

Revascularization of the Diabetic Patient in 2010

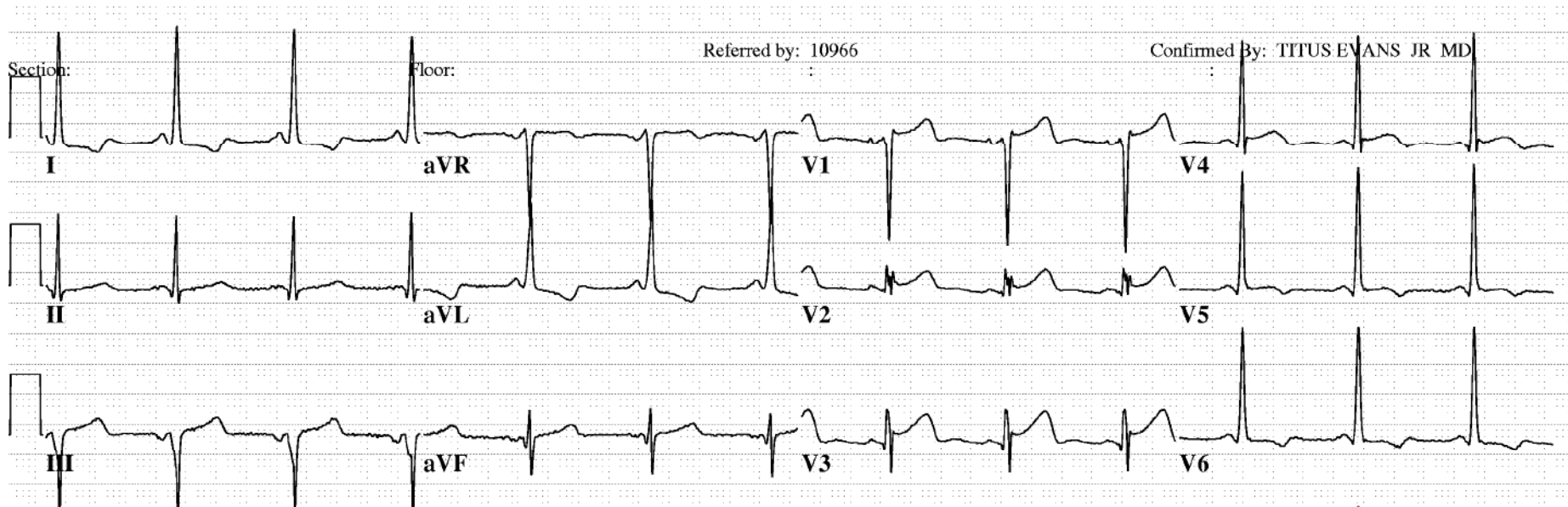
Charanjit S Rihal, MD

Chair, Division of Cardiovascular
Diseases

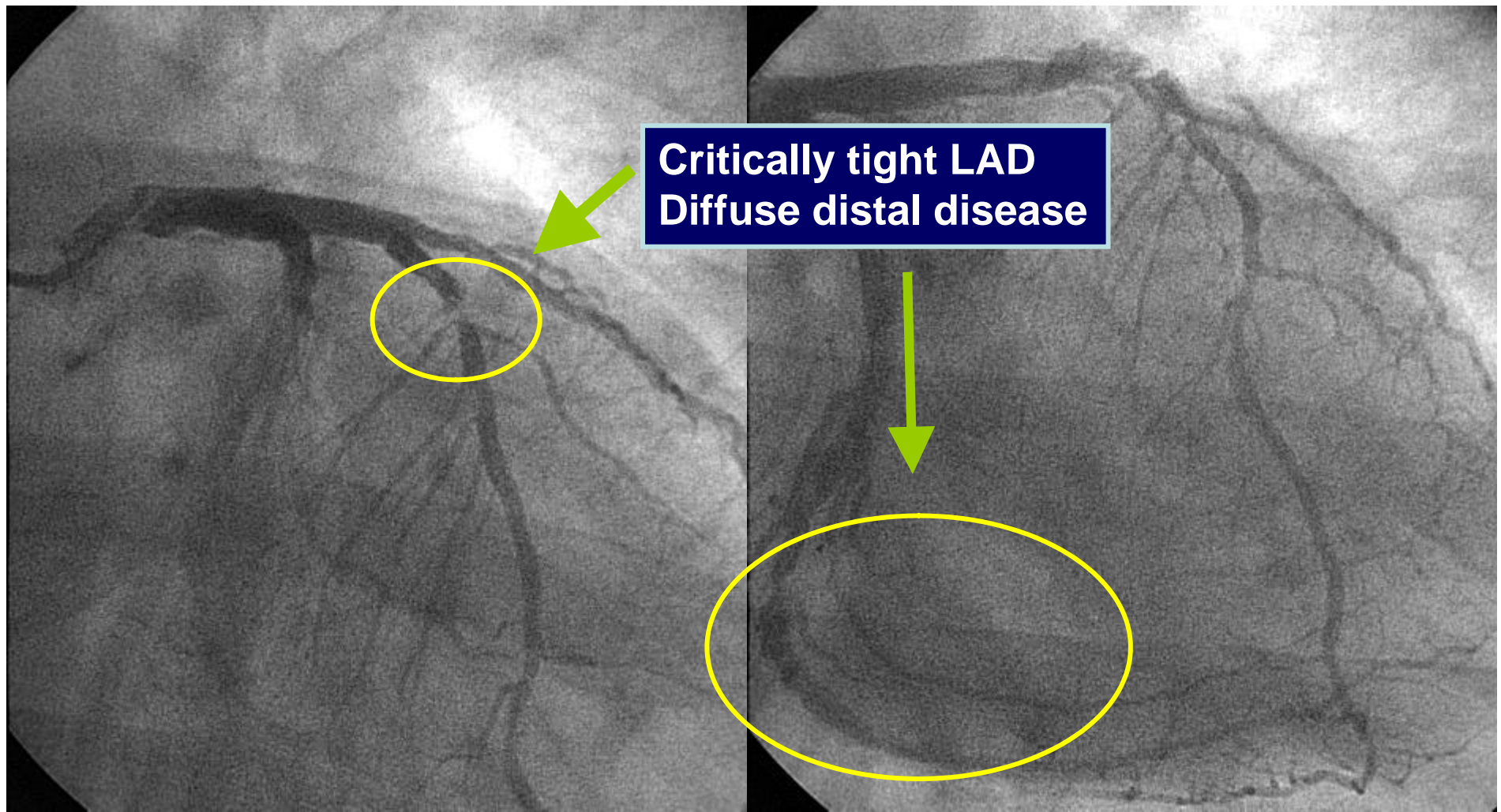
Mayo Clinic, Rochester MN

Case: 46M

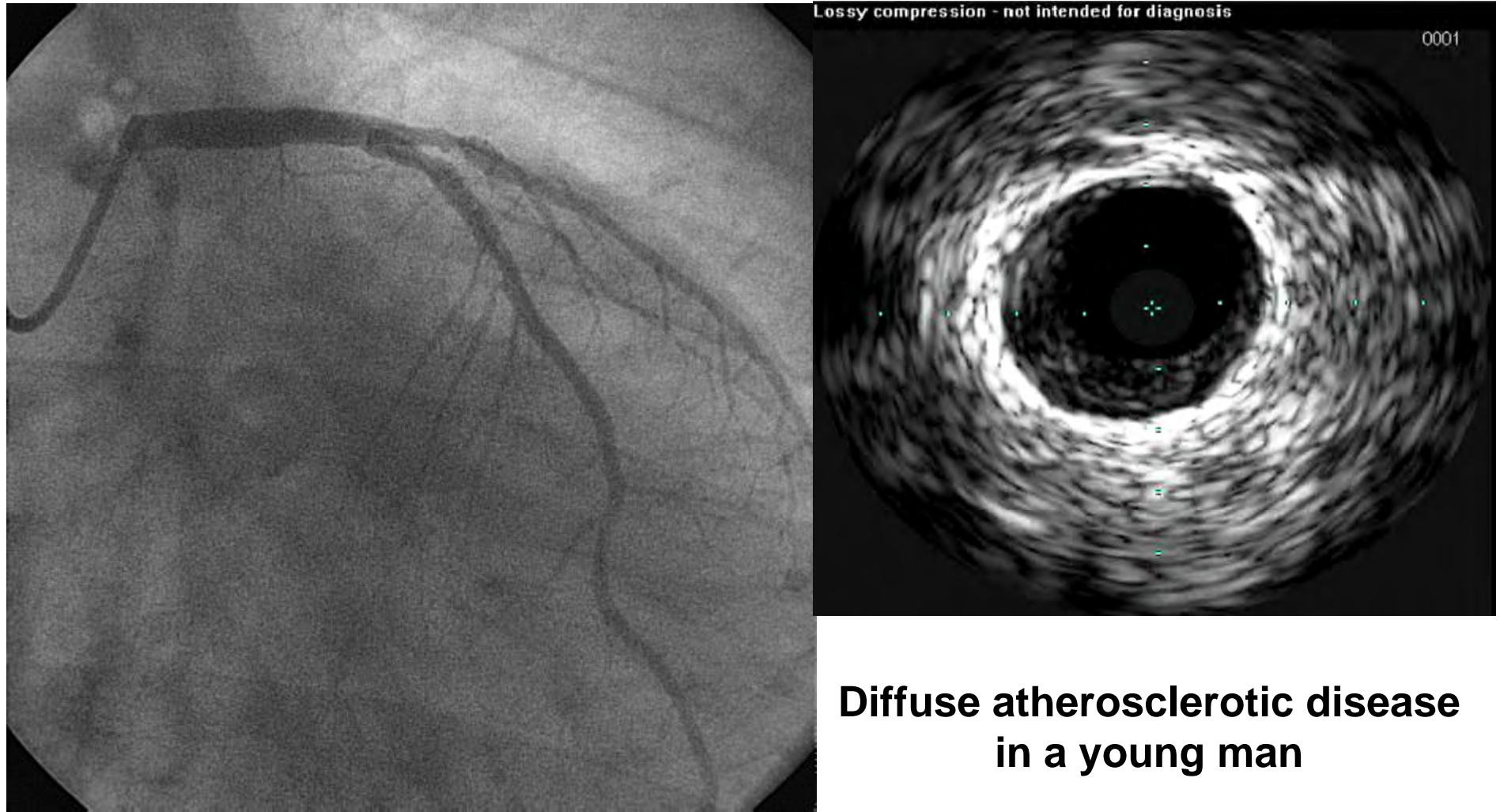
- BMI 42 kg/m²
- Mixed hyperlipidemia
- Smoker 35 pk yr
- 3 hours of acute chest pain
- TnT 3.25 (<0.03)
- CK 2234



Case: 46M



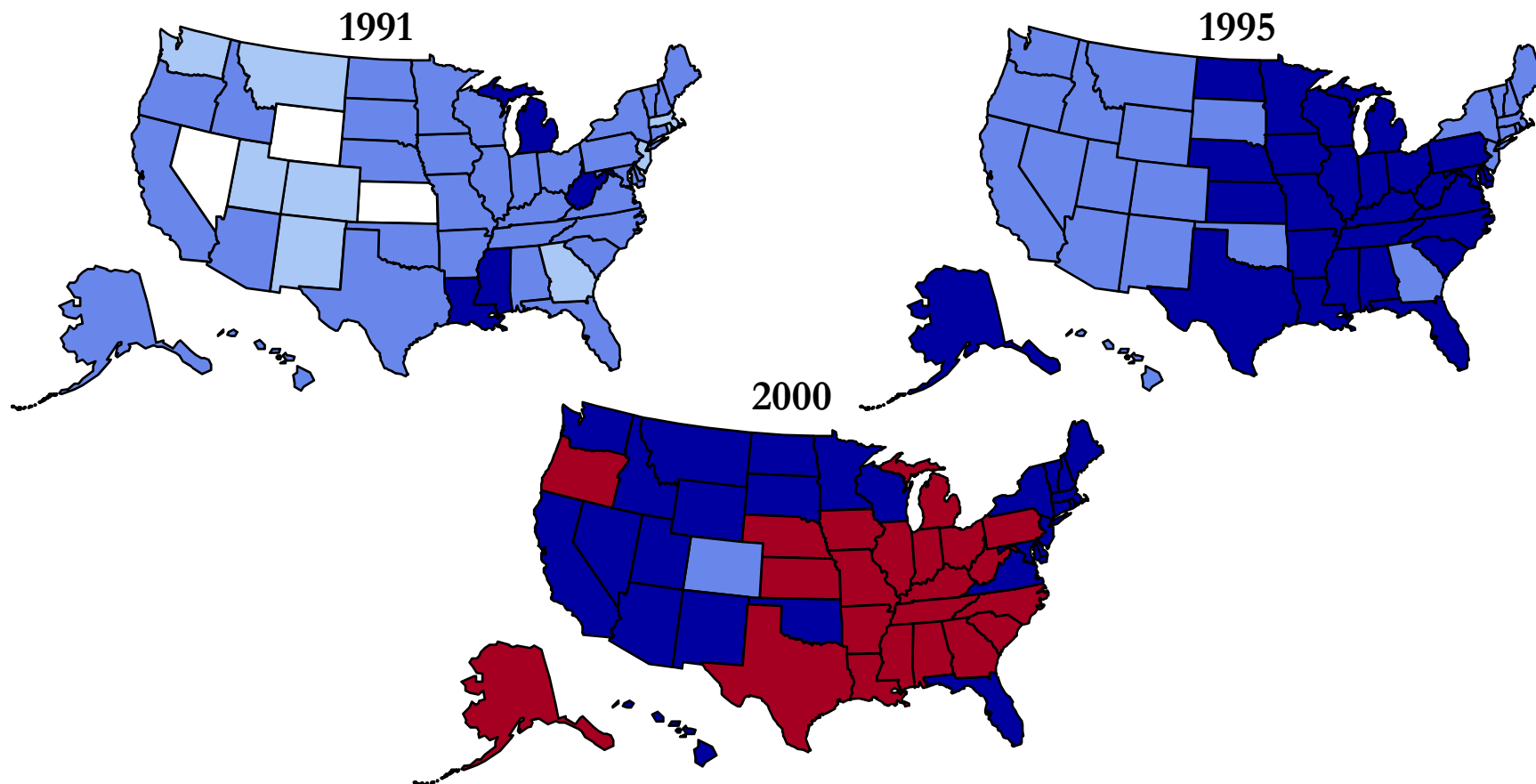
Case: 46M



Obesity Trends* Among U.S. Adults

BRFSS, 1991, 1995 and 2000

(*BMI ≥ 30 , or ~ 30 lbs overweight for 5'4" woman)



No Data ☐

<10% ☐

10%-14% ☐

15-19% ☐

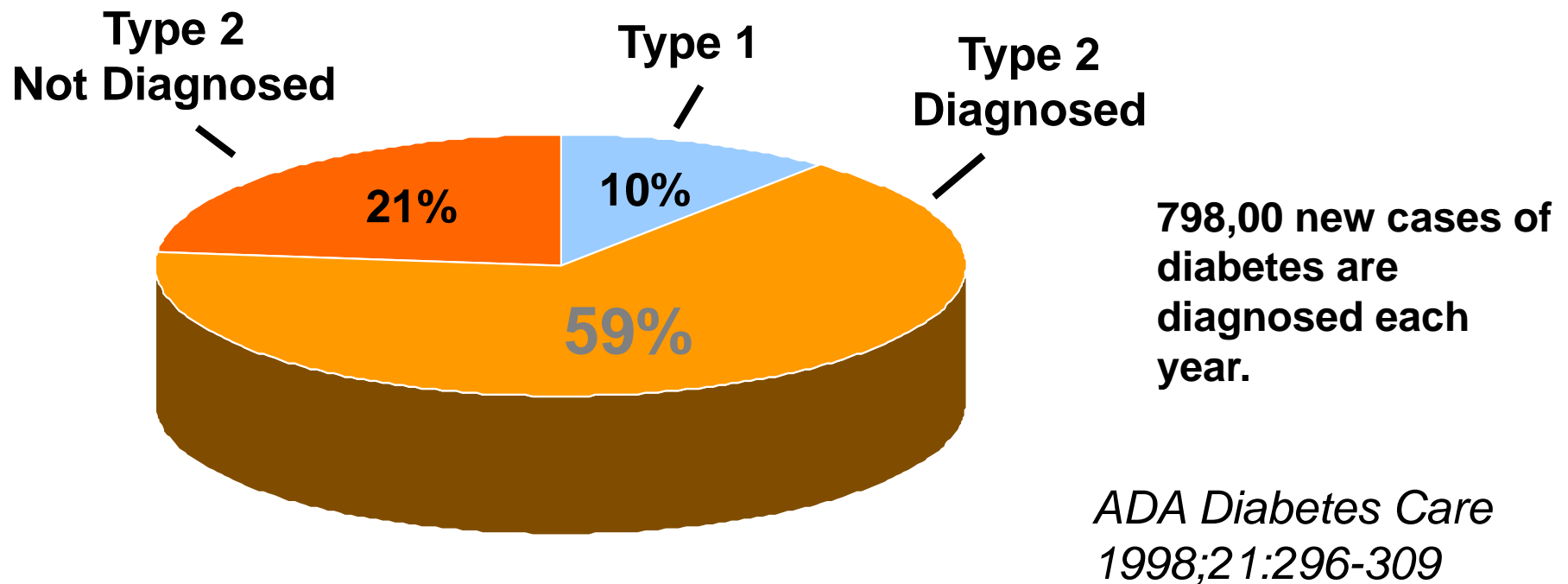
$\geq 20\%$ ☐



Source: Mokdad A H, et al. *J Am Med Assoc* 1999;282:16, 2001;286:10.

