PCI for Small Vessel Disease

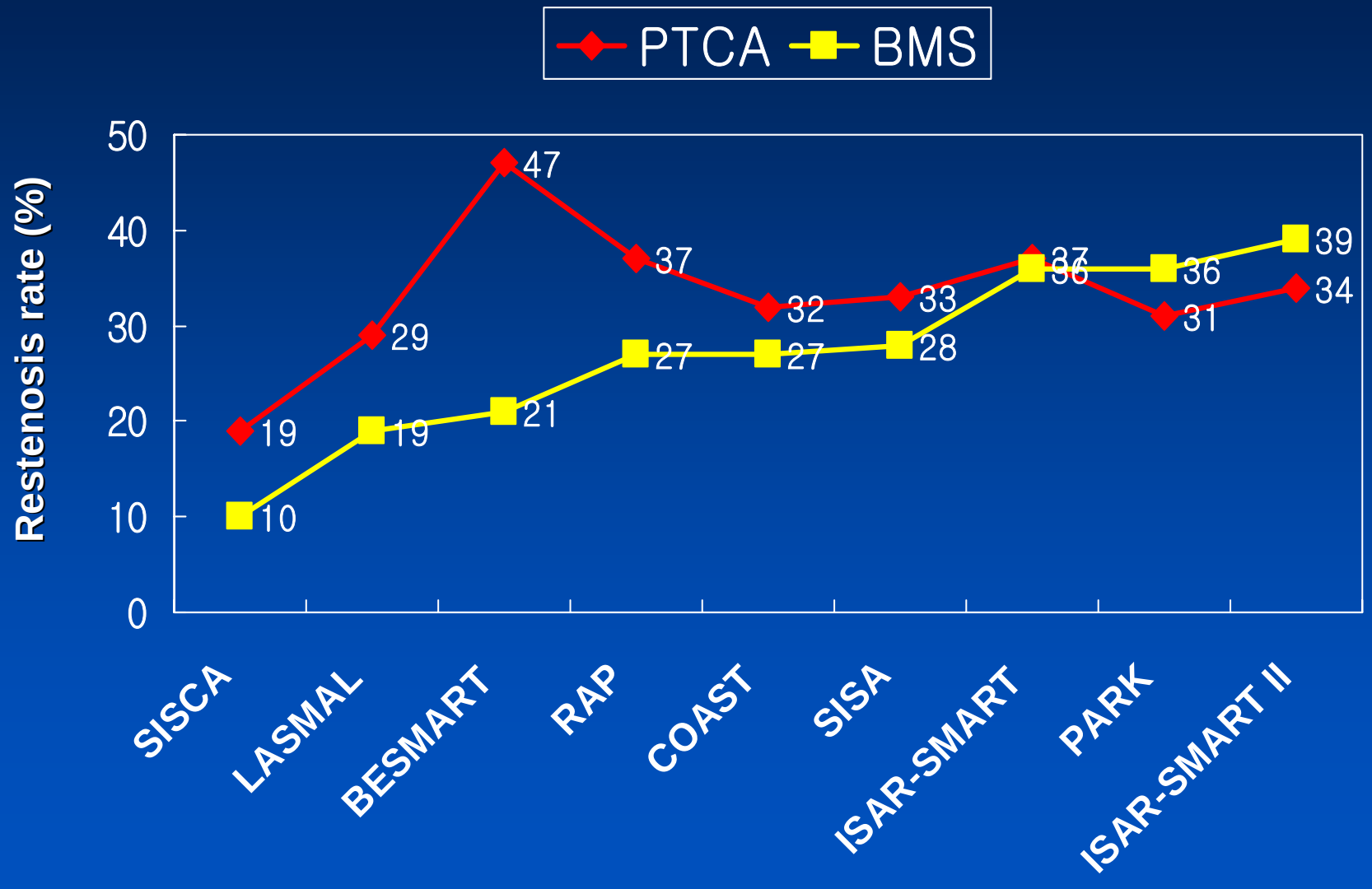
Small Vessel Disease

BMS vs. PTCA

Randomized Trials of BMS vs. PTCA in Small Vessel Disease

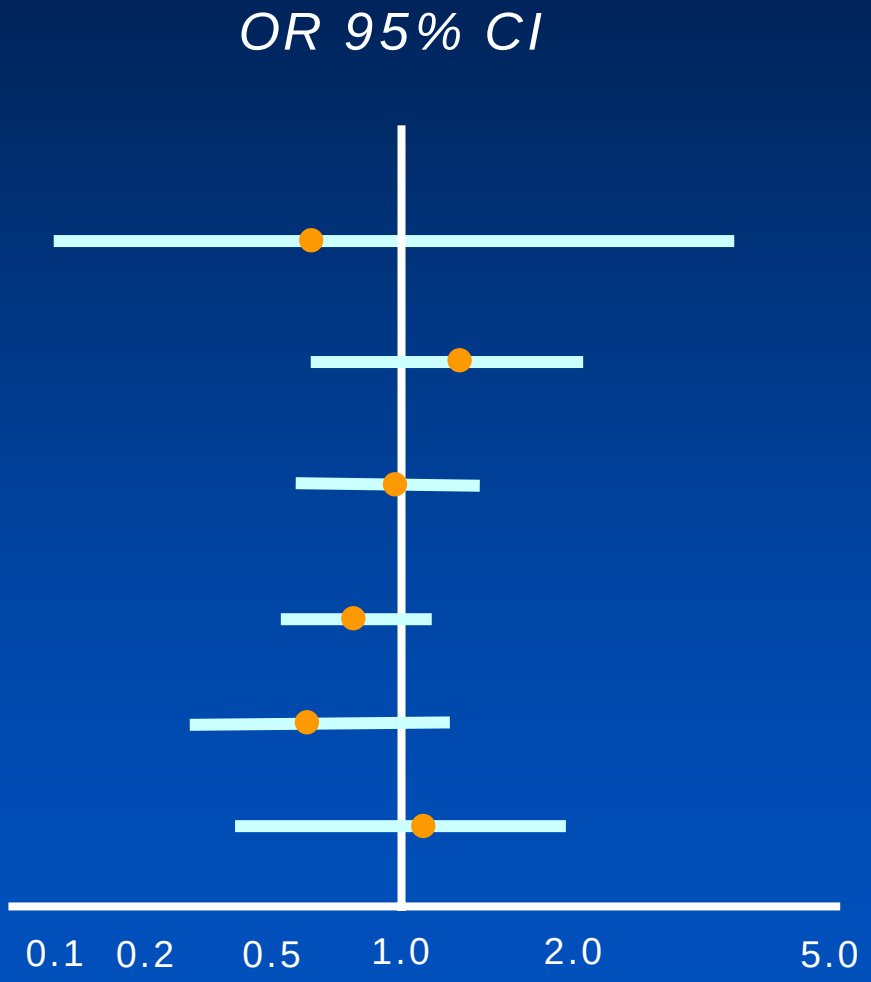
Trial	Stent type	Numbers
ISAR-SMART	Multi-Link	381
N/A	NIR	120
BESMART	BeStent	381
SISA	BeStent	351
SISCA	BeStent	145
RAP	BeStent	426
LASMAL	BiodivYsio	246
COAST	JoStent	588
ISAR-SMART II	BiodivYsio	502

Restenosis Rate of BMS vs. PTCA in Small Vessel Disease



TLR Rate at 8 Months

TRIALS	Stent	PTCA
SW Park et al.	2/60	3/60
ISAR-SMRT	41/204	33/200
ISAR-SMRT II	51/253	51/249
COAST	42/393	28/195
LASML	19/124	25/122
LASML II	17/111	16/109



P Agostoni et al. Eur Heart J 2005;26:881

Small Vessel Disease in the BMS era

- The results of trials comparing BMS to PTCA were discordant compared to the other coronary lesions.
- Clinical and angiographic restenosis rates remain relatively high with either strategy.

Small Vessel Disease

DES vs. BMS

PCI for Small Vessels in the DES Era

- For complete lesion coverage in the DES era, the number of PCI for small coronary lesions has been increased despite of small perfusion territory and unfavorable long-term outcomes.

Evidences
DES in Small Vessels

- Subgroups of randomized studies
  - RAVEL, SIRIUS, New-SIRIUS (SES vs. BMS)
  - TAXUS (PES vs. BMS)
- Randomized studies
  - E-SIRIUS (SES vs. BMS)
  - SES-SMART (SES vs. BMS)
- Registries
  - SVELTE (SES vs. BMS)
  - REVOLUTION (thin strut SES)
  - RESEARCH & T-SEARCH (SES vs. PES)
  - ISAR-SMART 3 (SES vs. PES)
  - Asan Medical Center (SES vs. PES)

SES=sirolimus-eluting stent, PES=paclitaxel-eluting stent, BMS=bare metal stent

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DES in Small Vessels

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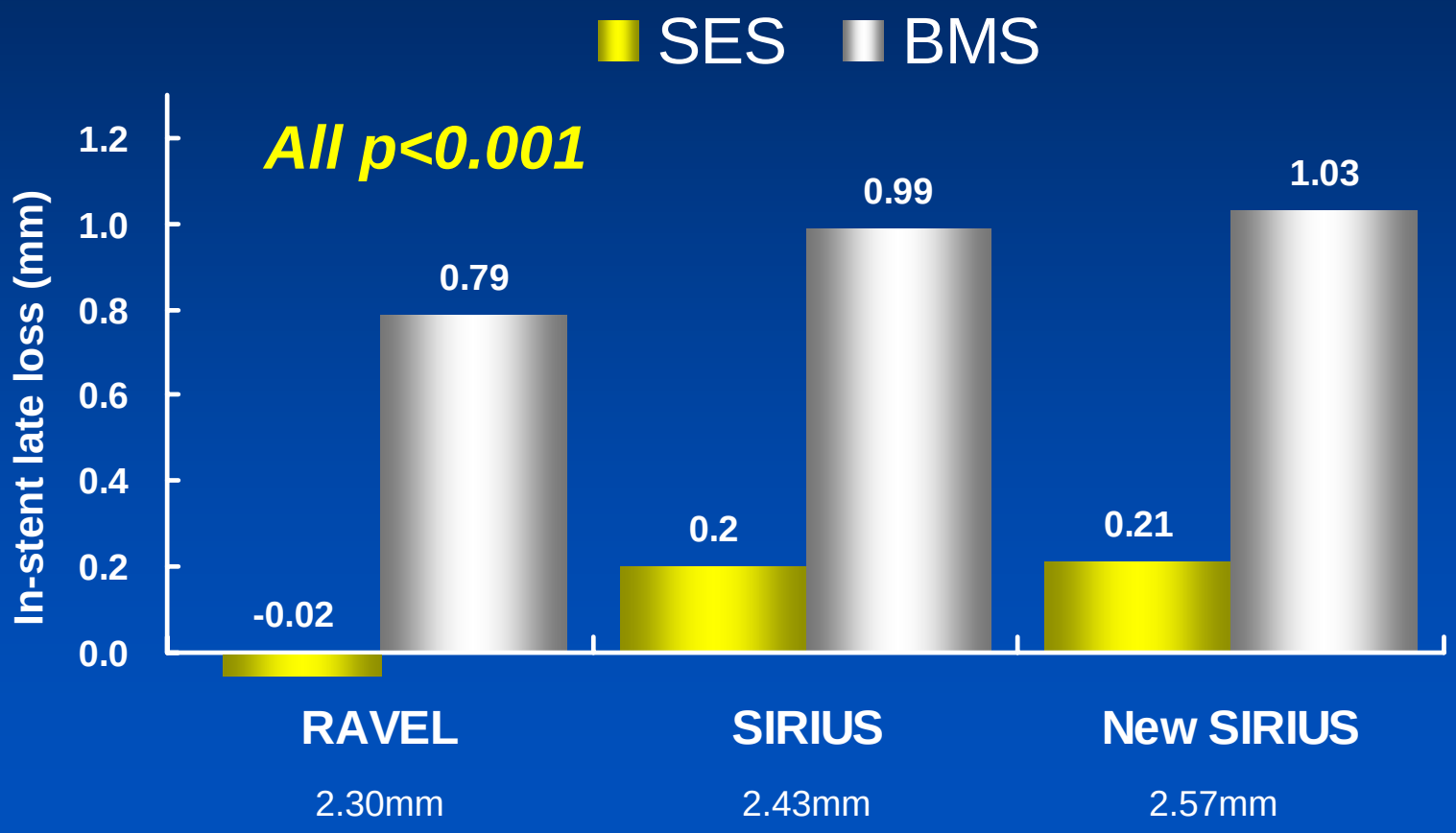
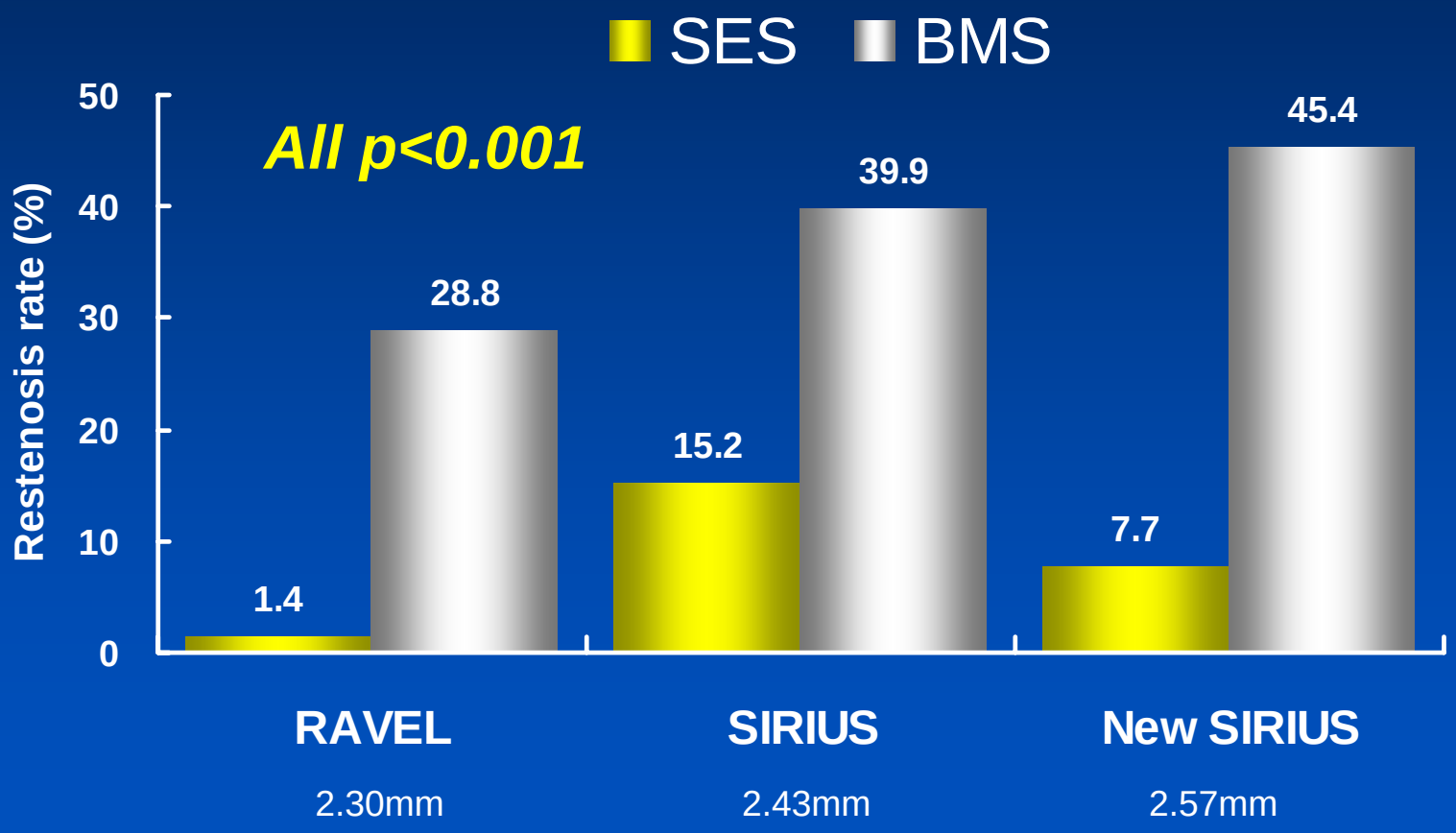
In-Stent Late Loss
SES vs. BMS in RVD<2.75mm

