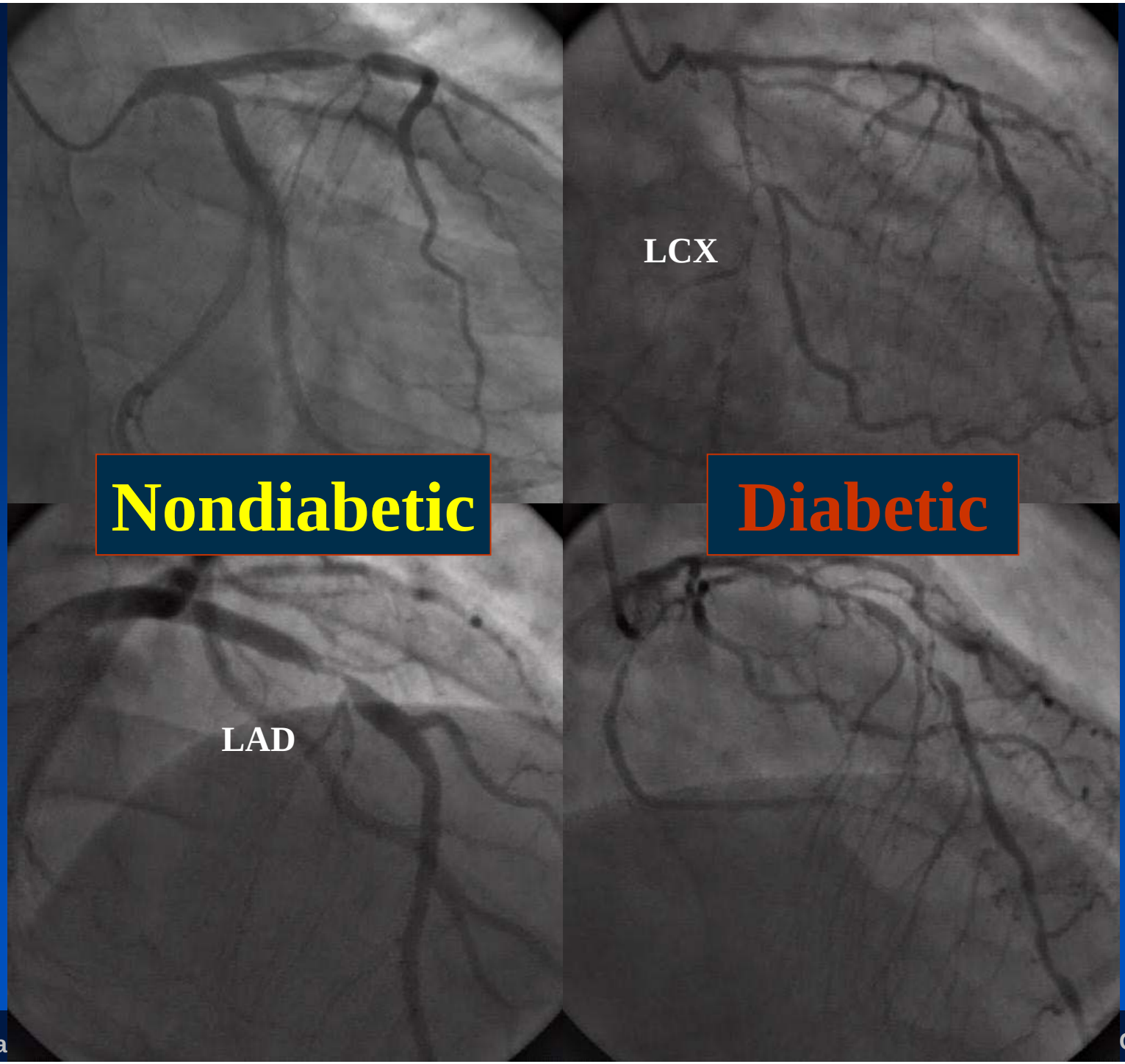
Impact of Diabetes on long-term outcomes of DES in Asian patients

Seung-Jung Park, MD, PhD,

Professor of Internal Medicine
Asan Medical Center, *Seoul, Korea*

Diabetes
; Different Disease Pattern


LCX
Nondiabetic
Diabetic
LAD

Characteristics of Coronary Artery Disease (CAD) in Diabetics

- Small vessel caliber (impaired remodeling or diffuse atherosclerosis)
- High incidence of multi-vessel disease
- High incidence of left main stem disease
- Complex lesion morphology; total occlusion
- Poor collateral development
- Increased coronary calcification

Diabetic patients tend to have a more aggressive form of CAD compared to non-diabetics

PCI in Diabetic Patients

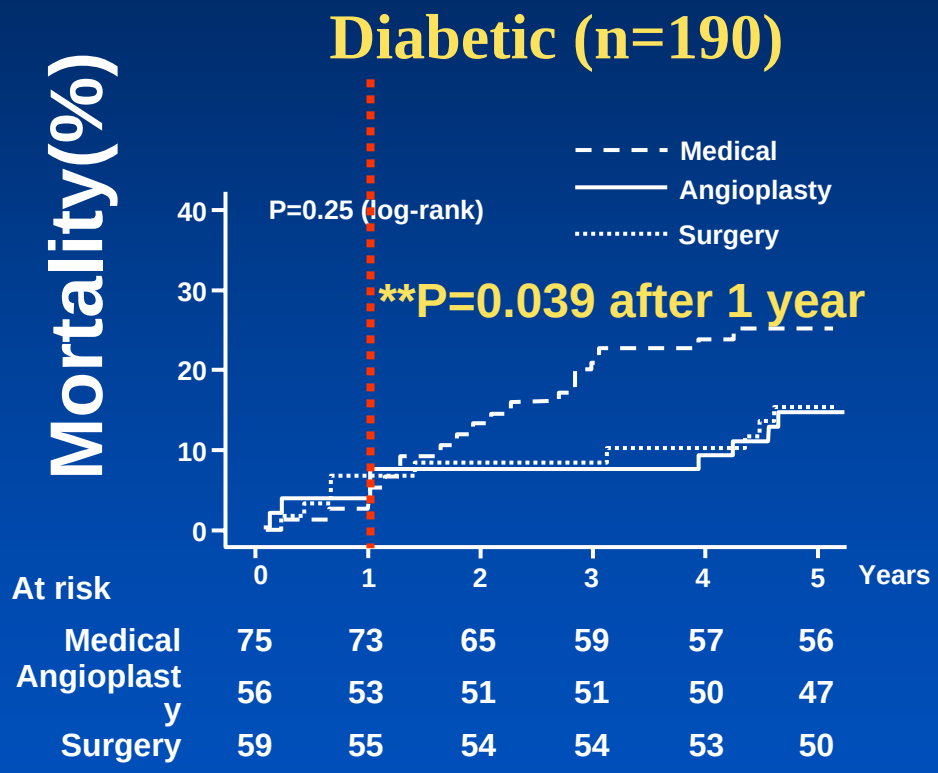
Why is it problem ?

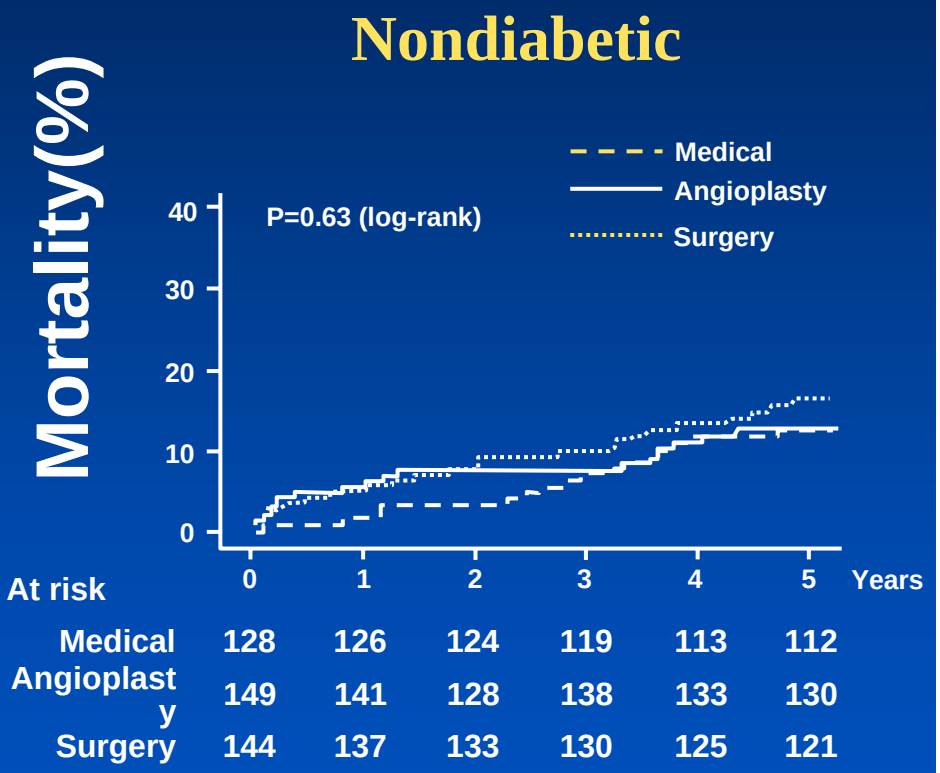
- Diabetic patients are prone to a diffuse and rapidly progressive form of atherosclerosis.
- A host of unfavorable pathophysiologic and anatomical features in diabetic patients contributed to worse outcomes
- Bypass surgery is the preferred revascularization strategy, because of increased risk of mortality and/or TLR rate after PCI in diabetic patients in the era of BMS.
- Drug-eluting stents (DES) markedly reduced restenosis and TLR compared with BMS, however we need more data for patients with diabetes.

Diabetes
; Treatment

Medical vs. PCI vs. CABG
in stable multi-vessel CAD (n=611pts)

MASS II RCT





*PCI = BMS era

Soares, PR et al. Circulation 2006; 114:I420

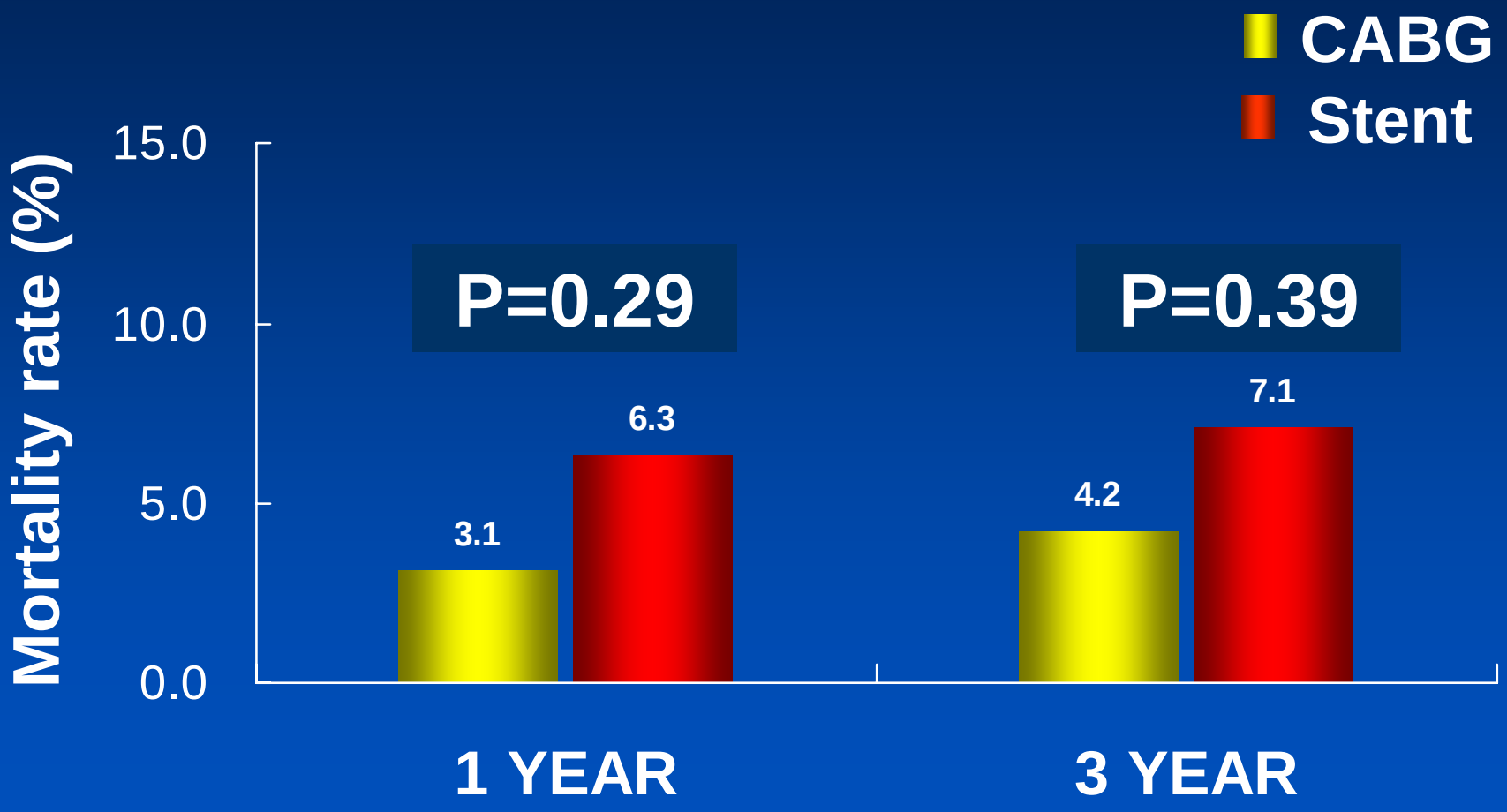
MASS II Study:
Revascularization in Diabetics

- For diabetic subjects, percutaneous or surgical revascularization was associated with a protective effect compared with medical treatment, significantly decreasing the risk of death after 1 year and up to 5 years.
- Therefore, aggressive invasive revascularization should be considered in diabetic patients to improve long-term outcomes

Diabetes
; PCI vs CABG

Mortality in Diabetics

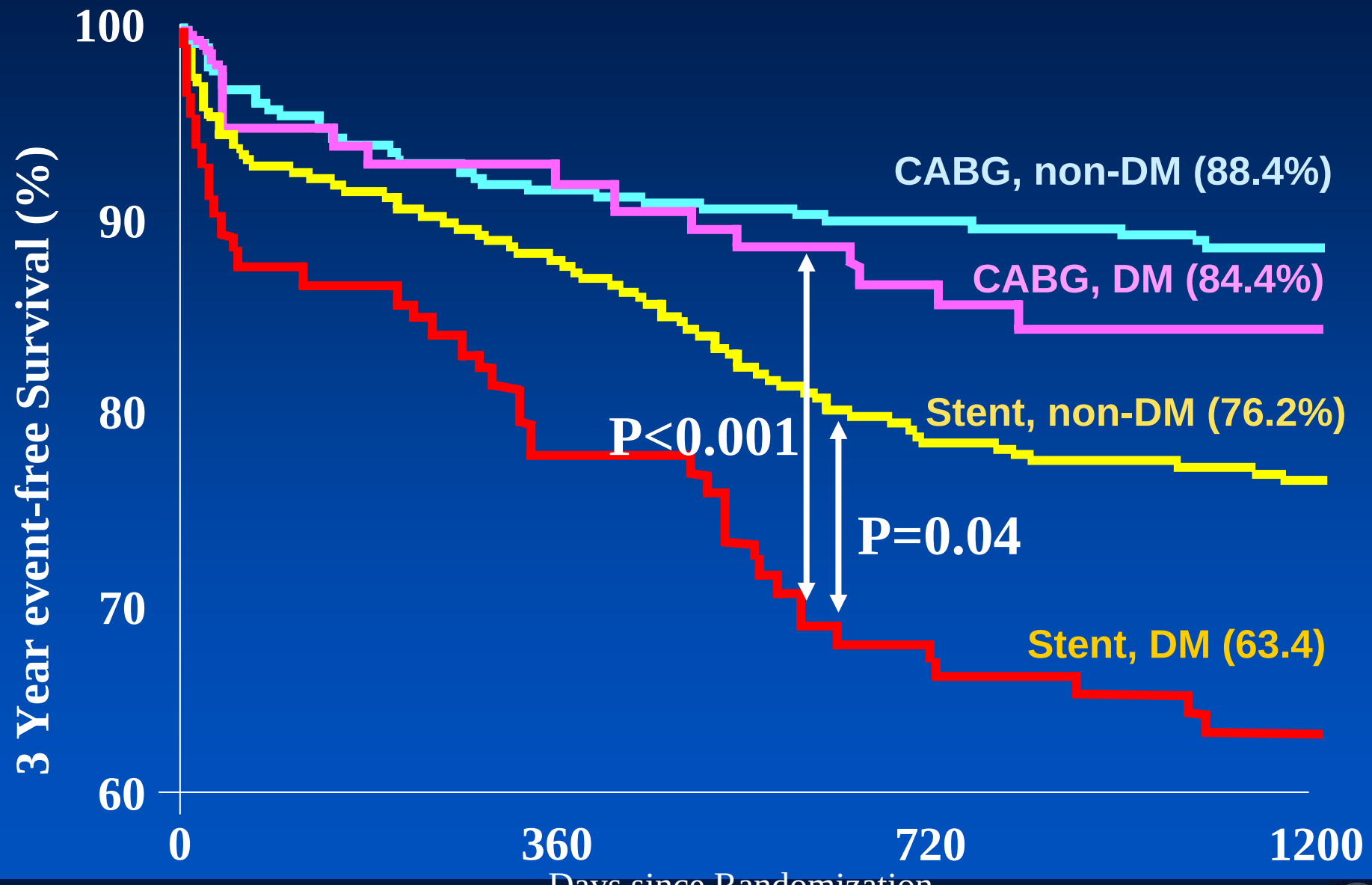
Data from ARTS Trials (n=208); Multivessel Disease study



Legrand VM, et al. Circulation 2004: 109

3 Year MACE-free Survival in Diabetics

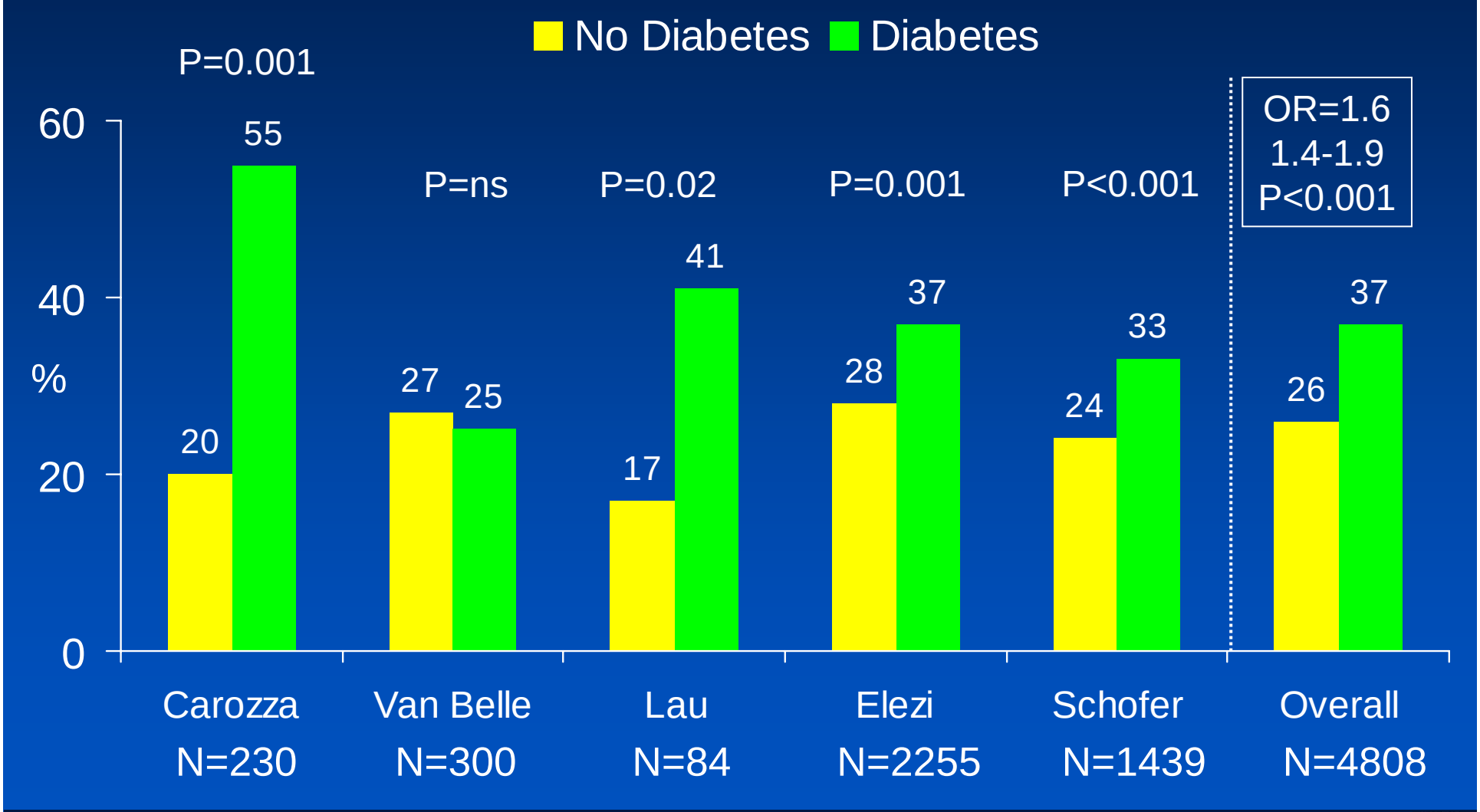
Data from ARTS Trials (n=208); Multivessel Disease study



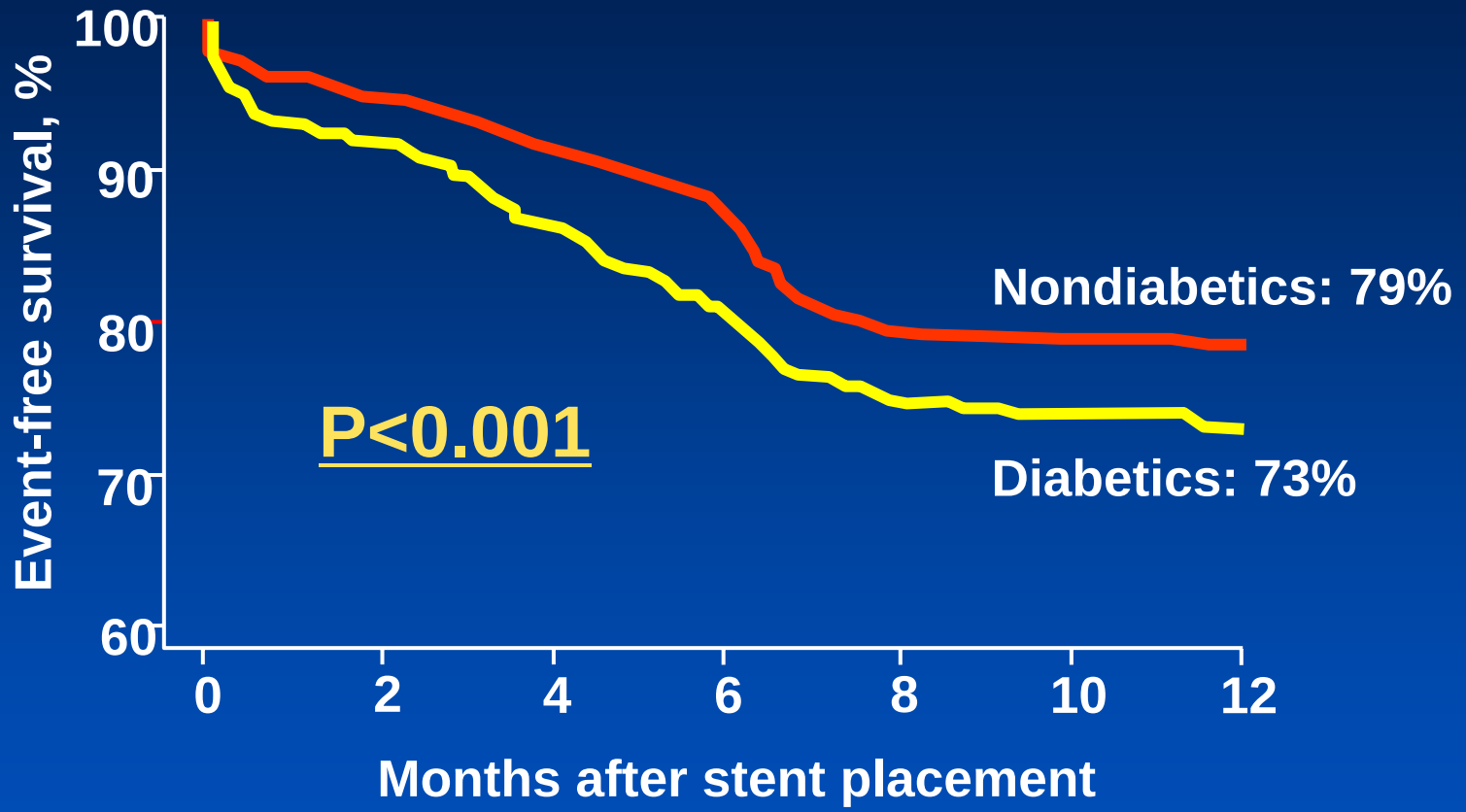
Diabetes
; PCI (BMS)

Risk of Restenosis in BMS

Diabetic vs Nondiabetic Patients



MACE (Death,MI,TLR) free Survival

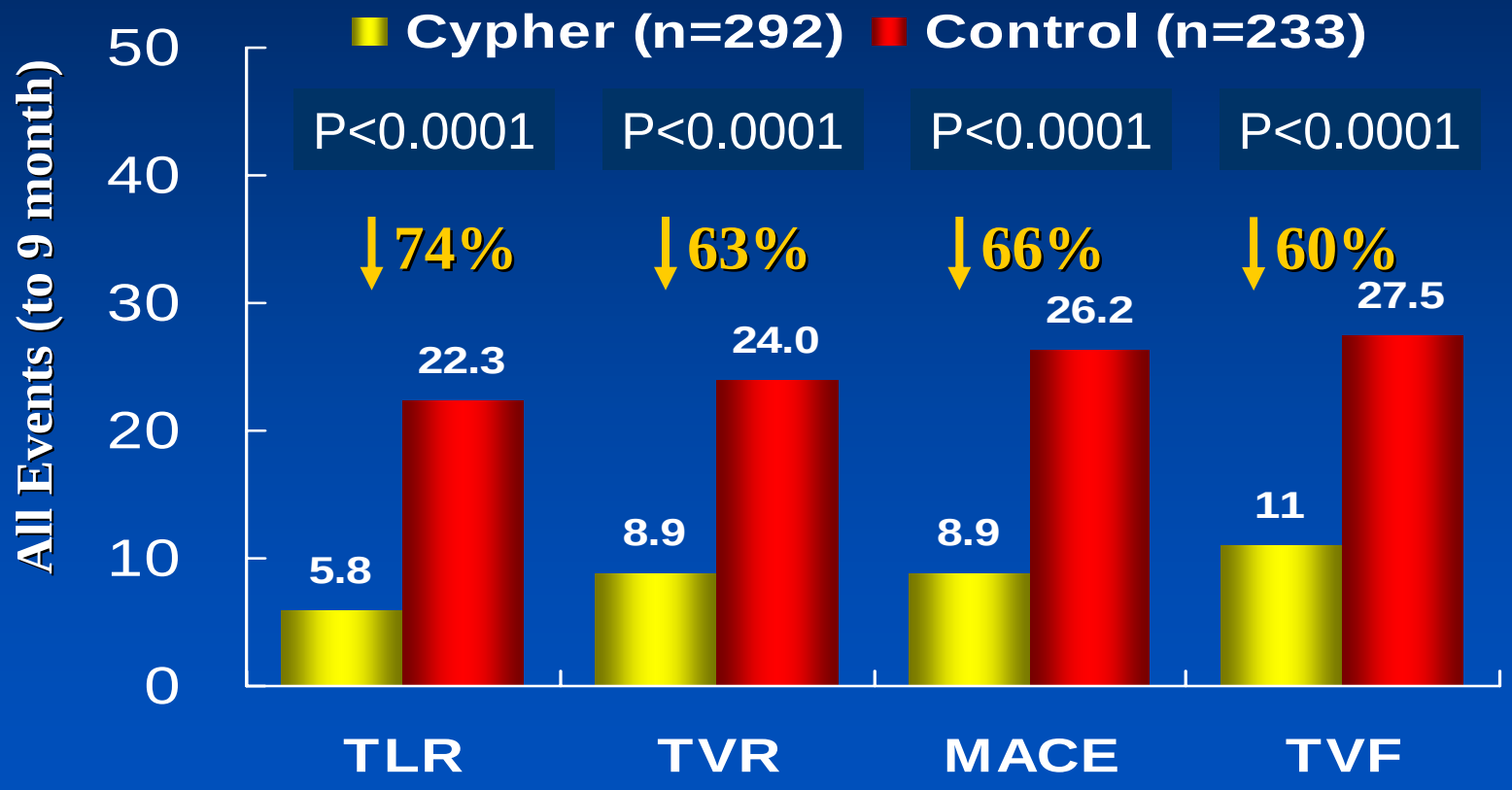


Kastrati A, et al. JACC 1998;32:1866

Diabetes
; PCI (DES)