Prevalence of Diabetes in the U.S.

More than 16 million Americans have diabetes



EUROASPIRE SURVEY ESC 2007

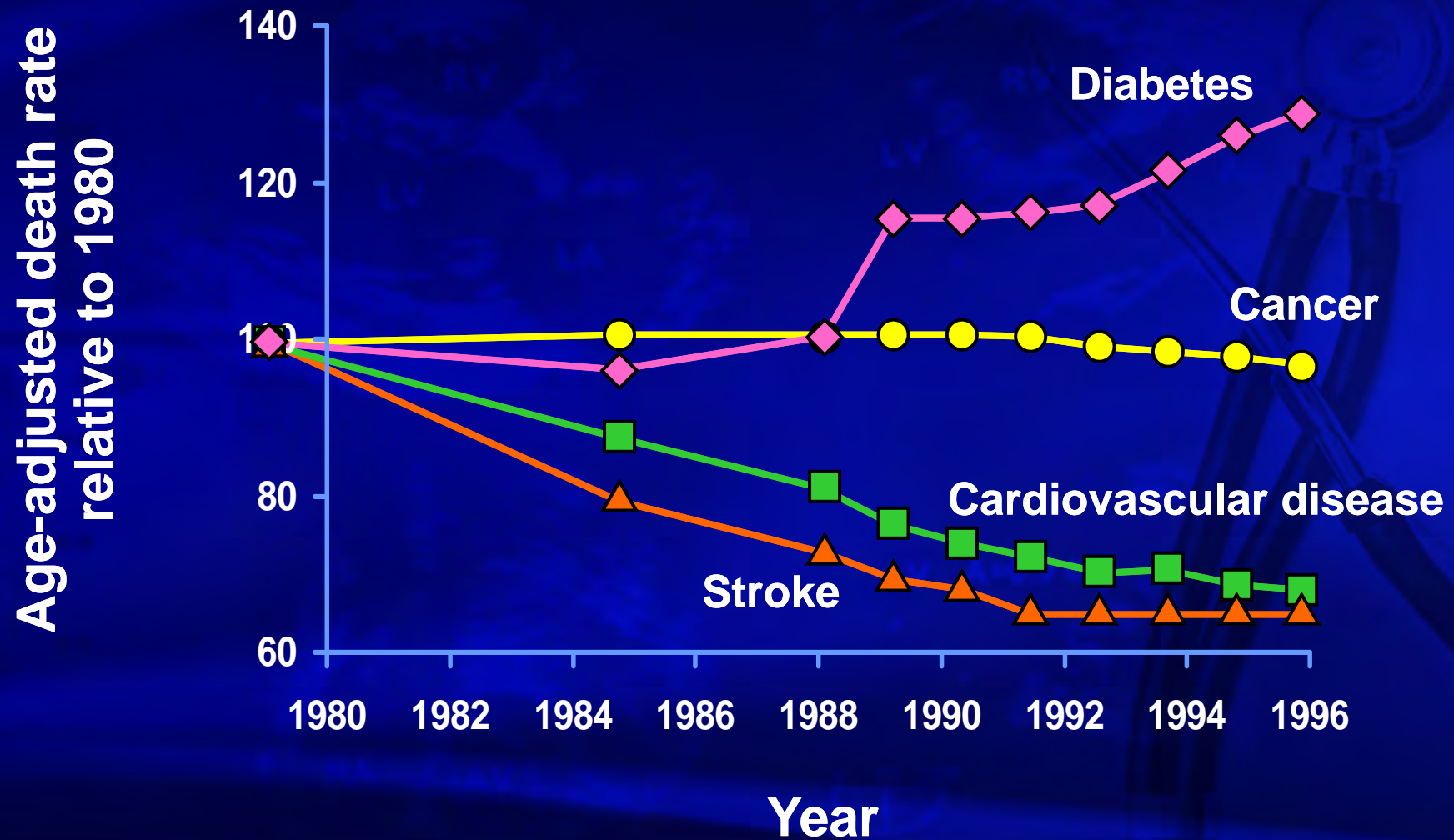
Prevalence of HTN, high cholesterol, and diabetes

EUROASPIRE surveys	Patients (%)			
	With raised BP ^a	With elevated TC ^b (%)	With elevated LDL-C ^c (%)	With diabetes
Survey 1	58.1	94.5	96.4	17.4
Survey 2	58.3	76.7	78.1	20.1
Survey 3	60.9	46.2	47.5	28.0

a. $\geq 140/90$ mm Hg or $\geq 130/80$ mm Hg among diabetics
b. 4.5 mmol/L or greater
c. 2.5 mmol/L or greater

Wood D. European Society of Cardiology Congress
2007; September 2, 2007; Vienna, Austria.

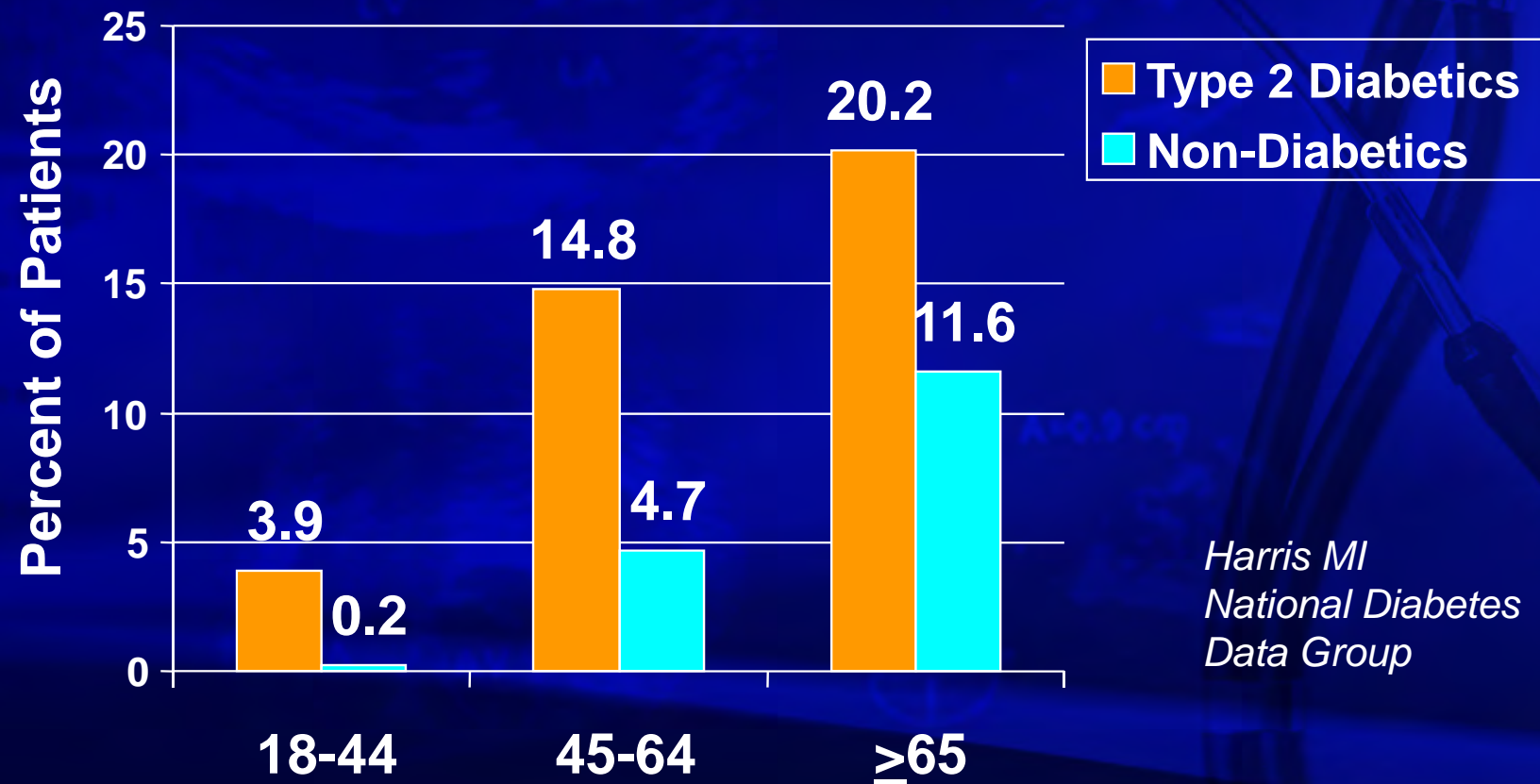
Increasing Deaths Due to Diabetes



Nature Medicine 5(4):364, 1999

Prevalence of Ischemic Heart Disease

2/3 of diabetics die from cardiovascular disease.



*Harris MI
National Diabetes
Data Group*

The Present

The US is already the most obese nation on earth, and we are getting bigger.



Western Acculturation





McAlooTikki™



McCurry Pan™

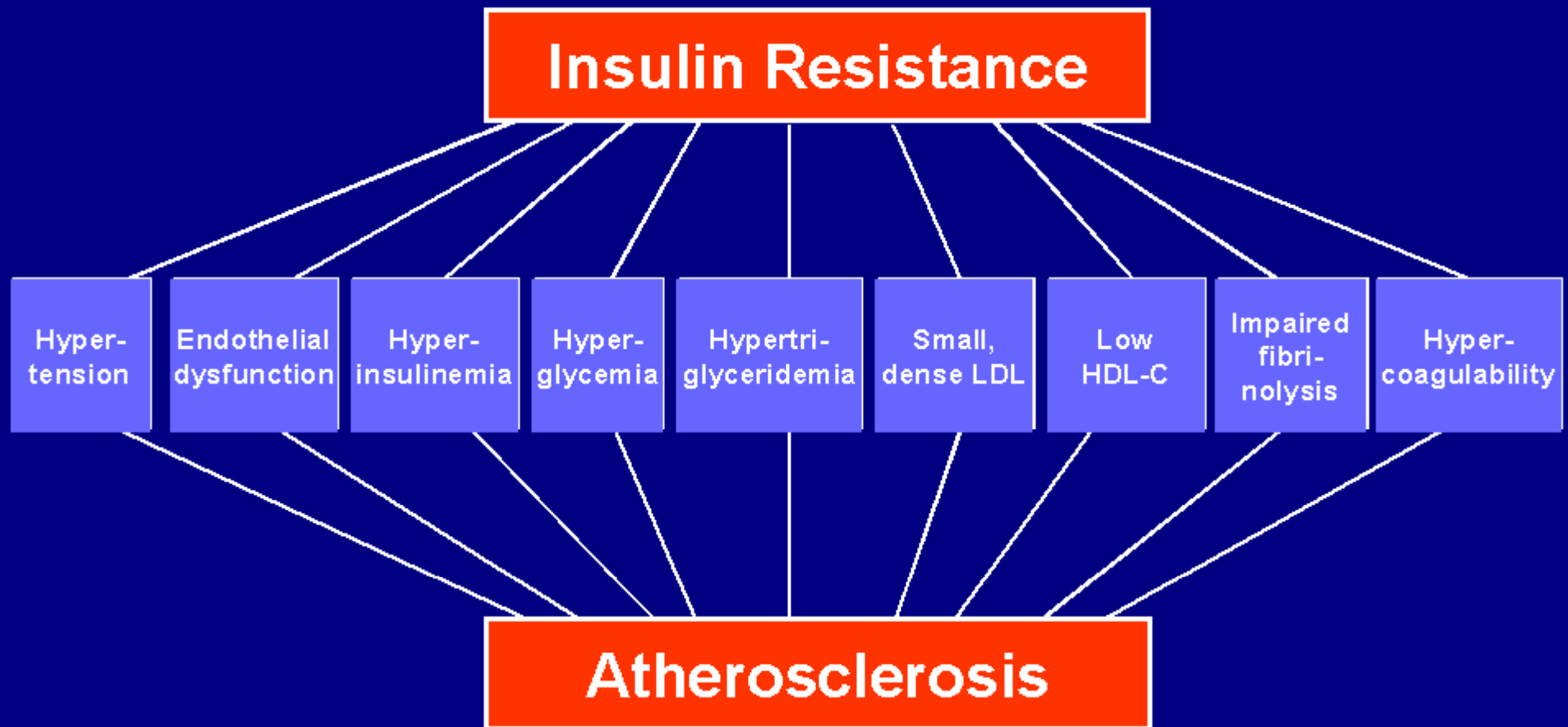


The Future





Interrelationship Between Insulin Resistance^c and Atherosclerosis



BARI Randomized Trial

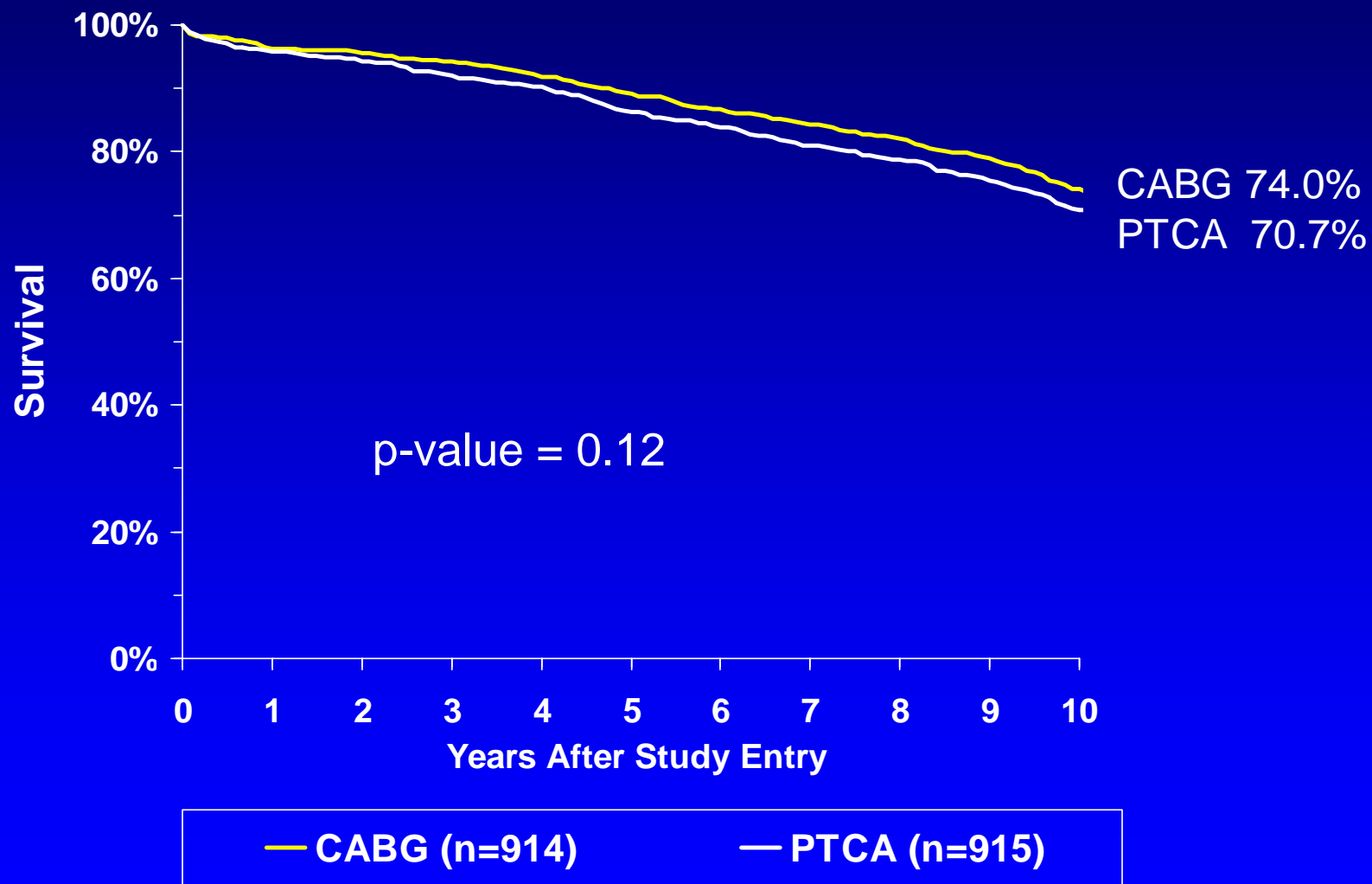
Designed to compare CABG and PTCA in patients who have:

- ◆ Multivessel coronary artery disease
- ◆ Angina or objective evidence of ischemia
- ◆ No prior revascularization procedures
- ◆ Eligible for both PTCA and CABG
- ◆ Complete revascularization NOT required

