Impact of Diabetes on Long Coronary Lesion Treated With Drug-Eluting Stents; Data from LONG-DES II

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Angiographic trials of BMS in diabetes

Characteristics	Van Belle		Carrozza		Elezi		Yokoi		Abizaid		
	DM (+)	DM (-)	DM (+)	DM (-)	DM (+)	DM (-)	DM (+)	DM (-)	ID DM	NID DM	DM (-)
No. of lesion	56	244	40	190	245	1223	263	768	706	151	97
RVD	2.96	3.0	3.24	3.40	NR	NR	3.23	3.24	2.86	2.93	2.99
Post-procedure MLD	2.55	2.53	3.27	3.46	NR	NR	2.86	2.88	2.71	2.75	2.81
Follow-up MLD	1.78	1.75	1.66	2.24	NR	NR	1.93	2.00	NR	NR	NR
Acute gain	1.77	1.77	2.59	2.64	2.18	2.23	NR	NR	NR	NR	NR
Late loss	0.77	0.79	1.66	1.23	1.35	1.05	NR	NR	NR	NR	NR
Restenosis (%)	55	27	34	20	44	24	31	23	44	35	16

Van Belle et al. Circualtion 1997;96:I454

Carrozza et al. Ann Int Med 1993; 118-34

Elezi et al. JACC 1997;29:188

Yokoi et al. JACC 1997;29:455

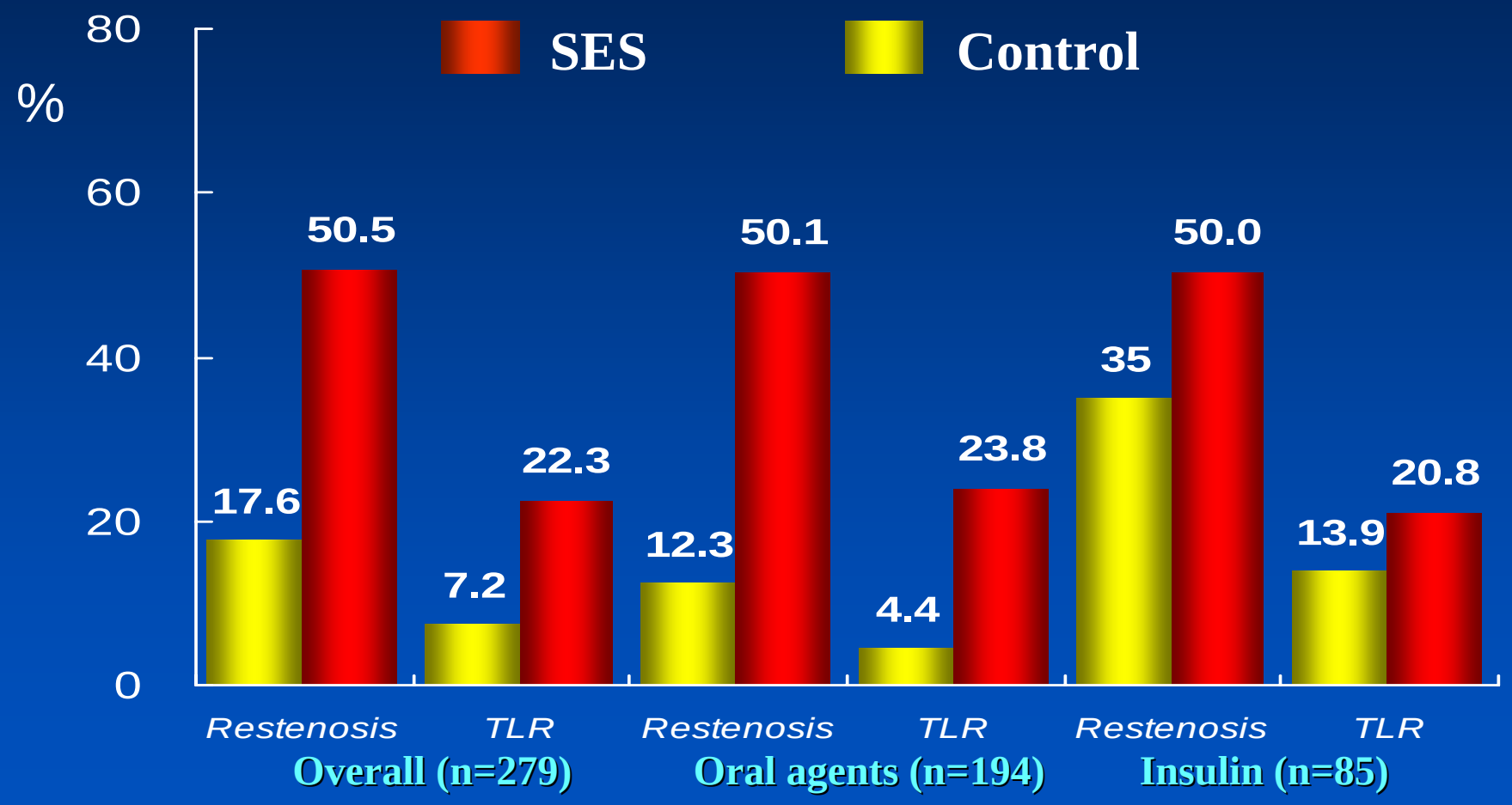
Abizaid et al. JACC1998;32:584

Mehran et al. JACC 2004;43:1348-1354

How about DES in Diabetic Patients

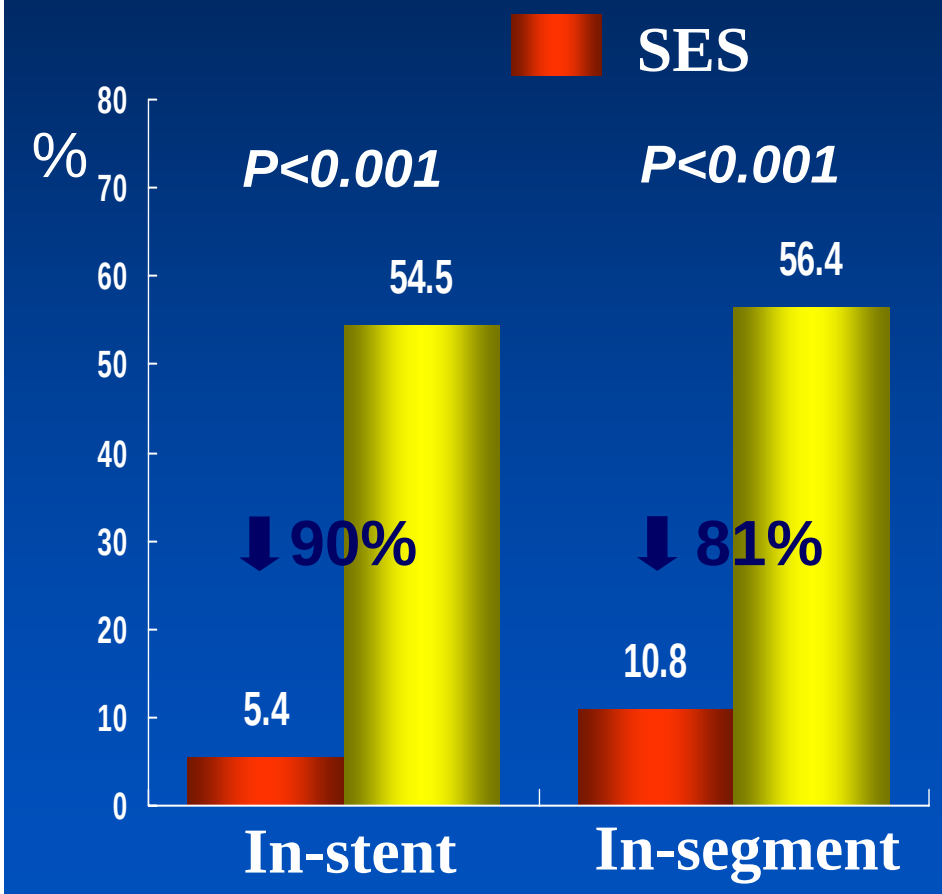
DES vs. BMS in Diabetes

SIRIUS-Diabetes

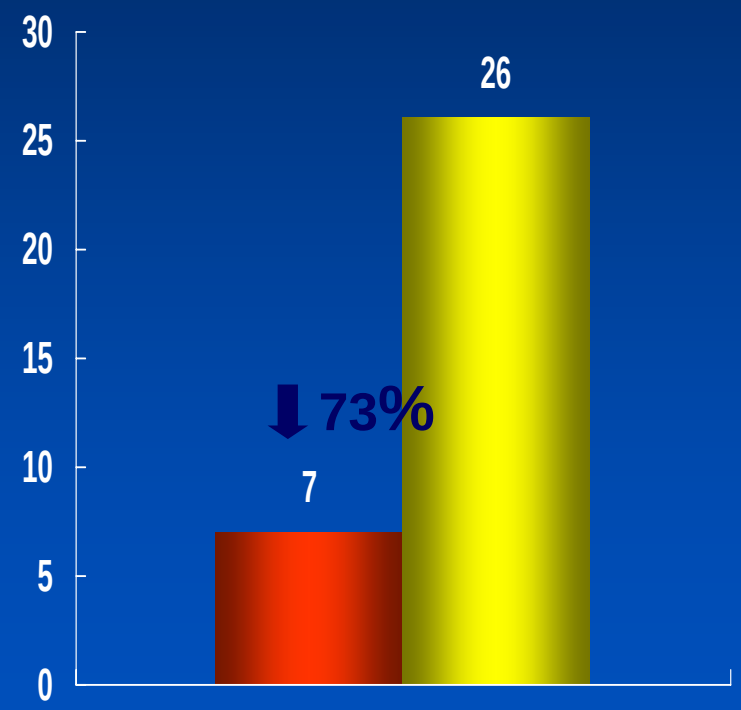


New SIRIUS - Diabetics

Binary Restenosis



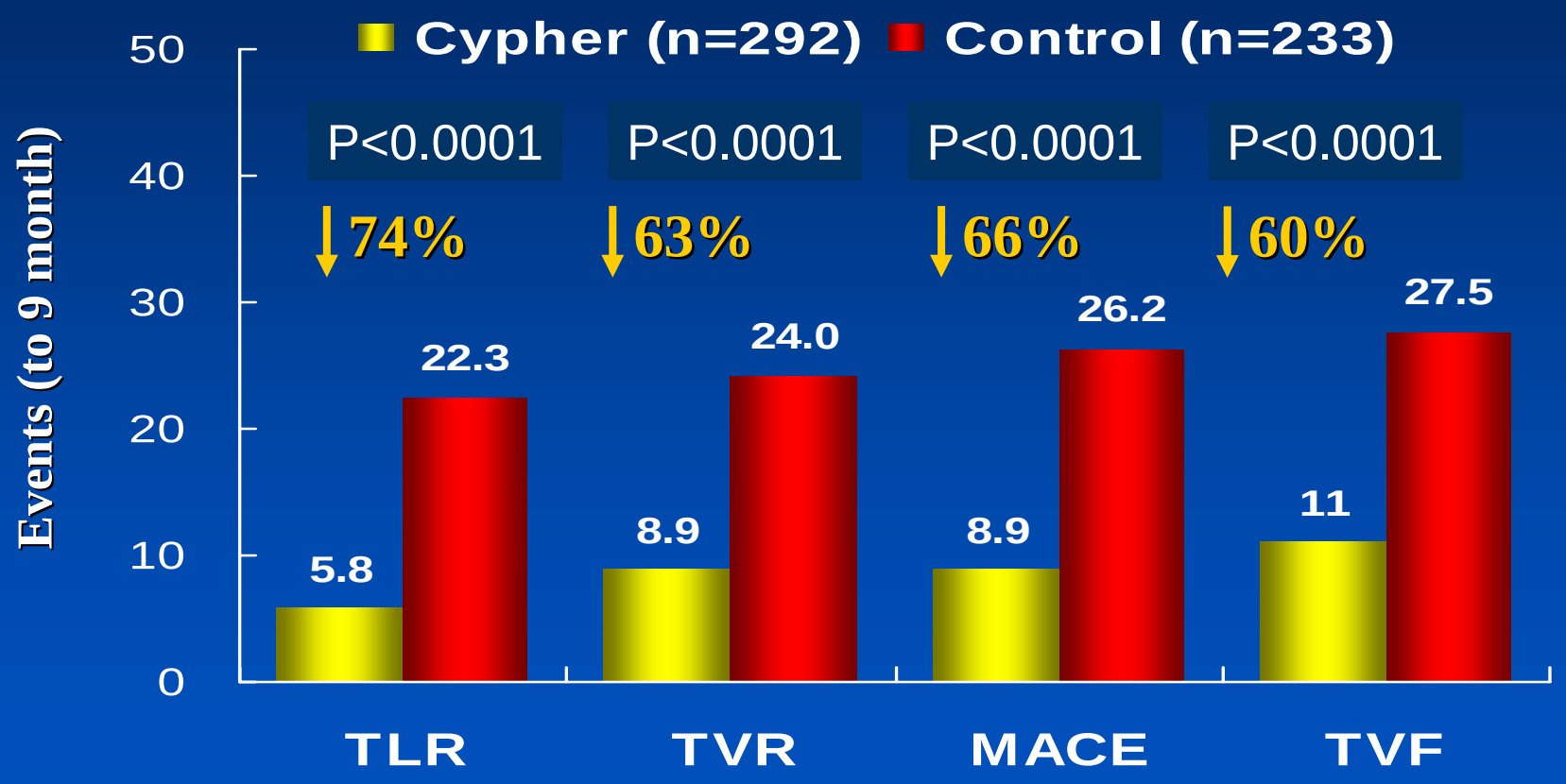
TLR



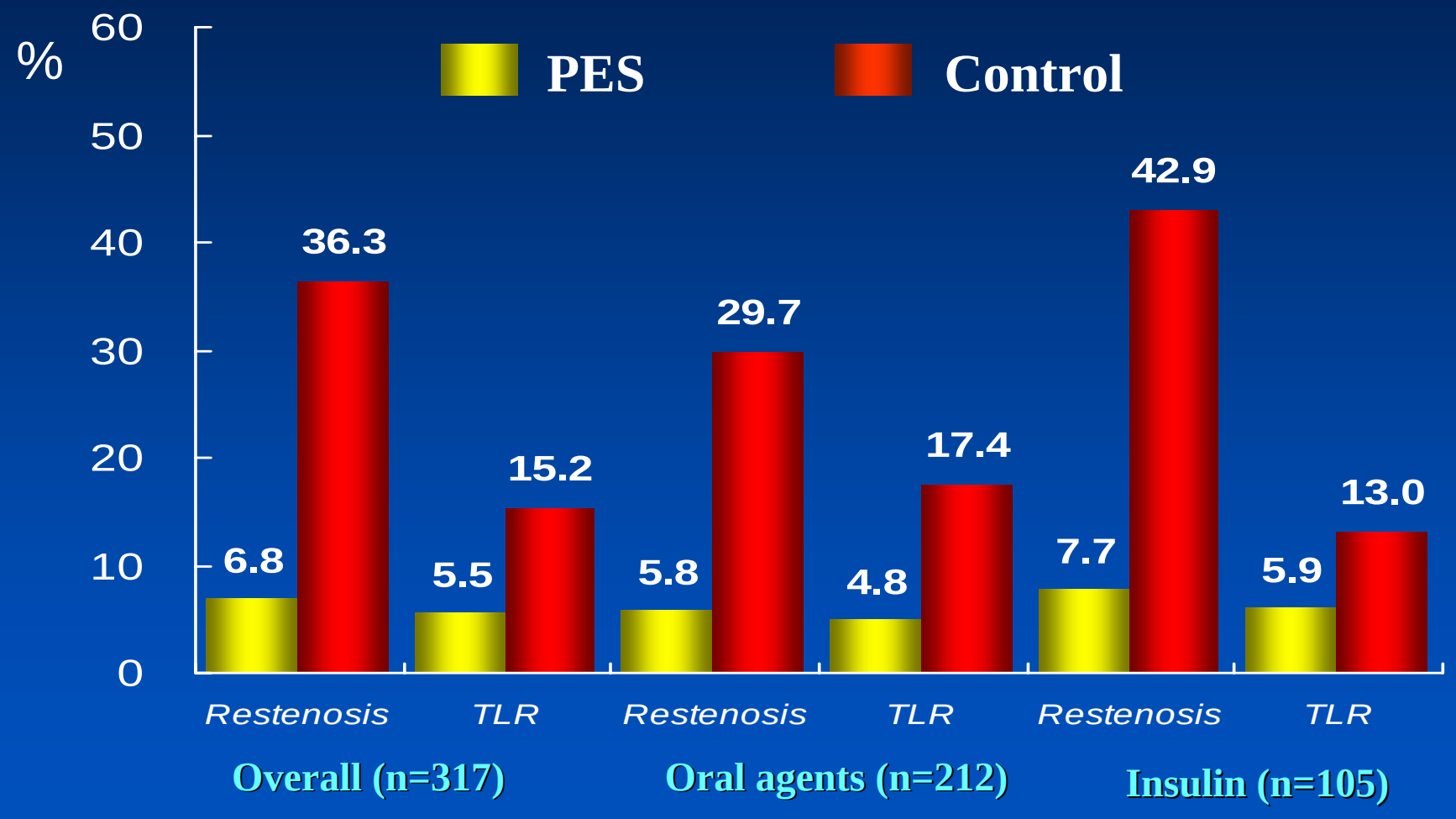
* Pooled data from the E- & C-SIRIUS trials

CYPHER Trials Meta-Analysis in Diabetes

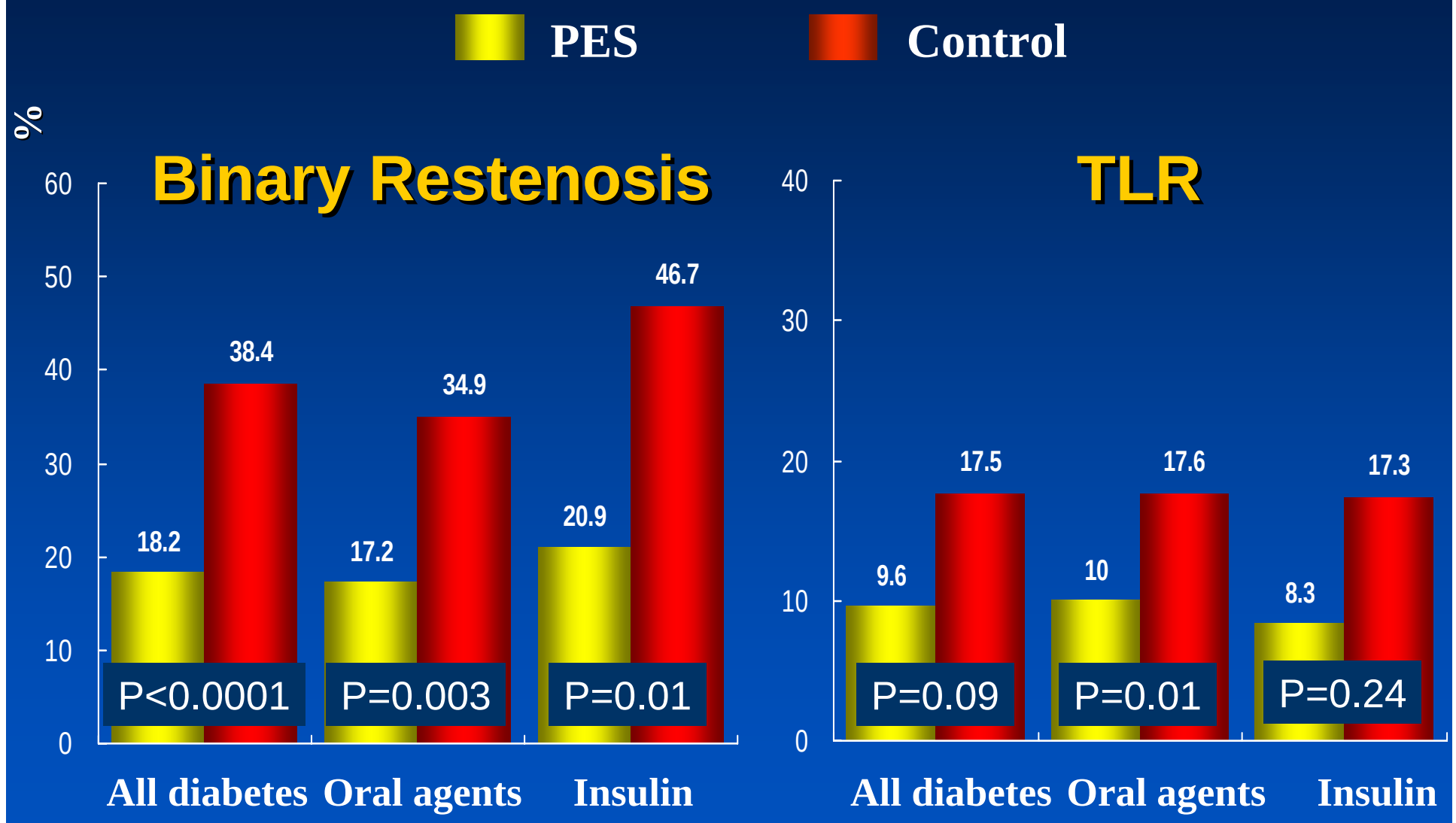
RAVEL, SIRIUS, E-SIRIUS, C-SIRIUS, DIRECT, SVELTE



