Impact of DM on PCI

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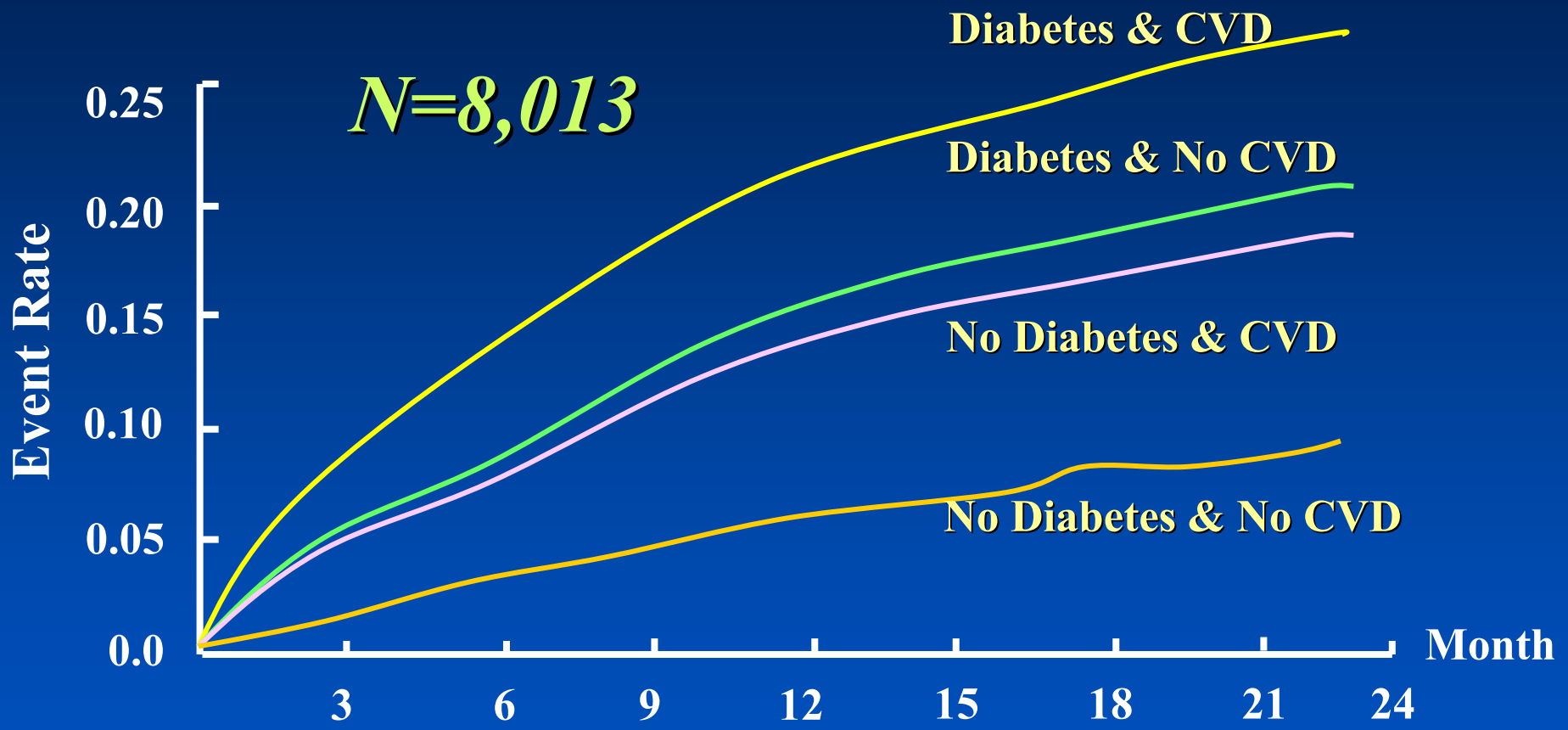
Diabetes & Risk of Cardiovascular Mortality

OASIS Registry



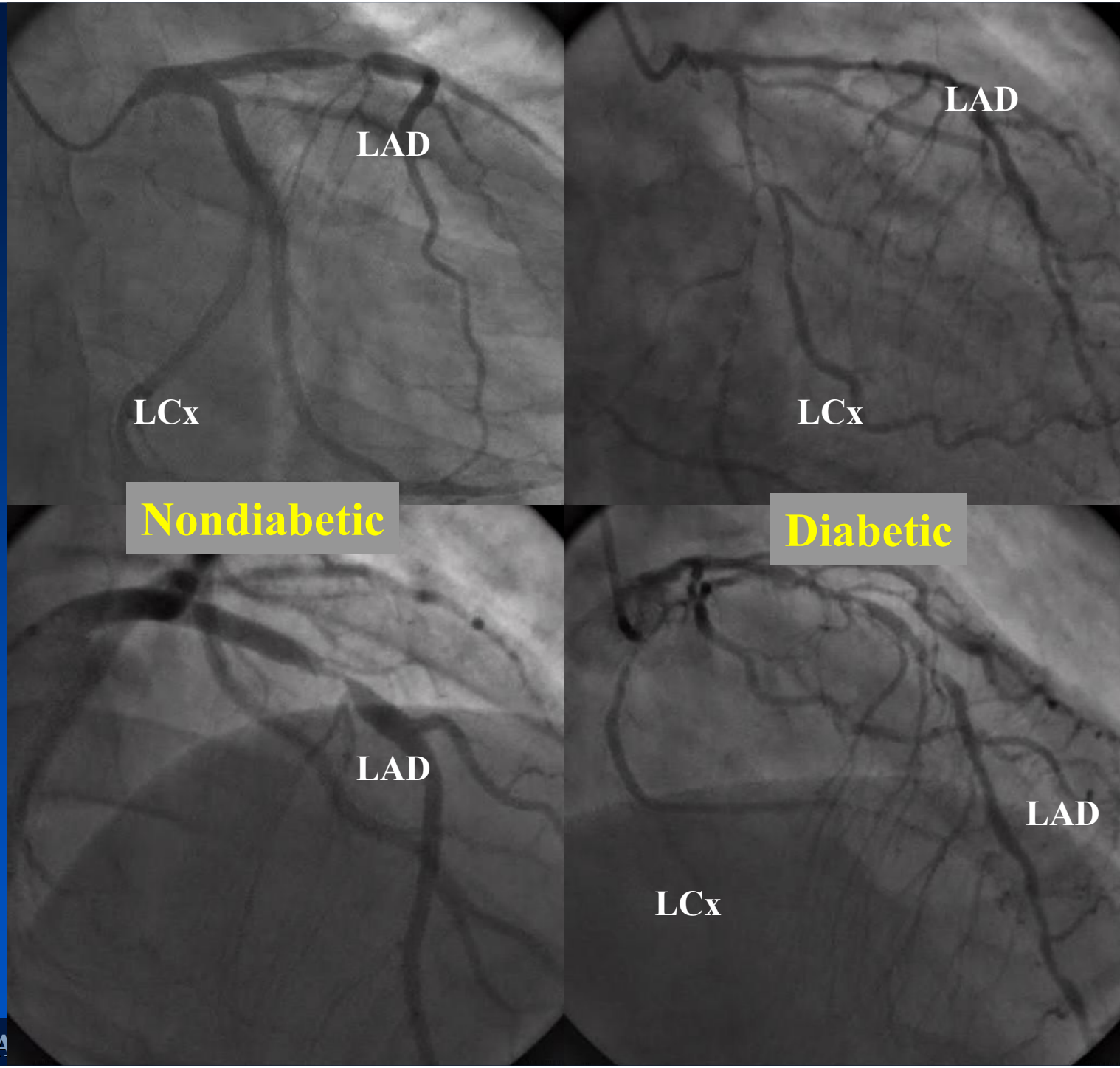
Diabetes & CVD; RR 2.85 (2.30-3.53)

Diabetes & No CVD; RR 1.71 (1.25-2.33)

No Diabetes & CVD; RR 1.71 (1.41-2.06)

No Diabetes & No CVD; RR 1.00

Malmberg K, et al. Circ 2000;102:1014-1019


LAD
LCx
LAD
LCx
Nondiabetic
Diabetic
LAD
LAD
LCx

Anatomy of Coronary Disease in Diabetic Patients

- Small vessel caliber (impaired remodeling or diffuse atherosclerosis)
- High incidence of multivessel 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 severe and diffuse pattern of coronary artery disease

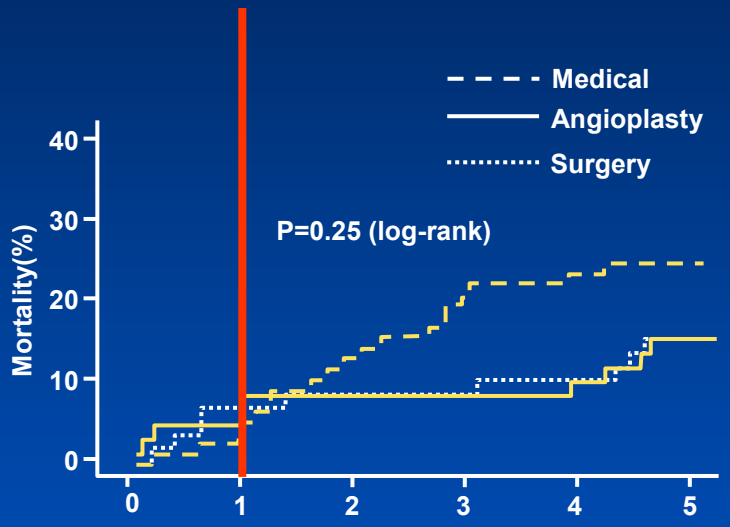
Mechanism of Increased Atherosclerosis in Diabetic Patients

- Endothelial dysfunction
- Dyslipidemia
- Thrombogenesis
- Oxidative stress
- Autonomic neuropathy

Ann Intern Med. 2003;139:824-834

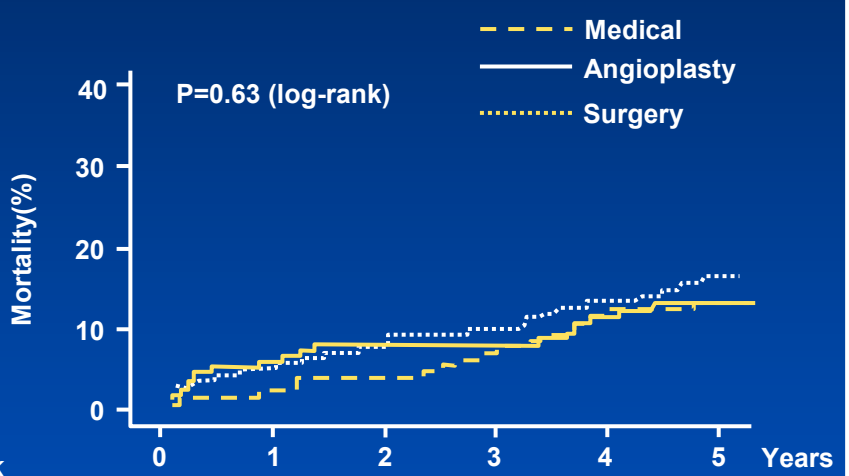
Medical vs. PCI or CABG in Stable MVD (MASS II)

Diabetic



At risk						
Medical	75	73	65	59	57	56
Angioplasty	56	53	51	51	50	47
Surgery	59	55	54	54	53	50

Nondiabetic



At risk						
Medical	128	126	124	119	113	112
Angioplasty		141	128	138	133	130
Surgery	144	137	133	130	125	121

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

Diabetes and Revascularization

- Surgery, angioplasty, and medical treatment did not influence the risk of death for nondiabetic subjects.
- For diabetic subjects, however, coronary revascularization (percutaneous or surgical) was associated with a protective effect compared with medical treatment alone, significantly decreasing the risk of death after 1 year and up to 5 years.
- Invasive revascularization strategy should be considered in stable diabetic patients

Post-PCI Outcomes

Diabetes vs. non-diabetics

Biological Consequences of Diabetes

Enhanced Platelet Activation and Release of Growth Factors

Accelerated Proliferation and Migration of Smooth Muscle Cells

Impaired Fibrinolysis (elevated t-pa, PAI-1, D-dimer)

Increased Inflammation (CRP, fibrinogen)

