

U.O. Cardiologia – UTIC

Emodinamica e Cardiologia Interventistica

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Dir. f.f. : F. Cassadonte

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Complesso Nausicaa – Itaca – Rossano Calabro (CS)

Il Ruolo della Rivascolarizzazione verso terapia medica nel paziente diabetico Tipo 2 e coronaropatia

Roberto CERAVOLO

Responsabile U.S. Emodinamica e Cardiologia Interventistica

DISCLOSURE STATEMENT

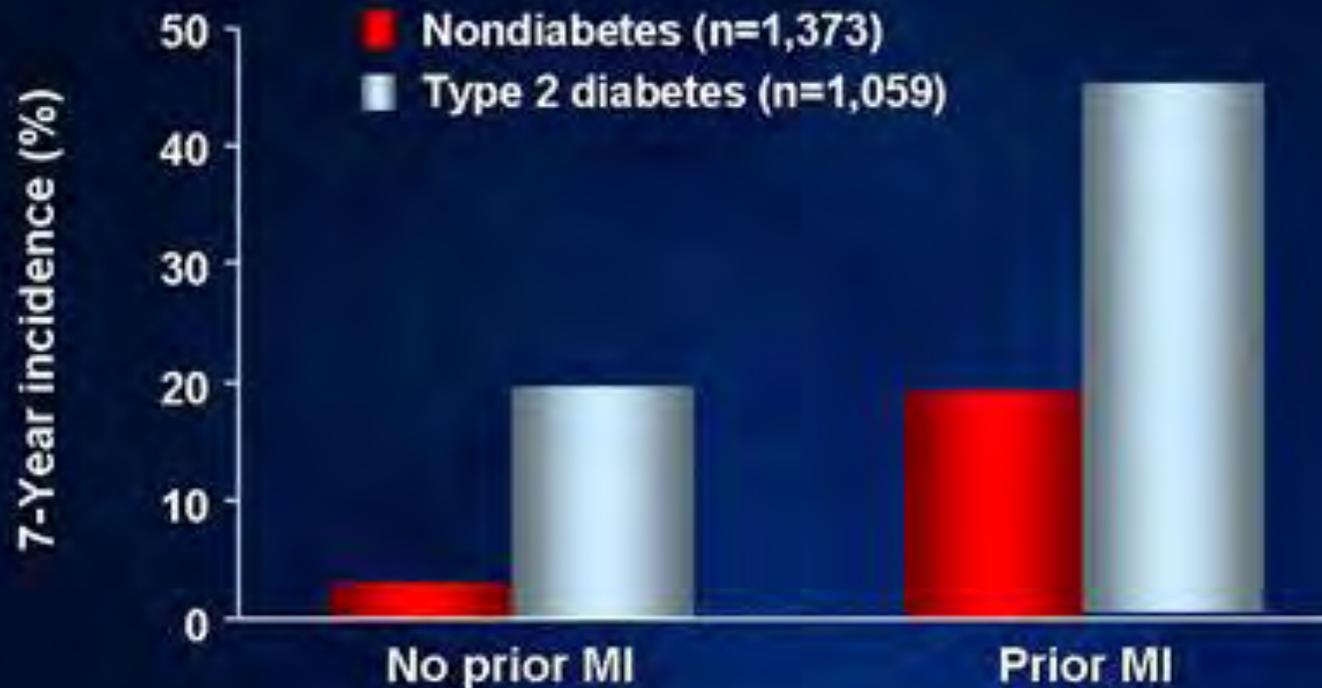
*I, Roberto Ceravolo **DO NOT** have a financial interest/arrangement or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation.*



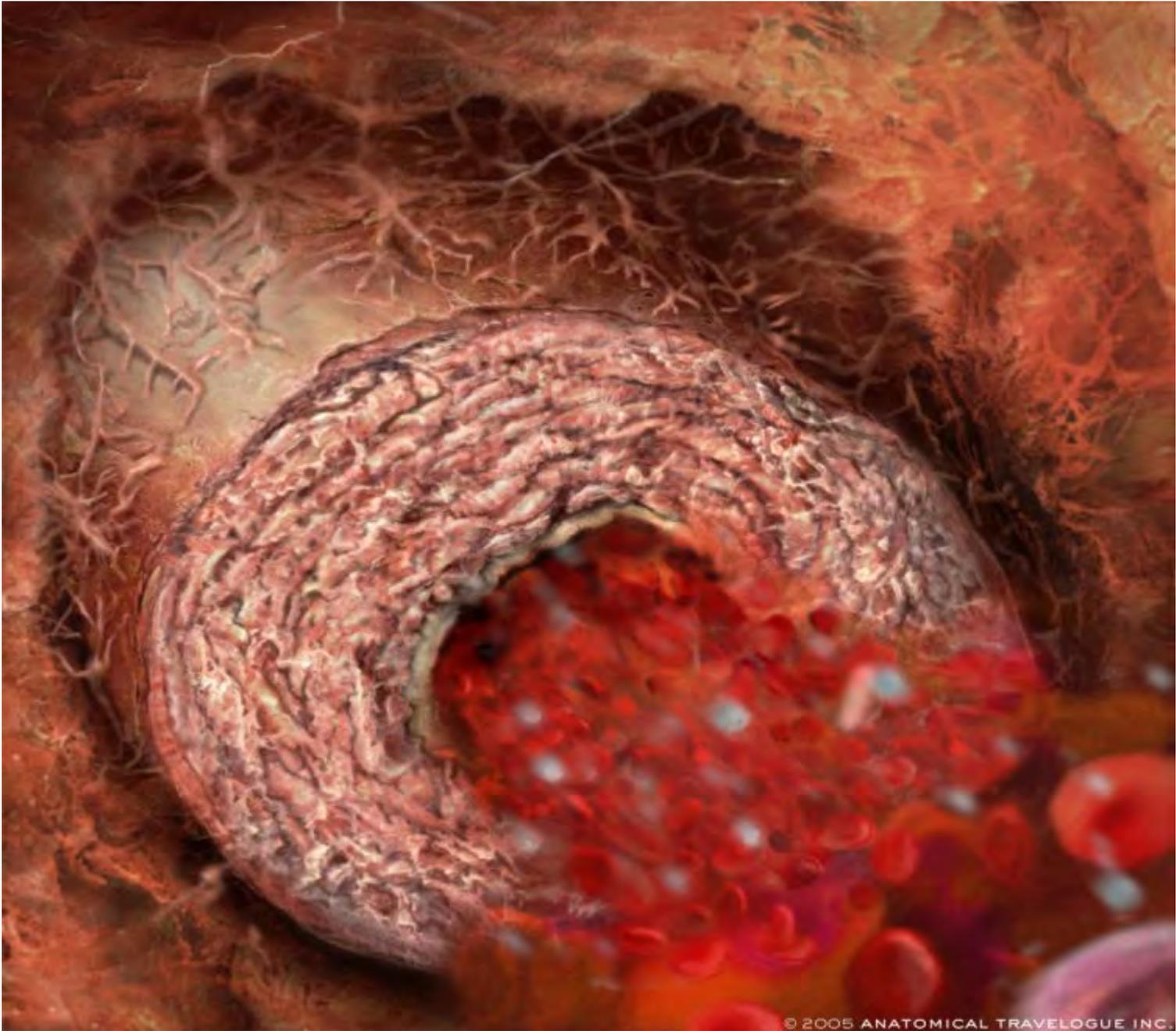
... I forgot to mention that I am an interventional cardiologist...

HAVE DIABETES OR HEART ATTACK IS THE SAME THING !

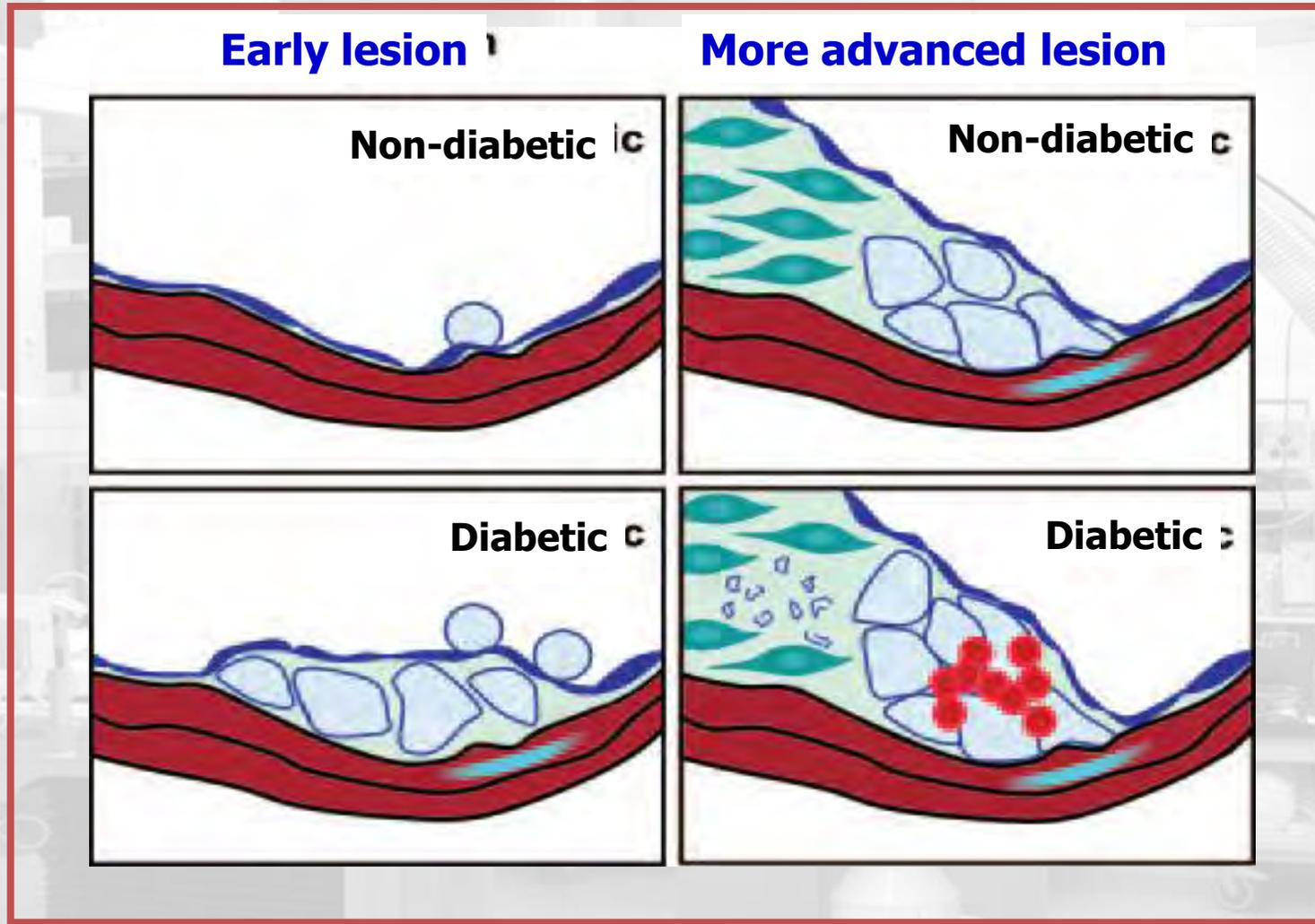
Incidence of Myocardial Infarction in People with Type 2 Diabetes



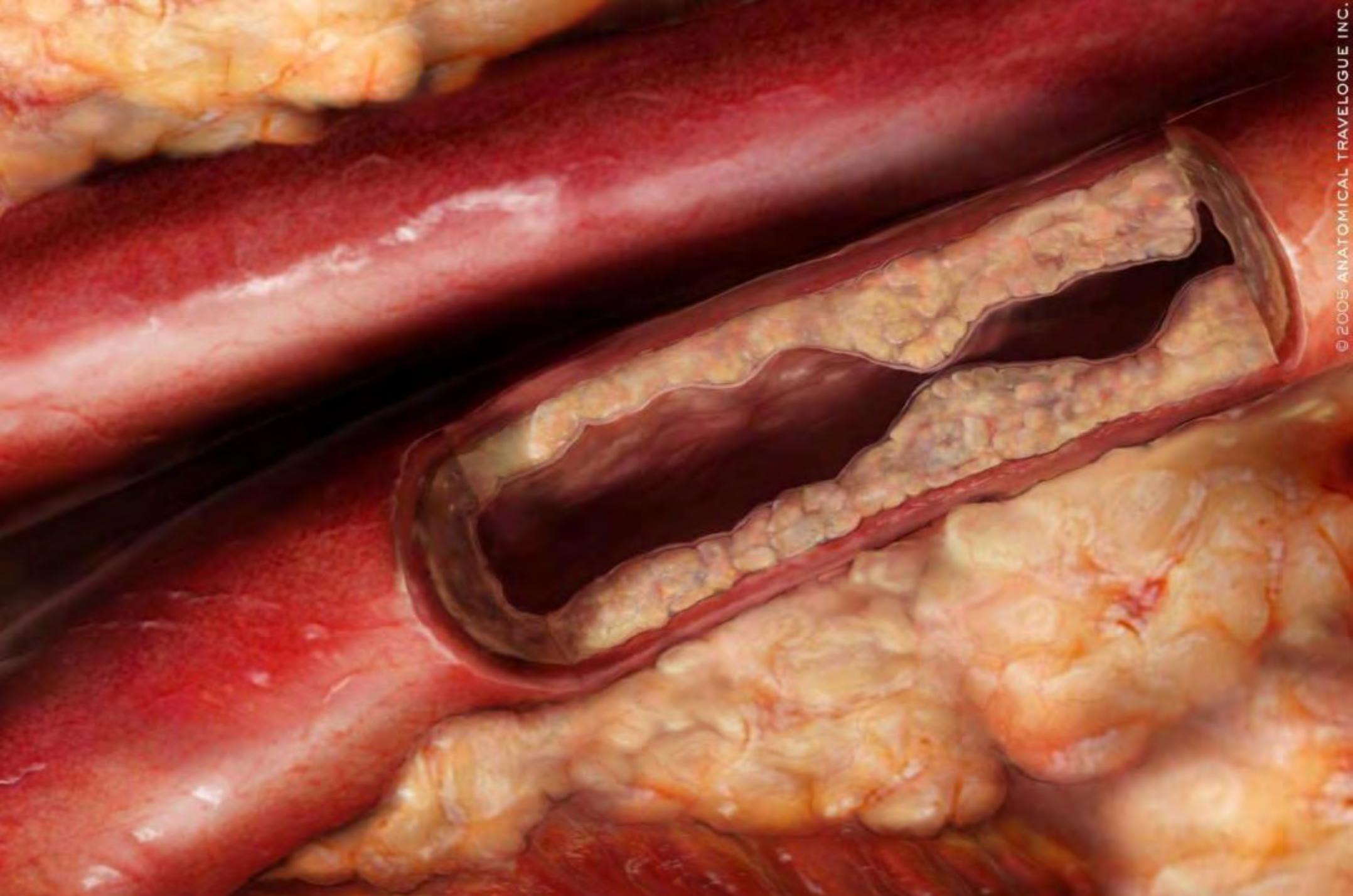
Haffner SM et al. *N Engl J Med.* 1998;339:229-234.



