"Long DES"
Multicenter Prospective Registry Study for DES Implantation in Long Coronary Lesion

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Background

- Stenting of long coronary lesions has traditionally yield poor immediate and long-term results.

- However, we expect that the remarkable benefit of drug-eluting stent observed in recent clinical trials may extend to the long coronary lesions.

Objective

- The present study was performed to evaluate the safety and efficacy of the sirolimus eluting stent (Cypher® stent; Cordis) and paclitaxel-eluting stent (Taxus™ stent;Boston Scientific) for long coronary lesion.
- And the results were compared to a control group composed of patients with long coronary lesions treated with long bare metal stents in the same study period.

Investigating Centers (8 centers)

Principal investigator

Asan Medical Center,	*Seung-Jung Park*

Participating hospitals and investigators

Ajou University Medical Center,	*SJ Tahk*
Catholic University of Korea, St Mary's Hospital,	*KB Seung*
Korea University Kuro Hospital,	*DJ Oh*
Samsung Medical Center,	*HC Gwon*
Seoul National University Hospital,	*Lee MM, Koo BK*
Yonsei University Severance Hospital,	*YS Jang*
Yonsei University Wonju Christian Hospital,	*JH Yoon*

Inclusion Criteria

- *De novo* lesion
- Angiographic evidence by visual estimation
  - Lesion length ≥ 24mm
  - Reference diameter ≥ 2.5mm
  - Diameter stenosis ≥ 70%
- Total stent length treated ≥ 28mm

Exclusion Criteria

- Contraindication to antiplatelet agents
- Left main disease
- Grafted lesions
- In-stent restenosis
- Chronic total occlusion
- AMI within 48 hrs
- Left ventricular dysfunction (EF< 40%)
- An inability to follow the protocol

Three Study Arms

From March 2003 - to February 2004

De-novo Lesions
(≥ 24mm)

637 patients, 739 lesions

CYPHER (≥ 28mm)	TAXUS (≥ 28mm)	Bare Metal (≥ 28mm)
294 patients	166 patients	177 patients
344 lesions	194 lesions	201 lesions

Study End Points

Primary end point

Six-month in-segment restenosis rate

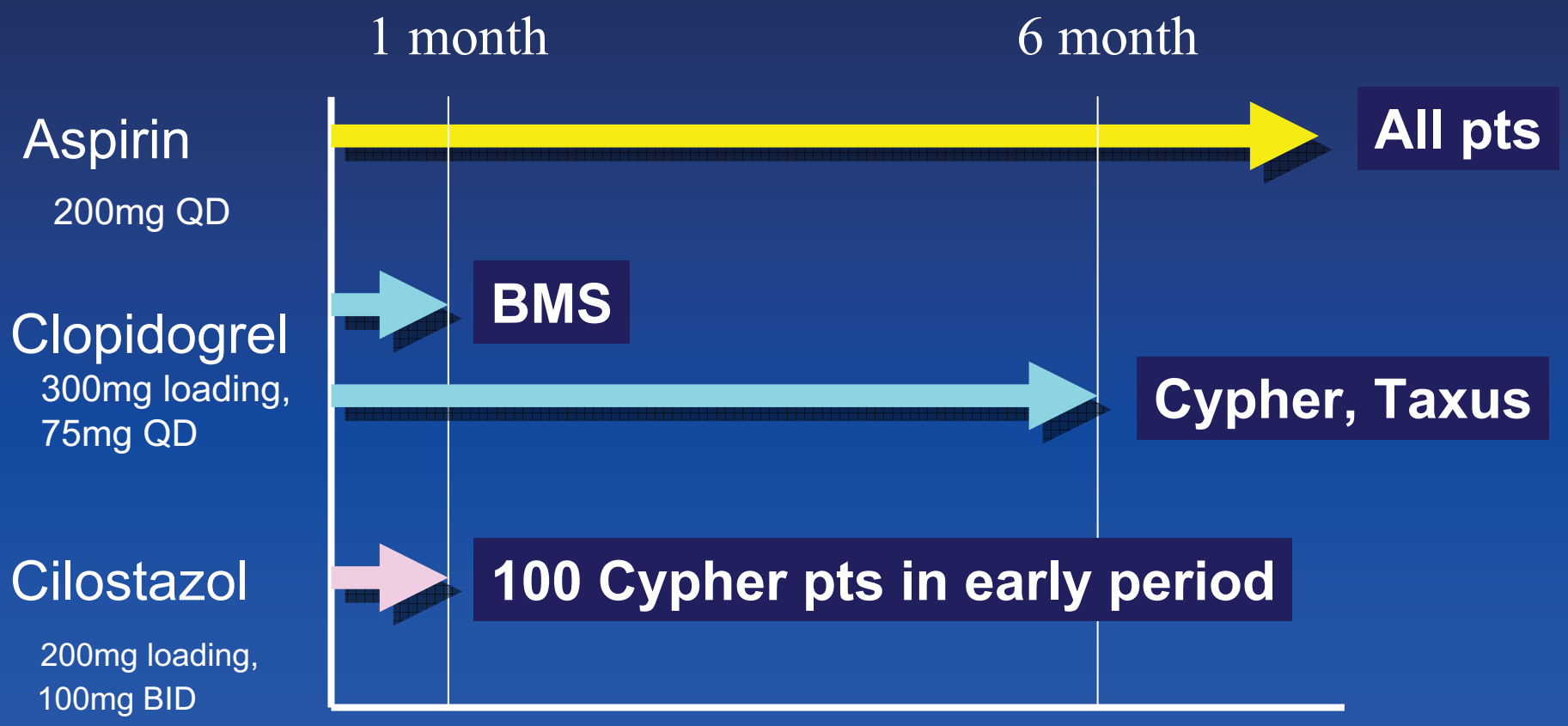
Secondary end points

1. In-segment late loss
2. Major adverse cardiac events including death, MI, or TLR

Follow Up

- Data were collected with a standardized case-report forms completed by the research coordinator at each site.
- All clinical events were monitored.
- Angiographic follow-up is being routinely performed at six months or earlier if a patient shows symptoms of recurrence.

Antiplatelet Regimens



Statistical Analysis

- Categorical variables are reported as value (%).
- Continuous variables are reported as mean±1SD.
- Comparison was performed with a Pearson's χ^2 test, unpaired *t* test, and standard ANOVA with post hoc comparisons using Bonferroni correction.

Baseline Demographics

	Cypher (n=294)	Taxus (n=166)	BMS (n=177)	P value
Age (years)	61.3±9.6	61.6±10.4	60.1±10.0	0.178
Man	206 (73)	115 (75)	136 (77)	0.662
Hypertension	168 (57)	93 (56)	97 (55)	0.863
Hypercholesterol ≥200mg/dL	83 (28)	52 (31)	61 (35%)	0.359
Diabetes mellitus	91 (31)	53 (32)	57 (32)	0.954
Smoking	83 (28) #	55 (31) **	88 (50)	**<0.001**

Between groups: * p<0.025 Cypher vs Taxus; # p<0.025 Cypher vs BMS;**, p<0.025 Taxus vs. BMS

Baseline Demographics

	Cypher (n=294)	Taxus (n=166)	BMS (n=177)	P value
LV EF (%)	58.7±9.1	59.4±9.6 **	56.6±9.6	**0.038**
Prior PCI	33 (11)	24 (15)	23 (13)	0.591
Prior CABG	4 (1)	6 (4) **	0 (0)	**0.025**
Clinical diagnosis				0.269
Stable angina	154 (52)	83 (50)	89 (50)	
Unstable angina	118 (40)	63 (38)	64 (36)	
Acute MI	22 (8)	20 (12)	24 (14)	
Multi-vessel disease	203 (69)	124 (75)	129 (73)	0.372

Between groups: * $p<0.025$ Cypher vs Taxus; # $p<0.025$ Cypher vs BMS;**, $p<0.025$ Taxus vs. BMS

Lesion Location

	Cypher (n=337)	Taxus (n=194)	BMS (n=201)	P value
Lesion location				0.005
LAD	201 (60) #	93 (48)	89 (44)	
LCX	46 (14)	31 (16)	41 (44)	
RCA	90 (27)	70 (36)	71 (35)	

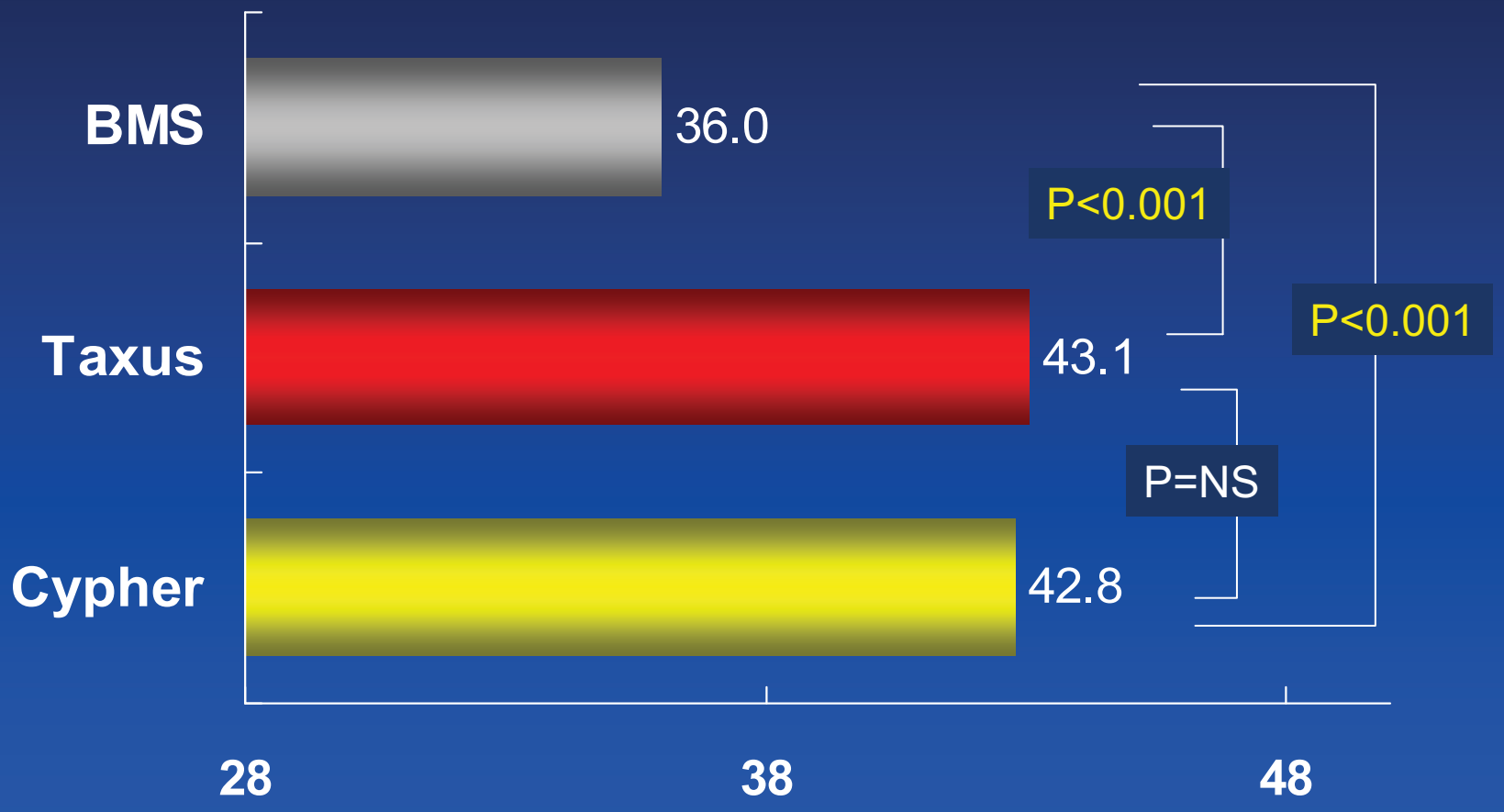
Between groups: * p<0.025 Cypher vs Taxus; # p<0.025 Cypher vs BMS;**, p<0.025 Taxus vs. BMS

