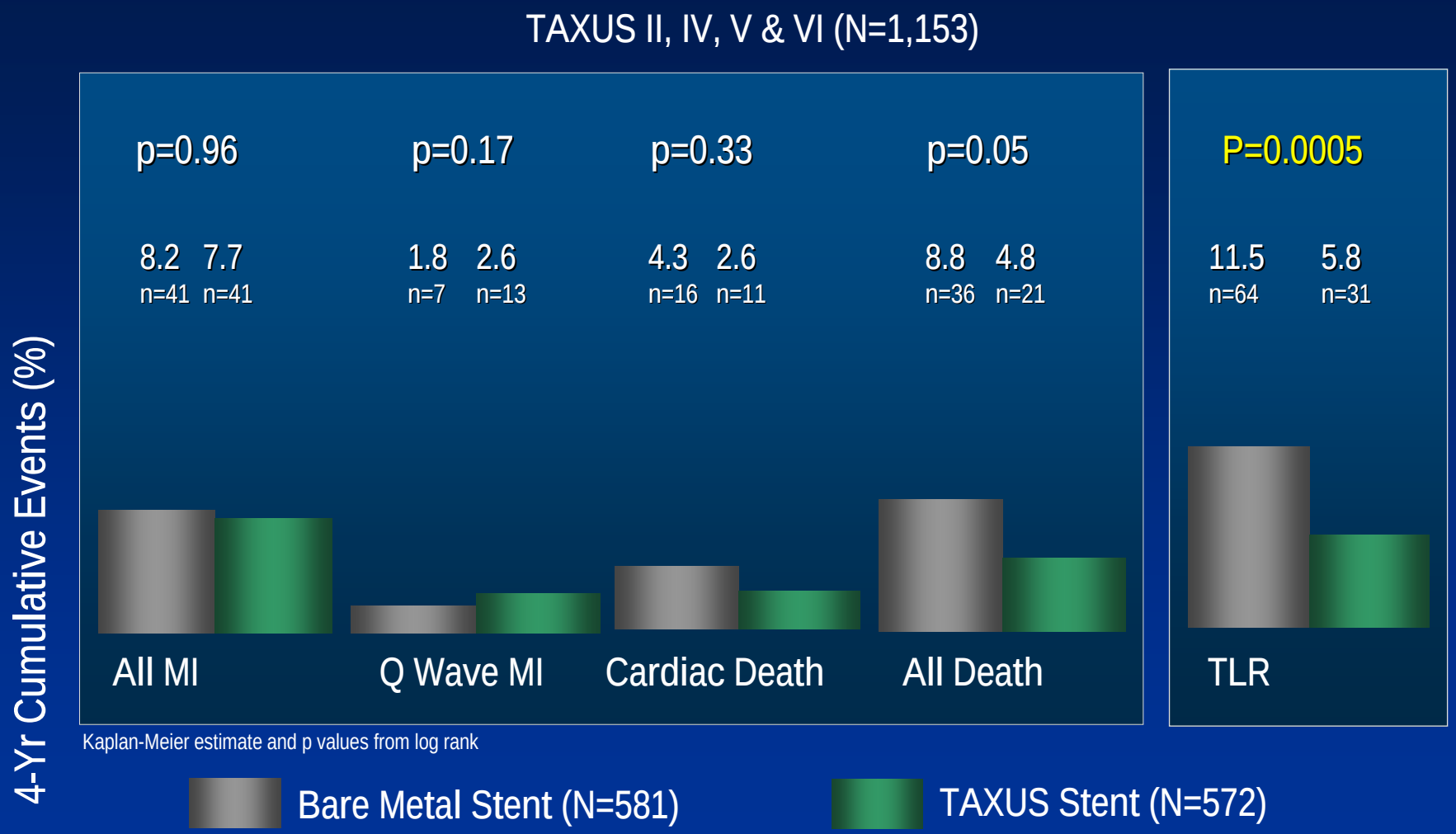
TAXUS 4.0 mm



CYPHER 4.0 mm



TAXUS Large Vessel 4-Year Outcome
Vessels ≥ 3.4 mm

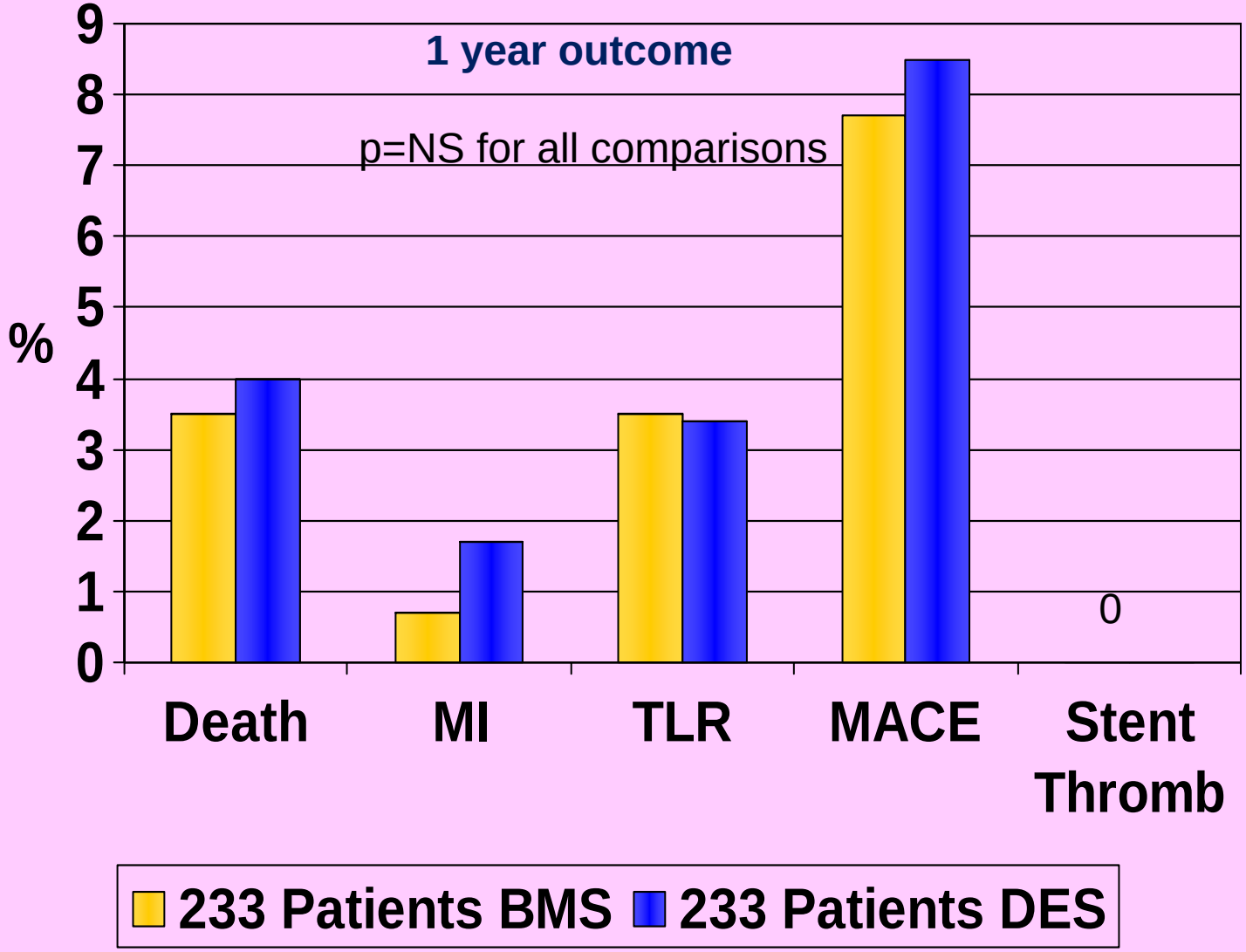


The safety and effectiveness of the TAXUS® Stent have not been established in patients for longer than 12 months or with coronary artery reference vessel diameters > 3.75mm.

BMS vs DES in Large Vessels (>3.5mm).

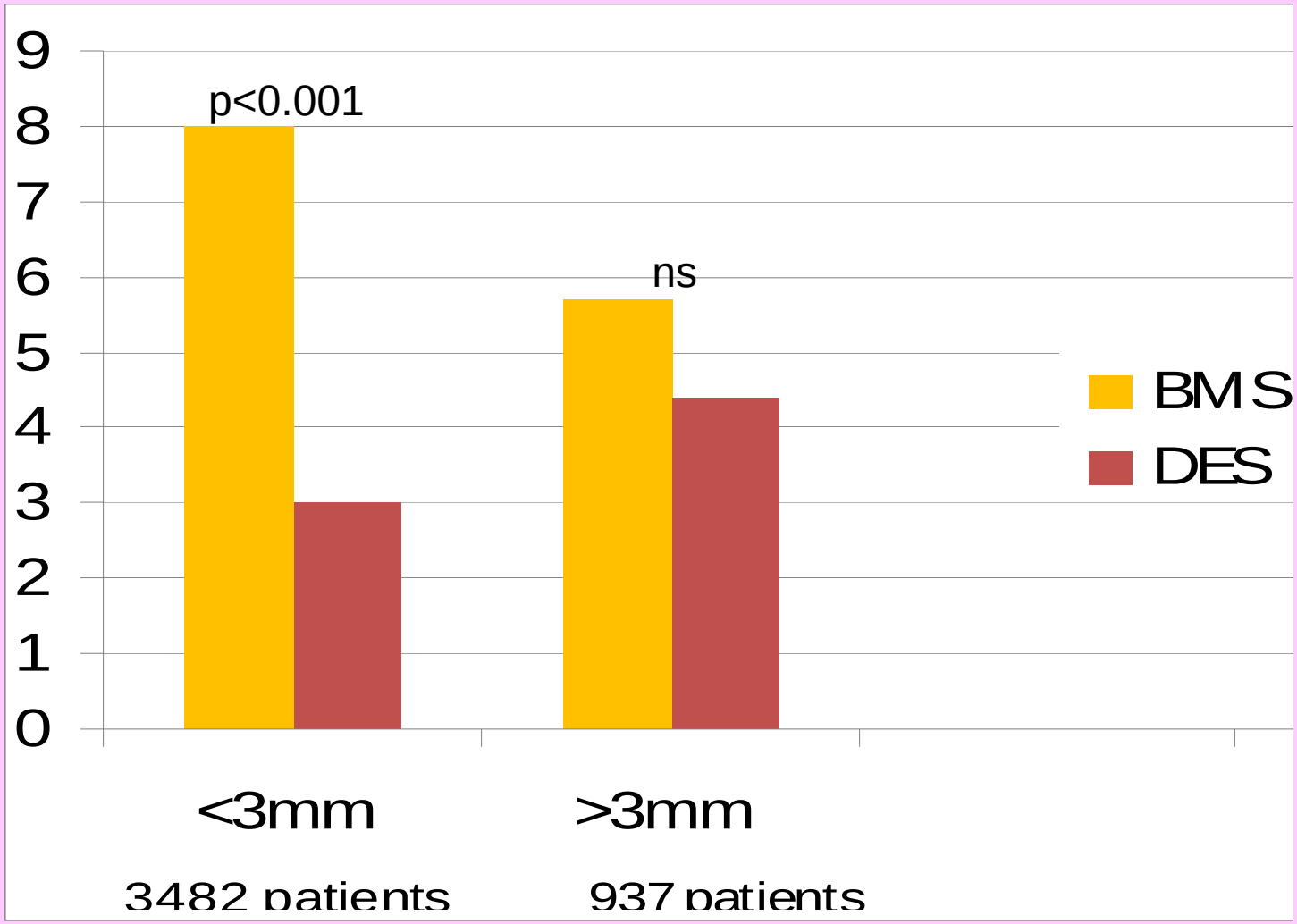
Washington Hospital Center

Steinberg et al. AJC 2007;99:599-602



DES vs BMS in >3mm Vessels.