Diabetes accelerates lesion initiation and progression

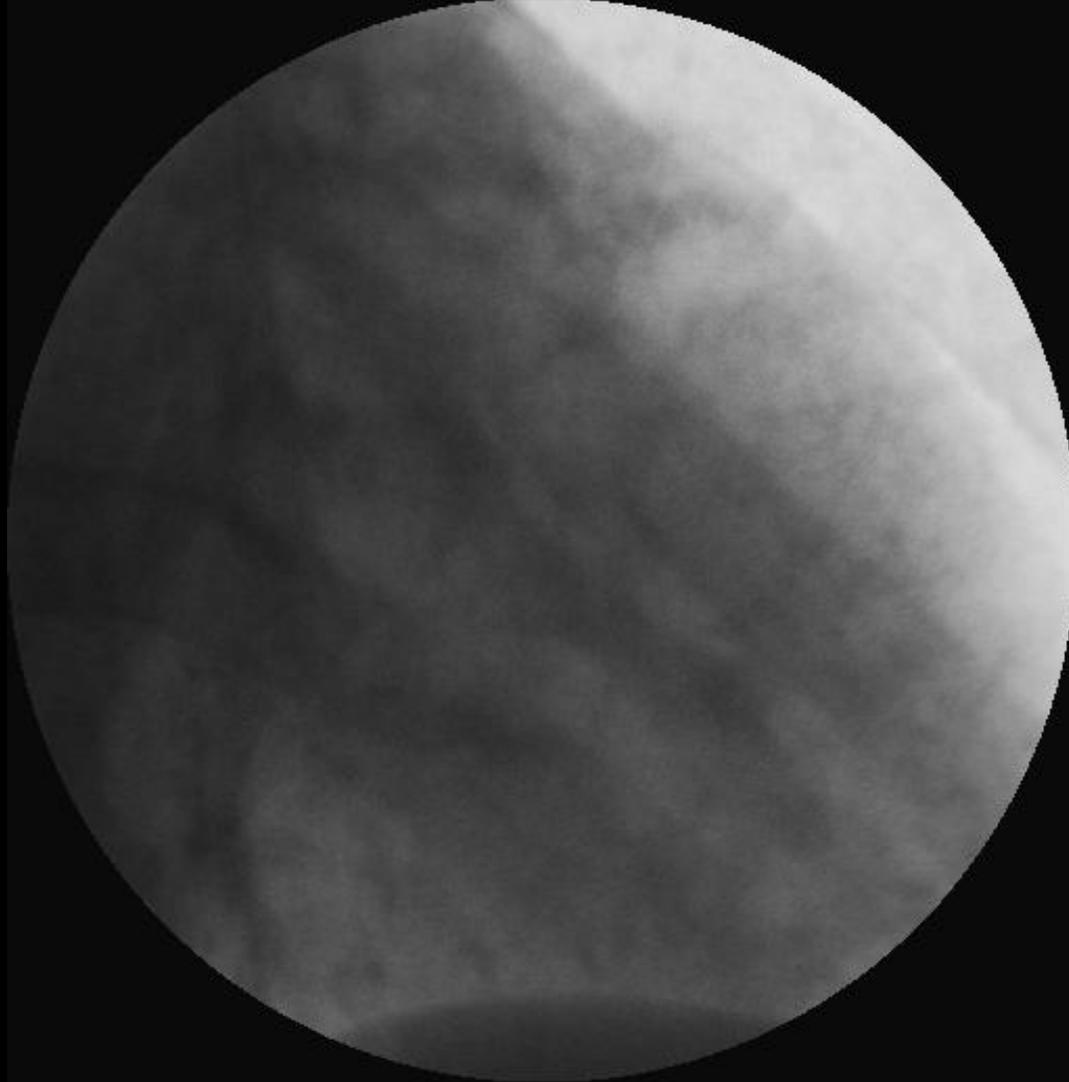


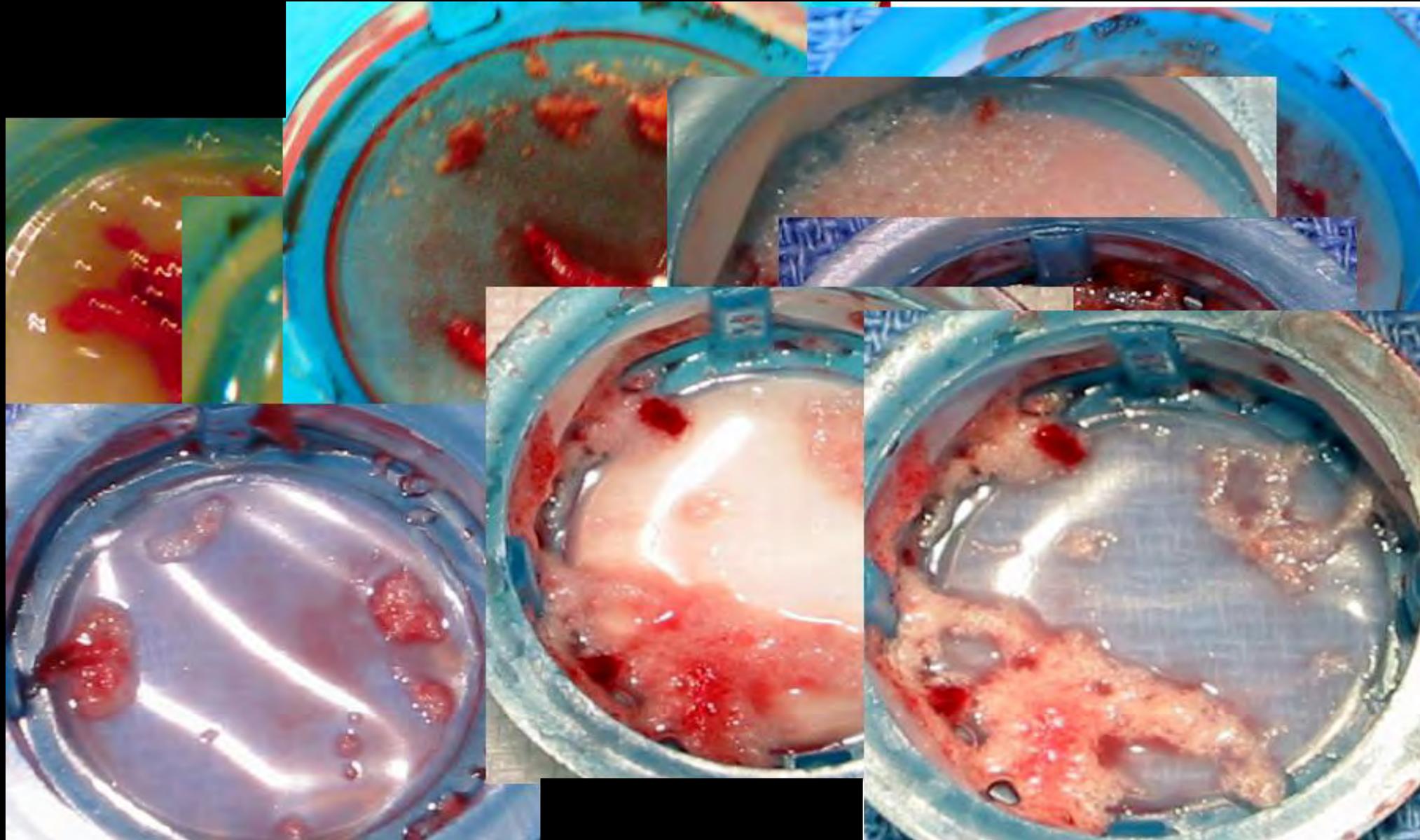




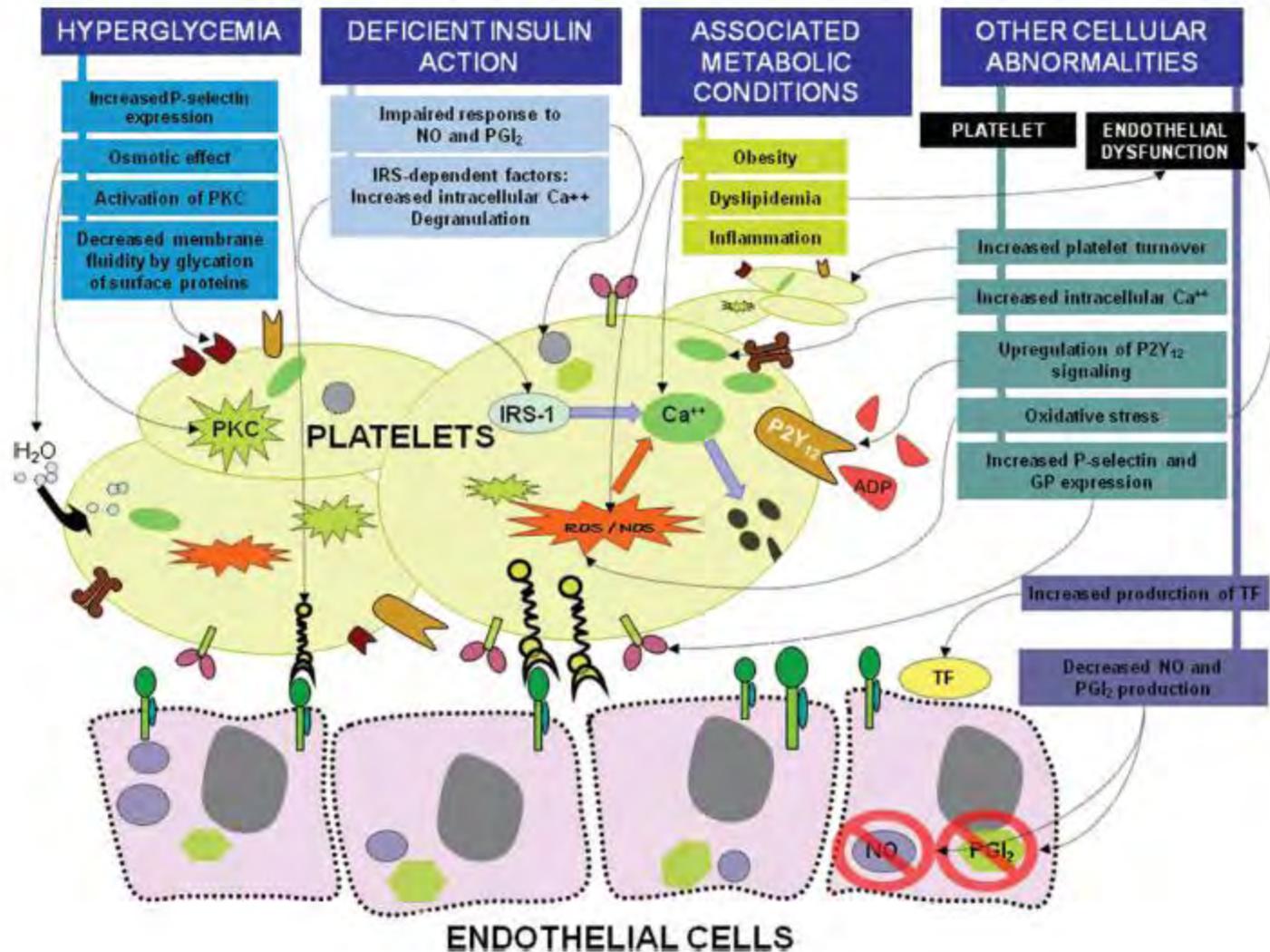


Thrombotic Risk

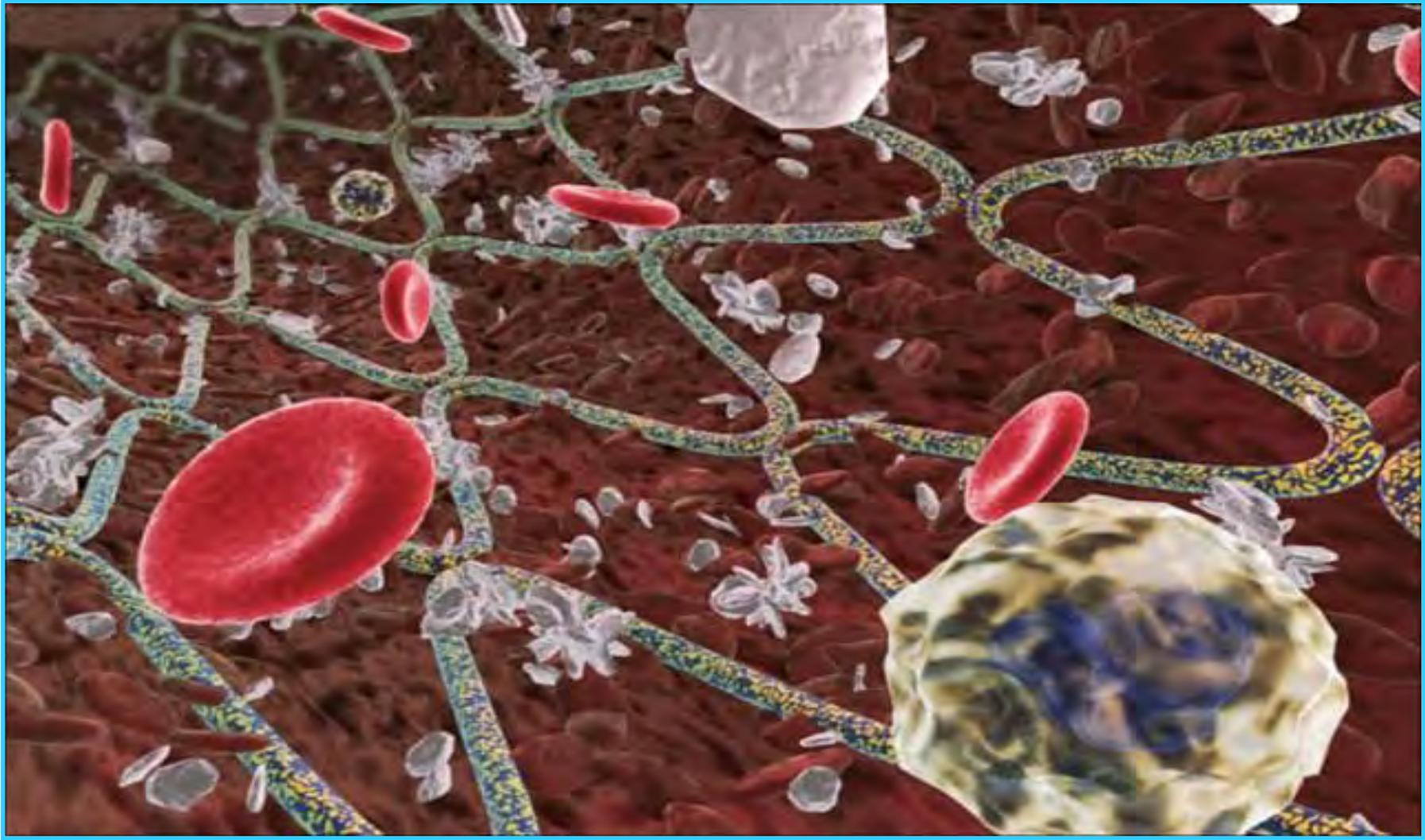




Mechanisms involved in platelet dysfunction in patients with DM



Platelet aggregation and activation



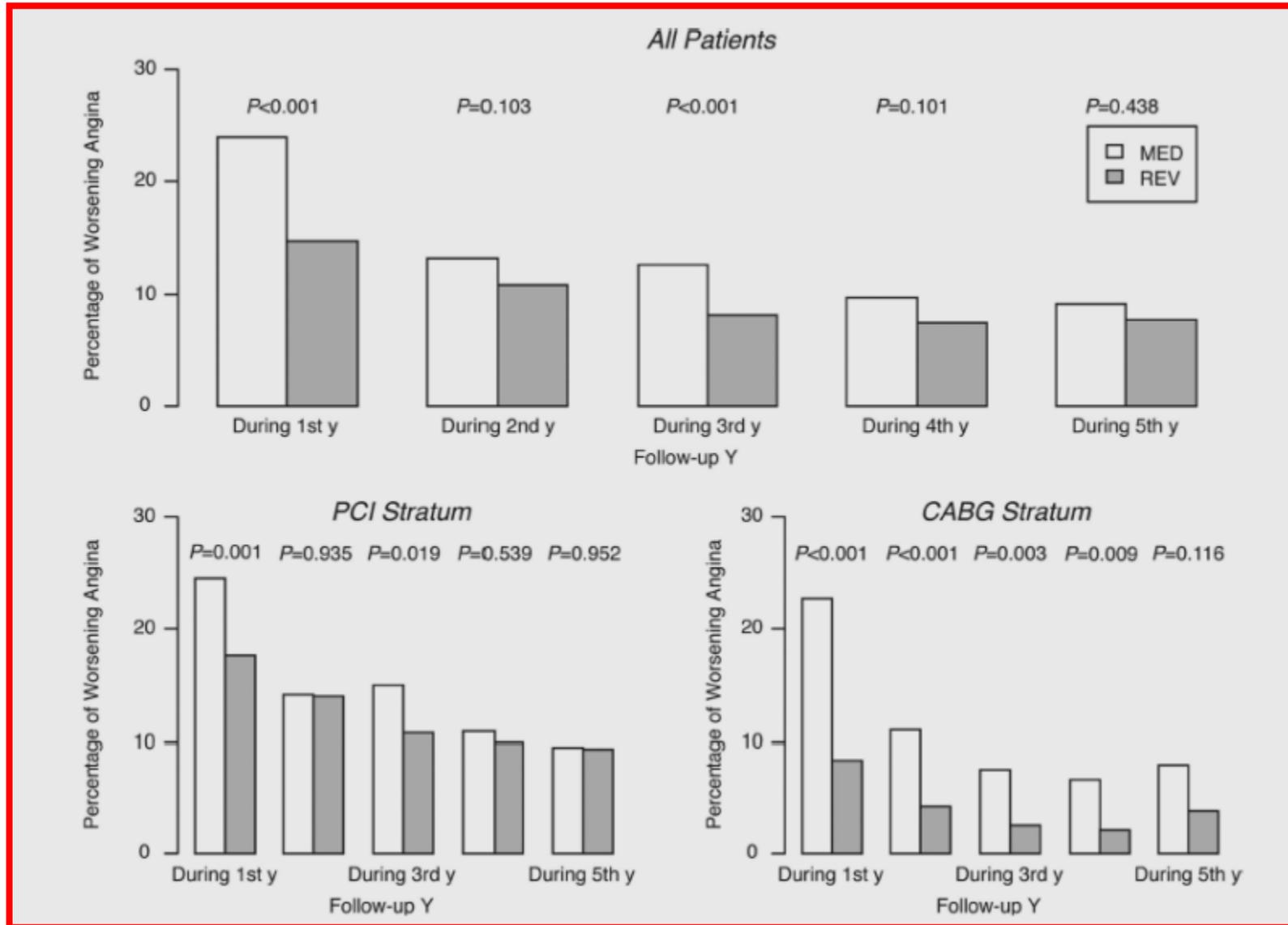
Platelet deposition and activation occur at the injury site, leading to the release of cell-signaling molecules.

Coronary Heart Disease

Effects of Optimal Medical Treatment With or Without Coronary Revascularization on Angina and Subsequent Revascularizations in Patients With Type 2 Diabetes Mellitus and Stable Ischemic Heart Disease

Gilbert E. DiGregorio, MD; Bing Liu, MD; David H. Evans, MD; Yaminli Yang, MD; Timothy M. Lapa, MD; Catha Loomis, MD; Waiyee Ho, MD; Norvin Weiss, MD; James Ryan, MD; Steven C. Frye, MD; and the Types 2 Angioplasty Revascularization Investigation 2 Group

