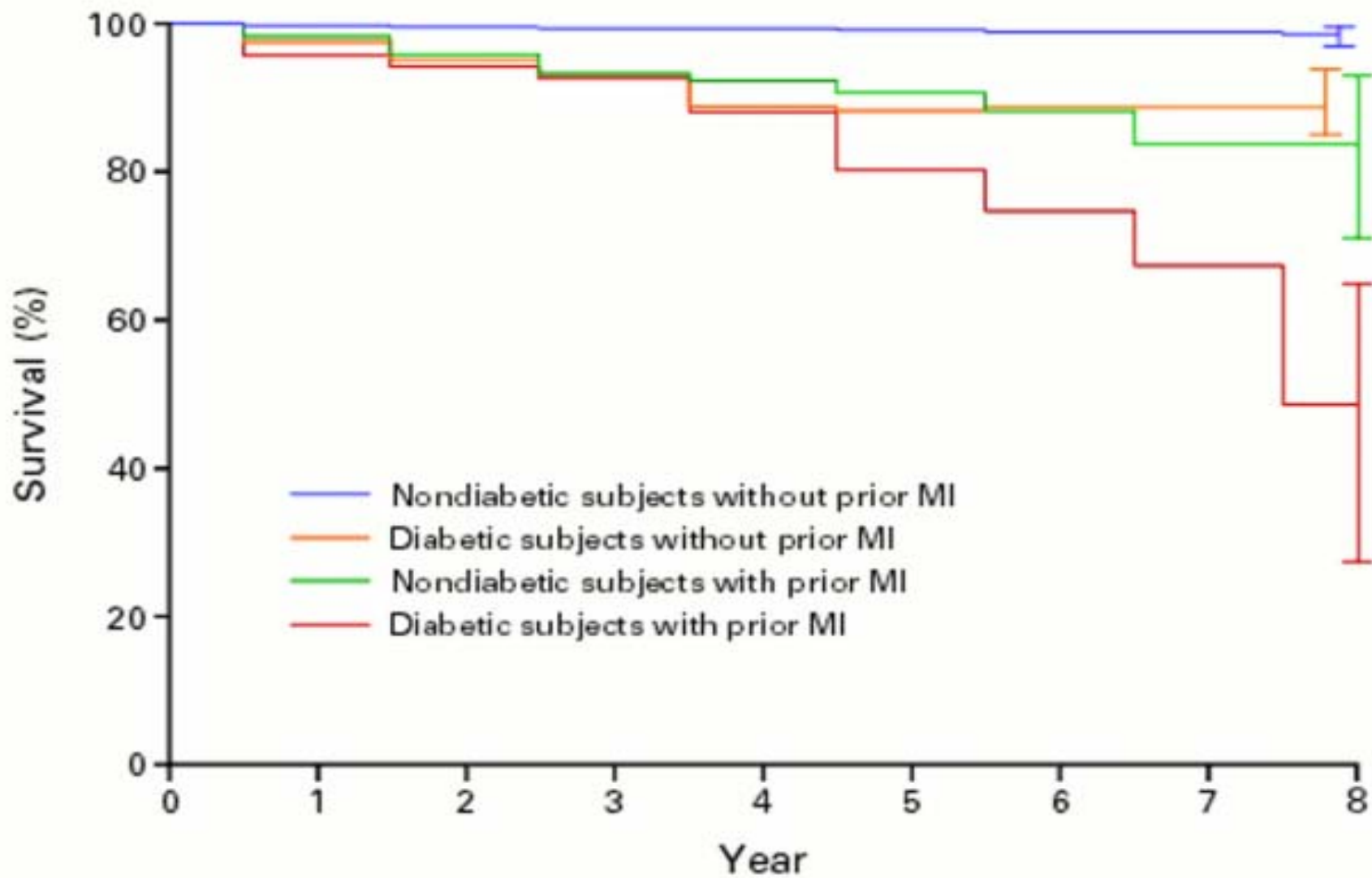


# **Diabetes and Atherosclerosis**

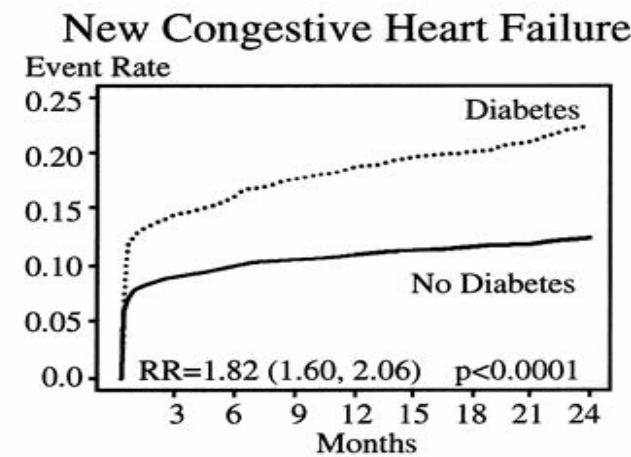
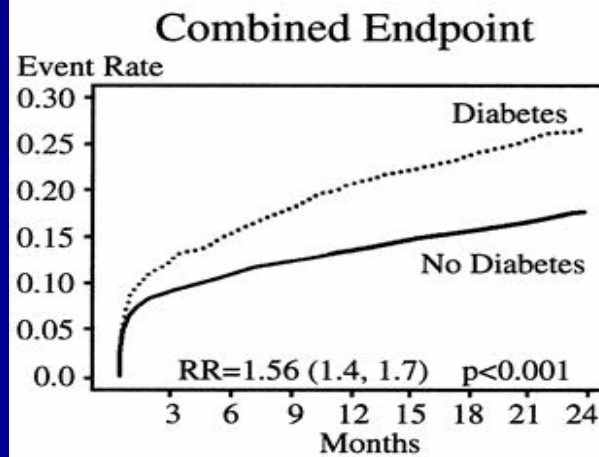
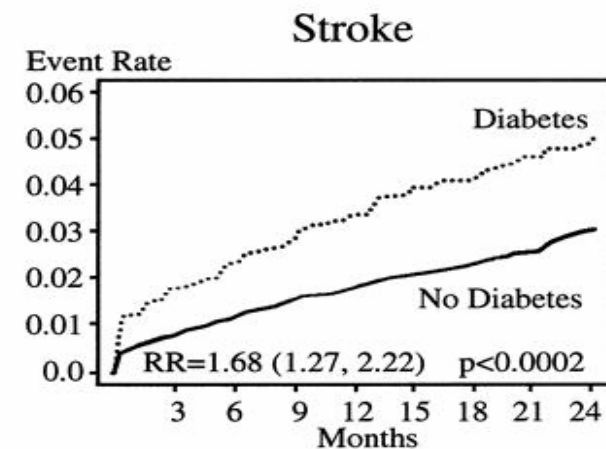
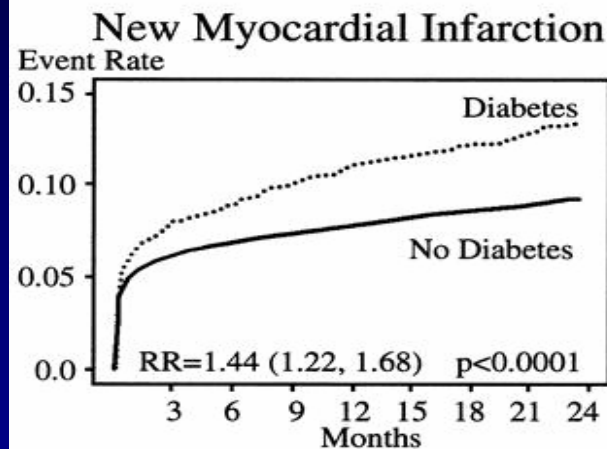
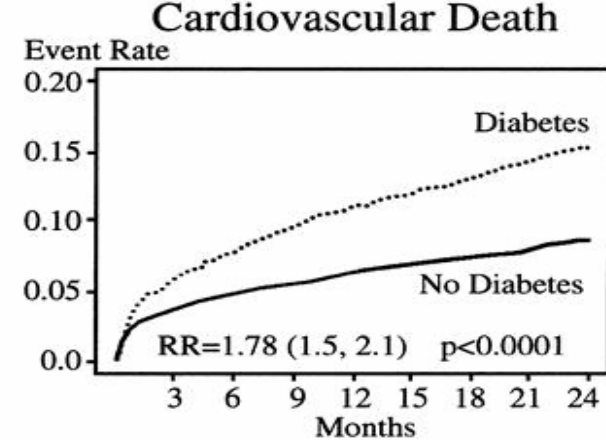
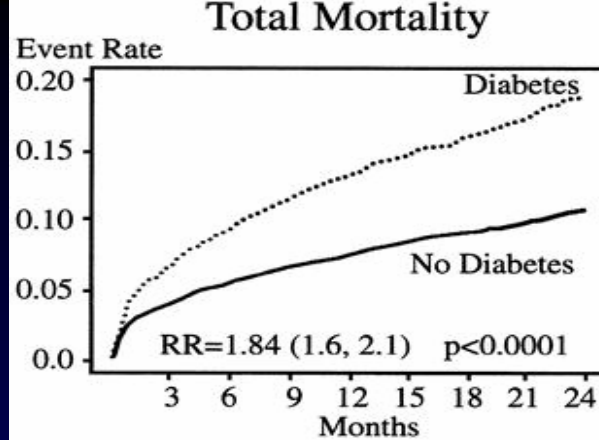
## **Coronary Artery Disease in Diabetic Patients**

# Type 2 Diabetes and CAD

- **Type 2 diabetes mellitus is a vascular disease.**
- **More than 3 out of 4 diabetic patients die of causes related to atherosclerosis, in most (75%) cases because of coronary artery disease.**
- **Yet, 70% of diabetic persons do not believe they are at serious risk for cardiovascular disease.**
- **Type 2 diabetes increases the risk for coronary artery disease by 2 to 4 times in the overall population.**



