Porto Alegre, RS
BRASIL

Angioplastia de Multiples Vasos:

Perspectiva

Dr. Gilberto L. Nunes

30º Congreso Uruguayo de Cardiologia

Declaração de Potencial Conflito de Interesse

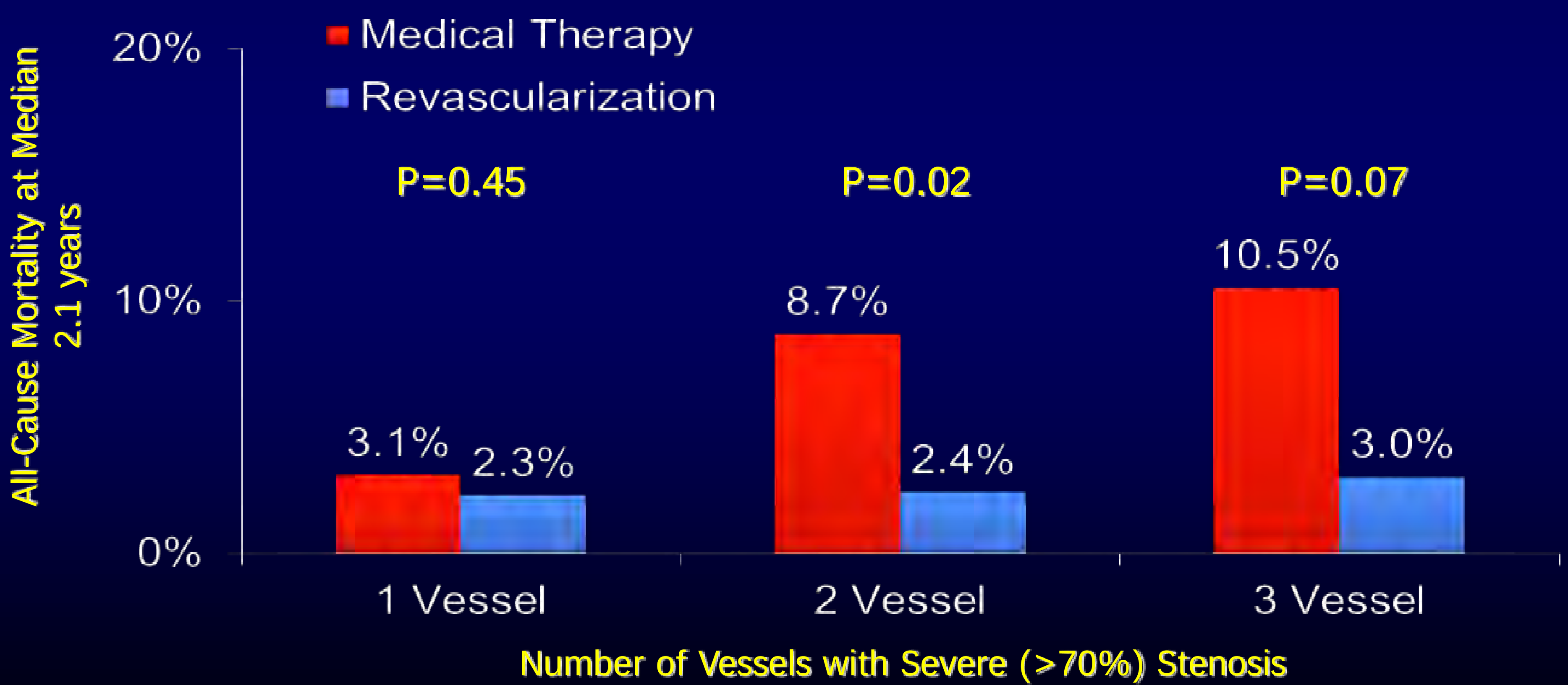
Nome do Palestrante: Gilberto Lahorgue Nunes
Título da Apresentação: Angioplastia de multiples vasos

CATEGORIAS DE POTENCIAL CONFLITO DE INTERESSE	INDÚSTRIA(S)
Patrocínio de transporte e/ou hospedagem em Congressos	Abbott, Biotronik,, Terumo
Patrocínio em estudos clínicos e/ou experimentais subvencionados pela indústria	-
Ser conferencista / palestrante em eventos patrocinados pela indústria	Terumo, BioSensors
Participar de comitês normativos de estudos científicos patrocinados pela indústria	-
Receber apoio institucional da indústria	Abbott, Biotronik, Terumo, Boston
Preparo de textos científicos em periódicos patrocinados pela indústria	-
Ter ações da indústria	-

CONFIRM: Association of Revascularization with All-Cause Mortality

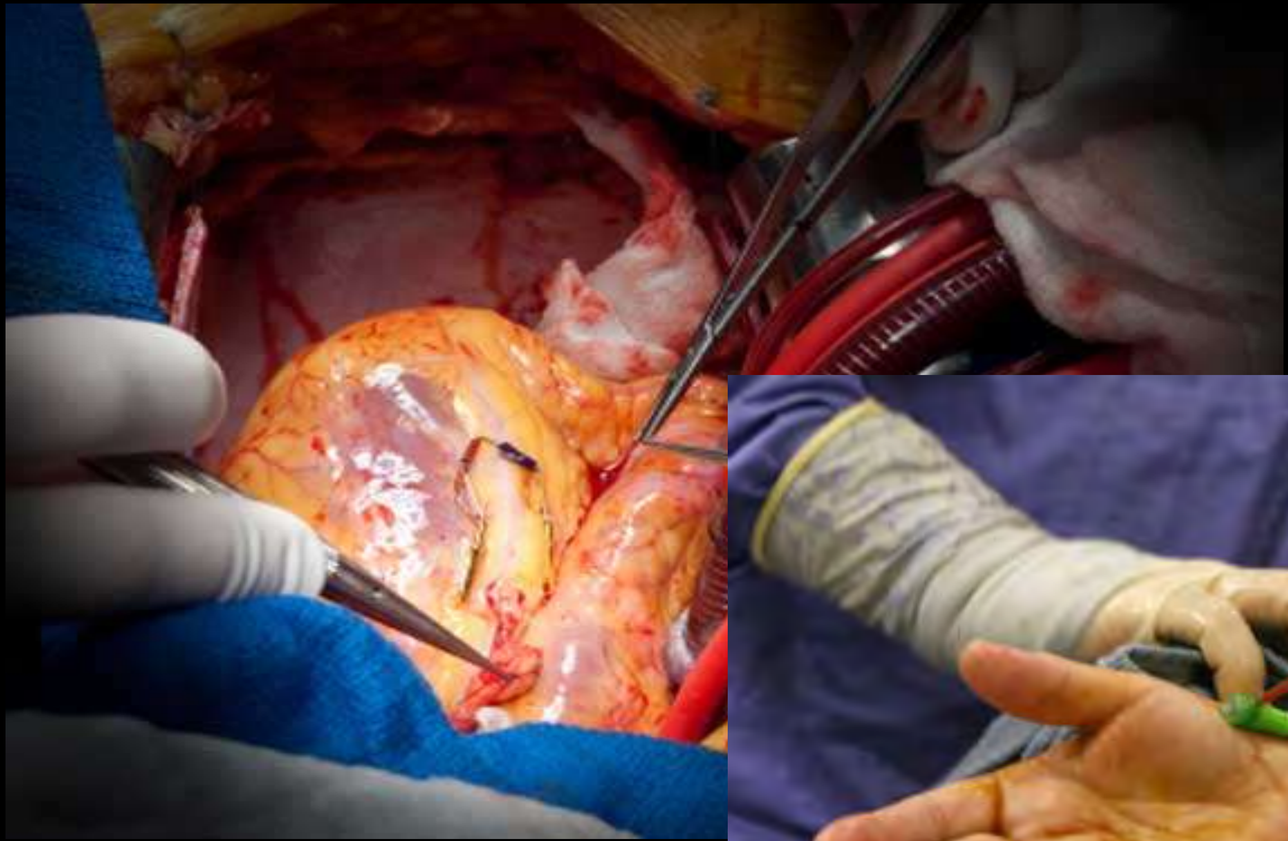
15,223 stable patients without known CAD undergoing CTA

Revascularization of "High-Risk" Anatomy (7.3%) was independently associated with 62% lower Mortality at 2.1 yrs (adjusted HR 0.38 [0.18,0.83])



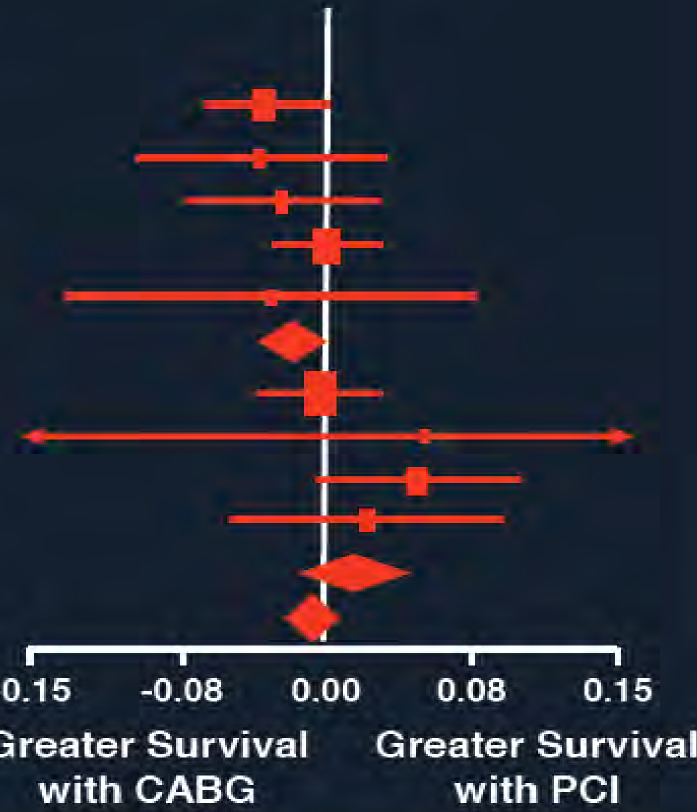
Min JK et al, Eur Heart J 2012

Two Very Different Procedures…



Five-year Survival with Balloon Angioplasty or Stents vs. Coronary Artery Bypass Grafting in Patients with Multivessel Disease

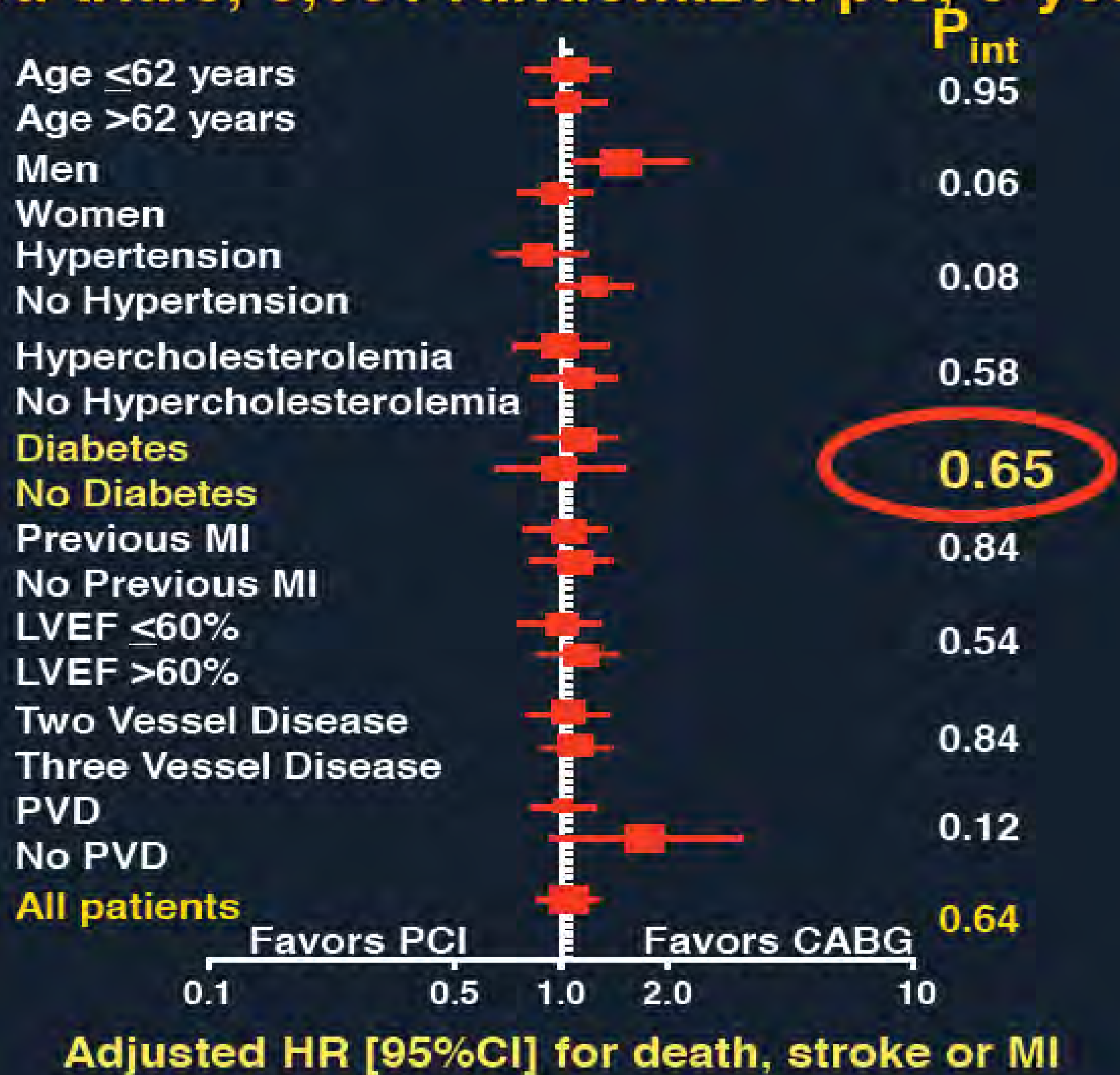
Study, Year (Reference)	Surviving Patients/All Patients, n/n		Risk Difference (95% CI)
	PCI	CABG	
BARI, 1996 (64)	790/915	816/914	
EAST, 2000 (80)	153/174	161/177	
GABI, 2005 (88)*	164/177	157/165	
RITA, 1998 (110)	483/510	474/501	
French Monocentric Study, 1997 (126)	66/76	68/76	
Balloon overall	1656/1852	1676/1833	
ARTS, 2005 (23)	542/590	538/584	
AWESOME, 2001 (28)	30/38	19/26	
ERACIII, 2005 (86)	209/225	199/225	
MASS II, 2006 (103)	177/205	171/203	
BMS overall	958/1058	927/1038	
MVD overall	2614/2910	2603/2871	



Bravata et al, *Ann Intern Med.* 2007;147.