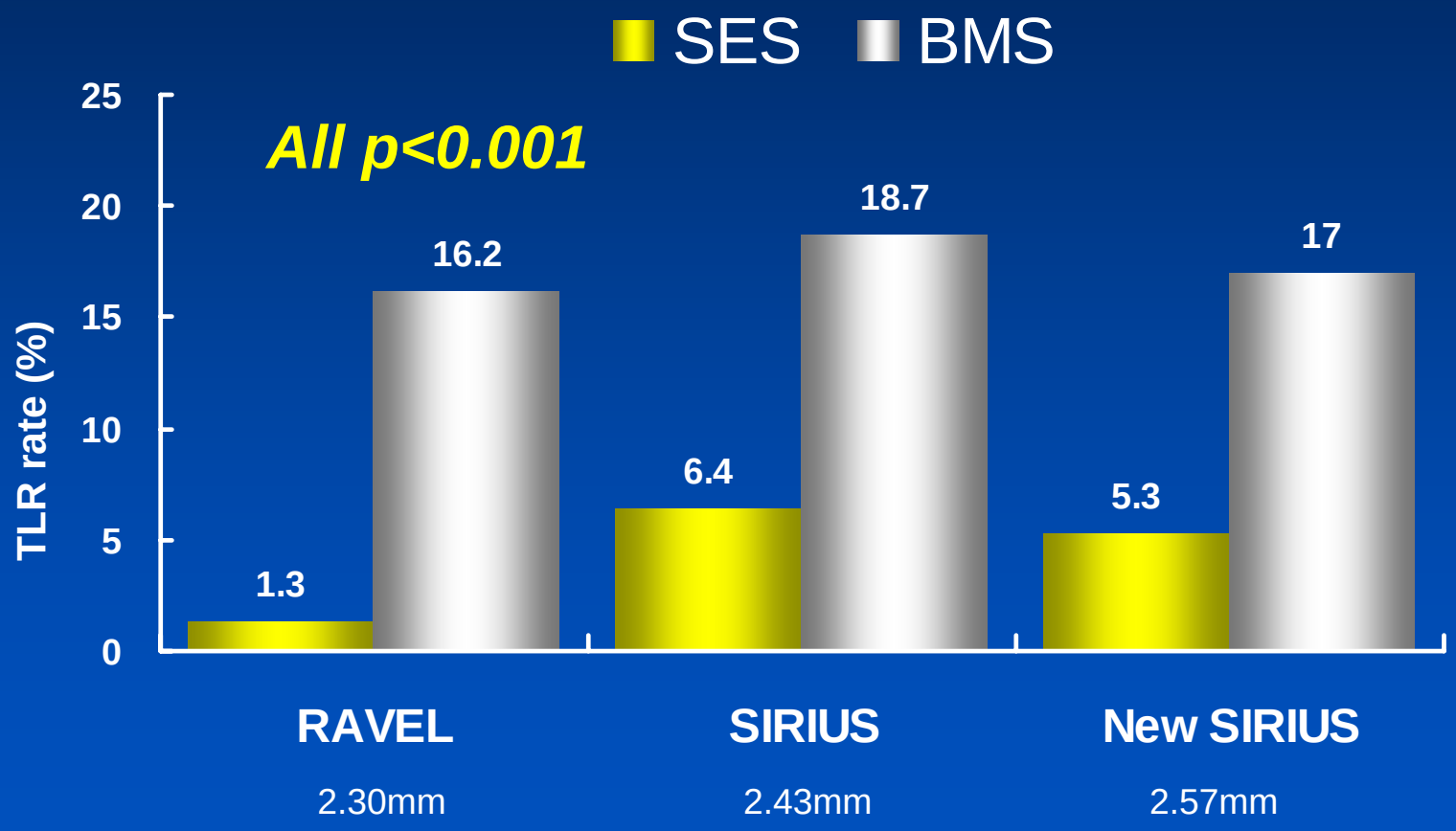


In-Segment Restenosis

SES vs. BMS in RVD<2.75mm



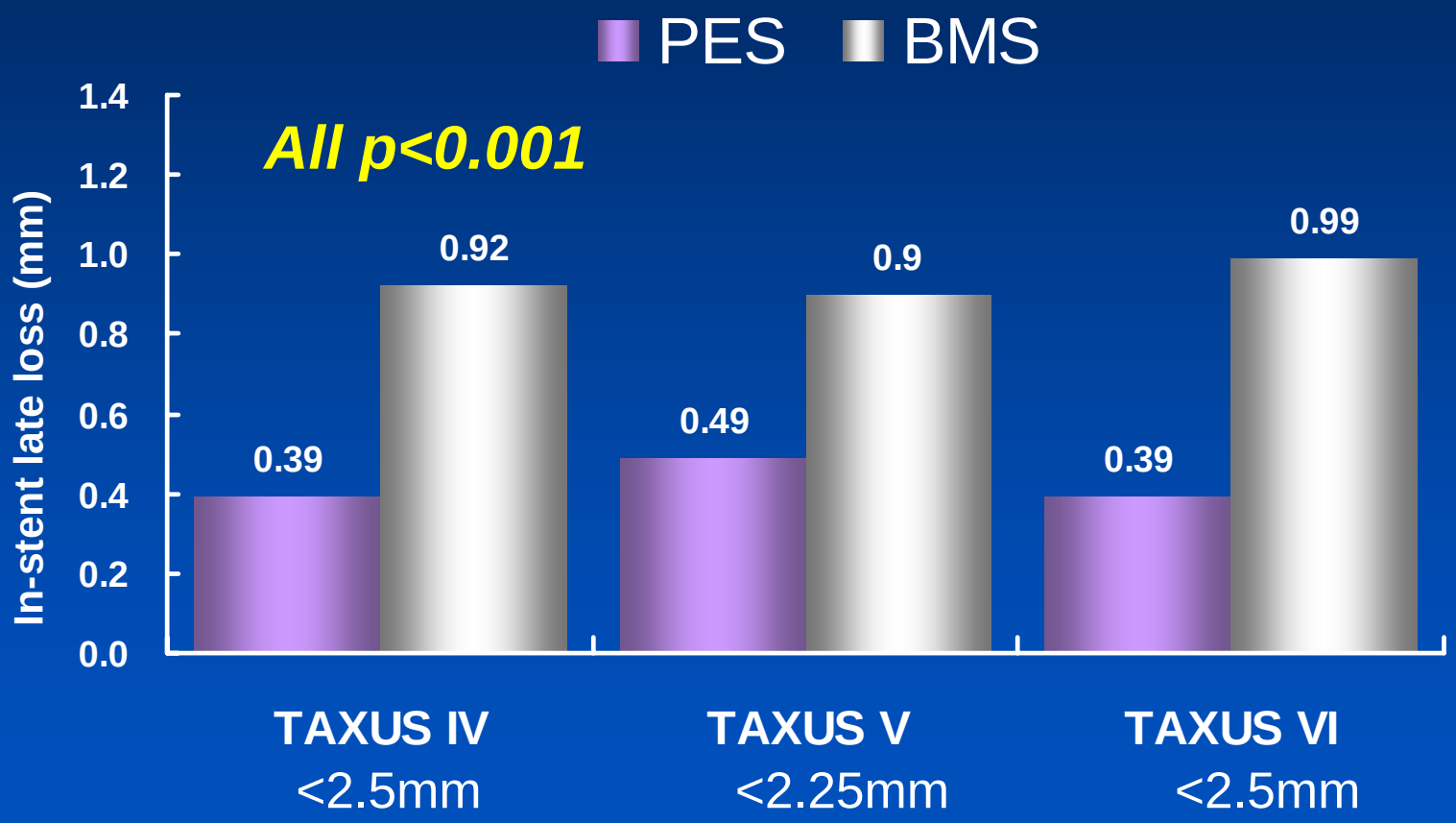
Nine-Month TLR Rates
SES vs. BMS in RVD<2.75mm



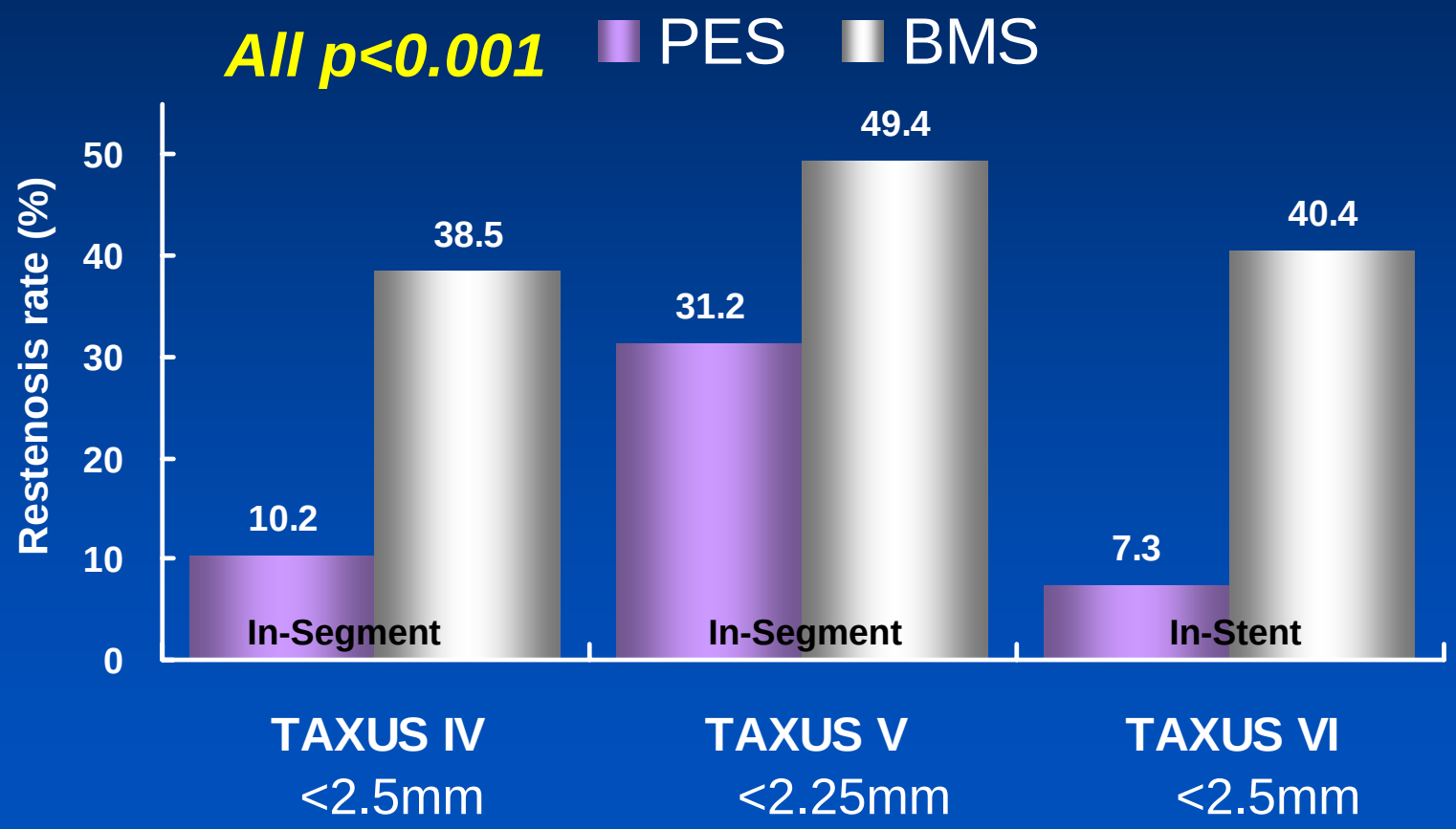
Paclitaxel-Eluting Stent
Taxus IV vs. V vs. VI