# Impact of Diabetes on Long-term Prognosis in Patients with UA/Non-Q-MI (OASIS Registry)

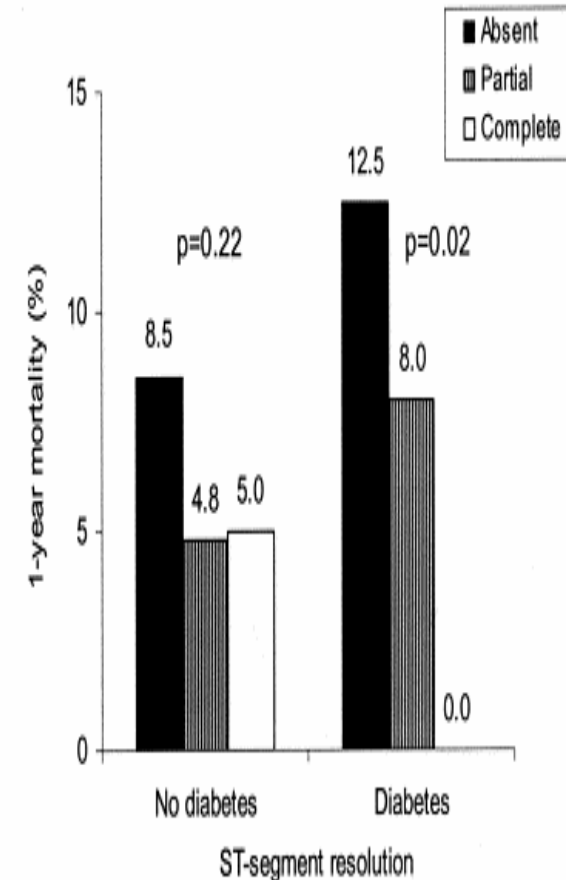
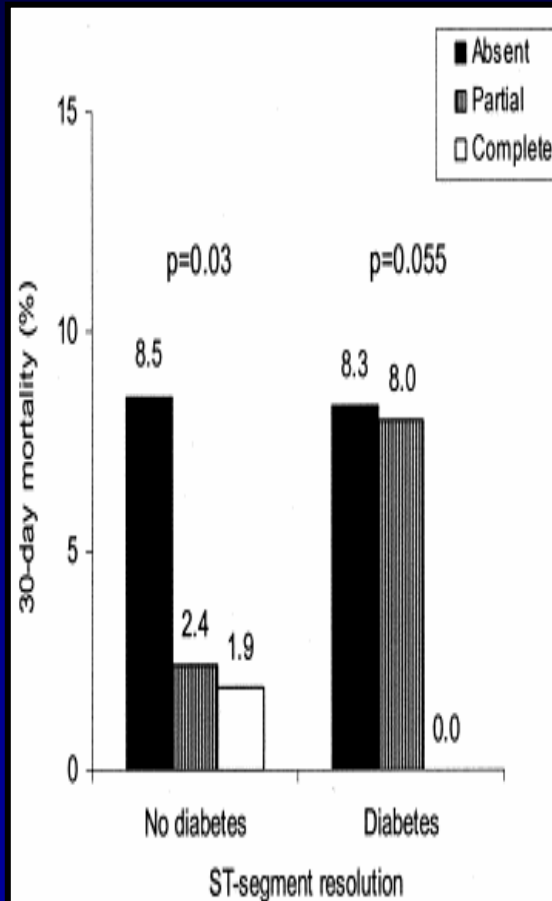
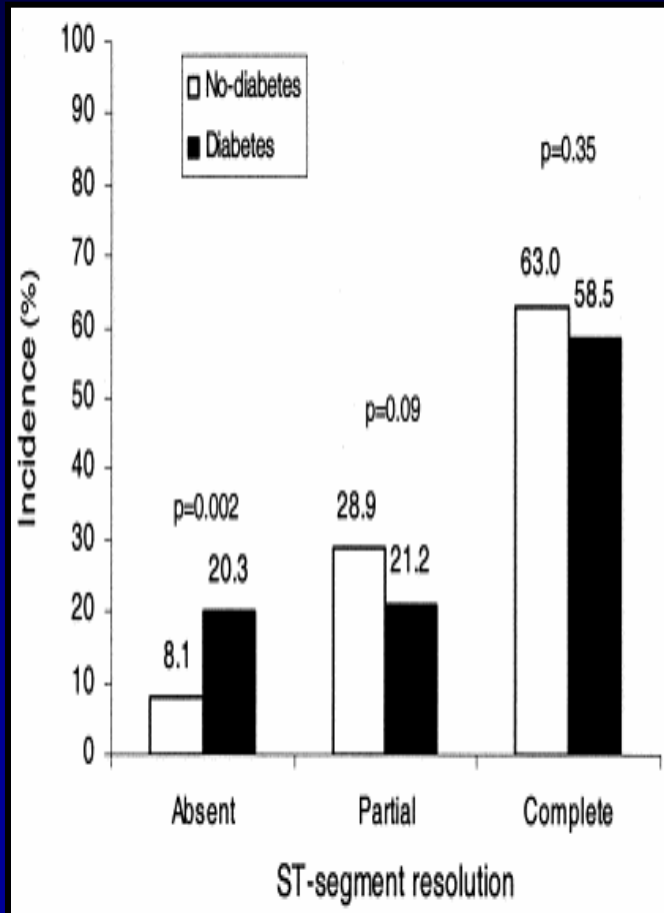


# Impact of DM on Myocardial Perfusion After Primary Angioplasty in AMI

ST-segment resolution

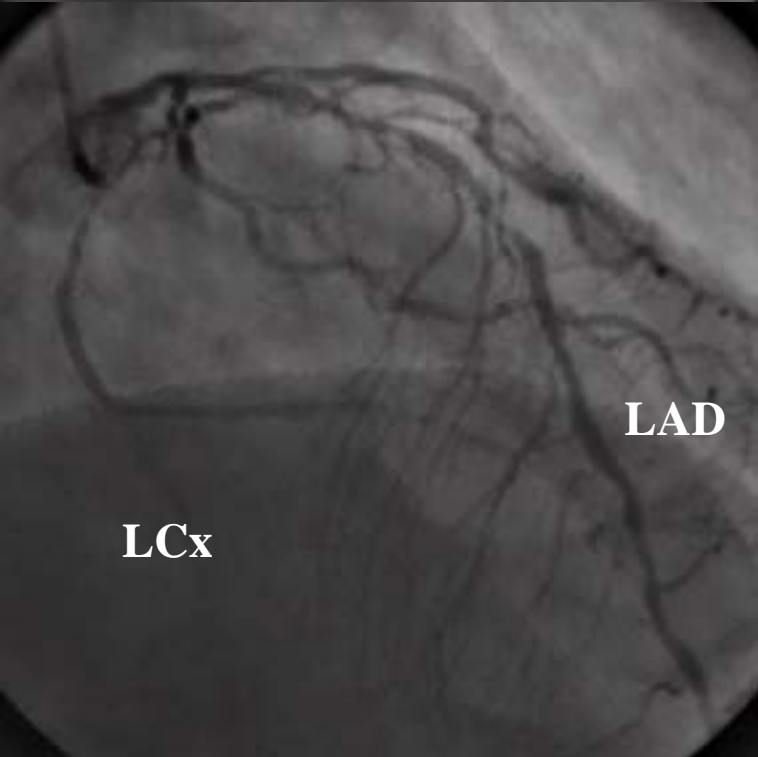
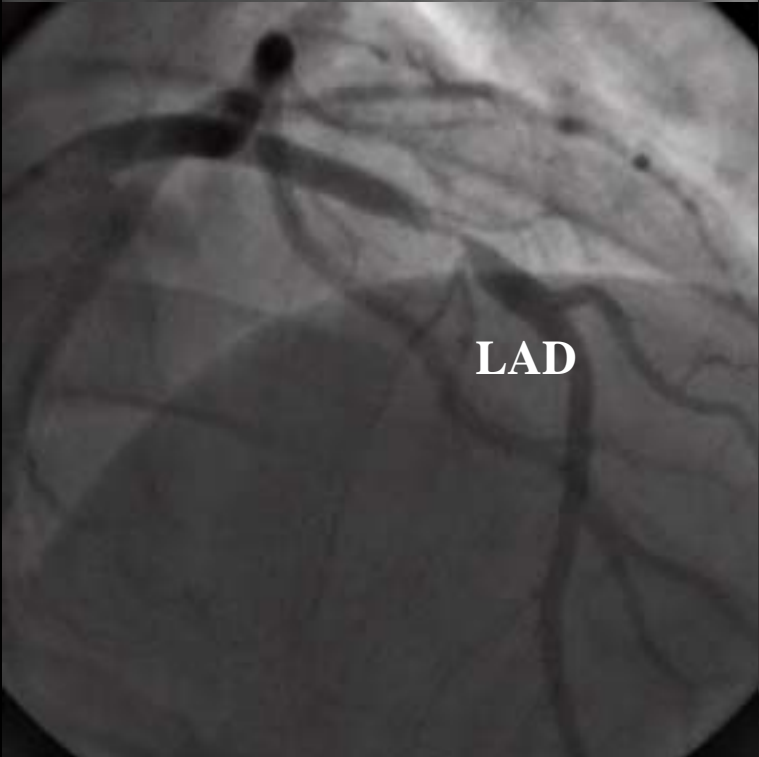
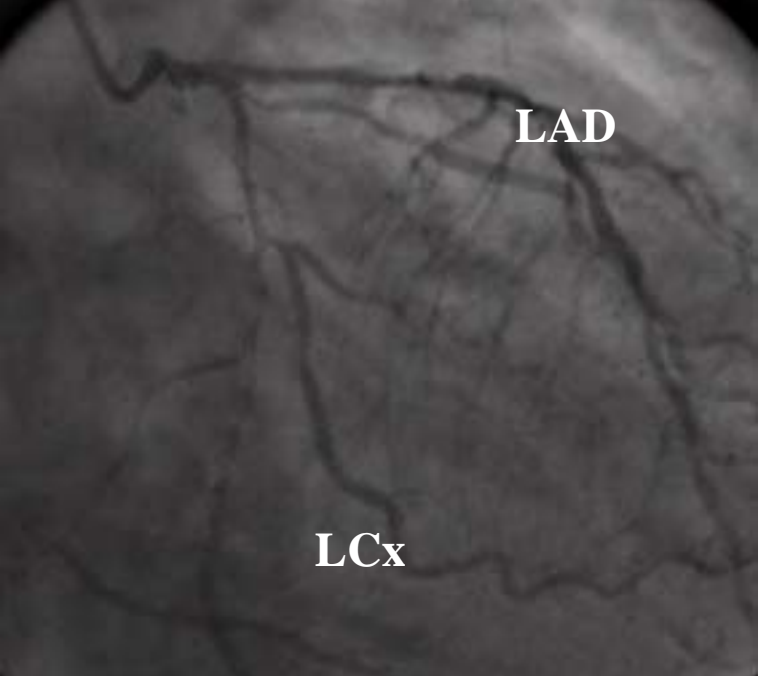
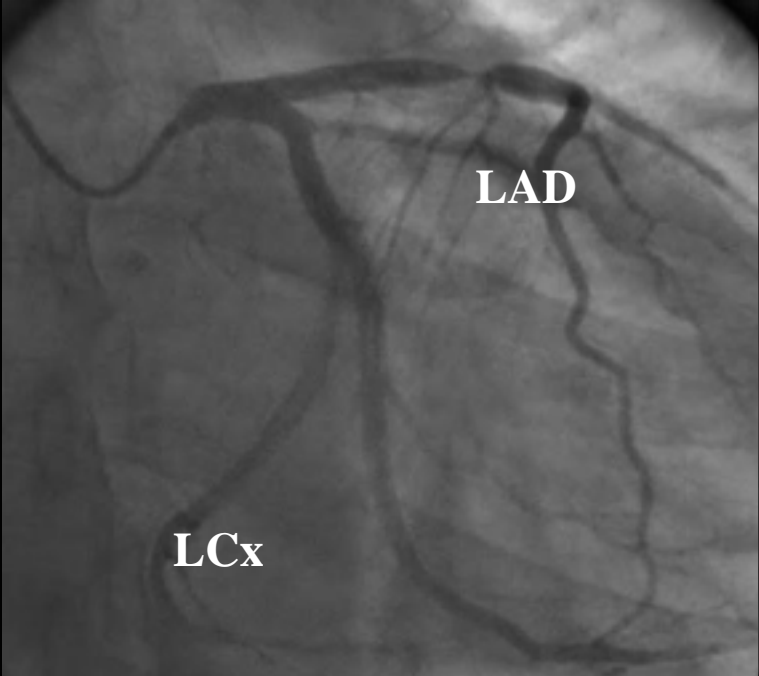
30-day mortality

