Impact of RCT's and AUC on CABG vs PCI

Craig R. Smith, M.D

Division of Cardiothoracic Surgery
Chairman, Department of Surgery
College of Physicians & Surgeons of Columbia University
Columbia University Medical Center
New York Presbyterian Hospital
New York, New York

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Conflicts: I am a Surgeon

(although I was once accused of being an Interventionalist)

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- Benefits
- Risks
- Impact of patient factors
- Impact of new and evolving technology

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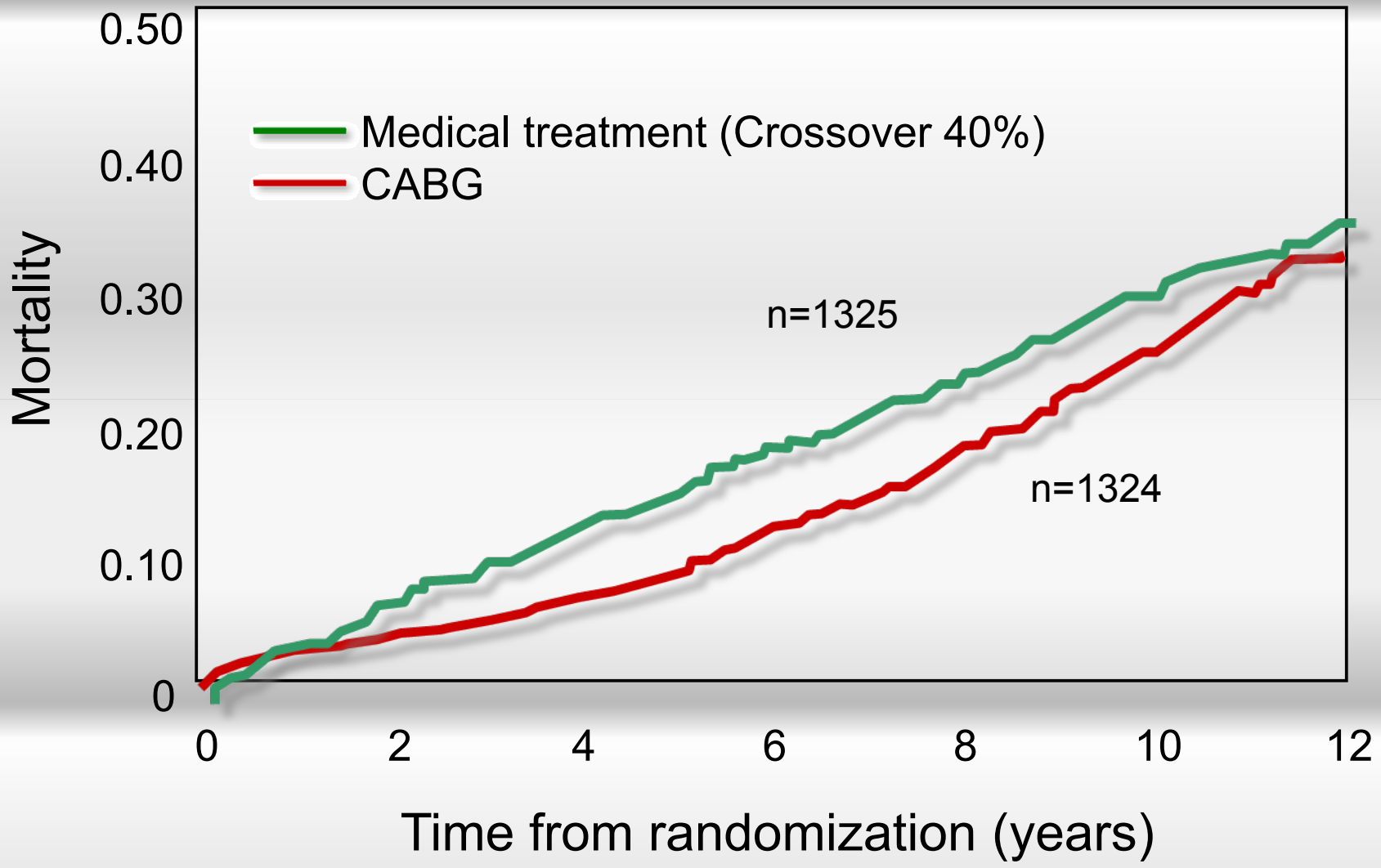
Appropriateness Studies

Meta-analysis of CABG vs. Medical Treatment
7 RCT's (CASS, European, VA, 4 smaller)



Yusef et al, Lancet 1994;344:563-70

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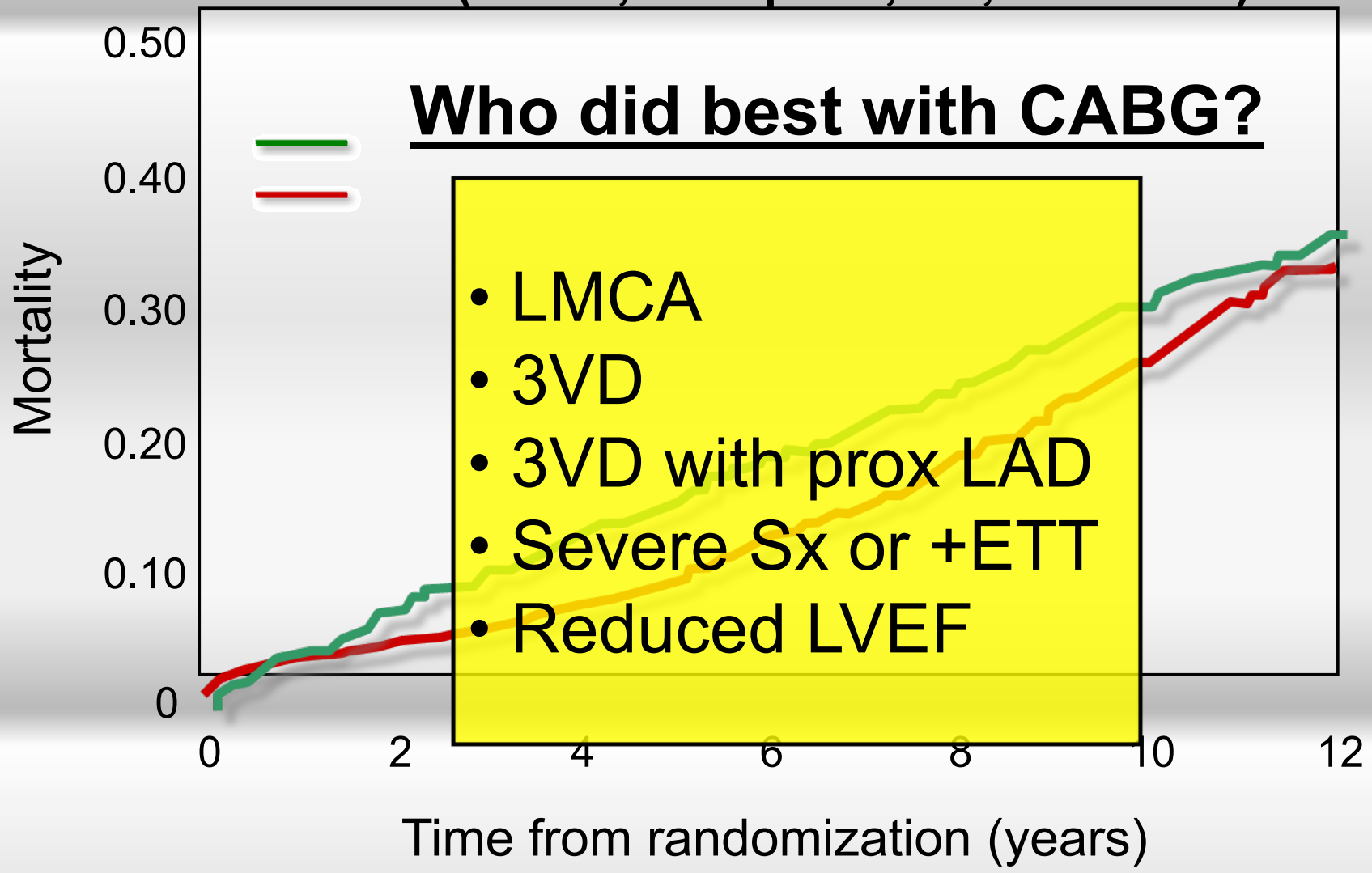

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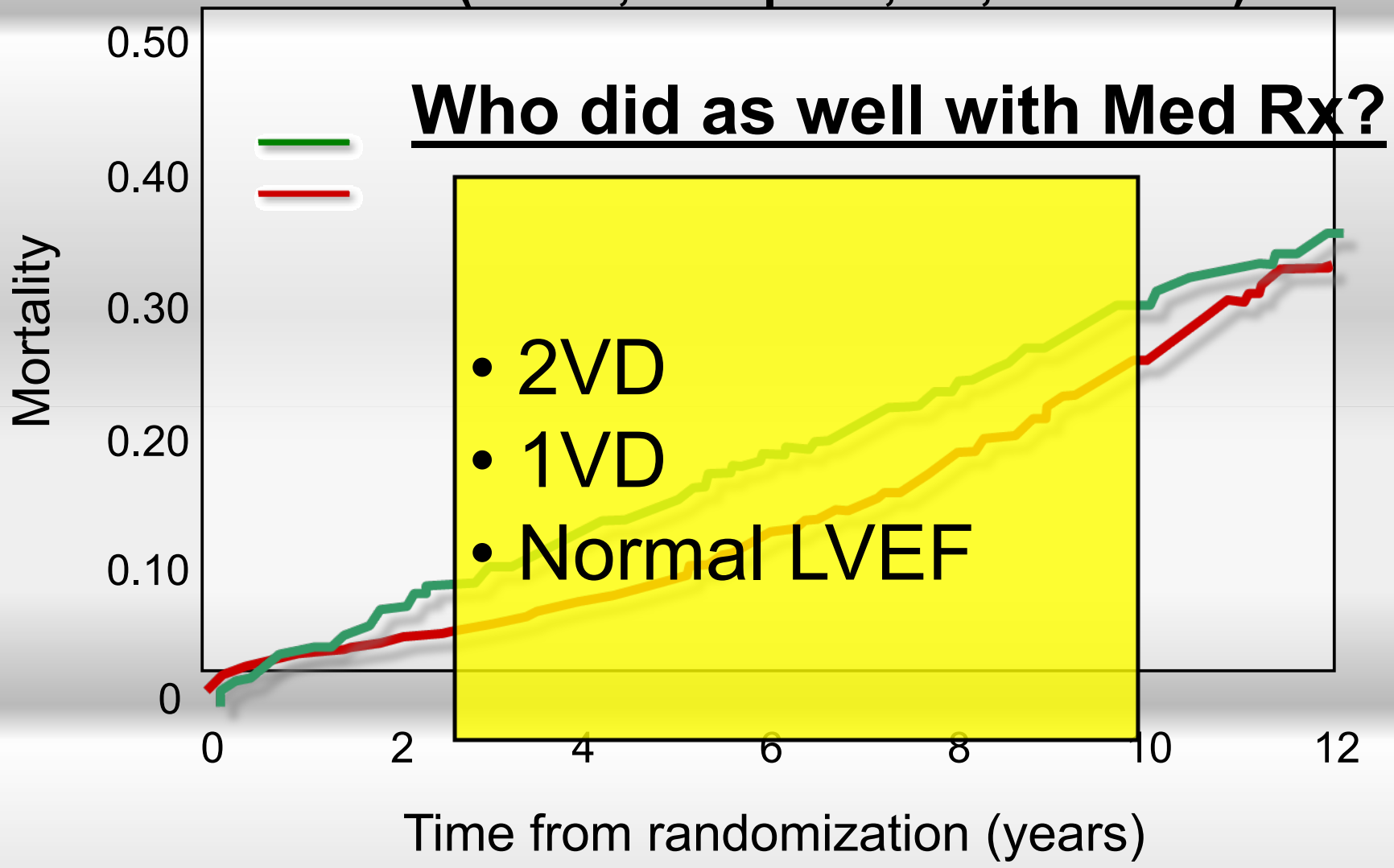
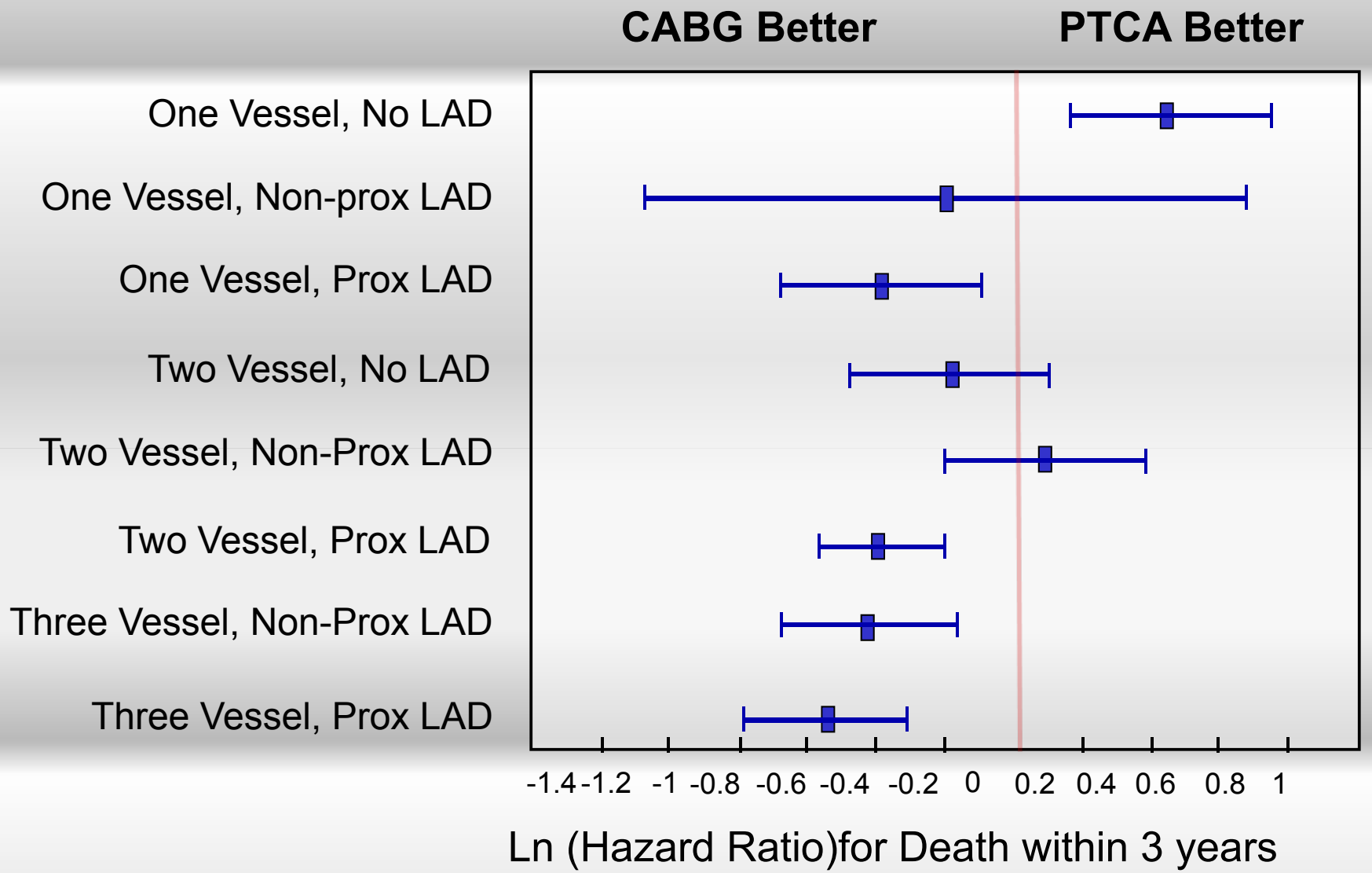


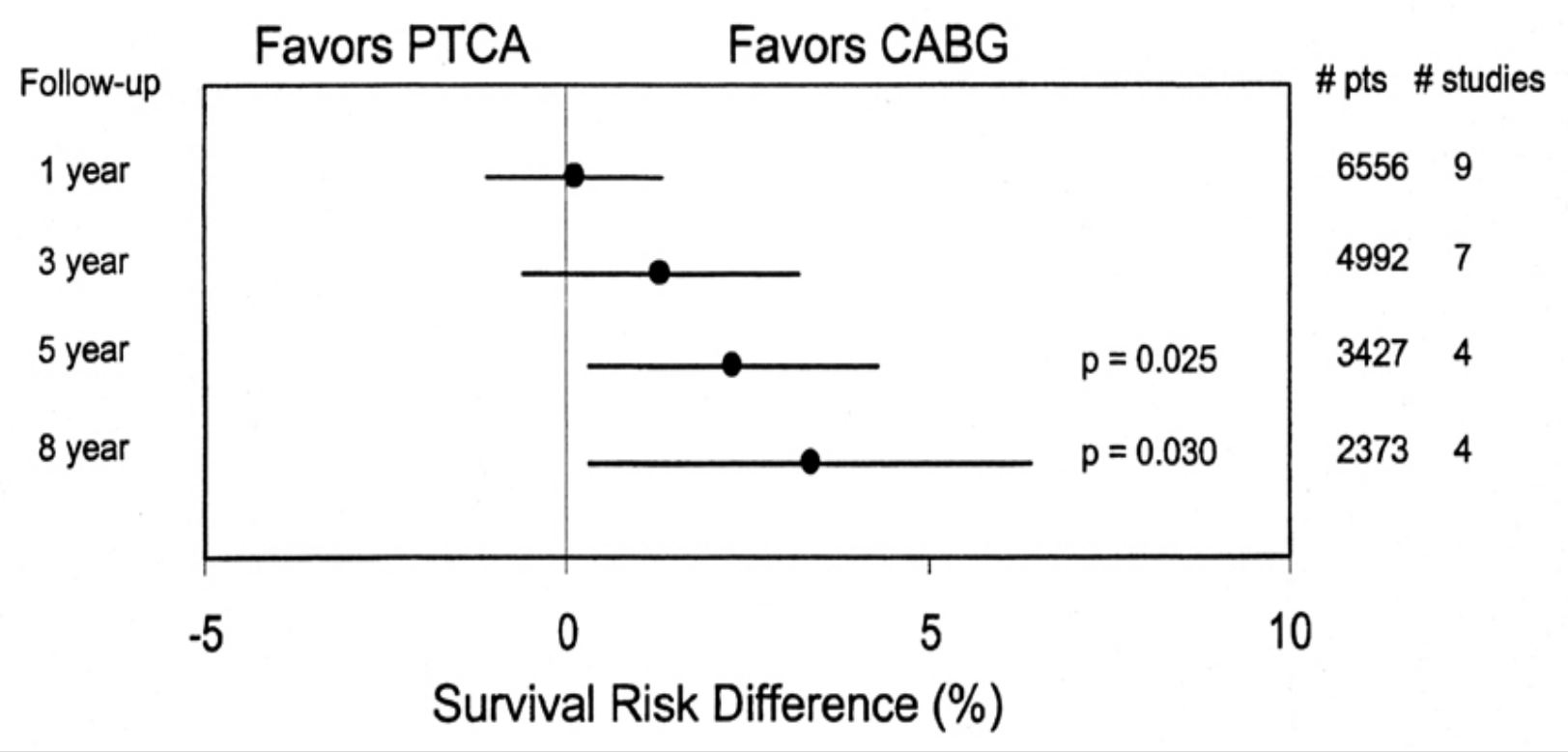
Yusef et al, Lancet 1994;344:563-70

Meta-analysis of RCT's comparing PCI to CABG



Hannan et al, J Am Coll Cardiol 1999;33:63-72

Meta-analysis of PTCA vs CABG: Multivessel Disease



13 randomized trials, 7,964 patients

2/3 2 VD
100% normal LVEF

Risk difference for all-cause mortality for years 1,3,5 and 8 post initial revascularization for multivessel coronary artery disease. The lines represent 95% confidence intervals. Event rates for the coronary bypass arm at 1,3,5 and 8 years were 3.49%, 5.3%, 8.99%, and 15.8%.

Hoffman et al, J *Am Coll Cardiol* 2003;41:1293-304

CABG vs Stent: New York State Registries

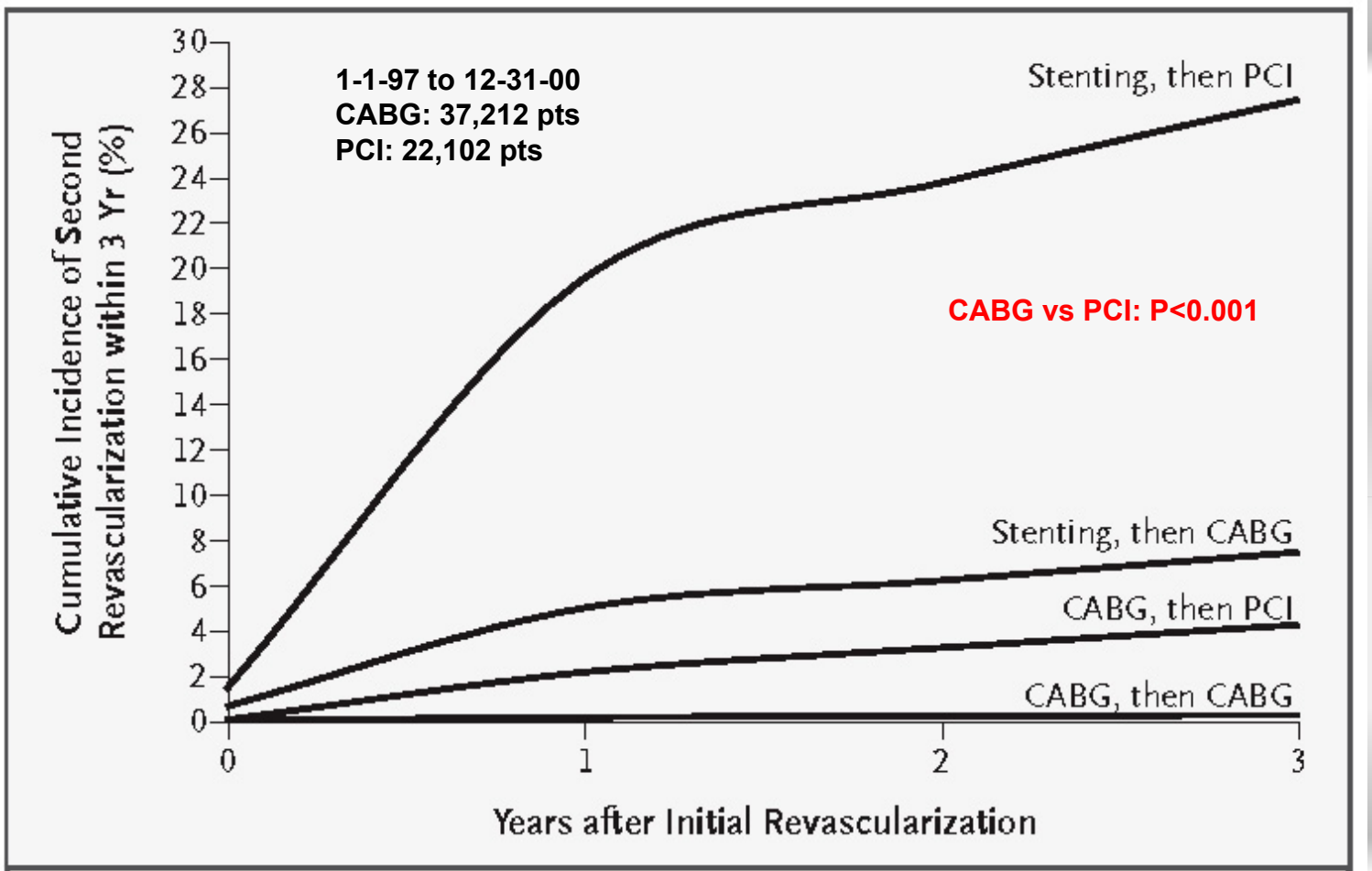
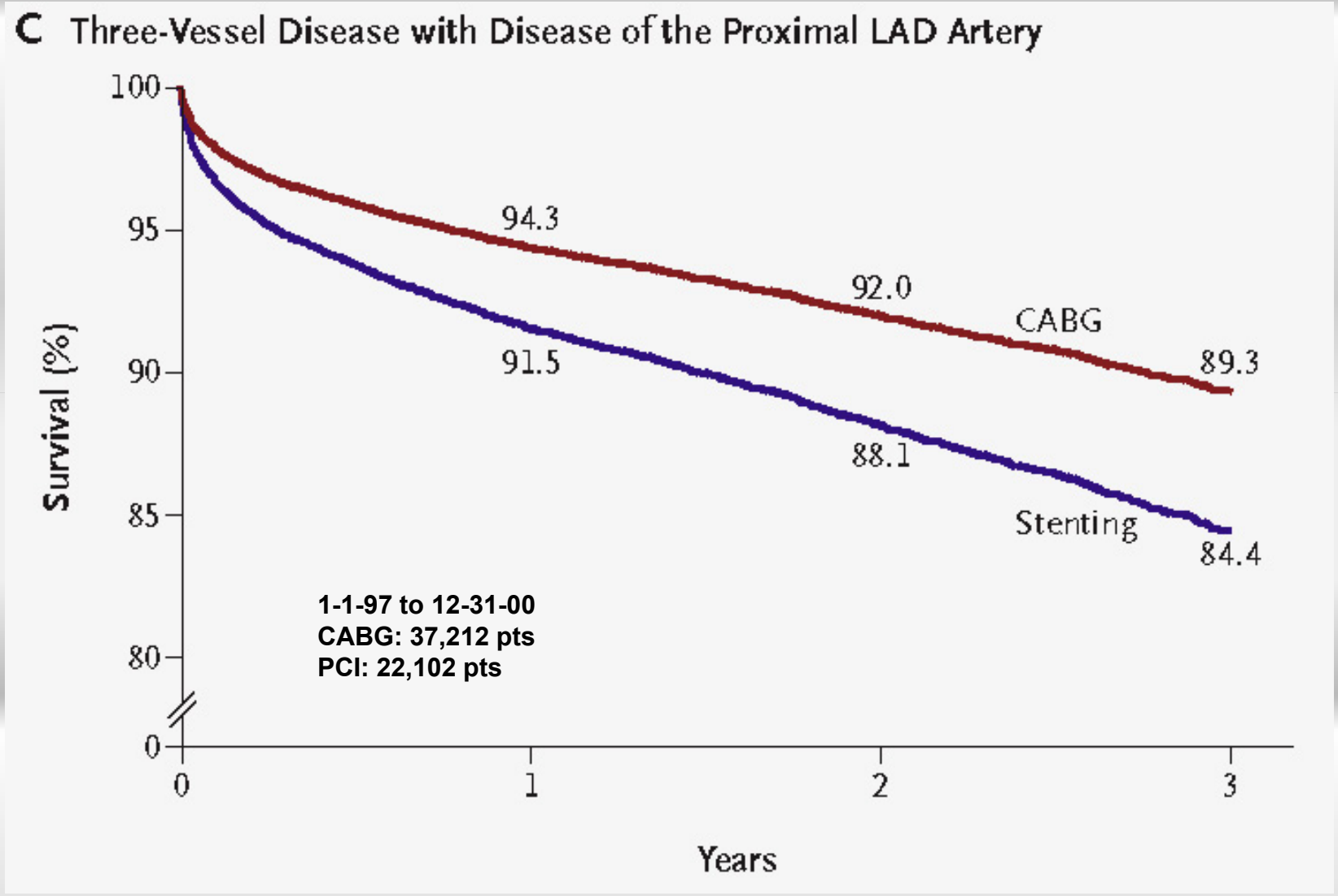


Figure 1. Percentage of Patients Undergoing a Second Revascularization Procedure within Three Years.

Hannan et al, N Engl J Med 2005;352

CABG vs Stent: New York State Registries



Hannan et al, N Engl J Med 2005;352

Original Article

Drug-Eluting Stents vs. Coronary-Artery Bypass Grafting in Multivessel Coronary Disease

Edward L. Hannan, Ph.D., Chuntao Wu, M.D., Ph.D., Gary Walford, M.D., Alfred T. Culliford, M.D., Jeffrey P. Gold, M.D., Craig R. Smith, M.D., Robert S.D. Higgins, M.D., Russell E. Carlson, M.D., and Robert H. Jones, M.D.

N Engl J Med
Volume 358(4):331-341
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CABG vs DES PCI: Risk Factors

Table 1. Risk Factors in Patients Treated with CABG or Drug-Eluting Stents.*

Risk Factor	CABG (N=7437)	Stent (N=9963)	P Value
Age (%)			<0.001
<50 yr	7.6	9.7	
50–59 yr	20.7	23.1	
60–69 yr	30.2	27.6	
70–79 yr	31.3	26.9	
≥80 yr	10.2	12.7	
Median age (yr)	67.0	66.0	<0.001
Mean age (yr)	66.0±10.9	65.4±11.9	<0.001
Sex (%)			<0.001
Male	72.5	67.2	
Female	27.5	32.8	
Hispanic ethnic background (%)†	6.9	9.3	<0.001
Race (%)†			<0.001
White	87.7	82.1	
Black	7.1	10.1	
Other	5.2	7.9	
Ejection fraction (%)			<0.001
<20%	2.0	0.8	
20–29%	6.8	3.3	
30–39%	12.9	6.6	
≥40%	77.7	84.2	
Data missing	0.6	5.1	
Previous myocardial infarction (%)			<0.001
1–7 days before treatment	20.5	18.9	
8–20 days before treatment	5.6	2.5	
≥21 days before treatment	21.4	12.3	
No previous myocardial infarction	52.5	66.3	
Cerebrovascular disease (%)	17.3	7.7	<0.001
Peripheral arterial disease (%)	10.7	7.0	<0.001
Hemodynamic instability or shock (%)	1.8	0.2	<0.001
Congestive heart failure (%)			<0.001
None	84.3	89.9	
At current admission	12.6	7.4	
Before current admission	3.1	2.7	
Malignant ventricular arrhythmia (%)	0.7	0.4	0.03
Chronic obstructive pulmonary disease (%)	17.4	6.6	<0.001
Diabetes (%)	38.2	32.7	<0.001
Renal failure (%)			0.01
Requiring dialysis	2.2	2.4	
Creatinine >2.5 mg/dl (220 μmol/liter)	2.0	1.4	
No renal failure	95.8	96.3	
No. of diseased vessels (%)‡			<0.001
3, with proximal LAD artery	51.5	11.8	
3, without proximal LAD artery	18.4	13.1	
2, with proximal LAD artery	20.0	26.1	
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* Plus–minus values are means ±SD. Because of rounding, percentages may not total 100. CABG denotes coronary-artery bypass grafting, and LAD left anterior descending.
† Race or ethnic group was reported by the Cardiac Surgery Reporting System and the Percutaneous Coronary Intervention Reporting System registries.
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Hannan EL et al. N Engl J Med 2008;358:331-341

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CABG patients were:
- **Older**
- **Had lower EF**

And had more:
- **previous MI**
- **Cerebrovascular disease**
- **Peripheral vascular disease**
- **Instability/shock**
- **CHF**
- **Malignant arrythmias**
- **COPD**
- **Diabetes**
- **Renal failure**
- **Number of diseased vessels**

Hannan EL et al. N Engl J Med 2008;358:331-341

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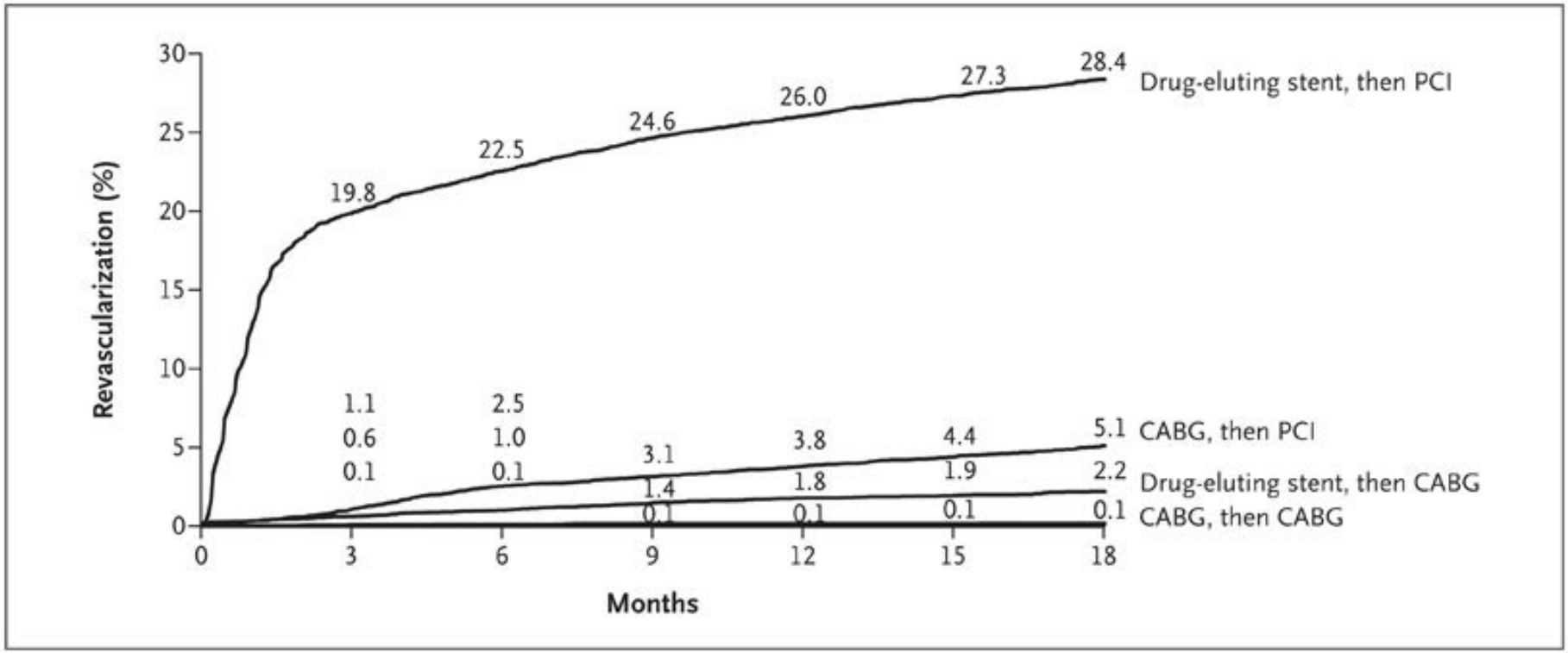
Revascularization within 18 Months after Initial Procedure



Hannan EL et al. N Engl J Med 2008;358:331-341

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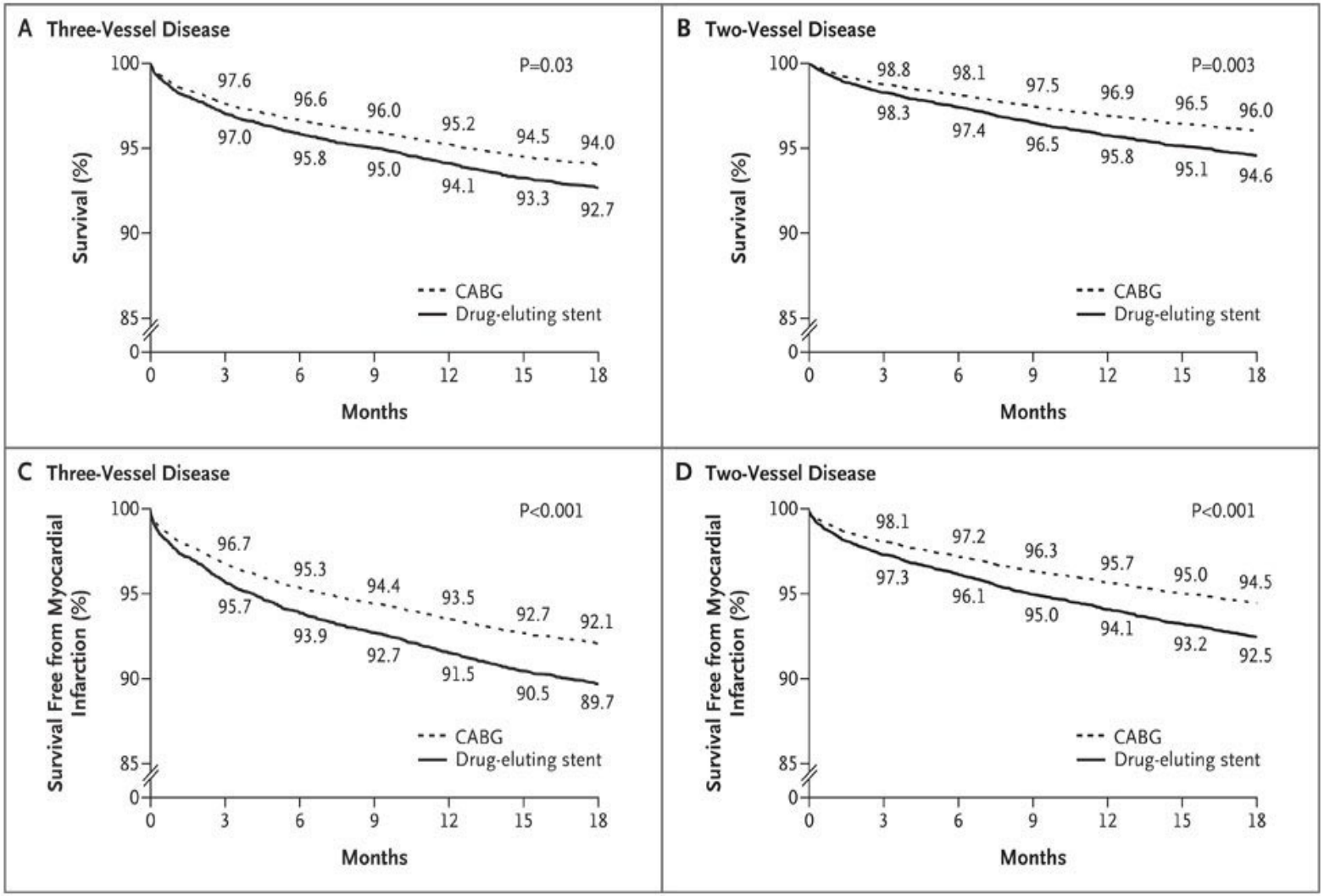
CABG vs DES PCI: 2VD and 3VD, Adjusted Survival Curves



Hannan EL et al. N Engl J Med 2008;358:331-341

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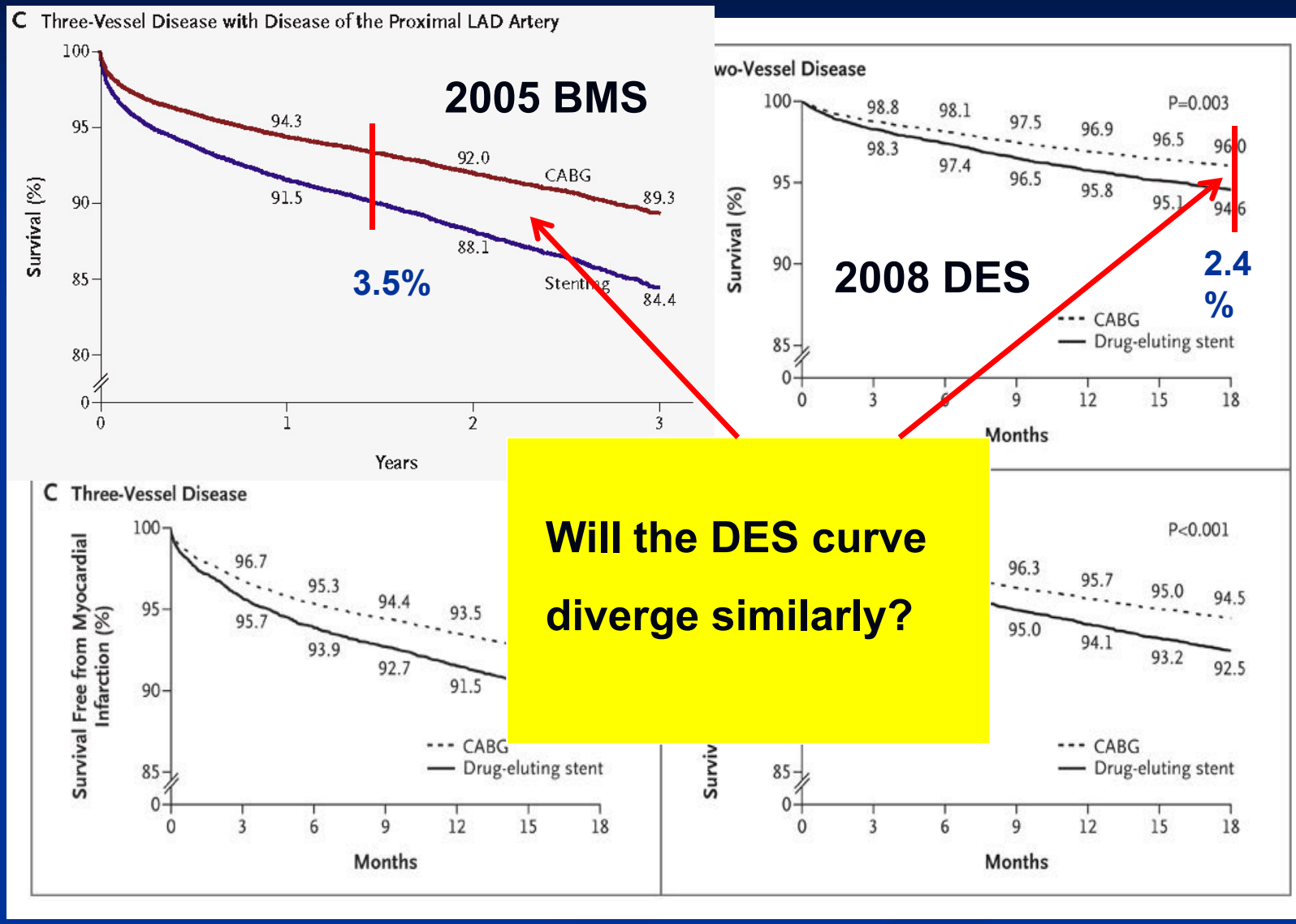
CABG vs PCI: BMS vs DES at 18 months, Adjusted Survival Curves



Hannan et al. N Engl J Med 2008;358:331-341
Hannan et al, N Engl J Med 2005;352

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Editorial Comment*

- Suggestion of decreased TLR/TVR with DES
- Unmeasured confounders (dementia?)
- Enrollment prior to widespread use of extended dual antiplatelet Rx for DES
- F/U too short to see vein graft failures
- But…"CABG remains the standard of care" for multivessel CAD

*Carozza, N Engl J Med 2008;358:405-7

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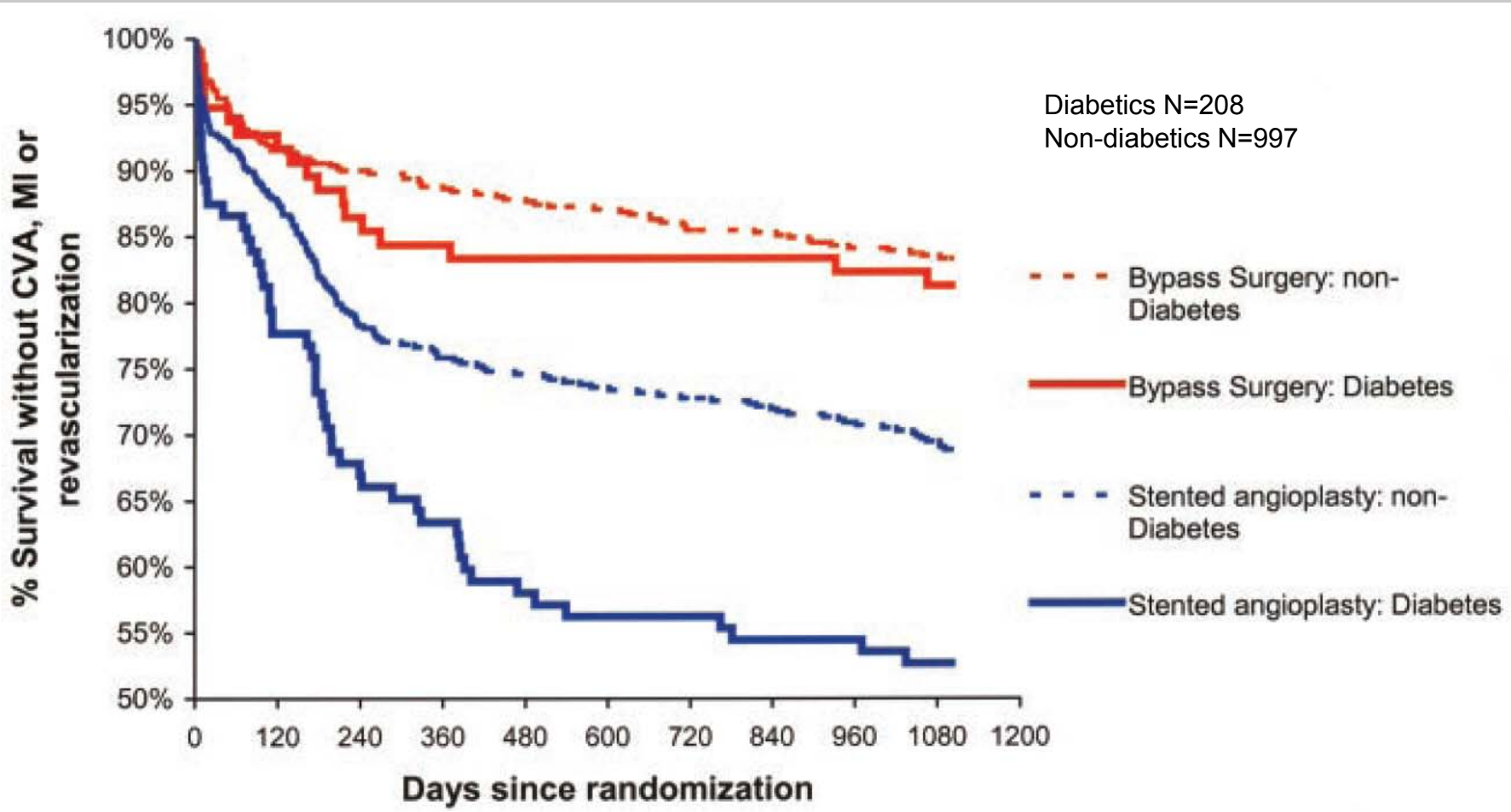
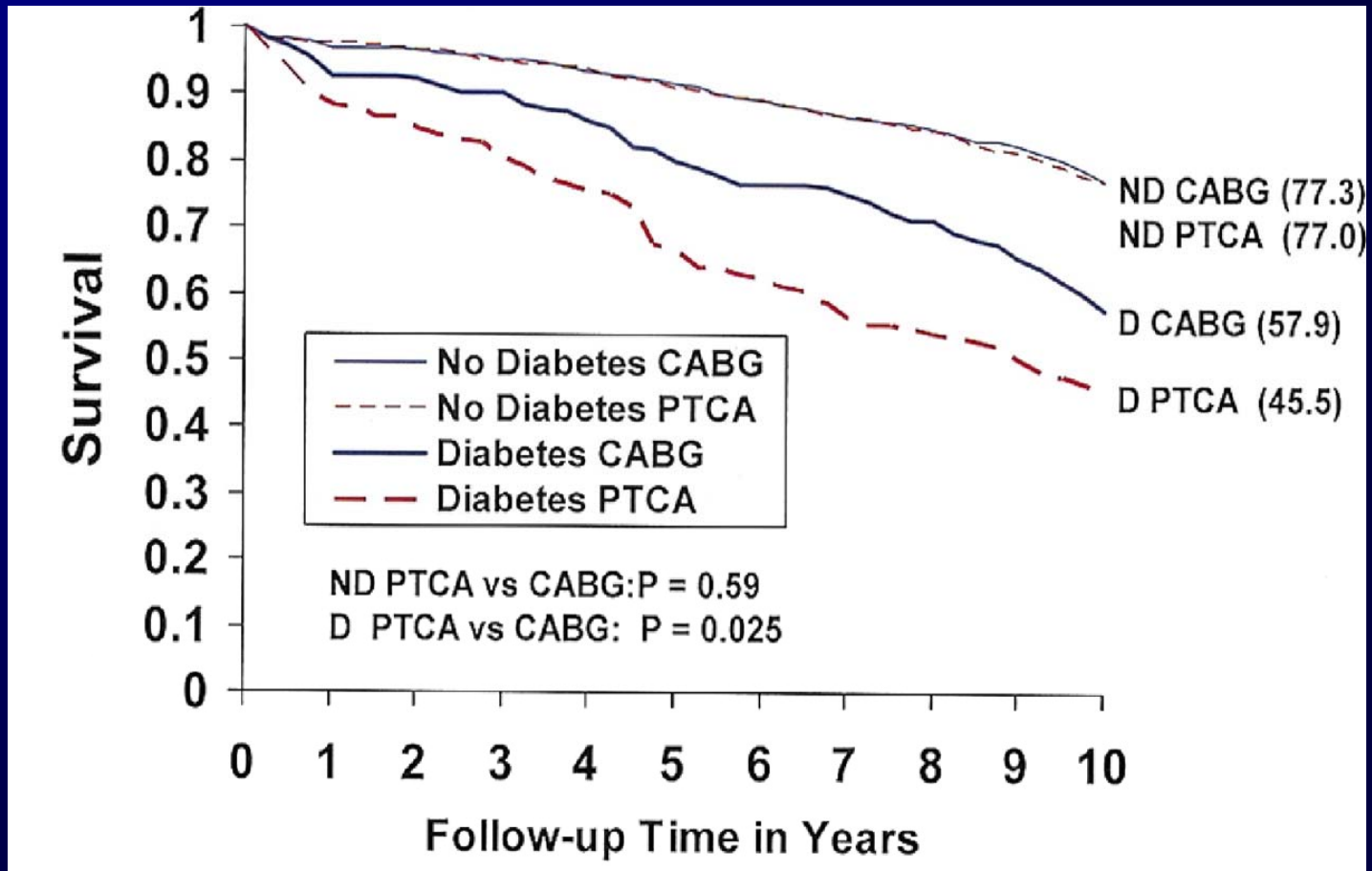
ARTS: 3-year Event-free Survival