Excessive Matrix Deposition

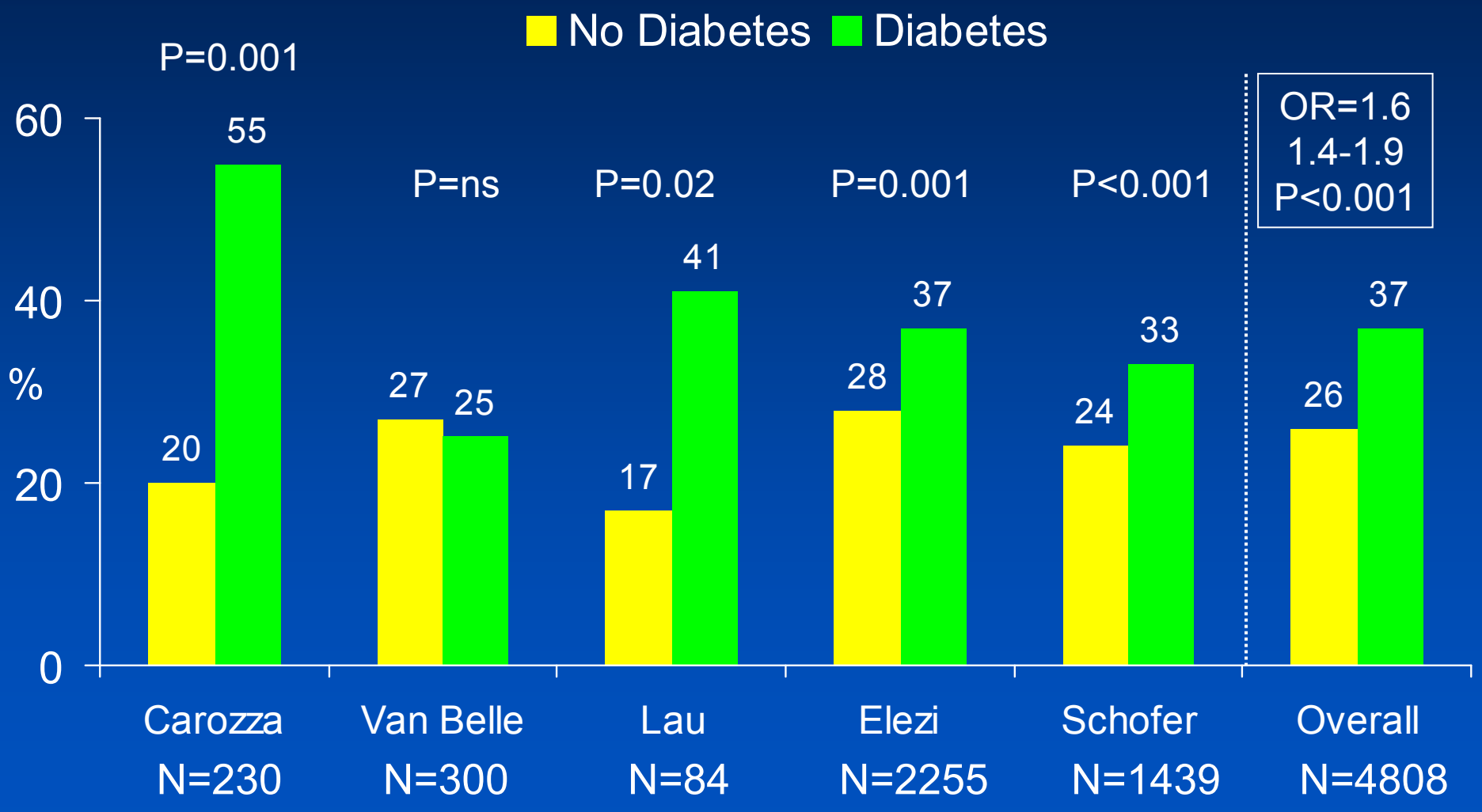
Delayed Wound Healing

Endothelial Dysfunction

Increased intimal proliferation at the stented site
Rapid progression of non-culprit lesions

Risk of Restenosis in BMS

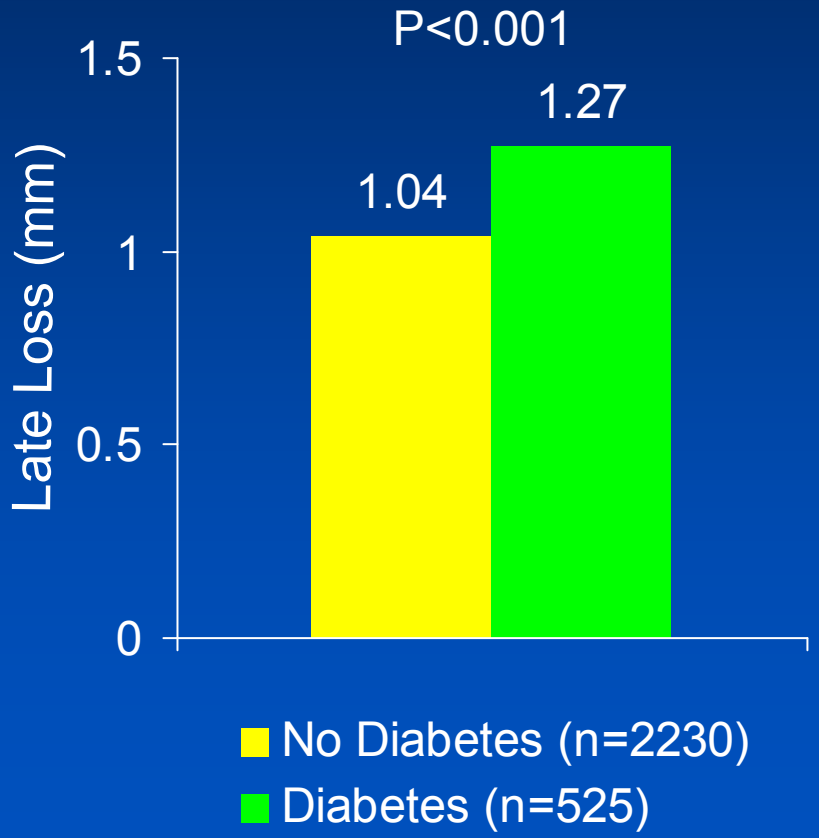
Diabetic vs Nondiabetic Patients



Mechanism of Restenosis in Diabetic Patients

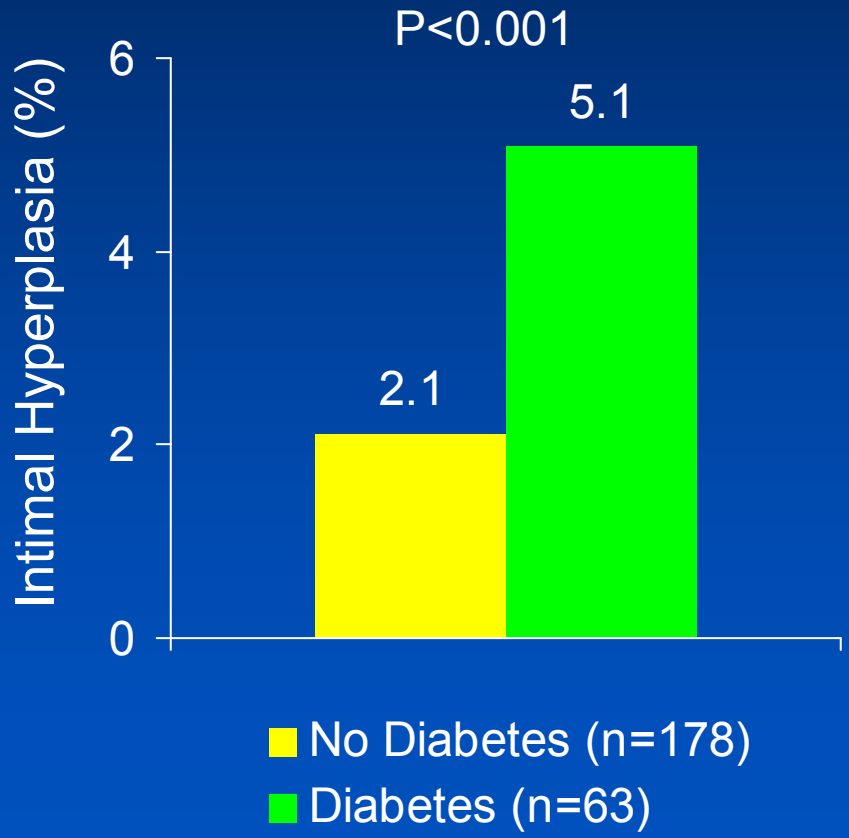
Late Loss

Elezi S et al. *JACC* 1998;32:1866



Neointimal Hyperplasia

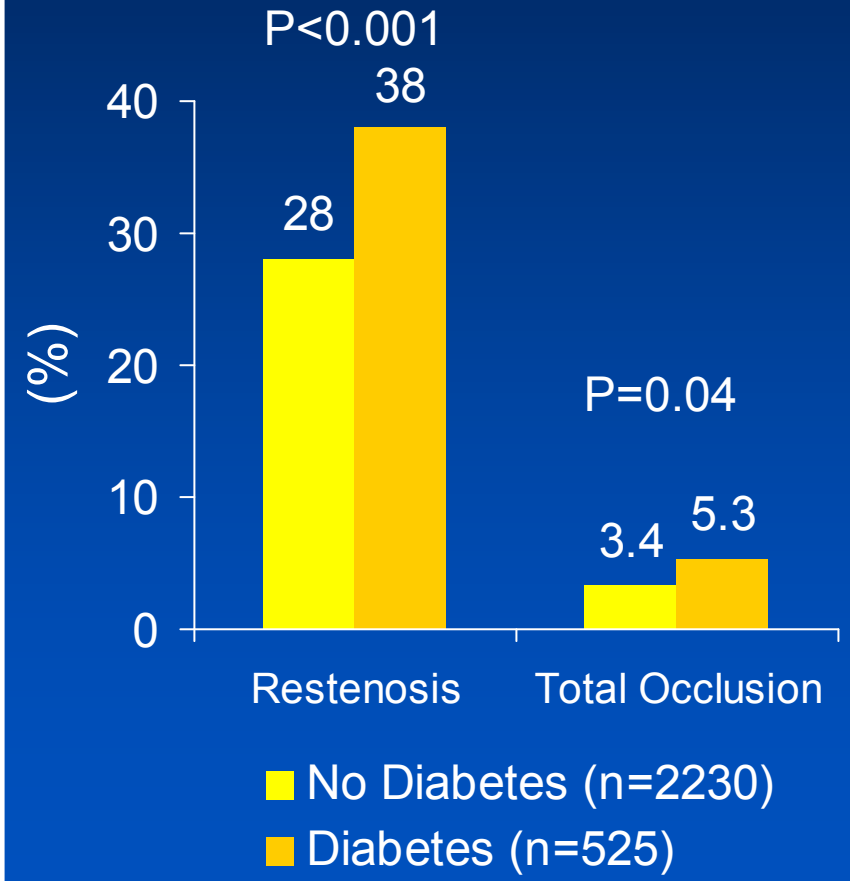
Kornowski et al. *Circulation* 1997;95:1366