Kosmicki. JACC 2006;47:43B

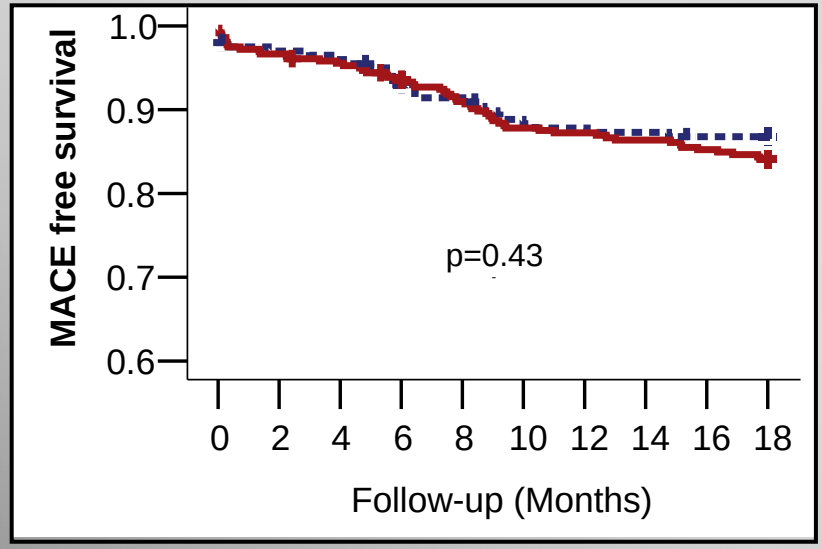


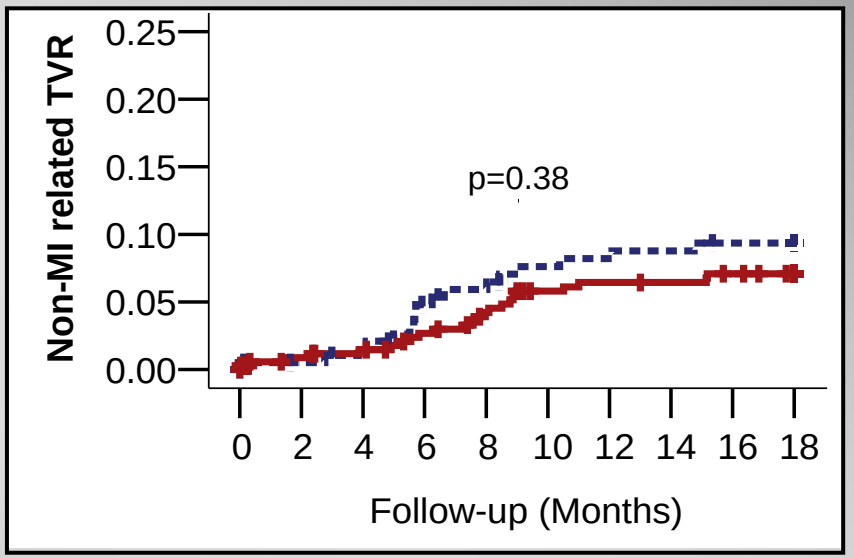
Vessels > 3mm (no bypass grafts)

Randomized to Cypher, Taxus or Vision.

Kaiser et al., ESC 2006.