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

Legrand et al, *Circulation*. 2004;109:1114-1120

BARI Randomized Trial 10-Year Survival Stratified by Diabetes Status



No. of Patients					
ND CABG	734	698	669	613	473
ND PTCA	742	703	675	621	477
D CABG	180	161	143	124	80
D PTCA	173	139	115	93	63

The BARI Investigators, J Am Coll Cardiol 2007;49:1600-1606

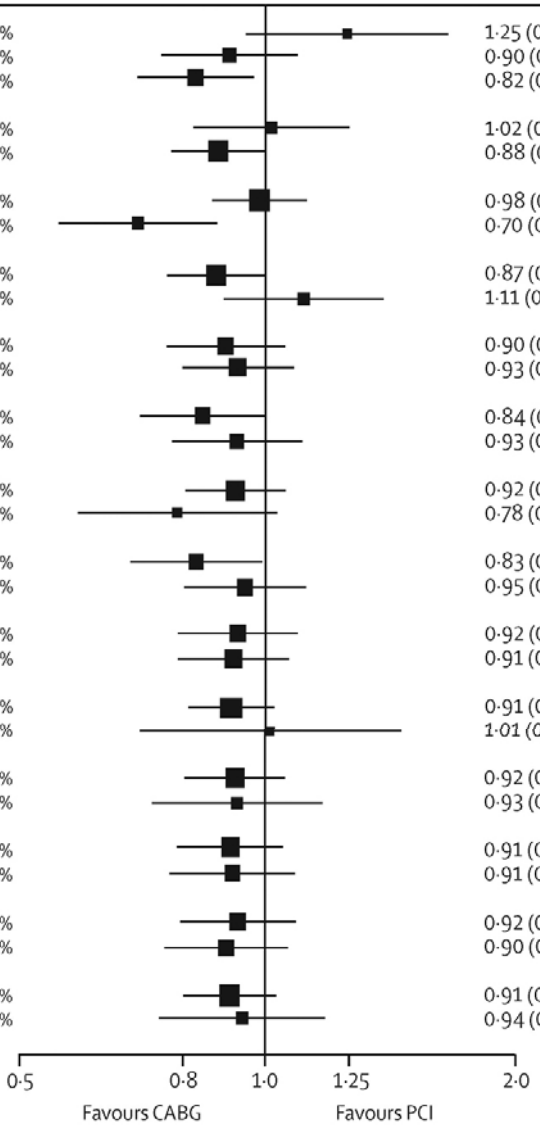
CABG vs. PCI in Multivessel CAD: A Collaborative Analysis of Mortality

	Overall (N=7812)	ARTS[1] (N=1205)	BARI[2] (N=1829)	CABRI[3] (N=1054)	EAST[4] (N=392)	ERACI-II[5] (N=450)	GABI[6] (N=323)	MASS-II[7] (N=408)	RITA-1[8] (N=1011)	SoS[9] (N=988)	Toulouse[10] (N=152)
Age											
<55 years	2185 (28%)	332 (28%)	442 (24%)	286 (27%)	94 (24%)	124 (28%)	107 (33%)	131 (32%)	403 (40%)	253 (26%)	13 (9%)
55–64 years	2933 (38%)	420 (35%)	678 (37%)	443 (42%)	143 (36%)	163 (36%)	130 (40%)	135 (33%)	442 (44%)	340 (34%)	39 (26%)
≥65 years	2688 (34%)	453 (38%)	709 (39%)	320 (31%)	155 (40%)	162 (36%)	86 (27%)	142 (35%)	166 (16%)	395 (40%)	100 (66%)
Female	1831 (23%)	283 (23%)	489 (27%)	234 (22%)	103 (26%)	93 (21%)	67 (21%)	125 (31%)	196 (19%)	206 (21%)	35 (23%)
Diabetes	1233 (16%)	208 (17%)	353 (19%)	124 (12%)	90 (23%)	78 (17%)	41 (13%)	115 (28%)	62 (6%)	142 (14%)	20 (13%)
Current smoker	1665 (25%)	323 (27%)	463 (25%)	NA	79 (20%)	233 (52%)	36 (11%)	134 (33%)	169 (17%)	149 (15%)	79 (52%)
Hypertension	3503 (45%)	540 (45%)	896 (49%)	378 (36%)	206 (53%)	318 (71%)	136 (42%)	253 (62%)	265 (26%)	447 (45%)	64 (42%)
Hypercholesterolaemia	3386 (52%)	694 (58%)	725 (44%)	460 (44%)	146 (40%)	275 (61%)	201 (63%)	322 (79%)	NA	509 (52%)	54 (36%)
Peripheral vascular disease	665 (10%)	64 (5%)	303 (17%)	72 (7%)	NA	103 (23%)	26 (8%)	0 (0%)	NA	66 (7%)	31 (20%)
Unstable symptoms	2653 (41%)	451 (37%)	1250 (68%)	166 (16%)	NA	412 (92%)	41 (13%)	0 (0%)	NA	202 (20%)	131 (86%)
Previous myocardial infarction	3506 (45%)	520 (43%)	987 (55%)	439 (43%)	160 (41%)	126 (28%)	150 (47%)	191 (47%)	428 (43%)	448 (45%)	57 (38%)
Heart failure	245 (3%)	0 (0%)	161 (9%)	0 (0%)	13 (3%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	62 (6%)	9 (6%)
Abnormal left ventricular function	1166 (17%)	189 (17%)	341 (19%)	138 (15%)	63 (16%)	88 (20%)	25 (13%)	13 (3%)	142 (26%)	153 (20%)	14 (9%)
Three-vessel disease	2853 (37%)	338 (29%)	754 (41%)	449 (43%)	156 (40%)	219 (49%)	119 (38%)	230 (56%)	125 (12%)	419 (42%)	44 (29%)
Proximal LAD disease	3391 (51%)	NA	668 (37%)	638 (61%)	283 (72%)	230 (51%)	92 (28%)	389 (95%)	567 (56%)	457 (46%)	67 (44%)
Follow-up (years)	5·9 (5·0–10·0)	5·1 (5·0–5·3)	10·4 (10·0–11·0)	3·0 (2·4–3·7)	8·2 (8·2–8·2)	5·0 (5·0–5·0)	13·0 (12·1–14·5)	5·1 (5·1–5·2)	10·0 (10·0–10·0)	6·0 (5·5–6·7)	4·9 (4·0–5·7)
Stent use in PCI*	1432 (37%)	580 (98%)	9 (1%)	0 (0%)	0 (0%)	221 (100%)	0 (0%)	157 (82%)	0 (0%)	465 (97%)	0 (0%)
IMA use in CABG†	2573 (83%)	539 (93%)	729 (82%)	NA	NA	198 (96%)	62 (39%)	188 (95%)	364 (74%)	451 (93%)	42 (55%)

Hlatky et al. Lancet 2009;373:1190-1197

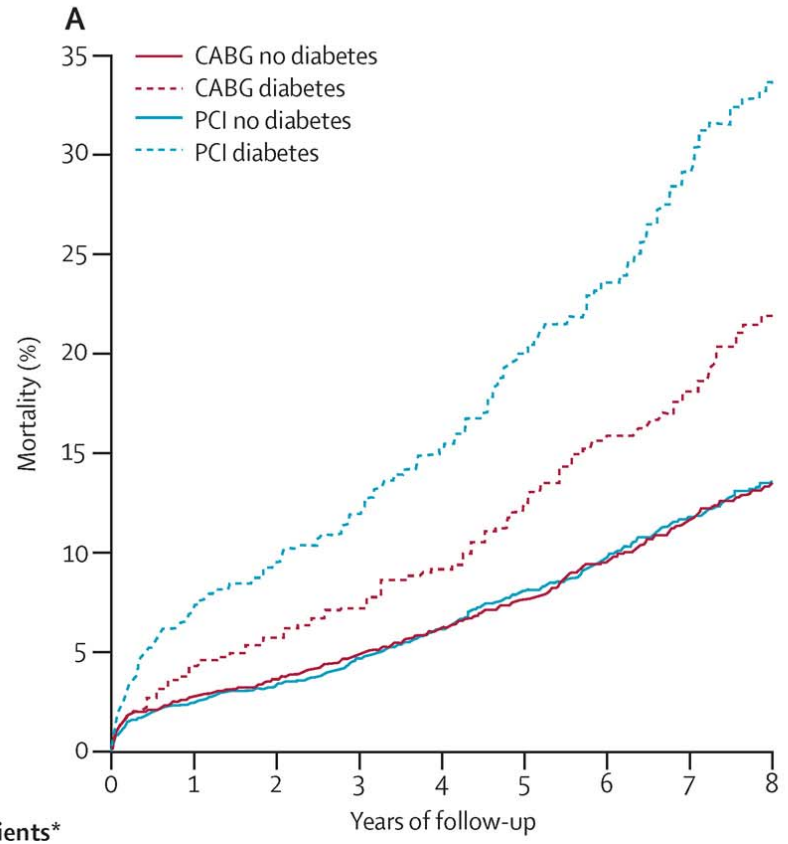
CABG vs. PCI in Multivessel CAD: A Collaborative Analysis of Mortality

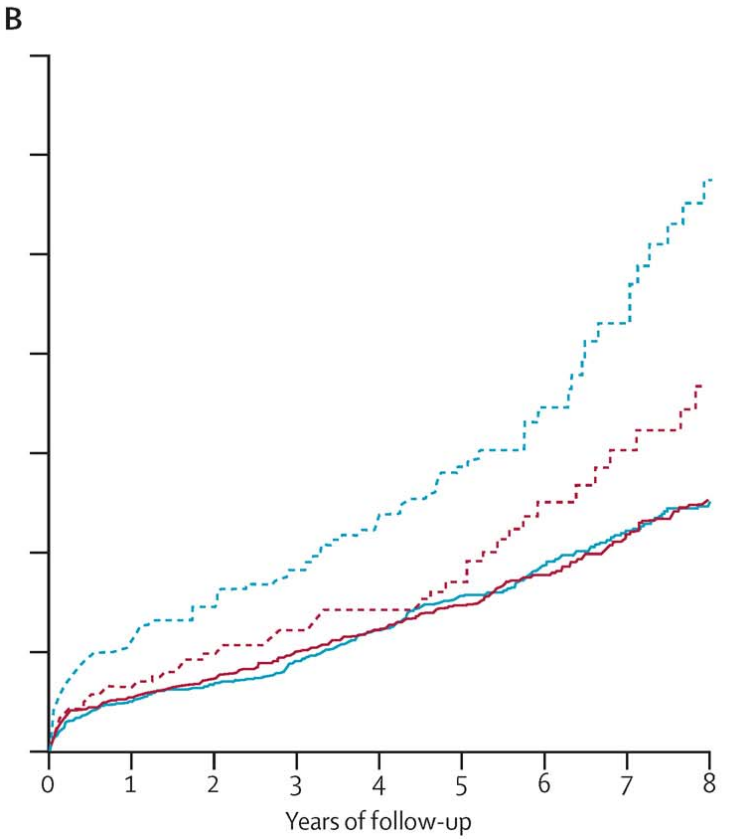
	Total mortality* (n/N)		5-year mortality (%)†		Hazard ratio (95% CI)*	p value‡
	CABG	PCI	CABG	PCI		
Age <55 years	107/1063	88/1122	5·5%	5·0%	1·25 (0·94–1·66)	0·002
Age 55–64 years	201/1477	220/1456	8·0%	9·4%	0·90 (0·75–1·09)	
Age >65 years	267/1347	319/1341	11·0%	14·7%	0·82 (0·70–0·97)	
Women	162/909	164/922	9·6%	12·0%	1·02 (0·82–1·27)	0·25
Men	413/2980	464/3001	8·0%	9·4%	0·88 (0·77–1·00)	
No diabetes	432/3263	448/3298	7·6%	8·1%	0·98 (0·86–1·12)	0·014
Diabetes	143/615	179/618	12·3%	20·0%	0·70 (0·56–0·87)	
Not smoking	393/2558	440/2526	7·9%	9·5%	0·87 (0·76–1·00)	0·073
Smoking	158/816	149/849	10·4%	10·9%	1·11 (0·89–1·39)	
No hypertension	268/2128	299/2167	7·1%	8·7%	0·90 (0·76–1·06)	0·73
Hypertension	306/1750	329/1753	9·9%	11·5%	0·93 (0·79–1·08)	
Normal cholesterol	236/1599	273/1588	9·0%	11·0%	0·84 (0·71–1·00)	0·46
Hypercholesterolaemia	221/1667	247/1719	8·4%	9·8%	0·93 (0·77–1·11)	
No PVD	374/2841	408/2872	8·1%	9·1%	0·92 (0·80–1·06)	0·33
PVD	91/334	110/331	15·0%	22·1%	0·78 (0·59–1·03)	
Stable symptoms	205/1840	256/1900	8·2%	10·2%	0·83 (0·69–0·99)	0·30
Unstable symptoms	262/1347	266/1306	9·6%	11·1%	0·95 (0·80–1·12)	
No previous MI	263/2123	286/2132	7·4%	9·3%	0·92 (0·78–1·09)	0·92
Previous MI	308/1742	334/1764	9·5%	10·8%	0·91 (0·78–1·07)	
No heart failure	513/3756	566/3800	7·5%	9·2%	0·91 (0·80–1·02)	0·46
Heart failure	59/126	58/119	30·1%	32·1%	1·01 (0·70–1·46)	
Normal LV function	375/2789	398/2791	7·6%	9·1%	0·92 (0·80–1·06)	0·87
Abnormal LV function	126/551	151/615	12·4%	14·4%	0·93 (0·73–1·18)	
Less than three diseased vessels	325/2386	371/2523	7·7%	8·8%	0·91 (0·78–1·06)	0·98
Three-vessel disease	248/1477	253/1376	9·5%	12·1%	0·91 (0·77–1·09)	
No proximal LAD	278/1567	310/1636	8·2%	10·2%	0·92 (0·79–1·09)	0·77
Proximal LAD	249/1707	268/1684	8·8%	10·5%	0·90 (0·75–1·07)	
Balloon angioplasty trials	436/2356	481/2405	8·5%	10·9%	0·91 (0·80–1·03)	0·19
Bare-metal stent trials§	139/1533	147/1518	8·2%	8·6%	0·94 (0·74–1·18)	



Hlatky et al. Lancet 2009;373:1190-1197

CABG vs. PCI in Multivessel CAD: A Collaborative Analysis of Mortality





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

CABG no diabetes	2529	2457	2382	2179	1992	1598	940	747	655
CABG diabetes	435	420	410	371	344	278	120	91	73
PCI no diabetes	2556	2493	2432	2215	2031	1606	946	750	655
PCI diabetes	445	421	408	369	344	258	110	81	66

Hlatky et al. Lancet 2009;373:1190-1197

FREEDOM Design (1)

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

Randomized 1:1

Multi-vessel PCI with DES

CABG w/wo CPB

Largest RCT of PCI vs CABG in diabetics
Intensive, state-of-the-art medical treatment

FREEDOM Trial Design (2)

Design: Superiority trial over 7 yrs

Minimum 2 yrs
Median 3.8 yrs

Sample Size: N= 1900, 131 Centers

953 PCI / DES
947 CABG

Primary Outcome: Composite of earliest occurring:

All cause mortality

Non-fatal MI

Non-fatal Stroke

FREEDOM Trial Design (3)

Secondary Outcomes

MACCE: Death, MI, Stroke, Repeat Revasc at 30 d and 1 Year

Survival: at 1,2,3 Years

Cost-Effectiveness: Quality of Life at 30 d, 6 Mos, 1, 2 & 3 yrs

FREEDOM: Inclusion Criteria

- Diabetes Mellitus (Type 1 or Type 2): Based on the American Diabetes Association.
- Angiographically: ≥70% stenosis in at least two major epicardial vessels
- Indication for revascularization: Angina and/or objective evidence of myocardial ischemia

FREEDOM – Exclusion Criteria

- Severe CHF (class III or IV)
- Simultaneous surgical procedure
- Prior CABG or PCI with stent within 6 months
- Prior Cardiac Valve Surgery
- LMCA stenosis, or 2+ CTO's in major territories
- Acute ST-elevation MI (Q-wave) within 72 hours
- CK > 2x normal and/or abnormal CK-MB levels
- Stroke within 6 mo. or > 6 mo. with residual deficit
- Concurrent enrollment in another clinical trial

Pre - Randomization

- All qualifying angiograms reviewed by a participating interventionalist and surgeon

Diabetes & Medical Management

- Target Hemoglobin A1C: < 7.0%
  - Therapy managed by MD/Diabetologist
  - Recommended ACCORD Protocol
- Target LDL- C: < 70 mg/dL
- Target BP: < 130/80 mm Hg

CABG Management

- IMA to the LAD strongly recommended in all patients
- On-pump vs OPCAB left to individual surgeon judgement

Interventional – Pre-Stent Process

- **Prior to PCI:** Clinical suitability of each lesion
  Certified operator
  PCI within 14 days of randomization

- **DES:** For all lesions, only one DES type per patient

- **Antithr:** Oral ASA 325 mg + Clopid. ≥ 300 mg load ,
  Unfractionated Heparin or Bivalirudin,
  Abciximab at initial PCI

  ASA 81-100 mg + Clopid. 75 mg/day 1-yr

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

947 Randomized to CABG

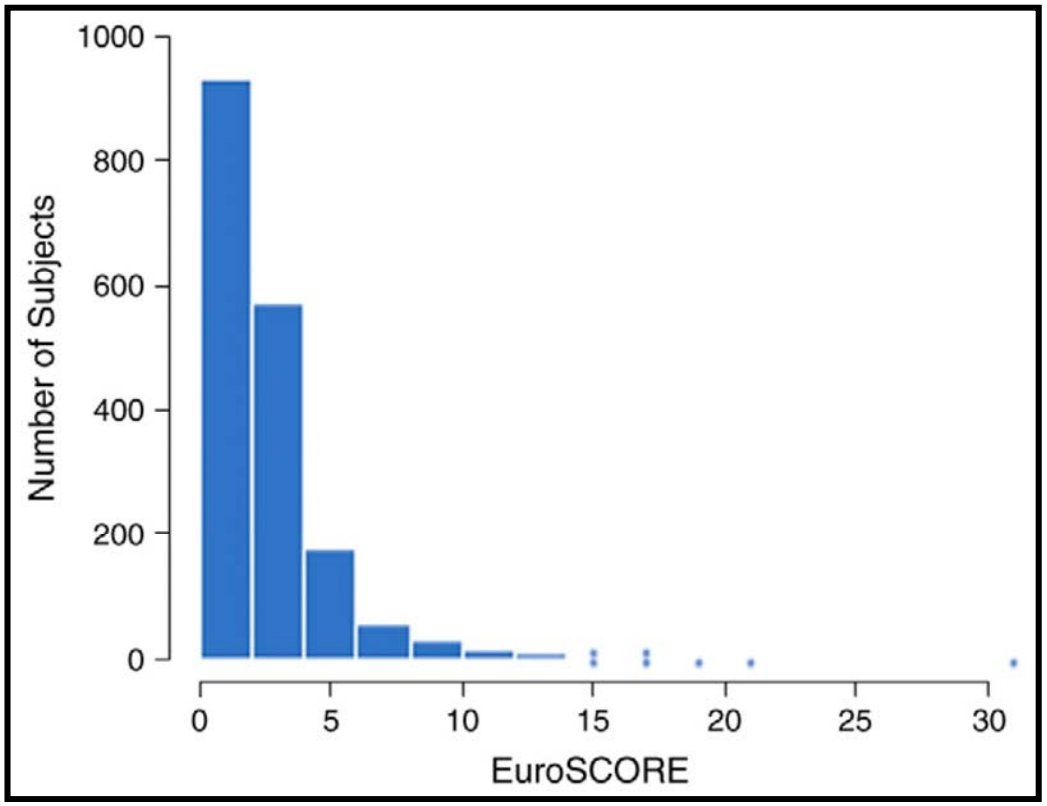
18 underwent PCI/DES
26 withdrew prior to procedure
3 died prior to procedure
7 underwent neither PCI/DES or CABG

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

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

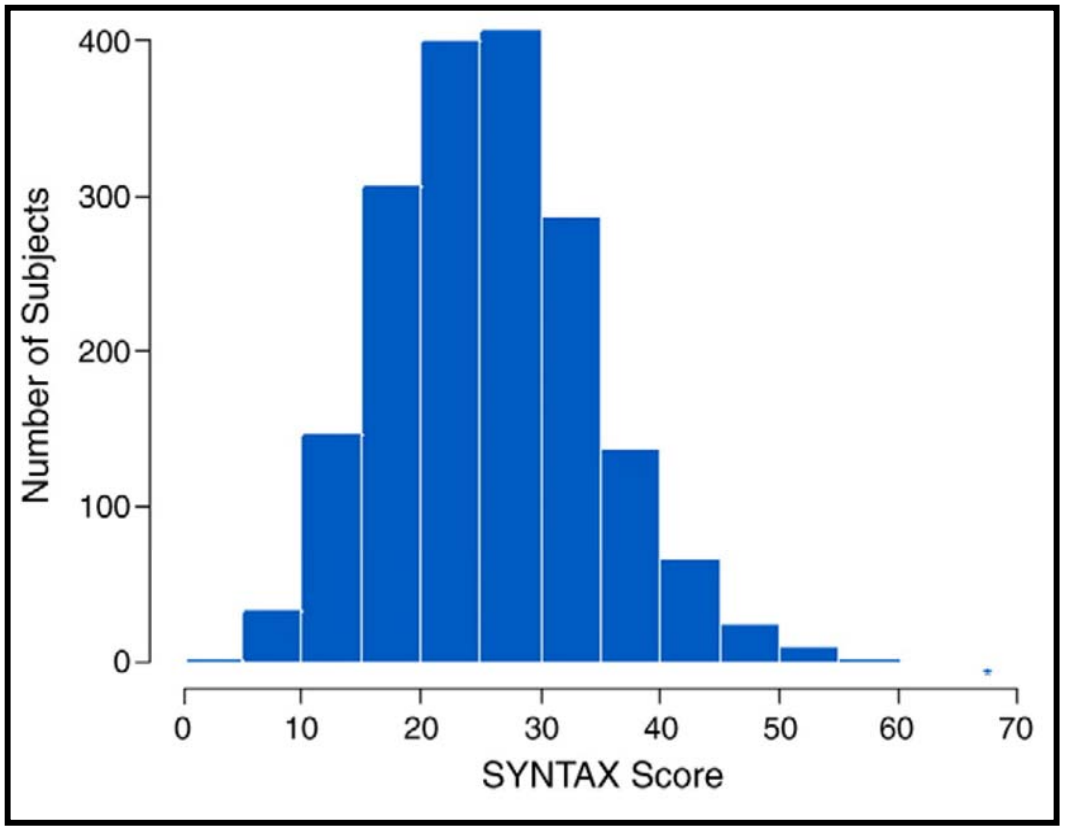
*953 and 947 included in ITT analysis using all available follow-up time post-randomization

FREEDOM Trial Clinical Characteristics
EuroSCORE



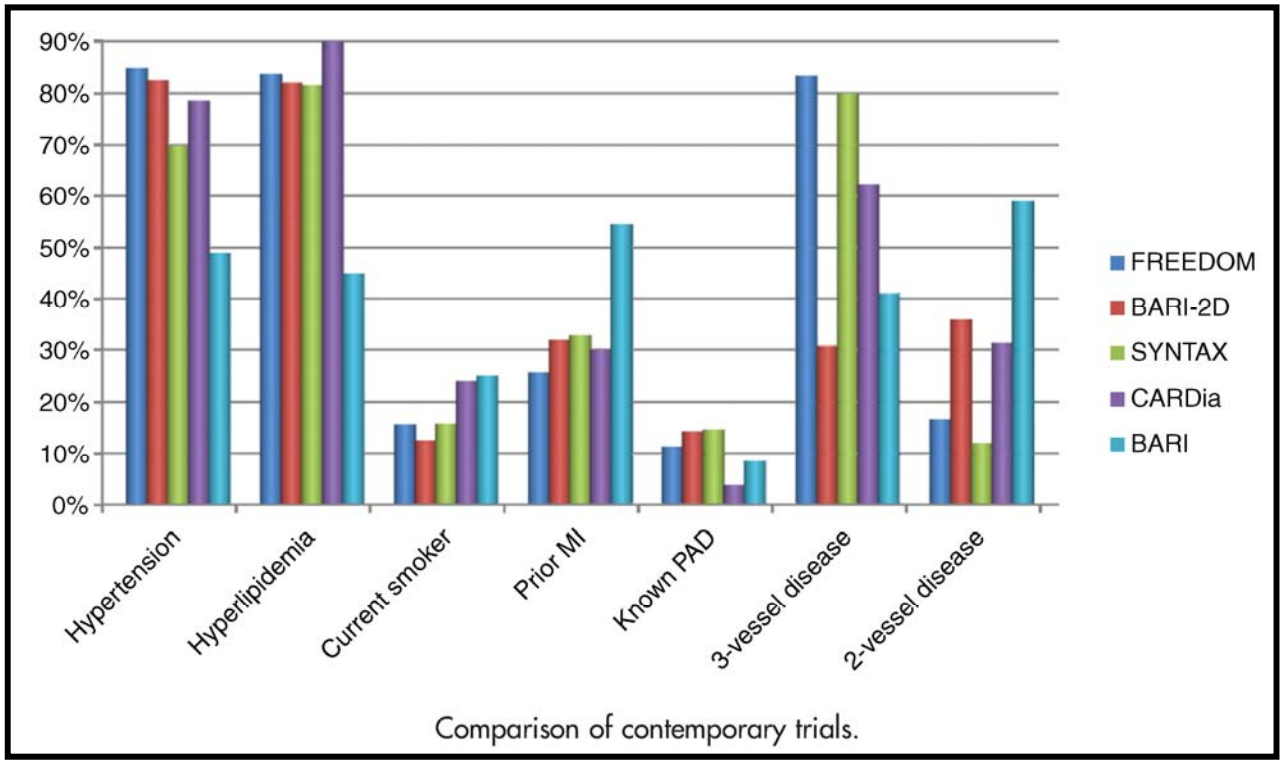
Bansilal, et al; AmHeartJ2012;164:591-9

FREEDOM Trial Clinical Characteristics
SYNTAX Score



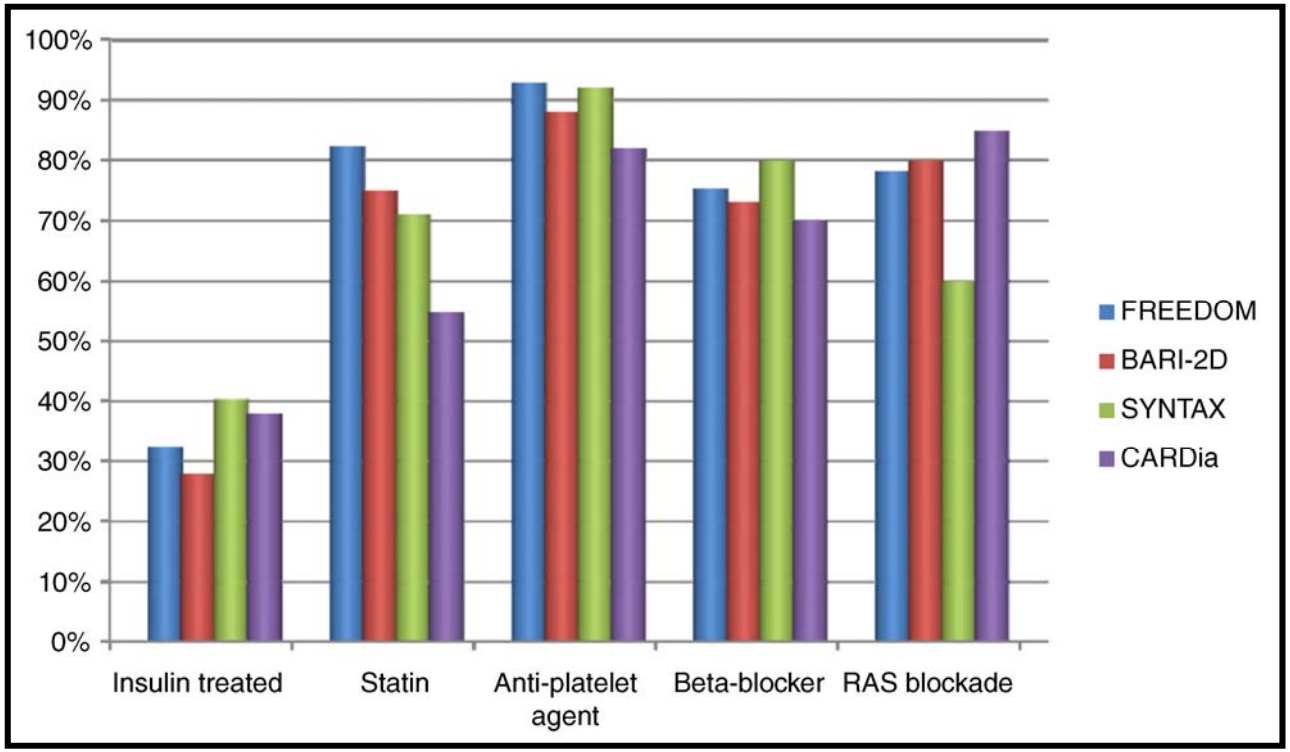
Bansilal, et al; AmHeartJ2012;164:591-9

FREEDOM Trial Clinical Characteristics Comparison to Similar Trials



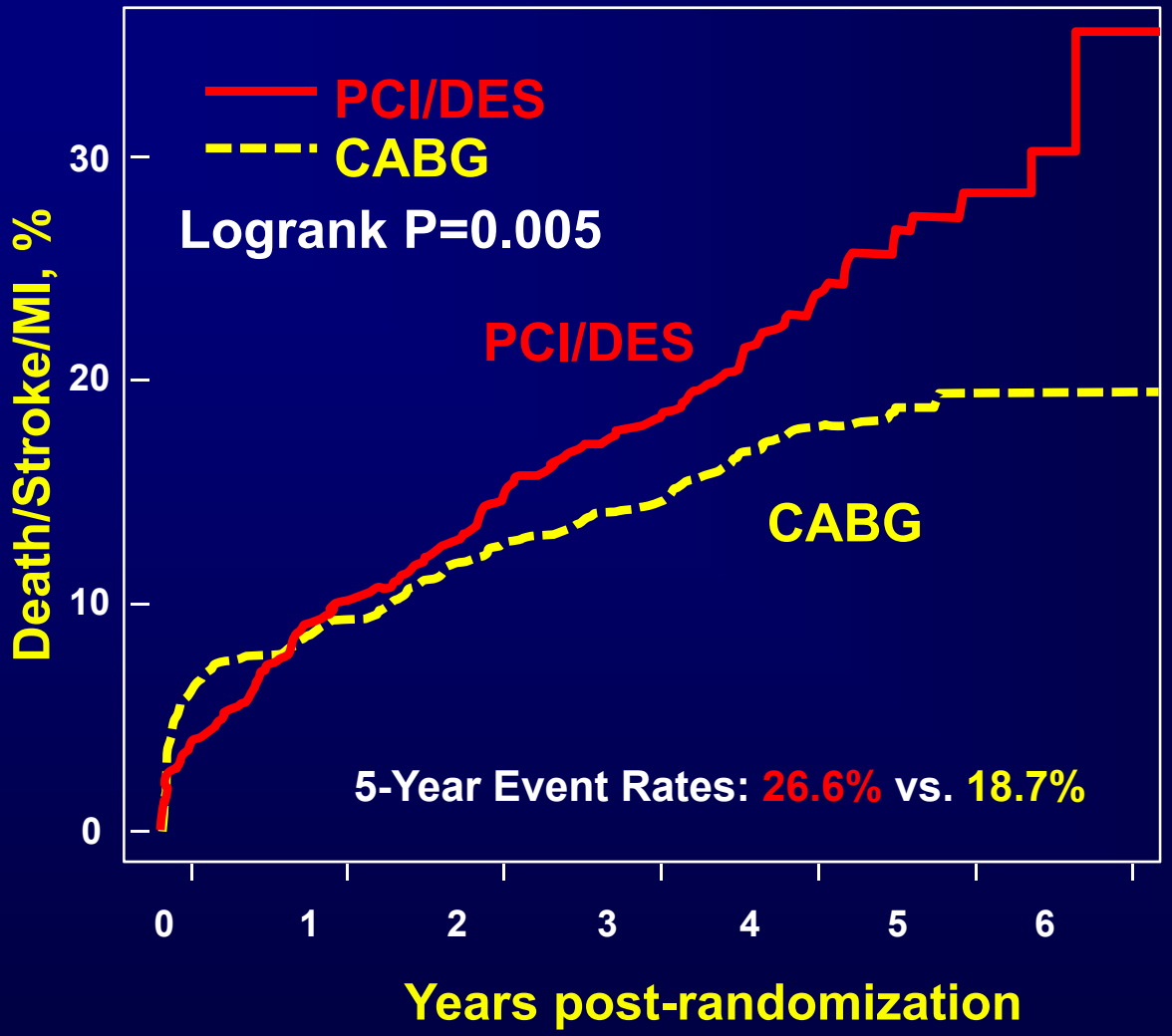
Bansilal, et al; AmHeartJ2012;164:591-9

FREEDOM Trial Clinical Characteristics Comparison to Similar Trials



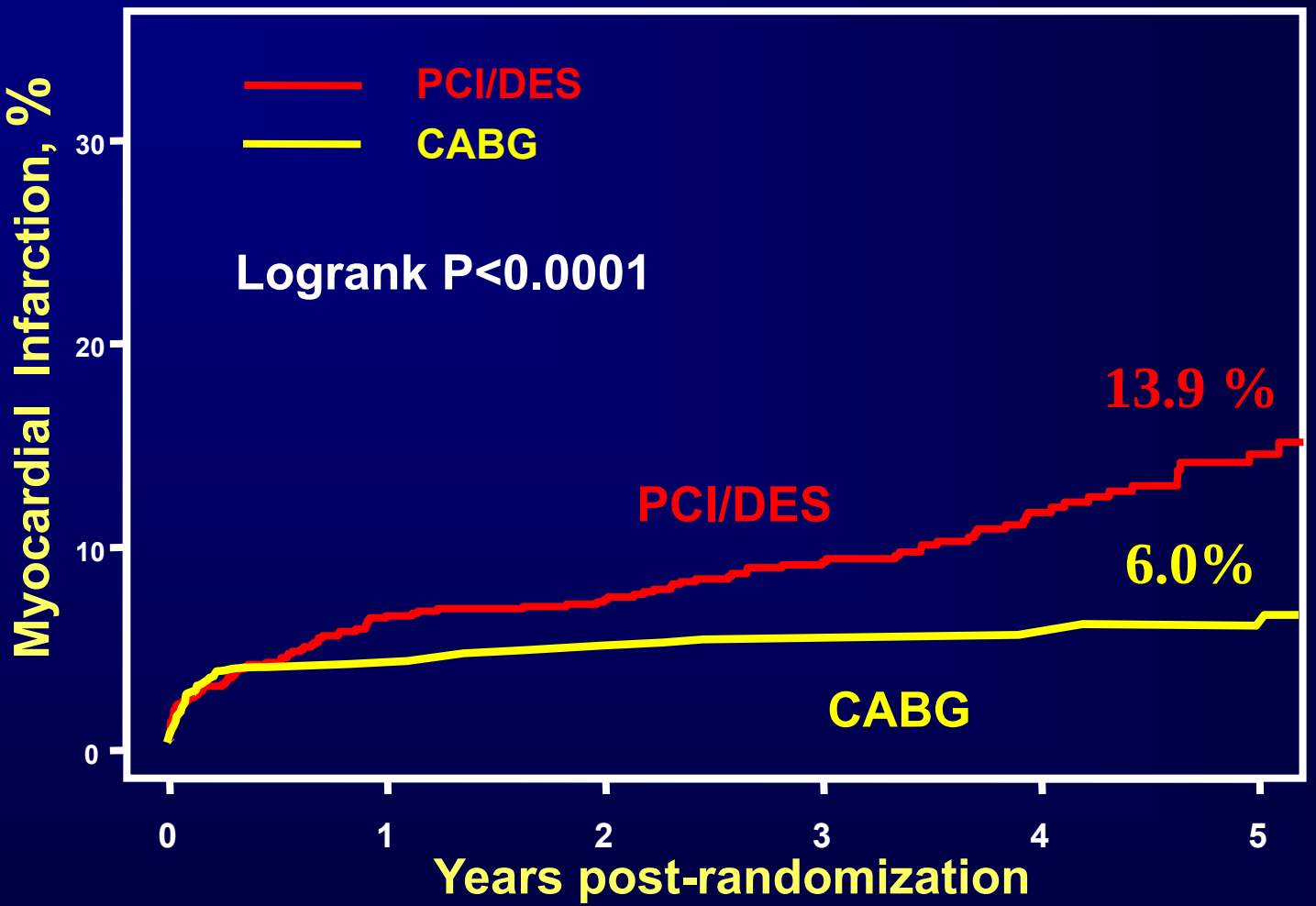
Bansilal, et al; AmHeartJ2012;164:591-9

PRIMARY OUTCOME – DEATH / STROKE / MI



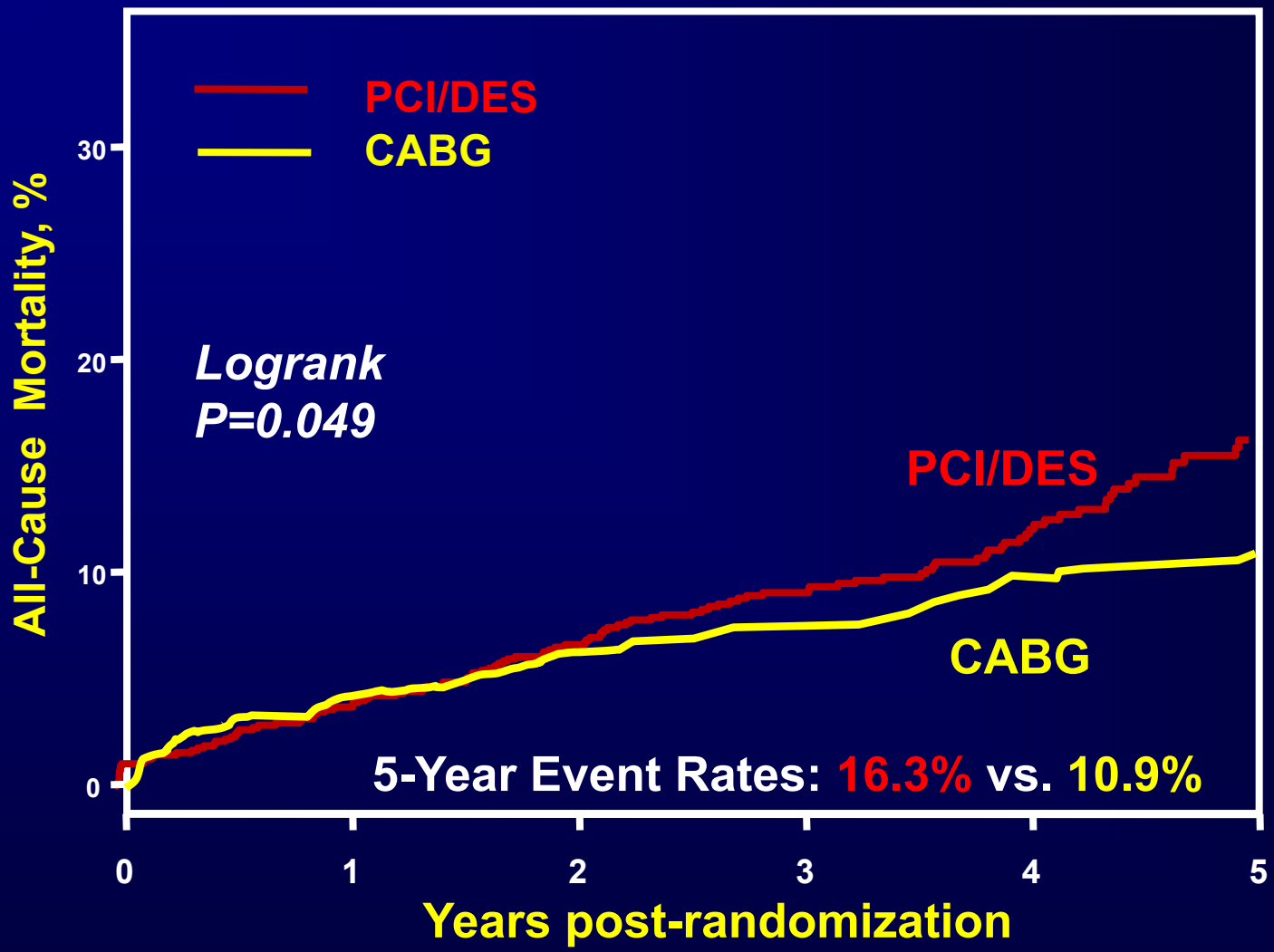
PCI/DES N	953	848	788	625	416	219	40
CABG N	943	814	758	613	422	221	44

MYOCARDIAL INFARCTION



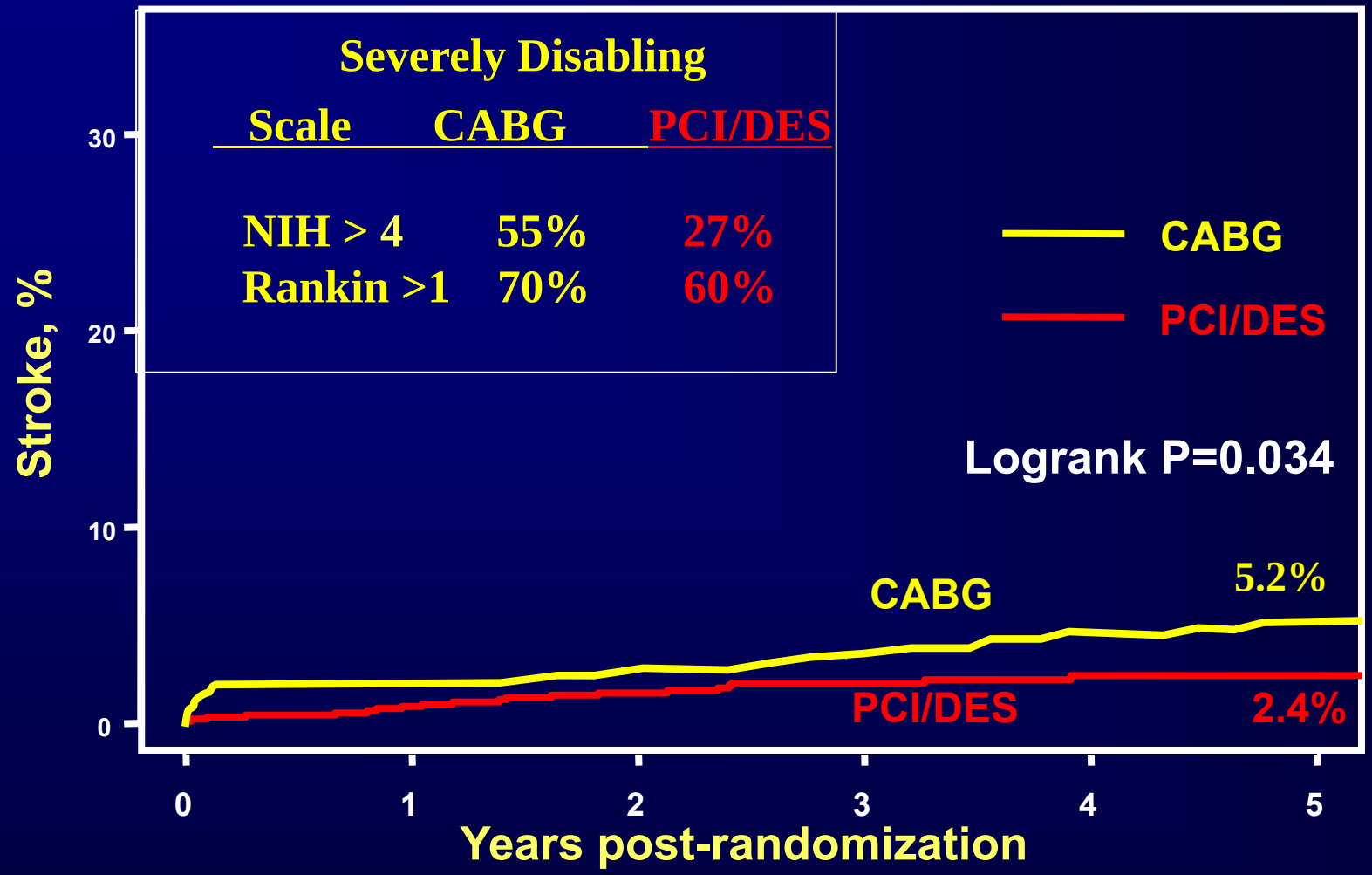
PCI/DES N 953	853	798	636	422	220
CABG N 947	824	772	629	432	229