1-year mortality



# **Mechanism of Increased Atherosclerosis in Diabetic Patients**

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

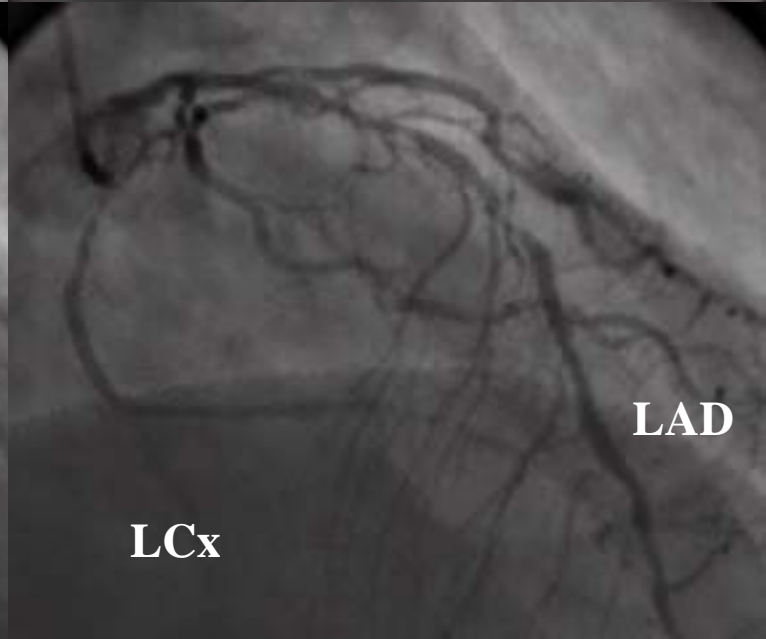
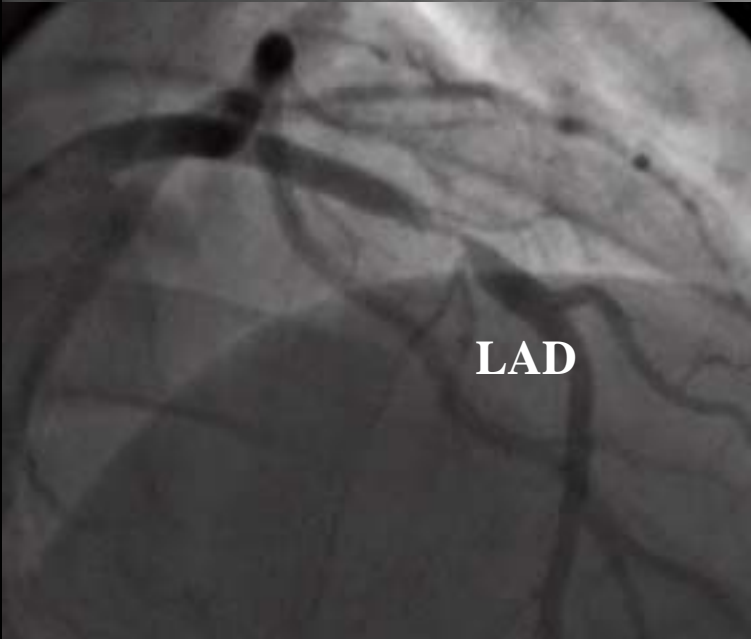
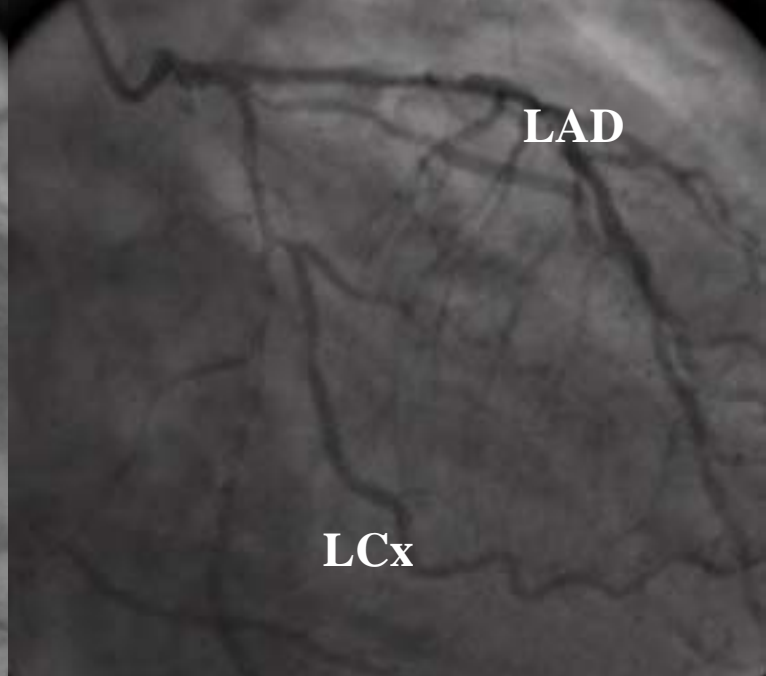
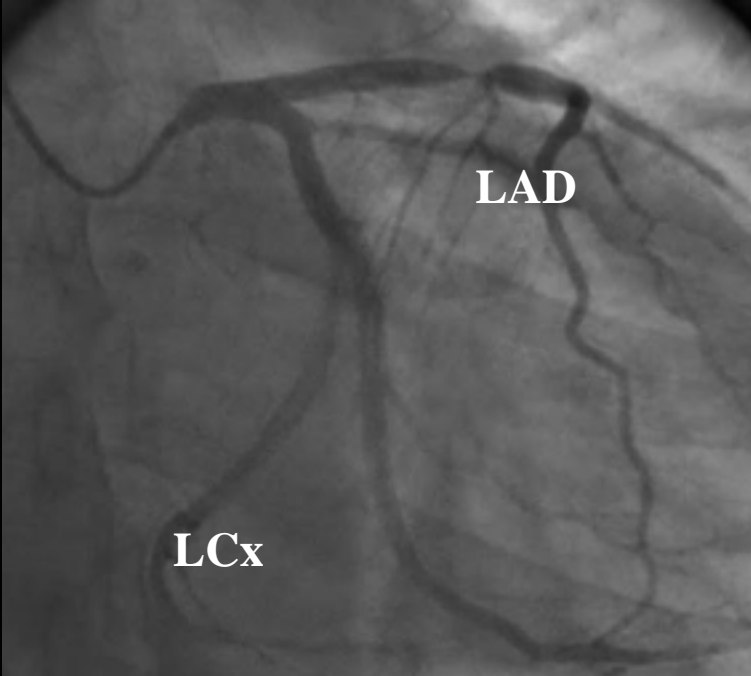


# **Anatomy of Coronary Disease in Diabetic Patients**

- **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**





**Nondiabetic**

**Diabetic**

# Treatment of CAD in Diabetic Patients

- **Modification of Risk Factors for Coronary Artery Disease**

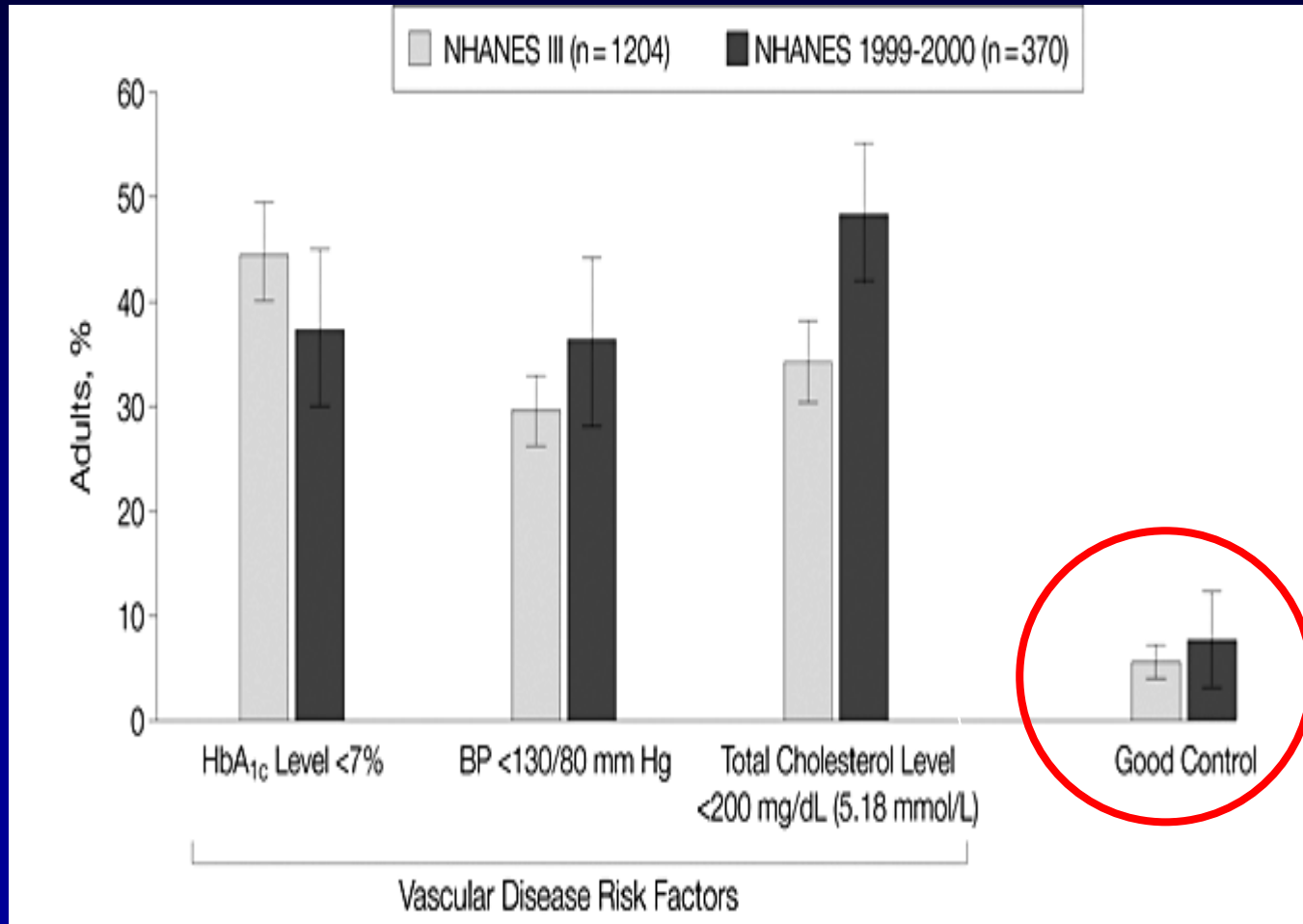
- **Glycemic Control: Oral agents, Insulin**