CYPHER Trials Meta-Analysis in Diabetes

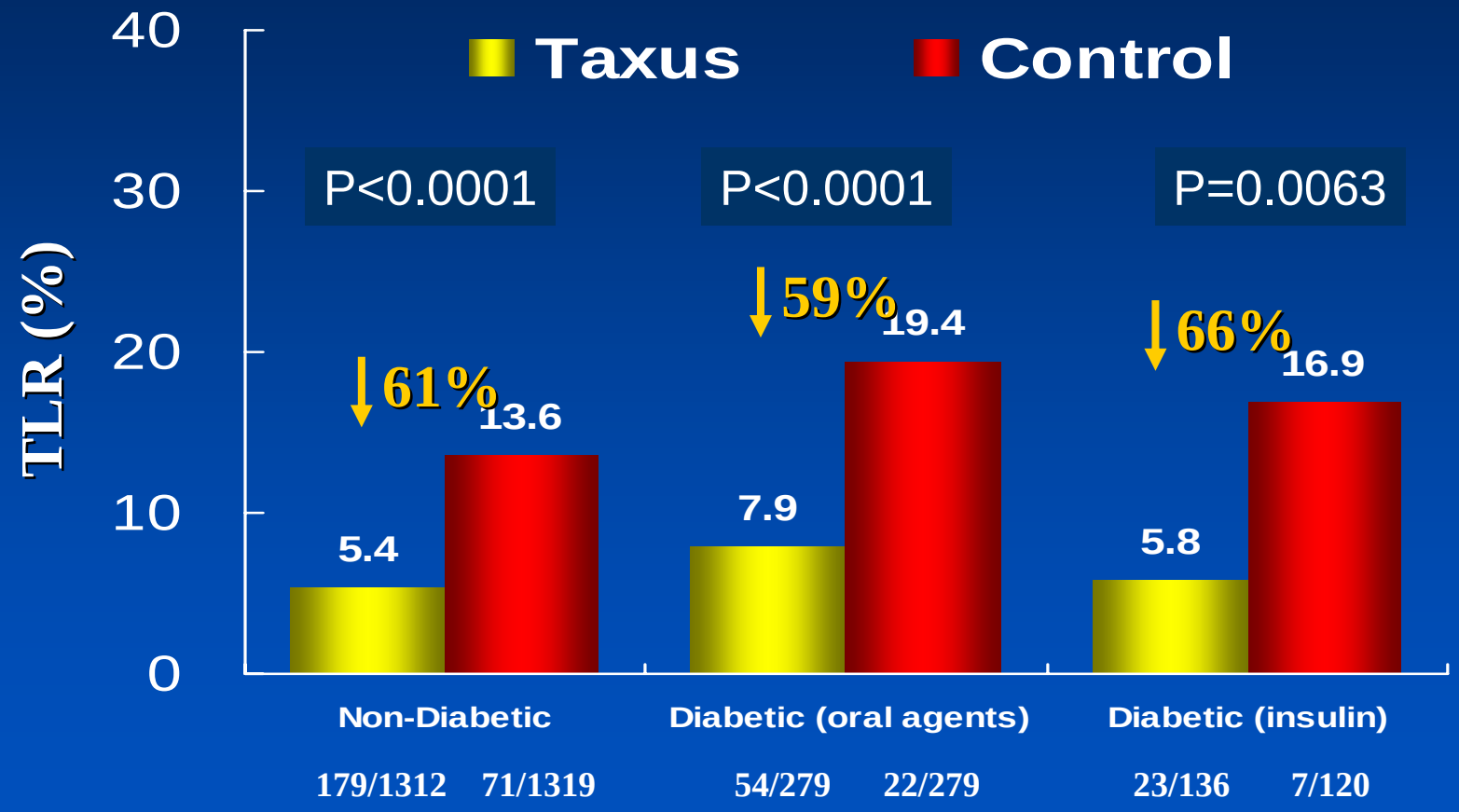
RAVEL, SIRIUS, E-SIRIUS, C-SIRIUS, DIRECT, SVELTE



Abizaid et al. Angioplasty Summit 2005

TAXUS Trials Meta-Analysis in Diabetes

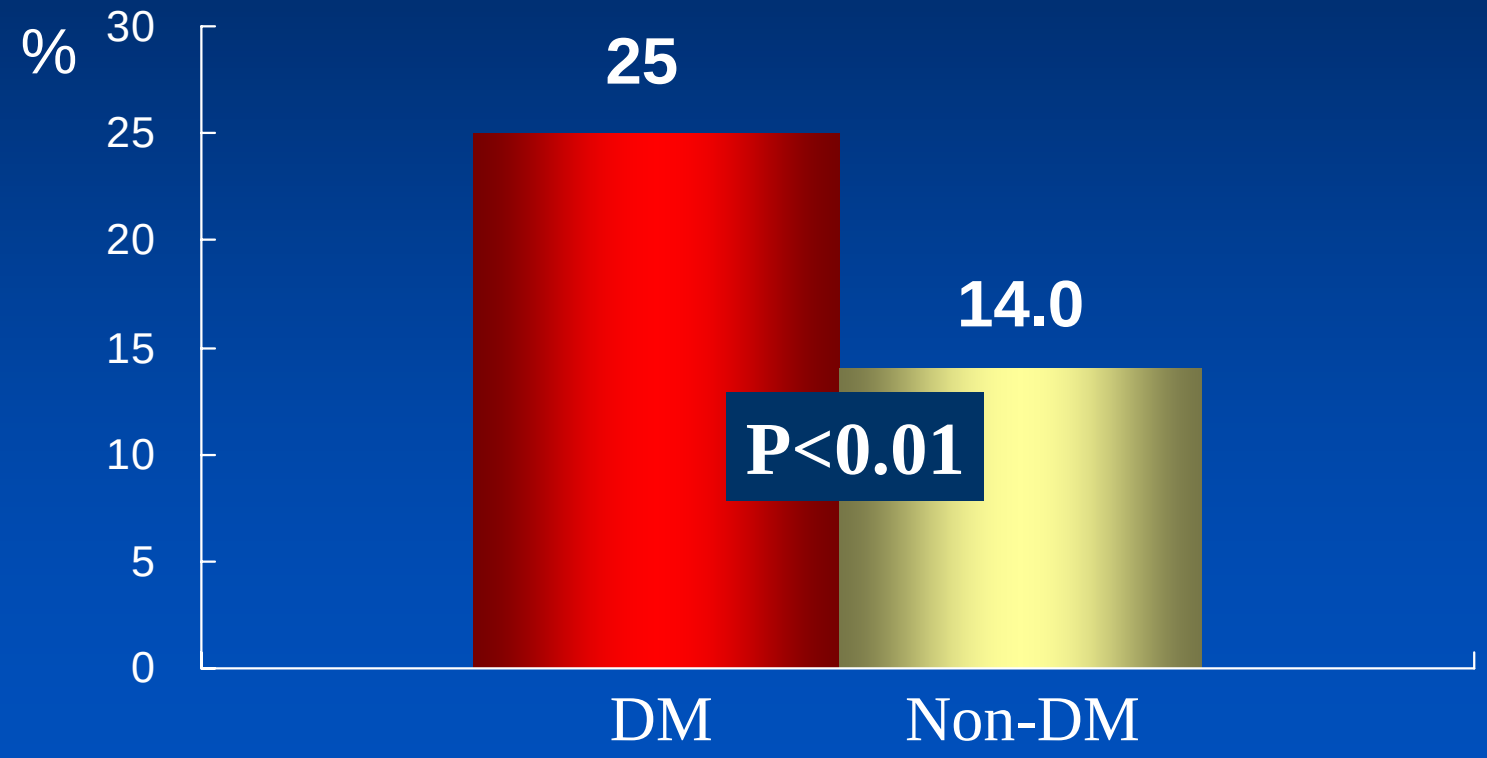
TAXUS II, IV, V, VI



Stone GW et al. Angioplasty Summit 2005

Impact of DM on Restenosis after DES Implantation

Matched comparison (192: 192)



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

Risk of Restenosis in DES

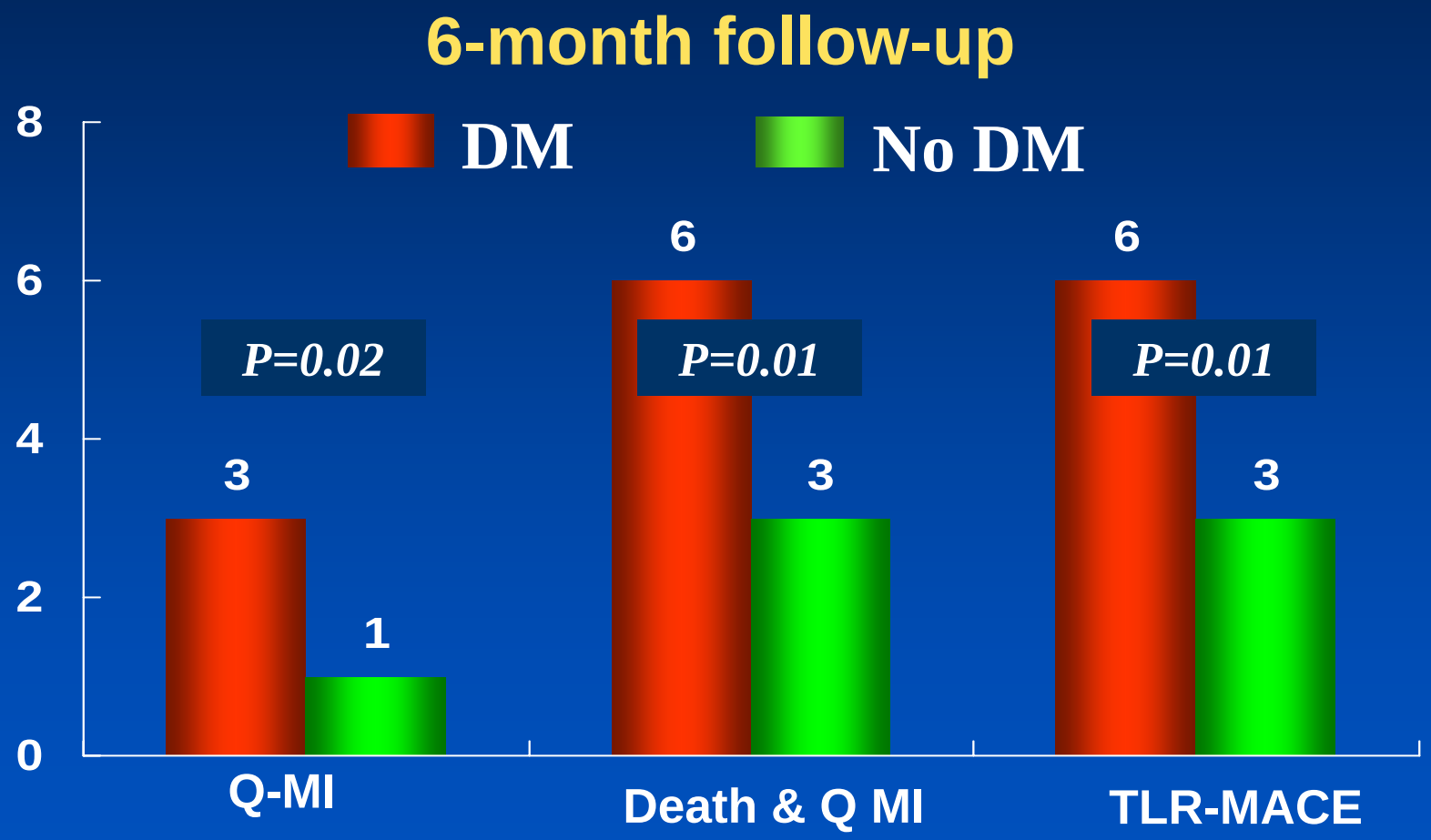
Diabetic vs Nondiabetic Patients

Multivariate Predictors of In-Segment Restenosis after SES

	OR	95% CI	p
ISR	4.16	1.63-11.01	<0.01
Ostial lesion	4.84	1.81-12.07	<0.01
Diabetes	2.63	1.14-6.31	0.02
Stent length	1.42	1.21-1.68	<0.01
Ref diameter	0.46	0.24-0.87	0.03
LAD	0.30	0.10-0.69	<0.01

Lemos PA et al. Circulation 2004;109:1366-1370

Higher MACE in Diabetics after SES



Kuchulakanti et al. Am J Cardiol 2005;96:1100

Impact of diabetes mellitus on long-term outcomes in the drug-eluting stent era

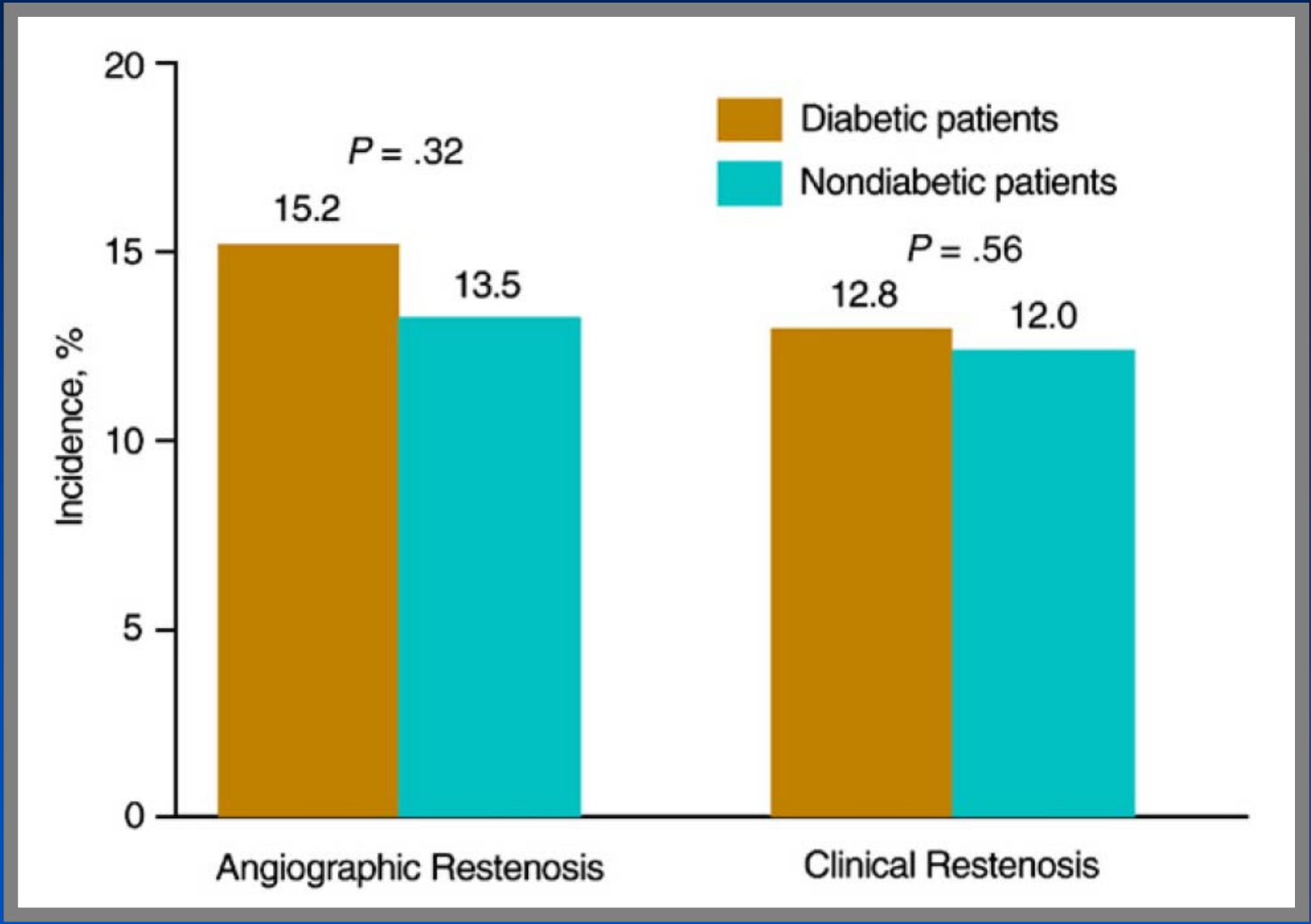
Raisuke Iijima, MD, Gjin Ndrepepa, MD, Julinda Mehilli, MD, Christina Markwardt, MD, Olga Bruskina, MD, Jürgen Pache, MD, Maryam Ibrahim, MD, Albert Schömig, MD, and Adnan Kastrati, MD *Munich, Germany*

Prospective database of 2557 patients in 2 centers

: Diabetes (n=727) vs. Non-diabetes (n=1830)

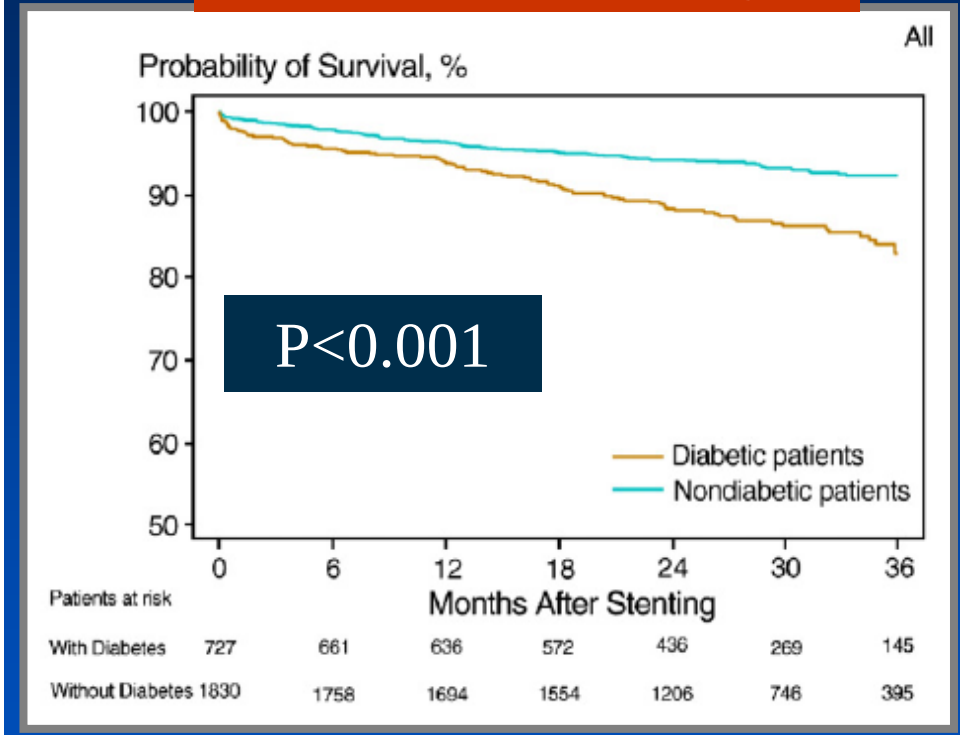
Am Hear J 2007;154:688-93

Angiographic and clinical restenosis (TLR)

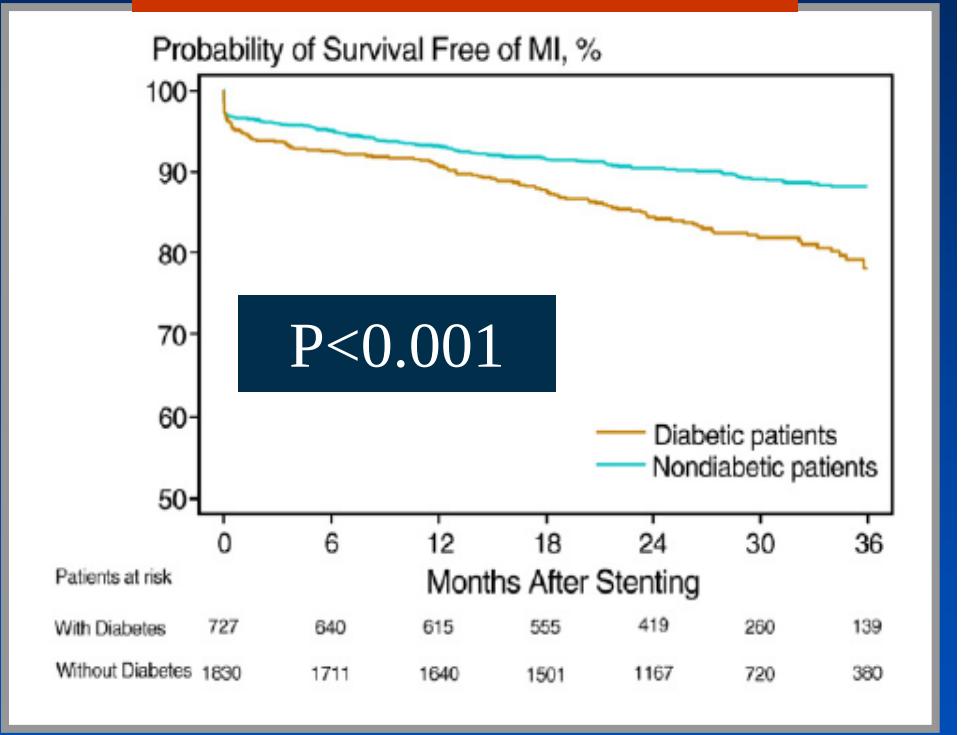


Impact of diabetes mellitus on long-term outcomes in the drug-eluting stent era

All-cause mortality



Death or MI



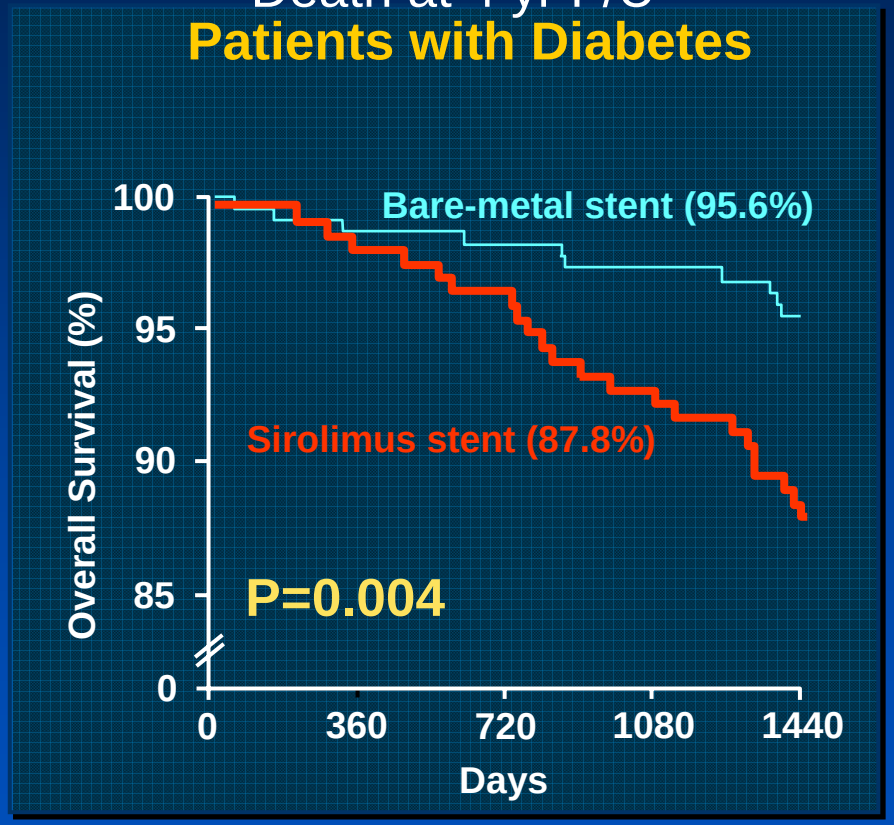
Prospective database of 2557 patients in 2 centers, Diabetes (n=727) vs. Non-diabetes (n=1830)

Raisuke Lijima, Am Hear J 2007;154:688-93

Significant difference in rates of deaths from both cardiovascular and noncardiovascular cause in Diabetic patients at 4 year F/U

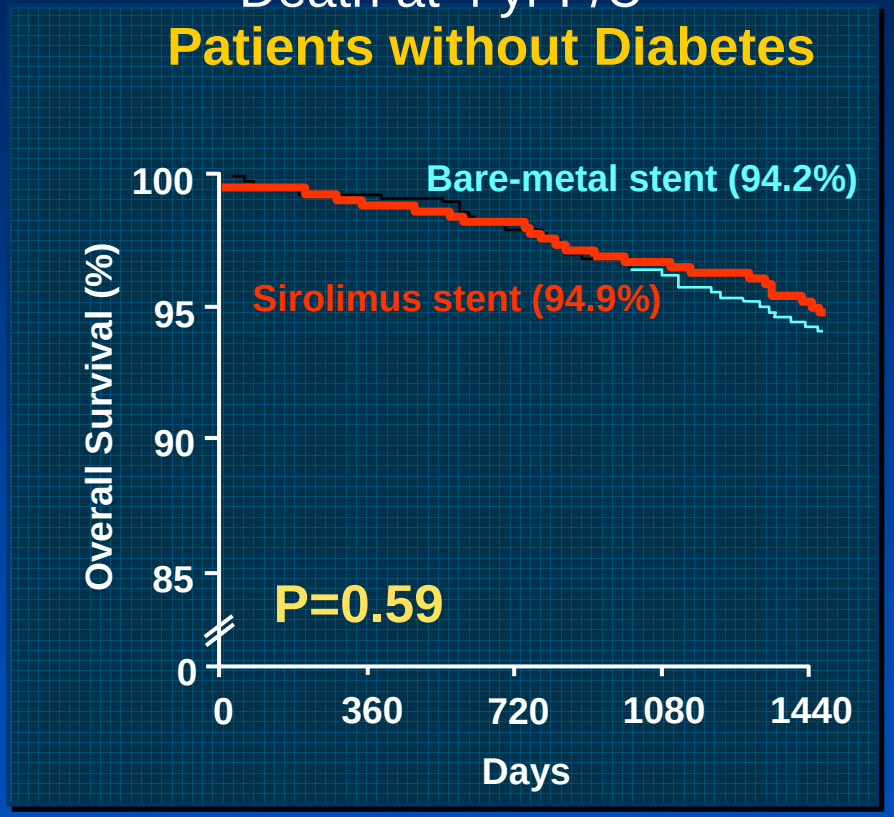
Death at 4 yr F/U

Patients with Diabetes



Death at 4 yr F/U

Patients without Diabetes



Pooled analysis of 1748 patients in 4 RCTs comparing SES with BMS
(Pivotal SES Trials: RAVEL, SIRIUS, E-SIRIUS, C-SIRIUS)