Baseline QCA

	Cypher (n=337)	Taxus (n=194)	BMS (n=201)	P value
Reference, mm				
Proximal	3.01±0.49 #	3.10±0.49 **	3.27±0.55	<0.001
Distal	2.59±0.45 * #	2.71±0.53	2.84±0.57	<0.001
Mean	2.80±0.41 * #	2.90±0.48 **	3.10±0.54	<0.001
Lesion length, (mm)	35.3±14.3 #	36.3±14.5 **	32.0±12.3	0.004
MLD, (mm)	0.76±0.47	0.77±0.49	0.78±0.54	0.942
DS, %	72.5±16.6	73.6±16.2	74.4±17.0	0.450

Between groups: * p<0.025 Cypher vs Taxus; # p<0.025 Cypher vs BMS;**, p<0.025 Taxus vs. BMS

Total Stent Length Treated



Procedural Characteristics

	Cypher (n=337)	Taxus (n=194)	Control (n=201)	P value
Used stents	1.65±0.71 #	1.63±0.70 **	1.28±0.49	**<0.001**
Overlapping	179 (53) #	100 (52) **	52 (26)	**<0.001**
Maximal pressure, (atm)	16.0±3.6 * #	13.2±3.9 **	12.0±3.3	**<0.001**
Maximal device diameter, (mm)	3.35±0.37 *	3.40±0.41	3.47±0.52	**0.014**
IVUS guidance	266 (79) #	144 (74) **	96 (48)	**<0.001**
Use of Abciximab	8 (3)	2 (1)	7 (4)	0.266

Between groups: * p<0.025 Cypher vs Taxus; # p<0.025 Cypher vs BMS;**, p<0.025 Taxus vs. BMS

In-Hospital Outcomes

	Cypher (n=294)	Taxus (n=166)	Control (n=177)	P value
Angiographic success (%)	329 (98)	191 (99)	193 (96)	0.296
Death	0 (0)	0 (0)	1 (0.6)	0.422
MI				
Q wave	0 (0)	0 (0)	1 (0.6)	0.272
Non-Q wave	26 (8.8)	16 (9.6)	14 (7.9)	0.852
Stent thrombosis	0 (0)	0 (0)	1 (0.6)	0.272
TLR	0 (0)	0 (0)	1 (0.6)	0.272
MACE	26 (8.8)	16 (9.6)	15 (8.5)	0.928

Between groups: * $p<0.025$ Cypher vs Taxus; # $p<0.025$ Cypher vs BMS;**, $p<0.025$ Taxus vs. BMS

QCA After Procedure

	Cypher (n=337)	Taxus (n=194)	BMS (n=201)	P value
Reference, mm				
Proximal	3.08±0.48 #	3.15±0.50 **	3.31±0.55	**<0.001**
Distal	2.57±0.46 * #	2.70±0.52 **	2.84±0.53	**<0.001**
Mean	2.81±0.42 * #	2.92±0.46 **	3.09±0.50	**<0.001**
MLD, mm	2.69±0.43 * #	2.78±0.43 **	2.90±0.55	**<0.001**
DS, %	3.42±12.89	3.81±12.3	5.65±12.21	0.128
Acute gain, mm	1.93±0.60 #	2.01±0.57	2.12±0.67	**0.002**

Between groups: * p<0.025 Cypher vs Taxus; # p<0.025 Cypher vs BMS;**, p<0.025 Taxus vs. BMS

IVUS Data After Procedure

Angiographically normal reference vessels actually had about 40% plaque burden when seen by IVUS

	Cypher (n=166)	Taxus (n=76)	P value
Proximal reference			
EEM, mm^2	14.8±3.7	15.4±3.7	0.281
Lumen, mm^2	8.2±2.5	8.6±2.8	0.445
Plaque area, mm^2	6.6±2.2	6.9±2.3	0.358
Plaque burden, %	44.4±9.2	45.1±11.3	0.662
Distal reference			
EEM, mm^2	10.1±3.2	10.5±3.8	0.325
Lumen, mm^2	6.2±2.1	6.4±2.6	0.408
Plaque area, mm^2	3.9±1.8	4.1±1.6	0.437
Plaque burden, %	38.4±8.5	39.2±7.3	0.465

Stent CSA
after procedure

	Cypher (n=166)	Taxus (n=76)	P value
Worst lumen site			
EEM, mm^2	12.2±3.8	12.4±3.8	0.690
Stent, mm^2	5.9±1.6	6.3±2.0	0.181
Plaque area, mm^2	6.3±2.3	6.1±2.2	0.706
Plaque burden, %	50.5±6.6	49.2±6.7	0.159

Follow-Up Study

CYPHER	TAXUS	Bare Metal
294 pts, 344 les	166 pts, 194 les	177 pts, 201 les

Six-Month Angiographic Follow-Up

271 les (80.4%)	150 les (77.3%)	160 les (79.6%)