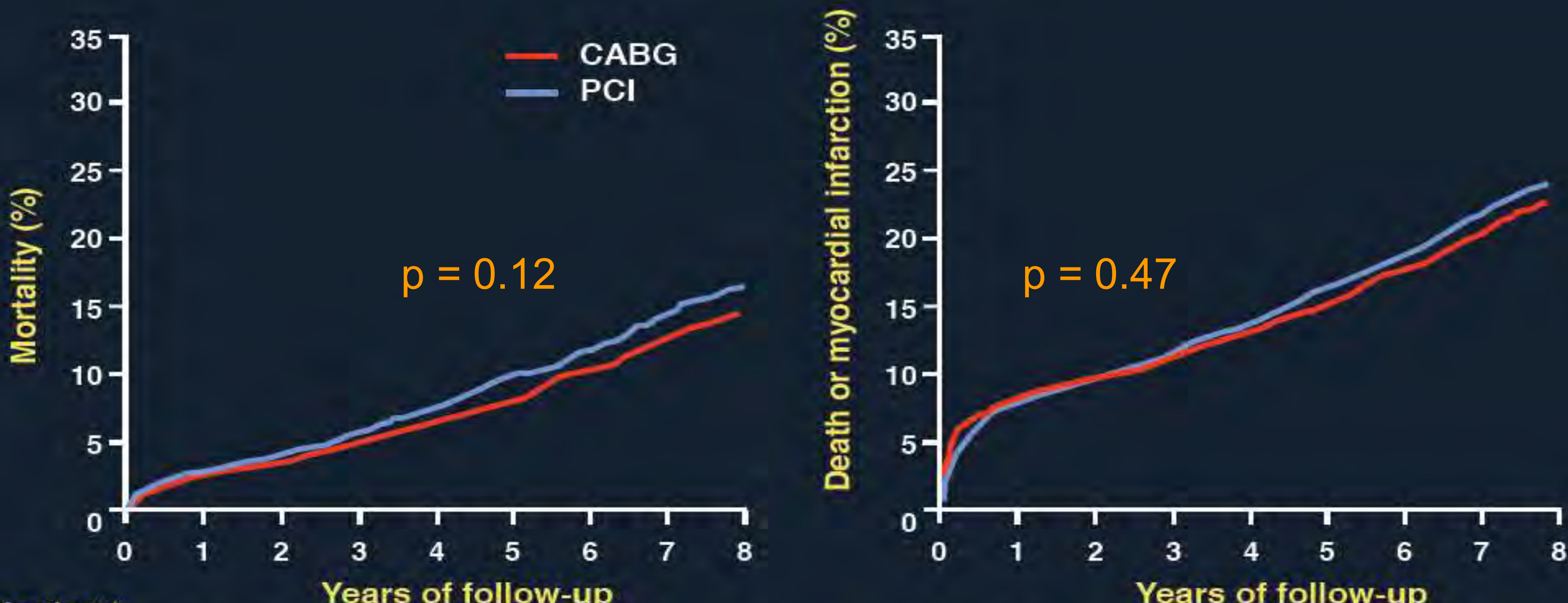
Bare Metal Stents vs. CABG

4 randomized trials, 3,051 randomized pts, 5-year follow-up



Daemen J et al. *Circulation* 2008; 118:1146-1154

10 RCTs 7812 Pts: CABG vs. PCI: No Difference in Death and MI



No. of patients*

	0	1	2	3	4	5	6	7	8
CABG	3889	3767	3675	3415	3180	2693	1853	1609	1477
PCI	3923	3798	3709	3431	3205	2658	1828	1576	1452

	0	1	2	3	4	5	6	7	8
CABG	3695	3369	3269	3001	2763	2294	1501	1269	1161
PCI	3725	3419	3310	3023	2797	2267	1491	1253	1150

POBA and BMS trials

Hlatky et al, *The Lancet* 2009;373:1190-1197

BARI 10 Year Follow-up

No. of Patients					
CABG	914	859	812	737	553
PTCA	915	842	790	714	540

Brooks et al, *JACC* 2007;49:1600-06

SYNTAX

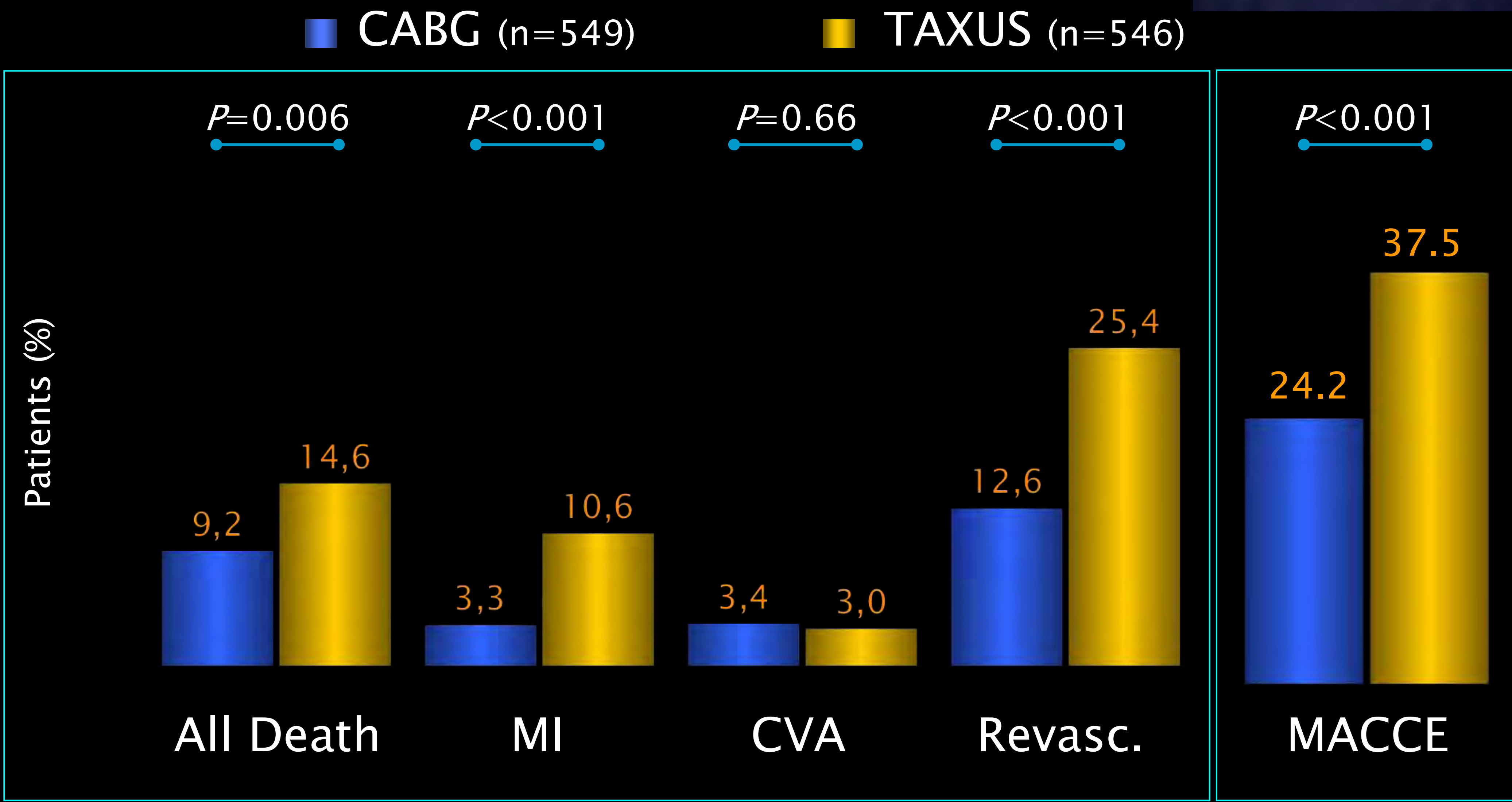
The Synergy between Percutaneous Coronary Intervention with TAXUS and Cardiac Surgery: The SYNTAX Study

Final Five-year Follow-up of the SYNTAX Trial: Optimal Revascularization Strategy in Patients with

Three-vessel Disease

3VD Disease

5-year Outcomes (N=1095)

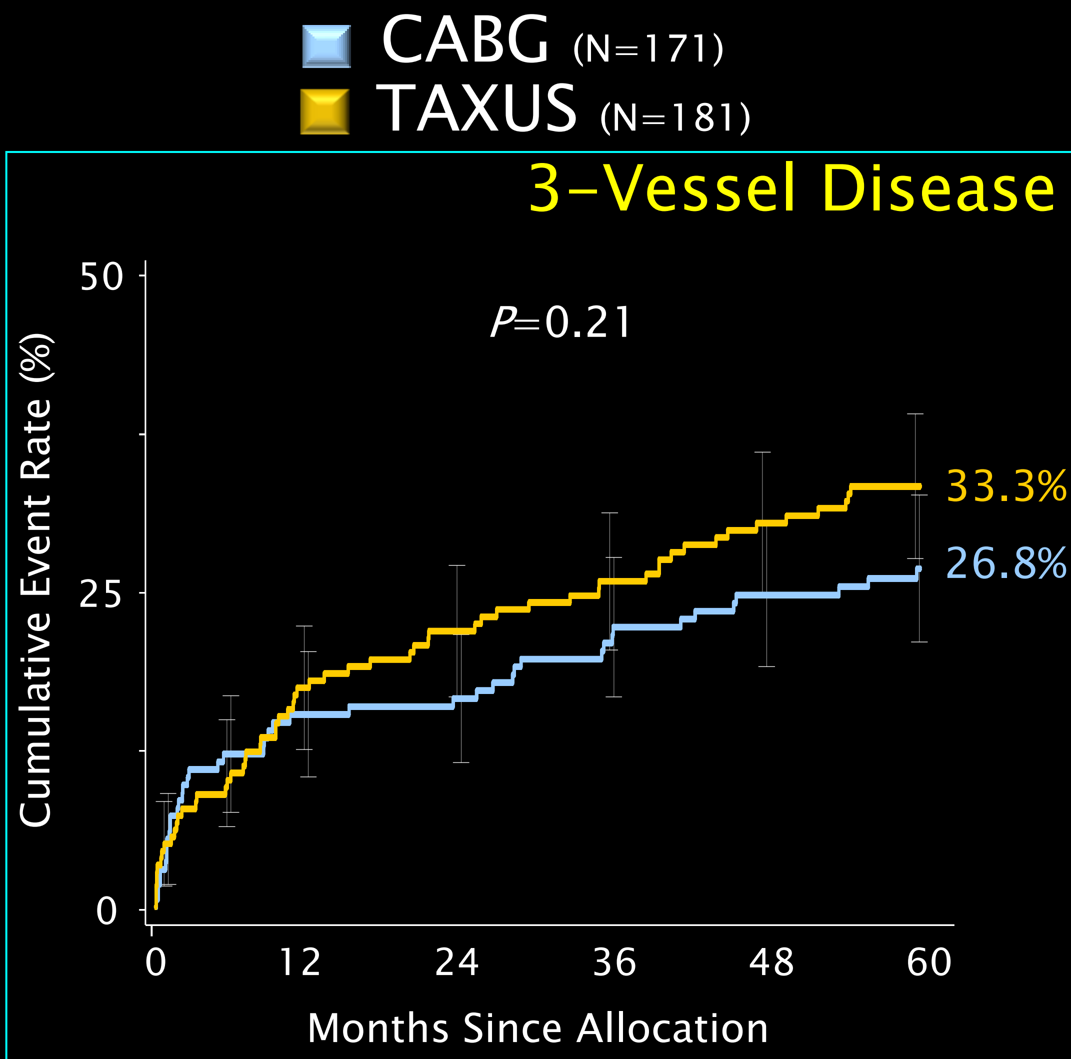


Cumulative KM Event Rate; log-rank *P* value

ITT population

MACCE to 5 Years by SYNTAX Score Tercile
3VD Subset Low Scores 0-22

SYNTAX



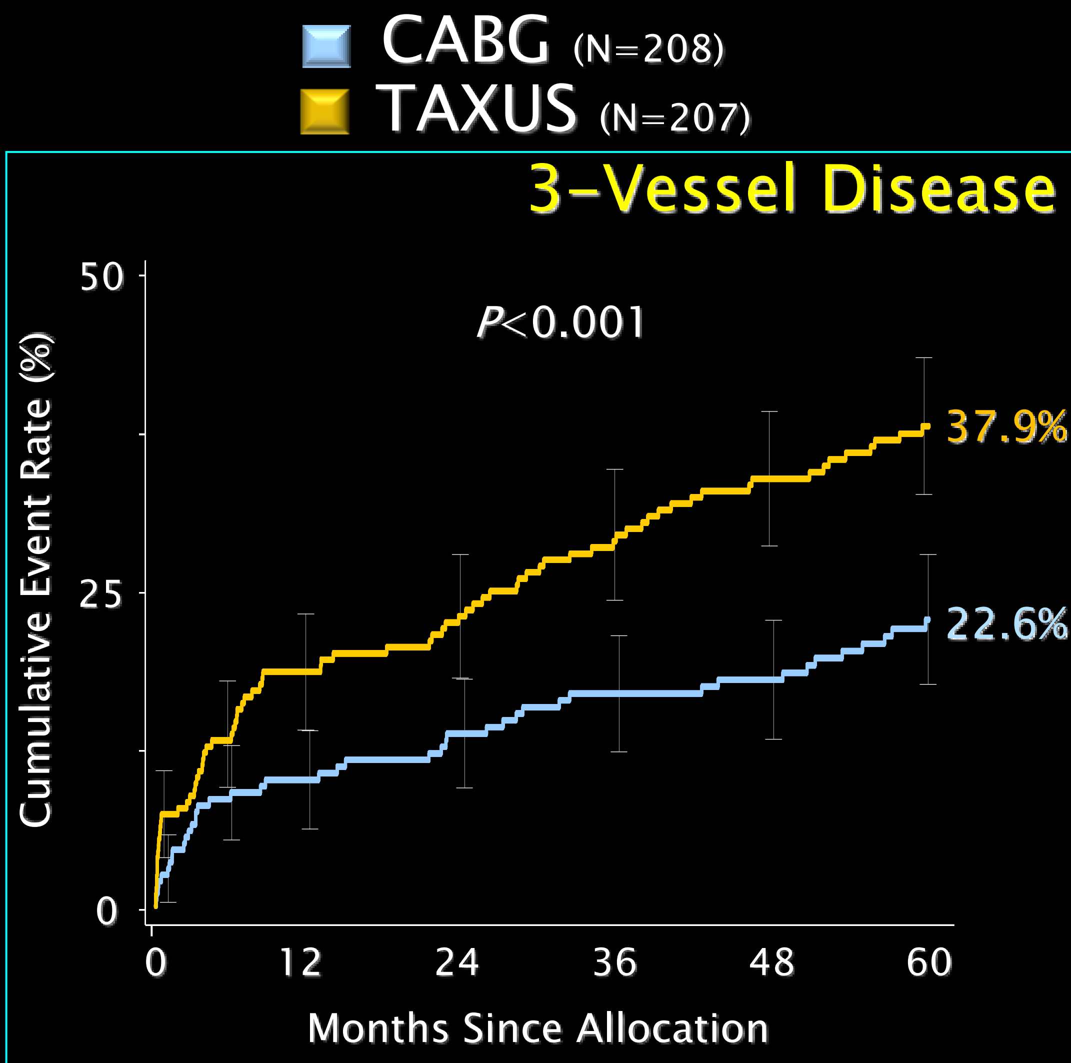
Cumulative KM Event Rate ± 1.5 SE; log-rank *P* value