Christian Spaulding, NEJM 2007;356:989-97

Independent predictors of stent thrombosis

Incidence, Predictors, and Outcome of Thrombosis After Successful Implantation of Drug-Eluting Stents

- **Diabetes (HR 3.71, 95% CI, 1.74–7.89).**

JAMA 2005;293:2126-2130

Early and late coronary stent thrombosis of sirolimus-eluting and paclitaxel-eluting stents in routine clinical practice: data from a large two-institutional cohort study

Joost Daemen, Peter Wenaweser, Keiichi Tsuchida, Linda Abrecht, Sophia Vaina, Cyrill Morger, Neville Kukreja, Peter Jüni, Georgios Sianos, Gerrit Hellige, Ron T van Domburg, Otto M Hess, Eric Boersma, Bernhard Meier, Stephan Windecker, Patrick W Serruys

- **Diabetes (HR 2.03, 95% CI, 1.07–3.83).**

Lancet 2007;369: 667–78

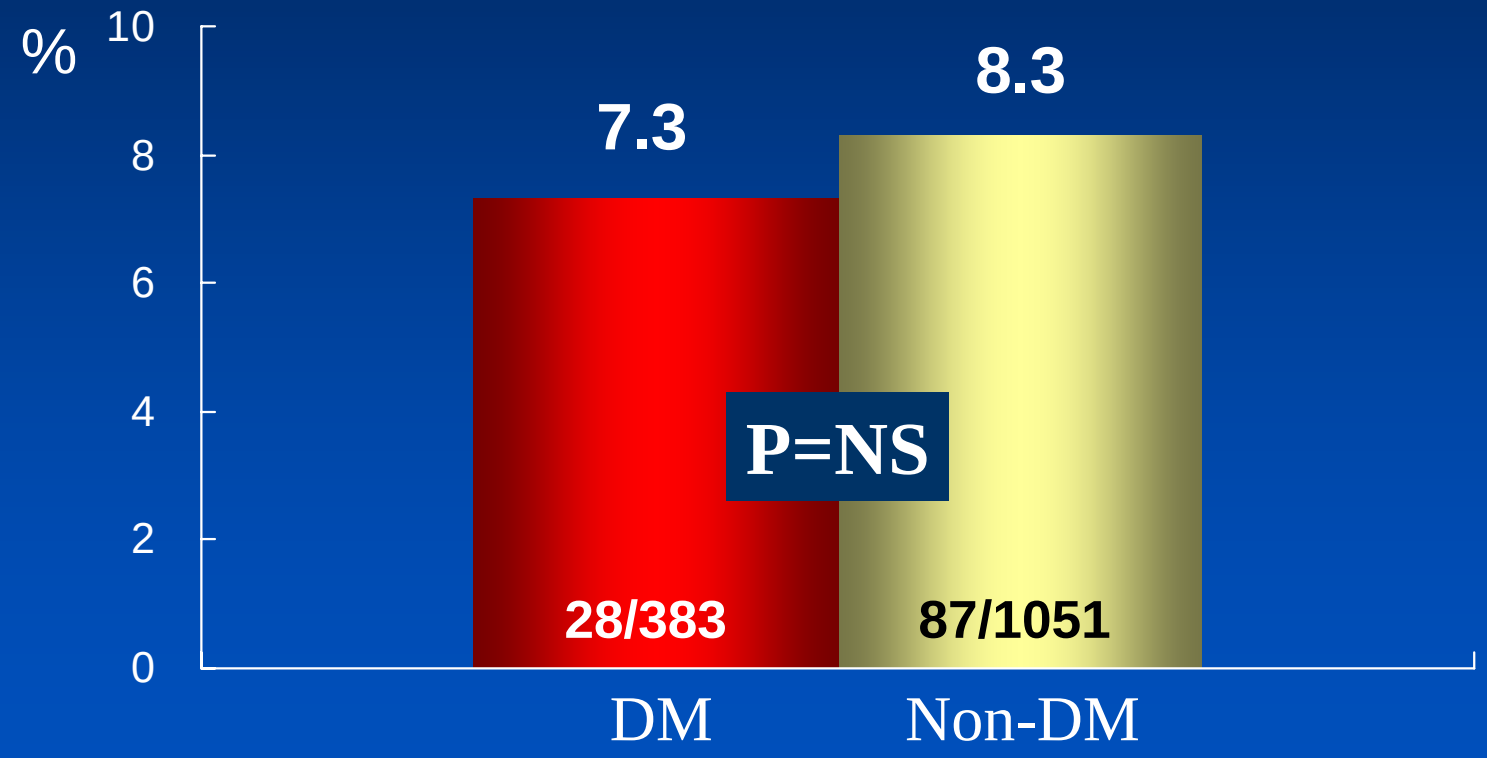
General Concerns
about Diabetic Influence
in Patients Undergoing PCI with DES

- Still higher restenosis rate and MACE in diabetics compare to non-diabetics
- Higher mortality after PCI with DES ?
- Higher incidence of stent thrombosis ?

Any Differences of Long-term Clinical Outcomes after DES Implantation in Asia vs. Western ?

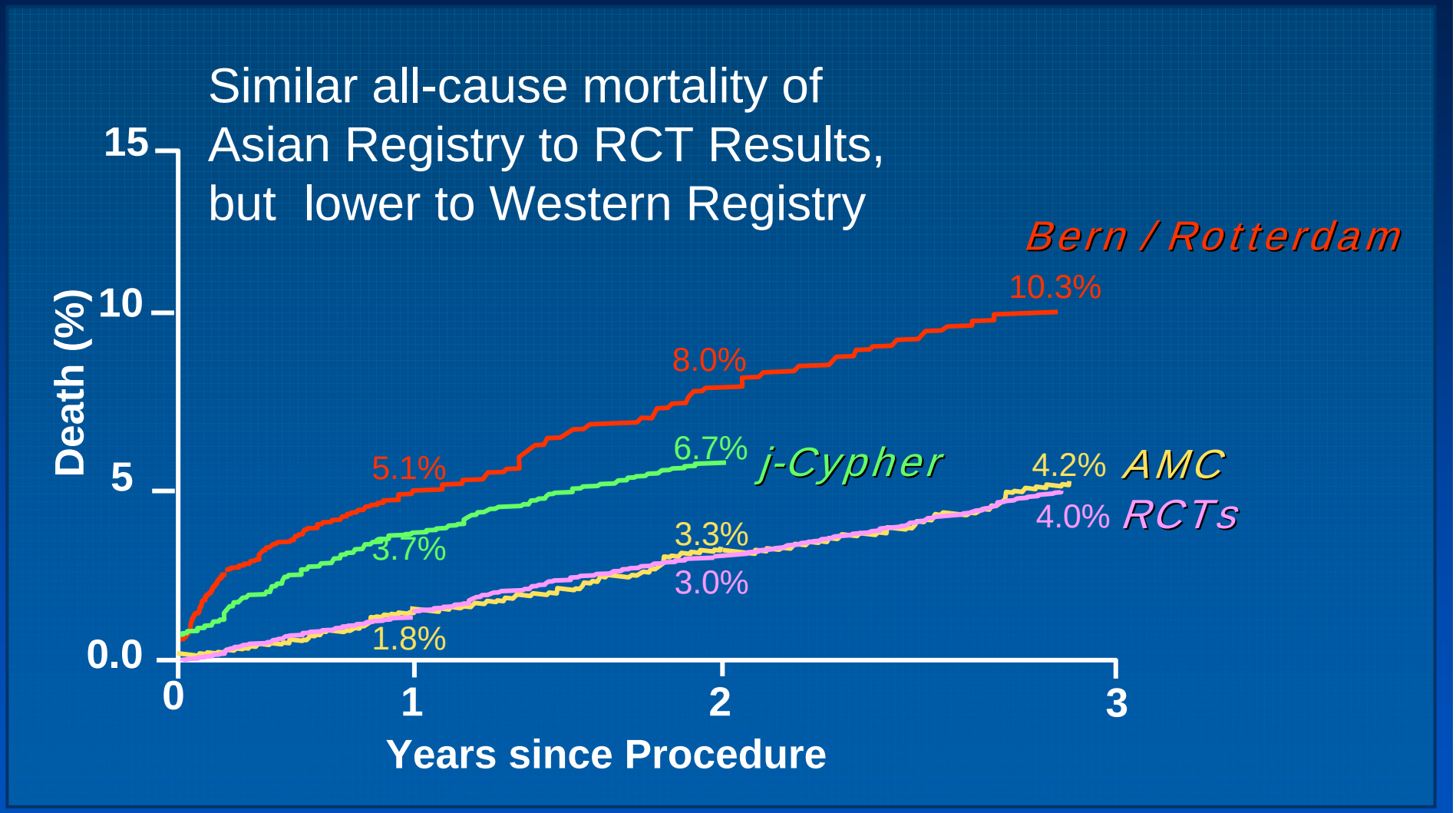
Impact of DM on Restenosis after DES Implantation

1126 Cypher lesions and 308 Taxus lesions



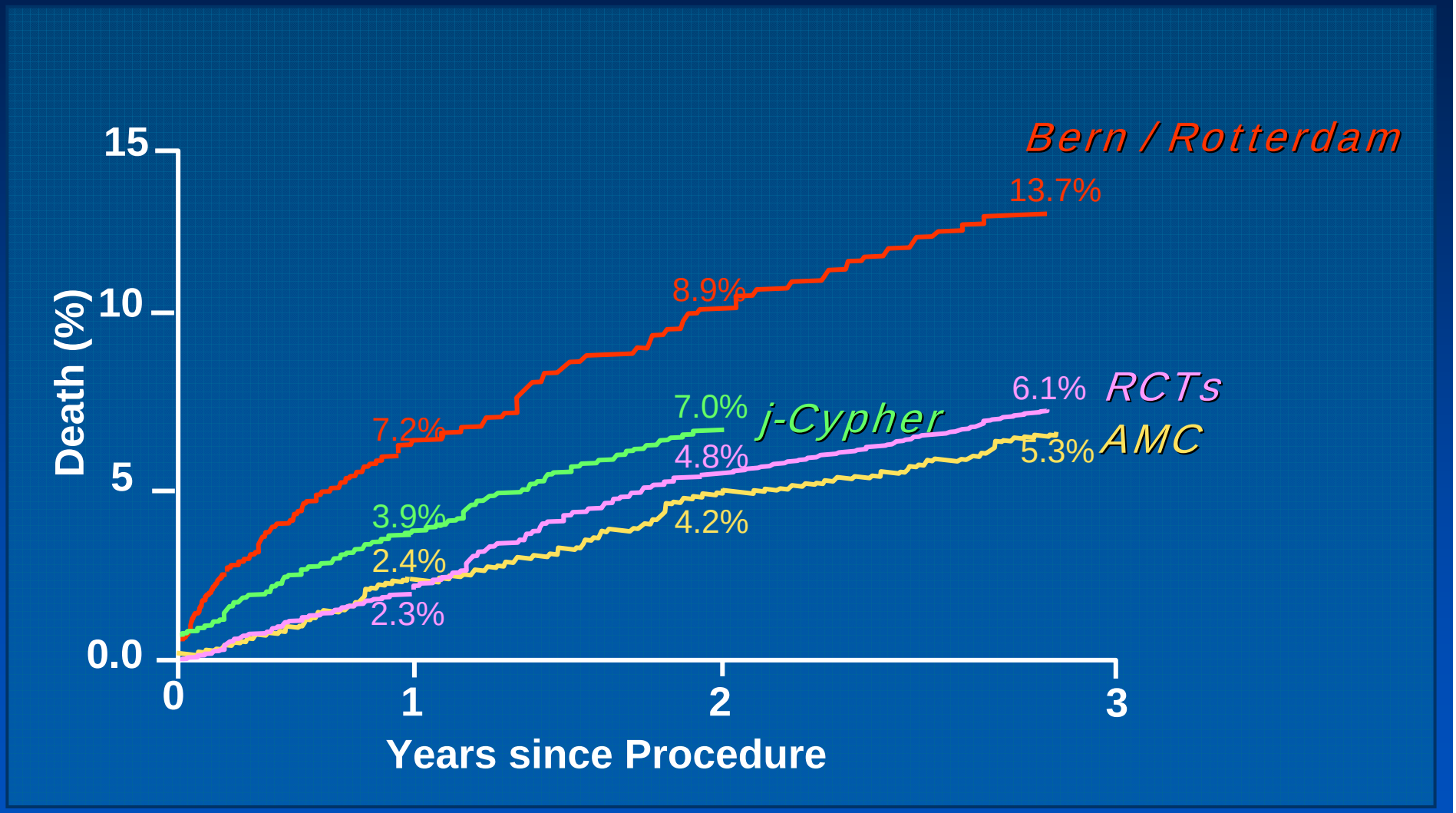
TH Y et al. Am J Cardiol 2005;96:1389

All-Cause Mortality



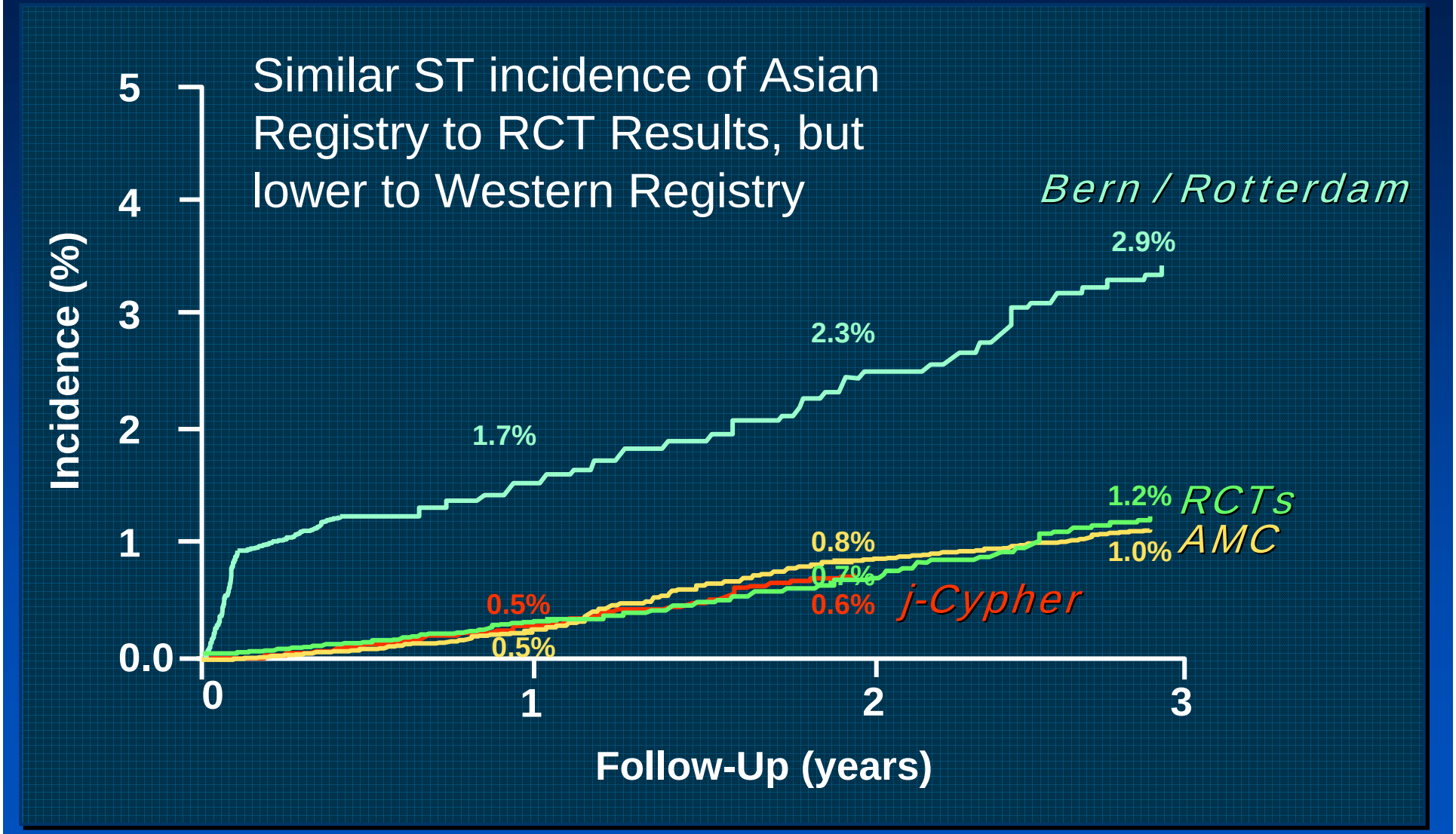
Park et al. *JACC:Cardiovascular Interventions* 2008

Death or MI



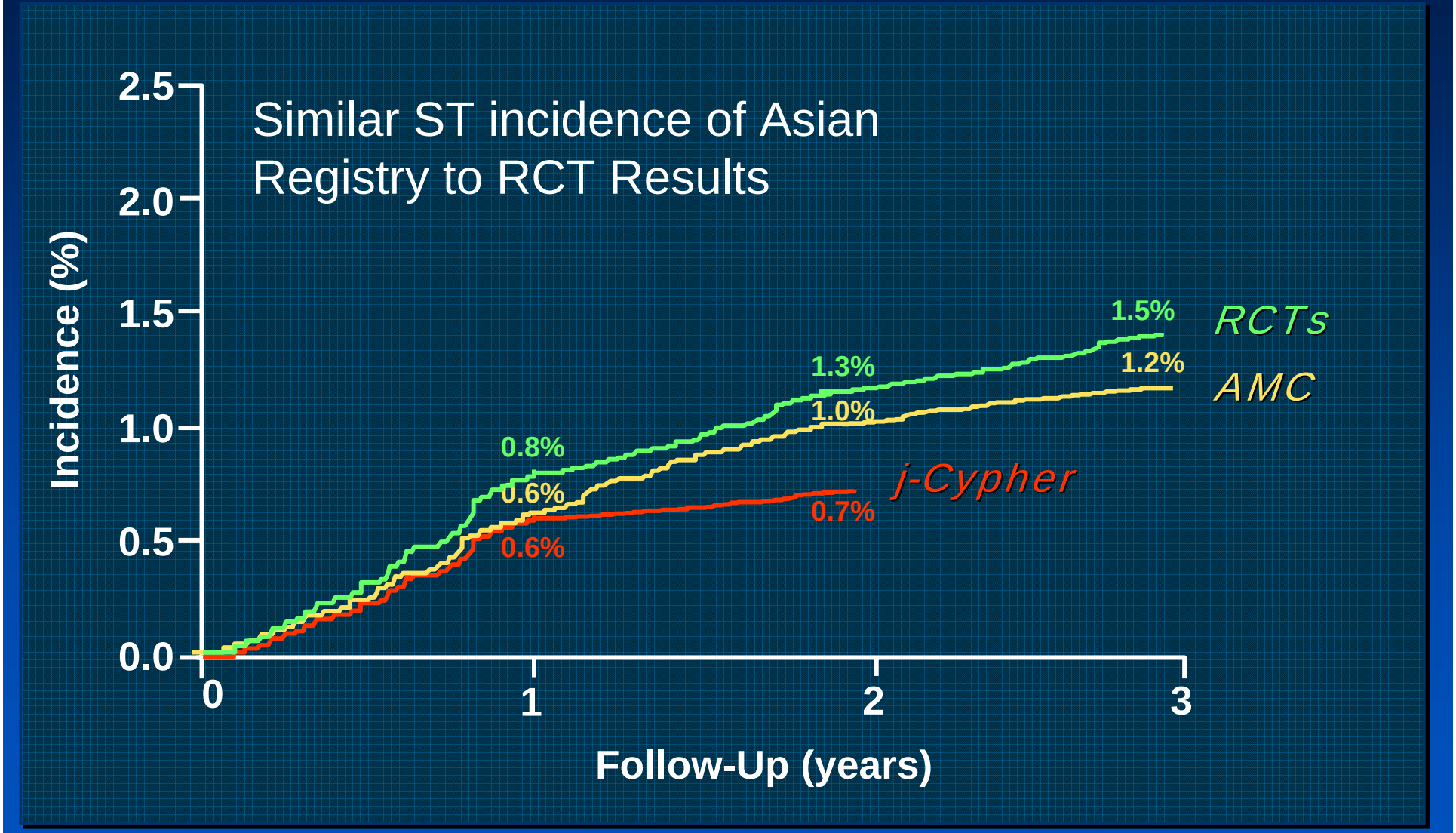
Park et al. *JACC:Cardiovascular Interventions* 2008

Incidence of Angiographic ST



Park et al. *JACC:Cardiovascular Interventions* 2008

Incidence of ST (Definite+Probable)



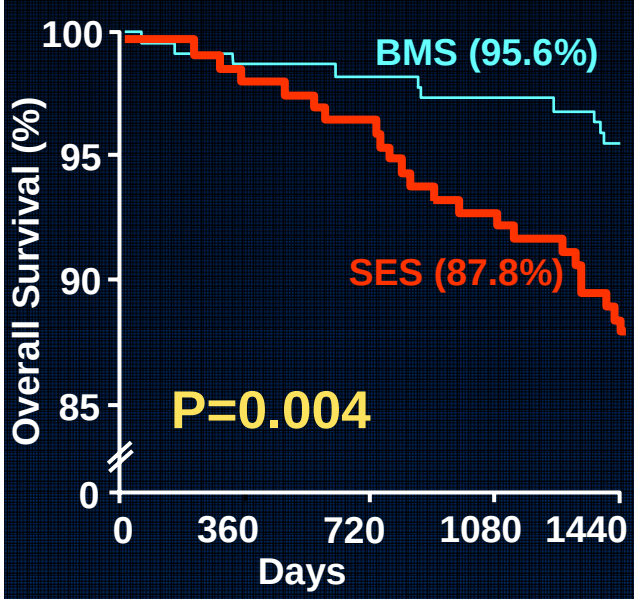
Park et al. *JACC:Cardiovascular Interventions* 2008

Impact of Diabetes

All-Cause Mortality

Death at 4 yr F/U

Patients with Diabetes

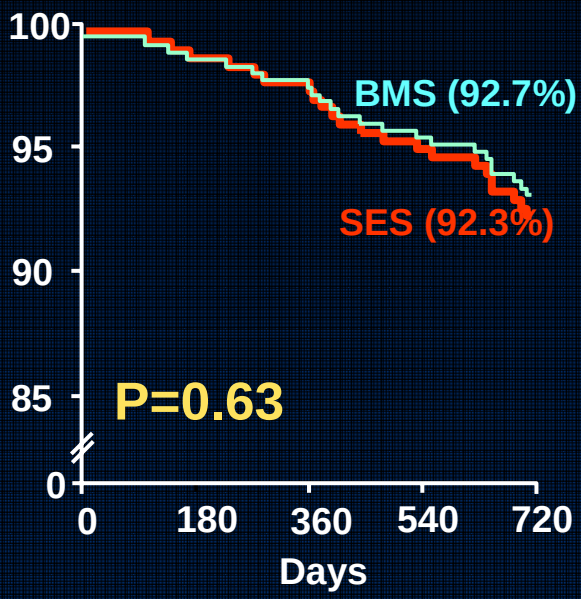


RCTs

(RAVEL, SIRIUS,
E-SIRIUS, C-SIRUS)

Death at 2 yr F/U

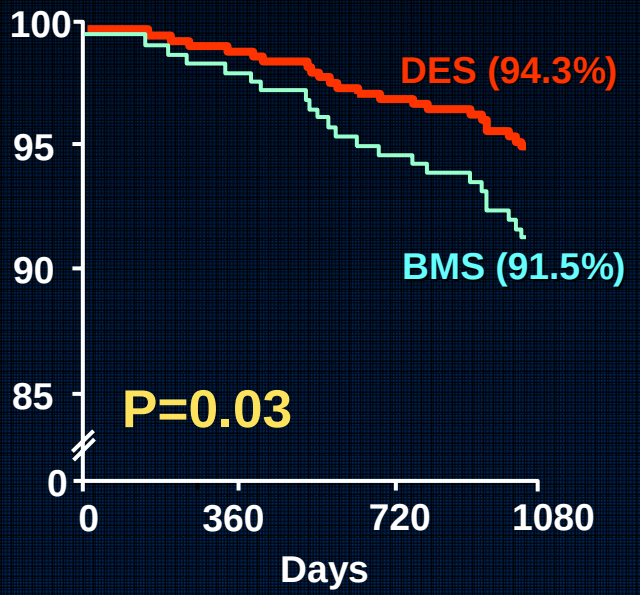
Patients with Diabetes



J-Cypher

Death at 3 yr F/U

Patients with Diabetes



AMC Registry

Independent risk factors of ST

-Multivariate Analysis-

Bern / Rotterdam

- Acute coronary syndrome
- Diabetes

AMC Registry

- Lower EF
- Renal failure
- Stent length

Mostly, clinical factors are involved in risk of ST. However, diabetes is not independent predictor of ST in AMC registry data.

Summary

- Incidence of ST and all-cause mortality of Asian registry was similar to those of RCT, but lower than results of western registry
- Important predictors of ST was mainly due to clinical factors.
- Impact of diabetes on the long-term outcomes in Asia was very modest, compared to the features from Western data.

Prognostic Influence of Diabetes Mellitus on Long-Term Clinical Outcomes and Stent Thrombosis Following DES Implantation in Asian Patients

Overall 3160 patients:

Diabetes (n=865) vs. Non-diabetes (n=2295)

during 3-year follow-up.

