

Are There Meaningful Differences Among FDA- Approved Drug-Eluting Stents?

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Disclosure Statement of Financial Interest

Consulting Fees/Honoraria

- Abbott
- Biosensor
- Biotronik
- Boston Scientific
- Johnson&Johnson
- Medtronic

Are There Meaningful Differences Among FDA-Approved Drug-Eluting Stents

DES Efficacy

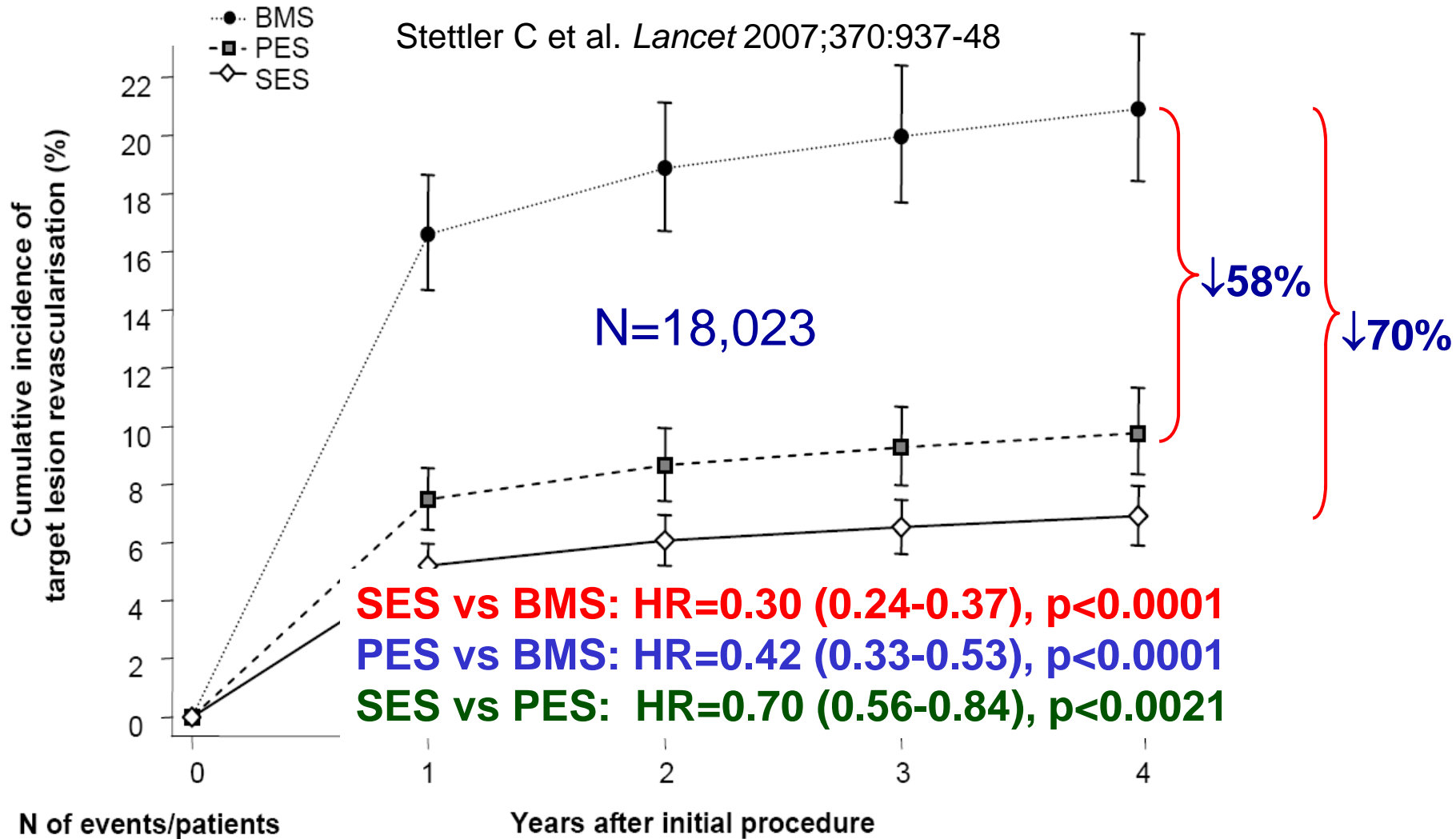
DES Safety

- Ischemic endpoints
- Stent thrombosis
- Endothelial function

Target Lesion Revascularization

SES vs PES vs BMS

Stettler C et al. *Lancet* 2007;370:937-48



N of events/patients

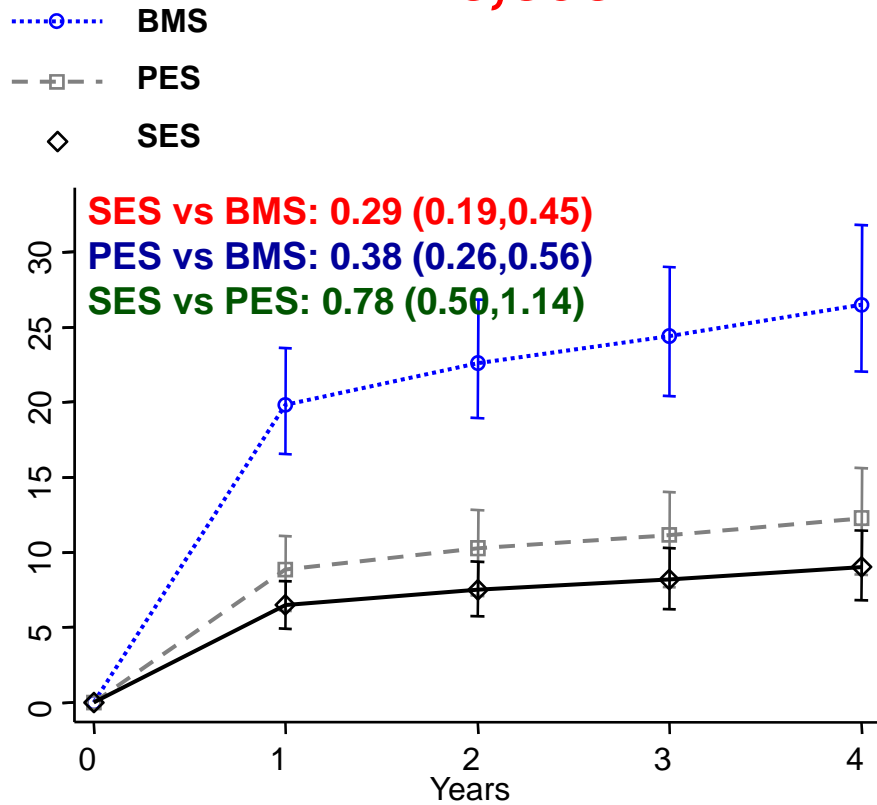
Years after initial procedure

BMS	4763	820/4746	53/2795	22/1871	10/1543
PES	6328	448/6280	98/3950	15/1999	6/832
SES	6621	356/6580	68/3801	16/2153	14/999

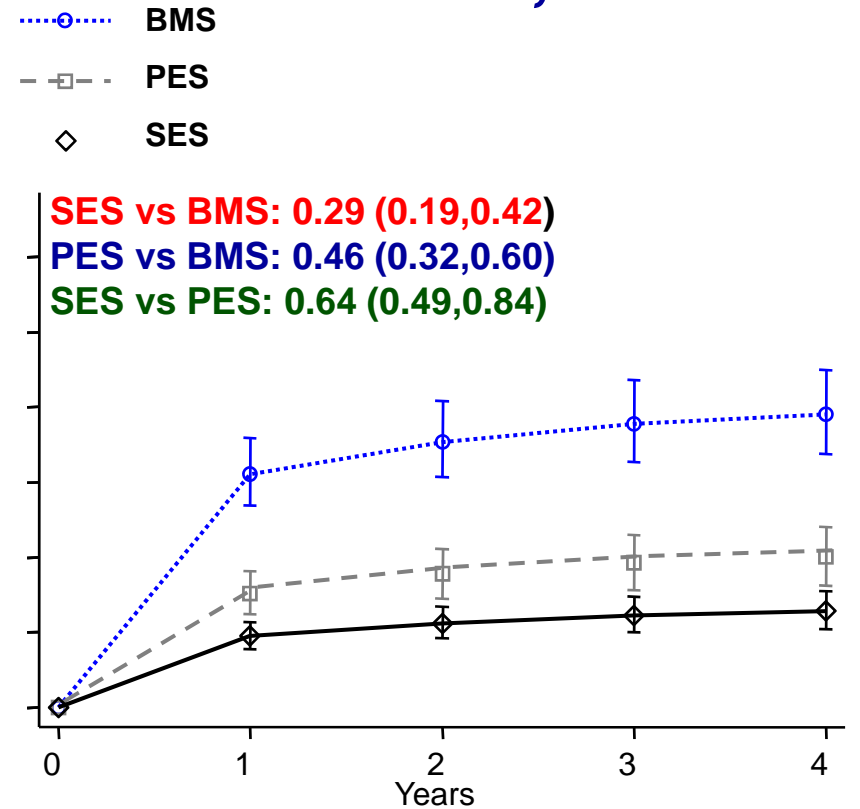
Target Lesion Revascularization SES vs PES vs BMS

Stettler C et al. *Brit Med J* 2008

Diabetic Patients N=3,853



Non-Diabetic Patients N=10,947



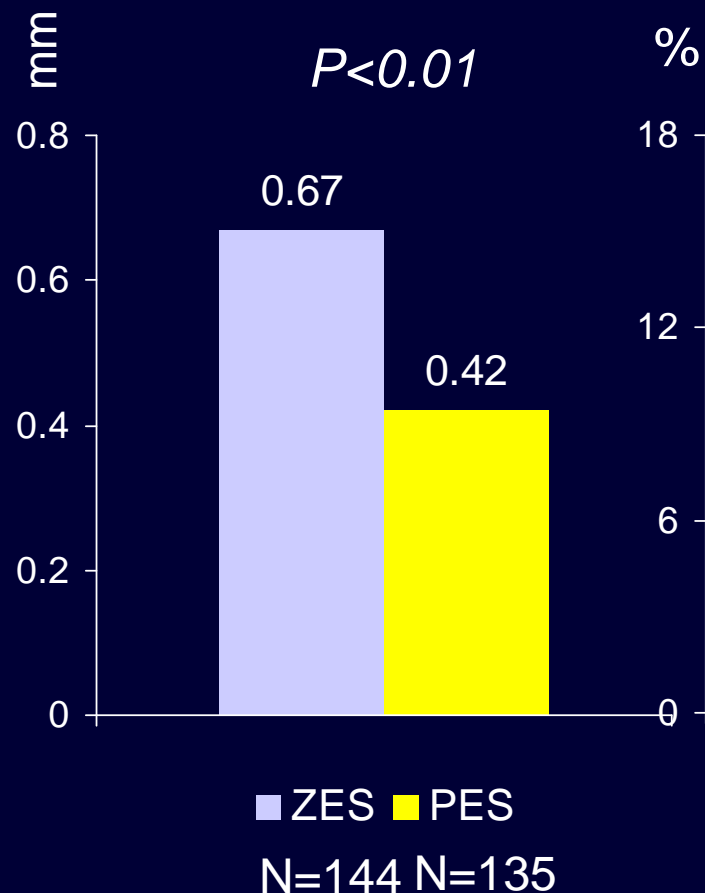
BMS	1228	1228	667	451	348
PES	1161	1161	942	486	146
SES	1373	1373	947	606	219

	3384	3384	2128	1420	1195
	3466	3466	2776	1477	660
	3505	3505	2614	1512	753

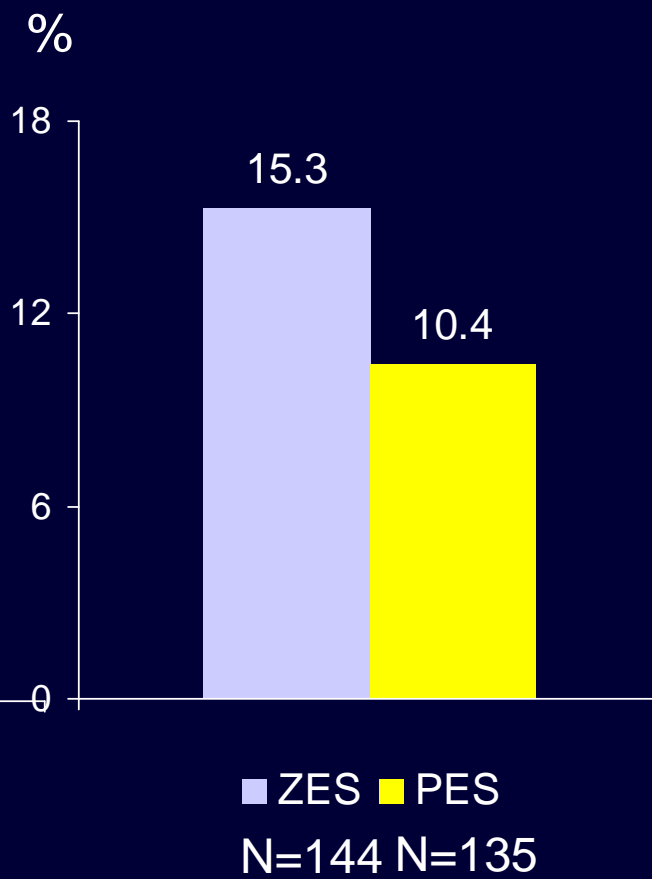
ENDEAVOR IV – Randomized Comparison Between Zotarolimus- and Paclitaxel-Eluting Stent