Seven-Month Clinical Follow-Up

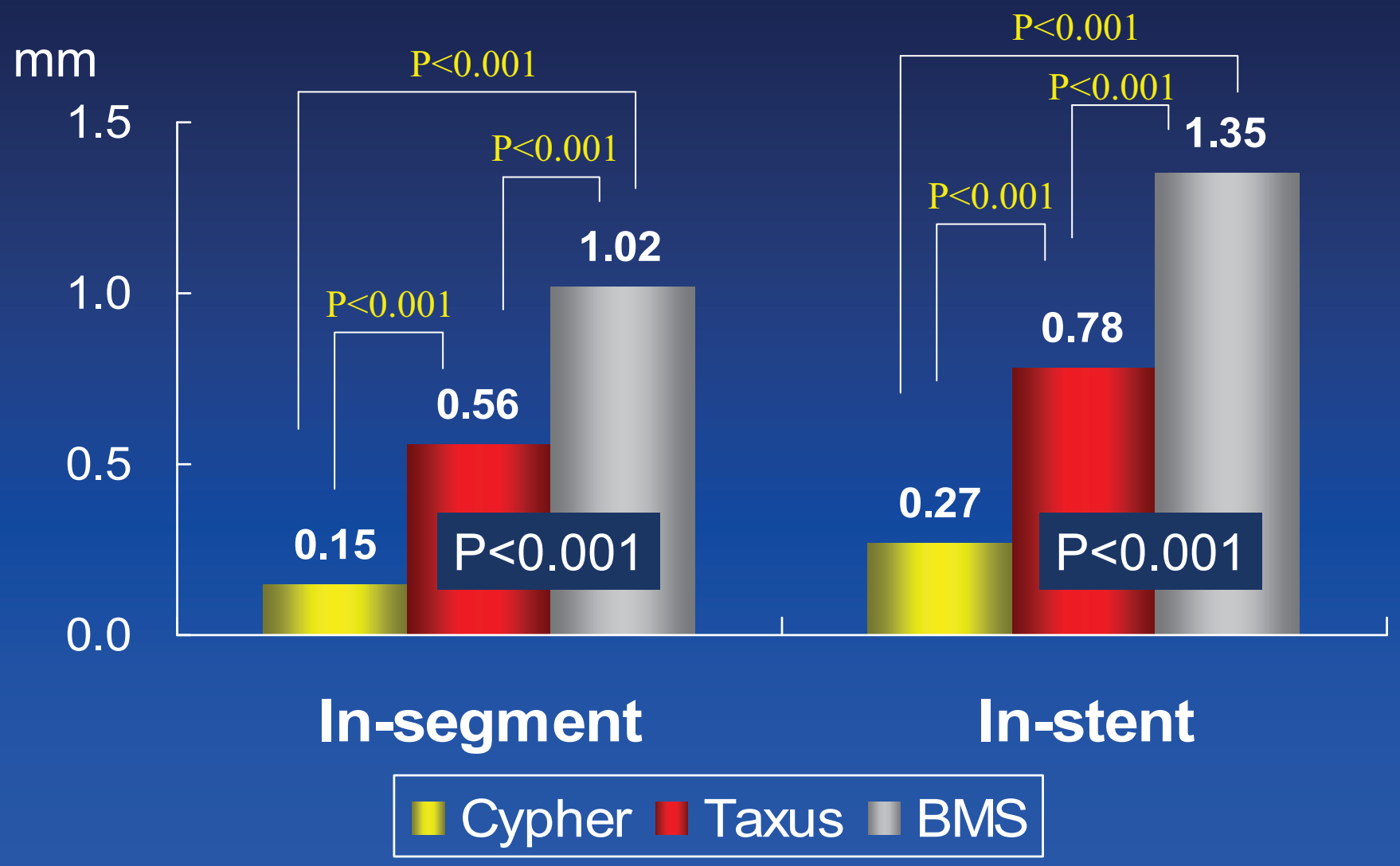
Available in all study patients

QCA at F/U

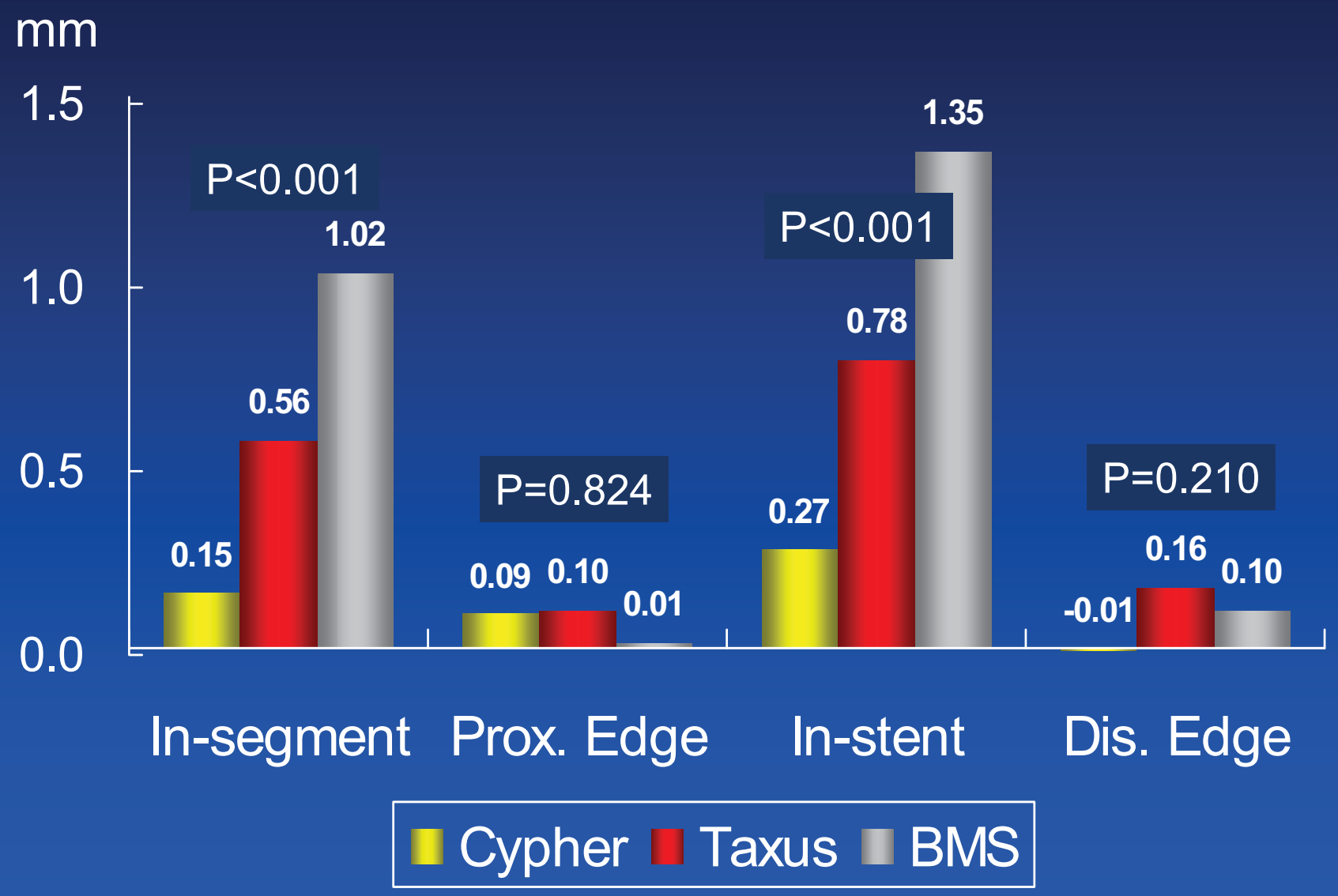
	Cypher (n=271)	Taxus (n=150)	BMS (n=160)	P value
Reference, mm	2.75±0.41 #	2.78±0.41	2.86±0.49	**0.046**
MLD, mm				
In-segment	2.24±0.58 * #	1.90±0.71 **	1.56±0.69	**<0.001**
In-stent	2.45±0.64 * #	1.98±0.77 **	1.58±0.71	**<0.001**
DS, %				
In-segment	15.1±19.1 * #	31.0±24.0 **	45.4±22.4	**<0.001**
In-stent	10.4±21.6 * #	29.3±25.8 **	45.0±22.7	**<0.001**
Late loss, mm				
In-segment	0.15±0.51 * #	0.56±0.62 **	1.02±0.67	**<0.001**
In-stent	0.27±0.61 * #	0.78±0.72 **	1.35±0.74	**<0.001**

Between groups: * p<0.025 Cypher vs Taxus; # p<0.025 Cypher vs BMS;**, p<0.025 Taxus vs. BMS

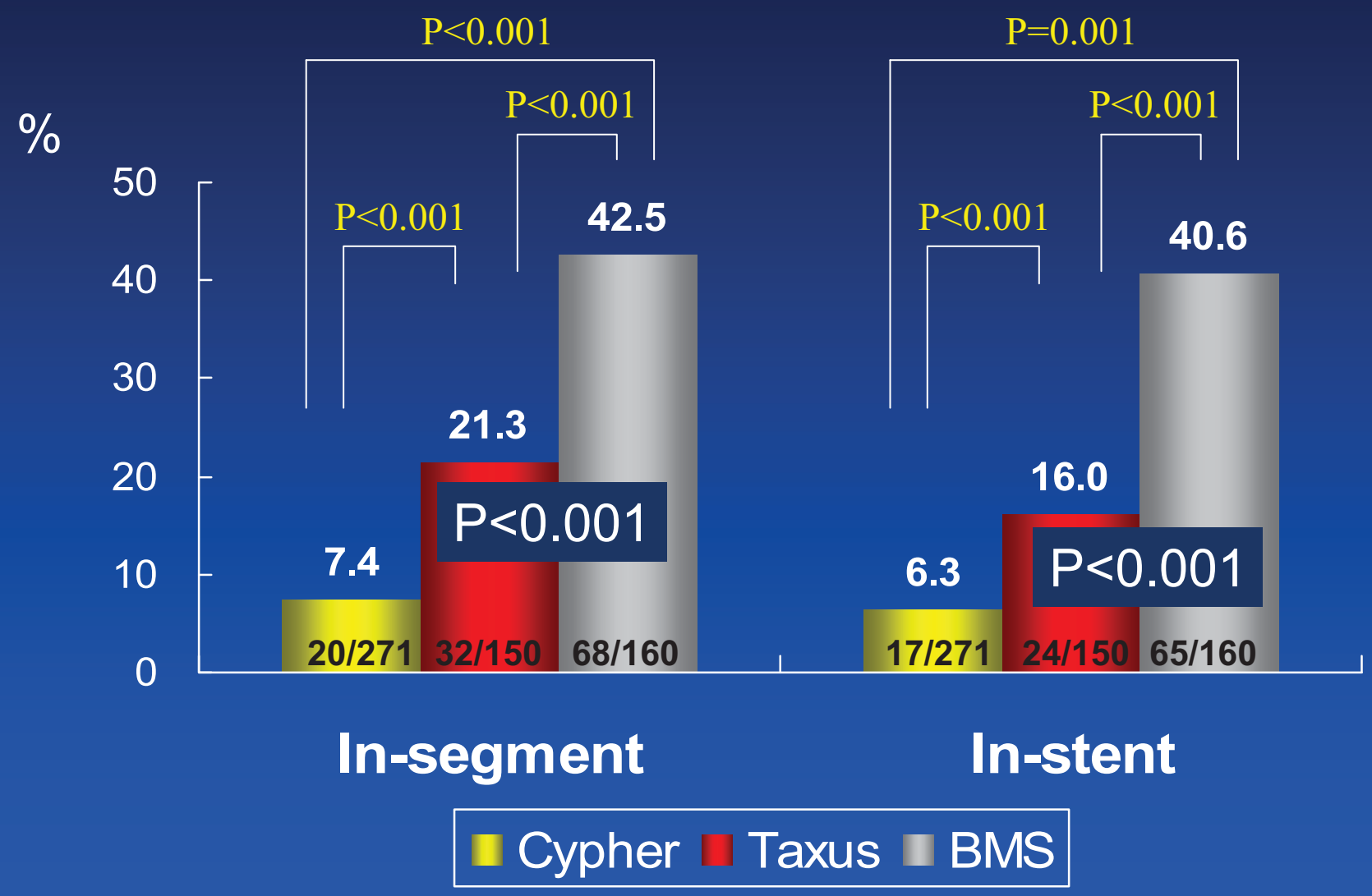
Late Loss


mm
1.5
1.0
0.5
0.0
P<0.001
P<0.001
P<0.001
P<0.001
P<0.001
P<0.001
0.15
0.56
1.02
0.27
0.78
1.35
P<0.001
P<0.001
In-segment
In-stent
Cypher
Taxus
BMS

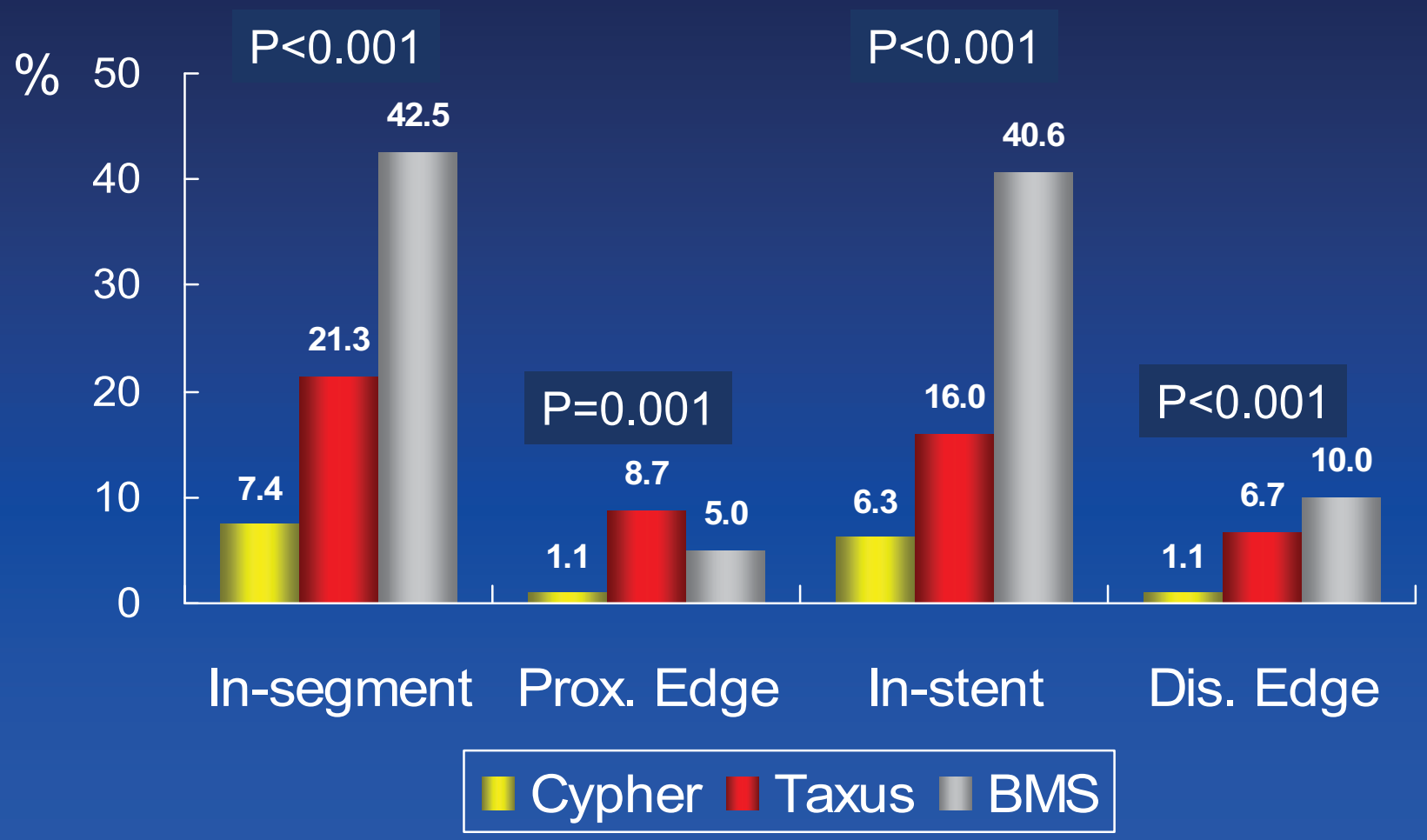
Late Loss


mm
1.5
1.0
0.5
0.0
P<0.001
1.02
0.56
0.15
P=0.824
0.09
0.10
0.01
P<0.001
1.35
0.78
0.27
P=0.210
0.16
0.10
-0.01
In-segment
Prox. Edge
In-stent
Dis. Edge
Cypher
Taxus
BMS