Outcomes of study

- Primary end-point
  ; Composite of death, nonfatal MI, or TVR

- Secondary end-points
  ; Death, MI, TLR, TVR, and stent thrombosis (ARC criteria)

Baseline characteristics

Variable	Diabetes (n=865)	Non-diabetes (n=2295)	*P*
Age (years)	62.7±9.1	59.7±10.6	<0.001
Female	312 (36.1)	619 (27.0)	<0.001
Hypertension	533 (61.6)	1066 (46.4)	<0.001
Lipid profiles			
Total cholesterol (mg/dl)	178.2±53.3	172.2±48.5	0.003
Triglyceride (mg/dl)	161.2±102.8	147.0±93.5	0.005
HDL cholesterol (mg/dl)	41.9±17.3	43.2±15.1	0.10
Current smoking	201 (23.2)	719 (31.3)	<0.001
Renal failure	50 (5.8)	30 (1.3)	<0.001
Previous myocardial infarction	99 (11.4)	198 (8.6)	0.02
Previous coronary angioplasty	161 (18.6)	383 (16.7)	0.20
Previous coronary artery bypass graft	31 (3.6)	53 (2.3)	0.05

Baseline characteristics

Variable	Diabetes (n=865)	Non-diabetes (n=2295)	*P*
Clinical indication			<0.001
Stable angina	450 (52.0)	1074 (46.8)	
Unstable angina	334 (38.6)	865 (37.7)	
Myocardial infarction	81 (9.4)	356 (15.5)	
Multivessel disease	585 (67.6)	1280 (55.8)	<0.001
Left ventricular ejection fraction (%)	57.9±9.3	58.6±8.7	0.04
Medications at discharge			
Warfarin	10 (1.2)	21 (0.9)	0.54
Statin	498 (57.6)	1240 (54.0)	0.07
β-Blocker	631 (72.9)	1629 (71.0)	0.28
Calcium Channel Blocker	417 (48.2)	1129 (49.2)	0.62
ACE inhibitor	536 (62.0)	1271 (55.4)	0.001

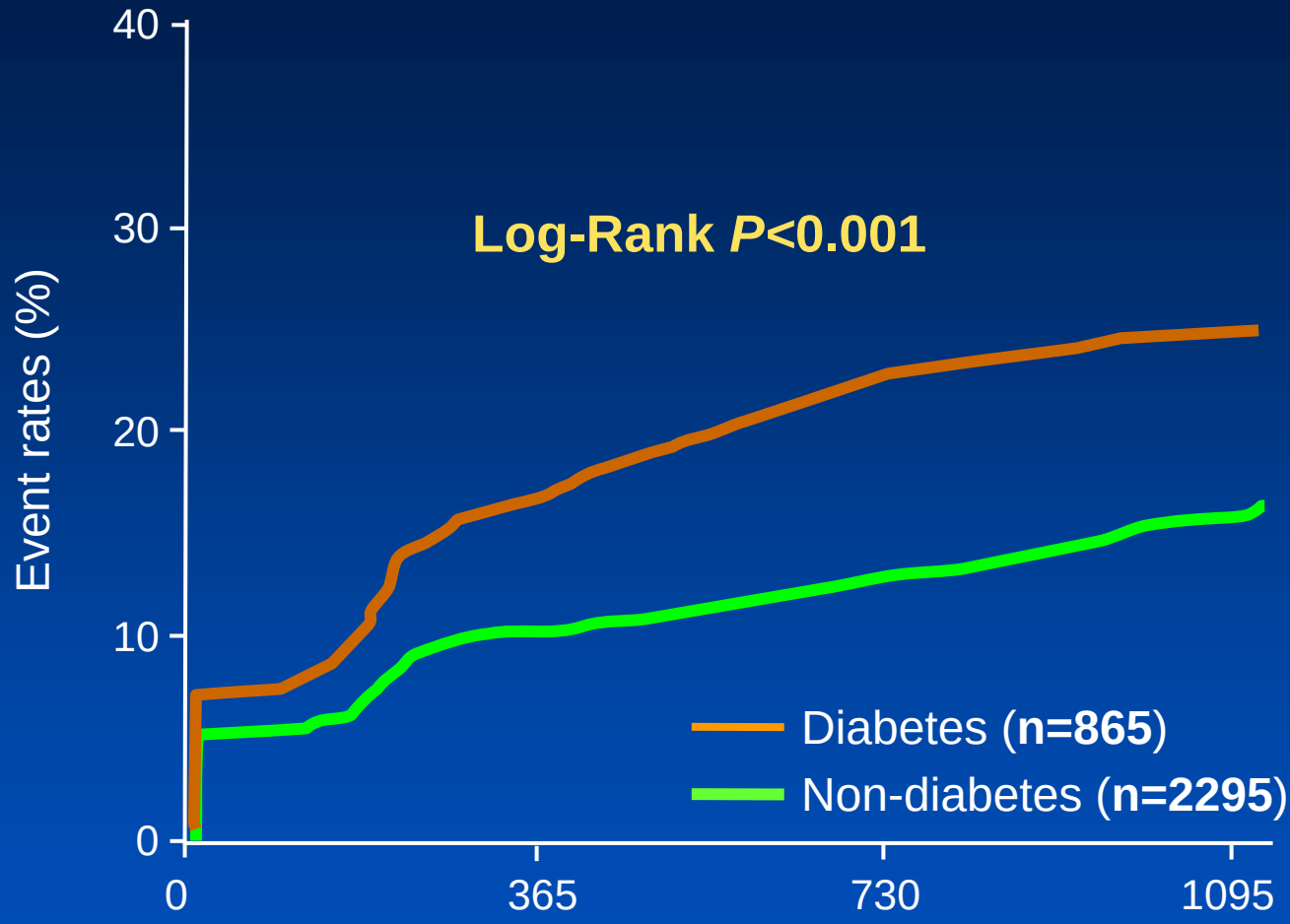
Baseline characteristics

Variable	Diabetes (n=865)	Non-diabetes (n=2295)	*P*
Treated lesions, No.	1301	3190	
Left anterior descending artery	637 (49.0)	1579 (49.5)	0.74
Left main artery	83 (6.4)	224 (7.0)	0.44
Lesion Characteristics			
ACC/AHA type B2 or C lesion	1008 (77.5)	2330 (73.0)	0.002
Ostial	84 (6.5)	271 (8.5)	0.02
Bifurcation	236 (18.1)	501 (15.7)	0.05
Total occlusion	70 (5.4)	181 (5.7)	0.70
Restenotic lesion	68 (5.2)	183 (5.7)	0.50

Procedural characteristics

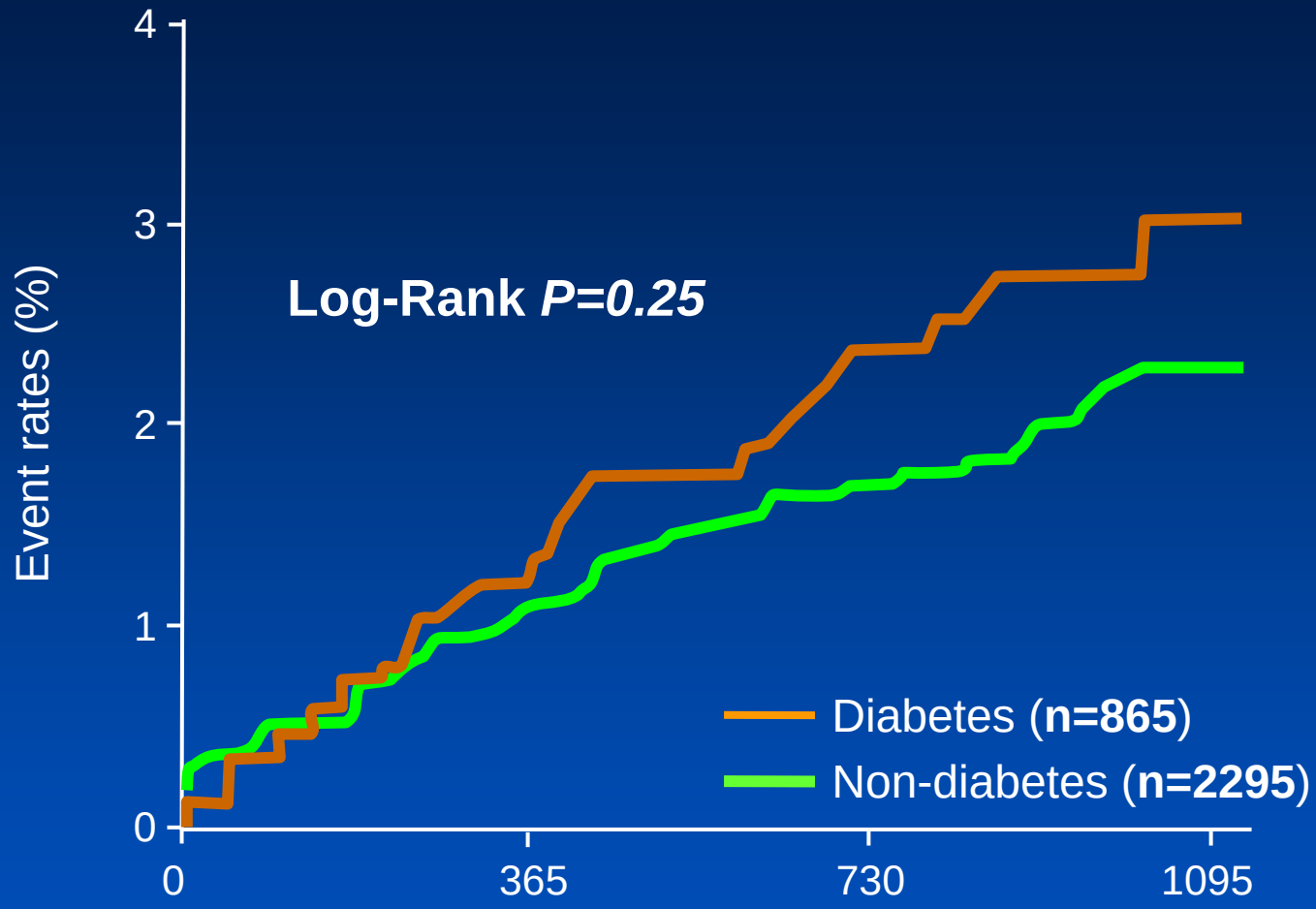
Variable	Diabetes (n=865)	Non-diabetes (n=2295)	*P*
Treated lesions, No.	1301	3190	
Direct stenting	174 (13.4)	553 (17.3)	0.001
IVUS guidance	798 (61.3)	2099 (65.8)	0.01
DES type			0.06
Sirolimus-eluting stent	976 (75.0)	2478 (77.7)	
Paclitaxel-eluting stent	325 (25.0)	712 (22.3)	
Number of stents per patient	2.1±1.2	1.8±1.1	<0.001
Total stent length per patient (mm)	53.5±33.3	46.0±29.8	<0.001
Average stent diameter per patient (mm)	3.1±0.3	3.2±0.3	<0.001
Use of Glycoprotein IIb/IIIa inhibitors	24 (2.8)	69 (3.0)	0.73

Composite of Death, MI, or TVR



No. at Risk				
Diabetes	865	730	457	195
Non-diabetes	2295	2057	1339	581

Stent Thrombosis

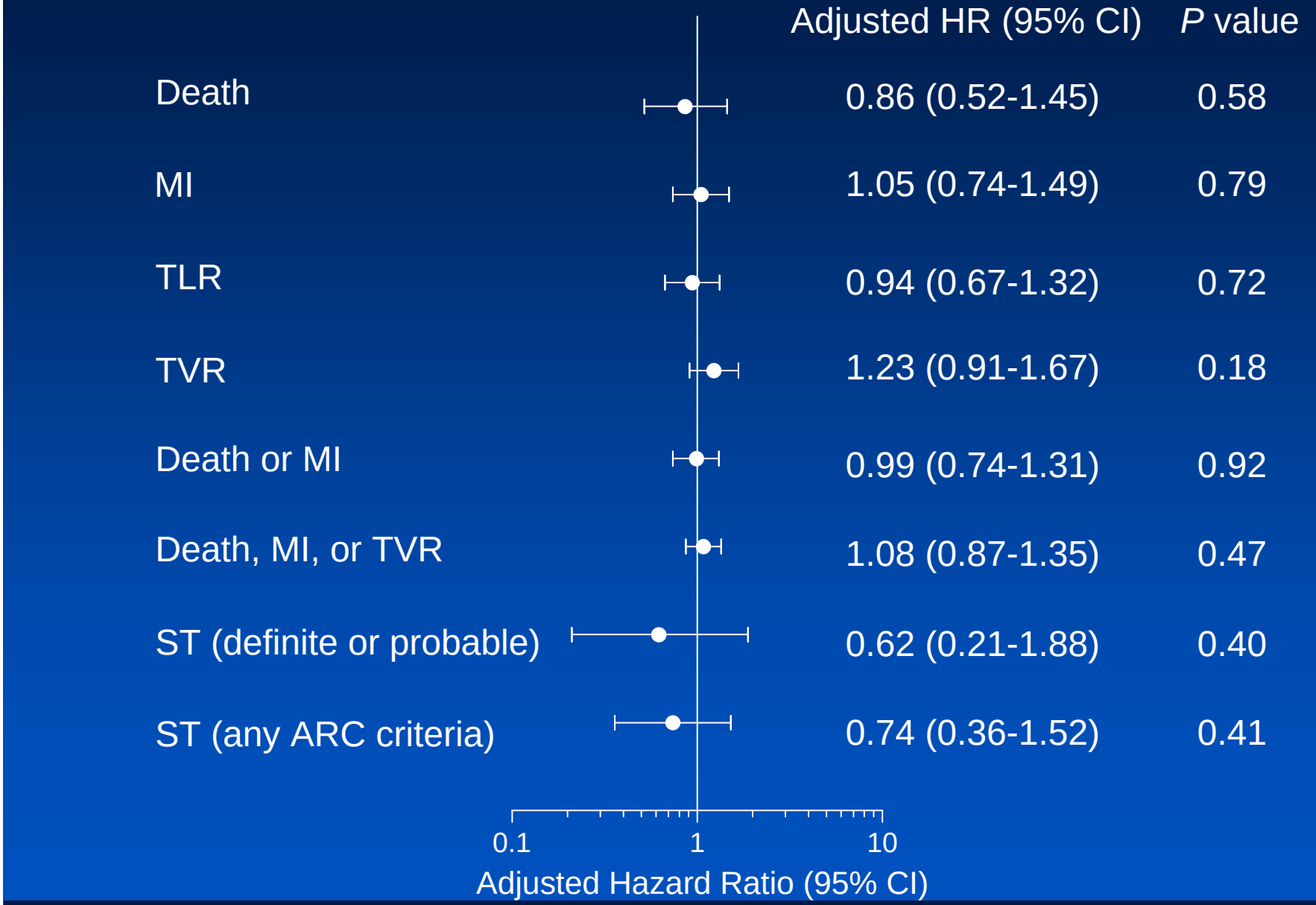


No. at Risk				
Diabetes	865	842	561	247
Non-diabetes	2295	2248	1521	674

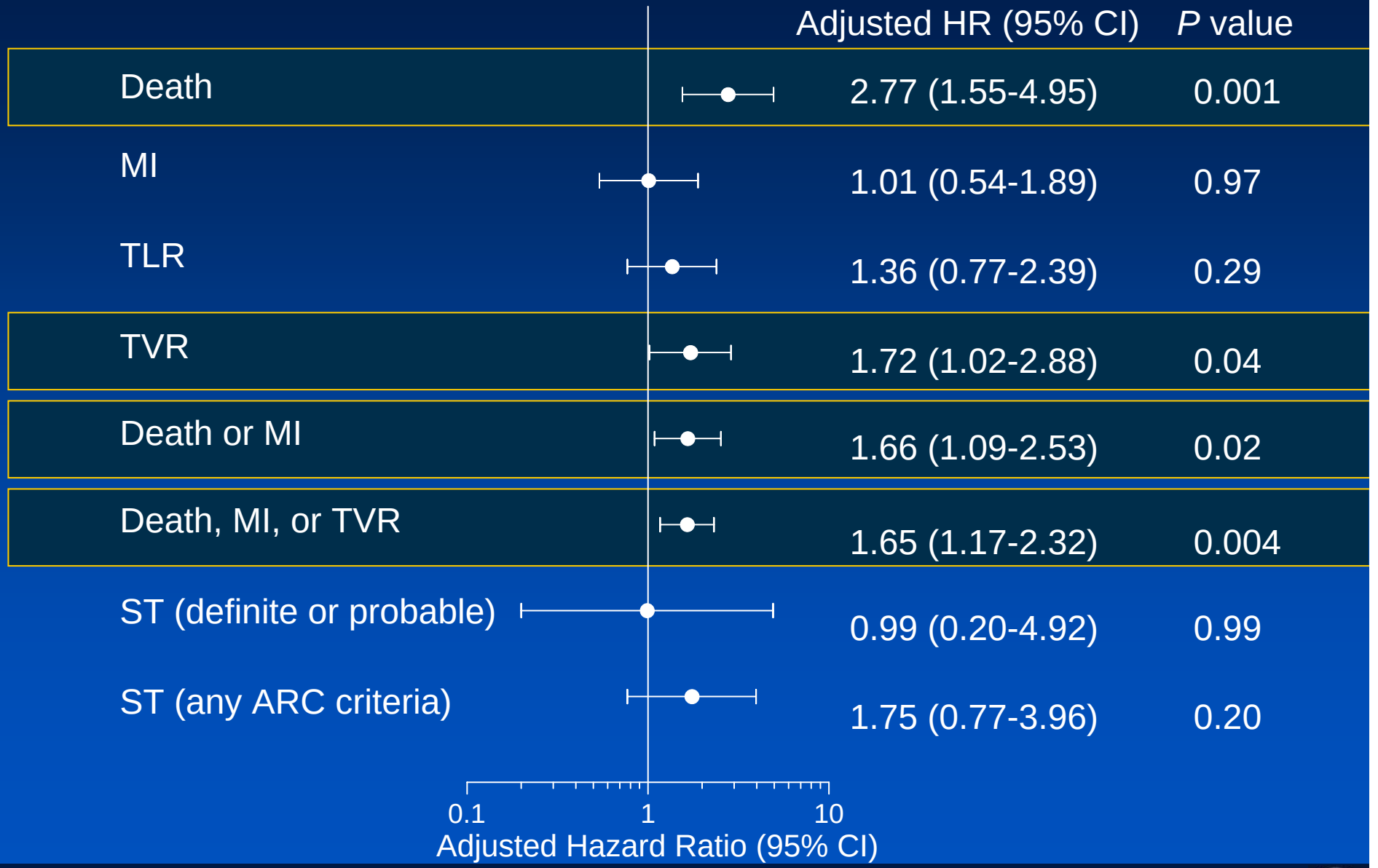
Adjusted HRs of Clinical Outcomes
Diabetic vs. Non-diabetics

Outcome	HR	95% CI	P
Death	1.35	0.89-2.05	0.16
MI	1.08	0.78-1.50	0.63
TLR	1.06	0.78-1.43	0.71
TVR	1.37	1.04-1.81	0.03
Death/MI	1.18	0.92-1.53	0.20
Death/MI/TVR	1.24	1.02-1.51	0.03
Stent thrombosis			
Definite	0.62	0.20-1.84	0.41
Definite/probable	0.87	0.37-2.06	0.77
Any	1.14	0.69-1.99	0.64

Non-diabetes vs. **Non-insulin-treated diabetes**



Non-diabetes vs. **Insulin-treated diabetes**



Summary:
Diabetic Impact in Asian Patients

- The overall mortality rate was similar in diabetic and non-diabetic patients
- Diabetic patients have a higher incidence of TVR, without a significantly increased rate of TLR
- There was no significant association between increased risk of stent thrombosis and diabetes, whether insulin-dependent or not
- Insulin-treated diabetes was independently associated with increased risk of death and TVR

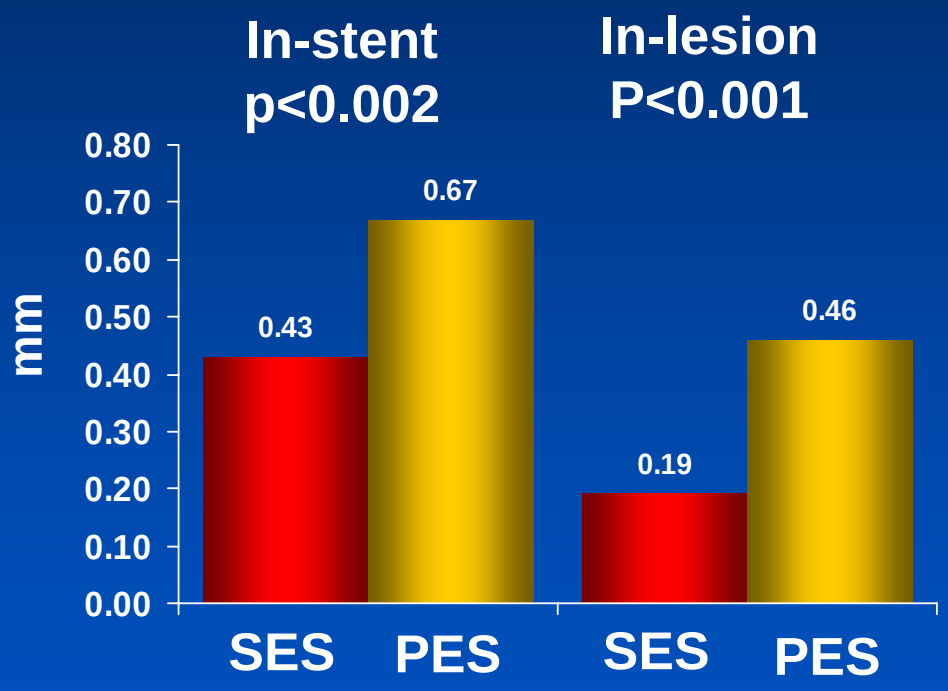
Impact of Diabetes on DES outcomes ; All DESs Are Equally Effective?