TAXUS IV-Diabetes



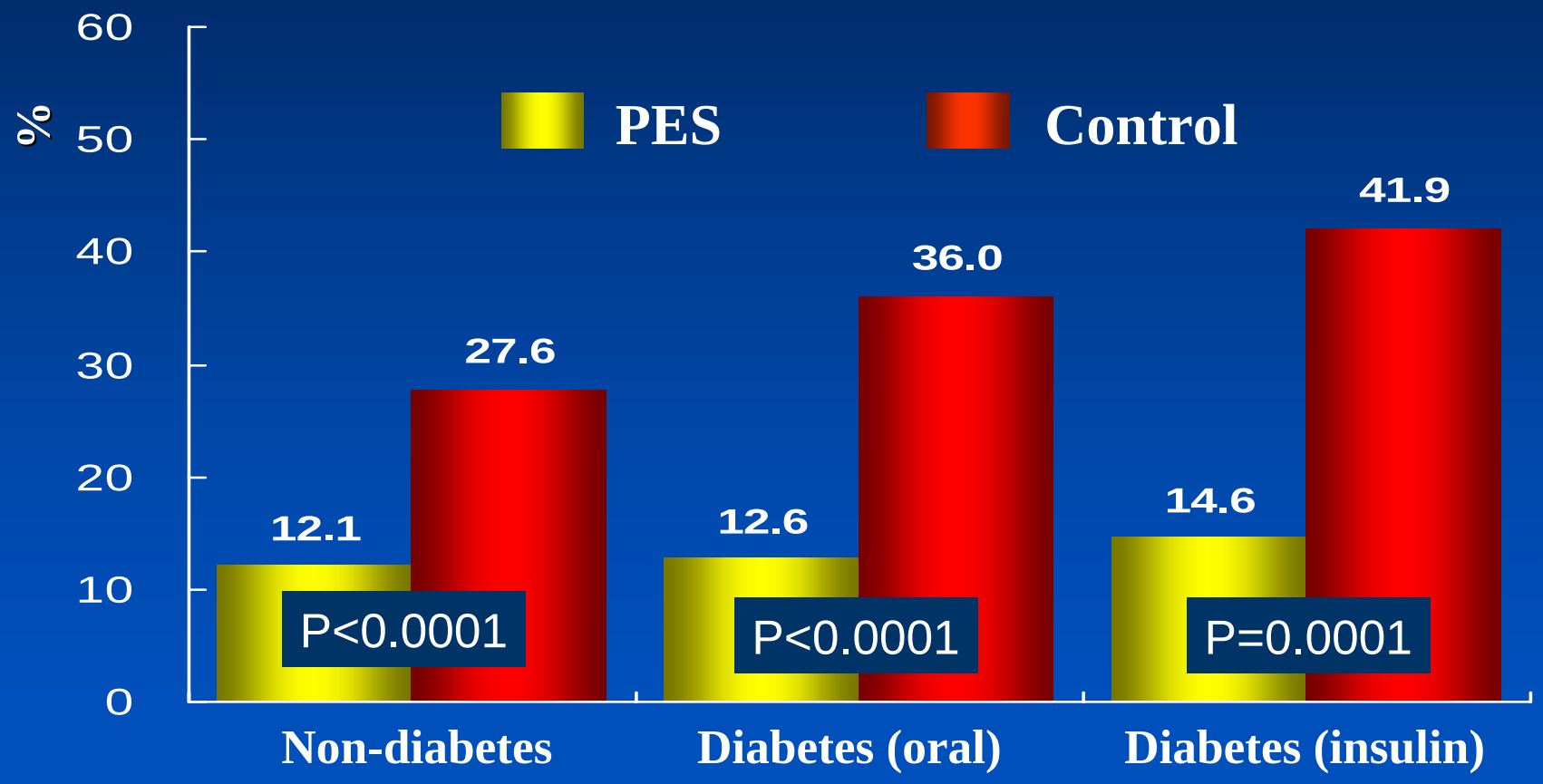
TAXUS V-Diabetes



TAXUS Trials Meta-Analysis in Diabetes

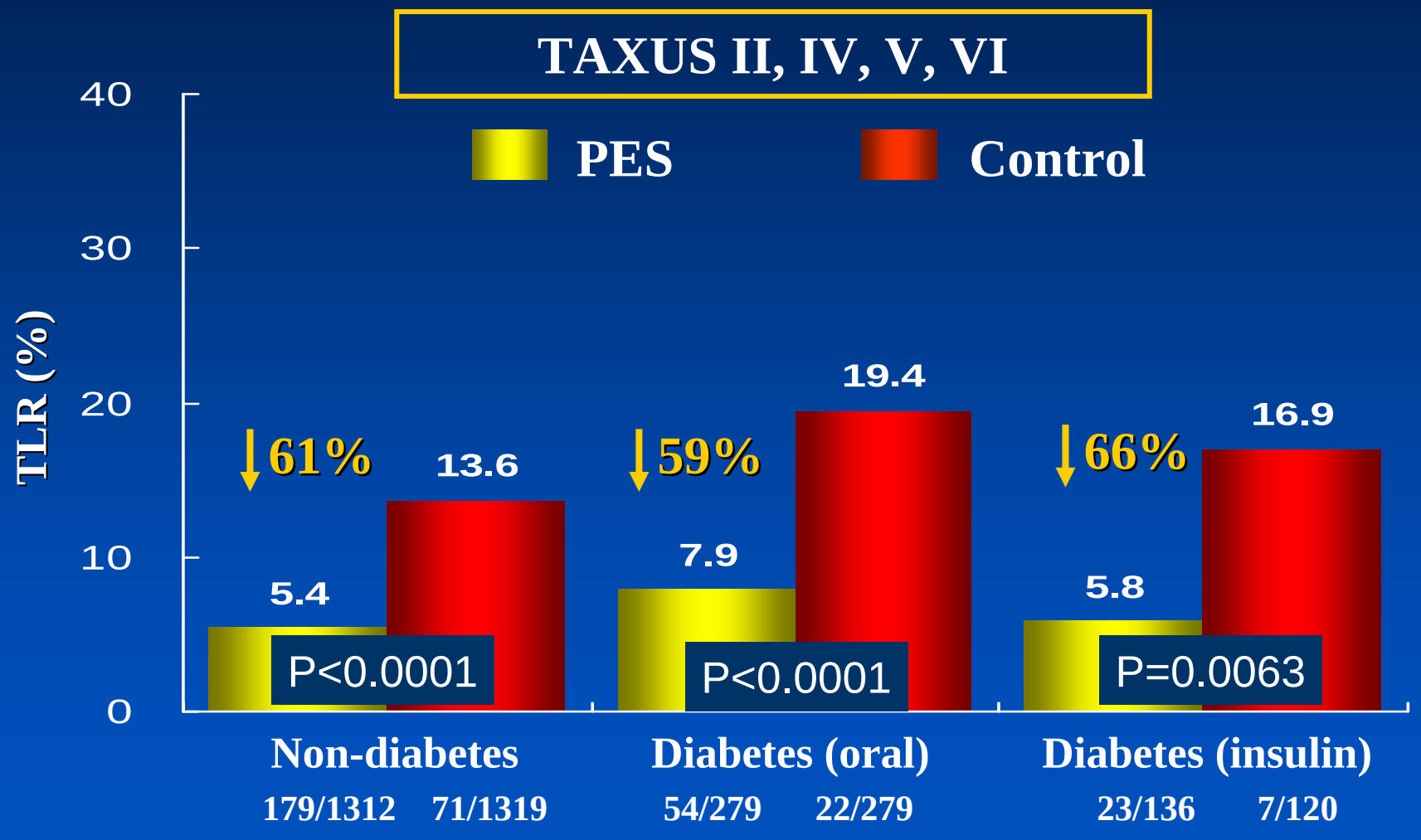
Binary Restenosis

TAXUS II, IV, V, VI



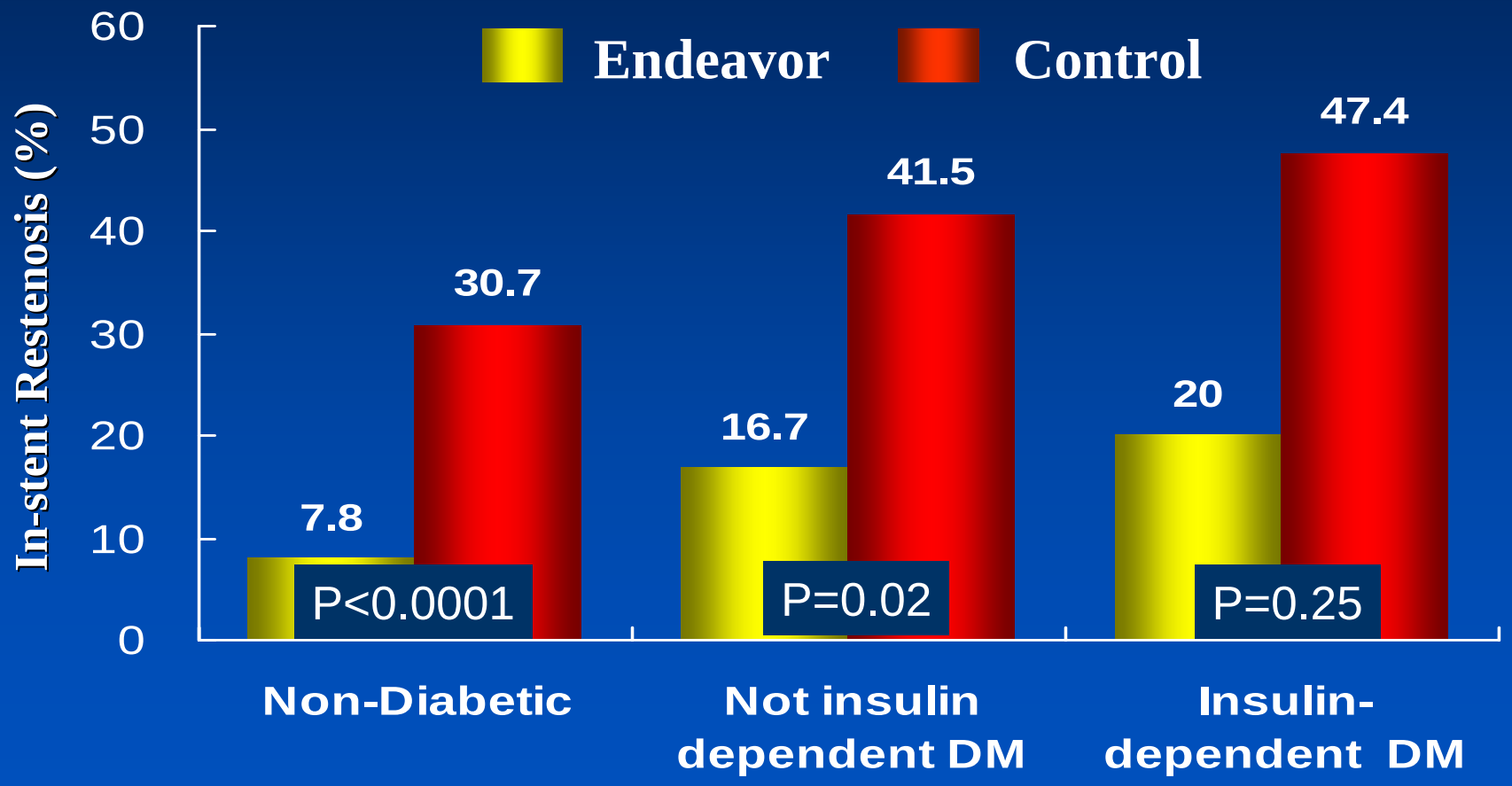
TAXUS Trials Meta-Analysis in Diabetes

Target lesion revascularization



ENDEAVOR II-Diabetes

Binary Restenosis

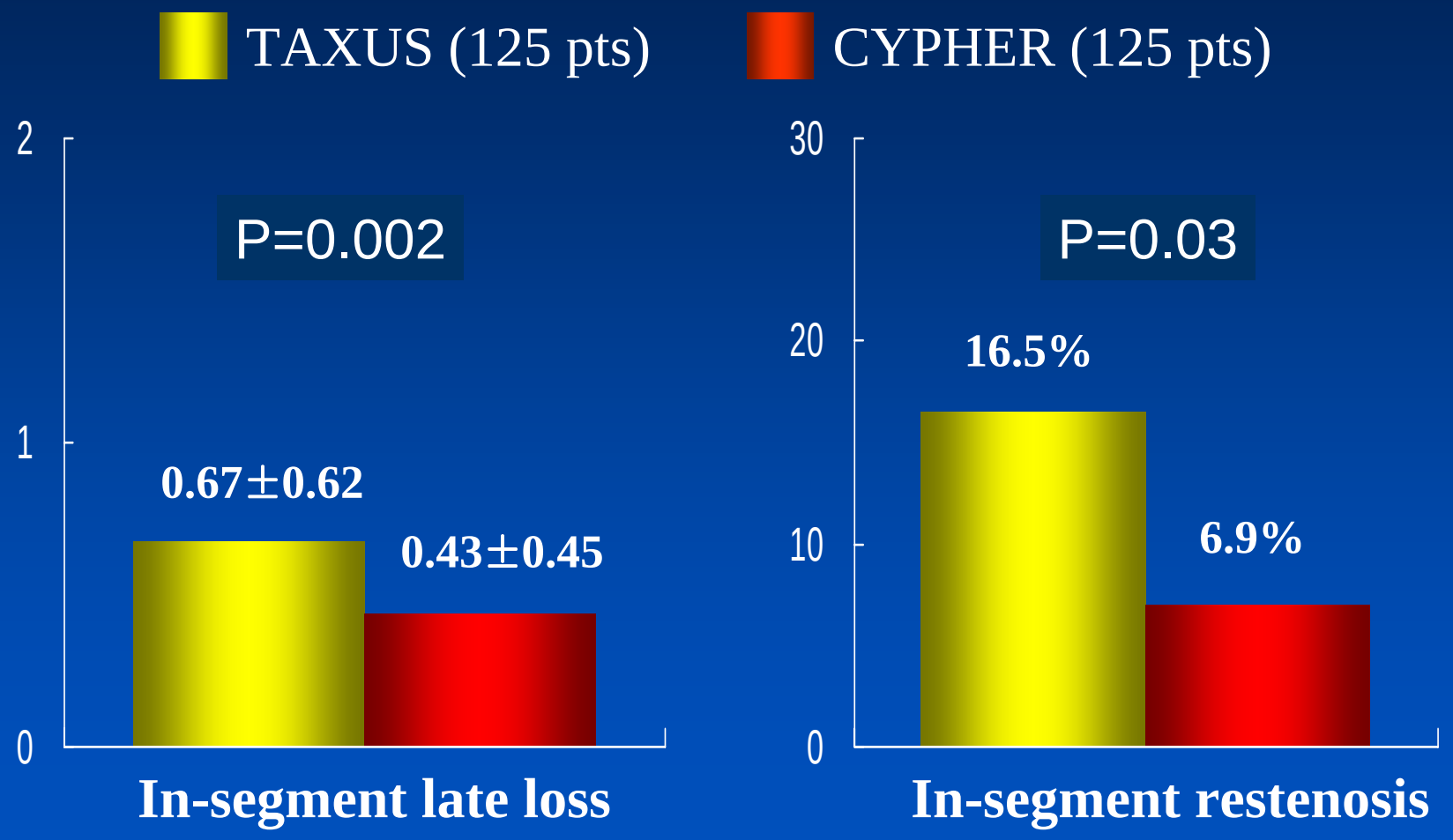


Fajadet J et al. Circulation 2006;114:798-806

Which DES is better in diabetic patients?