Leon M et al. *TCT 2007*

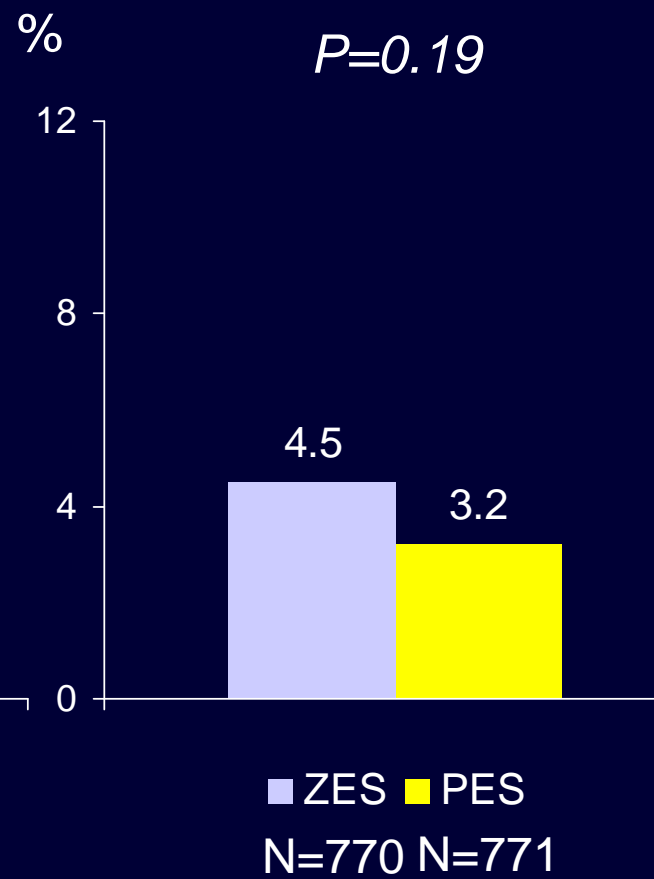
**Late Loss
@ 8 Months**



**Restenosis
@ 8 Months**



**TLR
@ 1 Year**



Zotarolimus-Eluting Stent (Endeavor)

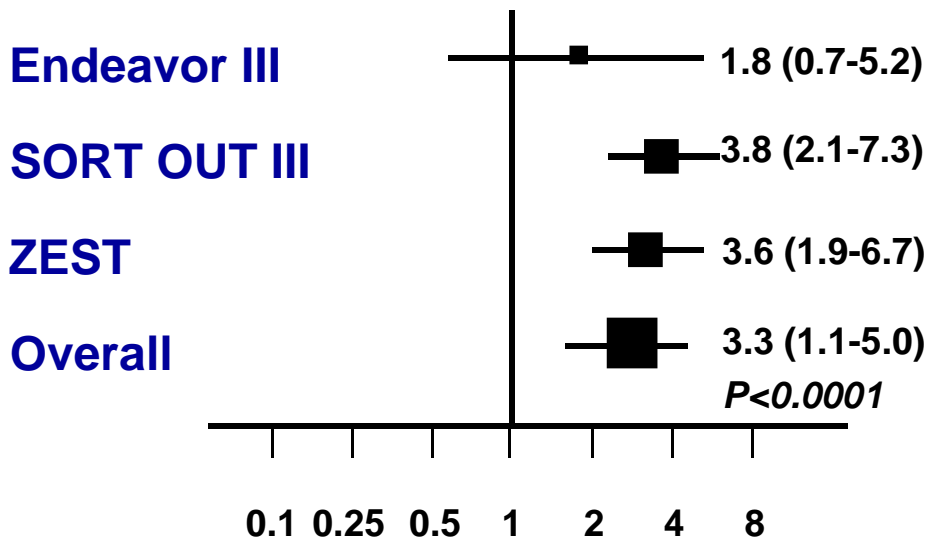
Target Lesion Revascularization @ 9-12 Mo

ZES versus SES

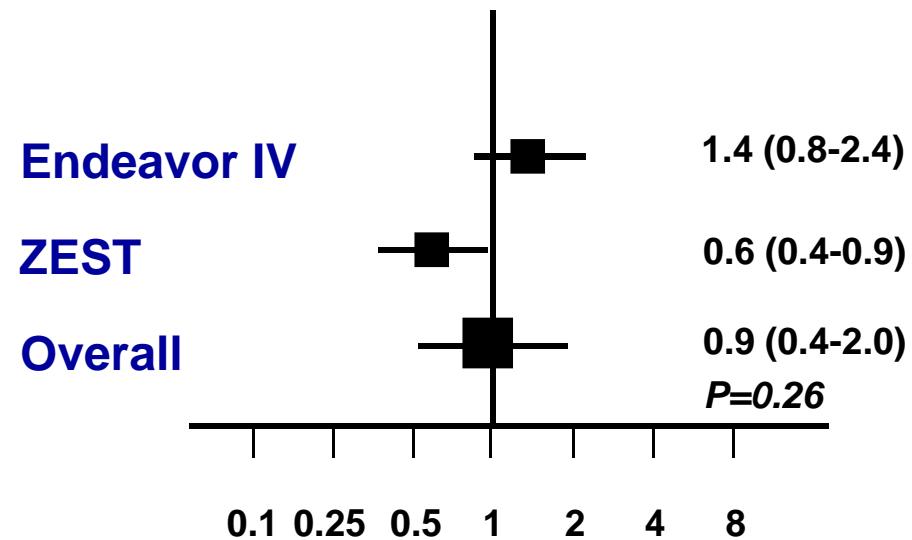
ZES versus PES

Relative Risk (95% CI)

Relative Risk (95% CI)



Favors ZES Favours SES



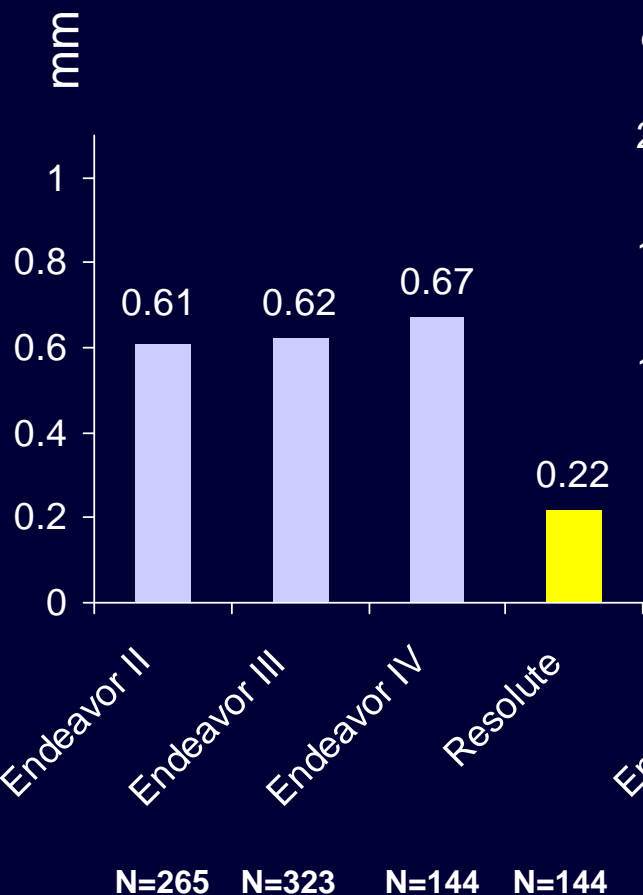
Favors ZES Favours PES

Zotarolimus-Eluting Stent

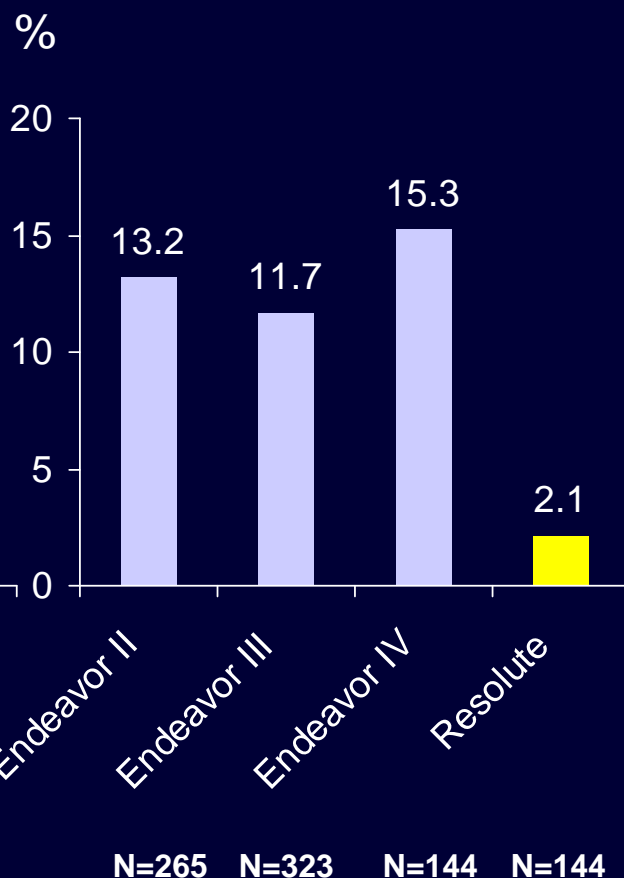
ENDEAVOR and RESOLUTE

Endeavor II Fajadet J et al. *Circulation* 2006;114:798-806; Meredith I et al. TCT 2007
Kandzari D et al. *J Am Coll Cardiol* 2006;48:2440-7; Leon M et al. TCT 2007

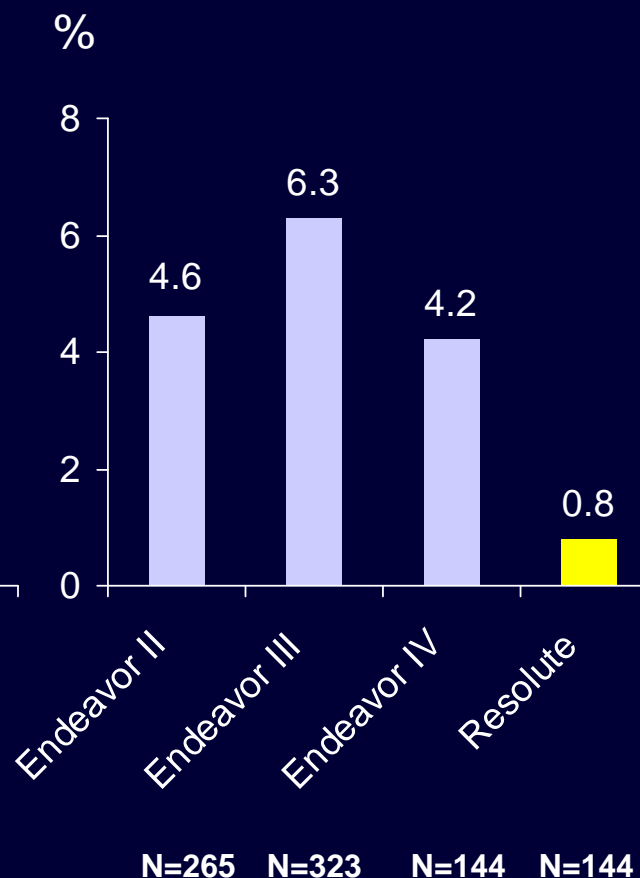
Late Loss (In-stent)



Restenosis (In-Segment)