- Early or Mid-Term Outcomes
- Long-Term Outcomes

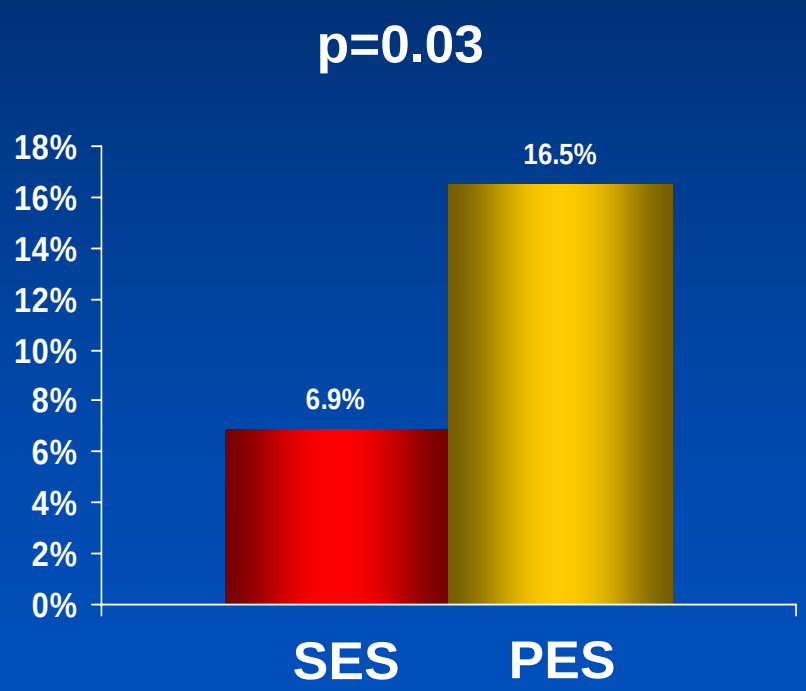
Diabetes
; CYPHER vs. TAXUS

ISAR-DIABETES Trial

Late Lumen Loss

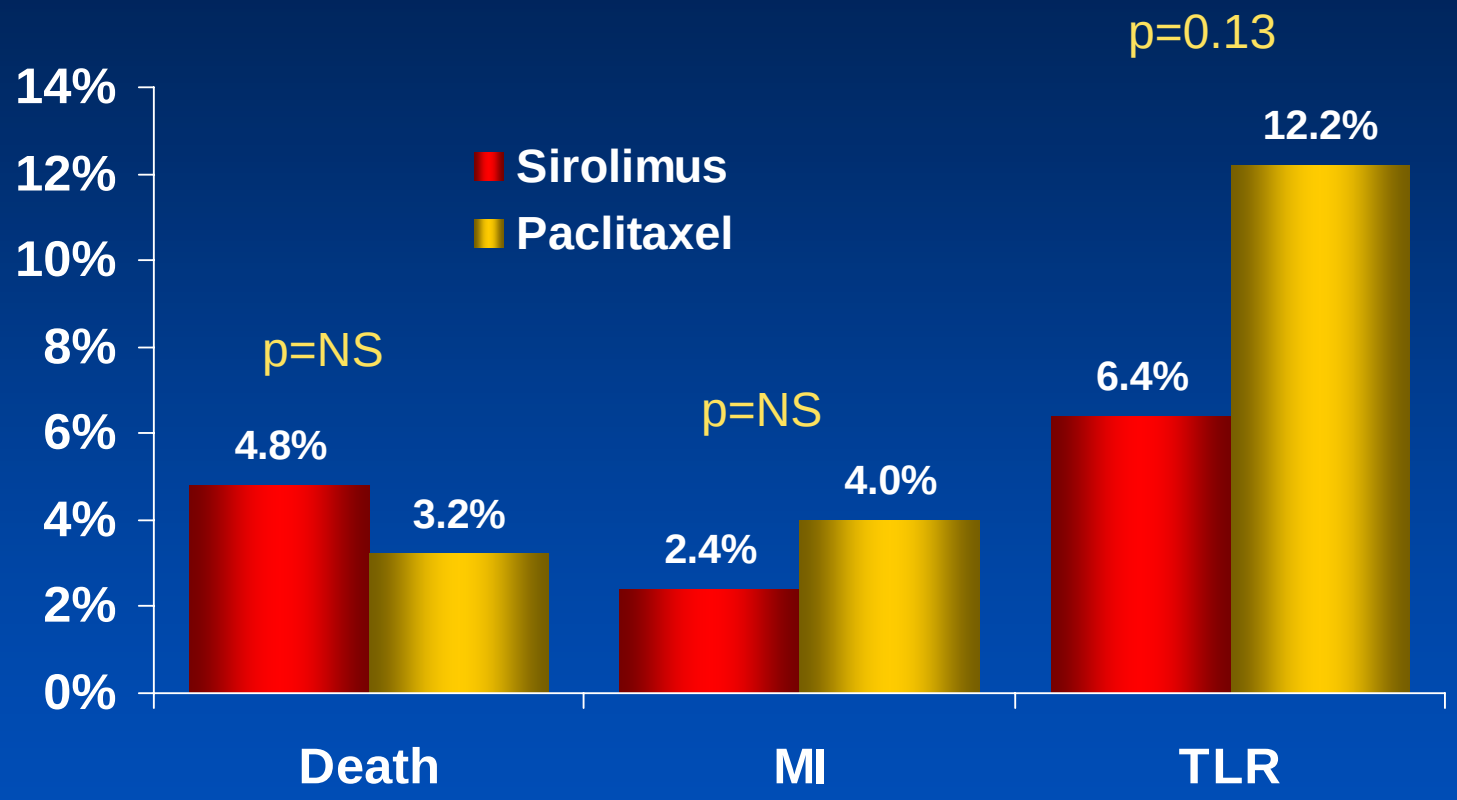


Re-stenosis



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

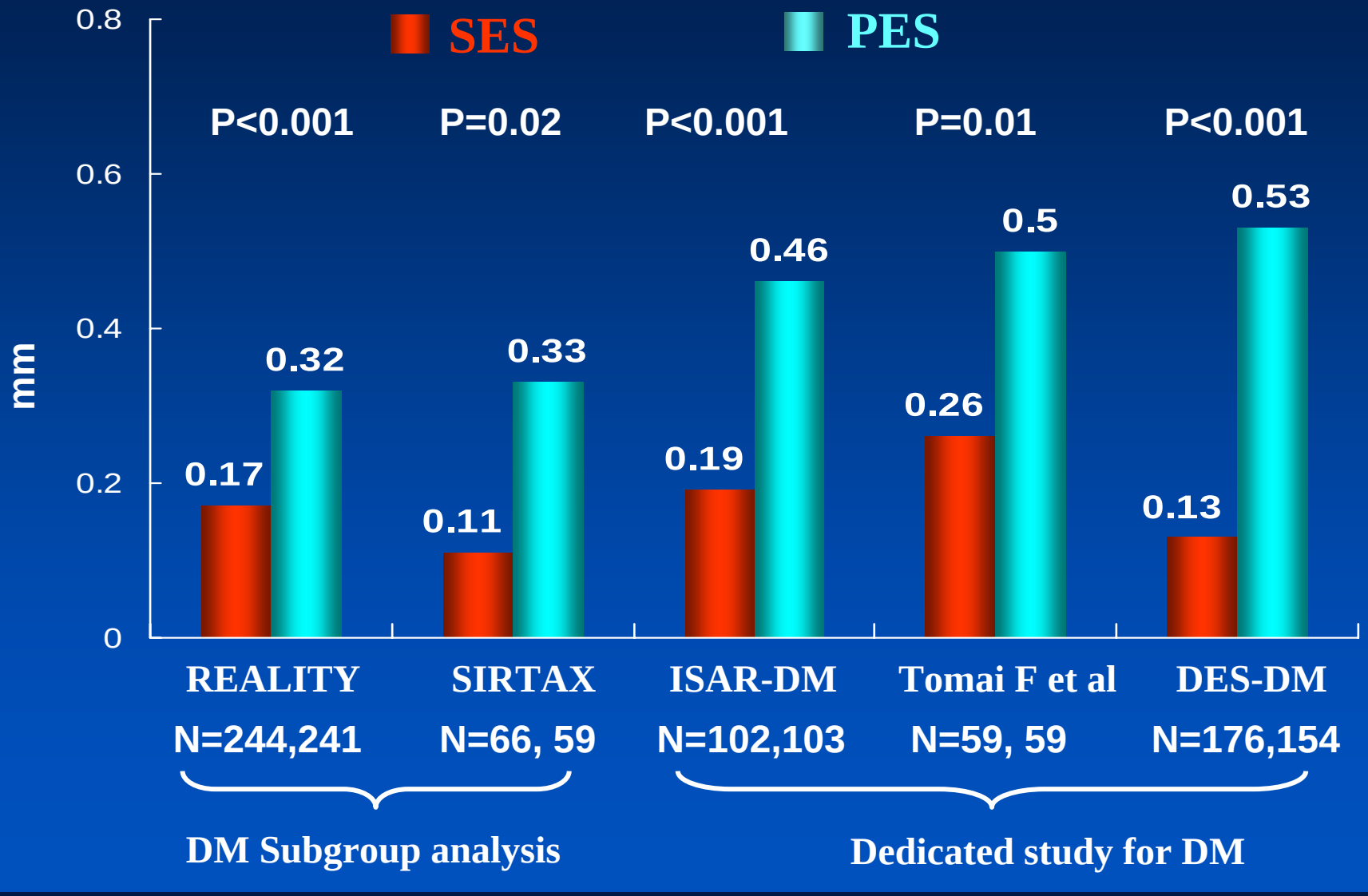
ISAR-DIABETES Trial



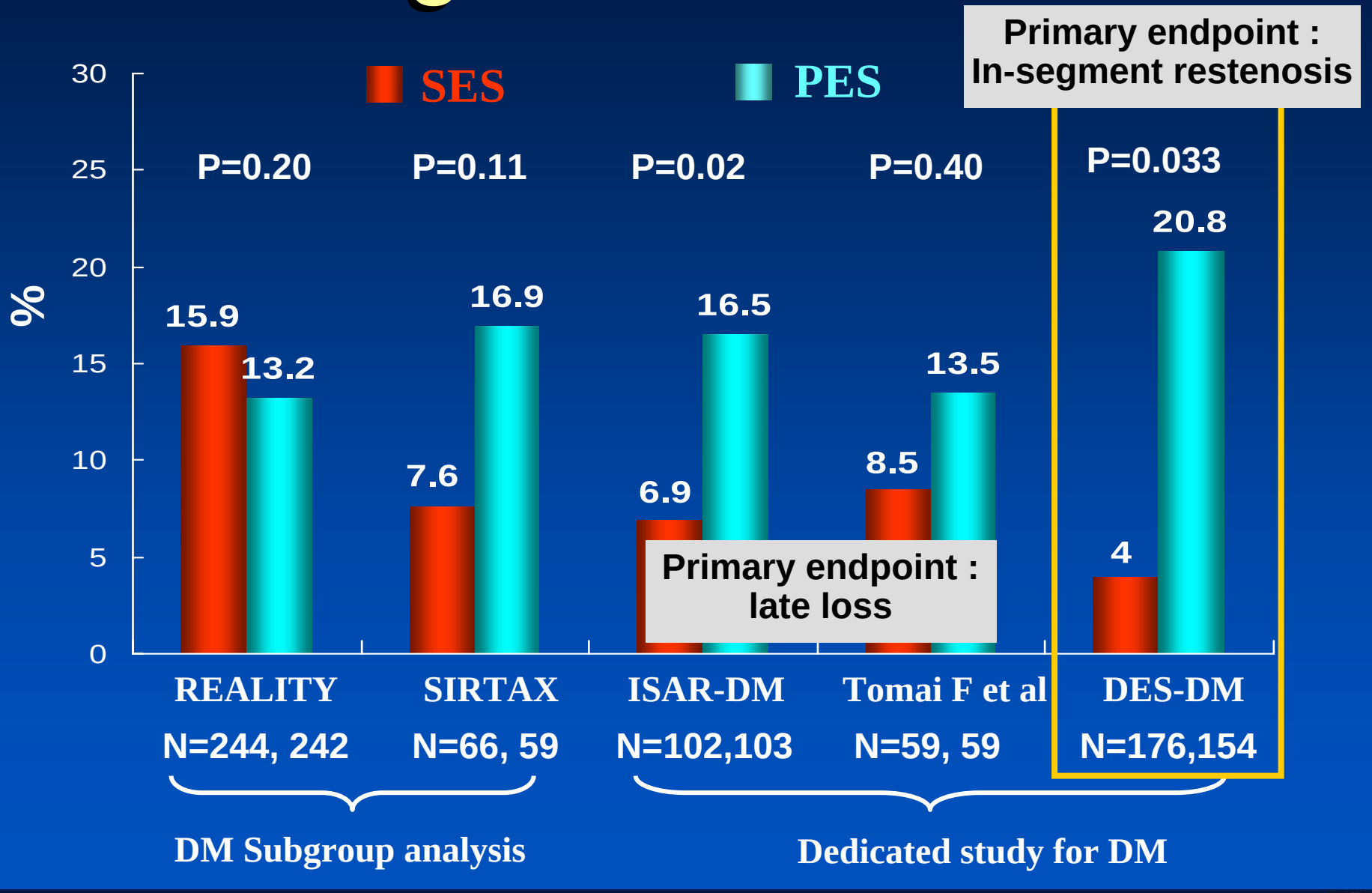
There was a trend towards a reduction in TLR (p=0.13)

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

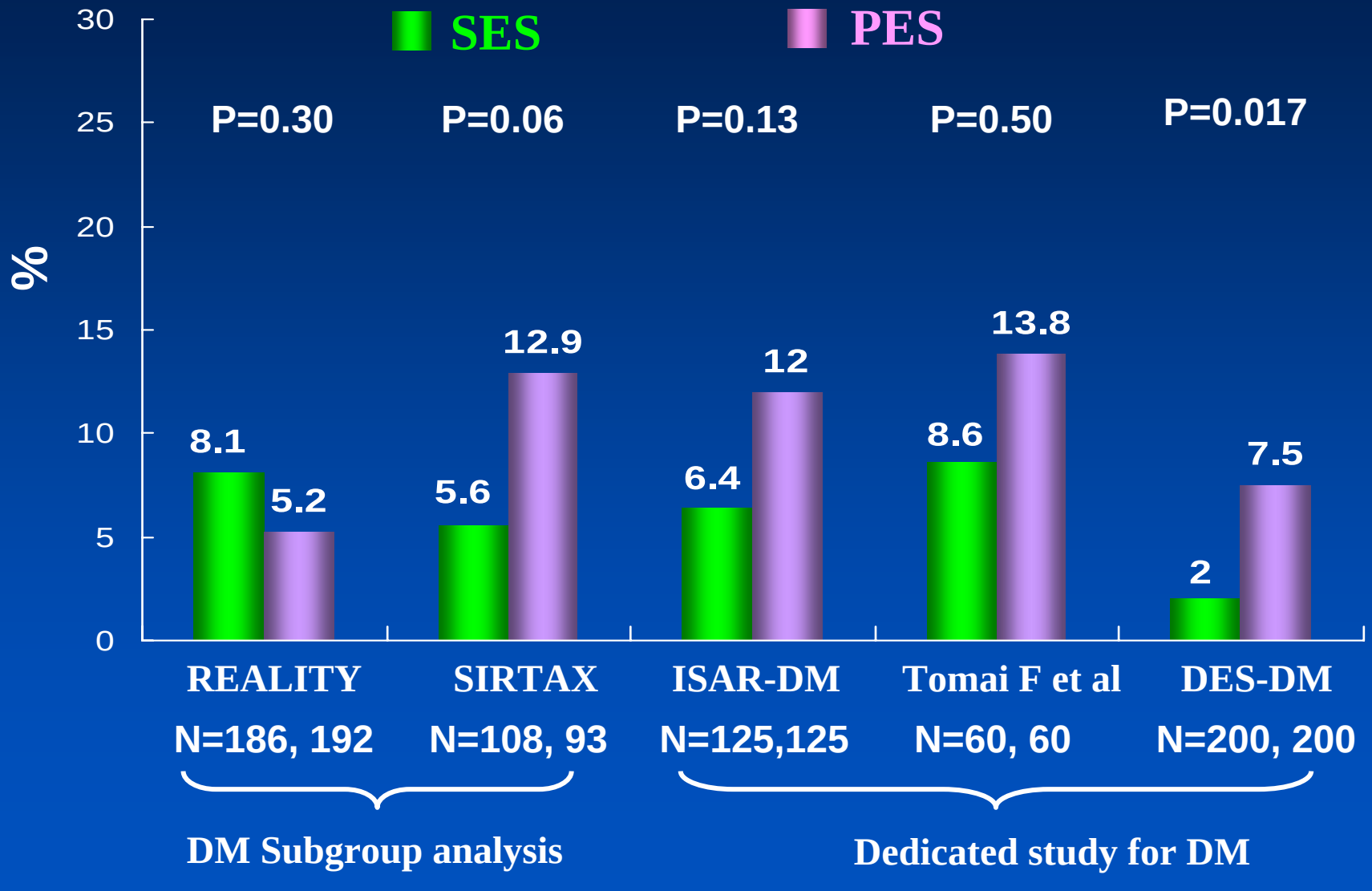
In-stent late loss



In-segment restenosis



TLR at 9 to 12 months



SES vs. PES

Long-term Clinical outcomes

SES vs. PES

Two-year outcomes

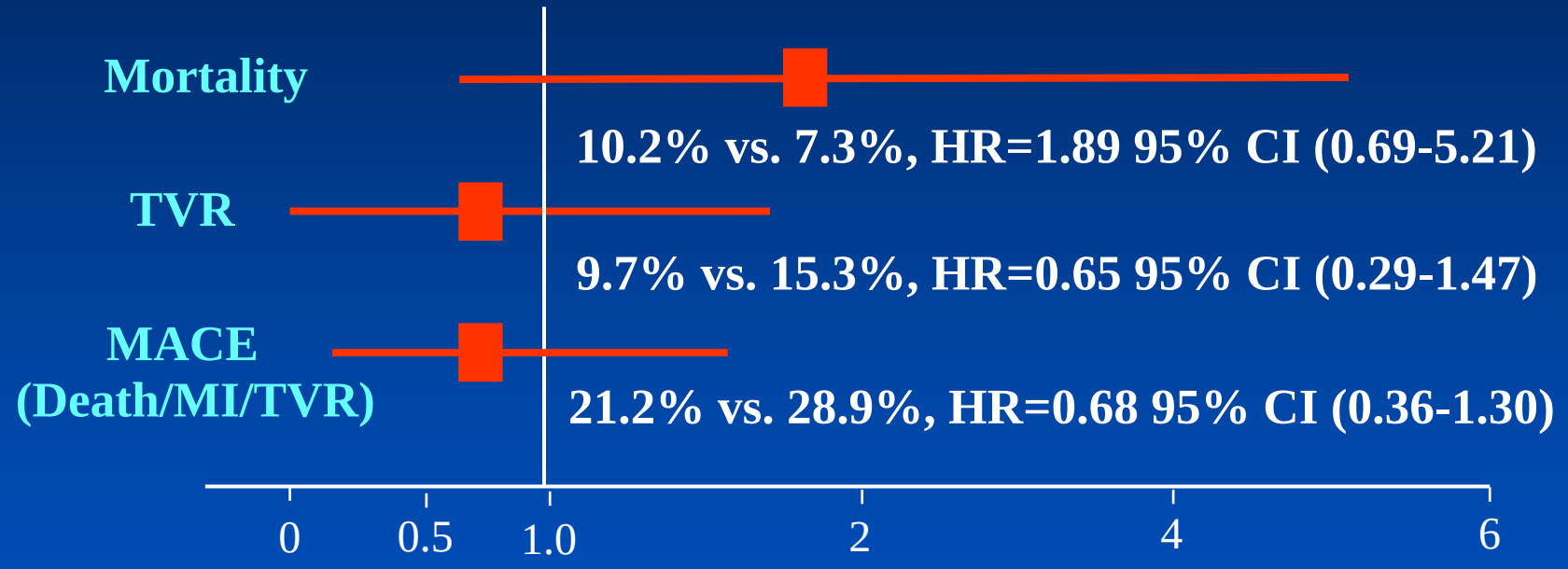
- RESEARCH and T-SEARCH } **REGISTRY**
- SIRTAX subgroup analysis } **RANDOMIZED STUDY**
- DECLARE-DIABETES } **RANDOMIZED STUDY**

Four-year outcomes

- Network meta-analysis

Adjusted Hazard Ratios for 2-year Outcomes Comparing PES and SES

Adjustment with propensity score

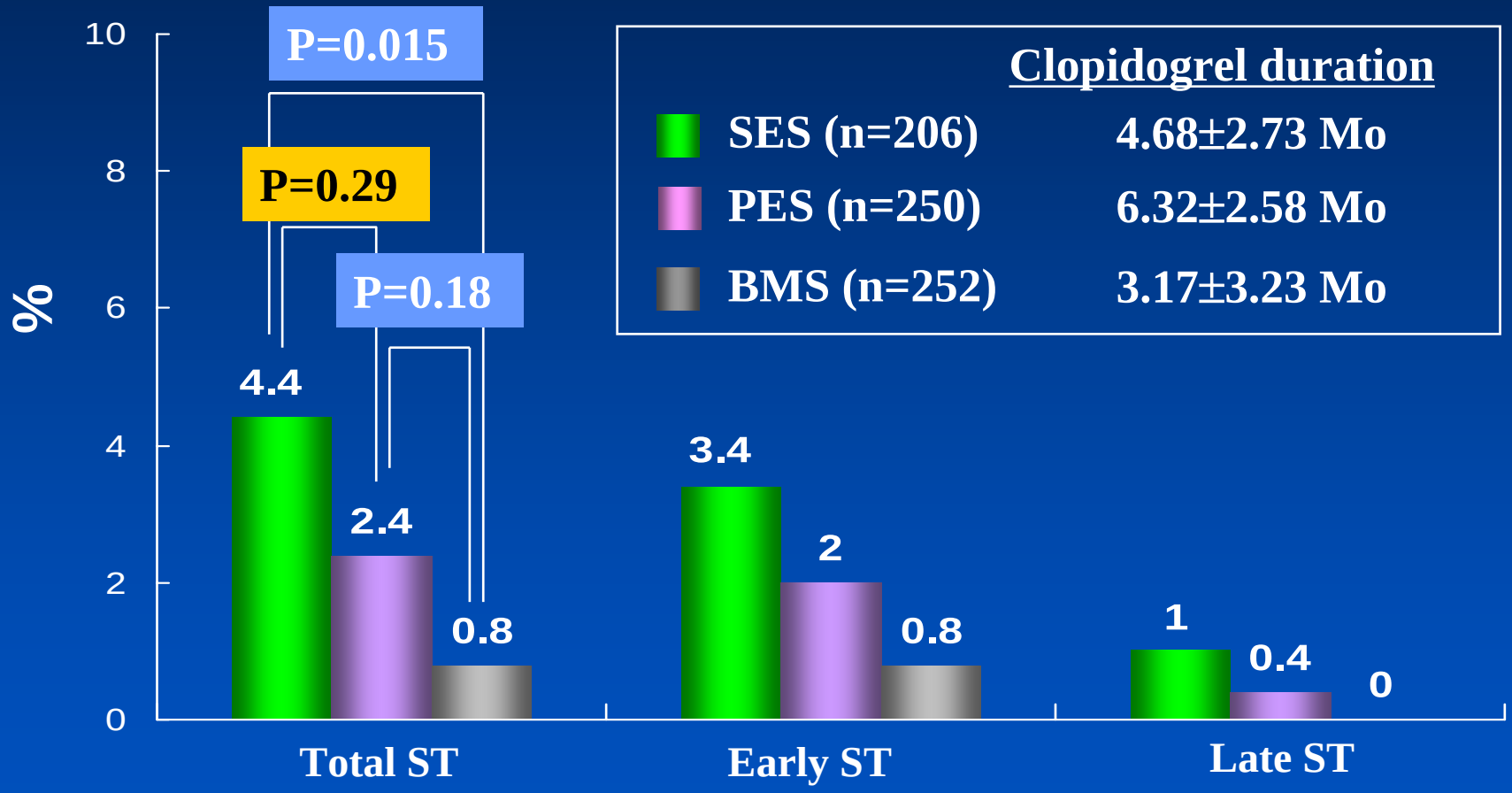


Favors PES (n=250) **Favors SES (n=206)**

Daemen J et al., Eur H Journal 2008;28:26-32

Two-year stent thrombosis

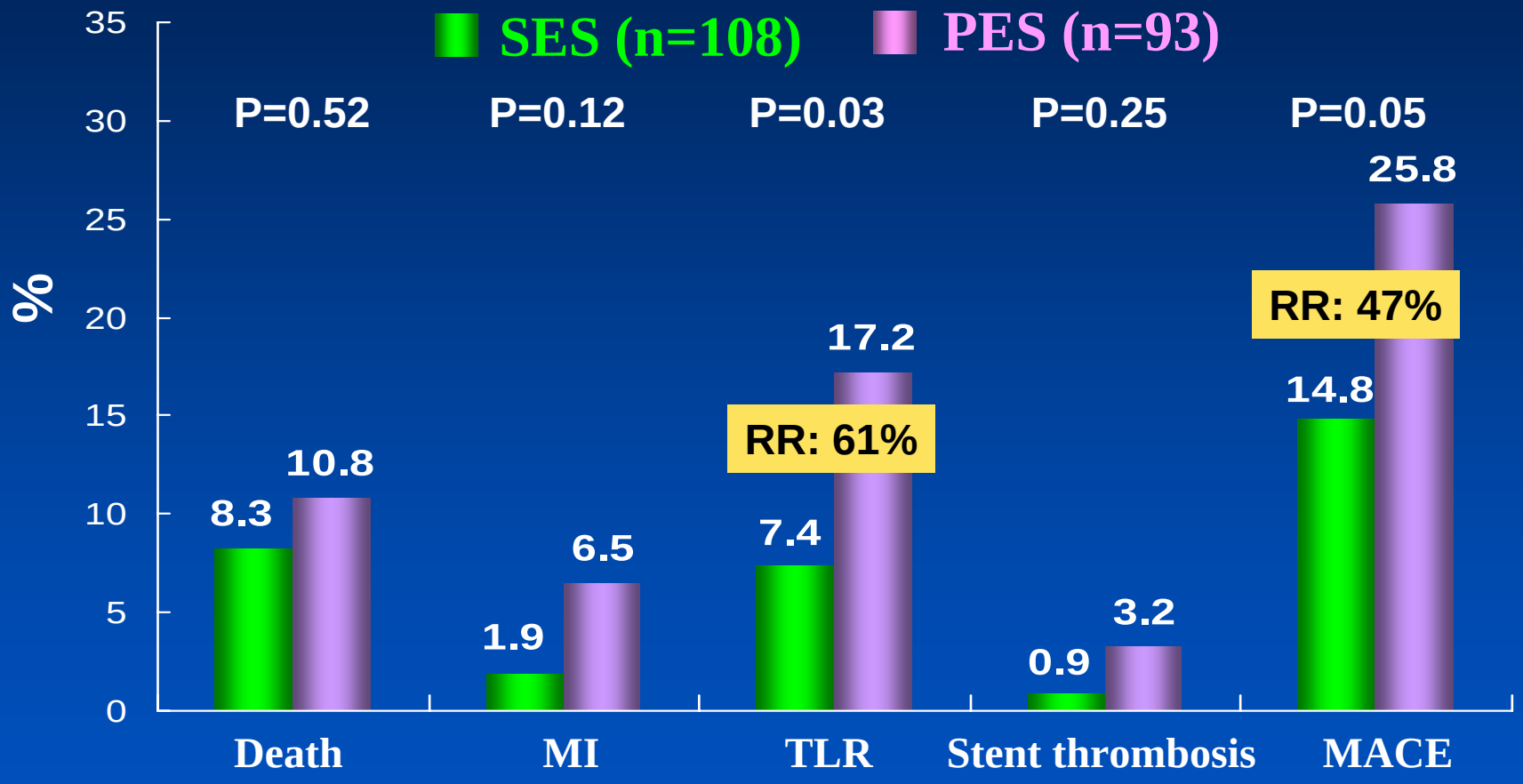
SES appeared to have high incidence of ST, but risk of stent thrombosis was not adjusted according to clinical and angiographic factors



Daemen J et al., Eur H Journal 2008;28:26-32

SIRTAX Trial

Two-year outcomes in diabetic subgroup



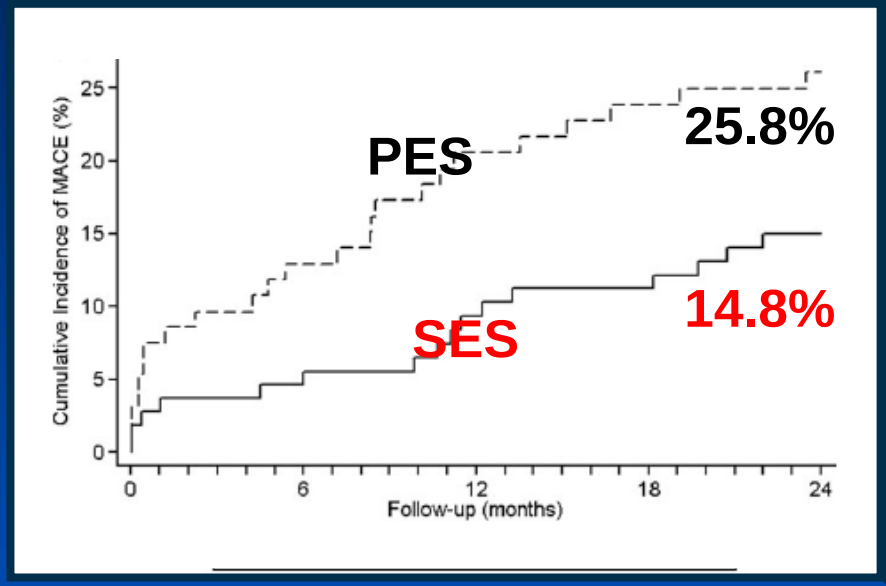
MACE: Death/MI/TLR

Billinger M et al., Eur H Journal 2008;29:718-25

SIRTAX Trial

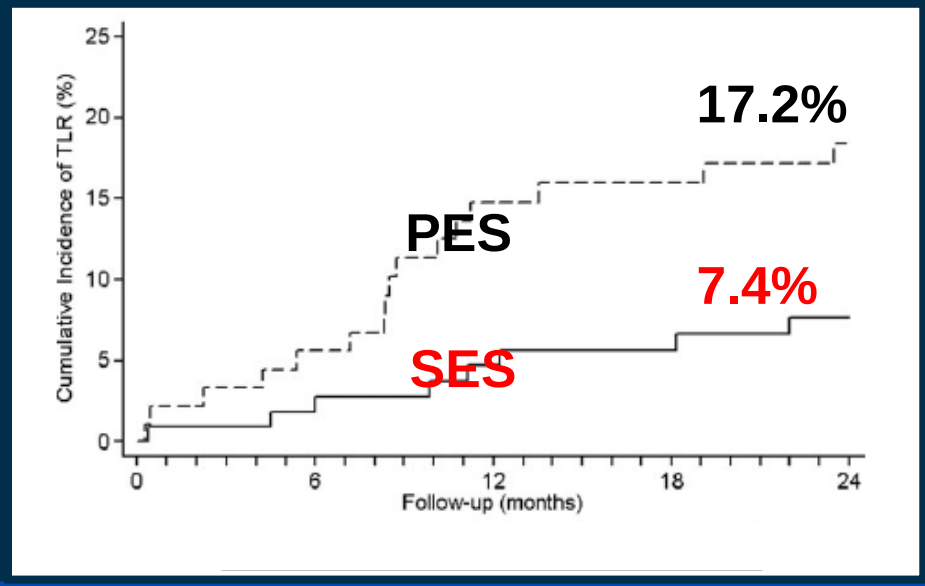
Two-year outcomes in diabetic subgroup

MACE



HR=0.52; 95% CI 0.28–0.99; P=0.05

TLR



HR=0.39; 95% CI 0.17–0.90; P=0.03

Billinger M et al., Eur H Jr 2008;29:718-25

A Randomized Comparison of SES vs. PES in Diabetic Patients

Lee et al, JACC 2008;52:727-33

A Randomized Comparison of triple antiplatelet therapy With dual antiplatelet therapy After drug-eluting stent implantation

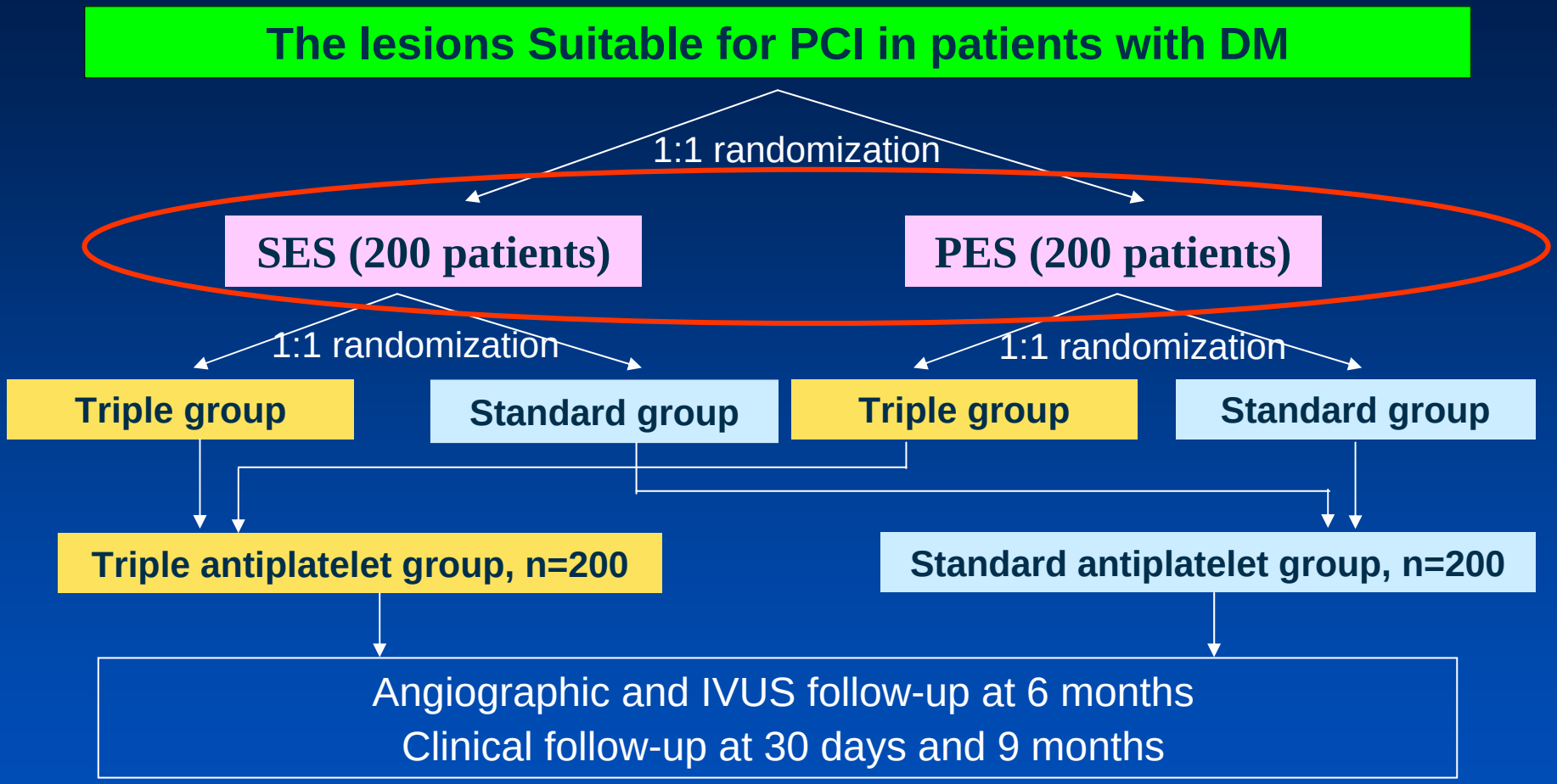
:*D*rug-*E*luting stenting followed by *C*ilostazol treatment reduces *LA*te *Re*stenosis in Patients with *Diabetes* mellitus

The DECLARE-DIABETES Trial

Seong-Wook Park, Seung-Whan Lee, Duk-Woo Park, Young-Hak Kim, Cheol Whan Lee, Myeong-Ki Hong, Jae-Joong Kim, Seung-Jung Park for the DECLARE-DIABETES Study investigators