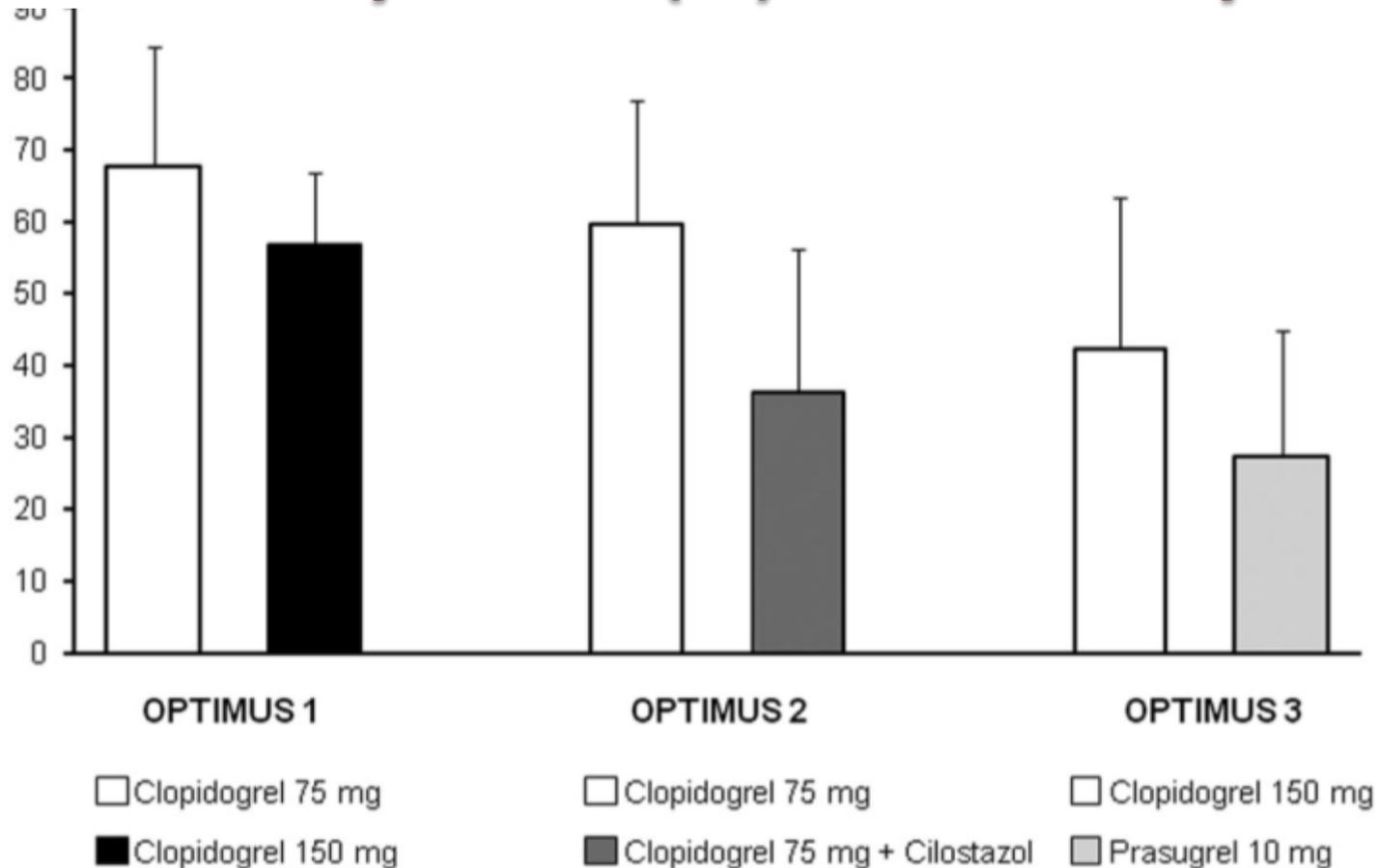
Circulation 2011;123:1492-1500



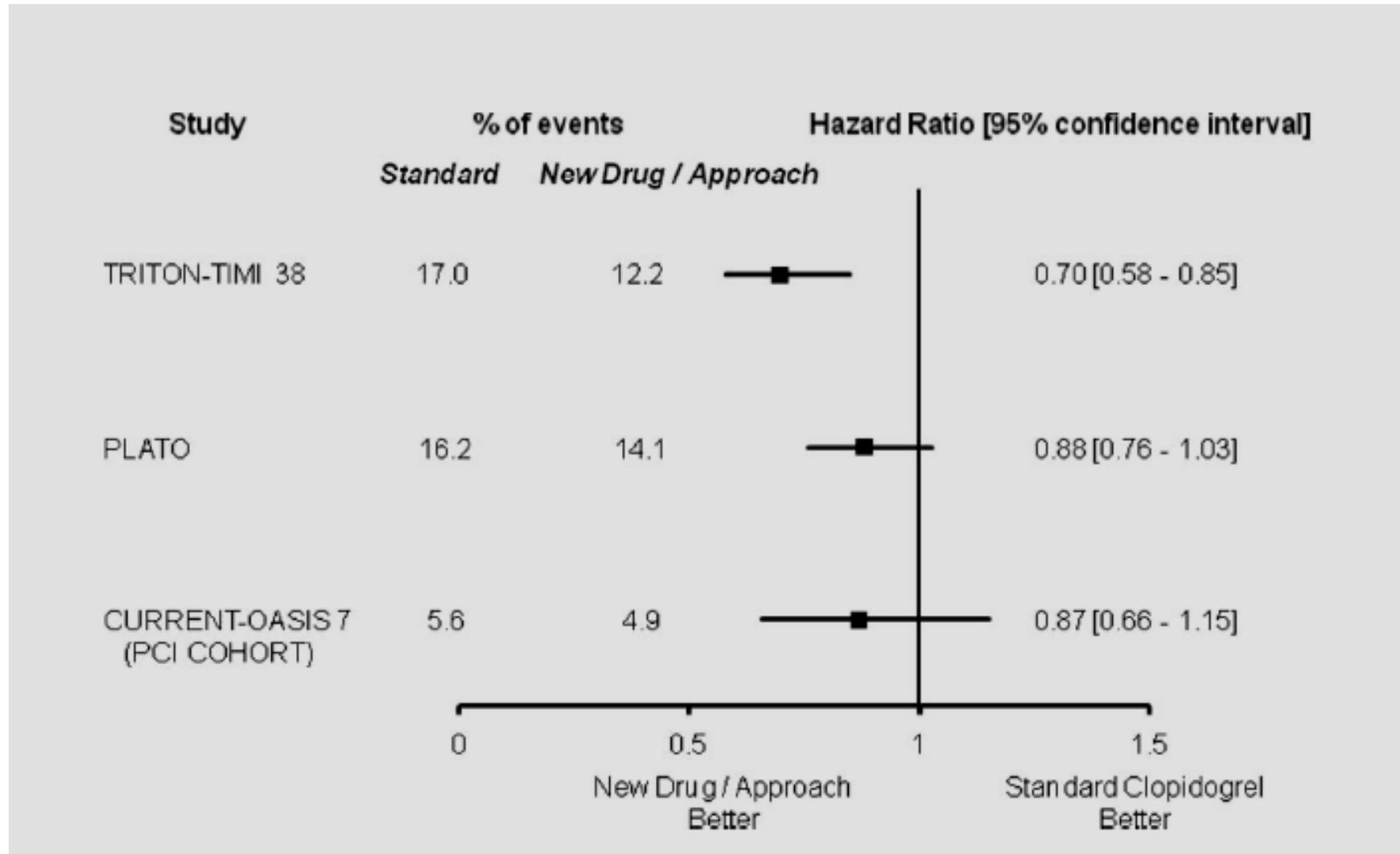
Effects of Optimal Medical Treatment With or Without Coronary Revascularization on Angina and Subsequent Revascularizations in Patients With Type 2 Diabetes Mellitus and Stable Ischemic Heart Disease

Gilbert R. Dimaria, MD; Jing Liu, MD; David H. Evans, MD; Yaminli Yang, MD; Timothy M. Lipp, MD; Catha Loomis, MD; Waiyee Ho, MD; Robert Weiss, MD; James Ryan, MD; Steven C. Frye, MD; and the Optimal Medical Treatment With or Without Coronary Revascularization Investigation 2 Guideline (ORAWI 2) Study Group

Platelet Reactivity index (%) assessed by VASP Assay



Efficacy in reducing adverse outcomes of new drugs and approaches tested in large-scale clinical trials in diabetes mellitus (DM) patients.