Target Lesion Revascularization

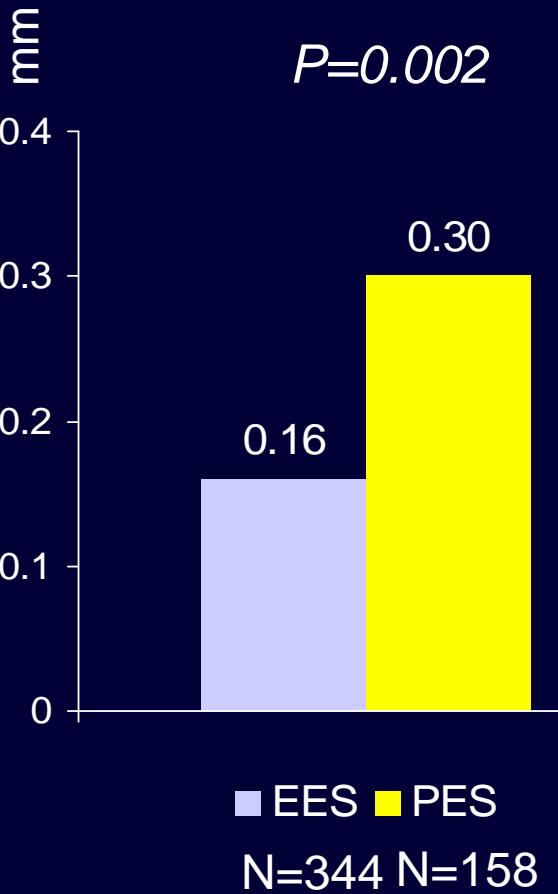


SPIRIT III - Randomized Comparison

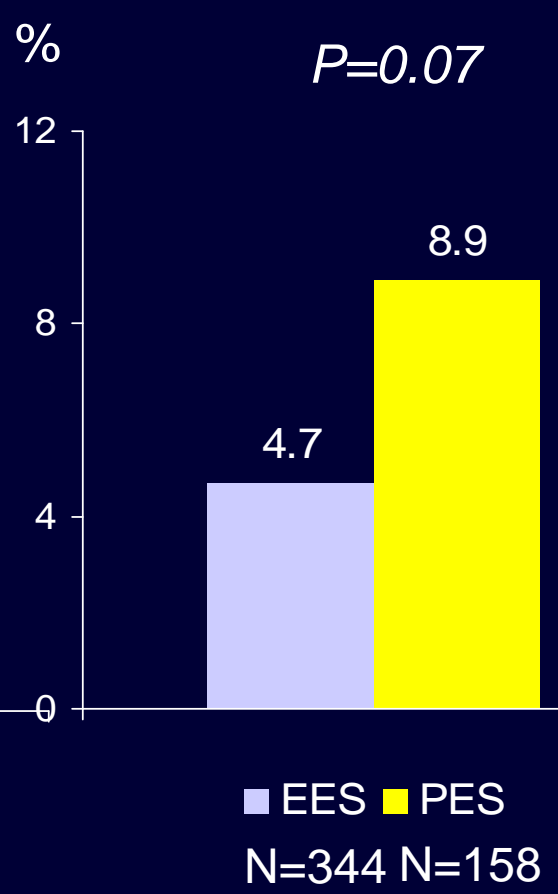
Between Everolimus- and Paclitaxel-Eluting Stent

Stone G et al. *JAMA* 2008;299:1903-13

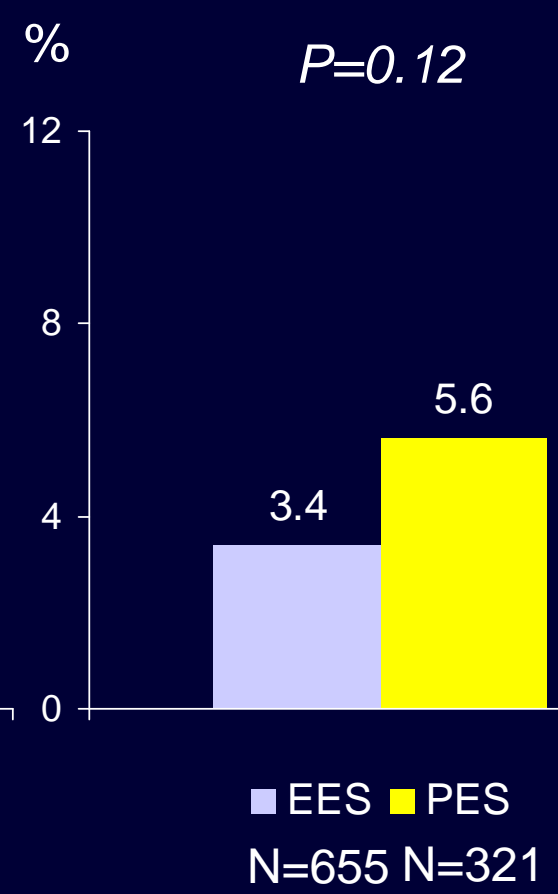
Late Loss @ 8 Months



Restenosis @ 8 Months



MACE @ 1 Year



Comparison of Everolimus-Eluting and Paclitaxel-Eluting Stents

Meta-Analysis of SPIRIT II and III

Windecker, Juni. *Circulation* 2009;119:653-6

Target Lesion Revascularization up to 2 Years

Clinically indicated TLR

Year 1

Year 2

Overall

0.51 (0.26, 0.97)

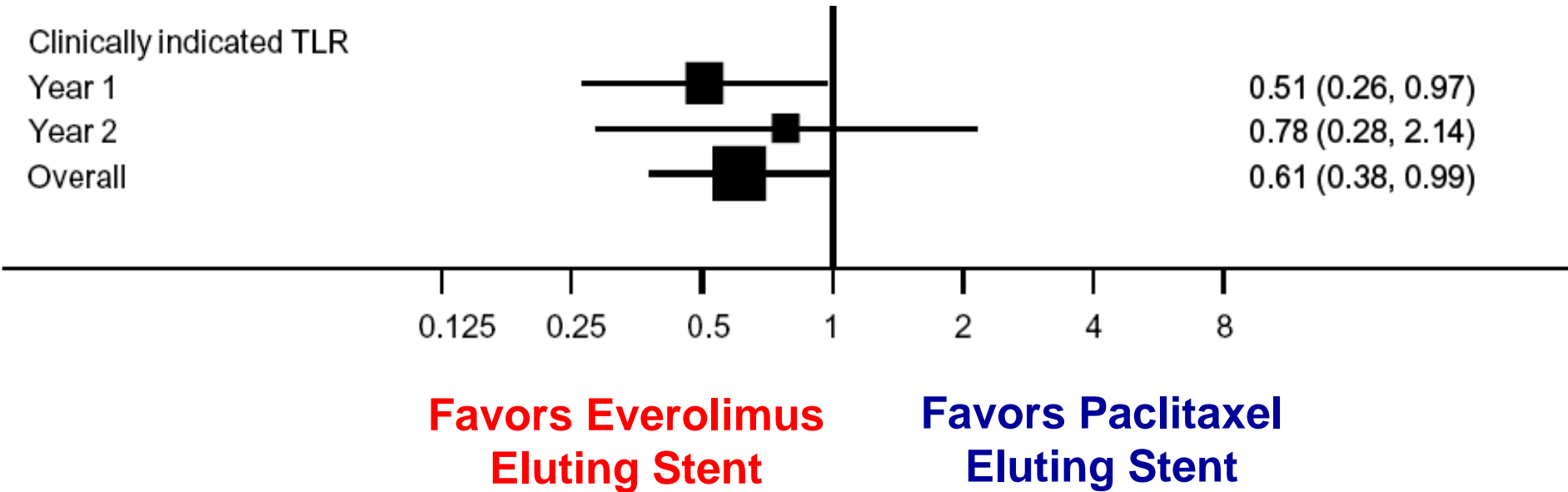
0.78 (0.28, 2.14)

0.61 (0.38, 0.99)

0.125 0.25 0.5 1 2 4 8

**Favors Everolimus
Eluting Stent**

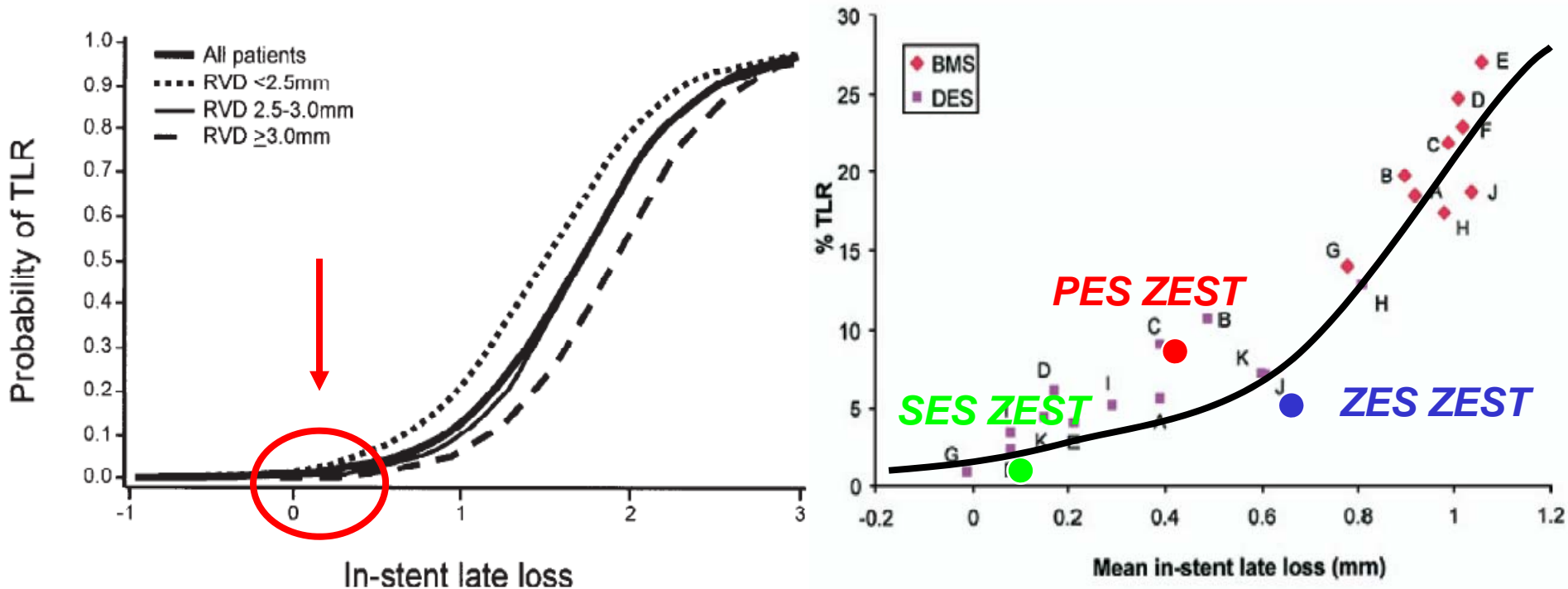
**Favors Paclitaxel
Eluting Stent**



Late Loss vs. TLR Relationship

Pocock S et al. *J Am Coll Cardiol* 2008;51:23-32

11 RCTs (N=5,381 pts) comparing SES, PES, ZES and BMS



There Are Meaningful Differences Among FDA-Approved Drug-Eluting Stents !

- ***Efficacy***

- SES more effective than PES
- SES more effective than ZES (Endeavor)
- ZES (Endeavor) as effective as PES
- EES more effective than PES
- EES versus SES?