Asan Medical Center,
University of Ulsan College of Medicine, Seoul, Korea

DECLARE-DIABETES Trial Design



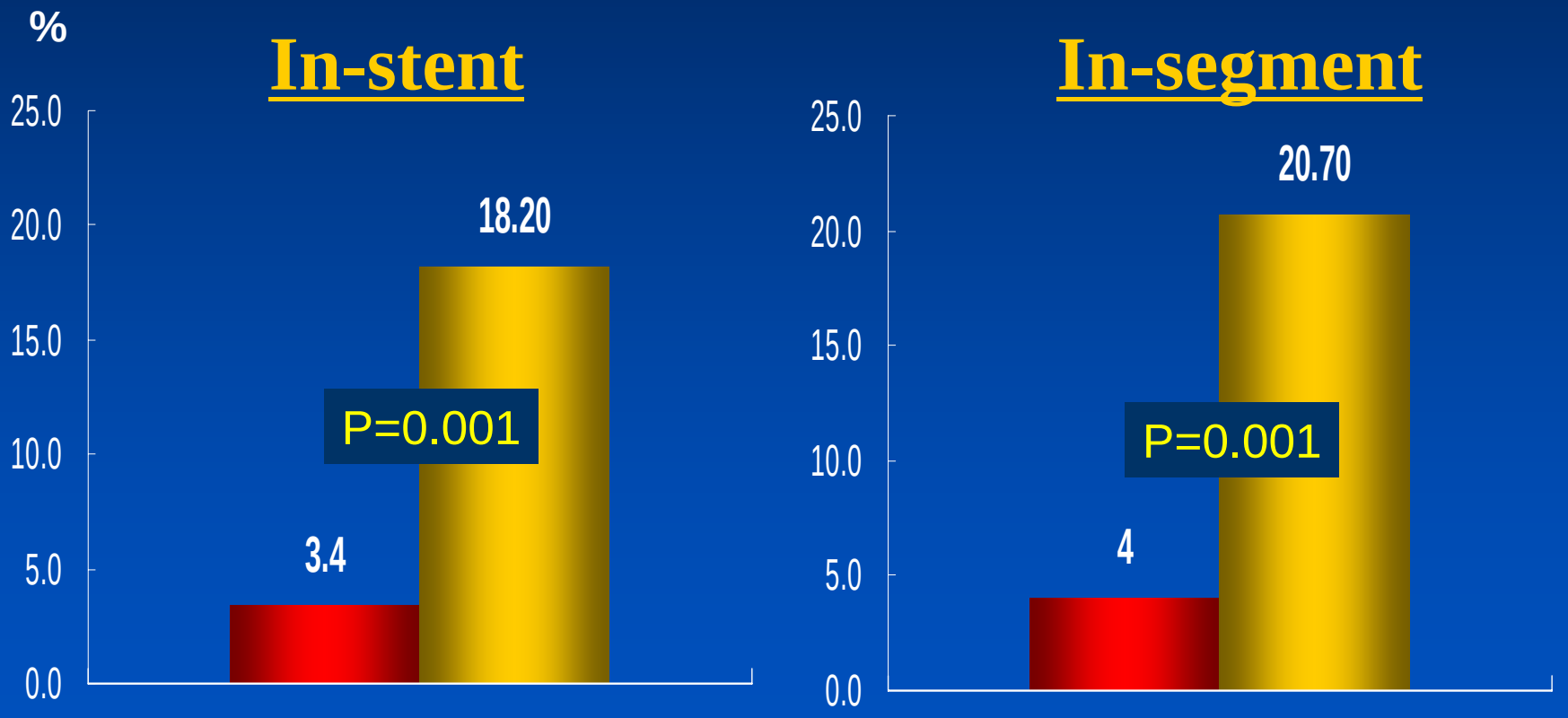
* Randomization – Stratification according to DES types
* Blinding – Patients, Outcome assessors
* Pre-specified angiographic primary endpoint
* Intention-to-treat analysis

DECLARE-DIABETES

Restenosis rate

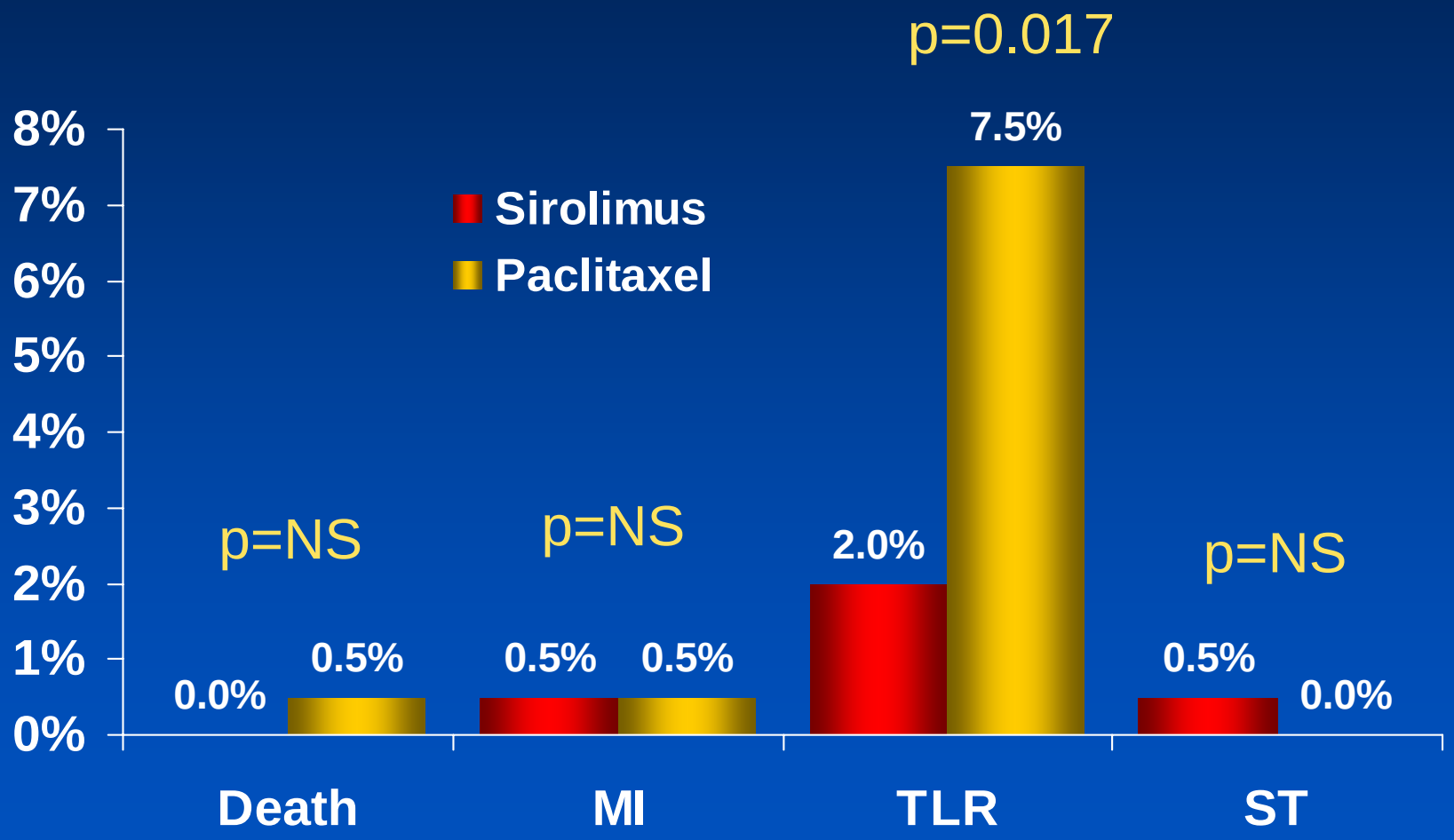
CYPHER vs. TAXUS in DM

Sirolimus Paclitaxel



Lee et al, JACC 2008;52:727-33

Clinical Outcomes at 9-Months
CYPHER vs. TAXUS in DM



Lee et al, JACC 2008;52:727-33

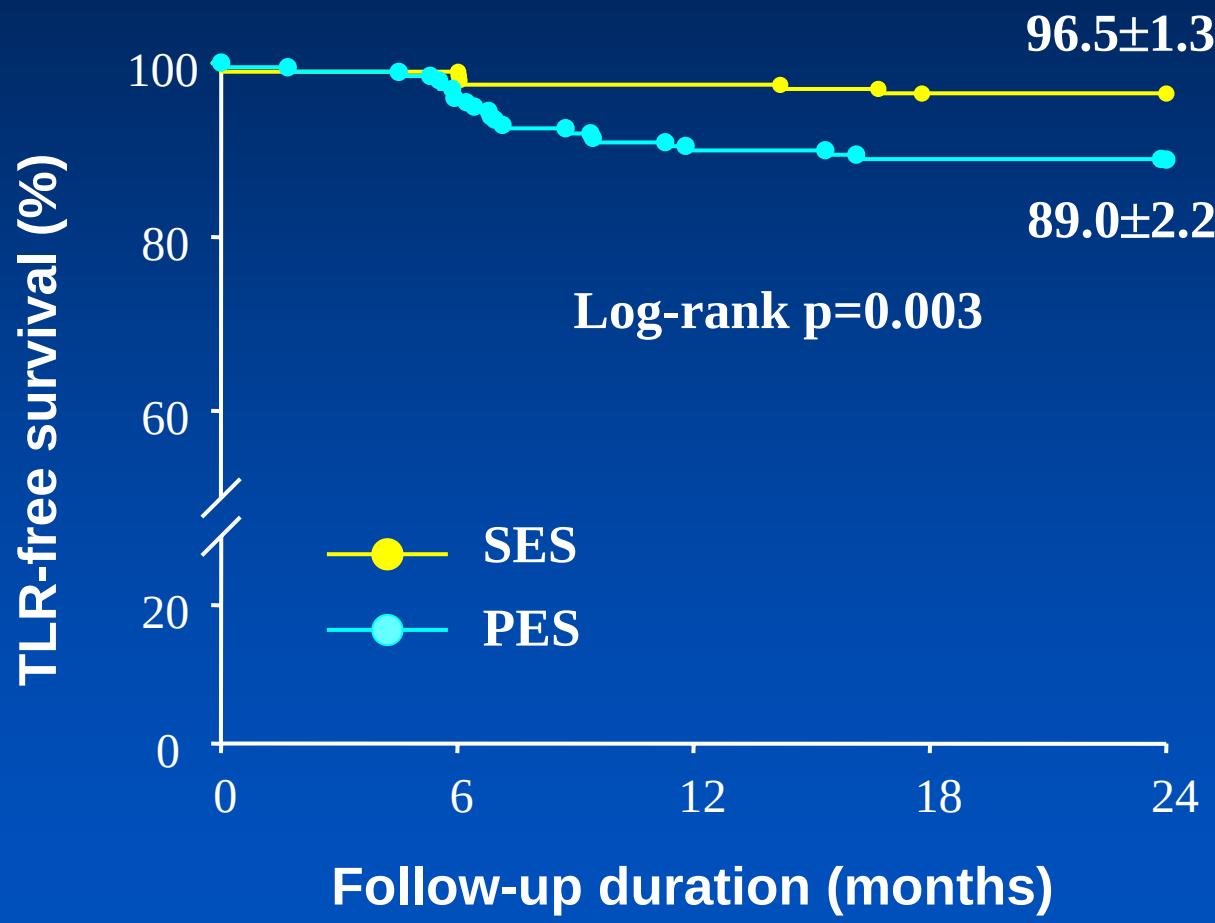
Clinical Outcomes at 9 Months

AMC data

Patients	SES (N=200)	PES (N=200)	P
Death	0	1 (0.5%)	0.999
Cardiac	0	1 (0.5%)	
Non-cardiac	0	0	
MI	1 (0.5%)	1 (0.5%)	0.999
TLR	4 (2.0%)	15 (7.5%)	0.017
TVR	7 (3.5%)	16 (8.0%)	0.053
Death/MI/TLR	4 (2.0%)	16 (8.0%)	0.010
Death/MI/TVR	7 (3.5%)	17 (8.5%)	0.035
Stent thrombosis	1 (0.5%)	0	0.999
Acute	1 (0.5%)	0	
Subacute & Late	0	0	

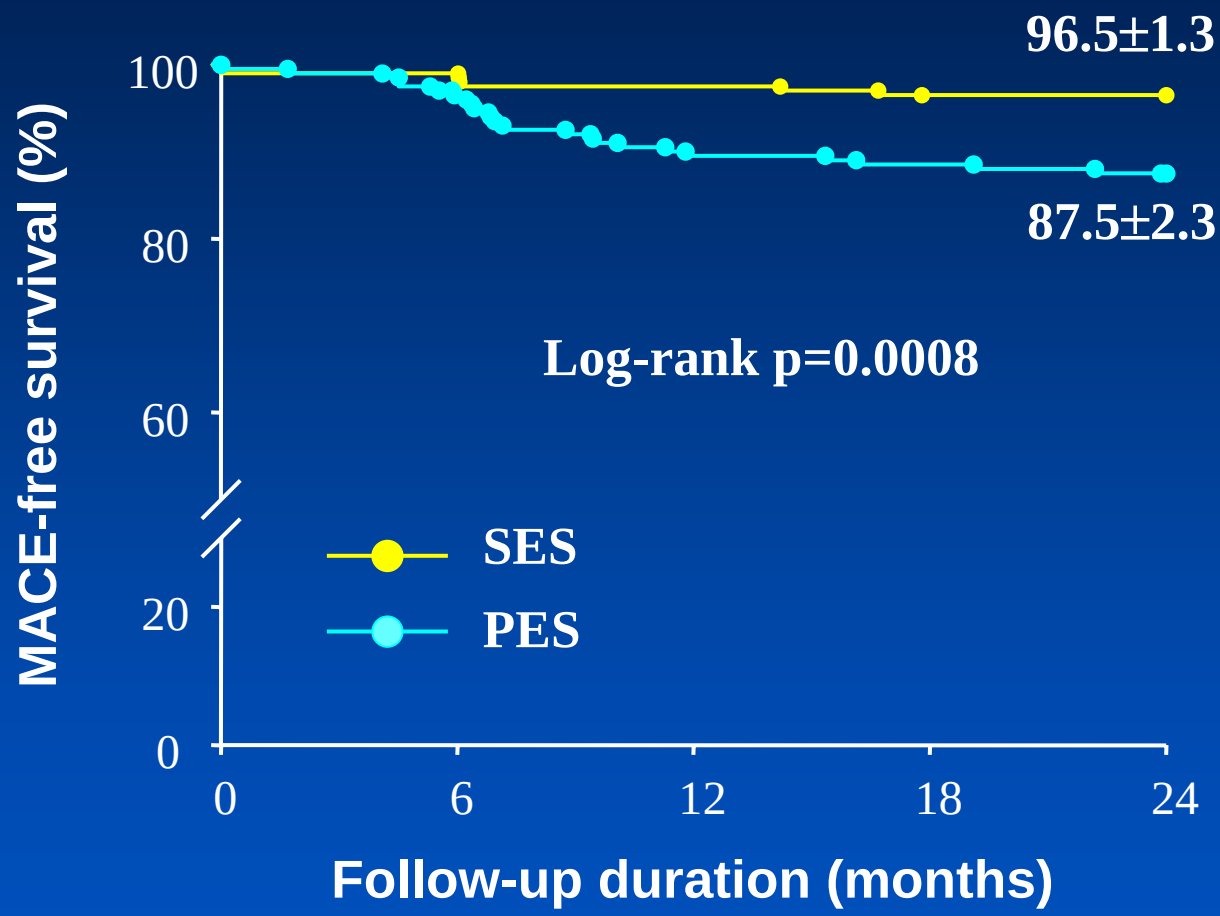
Lee et al, JACC 2008;52:727-33

Long-Term Outcomes: Two-year TLR-free survival



Lee et al, JACC 2009;53:812-813

Two-year MACE-free survival



MACE: Death/MI/TLR

Lee et al, JACC 2009;53:812-813

MACE at 2-years

	SES	PES	P
Patients	200	200	
Death	0	3(1.5%)	0.248
Cardiac	0	2(1.0%)	
Non-cardiac	0	1(0.5%)	
MI	1 (0.5%)	2 (1.0%)	0.999
Stent thrombosis	2 (1.0%)	0	0.499
Acute	1 (0.5%)	1	
Subacute	0	0	
Late	1 (0.5%)	0	
TLR	7 (3.5%)	22 (11.0%)	0.004
Death/MI/TVR	11 (5.5%)	28 (14.0%)	0.004
MACE (Death/MI/TLR)	7 (3.5%)	25 (12.5%)	0.001

Lee et al, JACC 2009;53:812-813

Conclusions

- SES implantation is associated with reduced angiographic restenosis and 9-month TLR and MACE, and showed sustained reduction of 2-year TLR and MACE compared to PES implantation with no difference of death or MI

- The use of SES was negative independent predictors of angiographic restenosis, 2-year risks of TLR and MACE.

Lee et al, JACC 2008;52:727-33
Lee et al, JACC 2009;53:812-813

NETWORK META-ANALYSIS
UpTo 4 Years

BMJ

RESEARCH

Drug eluting and bare metal stents in people with and without diabetes: collaborative network meta-analysis

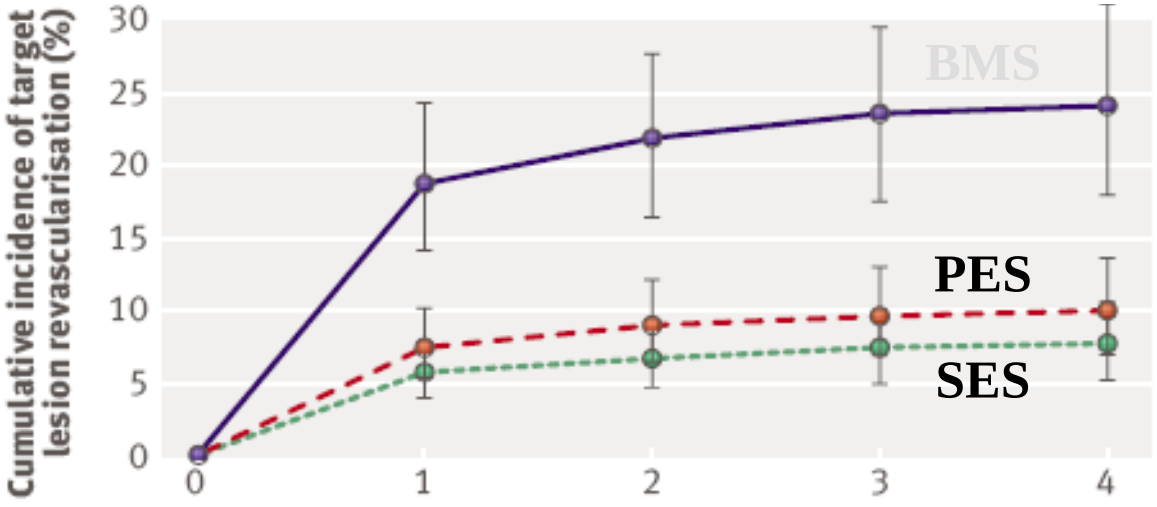
Stettler et al, BMJ. 2008;337:a1331

Cumulative incidence of TLR in Diabetic Patients

SES vs. BMS: Hazard Ratio 0.29 (0.19 to 0.45)

PES vs. BMS: Hazard Ratio 0.38 (0.26 to 0.56)

SES vs. PES: Hazard Ratio 0.78 (0.50 to 1.14)



		No of events/No of patients			
BMS	935	193/935	10/496	4/282	2/185
PES	1171	99/1171	21/946	3/487	3/146
SES	1122	80/1122	14/780	1/446	2/66

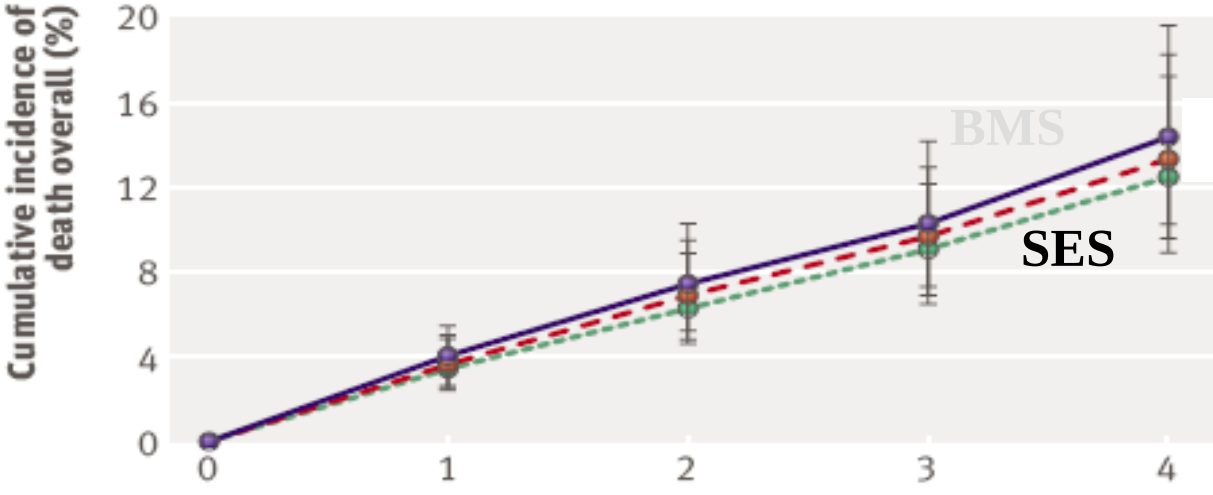
Stettler et al, BMJ. 2008;337:a1331

Cumulative incidence of Death in Diabetic Patients

SES vs. BMS: Hazard Ratio 0.88 (0.55 to 1.30)

PES vs. BMS: Hazard Ratio 0.91 (0.26 to 1.38)

SES vs. PES: Hazard Ratio 0.95 (0.50 to 1.43)



		No of events/No of patients			
BMS	904	37/904	15/632	7/358	10/224
PES	1162	35/1162	40/1020	11/535	3/158
SES	1078	39/1078	26/830	12/497	1/73

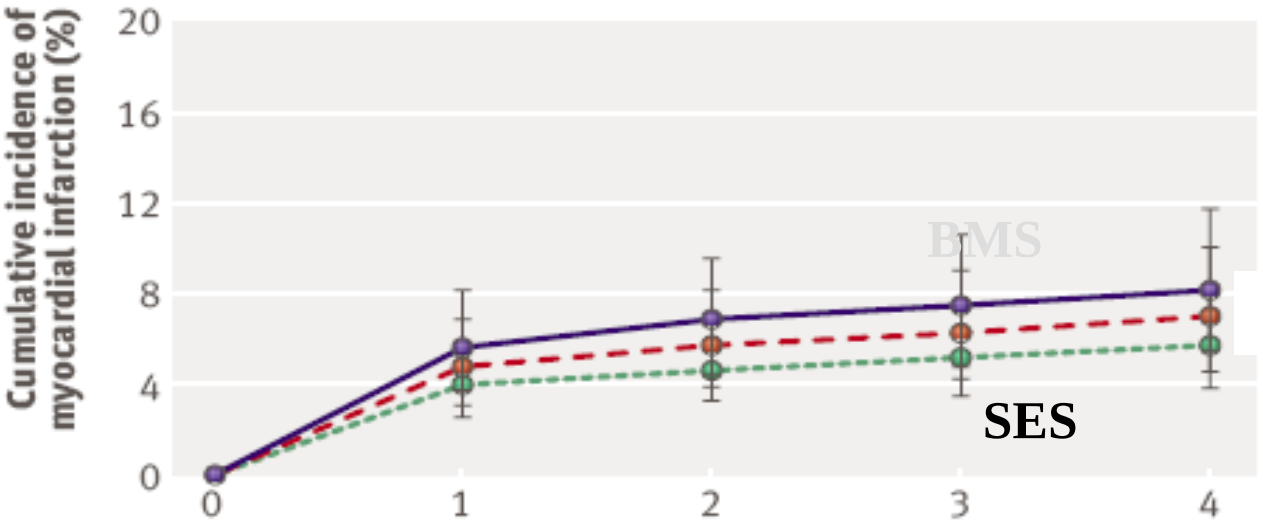
Stettler et al, BMJ. 2008;337:a1331

Cumulative incidence of MI in Diabetic Patients

SES vs. BMS: Hazard Ratio 0.68 (0.43 to 1.12)

PES vs. BMS: Hazard Ratio 0.85 (0.54 to 1.43)

SES vs. PES: Hazard Ratio 0.80 (0.55 to 1.27)



		No of events/No of patients			
BMS	867	54/867	6/585	2/336	2/209
PES	1160	55/1160	12/980	5/508	2/142
SES	1054	51/1054	2/792	1/460	0/56

Risk of stent thrombosis in diabetic patients

Variable	Events				Relative risks (95% credibility interval)		
	BMS	PES	SES	Total	SES *v* BMS	PES *v* BMS	
ARC definite stent thrombosis*							
	557	874	753	2184			
	13	17	9	39	0.33 (0.09 to 1.09)	0.82 (0.23 to 3.09)	
	11	9	6	26	0.25 (0.04 to 1.11)	0.39 (0.05 to 2.36)	
	2	8	3	13	0.72 (0.04 to 10.8)	3.54 (0.23 to 78.6)	
Patients without diabetes:							
No of patients at risk	2439	3130	2647	8216			
0 days to 4 years	34	56	46	136	1.24 (0.58 to 3.08)	1.48 (0.69 to 3.40)	0.84 (0.41 to 1.88)
0-30 days	19	22	28	69	1.19 (0.43 to 3.09)	1.11 (0.38 to 2.97)	1.06 (0.41 to 2.90)
>30 days to 4 years	15	34	18	67	1.19 (0.43 to 4.13)	1.83 (0.67 to 5.85)	0.65 (0.26 to 1.70)
Per protocol definition of stent thrombosis†							
	723	912	870	2505			
	16	18	7	41	0.20 (0.05 to 0.68)	0.73 (0.19 to 2.80)	
	11	10	5	26	0.23 (0.03 to 1.08)	0.55 (0.09 to 3.05)	
	5	8	2	15	0.10 (0.01 to 0.93)	0.87 (0.06 to 10.3)	
Patients without diabetes:							
No of patients at risk	2577	3382	2625	8584			
0 days to 4 years	29	58	46	133	1.48 (0.74 to 3.41)	1.80 (0.89 to 3.67)	0.82 (0.44 to 1.73)
0-30 days	22	24	28	74	1.11 (0.47 to 2.81)	0.99 (0.44 to 2.33)	1.15 (0.48 to 2.72)
>30 days to 4 years	7	34	18	59	2.29 (0.83 to 7.77)	4.12 (1.55 to 13.1)	0.55 (0.25 to 1.27)

SES vs. PES

- There has been heterogeneous clinical outcomes, but SES showed consistent superiority of late loss and angiographic restenosis, which is translated to improved clinical outcomes (SIRTAX, DECLARE-DIABETES) without difference of death, MI, and stent thrombosis.