Restenosis Rate

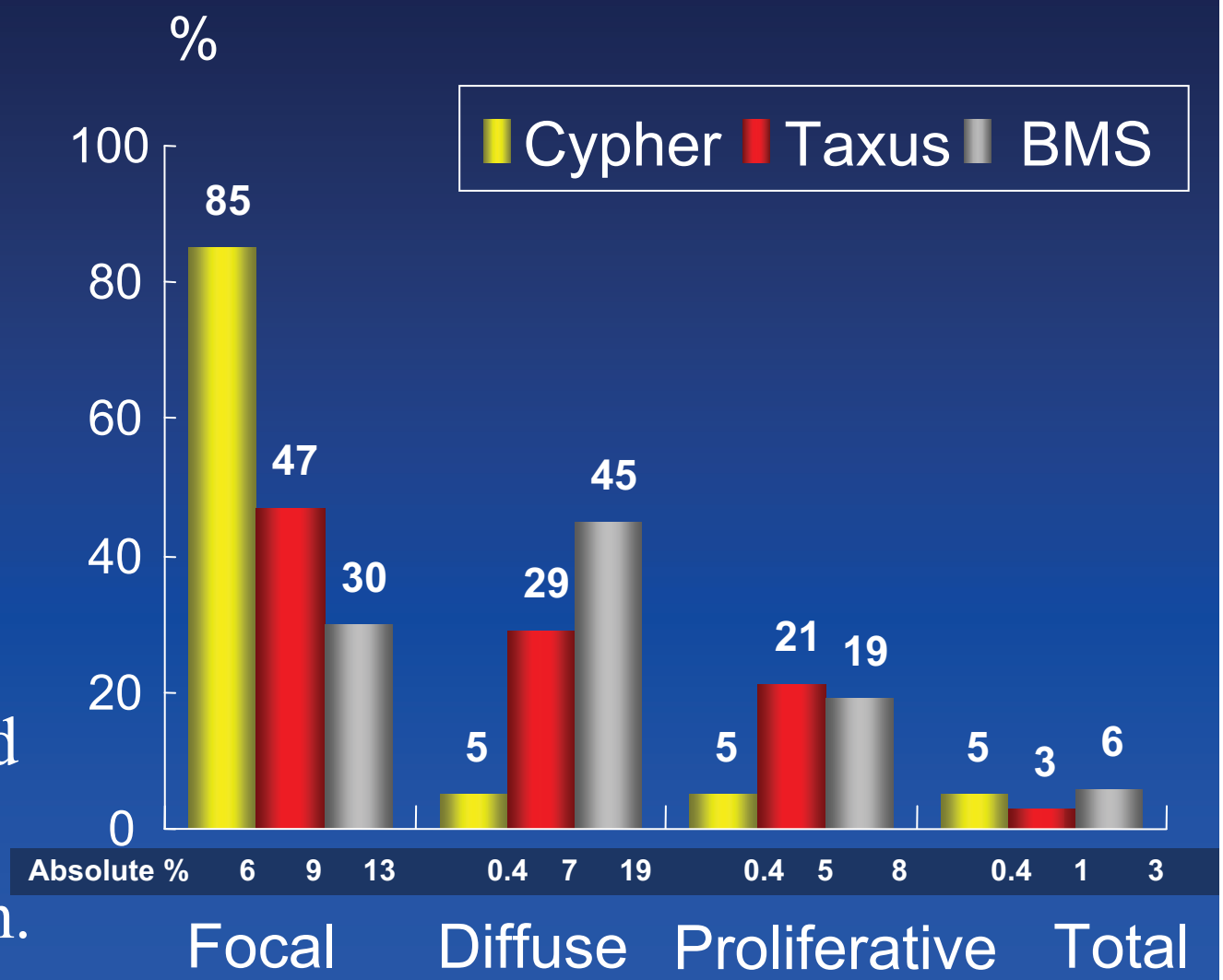


Restenosis Rate



Restenosis Pattern

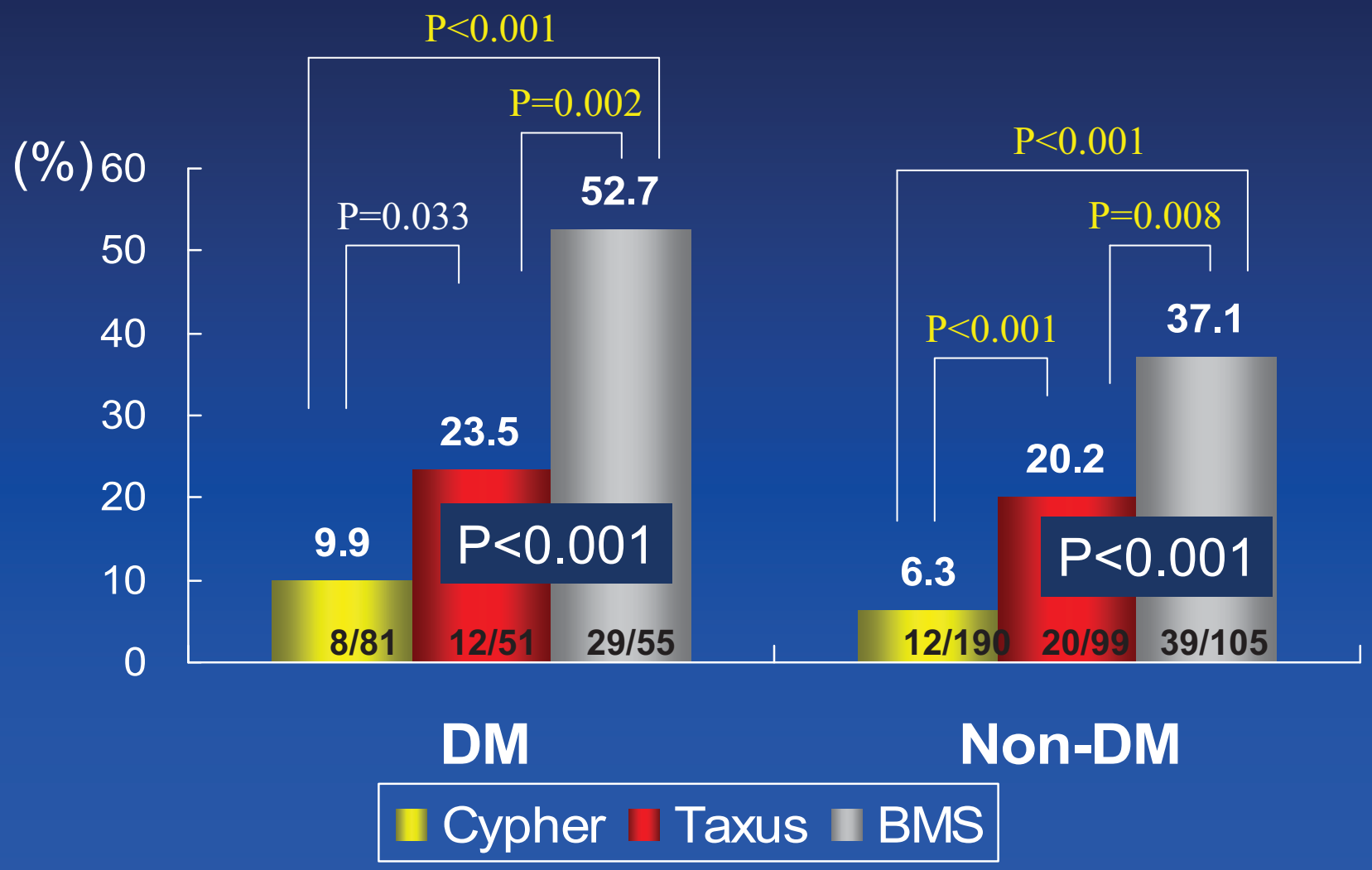
- The majority of restenosis in the Cypher occurred as a localized lesion.
- However, the Taxus and BMS restenosis commonly occurred as a diffuse or proliferative pattern.