Are There Meaningful Differences Among FDA-Approved Drug-Eluting Stents

DES Efficacy

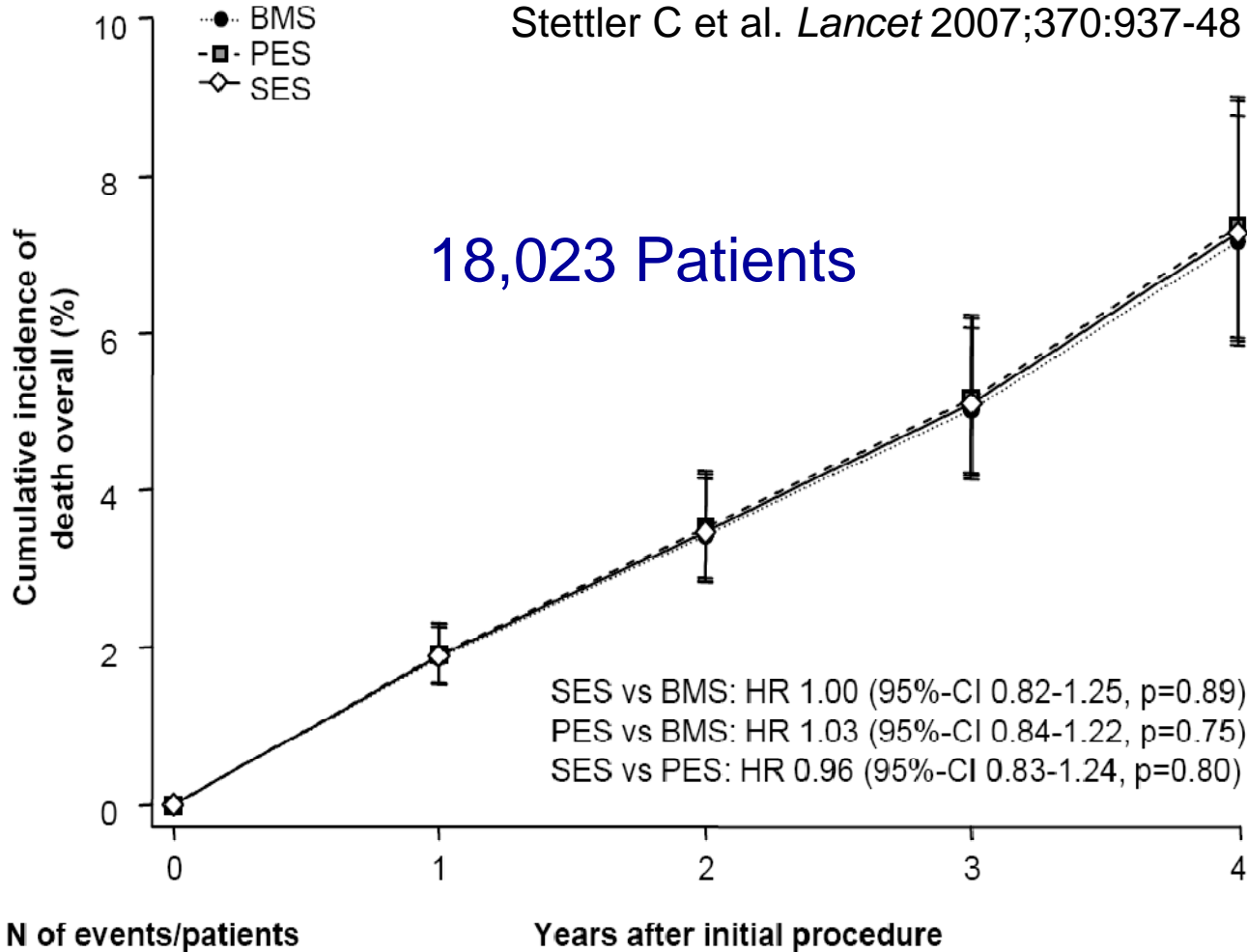
DES Safety

- Ischemic endpoints
- Stent thrombosis
- Endothelial function

All Cause Mortality - Network Meta-Analysis

SES vs PES vs BMS

Stettler C et al. *Lancet* 2007;370:937-48



38 RCTs comparing DES with BMS

Off-label: 19 trials with 9,881 pts

On-label: 19 trials with 8,142 pts

N of events/patients

Years after initial procedure

BMS	4921	109/4904	48/3340	31/2264	44/1875
PES	6331	138/6283	78/4263	32/2187	15/869
SES	6771	139/6730	72/4041	38/2340	24/1081

Zotarolimus-Eluting Stent (Endeavor)

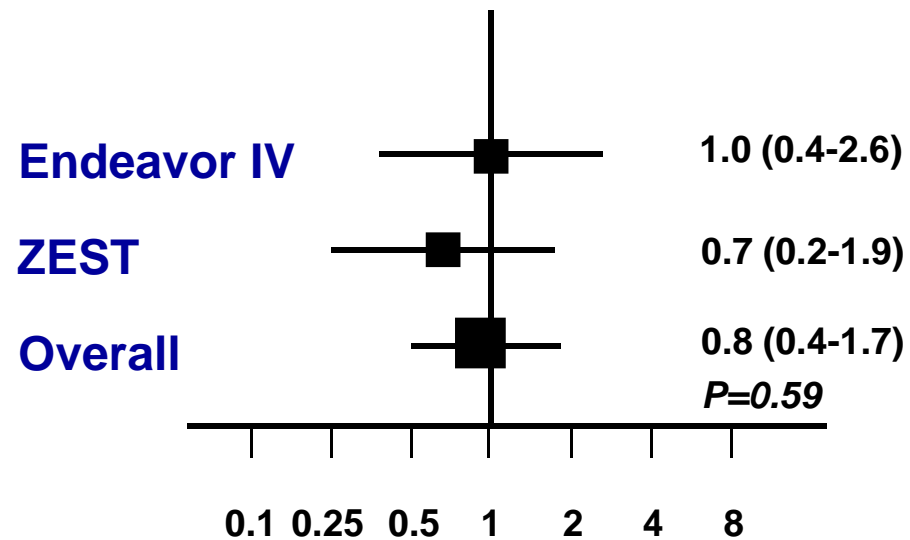
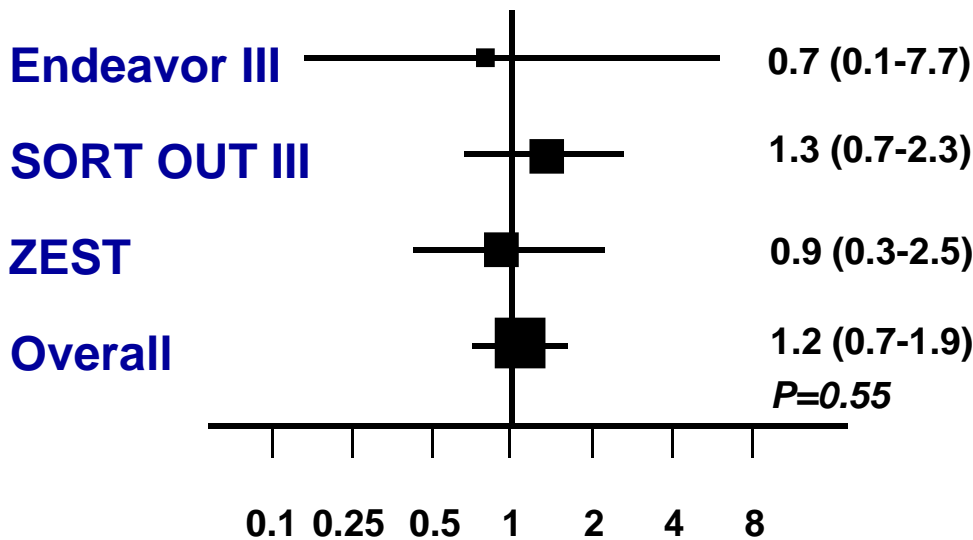
All Cause Death @ 9-12 Mo

ZES versus SES

ZES versus PES

Relative Risk (95% CI)

Relative Risk (95% CI)



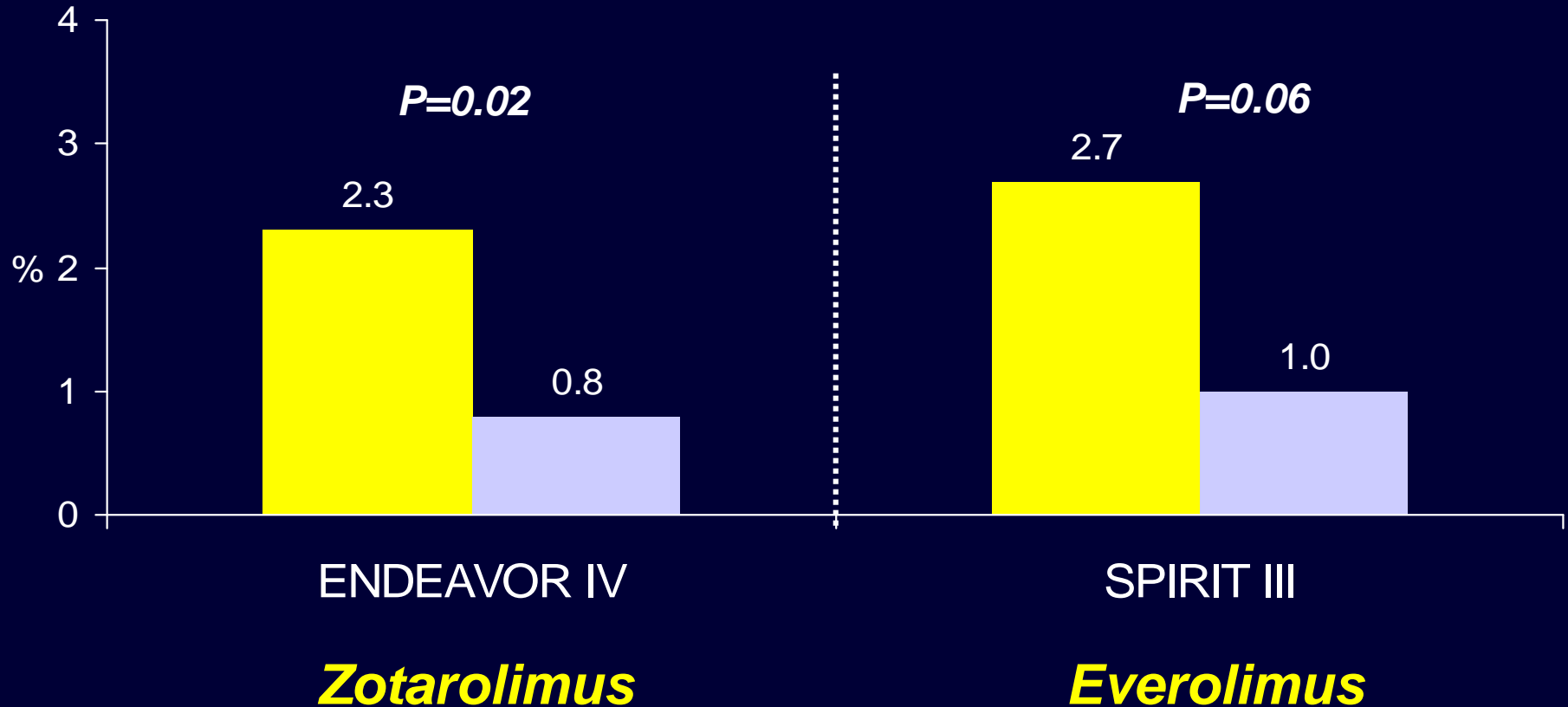
Favors ZES Favors SES

Favors ZES Favors PES

Comparison of Early Clinical Outcome Between First and Newer Generation DES

Rates of Myocardial Infarction @ 30 Days

■ First Generation DES (TAXUS) ■ New Generation DES



Frequency and Sequelae of Sidebranch Occlusion

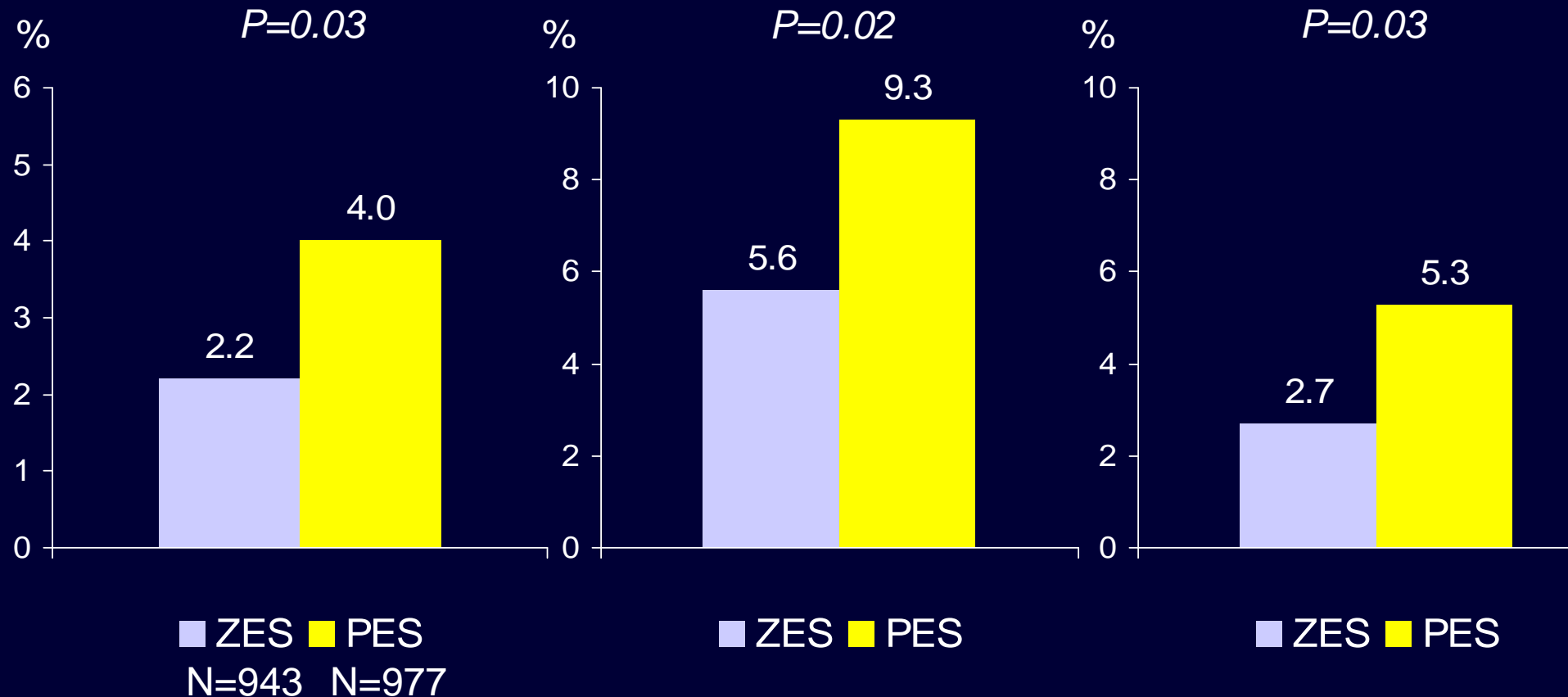
Angiographic Analysis of Endeavor IV (ZES vs PES)