- Network meta-analysis showed similar TLR up to 4 years (HR 0.78, 95% CI,0.50 to 1.14), but HR favoring SES explained possible superiority of SES over PES, which was demonstrated in randomized trial (DECLARE-DIABETES) dedicated for diabetic patients

Comparison of the Efficacy and Safety of *Z*otarolimus-*E*luting Stent versus *S*irolimus-Eluting Stent and Pacli*T*axel-Eluting Stent for Coronary Lesions:

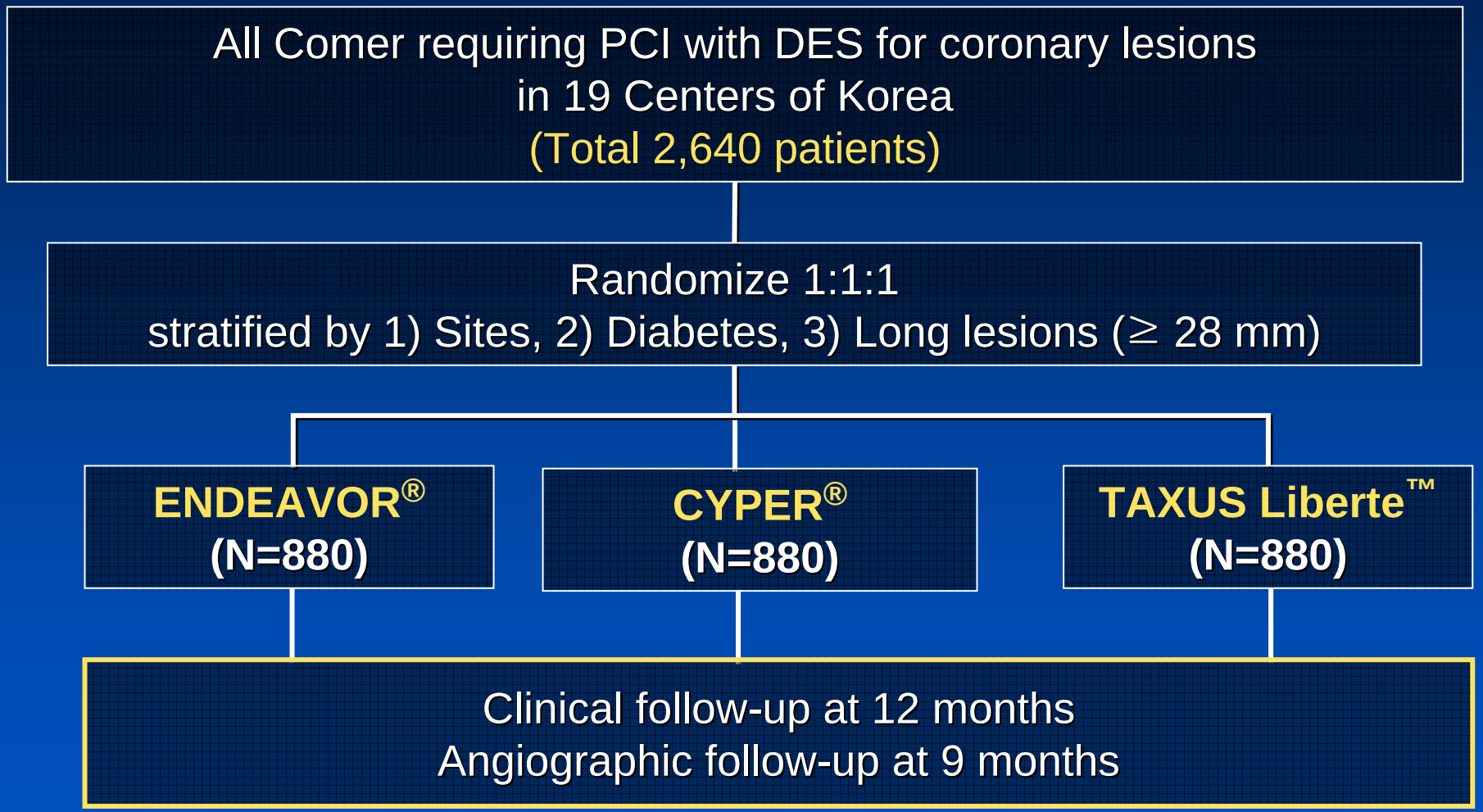
The ZEST Trial

ZEST-Diabetic Subgroup

Seung-Jung Park, MD, PhD
on behalf of the ZEST investigators

Intention-to-Treat Analyses

Study Design



Primary Study Endpoint

- The composite clinical outcome of
  - Death from any cause
  - Myocardial infarction (MI)
  - Ischemia-driven target-vessel revascularization (TVR)

  at 12 months after the index procedure.

Study Endpoints

- Secondary Endpoint
  : Death (all-cause or cardiac)
  : MI
  : Composite of death or MI
  : TVR (all- and ischemia-driven)
  : TLR (all- and ischemia-driven)
  : Composite of death, MI, ischemia-driven TLR
  : Stent thrombosis by ARC definition
  : Late loss in both in-stent and in-segment at 9 months
  : Restenosis in both in-stent and in-segment at 9 months
  : Procedural success rate

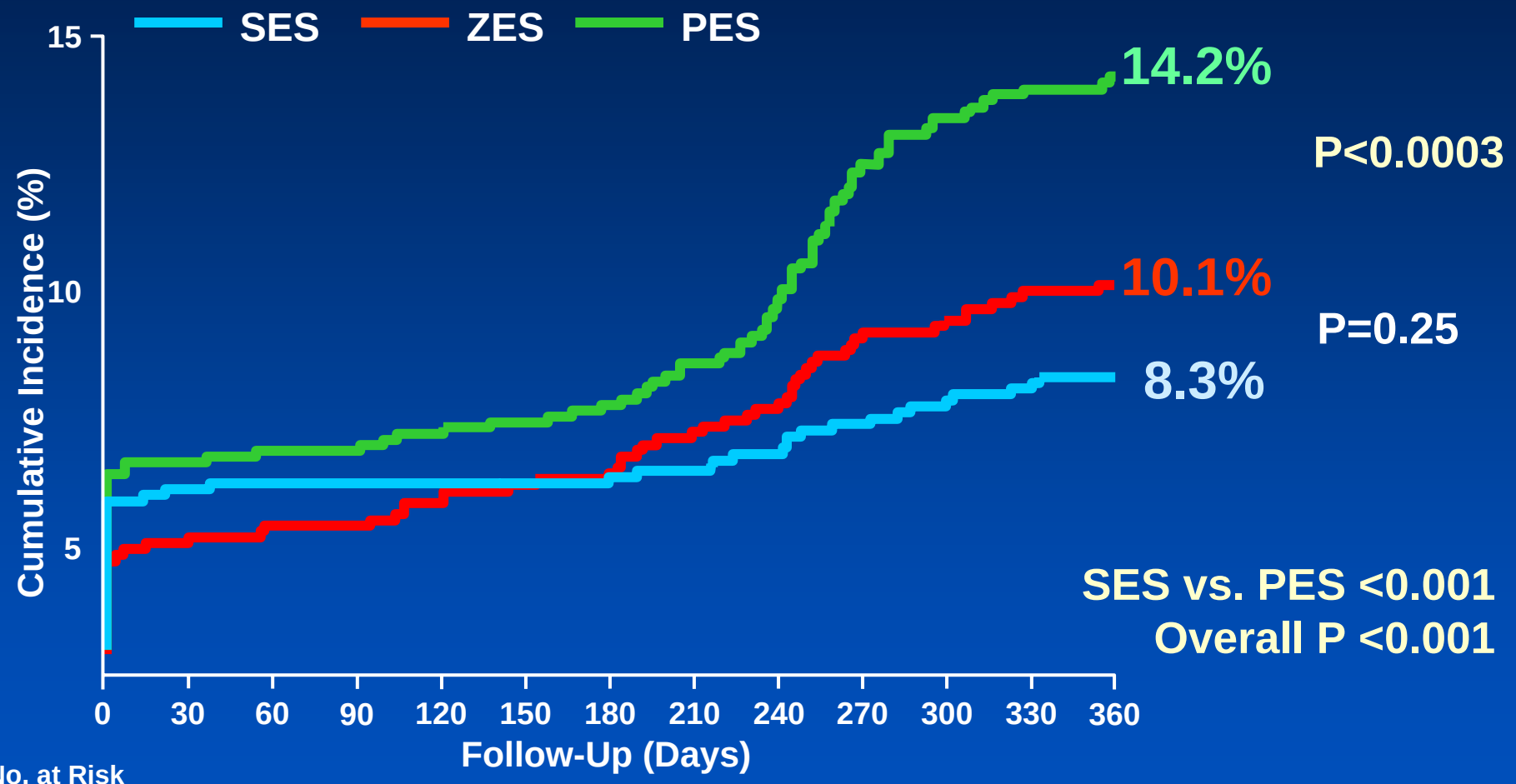
Baseline Characteristics

Patients	ZES (n=883)	SES (n=878)	PES (n=884)	P value
Age (yr)	62±9	62±10	62±10	0.80
Male sex	586 (66)	591 (67)	582 (66)	0.80
Body mass index	25±3	25±3	25±3	0.88
Diabetes mellitus				
Any diabetes	268 (30)	247 (28)	245 (28)	0.42
Requiring insulin	32 (4)	33 (4)	36 (4)	0.88
Hypertension	552 (63)	517 (59)	540 (61)	0.29
Hyperlipidemia	466 (53)	451 (51)	446 (51)	0.62
Current smoker	236 (27)	256 (29)	243 (28)	0.51
Family history of CAD	48 (5)	44 (5)	52 (6)	0.72

n (%)

Death, MI, Ischemia-driven TVR

Primary End Point at 12 month



No. at Risk

ZES	883	827	816	790	782
SES	878	816	813	802	792
PES	884	821	808	763	745

Baseline Characteristics

Patients	ZES (n=268)	SES (n=247)	PES (n=245)	P value
Age (yr)	63±9	63±8	62±10	0.65
Male sex	157 (59)	148 (60)	157 (64)	0.42
Body mass index	25±3	25±3	25±3	0.89
Insulin-requiring	32 (12)	33 (13)	36 (15)	0.66
Hypertension	199 (74)	176 (71)	174 (71)	0.66
Hyperlipidemia	133 (50)	119 (48)	117 (48)	0.91
Current smoker	59 (22)	59 (24)	70 (29)	0.21
Family history of CAD	12 (5)	9 (4)	13 (5)	0.67

n (%)

Lesion Characteristics

Lesions	ZES (n=435)	SES (n=448)	PES (n=441)	P value
Location				0.39
LAD	52%	53%	51%	
LCX	21%	19%	21%	
RCA	27%	29%	28%	
ACC-AHA B2 or C type	72%	76%	74%	0.24
Total occlusion	6%	6%	8%	0.17
Thrombus-containing	3%	3%	3%	0.78
Bifurcation lesion	20%	18%	16%	0.24
Ostial lesion	7%	6%	7%	0.56
Restenotic lesion	1%	1%	1%	0.86

n (%)

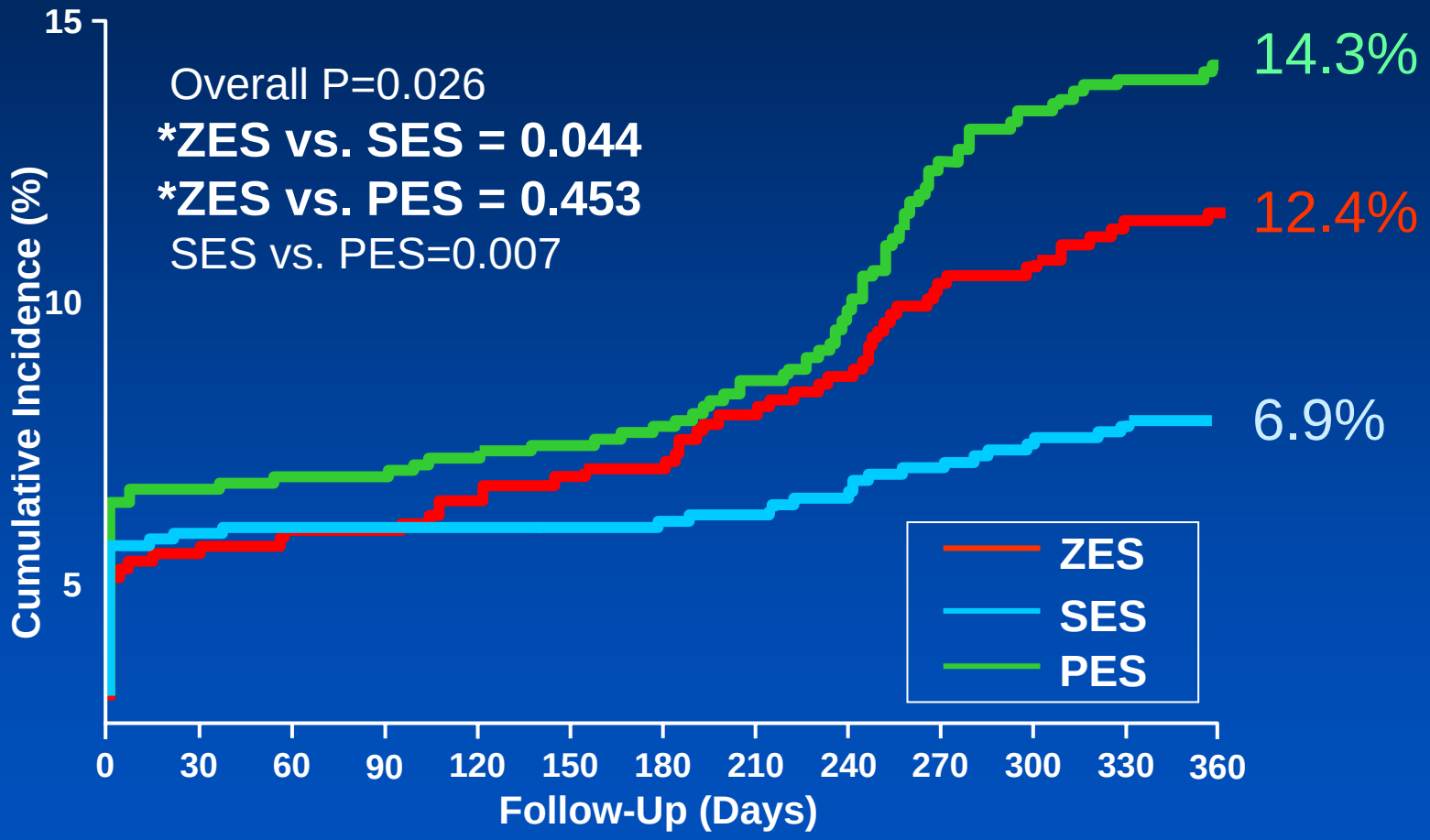
Procedural Characteristics

Lesions	ZES (n=435)	SES (n=448)	PES (n=441)	P value
No. of stents per lesion	1.3±0.4	1.3±0.4	1.3±0.4	0.45
No. of stents per patient	1.8±0.9	1.8±0.9	1.8±0.9	0.92
Length of stents per lesion	30.9±13.1	31.9±13.5	30.9±14.3	0.22
Length of stents per patients	42.7±26.8	41.3±24.3	41.9±25.2	0.55
Maximal stent diameter	3.4±0.7	3.4±0.7	3.5±0.6	0.29
Maximal pressure	16.3±4.2	16.3±4.1	16.2±4.2	0.95
Direct stenting	7%	9%	7%	0.34
Use of IVUS	40%	42%	41%	0.62

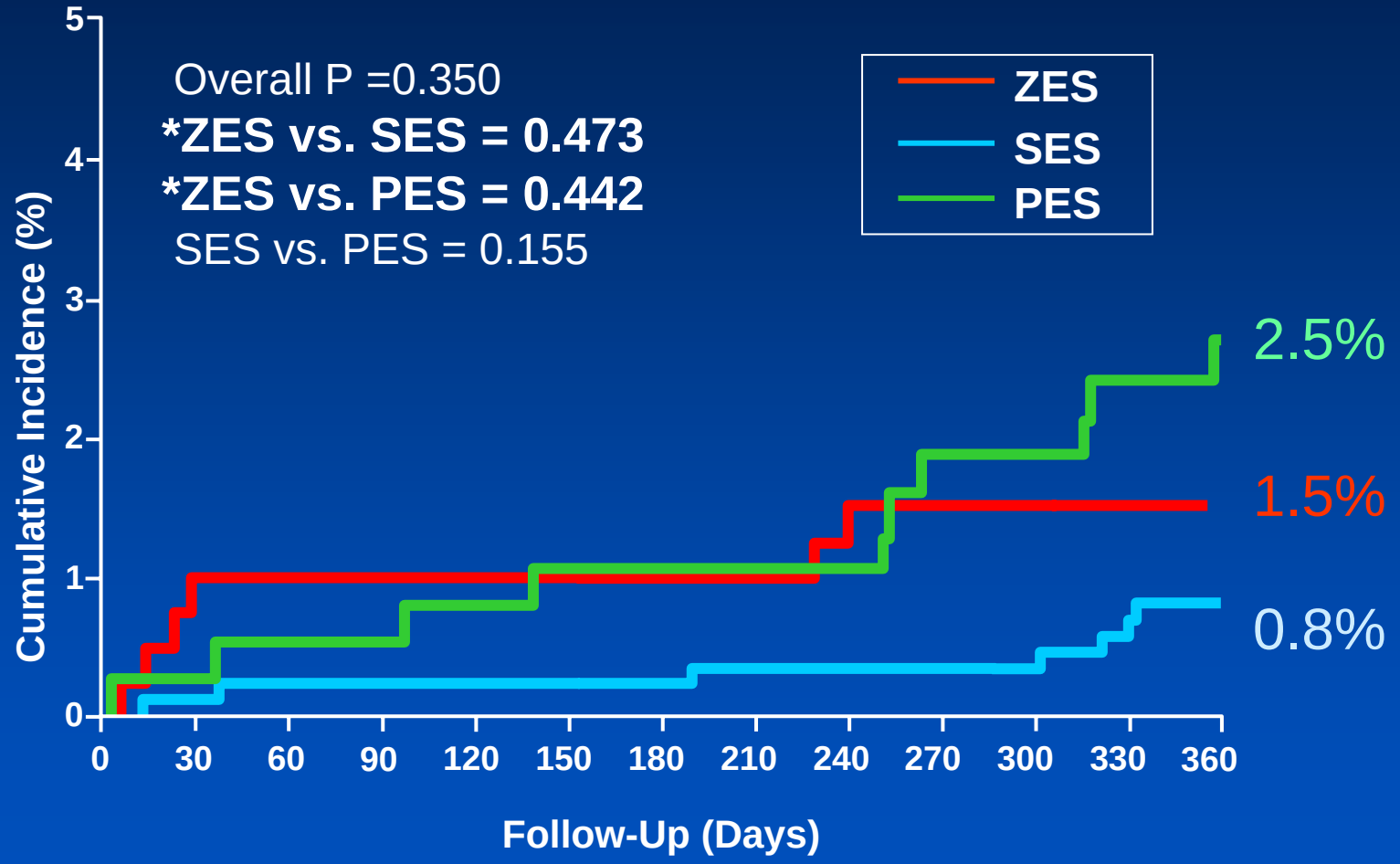
Clinical Events During 12 Months of Follow-Up