QCA Subgroup Analysis

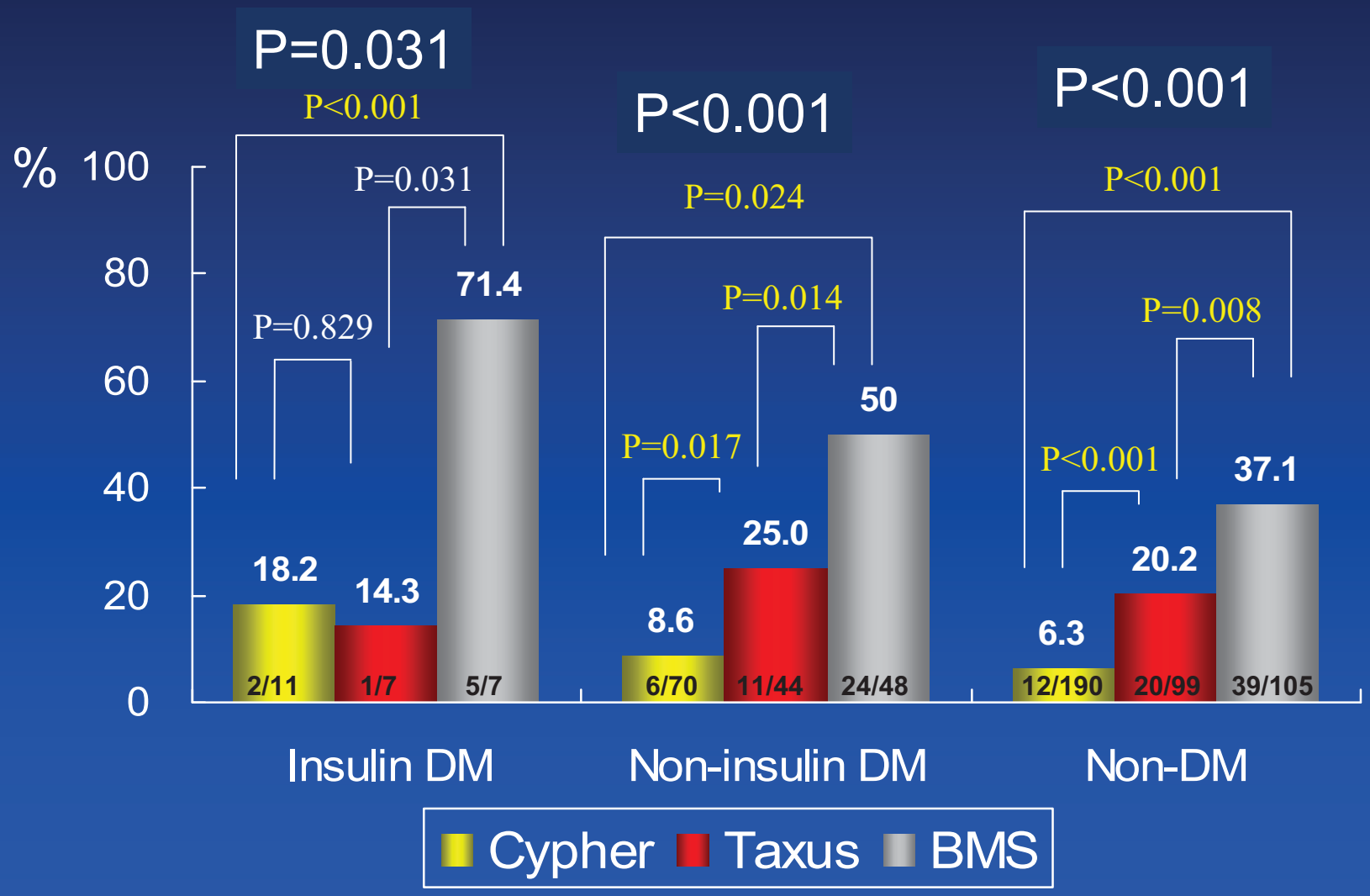
Impact of DM

In-segment Restenosis Rate



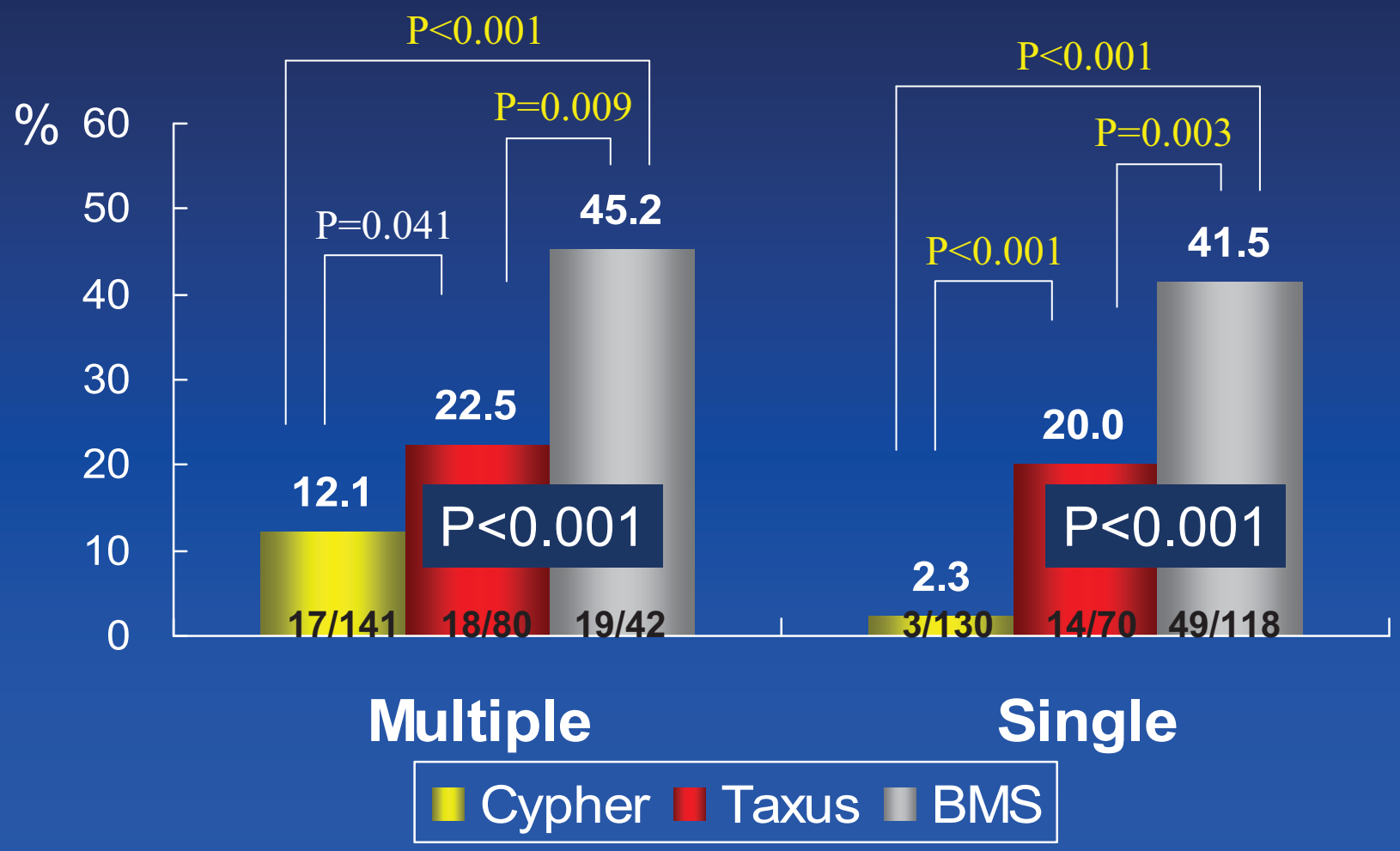
Impact of DM

In-segment Restenosis Rate



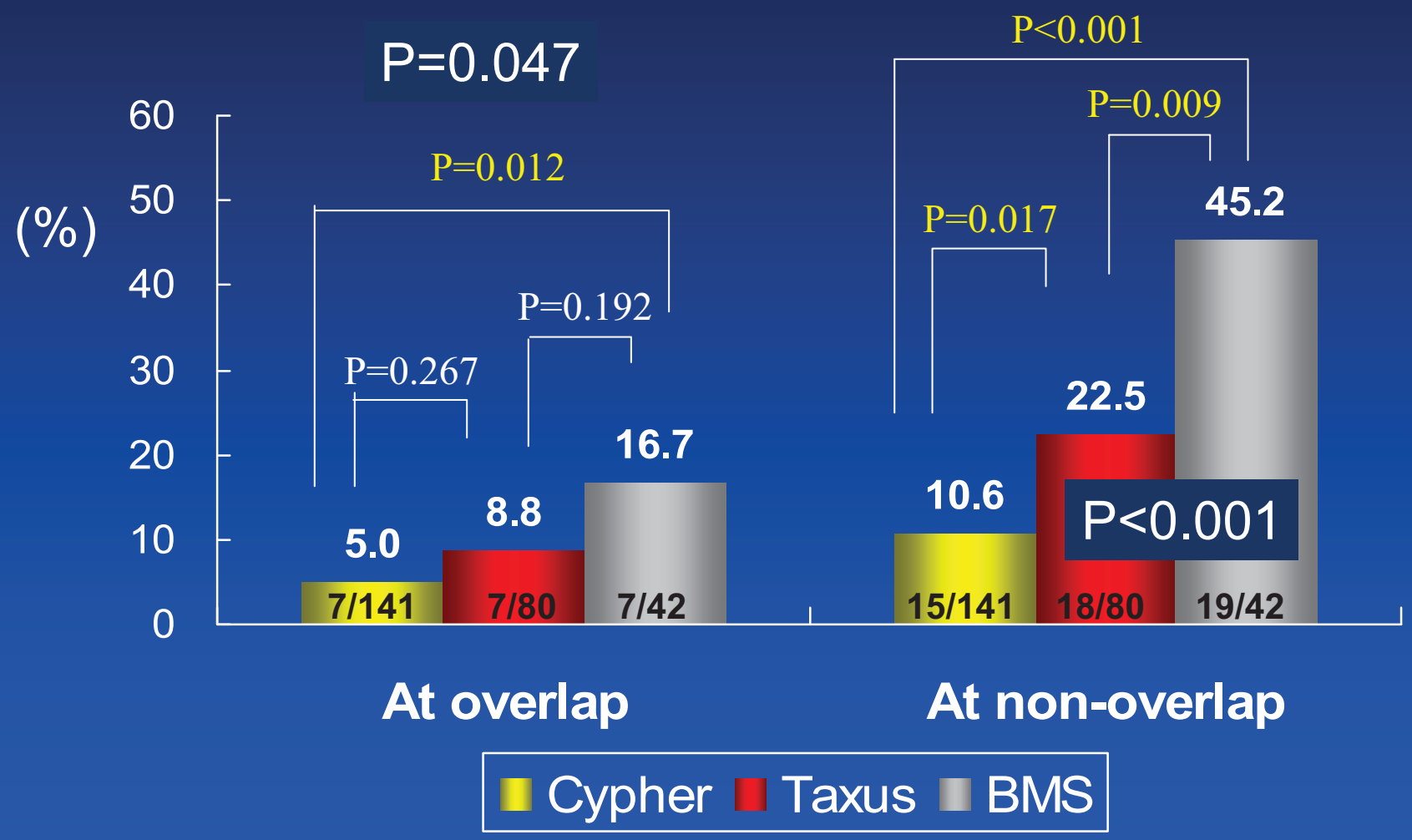
Impact of Multiple Stent

In-segment Restenosis Rate



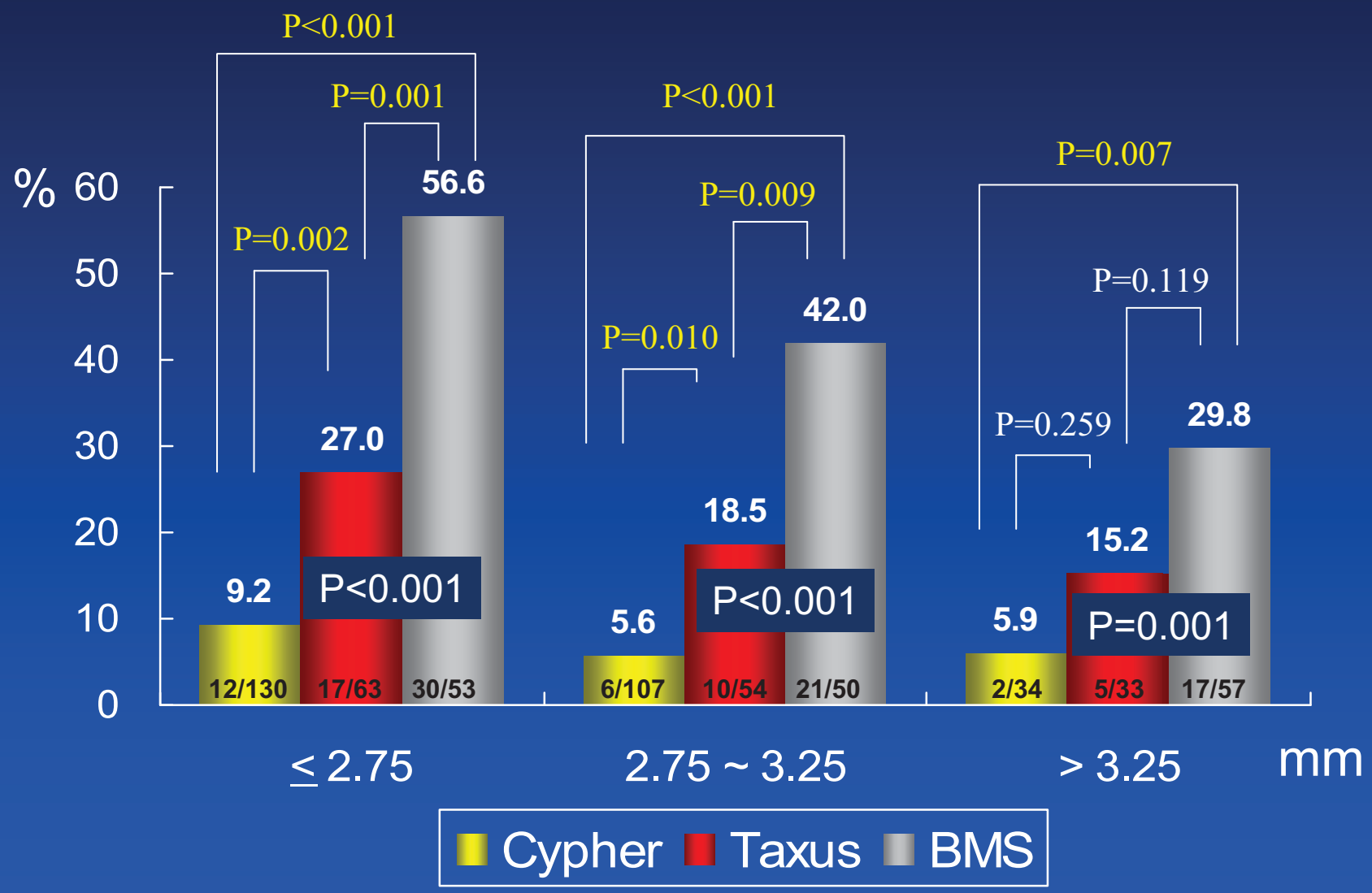
Impact of Stent Overlapping

In-segment Restenosis Rate in Multiple Stenting



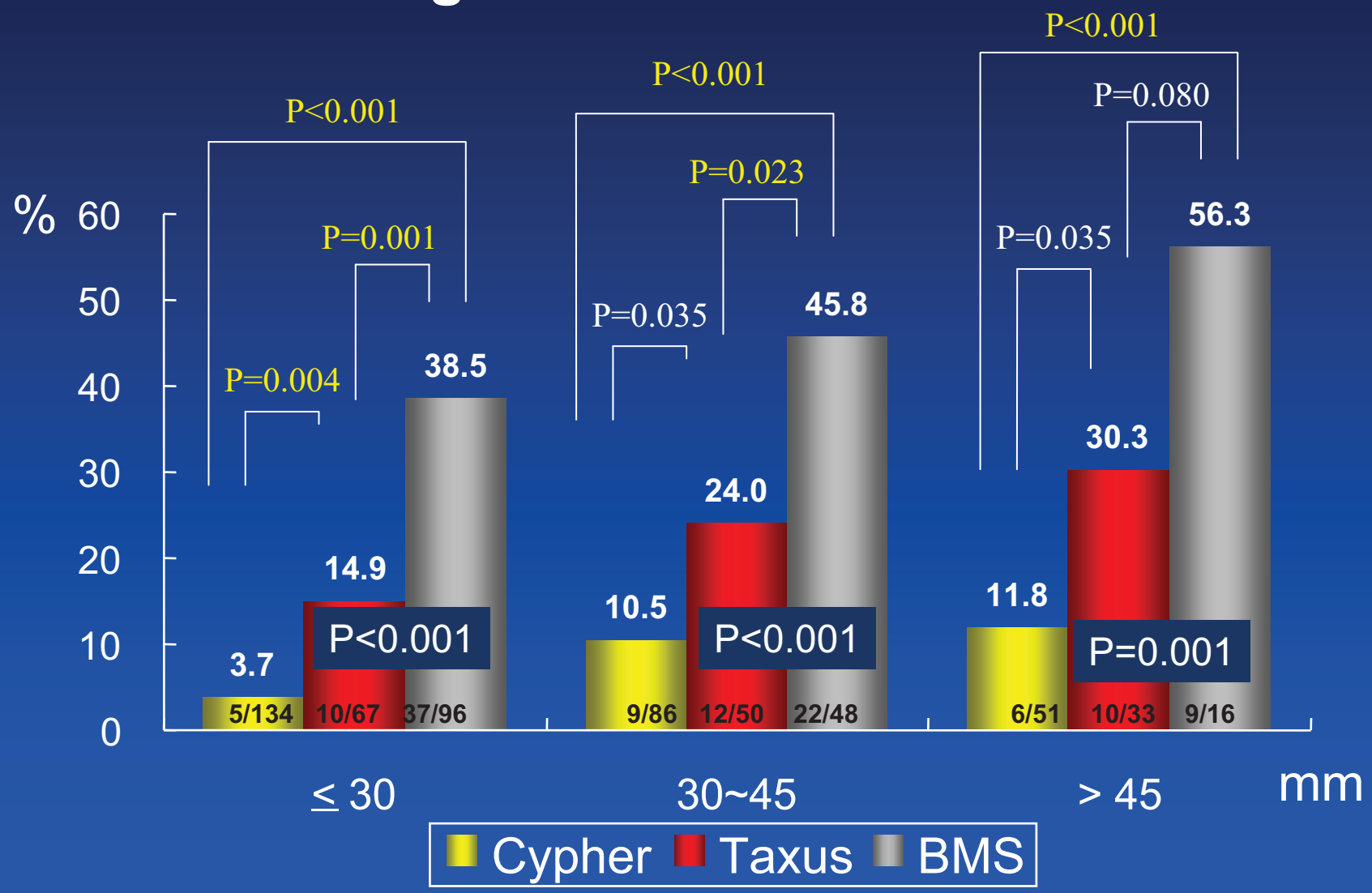
Impact of Reference Diameter

In-segment Restenosis Rate



