# Diabetes in Interventional Cardiology

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# Background

- CHD is a major cause of morbidity and mortality among patients with DM.
- Mortality due to heart disease is 2 to 4 times higher than in patients without diabetes.
- Patients with DM account for >25% of all PCIs
- Diabetic patients are at increased risk of adverse outcome after PCI.

- **Factors related with adverse outcome after PCI**
  - Diabetes-related
  - Procedure-related
- **DES vs. BMS**
- **SES vs. PES**
- **Safety concern : DES**
- **PCI vs. CABG**

## Why Do Patients With Diabetes Have Worse Outcomes After PCI?

- More extensive atherosclerosis and diffuse disease
- Multivessel, smaller, calcified lesion
- Longer, LM disease
- Greater plaque burden

# Adverse outcomes after PCI

- **Procedural Cx**. occur more frequently
- **Renal dysfunction** after PCI occurs more frequently
- DM was an independent predictor of **acute stent thrombosis**
- **Revascularization for restenosis** is more common
- Higher frequency of **new lesions** at 9 Months

# Diabetes-related factors for their impact on outcome after PCI

**65/Female**

C.C: severe chest pain

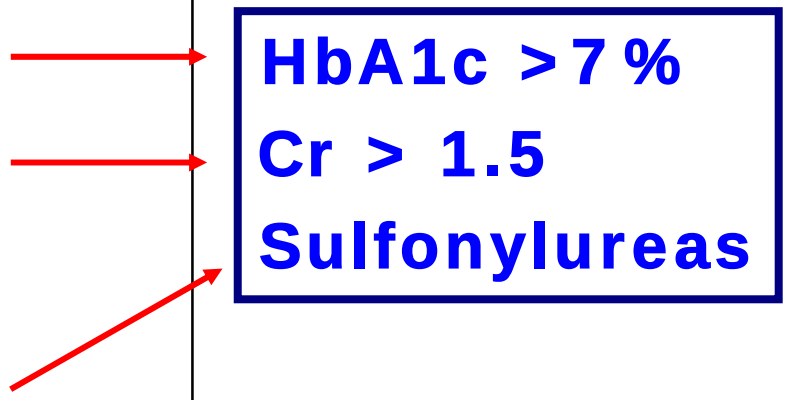
Bl.glucose : 265 mg/dl

$HbA1_C$ : 7.9%

Cr : 2.1 mg/dl

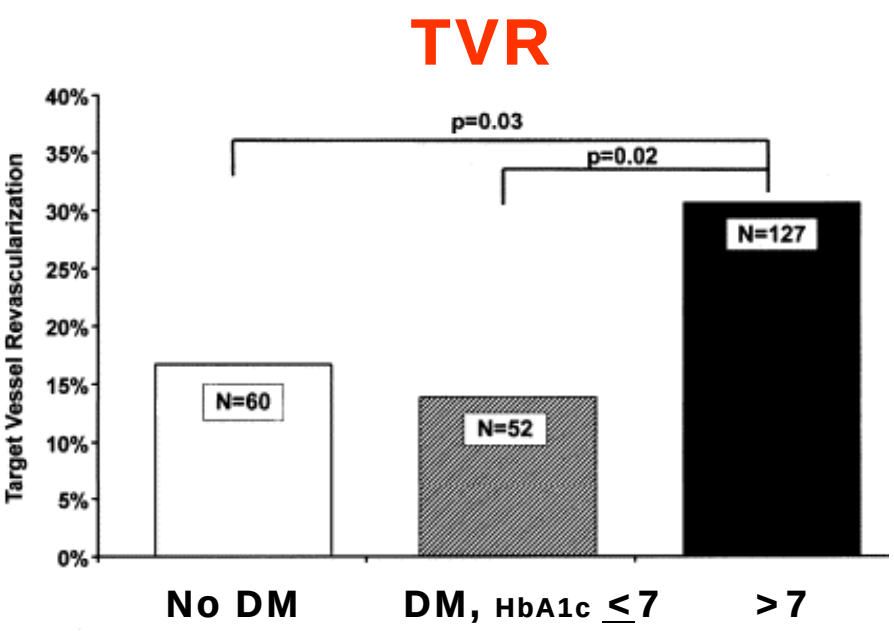
proteinuria

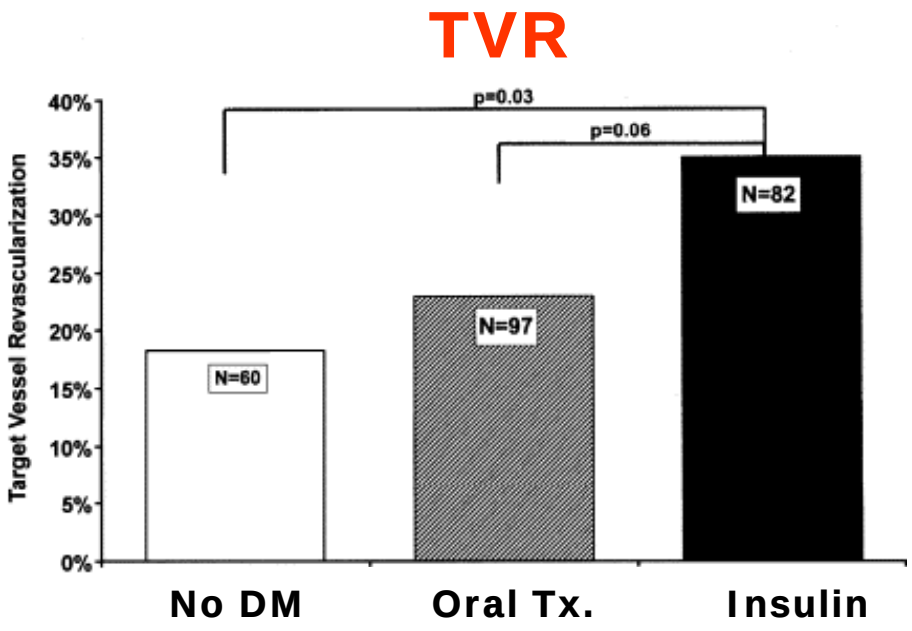
Rx: sulfonylurea



# Metabolic control and outcomes after PCI

## Glycemic control and outcomes 1 year after PCI




Corpus et al. JACC 2004:43:8

# Procedure-related factors for their impact on outcome after PCI

**65/Female**

C.C: severe chest pain

ECG : ST depression in inf.leads

Troponin I : 2.3 ng/ml

Impression : ACS

**GP IIb/IIIa blockade**

**DES vs BMS**

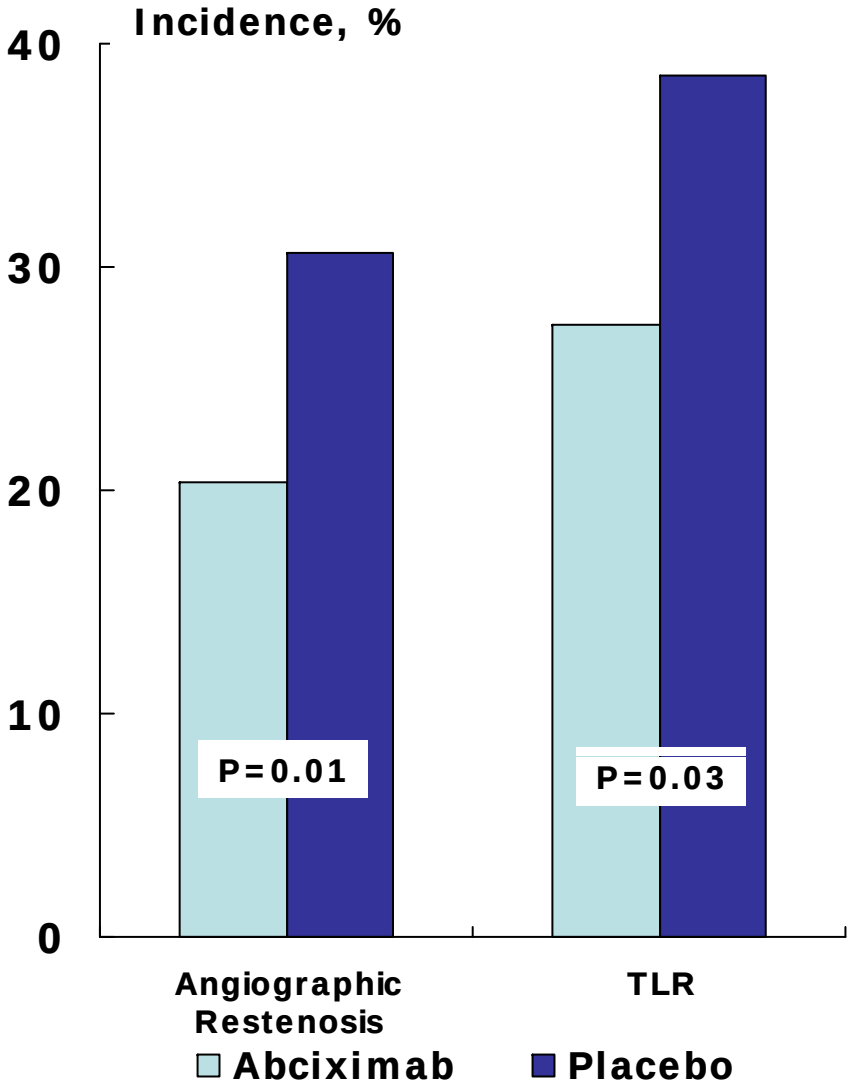
**SES vs PES**

**PCI vs CABG**

# GP IIb/IIIa blockade, Diabetes, and PCI

## ISAR-SWEET

- 701 diabetic patients
- Abciximab + heparin or placebo + heparin at PCI
- 600mg of clopodigrel
- POBA 10%
- BMS 80%
- DES 10%
- Primary endpoint :
  - Death or MI at one year
  - Mortality
  - No difference
- Secondary endpoint:
  - Angiographic restenosis