Impact of Restenosis on Prognosis in Diabetic Patients

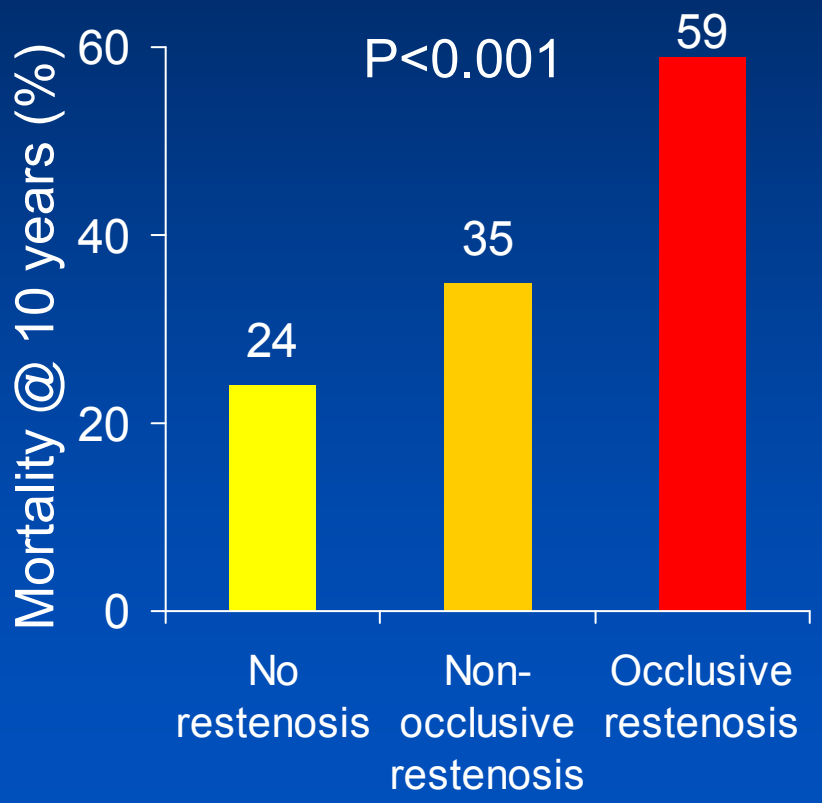
Restenosis

Elezi S et al. *JACC* 1998;32:1866



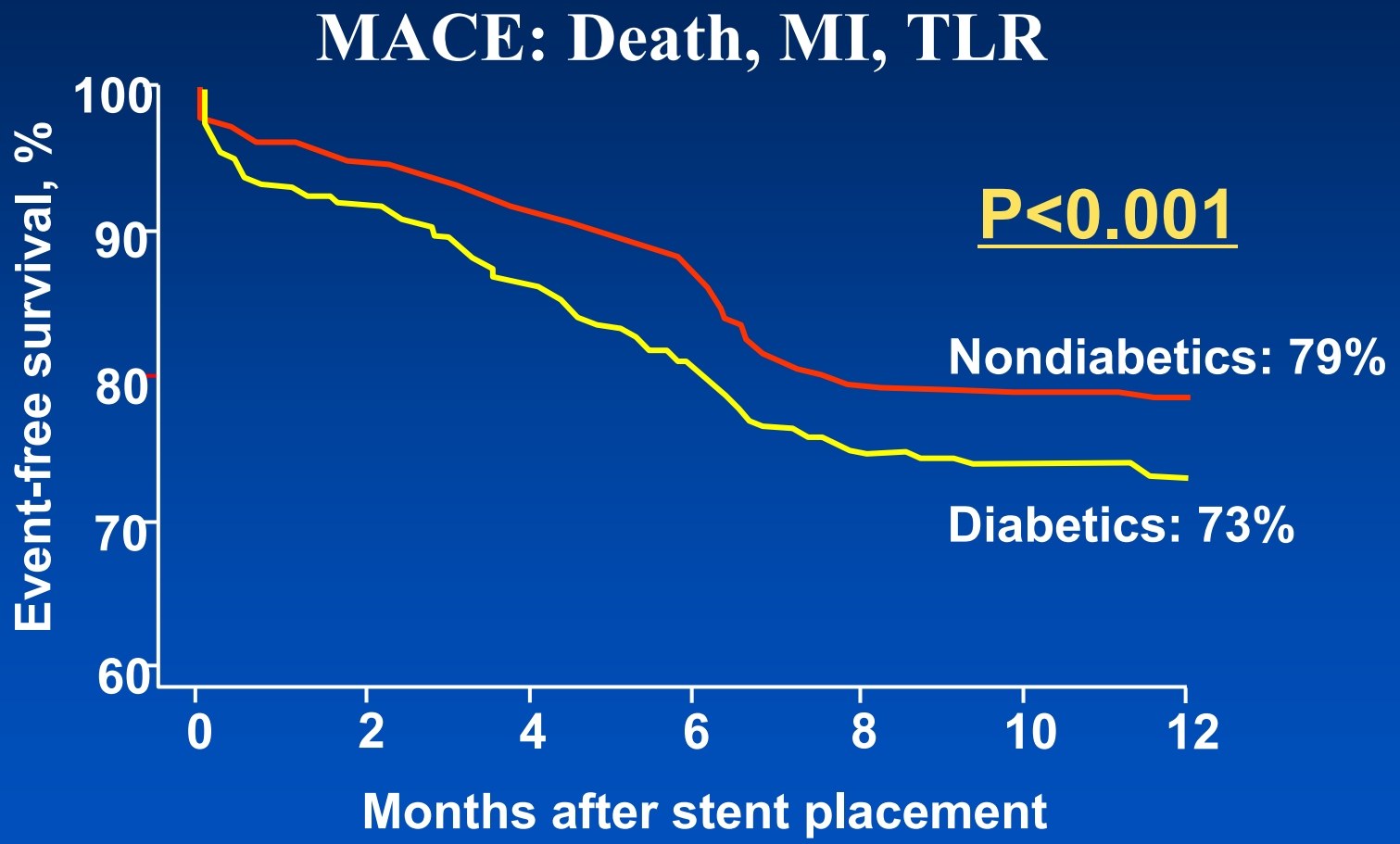
Mortality

Van Belle E et al. *Circulation* 2001;103:1218



Event-free survival after PCI

Diabetes vs. non-diabetics



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

Independent predictors of stent thrombosis

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

- **ACS (HR 2.28, 95% CI, 1.29–4.03)**
- **Diabetes (HR 2.03, 95% CI, 1.07–3.83)**

Lancet 2007; 369: 667–78

Independent predictors of SES thrombosis

EVASTENT Matched-Cohort Registry

- Renal failure (OR 3.6, 95% CI, 1.6-7.7, p=0.001)
- Insulin-requiring DM (OR 2.7, 95% CI, 1.4-5.2, p=0.004)
- Calcified lesion (OR 3.7, 95% CI, 1.8-7.7, p=0.001
- Lower EF (per U) (OR 0.95, 95% CI, 0.93-0.97, p<0.001)
- Length stented (per mm) (OR 1.01, 95% CI, 1.0-1.03, P=0.045)

JACC 2007; 50: 501-8

Clinical Consequences of Diabetes in Patients Undergoing PCI

- Larger disease burden at time of presentation
- High restenosis rate in the treated lesion
- Rapid progression of non-culprit coronary artery lesions
- Higher mortality after PCI
- Diabetic patients treated with insulin has the worst outcomes

JACC 1998. 32:584-590.

Post-PCI Outcomes in DM

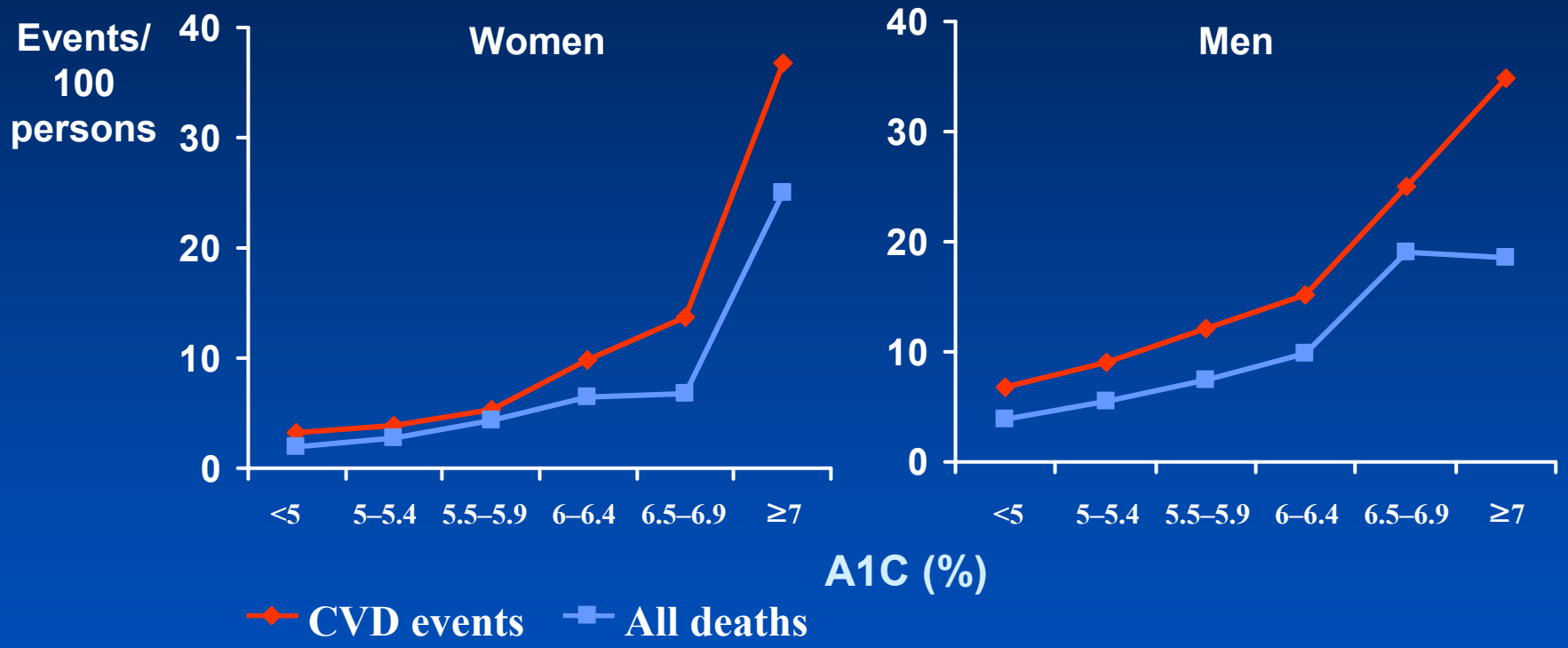
Associated factors

- Glycemic control
- Diabetic nephropathy
- Use of sulfonylurea ?
- In-stent restenosis

CV risk increases with HbA1C level

N = 10,232

EPIC-Norfolk



↑1% A1C associated with: ↑20% CVD events, ↑22% mortality

P_{Trend} < 0.001 across A1C categories for all endpoints

Khaw K-T et al. Ann Intern Med. 2004;141:413

HbA1c and Restenosis

75 patients with DM with 86 lesions

Predictors of angiographic restenosis after coronary intervention in patients with diabetes mellitus

Peter Mazeika, MD, Neeraj Prasad, MD, Sanh Bui, BSc, and Peter H. Seidelin, MD, FACC
Toronto, Ontario, Canada

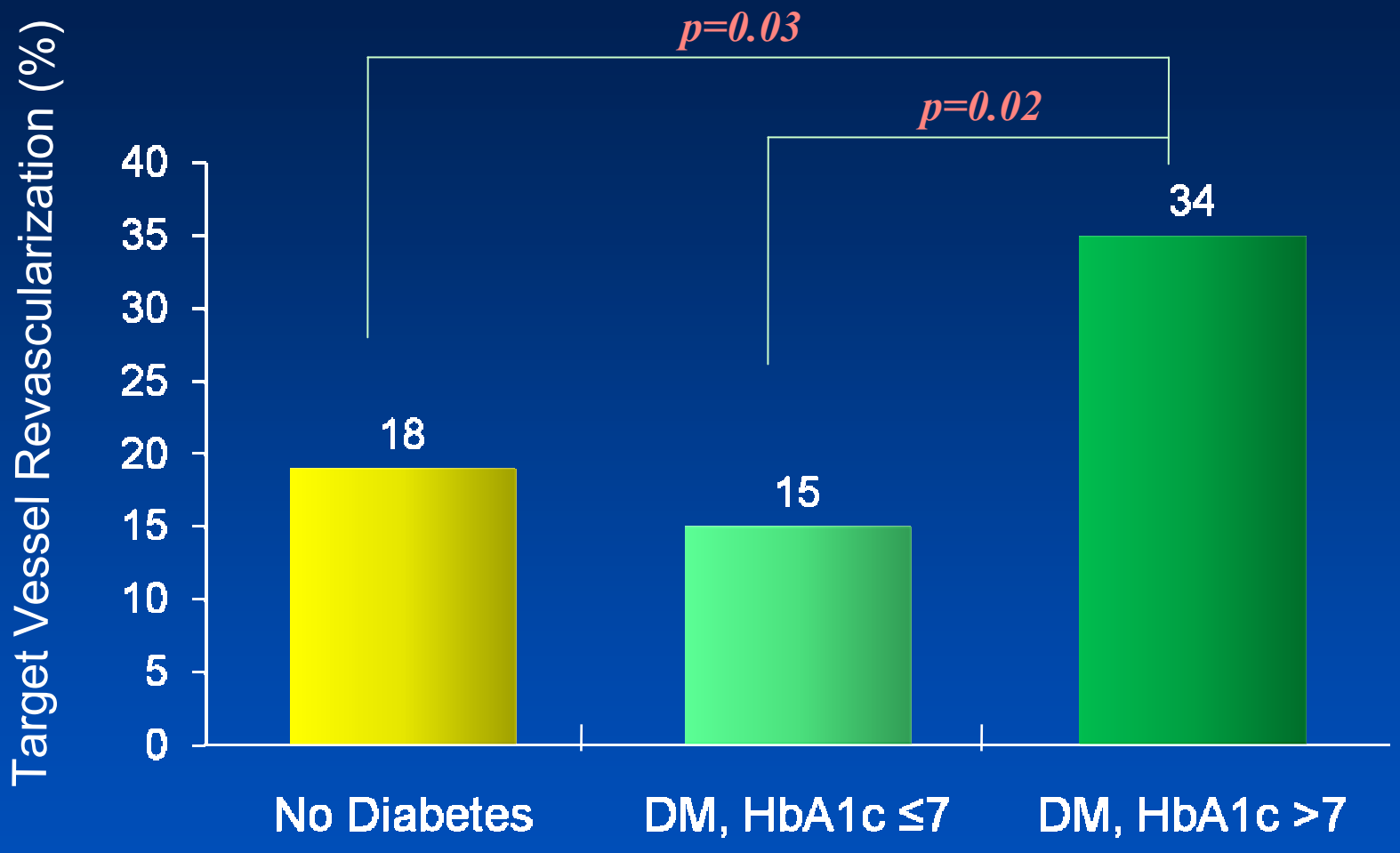
HbA1c level (OR 3.03, 95% CI 1.06–8.65, *P=0* .038)

Vessel reference diameter (OR 3.41, 95% CI 1.17–9.95, *P=0*.025)

Type of intervention (OR 3.12, 95% CI 1.08–9.00, *P=0*.036)

Mazeika P Am Heart J 2003;145:1013–1021.