- **Management of CAD**

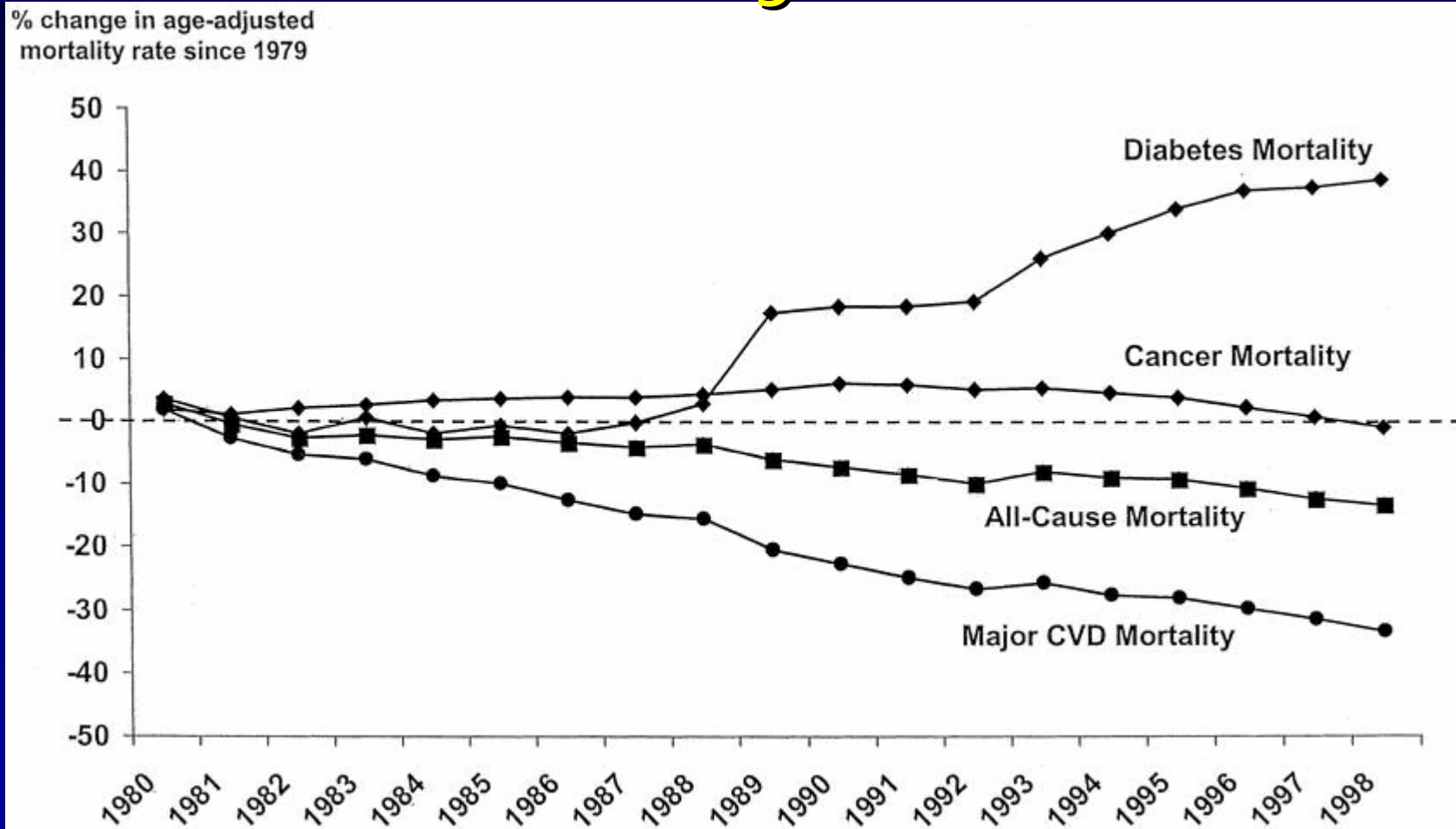
  - Acute coronary syndrome (ACS)**

  - Coronary Revascularization: Stent vs CABG**

# Poor Control of Risk Factors for Vascular Disease in Diabetic Patients



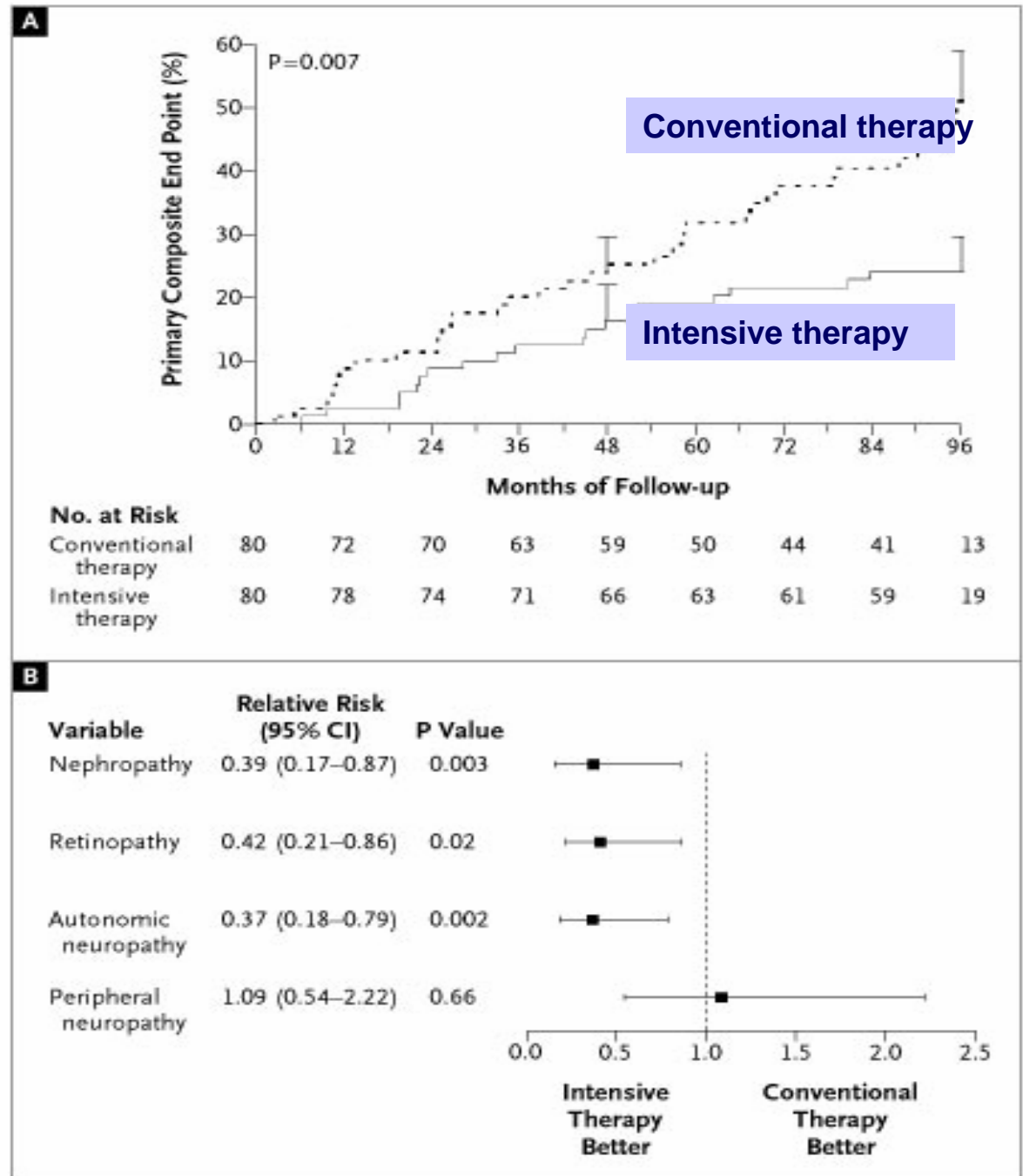
# Changes in age-adjusted mortality rates



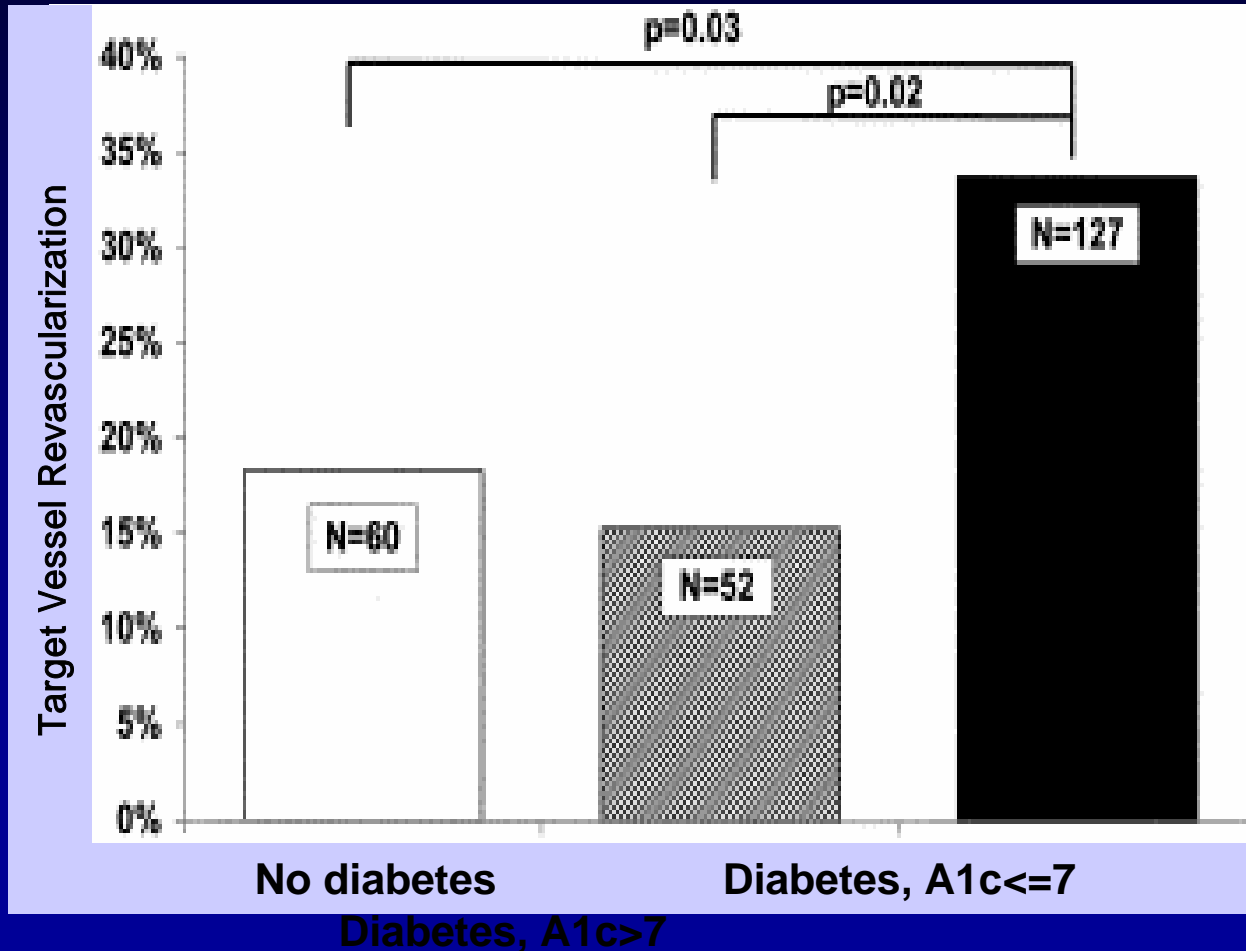
# Multifactorial Intervention In Type 2 Diabetes (STENO-2)

Composite end point of Cardiovascular Death, Nonfatal MI, CABG, PCI, Nonfatal Stroke, Amputation Surgery for PVD

NEJM 2003;348:383-93



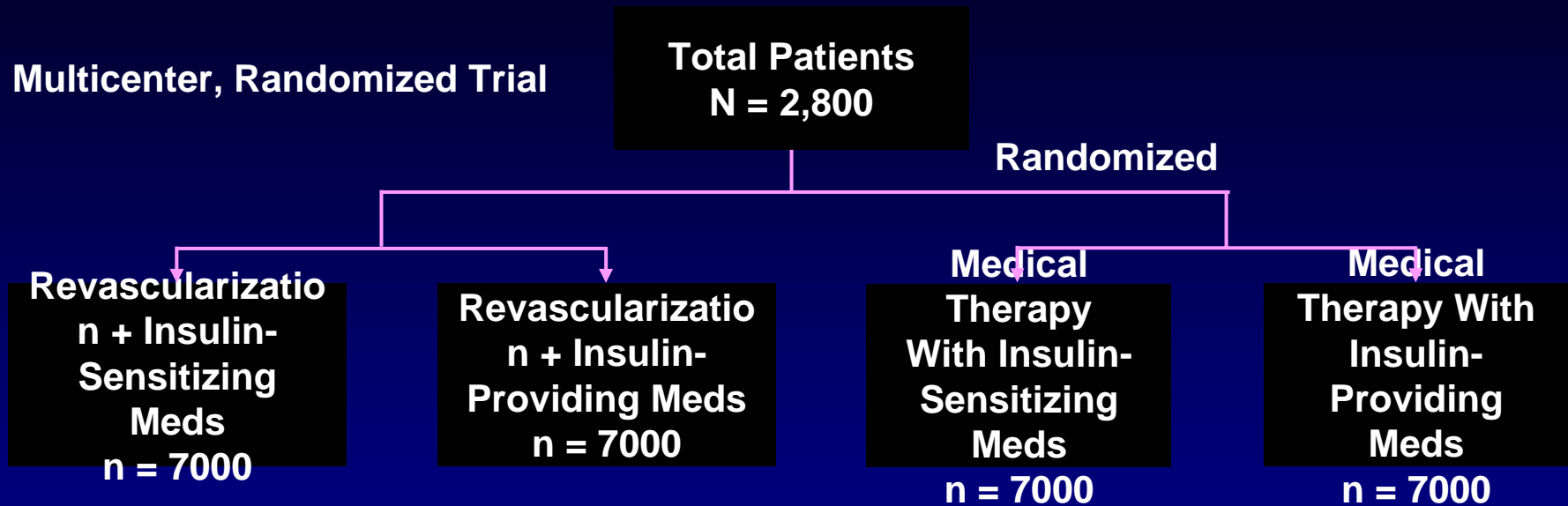
# Glycemic Control and TVR



# Treatment Modality of Diabetes and Outcomes of ACS

<b>Tx Modality Und-ECG</b>	<b>STE-ACS</b>	<b>NSTE-ACS</b>	
<b>Diet</b>	<b>1.0</b>	<b>1.0</b>	<b>1.0</b>
<b>OHA</b>	<b>0.8 (0.4-1.5)</b>	<b>2.2 (0.6-7.8)</b>	<b>0.9 (0.2-4.6)</b>
<b>Insulin</b>	<b>1.9 (1.0-3.8)</b>	<b>3.5 (1.0-12.5)</b>	<b>2.1 (0.5-9.5)</b>

# Bypass Angioplasty Revascularization Investigation 2D (BARI 2D)



Primary end point; 5-year mortality

## Inclusion Criteria

- Age ≥ 25 years
- Type 2 Diabetes
- CAD Suitable for Revascularization
- Myocardial Ischemia