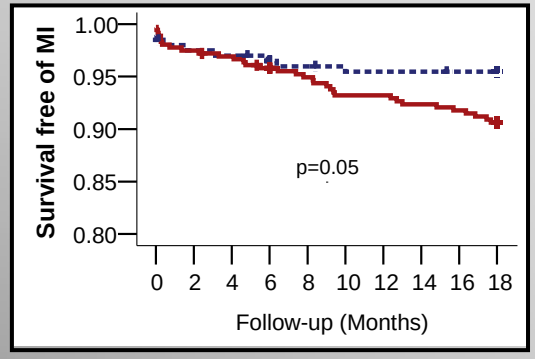
n=558 (68%)
18 months follow up





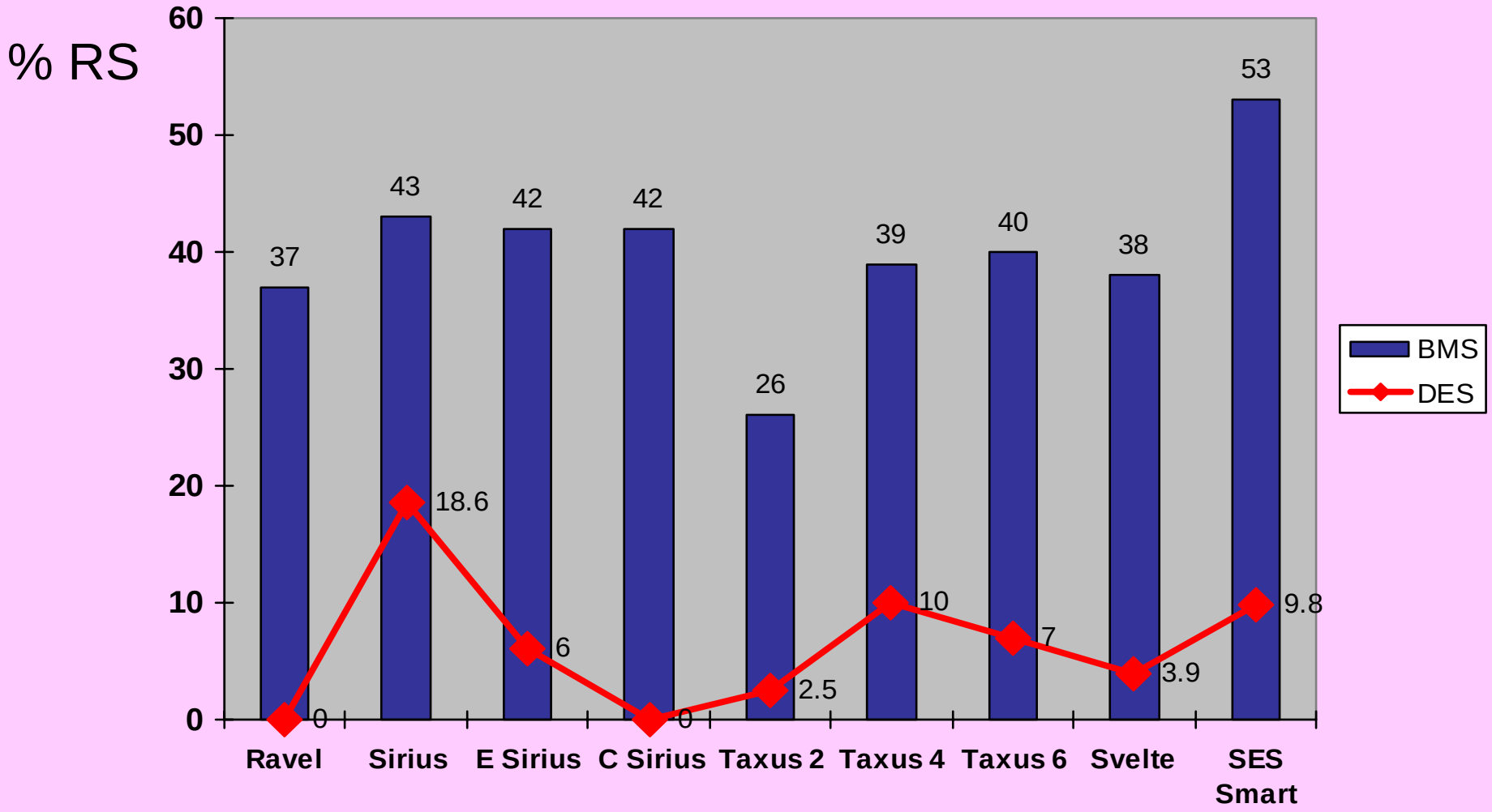
BMS

DES



Small vessels

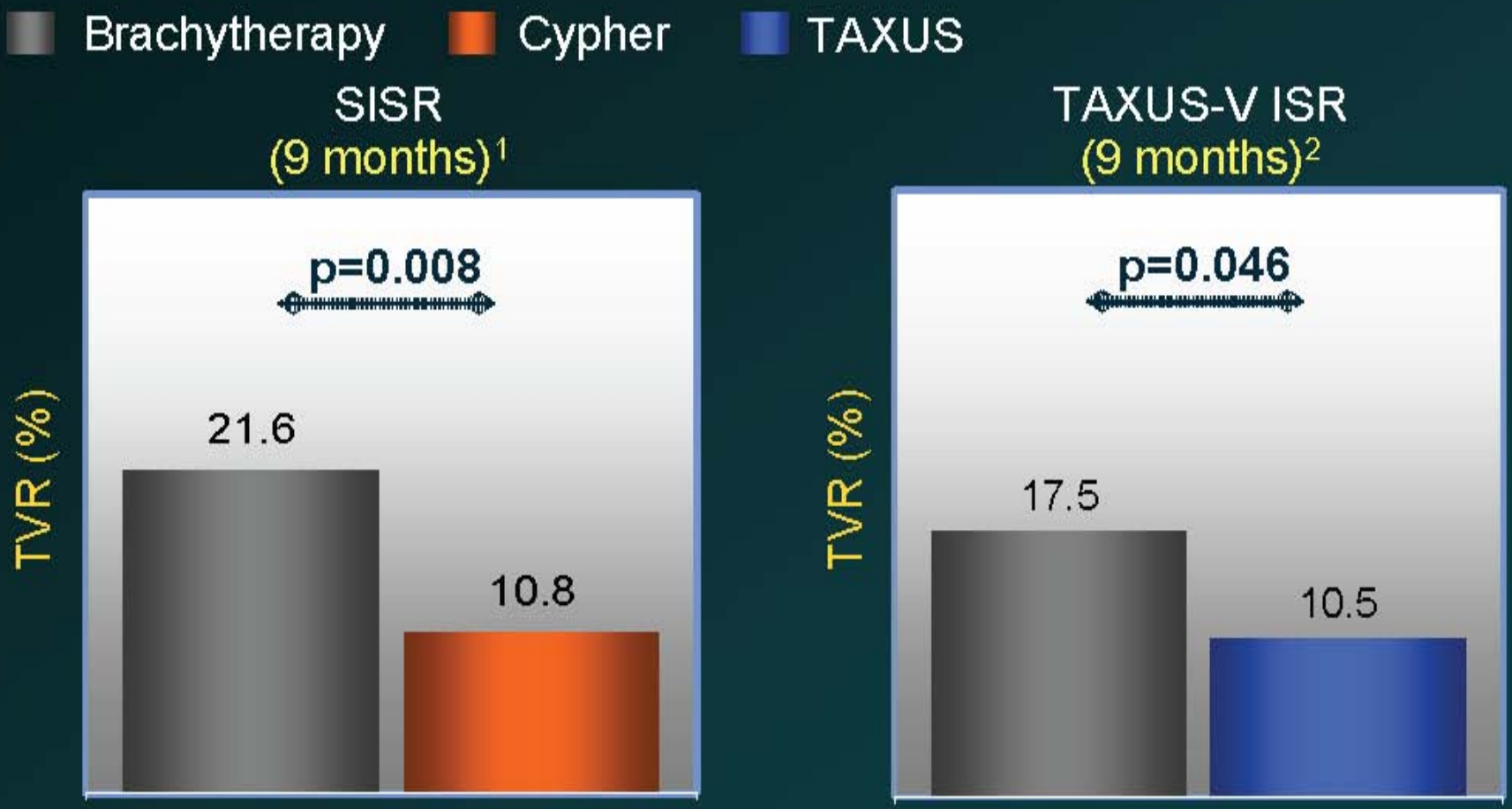
DES vs BMS in Small Vessels. Randomized Trials



In Stent Restenosis

Randomized ISR Trials

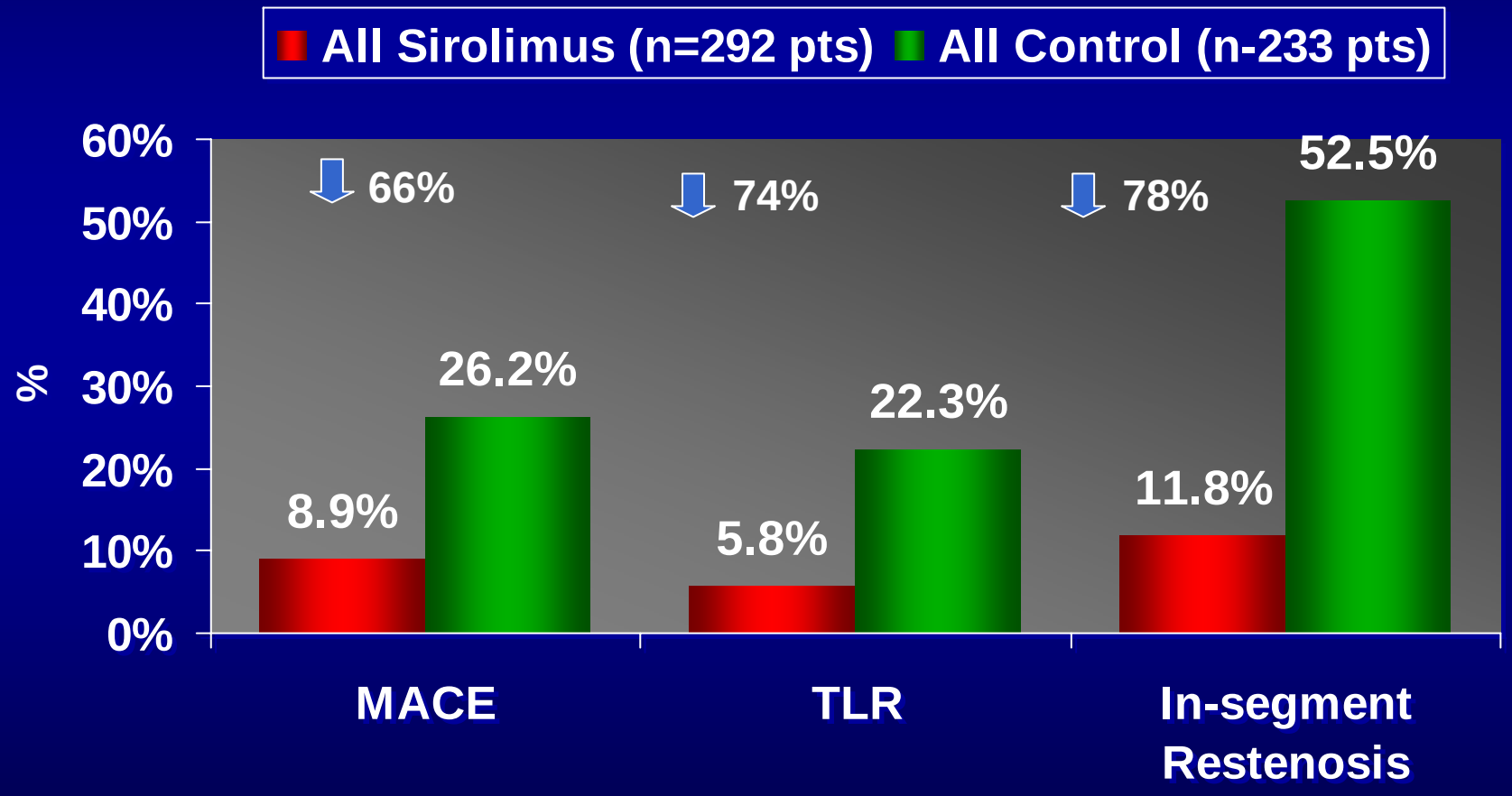
TVR at 9 Months: SISR and TAXUS-V ISR



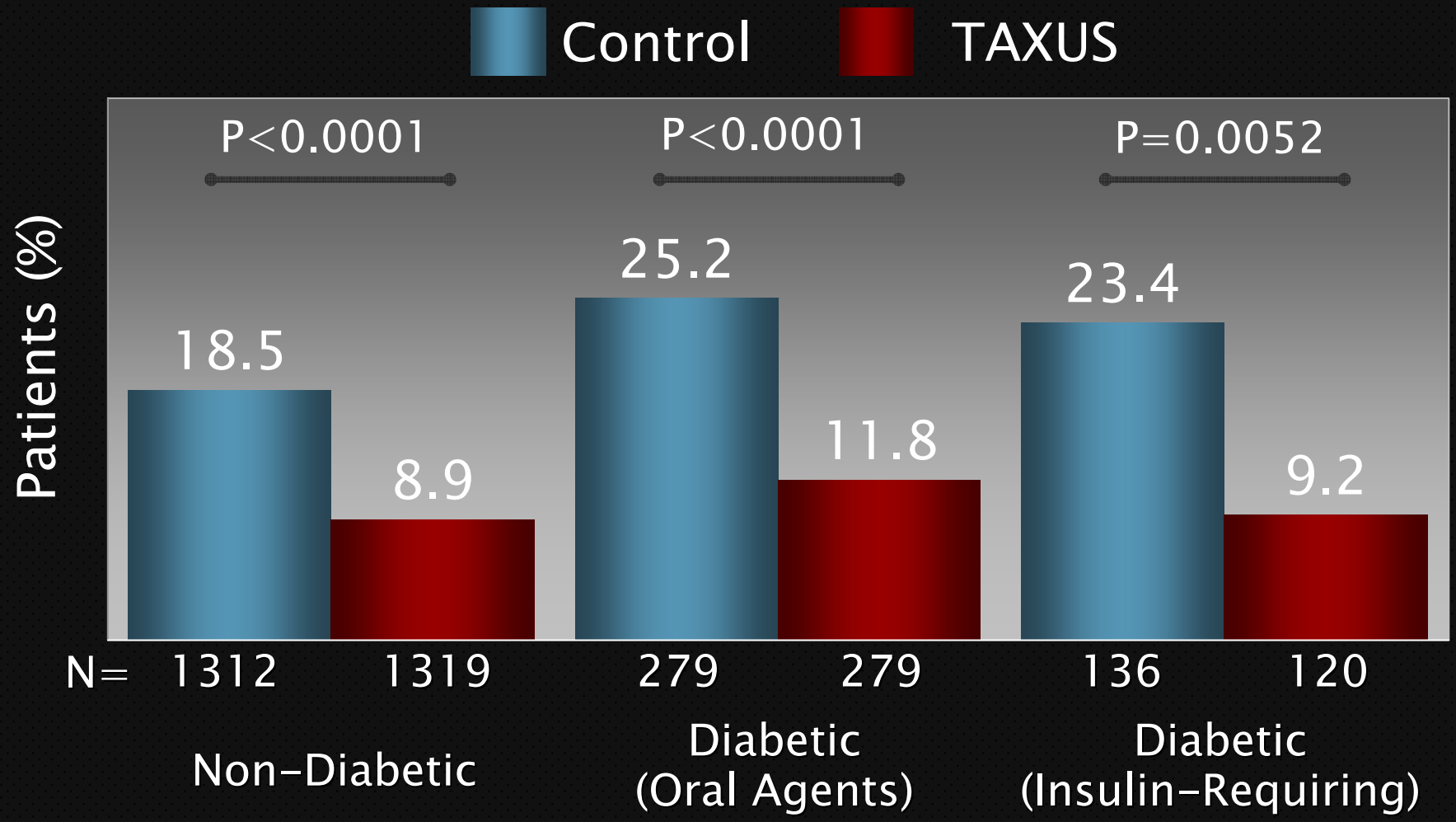
1. Holmes et al. *JAMA*. 2006;295:1264.
2. Stone et al. *JAMA* 2006;295:1253.