Circulation 2004

# DES vs. BMS

# Limitation of subgroup analysis of randomized trial and registry data

**Demographics**

- DM control
- Lipid concentration
- BP
- Inflammatory marker
- lack of information about anti-diabetic therapy

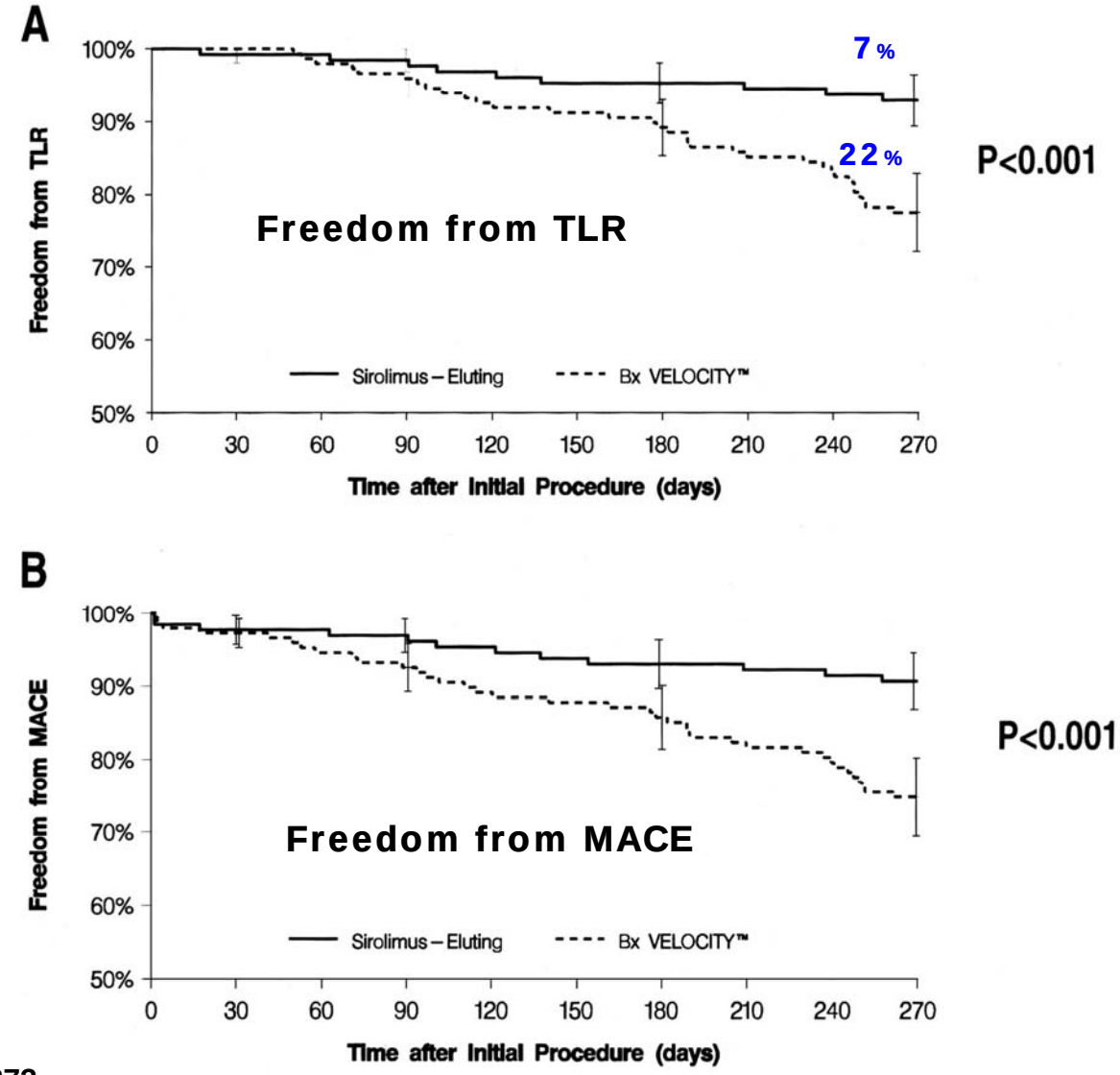
**Trial Design**

- Multicenter trial ?
- Primary endpoint ?
  - Clinical
- Required number of pts enrolled and followed ?
- Primary endpoint reached ?

# DES(SES) vs. BMS

A **SIRIUS** (**SIR**o**l**im**US**-coated Bx Velocity balloon-expandable stent in the treatment of patients with de novo coronary artery lesions) **Substudy**

279 DM pts
9 Mo F/U
TLR, MACE




Moussa, I. et al. Circulation 2004;109:2273-2278

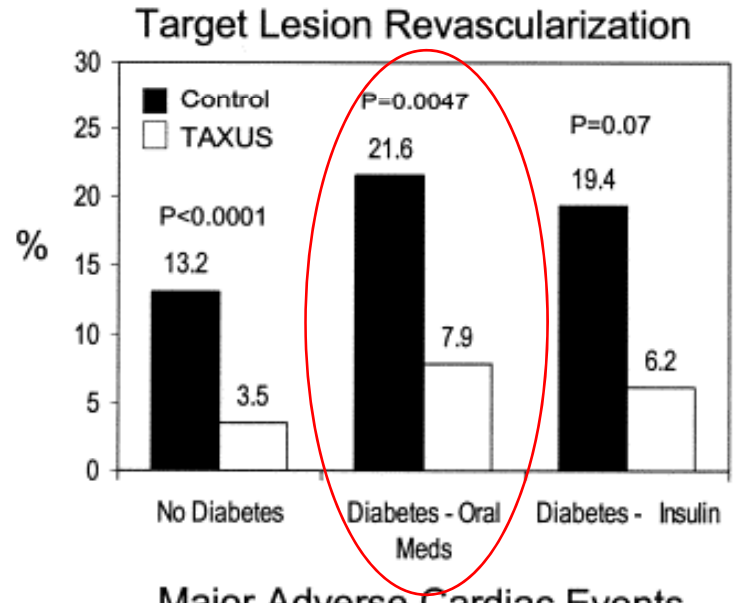
# DES(PES) vs. BMS

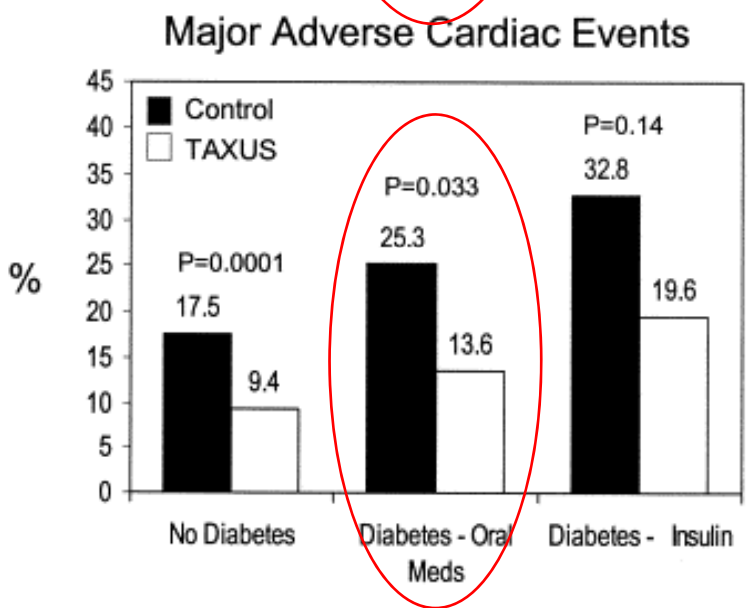
Outcomes with the polymer-based paclitaxel-eluting TAXUS stent in patients with DM