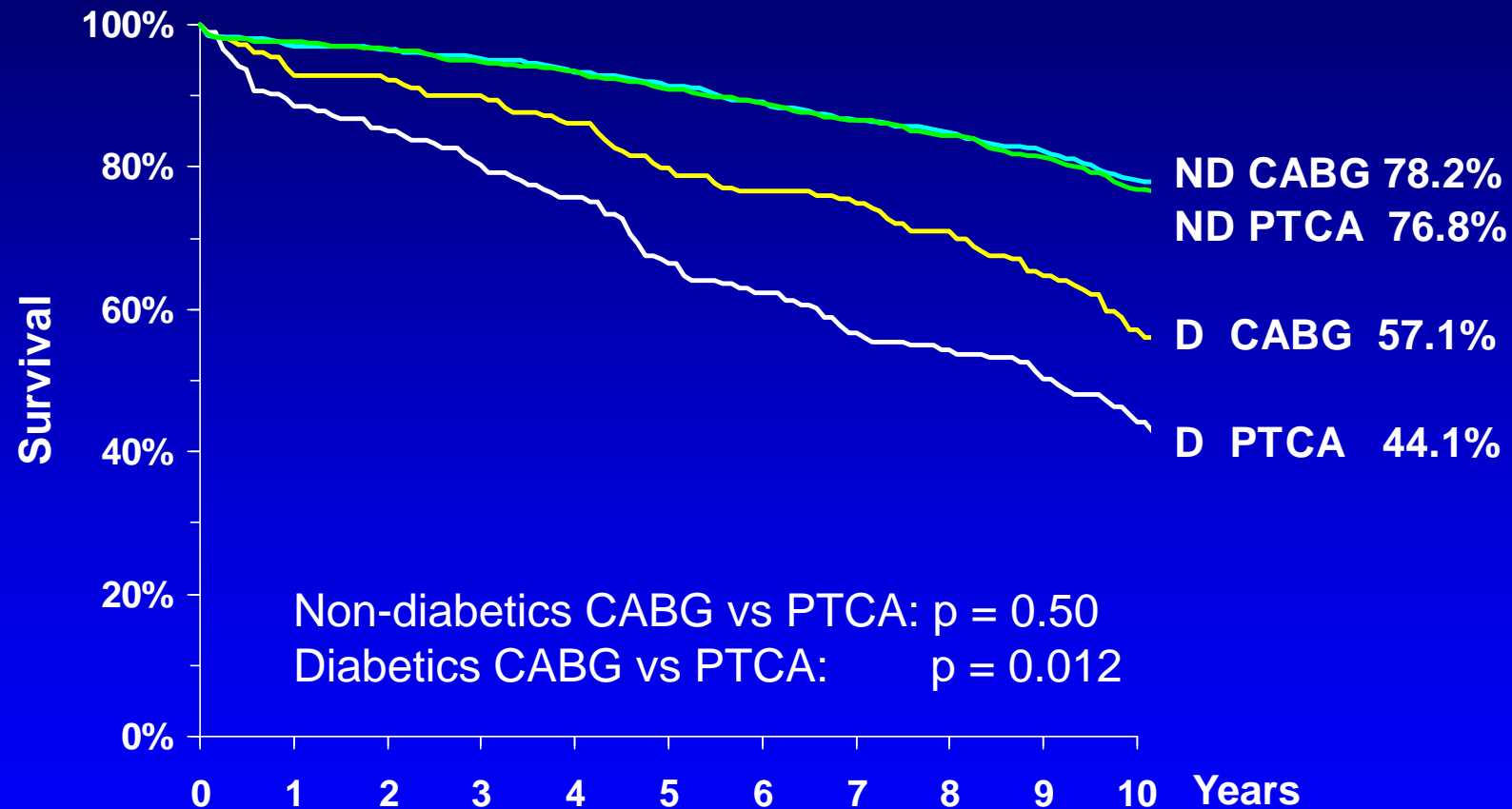
Survival analysis

BARI Randomized Trial

10-Year Survival

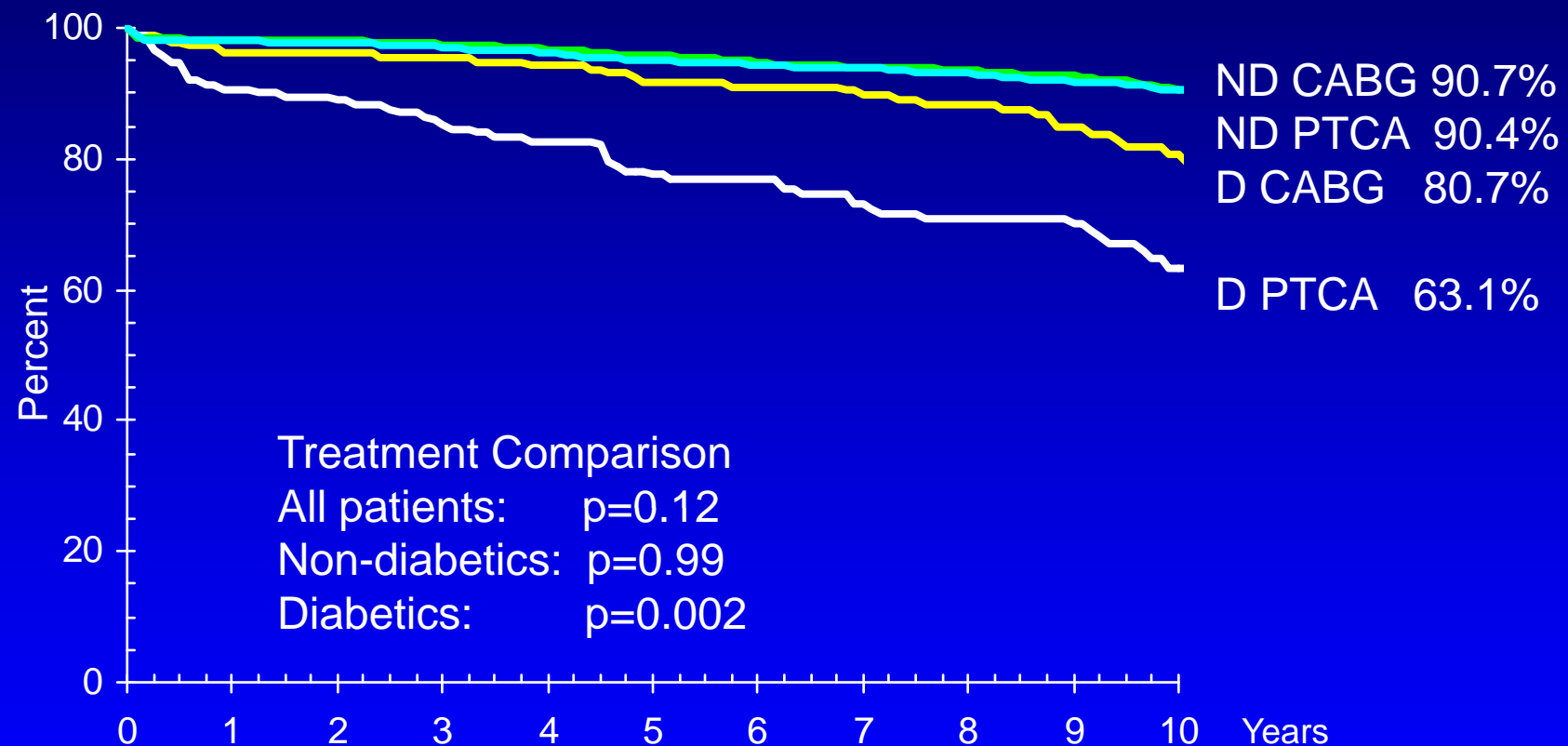


10-Year Survival Stratified by Diabetes Status



Diab CABG (n=180)	Diab PTCA (n=173)
Non-diab CABG (n=734)	Non-diab PTCA (n=742)

Freedom from Cardiac Death Stratified by Diabetes Status



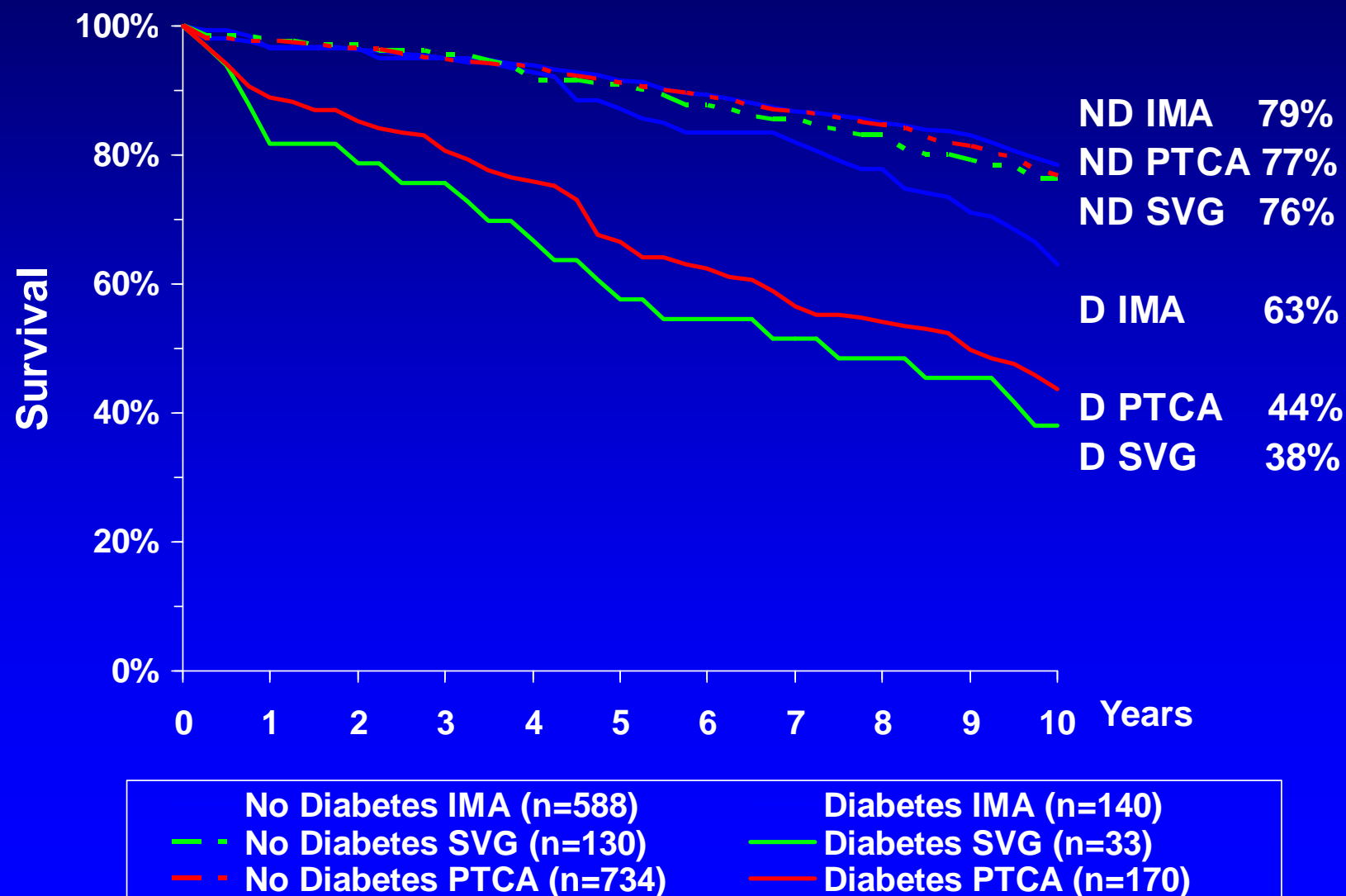
— Diab CABG (n=180)

— Diab PTCA (n=173)

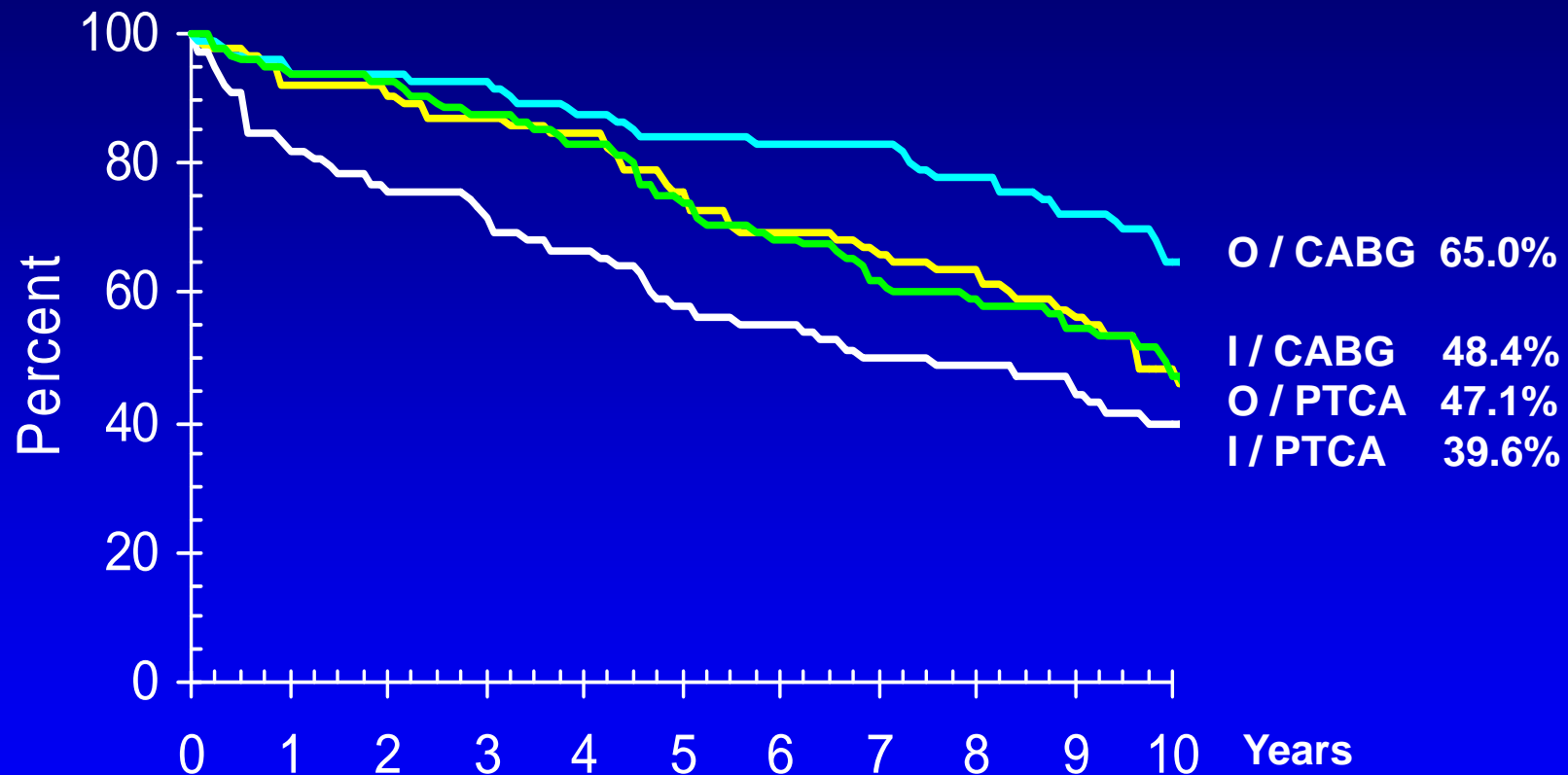
— Non-diab CABG (n=734)

— Non-diab PTCA (n=742)

Survival by Diabetes Status and by Revascularization Treatment Received



Survival among Patients with Diabetes Stratified by Diabetic Treatment at Baseline



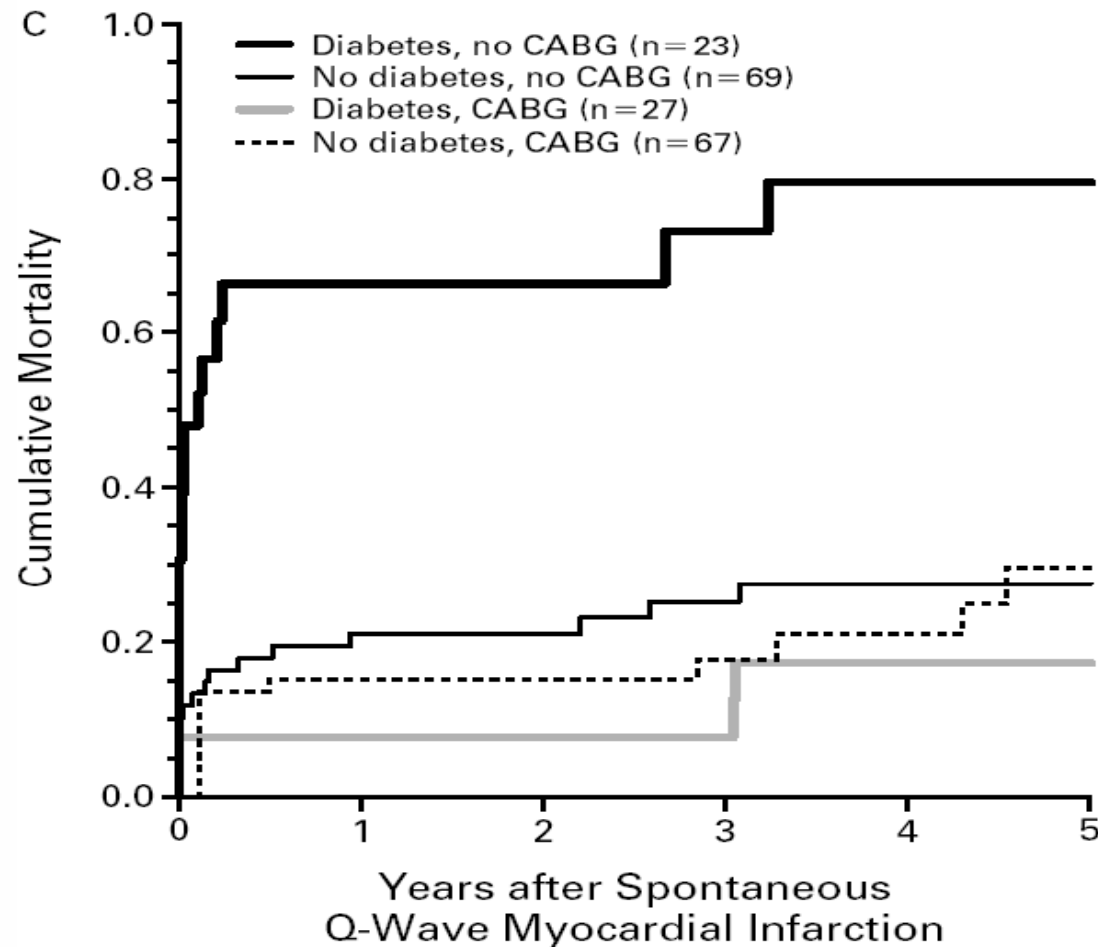
— Insulin CABG (n=85)