**SCIENCE TELLS US WHAT WE CAN DO;
GUIDELINES WHAT WE SHOULD DO;
REGISTRIES WHAT WE ARE ACTUALLY DOING.**



*Una medicina è una sostanza che
iniettata in un ratto produce un
articolo scientifico.*

Arthur Bloch



Li vorremmo così

Ma ...spesso sono così



Co-morbidità

Vorremmo un farmaco sicuro



Vorremmo una procedura senza complicanze

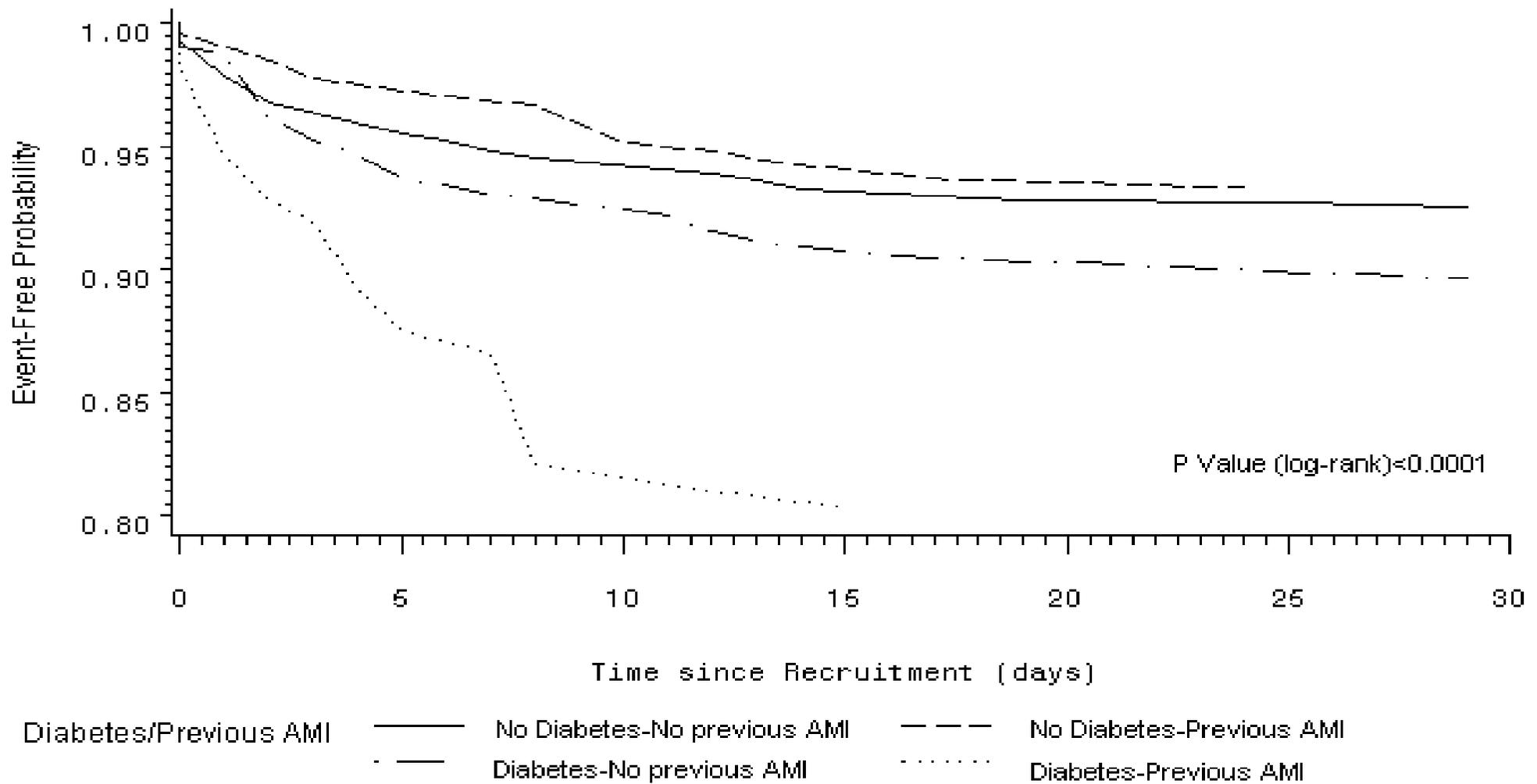


PCI VS CABG: WHO IS THE WINNER?

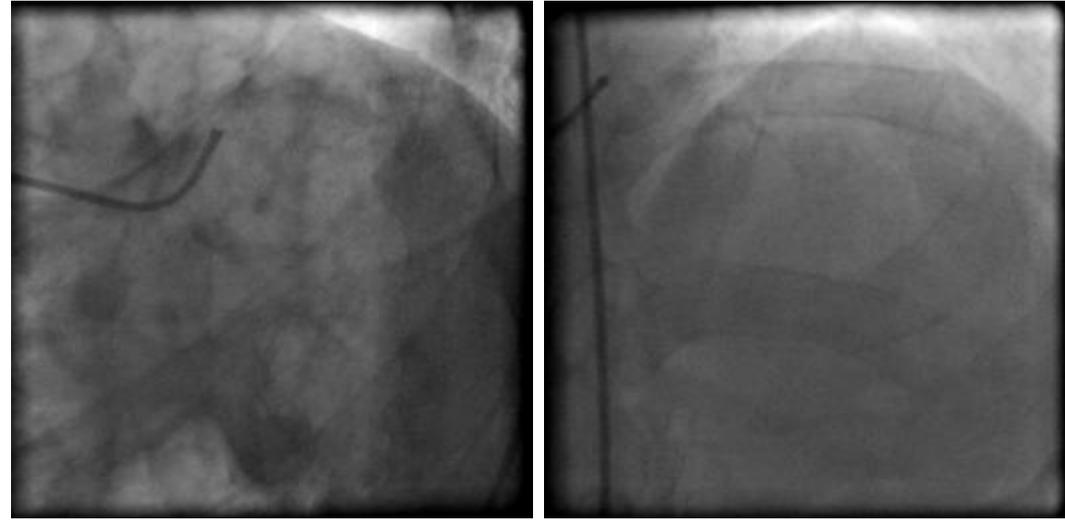
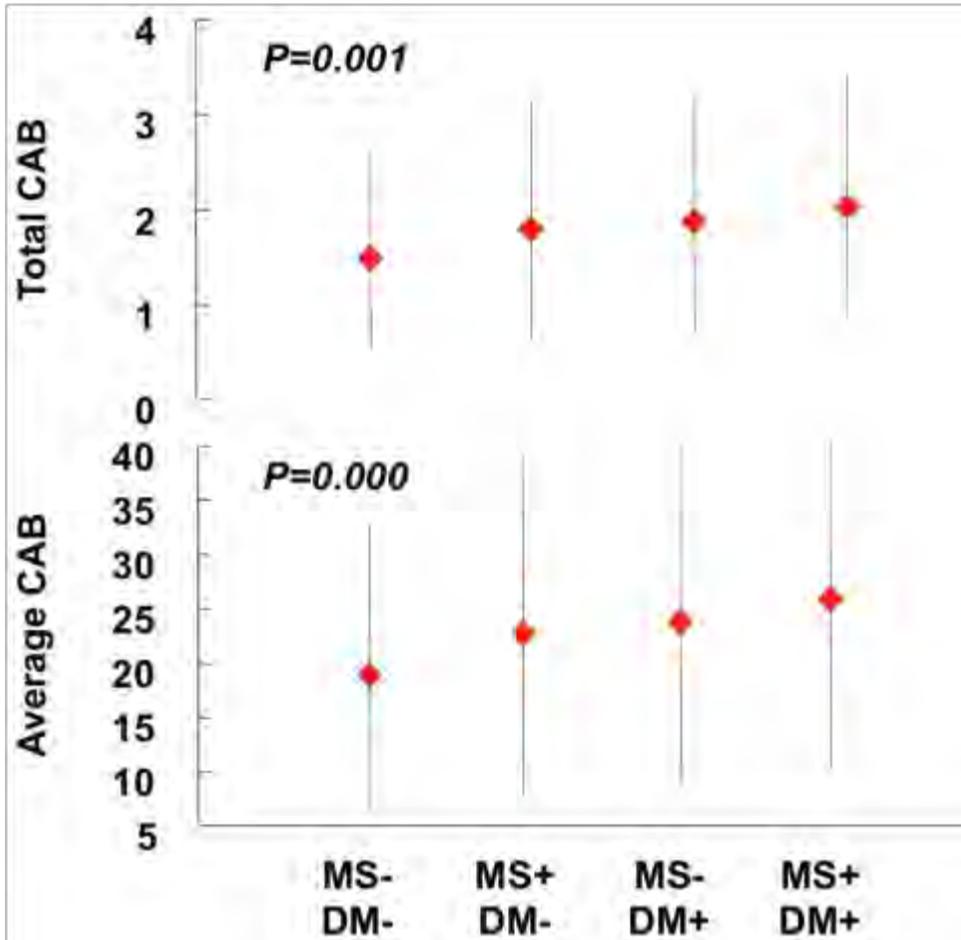


... and IN DIABETES?

Is better to have a heart attack or diabetes?



PATIENTS WITH AND WITHOUT GLYCO-METABOLIC FAILURE: INFLUENCE ON CORONARY ATHEROSCLEROTIC BURDEN.

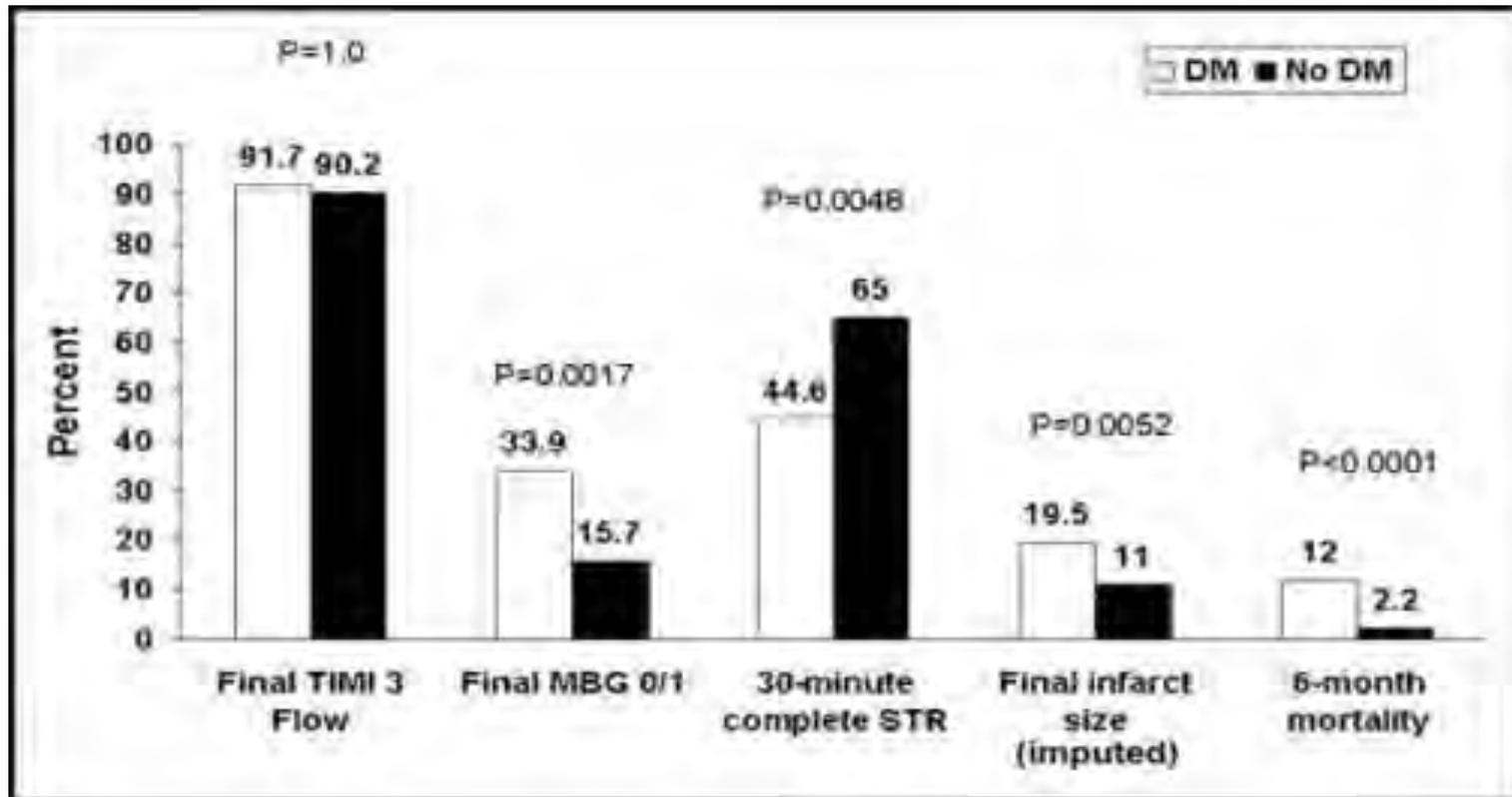




La riperfusione nel diabetico

“Limiti della PCI primaria nel diabetico”

Diabete predittore indipendente di:
minor riperfusione, infarti più estesi, maggior sviluppo di scompenso e maggior mortalità.