## Insulin-Providing Meds:

- Sulfonylureas
- Thiazolidinediones
- Repaglinide
- Nateglinide
- insulin

## Insulin-Sensitizing

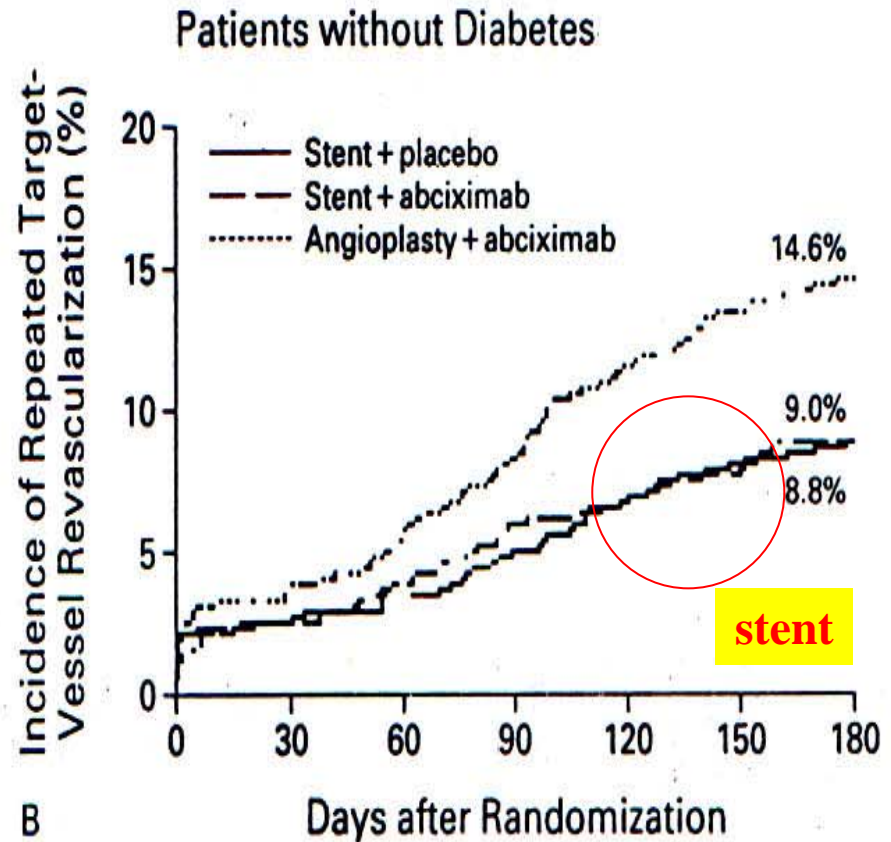
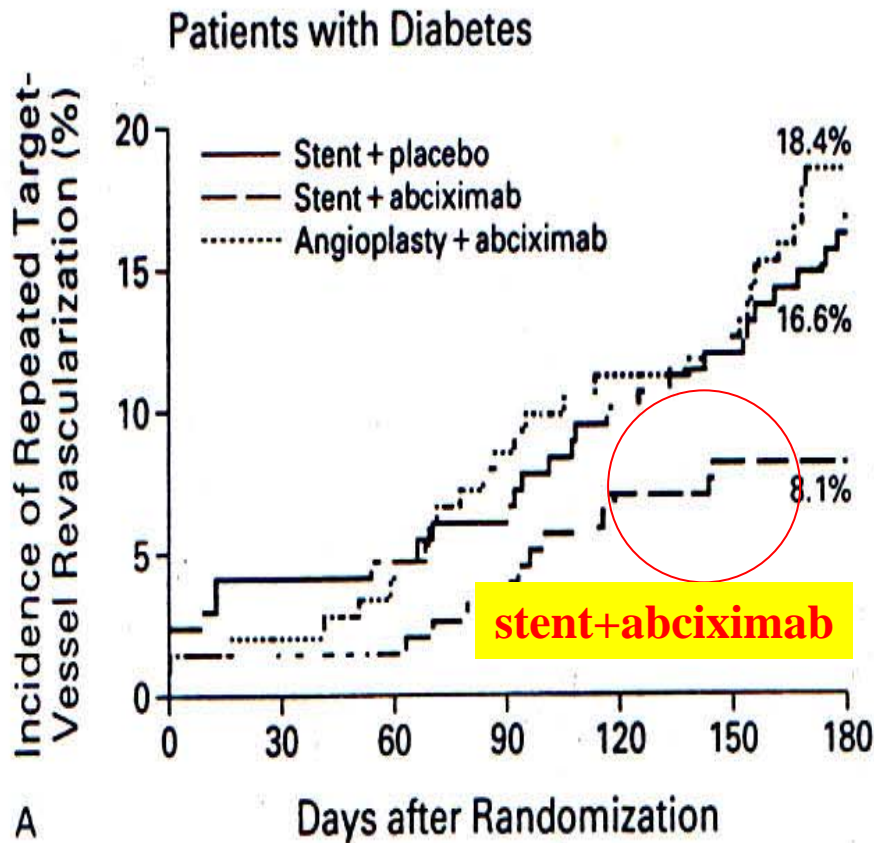
- 
- Metformin



# Management of ACS in Diabetics (= Nondiabetics)

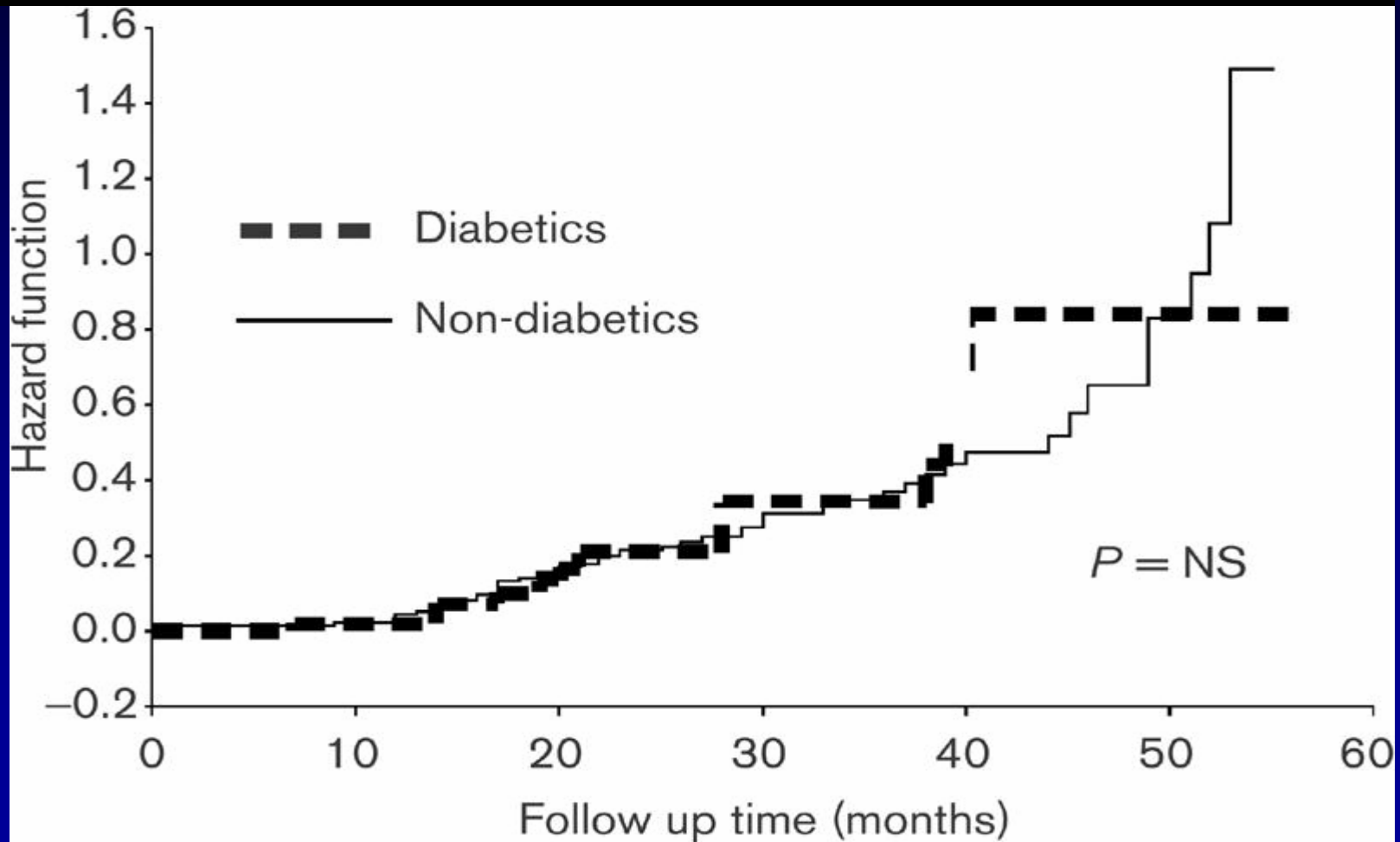
**STEMI: Primary PCI or Thrombolysis**

**NSTEMI or UA: Early invasive approach**



# Diabetes and Unstable CAD

(Stenting, IIb/IIIa Inhibitors, LLT)



# Coronary Revascularization

- **Percutaneous Coronary Intervention (PCI)**
- **Coronary Artery Bypass Grafting (CABG)**

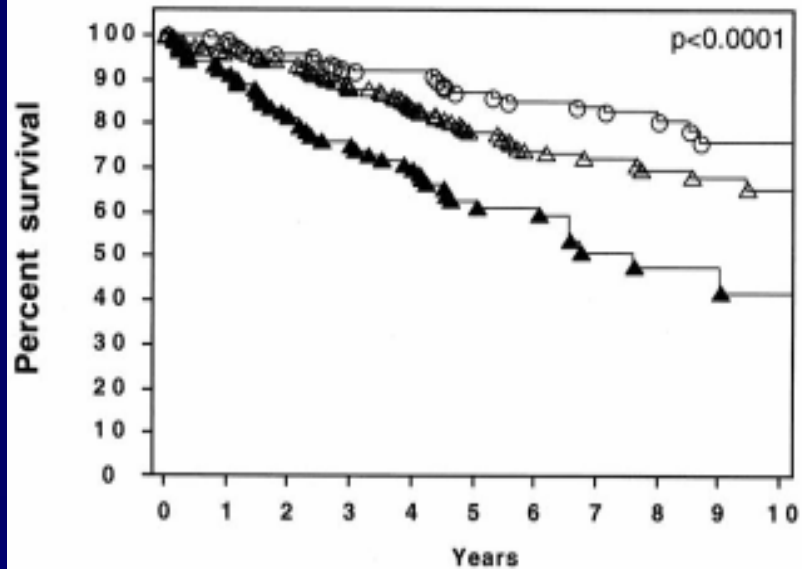
# PCI in Diabetic Patients

<b>Events</b>	<b>Nondiabetic (n=8798)</b>	<b>Diabetic (n=2684)</b>	<b>p</b>
<b>Death</b>	<b>75 (0.9)</b>	<b>57 (2.1)</b>	<b>&lt;0.01</b>
<b>MI</b>	<b>108 (1.2)</b>	<b>50 (1.9)</b>	<b>0.01</b>
<b>MI or Death</b>	<b>179 (2.0)</b>	<b>97 (3.6)</b>	<b>&lt;0.01</b>
<b>TVR</b>	<b>1128 (12.8)</b>	<b>480 (17.9)</b>	<b>&lt;0.01</b>