	CABG	PCI	*P* value
Death	9.3%	10.2%	0.81
CVA	3.9%	1.8%	0.24
MI	4.9%	8.8%	0.20
Death, CVA or MI	14.8%	17.5%	0.56
Revasc.	14.6%	23.1%	0.04

Site-reported Data; ITT population

MACCE to 5 Years by SYNTAX Score Tercile
3VD Subset Intermediate Scores 23–32

SYNTAX



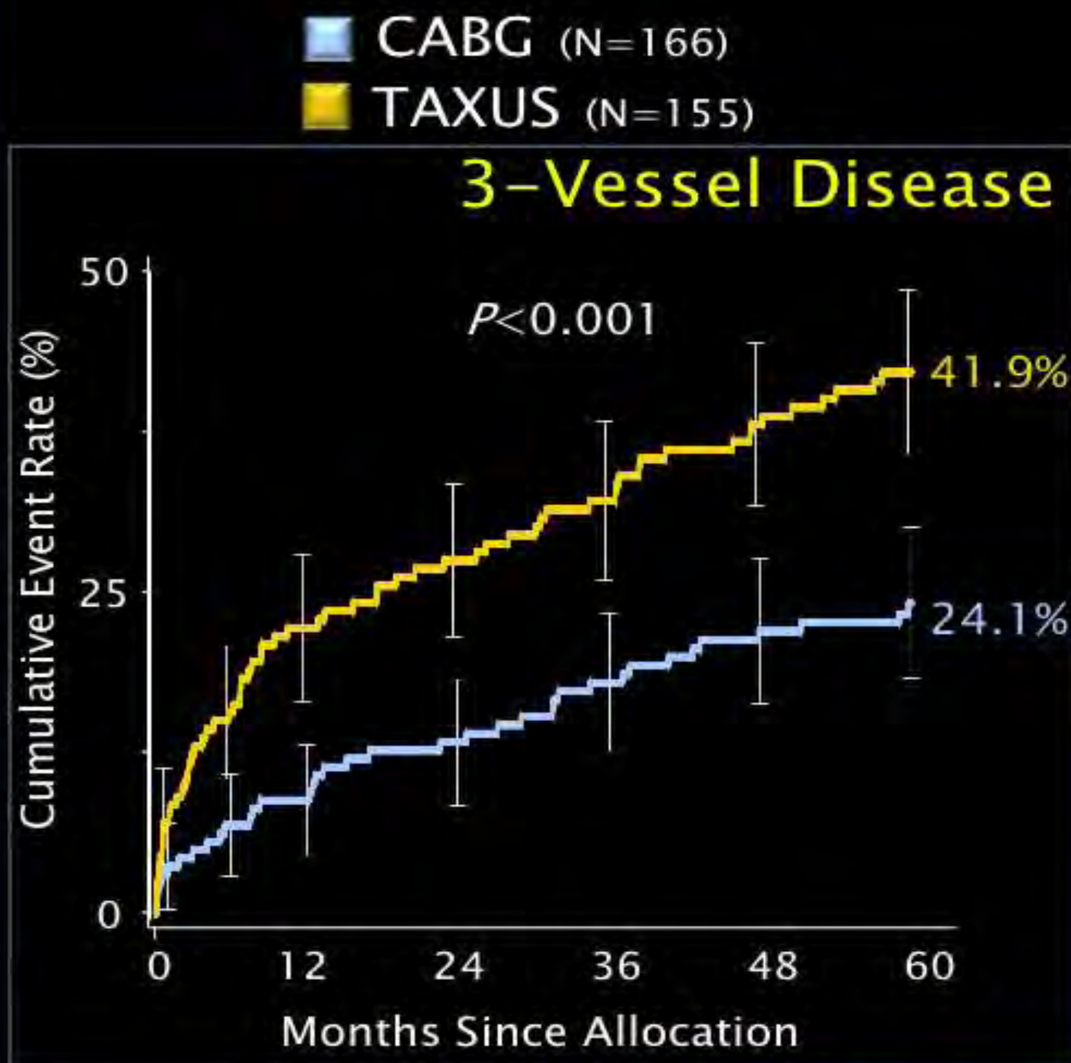
Cumulative KM Event Rate ± 1.5 SE; log-rank *P* value

	CABG	PCI	*P* value
Death	9.6%	16.3%	0.047
CVA	3.6%	2.5%	0.53
MI	3.1%	13.8%	<0.001
Death, CVA or MI	14.7%	23.2%	0.04
Revasc.	11.0%	25.1%	<0.001

Site-reported Data; ITT population

MACCE to 5 Years by SYNTAX Score Tercile
3VD Subset High Scores ≥33

SYNTAX



	CABG	PCI	*P* value
Death	8.8%	17.8%	0.02
CVA	2.6%	5.1%	0.31
MI	1.9%	8.7%	0.008
Death, CVA or MI	12.5%	26.2%	0.002
Revasc.	12.6%	28.2%	<0.001

Cumulative KM Event Rate ± 1.5 SE; log-rank *P* value

Site-reported Data; ITT population

Summary & Conclusions

SYNTAX

- The final 5-year results of the SYNTAX trial demonstrate that surgery remains the gold standard for patients with complex multivessel disease
- In patients with less complex disease, PCI is an acceptable alternative treatment
- Treatment decisions for an individual patient should continue to be made in consultation between the patient and the Heart Team, while considering the risks and benefits of the respective treatment options

Thank you to the SYNTAX Steering Committee and Investigators

Cost-Effectiveness of Percutaneous Coronary Intervention with Drug-Eluting Stents vs. Bypass Surgery for Patients with 3-Vessel or Left Main Coronary Artery Disease: Final Results from the SYNTAX Trial

- **Background**—The SYNTAX trial demonstrated that in patients with 3-vessel or left-main CAD, CABG was associated with a lower rate of cardiovascular death, MI, stroke, or repeat revascularization compared with DES-PCI. The long-term cost-effectiveness of these strategies is unknown.
- **Methods and Results**—Between 2005 and 2007, 1800 patients with left-main or 3-vessel CAD were randomized to CABG (n=897) or DES-PCI (n=903). Costs were assessed from a US perspective, and health state utilities were evaluated with the EuroQOL questionnaire. A patient-level micro-simulation model based on the 5-year in-trial data was used to extrapolate costs, life expectancy, and quality-adjusted life expectancy over a lifetime horizon. Although initial procedural costs were $3415/patient lower with CABG, total hospitalization costs were $10,036/patient higher. Over the next 5 years, follow-up costs were higher with DES-PCI, owing to more frequent hospitalizations, revascularization procedures, and higher medication costs. Over a lifetime horizon, CABG remained more costly than DES-PCI but the incremental cost-effectiveness ratio was favorable ($16,537/ QALY gained) and remained <$20,000/QALY in most bootstrap replicates. Results were consistent across a wide range of assumptions regarding the long-term effect of CABG vs. DES-PCI on events and costs. **In patients with left-main disease or a SYNTAX Score ≤22, however, DES-PCI was economically dominant compared with CABG** although these findings were less certain.
- **Conclusions**—For most patients with 3-vessel or left-main CAD, CABG is a clinically and economically attractive revascularization strategy compared with DES-PCI. **However, among patients with less complex disease, DES-PCI may be preferred on both clinical and economic grounds**.

Circulation 2014

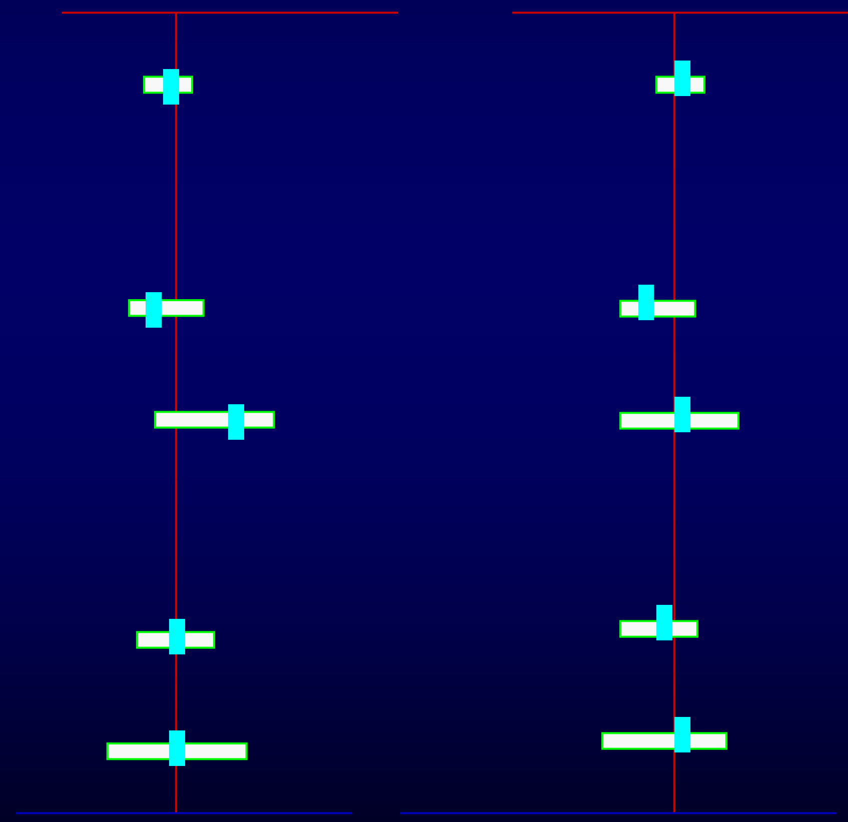
What About the Diabetics?

BARI Registry
PCI vs. CABG Relative Risk for Mortality

	Seven Year Survival		Relative Risk	
	CABG %	PTCA %	Unadj (p)	Adj (p)
OVERALL Registry	**85.8**	**86.1**	**.66**	**.86**
Eligibility Criteria				
UA/Non Q-MI	**83.2**	**86.4**	**.11**	**.29**
Stable Angina	**91.9**	**85.9**	**.079**	**.003**
Diabetes Status				
No Diabetes	**88.5**	**88.3**	**.88**	**.45**
Treated Diabetes	74.0	74.0	.96	.80

Unadjusted 99% CI for the Risk

Adjusted 99%

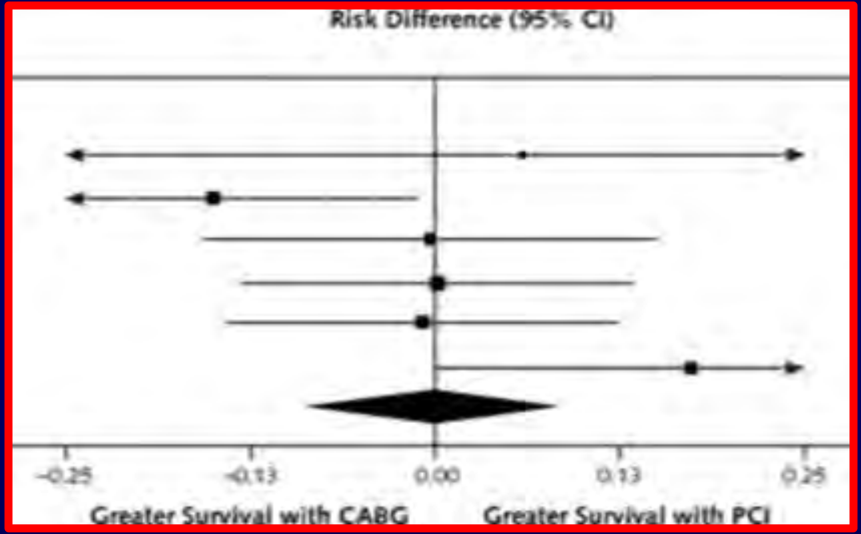


Feit F et al. Circulation 2000;101:2795

CABG vs PCI Diabetic Meta-analysis
5 Year Survival

Study, Year	Surviving Patients/All Patients PCI	CABG
AWESOME, 2002 (33)	8/11	8/12
BARI, 1997 (37), 1996 (64)	45/69	75/93
EAST, 2000 (83)	26/29	27/30
ERACI II, 2005 (86)	35/39	35/39
MASS II, 2006 (103)	47/56	50/59
RITA, 1998 (110)	27/29	25/33
Overall	188/233	220/266

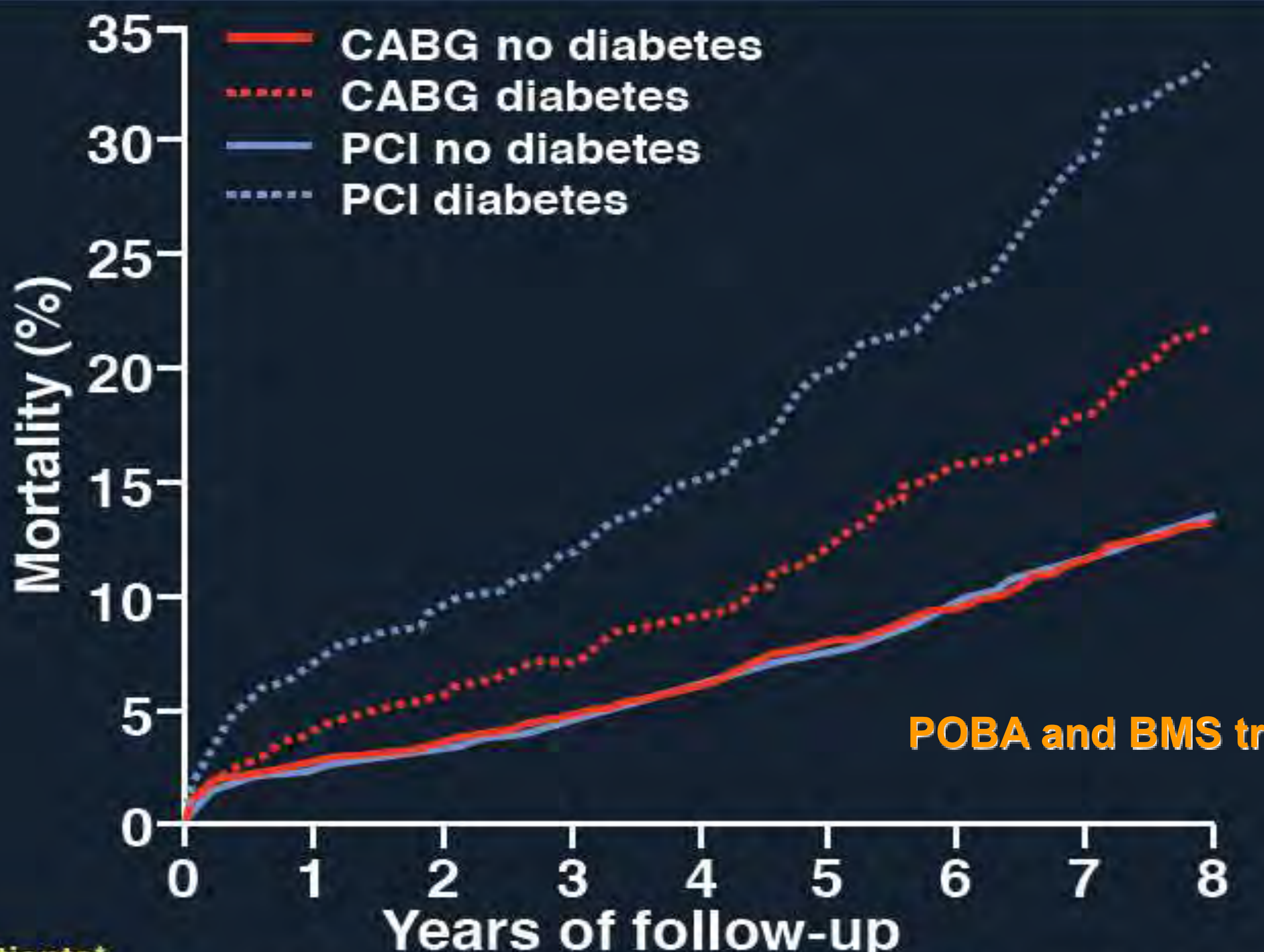
Risk Difference (95% CI)