Popma J et al. ACC/SCAI 2008

Frequency of SB Occlusion

Periprocedural MI, CK>2xULN

Periprocedural MI, CK>3xULN



Zotarolimus-Eluting Stent (Endeavor)

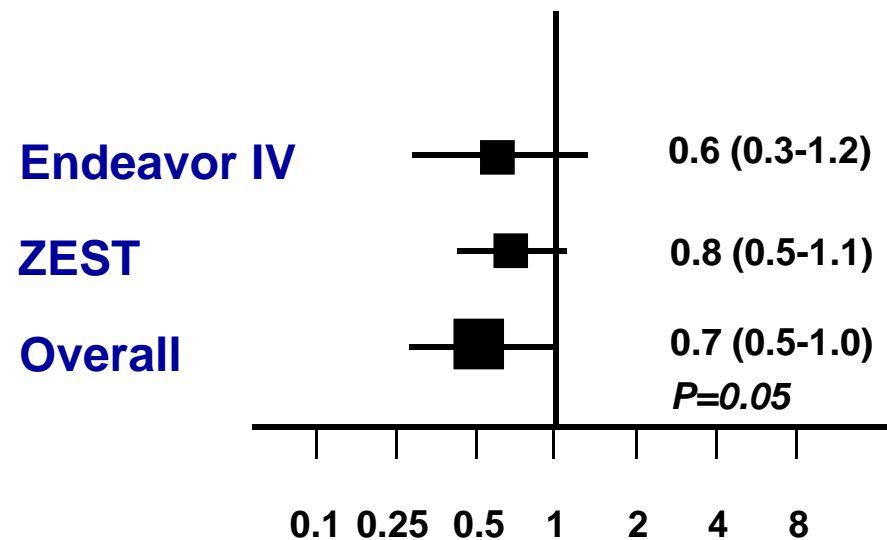
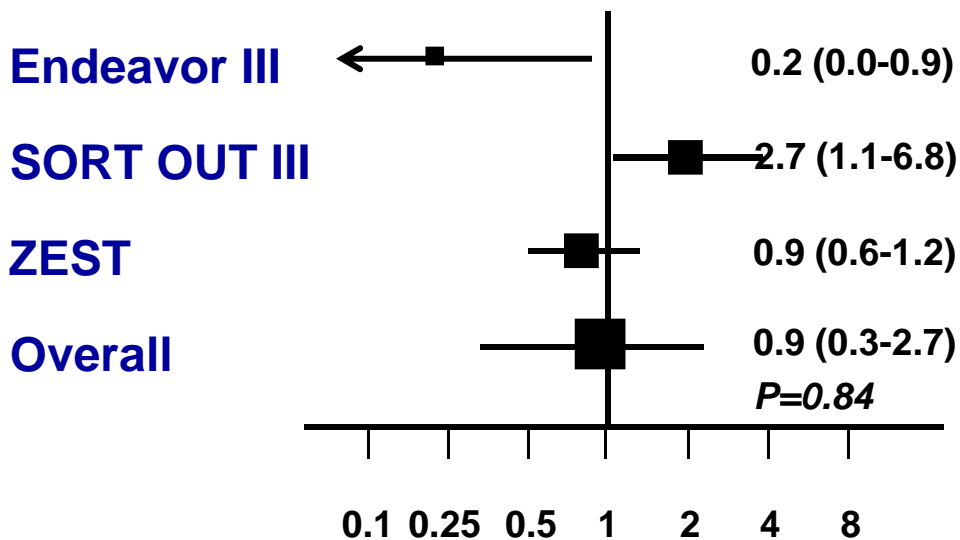
Myocardial Infarction @ 9-12 Months

ZES versus SES

ZES versus PES

Relative Risk (95% CI)

Relative Risk (95% CI)



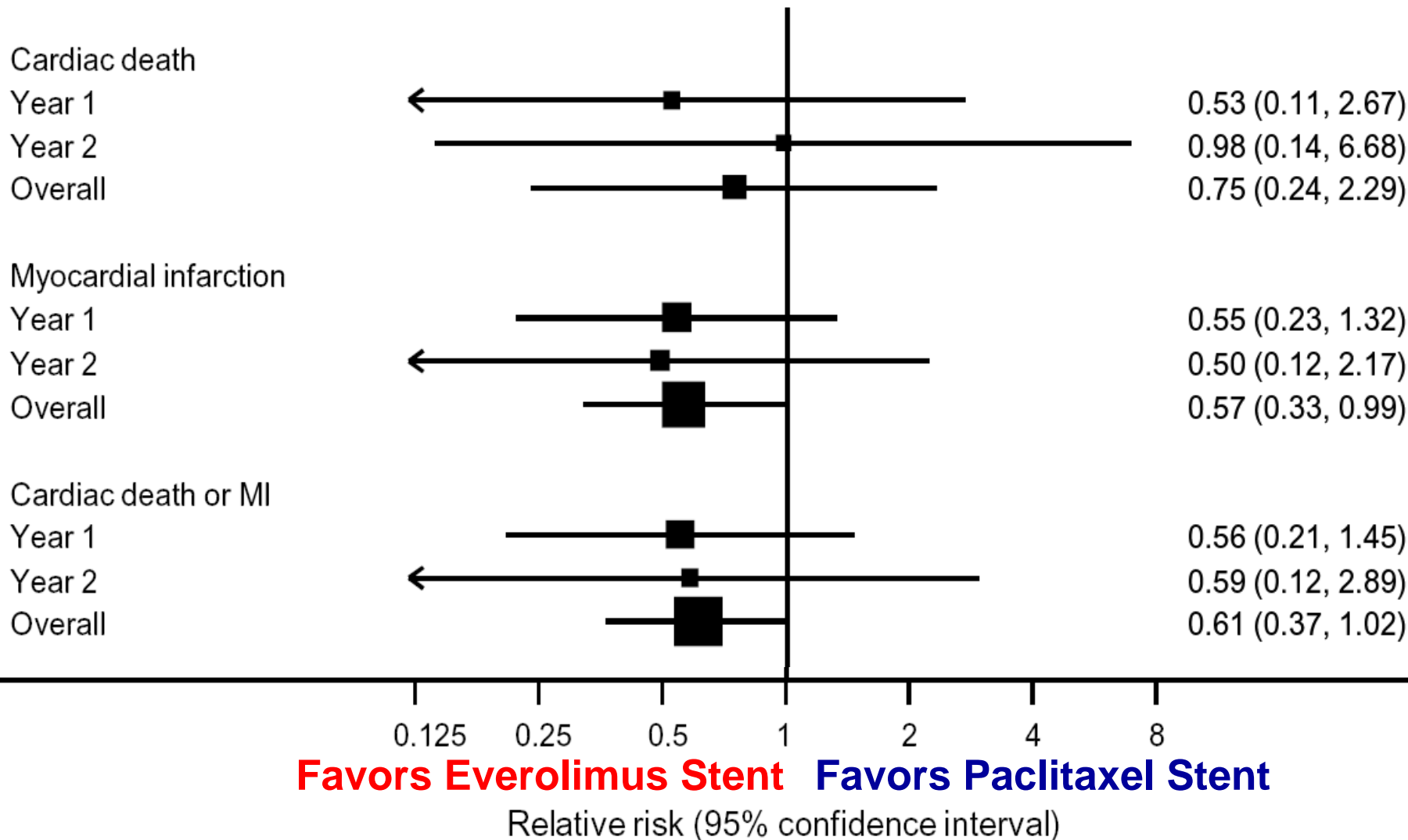
Favors ZES **Favors SES**

Favors ZES **Favors PES**

Comparison of Everolimus-Eluting and Paclitaxel-Eluting Stents

Meta-Analysis of SPIRIT II and III

Windecker, Juni. *Circulation* 2009;119:653-6



Are There Meaningful Differences Among FDA-Approved Drug-Eluting Stents

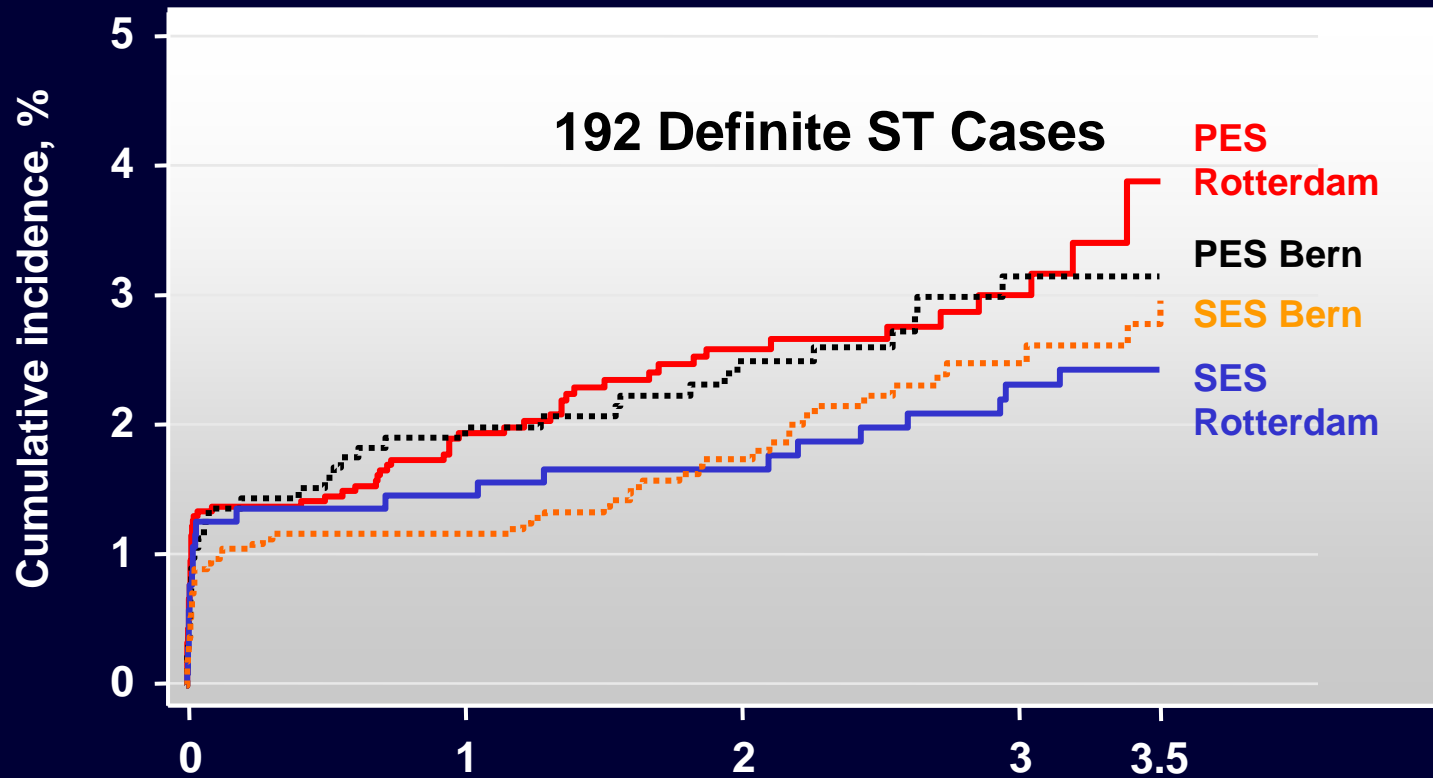
DES Efficacy

DES Safety

- Ischemic endpoints
- Stent thrombosis
- Endothelial function

Definite Stent Thrombosis and Stent Type Bern - Rotterdam Cohort Study

Wenaweser P et al. *J Am Coll Cardiol* 2008



PES: 3.6%

SES: 2.7%

HR=0.71
(0.53-0.95)