	TAXUS IV	TAXUS V	TAXUS VI
No of patients	1,314	1,156	446
Lesion length (mm)	14.4	17.3	20.6
Stent length (mm)	21.9	28.7	33.4
AHA/ACC type C lesions (%)	20.3	36.8	55.6
Small vessels (<2.5mm) (%)	32.1	18.7	27.8
Overlapping stent (%)	Not permit	29.1	27.8
Non-target vessel intervention (%)	20.8	NA	23.5
Diabetes mellitus (%)	23.4	31.7	20.0

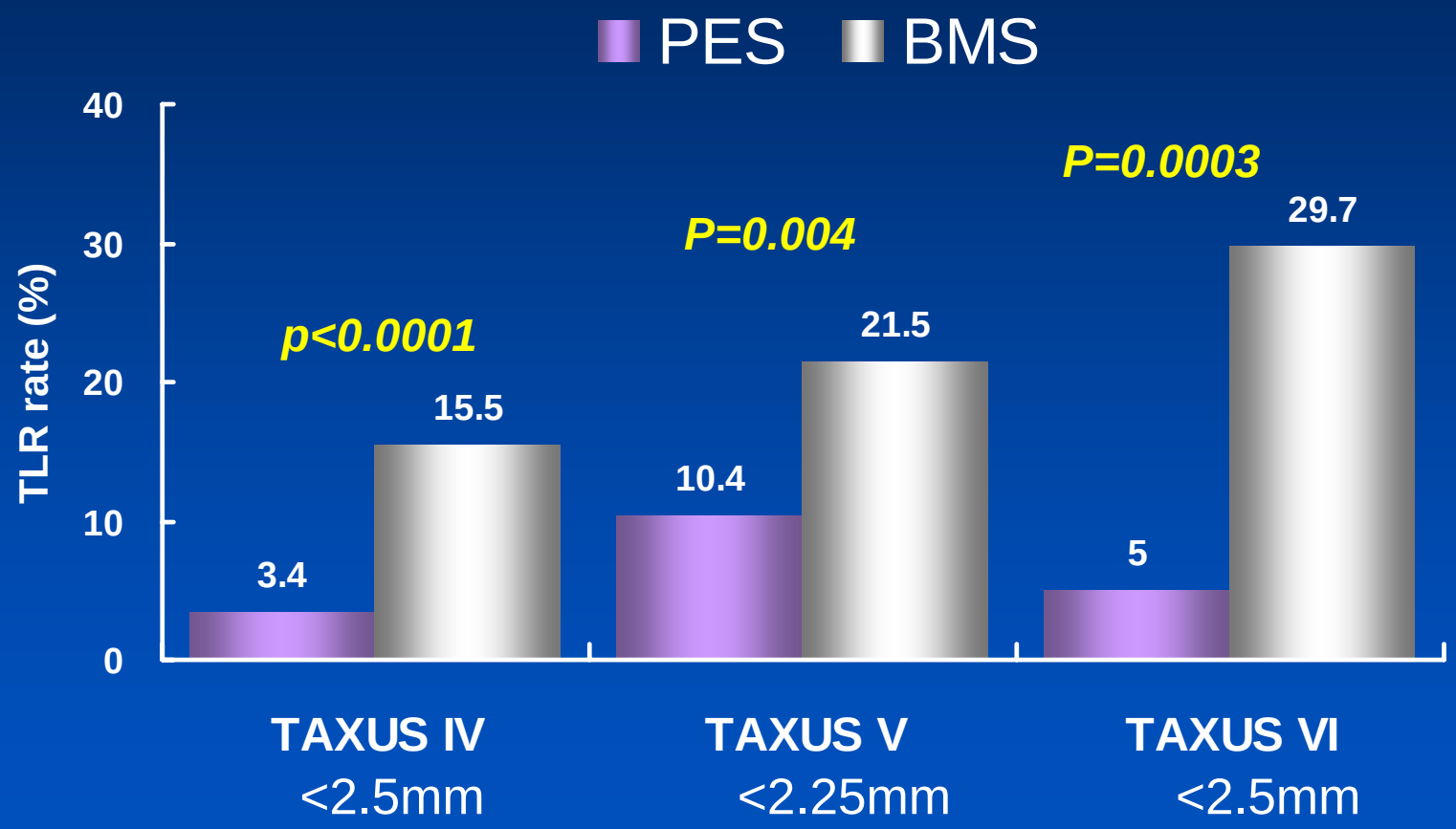
In-Stent Late Loss at 9 Mo
PES vs. BMS



Restenosis at 9 Mo
PES vs. BMS



TLR Rates at 9 Mo
PES vs. BMS



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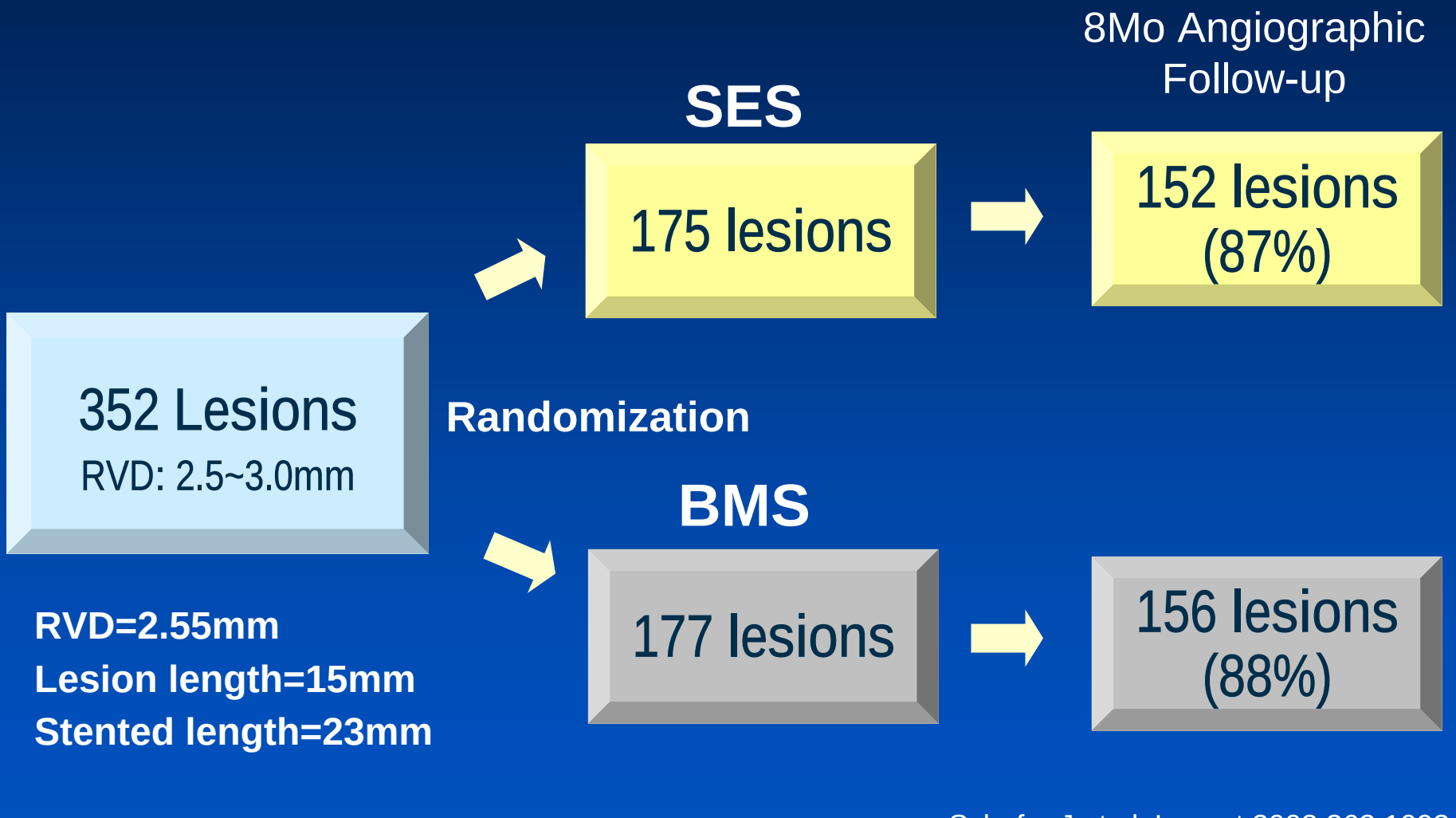
E-SIRIUS Study

2.5~3.0mm



Schofer J et al. Lancet 2003;362:1093

Angiographic Outcomes at 8 Mo

	SES	BMS	p
Reference size, mm	2.61±0.34	2.48±0.32	0.0006
In-stent MLD, mm	2.22±0.48	1.33±0.63	<0.0001
In-segment MLD, mm	1.97±0.48	1.29±0.61	<0.0001
In-stent late loss, mm	0.20±0.38	1.05±0.61	<0.0001
In-segment late loss, mm	0.19±0.38	0.80±0.57	<0.0001
In-stent restenosis	6/152 (3.9%)	65/156 (41.7%)	<0.0001
In-segment restenosis	9/152 (5.9%)	66/156 (42.3%)	<0.0001

Schofer J et al. Lancet 2003;362:1093

Clinical Outcomes at 9 Mo

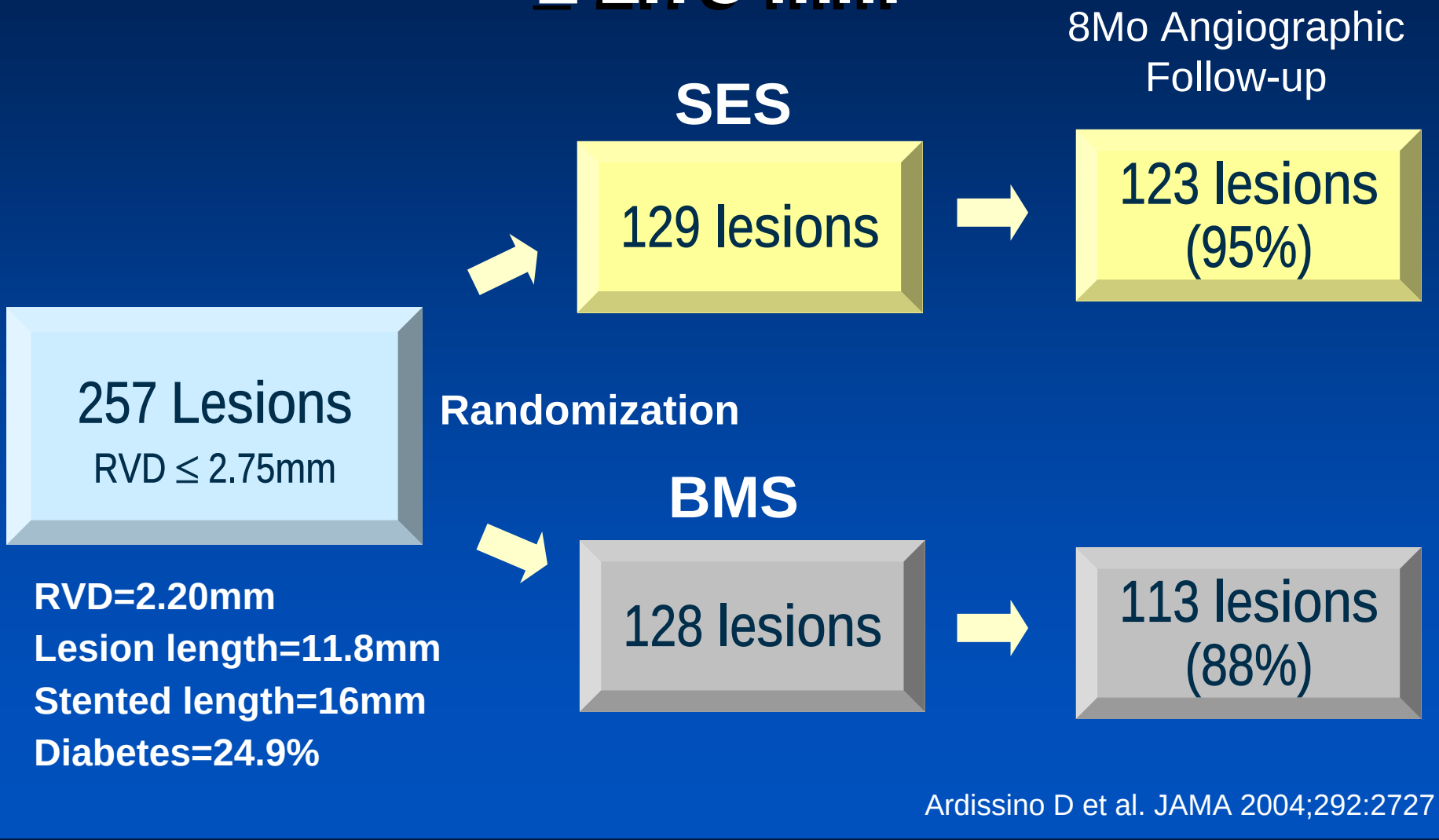
	SES (n=175)	BMS (n=177)	P
Death	2 (1.1)	1 (0.6)	0.62
MI	8 (4.6)	4 (2.3)	0.26
Q-MI	2 (1.1)	0 (0)	0.25
Non Q-MI	6 (3.4)	4 (2.3)	0.54
CABG	0 (0)	3 (1.7)	0.25
TLR	7 (4.0)	37 (20.9)	<0.0001
Total	14 (8.0)	40 (22.6)	0.0002