— Insulin PTCA (n=78)

— Oral CABG (n=95)

— Oral PTCA (n=95)

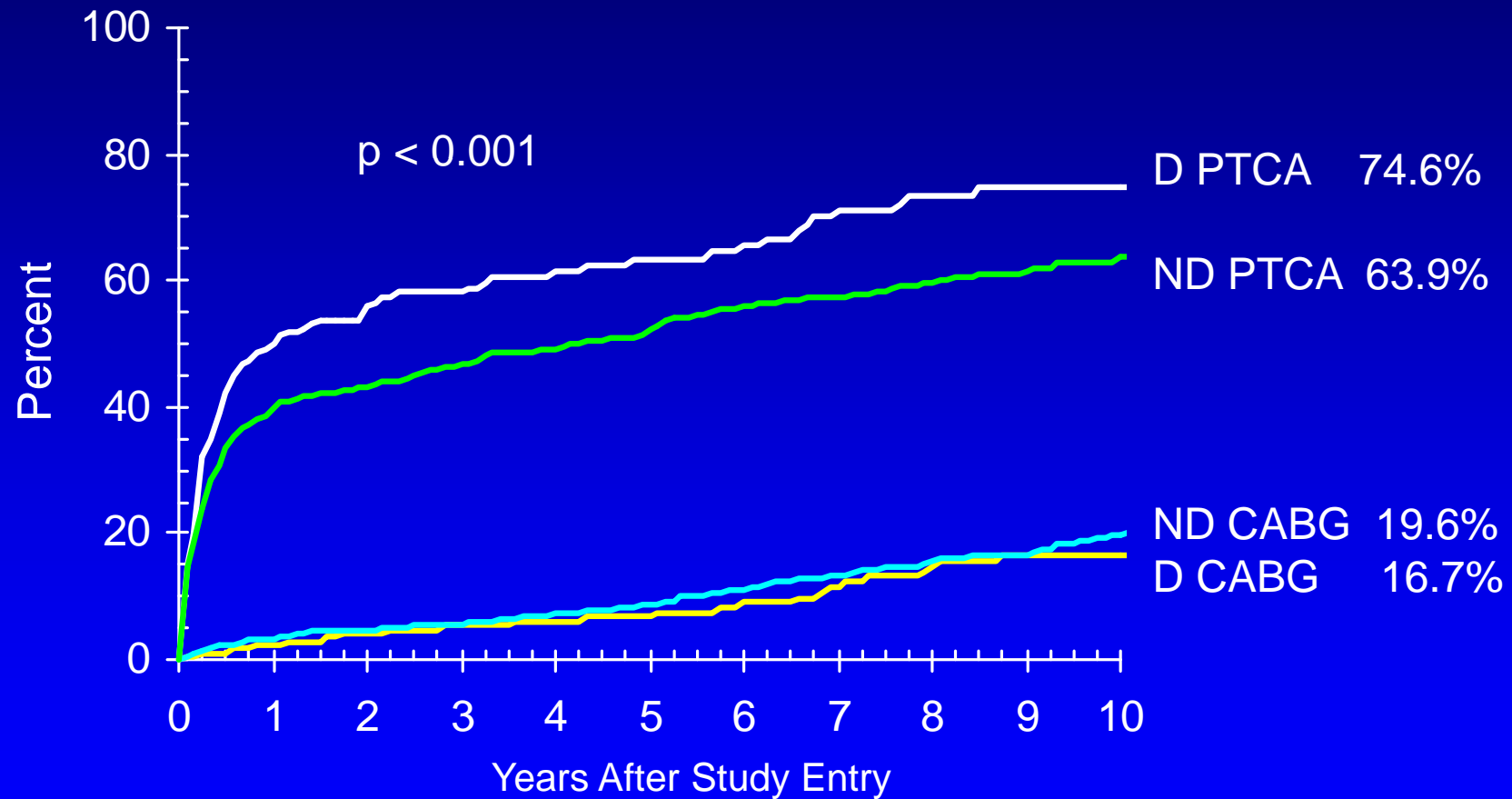
Prior CABG is Protective after AMI in Diabetic Patients



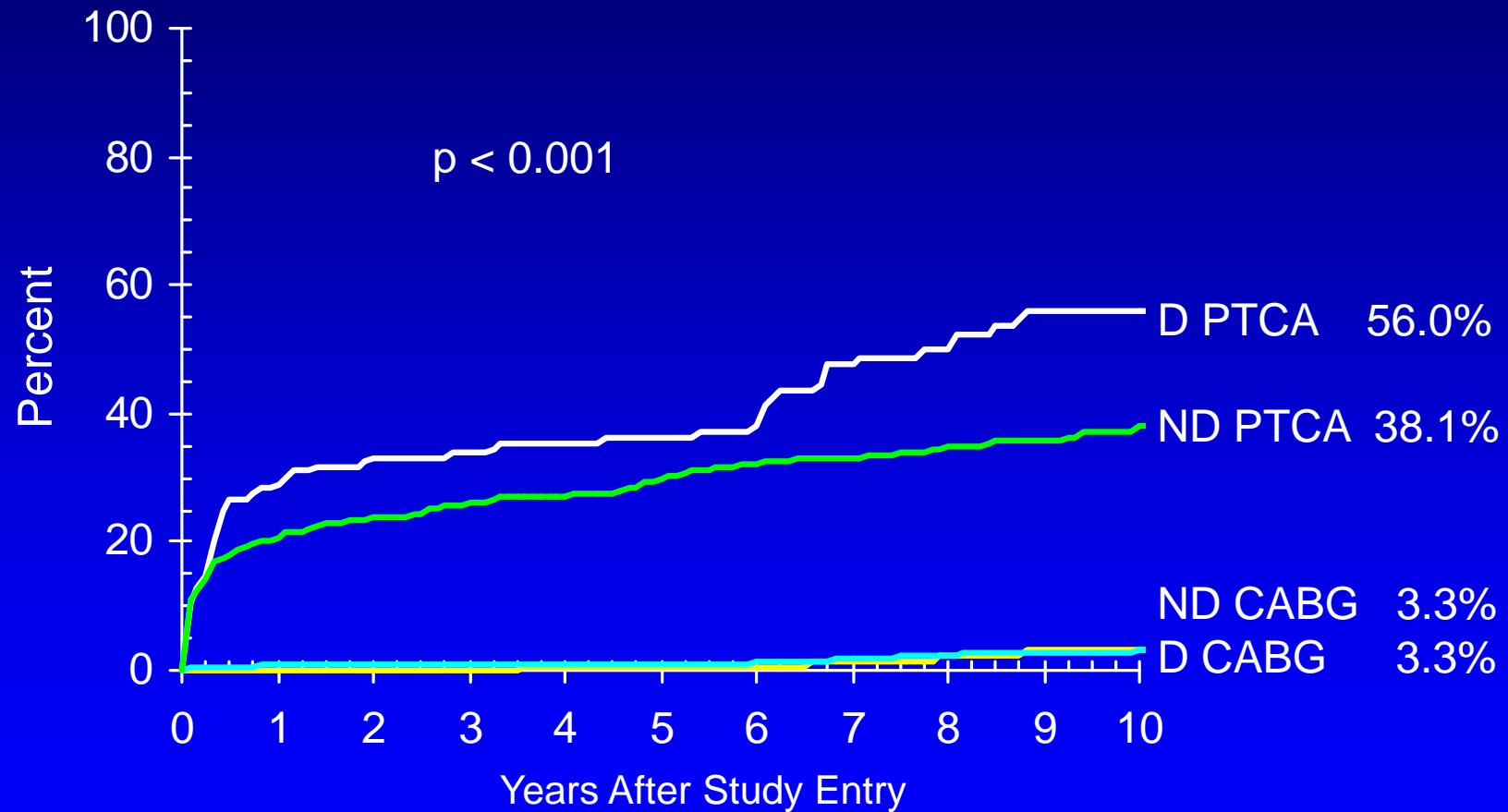
Detre et al. BARI Trial. NEJM. 2000

Repeat Revascularization

Subsequent Revascularization Stratified by Diabetes Status



Subsequent CABG Stratified by Diabetes Status



Coronary artery bypass surgery compared with percutaneous coronary interventions for multivessel disease: a collaborative analysis of individual patient data from ten randomised trials



Mark A Hlatky, Derek B Boothroyd, Dena M Bravata, Eric Boersma, Jean Booth, Maria M Brooks, Didier Carrié, Tim C Clayton, Nicolas Danchin, Marcus Flather, Christian W Hamm, Whady A Hueb, Jan Kähler, Sheryl F Kelsey, Spencer B King, Andrzej S Kosinski, Neuza Lopes, Kathryn M McDonald, Alfredo Rodriguez, Patrick Serruys, Ulrich Sigwart, Rodney H Stables, Douglas K Owens, Stuart J Pocock

Lancet 2009

Summary

Background Coronary artery bypass graft (CABG) and percutaneous coronary intervention (PCI) are alternative treatments for multivessel coronary disease. Although the procedures have been compared in several randomised trials, their long-term effects on mortality in key clinical subgroups are uncertain. We undertook a collaborative analysis of data from randomised trials to assess whether the effects of the procedures on mortality are modified by patient characteristics.

Methods We pooled individual patient data from ten randomised trials to compare the effectiveness of CABG with PCI according to patients' baseline clinical characteristics. We used stratified, random effects Cox proportional hazards models to test the effect on all-cause mortality of randomised treatment assignment and its interaction with clinical characteristics. All analyses were by intention to treat.

10 RCTs N=7812
POBA in 6 trials
BMS in 4 trials

Published Online

March 20, 2009

DOI:10.1016/S0140-6736(09)60552-3

See Online/Comment

DOI:10.1016/S0140-6736(09)60574-2

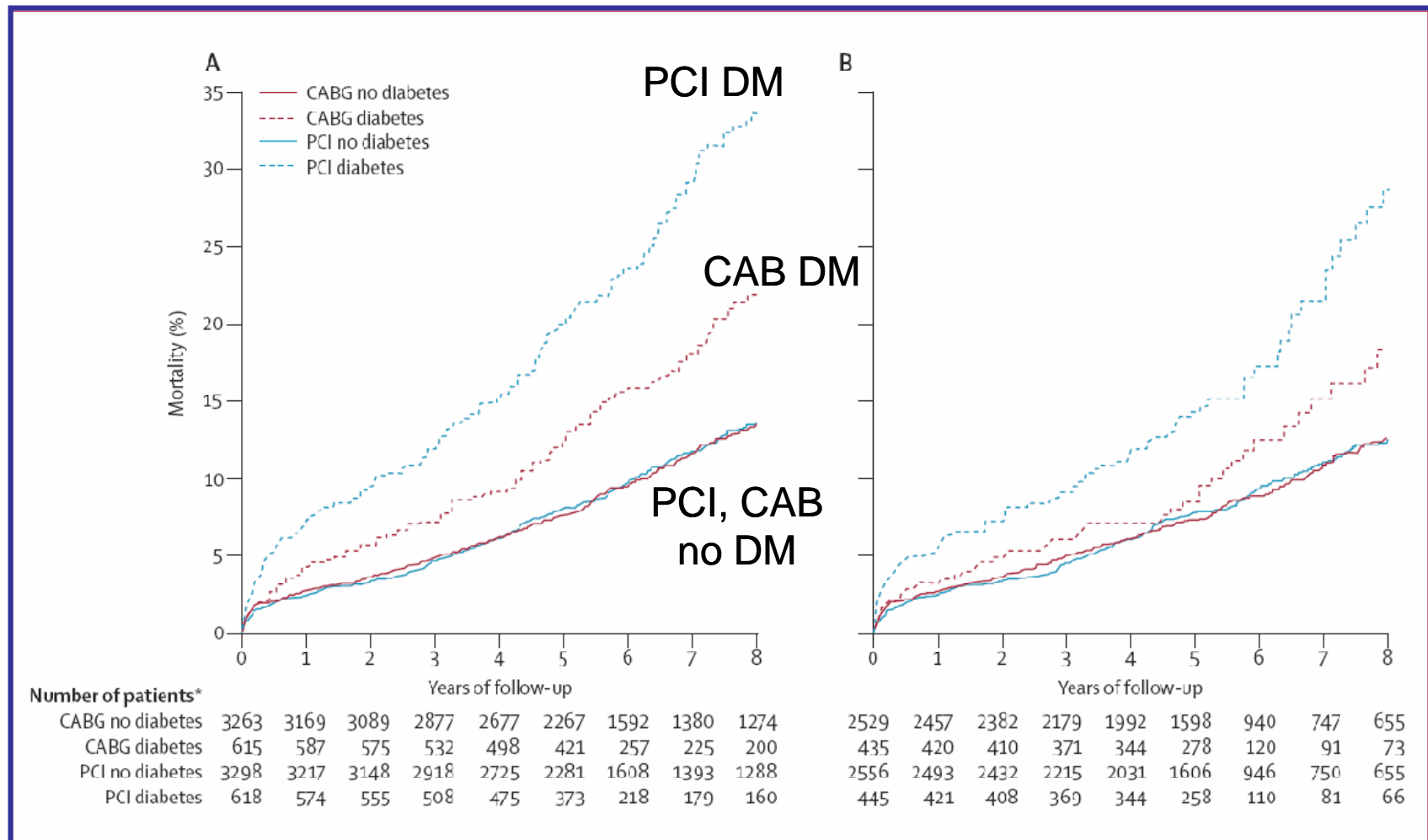
Stanford University School of Medicine, Stanford, CA, USA

(Prof M A Hlatky MD, D B Boothroyd PhD, D M Bravata MD, K M McDonald MM);

Department of Cardiology, Erasmus University, Rotterdam, Netherlands

(Prof E Boersma PhD, Prof P Serruys MD); Royal Brompton & Harefield NHS Trust, London, UK (J Booth MS, M Flather FRCP); Department of Epidemiology, University of Pittsburgh, Pittsburgh, PA, USA (M M Brooks PhD, Prof S F Kelsey PhD); Rangueil

Effect of Diabetes on Outcome



Hlatky Lancet 2009

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APRIL 12, 2007

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Optimal Medical Therapy with or without PCI for Stable Coronary Disease

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ABSTRACT

BACKGROUND

In patients with stable coronary artery disease, it remains unclear whether an initial management strategy of percutaneous coronary intervention (PCI) with intensive pharmacologic therapy and lifestyle intervention (optimal medical therapy) is superior

Affiliations for all authors are listed in the Appendix. Address reprint requests to Dr. Boden at the Division of Cardiology, Buffalo General Hospital, 100 High St., Buffalo, N.Y. 14203.