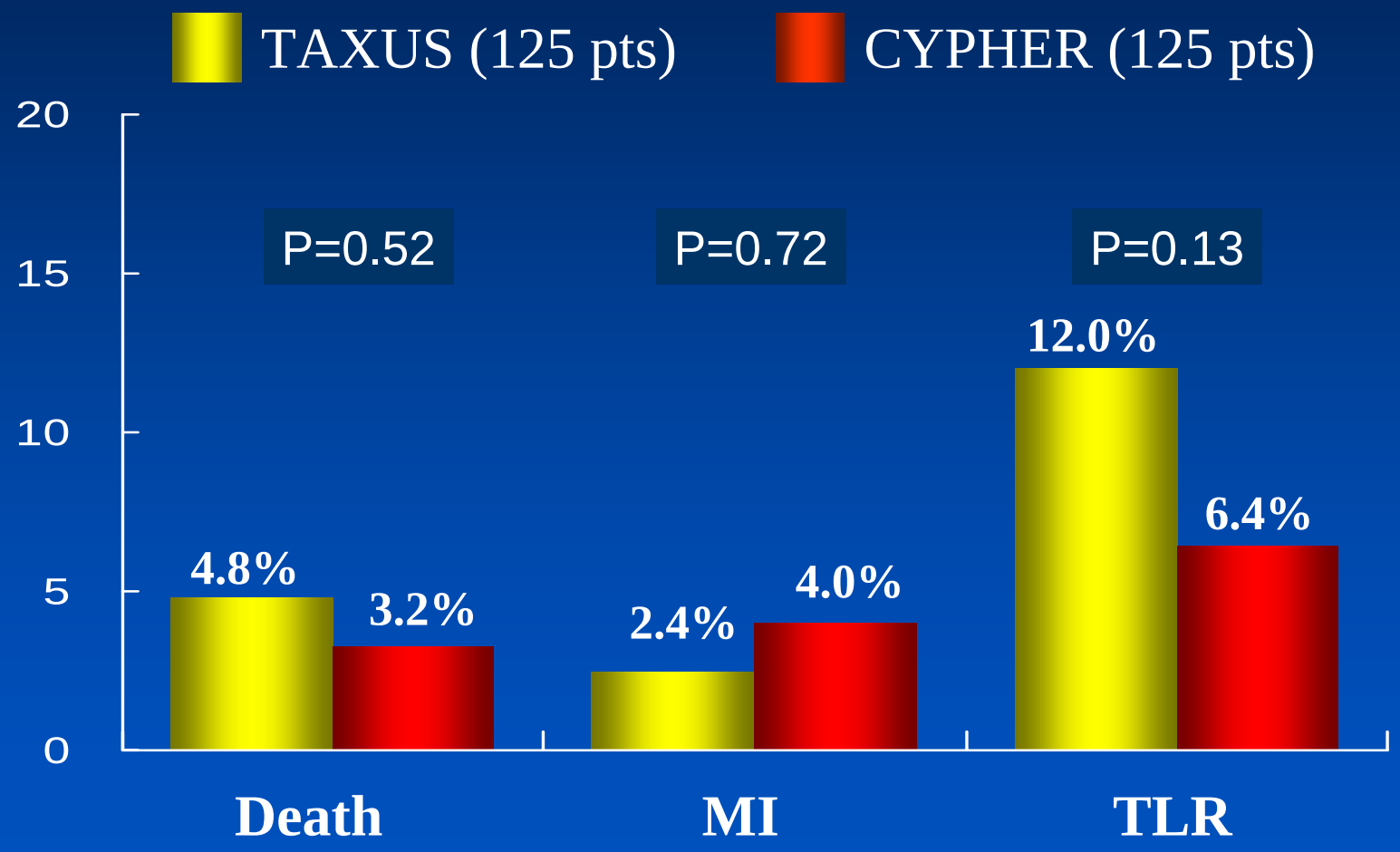
SES vs. PES in diabetes

ISAR-Diabetes



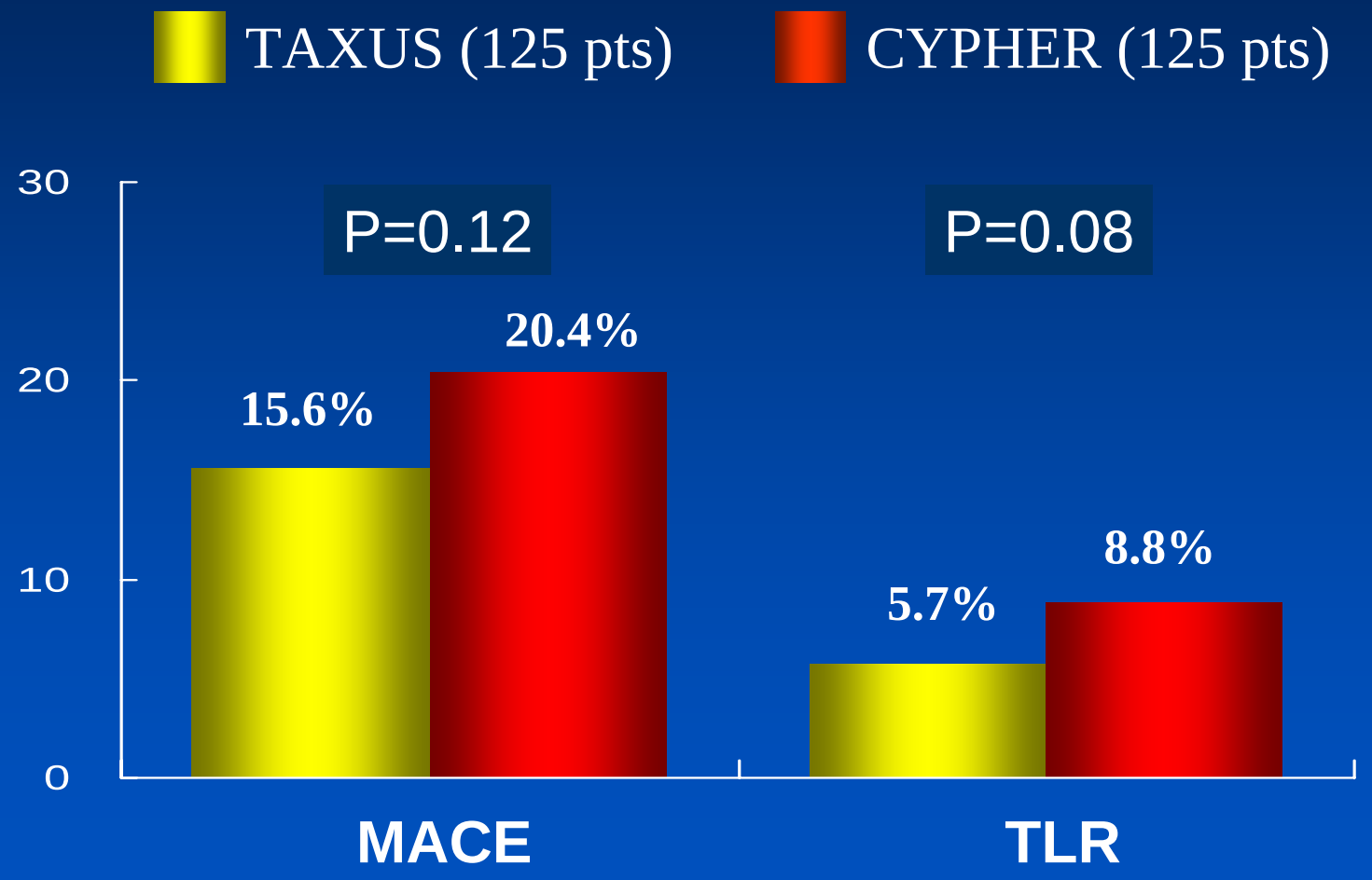
Kastrati et al., NEJM 2005;353:663-70

ISAR-Diabetes



Kastrati et al., NEJM 2005;353:663-70

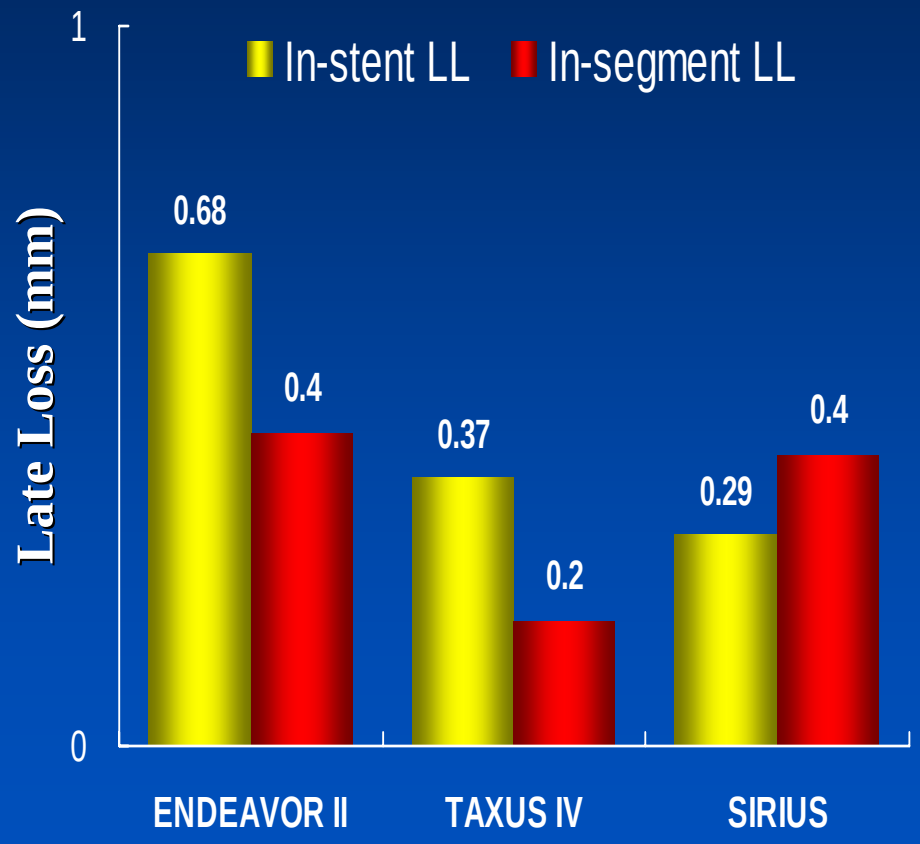
RESEARCH/T-SEARCH-Diabetes

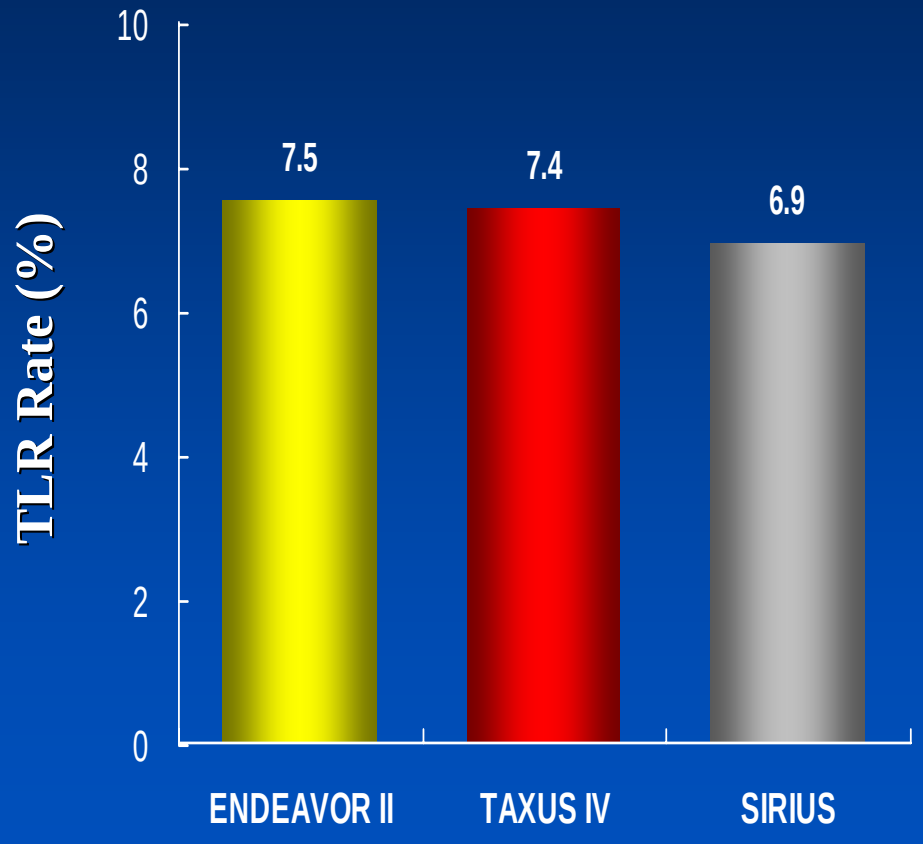


Ong AT et al., Am J Cardiol 2005;96:358-62

Comparison of DES Trials-Diabetes

ENDEAVOR II, TAXUS IV, SIRIUS





*Clinical results are not suitable for multiple comparison

Impact of Diabetes on DES efficacy

DM versus. Non-DM

Impact of Diabetes Mellitus on Angiographic and Clinical Outcomes in the Drug-Eluting Stents Era

AMC Experience

Overall 786 patients treated with DES

DM vs. Non-DM

T-H Yang, et al. Am J Cardiol *2005;96:1389-1392*

Baseline Characteristics

	DM (n=226)	No DM (n=560)	*p*
Age (yrs)	61.3±9.8	60.9±10.4	0.74
Men	160 (71%)	408 (73%)	0.56
Hypertension	129 (57%)	281 (50%)	0.11
Smoking	56 (25%)	175 (31%)	0.08
Previous MI	52 (23%)	114 (20%)	0.41
Previous PCI	60 (27%)	130 (23%)	0.36
Previous bypass surgery	9 (4%)	19 (3%)	0.69
Multi-vessel disease	154 (68%)	327 (58%)	0.01
LVEF (%)	57±10	59±10	0.21

T-H Yang, et al. Am J Cardiol *2005;96:1389-1392*

Baseline Characteristics

	DM (n=299)	No DM (n=705)	*p*
Lesion location			0.62
Left main	28 (9%)	69 (10%)	
LAD	141 (47%)	334 (47%)	
LCX	51 (17%)	97 (14%)	
RCA	77 (26%)	195 (28%)	
Ostial lesion	13 (4%)	39 (6%)	0.44
Bifurcation lesion	56 (19%)	149 (21%)	0.39
CTO	12 (4%)	42 (6%)	0.21
Type B2/C	222 (74%)	477 (68%)	0.18

T-H Yang, et al. Am J Cardiol *2005;96:1389-1392*

Procedural Findings

	DM (n=299)	No DM (n=705)	*p*
Use of sirolimus-eluting stent	208 (70%)	490 (70%)	0.99
Stent length (mm)	32.5±19.1	29.2±15.6	<0.01
Use of GP IIb/IIIa inhibitor	18 (8%)	58 (10%)	0.35

T-H Yang, et al. Am J Cardiol *2005;96:1389-1392*

QCA: pre- & post-procedure

	DM (n=299)	No DM (n=705)	*p*
Lesion length (mm)	26.6±15.6	23.4±13.2	<0.01
Reference diameter (mm)	2.86±0.49	2.97±0.49	<0.01
MLD (mm)			
Pre-procedure	0.93±0.49	0.95±0.54	0.65
Post-procedure	2.77±0.49	2.88±0.48	<0.01
Diameter stenosis (%)			
Pre-procedure	67.5±15.4	68.2±17.2	0.59
Post-procedure	2.2±13.9	2.1±13.5	0.89

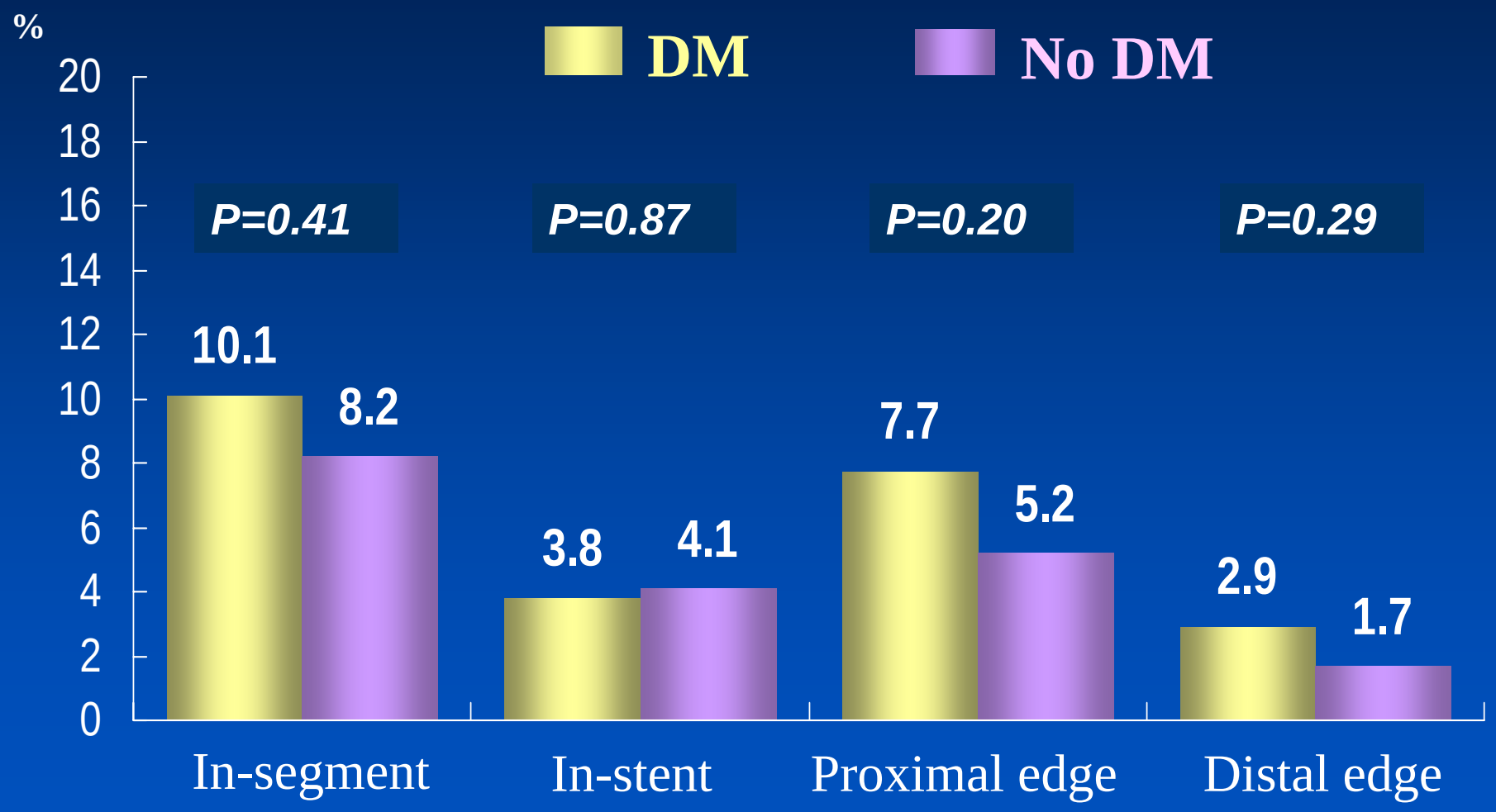
T-H Yang, et al. Am J Cardiol *2005;96:1389-1392*