**TAXUS-IV**

**Substudy**

318 DM pts
12 Mo F/U
MACE, TLR,




Hermiller et al. JACC 2005;109:1172

# DES(SES) vs. BMS

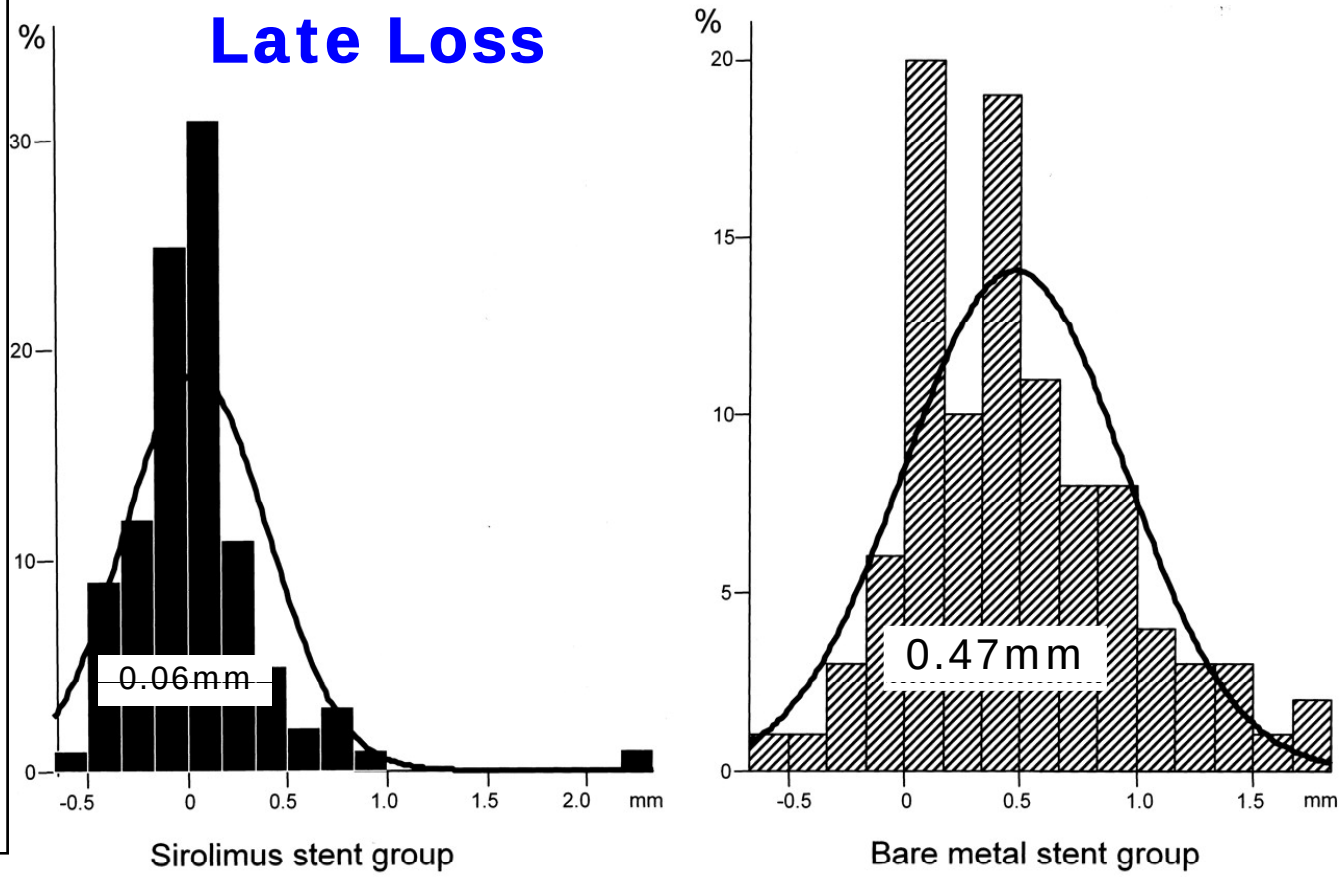
The Diabetes and Sirolimus-Eluting Stent (**DIABETES**) Trial

Multicenter, **Randomized**,

80 vs 80
**9mo** F/U

$1^0$ end point :
**In-segment LLL**
$2^0$ end point :
TLR,MACE

## Late Loss




Sabate, M. et al. Circulation 2005;112:2175-2183

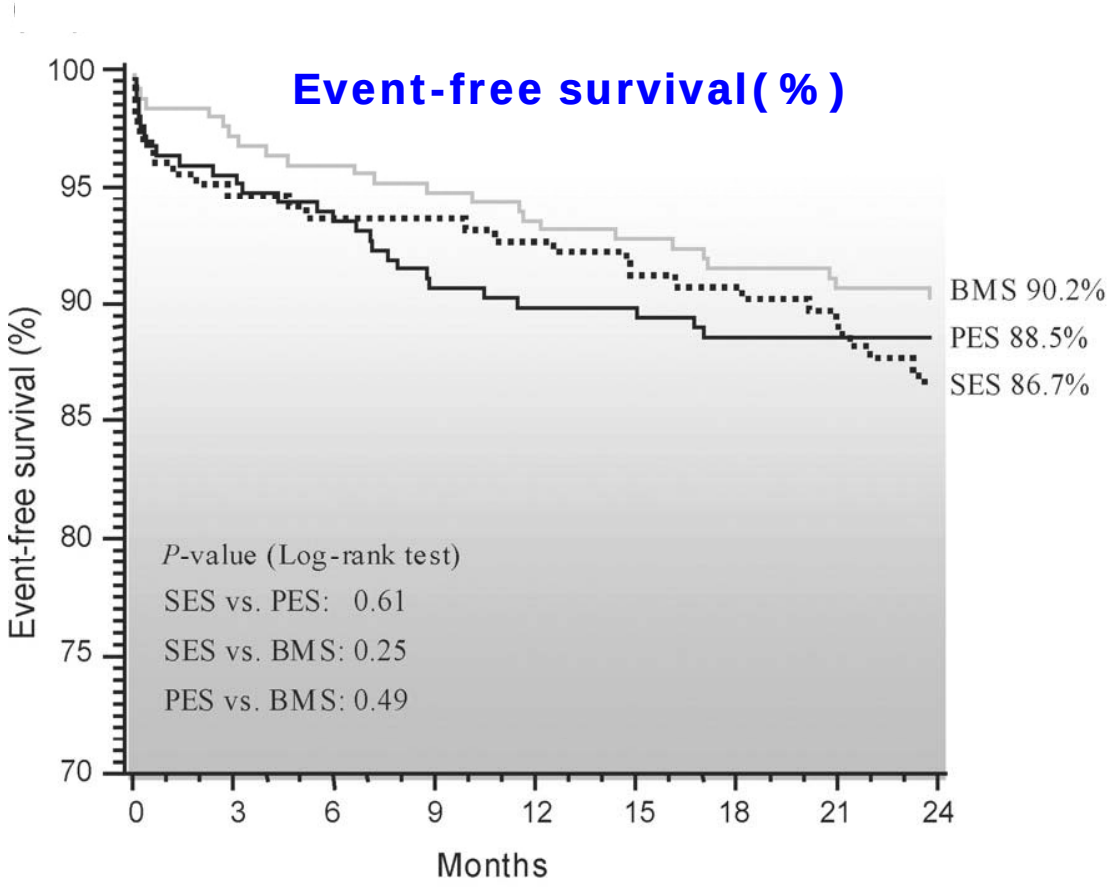
# DES(SES, PES) vs. BMS

As part of **RESEARCH** and **T-SEARCH** registries
**60 % high risk**

708 DM pts
**2 yr** F/U

$1^0$ end point :
**MACE at 2 Yrs**
*propensity analysis

Limitation :
Non-randomized , registry trial
Compared group : not completely identical