DES in Diabetics

CYPHER Trials DM Patients



1-3 year TLR in Diabetics.
Meta-AnalysisTAXUS II (3y), IV (3y), V (1y), VI (2y)



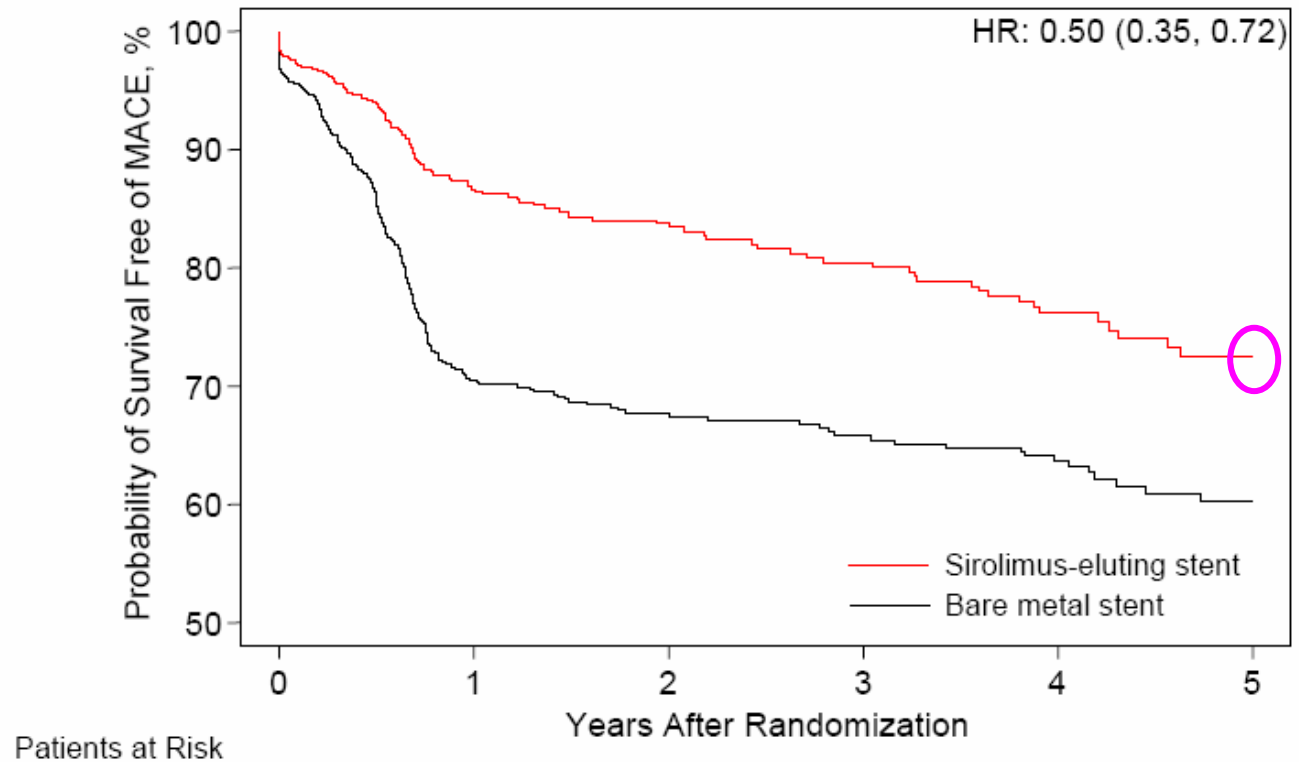
Event rate based on Kaplan Meier Estimate

Diabetes: Meta-analysis of RCTS (CYPHER vs. BMS)

Kastrati, FDA Panel Dec 2006

Cordis
a Johnson & Johnson company

Kaplan-Meier Curves of Survival Free of MACE
-Diabetic Patients-



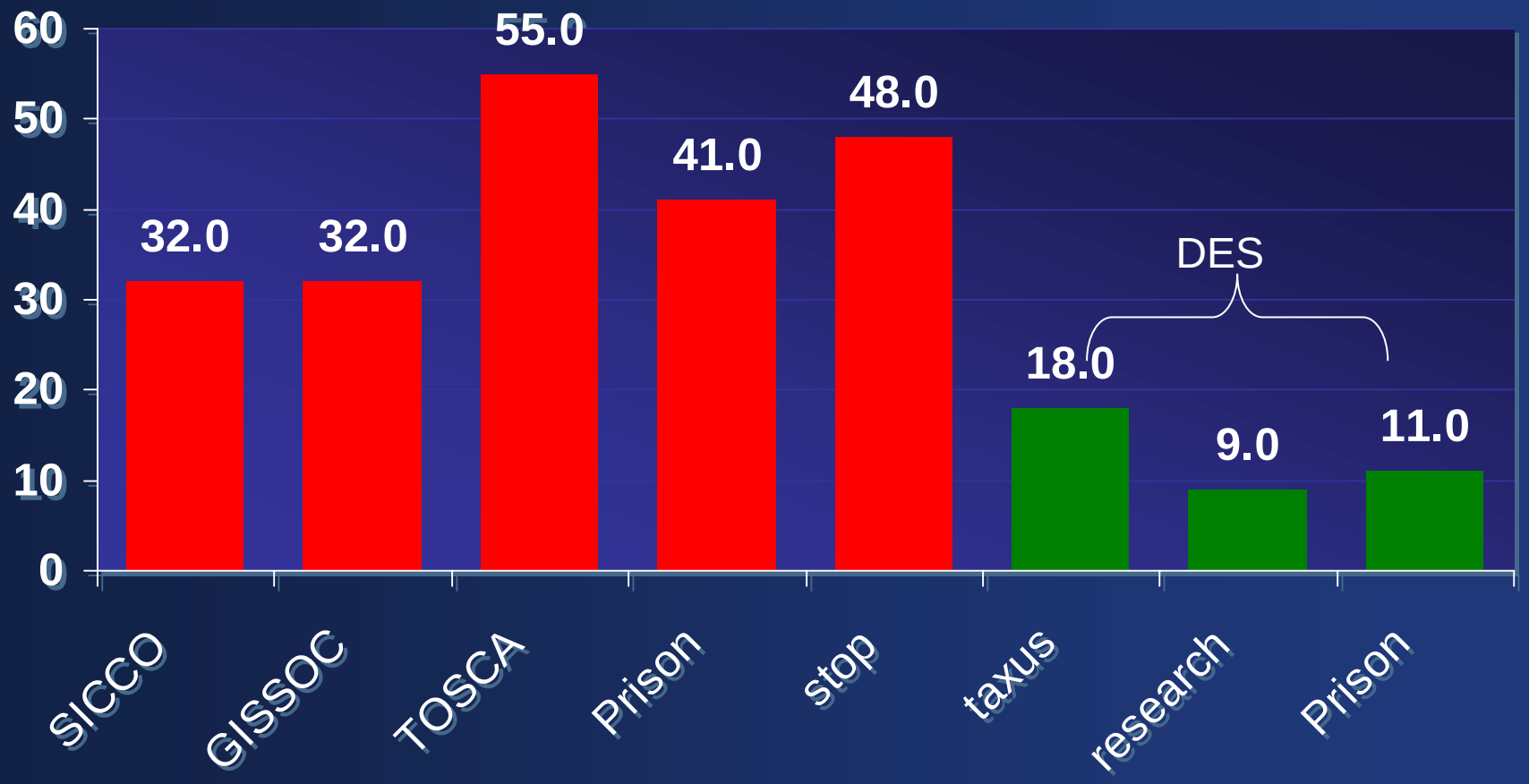
Patients at Risk

SES	675	492	294	207	144	100
BMS	736	449	260	198	157	88

FDA has not made any determination as to the safety & efficacy of the CYPHER® Stent in people with diabetes