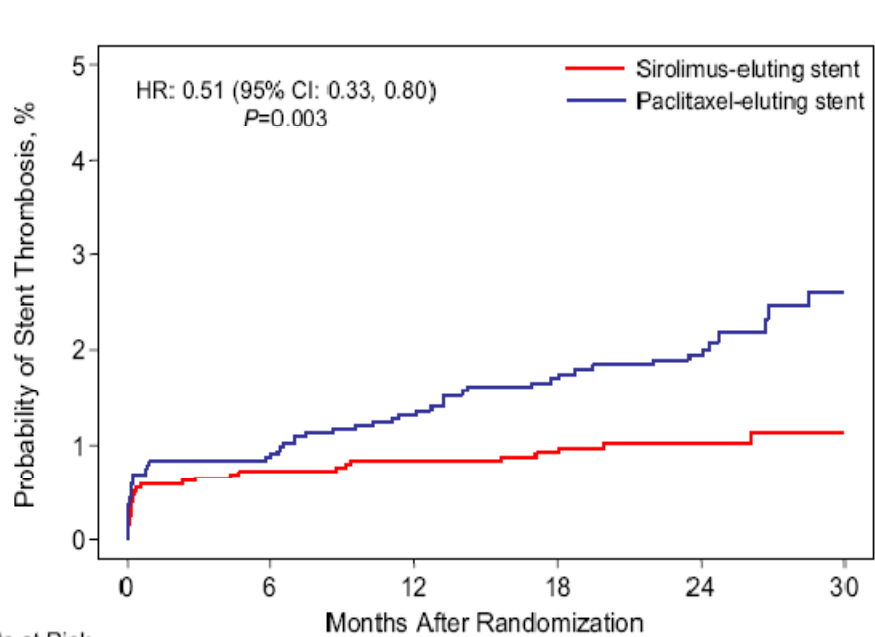
P=0.019

Months	1	12	24	36	42
Cumulative incidence SES, %	1.0	1.2	1.7	2.4	2.7
Cumulative incidence PES, %	1.3	1.9	2.5	3.1	3.6

Risk of Stent Thrombosis: SES vs PES

Kastrati et al. *J Am Coll Cardiol* 2007

16 Head-to-Head RCTs - 8,695 Patients

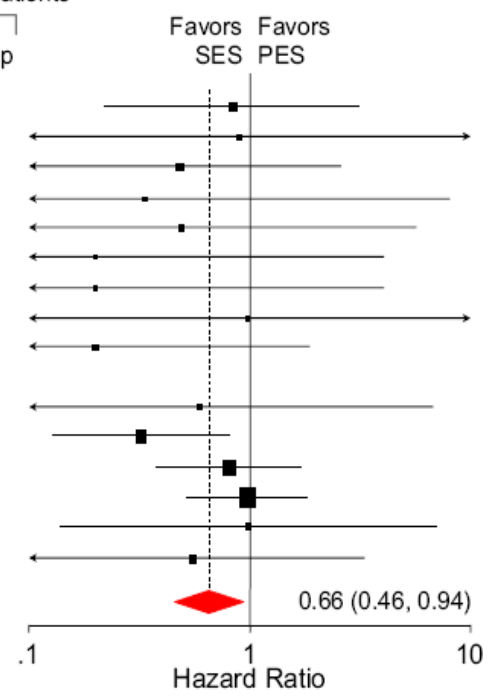


Patients at Risk

	0	6	12	18	24	30
SES	2783	2718	2546	2266	1752	676
PES	2779	2687	2526	2224	1693	632

Trial	No. of events / Total No. of patients	
	SES group	PES group
BASKET	4/264	5/281
Cervinka et al.	1/37	1/33
CORPAL	2/331	4/321
Di Lorenzo et al.	0/90	1/90
Han et al.	1/210	2/206
ISAR-DESIRE	0/100	2/100
ISAR-DIABETES	0/125	2/125
ISAR-SMART 3	1/180	1/180
LONG-DES II	1/250	5/250
Petronio et al.	0/50	0/50
PROSIT	2/154	2/151
REALITY	6/684	18/669
SIRTAX	12/503	15/509
SORT-OUT II	19/1065	19/1033
TAXI	2/102	2/100
Zhang et al.	2/246	3/203
Overall	53/4391	82/4304

$I^2=0\%$, $P_{(Heterogeneity)}=0.93$
 $P_{(Overall\ Effect)}=0.02$



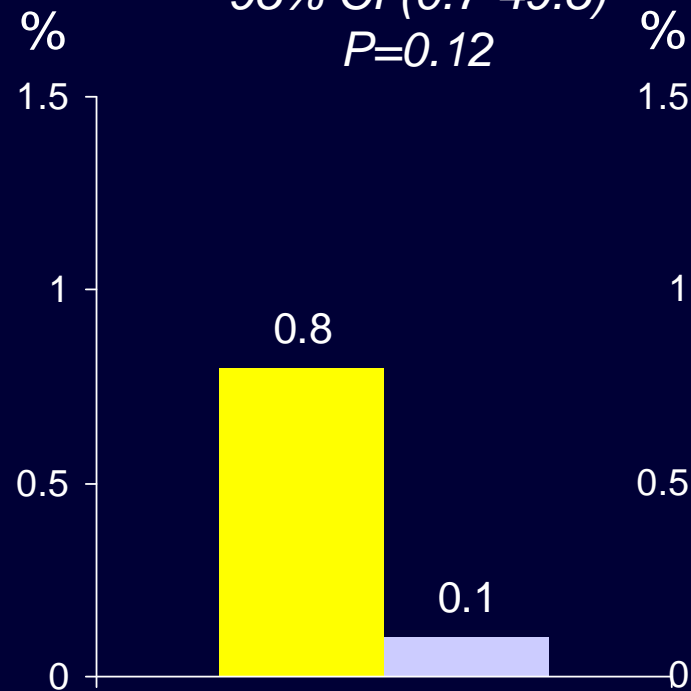
135 ST Cases

ZEST Trial – Definite Stent Thrombosis

Early and Late Definite ST \leq 12 Months

Endeavor IV

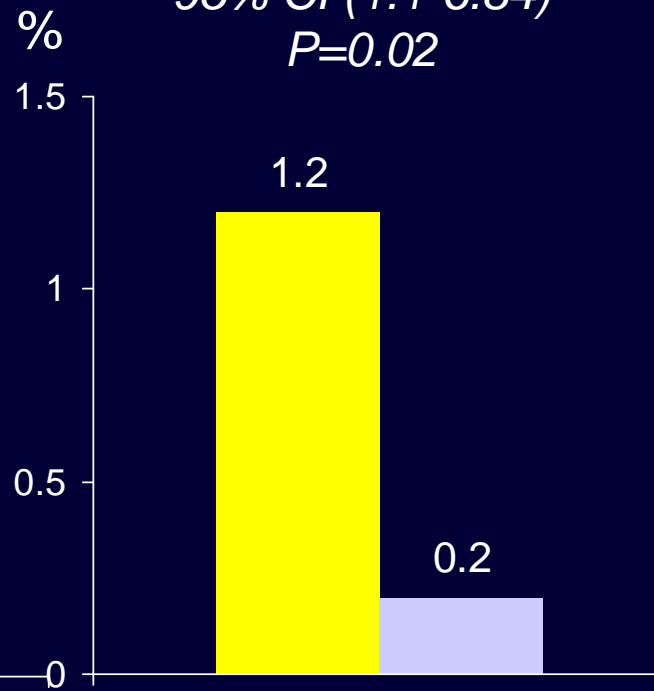
RR=5.98
95% CI (0.7-49.5)
P=0.12



■ ZES ■ PES
N=749 N=741

SORT OUT III

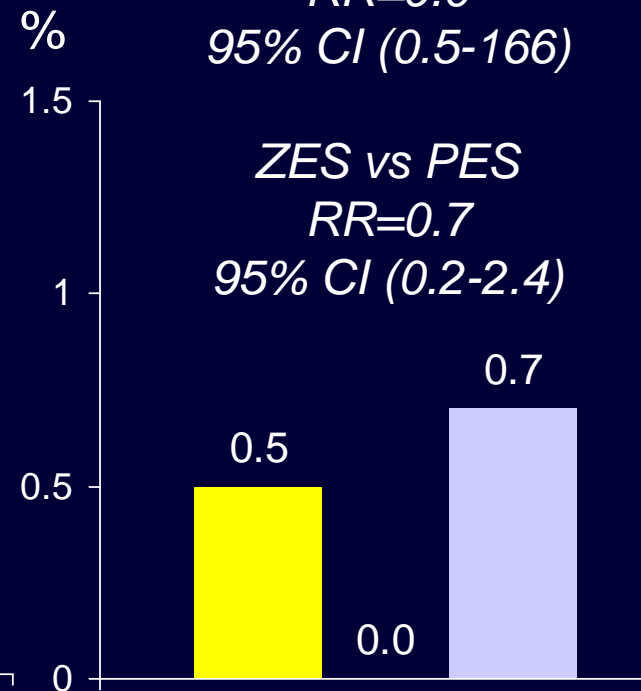
RR=2.69
95% CI (1.1-6.84)
P=0.02



■ ZES ■ SES
N=1162 N=1171

ZEST

ZES vs SES
RR=9.0
95% CI (0.5-166)

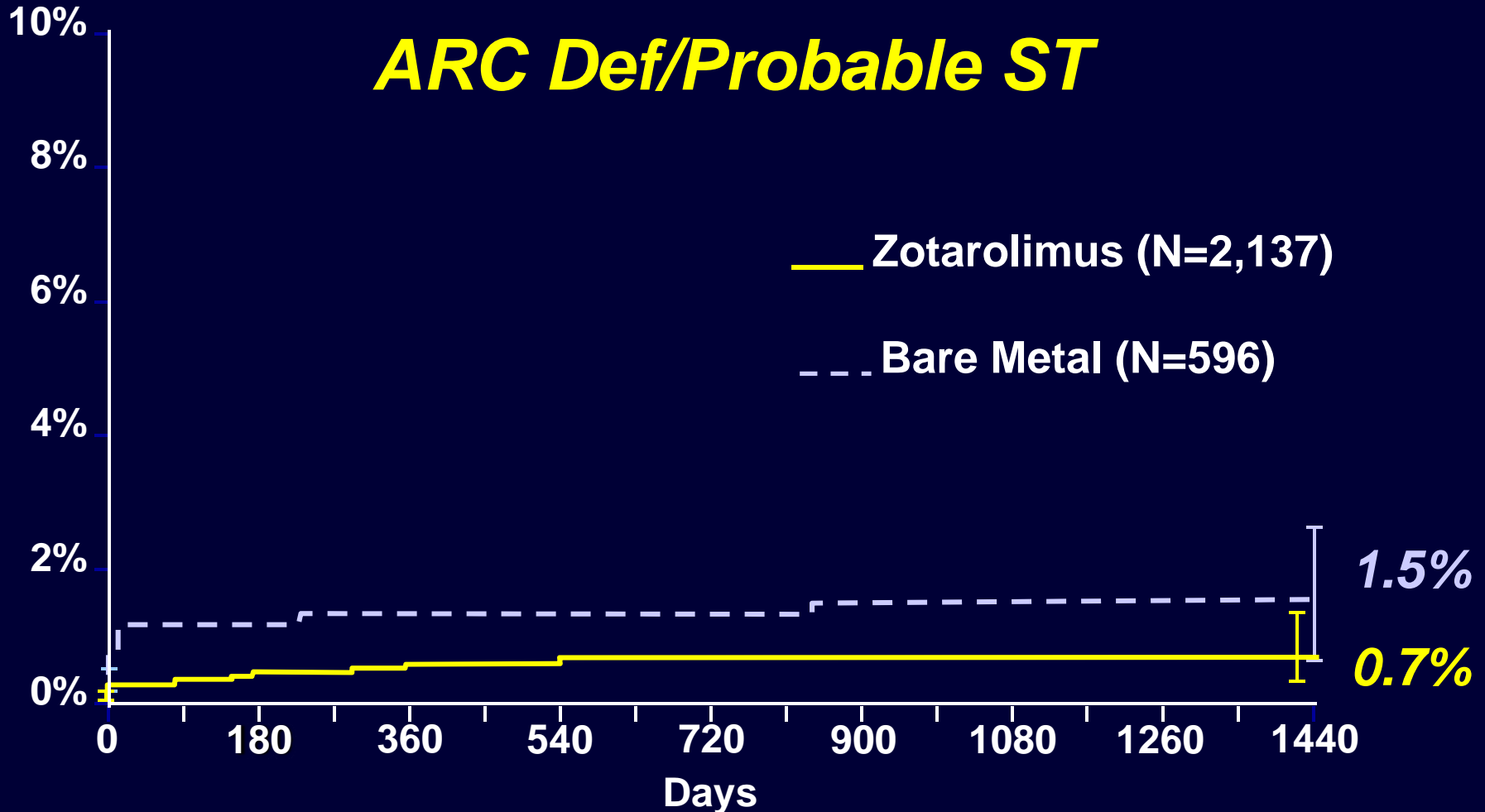


ZES vs PES
RR=0.7
95% CI (0.2-2.4)