Greater Survival with CABG **Greater Survival with PCI**

Bravata, D. M. et. al. Ann Intern Med 2007;147:703-716

CABG vs PCI :Death and Diabetic Status



Number of patients*									
CABG no diabetes	3263	3169	3089	2877	2677	2267	1592	1380	1274
CABG diabetes	615	587	575	532	498	421	257	225	200
PCI no diabetes	3298	3217	3148	2918	2725	2281	1608	1393	1288
PCI diabetes	618	574	555	508	475	373	218	179	160

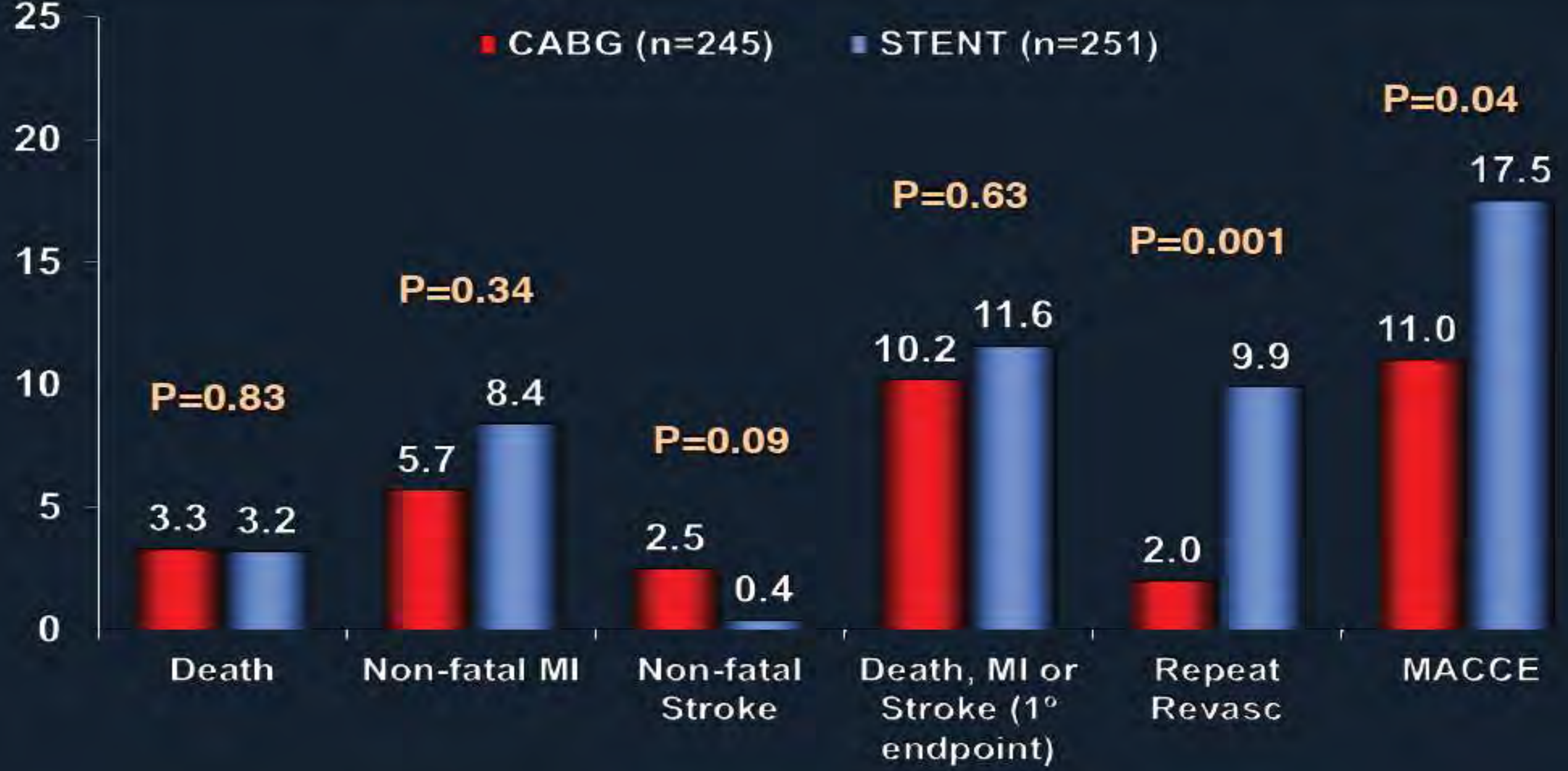
Hlatky et al, *The Lancet* 2009;373:1190-1197

Cardiovascular Research Foundation
A Passion for Innovation

Columbia University Medical Center
NewYork-Presbyterian

CARDia: 1-Year MACCE

61% 3VD (LM excluded) 31% IDDM



TRIAL SCREENING & ENROLLMENT

32,966 Patients were screened for eligibility

3,309 were eligible (10%)

1,409 did not consent

1,900 consented (57%)

953 Randomized to PCI/DES*

5 underwent CABG
3 withdrew prior to procedure
3 died prior to procedure
3 underwent neither PCI/DES or CABG

16 withdrew post-procedure
43 were lost to follow-up

947 Randomized to CABG

18 underwent PCI/DES
26 withdrew prior to procedure
3 died prior to procedure
7 underwent neither PCI/DES or CABG

36 withdrew post-procedure
51 were lost to follow-up

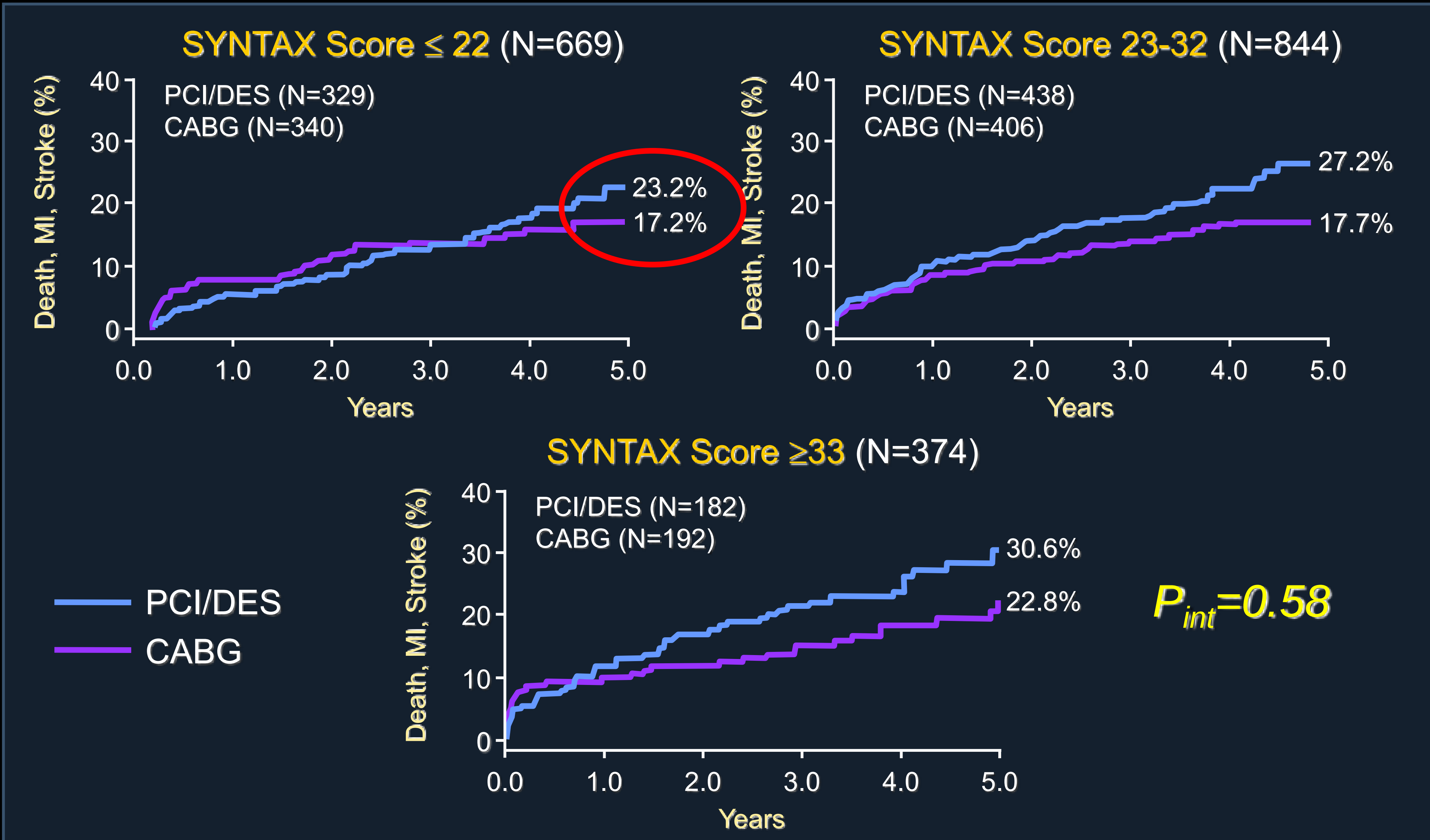
*953 and 947 included ITT analysis using all available follow-up time post-randomization

FREEDOM: 1900 pts with diabetes +MVD randomized to SES/PES vs. CABG

Characteristic	SES/PES (N=953)	CABG (N=947)	P-value
Age (years)	63.2 ± 8.9	63.1 ± 9.2	0.78
Male sex	73.2%	69.5%	0.08
Use of insulin	33.8%	30.9%	0.19
Duration of diabetes – yrs	10.1 ± 8.9	10.31 ± 9.0	0.49
Hemoglobin A1c – %	7.8 ± 1.7	7.8 ± 1.7	0.86
Unstable angina	31.9%	29.5%	0.25
3VD	82.3%	84.5%	0.22
No. of lesions	5.7 ± 2.2	5.7 ± 2.2	0.33
SYNTAX score	26.2 ± 8.4	26.1 ± 8.8	0.77
EuroSCORE	2.7 ± 2.4	2.8 ± 2.5	0.52

Farkouh ME et al. NEJM 2012

Death, Stroke, MI by Syntax Score



Farkouh ME et al. NEJM 2012

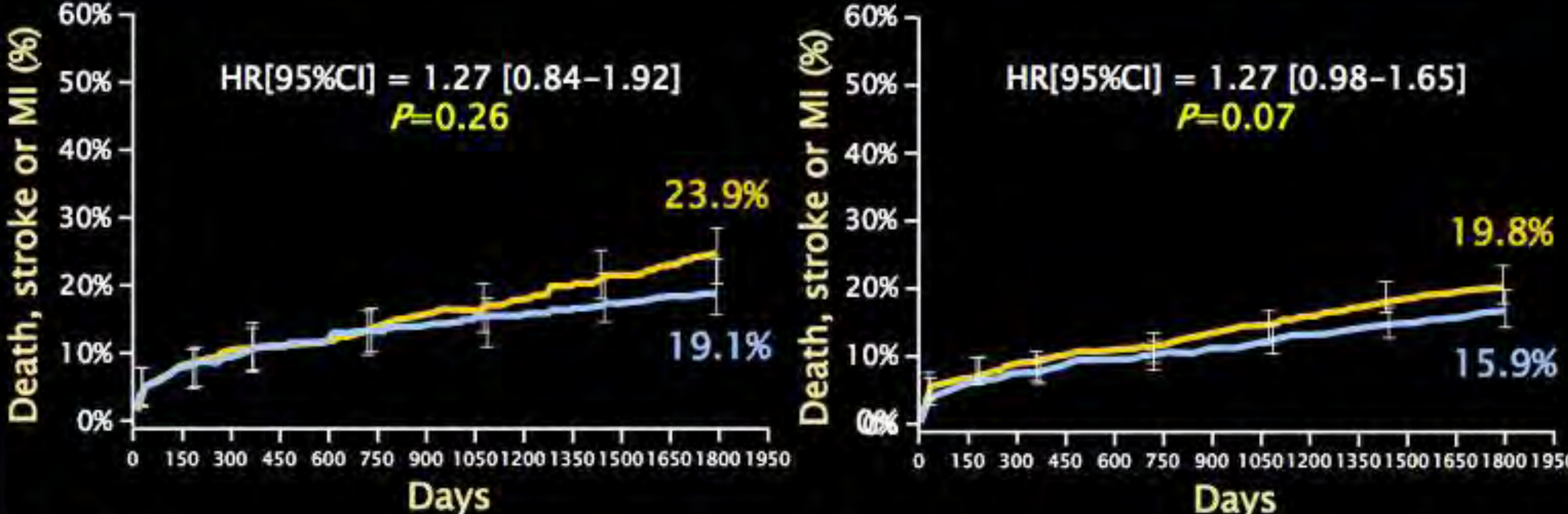
Death, CVA, MI to 5 Years: *Impact of Diabetes*

SYNTAX

— CABG — TAXUS

$P_{int} = 0.76$

Diabetes | No diabetes



No. at risk:

Days	0	180	365	730	1095	1460	1825
PCI	231	217	206	205	197	188	178
CABG	221	198	187	183	175	169	160

No. at risk:

Days	0	180	365	730	1095	1460	1825
PCI	672	634	624	620	597	572	539
CABG	676	626	602	598	578	555	529

Kappetein AP et al. EJCTS 2012

Effectiveness of Percutaneous Coronary Intervention With Drug-Eluting Stents Compared With Bypass Surgery in Diabetics With Multivessel Coronary Disease: Comprehensive Systematic Review and Meta-analysis of Randomized Clinical Data

Sensitivity Analysis

Variable		PCI	CABG	RR	p
MACE based on SYNTAX Score	<22 (n = 805)	22.2%	17.5%	1.27 (0.96 to 1.68)	0.09
	23 to 32 (n = 992)	26.1%	18.3%	1.32 (0.86 to 2.02)	0.21
	> 33 (n = 541)	**24.7%**	**14.4%**	**1.73 (1.21 to 2.46)**	**0.003**

J Am Heart Assoc 2013; 2(4): e000354.