Primary End Point at 12 month

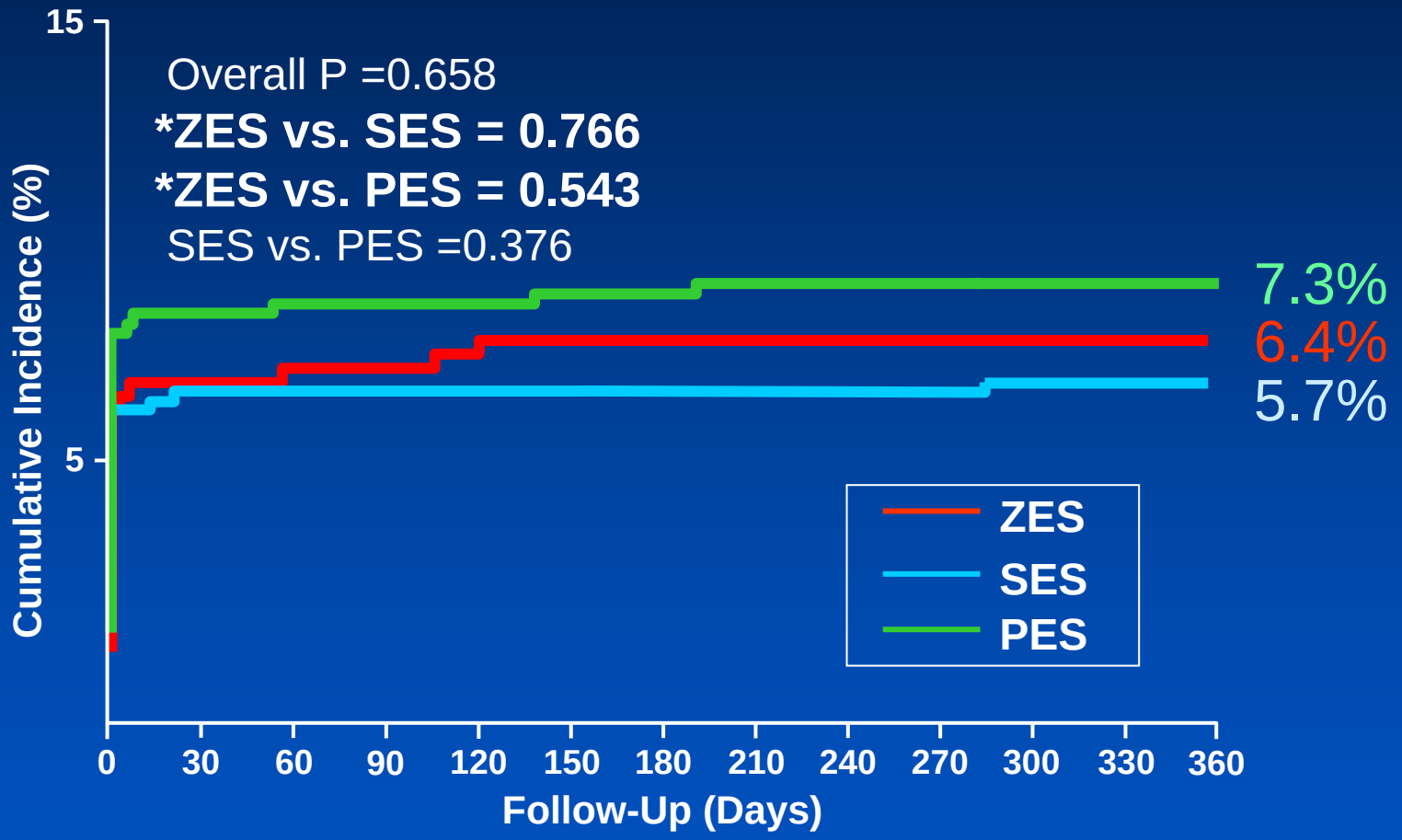
: Death, MI, Ischemia-driven TVR



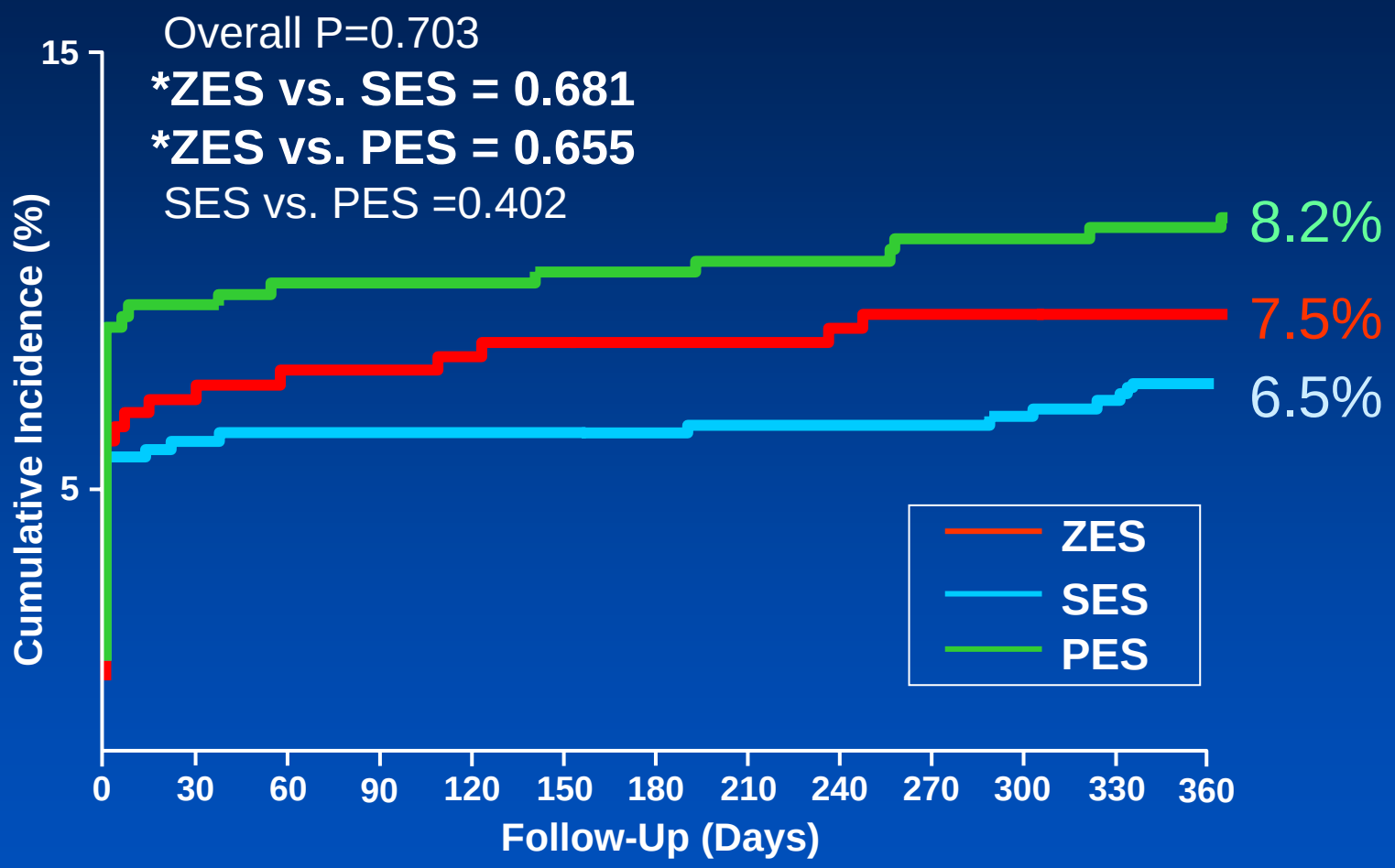
Death at 12 month



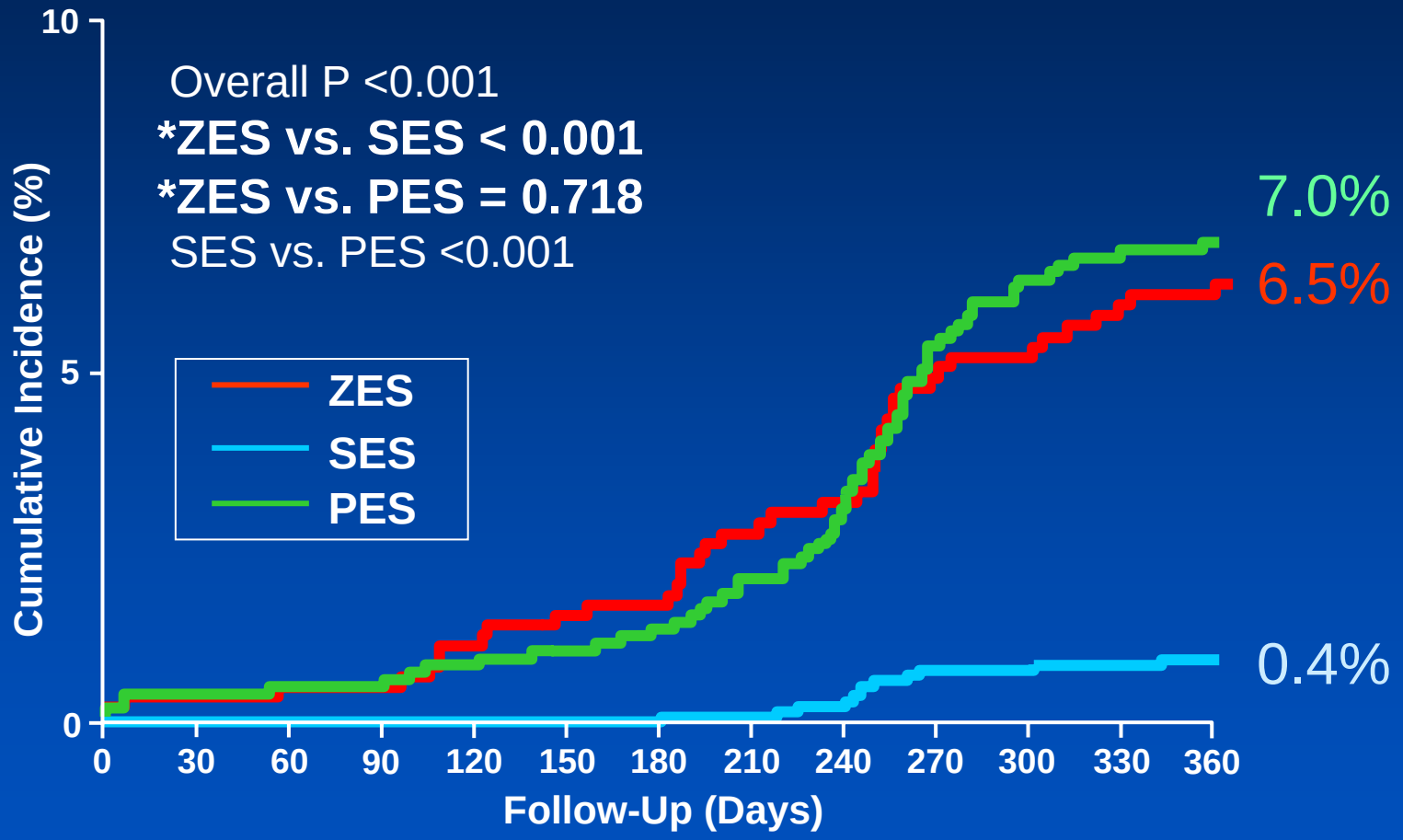
MI at 12 month



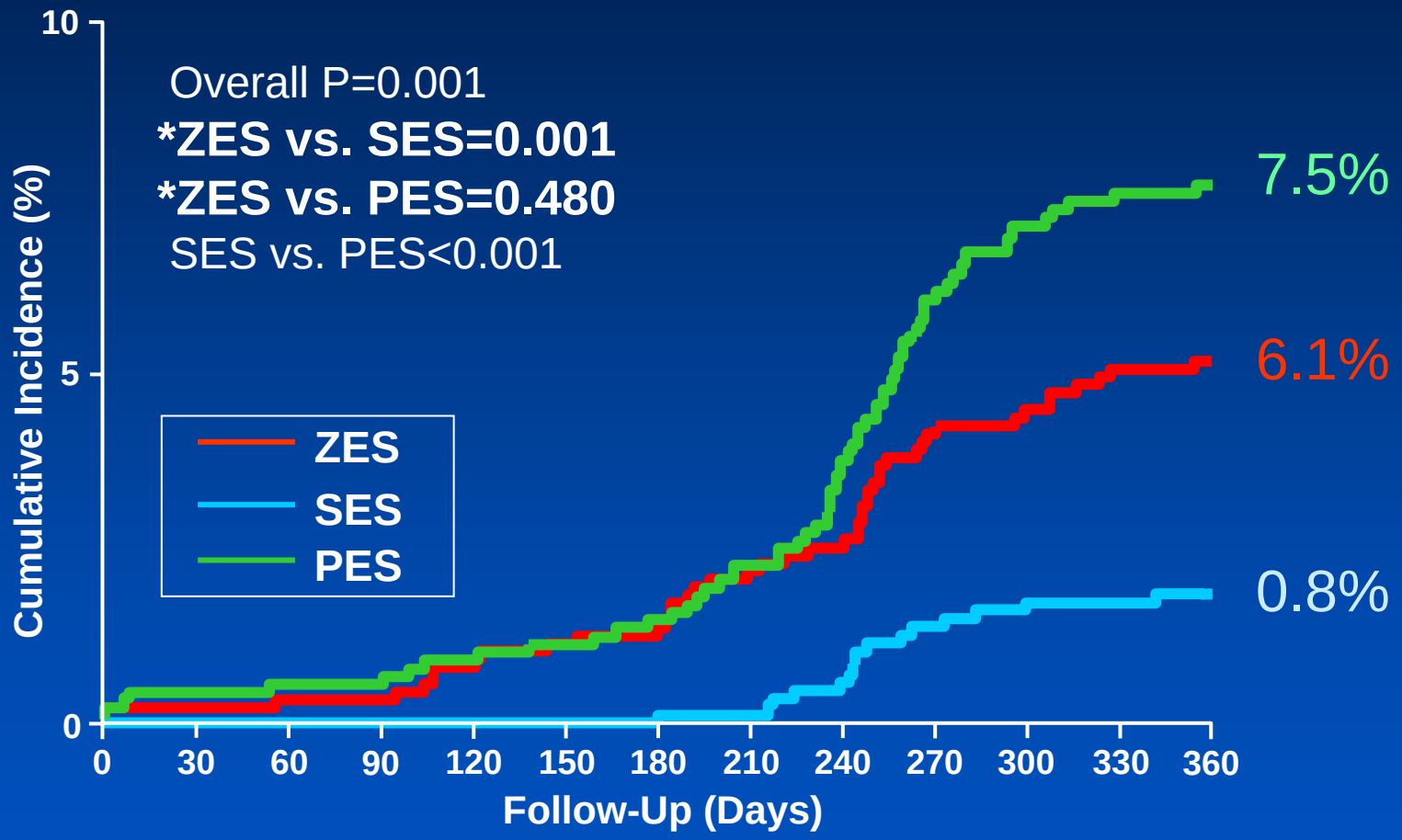
Death or MI at 12 month



Ischemia-Driven TLR at 12 month

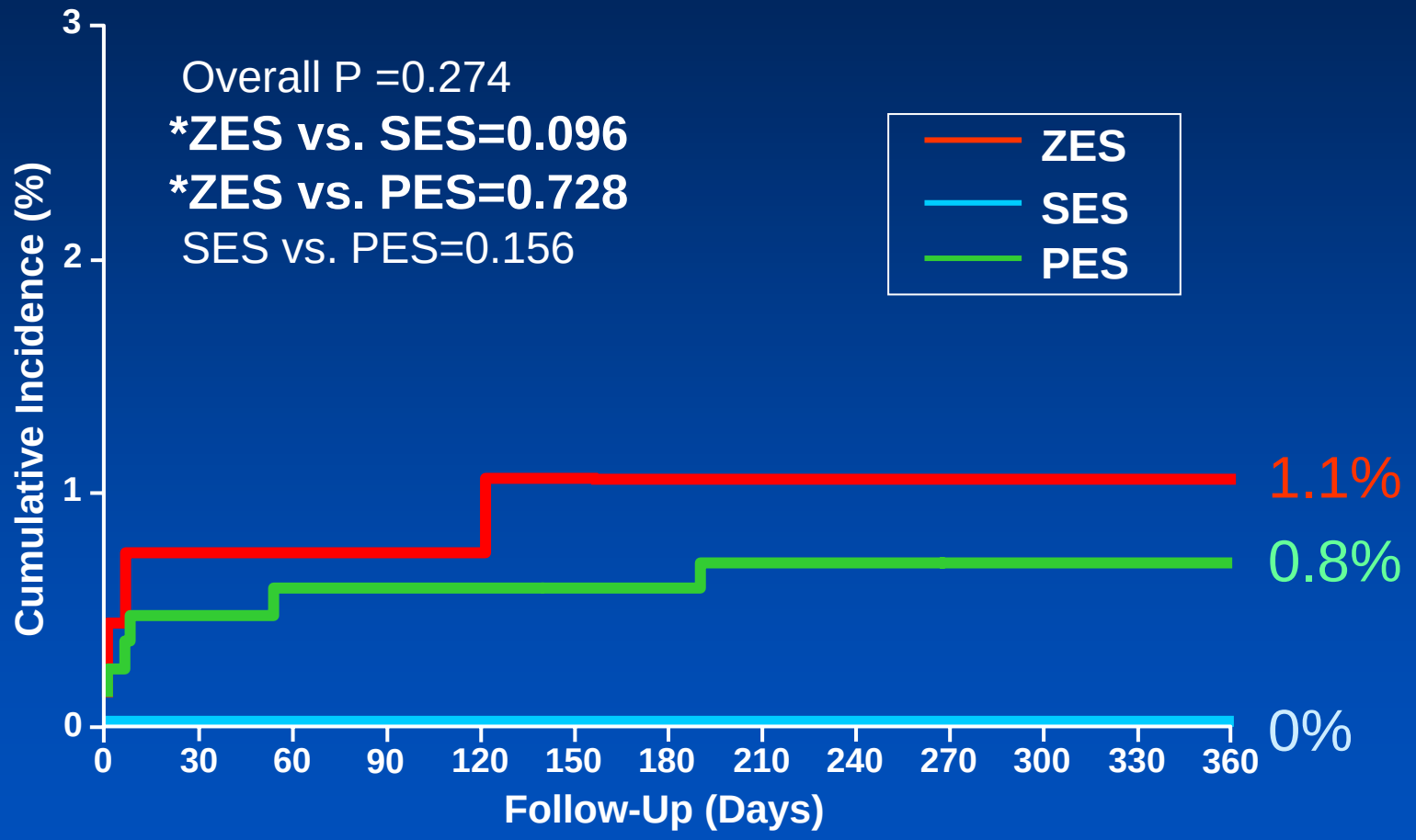


Ischemia-Driven TVR at 12 month



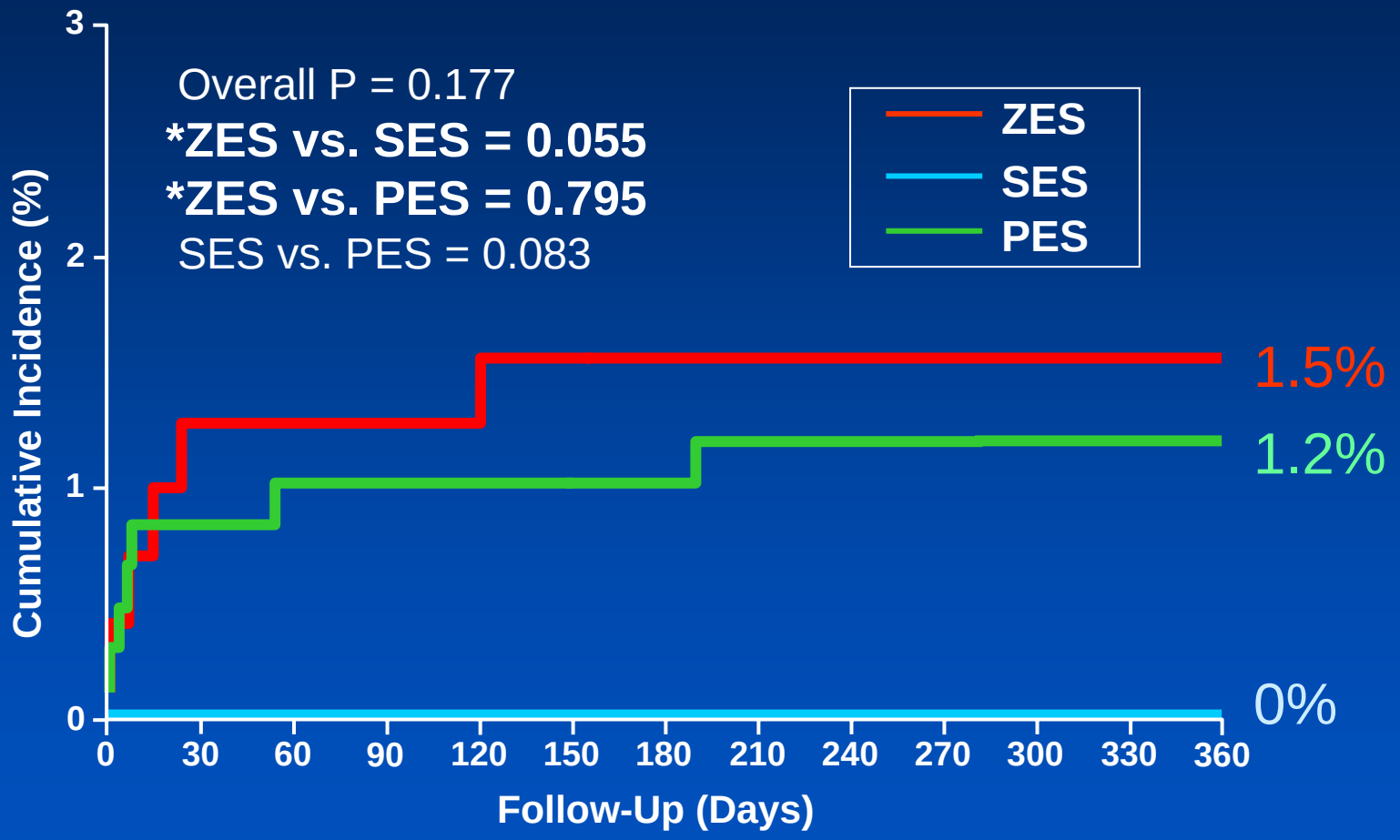
Stent thrombosis at 12 month

: ARC Definite Criteria



Stent thrombosis at 12 month

: ARC Definite or Probable Criteria



Summary:
ZEST Diabetic Subgroup

- The use of Cypher stent resulted in fewer major adverse cardiac events as compared with Taxus Liberte or Endeavor stent, mainly due to significant reduction of TLR and TVR.

- There were no significant differences in terms of death, MI, or stent thrombosis.

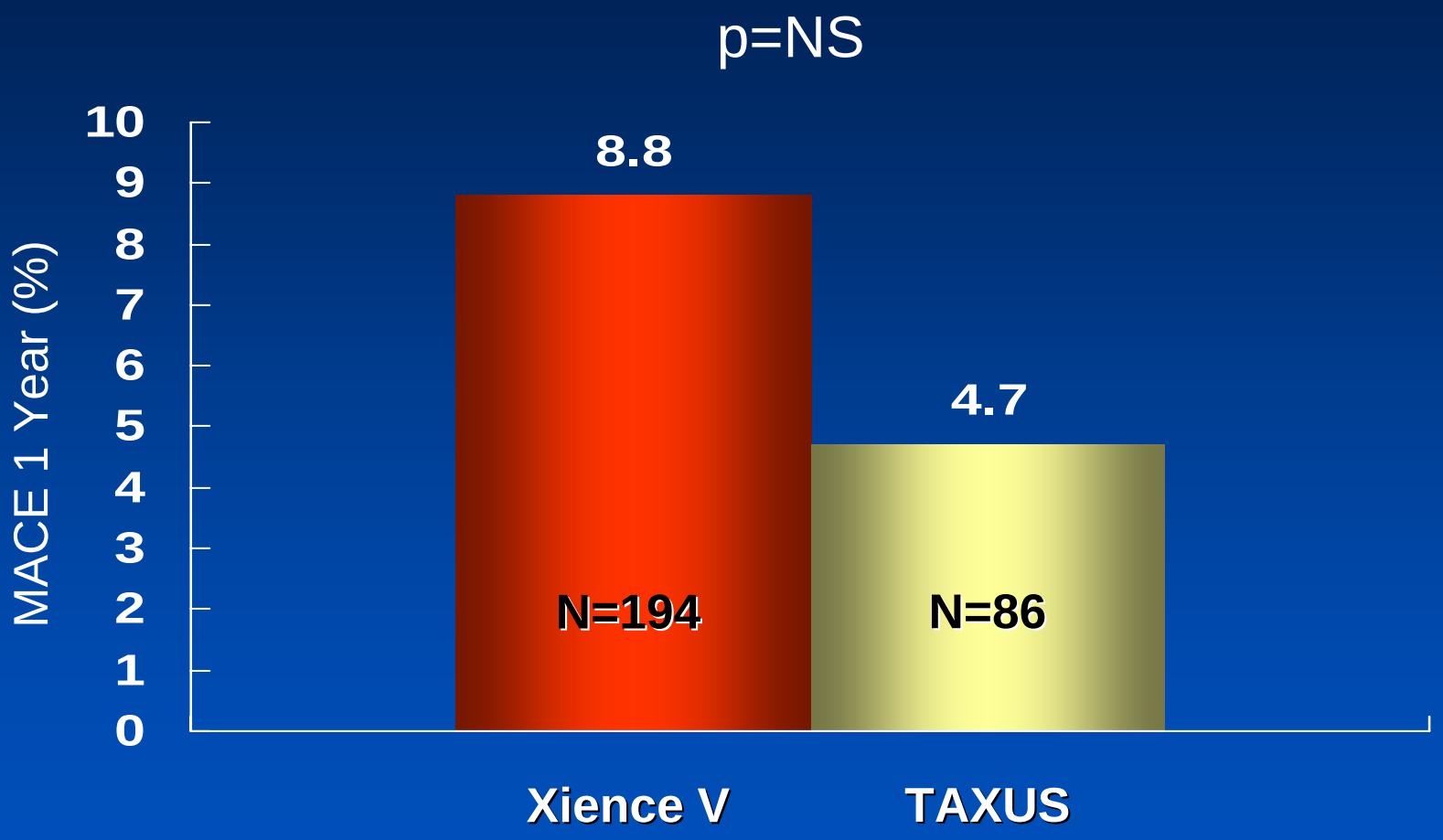
Diabetes

; Other second-generation DESs

→ very limited data

→ warrants more studies….

SPIRIT III in Diabetes



Evaluation of *D*iabetic *E*ffects on Clinical Outcomes After *S*irolimus-Eluting *S*tents in As*IAN* Population

The **DESSIAN** Registry

1. Prospective Enrollment of Consecutive **Diabetic Patients** Receiving Sirolimus-Eluting Stents (SES) in Routine Clinical Practice.
2. For Comparison, Concomitant Enrollment of **Non-diabetic Patients** Receiving SES

↓

Consecutive Enrollment Of Patients Treated With SES Up to 3600 Patients

Approximately DM vs. Non-DM = 30% vs. 70%

Diabetic Patients (n=1100)	**Nondiabetic patients (n=2500)**

Clinical follow-up at 1-, 6-, and 12-months

***Primary end point:** Composite of Death, MI, and TVR at 12-months `

ESSENCE-DIABETES Trial

AMC data

Patients with de novo coronary lesions requiring single or multiple stents in diabetic patients (Total patients, N=280)

18 Centers in Korea

1:1 randomization

XIENCE V (n=140)

CYPHER (n=140)

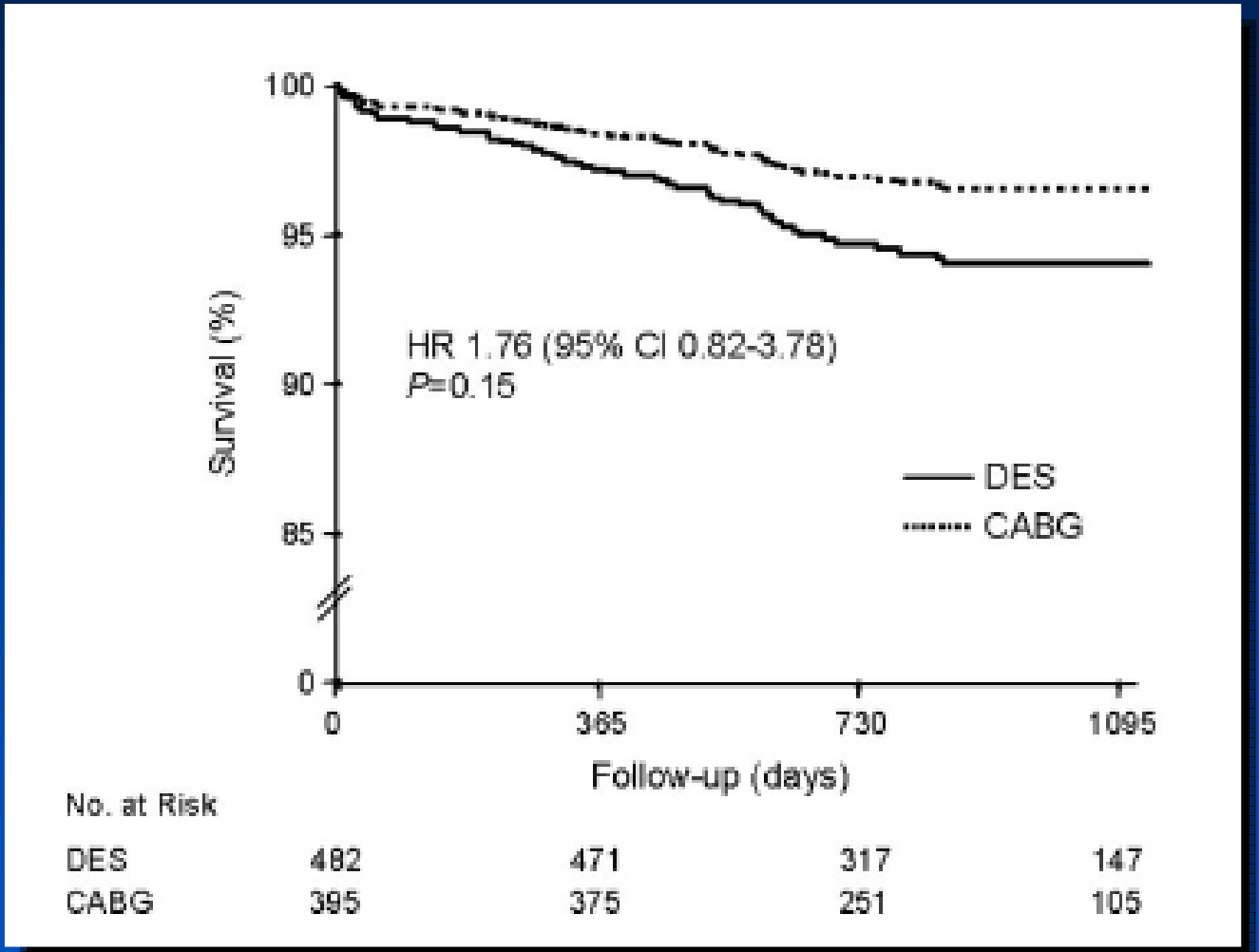
8 month angiographic follow-up
1-year clinical follow-up

Primary end-point: Angiographic in-segment late loss at 8-month angiography
Secondary end-point: Clinical outcomes at 12 month follow-up
IVUS results at 8 month angiographic follow-up (selected center)

PI: Seong-Wook Park, MD, PhD, FACC

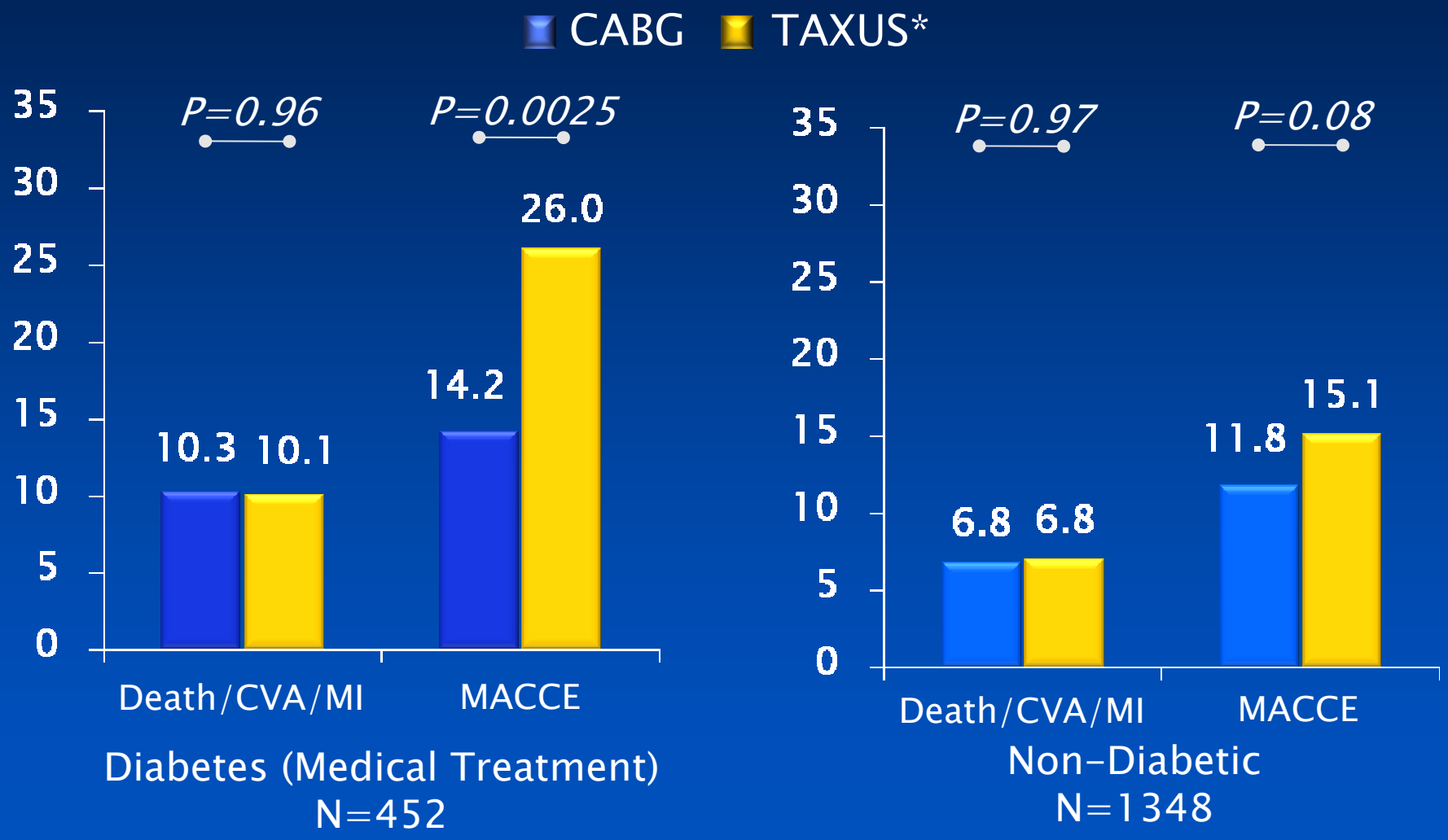
DES vs. CABG
in Diabetic Patients

DES vs. CABG
Three-year mortality in Diabetes



Park DW et al., Circulation 2008;117:2079-2086

Medically Treated Diabetes and Non-Diabetic (Syntax Subgroup)
All-Cause Death/CVA/MI and MACCE at 12 Months



ITT population

MACCE: death/CVA/MI/any revascularization

MAIN-COMPARE

Adjusted HRs of 3-year Outcomes

	HRs	95% CI	P	Interaction P
Oveall Patients				
Death	0.95	0.62,1.46	0.83	0.16
Death, QMI, CVA	0.96	0.65,1.42	0.85	0.93
TVR	4.31	2.28,8.15	<0.001	0.92
Diabetic Patients				
Death	0.55	0.24,1.25	0.15	
Death, QMI, CVA	0.78	0.38,1.62	0.51	
TVR	7.67	2.76,21.32	<0.001	
Non-Diabetic Patients				
Death	1.00	0.59,1.72	0.99	
Death, QMI, CVA	0.96	0.57,1.58	0.88	
TVR	2.94	1.36,6.38	0.006	

Summary (1)
DES in Diabetics

- Aggressive revascularization strategy improves the survival in diabetic patients compare to medical treatment.
- Diabetic patients treated with DES bring a reduced risk of TLR,TVR,TVF and MACE compared with BMS
- Diabetics still have higher TVR and Death/MI/TVR especially, insulin treated diabetics have a clear trend of poor clinical outcomes (Death, TVR and Death/MI/TVR) compared to non-diabetics even in the era of DES

Summary (2)
DES in Diabetics

- According to the ISAR-DIABETES and DECLARE-DIABETES Trial, SES appears to be more effective than PES in preventing restenosis in on-label lesions. However, in real practice, two stent had similar outcomes.
- Adjunctive pharmacologic therapy (Cilostazol, GP IIb/IIIa, Thiazolidinediones, ACEI, strict glycemic control) is likely to further improve PCI outcomes
- Efficacy concerns of DES compare to surgery should be evaluated in the future.


Thank You !!
summitMD.com