QCA at Follow-up

	DM (n=299)	No DM (n=705)	*p*
Patients	159 (70.4%)	428 (76.4%)	0.09
MLD	2.40±0.75	2.53±0.74	0.04
Diameter stenosis	9.9±28.0	10.3±23.7	0.87
Late loss (mm)	0.41±0.63	0.36±0.65	0.31
Loss index	0.23±0.38	0.18±0.37	0.11

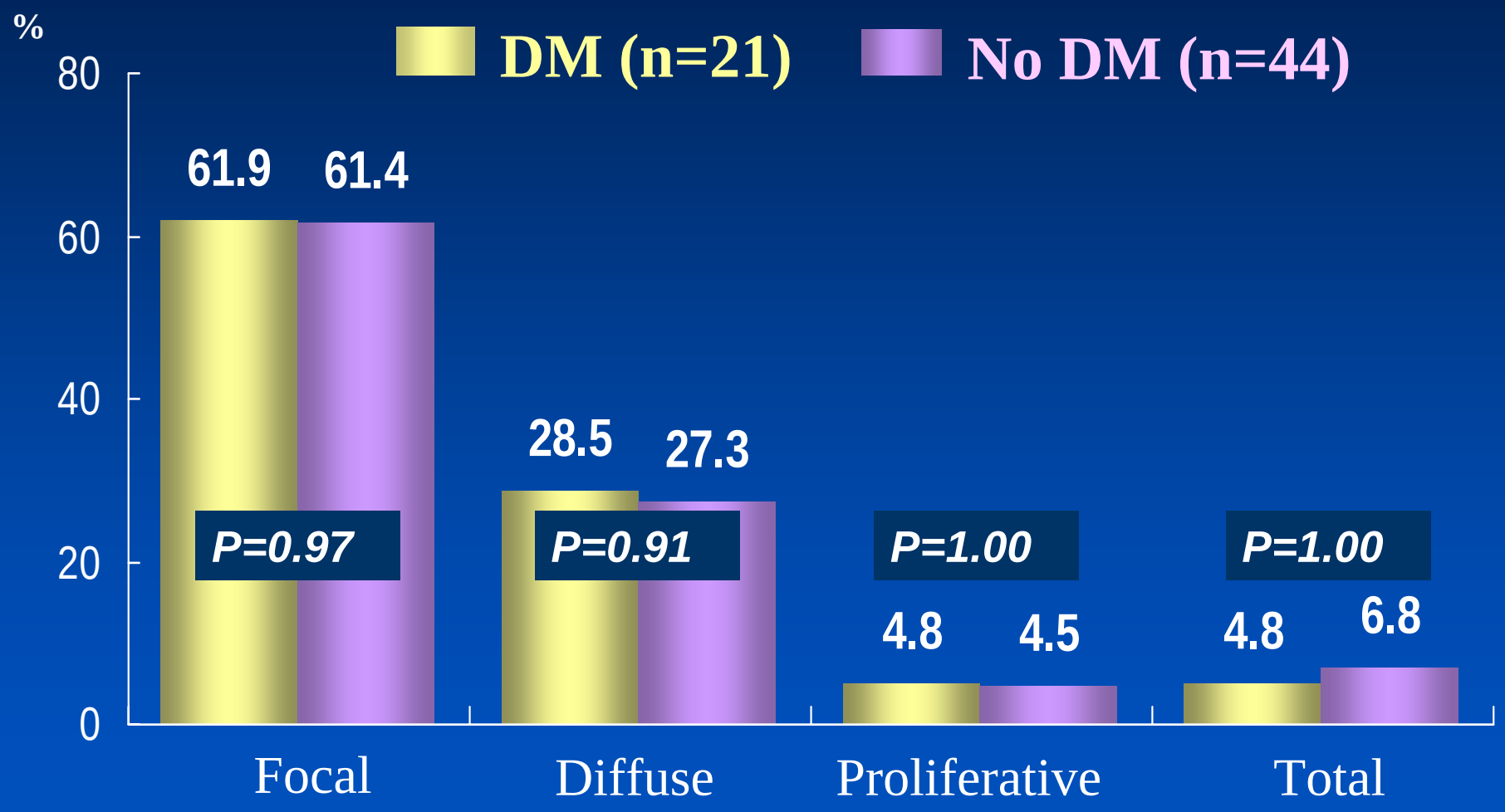
T-H Yang, et al. Am J Cardiol *2005;96:1389-1392*

Angiographic Restenosis



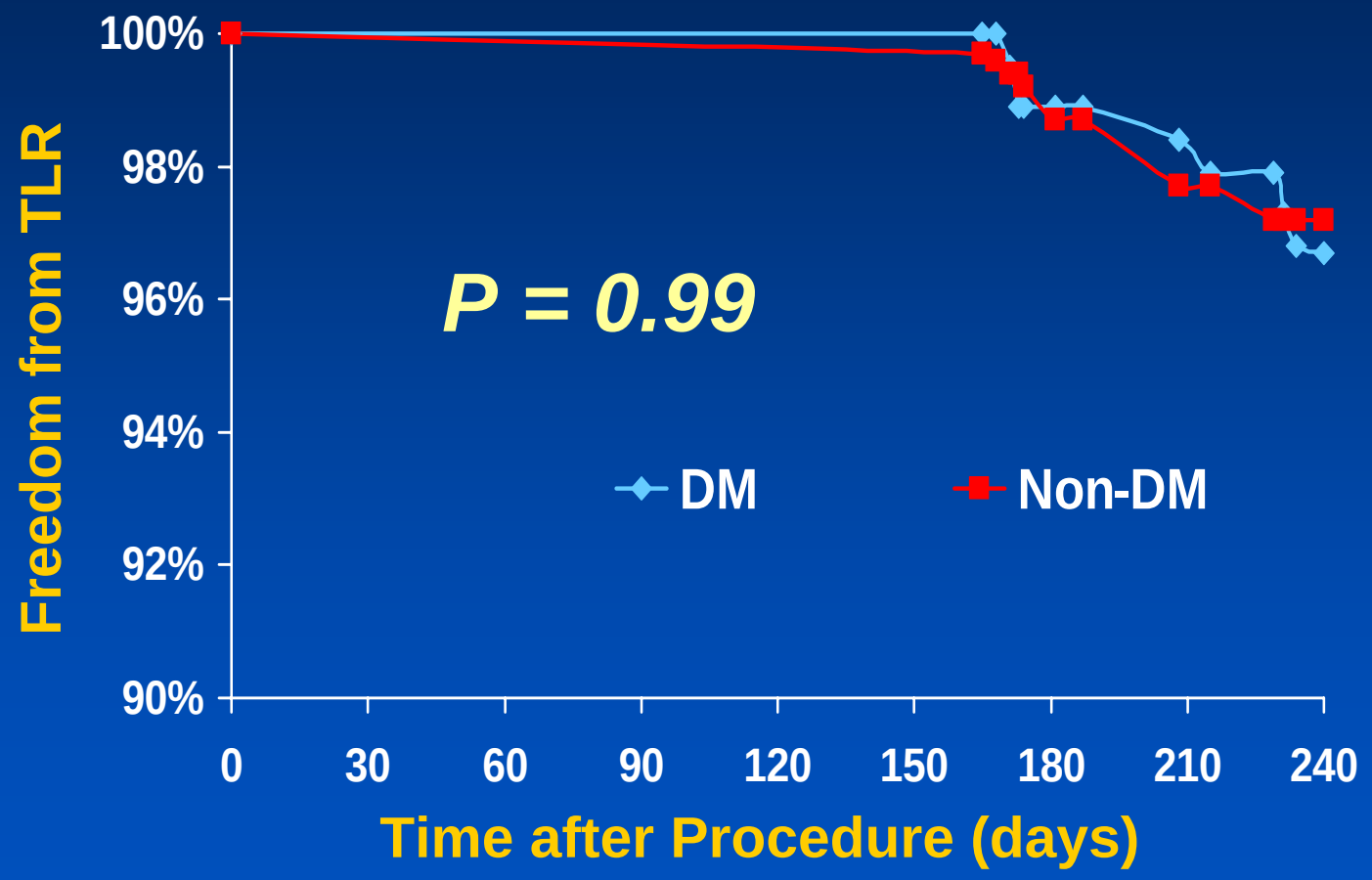
T-H Yang, et al. Am J Cardiol *2005;96:1389-1392*

Restenotic Pattern



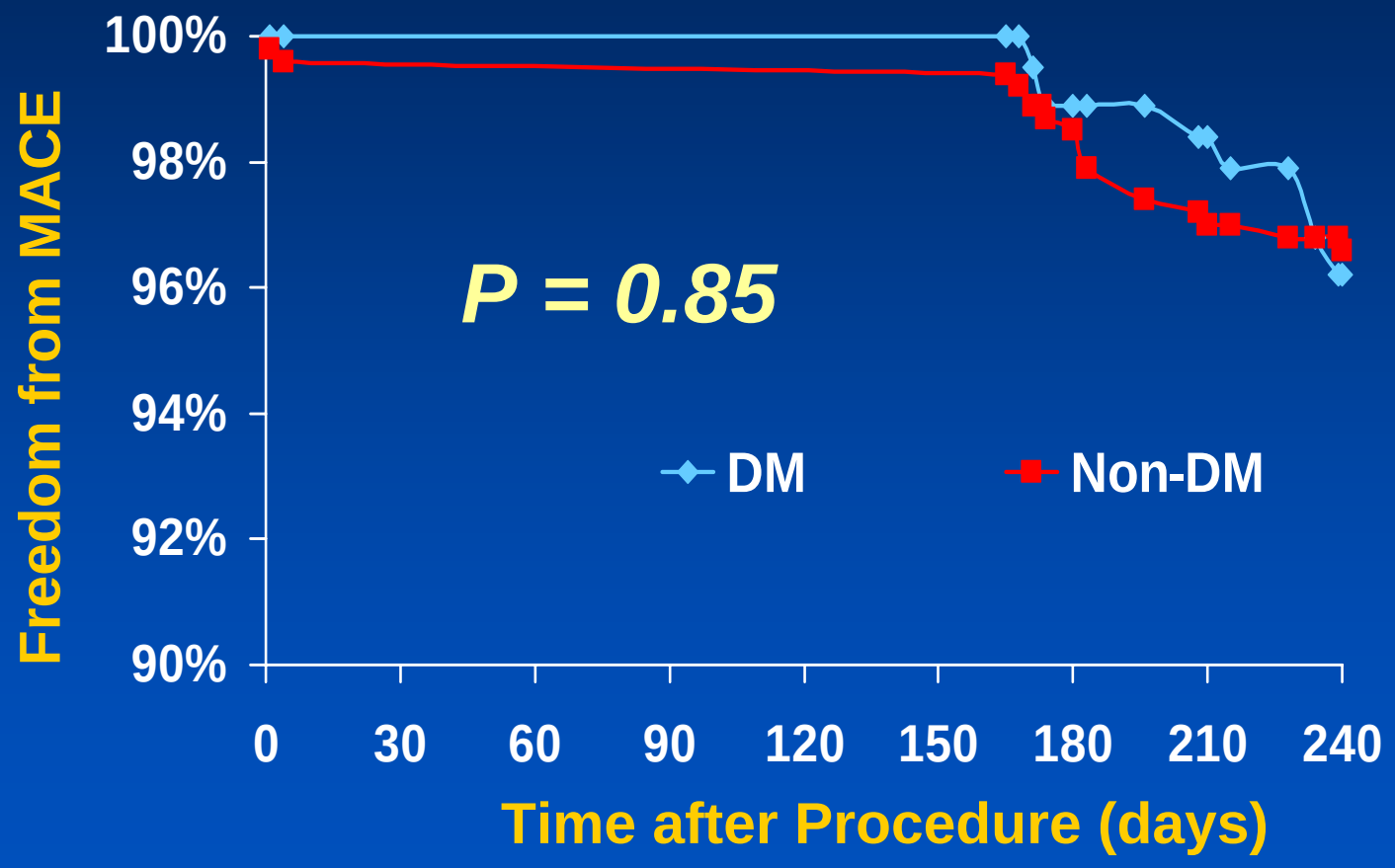
T-H Yang, et al. Am J Cardiol *2005;96:1389-1392*

Event-free survival at 9 months:
Target lesion revascularization



T-H Yang, et al. Am J Cardiol *2005;96:1389-1392*

Event-free survival at 9 months:
MACE (death, MI, TLR)



T-H Yang, et al. Am J Cardiol *2005;96:1389-1392*

Case-control study

DM vs. Non-DM treated with DES

Matched-pair analysis

DM and non-DM (n=384 lesions)

Stratifying for reference vessel, MLD, lesion length

DM
(113 patients, 192 lesions)

Non-DM
(182 patients, 192 lesions)