ALL-CAUSE MORTALITY



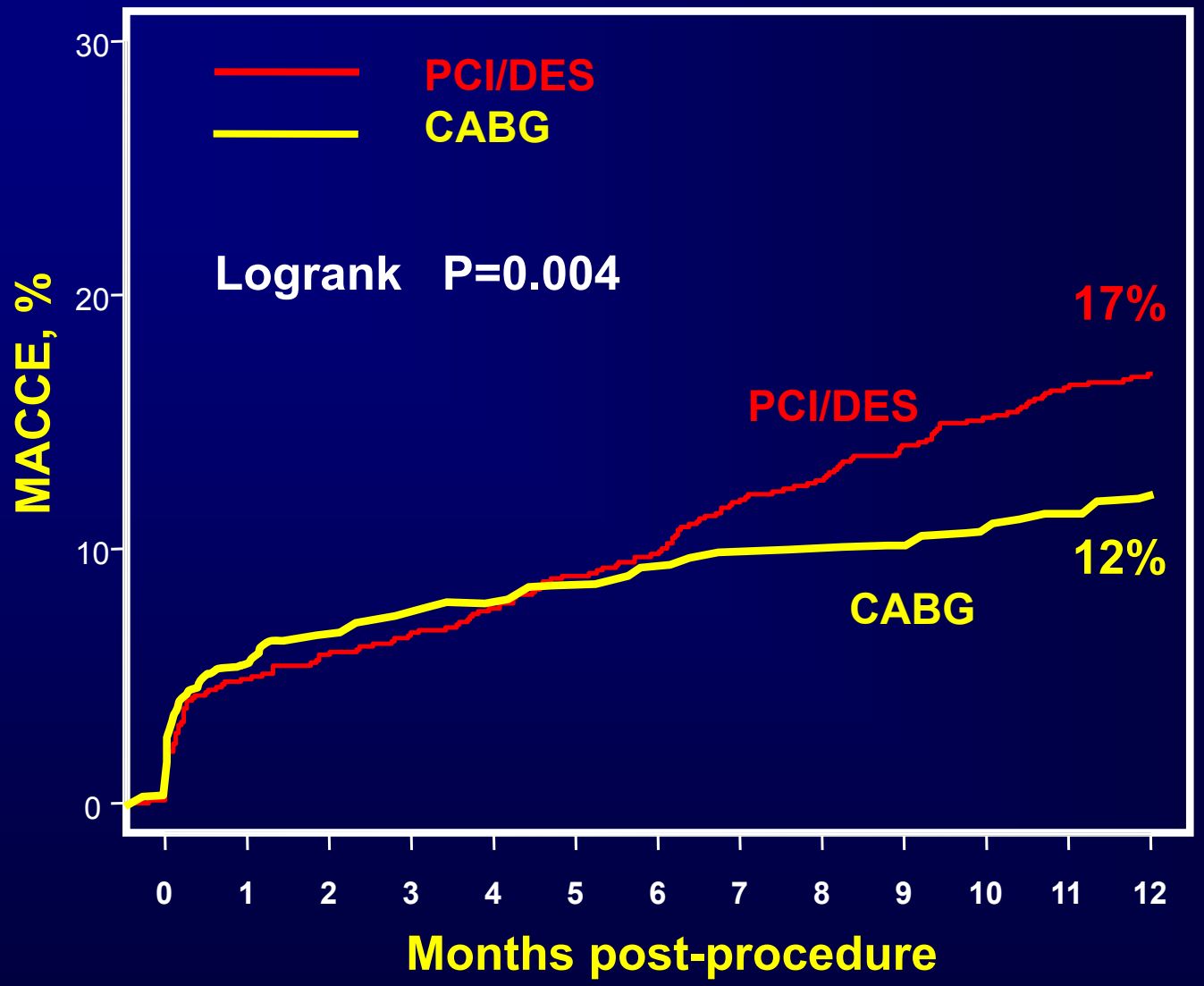
PCI/DES N	953	897	845	685	466	243
CABG N	947	855	806	655	449	238

STROKE



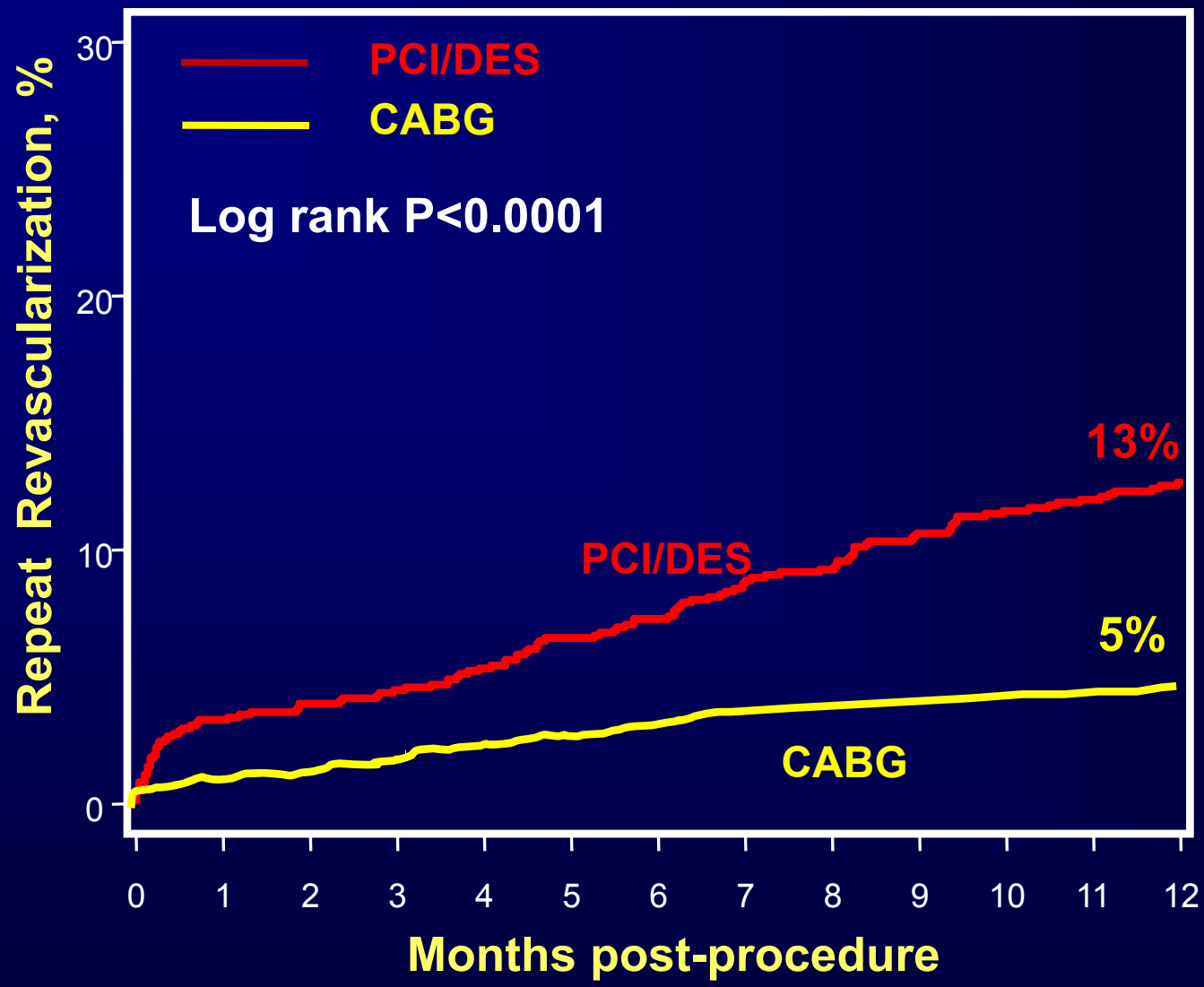
PCI/DES N	953	891	833	673	460	241
CABG N	947	844	791	640	439	230

MACCE (DEATH / STROKE / MI / REPEAT REV.)



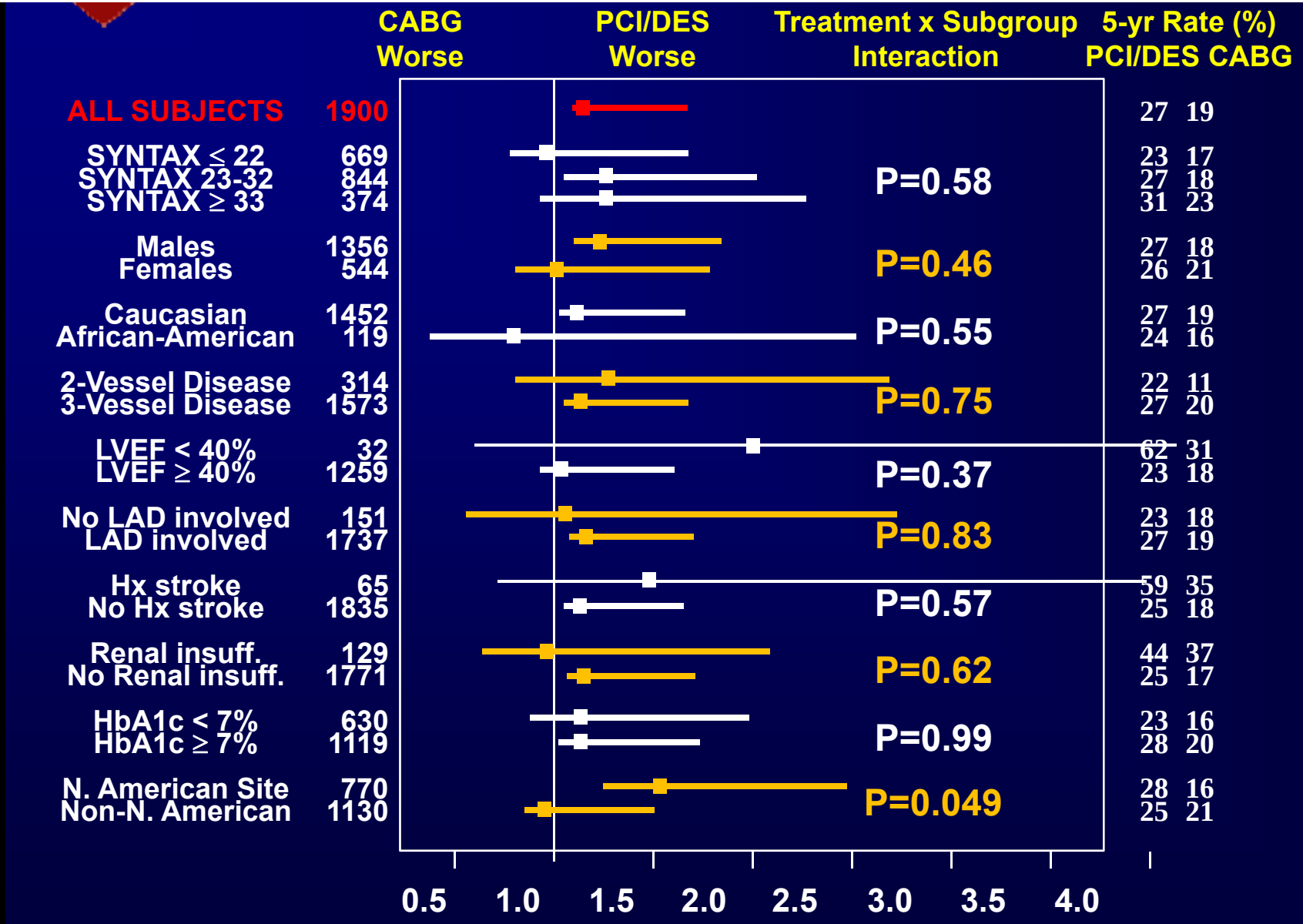
PCI/DES N	944	873	842	803	773
CABG N	911	825	805	794	773

REPEAT REVASCULARIZATION



PCI/DES N 944	887	856	818	792
CABG N 911	858	836	825	806

SUBGROUP ANALYSES



Conclusion

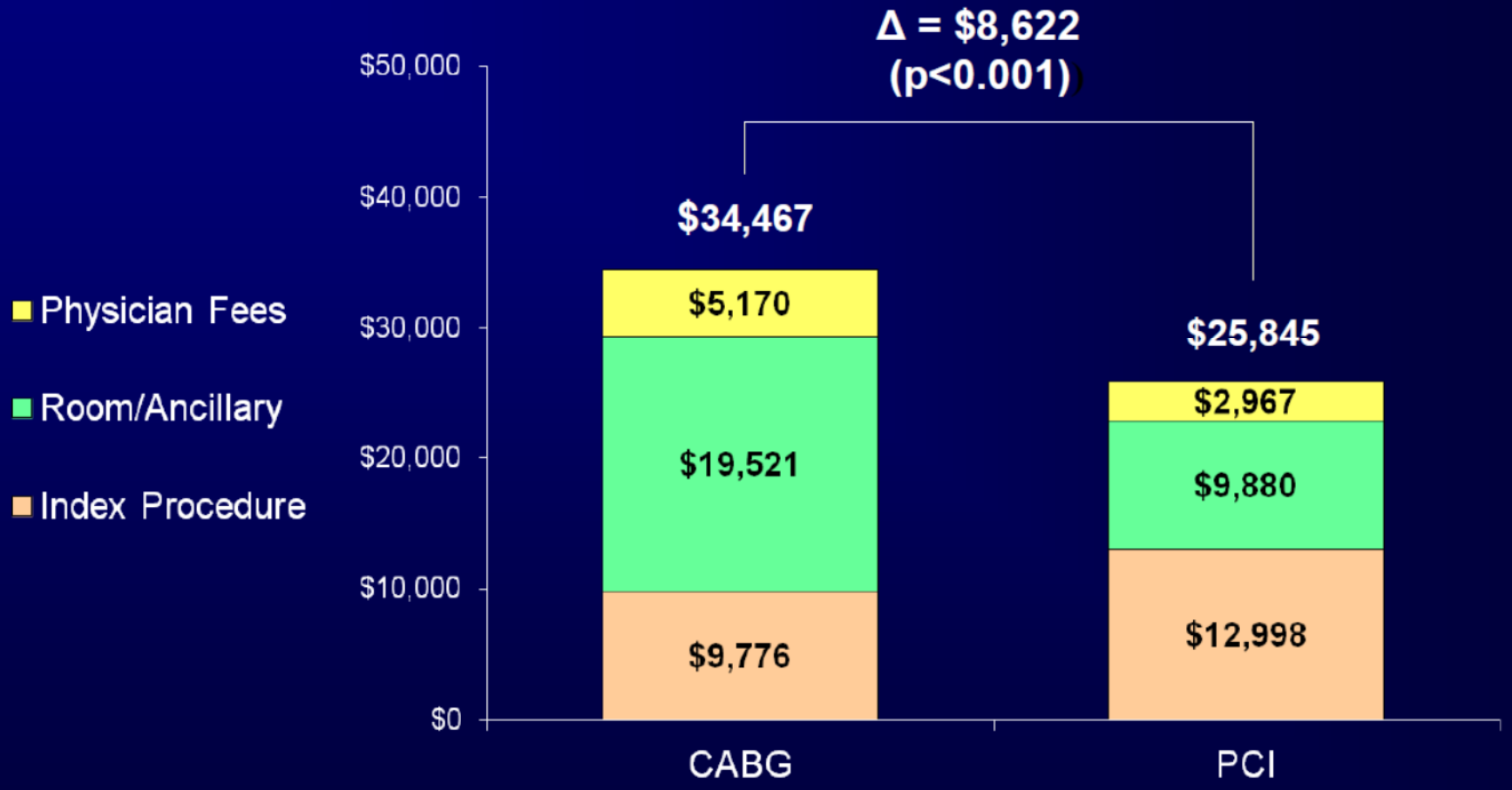
- Comparing CABG to PCI in patients with diabetes and advanced coronary disease, MI & all cause mortality were independently decreased, while stroke was slightly increased
- There was no significant interaction between the treatment effect of CABG on the primary endpoint according to SYNTAX score or any other prespecified subgroup.
- CABG surgery is the preferred method of revascularization for patients with diabetes & multi-vessel CAD.

Cost-Effectiveness of PCI with Drug Eluting Stents vs. Bypass Surgery for Patients with Diabetes and Multivessel CAD: *Results from the FREEDOM Trial*

Elizabeth A. Magnuson, Valentin Fuster, Michael E. Farkouh, Kaijun Wang, Katherine Vilain, Haiyan Li, Jaime Appelwick, Victoria Muratov, Lynn A. Sleeper, Mouin Abdallah, David J. Cohen

Saint Luke's Mid America Heart Institute
University of Missouri-Kansas City
Kansas City, Missouri

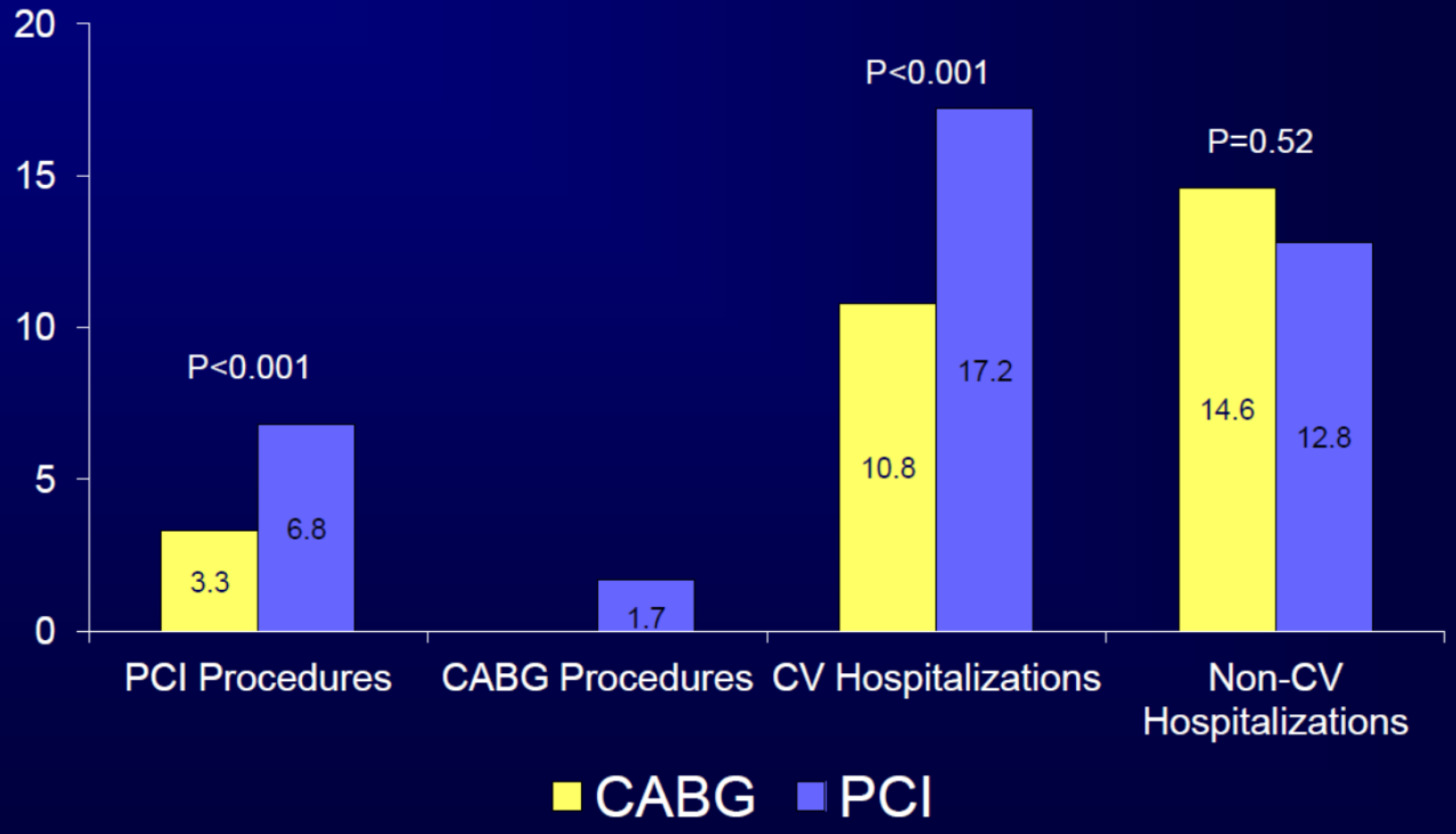
Index Hospitalization Costs



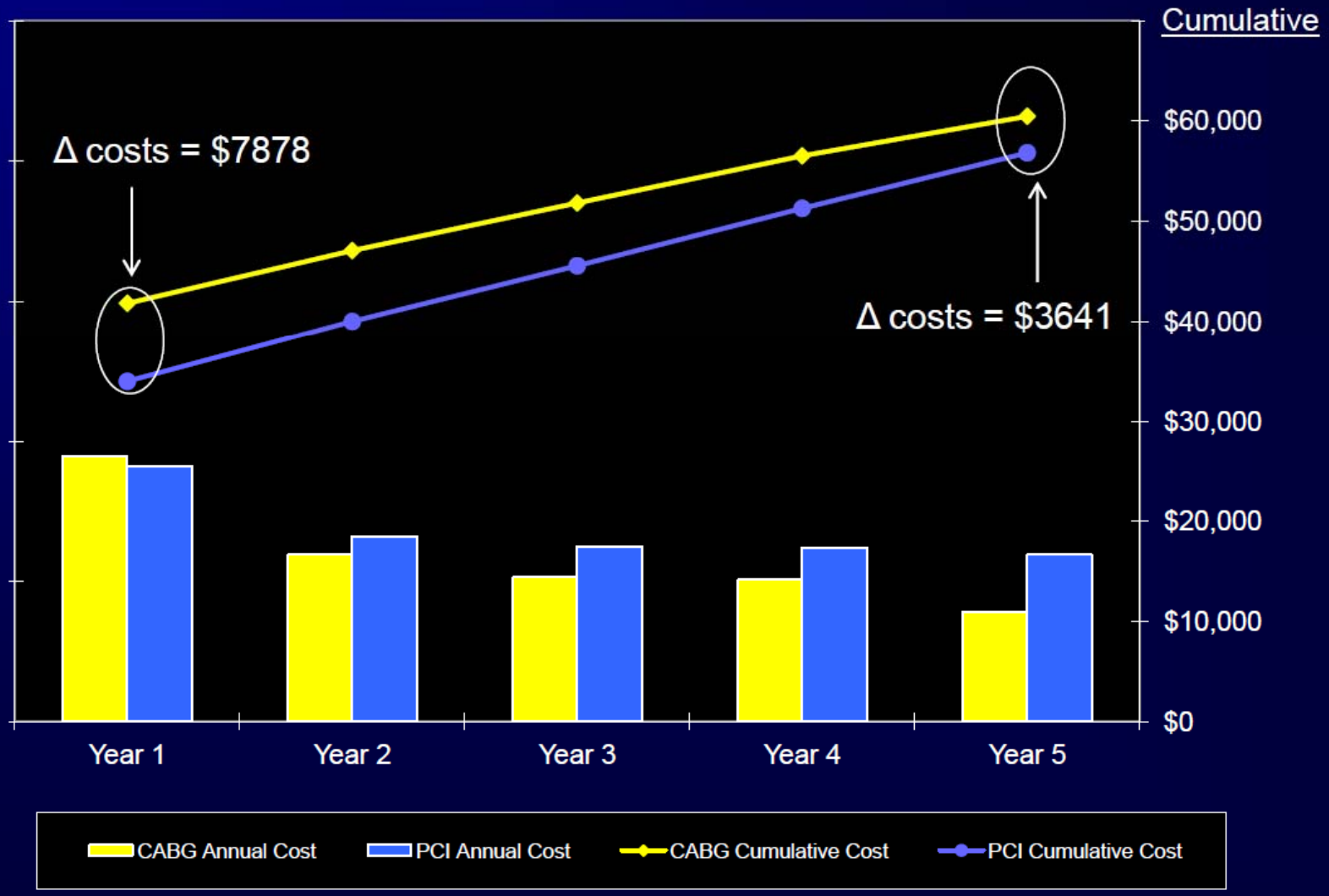
* ITT population (includes planned staged procedures)

5-Year Follow-up Resource Utilization

Rates per 100 person-years



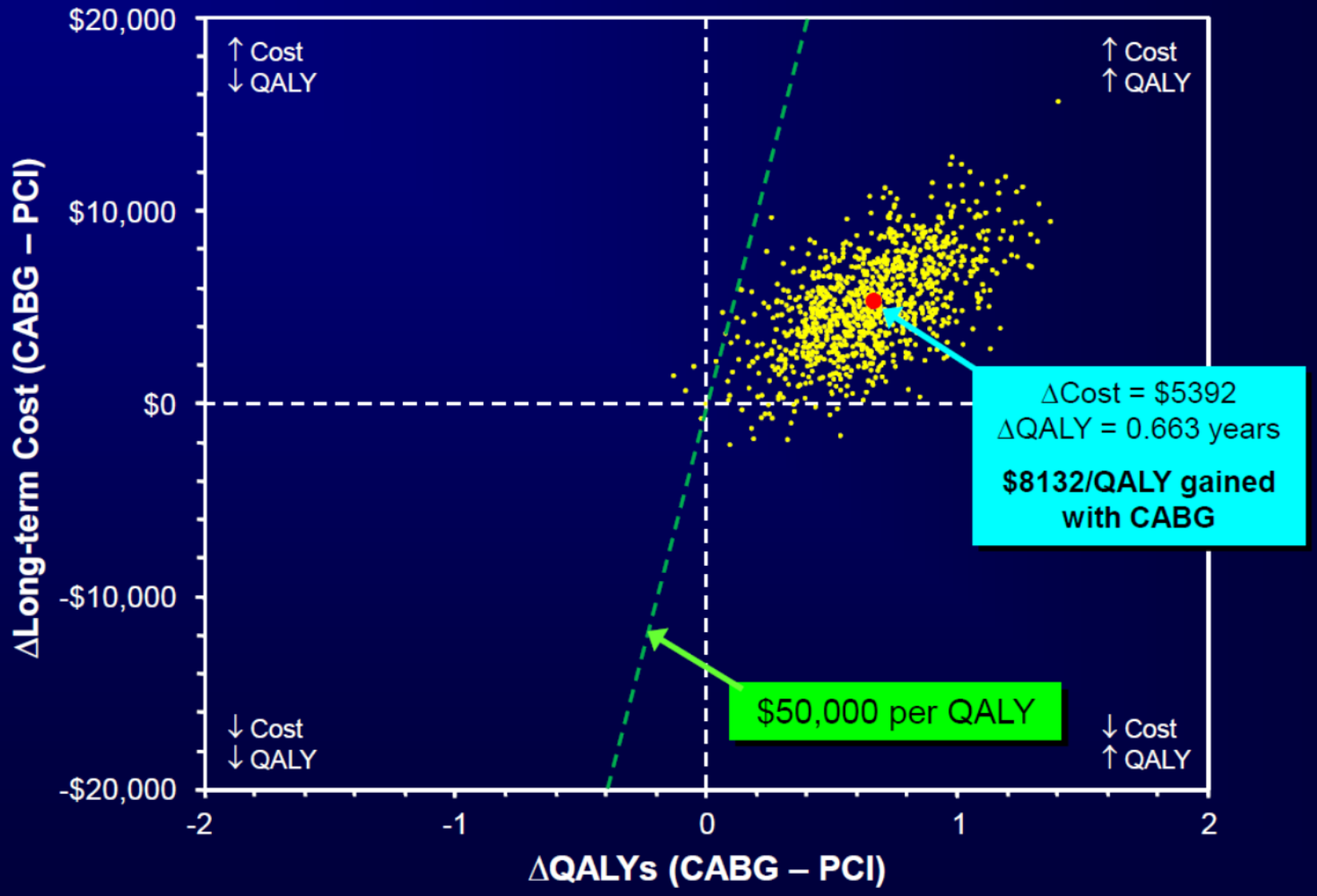
Annual and Cumulative Costs: Years 1- 5



Annual Differences in Life Years and QALYs

Time Since Randomization (Years)	Δ Life Years (CABG-PCI)	Δ QALYs (CABG-PCI)
1	-0.008	-0.033
2	-0.010	-0.034
3	-0.0006	-0.029
4	+0.015	-0.004
5	+0.053	+0.031

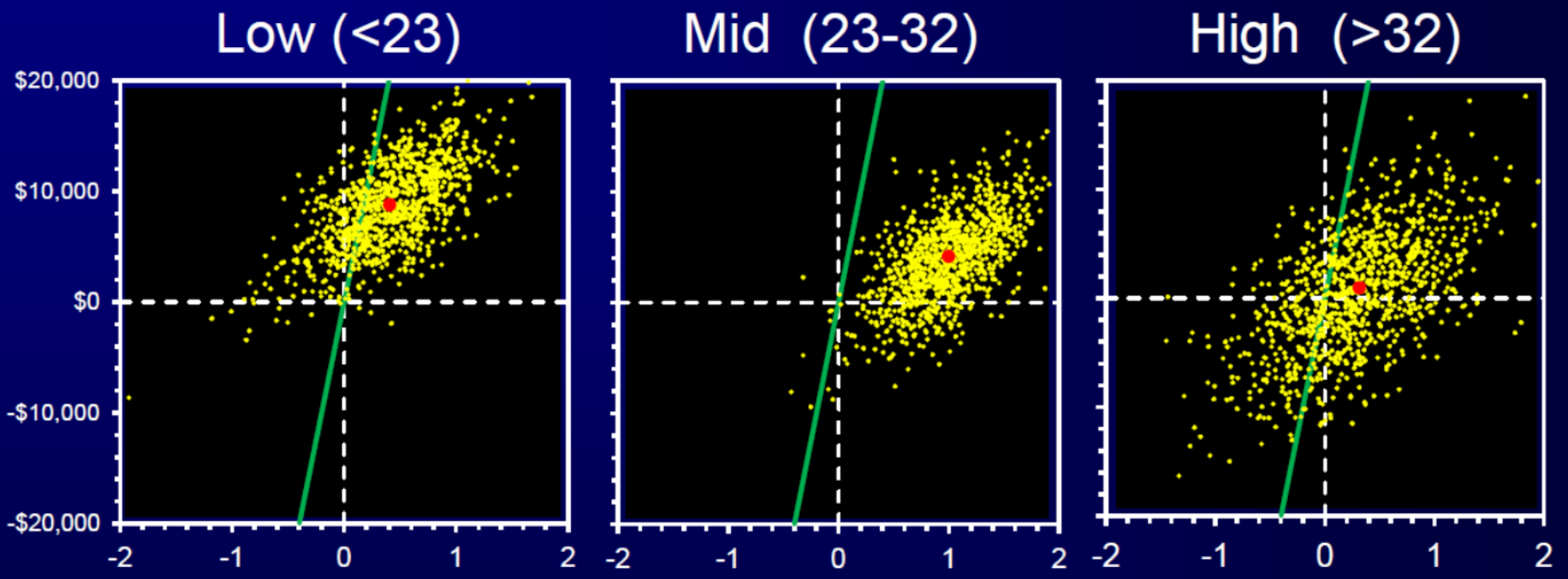
Lifetime Cost-Effectiveness Results



Costs and QALYs discounted 3% annually

Cost-Effectiveness of CABG vs. PCI

SYNTAX Score Tertiles



Δ Costs	$8,784
Δ QALYs	0.407
ICER	**$21,582**

Δ Costs	$4,160
Δ QALYs	0.997
ICER	**$4,172**

Δ Costs	$973
Δ QALYs	0.315
ICER	**$3,088**

Costs and QALYs discounted 3% annually

Conclusions

- For patients with diabetes and multivessel CAD, CABG provides not only better long-term clinical outcomes than DES-PCI but these benefits are achieved at an overall cost that represents an attractive use of societal health care resources
- These findings provide additional support for existing guidelines that recommend CABG for diabetic patients with multivessel CAD

CABG Again Outshines Stenting for Some Patients With Coronary Artery Blockage

Mike Mitka, MSJ

LOS ANGELES—A study of patients with diabetes in need of multivessel revascularization has shown that coronary artery bypass graft (CABG) surgery produces better outcomes than percutaneous coronary intervention (PCI). The study, highlighted here in November during the annual Scientific Sessions of the American Heart Association (AHA), adds to the growing list of investigations showing superiority of CABG over PCI in a variety of patient populations.

Yet mounting evidence suggests that PCI continues to be performed at rates higher than is appropriate. So why does it remain difficult for interventional cardiologists to embrace this corner of the evidence-based medicine world?

At the AHA meeting, attendees heard the results from the Future Revascularization Evaluation in Patients With Diabetes Mellitus: Optimal Management of Multivessel Disease (FREEDOM) trial. The FREEDOM researchers randomized 1900 patients with diabetes and

"CABG surgery is the preferred intervention for patients with diabetes and multivessel disease," said Valentin Fuster, MD, PhD, senior author of FREEDOM

Antonia Reeve/www.sciencesource.com

New findings suggest that coronary artery bypass graft surgery produces better outcomes than stenting in patients with diabetes who require multivessel revascularization.

103 549 patients who underwent PCI for treatment of 2-vessel or 3-vessel coronary artery disease without acute myocardial infarction from 2004 through 2008 (Weintraub WS et al. *N Engl J Med.* 2012;366[16]:1467-1476).

William S. Weintraub, MD, one of ASCERT's principal investigators and director of the Christiana Center for Outcomes Research in Wilmington, Del, said the FREEDOM trial should reinforce the superiority of CABG in revascularization of complicated patients. "Overall, surgery has been in decline for a number of years, and we've moved to less invasive procedures fairly easily," said Weintraub in an interview. "But with FREEDOM, you are moving the needle back toward surgery."

Fred H. Edwards, MD, another principal investigator with ASCERT and emeritus professor in the department of surgery at the University of Florida Academic Health Center in Jacksonville, said his trial and FREEDOM should give clinicians the evidence they need to make better-informed deci-

Final Five-Year Follow-up of the SYNTAX Trial:

Optimal Revascularization Strategy in Patients With Three-Vessel Disease and/or Left Main Disease

Friedrich W. Mohr, MD PhD
Herzzentrum Universität Leipzig
Leipzig, Germany
On behalf of the SYNTAX investigators

Conflicts of Interest: None

SYNTAX Trial Design

De novo disease (n=1800)

Limited Exclusion Criteria

- Previous interventions
- Acute MI with CPK>2x
- Concomitant cardiac surgery

Left Main Disease (isolated, +1, +2 or +3 vessels)	3 Vessel Disease (revasc all 3 vascular territories)
N=705	**N=1095**

Primary endpoint = death/MI/stroke/repeat revasc at 1 year

Serruys PW et al. NEJM 2009;360:961-72

Study Design & Patient Disposition

62 EU Sites + 23 US Sites

De novo 3VD and/or LM (isolated, +1,2,3 VD)

Heart Team (Surgeon & Interventional Cardiologist) Review
- Randomized if suitable for either CABG or PCI *or*
- Enrolled in nested registry if not equally suitable

CABG Reg. n=649*	CABG RCT n=897	*Enrolled*	PCI RCT n=903	PCI Registry n=198
CABG n=644**	CABG 849 (94.6%)	*Primary Endpoint 1 Year Follow-up*	PCI 891 (98.7%)	PCI n=192**
CABG 610 (94.7%)	CABG 805 (89.7%)	*Completed Study 5 Year Follow-up*	PCI 871 (96.5%)	PCI 188 (97.9%)

*N=649 followed for 5 years, N=1077 enrolled, **CABG N=644, PCI N=192 treated per protocol. PCI performed with TAXUS Express

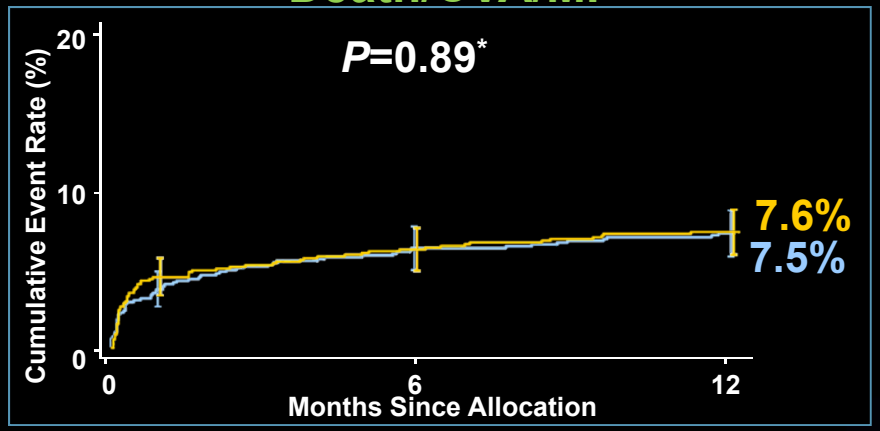
Patient Characteristics

	CABG RCT N=897	PCI RCT N=903	*P* value	CABG Registry N=644	PCI Registry N=192
Age* (y)	65.0±9.8	65.2±9.7	0.55	65.7±9.4	71.2±10.4
Male, %	78.9	76.4	0.20	80.7	70.3
Diabetes*†, %	24.6	25.6	0.64	26.4	30.2
Additive euroSCORE*	3.8±2.7	3.8±2.6	0.78	3.9±2.7	5.8±3.1
Total Parsonnet score*	8.4±6.8	8.5±7.0	0.76	9.0±7.1	14.4±9.5
Total SYNTAX Score	29.1±11.4	28.4±11.5	0.19	37.8±13.3	31.6±12.3
Mean # of lesions	4.4±1.8	4.3±1.8	0.44	4.6±1.7	4.5±1.8
3VD only, %	66.3	65.4	0.70	59.7	66.7
Left main, any, %	33.7	34.6	0.70	40.3	33.3
Total occlusion, %	22.2	24.2	0.33	56.4	36.5
Complete revasc, %	63.2	56.7	0.005	74.7	36.5

Values are mean±SD or %. Core laboratory reported unless *Site-reported †Medically treated

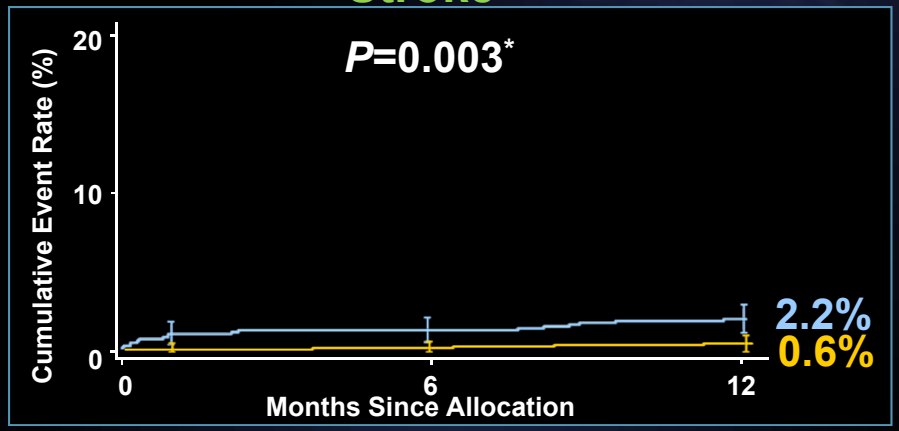
Summary of Primary Endpoint (1 Year)

Death/CVA/MI



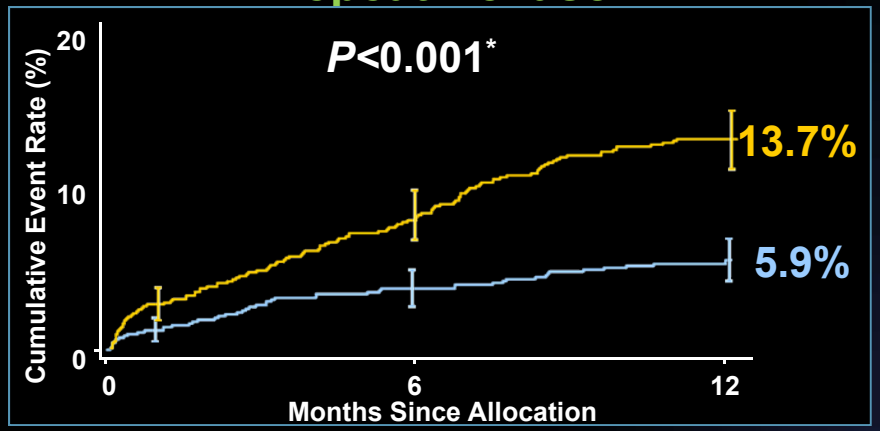
Cumulative KM Event Rate ± 1.5 SE; log-rank *P* value;*Binary rates ITT population

Stroke



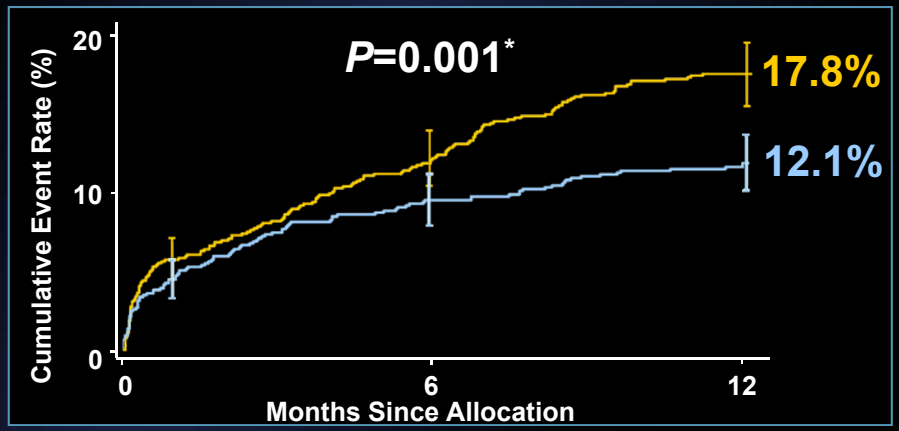
Cumulative KM Event Rate ± 1.5 SE; log-rank *P* value;*Binary rates ITT population

Repeat Revasc.