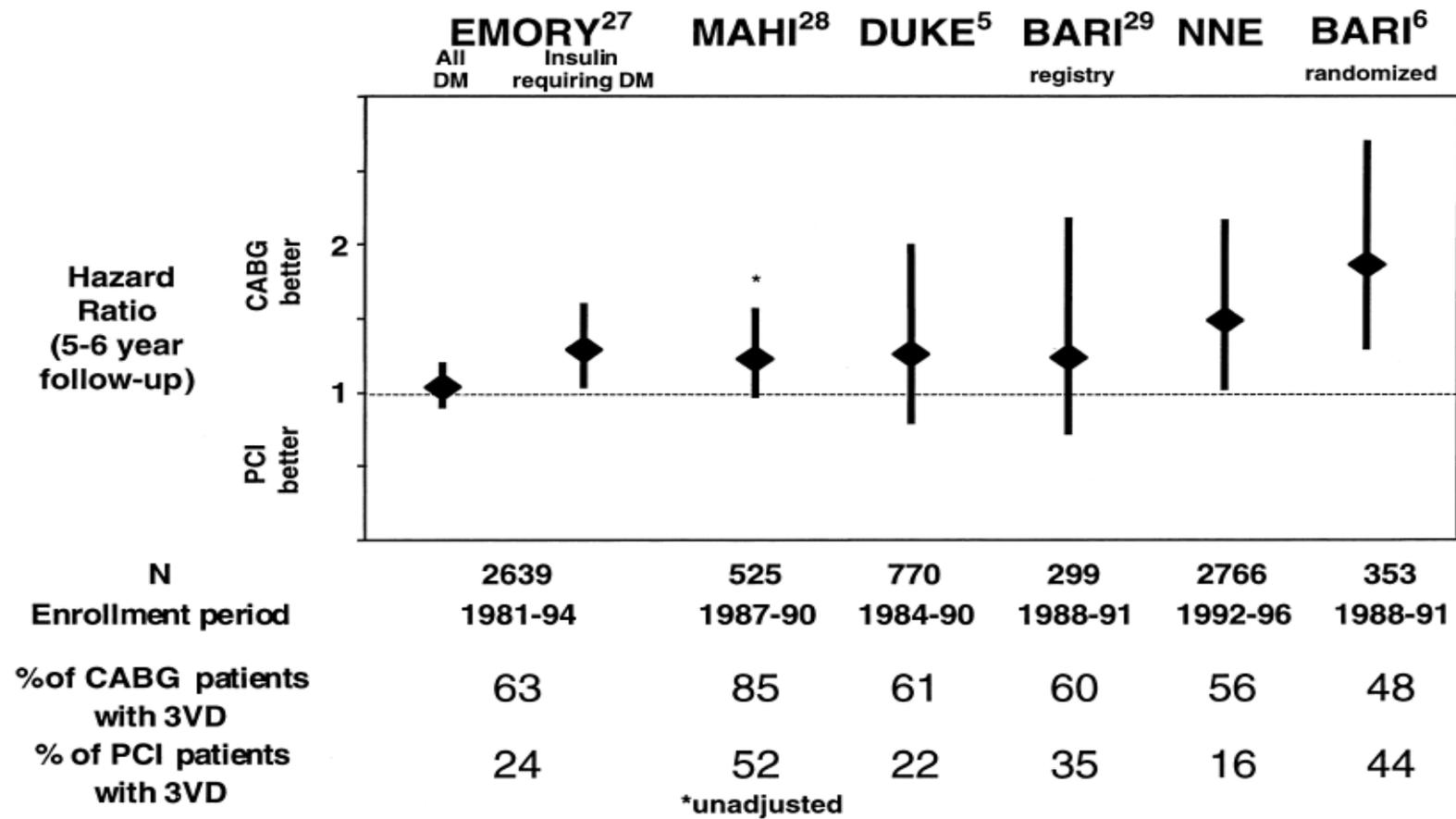


ALLORA, TESTA O CROCE?



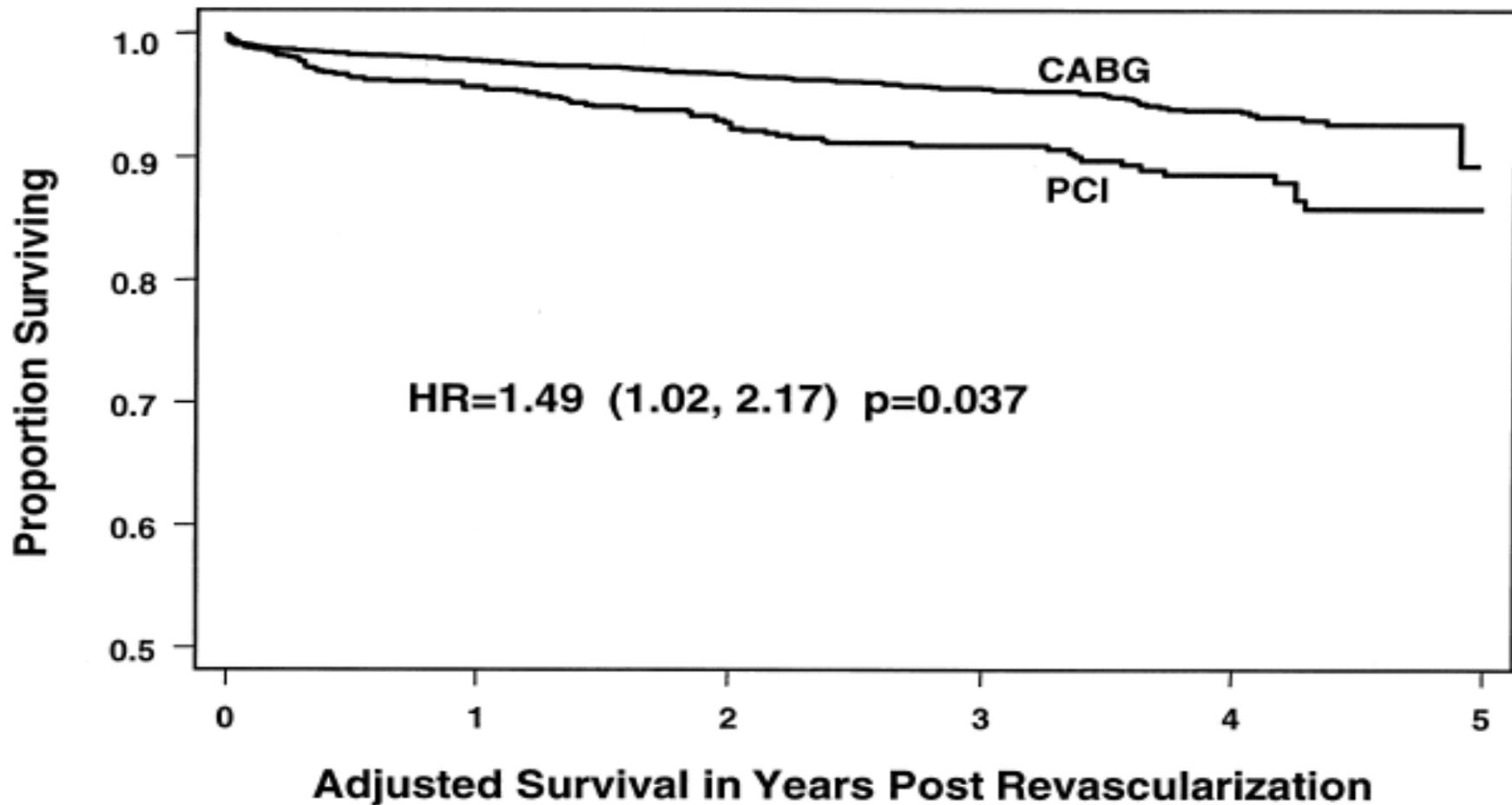


Hazard ratio at five to six-years of follow-up for initial PCI compared with CABG among patients with diabetes and multivessel disease





SURVIVAL OF PATIENTS WITH DIABETES AND MULTIVESSEL CORONARY ARTERY DISEASE AFTER SURGICAL OR PERCUTANEOUS CORONARY REVASCULARIZATION

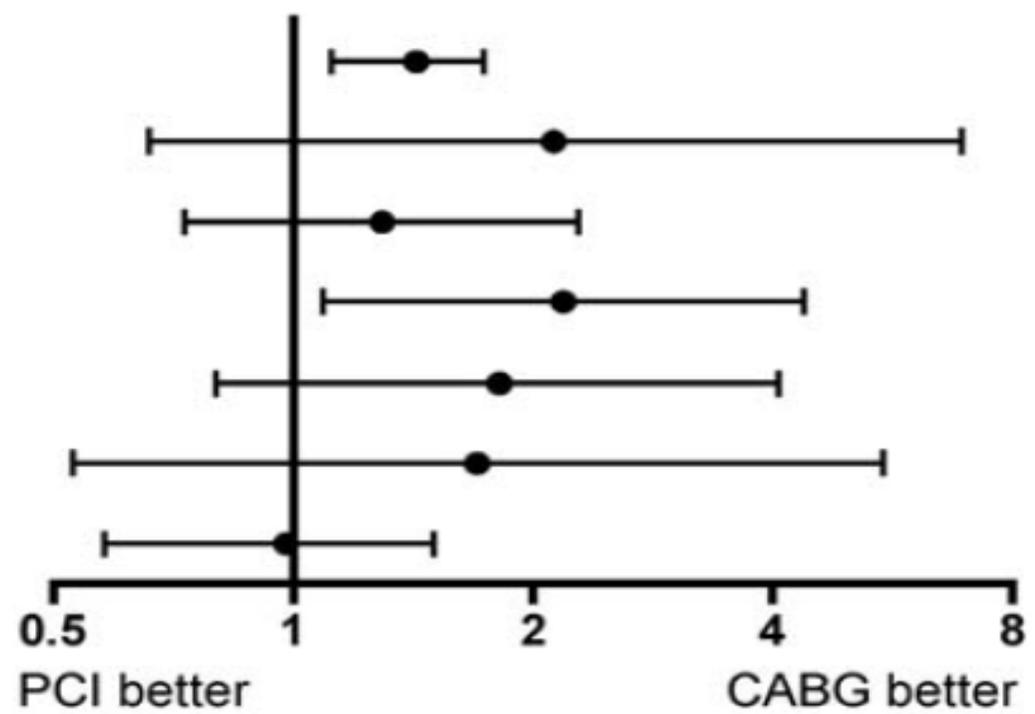




CABG OR PCI IN DIABETIC PATIENT

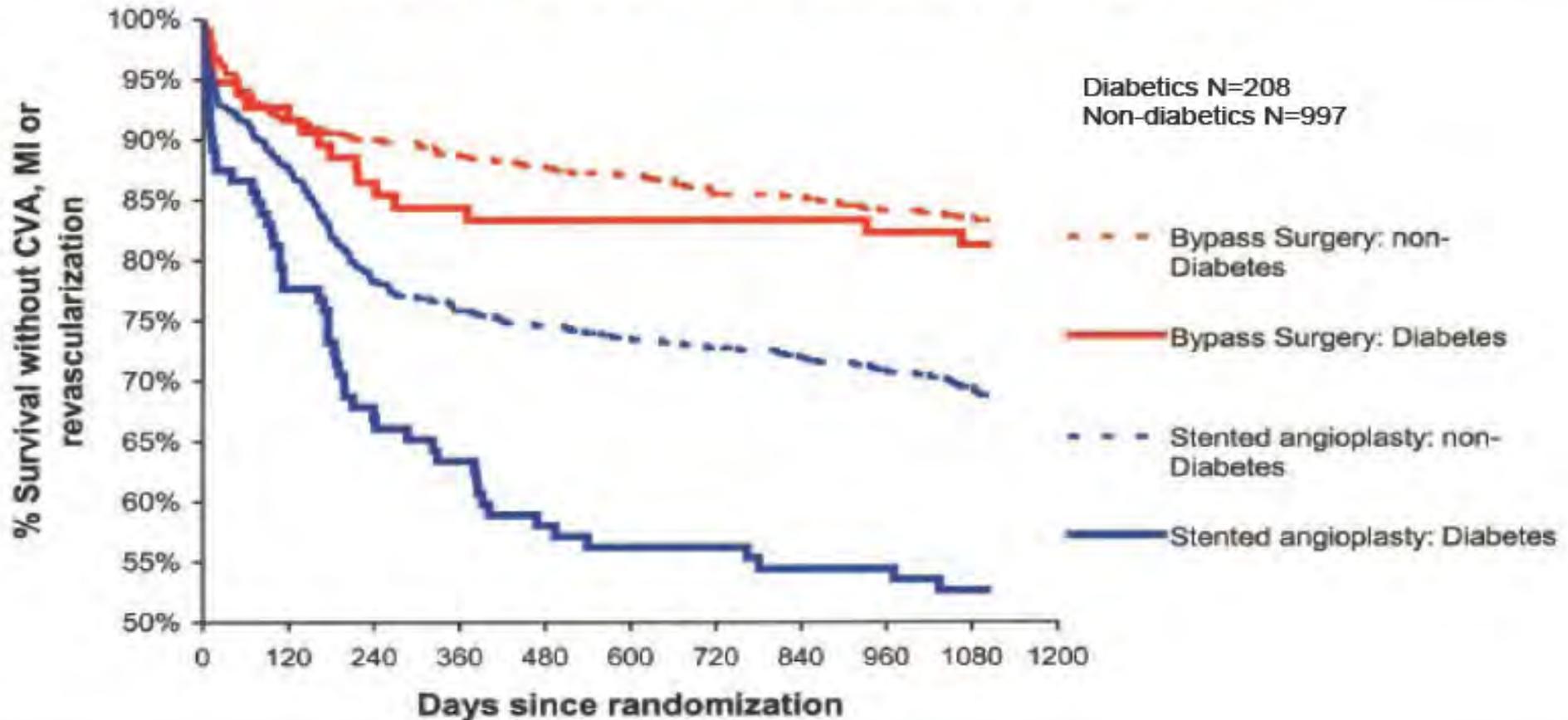
Mortality in diabetics undergoing revascularization

	patients	enrollment period
BARI	353	88-91
BARI Reg	299	88-91
EAST	59	87-90
MAHI	525	87-90
CABRI	125	88-92
ARTS	208	97-98
AWESOME	144	95-00