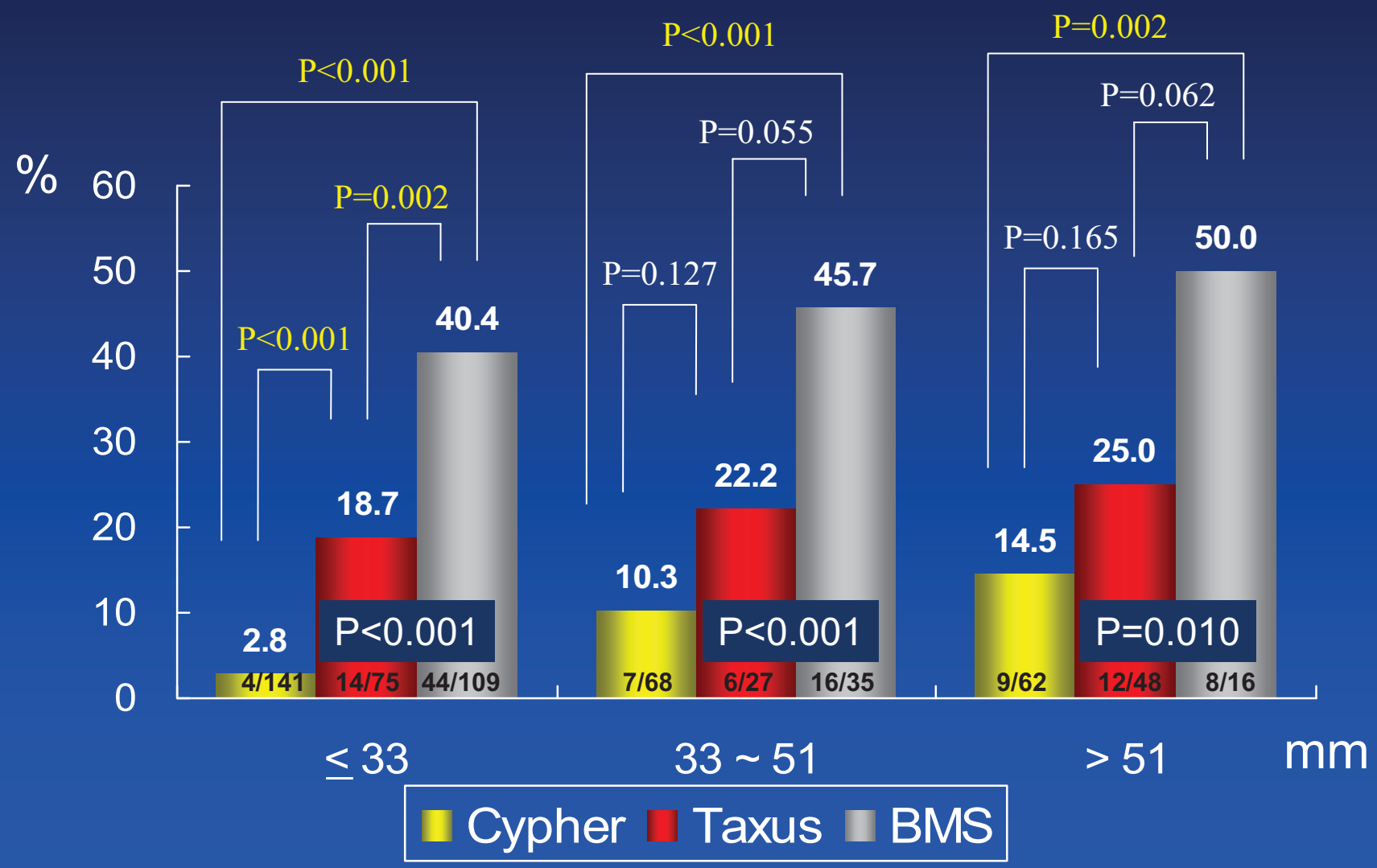
Impact of Lesion Length

In-segment Restenosis Rate



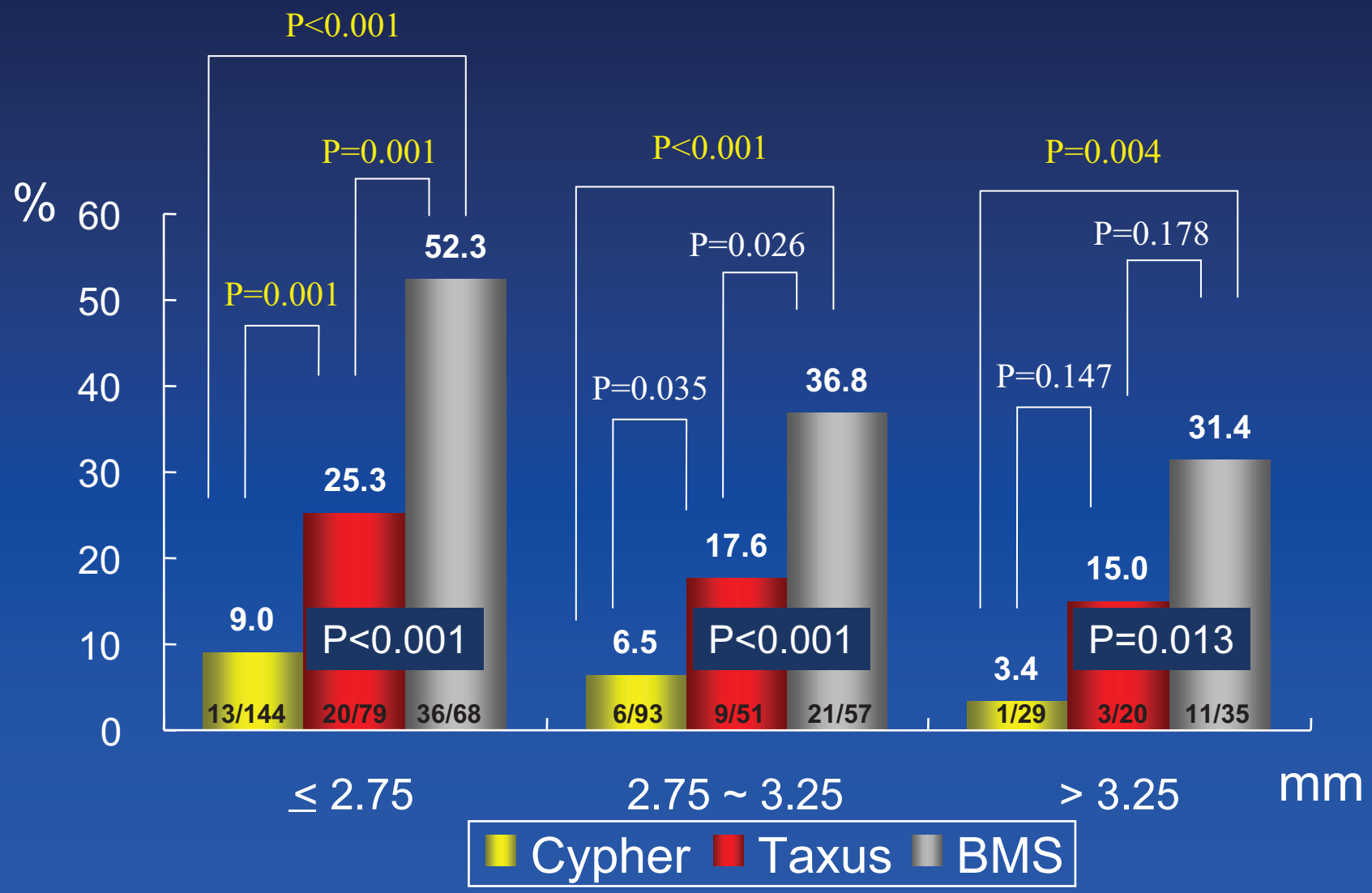
Impact of Stent Length

In-segment Restenosis Rate



Impact of Post-procedural MLD

In-segment Restenosis Rate



In subgroup analysis…

- The superior benefits of the DES over the BMS was extended to the patients with traditional high risks of restenosis, such as diabetes mellitus with or without insulin-dependency, very long lesions, very long-stented segment, multiple stents, and small post-procedural MLD.