Cumulative KM Event Rate ± 1.5 SE; log-rank *P* value;*Binary rates ITT population

MACCE

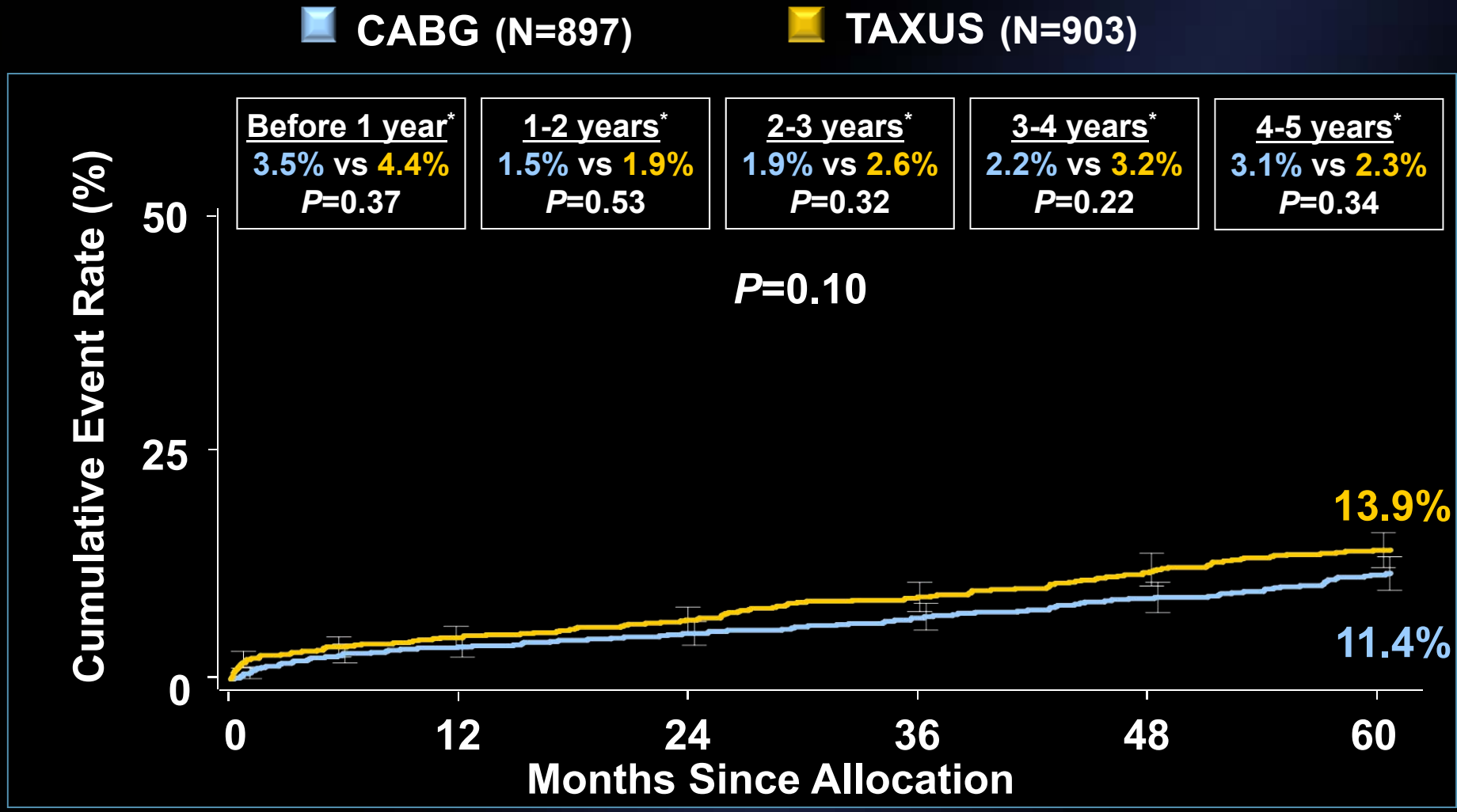


Cumulative KM Event Rate ± 1.5 SE; log-rank *P* value;*Binary rates ITT population

- Death/CVA/MI rates were similar between CABG and PCI
- Stroke was increased in CABG vs PCI
- Repeat revascularization and MACCE were increased in PCI vs CABG

CABG (N=897) PCI (N=903)

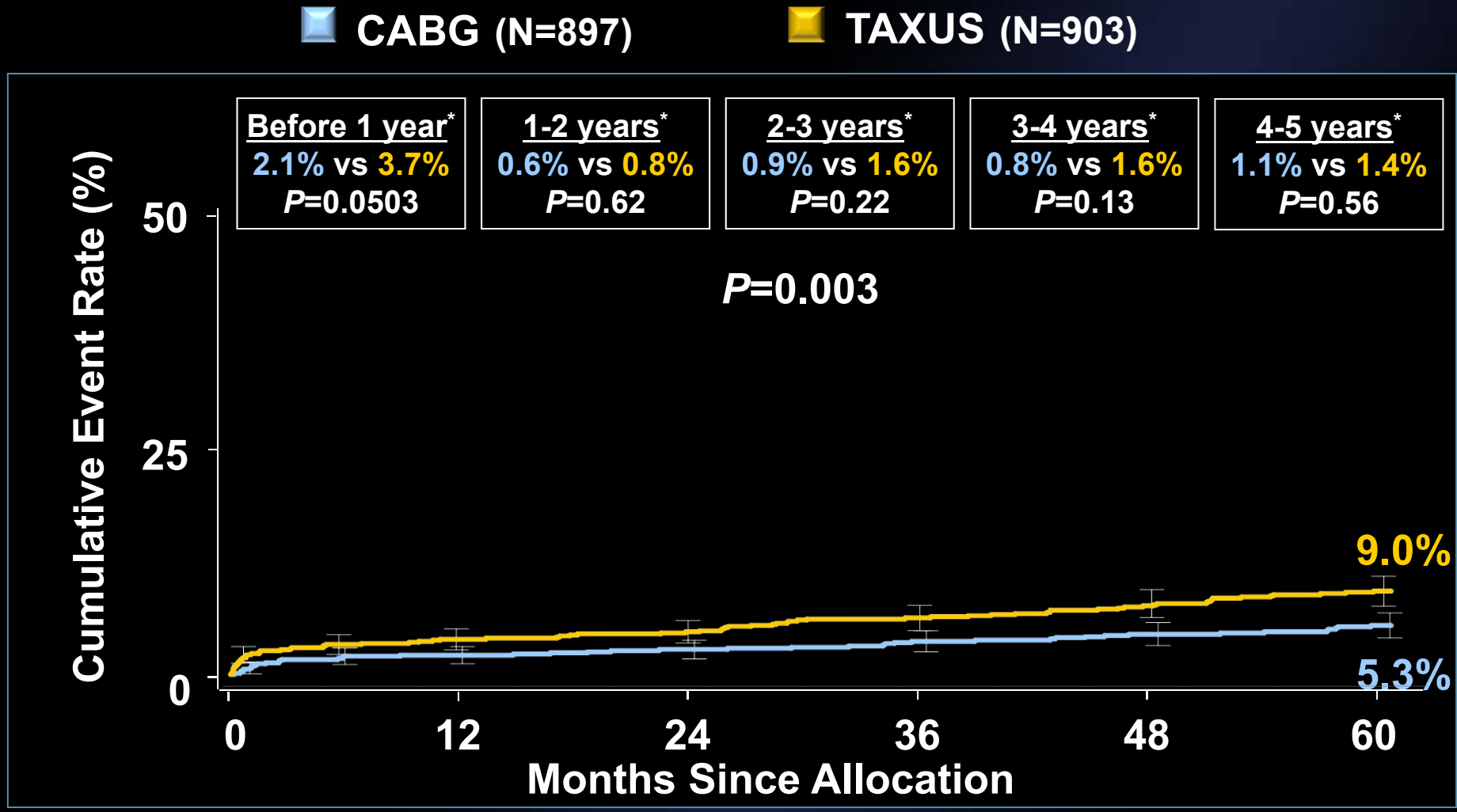
All-Cause Death to 5 Years



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

ITT population

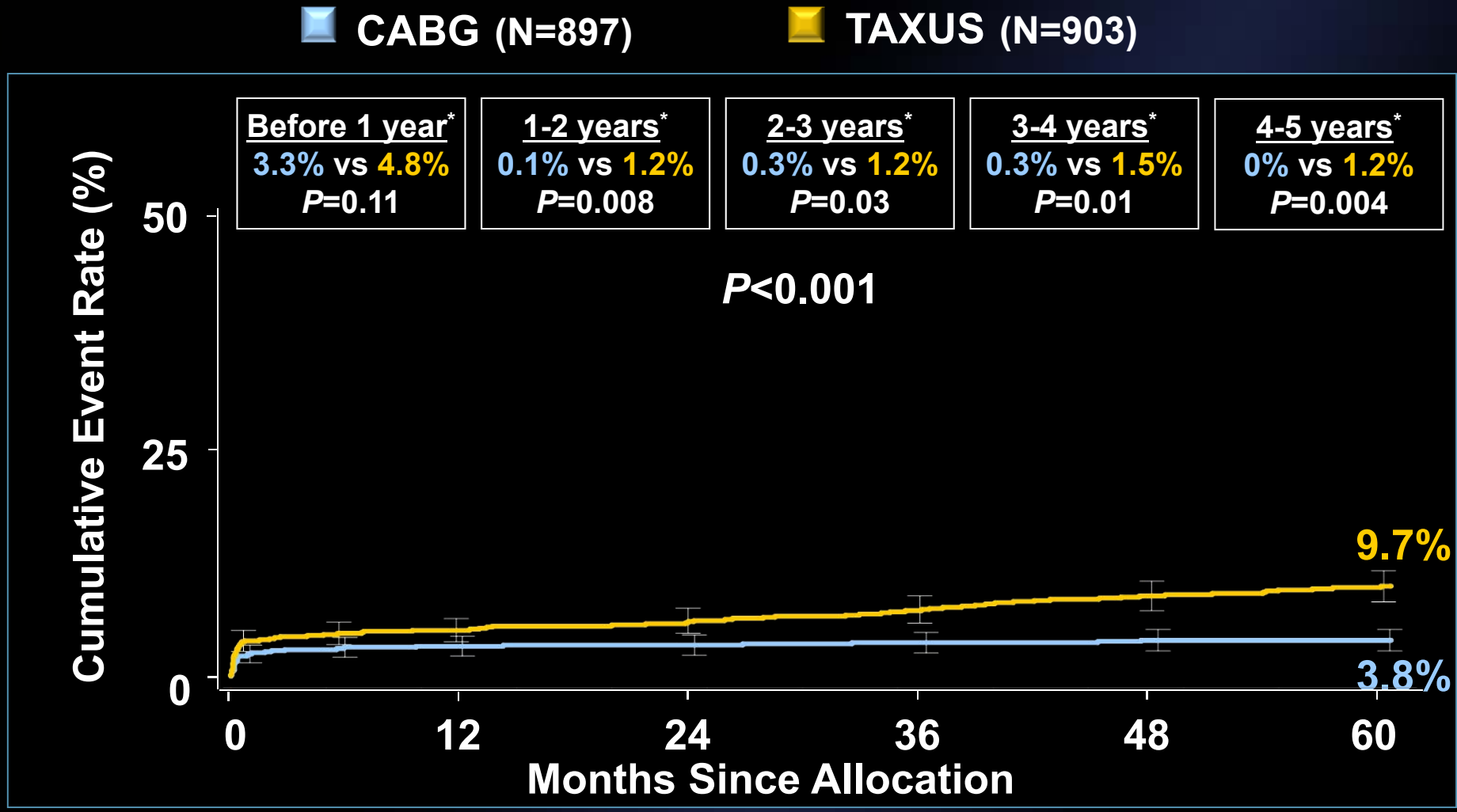
Cardiac Death to 5 Years



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

ITT population

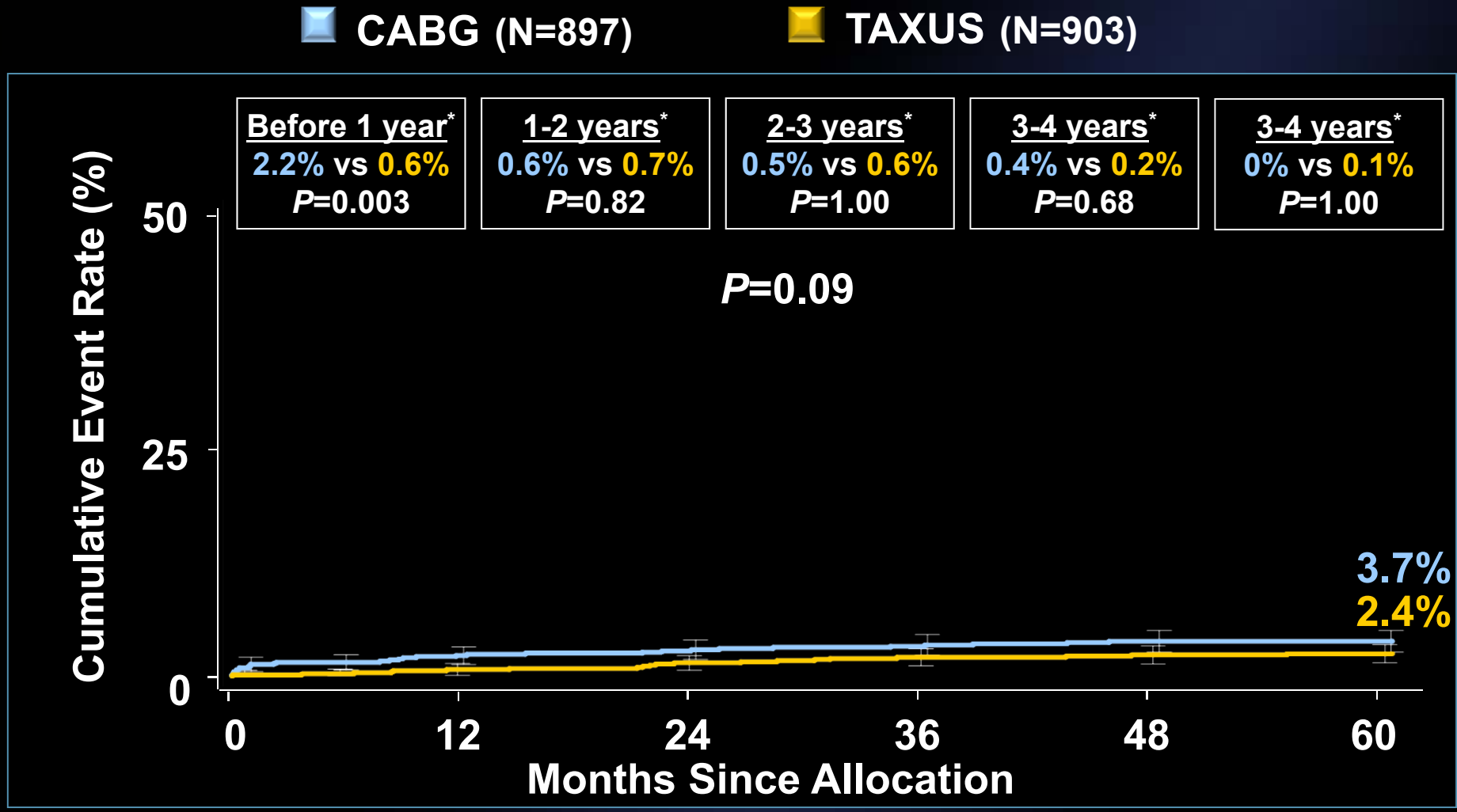
Myocardial Infarction to 5 Years



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

ITT population

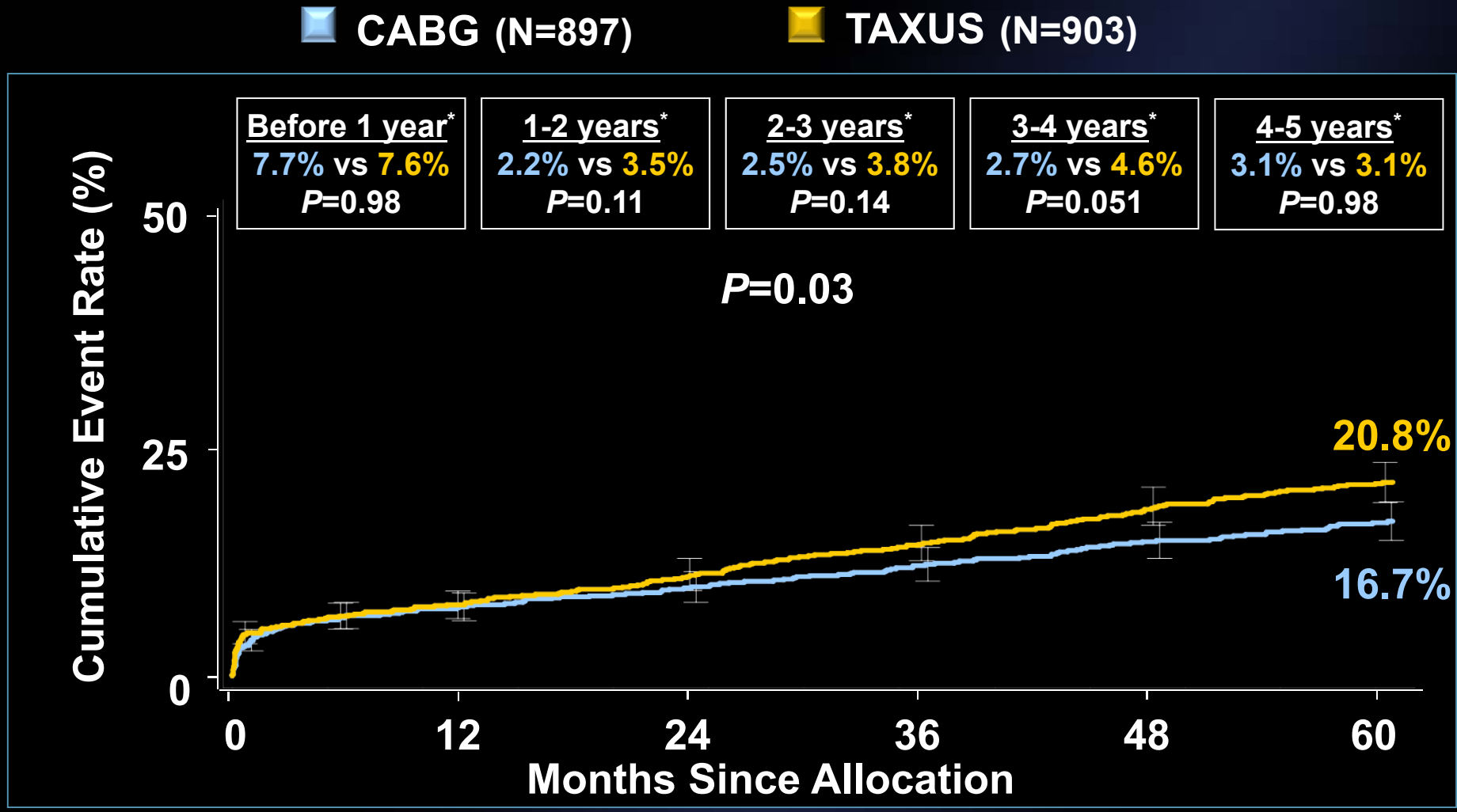
CVA to 5 Years



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

ITT population

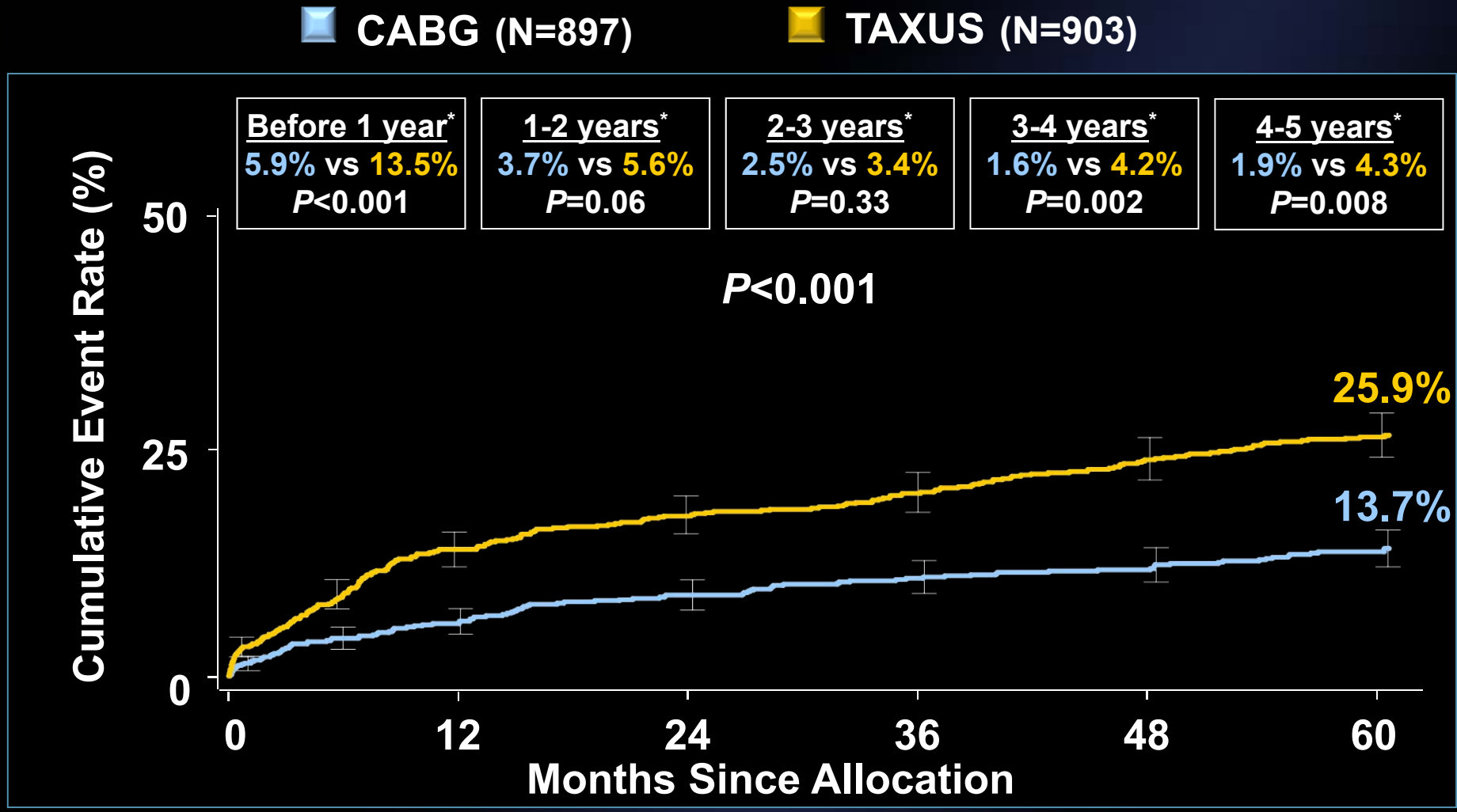
All-Cause Death/CVA/MI to 5 Years



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

ITT population

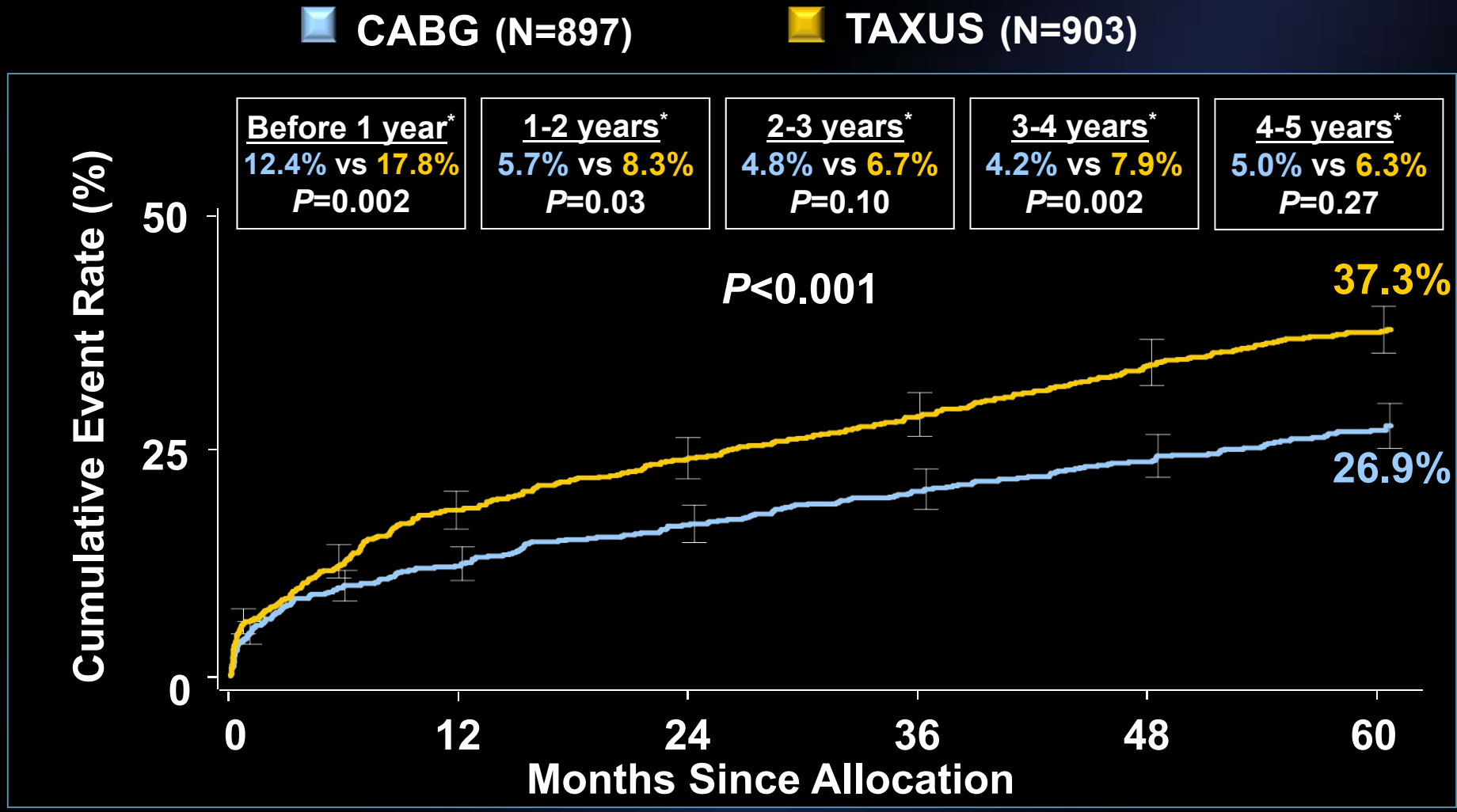
Repeat Revascularization to 5 Years



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

ITT population

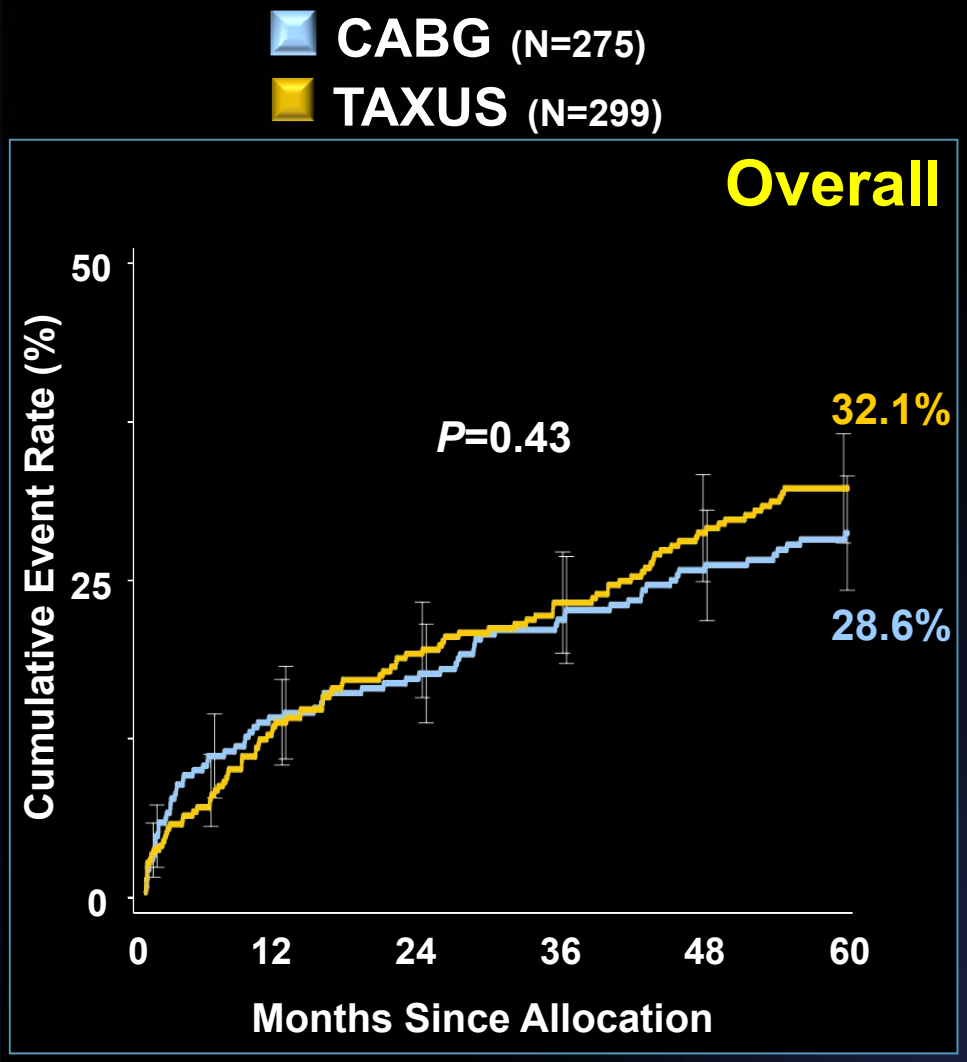
MACCE to 5 Years



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

ITT population

MACCE to 5 Years by SYNTAX Score Tercile *Low Scores (0–22)*



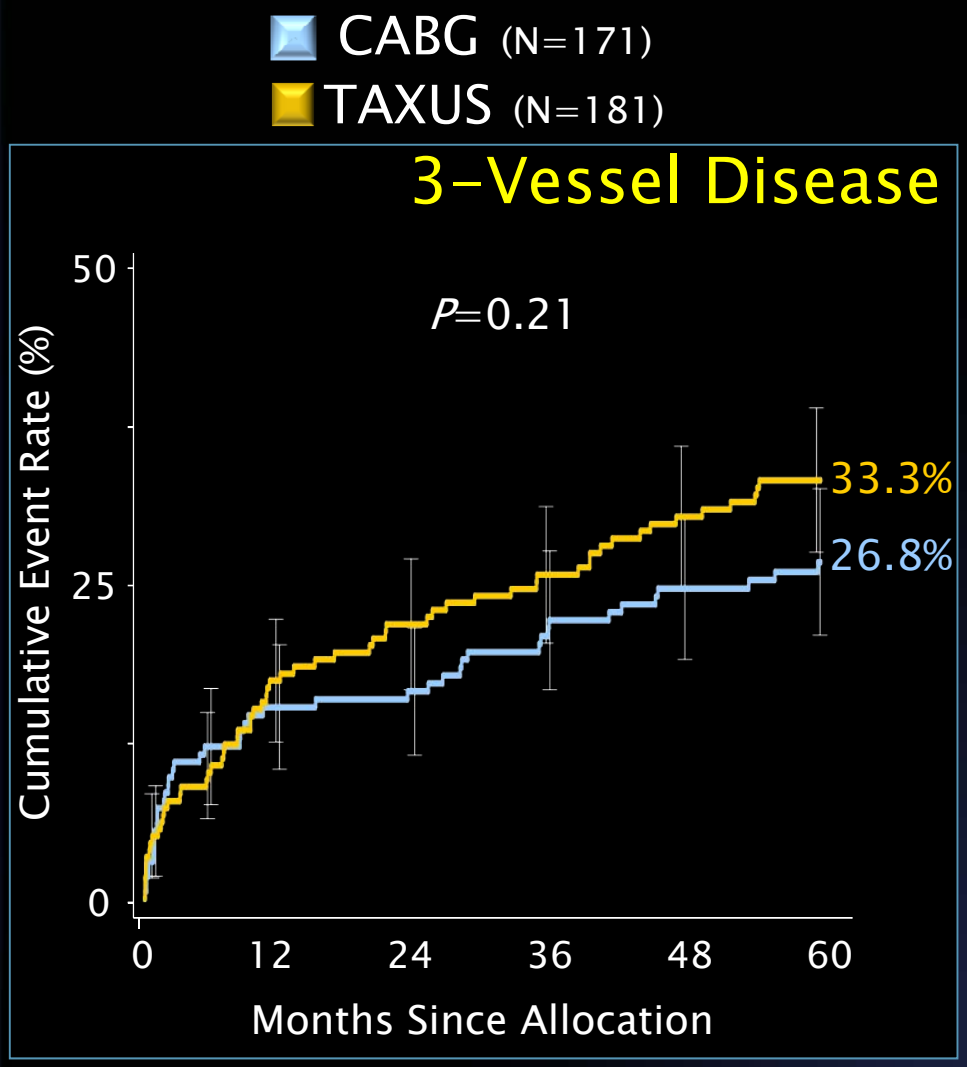
	CABG	PCI	*P* value
Death	10.1%	8.9%	0.64
CVA	4.0%	1.8%	0.11
MI	4.2%	7.8%	0.11
Death, CVA or MI	14.9%	16.1%	0.81
Revasc.	16.9%	23.0%	0.06

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

Core lab-reported Data; ITT population

MACCE to 5 Years by SYNTAX Score Tercile

3VD Subset Low Scores 0–22

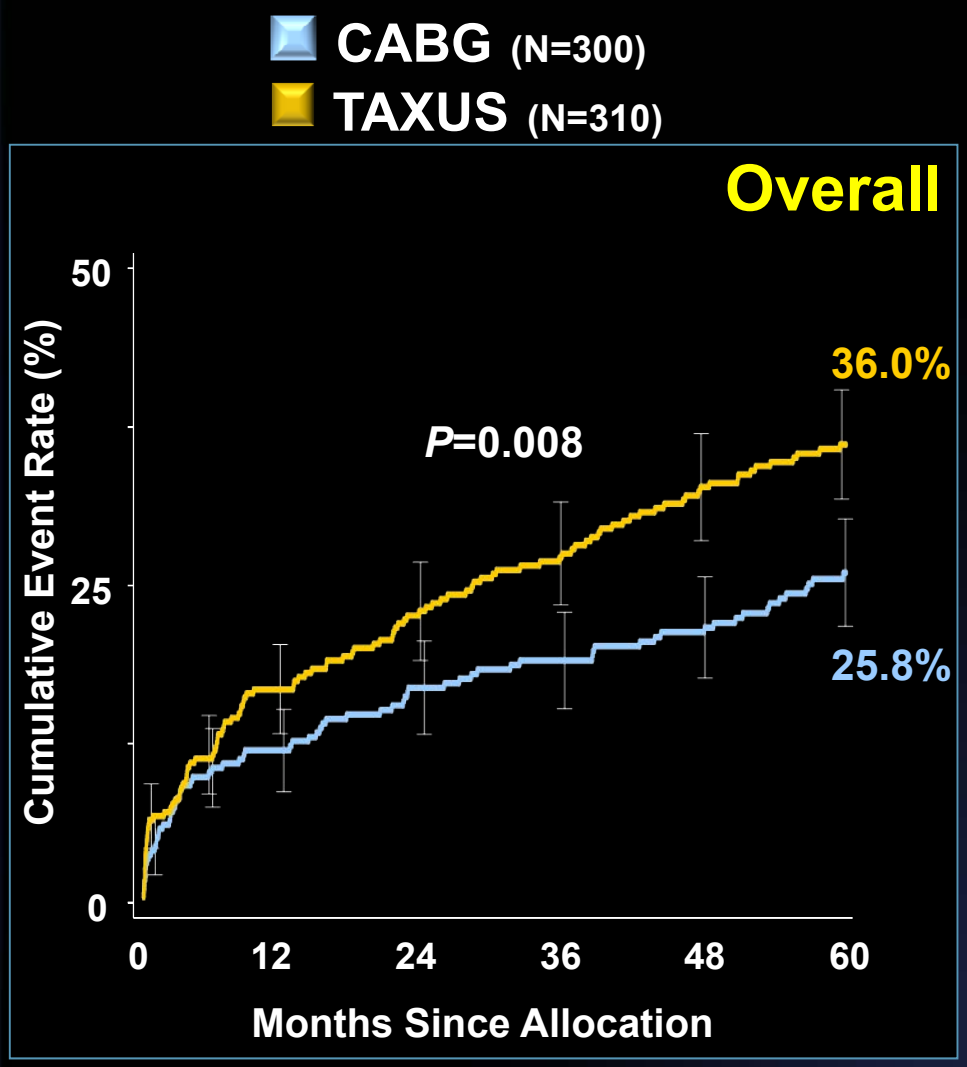


	CABG	PCI	*P* value
Death	9.3%	10.2%	0.81
CVA	3.9%	1.8%	0.24
MI	4.9%	8.8%	0.20
Death, CVA or MI	14.8%	17.5%	0.56
Revasc.	14.6%	23.1%	0.04

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

Site-reported Data; ITT population

MACCE to 5 Years by SYNTAX Score Tercile *Intermediate Scores (23–32)*



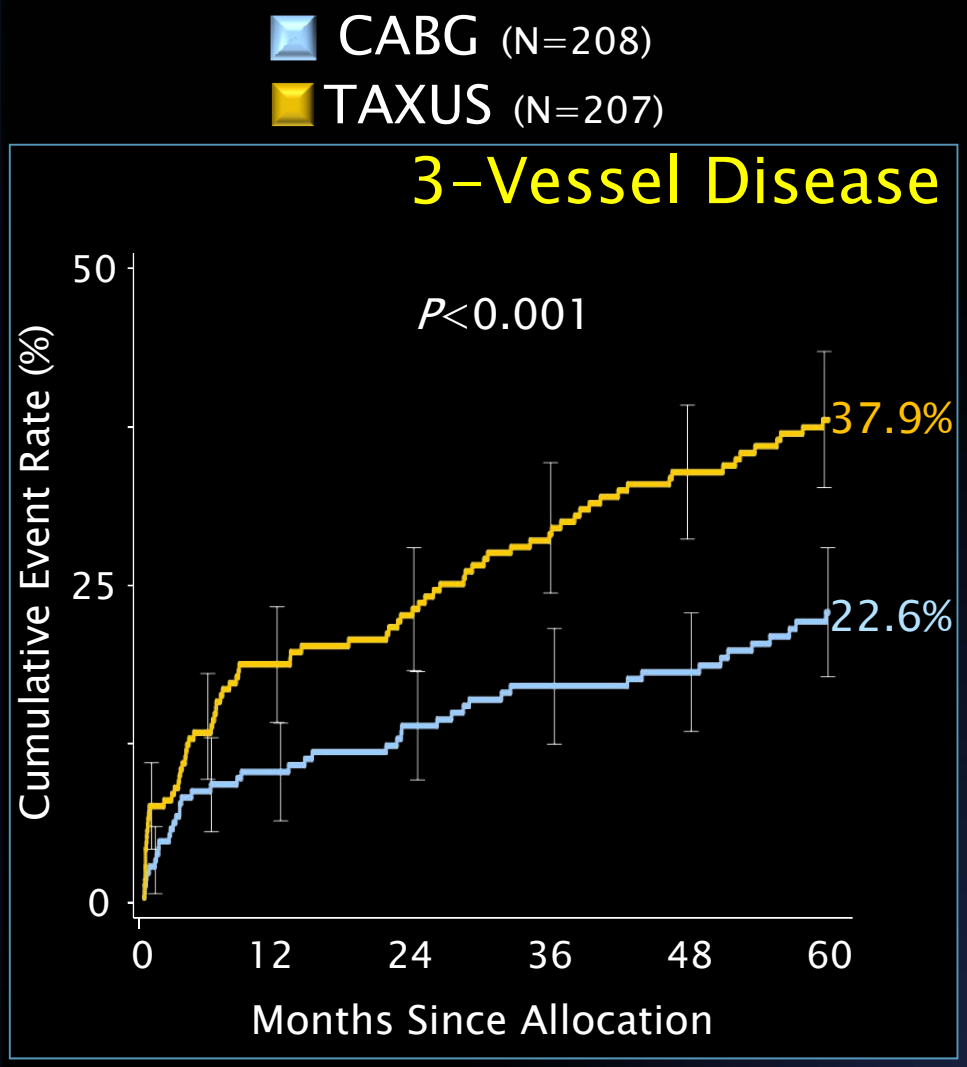
	CABG	PCI	*P* value
Death	12.7%	13.8%	0.68
CVA	3.6%	2.0%	0.25
MI	3.6%	11.2%	<0.001
Death, CVA or MI	18.0%	20.7%	0.42
Revasc.	12.7%	24.1%	<0.001

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

Core lab-reported Data; ITT population

MACCE to 5 Years by SYNTAX Score Tercile

3VD Subset Intermediate Scores 23–32

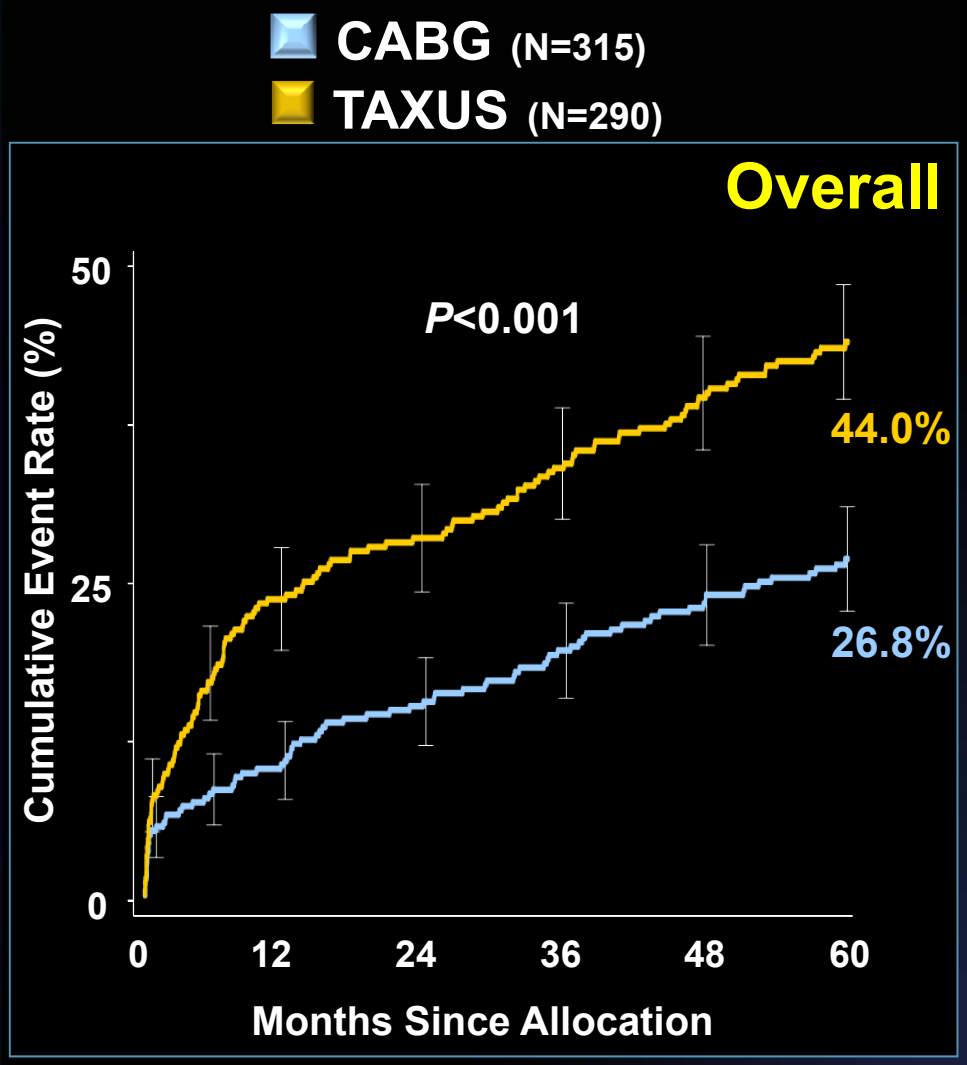


	CABG	PCI	*P* value
Death	9.6%	16.3%	0.047
CVA	3.6%	2.5%	0.53
MI	3.1%	13.8%	<0.001
Death, CVA or MI	14.7%	23.2%	0.04
Revasc.	11.0%	25.1%	<0.001

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

Site-reported Data; ITT population

MACCE to 5 Years by SYNTAX Score Tercile *High Scores (≥33)*



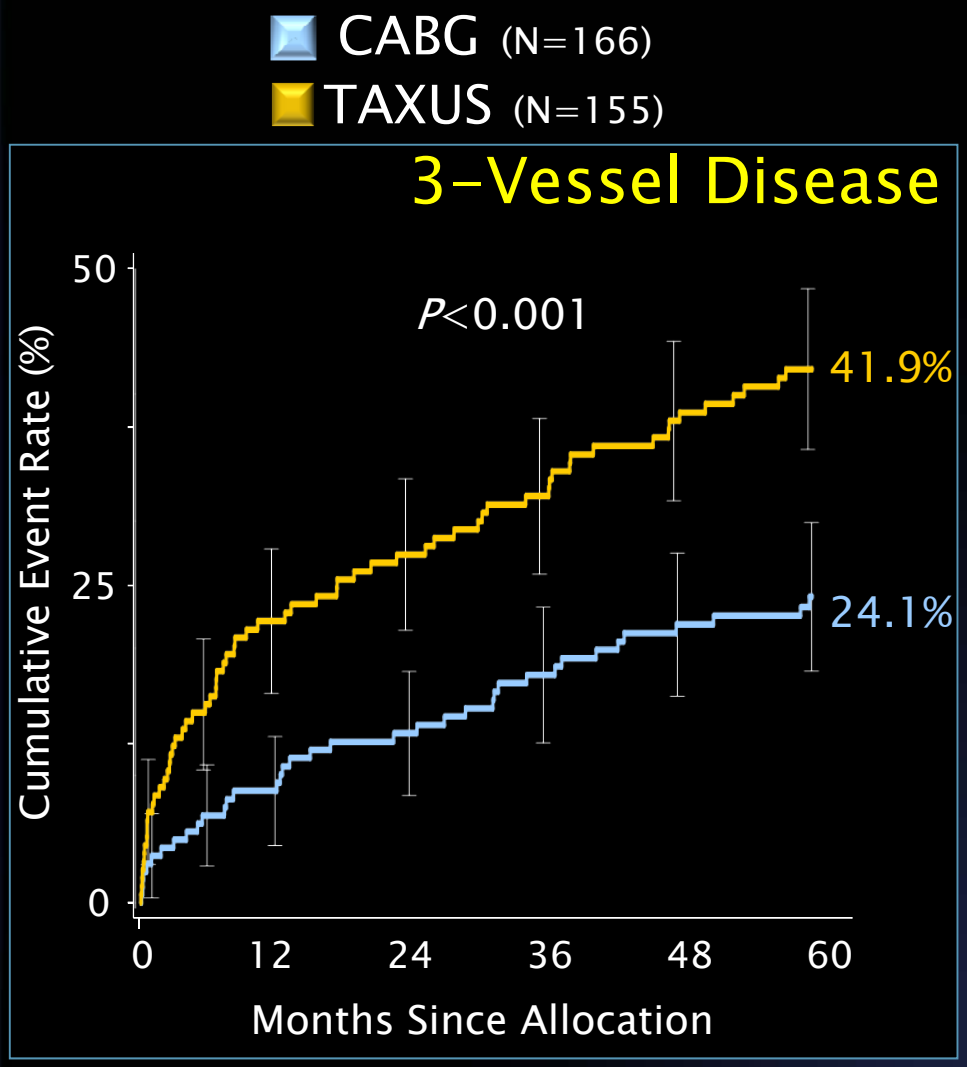
	CABG	PCI	*P* value
Death	11.4%	19.2%	0.005
CVA	3.7%	3.5%	0.80
MI	3.9%	10.1%	0.004
Death, CVA or MI	17.1%	26.1%	0.007
Revasc.	12.1%	30.9%	<0.001

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

Core lab-reported Data; ITT population

MACCE to 5 Years by SYNTAX Score Tercile

3VD Subset High Scores ≥33

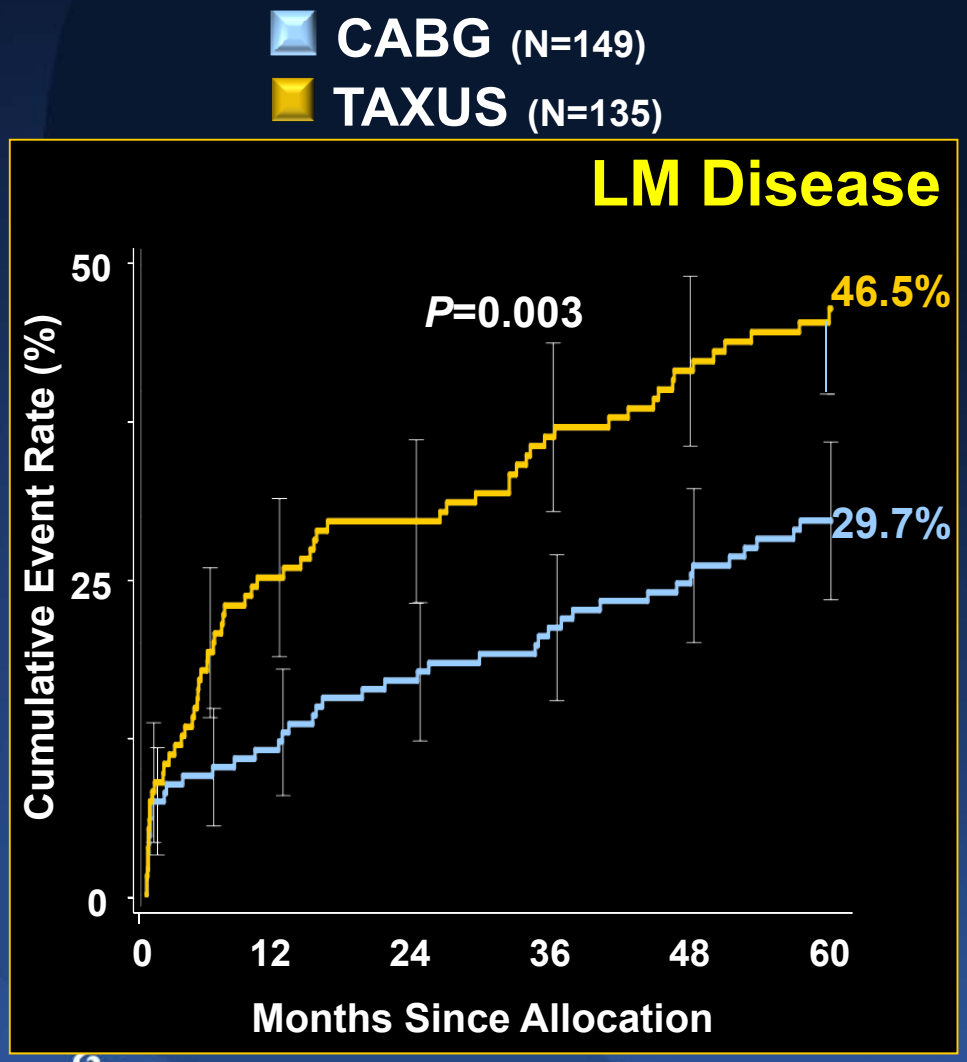


	CABG	PCI	*P* value
Death	8.8%	17.8%	0.02
CVA	2.6%	5.1%	0.31
MI	1.9%	8.7%	0.008
Death, CVA or MI	12.5%	26.2%	0.002
Revasc.	12.6%	28.2%	<0.001

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

Site-reported Data; ITT population

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



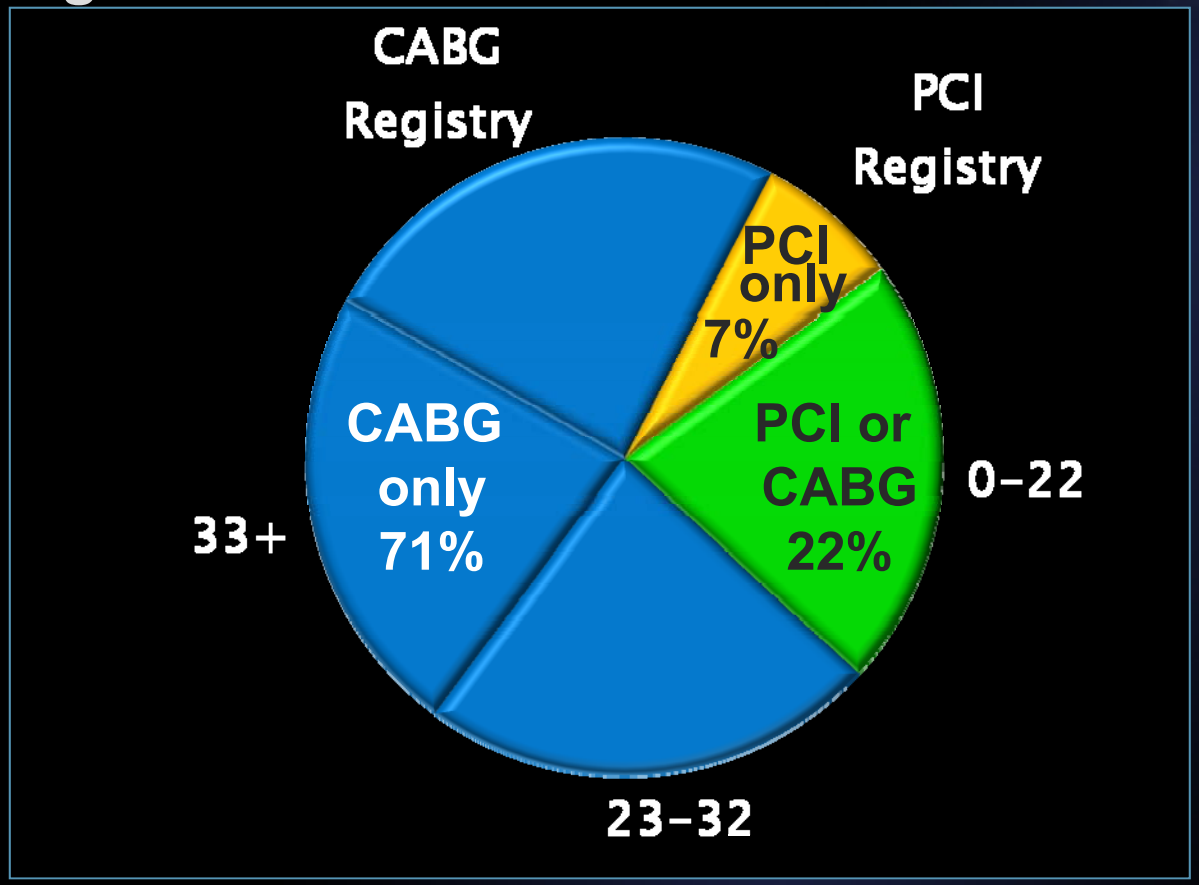
	CABG	PCI	*P* value
Death	14.1%	20.9%	0.11
CVA	4.9%	1.6%	0.13
MI	6.1%	11.7%	0.13
Death, CVA or MI	22.1%	26.1%	0.40
Revasc.	11.6%	34.1%	<0.001

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

Site-reported Data; ITT population

MACCE to 5 Years

Interpreting Results Based on SYNTAX Score



Five-year results of the SYNTAX trial suggest that 71% of all patients are still best treated with CABG; however, for the remaining patients PCI is an alternative to surgery

Summary & Conclusions

- 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

Are FREEDOM and SYNTAX conclusions consistent with real-world experience?