2005

Arterial Revascularization Therapies Study (ARTS) Randomized Trial: *3-years event-free survival*



Repeat revascularization rate at 3y: 26.7% (PCI) vs 6.6% (CABG)



FIVE-YEAR OUTCOMES AFTER CORONARY STENTING VERSUS BYPASS SURGERY FOR THE TREATMENT OF MULTIVESSEL DISEASE

The Final Analysis Of The Arterial Revascularization Therapies Study (ARTS) Randomized Trial in patients with diabetes stratified according to treatment

	Stent Diabetes n = 112 n* (%*)	Bypass Diabetes n = 96 n* (%*)	Relative Risk (95% CI)	Stent Versus CABG p Value†
Death	15 (13.4)	8 (8.3)	1.61 (0.71–3.63)	0.27
CVA	7 (6.3)	7 (7.3)	0.86 (0.31–2.36)	0.79
MI	12 (10.7)	7 (7.3)	1.47 (0.60–3.59)	0.47
Q-wave MI	9 (8.0)	4 (4.2)	1.93 (0.61–6.07)	0.39
Non-Q-wave MI	3 (2.7)	3 (3.1)	0.86 (0.18–4.15)	1.00
Composite death/CVA/MI	28 (25.0)	19 (19.8)	1.26 (0.76–2.11)	0.41
(re) CABG	17 (15.2)	2 (2.1)	7.29 (1.73–30.7)	0.001
(re) PTCA	34 (30.4)	9 (9.4)	3.24 (1.64–6.41)	<0.001
Any revascularization	48 (42.9)	10 (10.4)	4.11 (2.20–7.68)	<0.001
Any MACCE	61 (54.5)	24 (25.0)	2.18 (1.48–3.20)	<0.001

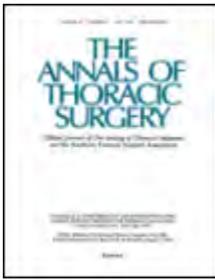
*Number of patients and percentage of patients with at least one occurrence of the specified clinical event during the time interval indicated in the table. †p value calculated using the Fisher exact test.

PCI DES vs CABG: “running game”

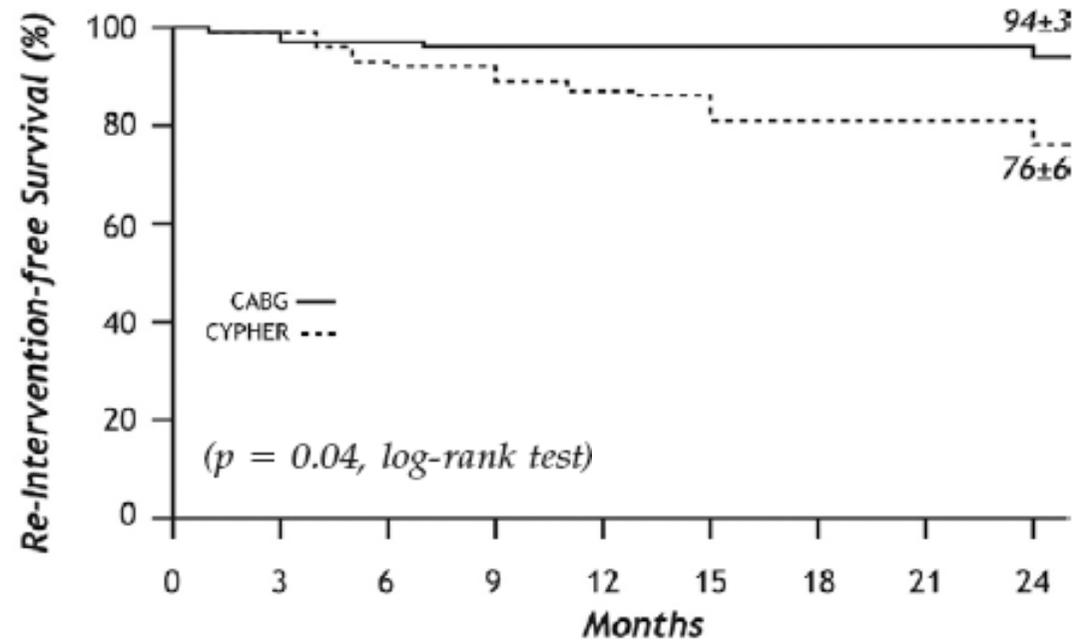
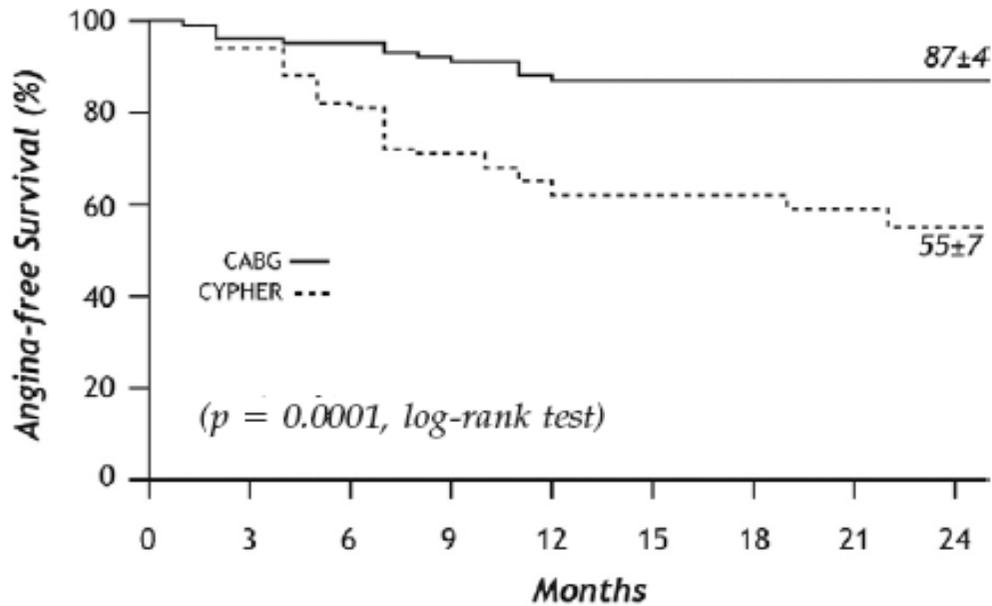
PCI BMS vs CABG: 1 - 2

PCI Balloon vs CABG: 0 - 2





DRUG-ELUTING STENT VERSUS CORONARY ARTERY BYPASS GRAFTING IN PATIENTS WITH DIABETES MELLITUS



OUTCOMES OF CORONARY ARTERY BYPASS GRAFTING VERSUS PERCUTANEOUS CORONARY INTERVENTION WITH DRUG-ELUTING STENT FOR PATIENTS WITH MULTIVESSEL CORONARY ARTERY DISEASE

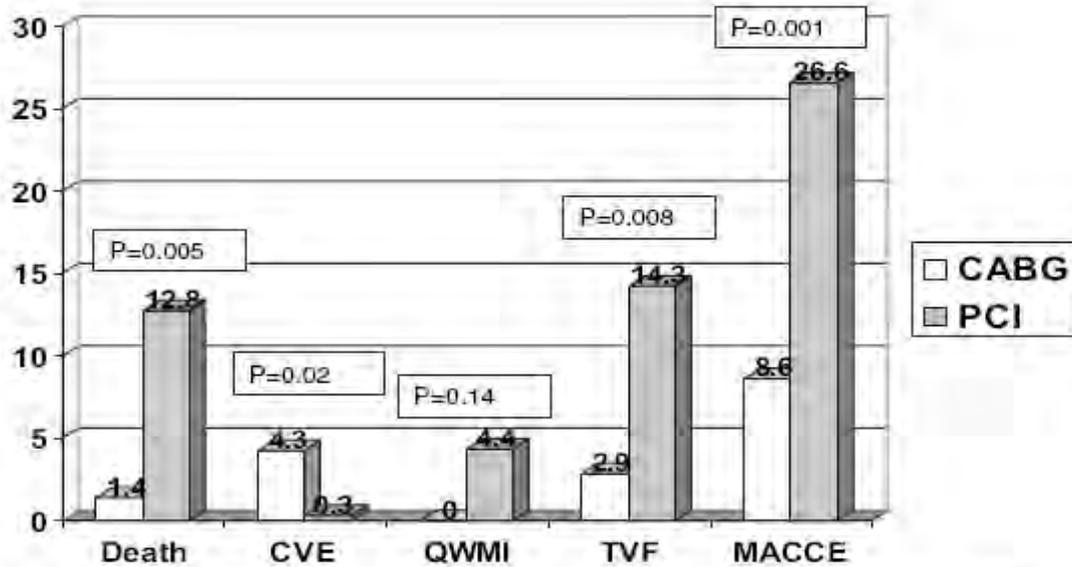


Figure 3. Clinical 12-month outcomes for 2-vessel CAD with diabetes mellitus.

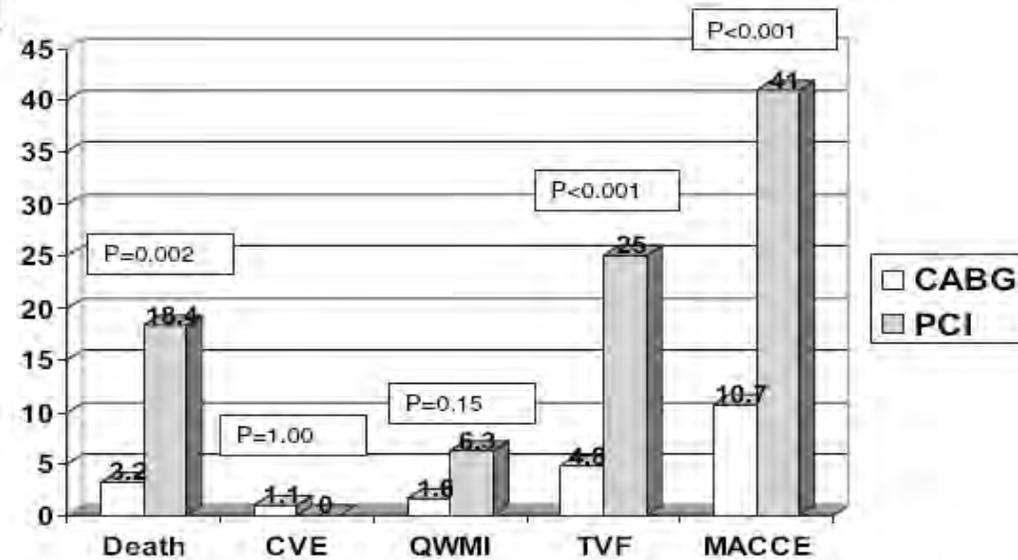
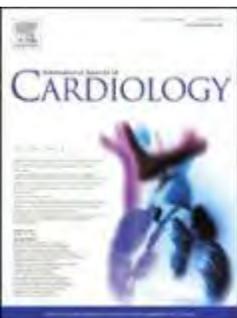


Figure 4. Clinical 12-month outcomes for 3-vessel CAD with diabetes mellitus.



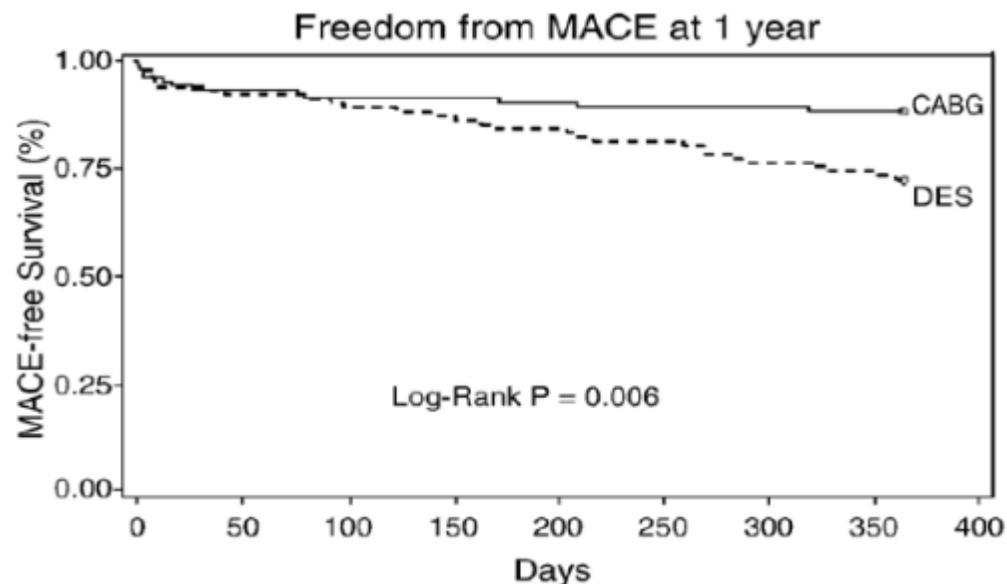
COMPARISON OF BYPASS SURGERY WITH DRUG-ELUTING STENTS FOR DIABETIC PATIENTS WITH MULTIVESSEL DISEASE