Glycemic control and TVR in Diabetic Patients

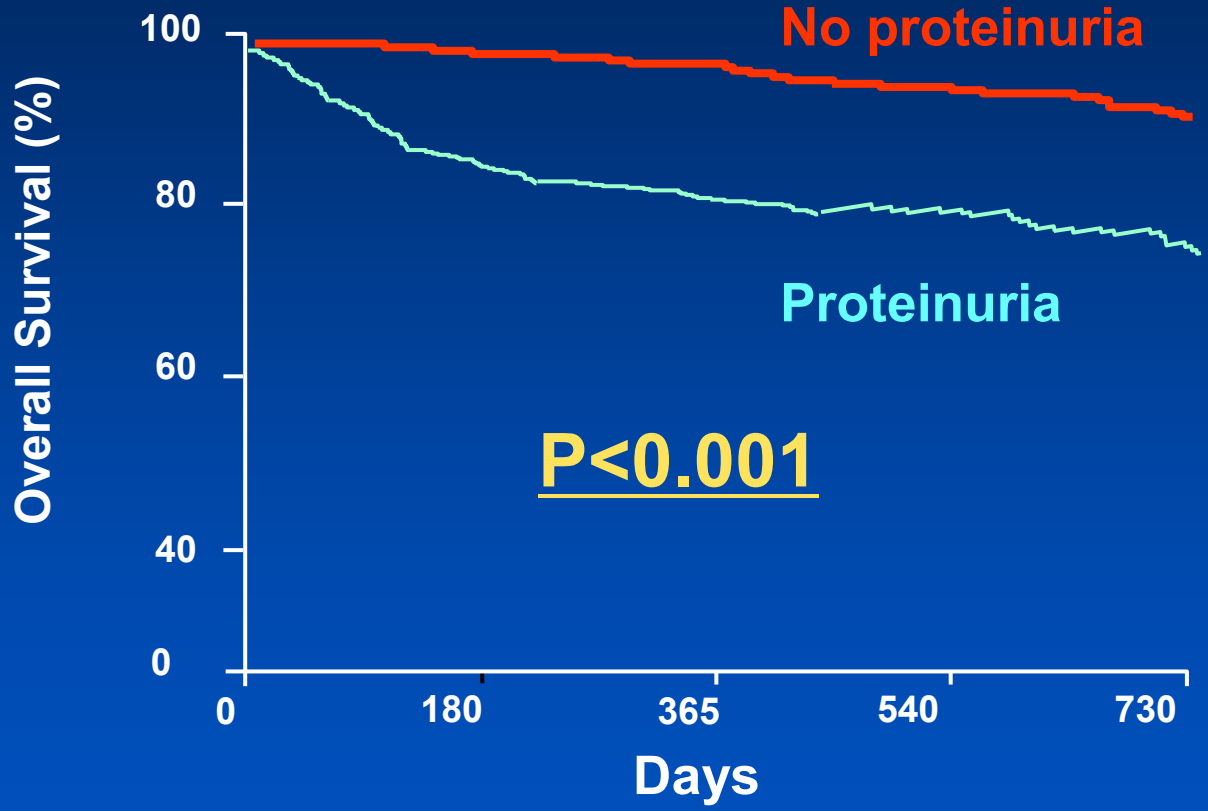


"Improved glycemic control might improve PCI outcomes"

Corpus RA et al. JACC 2004;43:8-14

Influence of Proteinuria in Diabetes

All-Cause Mortality



Marso SP et al. J Am Coll Cardiol 1999;33:1269 –77

How to improve the clinical outcomes after PCI in DM

- Drug-eluting stent
- Thiazolidinediones
- Cilostazol
- Glycoprotein IIb/IIIa inhibitors

How to improve the clinical outcomes after PCI in DM

- Drug-eluting stent
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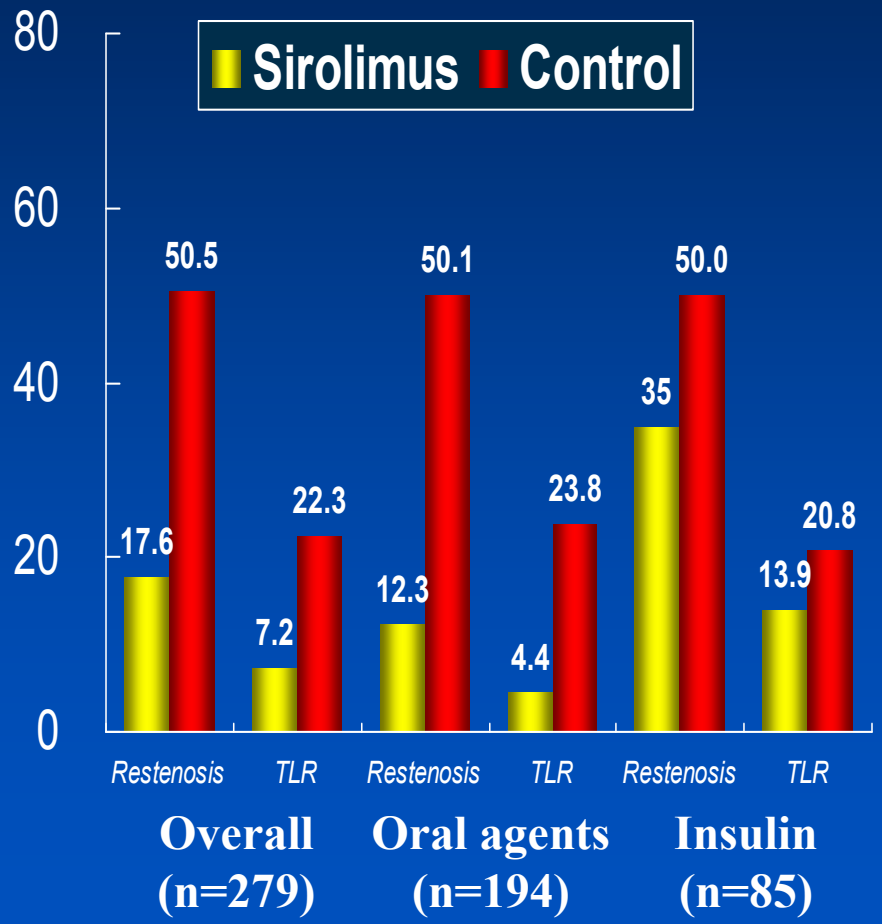
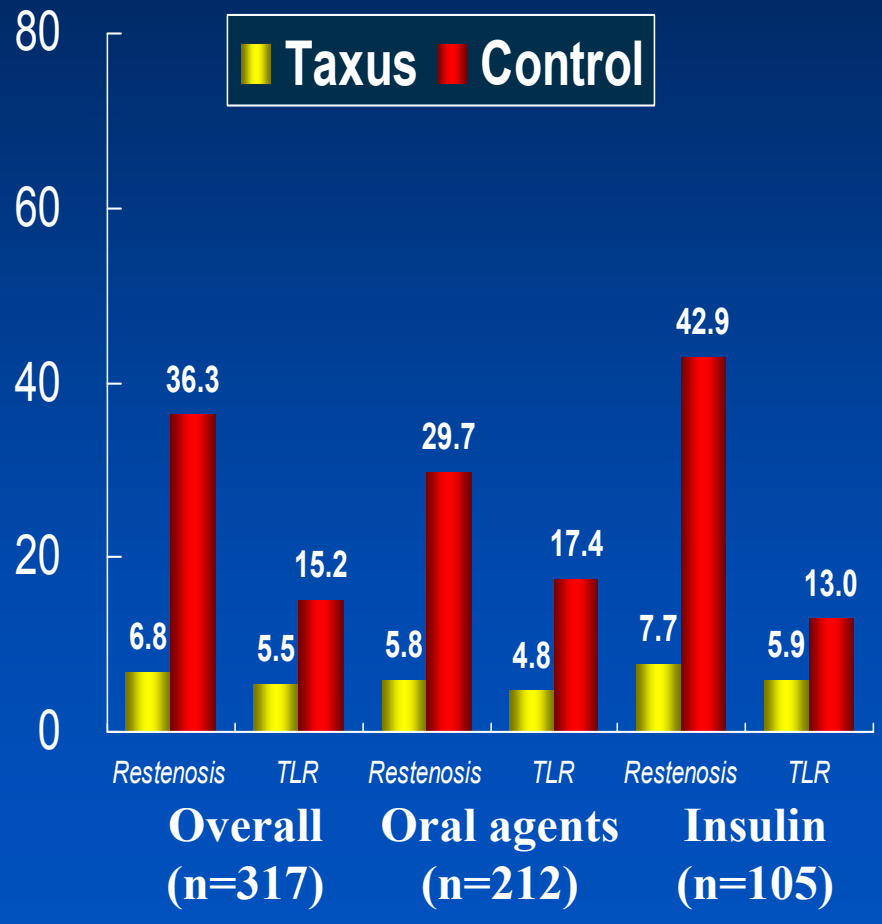
Outcomes with DES vs BMS in Diabetic patients

SIRIUS Trial Diabetic Sub-analysis



Moses et al. NEJM 2003;349:1315

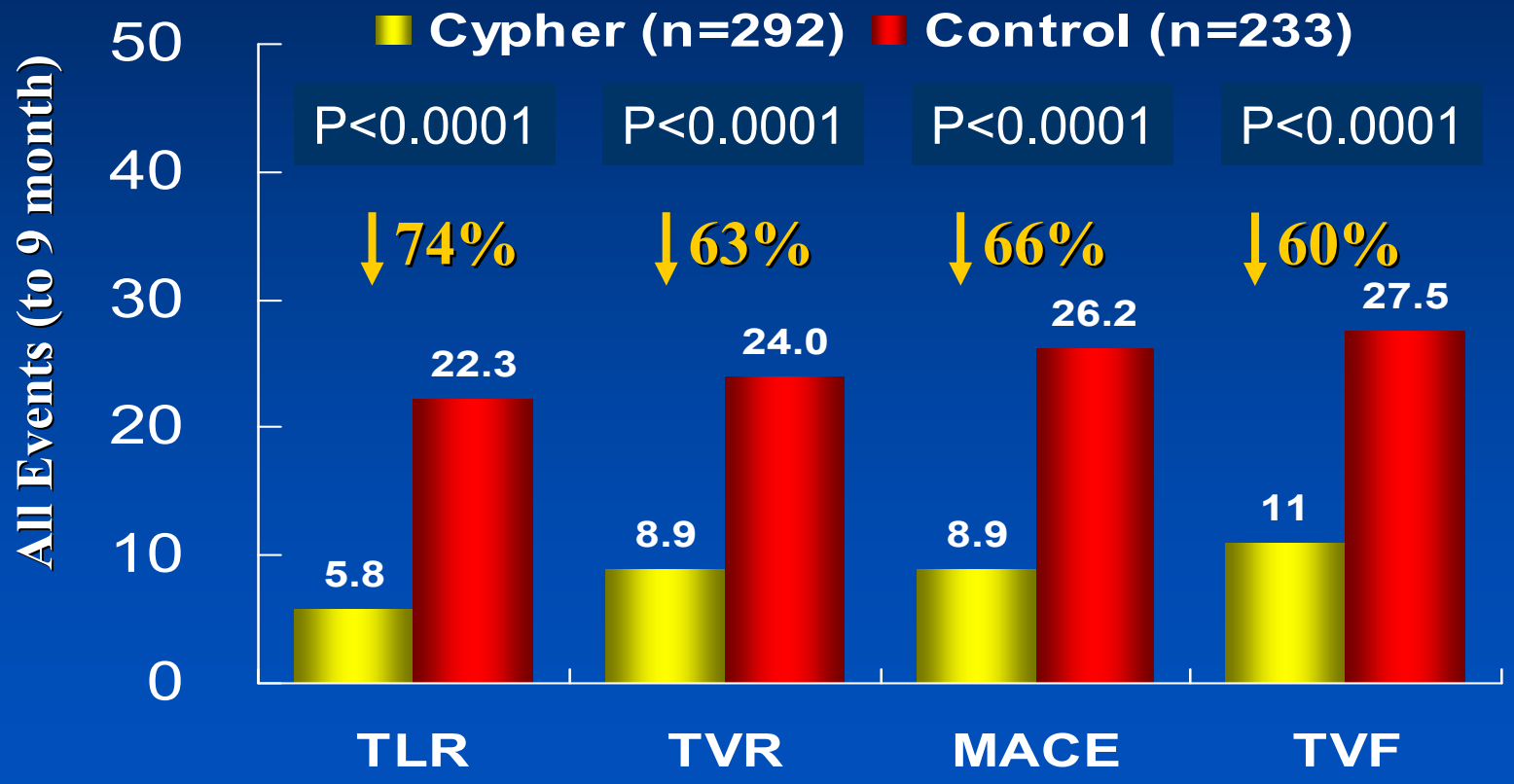
TAXUS IV Trial Diabetic Sub-analysis



Stone et al. NEJM 2004;350:221.