Daemen et al. Eur Heart J 2007;28:26

# DES(SES) vs. BMS

**Real-world Multicenter registry**

**Off-label**
- Multi-vessel lesion
- Complex lesion
- s/p MI lesion

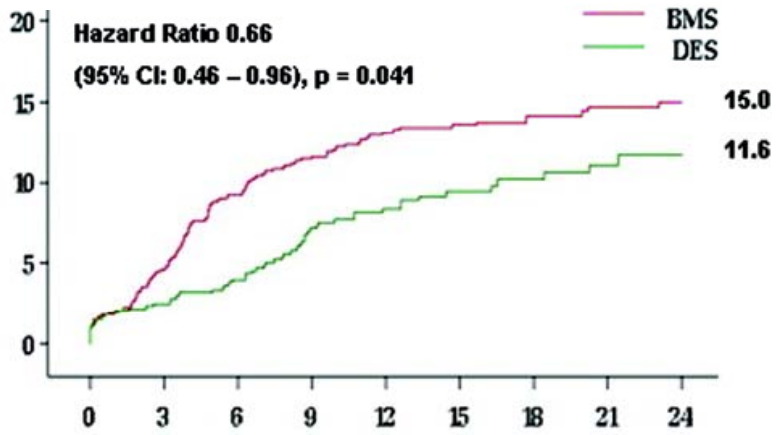
559 DM pts
**2 yr** F/U

$1^0$ end point : **TVR,MACE**

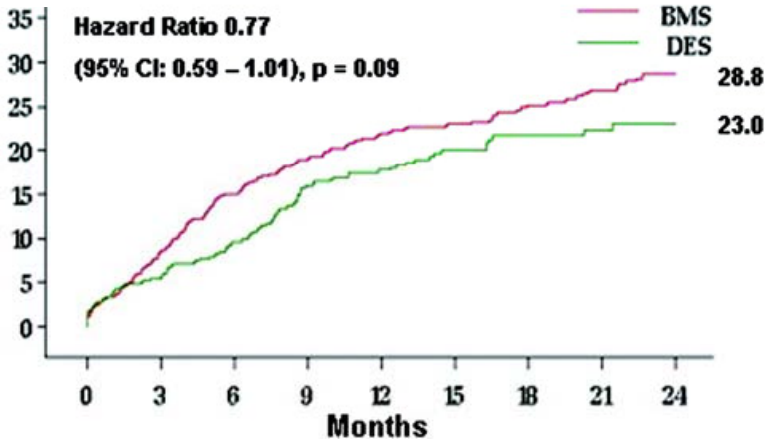
*after propensity score adjustment

Limitation :
Nonrandomized comparison

**TVR %**

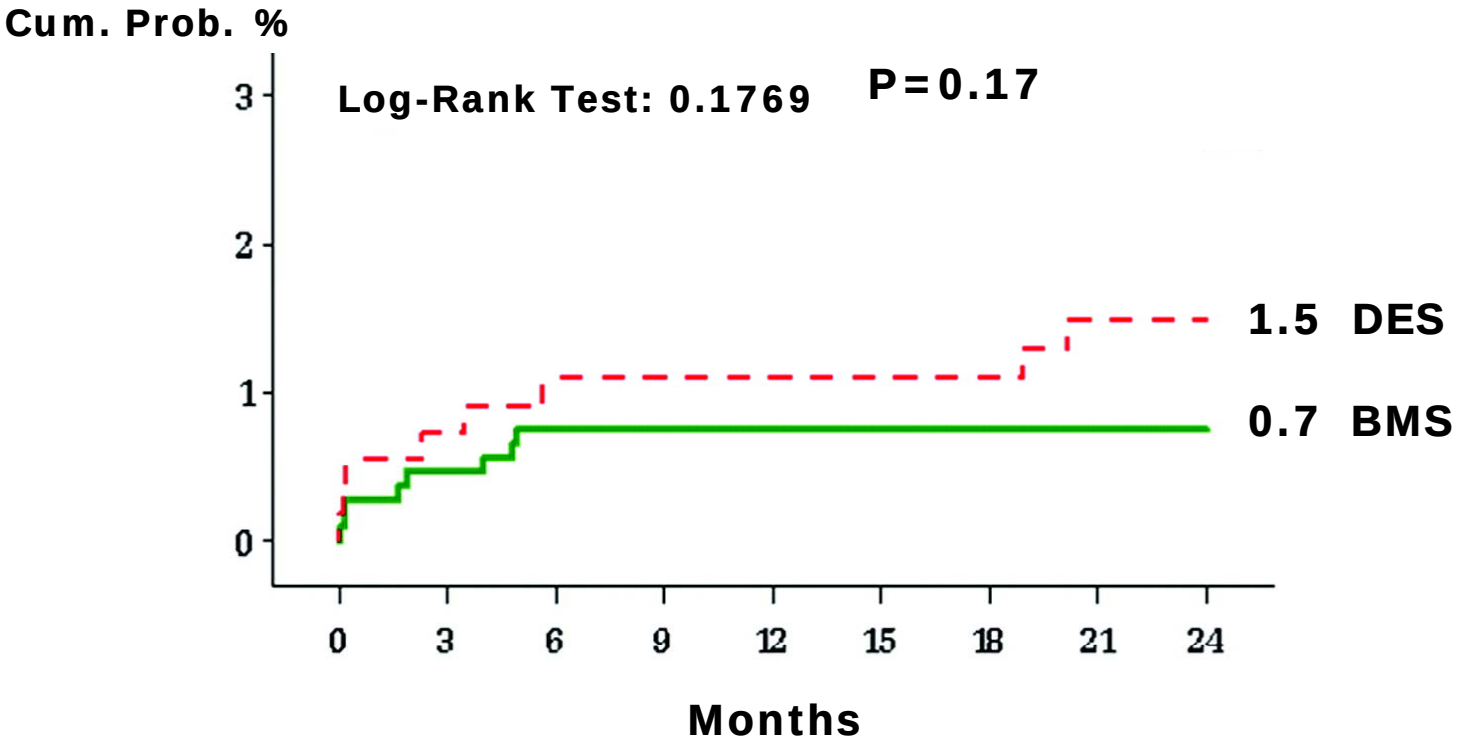



**MACE %**




Ortolani et al. Circulation 2008;117:923

# 2-year incidence of angiographically proven stent thrombosis




Ortolani et al. Circulation 2008;117:923

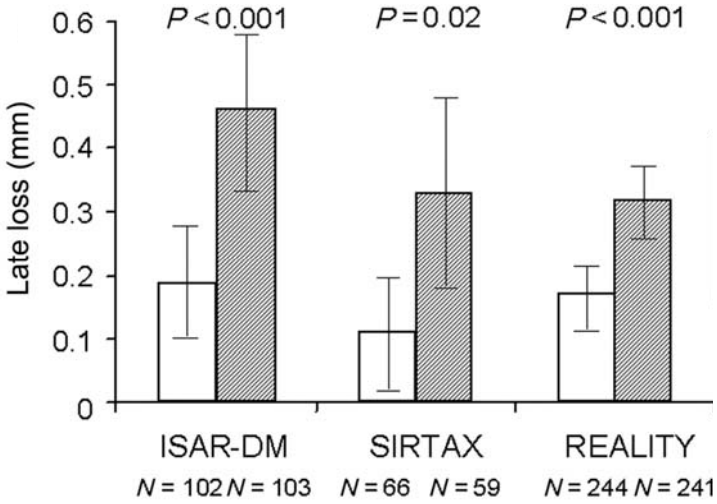
# SES vs. PES

# SES vs. PES

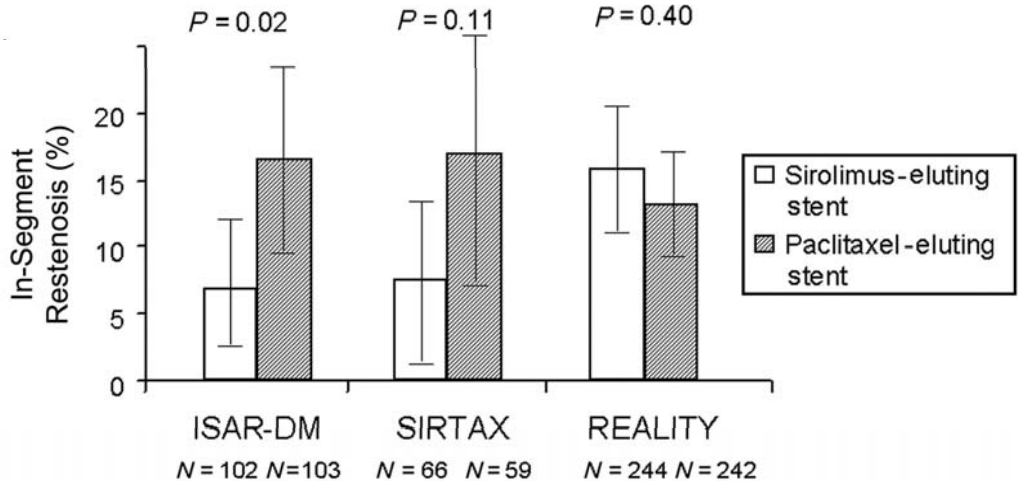
## ISAR-DIABETES, REALITY, SIRTAX trial

## Late Loss and In-Segment Restenosis

### Late Loss




### In-Segment Restenosis




**Randomized, Controlled Studies Comparing Cypher Stents to Taxus Stents**

Billinger, M. et al. Eur Heart J 2008

**Randomized, Controlled Studies Comparing Cypher Stents to Taxus Stents**

| | ISAR-Diabetes | SIRTAX | REALITY |
|---|---|---|---|
| Study Design | non-inferior | Cypher superior | Cypher superior |
| Multicenter | no | no | yes |
| Clinical primary endpoint | no | yes | no |
| Primary endpoint | Angiographic | clinical | angiographic |
| Time of PE | 6 mo | 9 mo | 8 mo |
| Parameter | In-segment LLL | MACE | In lesion RR |
| Patients | 125/125 | 503/509 | 684/669 |
| Lesion length | 13.8/12.4 | 12.4/13.4 | 17.0/17.3 |
| Vessel diameter | 2.7/2.8 | 2.25-4.0 | 2.25-3.02 |
| Restenosis in segment | 6.9/16.5* | 6.7/11.9* | 9.6/11.1 |
| Late lumen loss in stent | 0.43/0.67* | 0.13/0.25* | 0.09/0.31 |
| TVR | 6.4/12.2 | 6/0/9.2* | 1.6/1.2 |
| MACE | | 6.2/10.8* | 9.2/10.8 |
| Primary endpoint reached | (No) in seg LL | yes | no |
| Major limitation | No clinical primary endpoint | No multicenter trial | No clinical primary endpoint |