Data are shown as the number (%)

Schofer J et al. Lancet 2003;362:1093

SES-SMART Study

≤ 2.75 mm



Ardissino D et al. JAMA 2004;292:2727

Angiographic Outcomes at 8 Mo

	SES	BMS	p
In-stent MLD, mm	2.01±0.43	1.20±0.64	<0.001
In-segment MLD, mm	1.70±0.48	1.09±0.60	<0.001
In-stent late loss, mm	0.16±0.38	0.90±0.62	<0.001
In-segment late loss, mm	0.16±0.46	0.69±0.61	<0.001
In-stent restenosis	6/123 (4.9)	55/113 (49.1)	<0.001
In-segment restenosis	12/123 (9.8)	60/113 (53.1)	<0.001

Data are shown as the number (%)

Ardissino D et al. JAMA 2004;292:2727

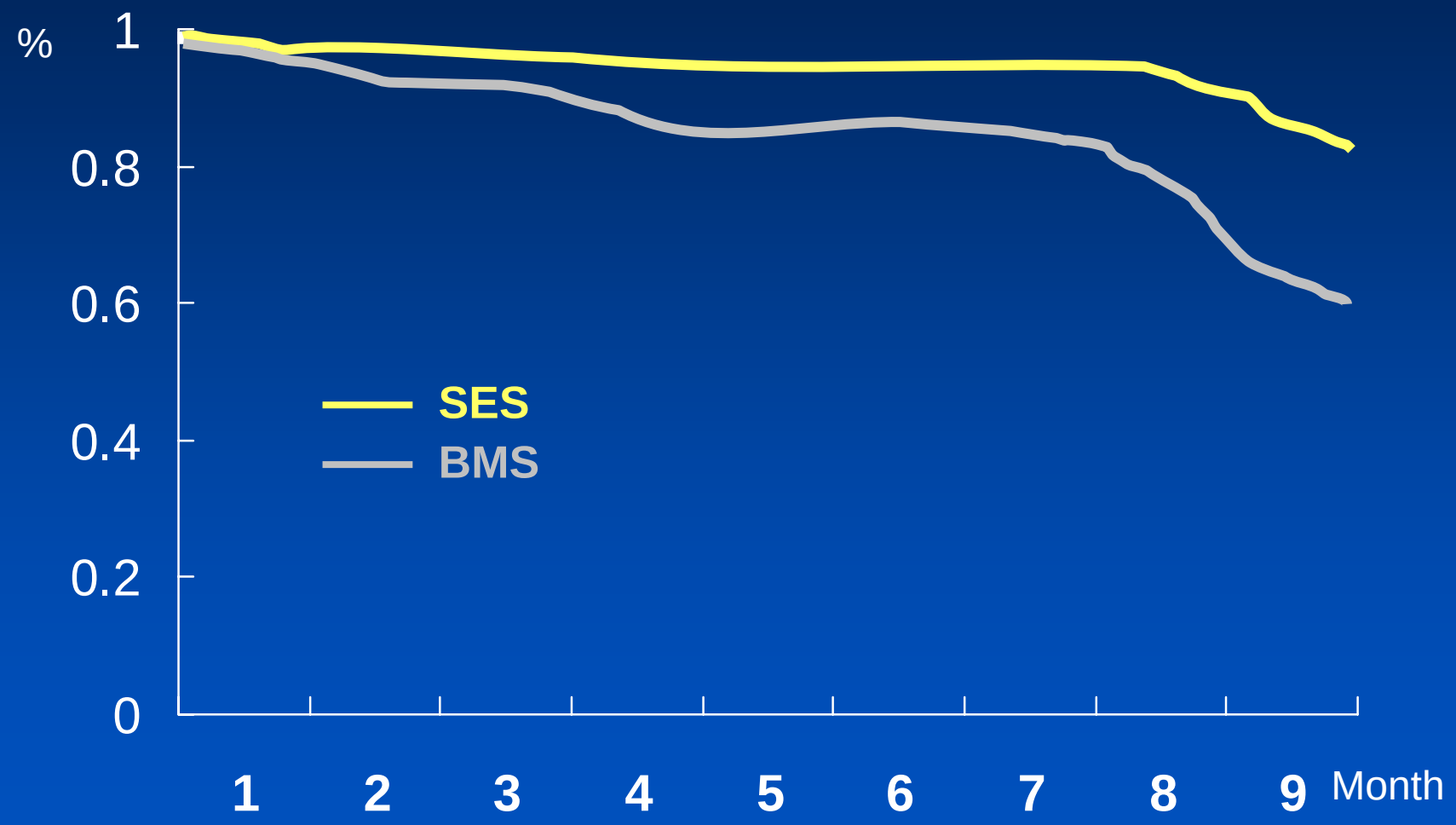
Clinical Outcomes at 8 Mo

	SES (n=129)	BMS (n=128)	P
Death	0	2 (1.6)	0.24
MI	2 (1.6)	10 (7.8)	0.04
Q-MI	0	2 91.6)	0.24
Non Q-MI	2 (1.6)	8 (6.3)	0.06
CVA	1 (0.8)	1 (0.8)	>0.99
TLR	9 (7)	27 (21.1)	0.002
Total	12 (9.3)	40 (31.3)	<0.001

Data are shown as the number (%)

Ardissino D et al. JAMA 2004;292:2727

Event-free Survival at 9 Mo



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DES in Small Vessels

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SVELTE Study

8Mo Angiographic Follow-up

101 Lesions
RVD = 2.25~2.75mm

SES-SVELTE

101 lesions

94.1%

- **Full-lesion coverage**
- **No edge injury**

Non-randomized historical comparison

101 Lesions
RVD=Lowest tertile from SIRIUS

SES from SIRIUS

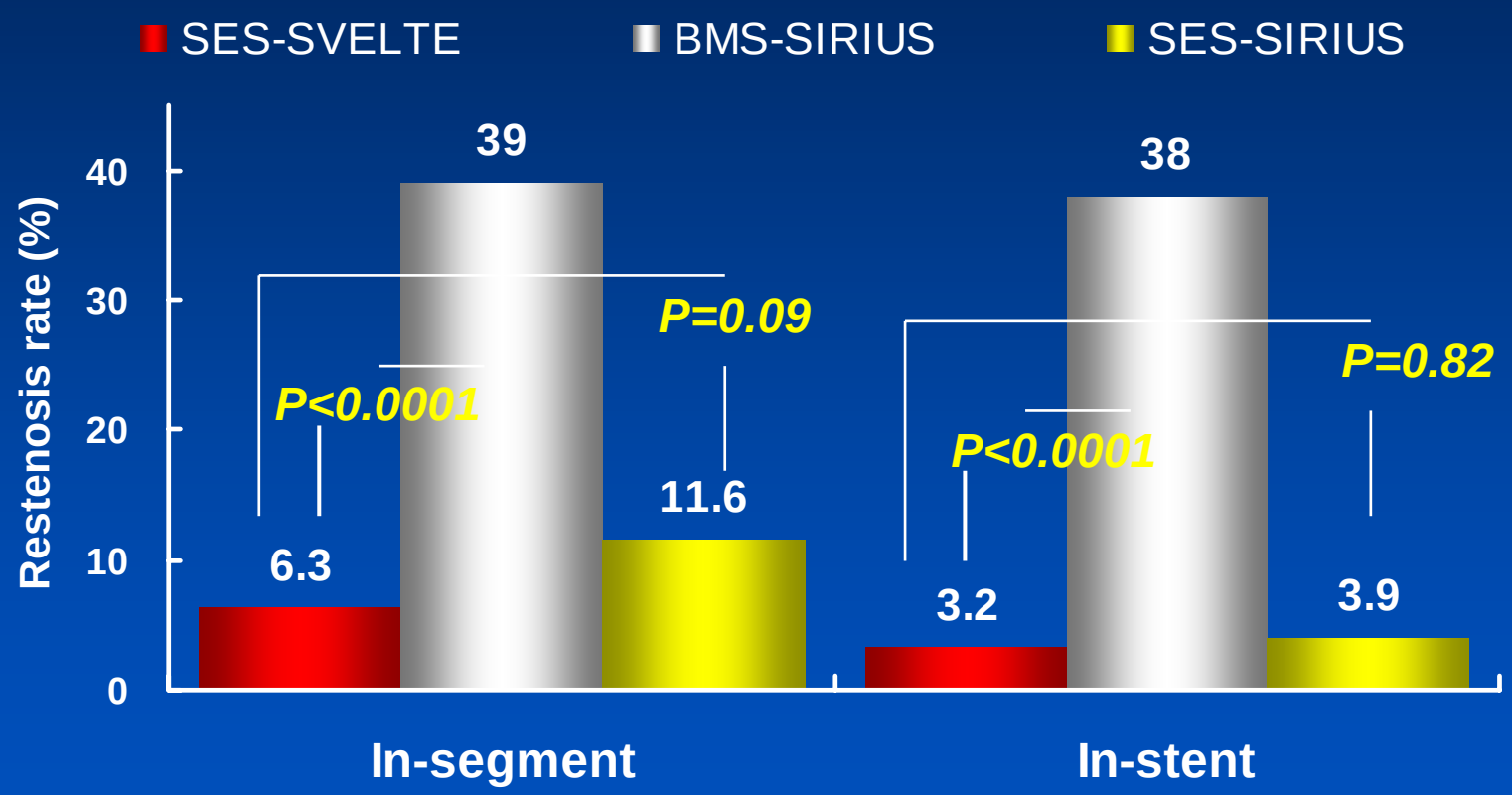
101 lesions

91%

Guagliumi G. TCT 2004

Restenosis Rate at 8 Mo

SES-SVELTE vs. BMS-SIRIUS vs. SES-SIRIUS



EVOLUTION Study
2.0-2.5mm

Multicenter registry
52 patients

- RVD= 2.0 ~ 2.5 mm
- Lesion length < 18mm
- SES heparin coated cobalt-Cr stent

In-stent restenosis	**4 (8.0%)**
In-segment restenosis	**5 (10.0%)**
In-stent late loss	**0.30 ± 0.44 mm**
In-segment late loss	**0.28 ± 0.45 mm**

Abizaid. TCT 2004

Integrate Analysis of SES studies

Angiographic Results

Small Vessels in Ravel, Sirius, New-Sirius, Direct and Svelte

	SES (n=909)	BMS (n=631)	p
In-stent late loss, mm	0.18	1.02	<0.0001
In-segment late loss, mm	0.21	0.81	<0.0001
In-stent restenosis, %	3.2%	38.5%	<0.0001
In-segment restenosis, %	6.9%	39.8%	<0.0001

Abizaid. TCT 2004

Integrate Analysis of SES studies

Clinical Results

in Small Vessels of Ravel, Sirius, New-Sirius, Direct and Svelte

	SES (n=909)	BMS (n=631)	p
Death	1.0%	0.7%	0.633
Q-MI	0.8%	0.3%	0.259
Non-Q MI	1.9%	2.9%	0.183
TVR	2.8%	3.4%	0.442
TLR	3.5%	17.1%	<0.0001
MACE	6.4%	19.4%	<0.0001