- The Cypher was associated with lower restenosis rate than the Taxus stent in such complex lesion subsets.

Predictors of Restenosis

by Multivariate Analysis

Predictors of Restenosis
Overall

Variables	Relative Risk	95% C.I.	P value
Bare metal stent	8.01	4.90-13.11	<0.001
Lesion length (10mm)	1.29	1.10-1.51	0.002
MLD after procedure (mm)	0.32	0.19-0.53	<0.001

Predictors of Restenosis
DES subgroup

Variables	Relative Risk	95% C.I.	P value
Taxus stent	3.65	1.96-6.79	<0.001
Lesion length (10mm)	1.31	1.08-1.60	0.006
MLD after procedure (mm)	0.29	0.13-0.61	0.001

Predictors of Restenosis
Cypher or Taxus subgroup

		R.R	95% C.I.	P value
Cypher	▪ Multiples stent	5.62	1.60-19.68	0.007
Taxus	▪ MLD after procedure (mm)	0.19	0.05-0.57	0.004
	▪ Lesion length (10mm)	1.36	1.02-1.82	0.037
BMS	▪ MLD after procedure (mm)	0.31	0.15-0.64	0.001
	▪ Diabetes mellitus	2.00	1.01-3.98	0.048

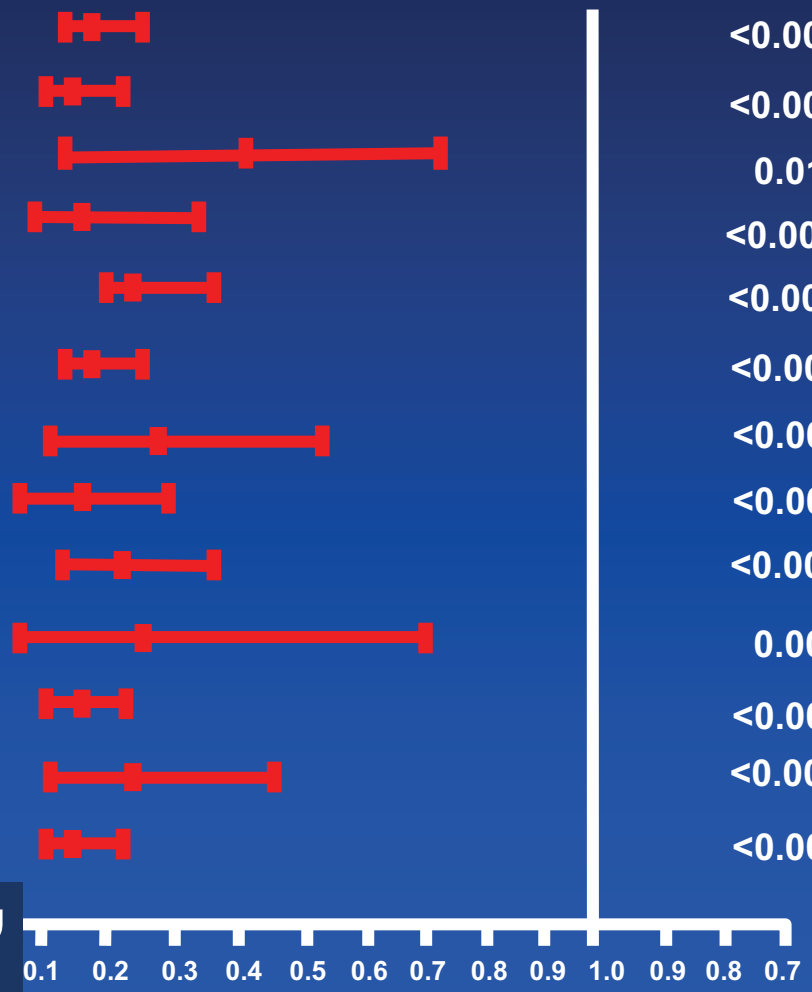
Summary : Restenosis Predictors

- The traditional risk factors of restenosis in the BMS era (multiple stents, lesion length, MLD after procedure) remained important determinants of restenosis in long DES implantation.

- The principles of coronary intervention in the BMS era - “the bigger, the better” or “the shorter, the better”- may be applied to the DES era in long lesion intervention. However, the clinical impact of such risk factors in the DES may not be as large as the BMS because of low absolute number of restenosis.

Angiographic Restenosis : **DES vs BMS**

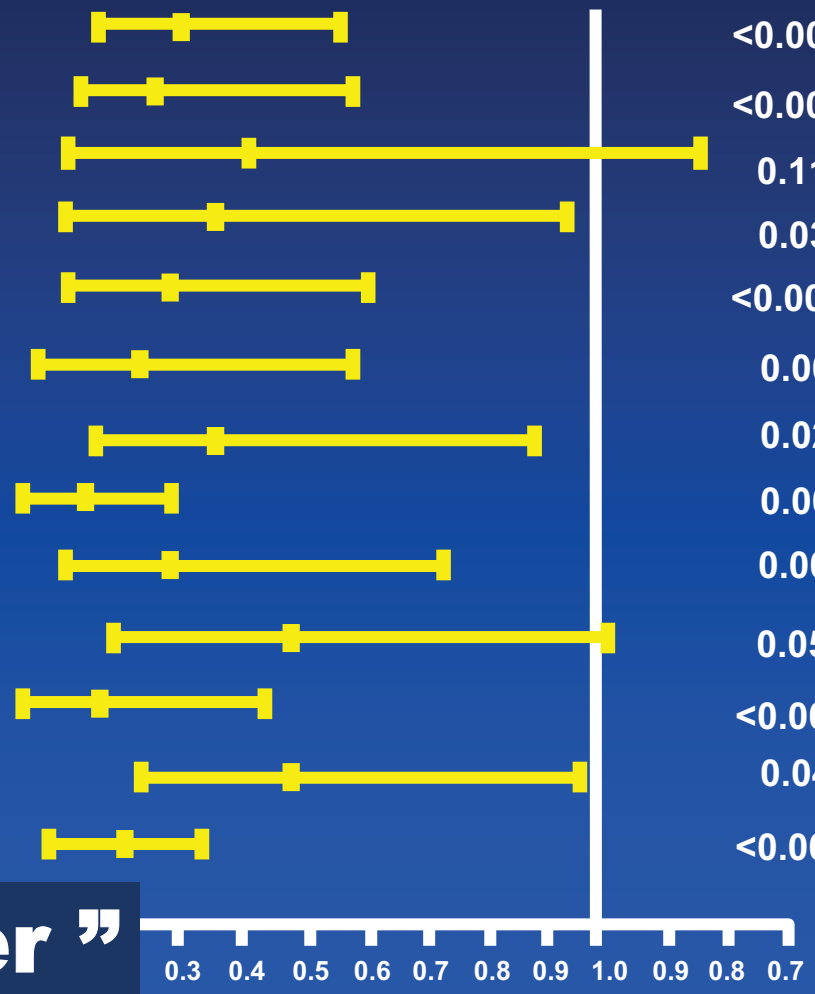
	DES	BMS	P-value
Overall	12.4	42.5	<0.0001
Male	12.1	45.6	<0.0001
Female	13.9	31.4	0.019
Diabetes	15.2	52.7	<0.0001
No Diabetes	11.1	37.1	<0.0001
LAD	10.3	45.9	<0.0001
Non-LAD	14.8	34.7	<0.0001
Small Vessel (≤2.75)	15.0	56.6	<0.0001
Large Vessel	10.1	35.5	<0.0001
Stent length>45mm	18.4	44.0	0.004
Stent length≤45mm	8.5	42.2	<0.0001
Multiple stent	15.8	45.2	<0.0001
Single	8.5	41.5	<0.0001



" DES Better "

Angiographic Restenosis : **Cypher** vs **Taxus**

	Cypher	Taxus	P-value
Overall	7.4	24.3	<0.0001
Male	6.6	21.3	<0.0001
Female	10.5	21.9	0.119
Diabetes	9.9	23.5	0.033
No Diabetes	6.3	20.2	<0.0001
LAD	5.7	20.5	0.001
Non-LAD	9.8	22.1	0.020
Small Vessel (≤2.75)	9.2	27.0	0.001
Large Vessel	5.7	17.2	0.005
Stent length>45mm	13.9	25.8	0.056
Stent length≤45mm	3.5	18.2	<0.0001
Multiple stent	12.1	22.5	0.041
Single	2.3	20.0	<0.0001