A North American Trial



19 US Non-VA Hospitals

50 Hospitals



15 VA Hospitals

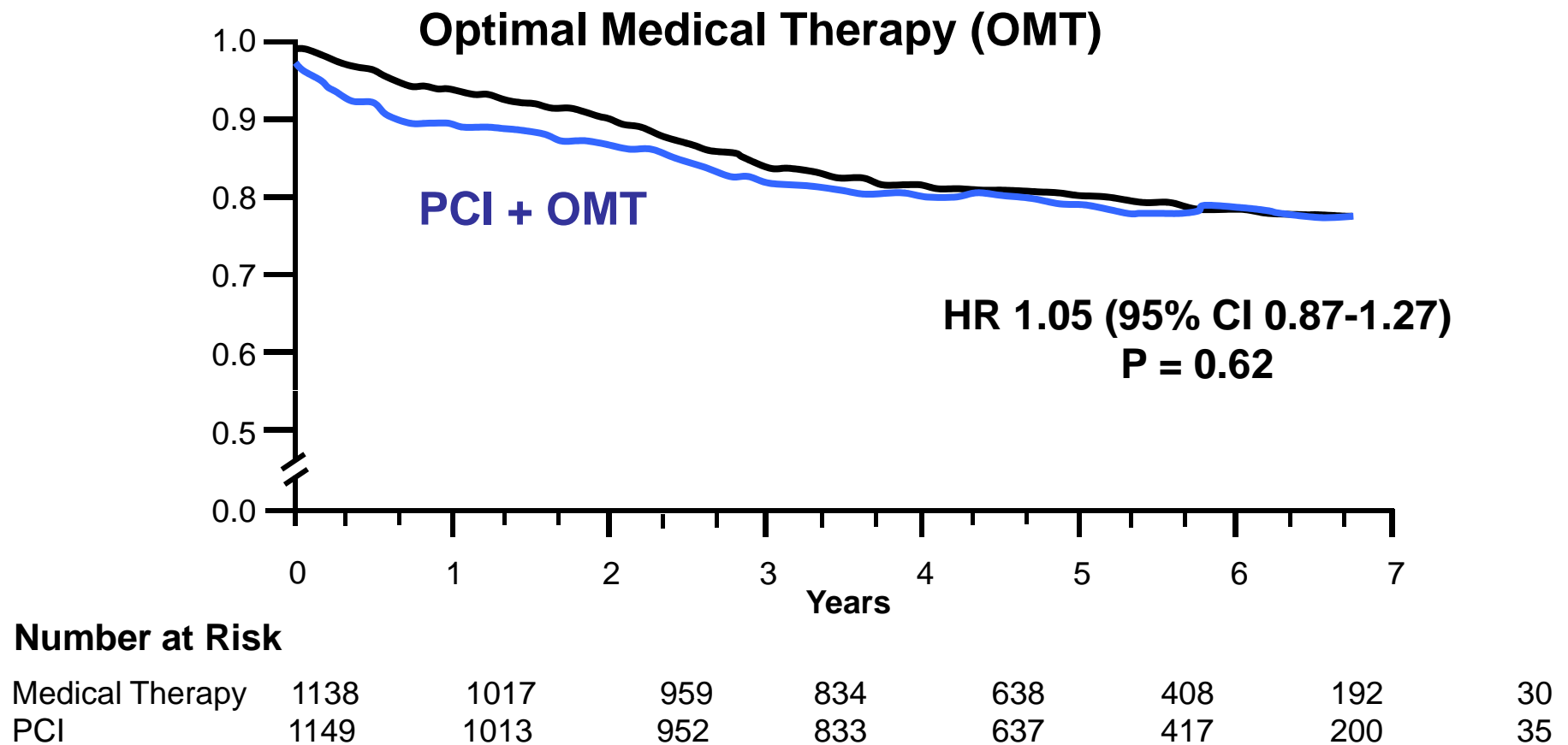
2,287 patients
enrolled between
6/99-1/04

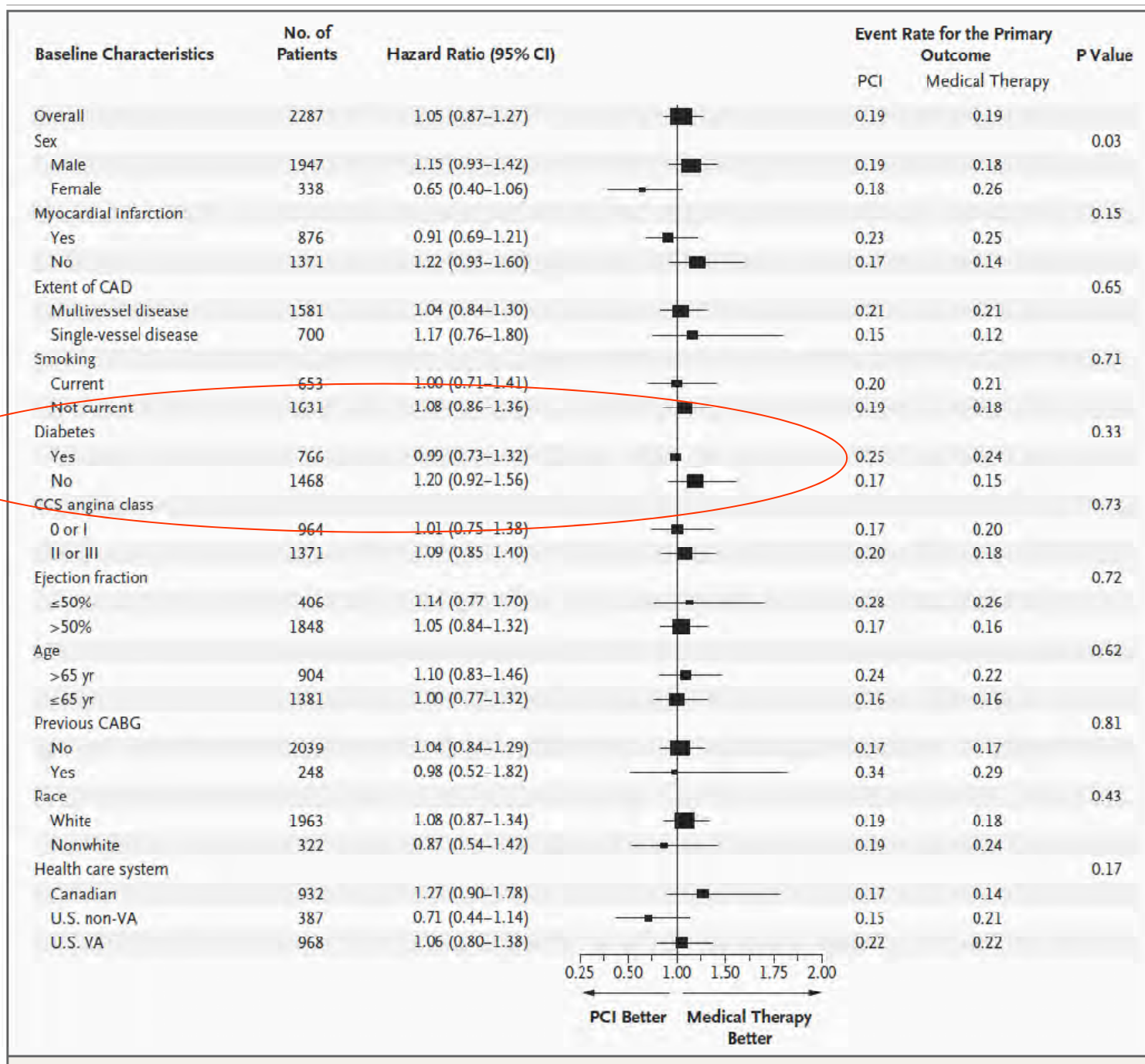


16 Canadian Hospitals

32 % Diabetes

Survival Free of Death from Any Cause and Myocardial Infarction





**Bypass Angioplasty
Revascularization Investigation
2 Diabetes (BARI 2D) tested
the hypothesis that early
revascularization would improve
mortality.**



BARI 2D Randomization: 2 x 2 Factorial Design

Ischemia Control Strategy

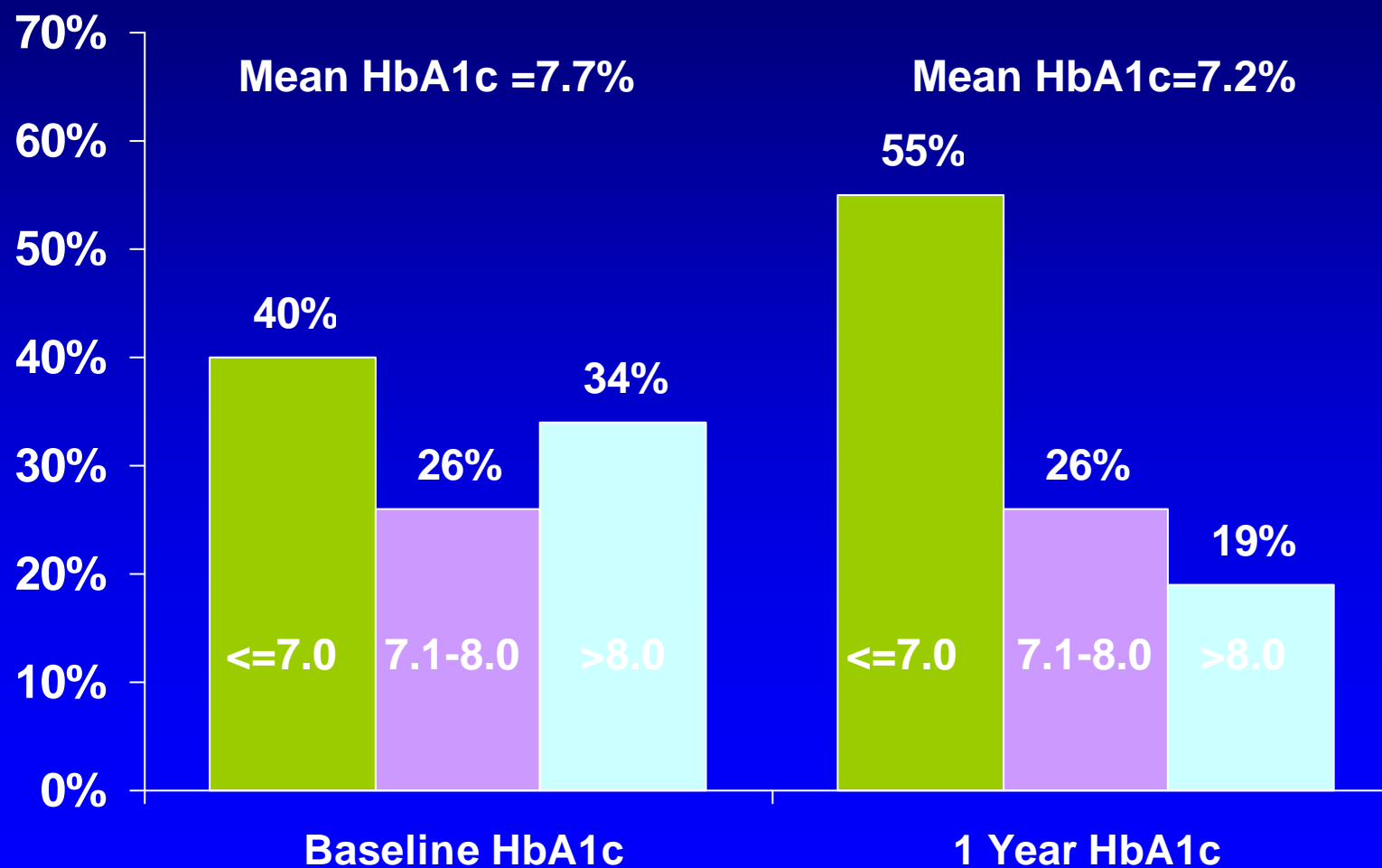
**Glucose
Control
Strategy**

	Ischemia Control Strategy		
	Prompt Revasc	Medical	
Insulin Provision	592	593	1185
Insulin Sensitization	584	599	1183
	1176	1192	2368



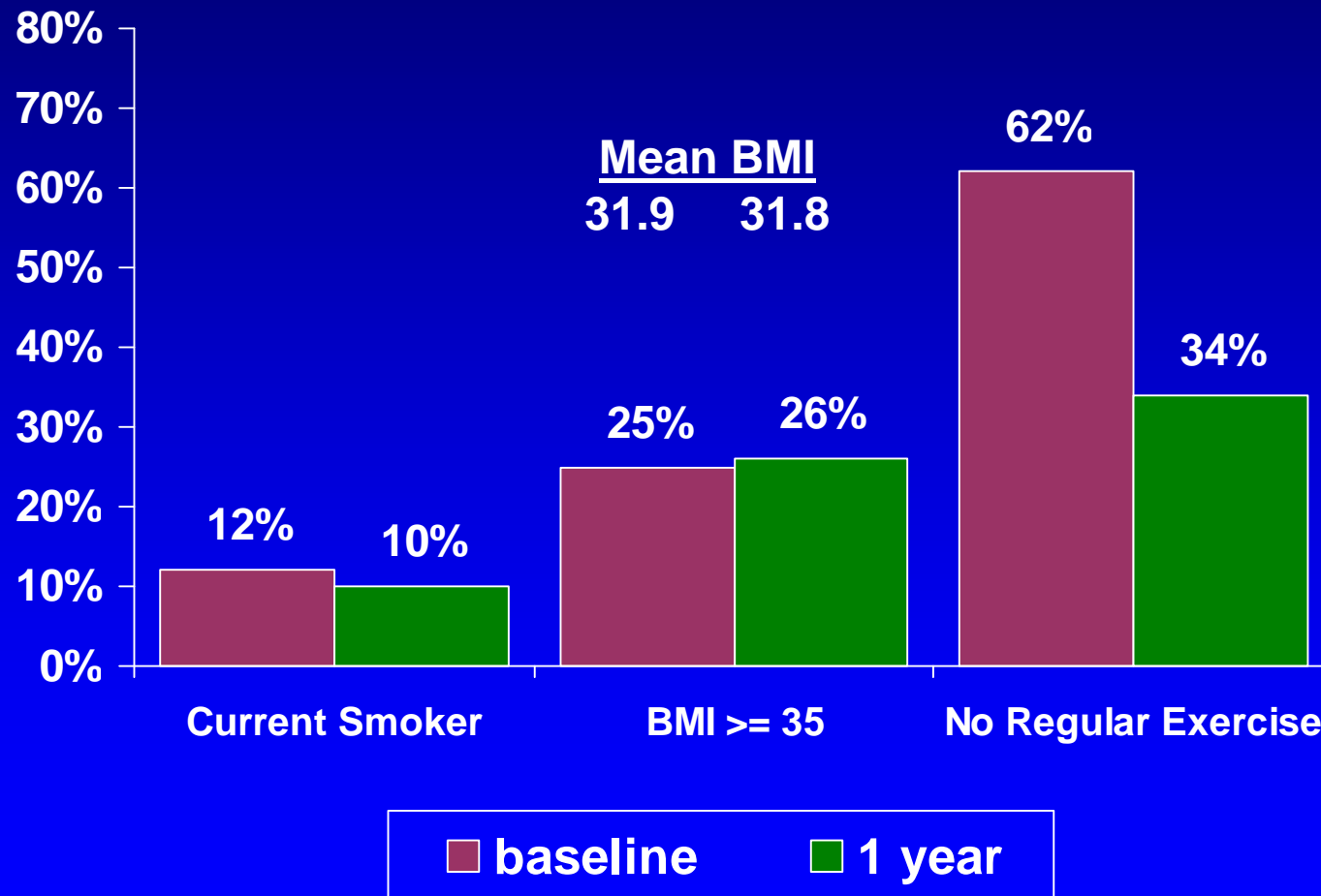
One-Year Glycemic Management

(N=1721 Patients with One Year of Follow-up)