CYPHER Trials Meta-Analysis in Diabetes

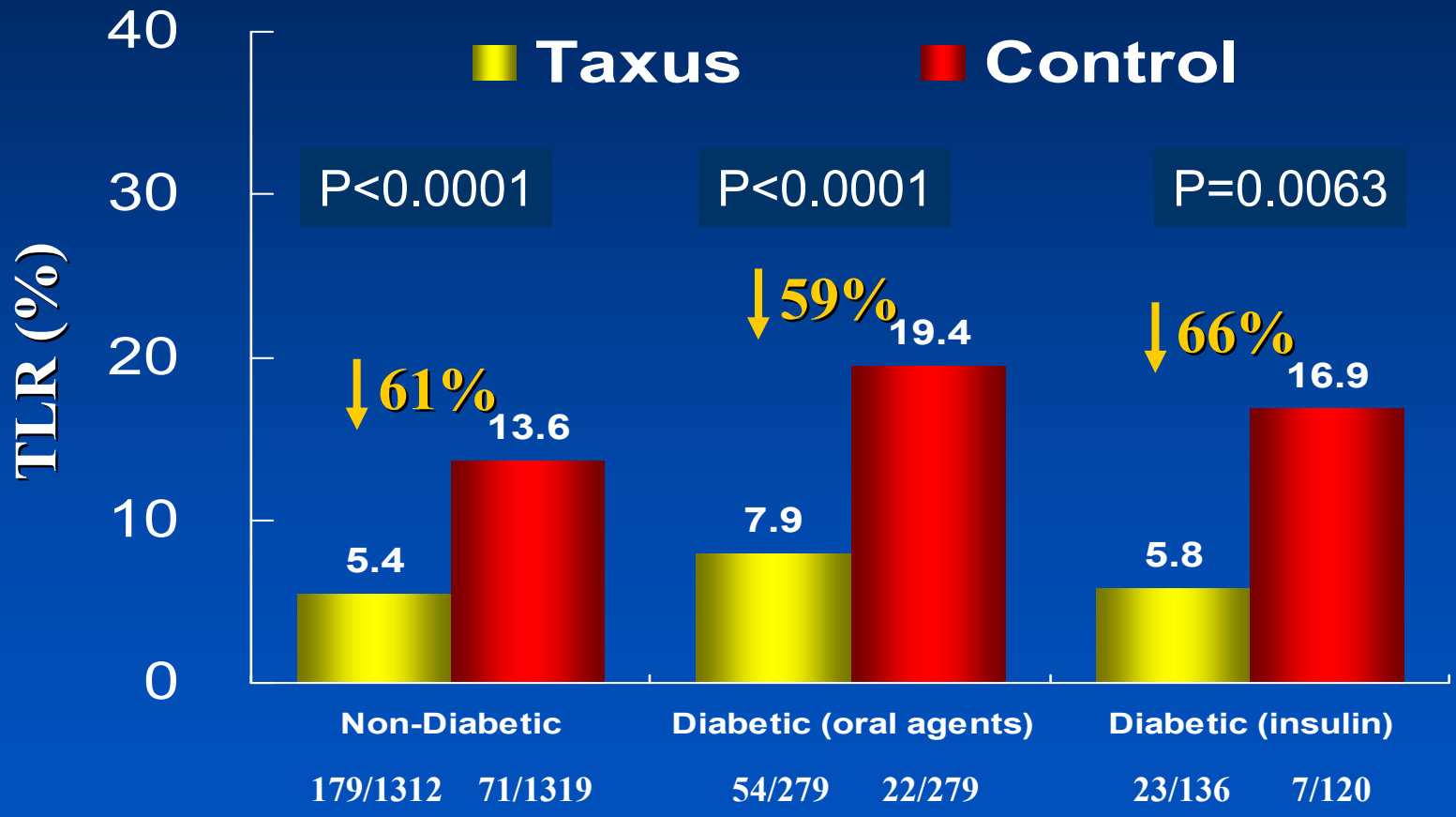
RAVEL, SIRIUS, E-SIRIUS, C-SIRIUS, DIRECT, SVELTE