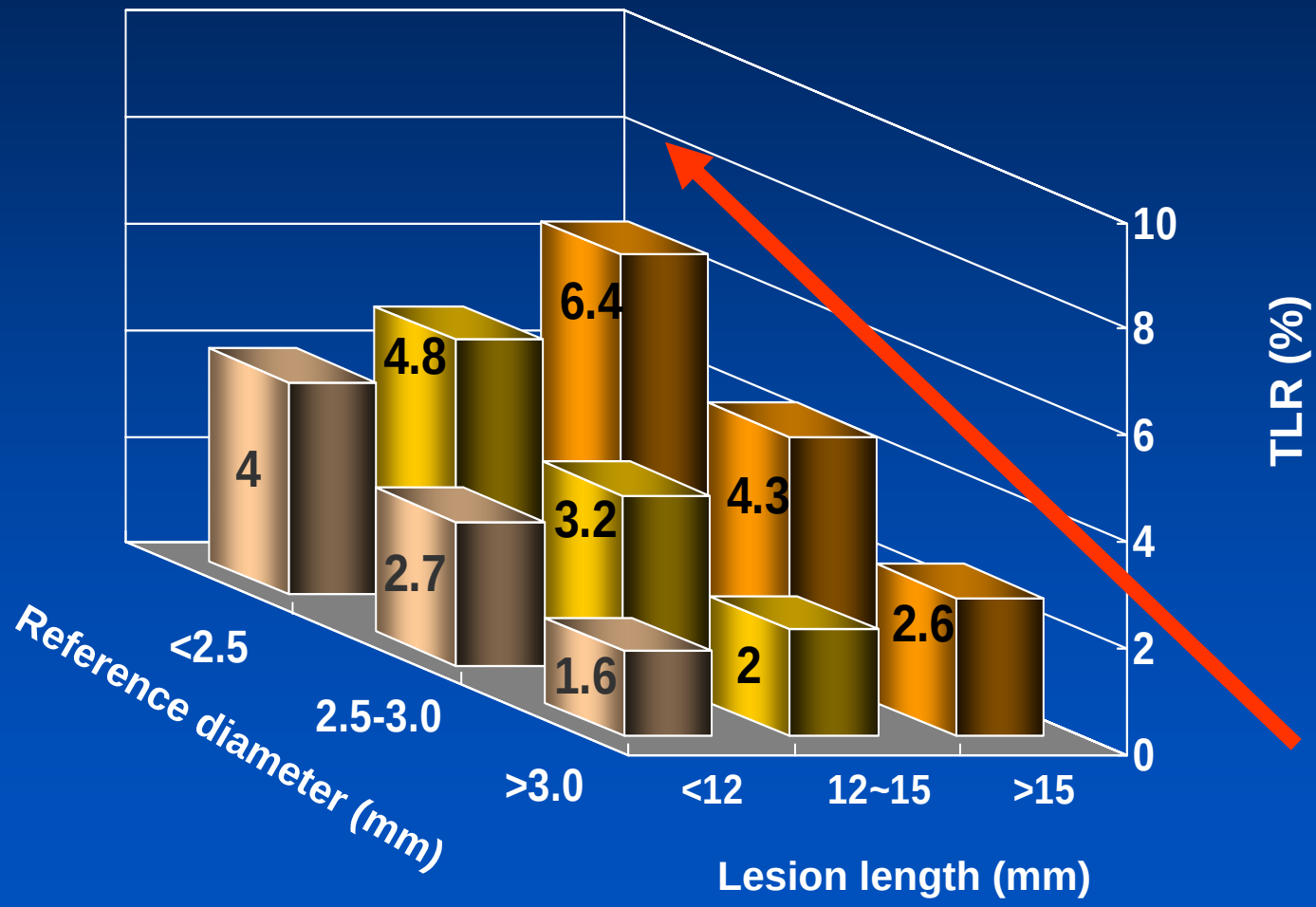
Abizaid. TCT 2004

DES in Small Coronary Lesions

Impact of Small Diameter

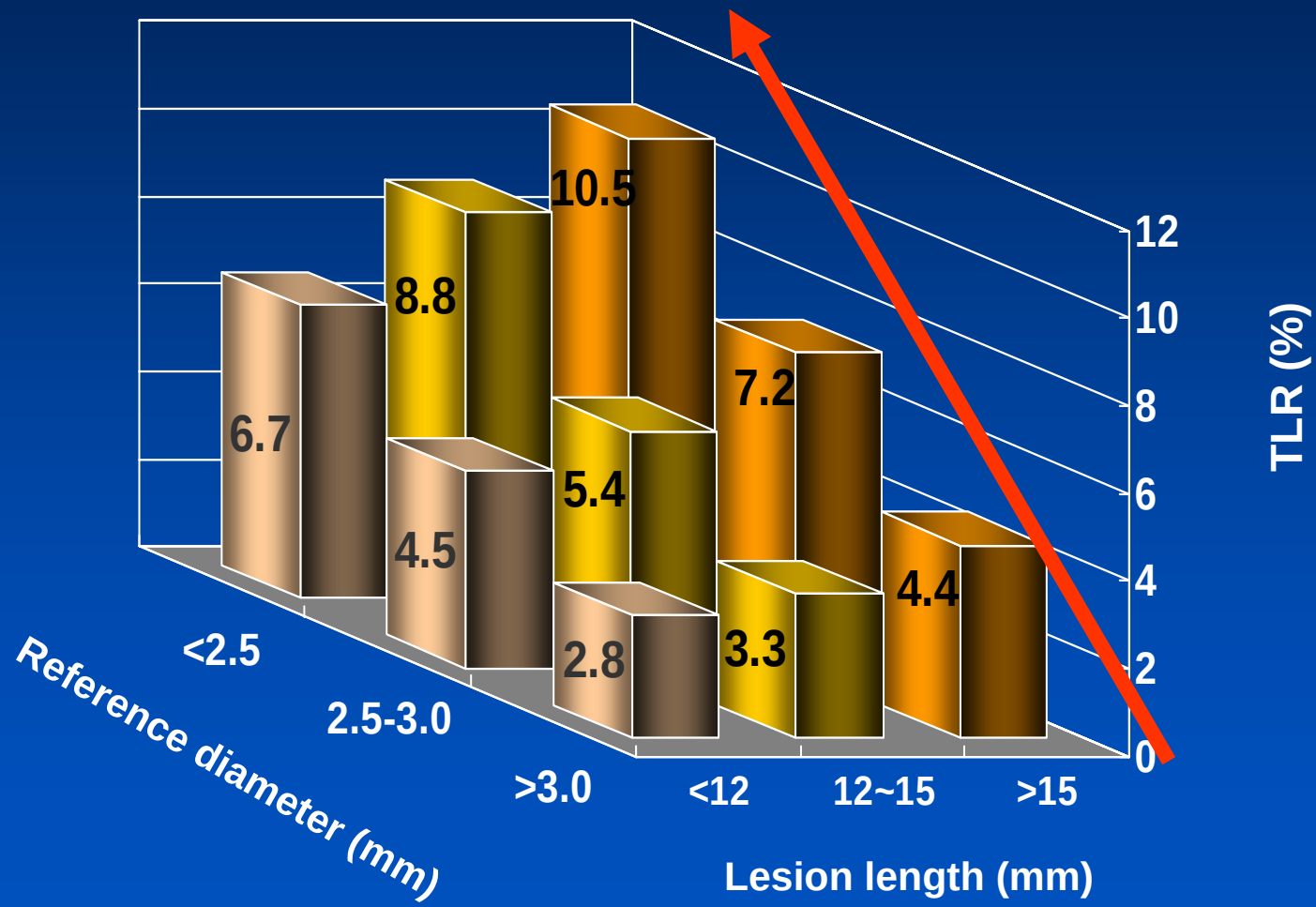
Predictors of TLR

In non-diabetics from Ravel, Sirius, New-Sirius, Direct and Svelte



Predictors of TLR

In diabetics from Ravel, Sirius, New-Sirius, Direct and Svelte



DES vs. BMS in Small Vessels

- In patients with small coronary lesions, the treatment with DES (either Cypher or Taxus), compared to the BMS, is associated with a dramatic reduction of angiographic and clinical events as the other coronary lesion subsets.
- However, the small coronary vessel remains an independent predictor of angiographic restenosis even in the DES era.