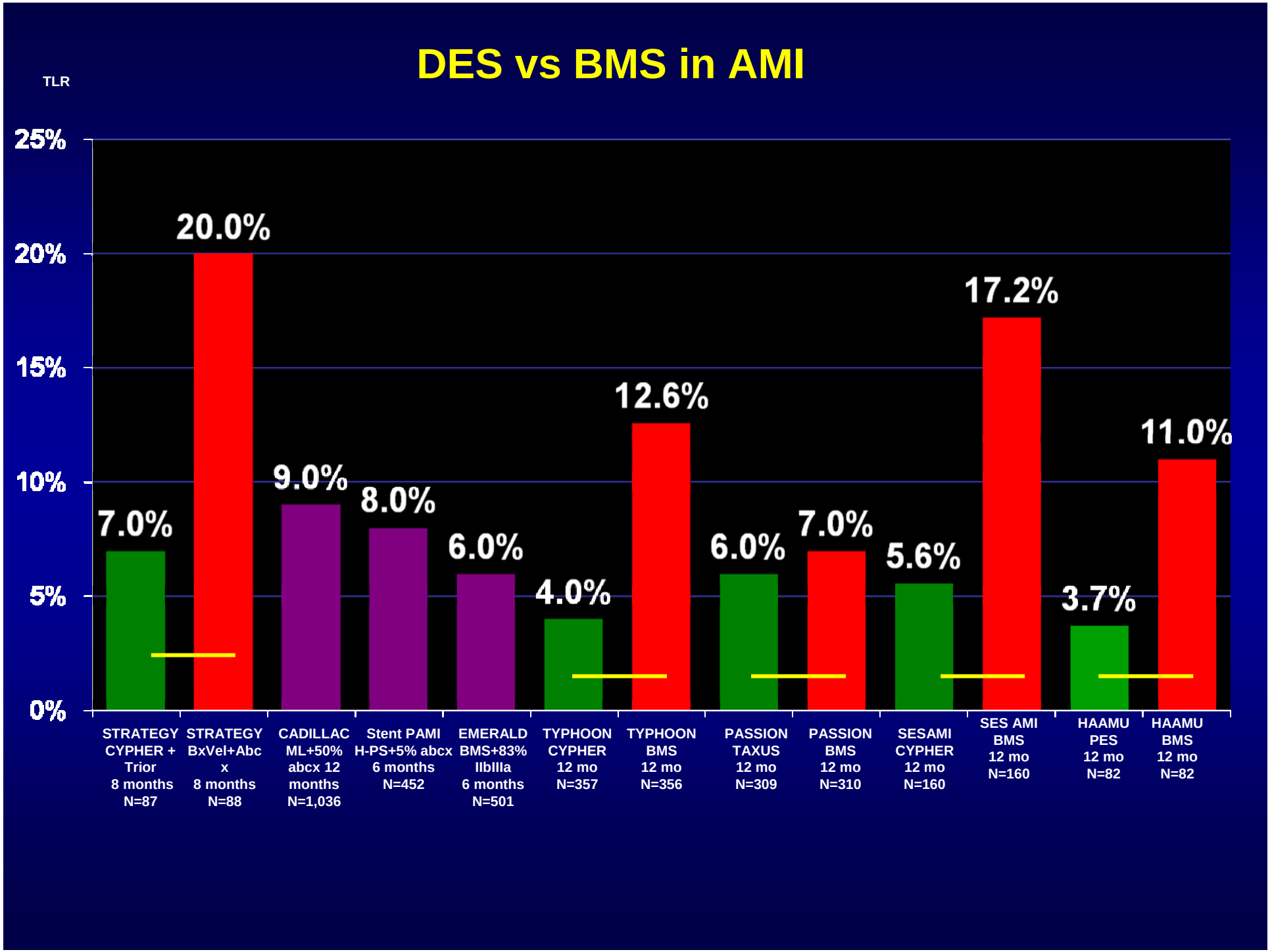
Chronic Total Occlusion

Restenosis Rates for Stenting in CTO



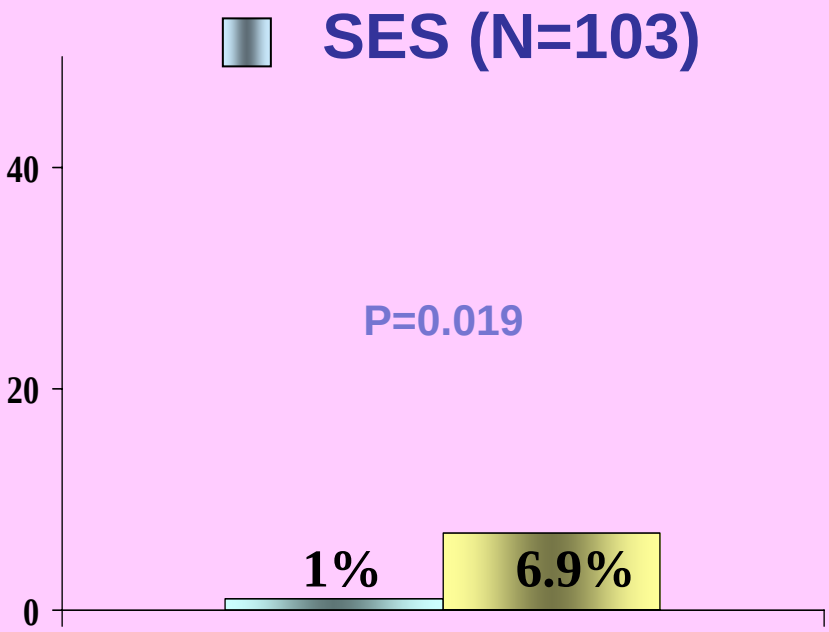
Acute MI

DES vs BMS in AMI

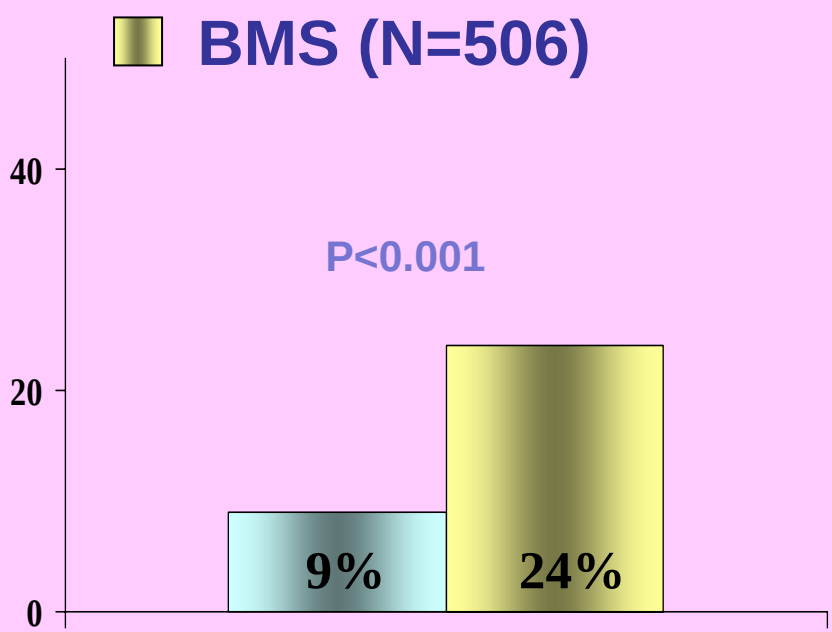


Cypher in Acute Myocardial Infarction.

Washington Hospital Center. Cheneau CCI 2005;65:469-72



6 monthsTLR



6 months MACE

BMS and DES in AMI.

Research, T Search Registries. 505 pts.
Daemen, Serruys et al. AJC 2007;99;1057-62

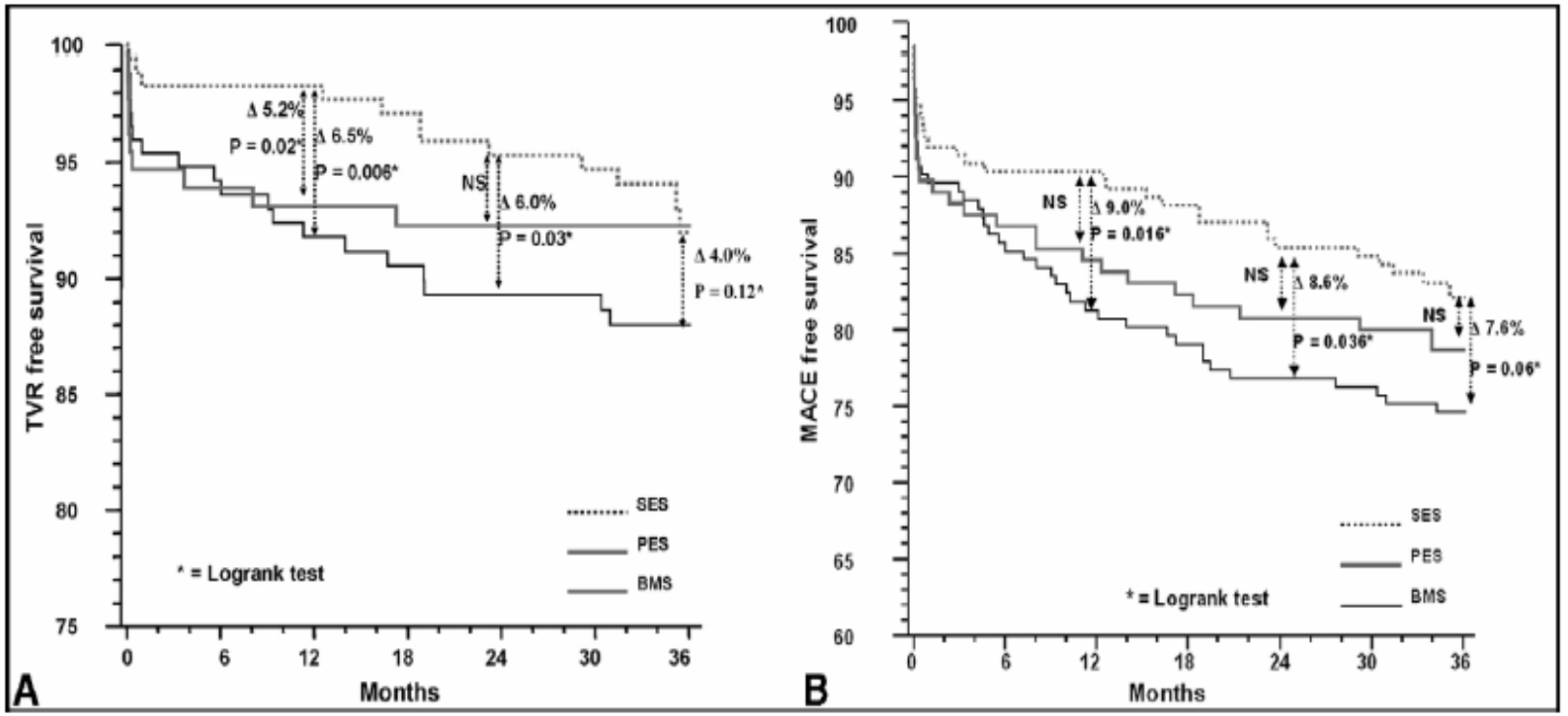


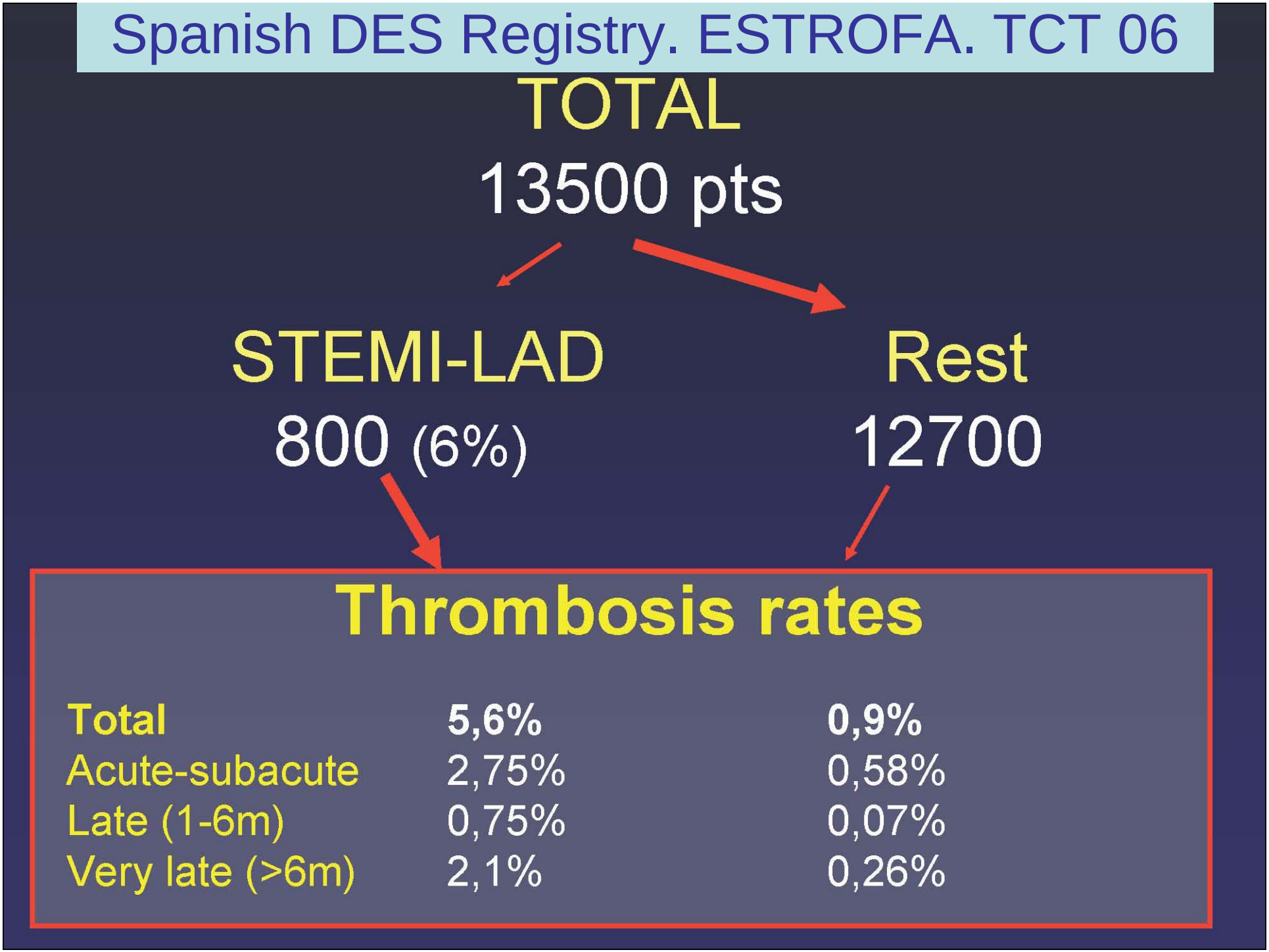
Figure 1. Kaplan-Meier survival curves of *(A)* TVR and *(B)* combined cumulative incidence of major adverse cardiac events (MACE; death, MI, and TVR). Δ = change.