Primary endpoint: binary restenosis at 5-month follow-up

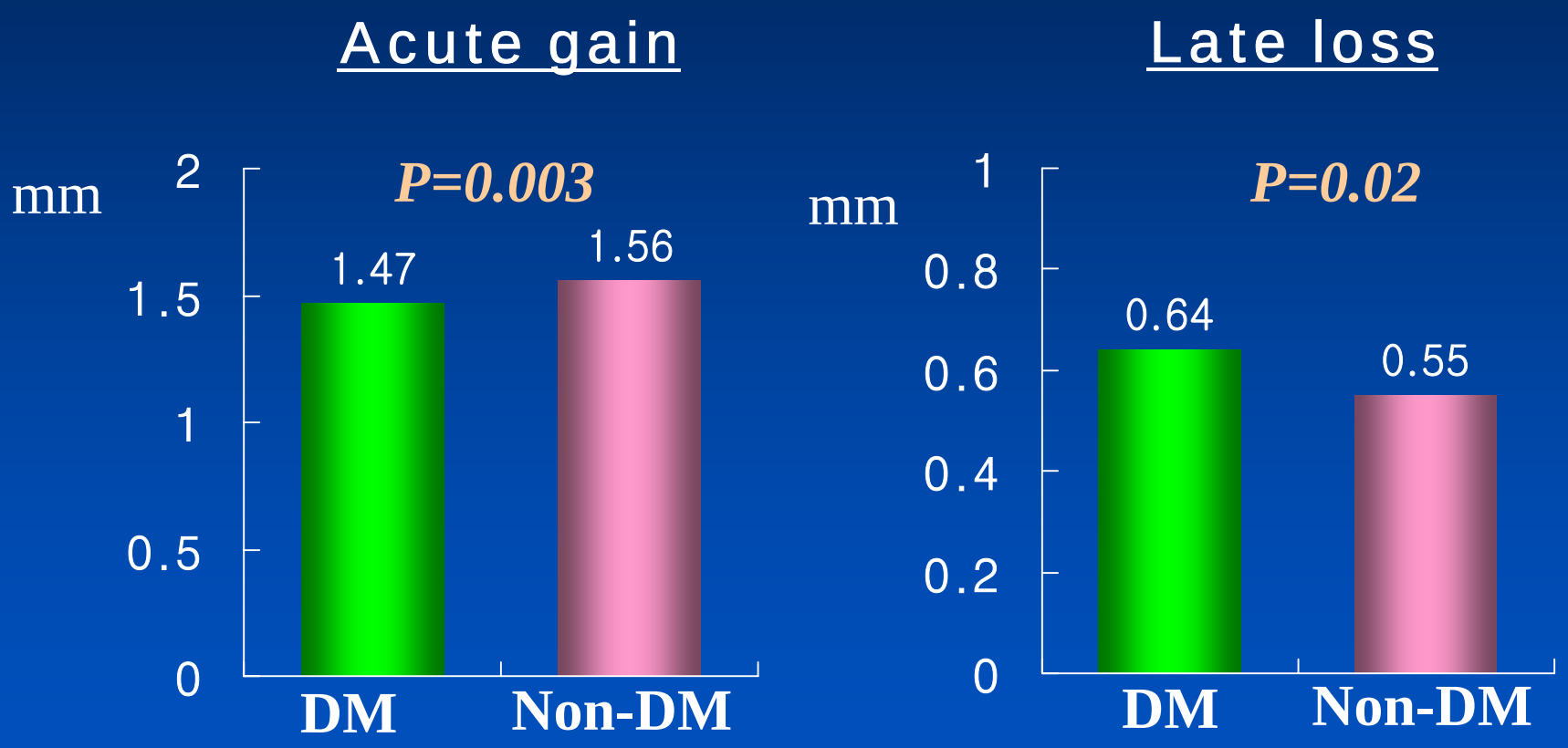
Radke PW, et al. Am J Cardiol 2006;98:1218-1222

Case-control study

DM vs. non-DM

QCA findings

Smaller acute gain and higher late loss in DM group

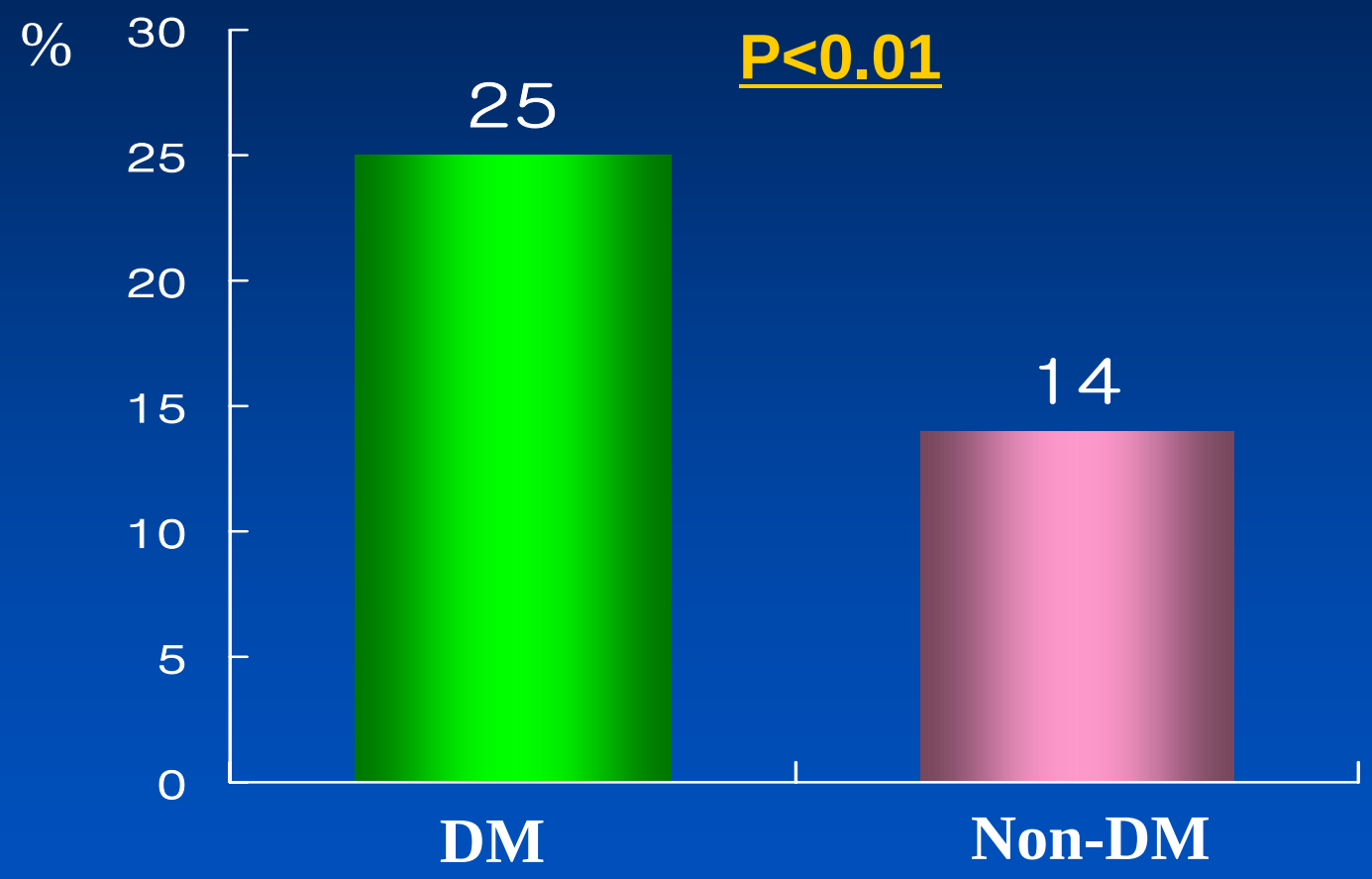


Radke PW, et al. Am J Cardiol 2006;98:1218-1222

Case-control study

DM vs. non-DM

Restenosis rate at 5 months



Radke PW, et al. Am J Cardiol 2006;98:1218-1222

DM vs. Non-DM treated with SES

Prospective registry

DM and non-DM (n=1,407 patients)

April 2003 to August 2004 consecutive patients

DM (496 patients)	Non-DM (915 patients)

-To evaluate the outcomes of IDDM (n=160) patients and NIDDM (n=332) patients with non-DM patients treated SESs
-To examine whether the reported reduction in the revascularization rate affect overall MACE in the diabetics

Kuchulakanti P, et al. Am J Cardiol 2005;96:1100-1106

Procedural and in-hospital outcomes

	DM (n=496)	No DM (n=915)	*p*
IABP	7(1.5%)	4 (0.4%)	0.04
Death	2 (0.4%)	0	0.05
Acute renal failure	14 (2.9%)	8 (0.9%)	0.004
Myocardial infarction			
Q-wave	0	3 (0.3%)	0.20
Non-Q wave	44 (9%)	96(11%)	0.27

Kuchulakanti P, et al. Am J Cardiol 2005;96:1100-1106

6-Month follow-up outcomes

	DM (n=360)	No DM (n=673)	*p*
Death	14(4%)	15(2%)	0.12
Myocardial infarction			
Q-wave	10 (3%)	6 (1%)	0.02
Non-Q wave	41 (11%)	84 (13%)	0.61
Death/Q-MI	21(6%)	18 (3%)	0.01
TLR/MACE	21 (6%)	18(3%)	0.01
TVR/MACE	28(8%)	41(6%)	0.29

Kuchulakanti P, et al. Am J Cardiol 2005;96:1100-1106

Percutaneous Treatment of *LONG* native Coronary Lesions with *D*rug-*E*luting *S*tent-*II*: Cypher versus Taxus in patients with diabetes

Long-DES II Trial

(Diabetes Subgroup Analysis)

for the Long-DES II Study investigators

Study Design (Long-DES II)

Long coronary lesions (>25mm) requiring single or multiple DES (planned total stent length ≥32mm)

1:1 randomization

SES (250 patients)

PES (250 patients)

1:1 randomization

Triple antiplatelet*

Standard antiplatelet#

1:1 randomization

Triple antiplatelet

Standard antiplatelet

Angiographic and IVUS follow-up at 6 months
Clinical follow-up at 30 days and 9 months

* Triple antiplatelet : aspirin plus clopidogrel plus cilostazol for 6 months

Standard antiplatelet : aspirin plus clopidogrel for 6 months

Primary endpoint:

1. Comparison of SES or PES: binary in-segment restenosis at 6 months
2. Comparison of triple and standard antiplatelet: in-stent late loss at 6 months

Subgroup Analysis

Diabetes

Long coronary lesions (>25mm) requiring single or multiple DES (planned total stent length ≥32mm)

1:1 randomization

SES (250 patients) → SES (82 patients)

PES (250 patients) → PES (84 patients)

Baseline Characteristics

	SES (n=82)	PES (n=84)	*p*
Age (yrs)	61±9	61±8	0.522
Men	44 (53.7%)	40 (47.6%)	0.436
Hypertension	42 (51.2%)	53 (63.1%)	0.112
Smoking	20 (24.4%)	20 (23.8%)	0.958
Hypercholesterolemia (≥ 200mg/dL)	15 (18.3%)	26 (31.0%)	0.059
LVEF (%)	59±10	59±10	0.984

Baseline Characteristics

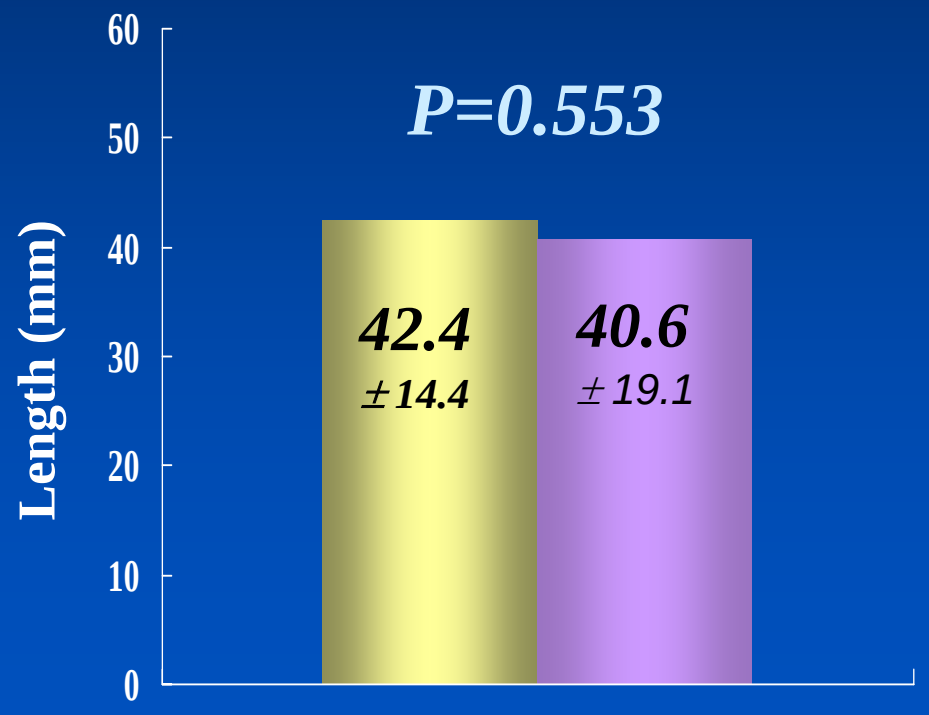
	SES (n=82)	PES (n=84)	*p*
Stented site			0.408
LAD	55 (67.1%)	53 (63.1%)	
LCX	8 (9.8%)	5 (6.0%)	
RCA	19 (23.2%)	26 (31.0%)	
Diagnosis			0.398
Stable angina	36 (43.9%)	33 (39.3%)	
Unstable angina	35 (42.7%)	33 (39.3%)	
AMI	11 (13.4%)	18 (21.4%)	

Procedural Findings

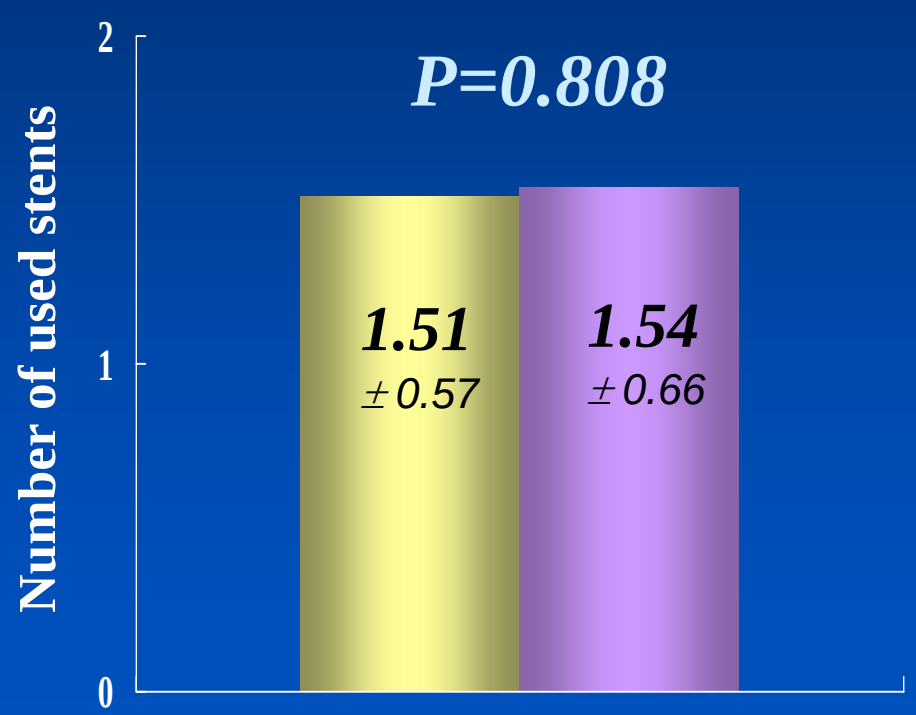
	SES (n=82)	PES (n=84)	*p*
Maximal device diameter (mm)	3.2±0.2	3.2±0.2	0.821
Maximal pressure (atm)	15.4±3.5	14.9±3.5	0.322
Use of IVUS	33 (40.2%)	30 (35.7%)	0.548
Use of GP IIb/IIIa inhibitor	0	3 (3.6%)	0.225