Abizaid et al. Angioplasty Summit 2005

TAXUS Trials Meta-Analysis in Diabetes

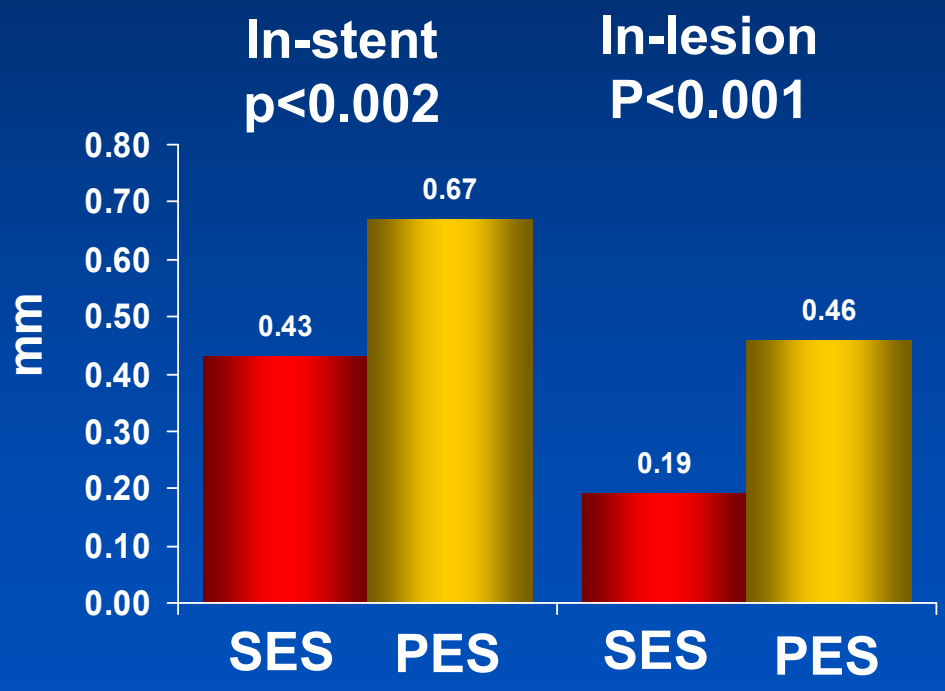
TAXUS II, IV, V, VI



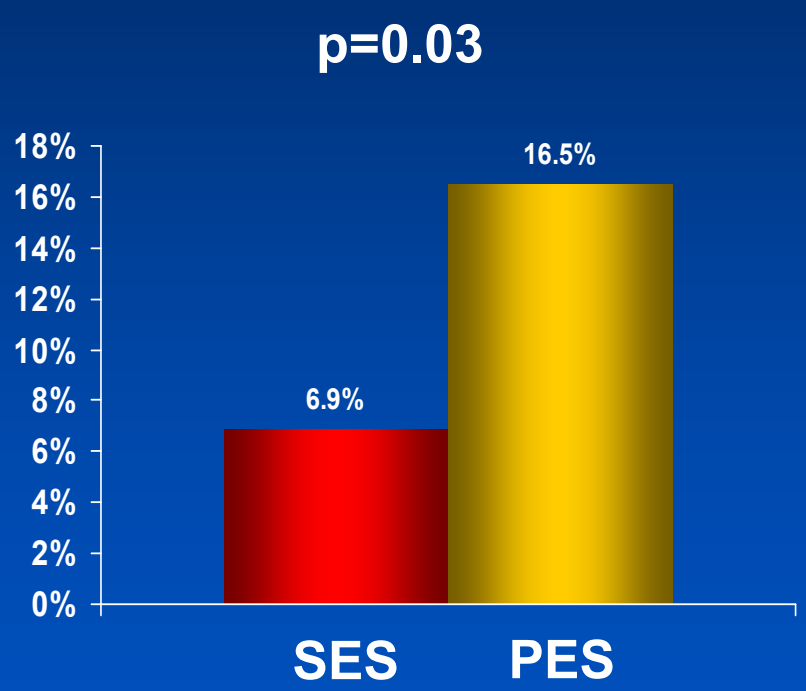
Stone GW et al. Angioplasty Summit 2005

ISAR-DIABETES Trial

Late Lumen Loss

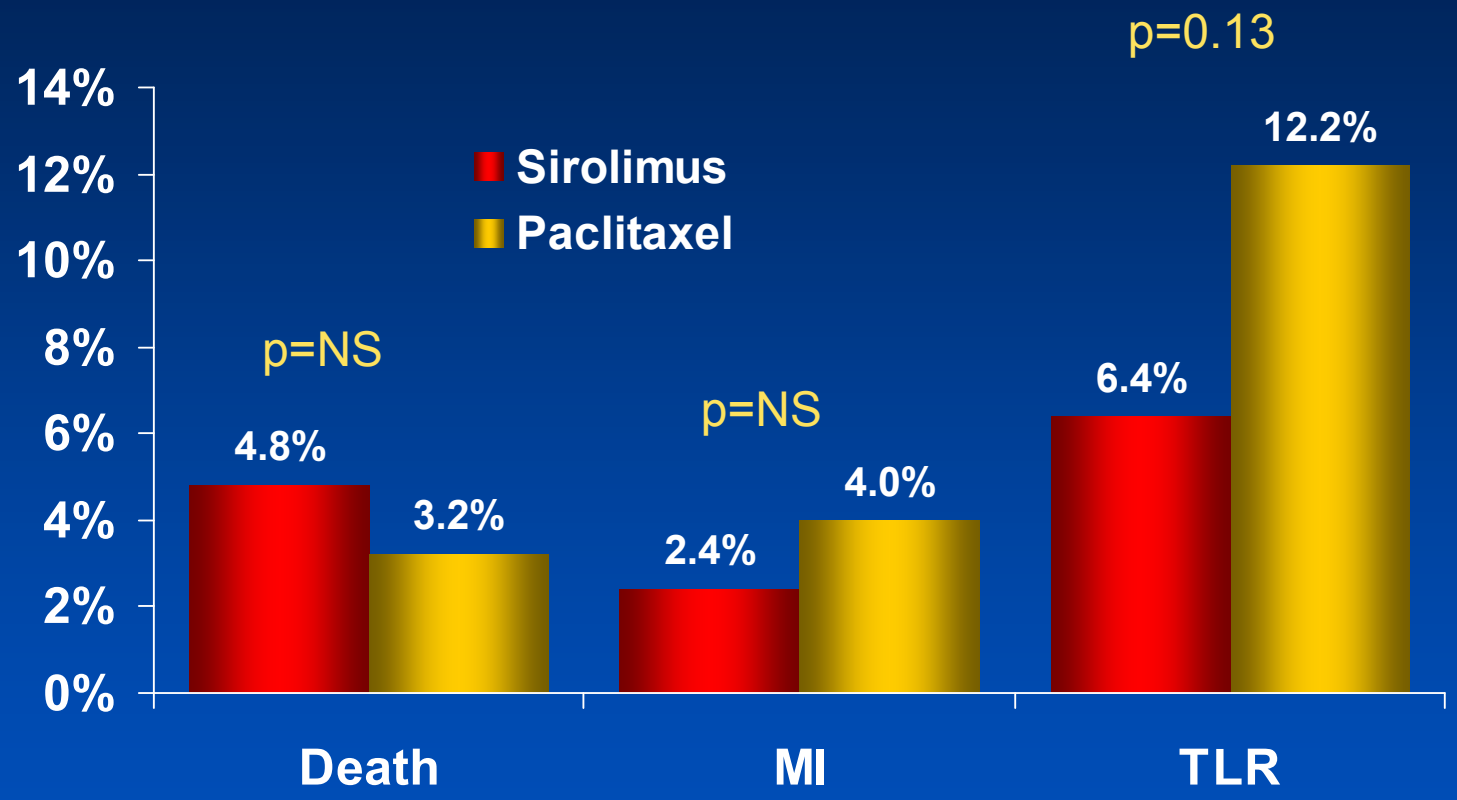


Re-stenosis



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

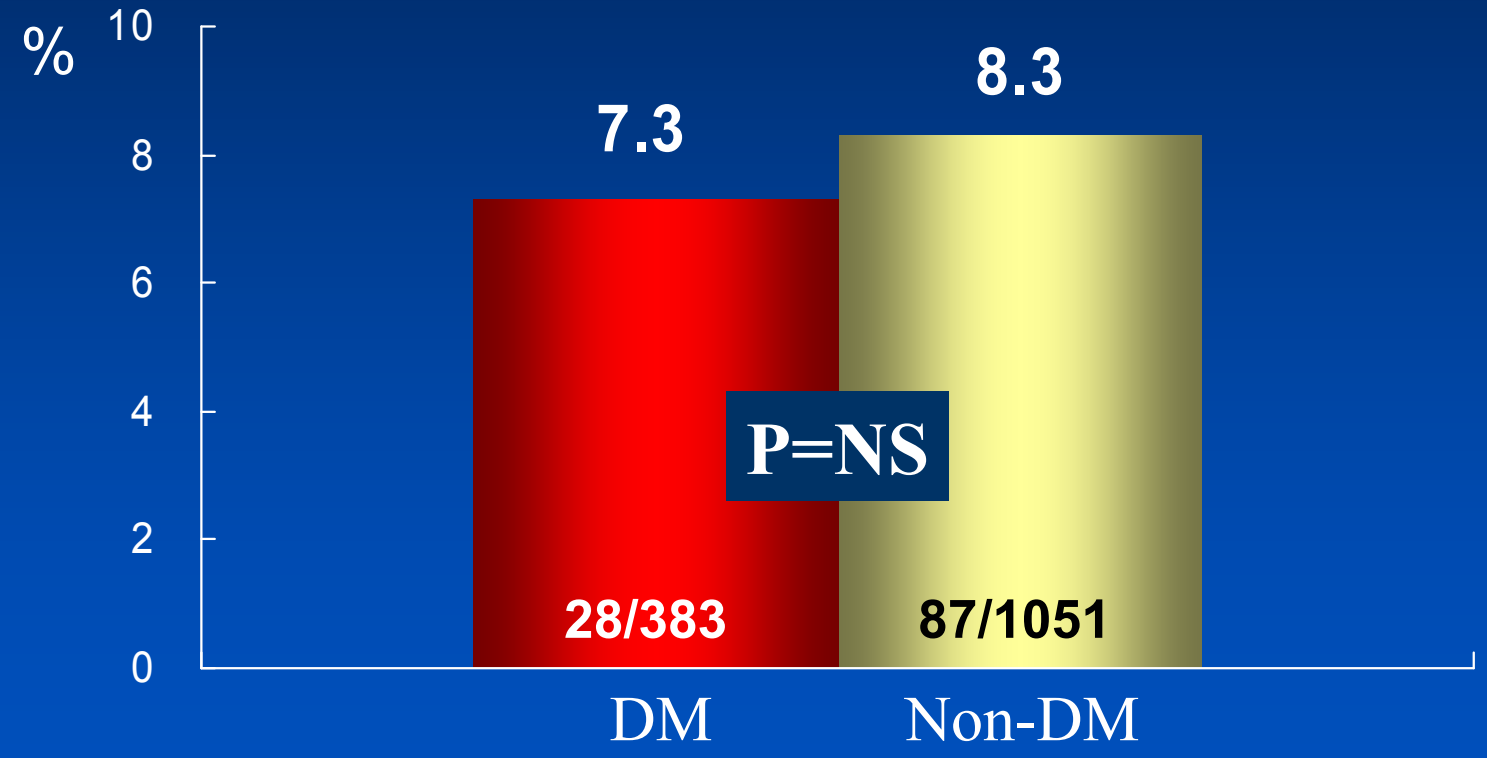
Multivariate Predictors of In-Segment Restenosis after SES

	OR	95% CI	p
ISR	4.16	1.63-11.01	<0.01
Ostial lesion	4.84	1.81-12.07	<0.01
DM	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

Impact of DM on Restenosis after DES Implantation

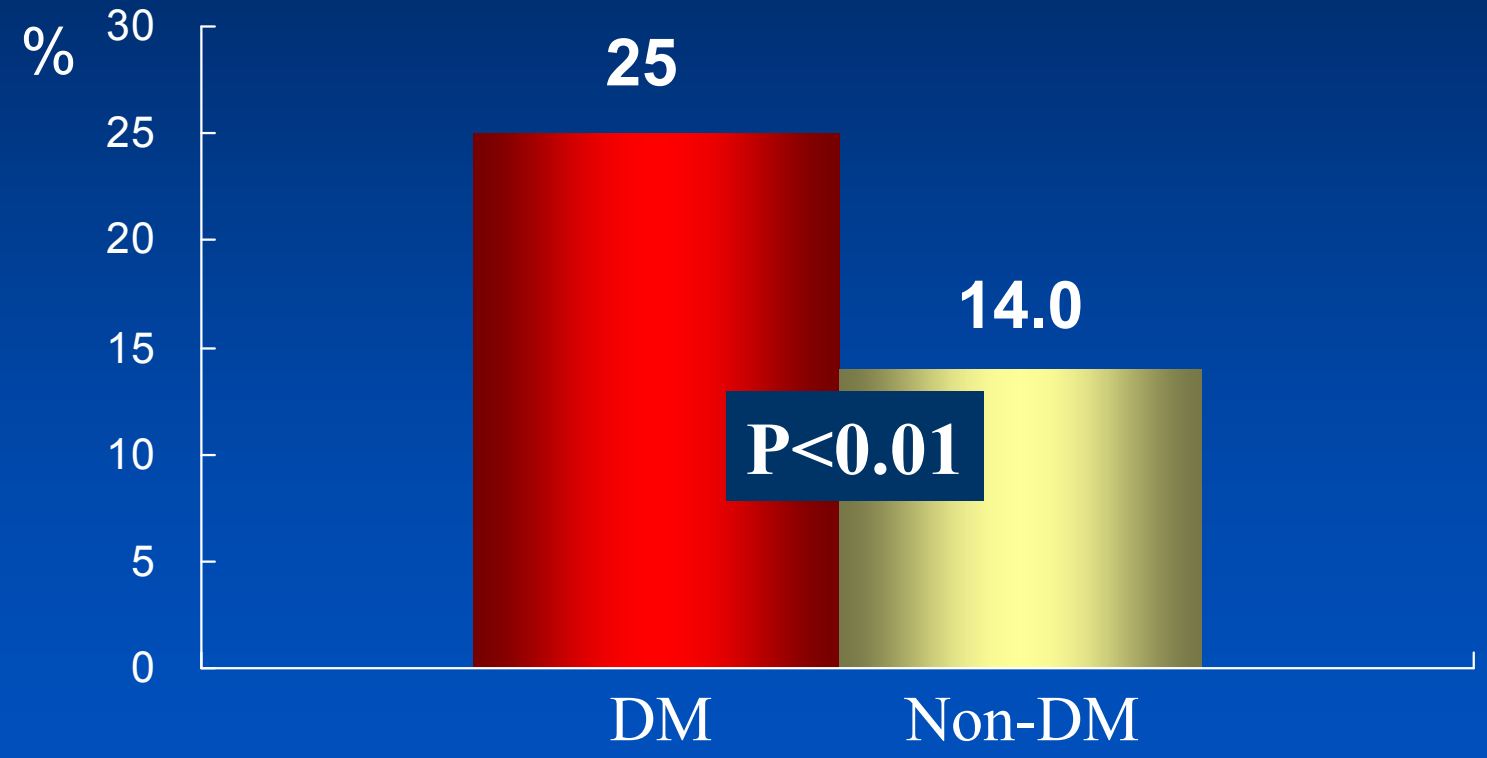
1126 Cypher lesions and 308 Taxus lesions



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

Impact of DM on Restenosis after DES Implantation

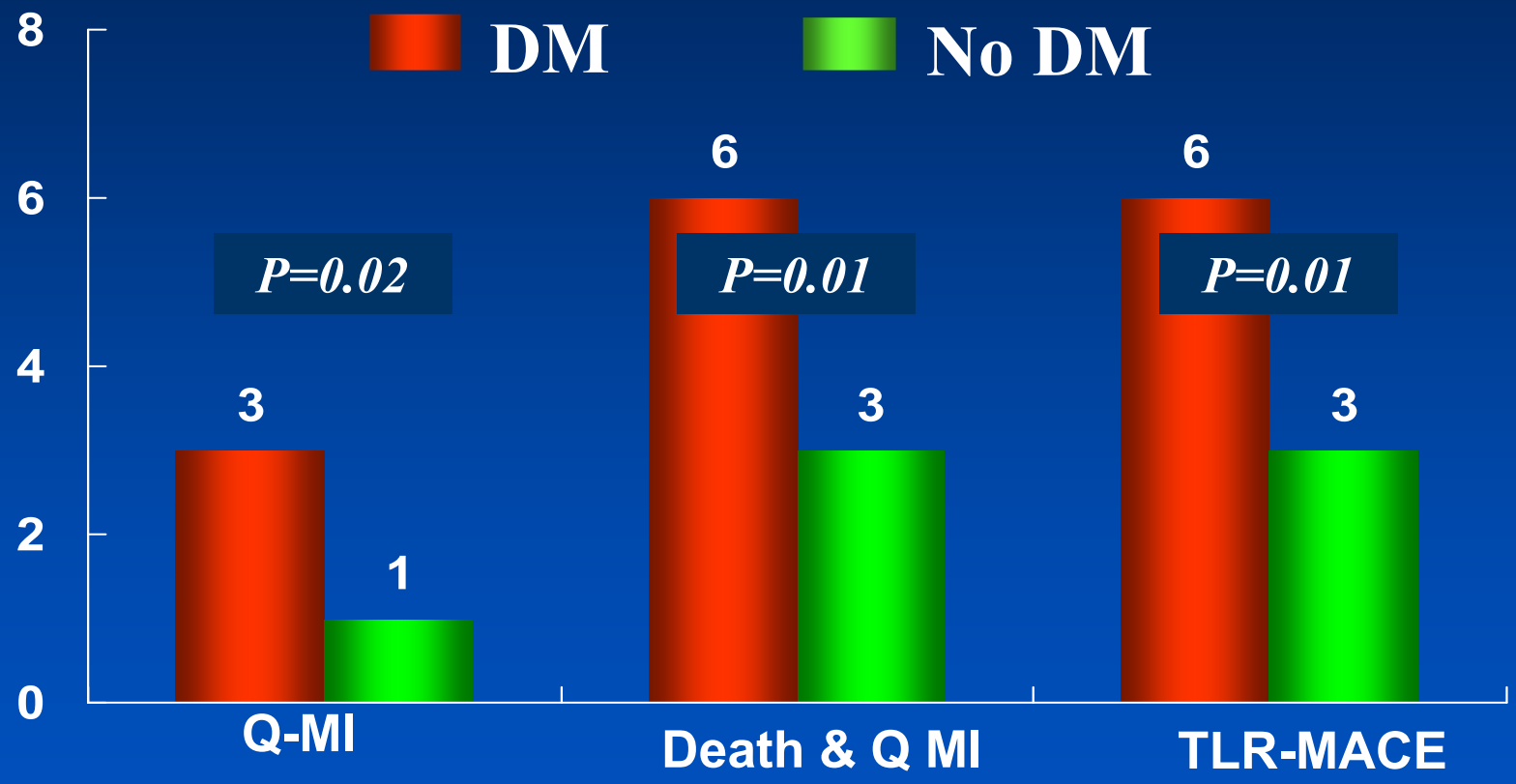
Matched comparison (192: 192)



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

Impact of DM on SES performance

6-month follow-up

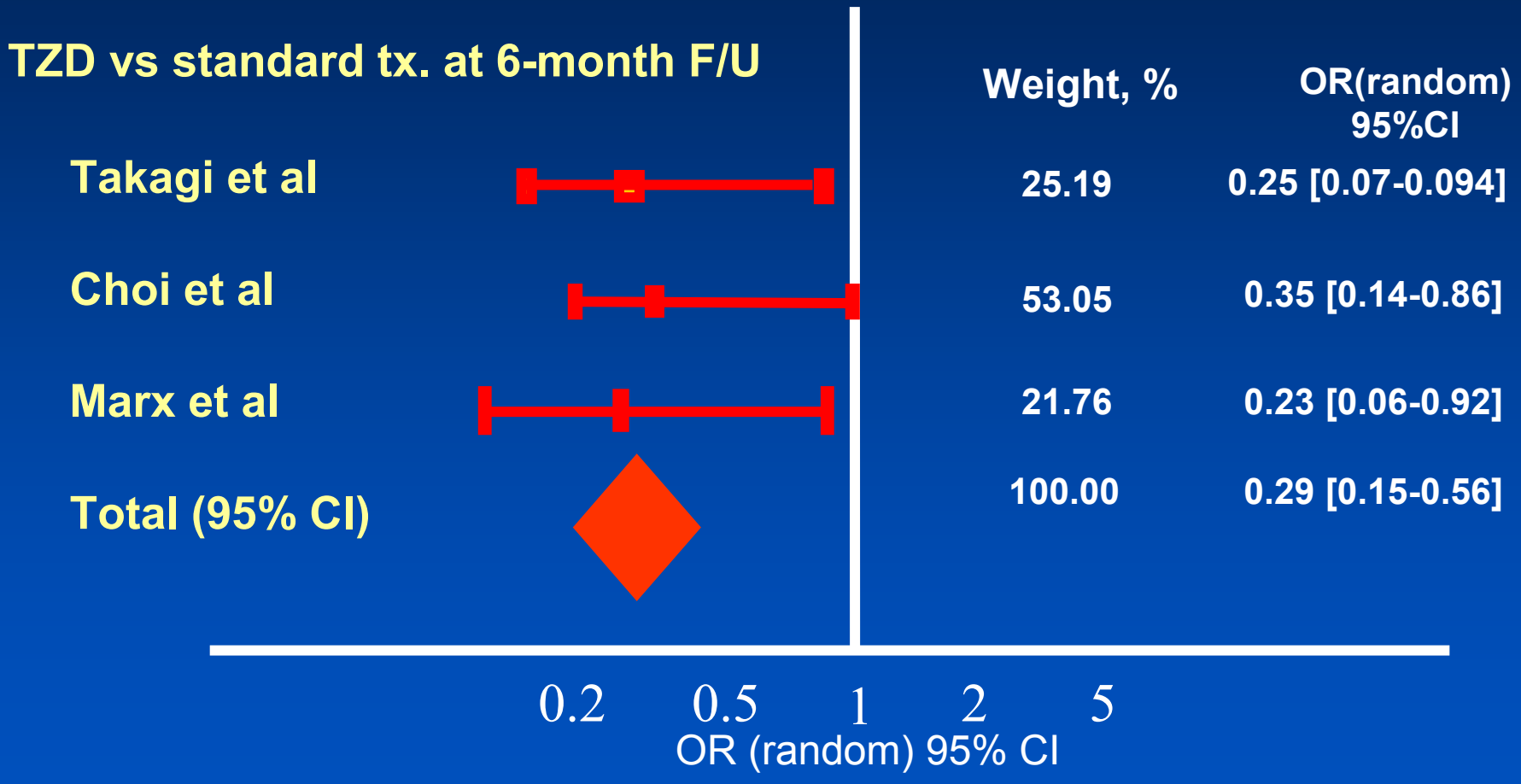


Kuchulakanti et al. Am J Cardiol 2005;96:1100

How to improve the clinical outcomes after PCI in DM

- Drug-eluting stent
- Thiazolidinediones
- Cilostazol
- Glycoprotein IIb/IIIa inhibitors