Small Vessel Disease

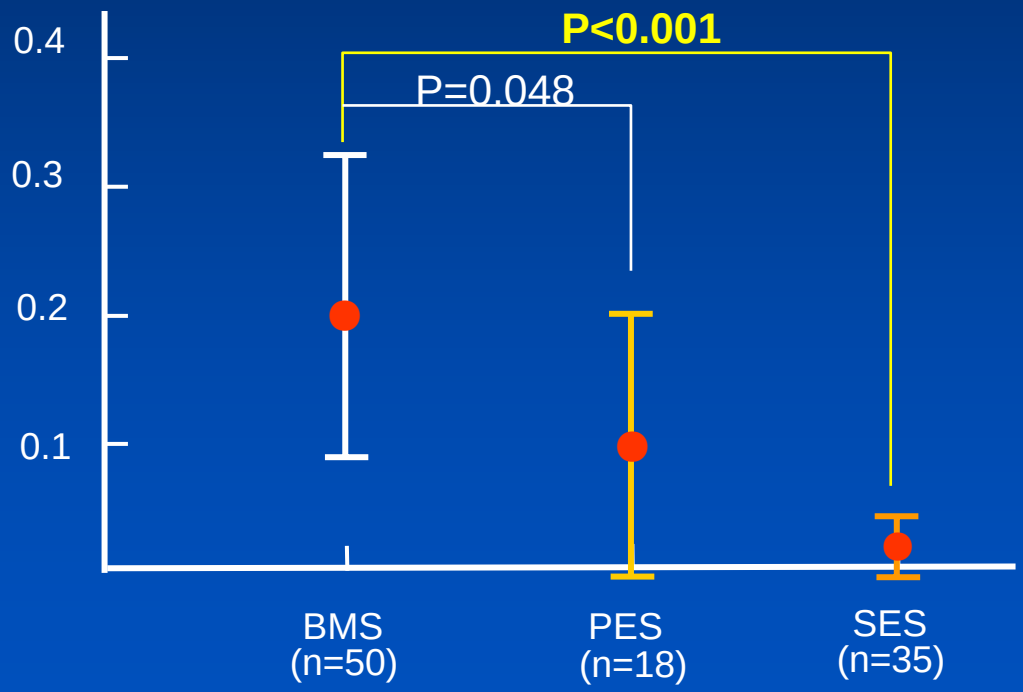
DES vs. BMS

IVUS Comparison of IH

BMS (Multi-Link) vs. PES (ACHIEVE) vs. SES

LL: 11.7mm, RVD: 2.6mm, DS:68.3%

6Mo Intimal Hyperplasia Thickness

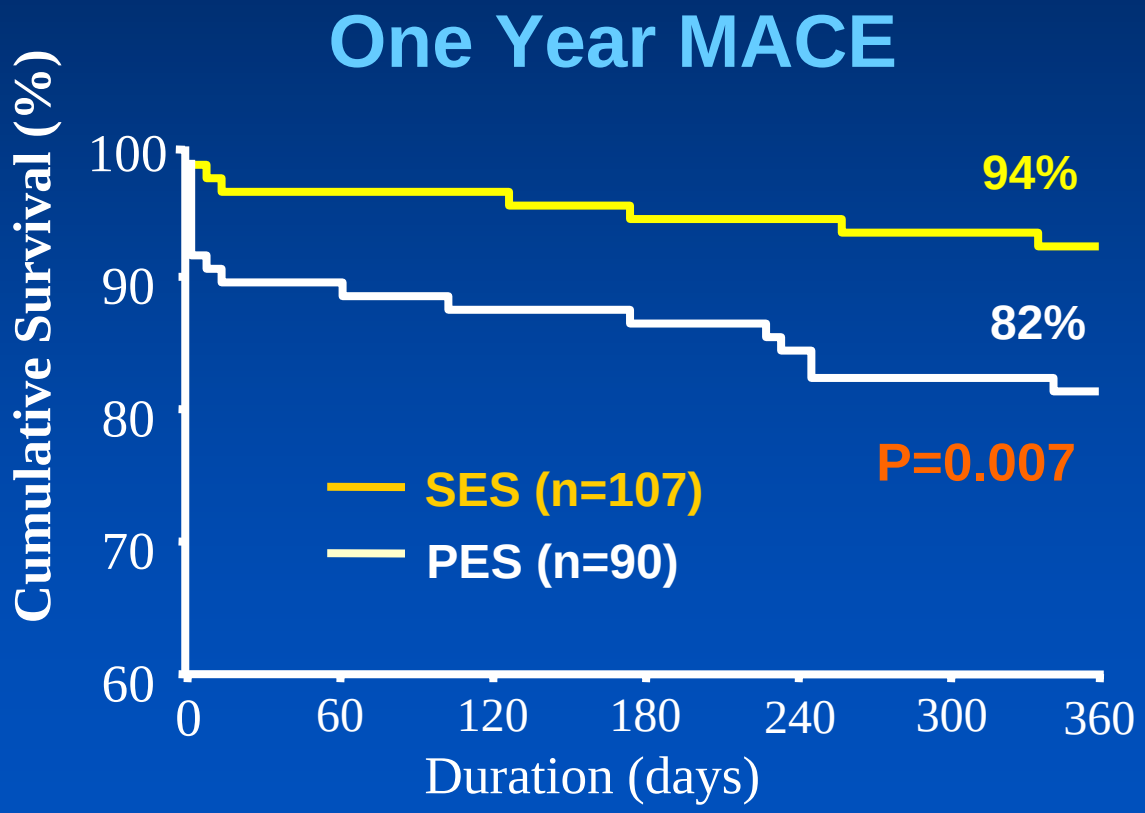


Hoffmann R. et al. Am J Cardiol 2004

Comparison of Very Small Vessels in RESEARCH vs. T-SEARCH Registries

2.25mm SES and PES stents

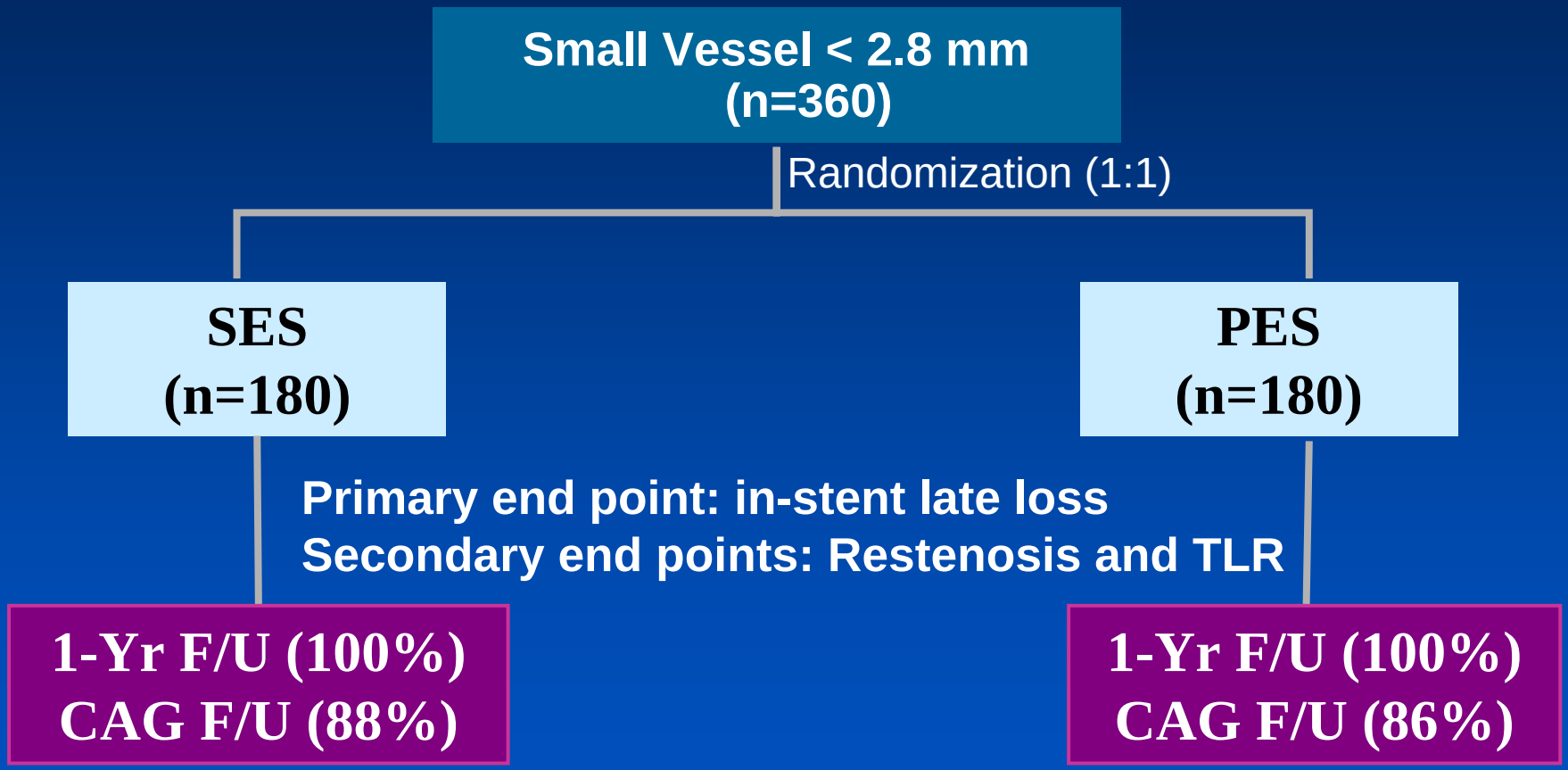
RVD: 1.90mm, MLD: 0.52mm, DS:72.4%, Stent length: 17.8mm



Rodriguez-Granillo GA. et al. J Invasive Cardiol 2005

SES vs PES for Small Vessels

ISAR-SMART 3 study



Mehilli J. et al Eur Heart J 2006;27:260

Angiogrpahy before Procedure

	TAXUS (n=204)	CYPHER (n=198)	P
Vessel size (mm)	2.40±0.38	2.44±0.38	0.34
Lesion length (mm)	11.7±6.7	12.9±8.0	0.12
MLD (mm)	10.3±0.39	0.99±0.40	0.33
DS (%)	57.2±14.4	59.4±15.3	0.15
Type B2/C lesions, n (%)	151 (74)	142 (72)	0.60

Mehilli J. et al Eur Heart J 2006;27:260

Angiogrpahy after Procedure

	TAXUS (n=204)	CYPHER (n=198)	P
Length of stent (mm)	21.0±7.8	21.4±9.8	0.65
MLD			
in-stent (mm)	2.44±0.37	2.44±0.36	0.80
in-segment (mm)	2.00±0.47	2.04±0.47	0.41
DS			
in-stent (%)	6.3±7.7	5.6±7.5	0.36
in-segment (%)	18.5±7.2	16.7±7.7	0.05

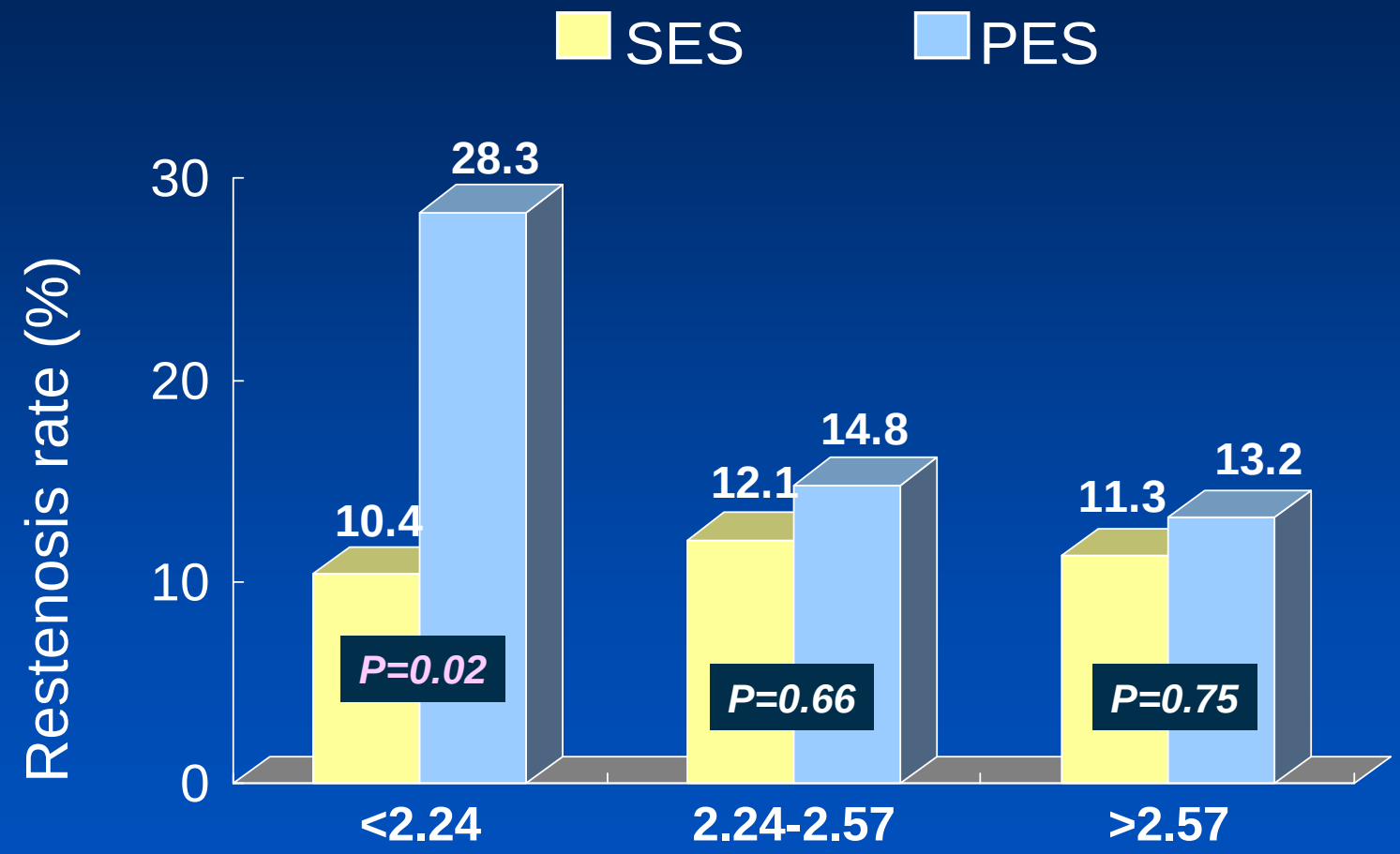
Mehilli J. et al Eur Heart J 2006;27:260

Angiogrpahy at Follow-up

	TAXUS (n=204)	CYPHER (n=198)	P
MLD			
in-stent (mm)	1.88±0.67	2.21±0.66	<0.001
in-segment (mm)	1.67±0.63	1.91±0.61	<0.001
Late lumen loss			
in-stent (mm)	0.56±0.59	0.25±0.55	<0.001
in-segment (mm)	0.34±0.57	0.13±0.56	<0.001
Binary restenosis			
in-stent, n (%)	26 (14.9)	14 (8.0)	0.04
in-segment, n (%)	33 (19.0)	20 (11.4)	0.047

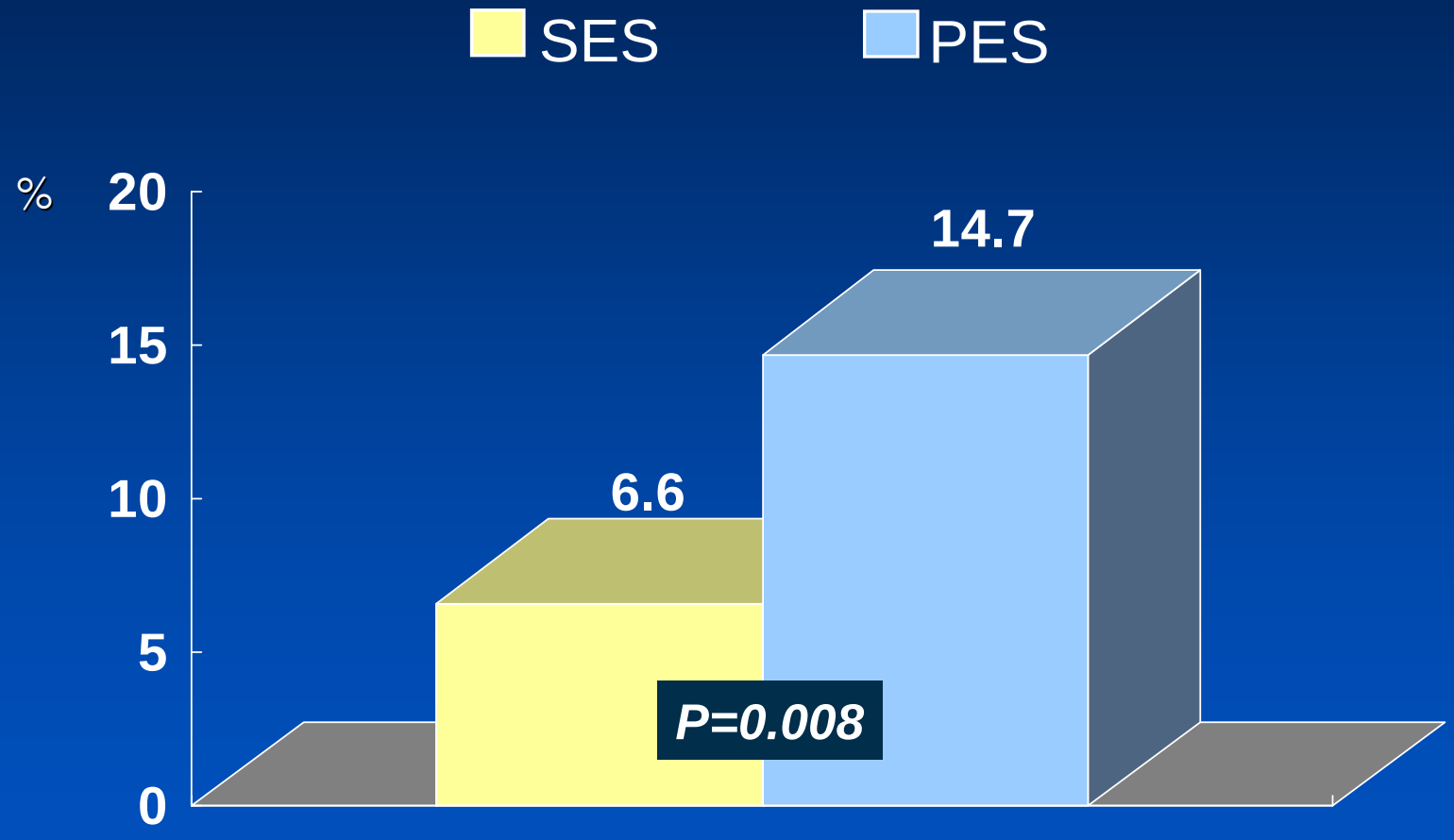
Mehilli J. et al Eur Heart J 2006;27:260