Length and No. of Used DESs

Length of stented segment



No. of stents per lesion



QCA before Procedure

	SES (n=82)	PES (n=84)	*p*
Proximal reference (mm)	3.13±0.40	3.08±0.44	0.485
Distal reference (mm)	2.36±0.39	2.45±0.36	0.156
Mean reference (mm)	2.73±0.40	2.76±0.42	0.694
Lesion length (mm)	33.9 ±11.3	35.1 ±12.0	0.536
MLD (mm)	0.73±0.45	0.75±0.44	0.768
Diameter stenosis (%)	72.0±15.2	71.4±15.3	0.789

QCA after Procedure

	SES (n=82)	PES (n=84)	*p*
Reference vessel (mm)	2.61±0.49	2.65±0.48	0.797
MLD (mm)			
In-stent	2.40±0.40	2.49±0.36	0.126
In-segment	2.10±0.43	2.17±0.47	0.330
Acute gain (mm)			
In-stent	1.66±0.49	1.74±0.51	0.368
In-segment	1.37±0.55	1.41±0.57	0.581
Diameter stenosis (%)			
In-stent	6.5±16.0	4.2±16.7	0.360
In-segment	16.4±12.3	15.3±12.0	0.570

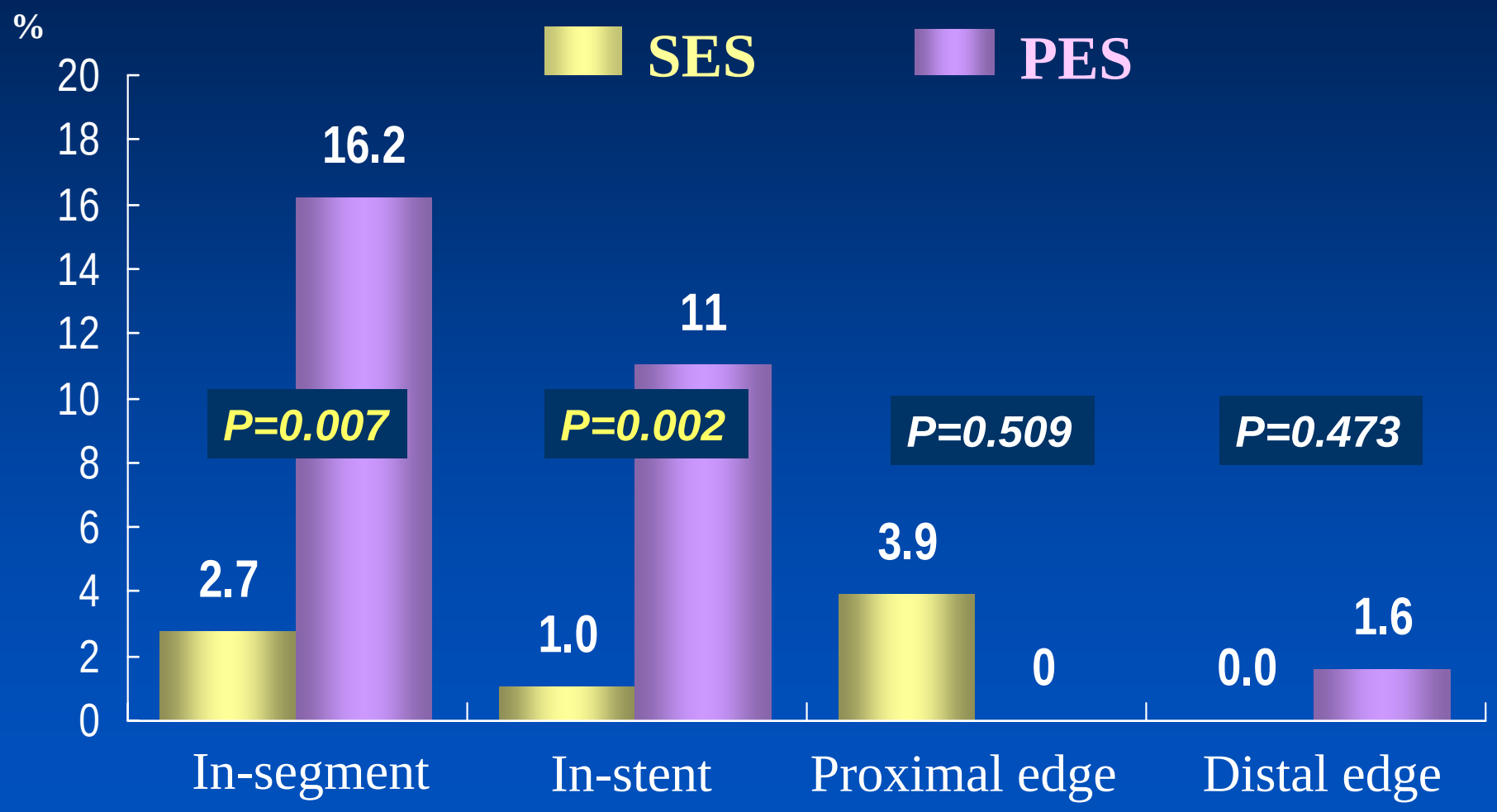
QCA at Follow-up

	SES (n=74)	PES (n=68)	*p*
Patients	74 (90.2%)	68(81%)	0.089
Reference vessel (mm)	2.71±0.46	2.66±0.49	0.577
MLD (mm)			
In-stent	2.30±0.44	1.83±0.65	<0.001
In-segment	2.10±0.45	1.67±0.55	<0.001
Diameter stenosis (%)			
In-stent	14.0±16.6	30.2±24.4	<0.001
In-segment	20.1±14.2	33.9±21.3	<0.001

QCA at Follow-up

	SES (n=74)	PES (n=68)	*p*
Late loss (mm)			
In-stent	0.08±0.34	0.60±0.54	<0.001
In-segment	0.24±0.37	0.75±0.54	<0.001
Loss index			
In-stent	0.04±0.22	0.34±0.34	<0.001
In-segment	0.21±0.41	0.66±0.74	<0.001

Angiographic Restenosis



Clinical Outcomes at 9 Months

	SES	PES	P
Patients	82	84	
Death	1(1.2%)	0	0.498
Cardiac	0	0	
Non-cardiac	1(1.2%)	0	
MI*	6 (7.3%)	10 (11.9%)	0.317
Stent thrombosis	0	0	1.0
TLR	1 (1.2%)	7 (8.3%)	0.064
TVR	2 (2.4%)	7 (8.3%)	0.168
MACE	8 (9.8%)	15 (17.9%)	0.131

* MI at post-procedural period (enzyme elevation > 3 times normal) and 9 months

How about impact of diabetes on long lesion treated with DES?

DM vs. Non DM

Long-DES II-Subgroup analysis

Baseline Characteristics

	DM (n=166)	Non DM (n=334)	*p*
Age (yrs)	61±9	61±9	0.888
Men	84 (50.6%)	237 (71.0%)	<0.001
Hypertension	95 (57.2%)	180 (54.1%)	0.502
Smoking	40 (32.3%)	99 (39.9%)	0.150
Hypercholesterolemia (≥ 200mg/dL)	41 (24.7%)	105 (31.5%)	0.059
LVEF (%)	59±10	58±9	0.558

Baseline Characteristics

	DM (n=166)	Non-DM (n=334)	*p*
Stented site			0.329
LAD	108 (65.1%)	199 (59.6%)	
LCX	13 (7.8%)	39 (11.7%)	
RCA	45 (27.1%)	96 (28.7%)	
Diagnosis			0.121
Stable angina	69 (41.6%)	158 (47.3%)	
Unstable angina	68 (41.0%)	108 (32.3%)	
AMI	29 (17.5%)	68 (20.4%)	

QCA before Procedure

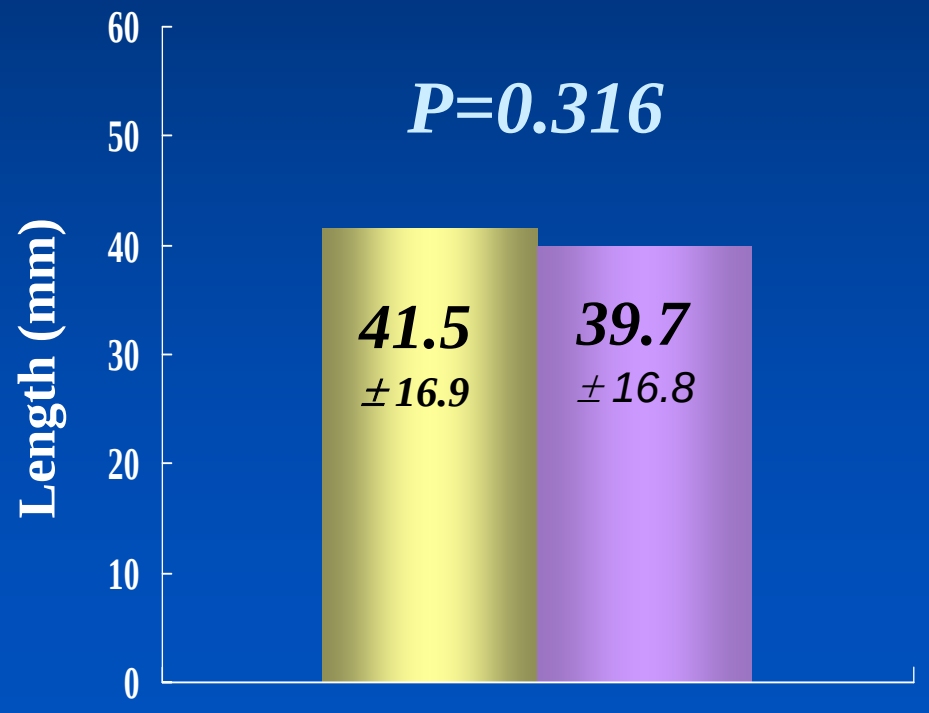
	DM (n=166)	Non-DM (n=334)	*p*
Proximal reference (mm)	3.11±0.42	3.16±0.54	0.369
Distal reference (mm)	2.41±0.38	2.53±0.51	0.014
Mean reference (mm)	2.74±0.41	2.87±0.49	0.006
Lesion length (mm)	34.5 ±11.6	33.9 ±12.4	0.620
MLD (mm)	0.74±0.44	0.67±0.49	0.164
Diameter stenosis (%)	71.7±15.3	74.4±16.7	0.086

Procedural Findings

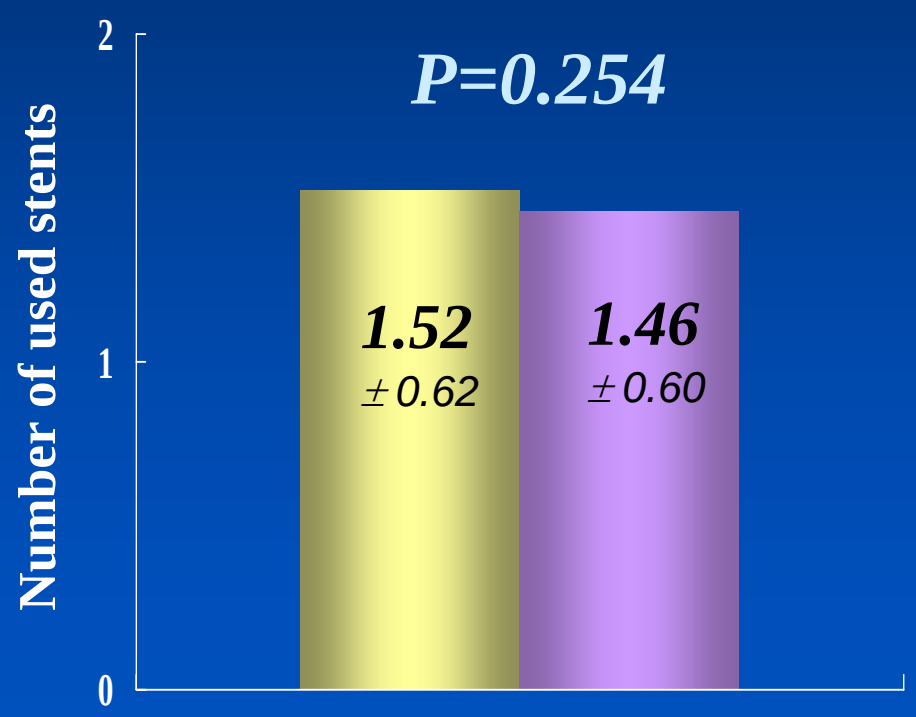
	DM (n=166)	Non-DM (n=334)	*p*
Maximal device diameter (mm)	3.2±0.3	3.2±0.3	0.680
Maximal pressure (atm)	15.2±3.5	15.7±3.4	0.097
Use of IVUS	63 (38.0%)	141 (42.2%)	0.361
Use of GP IIb/IIIa inhibitor	3(1.8%)	8 (2.4%)	0.884