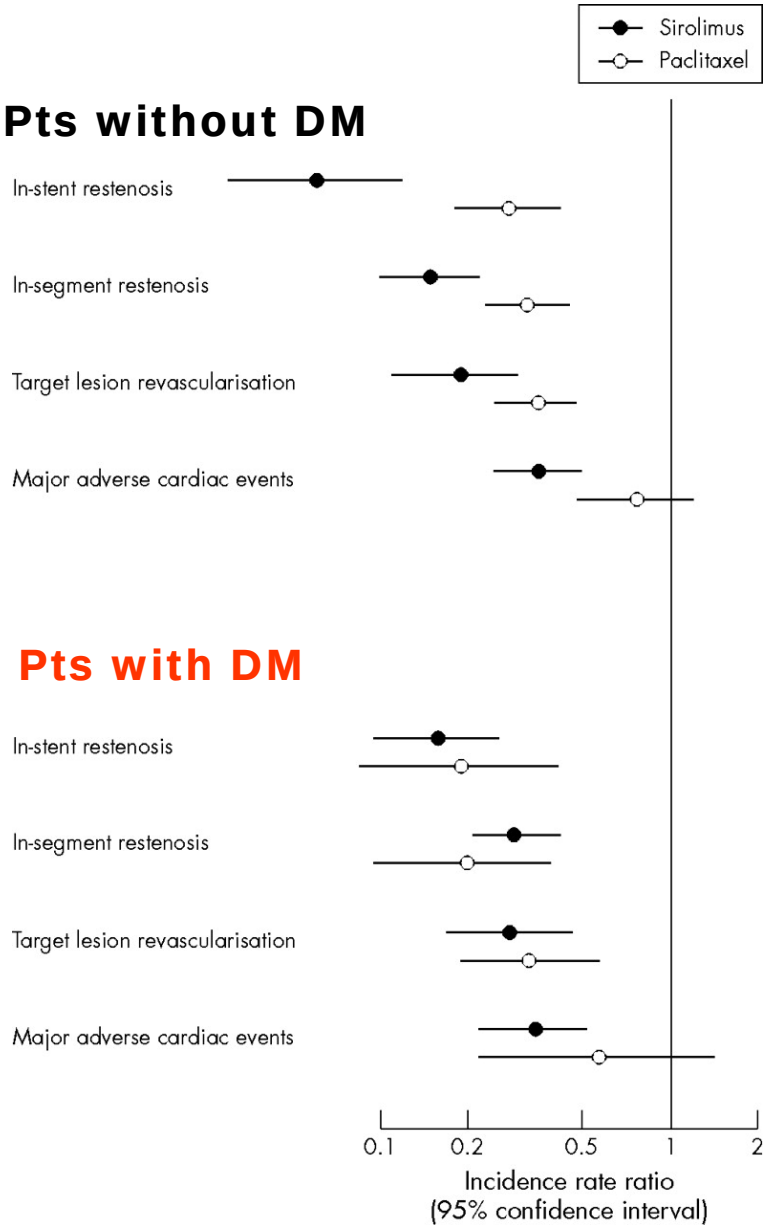
## Indirect comparision PES vs.DES

**Meta-analysis of**
**10 trials, RCT**
**(SIRIUS, E-SIRIUS, C-SIRUS, DiABETES, RAVEL, SES-SMART TAXUS I, II, IV, VI)**

1146 DM pts
6-9 Mo, 8-24Mo

In-stent restenosis,
in-segment restenosis,
TLR, MACE

Limitation :
not designed to examine the effectiveness of DES
0nly 10 trial was identified
Average f/u was relatively short
No data of glycemic control