Procedural and 30-Day outcomes

	CABG <i>n</i> = 103	DES <i>n</i> = 102	<i>p</i> -value
MACE (%)	8	5	0.40
Death (%)	5	3	0.48
Myocardial infarction ^a (%)	2	2	>0.9
Repeat revascularization (%)	1	3	0.32
Stroke (%)	3	0	0.08
VT/VF (%)	4	0	0.04
Requirement for permanent pacemaker (%)	8	0	0.004
Renal failure requiring dialysis (%)	3	1	0.32
Repeat surgery for bleeding (%)	5	NA	
Cardiac tamponade (%)	2	0	0.16
In-hospital length of stay (days±SD)	8.4±6.3	3.0±4.8	<0.001

One-year outcomes

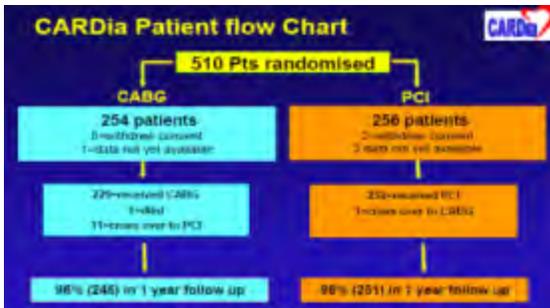
	CABG <i>n</i> = 103	DES <i>n</i> = 102	<i>p</i> -value
MACE (%)	12	27	0.006
Death (%)	8	10	0.6
Myocardial infarction ^a (%)	2	8	0.1
Repeat revascularization (%)	3	20	<0.001
Stroke (%)	4	0	0.04



CORONARY ARTERY REVASCULARIZATION IN DIABETES TRIAL (CARDia)



Hypothesis:
in diabetics patients with multivessel disease amenable to both CABG or PCI
Optimal PCI is not inferior to up-to-date CABG



CARDia: Main Conclusions

- No apparent difference between PCI and CABG at one year in:
 - Death
 - Composite of Death, MI and stroke
- More repeat revascularisation in the PCI group
- PCI may now be considered a reasonable strategy in diabetic patients with multivessel disease
- Longer follow up is needed

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, Neuzo Lopes, Kathryn M McDonald, Alfredo Rodriguez, Patrick Serruys, Ulrich Sigwart, Rodney H Stables, Douglas K Owens, Stuart J Pocock

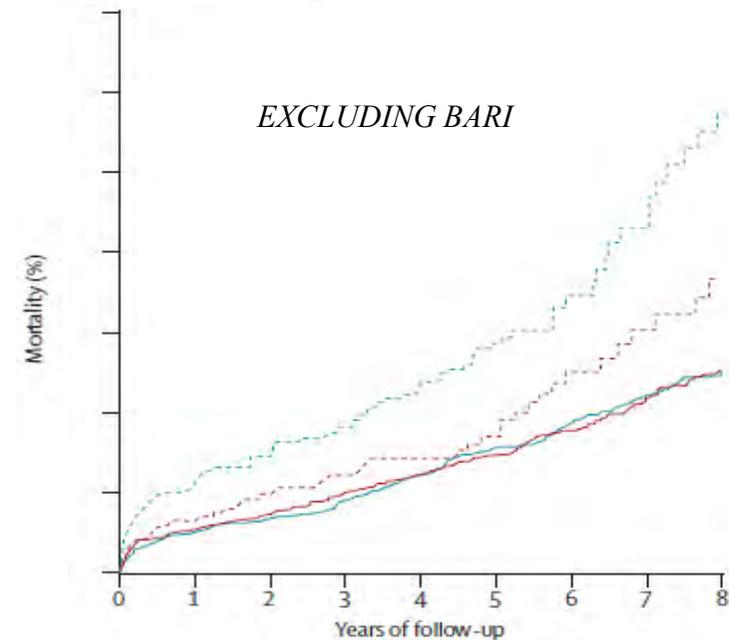
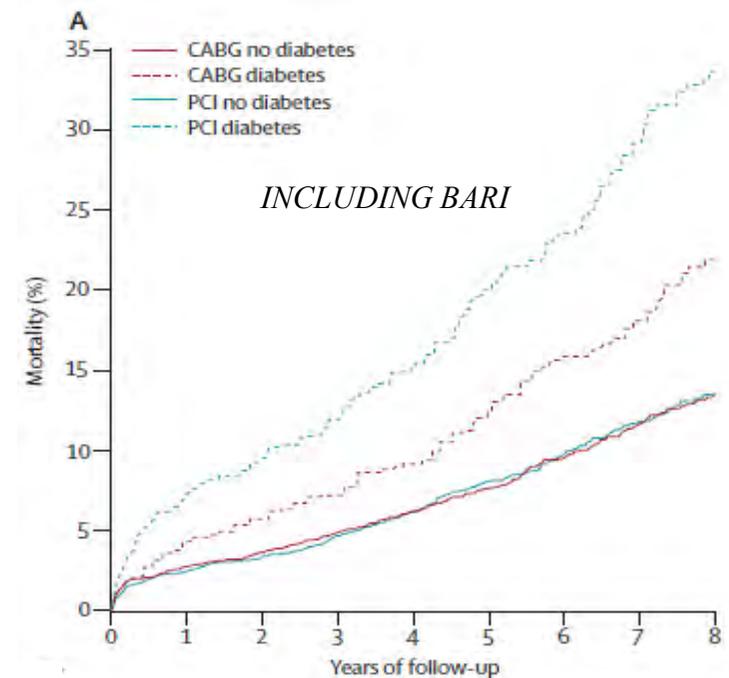
Summary

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.

Findings Ten participating trials provided data on 7812 patients. PCI was done with balloon angioplasty in six trials and with bare-metal stents in four trials. Over a median follow-up of 5.9 years (IQR 5.0–10.0), 575 (15%) of 3889 patients assigned to CABG died compared with 628 (16%) of 3923 patients assigned to PCI (hazard ratio [HR] 0.91, 95% CI 0.82–1.02; $p=0.12$). In patients with diabetes (CABG, $n=615$; PCI, $n=618$), mortality was substantially lower in the CABG group than in the PCI group (HR 0.70, 0.56–0.87); however, mortality was similar between groups in patients without diabetes (HR 0.98, 0.86–1.12; $p=0.014$ for interaction). Patient age modified the effect of treatment on mortality, with hazard ratios of 1.25 (0.94–1.66) in patients younger than 55 years, 0.90 (0.75–1.09) in patients aged 55–64 years, and 0.82 (0.70–0.97) in patients 65 years and older ($p=0.002$ for interaction). Treatment effect was not modified by the number of diseased vessels or other baseline characteristics.

Interpretation Long-term mortality is similar after CABG and PCI in most patient subgroups with multivessel coronary artery disease, so choice of treatment should depend on patient preferences for other outcomes. CABG might be a better option for patients with diabetes and patients aged 65 years or older because we found mortality to be lower in these subgroups.



A Randomized Trial of Therapies for Type 2 Diabetes and Coronary Artery Disease

The BARI 2D Study Group*

ABSTRACT

BACKGROUND

Optimal treatment for patients with both type 2 diabetes mellitus and stable ischemic heart disease has not been established.

METHODS

We randomly assigned 2368 patients with both type 2 diabetes and heart disease to undergo either prompt revascularization with intensive medical therapy or intensive medical therapy alone and to undergo either insulin-sensitization or insulin-provision therapy. Primary end points were the rate of death and a composite of death, myocardial infarction, or stroke (major cardiovascular events). Randomization was stratified according to the choice of percutaneous coronary intervention (PCI) or coronary-artery bypass grafting (CABG) as the more appropriate intervention.

RESULTS

At 5 years, rates of survival did not differ significantly between the revascularization group (88.3%) and the medical-therapy group (87.8%, $P=0.97$) or between the insulin-sensitization group (88.2%) and the insulin-provision group (87.9%, $P=0.89$). The rates of freedom from major cardiovascular events also did not differ significantly among the groups: 77.2% in the revascularization group and 75.9% in the medical-treatment group ($P=0.70$) and 77.7% in the insulin-sensitization group and 75.4% in the insulin-provision group ($P=0.13$). In the PCI stratum, there was no significant difference in primary end points between the revascularization group and the medical-therapy group. In the CABG stratum, the rate of major cardiovascular events was significantly lower in the revascularization group (22.4%) than in the medical-therapy group (30.5%, $P=0.01$; $P=0.002$ for interaction between stratum and study group). Adverse events and serious adverse events were generally similar among the groups, although severe hypoglycemia was more frequent in the insulin-provision group (9.2%) than in the insulin-sensitization group (5.9%, $P=0.003$).

CONCLUSIONS

Overall, there was no significant difference in the rates of death and major cardiovascular events between patients undergoing prompt revascularization and those undergoing medical therapy or between strategies of insulin sensitization and insulin provision. (ClinicalTrials.gov number, NCT00006305.)

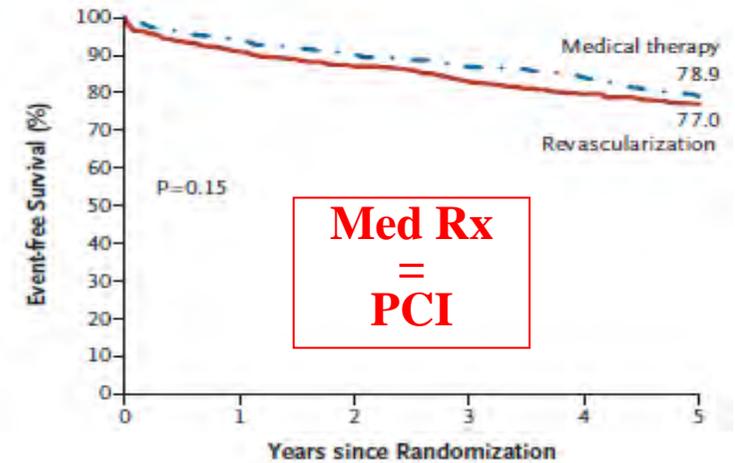
The members of the writing group (Robert L. Frye, M.D., Mayo Clinic, Rochester, MN; Phyllis August, M.D., M.P.H., New York Hospital Queens, Queens, NY; Maria Mori Brooks, Ph.D., Regina M. Harrison, M.S., Sheryl F. Kelsey, Ph.D., Joan M. MacGregor, M.S., and Trevor J. Orchard, M.B., B.Ch., University of Pittsburgh, Pittsburgh; Bernard R. Chaitman, M.D., Saint Louis University, St. Louis; Saul M. Genuth, M.D., Case Western Reserve University, Cleveland; Suzanne H. Goldberg, R.N., M.S.N., National Heart, Lung, and Blood Institute, Bethesda, MD; Mark A. Hlatky, M.D., Stanford University, Palo Alto, CA; Teresa L.Z. Jones, M.D., National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, MD; Mark E. Molitch, M.D., Feinberg School of Medicine, Northwestern University, Chicago; Richard W. Nesto, M.D., Lahey Clinic Medical Center, Burlington, MA; Edward Y. Sako, M.D., Ph.D., University of Texas Health Science Center, San Antonio; and Burton E. Sobel, M.D., University of Vermont, Burlington) assume responsibility for the overall content and integrity of the article. Address reprint requests to Dr. Brooks at the Department of Epidemiology, University of Pittsburgh Graduate School of Public Health, 130 DeSoto St., Pittsburgh, PA 15261, or at mbrooks@pitt.edu.

*Members of the Bypass Angioplasty Revascularization Investigation 2 Diabetes (BARI 2D) Study Group are listed in the Supplementary Appendix, available with the full text of this article at NEJM.org.

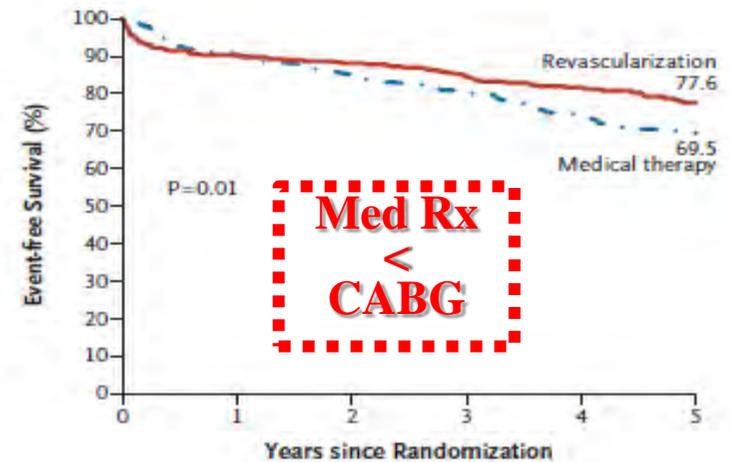
This article (10.1056/NEJMoa0805796) was published on June 7, 2009, at NEJM.org.