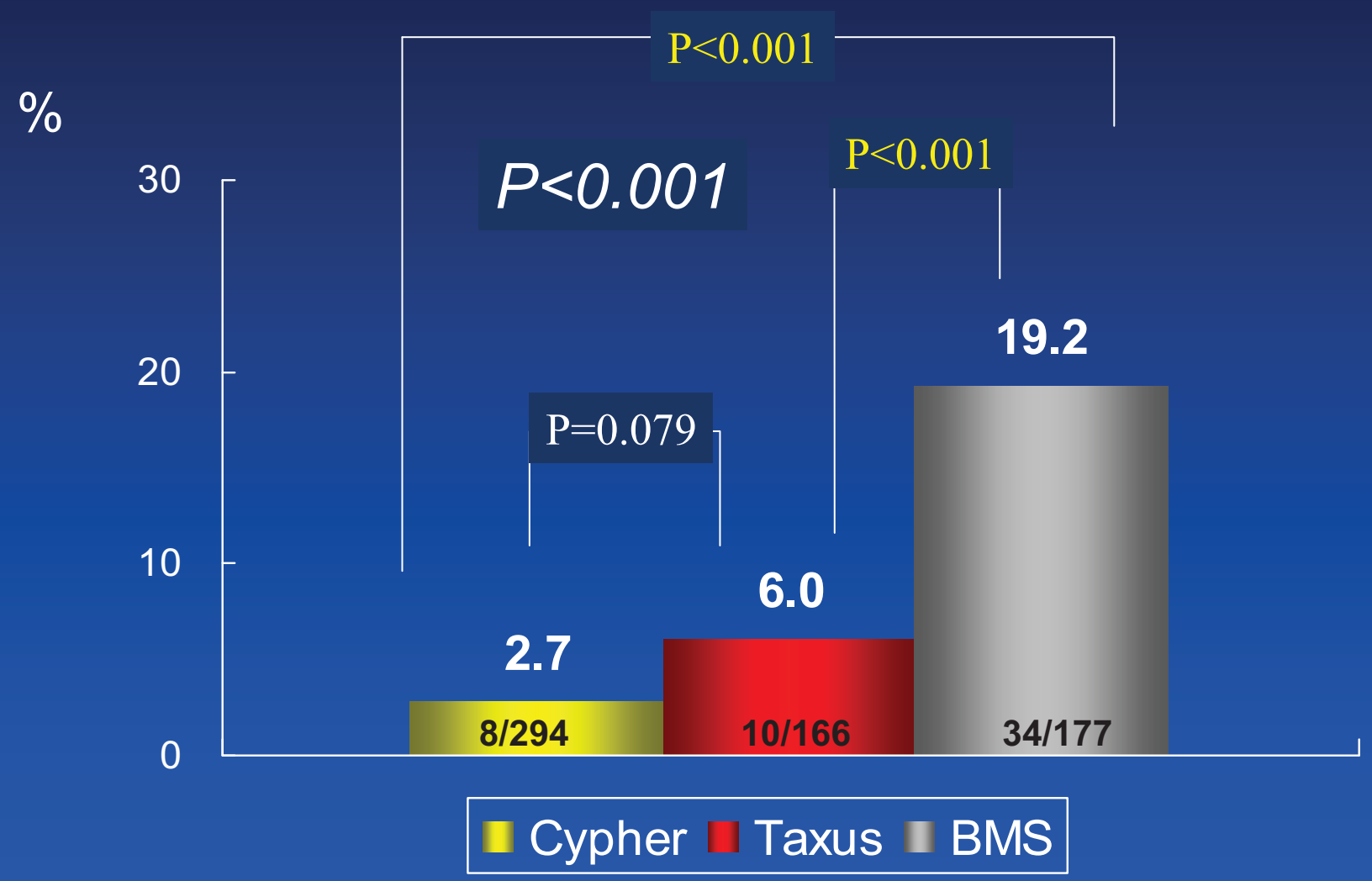
“ Cypher Better ”

Seven-Month Outcomes

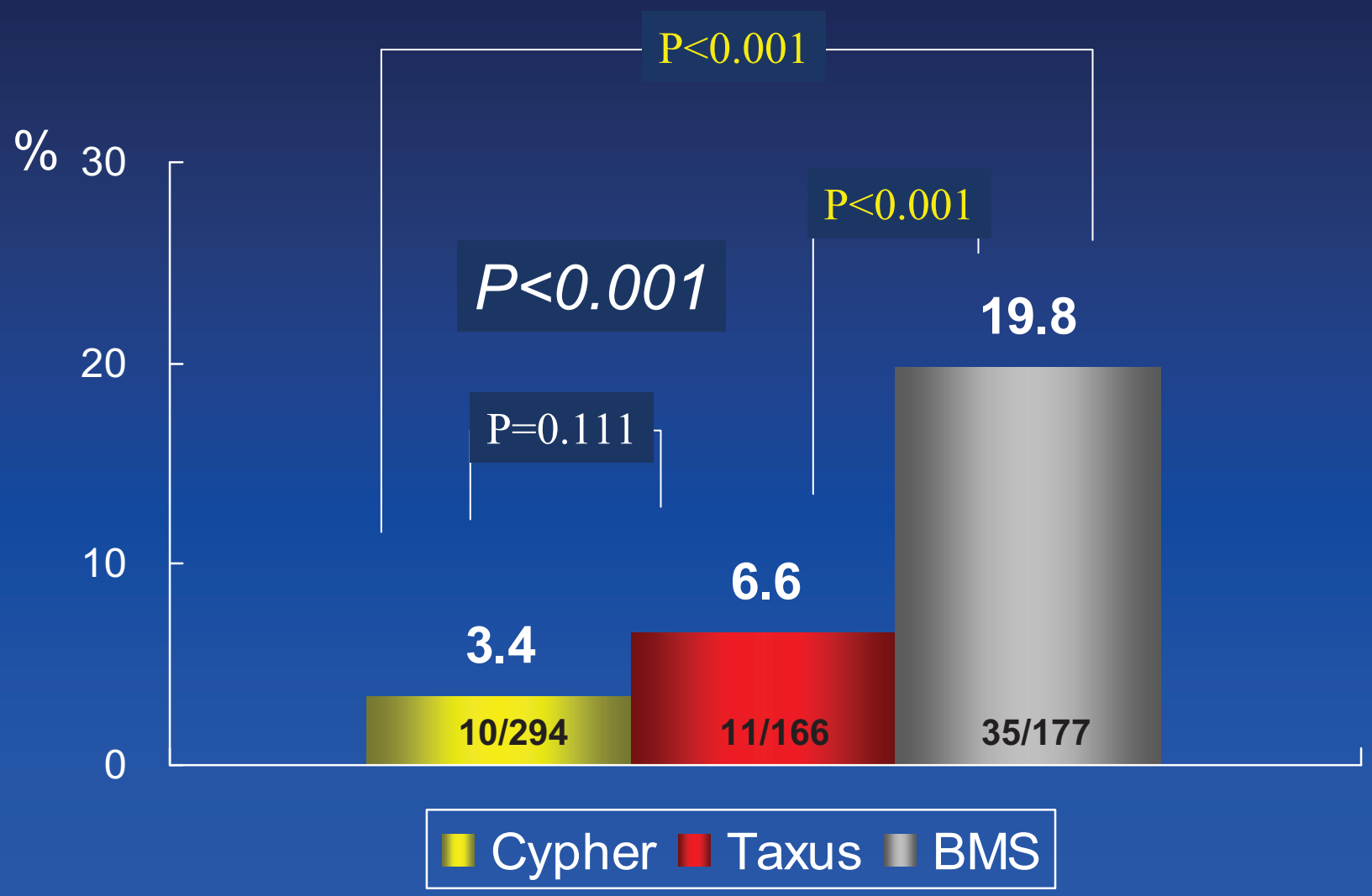
	Cypher (n=294)	Taxus (n=166)	Control (n=177)	P value
Death	2 (0.7)	1 (0.6)	1 (0.6)	0.987
MI	0 (0)	0 (0)	1 (0.6)	0.272
Q wave	0 (0)	0 (0)	1 (0.6)	
Non-Q wave	0 (0)	0 (0)	0 (0)	
Stent thrombosis	0 (0)	0 (0)	1 (0.6)	0.272
TLR	8 (2.7) #	10 (6.0) **	34 (19.2)	**<0.001**
Repeat PCI	7	7	32	
CABG	1	2	2	
MACE	10 (3.4) #	11 (6.6) **	35 (19.8)	**<0.001**

Between groups: * p<0.025 Cypher vs Taxus; # p<0.025 Cypher vs BMS;**, p<0.025 Taxus vs. BMS

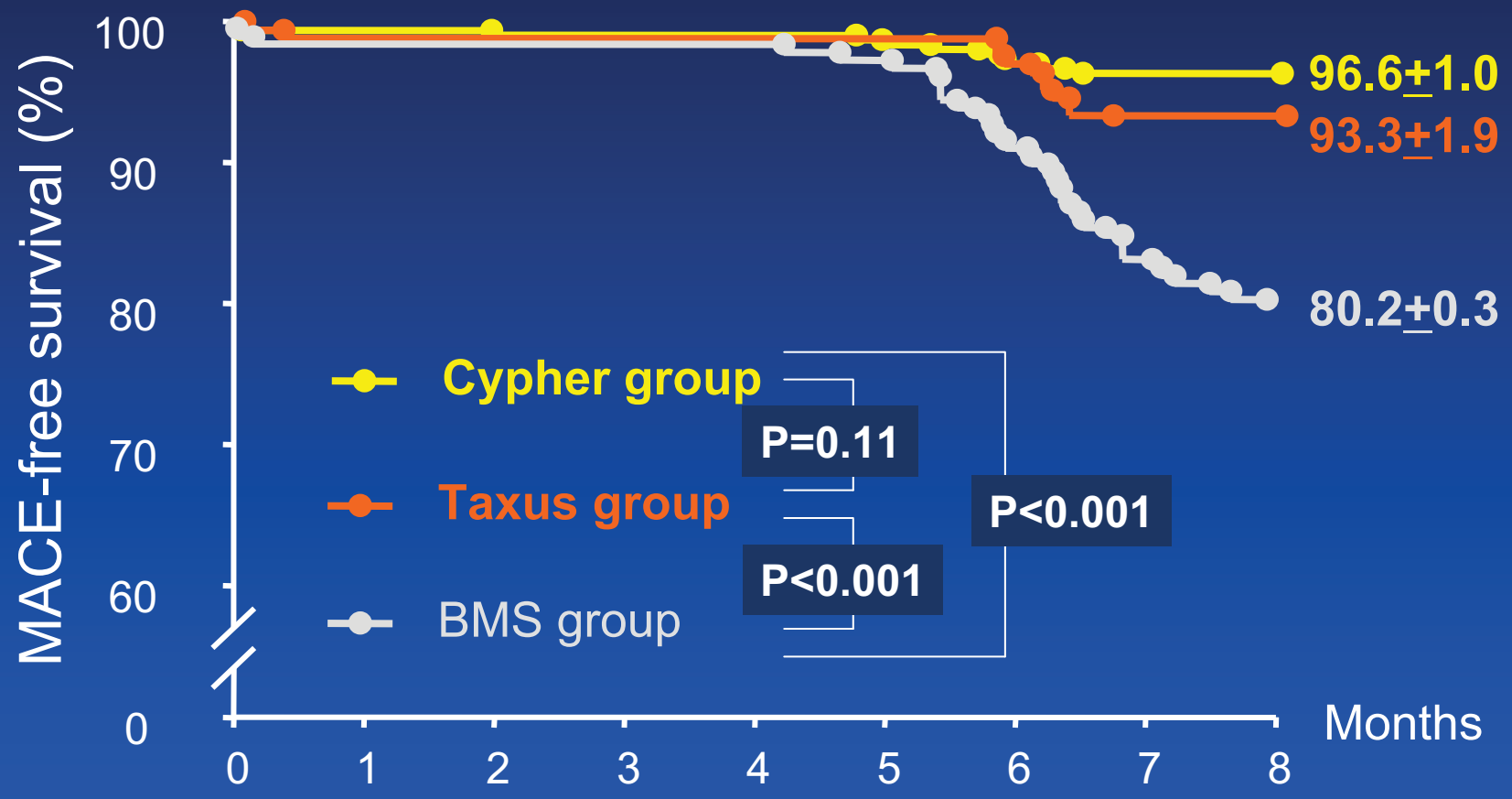
Seven-Month TLR



Seven-Month MACE



MACE-free Survival



Conclusions: DES vs. BMS

- Two leading DES including Cypher® sirolimus-eluting stent and Taxus™ paclitaxel-eluting stent implantation for long coronary lesions was safe with no incidents of death, stent thrombosis, or Q wave myocardial infarction.

- Both DES was associated with low rate of in-segment restenosis and TLR for long coronary lesions compared to BMS.

Conclusions: Cypher vs. Taxus

- Even though the Cypher group had narrower vessels at baseline and after procedure, those patients had less late loss and lower restenosis rate than the Taxus stent.

- However, the superior benefit of the Cypher stent in terms of late loss and restenosis rate was not translated into lower repeat revascularization rate, compared to the Taxus stent.