**Stettler et al. Heart 2006 :92:650-**

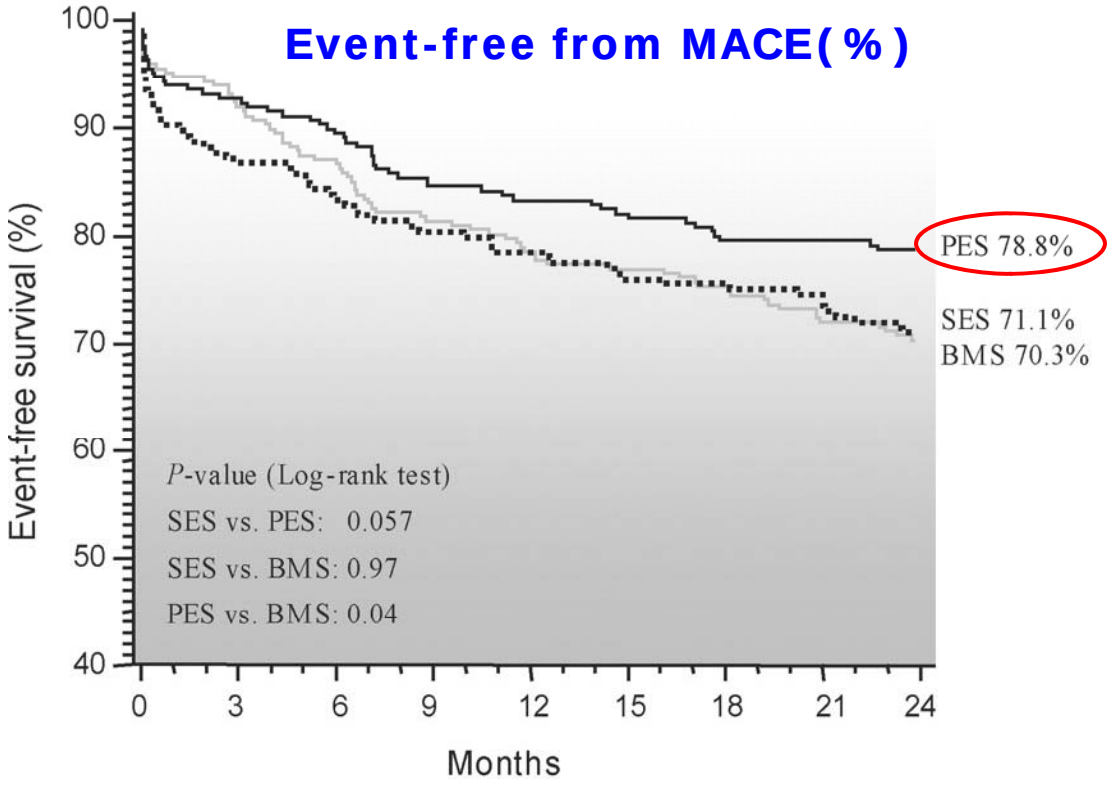
# SES vs. PES

As part of **RESEARCH** and **T-SEARCH** registries
**REAL WORLD**

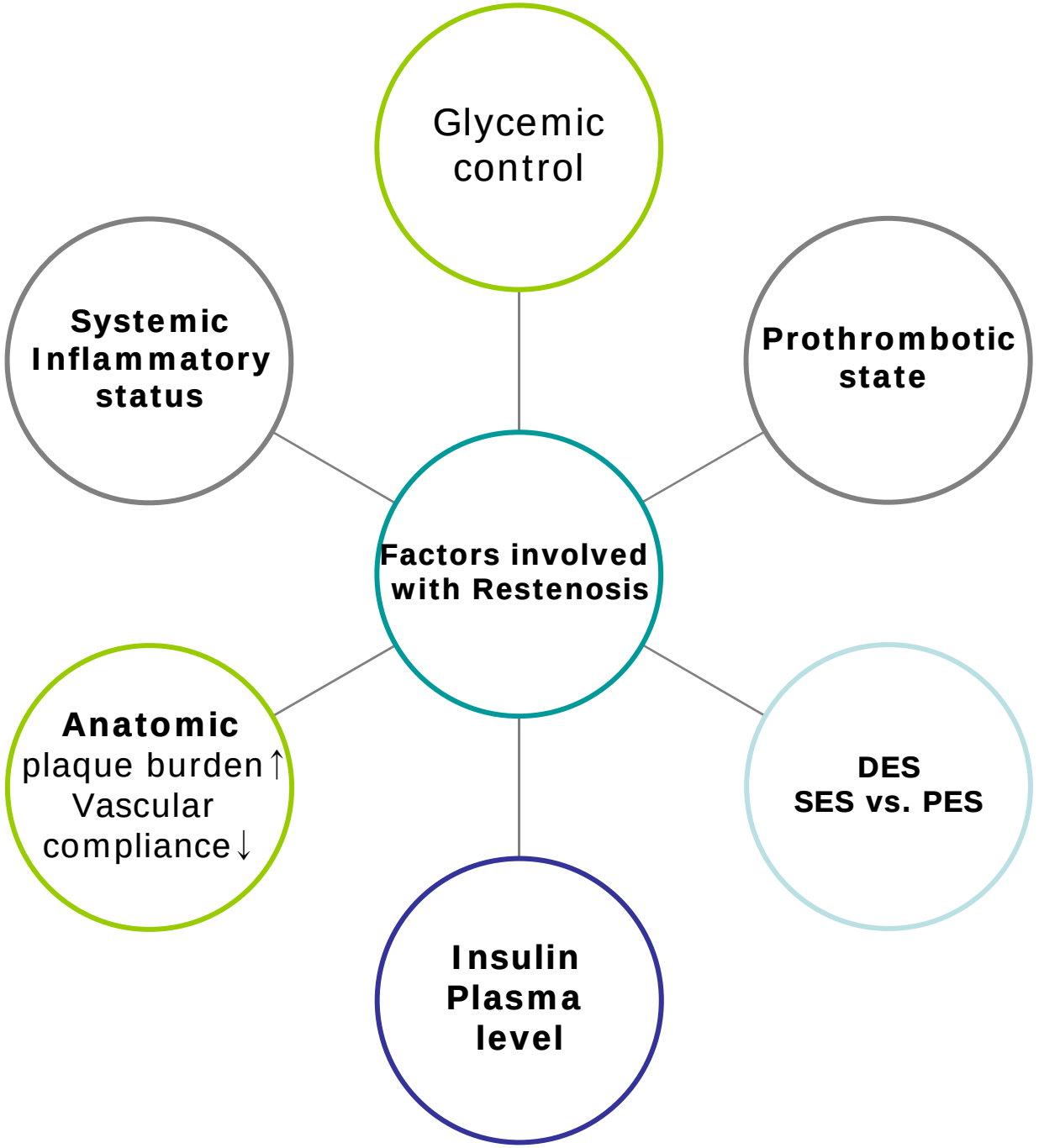
708 DM pts
**2 yr** F/U

$1^0$ end point :
**MACE at 2 Yrs**

Limitation :
Non-randomized , registry trial
Compared group : not completely identical




Daemen et al. Eur Heart J 2007;28:26

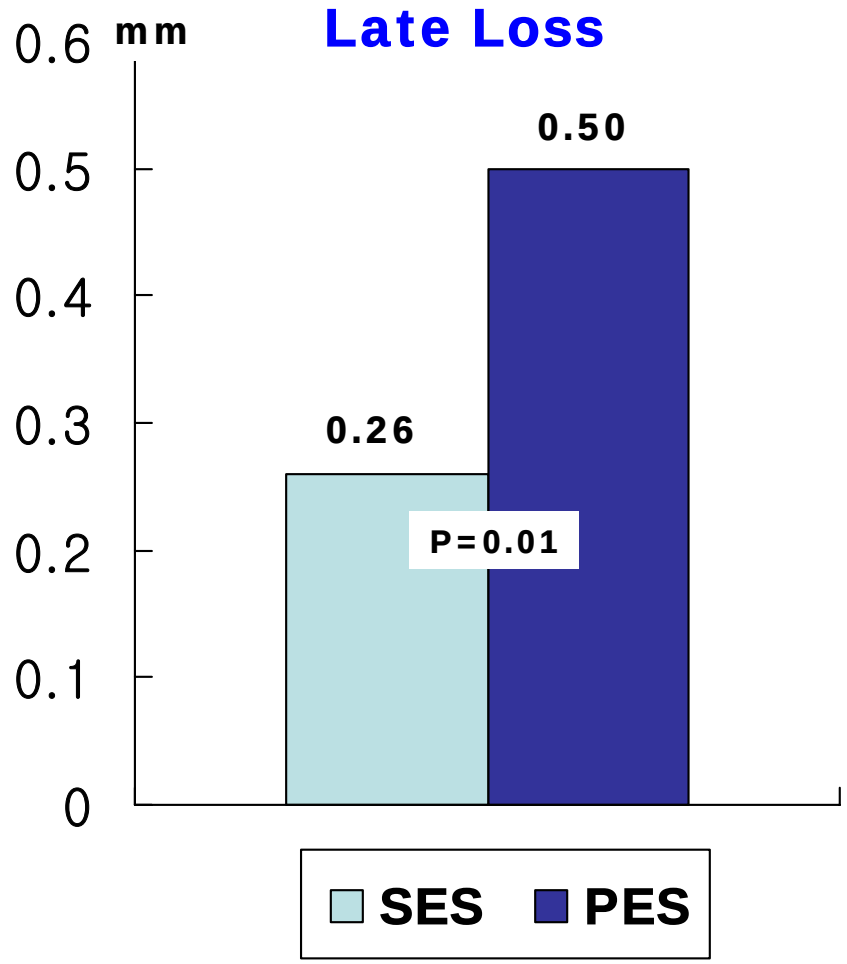

Glycemic control
Systemic Inflammatory status
Prothrombotic state
Factors involved with Restenosis
Anatomic
plaque burden↑
Vascular compliance↓
DES
SES vs. PES
Insulin
Plasma level

# SES vs. PES

**Head-to-Head comparison in the same diabetic pts with multiple coronary a. lesion**

**120 pts , 8 Mo**

**$1^0$ end point : in-stent LLL**




Tomai et al. Diabetes Care,31:15,2008

# Safety Concern of DES

# DES(SES) vs. BMS

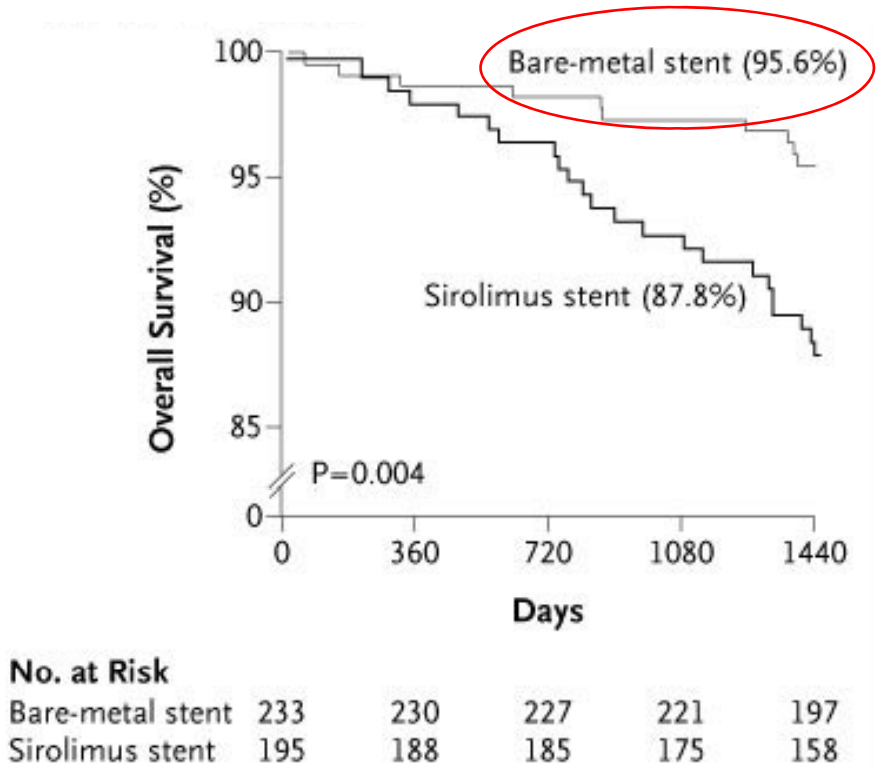
A pooled analysis, 4 Randomized trials (**RAVEL, SIRIUS, C-SIRIUS, E-SIRIUS**)

**Subgroup analysis**

Excessive Death:
d/t cardiac and noncardiac cause

Limitation :

Clopidogrel at least 2 or 3 Mo
No of fatal event so small due to by chance
Lower than mortality in BMS group
No mortality difference /c DM /s DM