From PRESTO Trial, Circulation 2004;109:476-480

# Vessel Patency and Survival In Diabetics After PTCA

## Total mortality

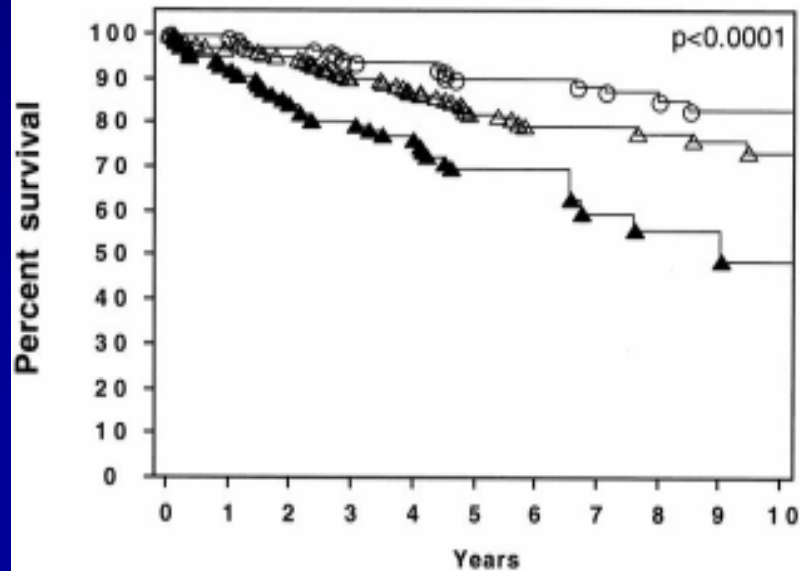


No restenosis

Restenosis

Occlusion

## Cardiac mortality



○ Patients without restenosis

△ Patients with non-occlusive restenosis

▲ Patients with occlusive restenosis

# BARI

## Bypass Angioplasty Revascularization Investigation

*PI: Robert L. Frye*

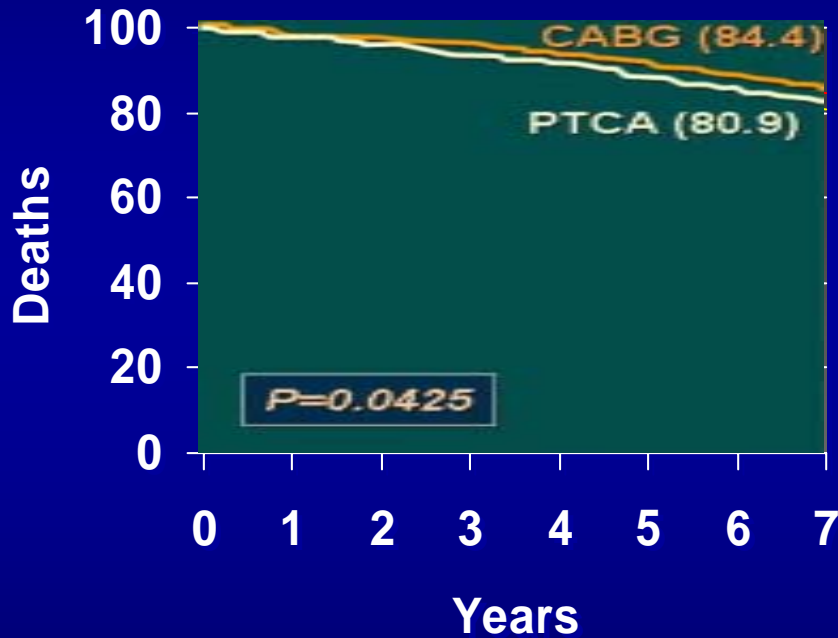
**Inclusion:** MVD, severe angina, suitable for PTCA, eligible for CABG



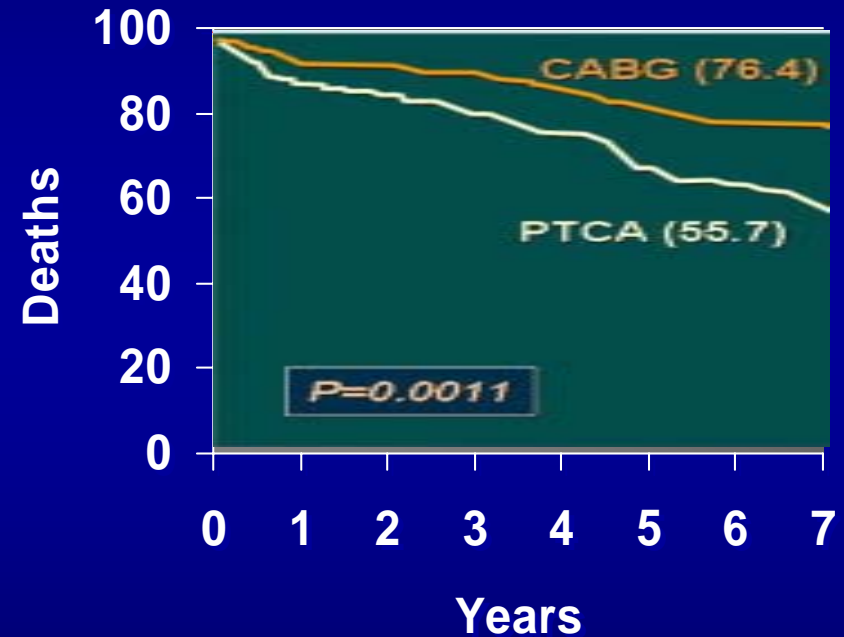
**Primary Endpoint:** Mortality @ 5 years, MACE @ 5 years

# BARI – Late Mortality

## Survival-All Patients



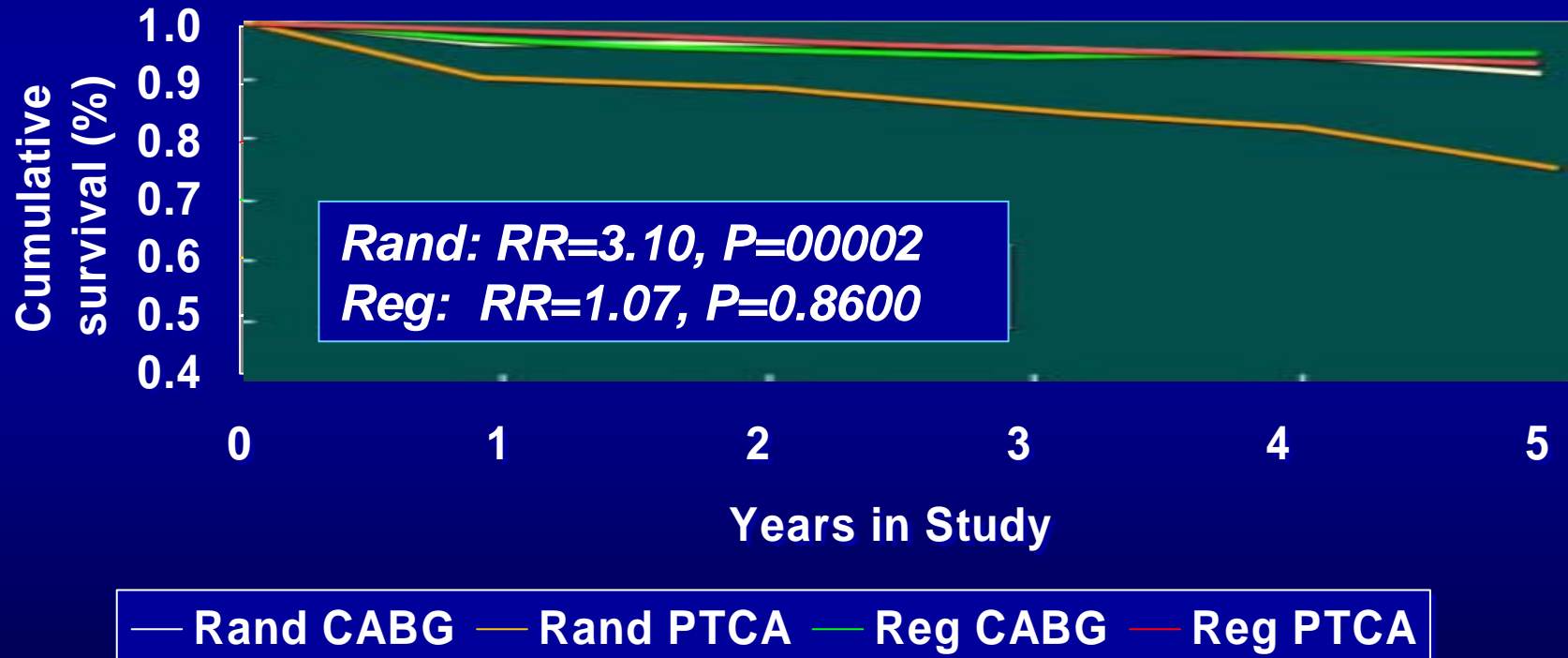
## Survival-Treated Diabetes



7-year Survival-diabetics	CABG		PTCA	
	Insulin treated (%)	84.1	60.6	
Oral hypoglycemics (%)	67.6	49.4		

# Cumulative Survival Among Diabetic Patients by Treatment in BARI Randomized and Registry Patients

## Cardiac Death





# BARI Criticisms

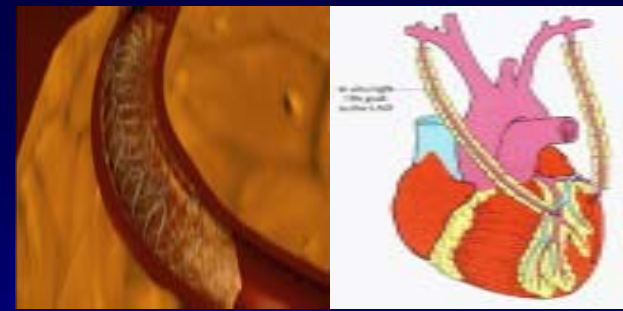
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- **Small number of diabetic patients (n=353)**
- **Diabetes was not a pre-specified subgroup for analysis**
- **PCI techniques pre-dated the “stent era”**
- **No glycoprotein IIb/IIIa inhibitors available**
- **PCI was associated with incomplete revascularization (cw CABG)**
- **The BARI registry more accurately reflected “real world” treatment patterns and results**

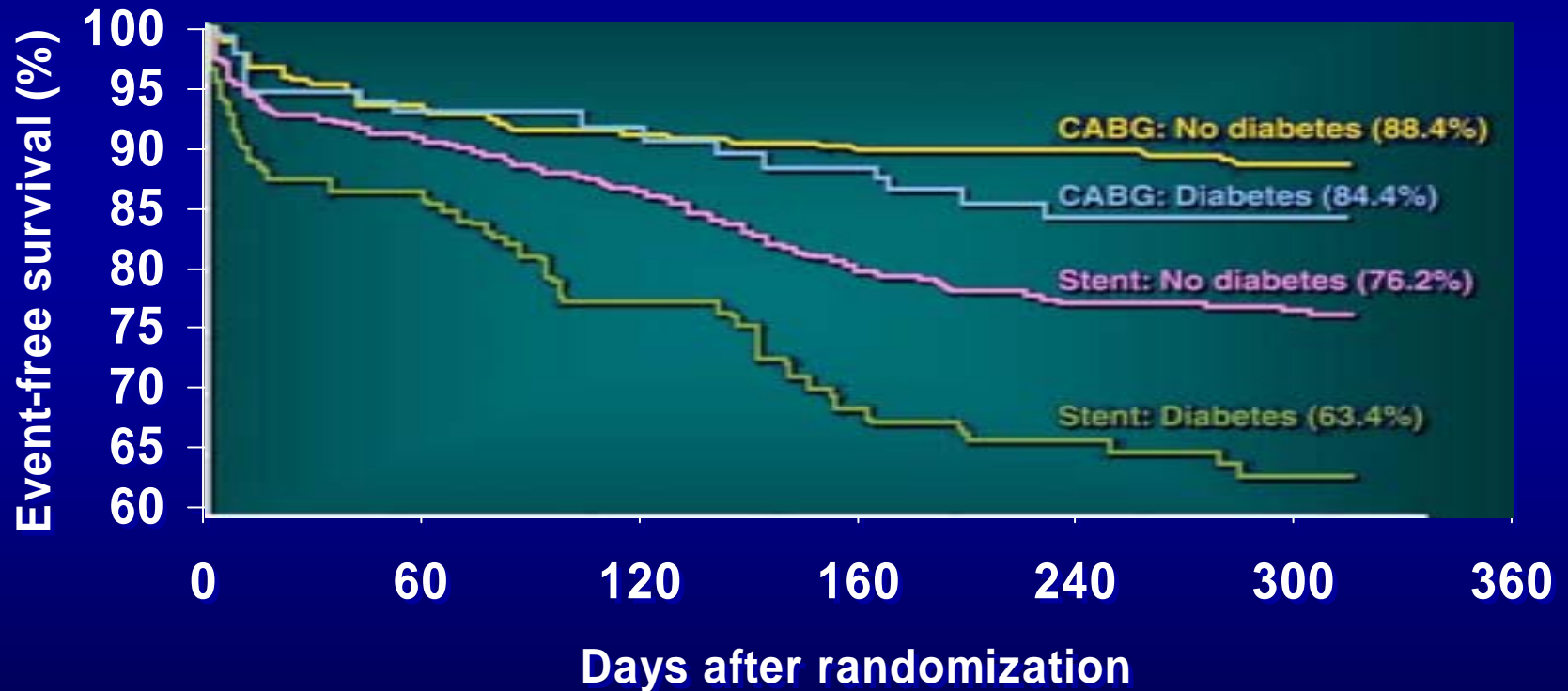
# Potential Mechanisms for Adverse Outcomes in Diabetes after PCI

- Different pathobiology (inflammatory) lesions with more frequent plaque rupture
- Increased thrombosis (increased platelet activity and other pro-coagulant effects)
- Increased CAD progression (more diffuse disease)
- Occlusive restenosis (impacts LVEF and mortality)
- Incomplete revascularization after PCI