3-year Outcomes Within PCI and CABG Registries Stratified by SYNTAX Score

3,075 pts in SYNTAX

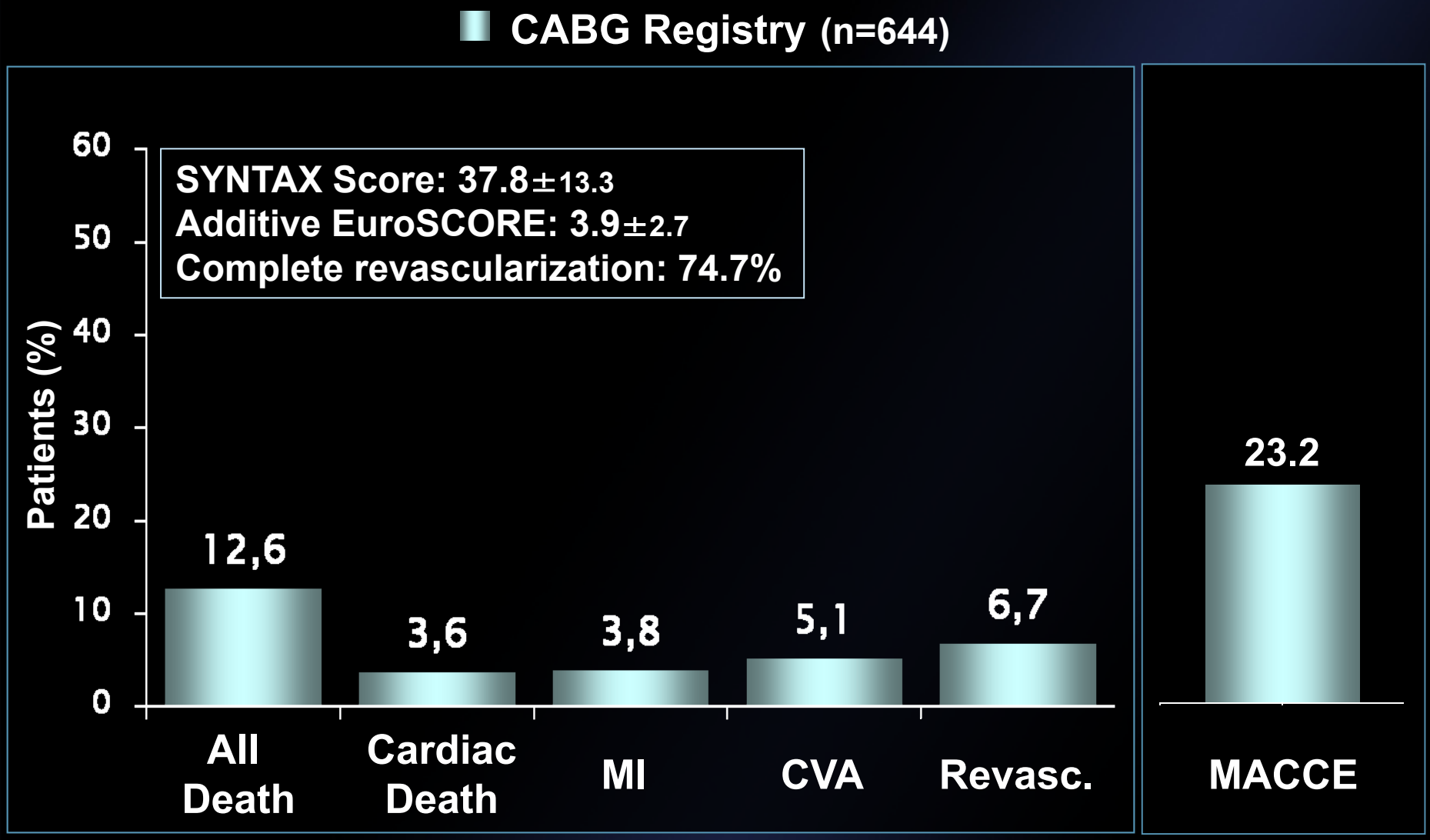
6.4% in PCI Registry
- 71% b/o too high risk for CABG

35% in CABG Registry
- 71% b/o too complex anatomy

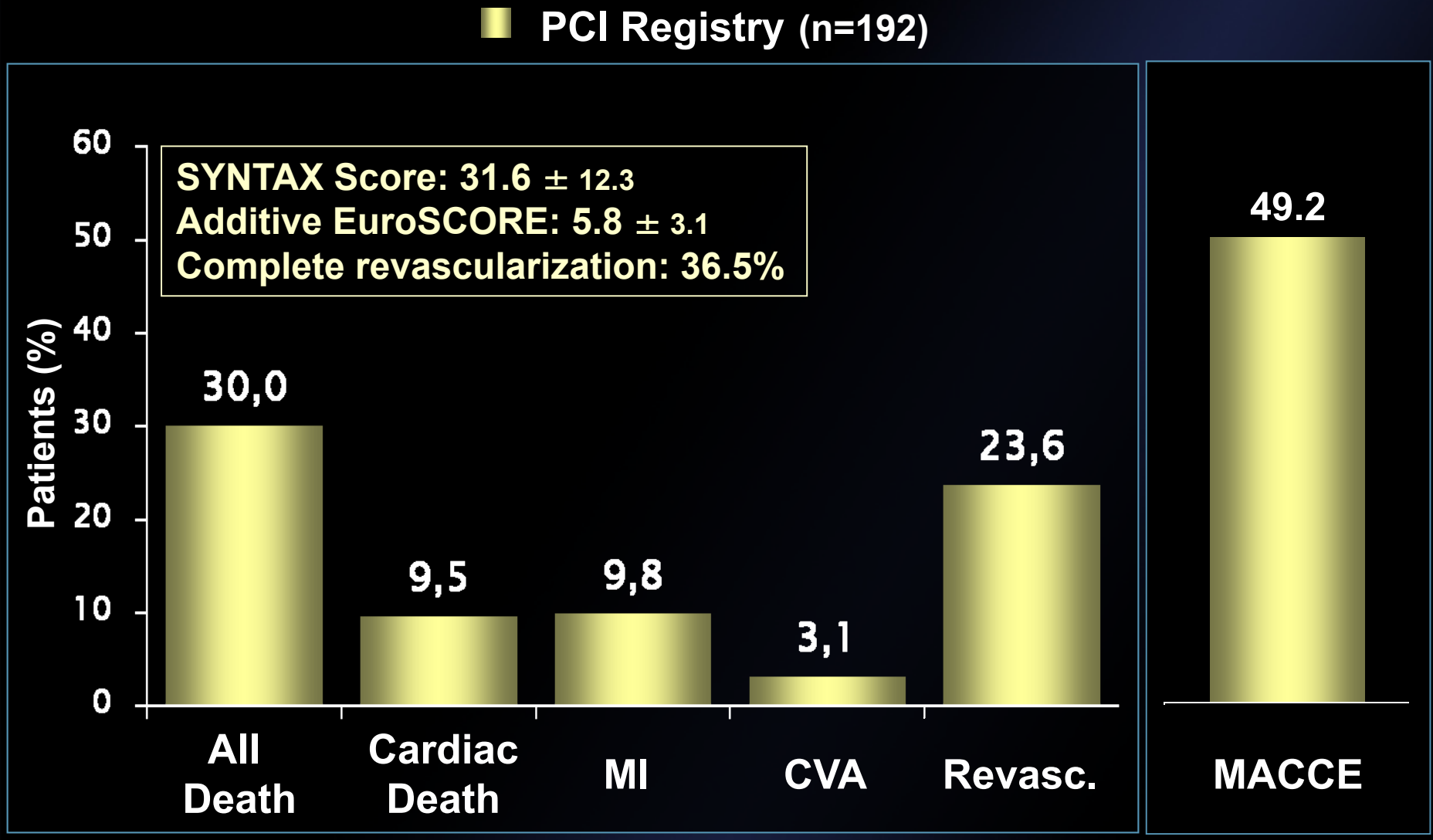
DM more prevalent in PCI
(35% vs 30% all, 15% vs 9% IDDM)

Head et al.; JACC: Cardiovascular Interventions,Vol.5,No.6,2012:618–25

MACCE to 5 Years
SYNTAX CABG Registry



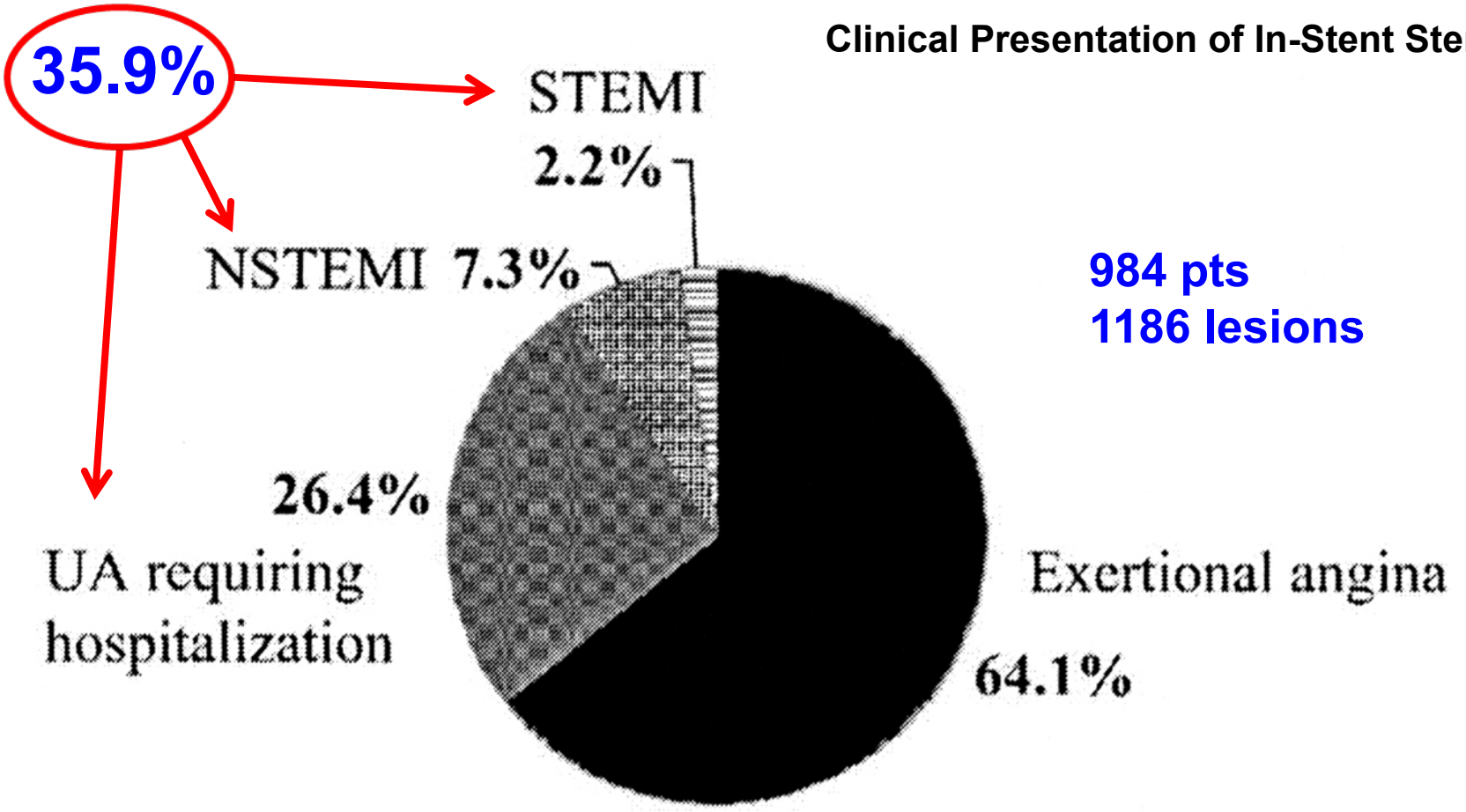
MACCE to 5 Years
SYNTAX PCI Registry



What's the big deal about Re-stenosis?

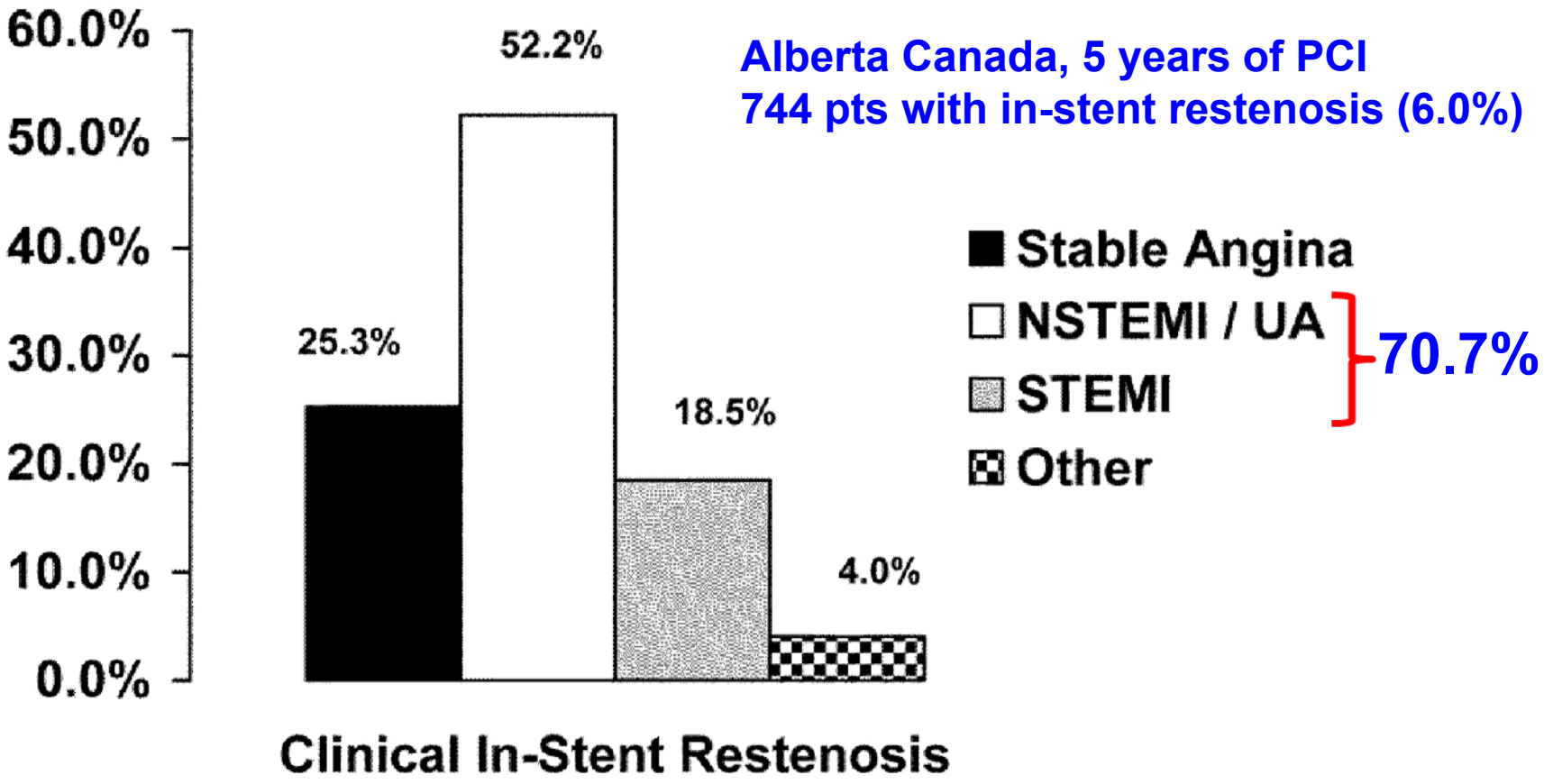
Just do PCI again!

Is In-stent Re-stenosis Benign?



Chen et al, Am Heart J 2006;151:1260-4

Is In-stent Restenosis Benign?



Patient presentation with clinical ISR ($n=744$)

Bainey et al, Int J Cardiol 2008;128:378-82

Treatment of DES Re-stenosis

- PCI for DES re-stenosis
  - 24 pts
  - 82% had BMS
  - F/U 1 year
  - 23% re-re-stenosis

"…secondary failure rate *only* 23%…."

Moussa et al, Am J Cardiol 2006;97:1582-84

Treatment of DES In-Stent Re-stenosis

Quantitative coronary angiographic data

Variable	Same DES	Different DES	P
Preprocedure	107	94	
RVD (mm)	3.04 ± 1.04	2.81 ± 0.62	
MLD (mm)	0.98 ± 0.55	0.86 ± 0.55	
DS (%)	67.3 ± 13.8	70.1 ± 17.2	
Lesion length (mm)	12.9 ± 9.6	11.7 ± 7.4	
Postprocedure			
RVD (mm)	3.26 ± 0.54	3.16 ± 0.51	.19
MLD (mm)	2.86 ± 0.54	2.77 ± 0.53	.22
DS (%)	12.4 ± 7.7	12.3 ± 8.4	.88
Follow-up	72	66	
RVD (mm)	3.09 ± 0.46	3.1 ± 0.58	.95
MLD (mm)	2.2 ± 0.89	2.0 ± 1.1	.32
DS (%)	29.6 ± 25	37.1 ± 30	.18
Restenosis	26.4% (19)	25.8% (17)	1.0

Data are presented as percentages and absolute numbers or means and SD. *RVD*, Reference vessel diameter; *MLD*, minimal lumen diameter; *DS*, diameter stenosis.

DES ISR
201 lesions
174 pts
Angio at 9 mos in 70%

Cosgrave et al, Am Heart J 2007;153:354-9

Outcomes of PCI to treat In-Stent Re-stenosis or Thrombosis

Kaplan-Meier Estimates	Overall (n = 92)	Homo-Stents (n = 59)	Hetero-Stents (n = 18)	Other (n = 15)
6 Month	**Percent of Patients (95% CI)**			
Death	4.4 (1.7–11.3)	3.4 (0.9–12.9)	5.9 (0.9–35.0)	6.7 (0.9–38.7)
Myocardial infarction	0	0	0	0
Target lesion revascularization†	9.7 (5.3–17.3)	8.1 (3.4–18.3)	14.3 (4.8–38.0)	10.0 (2.6–34.4)
All MACE, % of patients (95% CI)	12.7 (7.2–21.7)	9.1 (3.9–20.6)	17.6 (6.1–45.3)	21.0 (7.3–52.1)
12 Month	**Percent of Patients (95% CI)**			
Death	6.7 (3.1–14.3)	6.8 (2.6–17.2)	5.9 (0.9–35.0)	6.7 (0.9–38.7)
Myocardial infarction	2.4 (0.3–16.1)	0	0	20.0 (3.1–79.6)
Target lesion revascularization†	28.2 (20.4–38.2)	28.5 (18.8–42.0)	19.0 (7.6–43.1)	36.5 (19.3–62.0)
All MACE, % of patients (95% CI)	42.9 (31.5–56.4)	43.0 (29.5–59.5)	25.1 (10.1–54.4)	76.3 (38.1–98.7)

All differences among study groups are statistically non-significant. *Three patients underwent 2 separate procedures for in-stent restenosis of different lesions; †total number of lesions = 108.

CI = confidence interval; MACE = major adverse cardiac events.

12 months:

6.7% Death

28.2% TLR

MACE 42.9%

Mishkel et al, J Am Coll Cardiol 2007;49:181-4

Consequences of Re-Re-stenosis

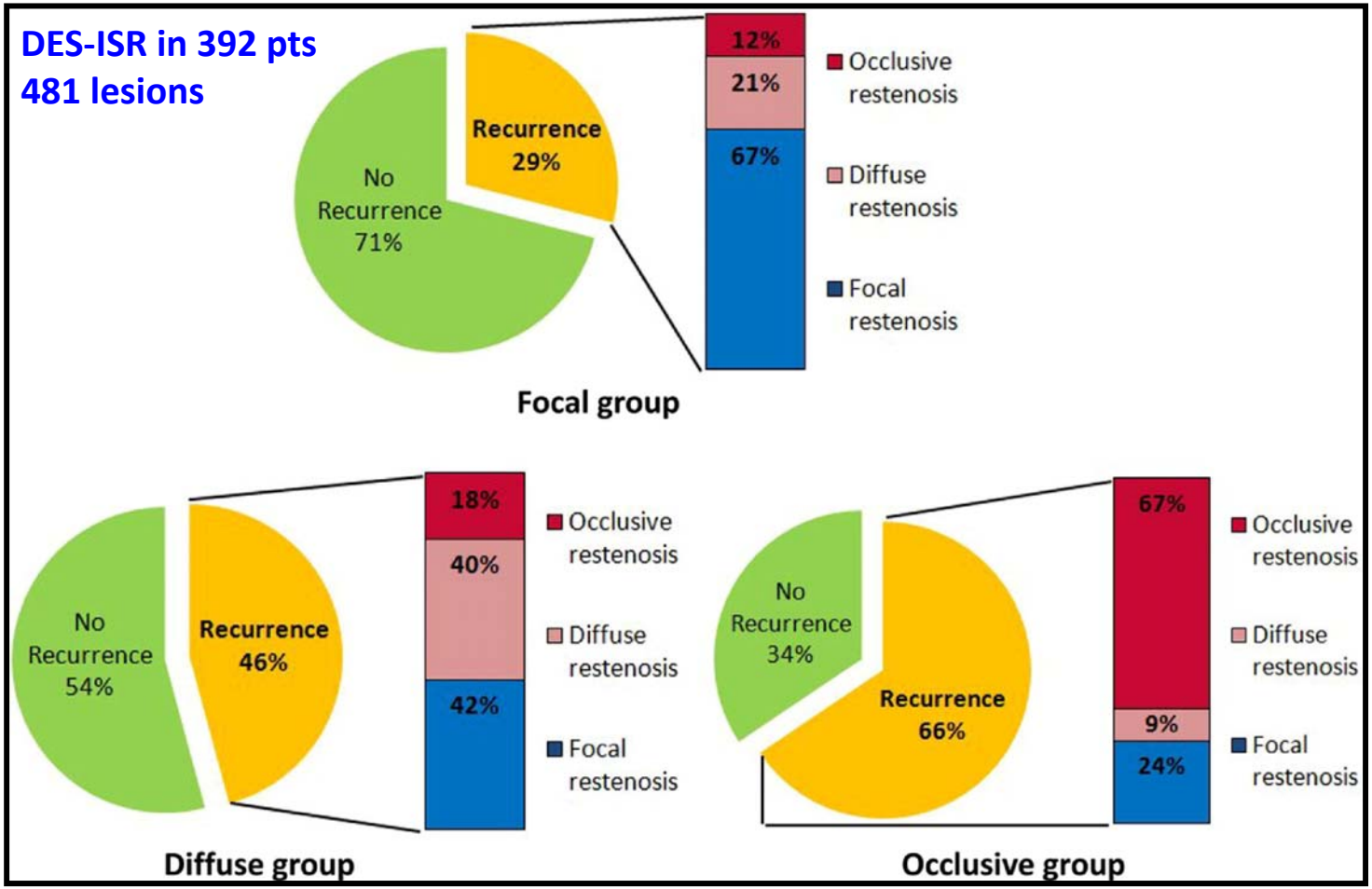
Clinical Outcomes at 2 Years after PCI for SES

114 pts with restenosis
101 treated and restudied

	Restenosis
Total number of patients	101
MI (%)	4 (3.9)
SAT (%)	0 (0)
LST (%)	0 (0)
CHF (%)	2 (2.0)
TLR (%)	36 (35.6)
PCI (%)	34 (33.7)
CABG (%)	2 (1.9)
Death (%)	8 (7.9)
Noncardiac (%)	4 (3.9)
Cardiac (%)	4 (3.9)
Total MACE (%)	44 (43.5)

Chatani et al, J Interven Cardiol 2009;22:354-61

Outcomes After PCI for DES-ISR According to Initial Pattern of Restenosis



Patterns of Recurrent Angiographic Restenosis According to the Initial Pattern of Restenosis. For each of the initial patterns of restenosis, the rate of recurrent restenosis after treatment of DES-ISR is shown as a pie chart with the pattern of recurrence in the bar graph.

Azeem Latib, et al.; JACC: Cardiovascular Interventions: Vol. 4, No. 2, 2011, February 2011:155–64

Impact of Stenosis after PCI on Survival

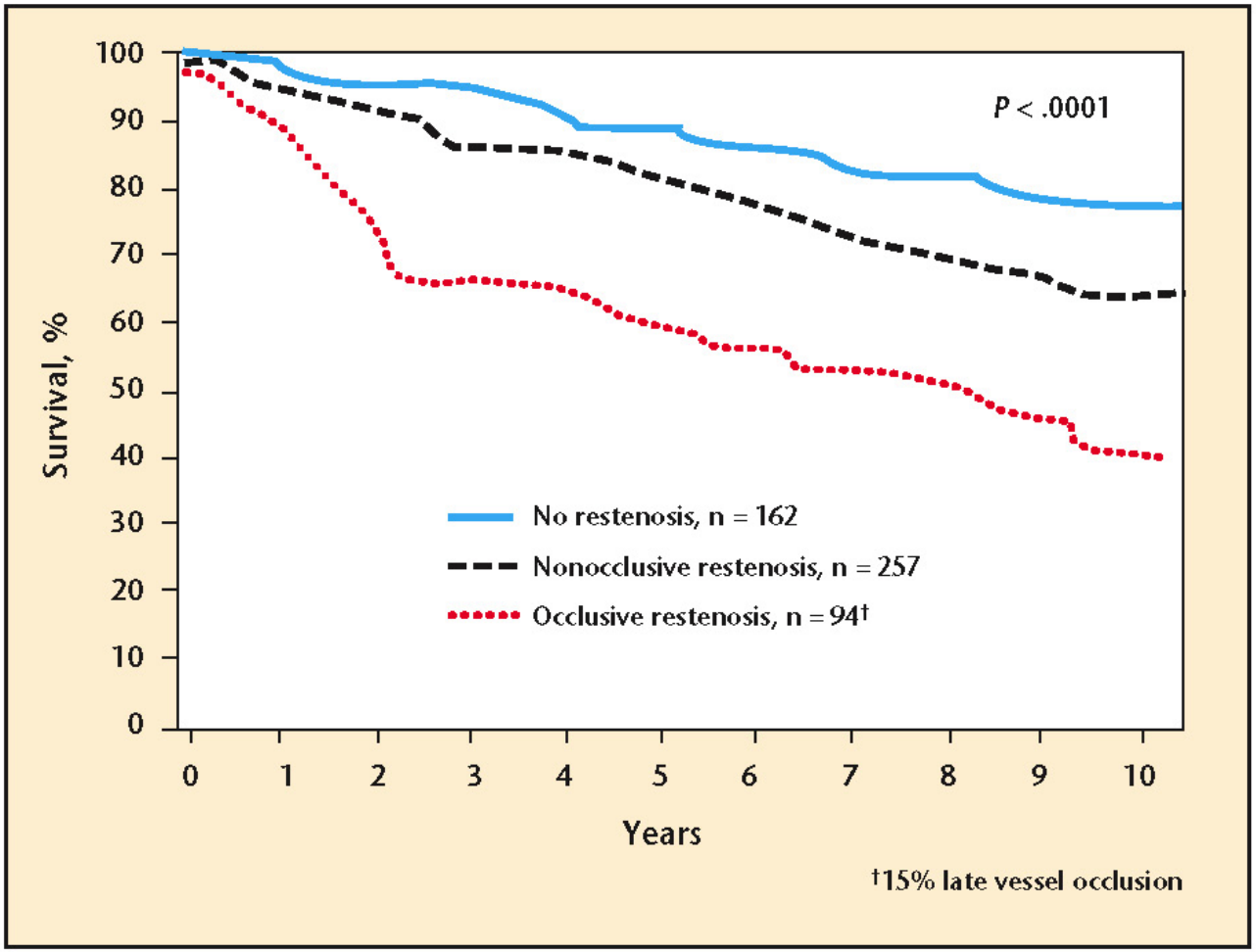


Figure 3. *Survival at late follow-up (mean 6.5 ± 2.4 yrs [SD]) by vessel patency following percutaneous coronary intervention. Survival is reduced in patients who have occlusive restenosis, which was observed in 15% of the total population. Both restenosis and occlusive restenosis were increased in diabetic patients. SD, standard deviation. Reproduced with permission from Van Belle et al.*[22]

Keriakes and Young, Rev Cardiovasc Med 2005;6(suppl 1):S48-58

Assessing Appropriate Use

Appropriateness: Health benefits exceed the risks by a sufficiently wide margin that the procedure is worth doing

Overuse: Patients who received a treatment that was graded "inappropriate"

Underuse: Patients for whom denial of an indicated treatment was graded "inappropriate"

Assessing Appropriate Use

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Overuse: Patients who received a treatment that was graded "inappropriate"

Underuse: Patients who did not receive treatment graded "appropriate"

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Assessing Appropriate Use

Establish criteria

- Literature review
- Expert panel

Test use in real patients against criteria

- Review of medical records
- Expert panel scoring of each record

Variations

- Published evidence only
- Include expert opinion (Rand-UCLA, 1984)
- Include experienced practitioners

2012 Appropriate Use Criteria for Coronary Revascularization: Focused Update

Indication		Appropriate Use Score (1–9)	
		PCI	CABG
62.	• Two-vessel CAD with proximal LAD stenosis	A (7)	A (8)
63.	• Three-vessel CAD with low CAD burden (ie, 3 focal stenoses, low SYNTAX score)	A (7)	A (9)
64.	• Three-vessel CAD with intermediate to high CAD burden (ie, multiple diffuse lesions, presence of CTO, or high SYNTAX score)	U (4)	A (9)
65.	• Isolated left main stenosis	U (6)	A (9)
66.	• Left main stenosis and additional CAD with low CAD burden (ie, 1- to 2-vessel additional involvement, low SYNTAX score)	U (5)	A (9)
67.	• Left main stenosis and additional CAD with intermediate to high CAD burden (ie, 3-vessel involvement, presence of CTO, or high SYNTAX score)	I (3)	A (9)
68.	• Prior bypass surgery with native 3-vessel disease and failure of multiple bypass grafts • LIMA remains patent to a native coronary artery • Depressed LVEF	U (6)	A (7)
69.	• 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	A (8)	U (6)

Blue shading: New and updated indications

Patel, et al., J Thorac Cardiovasc Surg.2012;143:780–803

2012 Appropriate Use Criteria for Coronary Revascularization: Focused Update

	CABG	PCI
Two-vessel CAD with proximal LAD stenosis	A	A
Three-vessel CAD with low CAD burden (i.e., three focal stenosis, 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., one to two vessel additional involvement, low SYNTAX score)	A	U
Left main stenosis and additional CAD with intermediate to high CAD burden (i.e., three vessel involvement, presence of CTO, or high SYNTAX score)	A	I

Patel, et al., J Thorac Cardiovasc Surg.2012;143:780–803

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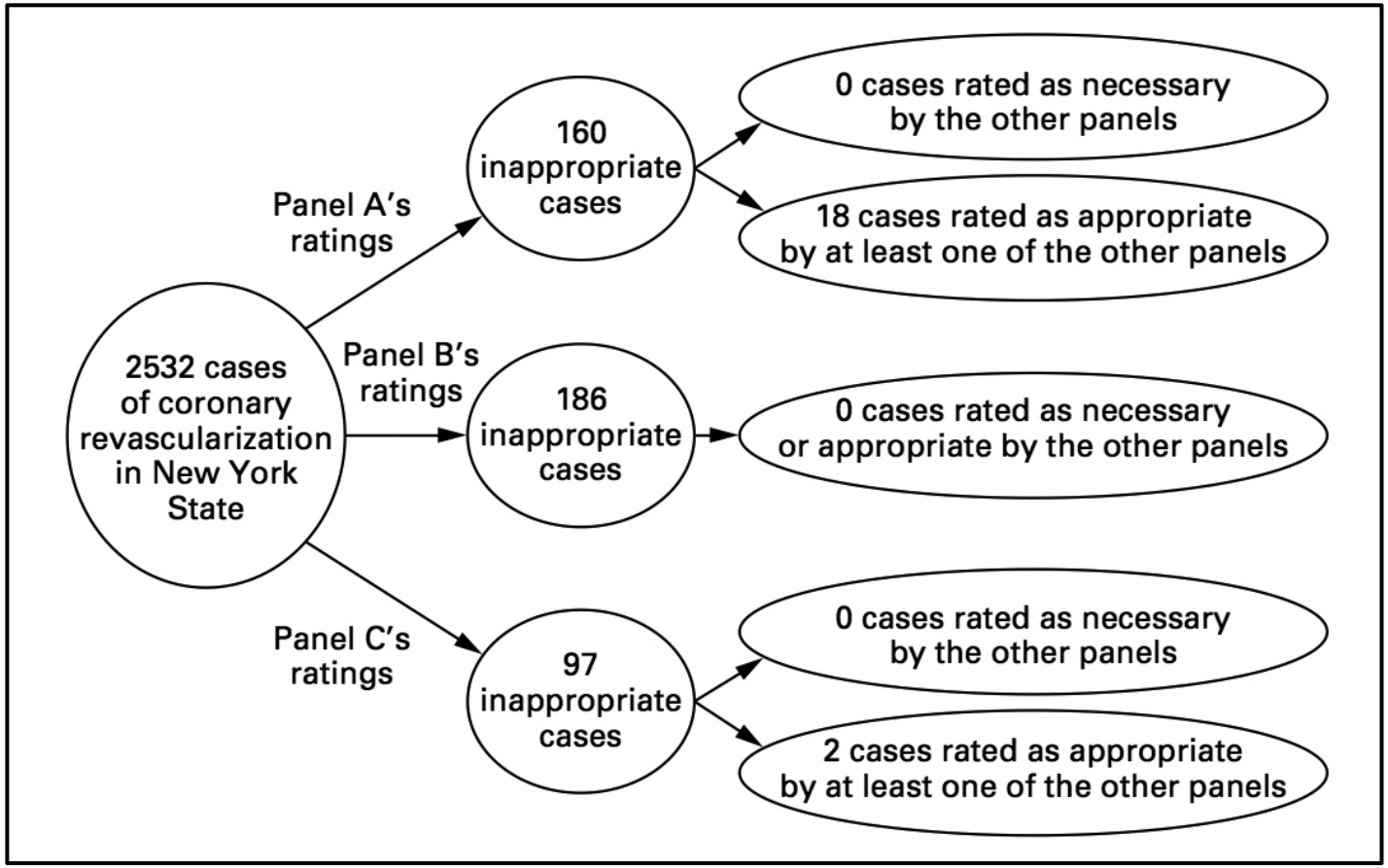
Underuse: Patients who did not receive treatment graded "appropriate"

Reproducibility of Appropriateness Ratings

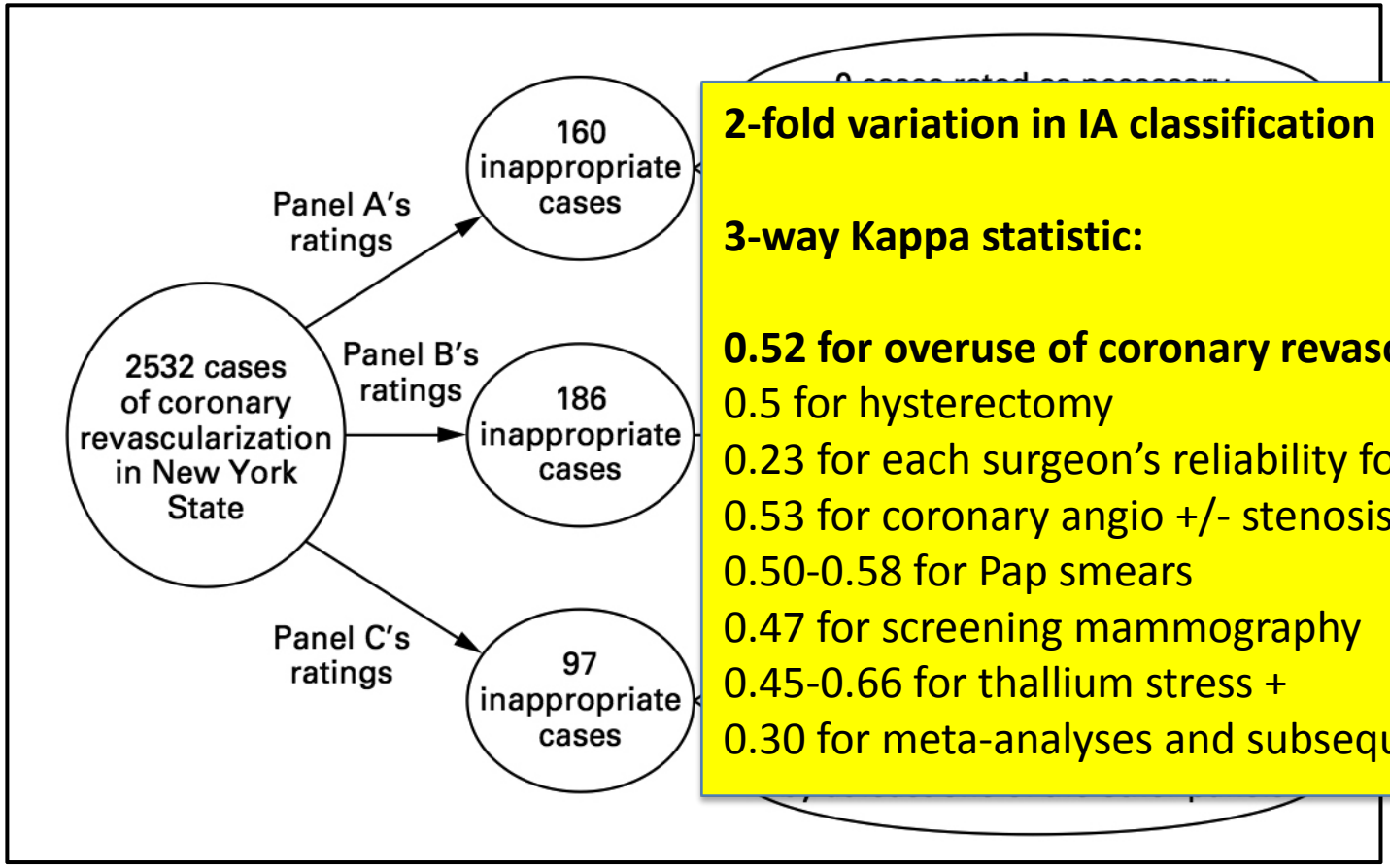
Overuse of Coronary Revascularization



Shekelle et al. N Engl J Med 1998;338:1888-95

Reproducibility of Appropriateness Ratings

Overuse of Coronary Revascularization



2-fold variation in IA classification

3-way Kappa statistic:

0.52 for overuse of coronary revasc
0.5 for hysterectomy
0.23 for each surgeon's reliability for hyst
0.53 for coronary angio +/- stenosis
0.50-0.58 for Pap smears
0.47 for screening mammography
0.45-0.66 for thallium stress +
0.30 for meta-analyses and subsequent RCT's

Shekelle et al. N Engl J Med 1998;338:1888-95

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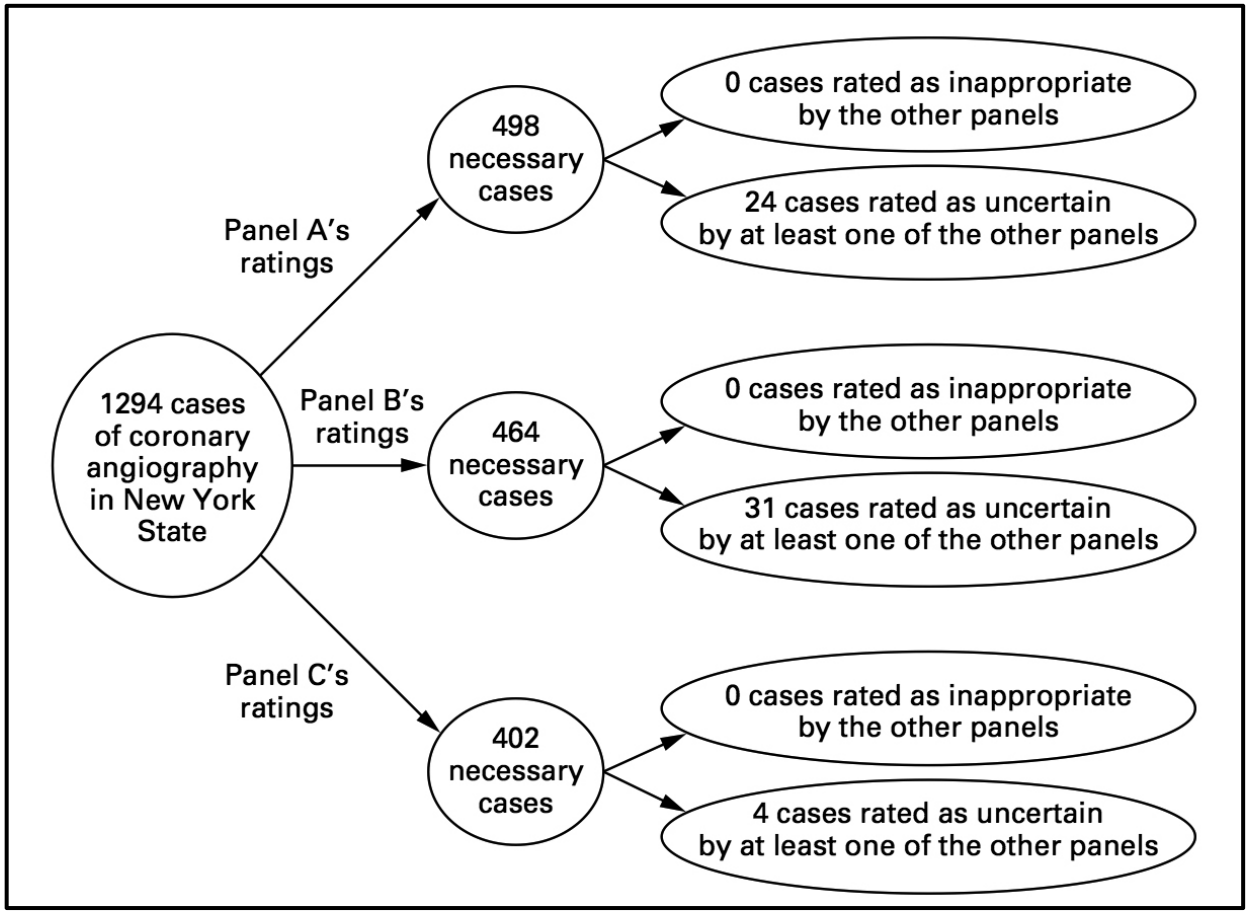
Reproducibility of Appropriateness Ratings

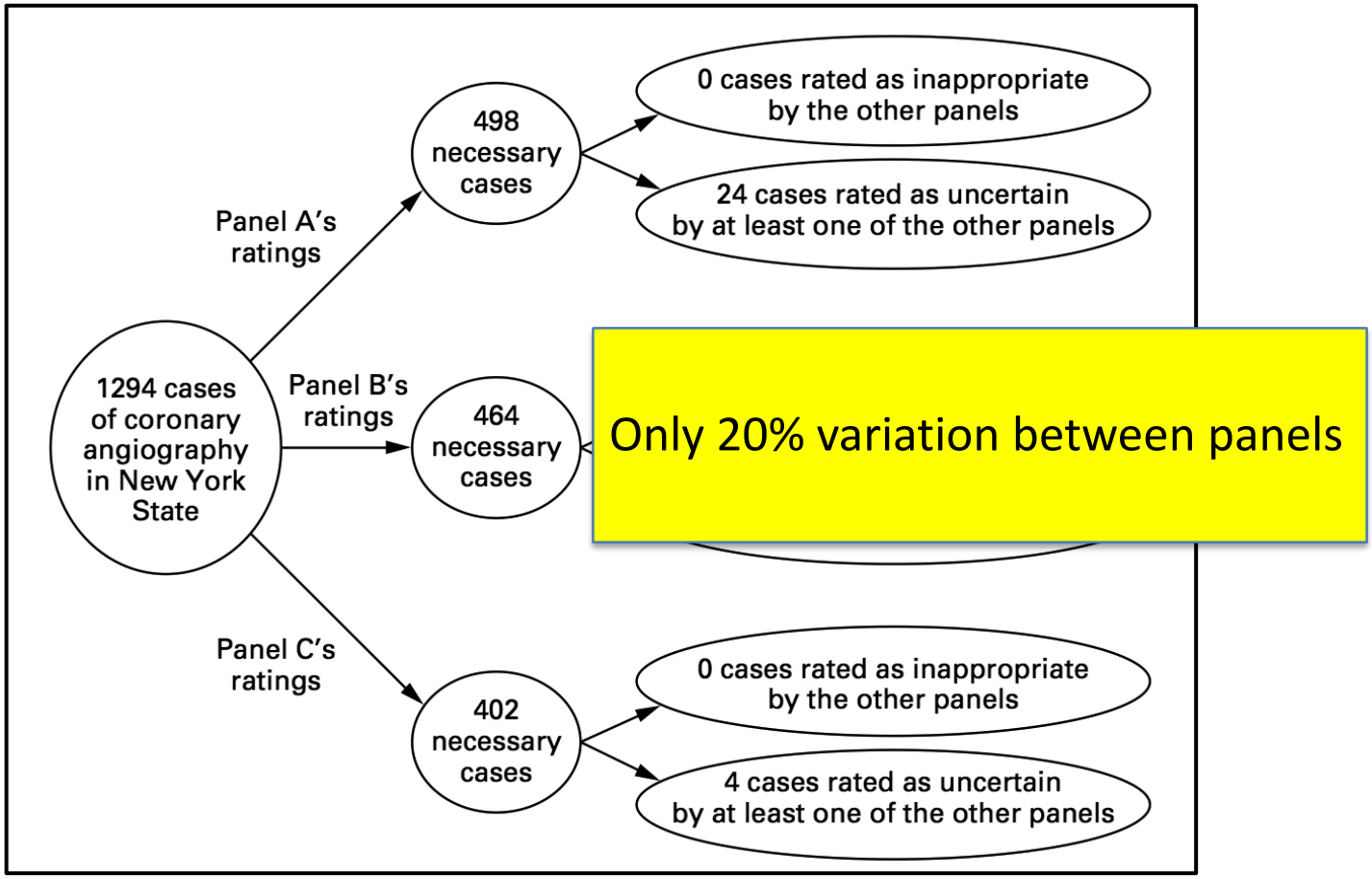
Underuse of Coronary Revascularization



Shekelle et al. N Engl J Med 1998;338:1888-95

Reproducibility of Appropriateness Ratings

Underuse of Coronary Revascularization



Shekelle et al. N Engl J Med 1998;338:1888-95

Appropriateness of Referral for Coronary Revascularization in Sweden in 1994

By treatment for which they were referred

		Appropriateness of coronary revascularisation (%)			
Referral	*n*	*Appropriate and necessary*	*Appropriate*	*Uncertain*	*Inappropriate*
CABG	1387	77.6	0.4	12.3	9.7
PTCA	687	21.3	10.5	30.0	38.3
Medical*	693	8.2	—	—	—

**For patients referred for continued medical therapy we only determined the necessity of undergoing coronary revascularization*.