**very late ST**

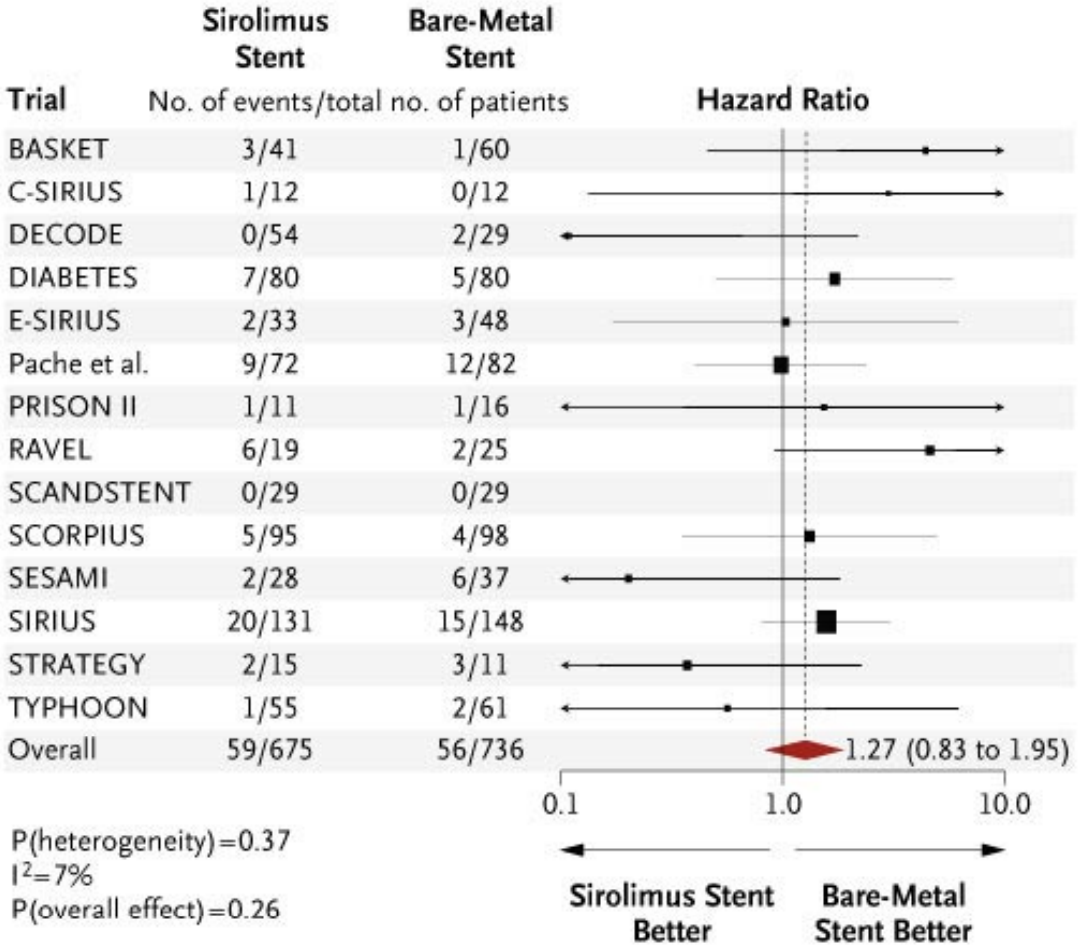
**3 cases**

**11 cases**

**Spaudling et al. NEJM 2007;356110**

# DES(SES) vs. BMS
## meta-analysis of 14 RCT

mean follow-up interval, 12.1 to 58.9 months
primary end point : death from any cause.
other outcomes : stent thrombosis, the composite end point of death or myocardial infarction, and the composite of death, myocardial infarction, or reintervention.




Kastrati et al. NEJM 2007; 356:1030356110

# DES(PES) vs. BMS

## Pooled analysis from 5 RCT(TAXUS I,II,,IV,V,VI)

## 3,513(827 DM), safety outcome , 4 yrs

| | PES | BMS | HR(95% CI) | p Value |
|---|---|---|---|---|
| **Death** | 8.4%(28) | 10.3%(33) | 0.88(0.53-1.45) | 0.61 |
| Cardiac | 4.0%(15) | 3.7%(14) | 1.10(0.53-2.28) | 0.80 |
| Noncardiac | 4.5%(13) | 6.8%(19) | 0.71(0.35-1.44) | 0.34 |
| **MI** | 6.9%(24) | 8.9%(35) | 0.70(0.41-1.17) | 0.17 |
| **Stent thrombosis** | 1.4%(4) | 1.2%(5) | 0.83(0.22-3.09) | 0.92 |

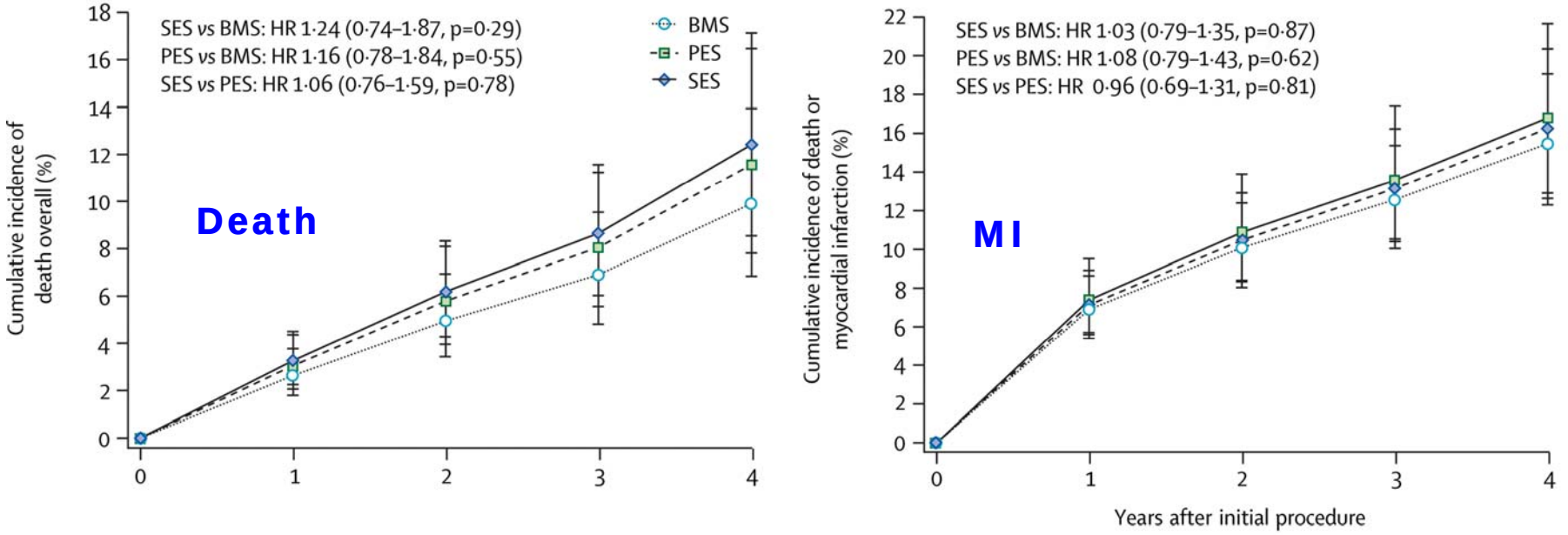
**Limitation**

Single discrete de-novo native coronary artrial lesions in relatively stable pts

Kirtane et al. JACC 2008:51;708

# DES(SES,PES) vs. BMS

**Meta-analysis** : RCT in DES, BMS and SES,PES
30 trials, 14153 (3762 DM) , **4yr** F/U
**Safety outcome** : mortality, MI, stent thrombosis, TLR