# ARTS Trial: 1-Year MACCE



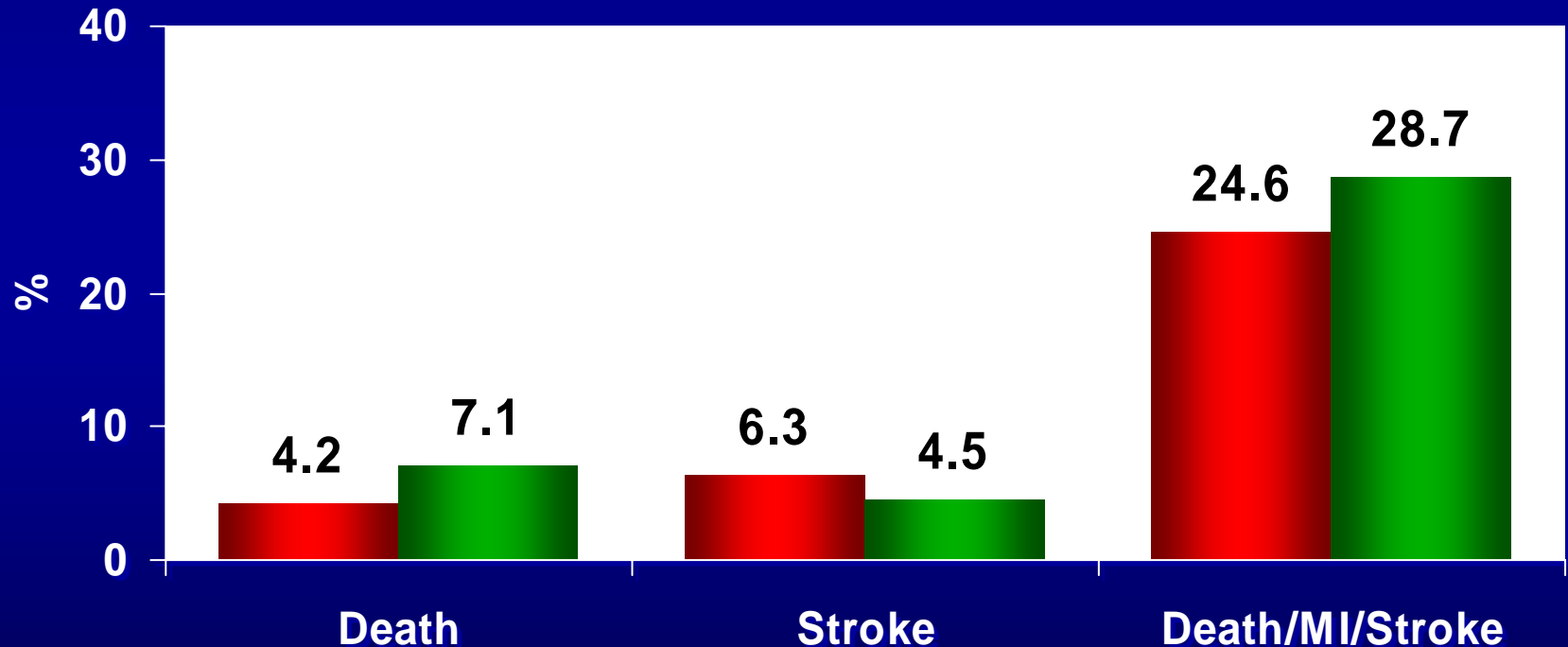
**MACE = Death/MI/Stroke/Revascularization**



# ARTS Trial: 3-Year Death/MI/Stroke

*Even without DES, "hard"  
Endpoints in DM @ 3 years:  
CABG = Stents*

**CABG** **Stent**

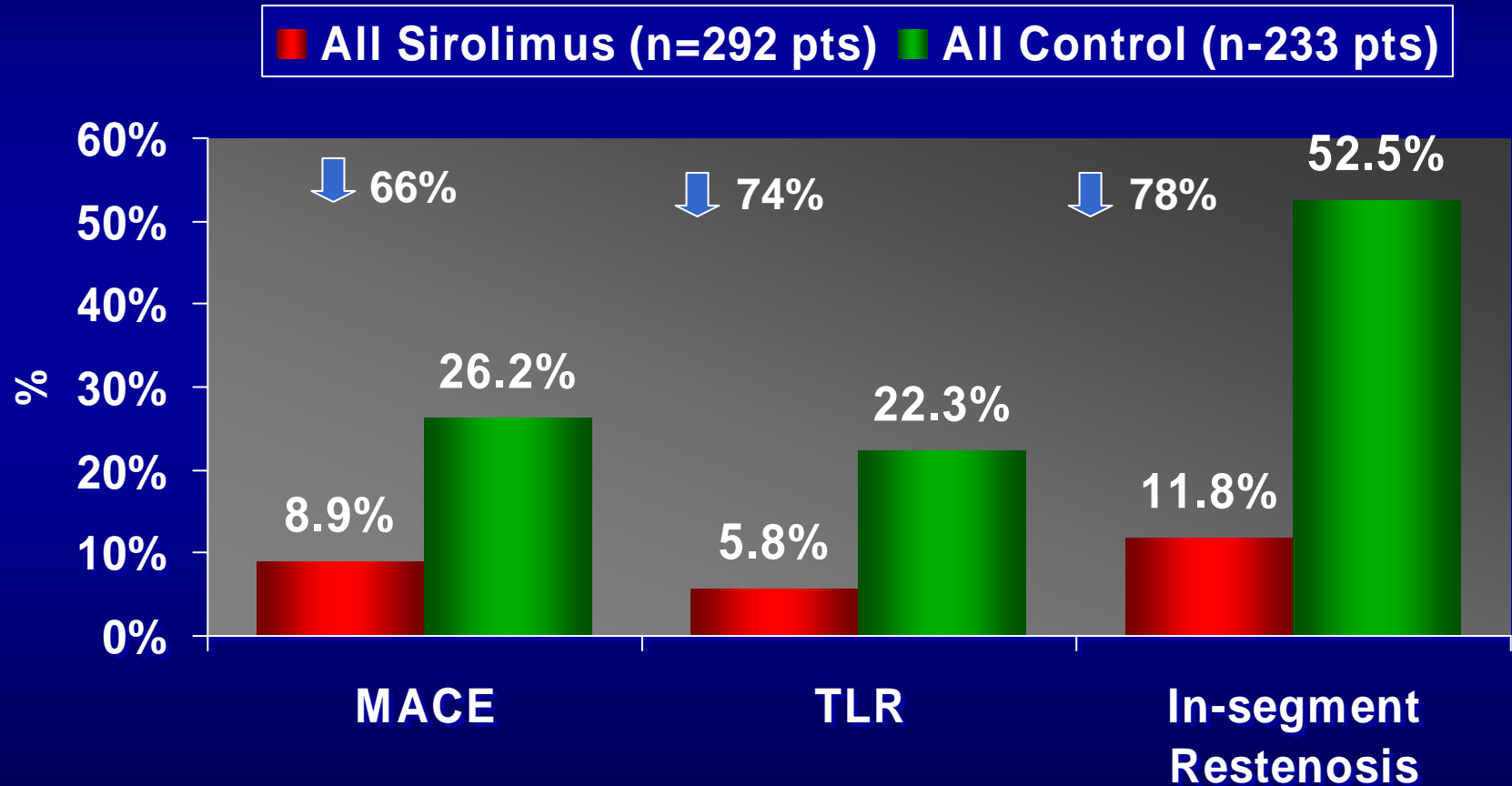


# CYPHER Trials in DM Patients

	DM Patients		Gender (M%)		Age (yrs)		IDDM pts	
	Cypher	Control	Cypher	Control	Cypher	Control	Cypher	Control
SIRIUS	131	148	64%	59%	63.4	62.1	38	44
E - SIRIUS	33	48	64%	60%	62.7	62.7	7	11
C - SIRIUS	12	12	50%	83%	64.9	58.8	1	2
DIRECT	70	-	73%	-	61.9	-	16	-
SVELTE	27	-	74%	-	63.4	-	2	-
RAVEL	19	25	68%	80%	63.6	63.0	5	5
Integrated	292	233	67%	63%	63.0	62.2	69	62