Effect of Thiazolidinedione on Restenosis
: A meta-analysis of randomized controlled trials



Rosmarakis et al. Am Heart J 2007;154:144

How to improve the clinical outcomes after PCI in DM

- Drug-eluting stent
- Thiazolidinediones
- Cilostazol
- Glycoprotein IIb/IIIa inhibitors

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

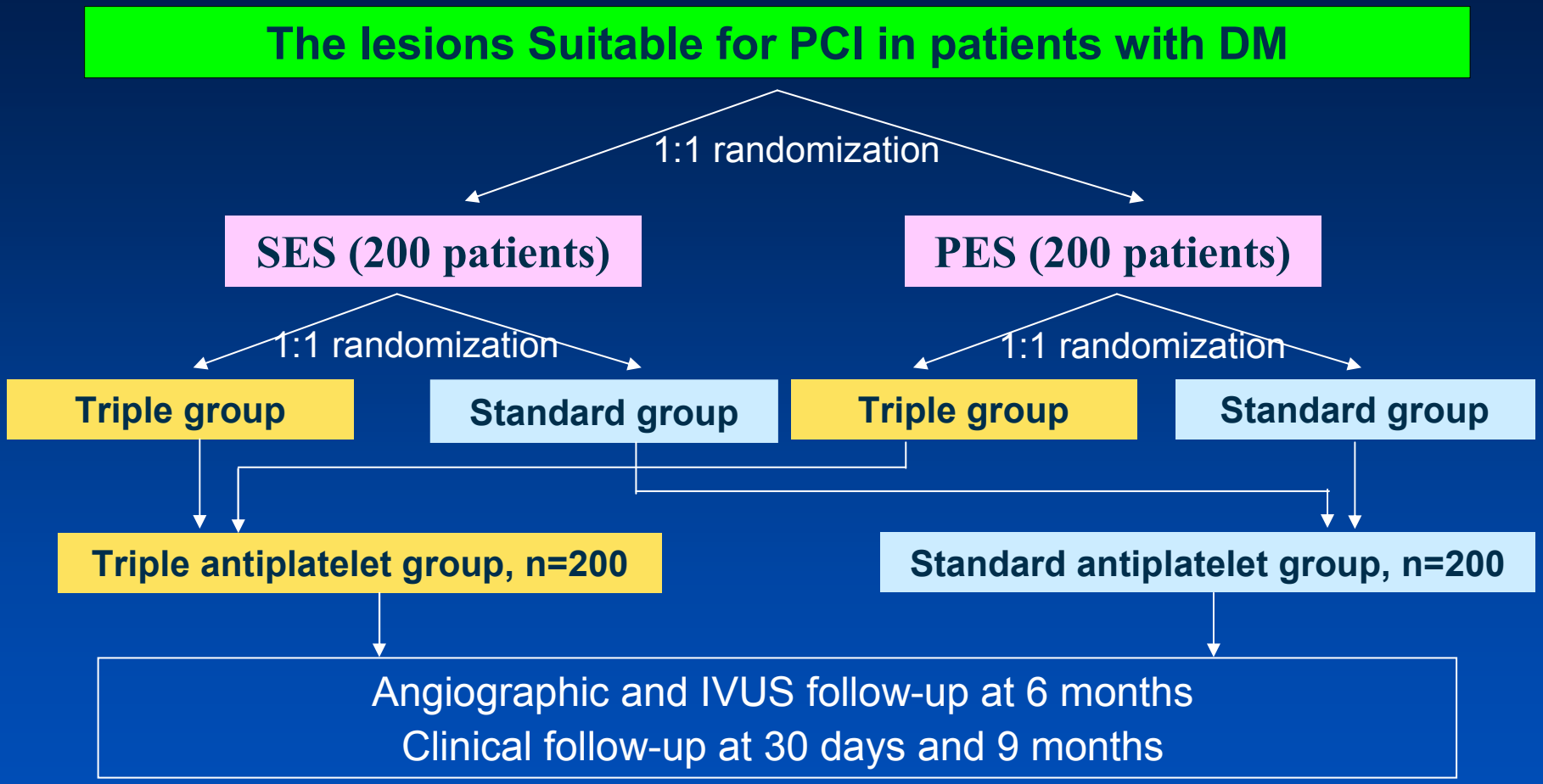
:*D*rug-*E*luting stenting followed by *C*ilostazol treatment reduces *LA*te *Re*stenosis in Patients with *Diabetes* mellitus

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

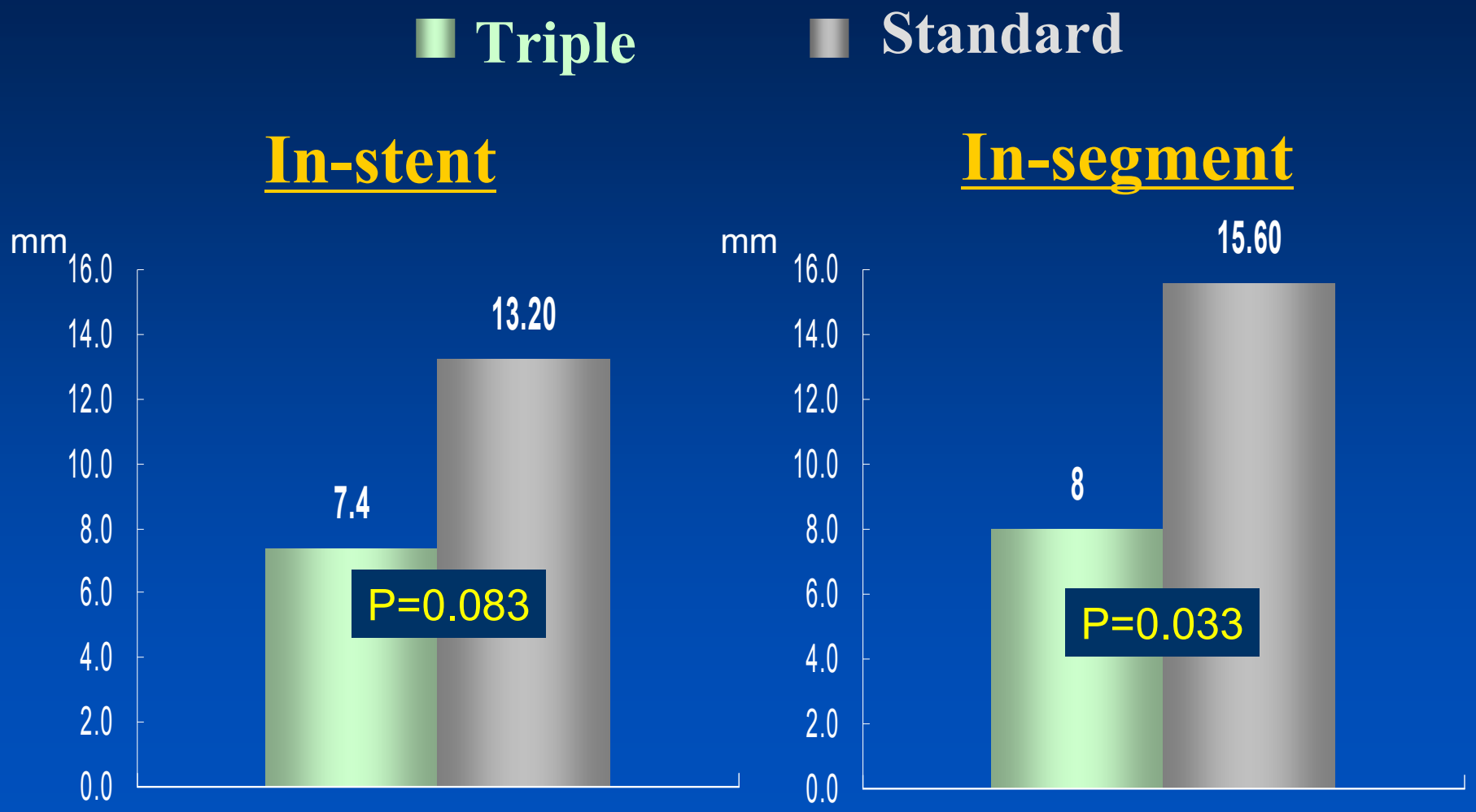
Asan Medical Center,
University of Ulsan College of Medicine, Seoul, Korea

DECLARE-DIABETES Trial Design



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

Restenosis rate



DECLARE-DIABETES

MACE at 9-Months

	Triple	Standard	P
Patients	**200**	**200**	
Death	1(0.5%)*	0	0.999
Cardiac	1	0	
Non-cardiac	0	0	
MI	1 (0.5%)*	1 (0.5%)	0.999
Stent thrombosis	0	1 (0.5%)	0.999
Acute	0	1	
Subacute	0	0	
Late	0	0	
TLR	5 (2.5%)	14 (7.0%)	0.034
Death/MI/TVR	8 (4.0%)	16 (8.0%)	0.092
MACE (Death/MI/TLR)	6 (3.0%)	14 (7.0%)	0.066

* This patient was dead due to non-target vessel AMI 6 months after index procedure.

Predictors of angiographic restenosis and clinical outcomes on multivariate analysis

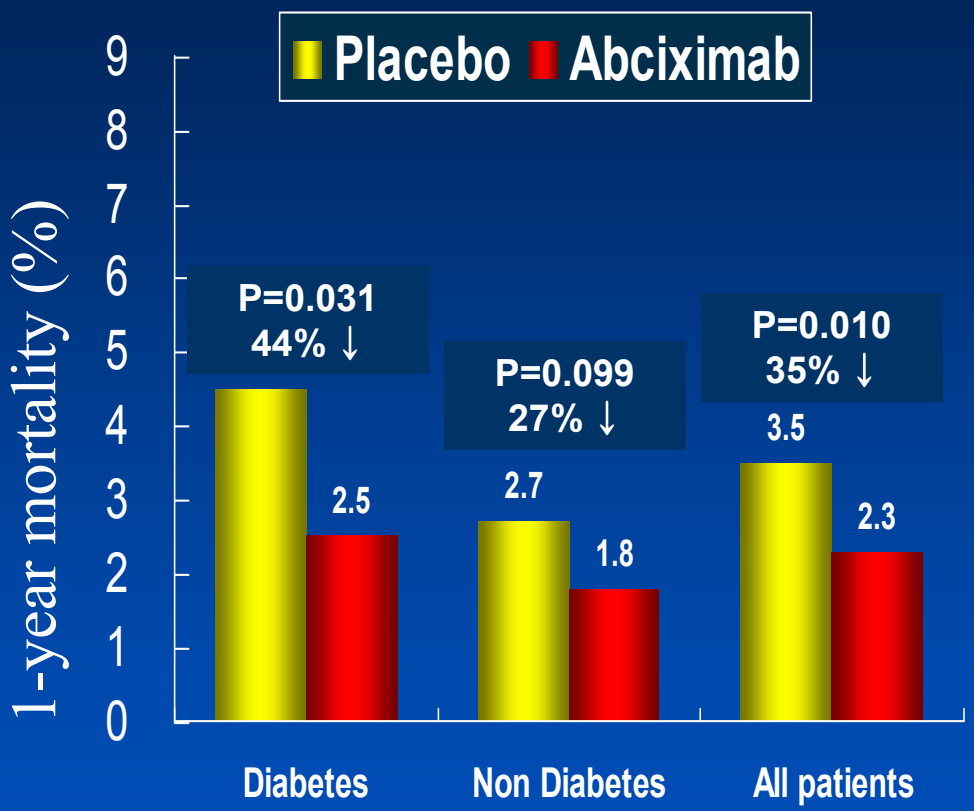
	OR	95% CI	p
Angiographic restenosis			
SES	0.15	0.06-0.40	0.0001
Cilostazol	0.32	0.11-0.89	0.029
Lesion length	1.03	1.01-1.06	0.013
Post-MLD	0.17	0.05-0.28	0.005
TLR			
SES	0.24	0.07-0.81	0.021
Cilostazol	0.26	0.07-0.95	0.042
MACE			
SES	0.21	0.06-0.71	0.012