N Engl J Med 2009;360:2503-15.
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C Freedom from Major Cardiovascular Events in PCI Stratum



D Freedom from Major Cardiovascular Events in CABG Stratum



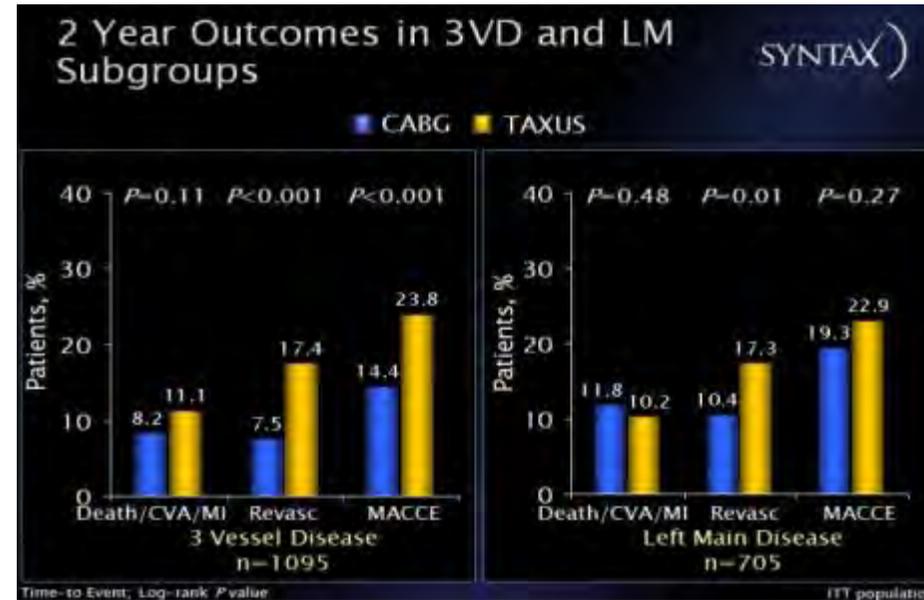
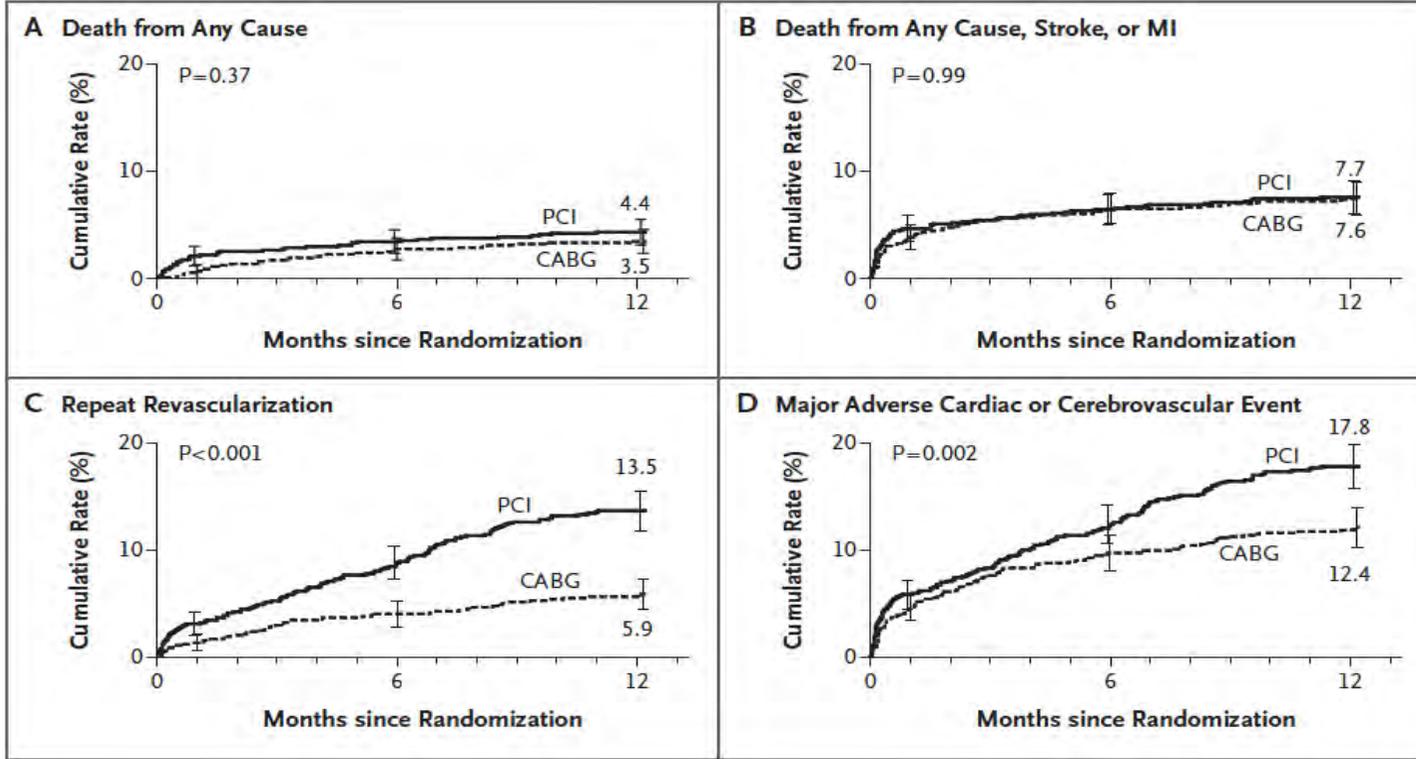
THE SYNTAX TRIAL

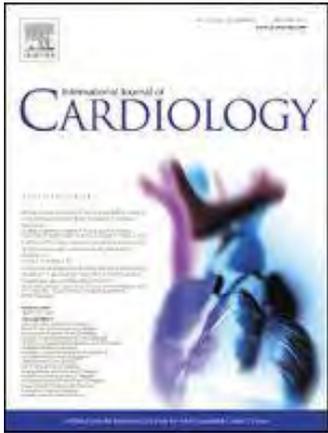
1 and 2 YEARS

The SYNTAX trial of CABG versus PCI with paclitaxel drug eluting stents in patients with left main or three vessel coronary disease included:

452 people with diabetes.

2009 ...





Revascularization strategies for stable multivessel and unprotected left main coronary artery disease:

From BARI to SYNTAX

1. Emerging evidence suggests that patients with higher atheroma burden, as indicated by older age, **presence of diabetes mellitus** and extensive MVD in combination with LV dysfunction may derive the greatest benefit from CABG.
2. PCI for unprotected LM with limited additional disease has been revised to a class II recommendation in the recent U.S. and European guidelines.
3. An interdisciplinary team of both cardiac surgeons and cardiologists may optimize treatment in patients with intermediate-to-high disease severity characteristics.

... from 1988 to 2011

TAKE HOME MESSAGES



Appropriateness of Revascularization

Indication	PCI Appropriateness Rating	CABG Appropriateness Rating
60. <ul style="list-style-type: none"> • 2-vessel CAD with proximal LAD stenosis • No diabetes and normal LVEF 	A ₍₈₎ *	A ₍₈₎
61. <ul style="list-style-type: none"> • 2-vessel CAD with proximal LAD stenosis • Diabetes 	A ₍₇₎	A ₍₈₎
62. <ul style="list-style-type: none"> • 2-vessel CAD with proximal LAD stenosis • Depressed LVEF 	A ₍₇₎	A ₍₈₎
63. <ul style="list-style-type: none"> • 3-vessel CAD • No diabetes and normal LVEF 	U ₍₆₎	A ₍₈₎
64. <ul style="list-style-type: none"> • 3-vessel CAD • Diabetes 	U ₍₅₎	A ₍₉₎
65. <ul style="list-style-type: none"> • 3-vessel CAD • Depressed LVEF 	U ₍₄₎	A ₍₉₎
66. <ul style="list-style-type: none"> • Isolated left main stenosis • No diabetes and normal LVEF 	I ₍₃₎	A ₍₉₎
67. <ul style="list-style-type: none"> • Isolated left main stenosis • Diabetes 	I ₍₃₎	A ₍₉₎
68. <ul style="list-style-type: none"> • Isolated left main stenosis • Depressed LVEF 	I ₍₃₎	A ₍₉₎
69. <ul style="list-style-type: none"> • Left main stenosis and additional CAD • No diabetes and normal LVEF 	I ₍₃₎	A ₍₉₎
70. <ul style="list-style-type: none"> • Left main stenosis and additional CAD • Diabetes 	I ₍₂₎	A ₍₉₎
71. <ul style="list-style-type: none"> • Left main stenosis and additional CAD • Depressed LVEF 	I ₍₂₎	A ₍₉₎
72. <ul style="list-style-type: none"> • Prior bypass surgery with native 3-vessel disease and failure of multiple bypass grafts • LIMA remains patent to a native coronary artery • Depressed LVEF 	A ₍₇₎	U ₍₆₎
73. <ul style="list-style-type: none"> • Prior bypass surgery with native 3-vessel disease and failure of multiple bypass grafts • LIMA was used as a graft but is no longer functional • Depressed LVEF 	U ₍₆₎	A ₍₈₎

Box. Strategies to Improve Outcomes in Diabetic Patients Undergoing Coronary Revascularization

CABG

If possible, use ≥ 1 arterial conduit, preferably an internal mammary artery, with preference given to anastomoses to the left anterior descending artery

Maintain rigid perioperative glycemic control (serum glucose < 200 mg/dL [11.1 mmol/L]) with a continuous insulin infusion

PCI

Drug-eluting stents, with either rapamycin or paclitaxel, are strongly recommended

Glycoprotein IIb/IIIa inhibitors are strongly recommended, especially during an acute coronary syndrome

Abbreviations: CABG, coronary artery bypass graft surgery; PCI, percutaneous coronary intervention.

PRACTICAL FLOWCHART

ULM or 3VD with any of the following unfavorable features:

- True bifurcational disease of ULM
- 1 or > clinically relevant CTO
- LV dysfunction (LVEF < 40%)
- Diabetes mellitus
- Other surgical indications

CABG as first choice!

Attempt PCI if:

- CABG contraindicated
- Patient/family and cardiac surgeon agree on PCI

ULM or MVD without any of above unfavorable features

CABG favored, but PCI reasonable

Protected LM or 2VD with any of these "favorable" features :

- Ostial LAD ok
- Lack of diffuse disease
- No true bifurcations
- No CTO
- No diabetes
- Ongoing STEACS

Risk-benefit balance fine for PCI, but CABG can still be appropriate and thus should be discussed with patient and family

1VD without other surgical indications

PCI recommended (CABG should be considered only for proximal LAD)

**1ST STEP IN CRISIS MANAGEMENT IS
PREVENTING IT: FOLLOW GUIDELINES UNLESS
YOU ARE JUSTIFIED...**



**2th Step: COLLABORATIVE DECISION-MAKING
IN ALL BUT CLEAR-CUT CASES:
*INVOLVE OTHER INTERVENTIONAL COLLEAGUES,
NON-INVASIVE CARDIOLOGISTS, AND SURGEONS***



Do all patients with diabetes and multivessel disease need CABG?



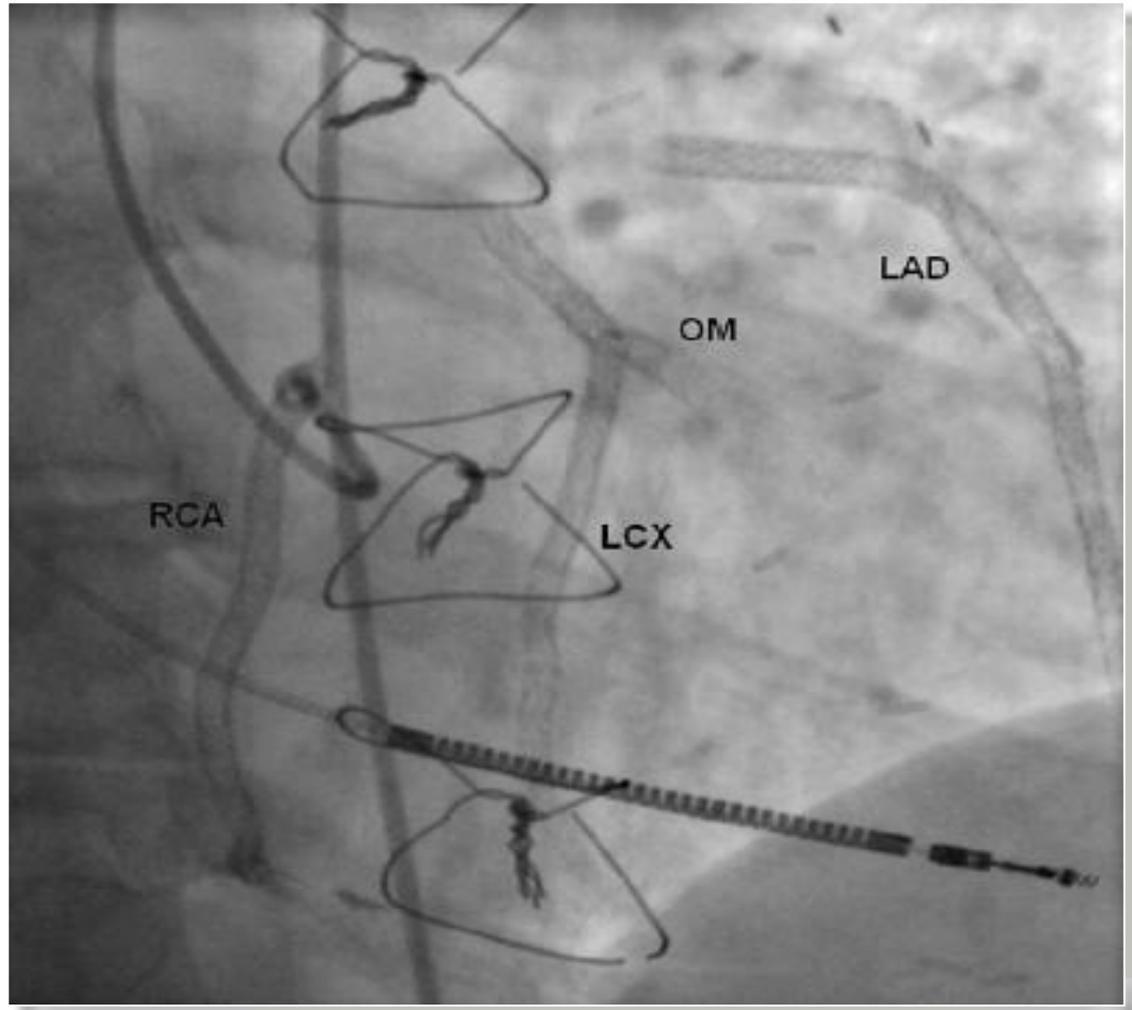
Patient with stable symptoms and only a small percentage of the myocardium that is ischaemic will do well with medical therapy.

Both stable and acute patients with large areas of ischaemia should have angiography and prompt revascularisation.

Data from both trials and registries confirm that CABG offers a more permanent solution to angina, reducing repeat revascularisation rates. However, recent data suggest, at least at one to two years, the overall stroke rate is higher with CABG than PCI with the death and myocardial infarction rates equivalent.

Patients need to be given adequate information to enable them to balance the risks and benefits.

67 stent



KHOUZAM R. ET AL. JACC 2010;56:1605

24 h post CABG



24 h post multivessel PCI



DANKSCHEEN
TASHAKKUR ATU
GRACIAS
ARIGATO
SHUKURIA
JUSPAKAR
BİYAN
SHUKRIA
THANK
YOU
BOLZIN
MERCİ