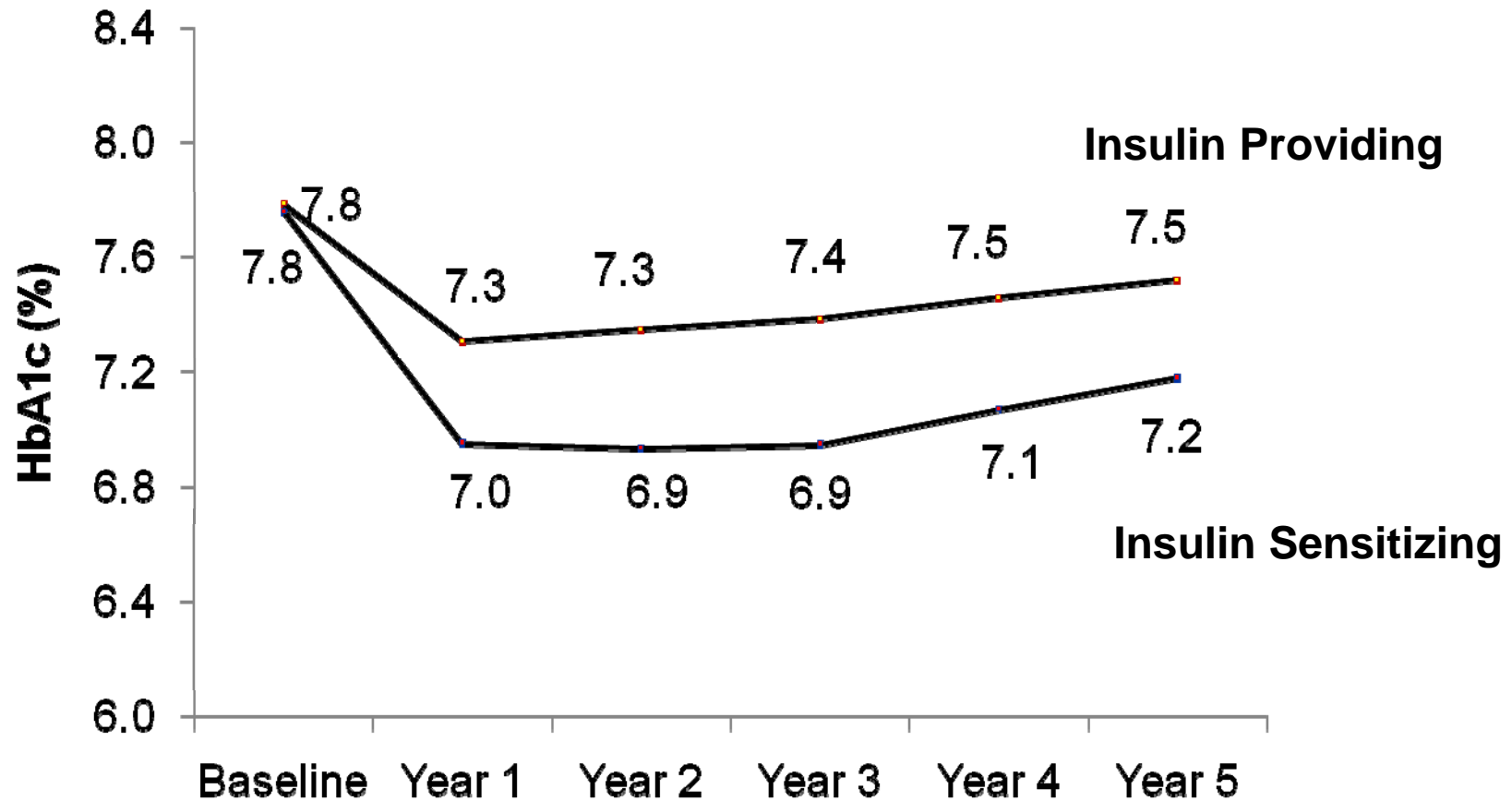


One-Year Lifestyle Factor Management

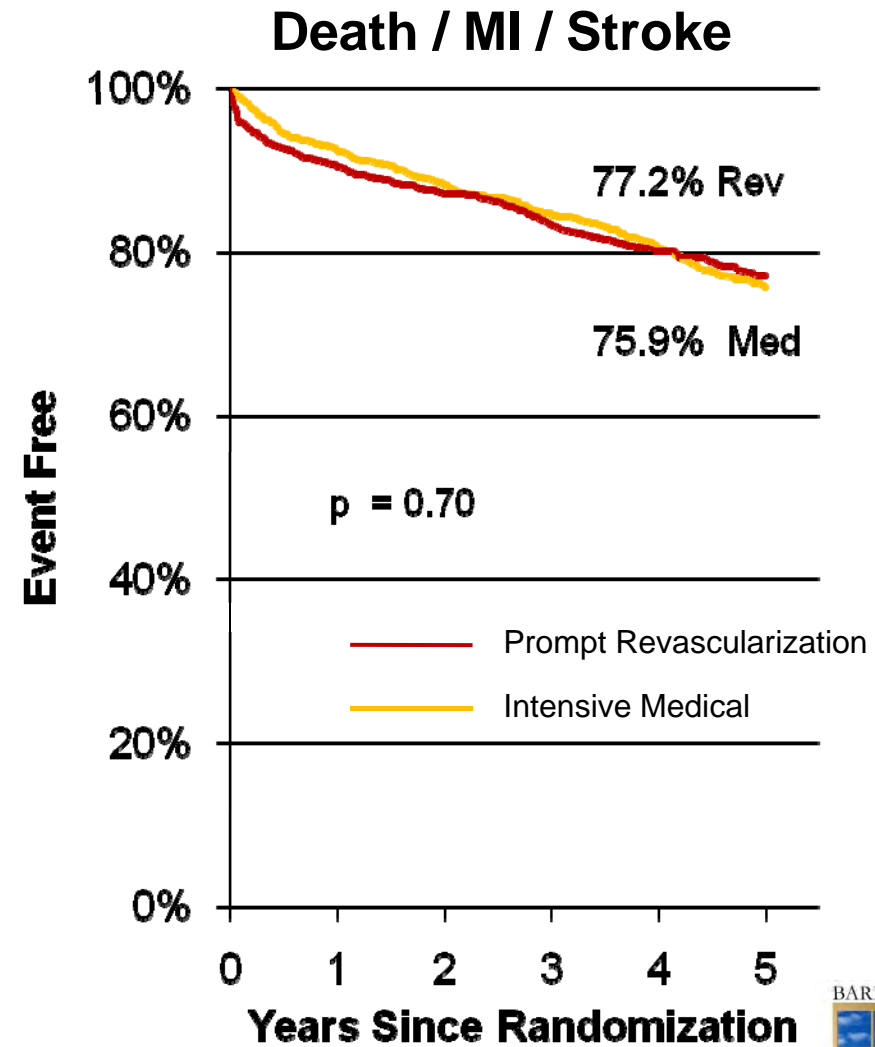
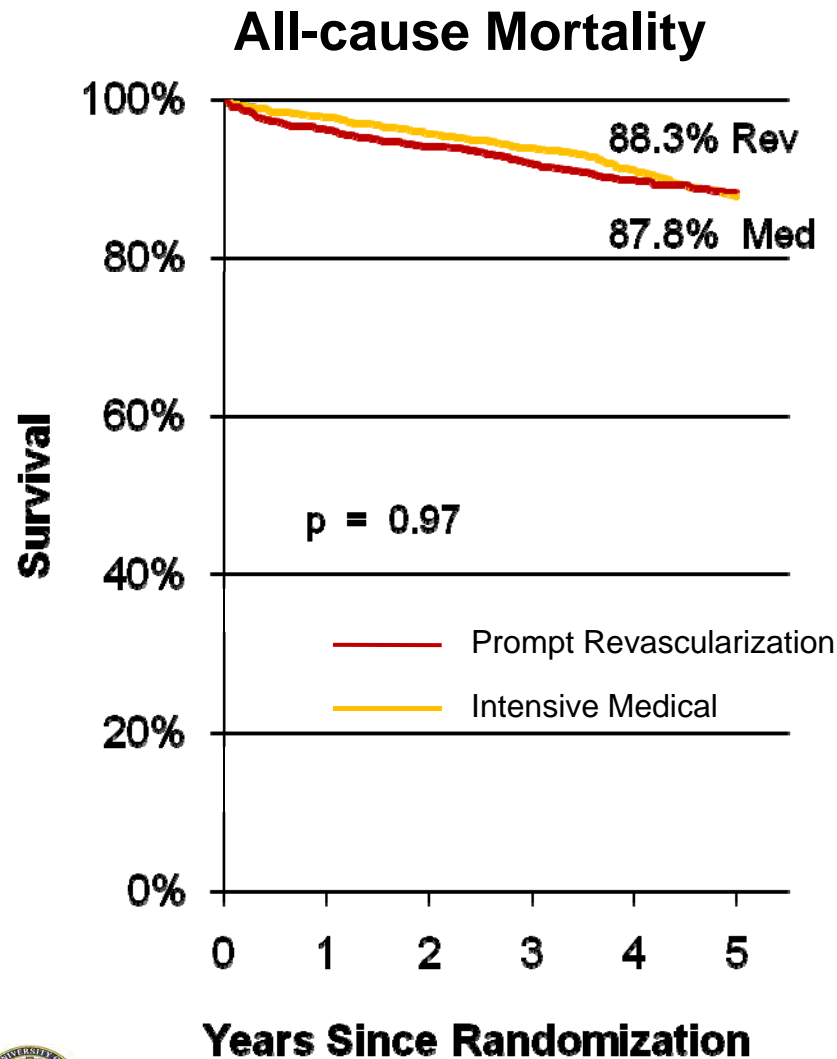
(N=1732 Patients with One Year of Follow-up)



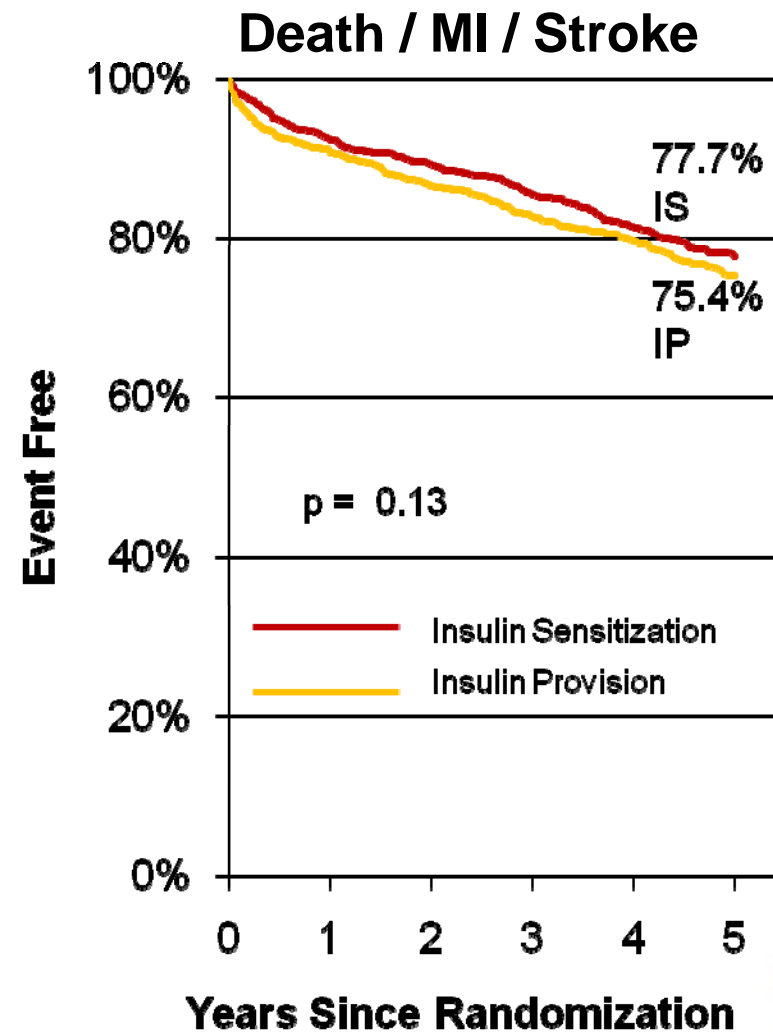
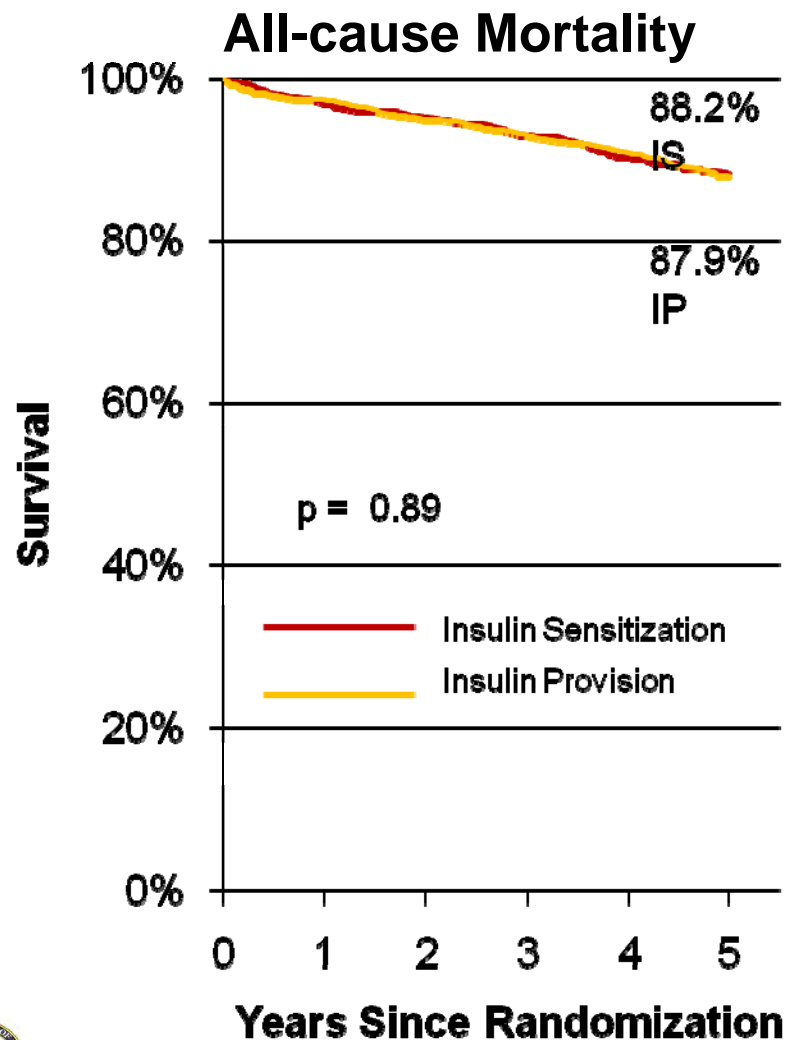
HbA1c Mean Over Time



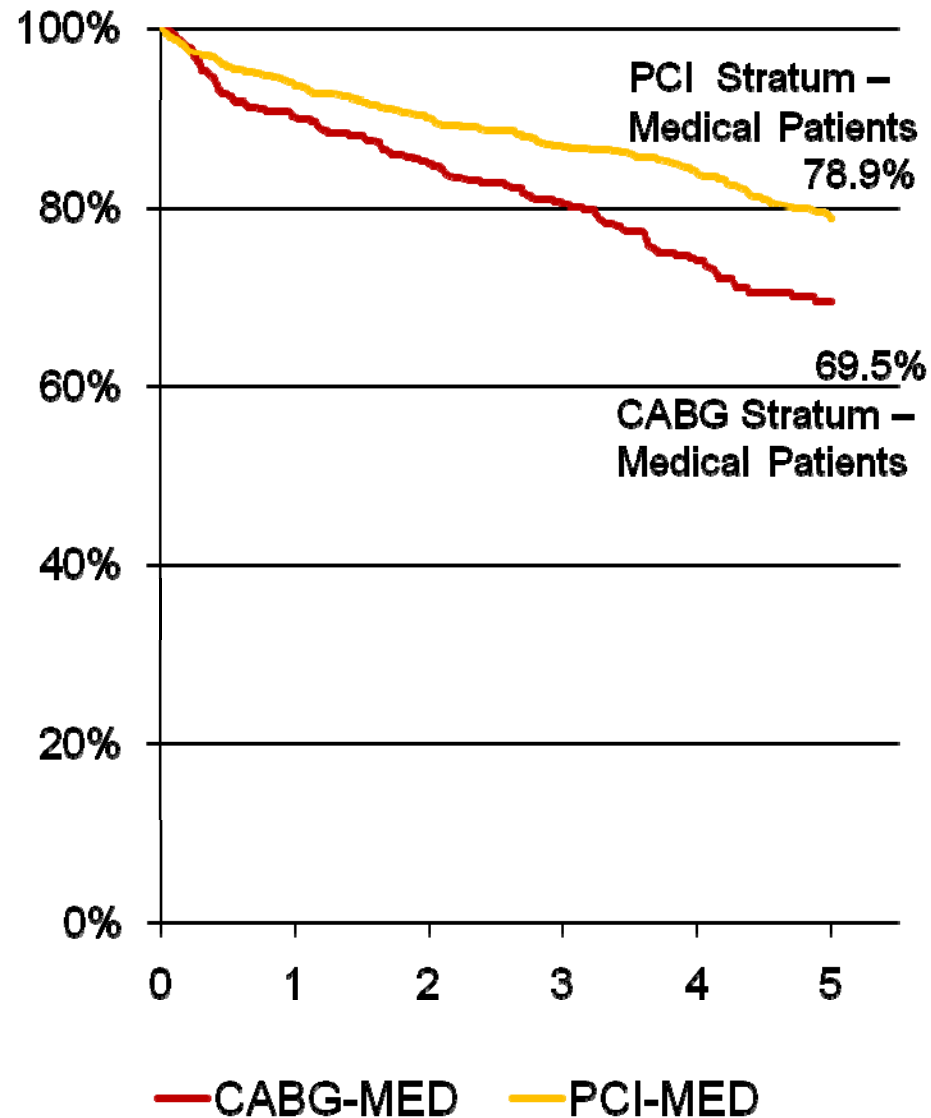
Prompt Revascularization vs Medical Therapy



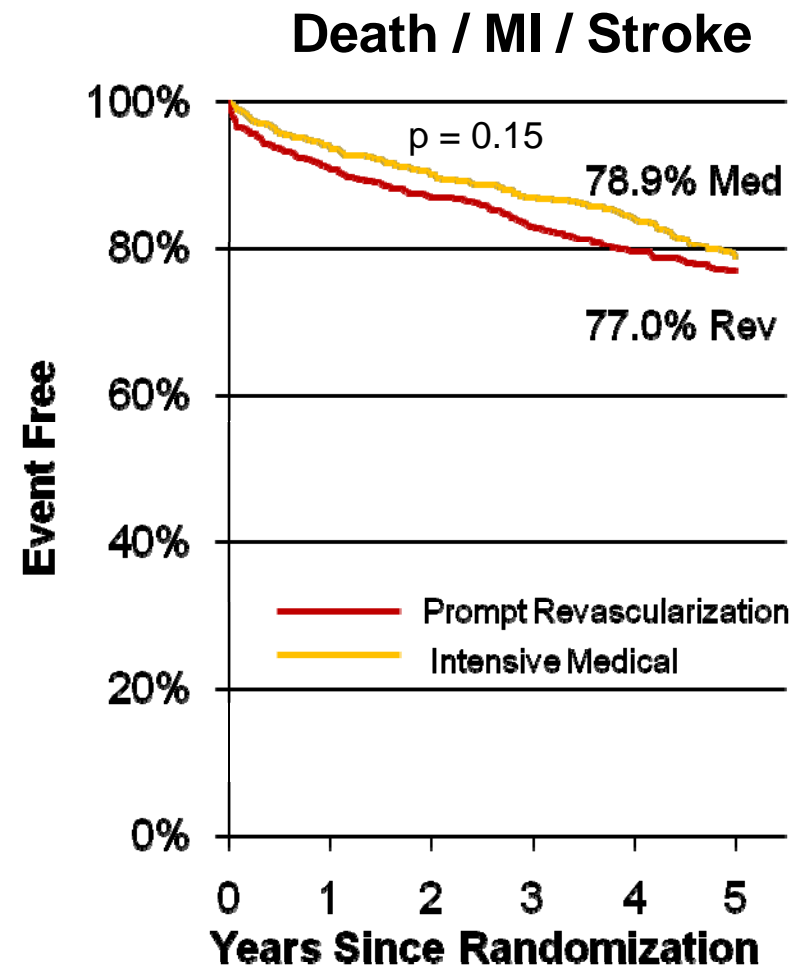
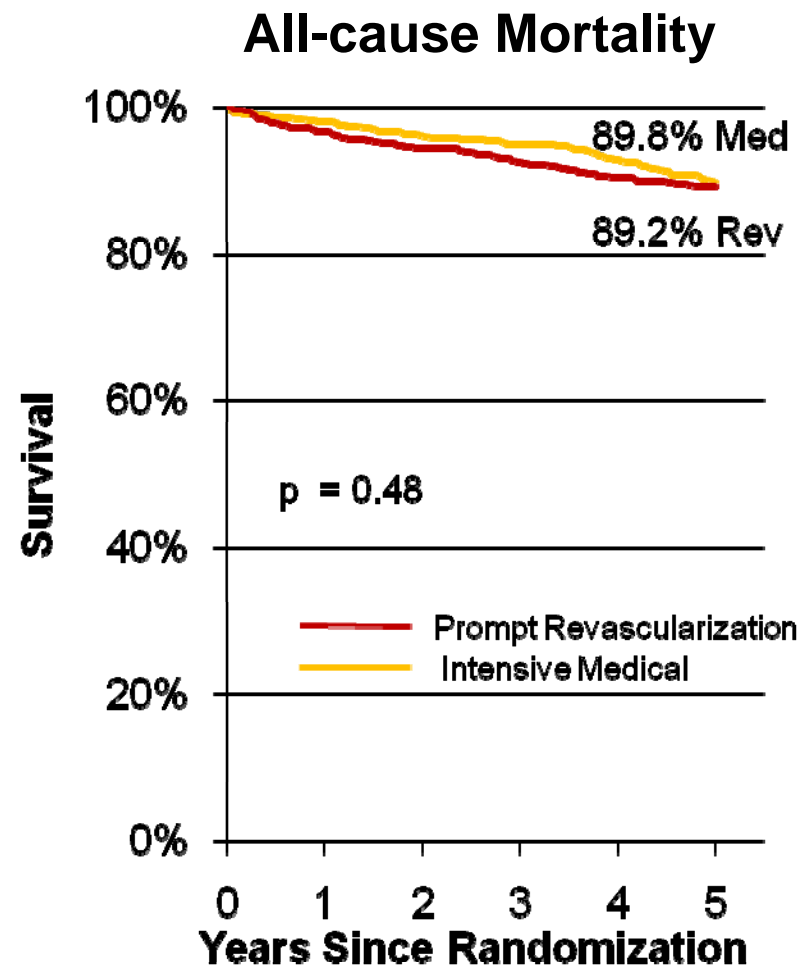
Insulin Sensitization versus Insulin Provision