2767 consecutive patients
50% referred for CABG
25% referred for PCI
25% referred for medical rx

S J Bernstein, et al.; Heart 1999; 81:470–477

Appropriateness of Referral for Coronary Revascularization in Sweden in 1994

By procedure and clinical indication

Indication	*n*	*Appropriateness (%)*			
		Appropriate and necessary	*Appropriate*	*Uncertain*	*Inappropriate*
CABG					
Asymptomatic	28	64.3	0	21.4	14.3
Chronic stable angina	1038	78.3	0	13.2	8.5
Unstable angina	204	73.0	0	10.3	16.7
Postmyocardial infarction	117	82.1	5.1	6.0	6.8
PTCA					
Asymptomatic	9	0	0	44.4	55.6
Chronic stable angina	447	12.3	13.2	37.8	36.7
Unstable angina	150	24.7	6.7	12.7	56.0
Postmyocardial infarction	81	66.7	3.7	17.3	12.4

2767 consecutive patients
50% referred for CABG
25% referred for PCI
25% referred for medical rx

S J Bernstein, et al.; Heart 1999; 81:470–477

Appropriateness of Referral for CABG and PCI: Multinational vs Dutch Criteria

Chronic Stable Angina

		Appropriateness rating [% (95% CI)]		
Procedure	Criteria	Inappropriate	Uncertain	Appropriate
PTCA	Dutch	34.8 (31.7–37.9)	35.6 (32.5–38.7)	29.6 (26.6–32.6)
	Multinational	6.1 (4.5–7.6)	24.1 (21.2–26.9)	69.8 (66.8–72.8)
CABG	Dutch	3.7 (2.6–4.9)	13.2 (11.1–15.3)	83.0 (80.7–85.3)
	Multinational	1.5 (0.7–2.2)	9.9 (8.1–11.7)	88.6 (86.7–90.6)

1137 PCI
1226 CABG
10 Dutch hospitals

S J Bernstein, et al.; International Journal for Quality in Health Care 2002; Volume 14, Number 2: pp. 103–109

Appropriateness of Referral for CABG and PCI: Multinational vs Dutch Criteria

Following Recent MI

		Appropriateness rating [% (95% CI)]		
Procedure	Criteria	Inappropriate	Uncertain	Appropriate
PTCA	Dutch	28.1 (22.3–33.9)	40.9 (34.5–47.2)	31.1 (25.1–37.0)
	Multinational	0.9 (0.0–2.0)	23.8 (18.3–29.3)	75.3 (69.7–80.9)
CABG	Dutch	3.9 (1.2–6.5)	14.6 (9.7–19.4)	81.6 (76.2–86.9)
	Multinational	2.4 (0.3–4.5)	11.1 (6.8–15.5)	86.4 (81.7–91.1)

1137 PCI
1226 CABG
10 Dutch hospitals

S J Bernstein, et al.; International Journal for Quality in Health Care 2002; Volume 14, Number 2: pp. 103–109

Appropriateness of Referral for CABG and PCI: Multinational vs Dutch Criteria

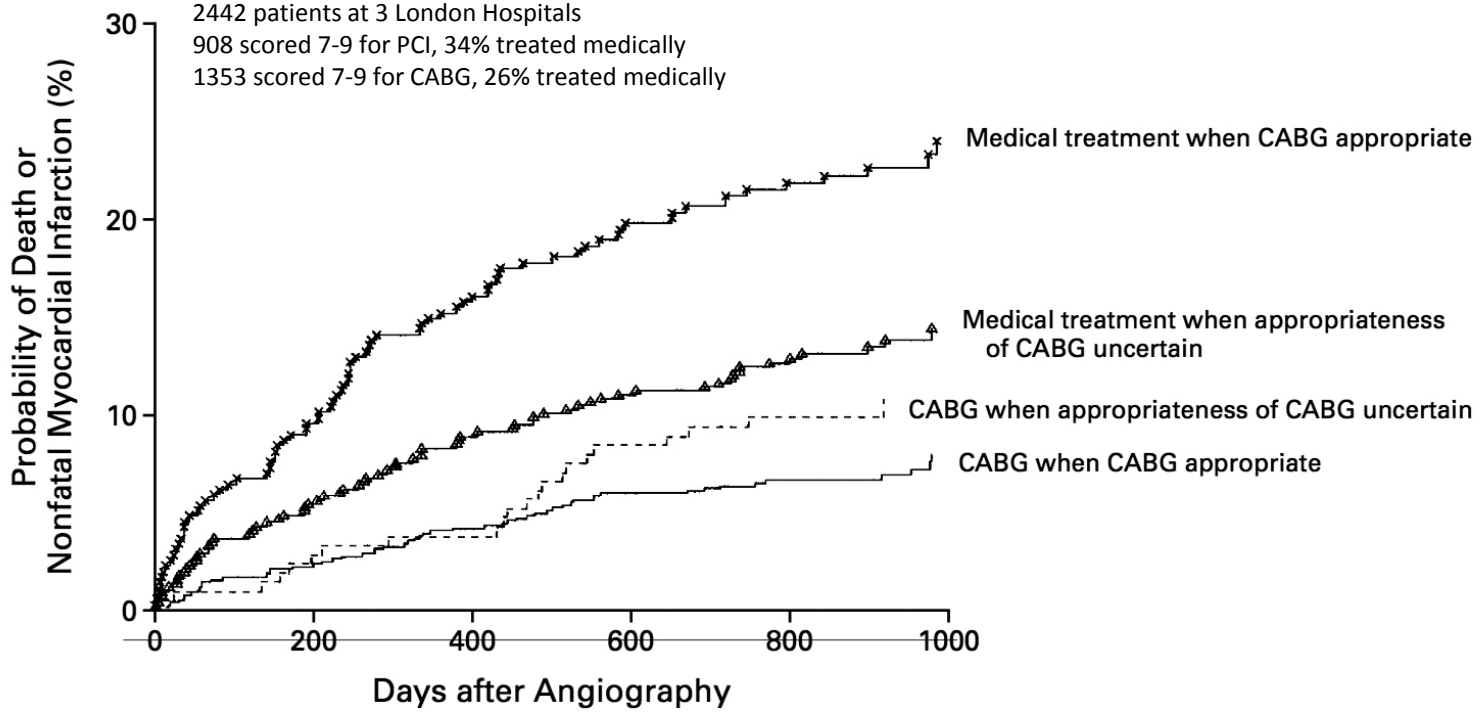
Sensitivity Analysis
With Lesion Morphology and Intensity of Medical Rx Reclassified

		Appropriateness rating [% (95% CI)]		
Procedure	Criteria	Inappropriate	Uncertain	Appropriate
PTCA	Dutch	6.5 (5.1–7.9)	9.2 (7.5–10.9)	84.3 (82.1–86.4)
	Multinational	5.0 (3.7–6.3)	24.0 (21.5–26.5)	71.0 (68.3–73.6)
CABG	Dutch	2.1 (1.3–2.9)	7.6 (6.1–9.1)	90.3 (88.6–92.0)
	Multinational	1.6 (0.9–2.3)	10.1 (8.4–11.8)	88.2 (86.4–90.1)

1137 PCI
1226 CABG
10 Dutch hospitals

S J Bernstein, et al.; International Journal for Quality in Health Care 2002; Volume 14, Number 2: pp. 103–109

Consequences of Medical Treatment when CABG Appropriate



No. at Risk						
Medical treatment						
CABG appropriate (×)	354	320	297	283	240	92
CABG uncertain (△)	514	486	468	457	366	118
CABG						
CABG uncertain (- -)	213	206	204	194	162	51
CABG appropriate (—)	765	747	733	719	584	198

H Hemingway, et al.; N Engl J Med, Vol. 344, No. 9 · March 1, 2001

Assessing Appropriate Use

Appropriateness: Health benefits exceed the risks by a sufficiently wide margin that the procedure is worth doing

Overuse: Patients who received a treatment that was graded "inappropriate"

Underuse: Patients who did not receive treatment graded "appropriate"

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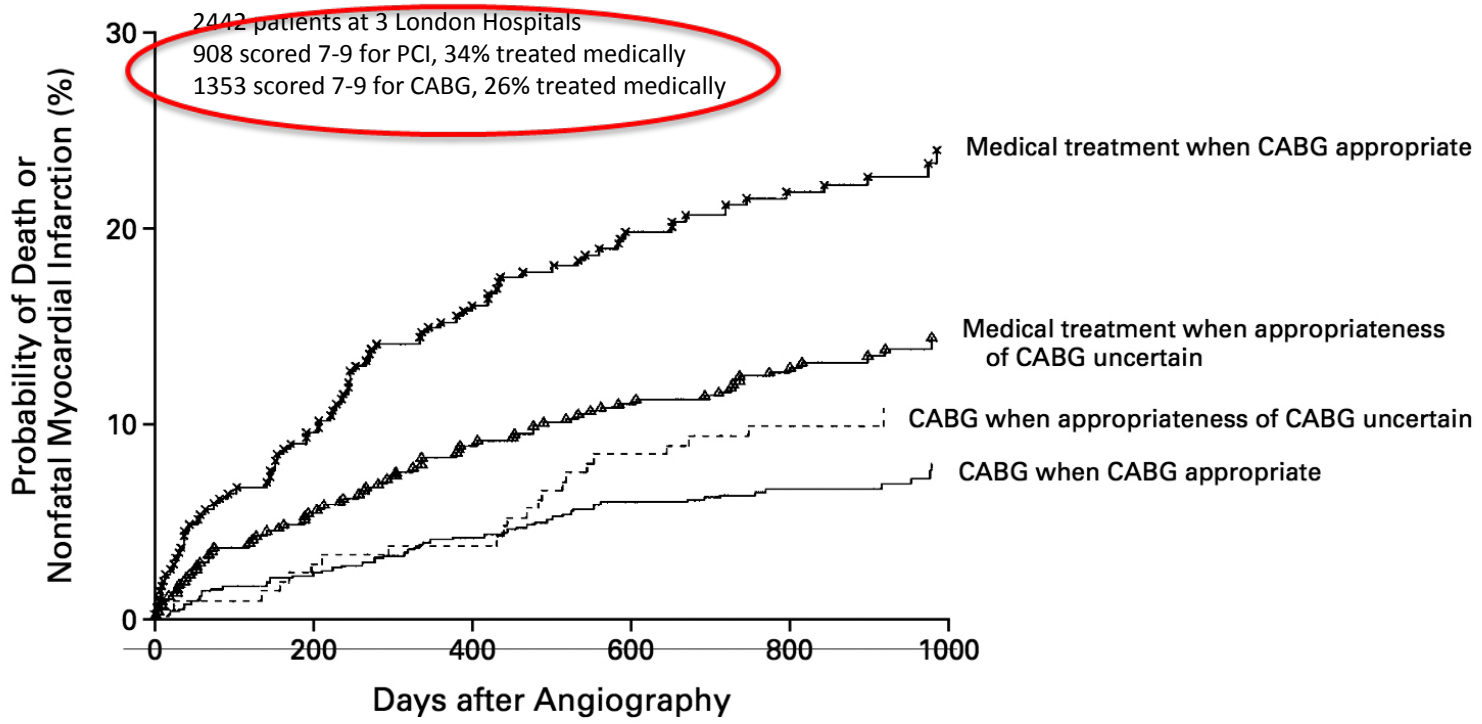

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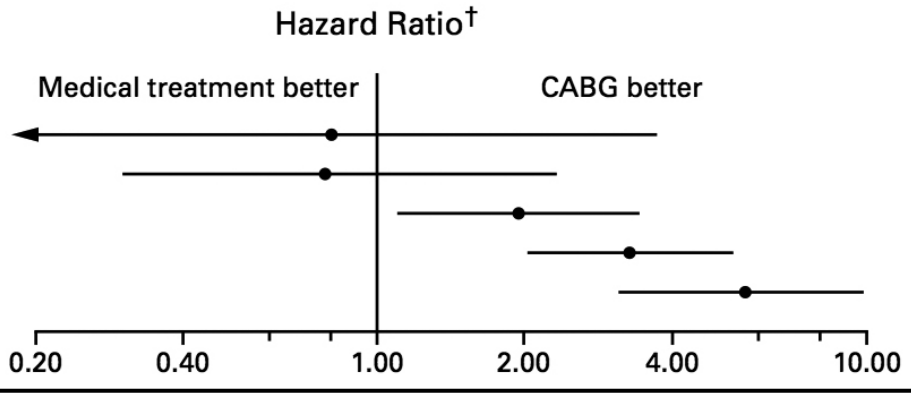
Relationship between Appropriateness Category and Outcome following Medical Treatment or CABG

5-Level Appropriateness Category (Range of Ratings)	Death from Any Cause or Nonfatal MI	Hazard Ratio (95% CI)	P Value
	no. with event/ total no.		
1–2	13/68	0.80 (0.18–3.67)	0.78
3–4	38/293	0.78 (0.27–2.27)	0.65
5–6	62/489	1.94 (1.09–3.44)	0.023
7–8	80/623	3.27 (2.01–5.33)	<0.001
9	56/496	5.58 (3.13–9.96)	<0.001

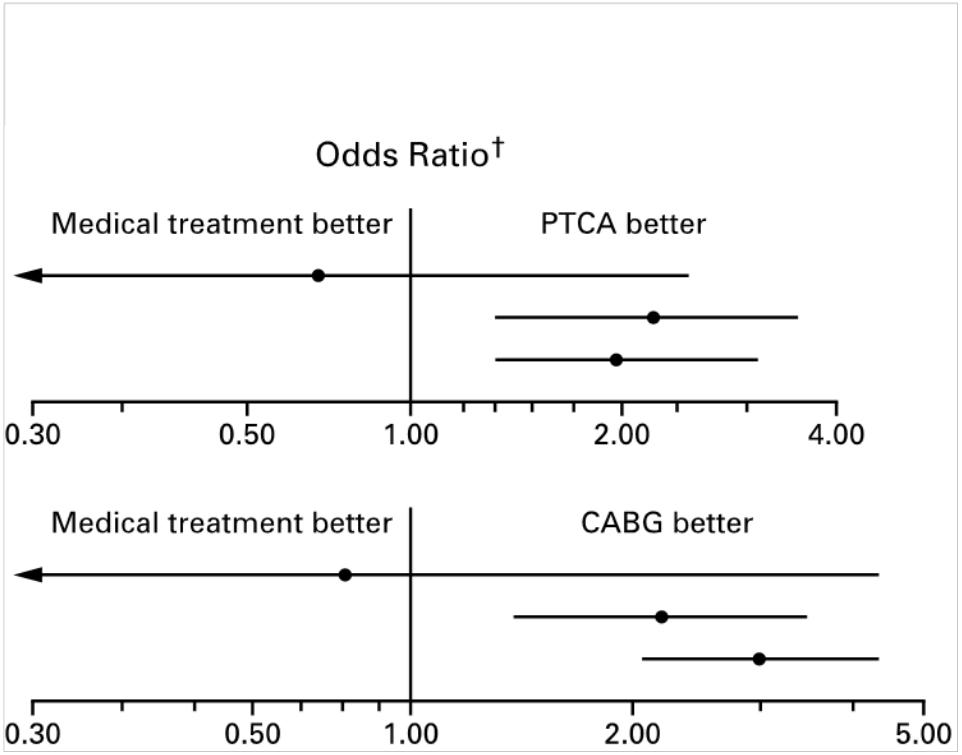


2442 patients at 3 London Hospitals
908 scored 7-9 for PCI, 34% treated medically
1353 scored 7-9 for CABG, 26% treated medically

H Hemingway, et a.l; N Engl J Med, Vol. 344, No. 9 · March 1, 2001

Relationship between Appropriateness Category and Outcome following Medical Treatment or CABG

Appropriateness Category	Angina at Follow-up		Odds Ratio (95% CI)
	Medical Treatment	Revascular-ization	
	no. with angina/total no.		
PTCA			
Inappropriate	56/110	9/14	0.73 (0.22–2.42)
Uncertain	172/317	67/142	2.15 (1.34–3.44)
Appropriate	143/205	114/210	1.97 (1.29–3.00)
CABG			
Inappropriate	49/70	6/8	0.82 (0.15–4.40)
Uncertain	189/348	60/136	2.23 (1.40–3.55)
Appropriate	137/208	213/547	3.03 (2.08–4.42)



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2012 Appropriate Use Criteria for Coronary Revascularization: Focused Update

	CABG	PCI
Two-vessel CAD with proximal LAD stenosis	A	A
Three-vessel CAD with low CAD burden (i.e., three focal stenosis, 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., one to two vessel additional involvement, low SYNTAX score)	A	U
Left main stenosis and additional CAD with intermediate to high CAD burden (i.e., three vessel involvement, presence of CTO, or high SYNTAX score)	A	I

Patel, et al., J Thorac Cardiovasc Surg.2012;143:780–803

Assessing Appropriate Use

Establish criteria

- Literature review
- Expert panel

Test use in real patients against criteria

- Review of medical records
- Expert panel scoring of each record

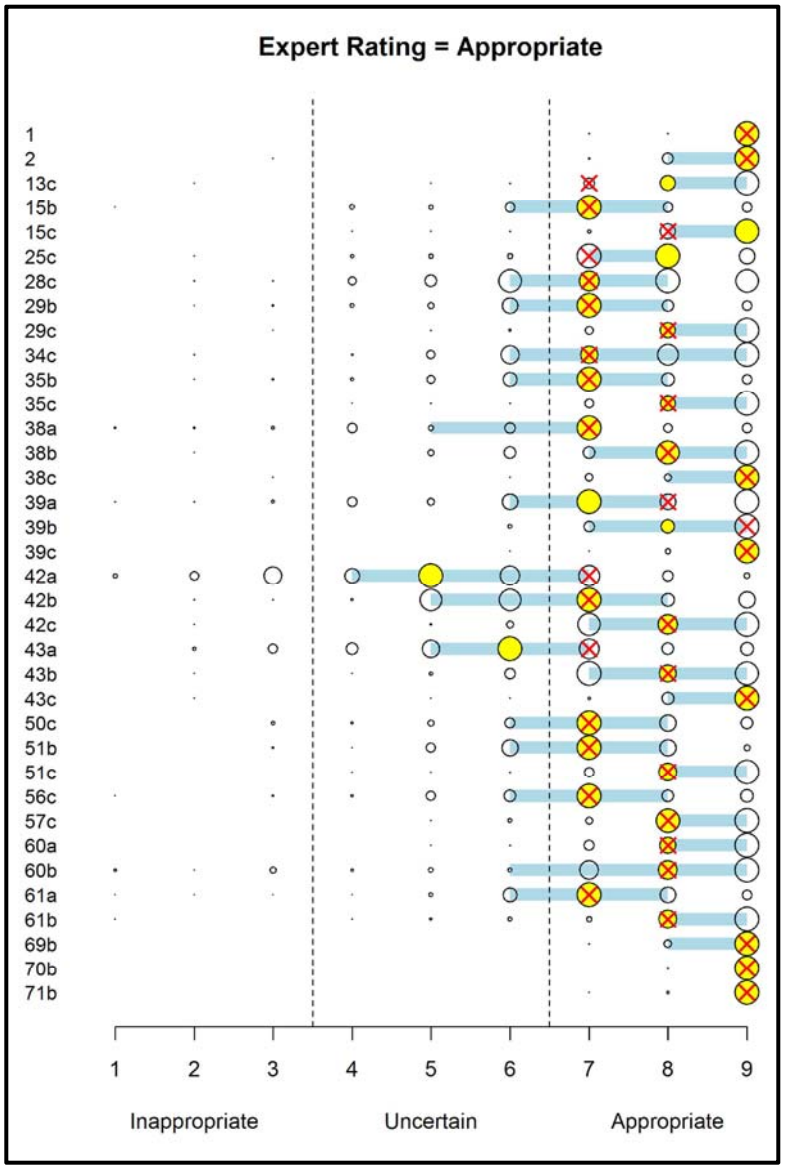
Variations

- Published evidence only
- Include expert opinion
- Include experienced practitioners

Concordance of Physician Ratings with AUC

Technical Panel:
- 17 members
- 174 scenarios

Physician Group:
- 85 Physicians
- 10 institutions
- 68 scenarios
- Blind to TP results



Red X = median rating of Technical Panel
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Chan et al, J Am Coll Cardiol 2011;57:1546-53

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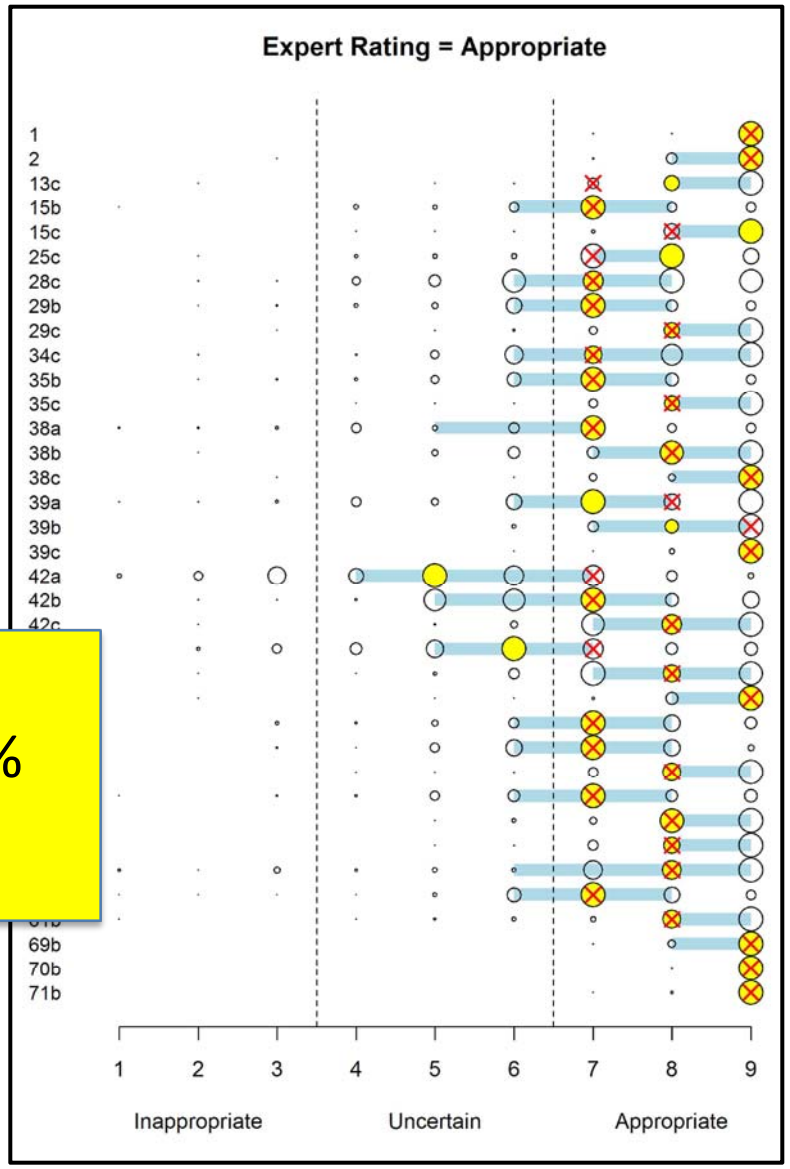
Concordance 94%



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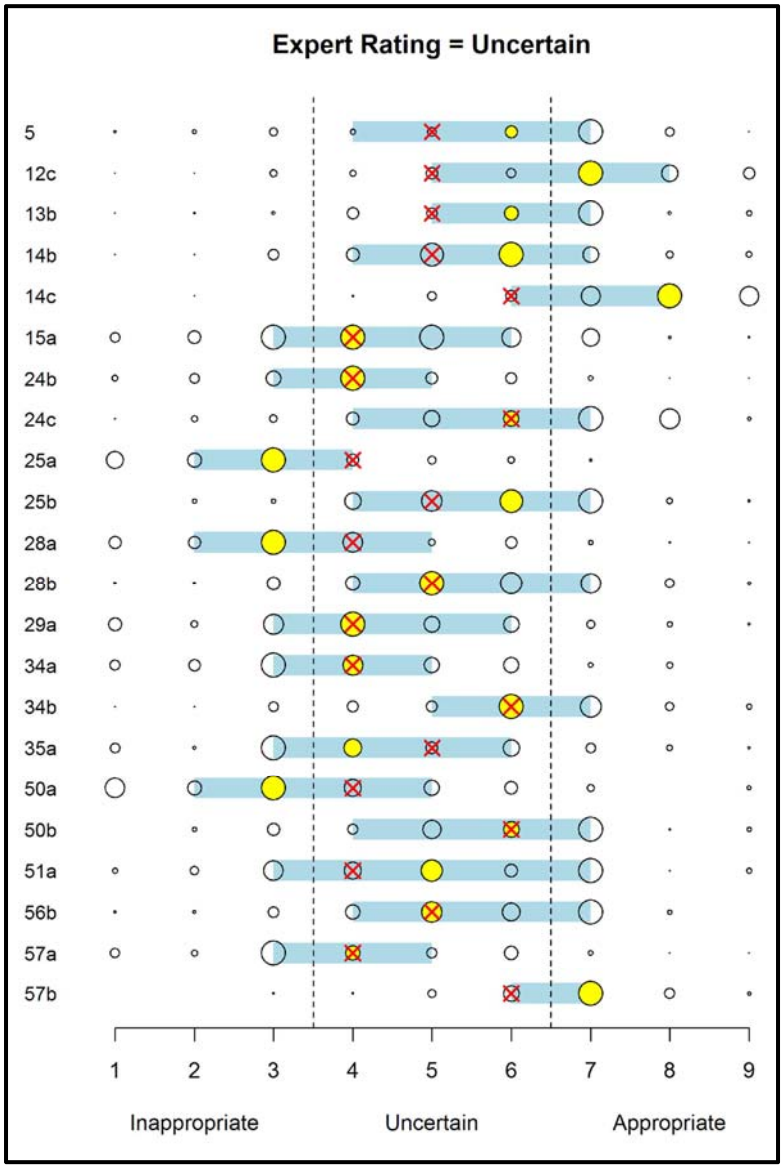

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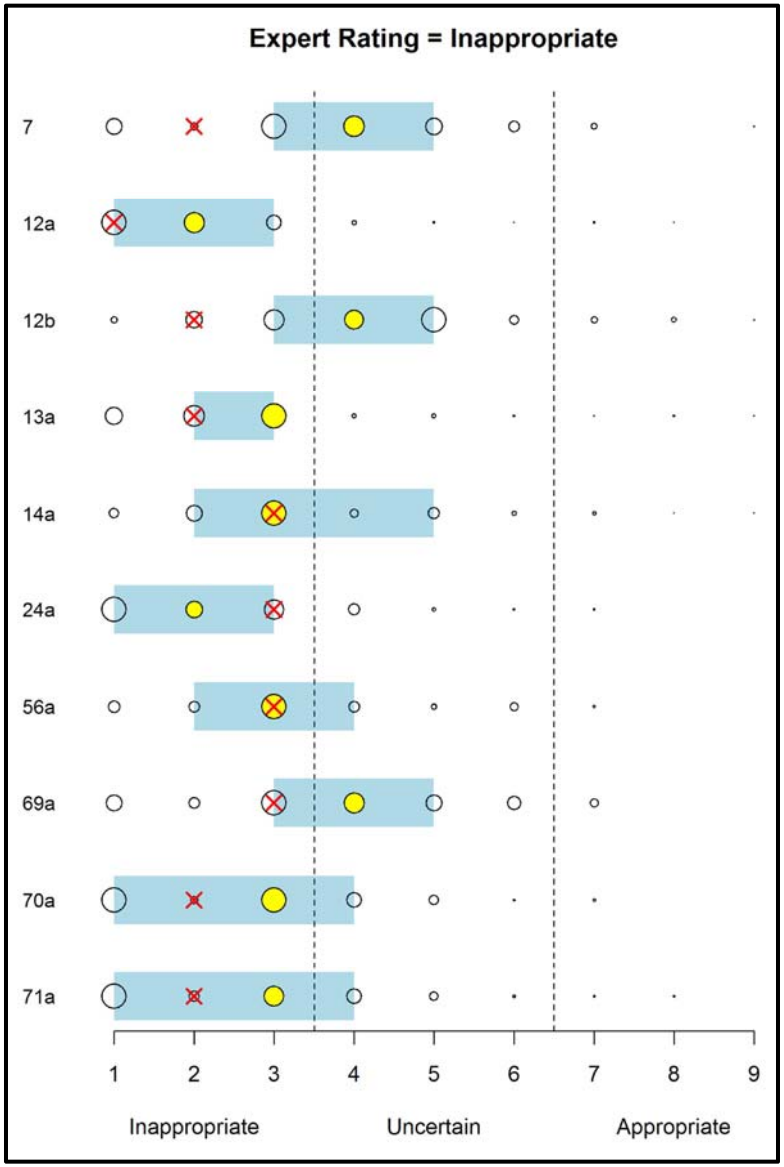

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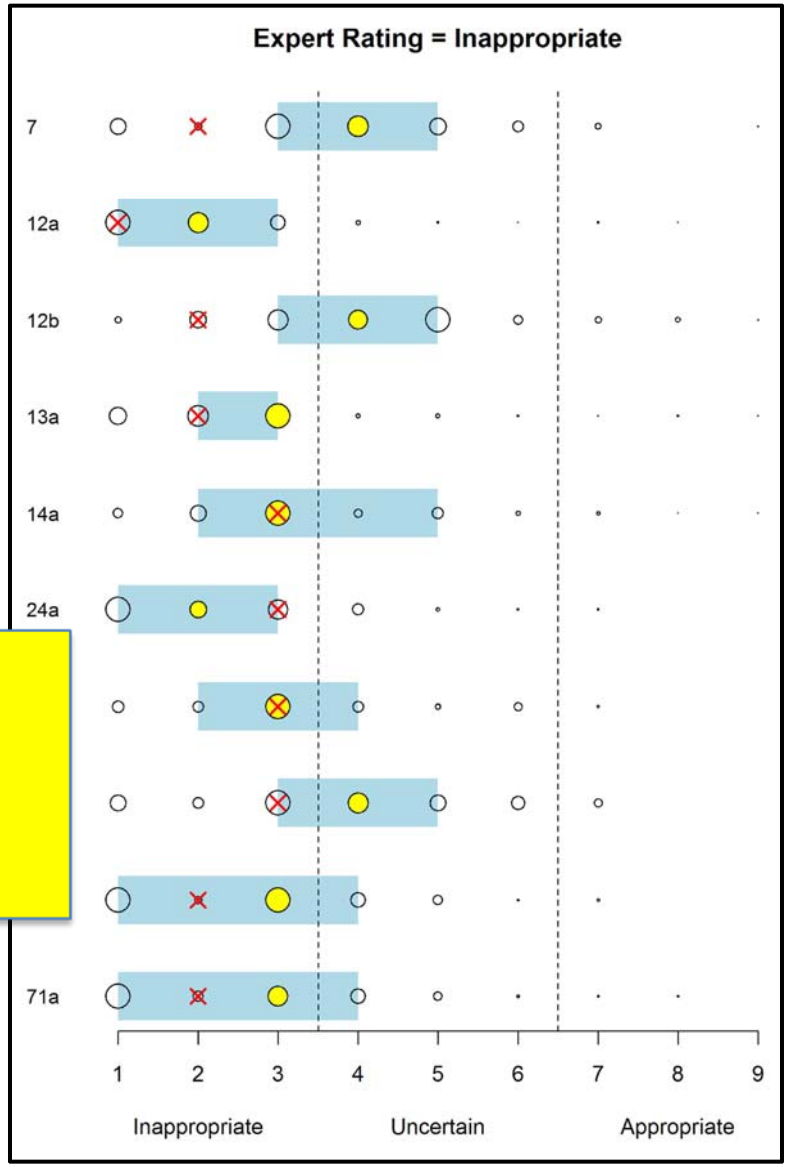

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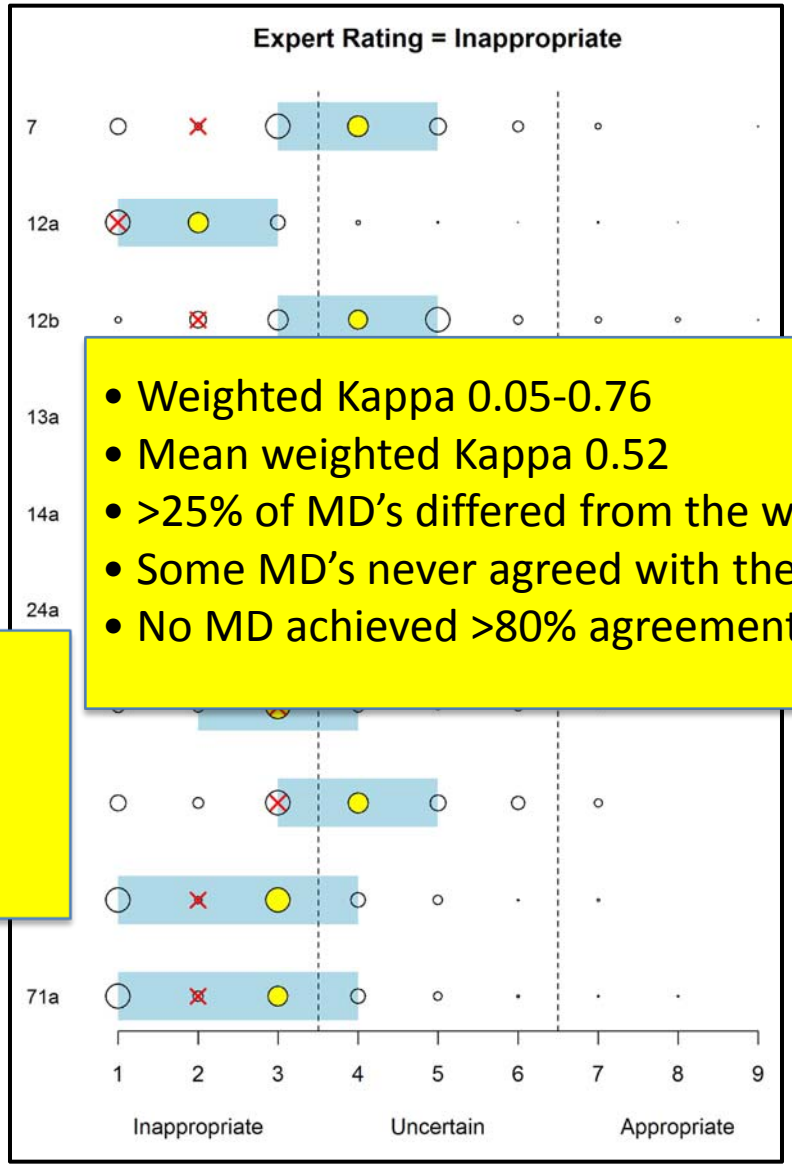

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- Weighted Kappa 0.05-0.76
- Mean weighted Kappa 0.52
- >25% of MD's differed from the whole in 2/3 scenarios
- Some MD's never agreed with the Technical Panel
- No MD achieved >80% agreement with the Technical Panel

Concordance 70%

Chan et al, J Am Coll Cardiol 2011;57:1546-53

Appropriateness of Coronary Revascularization in New York State

18 mos (2009-2010)
2009 AUC applied

Case Description	Procedure Performed	
	CABG	PCI
Total cases reported	14,519	81,407
Eligible cases—no ACS, no previous CABG (% of all cases reported that are eligible)	10,460 (72.04)	33,970 (41.73)
Eligible cases where rating cannot be determined	2,292	9,425
Cases rated for appropriateness of revascularization	8,168	24,545
Revascularization (CABG or PCI) is		
Appropriate	7,372	8,856
	90.25%	36.08%
Inappropriate	91	3,508
	1.11%	14.29%
Uncertain	705	12,181
	8.63%	49.63%

Hannan et al., JACC Vol. 59, No. 21, 2012 May 22, 2012:1870–6

Appropriateness of Coronary Revascularization in New York State

Most common scenarios for CABG patients rated IA or U

Rating	Anatomy	Symptoms	Stress Test	Anti-Ischemic Therapy	n (%)
Inappropriate					
	1-, 2-vessel non-PLAD	Asymptomatic	Intermediate risk	None/minimal	51 (55.4)
	1-, 2-vessel non-PLAD	CCS class I–II	Low risk	None/minimal	20 (21.7)
Uncertain					
	1-, 2-vessel non-PLAD	CCS class I–II	Intermediate risk	None/minimal	113 (16.0)
	1-, 2-vessel non-PLAD	CCS class III–IV	Intermediate risk	None/minimal	131 (18.5)
	1-, 2-vessel non-PLAD	CCS class I–II	Not done	No mention	154 (21.7)

Hannan et al., JACC Vol. 59, No. 21, 2012 May 22, 2012:1870–6

Appropriateness of Coronary Revascularization in New York State

Most common scenarios for PCI patients rated A, IA or U

Rating	Anatomy	Symptoms	Stress Test	Anti-Ischemic Therapy	n (%)
Inappropriate					
	1-, 2-vessel non-PLAD	Asymptomatic	Intermediate risk	None/minimal	1,583 (45.1)
	1-, 2-vessel non-PLAD	CCS class I–II	Low risk	None/minimal	1,203 (34.3)
	1-, 2-vessel non-PLAD	Asymptomatic	Low risk	None/minimal	488 (11.6)
Uncertain					
	1-, 2-vessel non-PLAD	CCS class I–II	Not done	No mention	5,019 (46.3)
	1-, 2-vessel non-PLAD	CCS class I–II	Intermediate risk	None/minimal	3,132 (28.9)
Appropriate					
	1-, 2-vessel non-PLAD	CCS class I–II	High risk	None/minimal	1,248 (14.1)
	1-, 2-vessel non-PLAD	CCS class III–IV	Not done	No mention	1,170 (13.2)
	1-, 2-vessel non-PLAD	CCS class I–II	Intermediate risk	Maximal	950 (10.7)

Hannan et al., JACC Vol. 59, No. 21, 2012 May 22, 2012:1870–6

Appropriateness of Coronary Revascularization in New York State

Cases for which no rating could be determined

Case Description	Procedure Performed	
	CABG	PCI
Eligible cases where rating cannot be determined	2,292	9,425
Scenario 18: 1- or 2-vessel disease, no PLAD, no noninvasive testing. Asymptomatic; AUC gives no rating	64	2,834
Scenario 19: 1- or 2-vessel disease, no PLAD, no IVUS/FFR; no noninvasive testing. Asymptomatic; AUC gives no rating	2	12
No vessels diseased (stenosis ≥50% for LM, 70% all others)	36	330
Stress test result = positive, risk unavailable	571	3,171
Noninvasive testing not done or results unknown (no high/moderate risk)	1,619	3,078

Hannan et al., JACC Vol. 59, No. 21, 2012 May 22, 2012:1870–6

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Appropriateness of Coronary Revascularization in New York State

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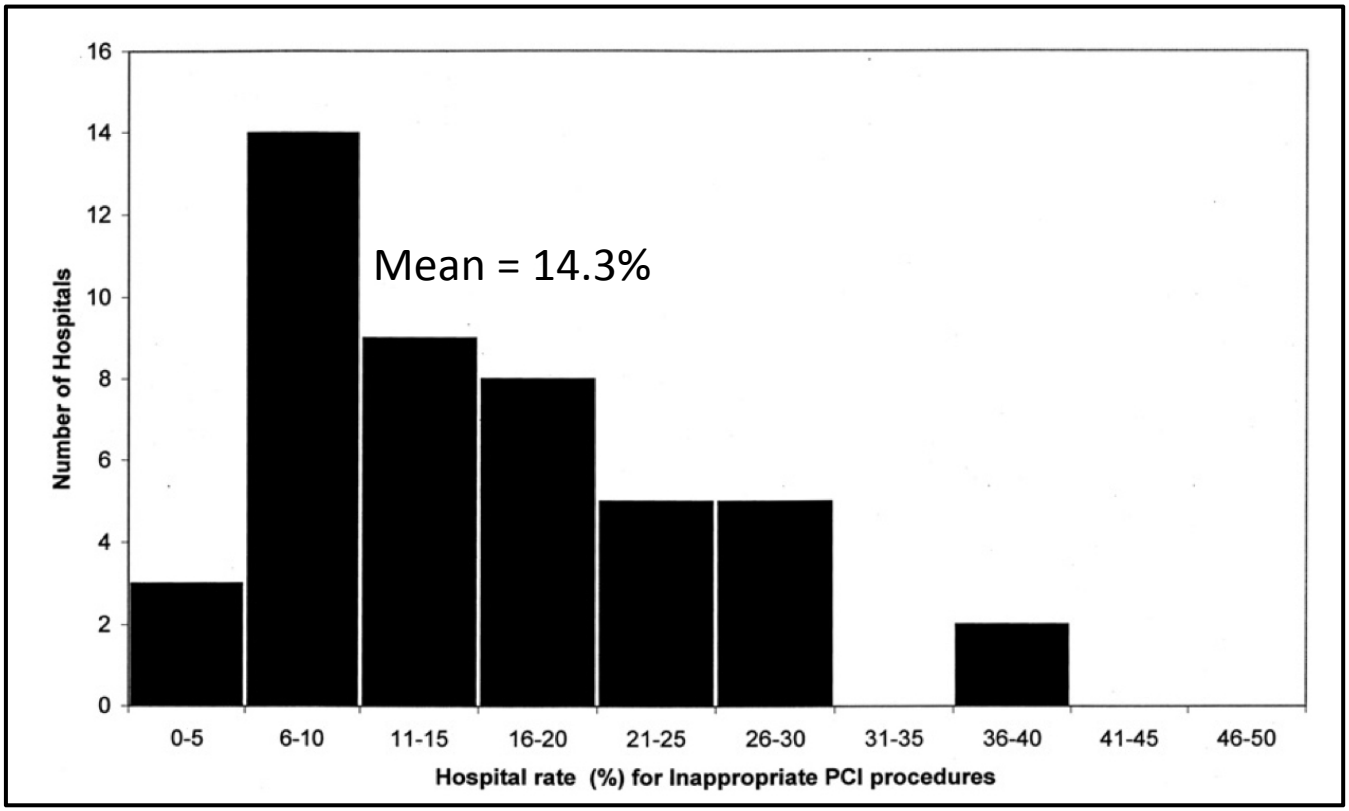
Scenario 19: 1- or 2-vessel disease, no PLAD, no IVUS/FFR; no noninvasive testing. Asymptomatic; AUC gives no rating	2	12
(no high/moderate risk)		

- Scenario 18 not rated by ACCF because writing group considered the likelihood so low that rating should not be done
- If added to IA cases, IA rate for PCI increases to 23.2%

Hannan et al., JACC Vol. 59, No. 21, 2012 May 22, 2012:1870–6

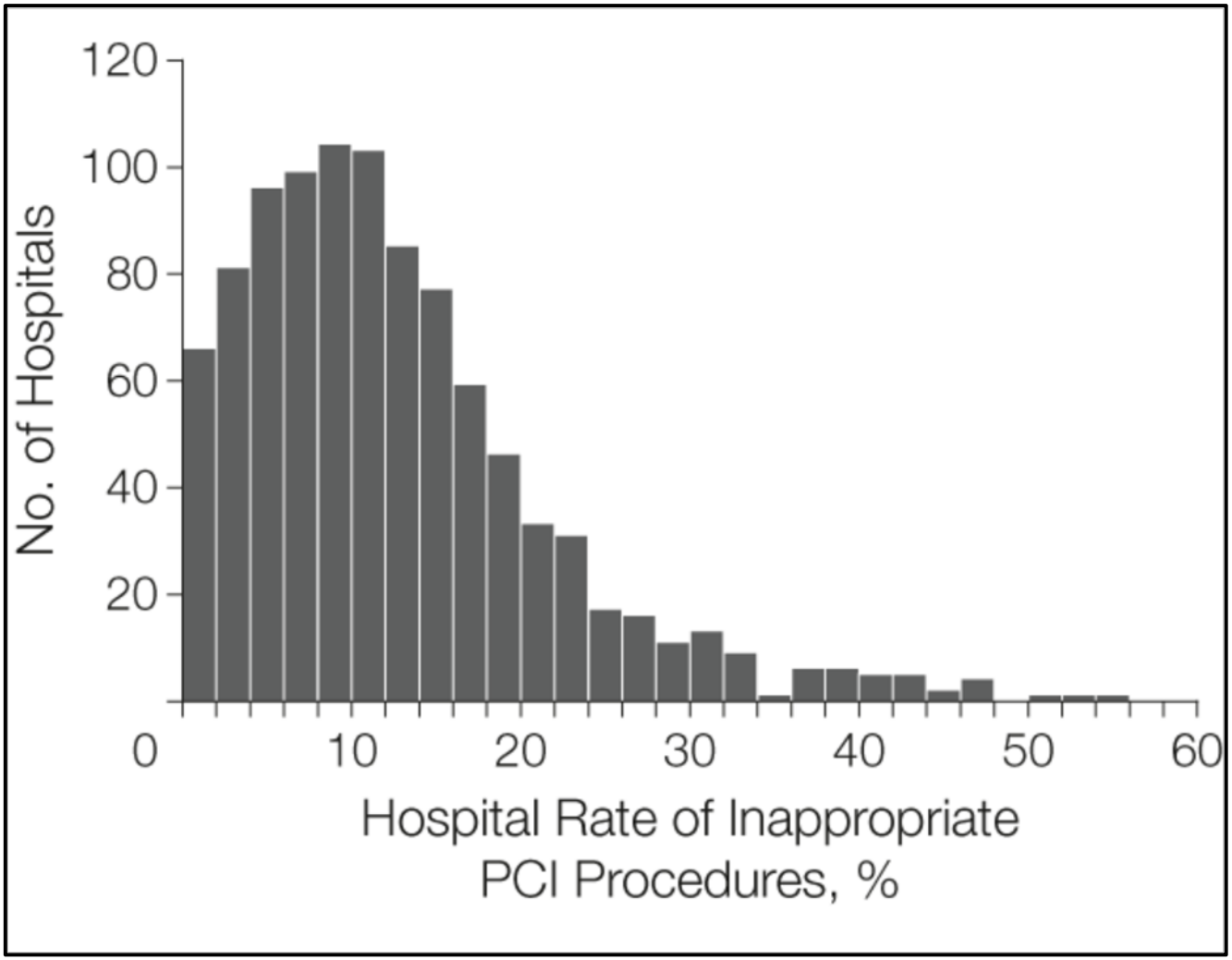
Appropriateness of Coronary Revascularization in New York State



Number of hospitals in different ranges of percutaneous coronary intervention (PCI) inappropriateness (for hospitals with volumes >400).