■ ZES ■ SES ■ PES
N=883 N=878 N=884

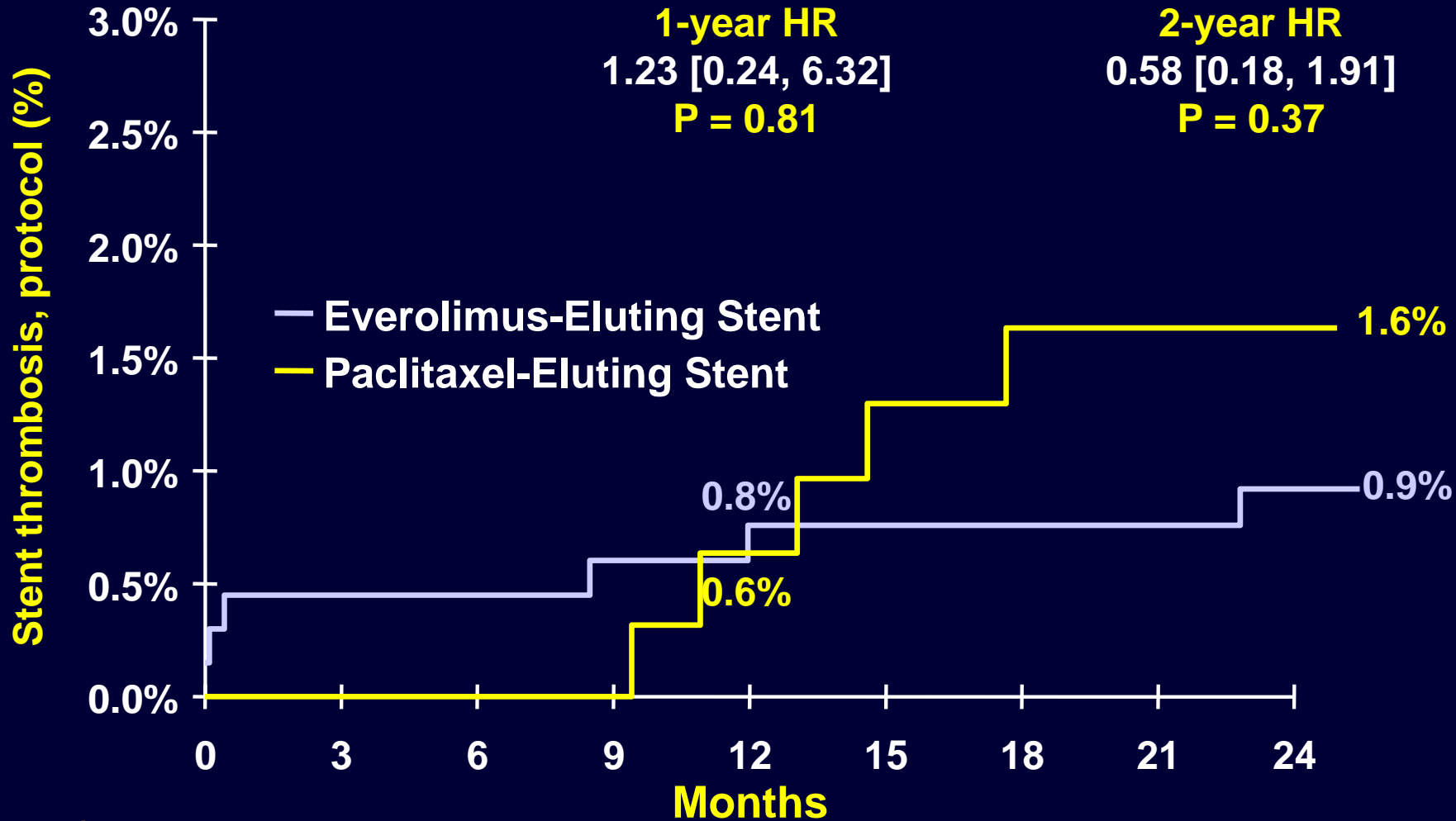
Stent Thrombosis

Pooled ZES versus BMS



SPIRIT III: Stent Thrombosis – Per Protocol

Stone G et al. *Circulation* 2009



Number at risk

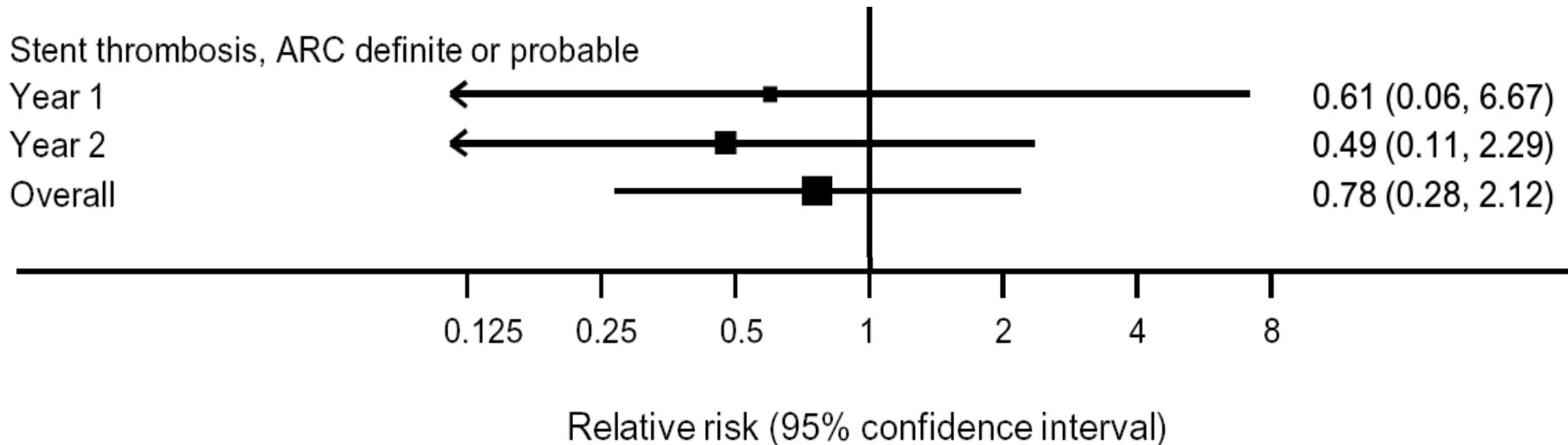
EES	669	661	658	650	642	627	627	624	619
PES	332	325	324	317	313	300	298	298	296

Comparison of Everolimus-Eluting and Paclitaxel-Eluting Stents

Meta-Analysis of SPIRIT II and III

Windecker, Juni. *Circulation* 2009;119:653-6

Definite or Probable Stent Thrombosis



**Favors Everolimus
Eluting Stent**

**Favors Paclitaxel
Eluting Stent**

Are There Meaningful Differences Among FDA-Approved Drug-Eluting Stents

DES Efficacy

DES Safety

- Ischemic endpoints
- Stent thrombosis
- Endothelial function

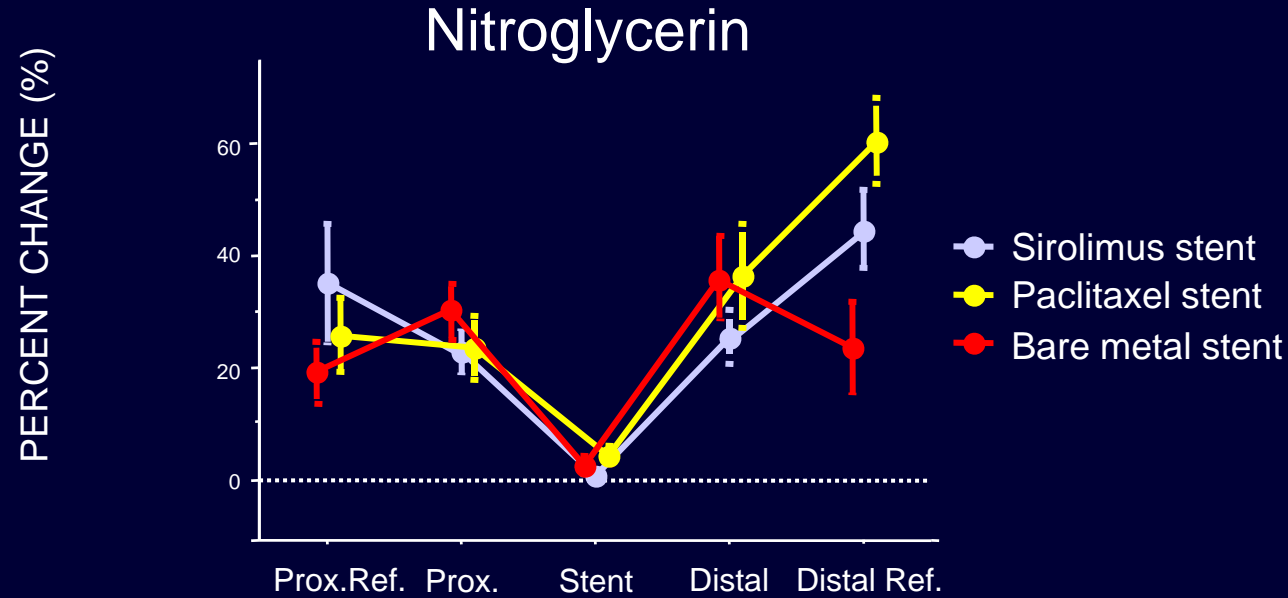
Sirolimus-Eluting Stents Associated With Impaired Exercise Induced Coronary Vasomotion

Togni M et al.
JACC 2005;46:231-6



Paclitaxel-Eluting Stents Associated With Impaired Exercise Induced Coronary Vasomotion

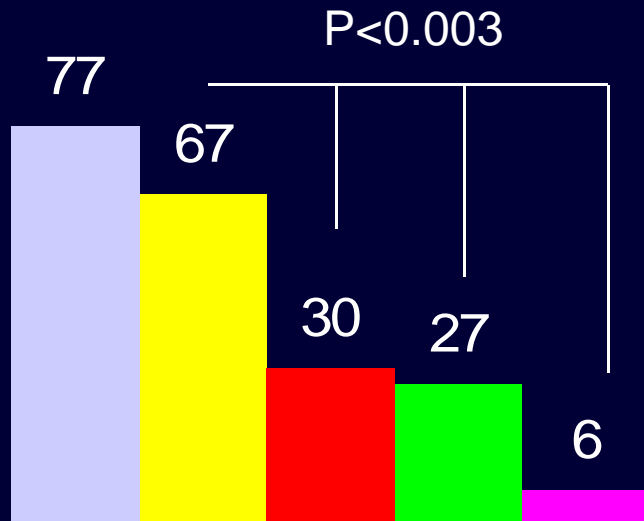
Togni M et al.
Int J Cardiol 2007;120:212-20



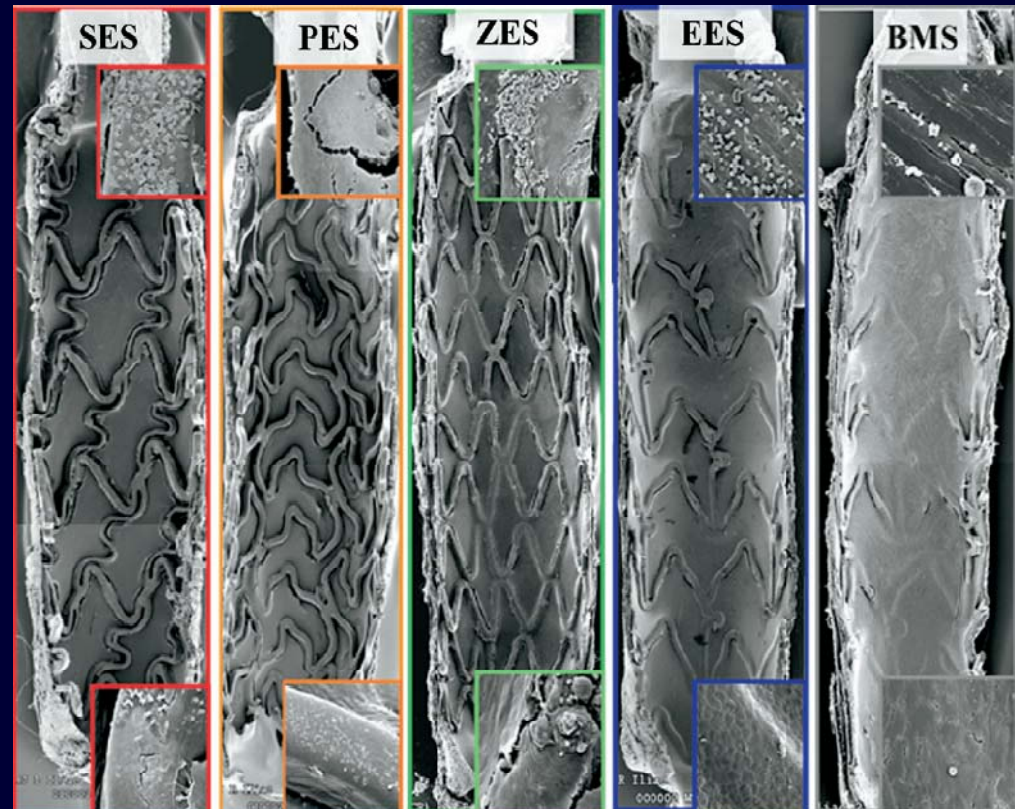
Comparison of Endothelial Recovery Between Different Drug-Eluting Stents