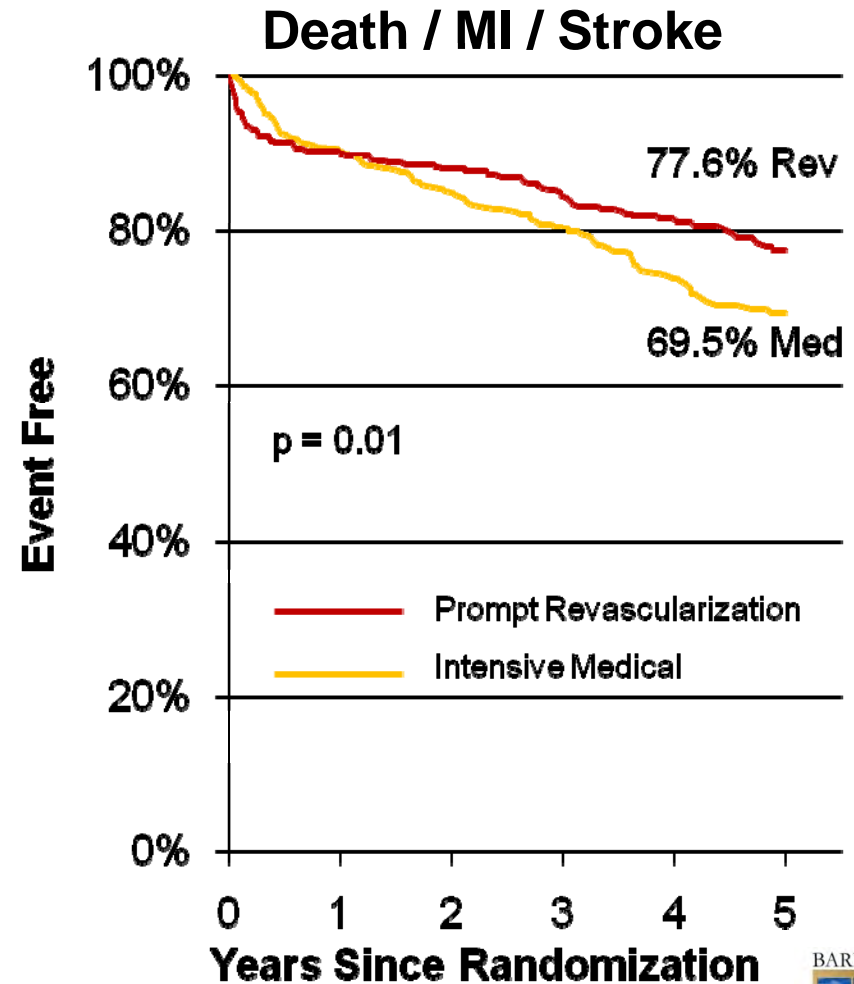
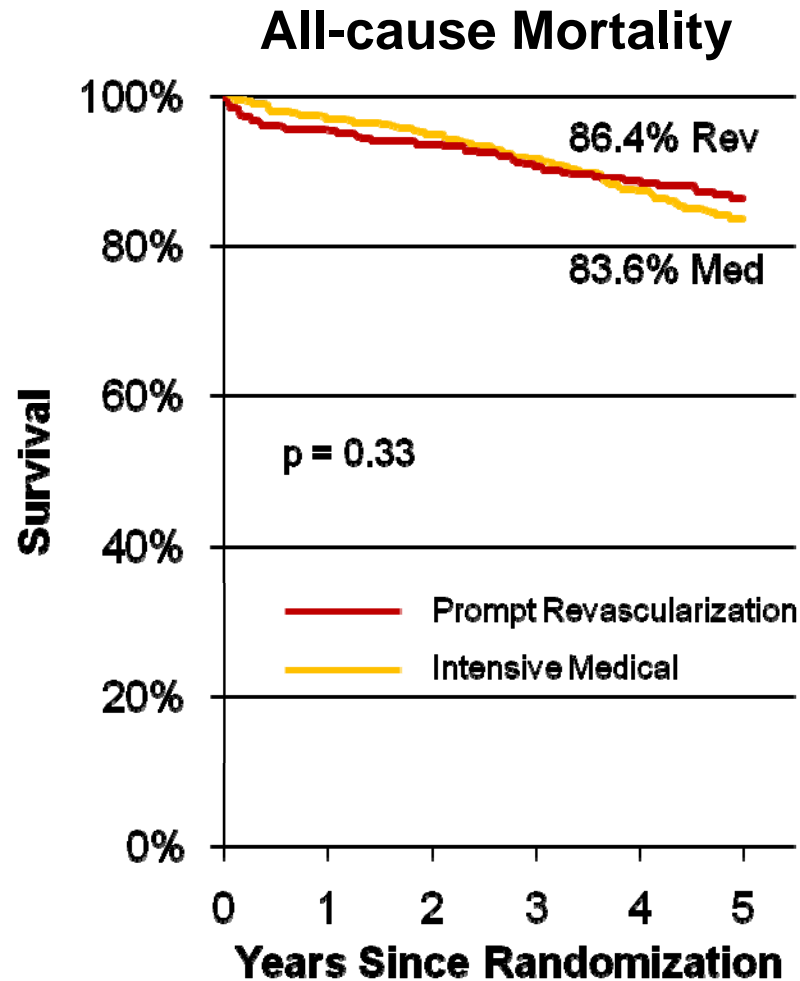
Freedom from Death / MI / Stroke *Among Medical Assigned Patients*



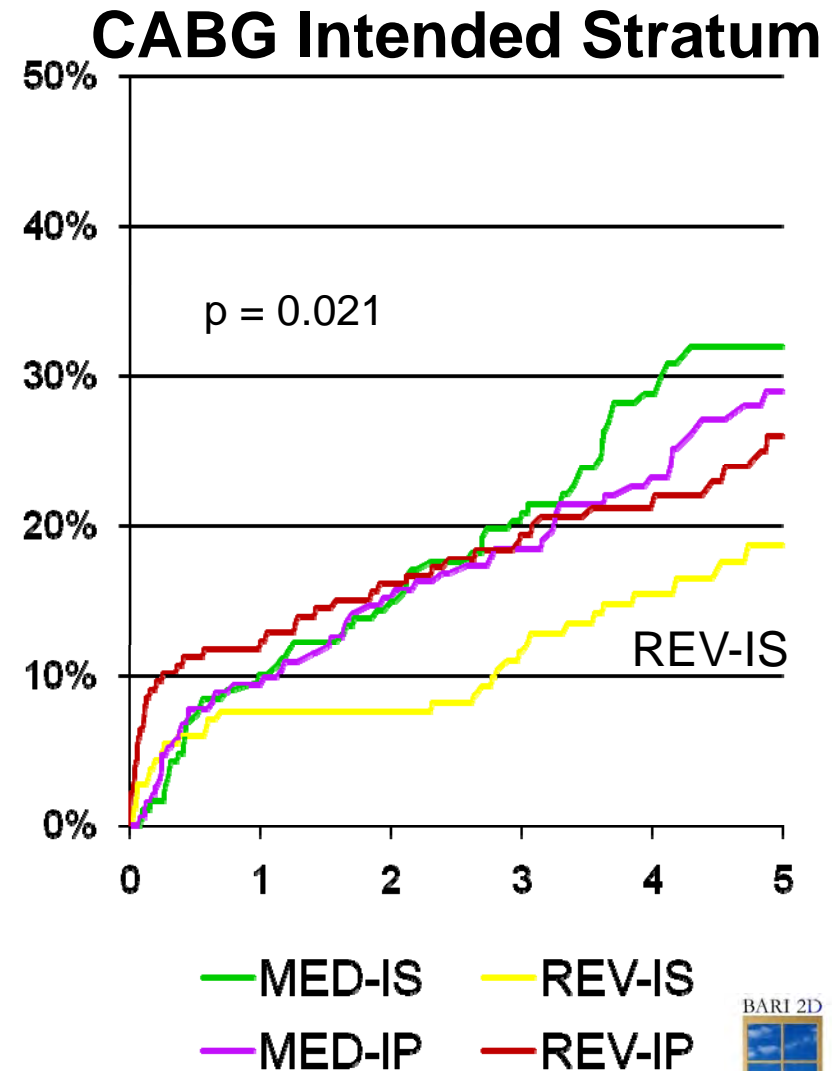
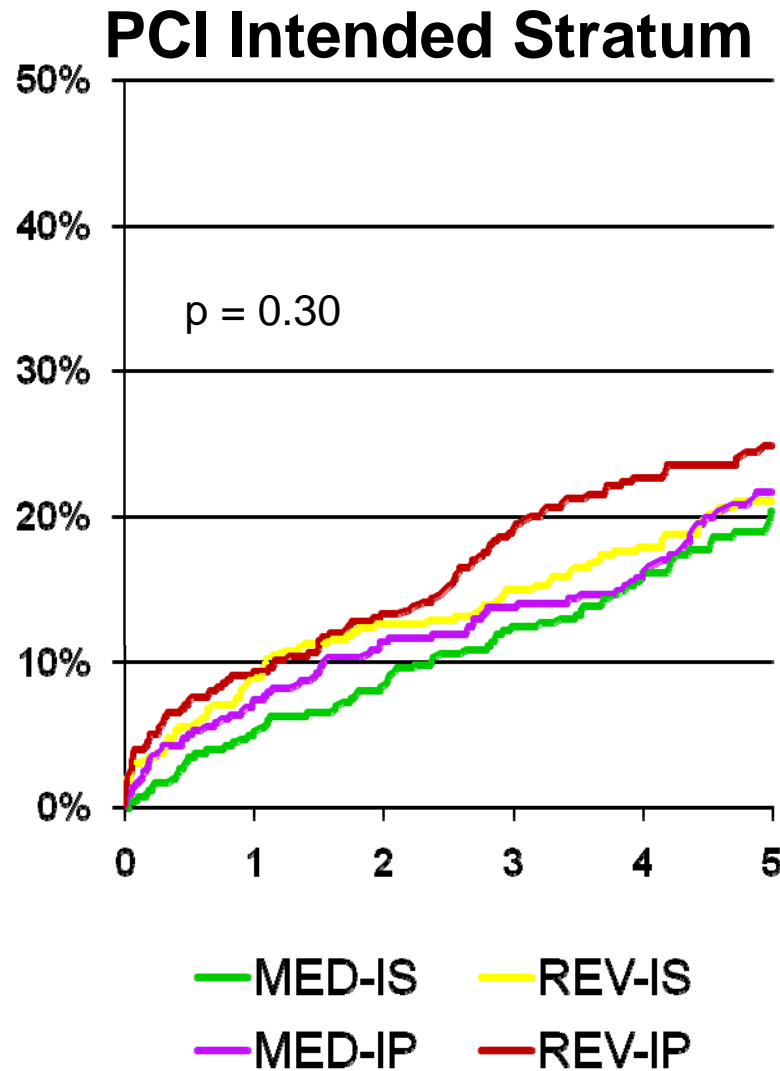
PCI Intended Revascularization Stratum (Lower Risk Patients)



CABG Intended Revascularization Stratum (Higher Risk Patients)

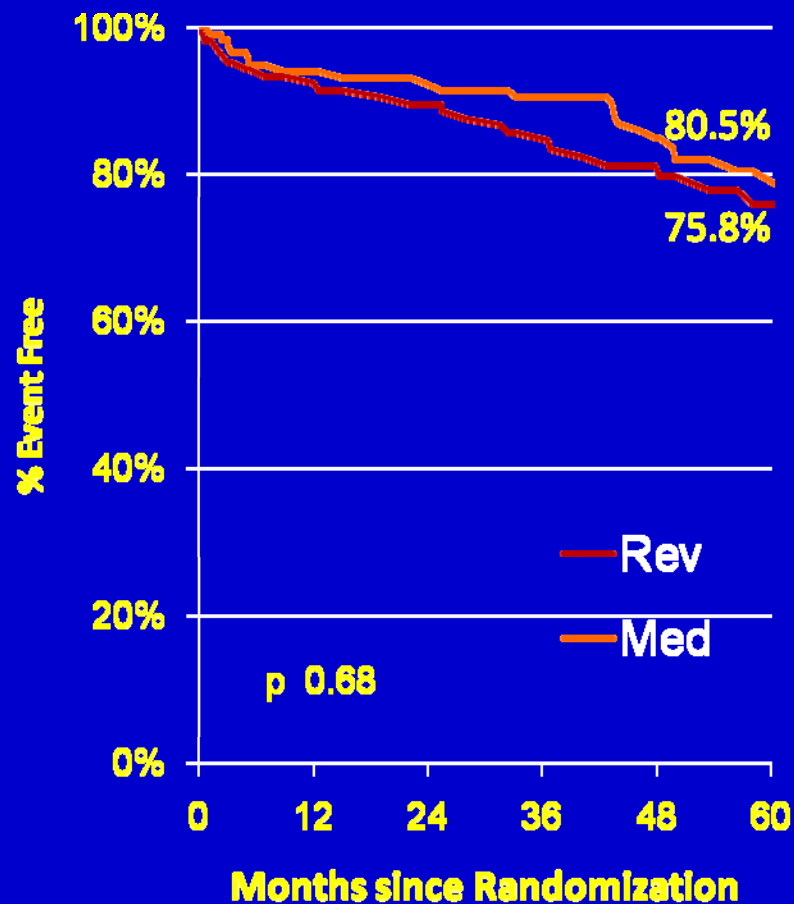


Major Cardiovascular Events

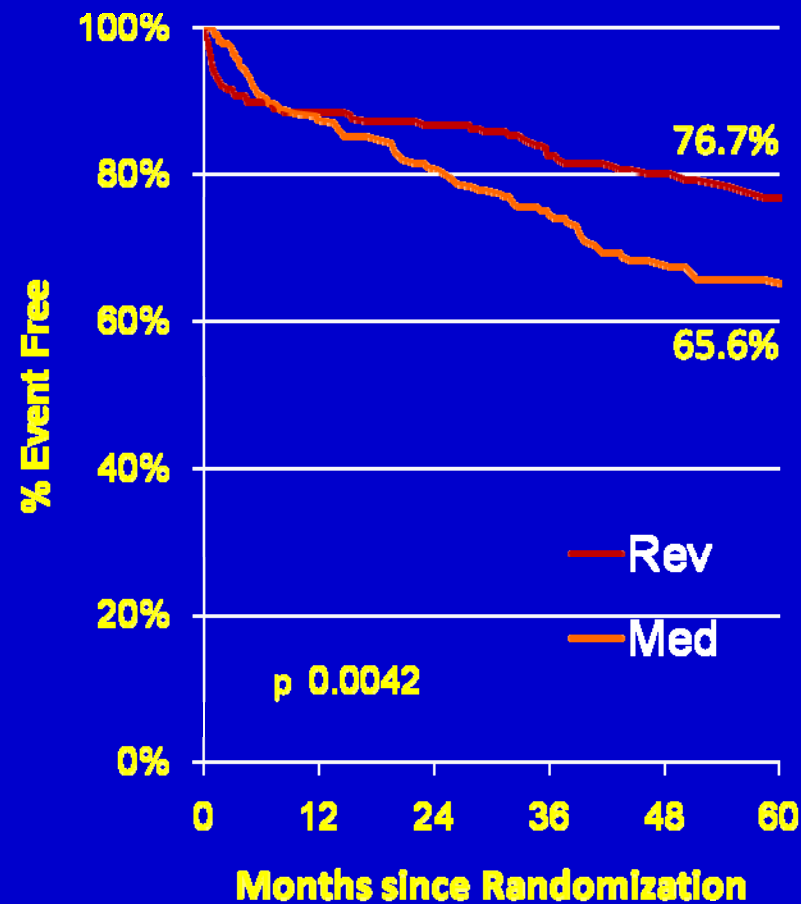


Freedom from Death/MI/Stroke Patients with Multi-vessel Disease CABG stratum

MJI < 55 (n=229)



MJI ≥ 55 (n=457)



BARI 2D Primary Conclusions

- **Among high risk patients selected for CABG**
 - **Prompt revascularization reduces major cardiovascular events compared with delayed/no revascularization ($p=0.01$).**
- **Among lower risk patients selected for PCI**
 - **Prompt revascularization and delayed/no revascularization had similar rates for major cardiovascular events.**



BARI 2D in the Context of Recent Trials

COURAGE Trial:

- Our PCI results are consistent with the results from COURAGE.
- The majority of participants in COURAGE did **not** have diabetes.
- COURAGE did not study CABG.