relatively small consecutive patient cohort, the use of SESs and PESs was no longer associated with significantly lower rates of TVR and major adverse cardiace events in patients with STEMI after 3 years of follow-up. A high frequency of stent thrombosis was observed in the 2 drug-eluting stent groups. (Am J Cardiol 2007;99:1027–1032)

Plavix Discontinuation in AMI Patients with DES. Premier Registry. Spertus et al.Circulation. 2006;113:2803-2809

- 500 patients from 19 centers treated with DES for acute MI.
- 68 **(13.6%) stopped Plavix within 30 days:**
  - **10 x more likely to die** during the next 11 months (7.5% versus 0.7%, *P*<0.0001)
  - **More likely to be rehospitalized** (23% versus 14%, *P*=0.08).
- The relatively high prevalence of thienopyridine discontinuation (1 in 7 patients) suggests that all DES recipients should be targeted for aggressive education to ensure high compliance with adjunctive dual-antiplatelet therapy.

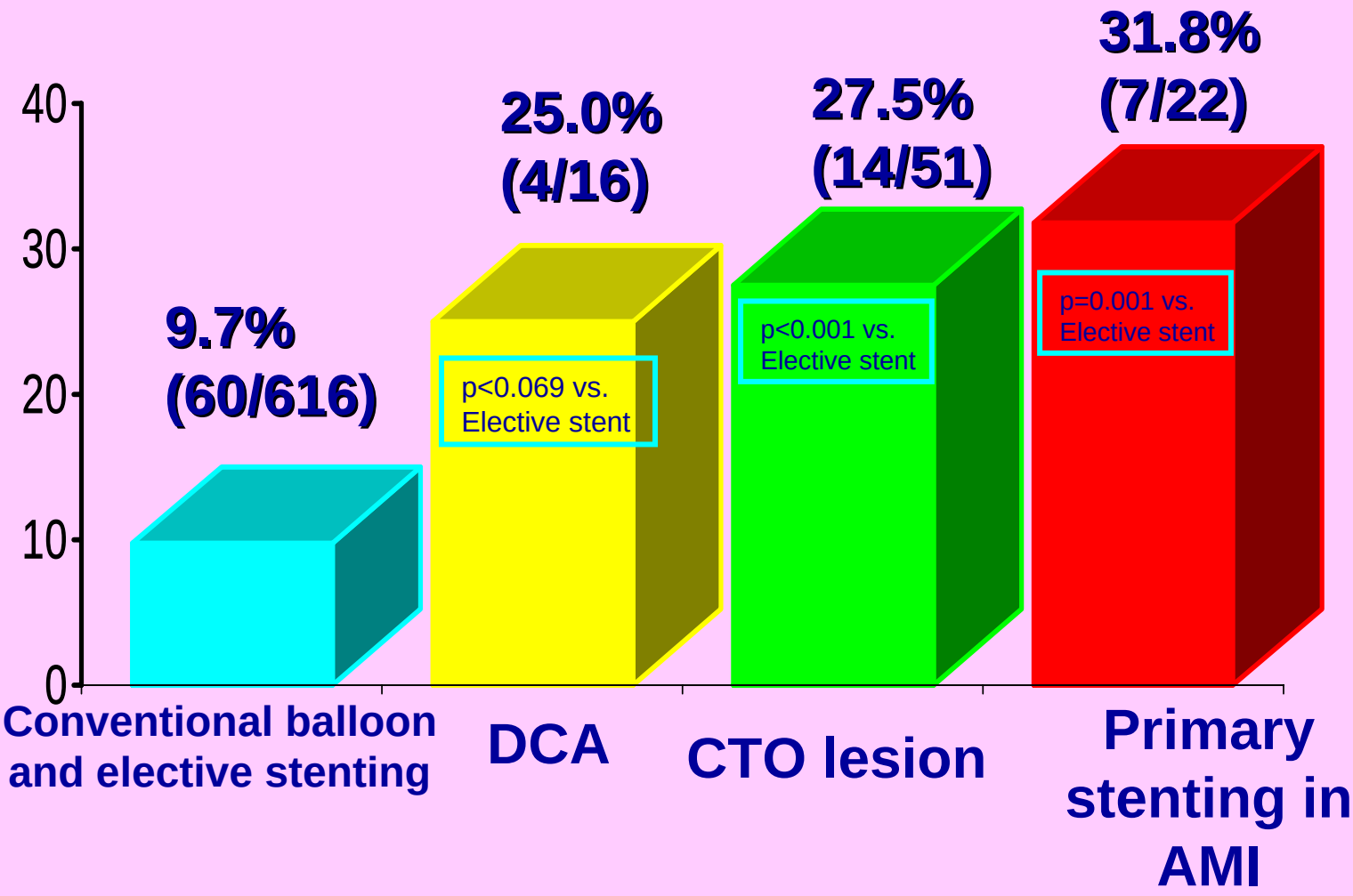
Spanish DES Registry. ESTROFA. TCT 06



Incidence of Late Stent Malapposition.

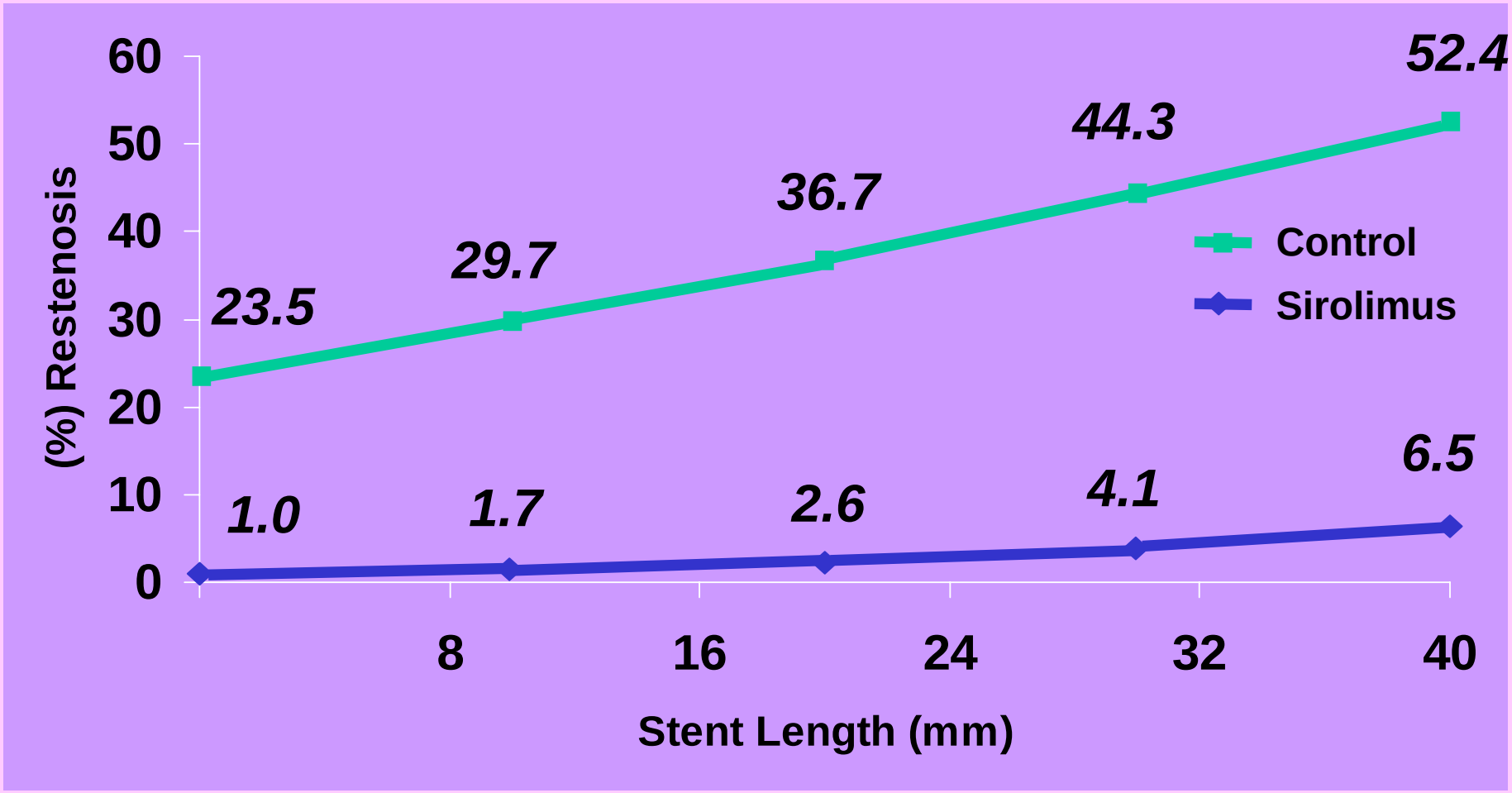
Hong MK, Circulation 2006;113:414-419

557 patients (705 lesions) with IVUS at 6 months (6.1±2.1 months).