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

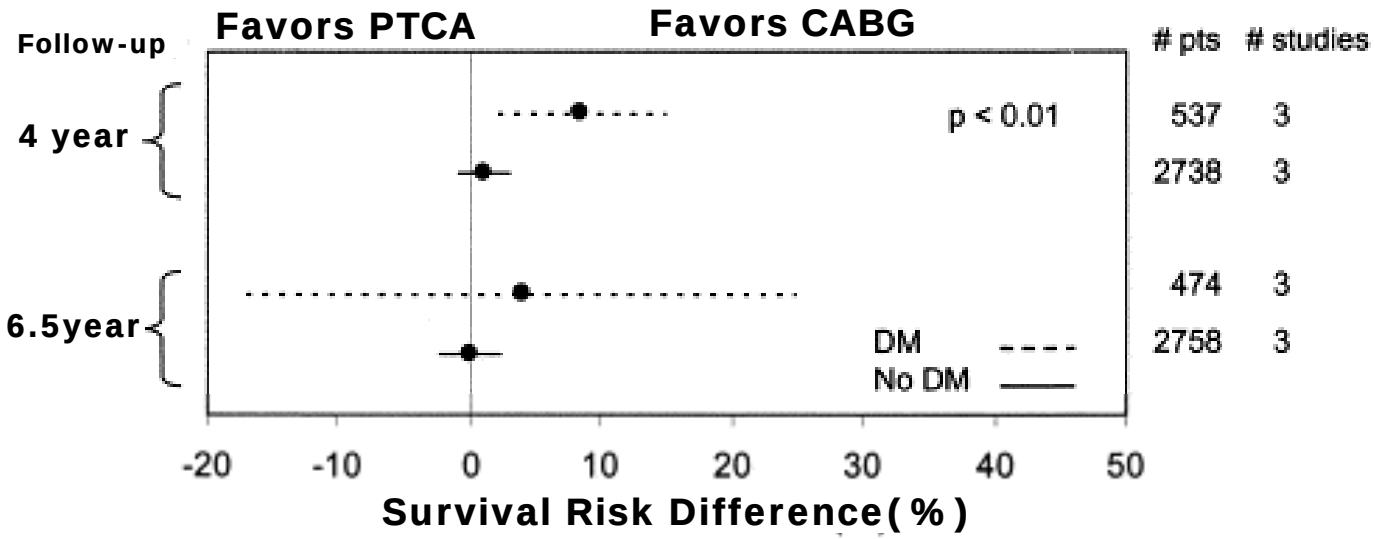
# PCI vs. CABG

# PCI vs.CABG

**Meta-analysis**
**13 RCTS**
- **BARI**
- **EAST**
- **CABRI**
- **RITA**

**Subgroup analysis of DM**

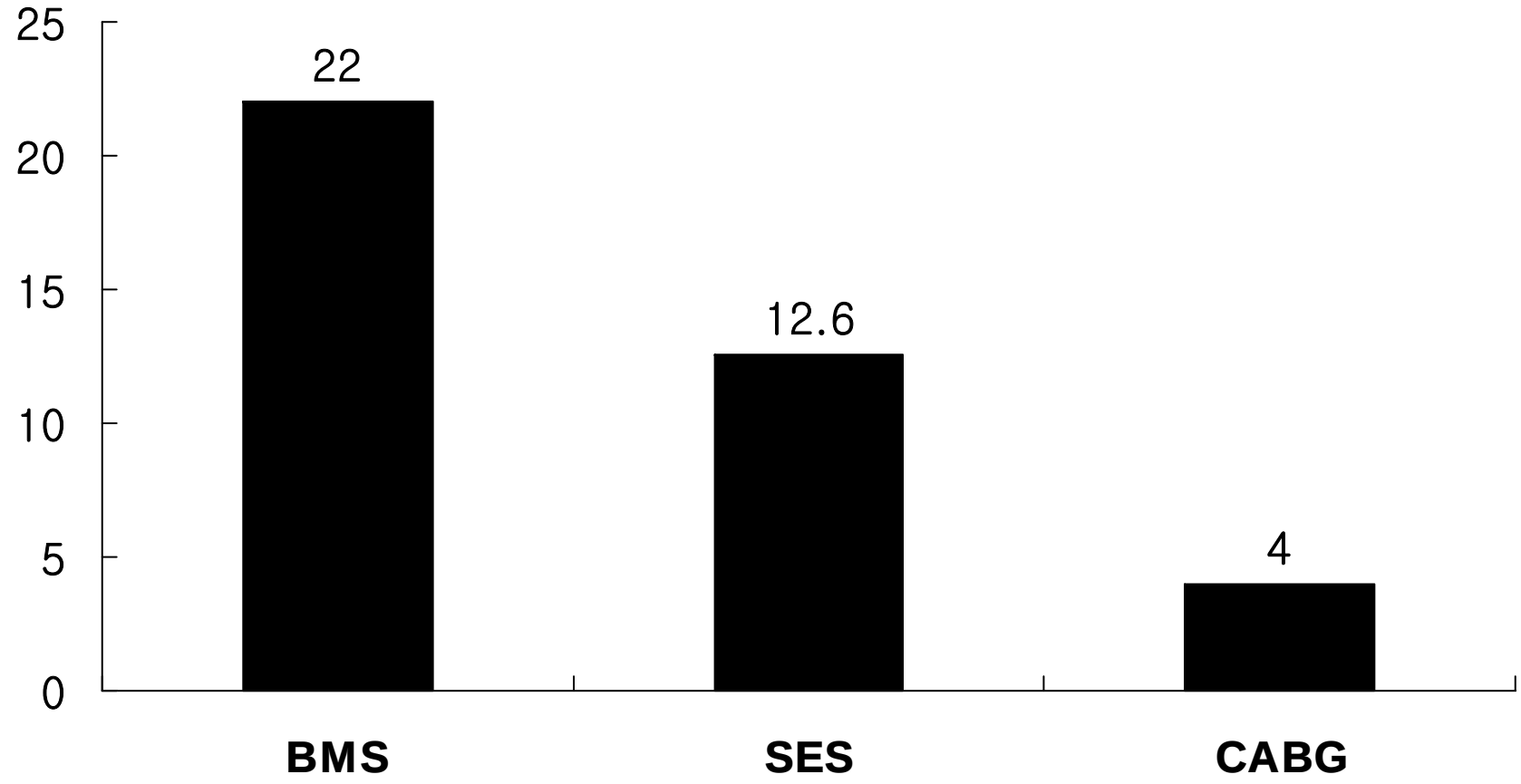
**1 to 8 years F/U**




Hoffman et al. JACC 2003:41;1293-

# PCI vs. CABG in multivessel disease in diabetic patients

**Rates of revascularization at one year**



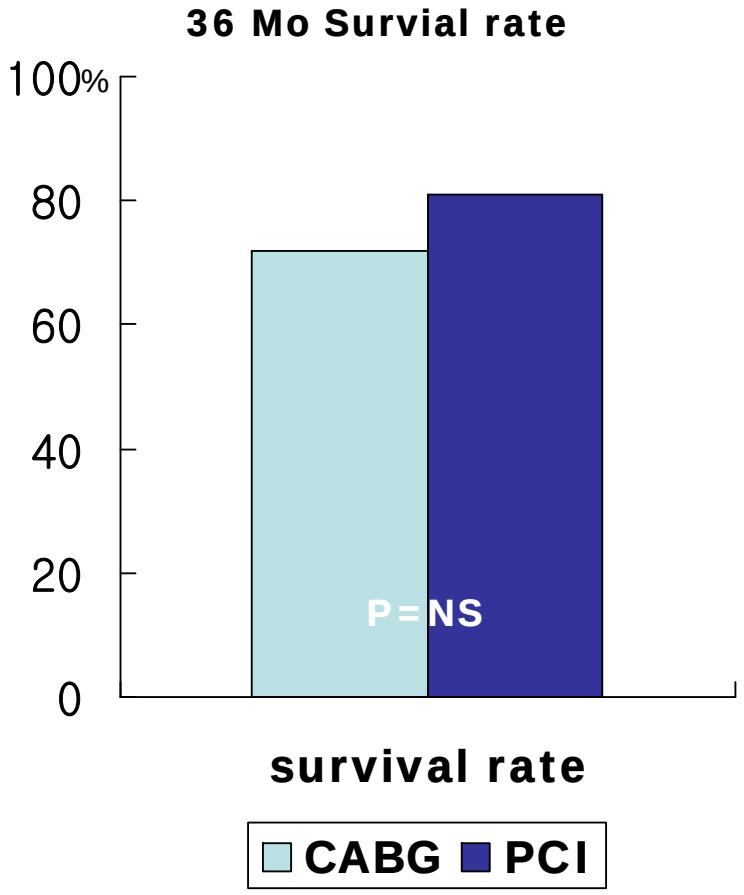

ART I, ART II trial 2005

# PCI vs. CABG in multivessel disease in diabetic patients

**High risk for CABG**

- age >70 years
- prior CABG
- MI within 7 days
- LVEF <0.35
- need for IABP

**144 DM pts**
**(79 CABG, 65 PCI)**




AWESOME trial 2002

# Ongoing Randomised Trials

- **BARI 2D trial**
  - **Revascularisation vs no revascularisation** in insulin requiring vs non-insulin requiring DM with mild to moderate coronary syndrome
- **FREEDOM trial**
  - **SES with abciximab vs CABG** in DM with multivessl disease
- **CARDIa trial**
  - Assessing the outcomes of diabetic pts with multivessel or single vessel disease eligible for revascularisation and treated with either a **DES or CABG surgery**

# Conclusion

- The diabetic population is particularly challenging for PCI because of specific high risk clinical and angiographic features.
- In the current era of DES, DM remains an independent risk factor for restenosis and TLR.
- DES represent a real advance in PCI for diabetics, and should be used as the first choice.
- Until results of ongoing RCTs, comparing DES with CABG are available, CABG is still a valid option for a progressive smaller diabetic population with multivessel disease.