BARI 2D in the Context of Recent Trials

Intensive Glycemic Control Trials: (ADVANCE, ACCORD and VADT)

BARI 2D does not address the question of intensive glycemic control as all subjects were treated with a target HbA1c of $< 7.0\%$.

TZD (Rosiglitazone) Therapy:

BARI 2D assessed therapeutic strategies rather than any specific drug.

No MI/Mortality differences were seen for the IS group in which over 60% were using TZDs, predominately rosiglitazone.

These results are thus consistent with RECORD.



BARI 2D: Cardiology Implications

- In patients with both Type 2 diabetes and stable CAD with documented ischemia:
 - Those with extensive multi-vessel CAD should be considered for CABG.
 - Those with less extensive CAD could be managed safely with intensive medical therapy until revascularization is clinically mandated.



BARI 2D

Diabetes Implications

- Overall both insulin sensitizing and insulin providing approaches appear appropriate in BARI 2D eligible patients.
- Further analyses will determine whether these strategies differ in other secondary outcomes.



Summary of BARI 2D Design

What BARI 2D is **NOT**:

- A test of PCI versus CABG.
- A test of individual diabetes drugs or a test of different HbA1c targets.

What BARI 2D **is**:

- A comparison of STRATEGIES for myocardial ischemia.
- A comparison of STRATEGIES for glycemic control.



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Percutaneous Coronary Intervention versus Coronary-Artery Bypass Grafting for Severe Coronary Artery Disease

Patrick W. Serruys, M.D., Ph.D., Marie-Claude Morice, M.D., A. Pieter Kappetein, M.D., Ph.D.,
Antonio Colombo, M.D., David R. Holmes, M.D., Michael J. Mack, M.D., Elisabeth Stähle, M.D.,
Ted E. Feldman, M.D., Marcel van den Brand, M.D., Eric J. Bass, B.A., Nic Van Dyck, R.N., Katrin Leadley, M.D.,
Keith D. Dawkins, M.D., and Friedrich W. Mohr, M.D., Ph.D., for the SYNTAX Investigators*

“In conclusion, the results of our trial show that CABG, as compared with PCI, is associated with a lower rate of major adverse cardiac or cerebrovascular events at 1 year among patients with three-vessel or left main coronary artery disease (or both) and should therefore remain the standard of care for such patients.”

SYNTAX Trial Design

 62 EU Sites +  23 US Sites

Heart Team (surgeon & interventionalist)

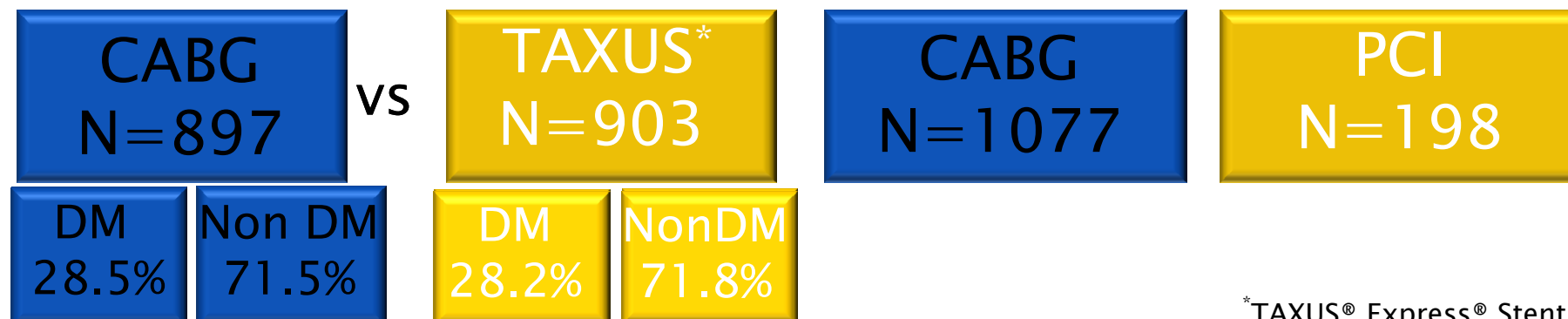
Amenable for both
treatment options

Amenable for only one
treatment approach

Stratification:
LM and Diabetes

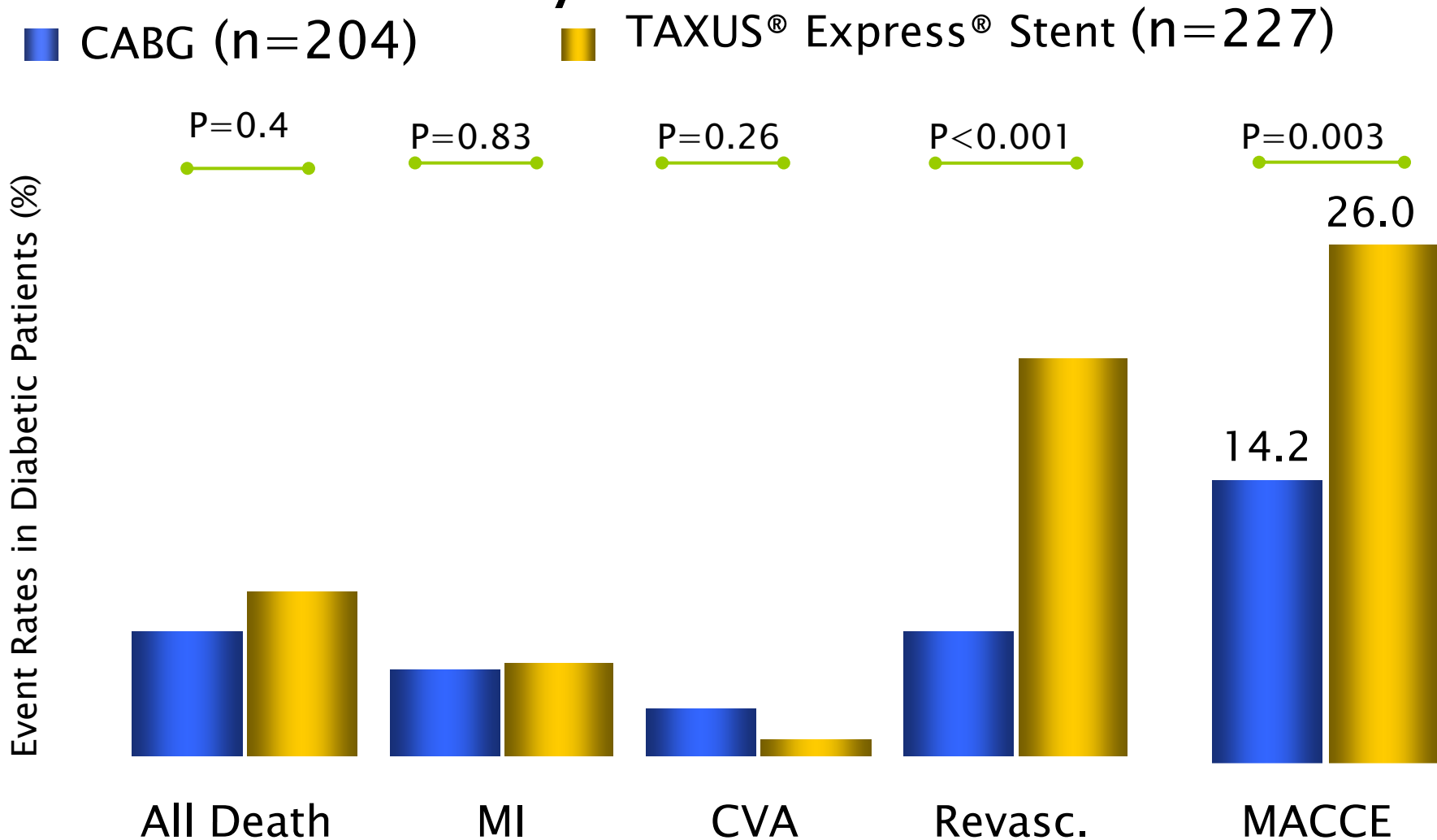
Randomized Arms
N=1800

Two Registry Arms
N=1275



*TAXUS® Express® Stent

Higher 12-Month MACCE in Diabetics* Driven by Revascularization

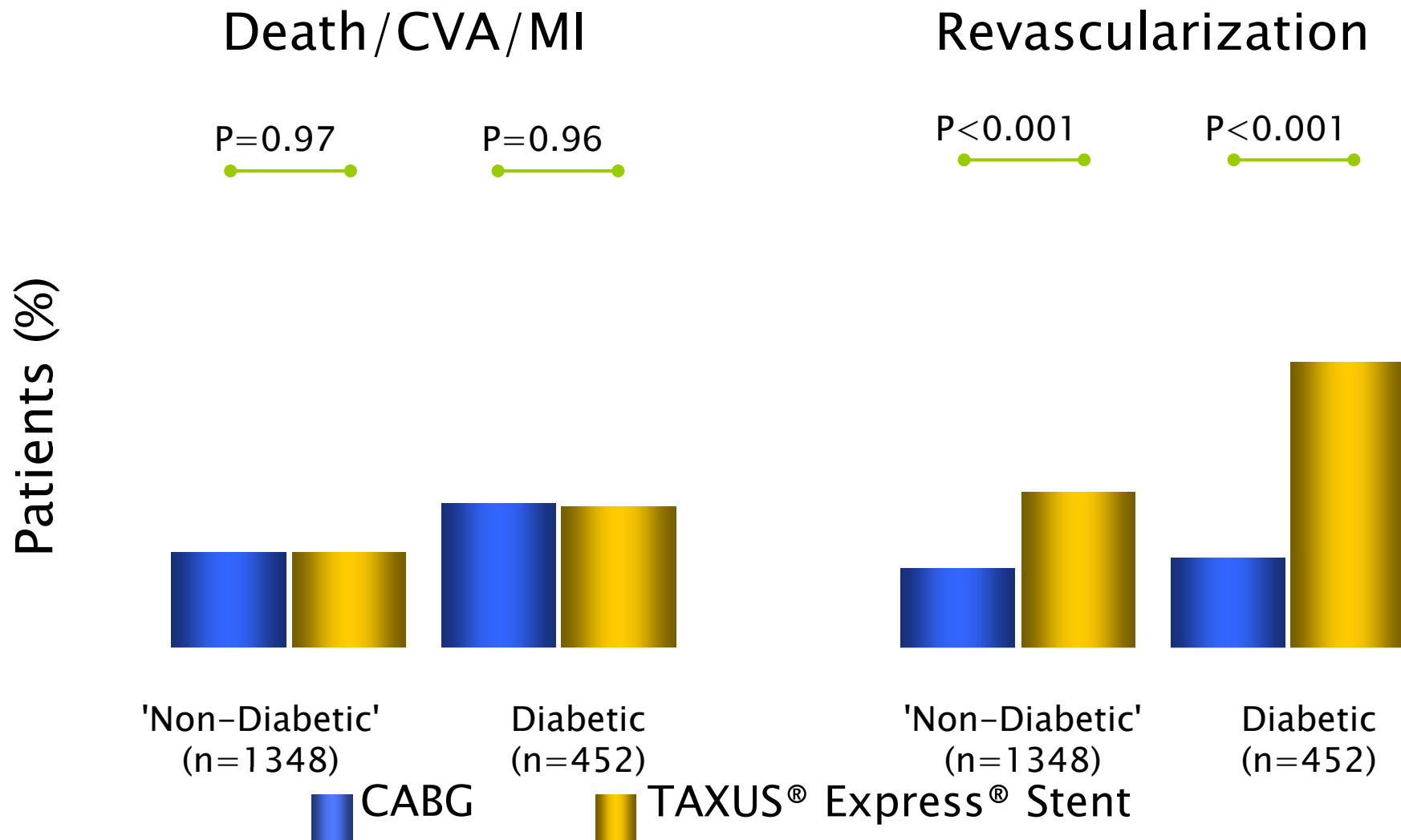


*Medically treated diabetes

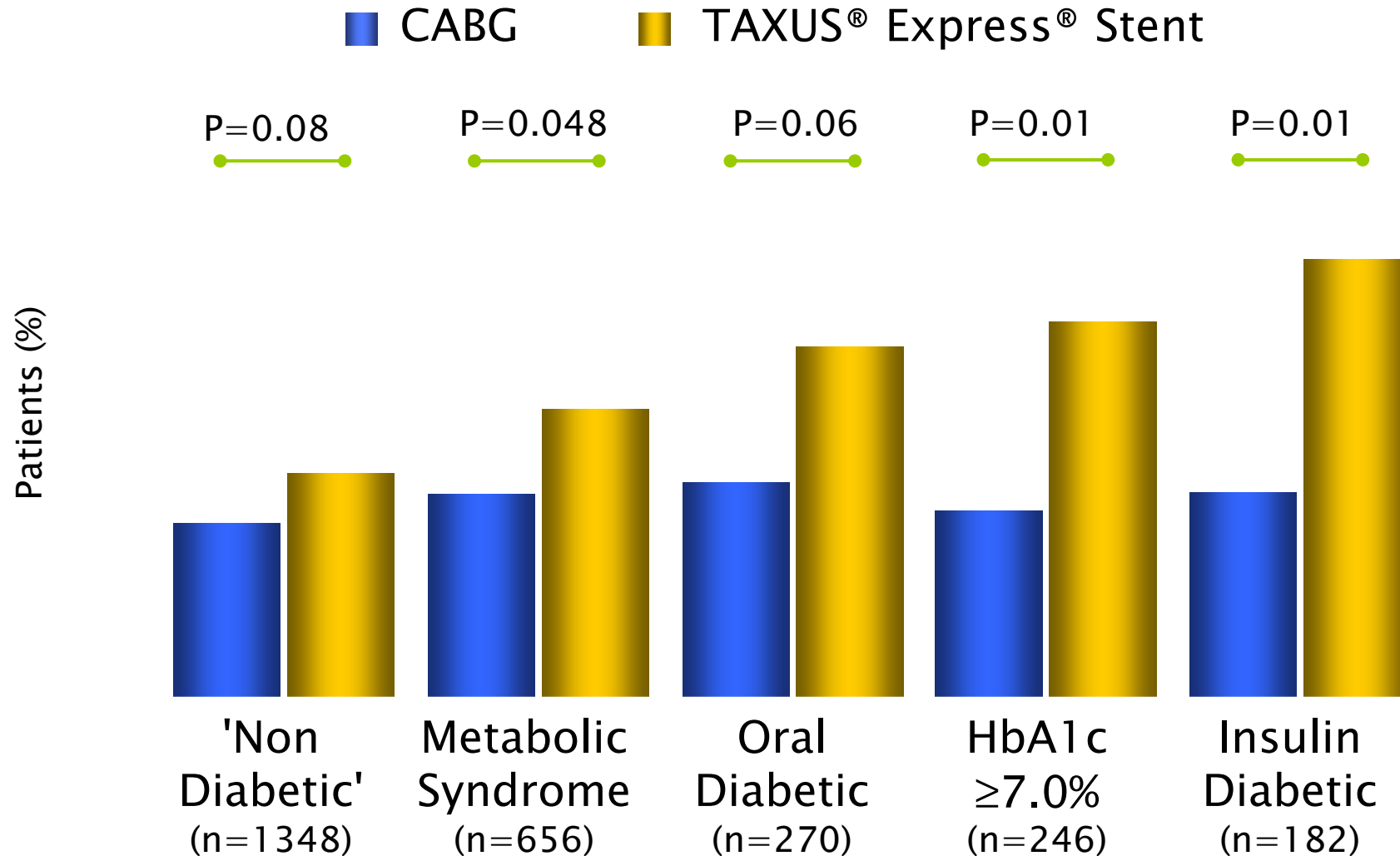
Presented by Dr. Dawkins; TCT 2008

The TAXUS Express Stent System has not been specifically indicated for patients with diabetes.

Outcome According to Diabetic Status at 12-Months



MACCE at 12-Months in Subgroups



Patients may belong to more than one group

Presented by Dr. Dawkins; TCT 2008

The TAXUS Express Stent System has not been specifically indicated for patients with diabetes.



FREEDOM Design

Patients with DM and multivesel CAD eligible for PCI or CABG

Randomized 1:1

**Contemporary PCI
with DES
N=1000**

**Contemporary CABG
with or without CPB
N=1000**

*Contemporary background therapy
for CAD and diabetes*



FREEDOM Recruitment