Long lesions

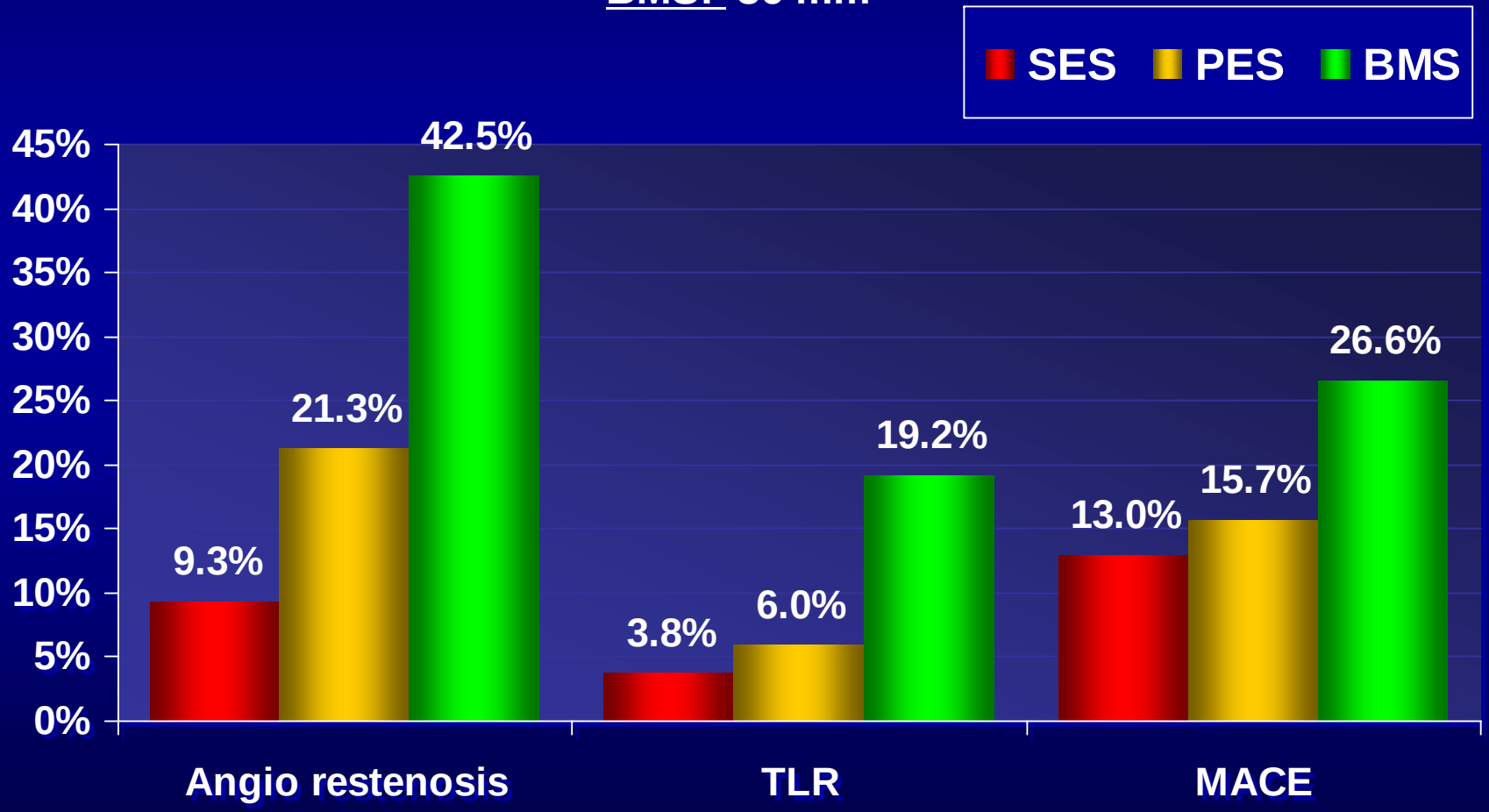
DES for Long Lesions



DES vs BMS in Long Lesions.

Kim, CCI 2006; 67:181-7

527 pts with 618 long lesions.
SES and PES: 43 mm
BMS: 36 mm



Angio Restenosis and IVUS Stent Area & Length.

Hong, Mintz et al. EHJ 2006:27:1305-11

Stent length (mm)	Stent CSA (mm^2)	Restenosis rates	*P* trend
≤40	≥5.5	1/284 (0.4%)	
≤40	<5.5	3/127 (2.4%)	<0.001
>40	≥5.5	6/70 (8.6%)	
>40	<5.5	11/62 (17.7%)	

Full Metal Jacket with DES

Matrix Registry

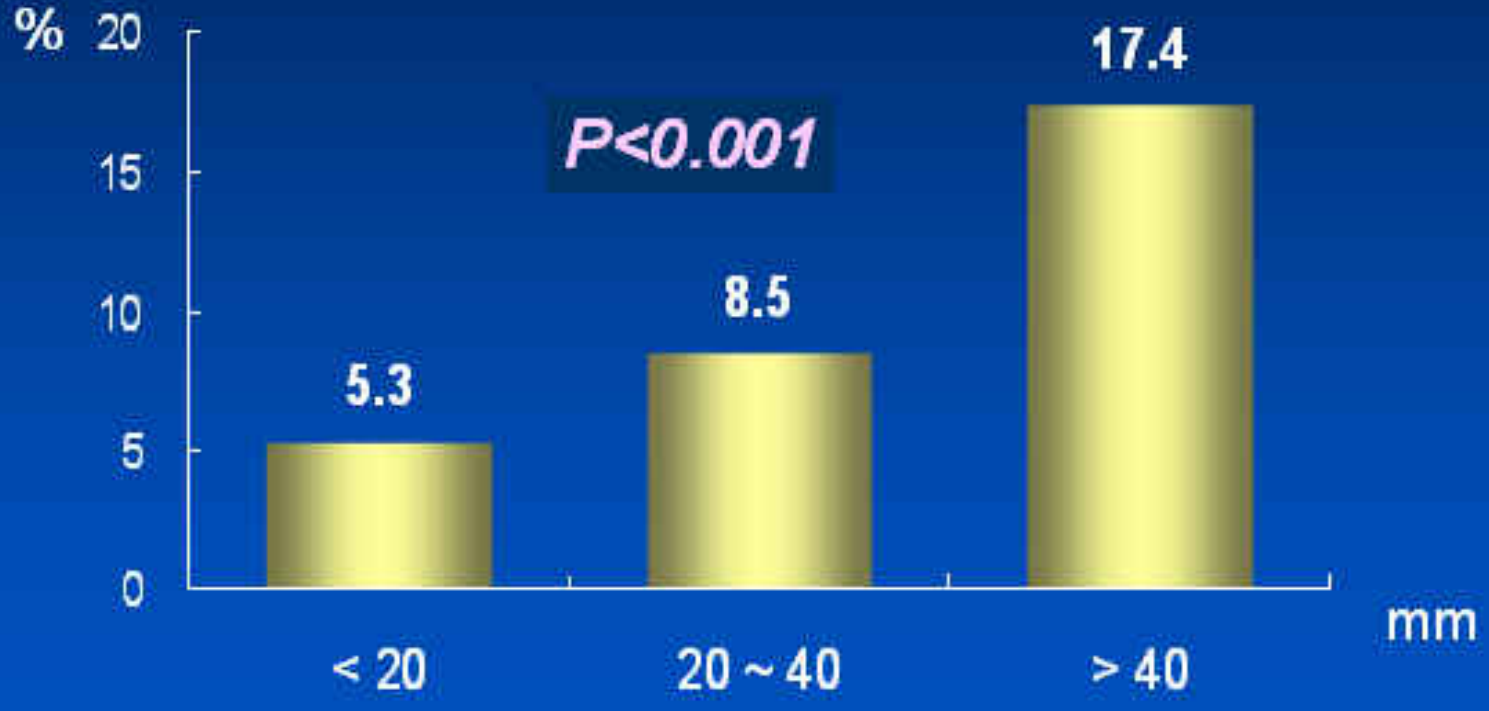
Stented segment length (mm)	≤35 (n=478)	36-70 (n=352)	>70 (n=145)	*p*
Ovelapping stents	4.9%	22.3%	34.1%	<0.0001
Procedural success	97.5%	94.9%	86.9%	<0.0001
In-hospital events				
NQMI	0.4%	2.3%	6.9%	<0.0001
TVF*	0.4%	2.3%	7.6%	<0.0001
6-months events				
NQMI	1.2%	3.0%	10.2%	<0.0001
TVF*	4.0%	8.0%	16.7%	<0.0001