Impact of Vessel Size on Restenosis



Mehilli J. et al Eur Heart J 2006;27:260

Target Lesion Revascularization



Mehilli J. et al Eur Heart J 2006;27:260

AMC Experience in Small Vessel Disease

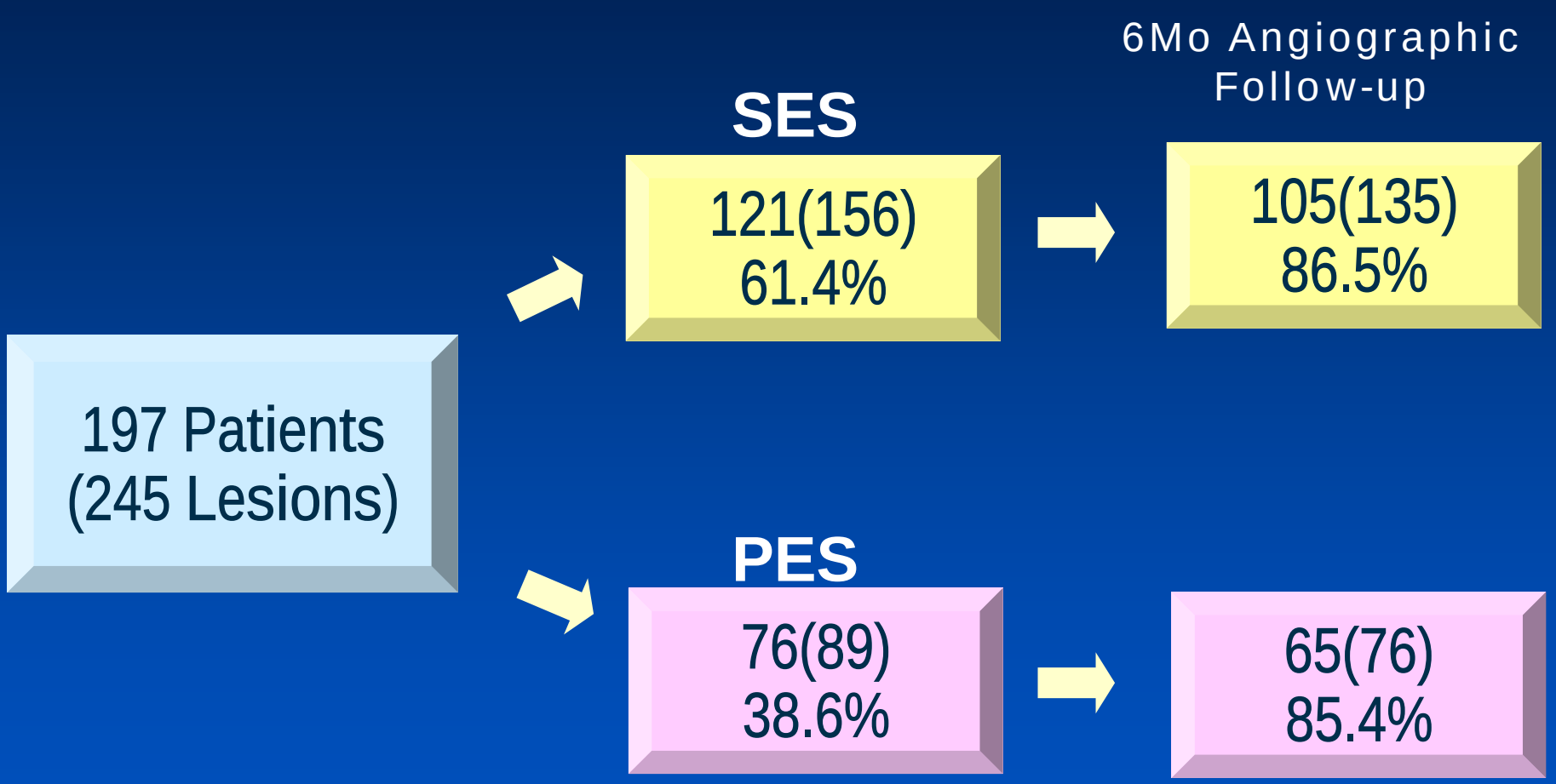
Subjects

- Between June 2003 and July 2004

- Inclusion criteria
  - Reference diameter ≤ 2.75mm
  - Diameter stenosis ≥ 70%
- Exclusion criteria
  - AMI within 48 hrs
  - LVEF ≤ 40%
  - LM, Bifurcation, CTO and ISR lesions
  - History. of PCI or CABG

KH Park. Catheter Cardiovasc Interv 2006;67:589

Subjects
≤ 2.75 mm



KH Park. Catheter Cardiovasc Interv 2006;67:589

Baseline Characteristics

	SES (n=121)	PES (n=76)	P- Value
Age, yrs	61.0±8.6	59.210.6	0.22
Male, n (%)	76 (62.8)	54 (71.0)	0.28
LVEF, %	59.1±8.5	58.8±7.6	0.79
Hypertension, n (%)	62 (51.2)	34 (44.7)	0.38
Diabetes mellitus, n (%)	39 (32.2)	21 (24.5)	0.53
Current smoker, n (%)	35 (28.9)	28 (36.8)	0.21
Hypercholesterolemia, n (%)	39 (32.2)	30 (39.5)	0.36
ACS	61 (50.4)	33 (43.3)	0.20

KH Park. Catheter Cardiovasc Interv 2006;67:589

Angiographic and Procedural Results

	SES (n=156)	PES (n=89)	P- Value
Multivessel, n (%)	62 (76.0)	63 (82.8)	0.51
Lesion location			0.21
LAD, n (%)	52 (52.6)	53 (59.6)	
LCX, n (%)	50 (32.0)	20 (22.4)	
RCA, n (%)	24 (15.3)	16 (18.0)	
Total stent length (mm)	31.4±17.5	32.8±14.4	0.69
Maximal pressure (atm)	15.9±3.0	15.1±2.9	0.09
Maximal device diameter (mm)	2.91±0.2	3.0±0.22	0.23

KH Park. Catheter Cardiovasc Interv 2006;67:589

Baseline QCA

	Cypher (n=156)	Taxus (n=89)	P- Value
Baseline			
Lesion length (mm)	25.2±14.7	27.1±12.7	0.34
Reference (mm)	2.47±0.21	2.44±0.25	0.19
MLD (mm)	0.86±0.33	0.81±0.42	0.31
Diameter stenosis (%)	65.4±13.0	67.5±16.0	0.22
After procedure			
MLD (mm)	2.52±0.33	2.42±0.35	0.45
Diameter stenosis (%)	3.7±7.1	5.8±8.3	0.06
Stent length (mm)	31.4±17.5	32.8±14.4	0.69

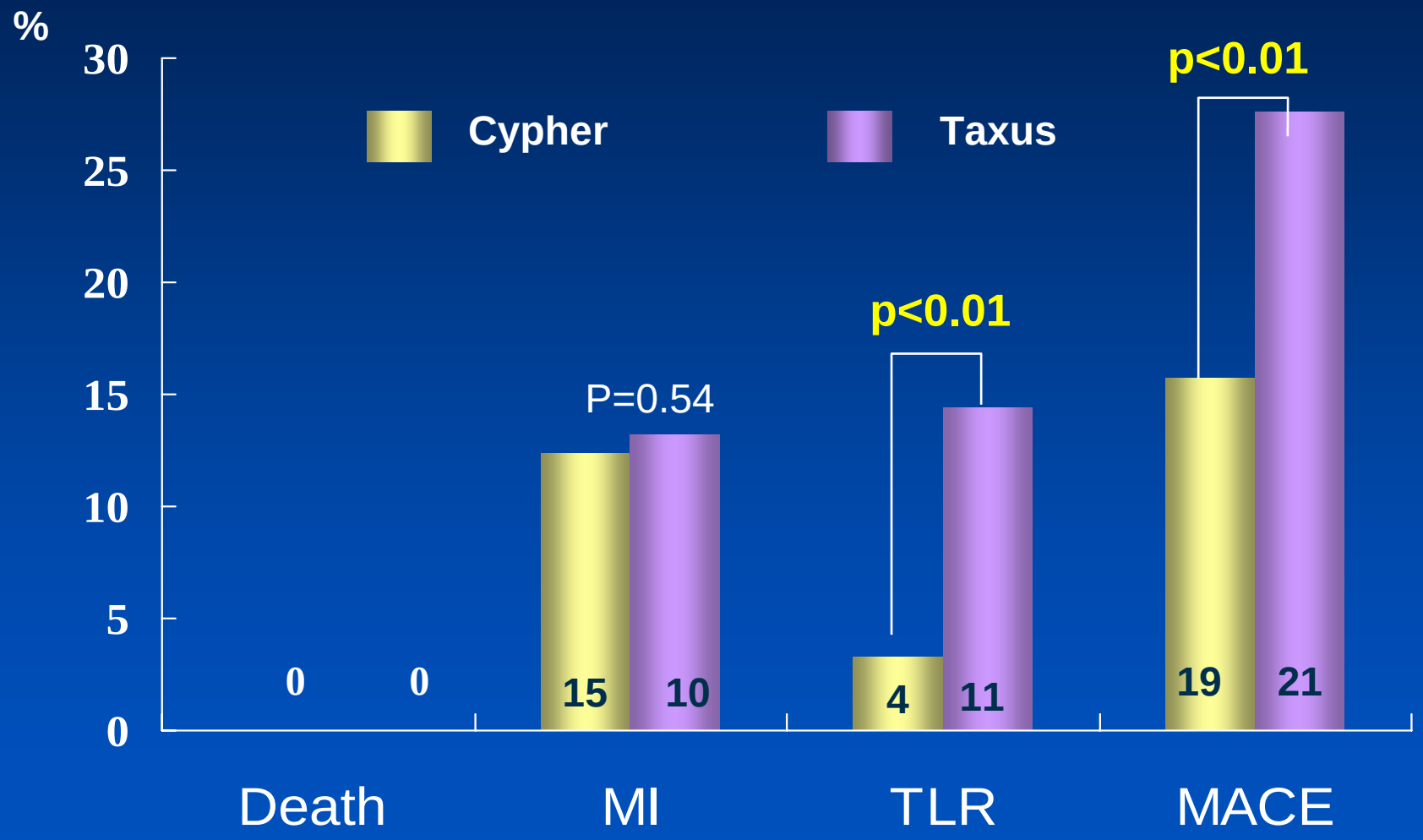
KH Park. Catheter Cardiovasc Interv 2006;67:589

QCA at 6 months

	Cypher	Taxus	P- Value
Lesions, n (%)	135 (86.5)	76 (85.4)	0.85
Reference (mm)	2.46±0.28	2.43±0.39	0.54
MLD (mm)	2.32±0.56	1.77±0.77	<0.001
DS (%)	5.38±22.5	31.7±34.9	<0.001
Late loss (mm)	0.29±0.42	0.69±0.62	<0.001
Restenosis, n (%)	9 (6.7)	21 (27.7)	<0.001