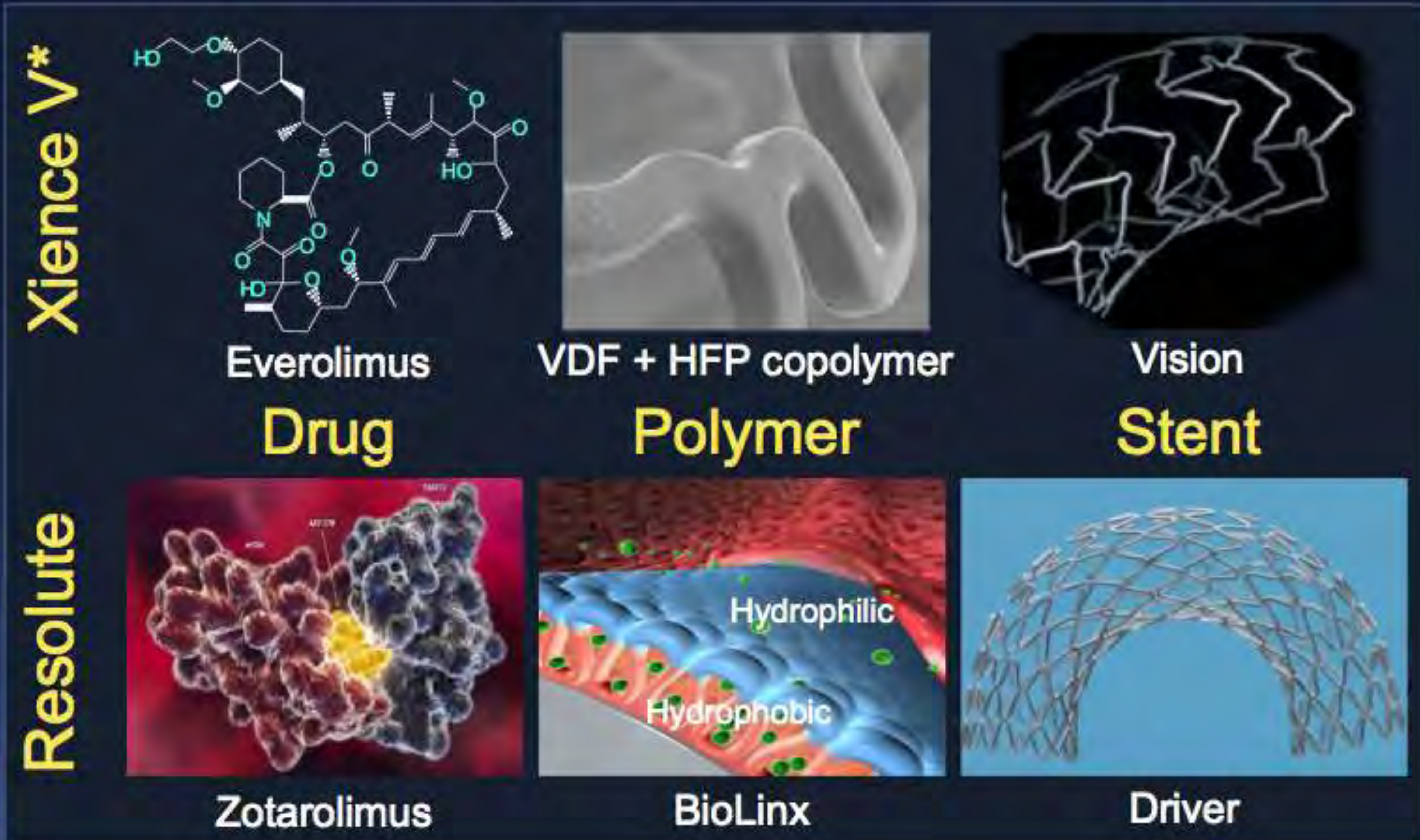
2014 ESC/EACTS Guidelines on myocardial revascularization
The Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)

Recommendation for the type of revascularization in patients with SCAD with suitable coronary anatomy for both procedures and low predicted surgical mortality

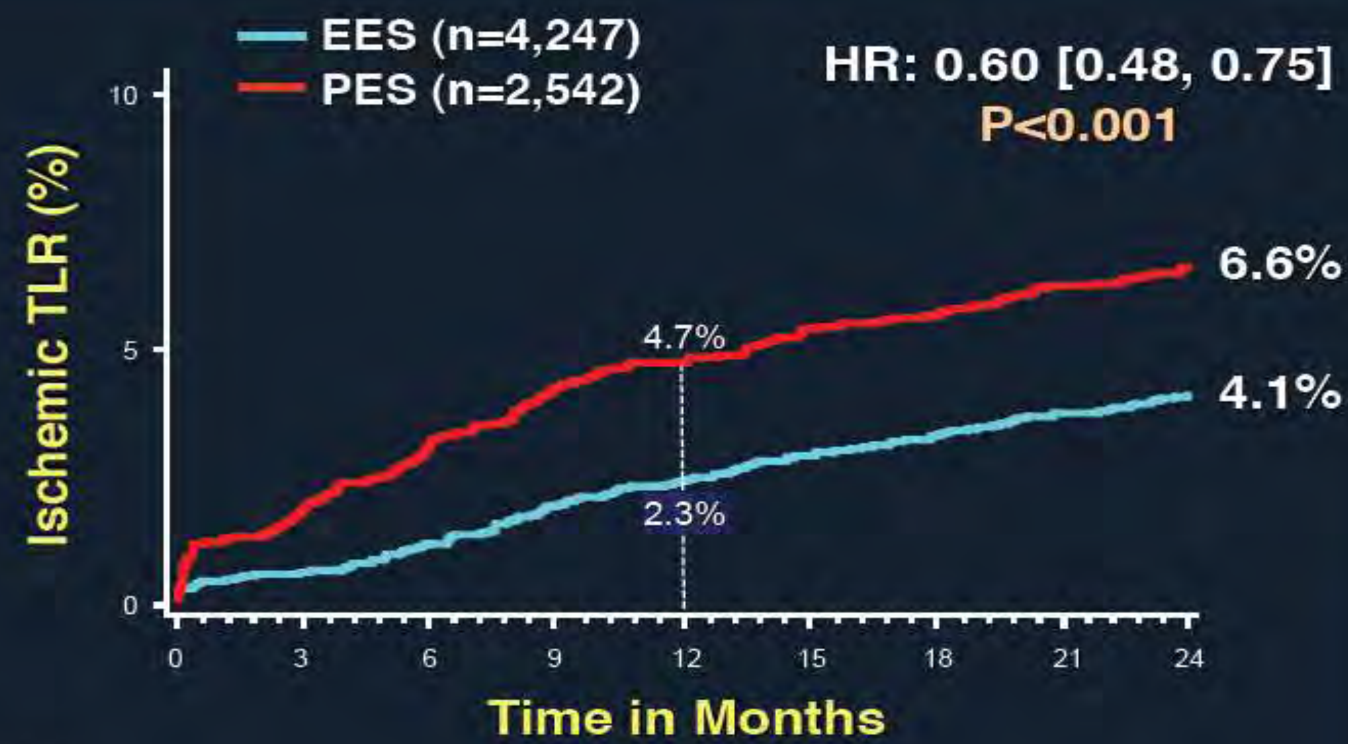
Recommendations according to extent of CAD	**CABG**		**PCI**	
	Class	**Level**	**Class**	**Level**
One or two-vessel disease without proximal LAD stenosis.	**IIb**	**C**	**I**	**C**
One-vessel disease with proximal LAD stenosis.	**I**	**A**	**I**	**A**
Two-vessel disease with proximal LAD stenosis.	**I**	**B**	**I**	**C**
Left main disease with a SYNTAX score 22.	**I**	**B**	**I**	**B**
Left main disease with a SYNTAX score 23–32.	**I**	**B**	**IIb**	**B**
Left main disease with a SYNTAX score >32.	**I**	**B**	**III**	**B**
Three-vessel disease with a SYNTAX score 22.	**I**	**A**	**I**	**B**
Three-vessel disease with a SYNTAX score 23–32.	**I**	**A**	**III**	**B**
Three-vessel disease with a SYNTAX score >32.	**I**	**A**	**III**	**B**

Has Percutaneous Coronary Intervention Evolved After SYNTAX and FREEDOM?

Stents Eluídos com Drogas: 2ª Geração

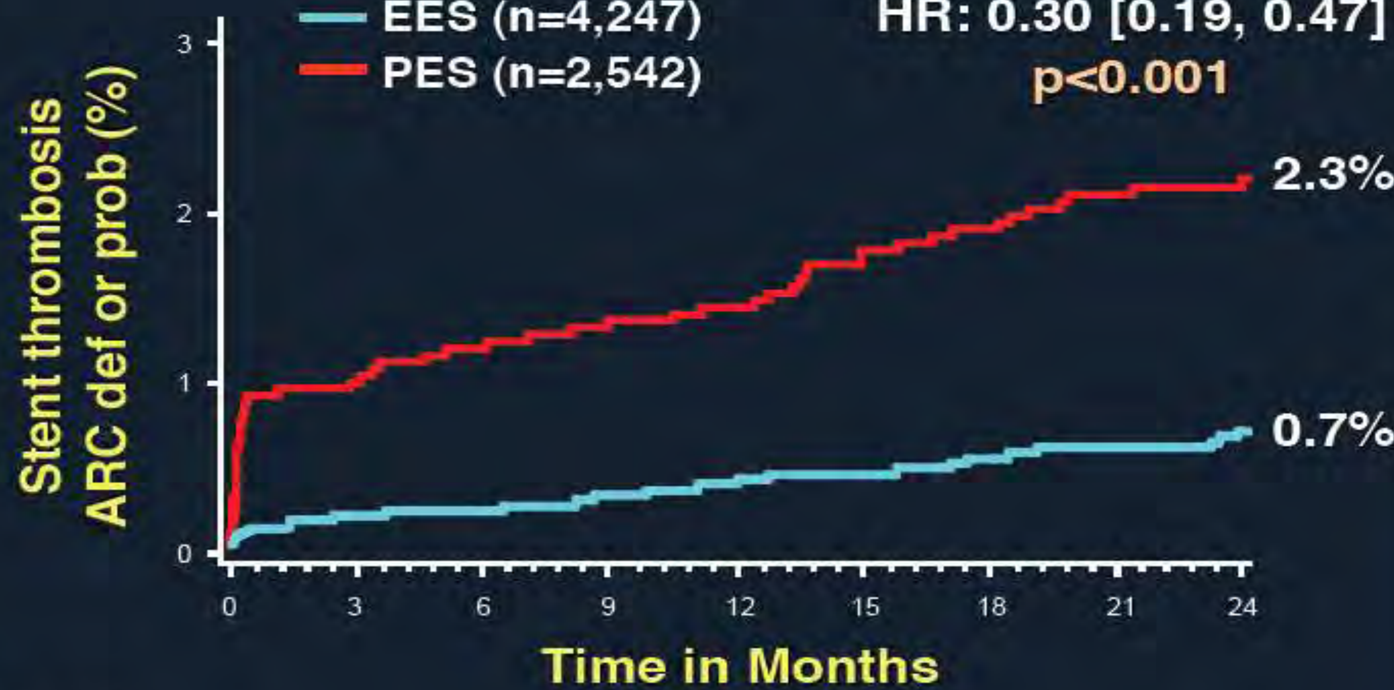


SPIRIT II, III, IV and COMPARE trials
Pooled database analysis (n=6,789)
Ischemic TLR



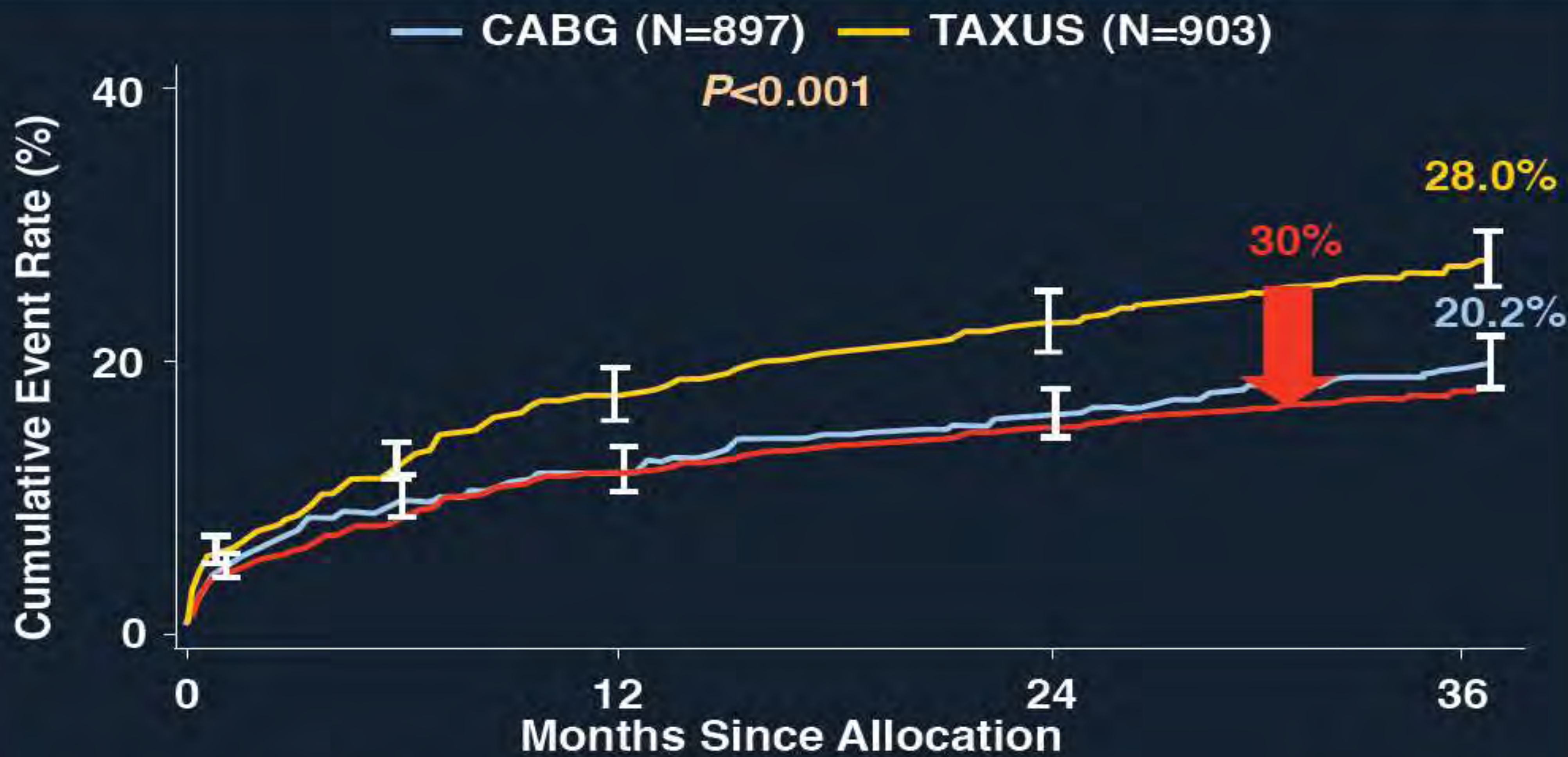
Number at risk					
XIENCE	4247	4143	4004	3891	3363
TAXUS	2542	2416	2328	2260	2018