TVF*; death, MI, TVR

Mehran R et al, TCT 2006

AMC

Restenosis Rate According to Lesion Length

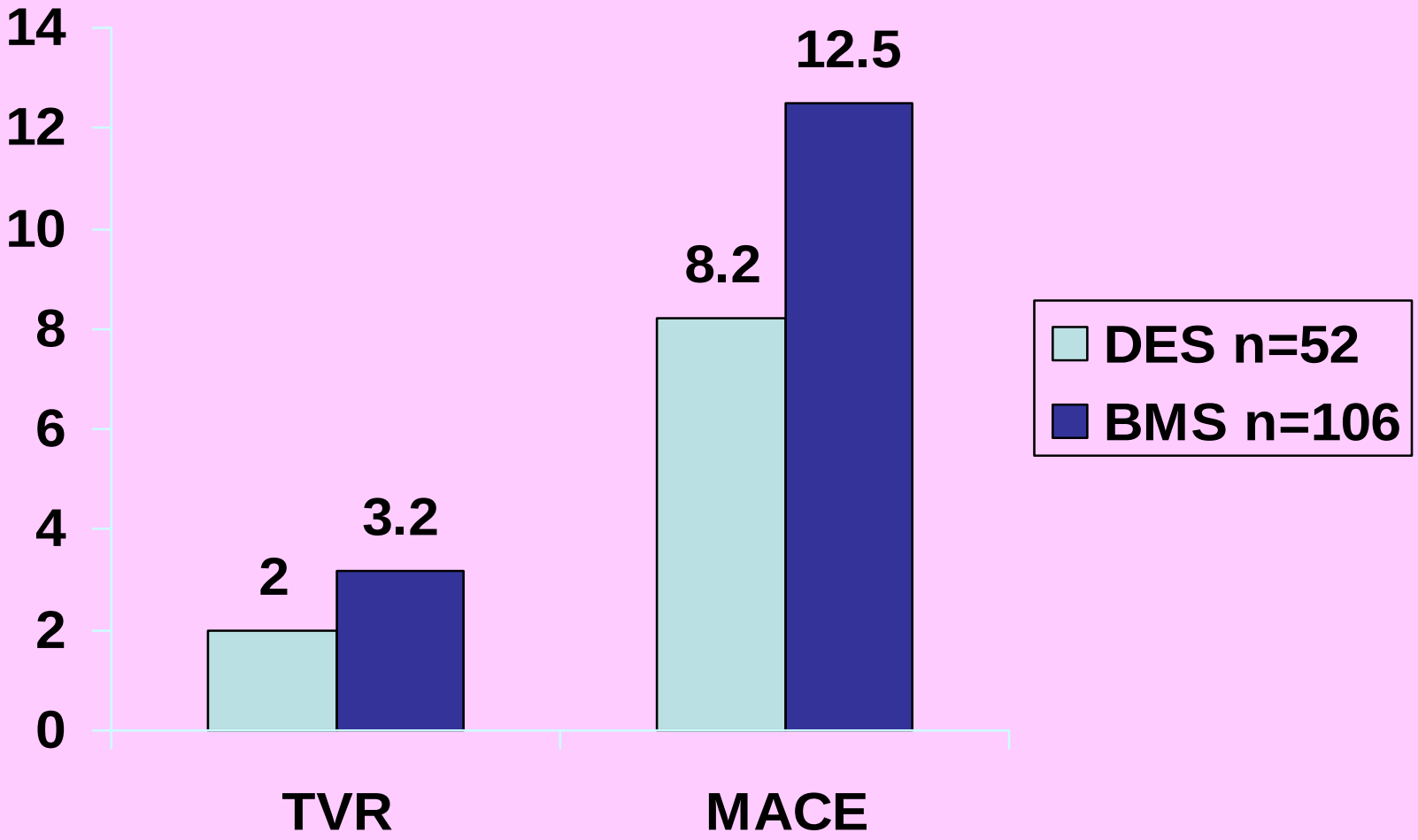


Lee CW et al. Am J Cardiol 2006;97:506-511

Ostial Location

DES in Ostial Lesions

Washington Hospital Center. 2004



DES vs BMS for Ostial Disease

Park et al. AJC 2007;99:760-5

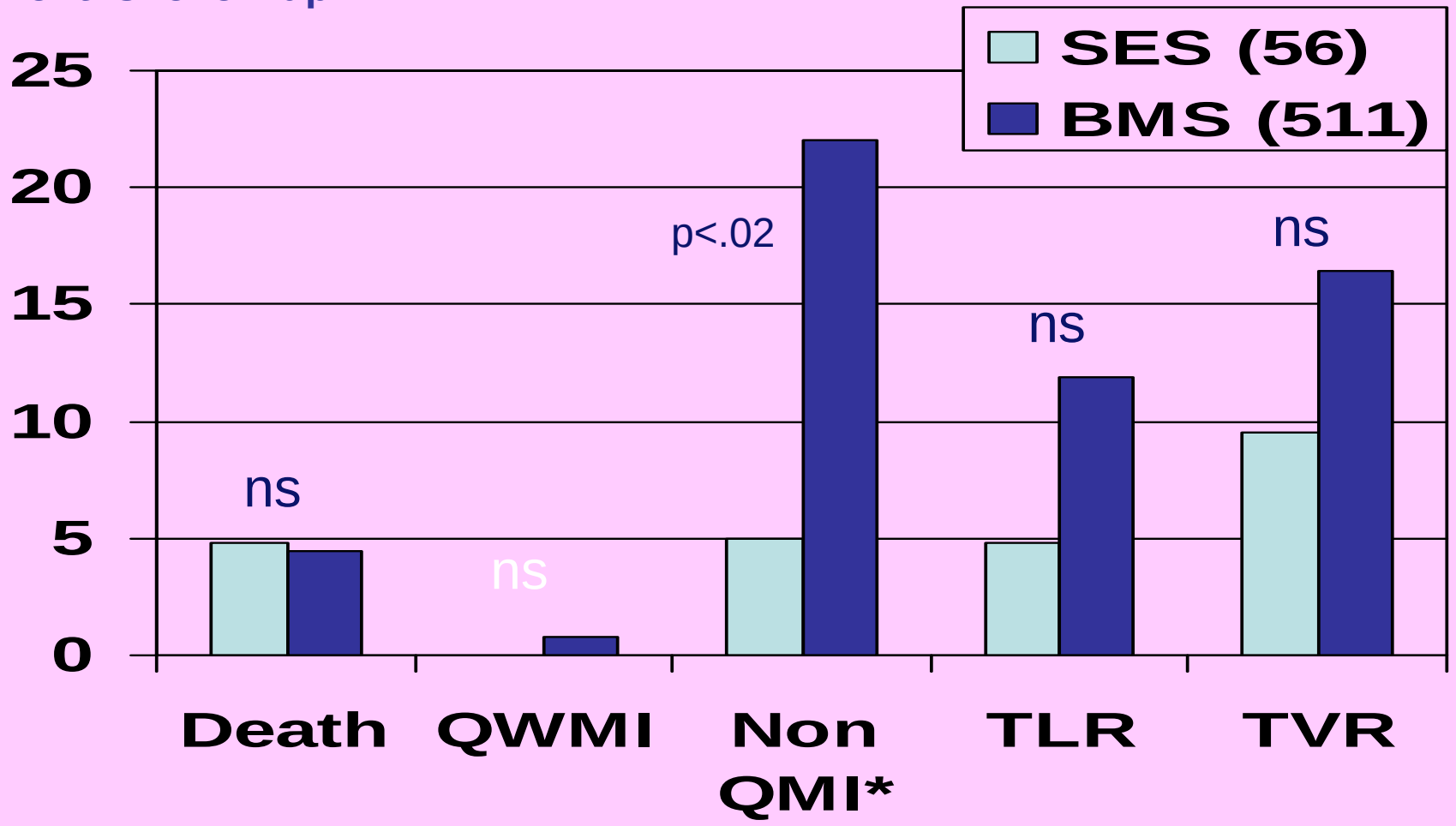
Variable	DES (n = 184)	Pre-DES (n = 172)	p Value
Cumulative 1-yr outcomes			
Death	3 (1.6)	4 (2.3)	0.7
Cardiac	3 (1.6)	3 (1.7)	1.0
Noncardiac	0	1 (0.6)	0.5
Q-wave myocardial infarction	1 (0.5)	2 (1.2)	0.6
TLR	8 (4.3)	20 (11.6)	0.011
Repeat intervention	4 (2.2)	10 (5.8)	0.1
Bypass surgery	4 (2.2)	10 (5.8)	0.1
Stent thrombosis	1 (0.5)	2 (1.2)	0.6
Total MACES	12 (6.5)	23 (13.4)	0.030

Saphenous Vein Graft

Cypher for SVG.

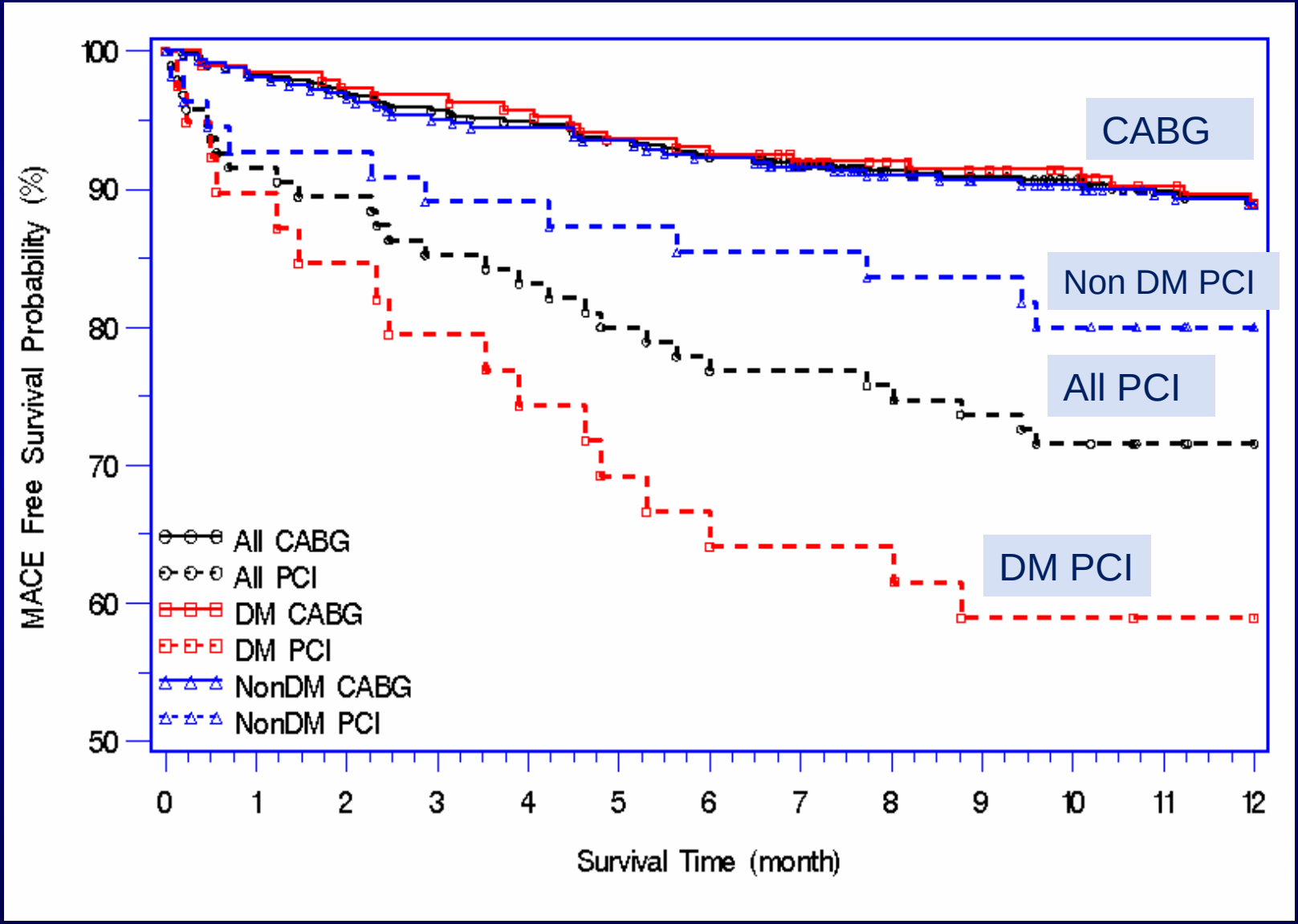
WHC. Chu et al. AJC 2006;97:34-37

6 months follow up



3 Vessel Disease. CABG vs PCI

WHC. Javaid et al. Circulation 2007 in press



- **For multiple complex lesions (long, small, bifurc, etc.), specially in diabetics, DES is not a permanent solution.**

- **Other alternatives need to be considered (medical therapy, coronary surgery, etc) before embarking in PCI.**

Conclusion

- **Drug eluting stents offer restenosis benefit in all lesion subsets.**
- **DES do not decrease MI or Death as compared with BMS.**
- **DES is the stent of choice in complex lesions (long lesions, diabetics, small vessels, CTO, etc.).**
- **New evidence for late adverse effects may decrease its universal use.**