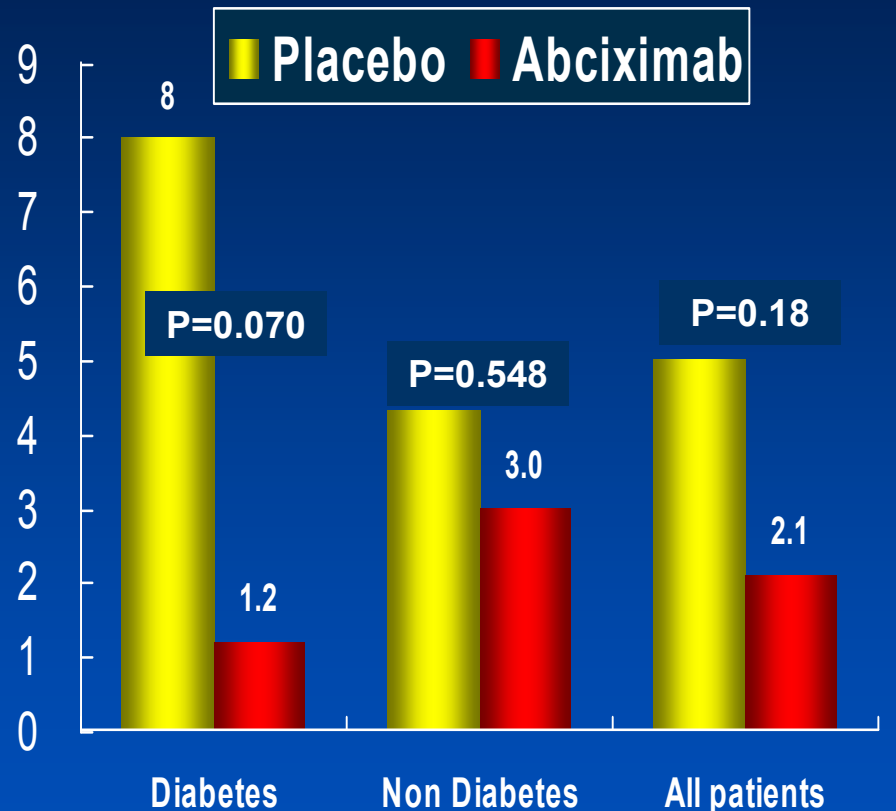
How to improve the clinical outcomes after PCI in DM

- Drug-eluting stent
- Thiazolidinediones
- Cilostazol
- Glycoprotein IIb/IIIa inhibitors

Diabetes-PCI-*GPIIb/IIIa* &1 Yr Mortality

EPIC, EPILOG, EPISTENT

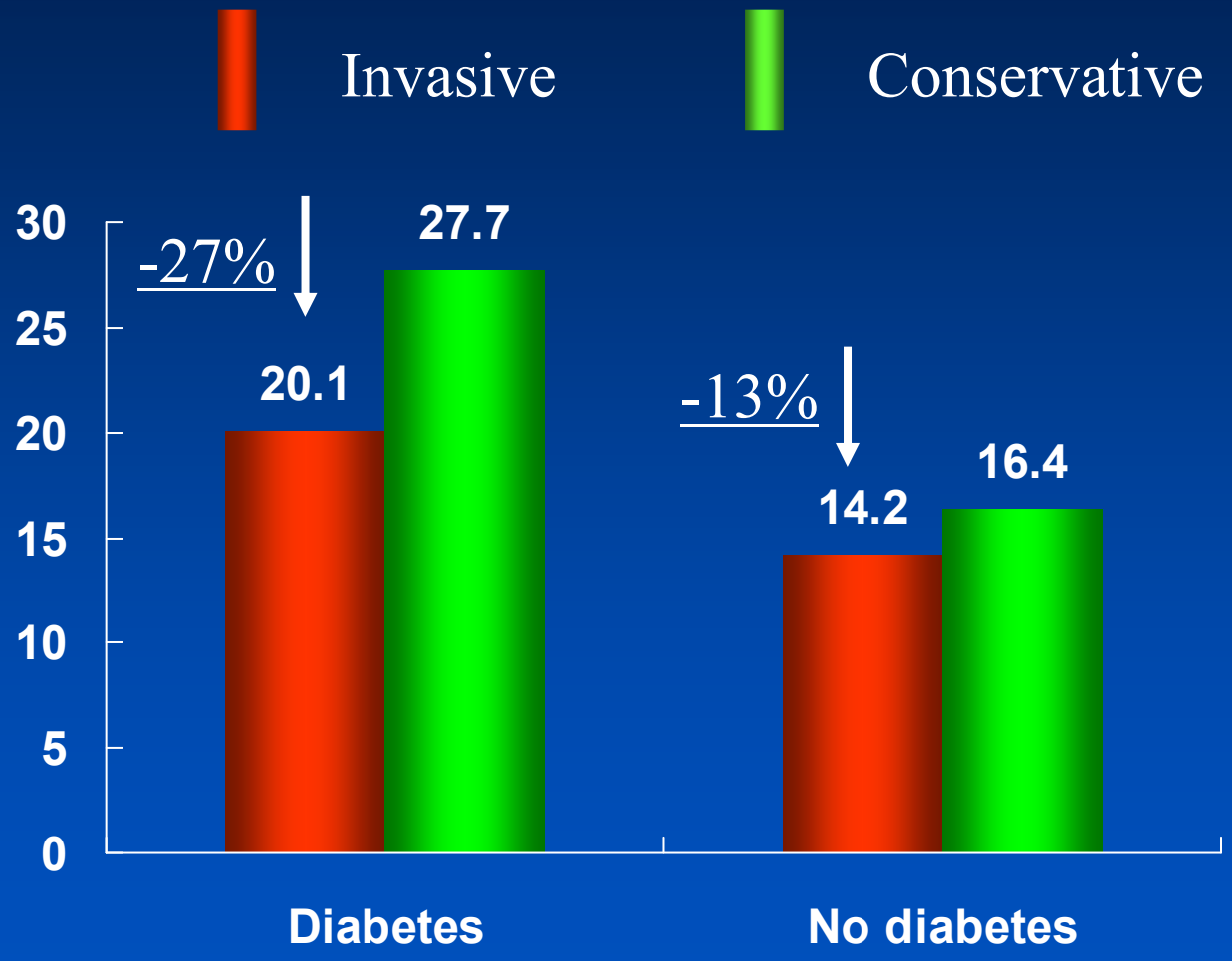




DL Bhatt et al., JACC 2000;35:922

GPIIb/IIIa inhibitor for ACS

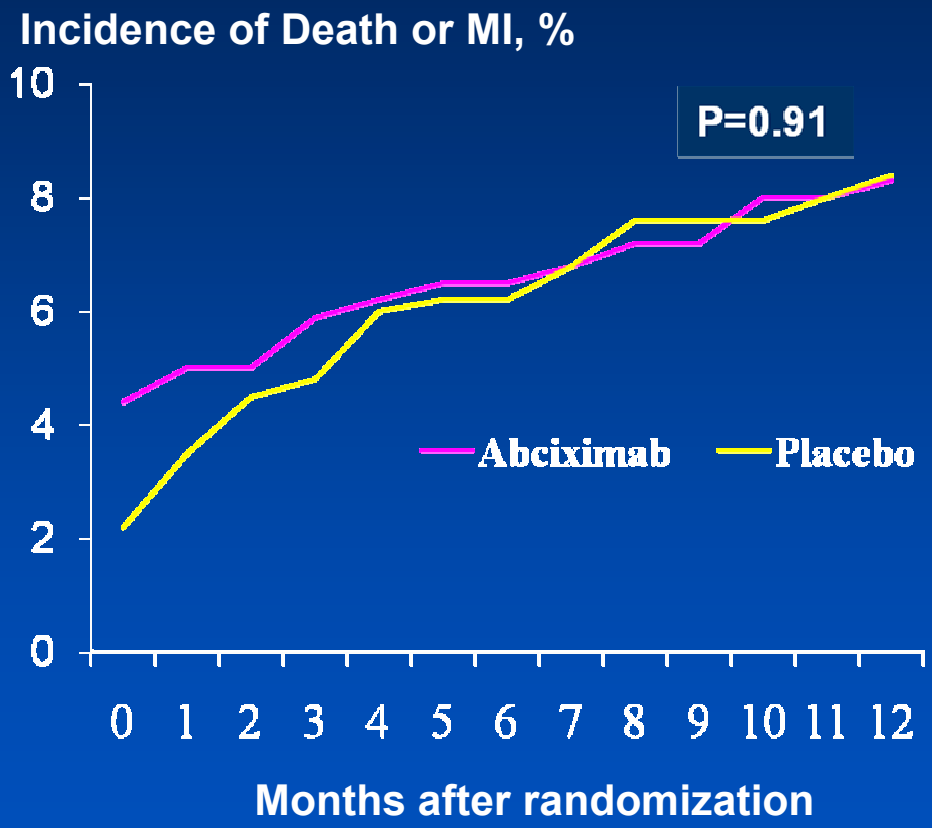
6-month death /MI /revascularization in TACTICS

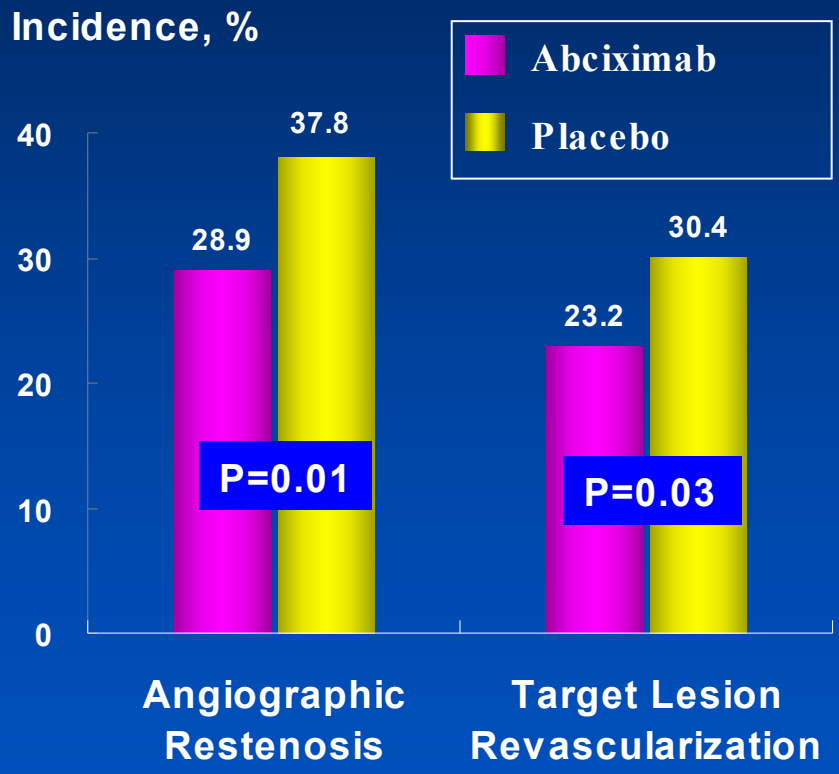


Cannon CP et al. N Engl J Med 2001;344:1879

Randomized Trial of Abciximab in Diabetes with PCI after High Loading Dose of Clopidogrel

ISAR-SWEET





Mehilli et al., Circ 2004;110:3627

Adjunctive Therapies Are Important for Improving Outcomes Following PCI in Diabetics

- HMG Co-A Reductase Inhibitors (Statins)
- ACE Inhibitors
- Angiotensin-Receptor Blockers
- Beta-Receptor Blockers
- Extended Thienopyridine Therapy

PCI in Diabetics: Summary

- Aggressive revascularization strategy improves the clinical outcomes in diabetics with multivessel disease.
- Diabetics has high restenosis rate and poor clinical outcomes compared to non-diabetics after PCI.
- Poor clinical outcomes in DM after PCI are associated with poor glucose control, higher restenosis, diabetic nephropathy.

PCI in Diabetics: Summary

- Diabetic patients treated with DES have a reduced risk of restenosis compared with BMS.
- Cypher versus Taxus: Conflicting data exist. In real-world practice, the two stents appear to have similar clinical outcomes.
- Adjunctive pharmacologic therapy (GP IIb/IIIa, ACEI, extended thienopyridines, tight glycemic control, cilostazol) is likely to further improve outcomes after PCI in diabetic patients.