SPIRIT II, III, IV and COMPARE trials
Pooled database analysis (n=6,789)
Stent thrombosis (ARC definite/probable)



Number at risk					
XIENCE	4247	4177	4082	3998	3479
TAXUS	2542	2463	2408	2350	2110

Potential SYNTAX MACCE with 2nd Gen DES

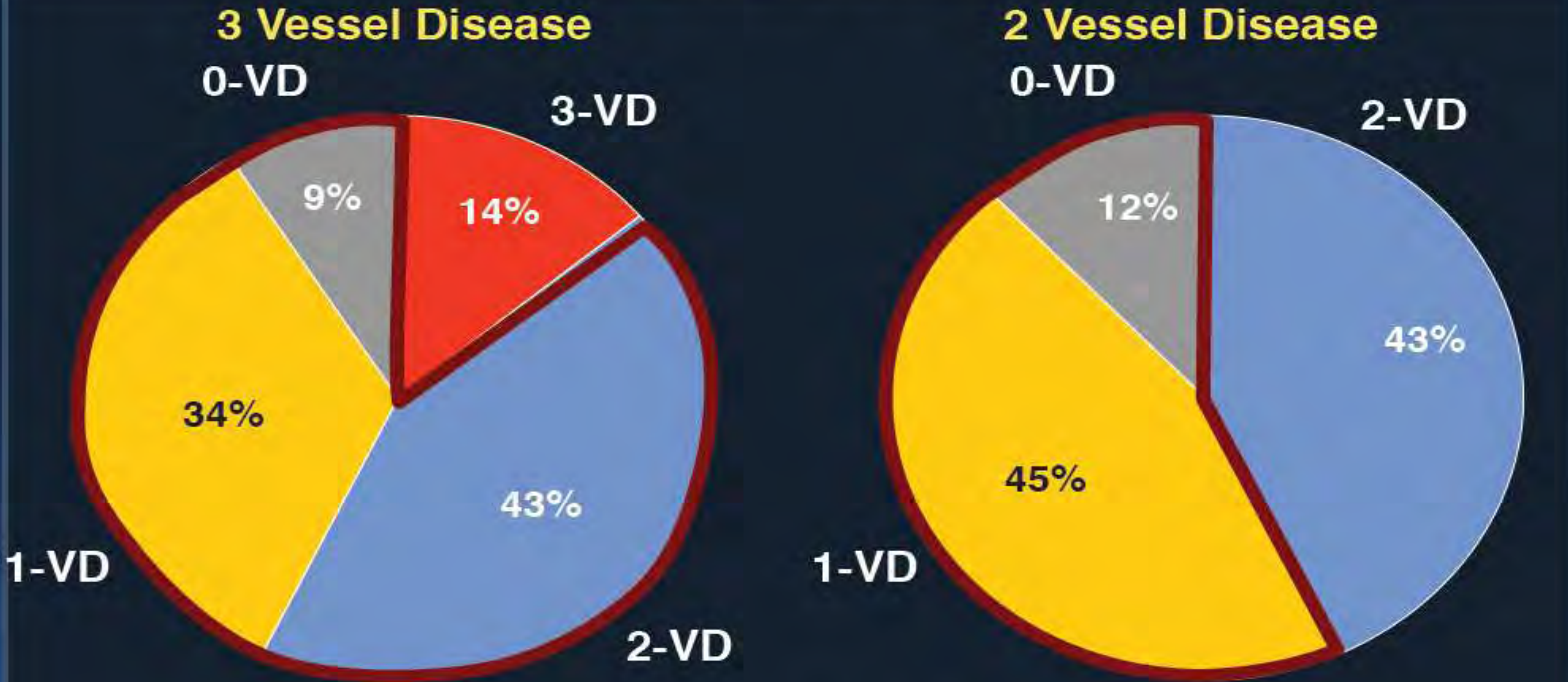


Cumulative KM Event Rate ± 1.5 SE; log-rank *P* value; * Binary rates
Event Rate ± 1.5 SE. ˙Fisher's Exact Test

ITT population

c/o J. Moses

FAME : "Downgrading" Multivessel Disease with FFR

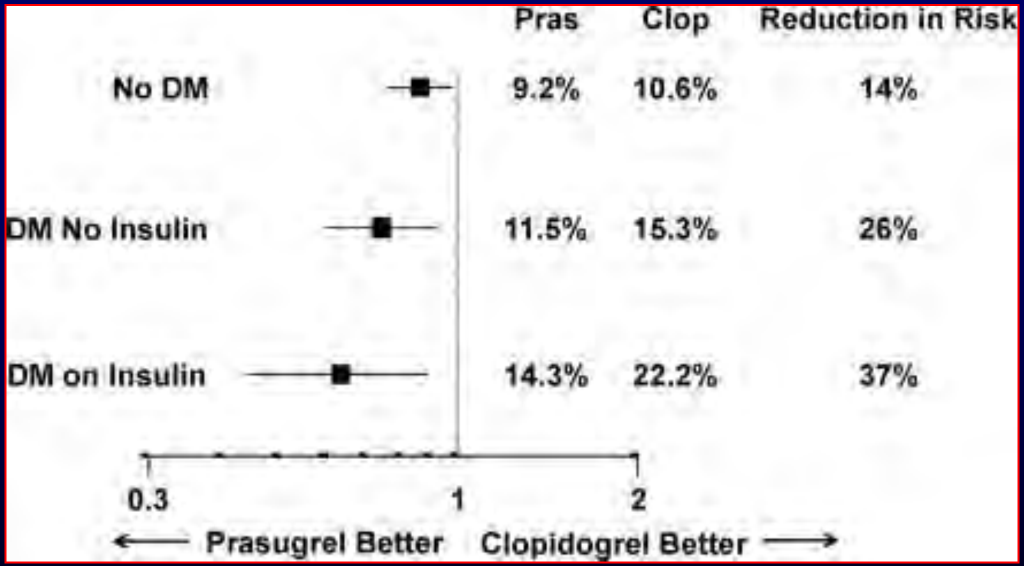


86% 3VD and 57% 2VD reclassified ≥1 vessel

Role of the New Antiplatelets Agents

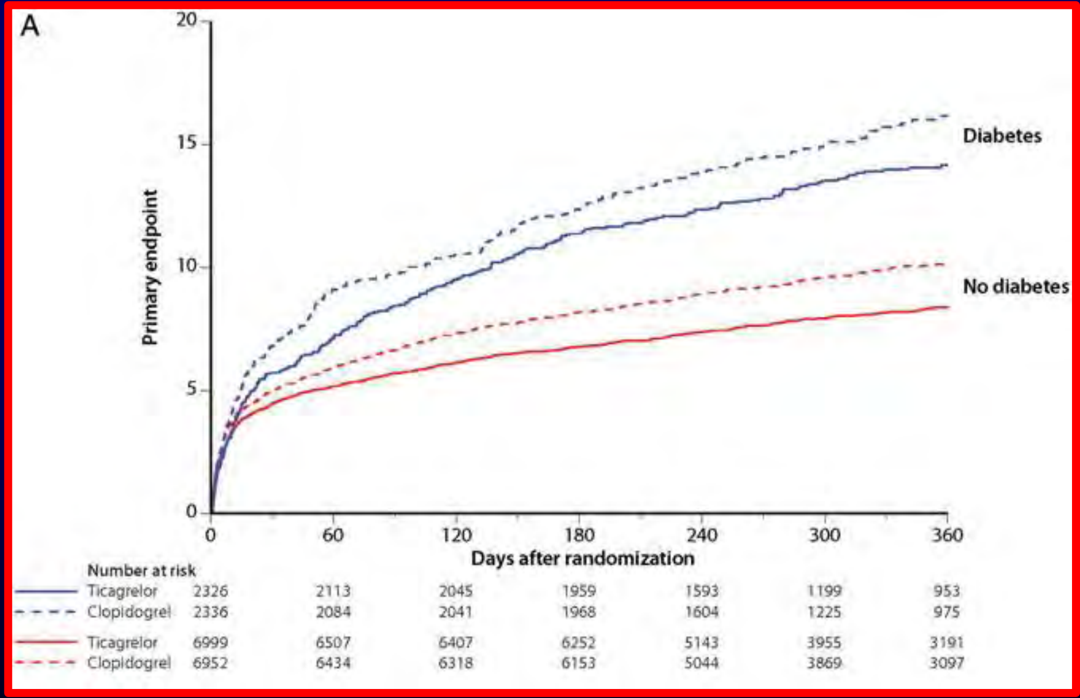
TRITON TIMI 38

Reduction in the primary end point (cardiovascular death/nonfatal MI, nonfatal stroke) by diabetes status and treatment group



PLATO Trial

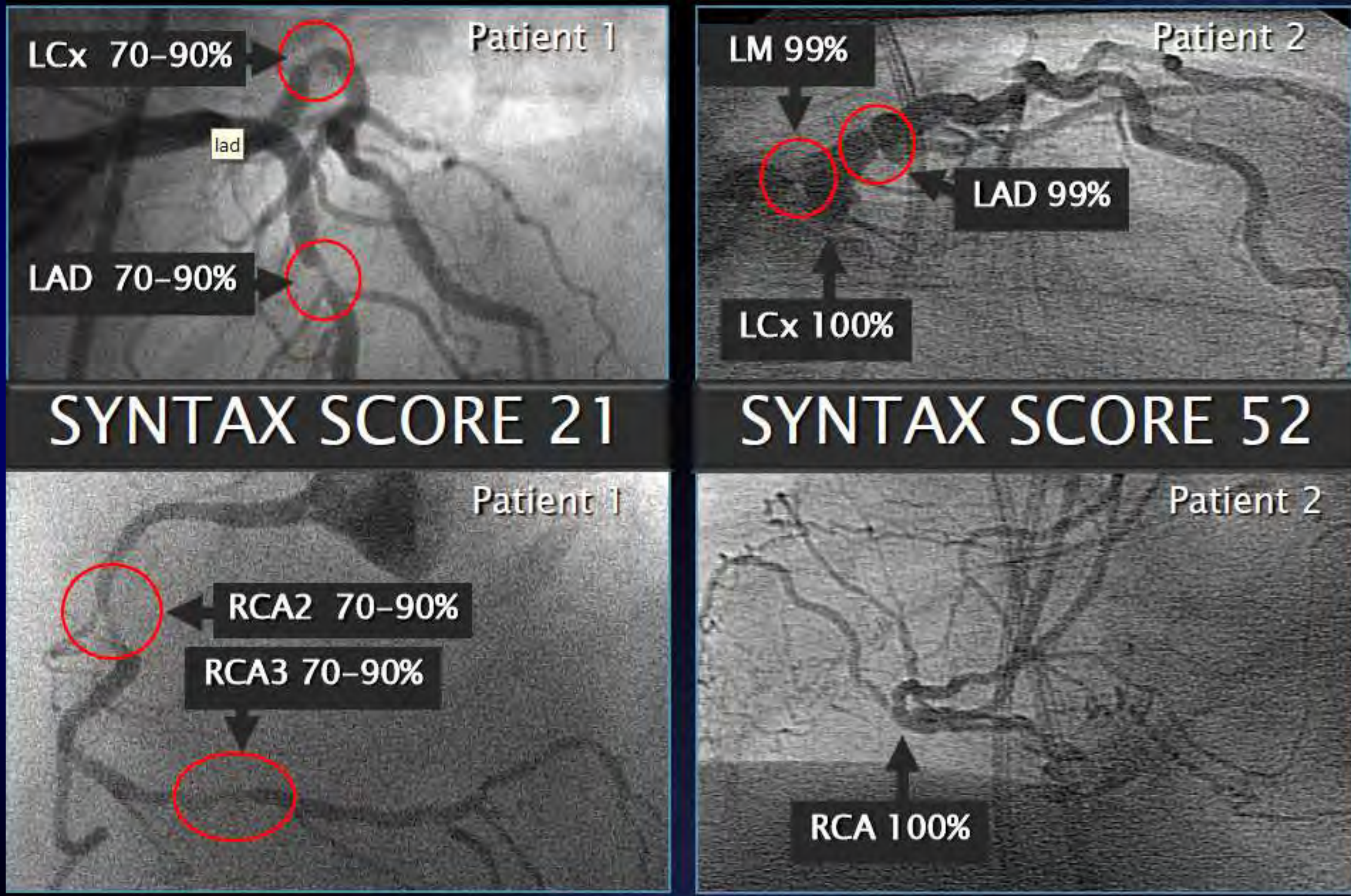
Ticagrelor vs. clopidogrel in patients with acute coronary syndromes and diabetes



Wiviott, S. D. et al. Circulation 2008;118:1626-1636

James S et al. Eur Heart J 2010;31:3006-3016

Existe "Doença de 3 Vasos" e "Doença de 3 Vasos" ....



Percutaneous Treatment of Multivessel Disease

- Choice of revascularization strategy must be individualized (Heart Team), taking into consideration current results of PCI and CABG;
- Aim for functional instead of anatomical complete revascularization;
- Use of new generation DES and best adjunctive pharmacology (statins, prasugrel/ticagrelor);
- Patients with low (<22) and possibly intermediate (<32) SYNTAX scores;
- Patients with high surgical risk/ineligible for CABG (EuroScore ≥ 6 / STS $\geq$ 5%).

Despite his distinguished career as a surgeon, Kirklin recognized the limitations of his specialty. He is cited in numerous reference sources for the following quotes:

"Surgery is always second best. If you can do something else, it's better."

Dr. John Kirklin, developer of the heart-lung machine, dead at the age of 86.