Hannan et al., JACC Vol. 59, No. 21, 2012 May 22, 2012:1870–6

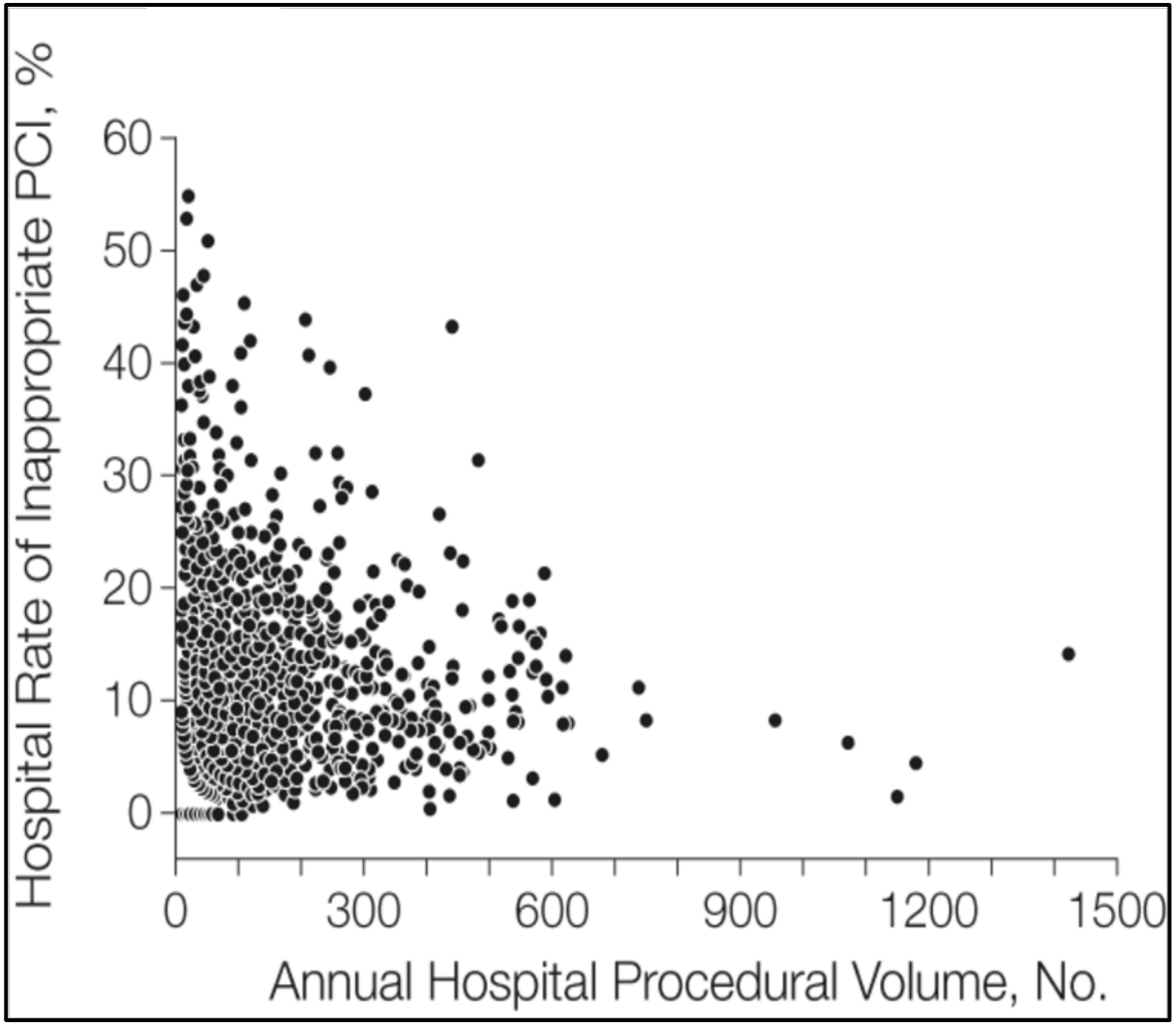
Appropriateness of PCI



500,154 PCI from NCDR; 144,737 nonacute (29%)

Chan et al, J Am Coll Cardiol 2011;57:1546-53

Appropriateness of PCI



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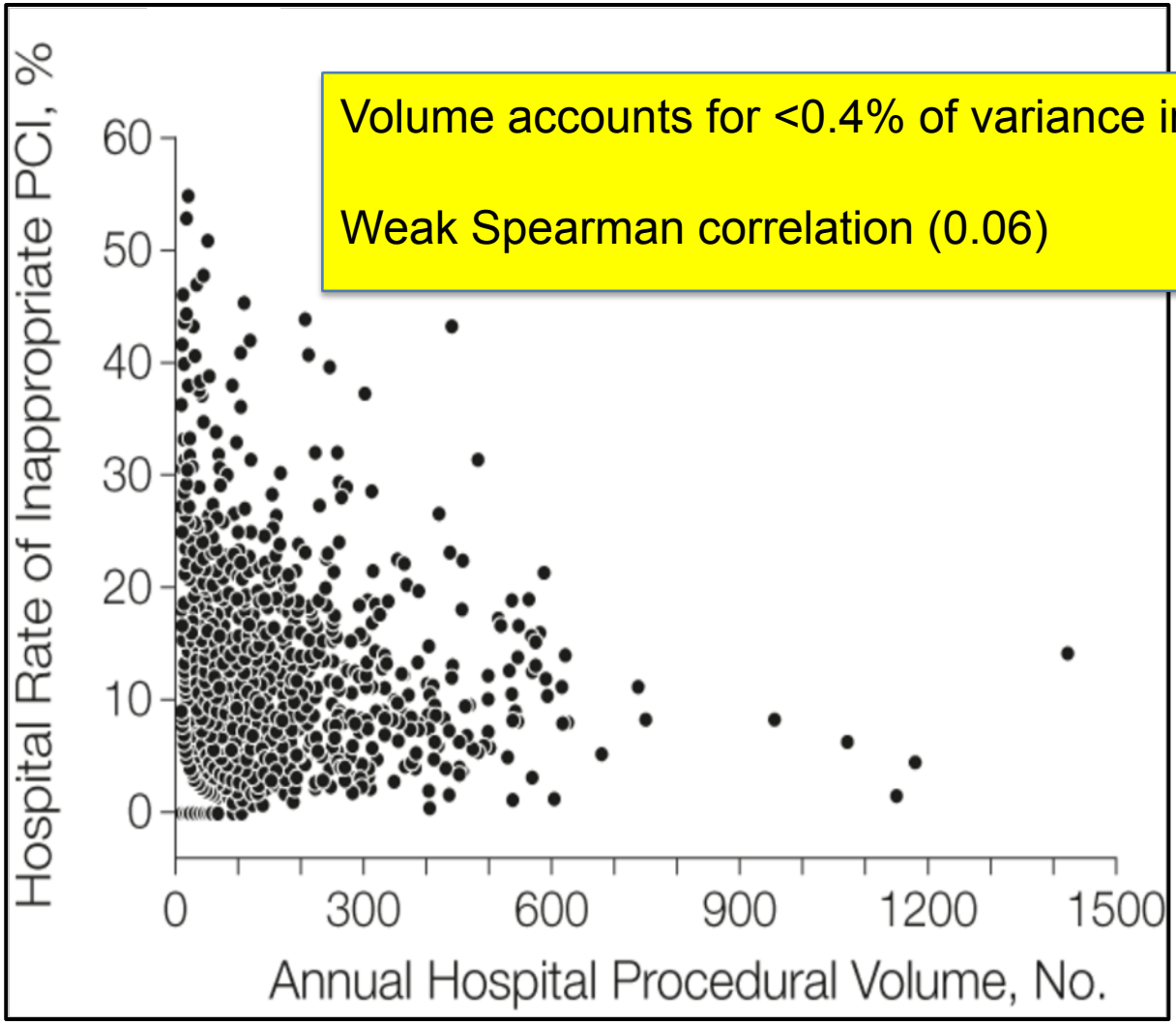

Volume accounts for <0.4% of variance in IA rates

Weak Spearman correlation (0.06)

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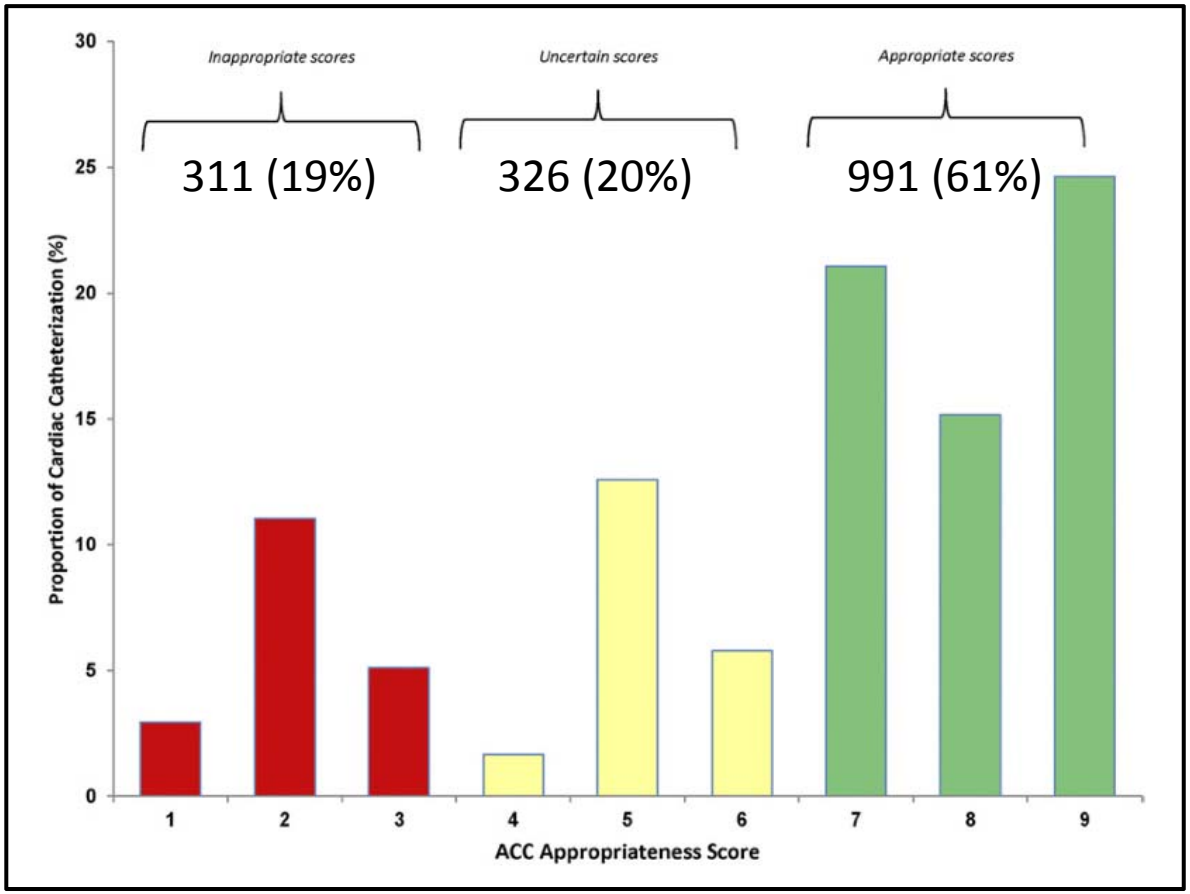
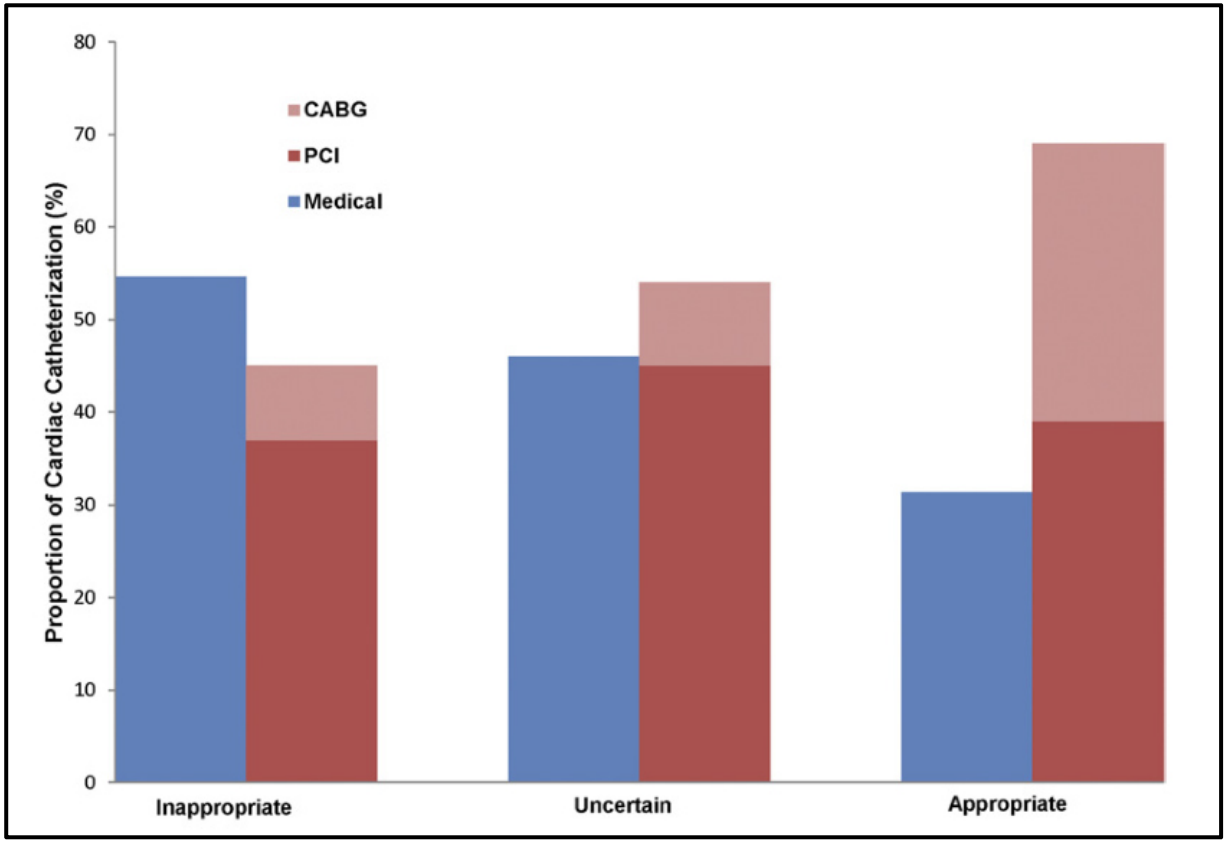
Appropriateness of Coronary Revascularization in Ontario



1,628 patients with coronary angiograms and data allowing assignment of AUC score

D Ko, et al., J Am Coll Cardiol 2012;60:1876–84)

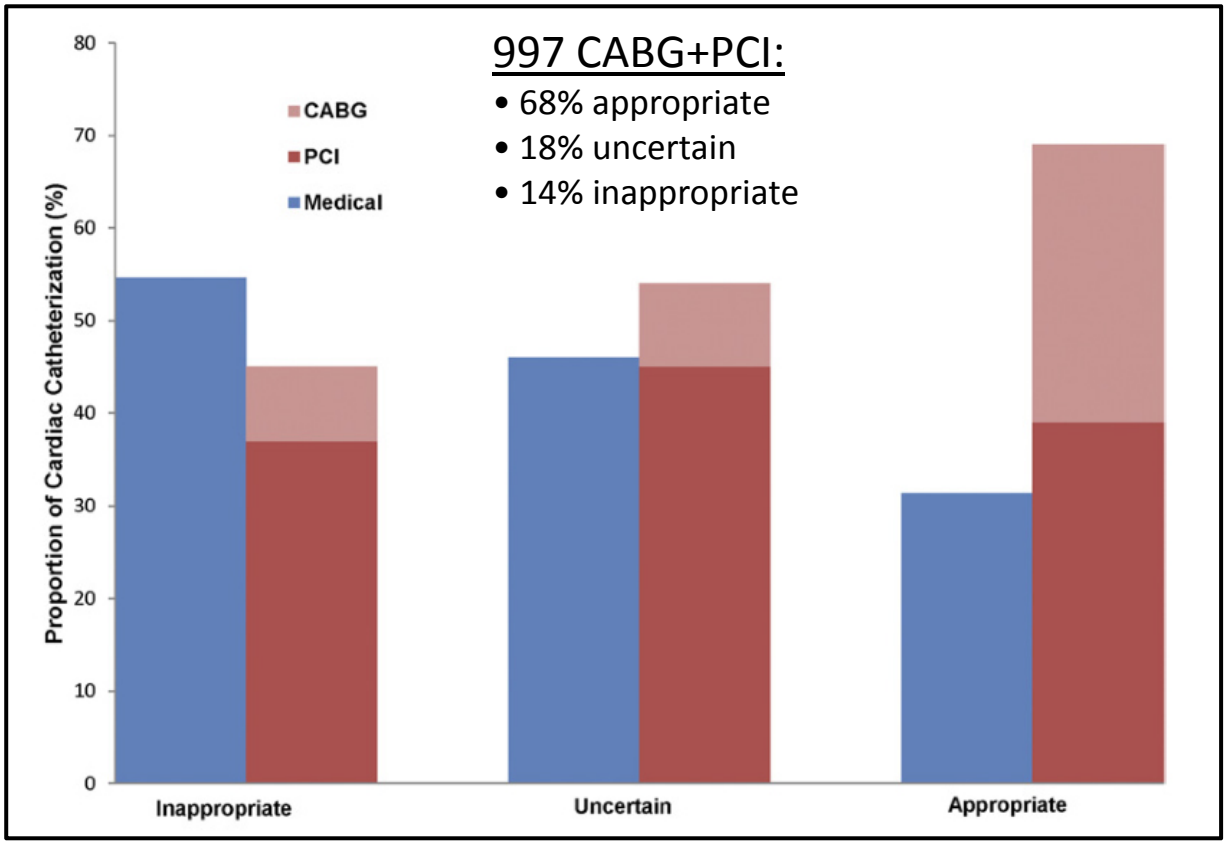
Appropriateness of Coronary Revascularization in Ontario



Proportions of patients undergoing medical therapy, PCI, or CABG in each appropriateness category

D Ko, et al., J Am Coll Cardiol 2012;60:1876–84)

Appropriateness of Coronary Revascularization in Ontario



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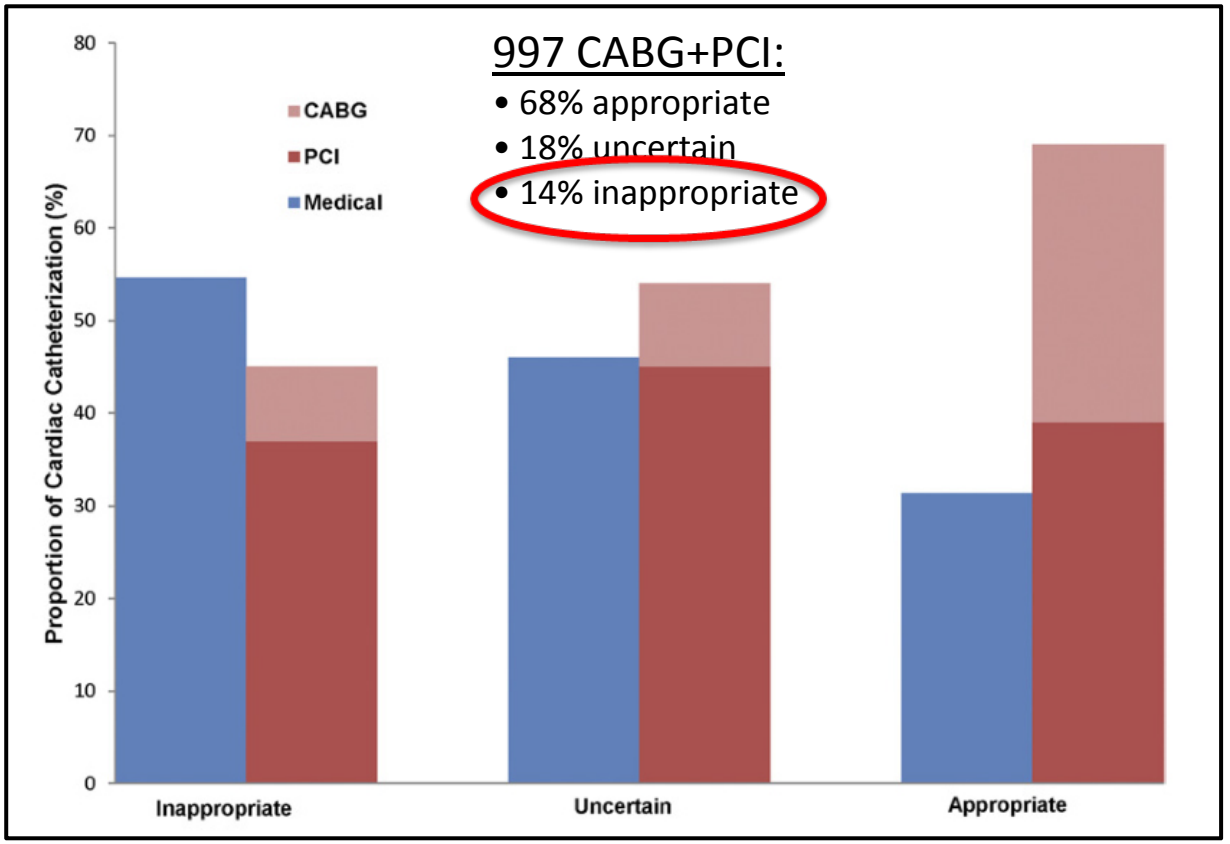
Appropriateness of Coronary Revascularization in Ontario



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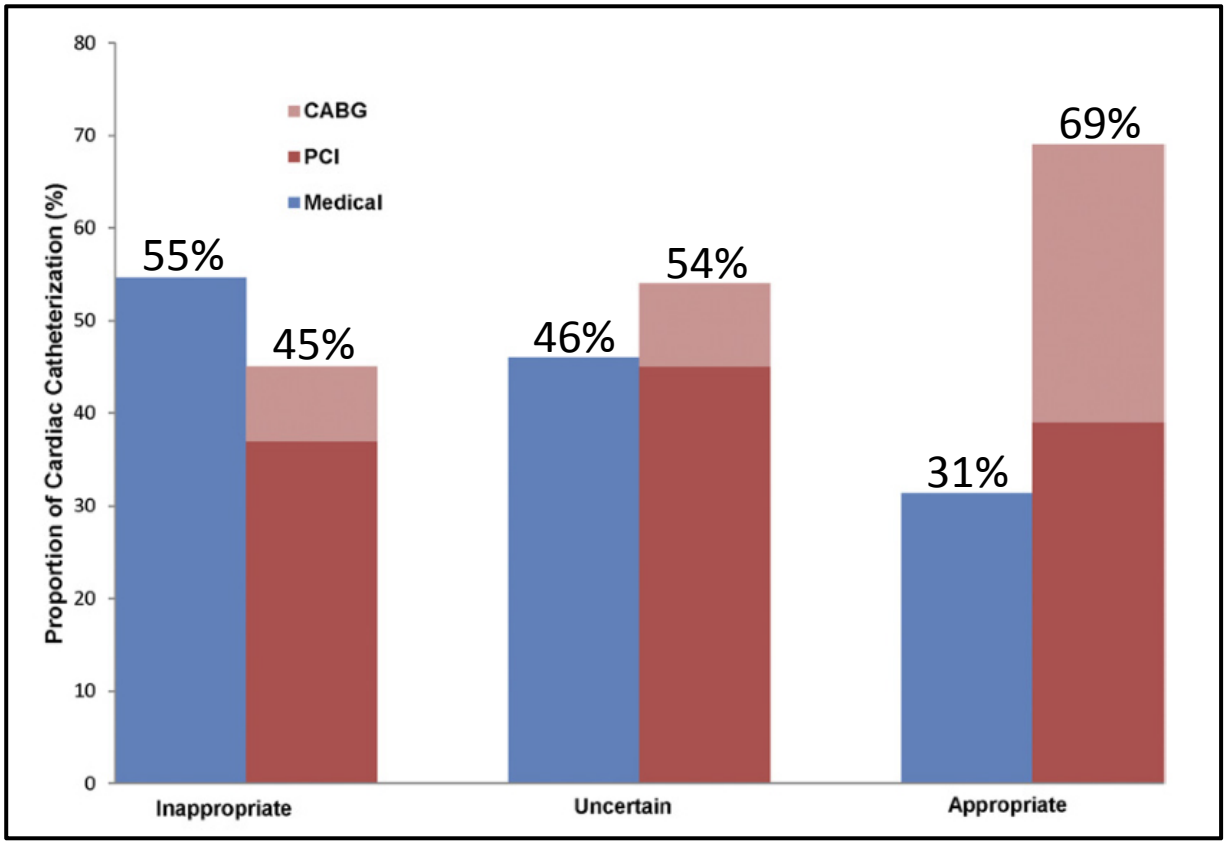

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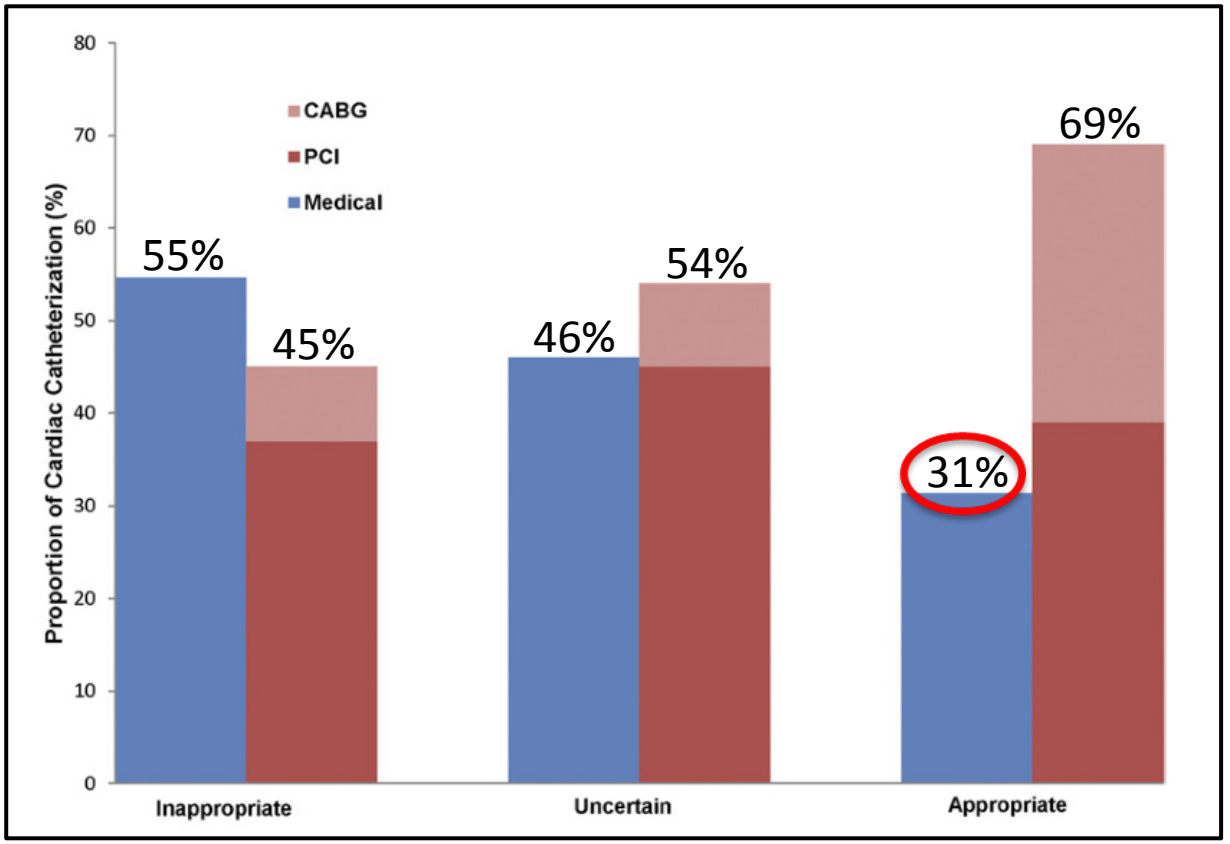

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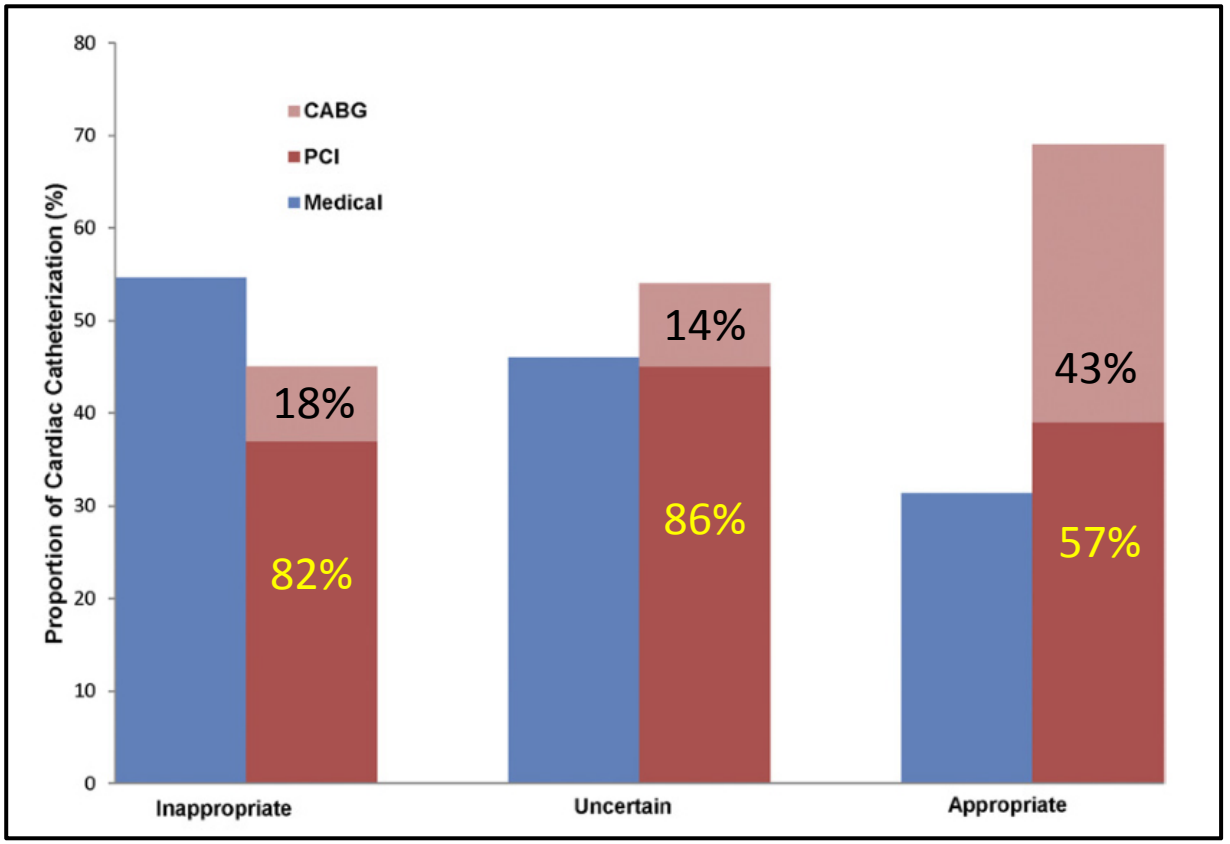

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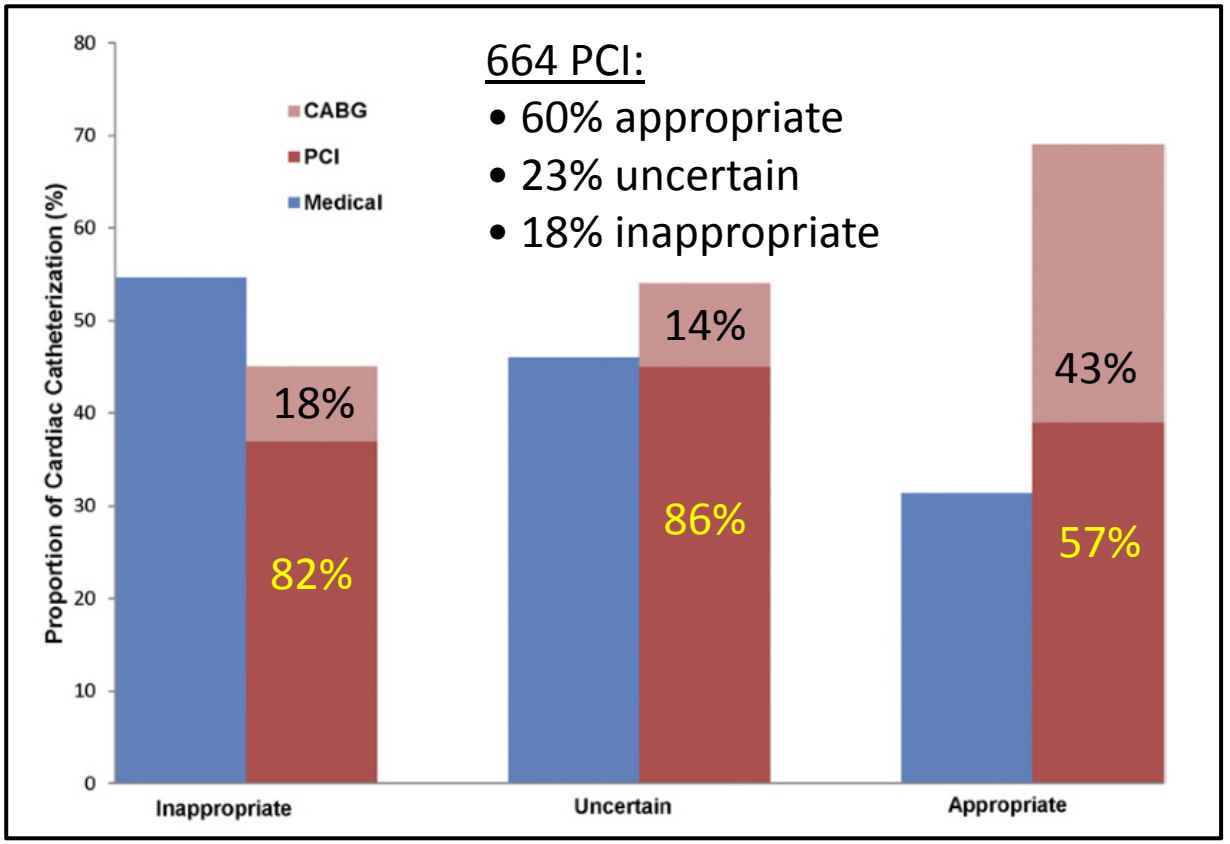

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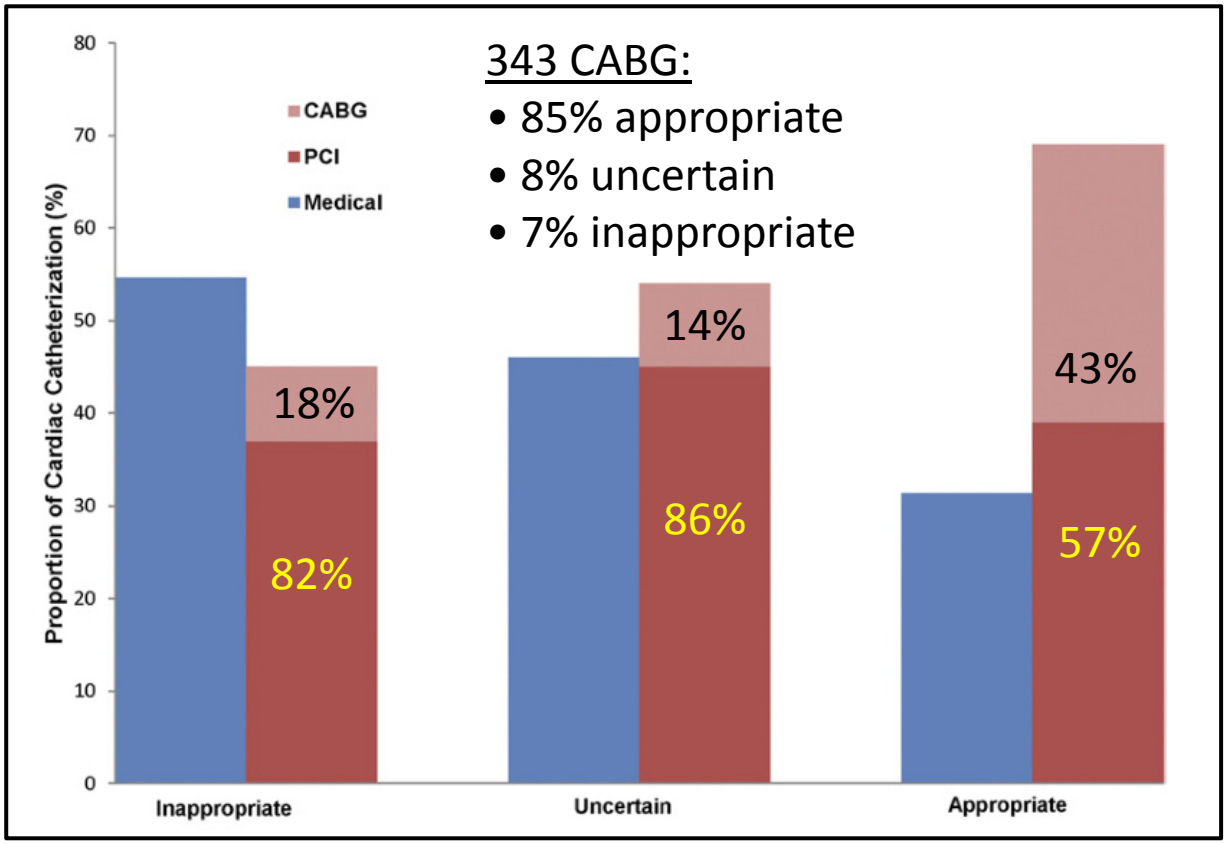

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Appropriateness of Coronary Revascularization in Ontario

Rate of Death plus Recurrent ACS

Appropriateness Category	n	Crude Rate %		HR (95% CI)	Adjusted p Value
		No Revascularization	Revascularization		
Inappropriate*	311	16 (9.4%)	20 (14.2%)	0.99 (0.48–2.02)	0.97
Uncertain*	326	23 (15.3%)	14 (8.0%)	0.57 (0.28–1.16)	0.12
Appropriate†	991	50 (16.1%)	80 (11.8%)	0.61 (0.42–0.88)	0.0087

Revascularization by method:

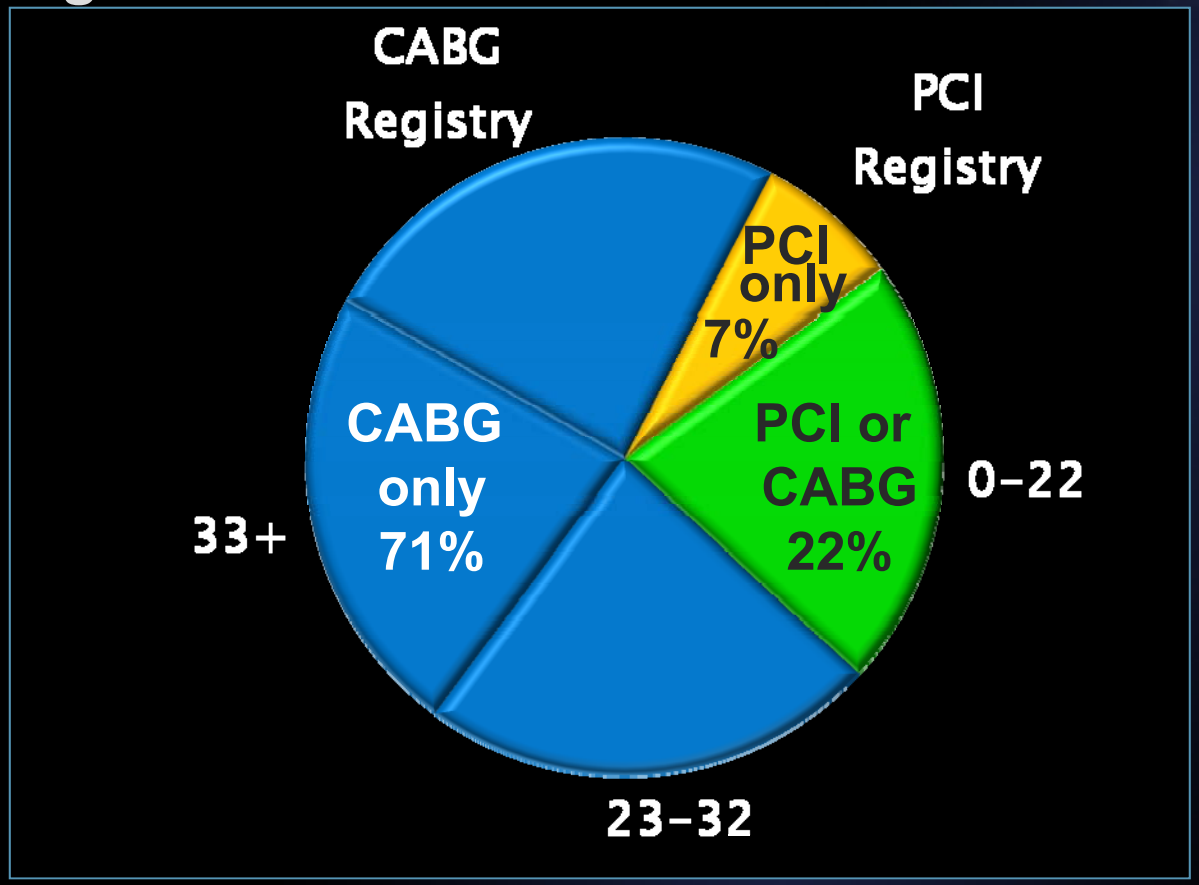
HR for CABG vs medical therapy = 0.33 (p=0.006)
HR for PCI vs medical therapy = 0.83 (p=NS)

D Ko, et al., J Am Coll Cardiol 2012;60:1876–84)

How do results of PCI and CABG compare?

MACCE to 5 Years

Interpreting Results Based on SYNTAX Score



Five-year results of the SYNTAX trial suggest that 71% of all patients are still best treated with CABG; however, for the remaining patients PCI is an alternative to surgery

Unfortunately, SYNTAX and FREEDOM do NOT Represent Current PCI Practice: Major changes since these trials

- **Importance of complete revascularization**
- **Ischemia-guided intervention**
- **2nd generation DES**

What Are We Really Fighting?


NO!
THE
ONE WORD
THAT
CAN SAVE
YOUR
LIFE

How are PCI and CABG being used?

- Appropriate Use Criteria are not perfect
- Substantial variability in assessment
- Underuse is more common than overuse
- Overuse of PCI >> CABG
- Heart Team approach may balance overuse

A Simple Choice

PCI vs. CABG

A Simple Choice

PCI vs. CABG

A Simple Choice

PCI vs. CABG

The Pickett's Charge Intervention (PCI): Why would it fail?