**All trials = 525 diabetics, 131 IDDM**

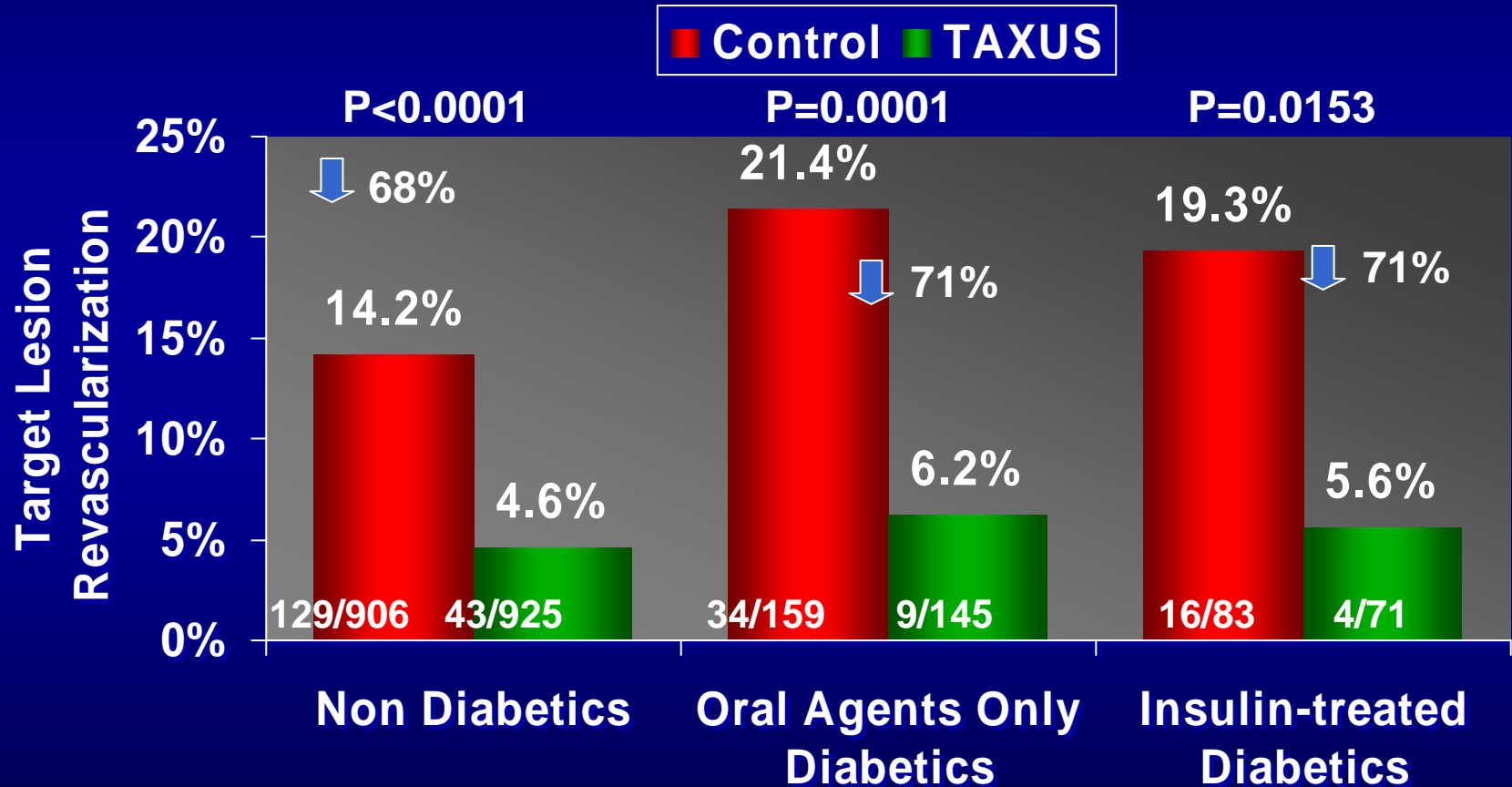
# CYPHER Trials in DM Patients



# The TAXUS Diabetic Meta-Analysis

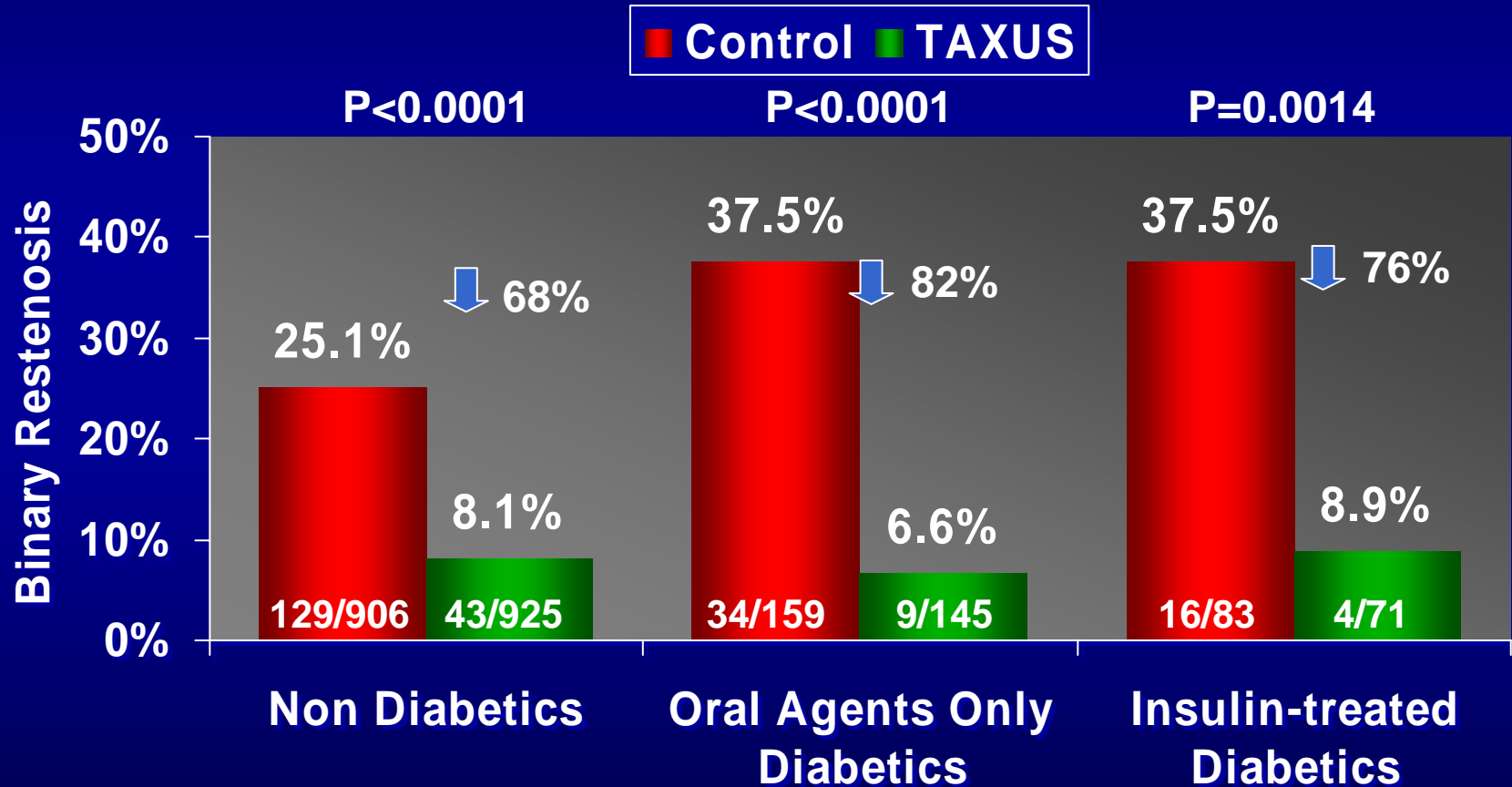
	Overall patients	Diabetic patients	Insulin-treated
TAXUS II SR	266	30	7
TAXUS IV MR	263	21	7
TAXUS IV SR	1314	318	105
TAXUS VI MR	446	89	35
Overall	2289	458	154
		242 Controls 216 TAXUS	83 Controls 71 TAXUS

# TAXUS DM: 12 month TLR



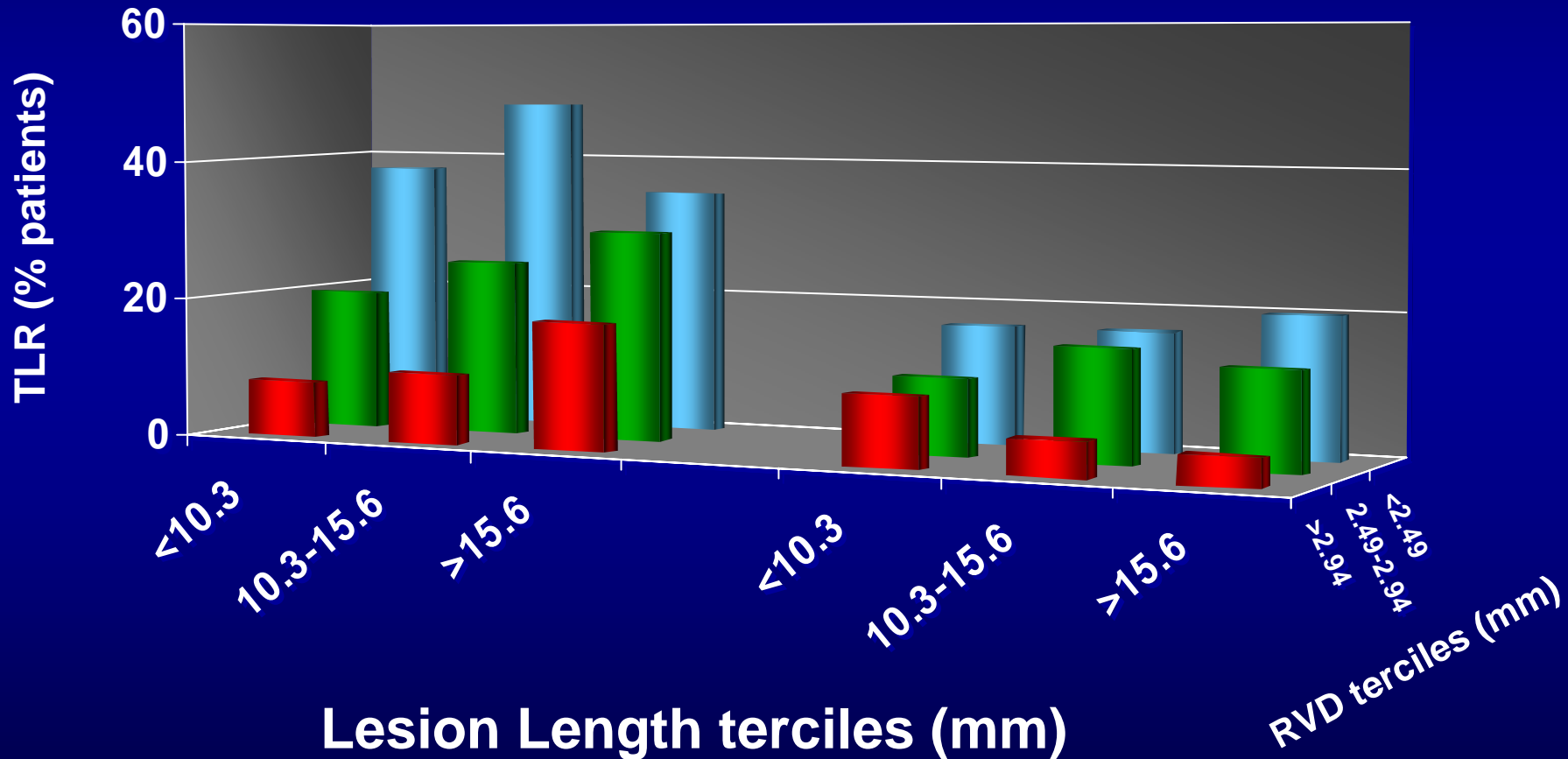


# TAXUS DM: In-Segment Restenosis



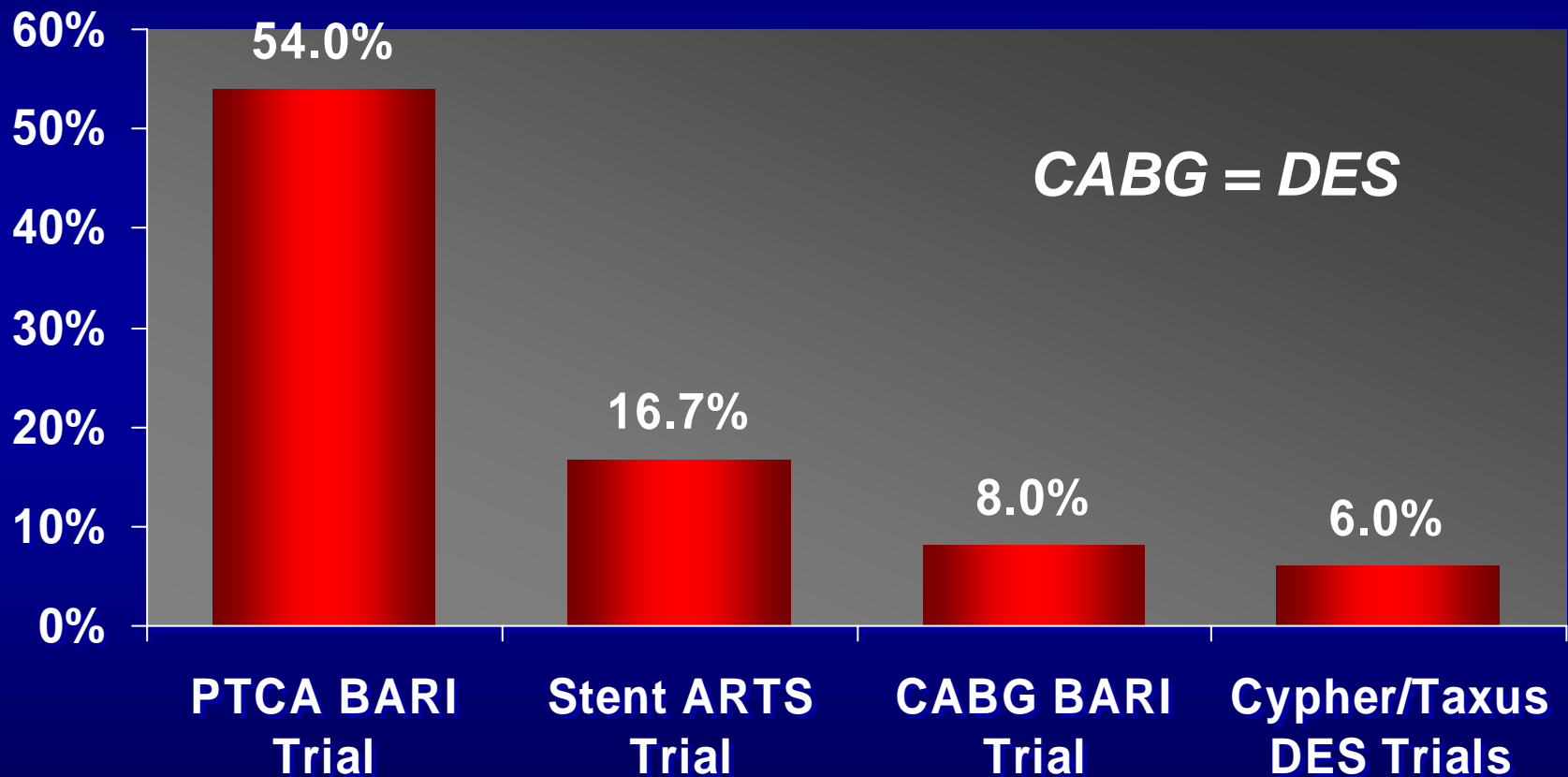
# TAXUS DM: Impact of Vessel Size and Lesion Length on TLR

Diabetic Patients



# PCI vs CABG

## Repeat Revascularization



# FREEDOM Trial

Eligibility: DM patients with MV-CAD eligible for stent or surgery  
Exclude: Patients with acute STEMI, cardiogenic shock

Randomized 1:1

MV-stenting  
With Drug-eluting stents  
And abciximab

CABG  
With or without CPB

All concomitant Meds shown to be beneficial are encouraged, including:  
Clopidogrel, ACE inhibitors, ARBs, B-blockers, statins

PRIMARY: 3-year death, MI, stroke  
SECONDARY: 12-month MACCE, 3-year Quality of Life