TheHeart.org, 27/04/2004

FREEDOM Trial (NHLBI)

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

N=1900 at 100 centers from NA, SA, EU, Rand. 1:1

MV DES stenting (Cypher or TAXUS) and abciximab

CABG with or without cardiopulmonary bypass

PRIMARY Endpoint: 3-year death, MI, stroke
SECONDARY Endpoints: 12-month MACCE, 3-year Quality of Life
PI: Valentin Fuster

2011 ACCF/AHA/SCAI Guideline for Percutaneous Coronary Intervention : A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines and the SCA&I

Revascularization to Improve Survival: Recommendations
Left Main CAD Revascularization

Class IIa

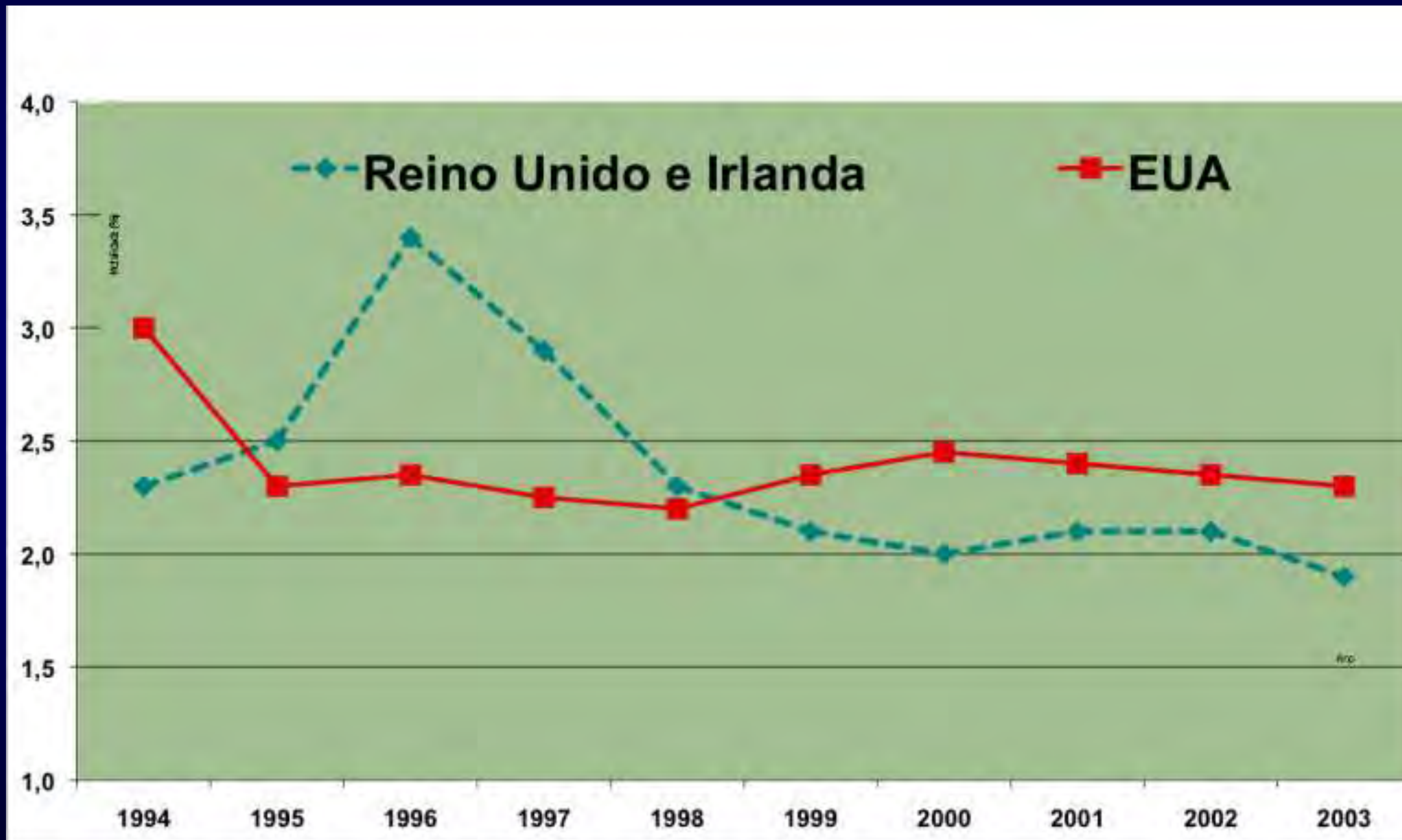
1. PCI to improve survival is reasonable as an alternative to CABG in selected stable patients with significant (>50% diameter stenosis) unprotected left main CAD with: 1) anatomic conditions associated with a low risk of PCI procedural complications and a high likelihood of good long-term outcome (eg, a low SYNTAX score [<22], ostial or trunk left main CAD); and 2) clinical characteristics that predict a significantly increased risk of adverse surgical out- comes (eg, STS-predicted risk of operative mortality >5%). (Level of Evidence: B)
2. PCI to improve survival is reasonable in patients with UA/NSTEMI when an unprotected left main coronary artery is the culprit lesion and the patient is not a candidate for CABG. (Level of Evidence: B)

Revascularization to Improve Symptoms
Non-Left Main CAD Revascularization

Class I

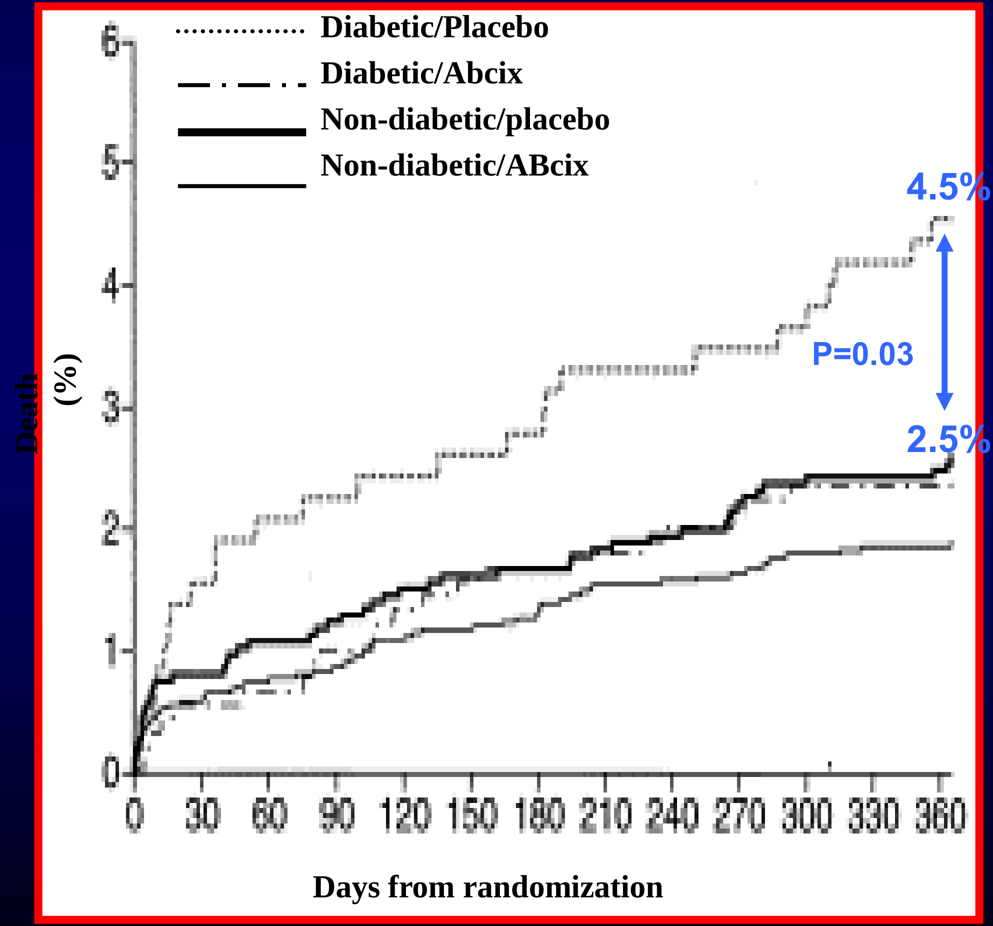
1. CABG or PCI to improve symptoms is beneficial in patients with 1 or more significant (>70% diameter) coronary artery stenoses amenable to revascularization and unacceptable angina despite GDMT. (Level of Evidence: A)

Mortalidade em CRM isolada, no Reino Unido e Irlanda vs EUA



BMJ 329:644, 2004

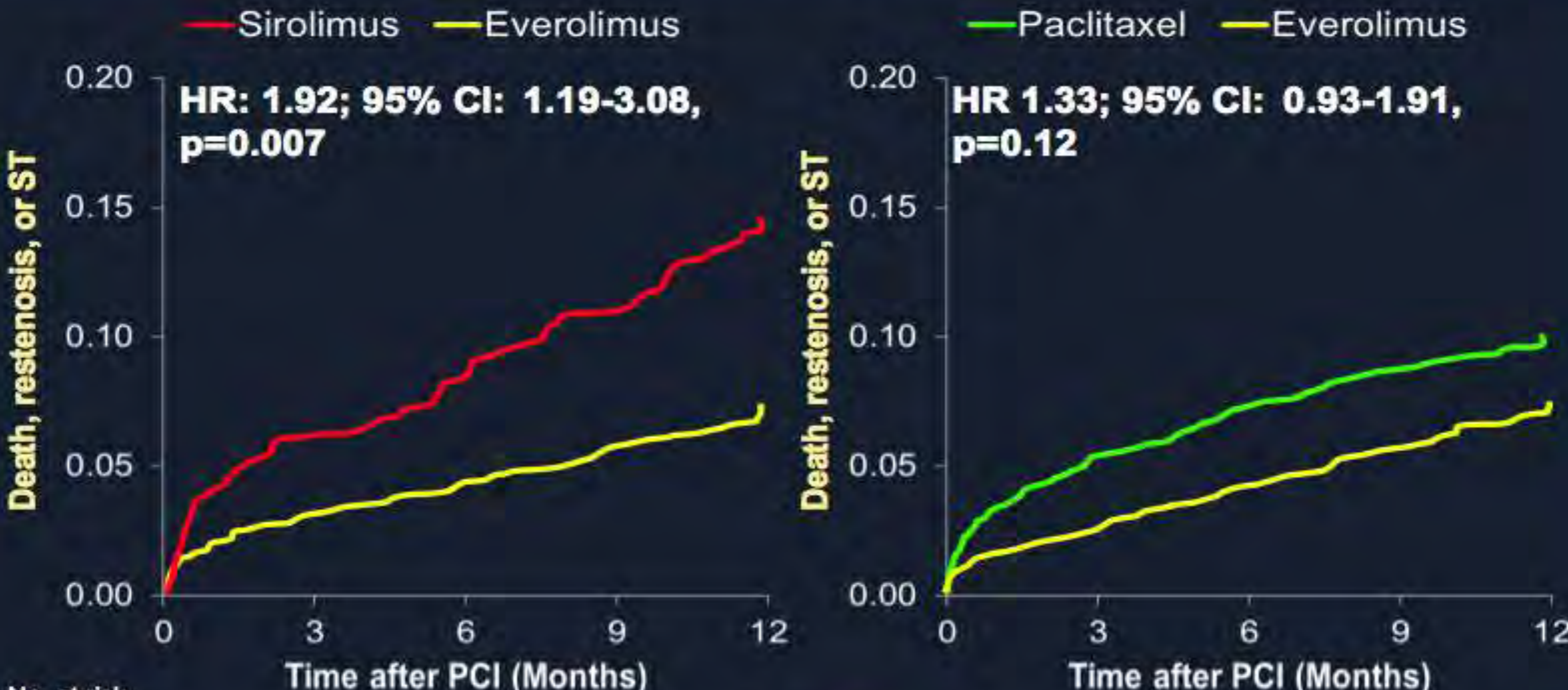
Redução da Mortalidade em Diabéticos Submetidos a ICP com Abciximab



- Pooled analysis of 1-year mortality from EPIC, EPILOG, and EPISTENT databases
- Among patients with diabetes (n=1420), abciximab reduced 1-year mortality by 45% (20 lives saved per 1000 pts; p=0.03)
- Mortality benefits particularly striking among diabetic patients with:
  - *IDDM (4.2% vs. 8.1%, p=0.07)*
  - *Multivessel PCI (0.9% vs. 7.7%; p=0.02)*

Bhatt, D. L. et al. J Am Coll Cardiol 2000;35:922-928

EES in Patients with Diabetes: SCAAR



No. at risk

SES	717	675	633	PES	1386	1290	1230
EES	1915	1552	984	EES	1915	1552	984

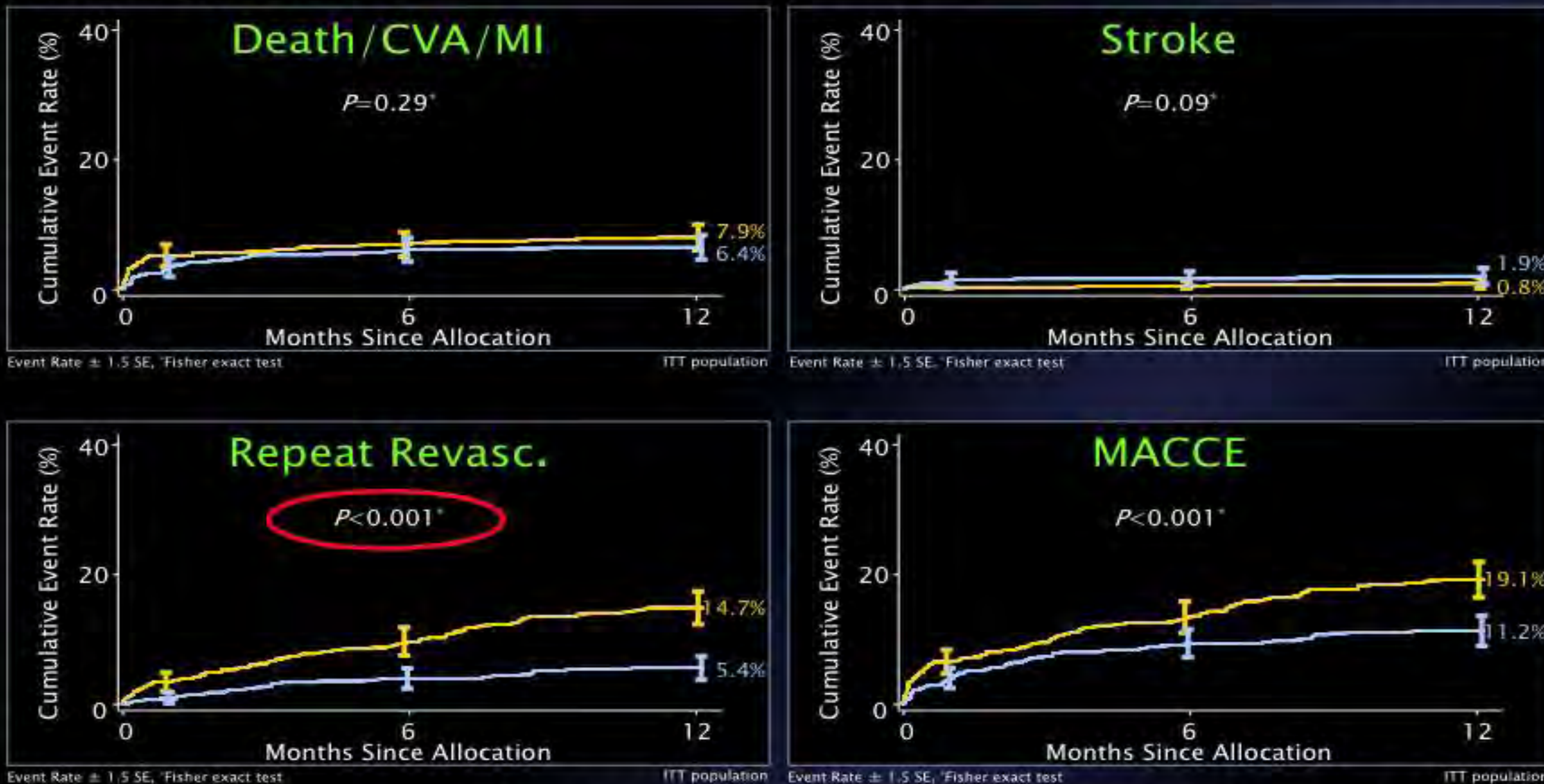
Kedhi et al. JACC Card Int 2012;5:1141-9