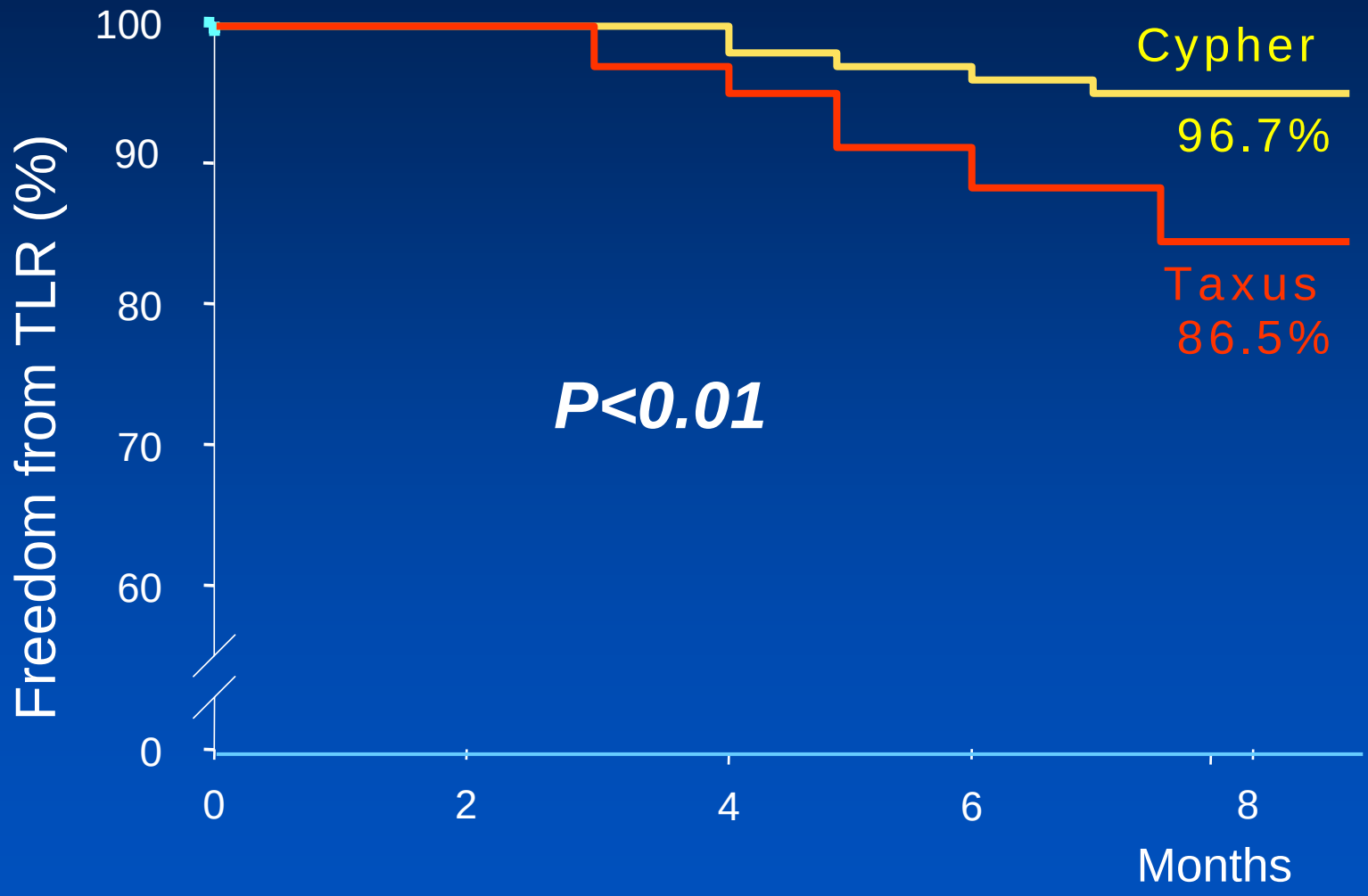
KH Park. Catheter Cardiovasc Interv 2006;67:589

Clinical outcomes at 9Mo



KH Park. Catheter Cardiovasc Interv 2006;67:589

Freedom from TLR at 9Mo



KH Park. Catheter Cardiovasc Interv 2006;67:589

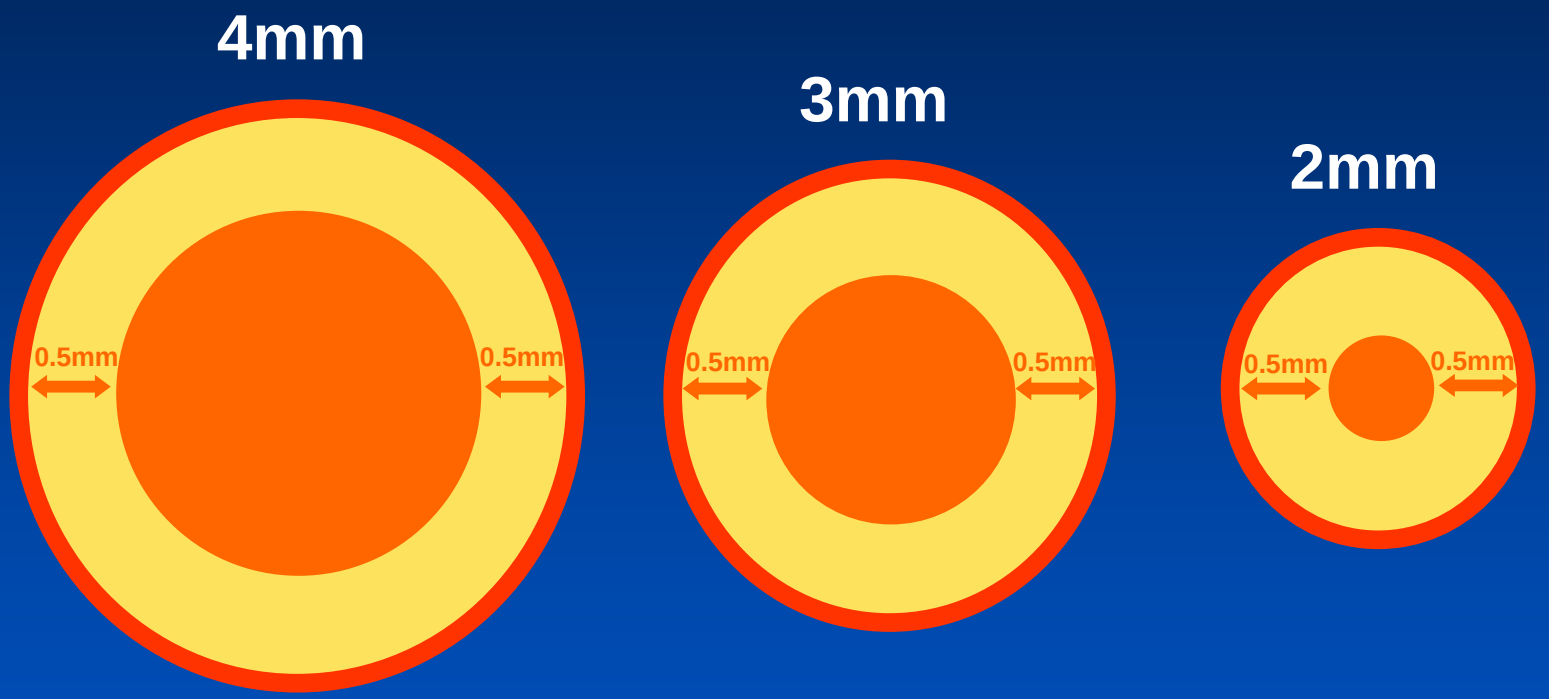
SES vs. PES in Small Vessels

- In patients with small vessels, use of the SES appears to be associated with a decrease in the extent of late luminal loss, angiographic restenosis, and the need of target lesion revascularization, as compared to use of the PES.
- Our finding in the AMC registry was in line with the recent randomized studies comparing the efficacy of SES versus PES.
- However, a randomized study for small coronary lesions is warranted to verity this registry result.

New DES for Small Vessels

Greater impact of late loss in small vessel

Late Loss 1mm



%DS	25%	33%	50%
%Decrease in CSA	44%	56%	75%

ISAR-STEREO-2

BMS Study

611 Lesions

Lesion length: 14.0mm
RVD: 2.92mm
DS: 69.5%

Randomization (1:1)

Multilink

309 Lesions (50um)

6Mo Angiographic Follow-up

229 Lesions 77%

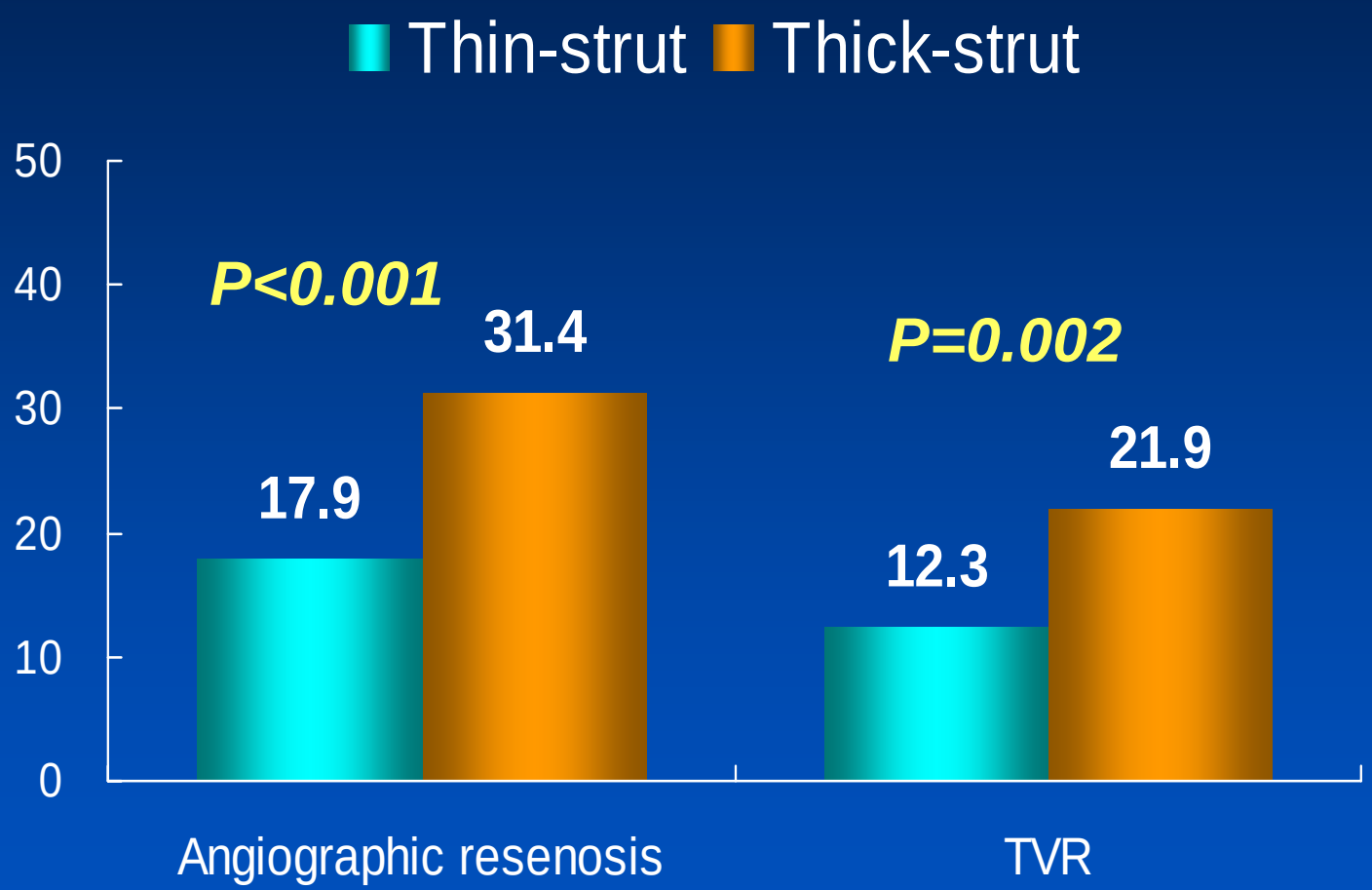
Bx Velocity

302 Lesions (140um)

236 Lesions 80%

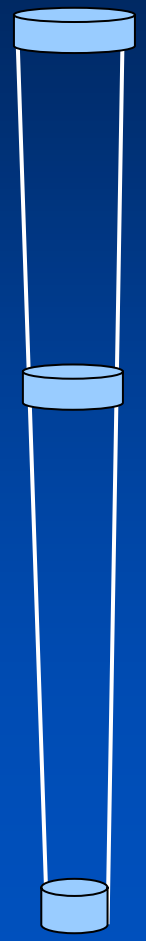
Pache J et al. J Am Coll Cardiol 2003;41:1283

Angiographic and Clinical Outcomes



Pache J et al. J Am Coll Cardiol 2003;41:1283

Thin Strut BMS vs. DES ?



μm

0.200 Jo-Graft stent

0.150 S 670

0.140 Bx Velocity

0.130 Multilink Tetra

Cypher

Taxus

0.120

0.100 NIR

0.090 Biodivysio

0.080 Tsunami

0.075 BeStent

0.070 Driver Vision

0.062

0.055

0.050 ACS Multilink

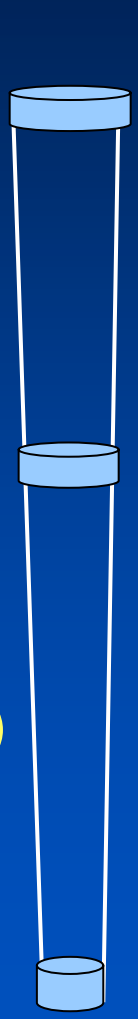
Strut Thickness and Restenosis in Small Vessel Disease

Thin-strut BMS (BeStent; 76μm) vs Thick-strut DES (Cypher; 140μm)

	Cypher	BeStent	P
Entire group (n=409)	9.0	22.5	<0.001
> 2.8mm (n=235)	7.0	34.2	<0.001
≤ 2.8mm (n=174)	10.0	13.1	0.52

Pache J. et al. Eur Heart J 2005

However, Thin-Strut DES ?



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Thin DES

New DES in Small Vessels

- In the studies with BMS, thinner strut has been shown to decrease neo-intimal hyperplasia.
- However, a recent randomized study failed to observe a similar efficacy of the thin-strut BMS compared to that of the SES in small coronary lesions.
- Nonetheless, a more smart DES stent platform with better conformability, trackability, and thinner stent strut is being investigated to improve the outcomes of small coronary interventions.