Joner M et al. *J Am Coll Cardiol* 2008;52:333-42

Rabbit Iliac Artery Model: SEM at 14 Days



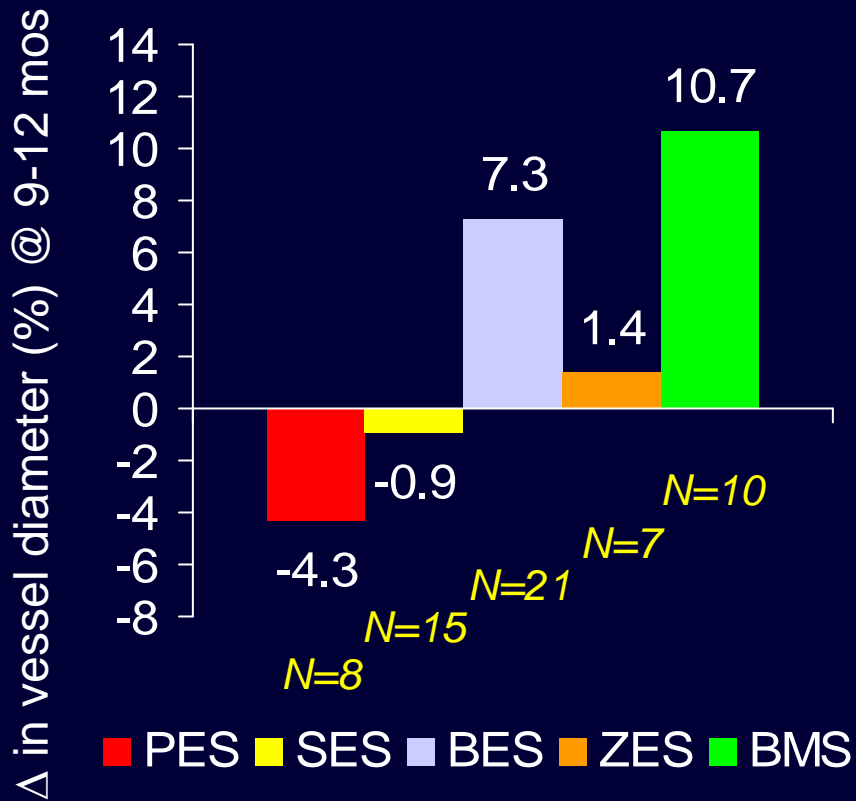
Endothelialization



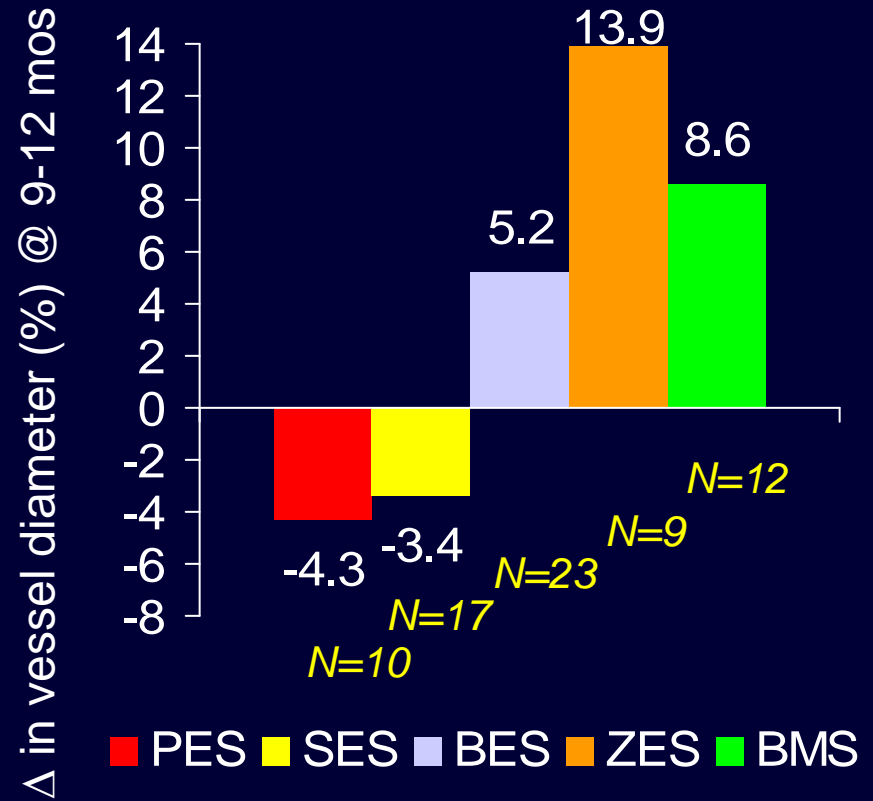
Comparison of Coronary Vasomotion Between Various Drug-Eluting and Bare Metal Stents

Hamilos MI et al. *Circulation Cardiovasc Intervention* 2009

Proximal Segment

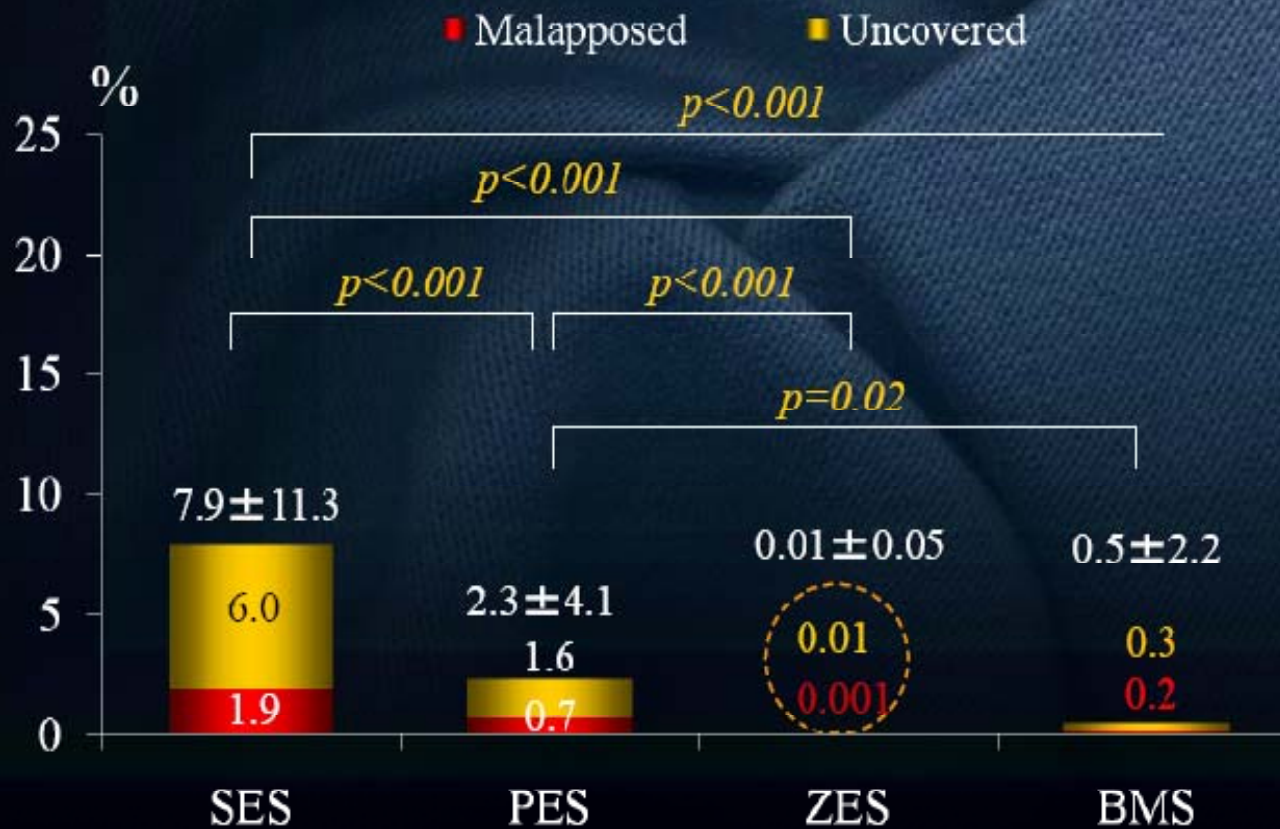


Distal Segment



ODESSA Non-overlap

Proportion of uncovered and/or malapposed struts by stent type

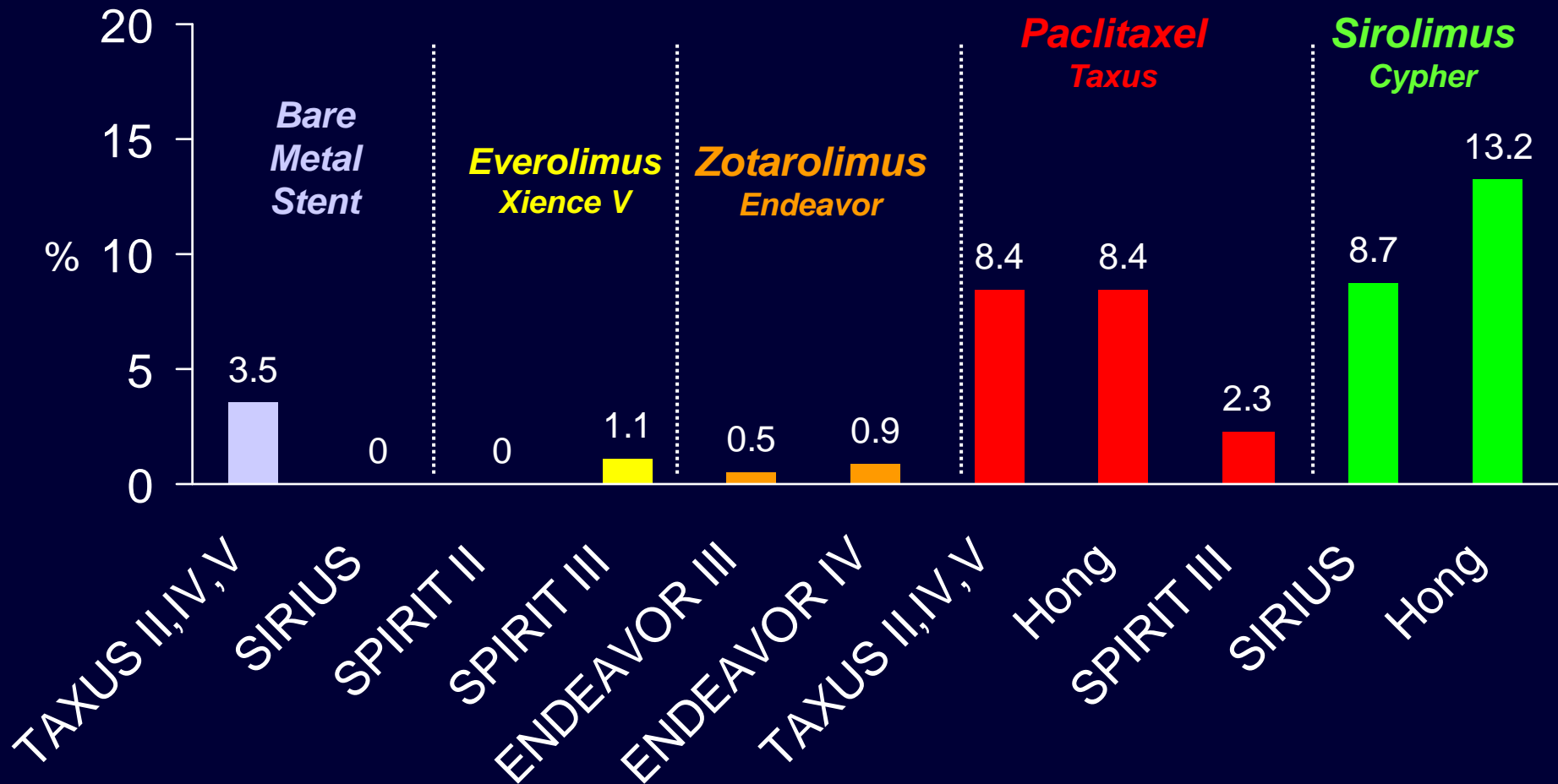


Late Acquired Stent Malapposition

Shah V et al. *Circulation* 2002;106:1753-55; Ako J et al. *JACC* 2005;46:1002-5

Mintz G et al. *JACC* 2006;48:421-9; Hong MK et al. *Circulation* 2006;113:414-19

Sakurai R et al. *Am J Card* 2007;100:818-23; Miyazawa A et al. *Am Heart J* 2008;155:108-13



There Are Meaningful Differences Among FDA-Approved Drug-Eluting Stents !

- Newer generation DES (ZES and EES) are associated with a lower rate of peri-procedural MI
- Newer generation DES (ZES and EES) are associated with a lower rate of MI up to 2 years compared with PES
- The risk of very late stent thrombosis with newer generation DES cannot be determined due to limited follow-up and underpowered studies
- Surrogate markers of safety have improved with newer generation DES (ZES and EES)
 - Improved strut coverage
 - Improved endothelial function
 - Lower rate of stent malapposition