ACCF/SCAI/STS/AATS/AHA/ASNC/HFSA/SCCT 2012 Appropriate Use Criteria for Coronary Revascularization Focused Update

Method of Revascularization of Multivessel Coronary Artery Disease	CABG		PCI
Two-vessel CAD with proximal LAD stenosis	A		A
Three-vessel CAD with low CAD burden (i.e., 3 focal stenoses, low SYNTAX score)	A		A
Three-vessel CAD with intermediate to high CAD burden (i.e., multiple diffuse lesions, presence of CTO, or high SYNTAX score)	A		U
Isolated left main stenosis	A		U
Left main stenosis and additional CAD with low CAD burden (i.e., 1- to 2-vessel additional involvement, low SYNTAX score)	A		U
Left main stenosis and additional CAD with intermediate to high CAD burden (i.e., 3-vessel involvement, presence of CTO, or high SYNTAX score)	A		U

Summary of 1-Year Results
3VD Subset

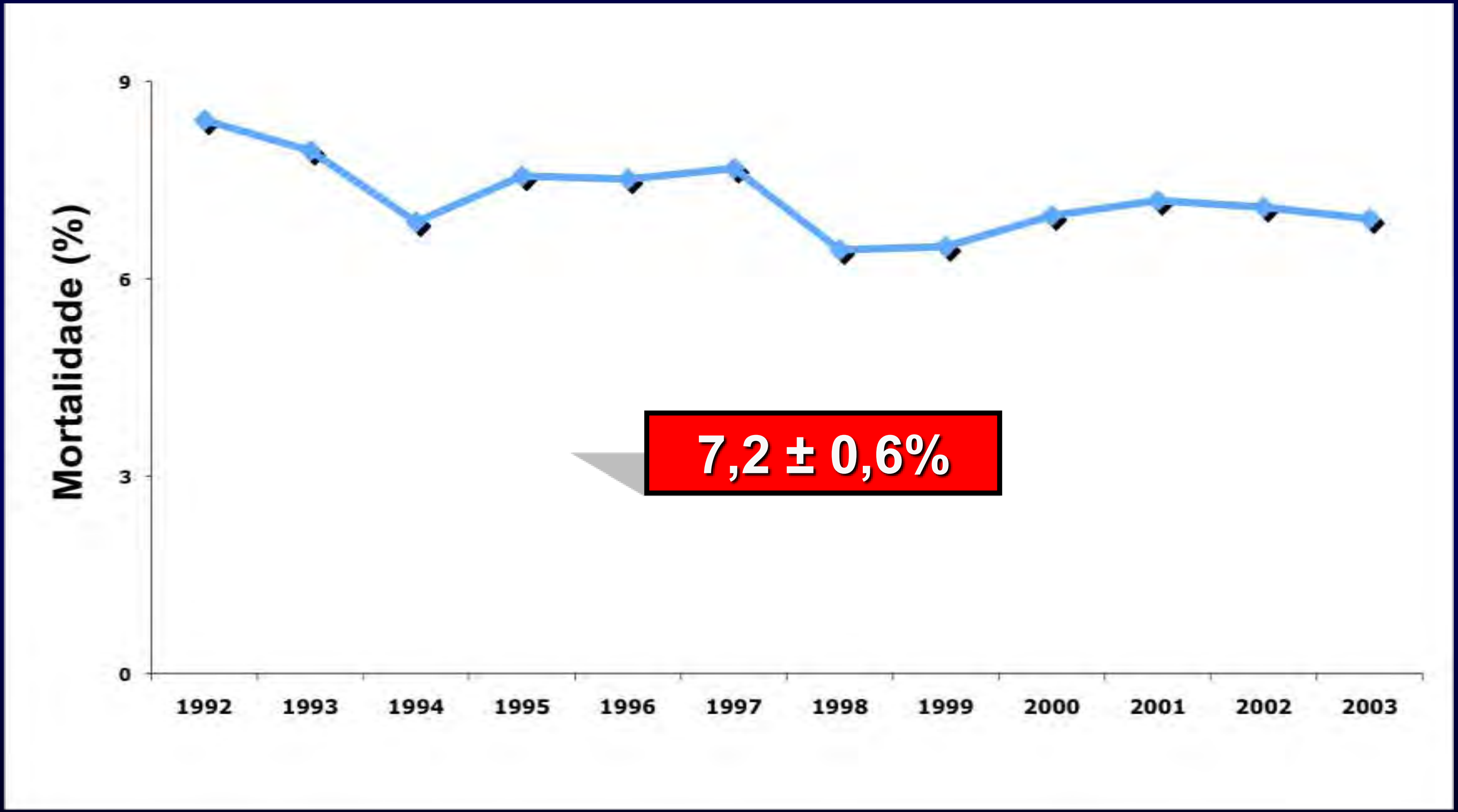
SYNTAX



- Death/Stroke/MI rates were similar between CABG and PCI
- Stroke was not significantly increased in CABG
- Repeat revascularization and MACCE increased in PCI vs CABG

CABG (N=549) PCI (N=546)

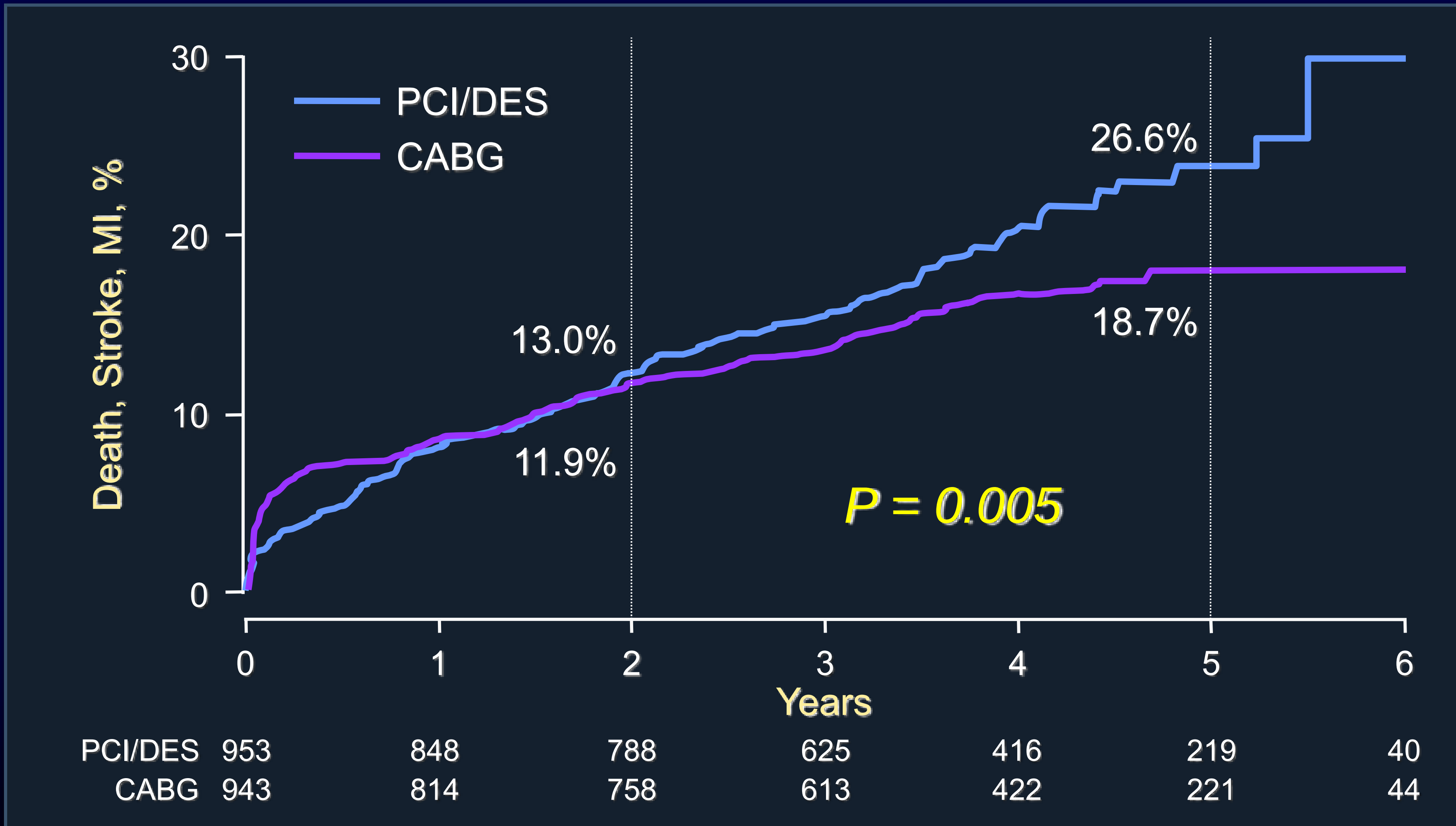
Mortalidade de RM Com CEC DATASUS (1992-2003)



Piegas LS e cols. Arq Bras Cardiol

FREEDOM: 1900 pts with diabetes +MVD randomized to SES/PES vs. CABG

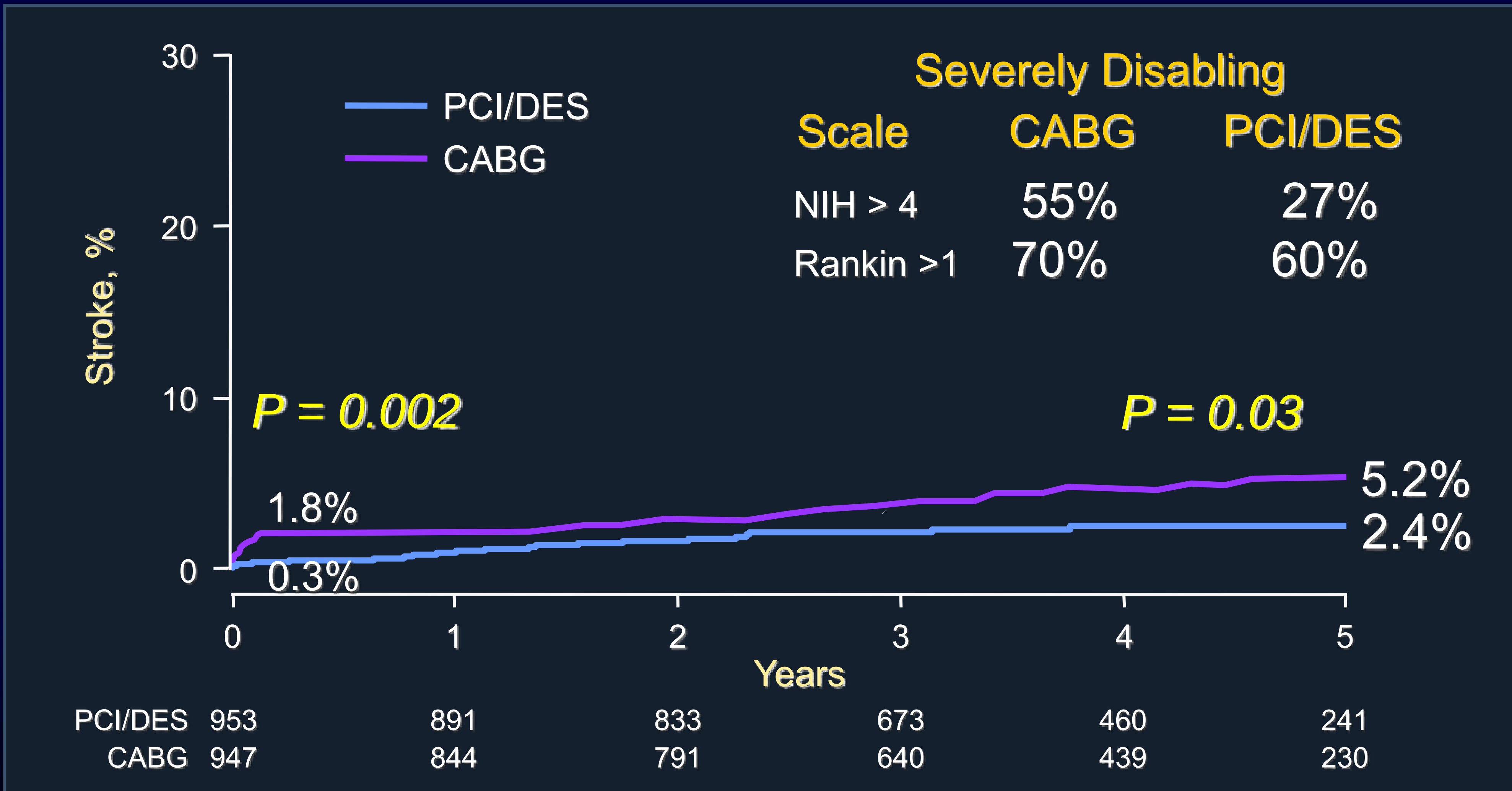
1° Endpoint: Death, Stroke, or MI



Farkouh ME et al. NEJM 2012

FREEDOM: 1900 pts with diabetes +MVD randomized to SES/PES vs. CABG

Stroke



Severely Disabling		
Scale	CABG	PCI/DES
NIH > 4	55%	27%
Rankin >1	70%	60%

Farkouh ME et al. NEJM 2012

Patient Disposition to 5 Years

3VD Subset Intent-to-Treat

SYNTAX

CABG n=549	RCT: *Enrolled* N=1095	PCI* n=546
CABG n=513	RCT: *1 Year Follow-up* CABG 93.4% PCI 98.2%	PCI* n=536
CABG n=505	RCT: *2 Year Follow-up* CABG 92.0% PCI 97.6%	PCI* n=533
CABG n=502	RCT: *3 Year Follow-up* CABG 91.4% PCI 98.2%	PCI* n=536
CABG n=495	RCT: *4 Year Follow-up* CABG 90.2% PCI 97.1%	PCI* n=530
CABG n=483	RCT: *5 Year Final Follow-up* CABG 88.0% PCI 96.2%	PCI* n=525

*TAXUS Express