Length and No. of Used DESs

Length of stented segment



No. of stents per lesion



QCA after Procedure

	DM (n=166)	Non-DM (n=334)	*p*
Reference vessel (mm)	2.63±0.48	2.74±0.52	0.034
MLD (mm)			
In-stent	2.44±0.38	2.51±0.38	0.074
In-segment	2.14±0.45	2.18±0.46	0.262
Acute gain (mm)			
In-stent	1.70±0.51	1.82±0.55	0.016
In-segment	1.39±0.56	1.50±0.62	0.059
Diameter stenosis (%)			
In-stent	5.4±16.4	6.4±16.1	0.522
In-segment	15.9±12.2	16.5±11.5	0.606

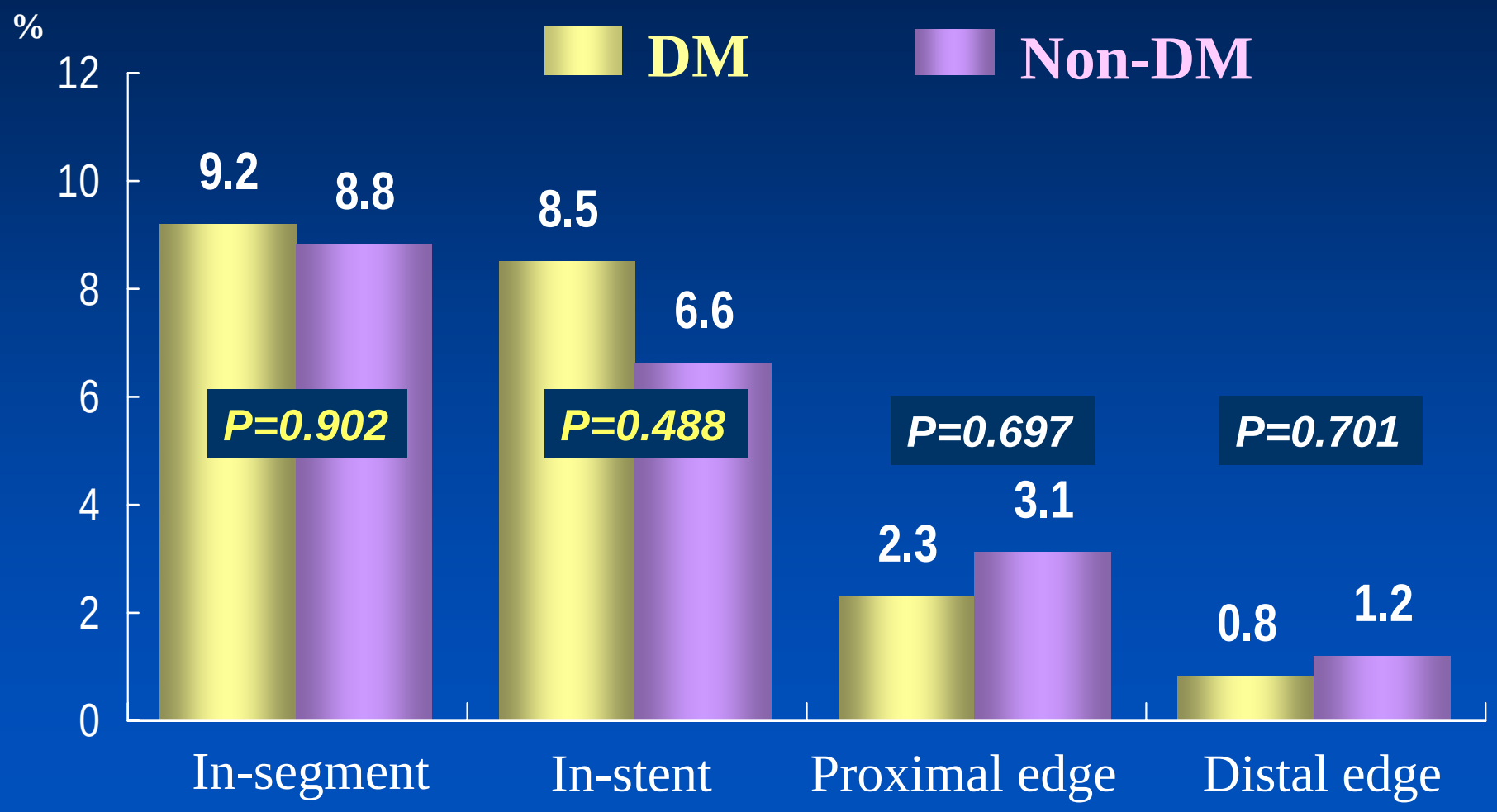
QCA at Follow-up

	DM (n=142)	Non-DM (n=273)	*p*
Patients	142 (85.5%)	273(81.7%)	0.286
Reference vessel (mm)	2.69±0.48	2.80±0.50	0.031
MLD (mm)			
In-stent	2.07±0.60	2.26±0.59	0.035
In-segment	1.89±0.54	2.05±0.57	0.004
Diameter stenosis (%)			
In-stent	21.8±22.2	18.3±22.3	0.132
In-segment	26.7±19.2	25.1±18.2	0.382

QCA at Follow-up

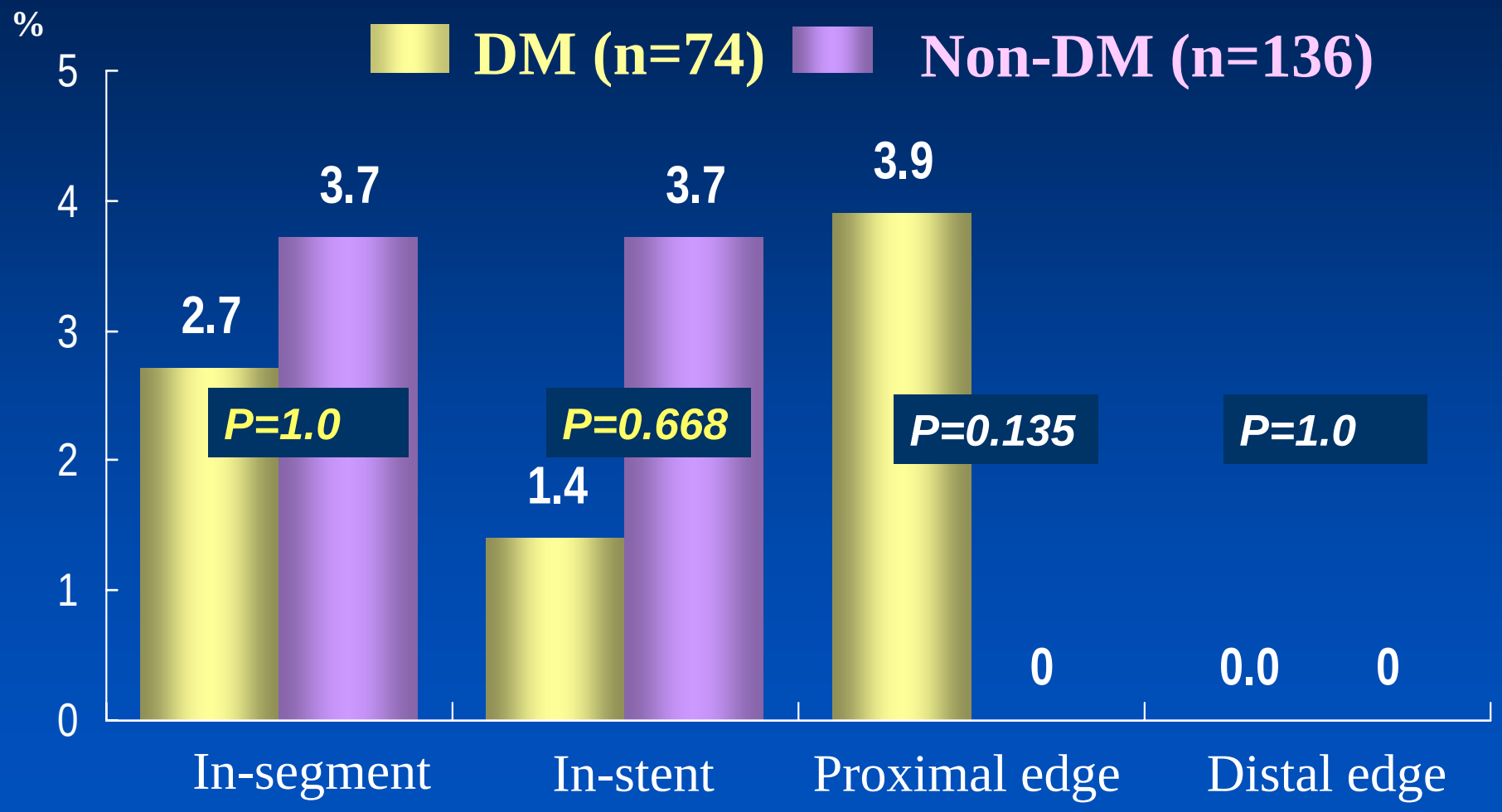
	DM (n=166)	Non-DM (n=334)	*p*
Late loss (mm)			
In-stent	0.33±0.52	0.23±0.48	0.072
In-segment	0.48±0.53	0.38±0.47	0.055
Loss index			
In-stent	0.18±0.32	0.13±0.31	0.128
In-segment	0.42±0.63	0.33±0.69	0.188

Angiographic Restenosis



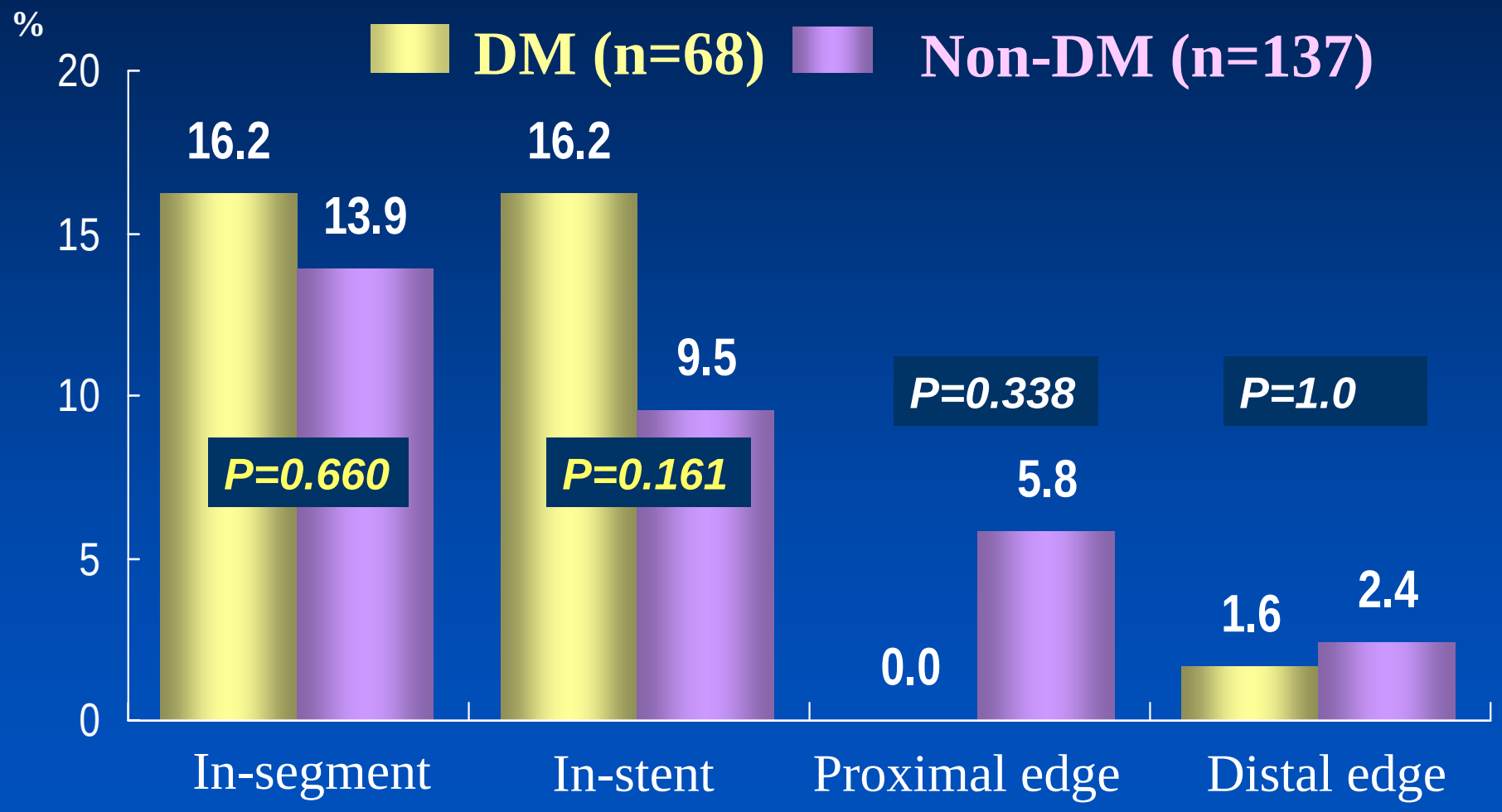
Angiographic Restenosis

In patients treated with SES



Angiographic Restenosis

In patients treated with PES



Clinical Outcomes at 9 Months

	DM	Non-DM	P
Patients	166	334	
Death	1(0.6%)	1(0.3%)	1.0
Cardiac	0	1(0.3%)	
Non-cardiac	1(1.2%)	0	
MI*	16 (9.6%)	33 (9.9%)	0.932
Stent thrombosis	0	2(0.6%)	1.0
TLR	8 (4.8%)	16 (4.8%)	0.989
TVR	9 (5.4%)	18 (5.4%)	0.988
MACE	23 (13.9%)	47 (14.1%)	0.948

* MI at post-procedural period (enzyme elevation > 3 times normal) and 9 months

Summary

- Compared to PES, SES appears to be more effective in inhibiting neointimal hyperplasia and result in a reduced risk of the angiographic restenosis and the need of repeat revascularization in patients with **diabetes and long coronary lesions.**

Summary

- Compared to non-DM patients, DM patients has a relatively smaller vessel size and acute gain and larger late loss.
- Compared to non-DM patients, DM patients has similar 6-month angiographic and 9-month clinical results after DES implantation in long coronary lesions without regard to types of DES.