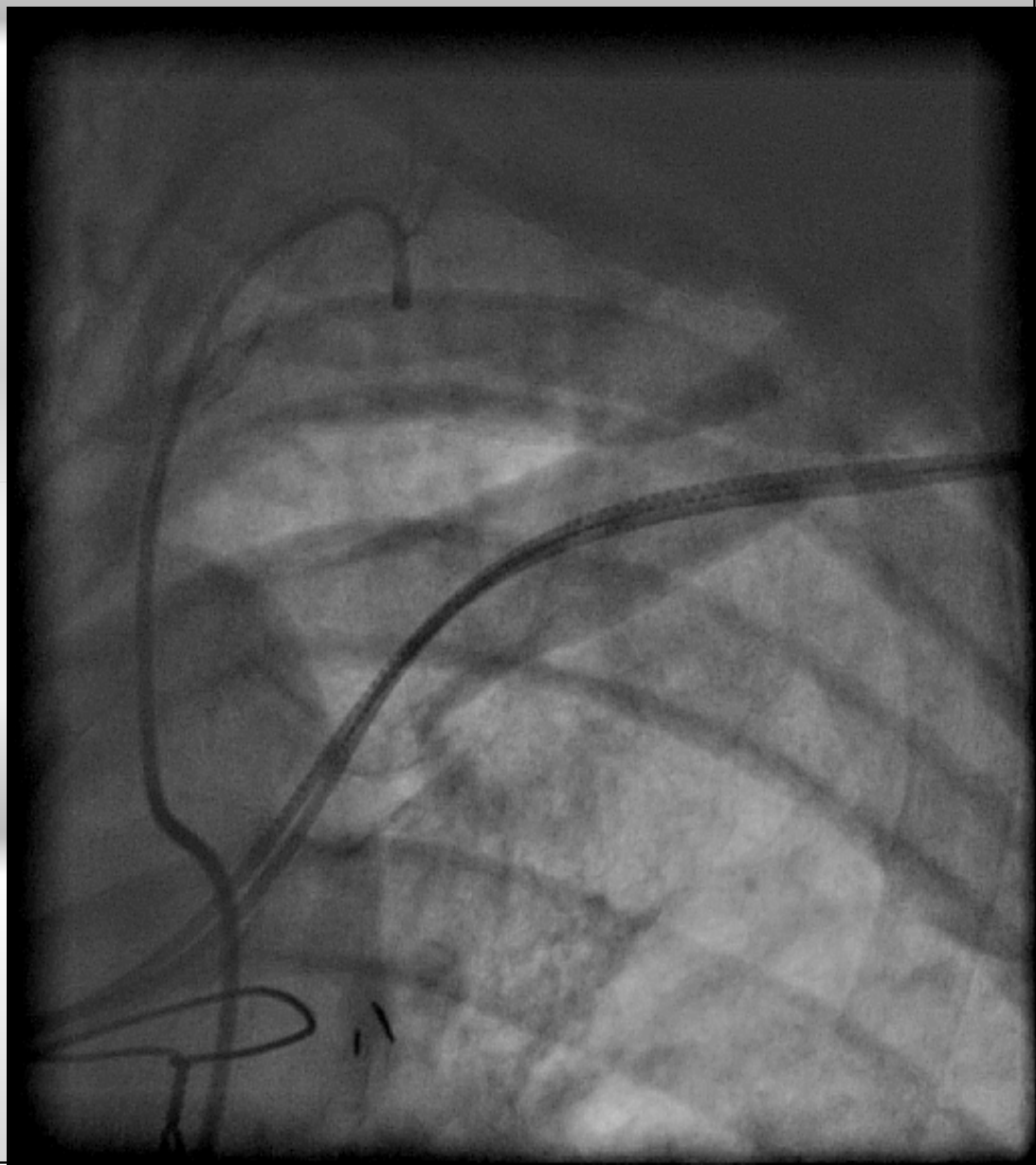
Post PCI, blood must pass through:

- A site prone to native disease
- A site that is rarely focal
- Now it contains a foreign body
- The foreign body includes drug and matrix
- The balance of drug-effect on healing is ??

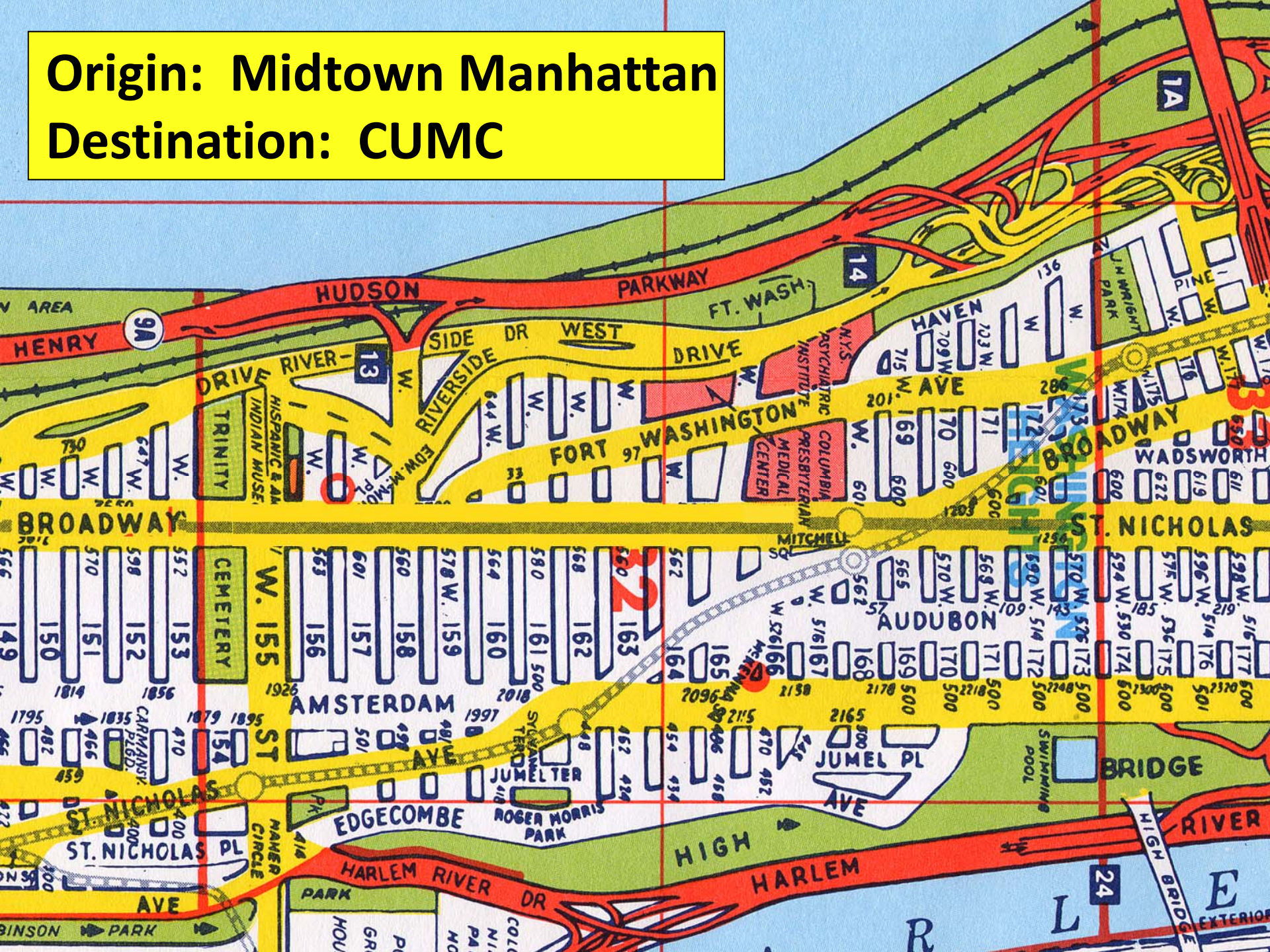
Why does CABG* succeed?

Blood must pass through:

- A relatively normal conduit
- One anastomosis
- The most normal segment of the coronary target



*Credible Advantage Beats Gatekeeping


Origin: Midtown Manhattan
Destination: CUMC
HUDSON PARKWAY
HENRY HUDSON PARKWAY
RIVERSIDE DRIVE
RIVERSIDE DR WEST
FT. WASH.
DRIVE
TRINITY CEMETERY
HISPANIC & AM. INDIAN MUSE.
N.Y.S. PSYCHIATRIC INSTITUTE
COLUMBIA PRESBYTERIAN MEDICAL CENTER
FORT WASHINGTON AVE
BROADWAY
WADSWORTH
ST. NICHOLAS
MITCHELL SQ
AUDUBON
W. 155 ST
AMSTERDAM AVE
JUMEL TER
JUMEL PL
ROGER MORRIS PARK
EDGECOMBE
ST. NICHOLAS PL
ST. NICHOLAS AVE
HARLEM RIVER DR
HARLEM RIVER
HIGH BRIDGE
SWIMMING POOL
JOHN WRIGHT PARK
PINE
HAVEN
CARMANSV. PLGD.
MAHER CIRCLE
1A
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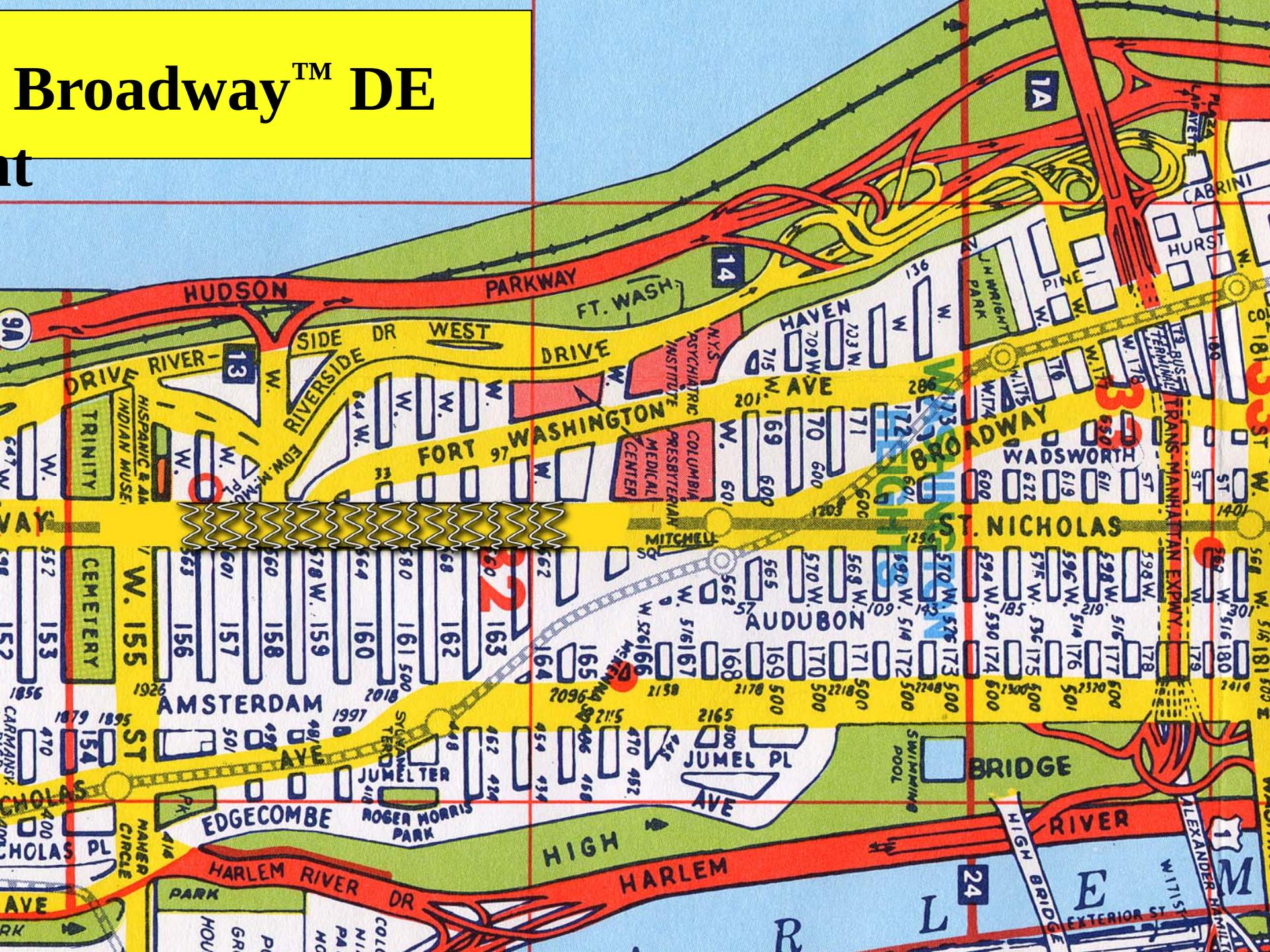
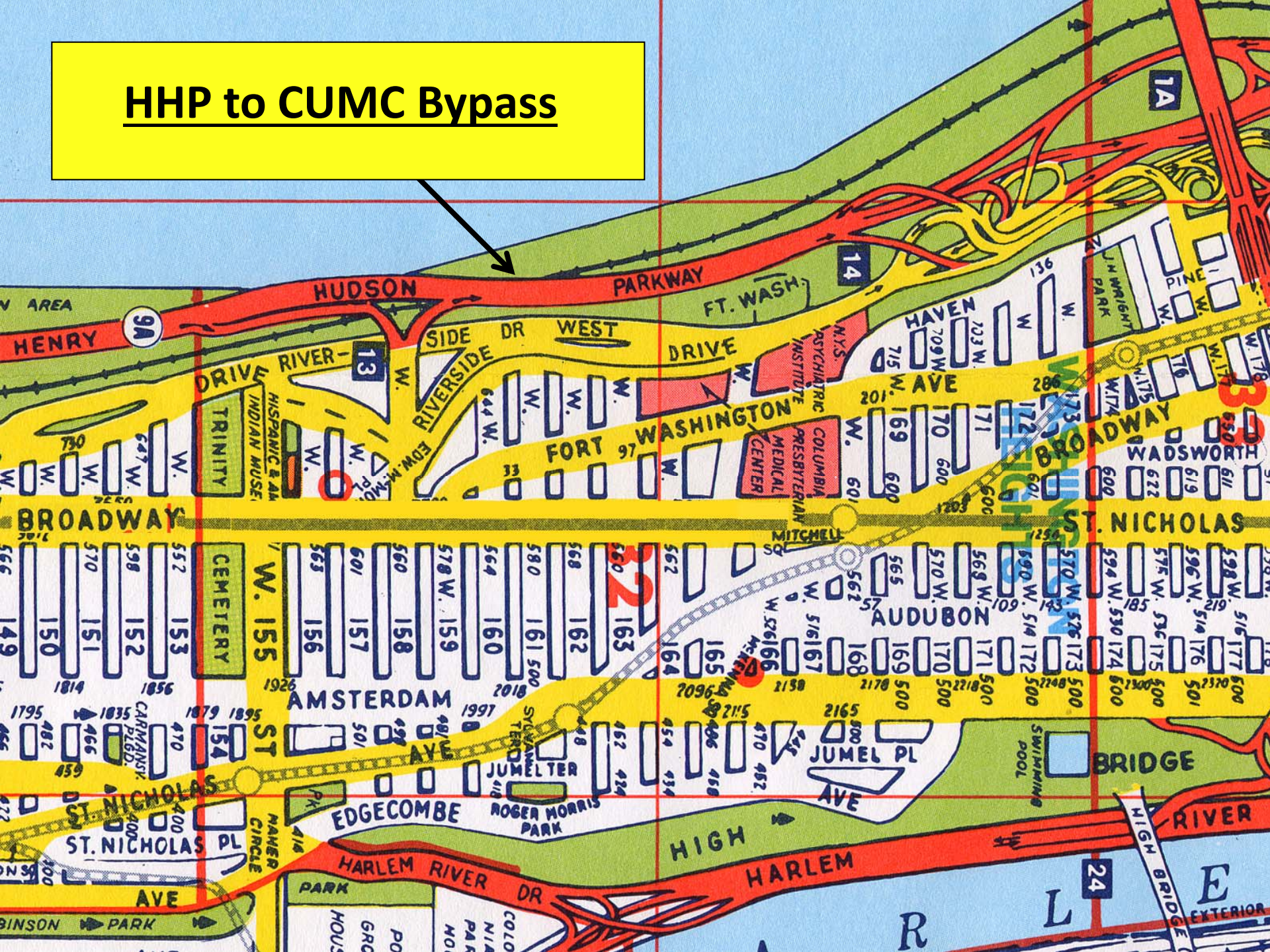
Broadway™ DE

nt




HHP to CUMC Bypass
HUDSON PARKWAY
HENRY HUDSON PARKWAY
RIVERSIDE DR WEST
RIVERSIDE DRIVE
DRIVE
FT. WASH.
HAVEN AVE
BROADWAY
FORT WASHINGTON AVE
WASHINGTON HEIGHTS
WADSWORTH
ST. NICHOLAS
MITCHELL SQ
AUDUBON
W. 155 ST
AMSTERDAM AVE
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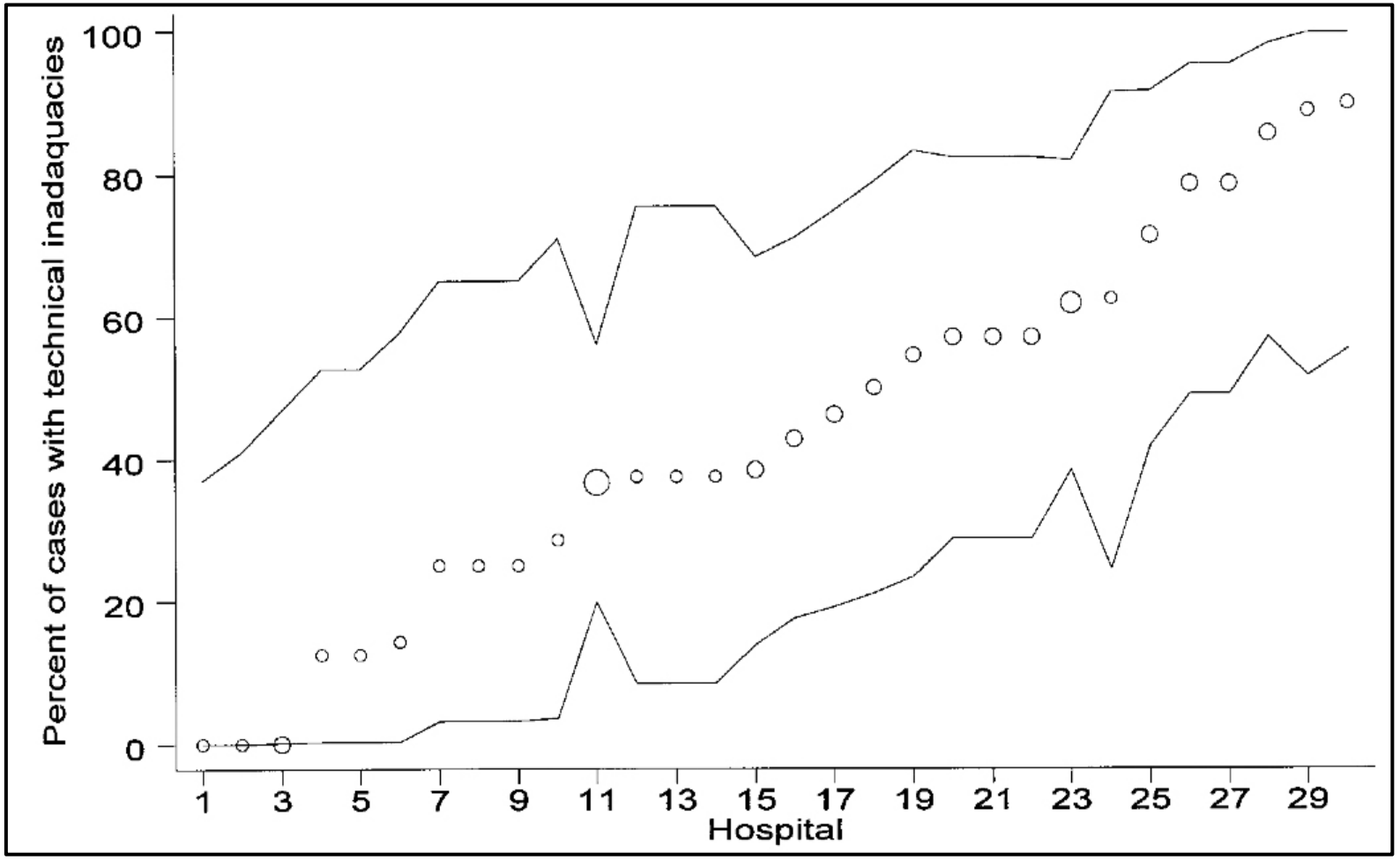
ST. NICHOLAS PL
HAMER CIRCLE
HARLEM RIVER DR
HIGH BRIDGE
HARLEM RIVER
PARK
EXTERIOR
1A
14
9A
13
32
24

Variability in Coronary Angiogram Interpretation: Effect on Appropriate Use Scoring



Circle size proportional to sample size (range 7-30). Solid lines are bound binomial CI's.

L L Leape, et al., Am Heart J 2000;139:106-13

Appropriateness of CABG

- Appropriateness criteria developed and updated for 16 surgical procedures including CABG.
- Appropriate use: 54% to 93%
- Overuse: 0% to 14%
- Underuse: 24% to 57%

Patel MR, J Am Coll Cardiol. 2009; Shekelle PG, N Engl J Med. 1998; Leape LL, JAMA. 1993; Park RE, Am J Public Health. 1986

Methodologic foundations of Appropriateness of medical interventions

- Appropriateness is defined as “the health benefits exceed the risks by a sufficiently wide margin that the procedure is worth doing”
- RAND/UCLA appropriateness method developed in 1984 by Rand Health Utilization Study
- 9-point scale with 1 being lowest and 9 being highest appropriateness
- 3 categories of appropriateness: appropriate/ necessary (7 to 9), equivocal (4 to 6), inappropriate (1 to 3)

Assessing Appropriateness

1. Define intervention, lit review, meta-analysis.
2. Panel of experts ranking scale of appropriateness
3. Abstraction and review of medical records for indication and intervention.
4. Each patient record independently reviewed by expert panel and assigned level of intervention appropriateness.

Analysis is performed by considering appropriateness similar to a diagnostic test

Phelps, NEJM 1993

The Pickett's Charge Intervention (PCI): Why would it fail?

Appropriateness of PCI

500,154 PCI from NCDR; 144,737 nonacute (29%)

Appropriate Use Criteria Scenario No.[b]	Indication: Anatomy	Prior CABG	Symptoms	Cardiac Risk (Stress Test)	Anti-ischemic Therapy	No. (%)
Inappropriate PCI						
12B	1- or 2-vessel CAD, no proximal LAD involvement	No	CCS class I or II	Low	None/minimal	6662 (39.6)
14A	1- or 2-vessel CAD, no proximal LAD involvement	No	Asymptomatic	Intermediate	None/minimal	4127 (24.5)
12A	1- or 2-vessel CAD, no proximal LAD involvement	No	Asymptomatic	Low	None/minimal	3083 (18.3)
54B	≥1 Stenoses in non-CABG territory, all bypass grafts patent	Yes	CCS class I or II	Low	None/minimal	568 (3.4)
56A	≥1 Stenoses in non-CABG territory, all bypass grafts patent	Yes	Asymptomatic	Intermediate	None/minimal	493 (2.9)

- >82% confined to only 5 AUC clinical scenarios
- Majority of inappropriates had no angina (54%), low-risk non-invasive testing (72%), or suboptimal medication (96%)

Chan et al, J Am Coll Cardiol 2011;57:1546-53

Appropriateness of PCI

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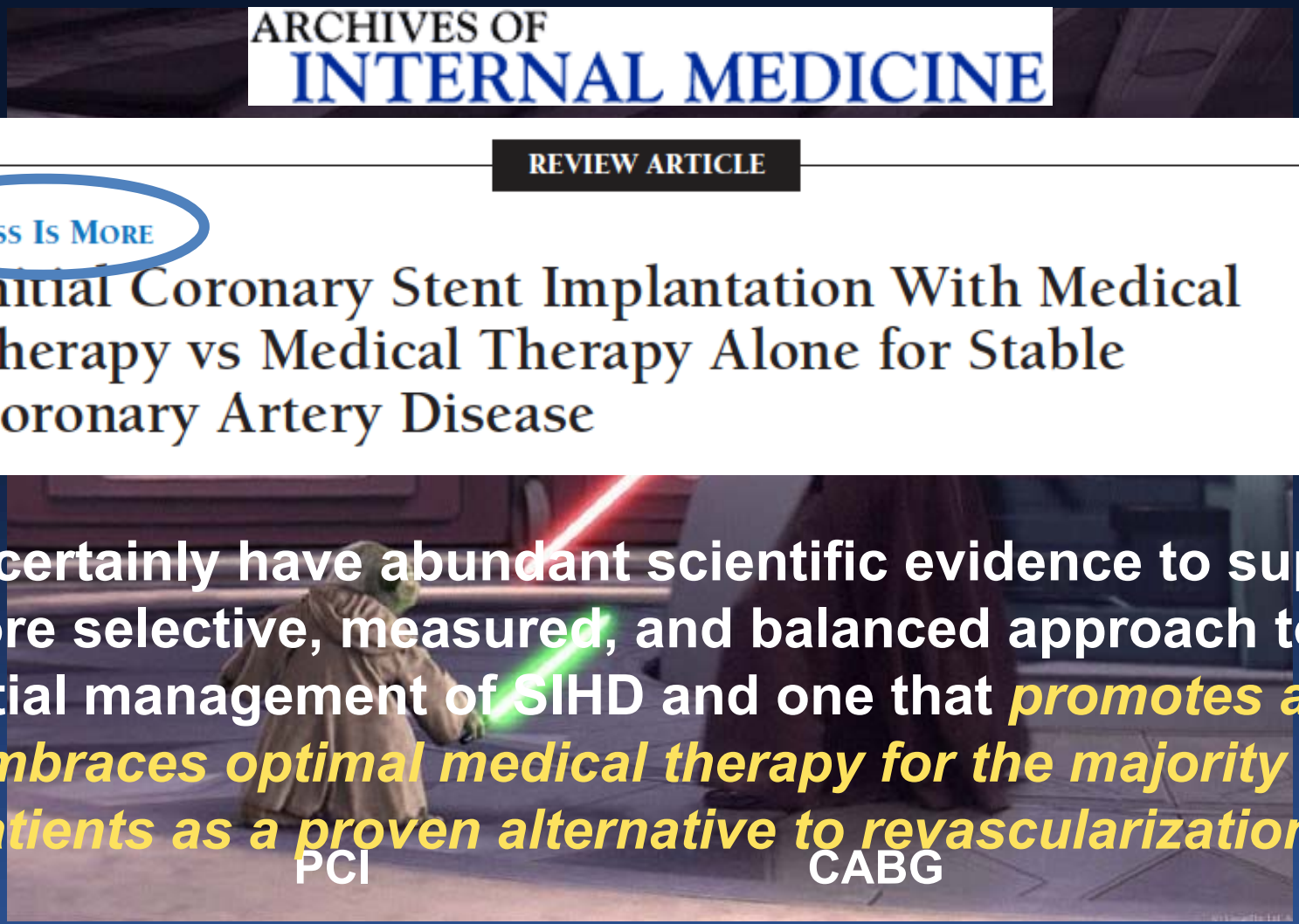
- Majority of inappropriates had no angina (54%), low-risk non-invasive testing (72%), or suboptimal medication (96%)

- 94,867 excluded b/o no stress test, or stress test with no ischemia specified
- IA rate increases to 21% if the 94,867 are included

Chan et al, J Am Coll Cardiol 2011;57:1546-53

What Are We Really Fighting?



ARCHIVES OF
INTERNAL MEDICINE

REVIEW ARTICLE

LESS IS MORE

Initial Coronary Stent Implantation With Medical Therapy vs Medical Therapy Alone for Stable Coronary Artery Disease

"We certainly have abundant scientific evidence to support a more selective, measured, and balanced approach to the initial management of SIHD and one that *promotes and embraces optimal medical therapy for the majority of patients as a proven alternative to revascularization.*"

PCI CABG

Editorial by W. Boden, 2012

Underestimating Medical Therapy for Coronary Disease . . . Again

James C. Fang, M.D.

The NEW ENGLAND JOURNAL of MEDICINE

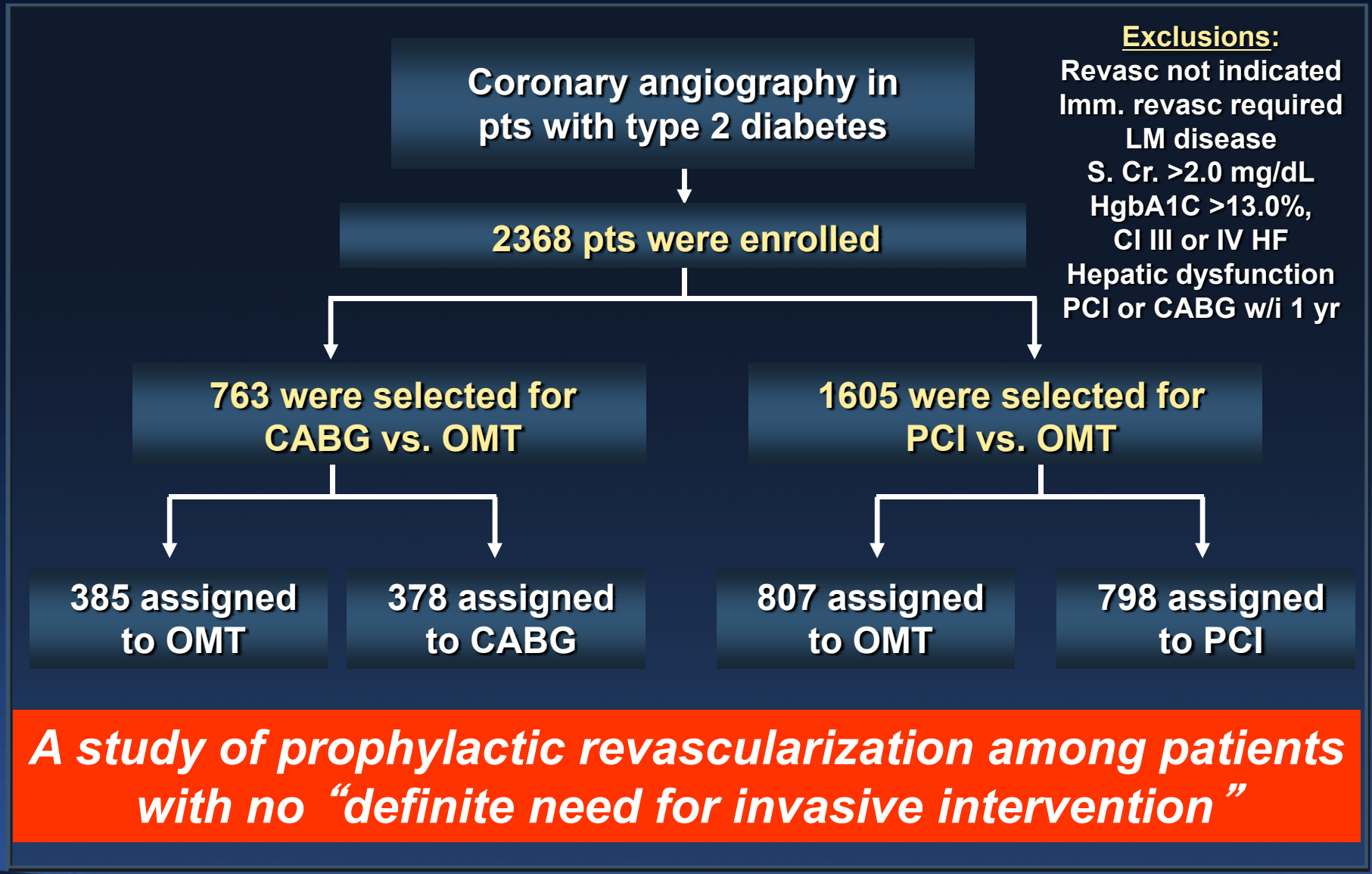
"With the results of the STICH trial, we should be comfortable with the notion that in general, *surgery is not superior to optimal medical therapy for ischemic left ventricular dysfunction*."

Except if you have prognostically important disease!

Two Goals of Therapy in Patients with Stable CAD

1. Improve Symptoms and Quality of Life
   - Measured by "soft endpoints" (i.e. angina/QOL scales)
2. Improve Prognosis
   - Measured by "hard endpoints" (i.e. death, MI)

BARI 2D: Patient Flow



A study of prophylactic revascularization among patients with no "definite need for invasive intervention"

CARDIOVASCULAR RESEARCH FOUNDATION
A Passion for Innovation

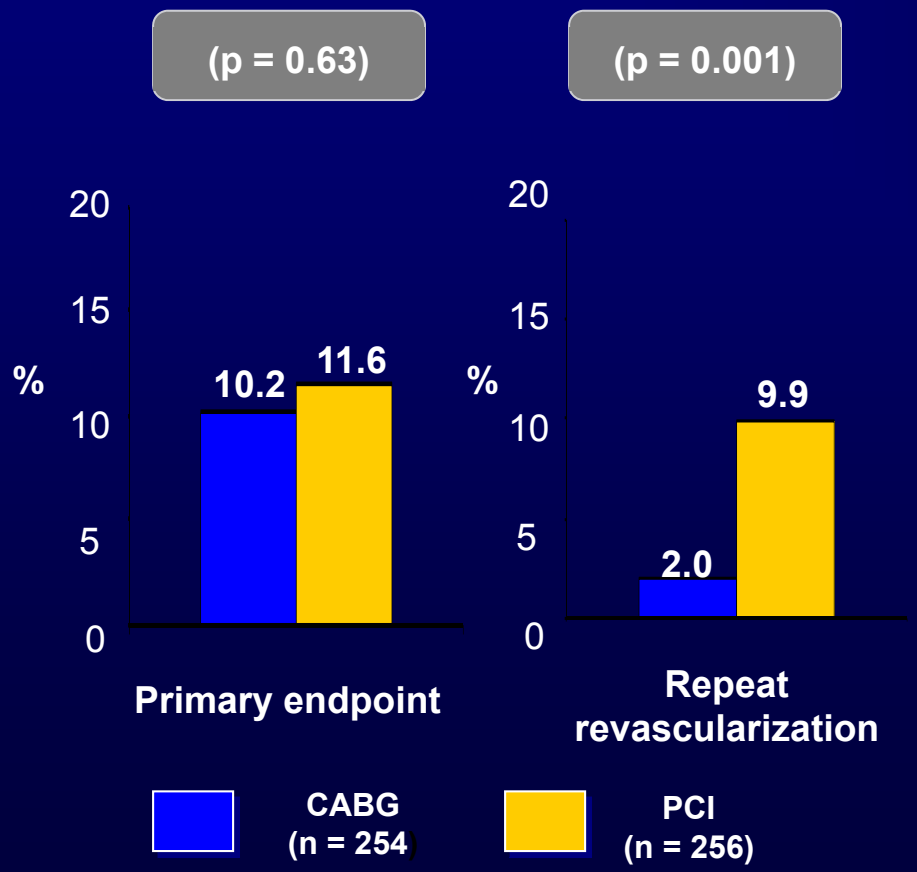
IP = insulin provision
IS = insulin sensitization

The BARI 2D Study Group.
NEJM 2009;360:2503-15

COLUMBIA UNIVERSITY MEDICAL CENTER
NewYork-Presbyterian

CARDIA

Trial design: Diabetic patients with multi-vessel disease or complex single-vessel disease, but not left main disease, were randomized to either CABG or PCI. Clinical outcomes were compared at 12 months.



Results

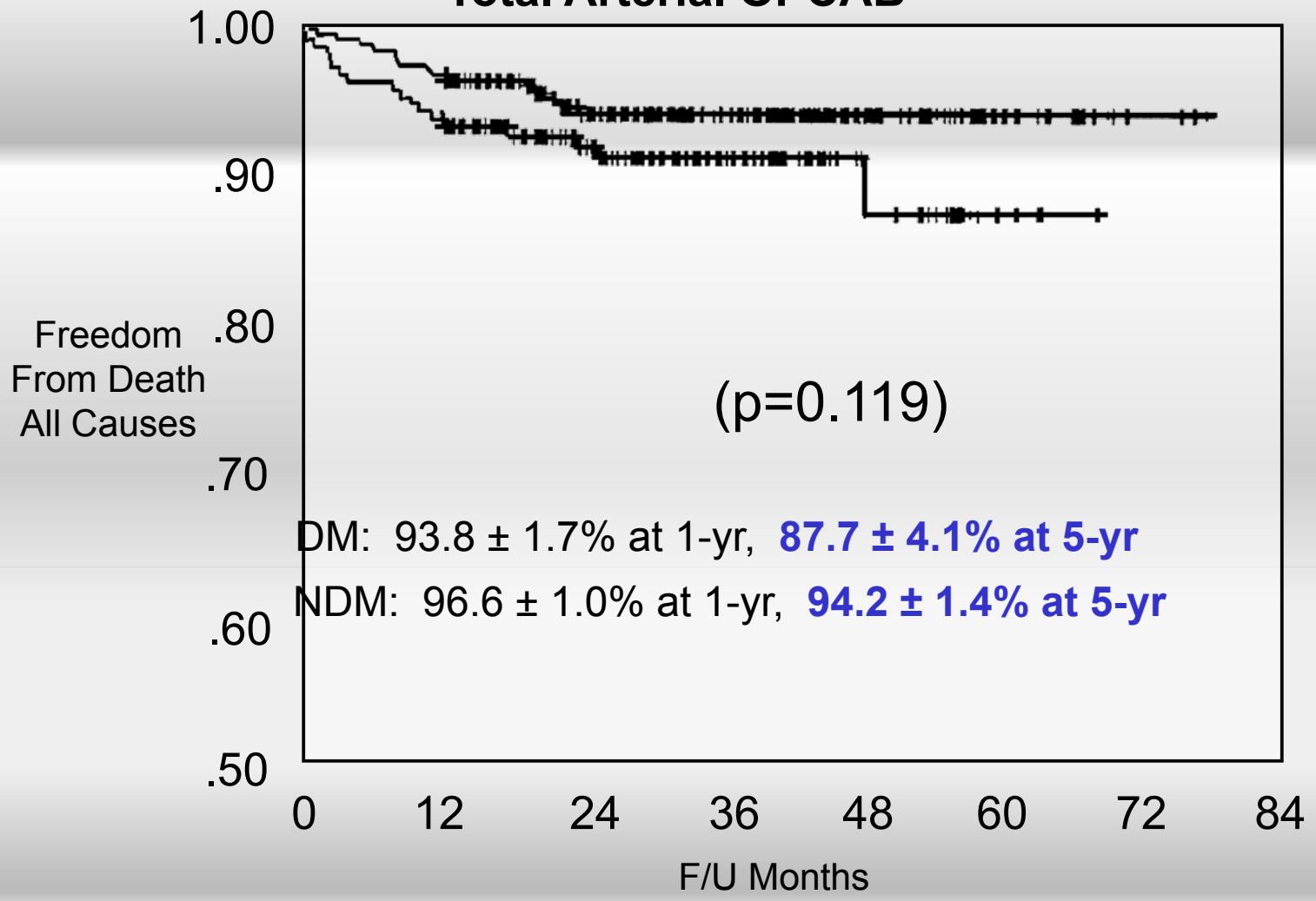
- Primary endpoint (death, MI, stroke) was similar between CABG and PCI (10.2% vs. 11.6%, p = 0.63)
- Significant ↓ in repeat revascularization in CABG arm (2% vs. 9.9%, p = 0.001). True in drug-eluting stent subset also
- Trend toward increased CVA in CABG arm (p = 0.09)

Conclusions

- Similar incidence of death, MI, or stroke in diabetics with CABG or PCI
- CABG was associated with fewer repeat revascularizations compared with PCI
- No difference in death, MI, but trend toward increased stroke with CABG, as suggested by other studies

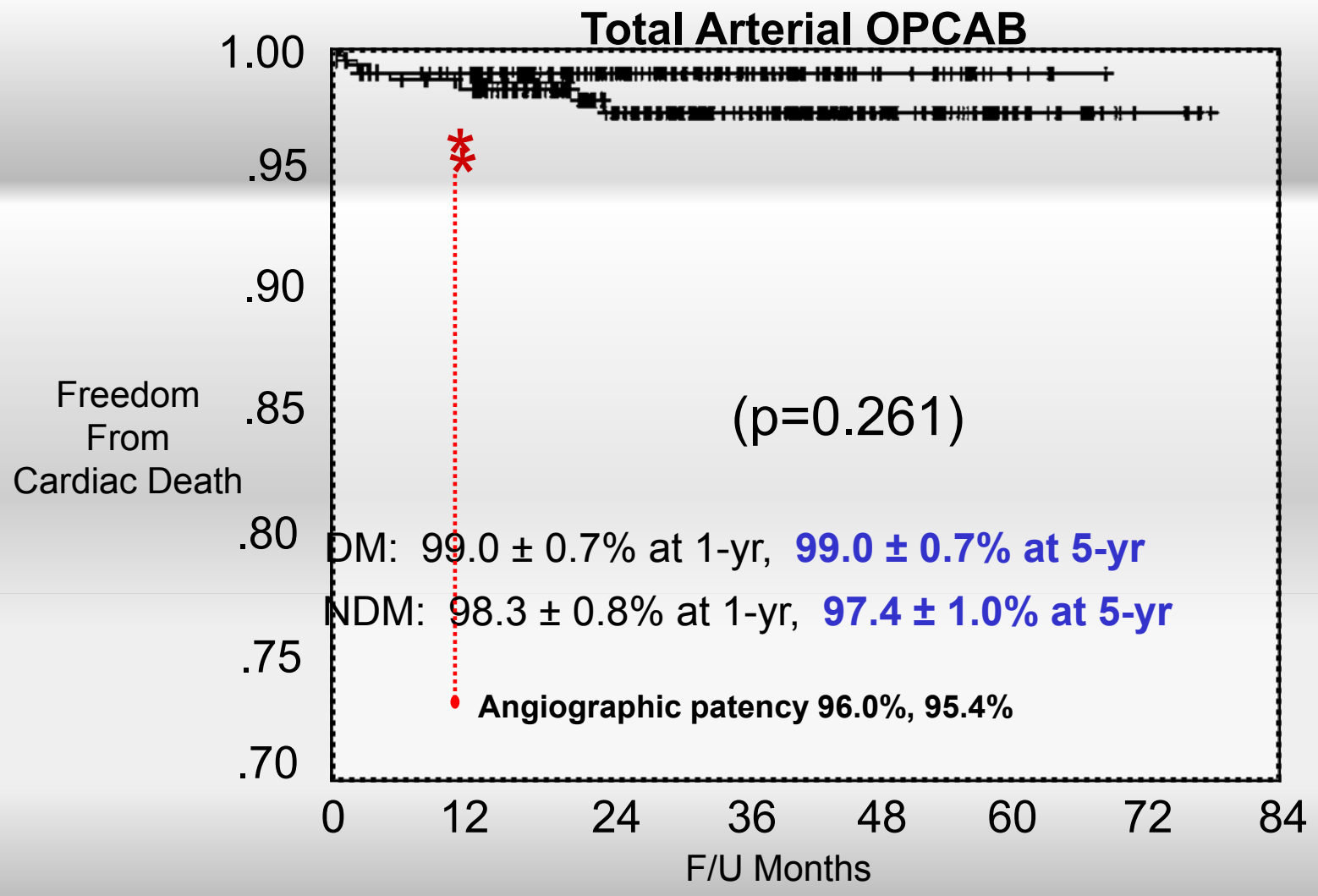
Presented by Dr. Akhil Kapur at ESC 2008

Total Arterial OPCAB



Postoperative months:	12	24	36	48	60	72
DM group (N):	194	134	77	26	5	
NDM group (N):	288	208	141	77	29	6

Choi et al, Ann Thorac Surg 2005;80:1353
Seoul, Korea



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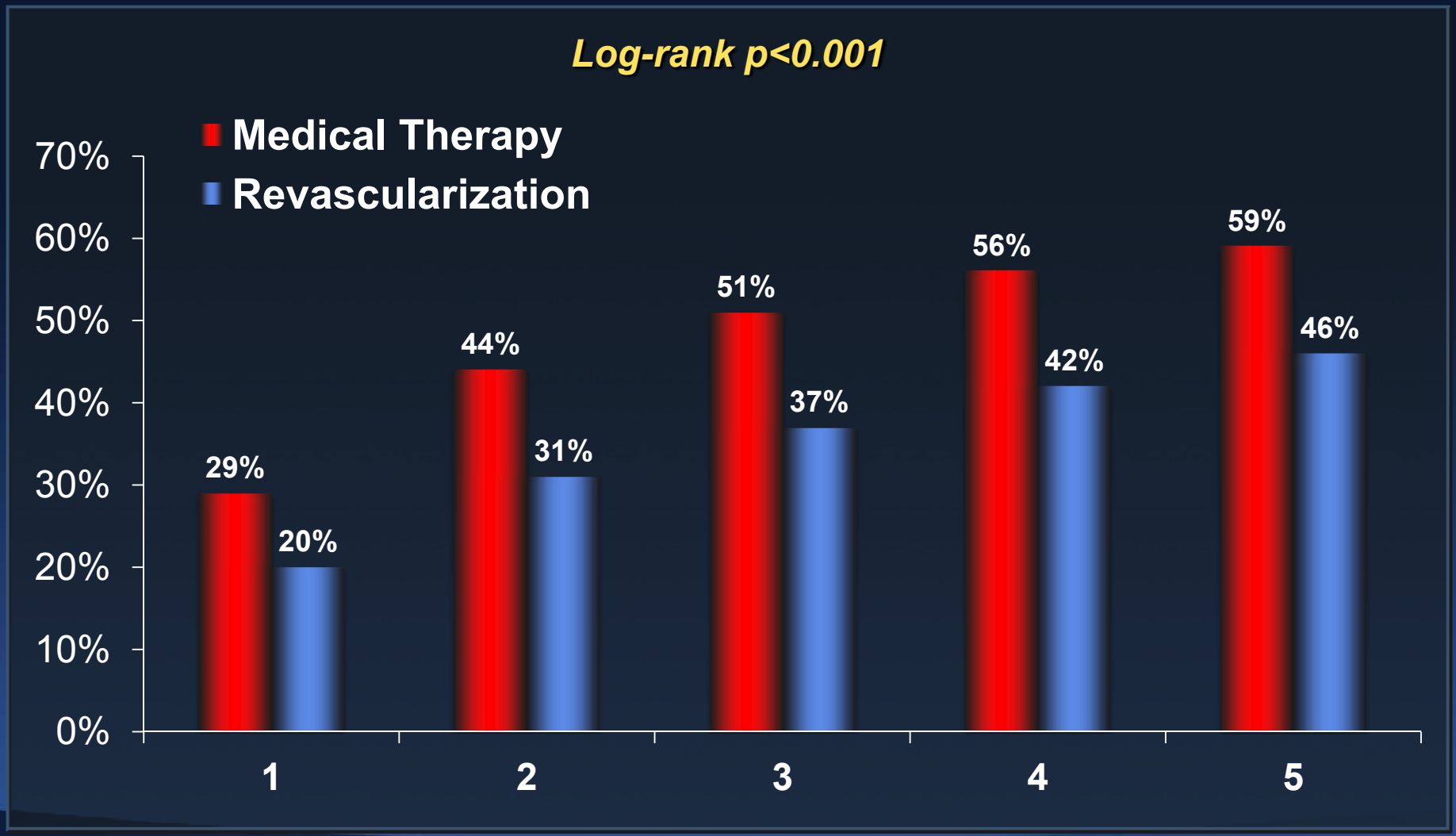
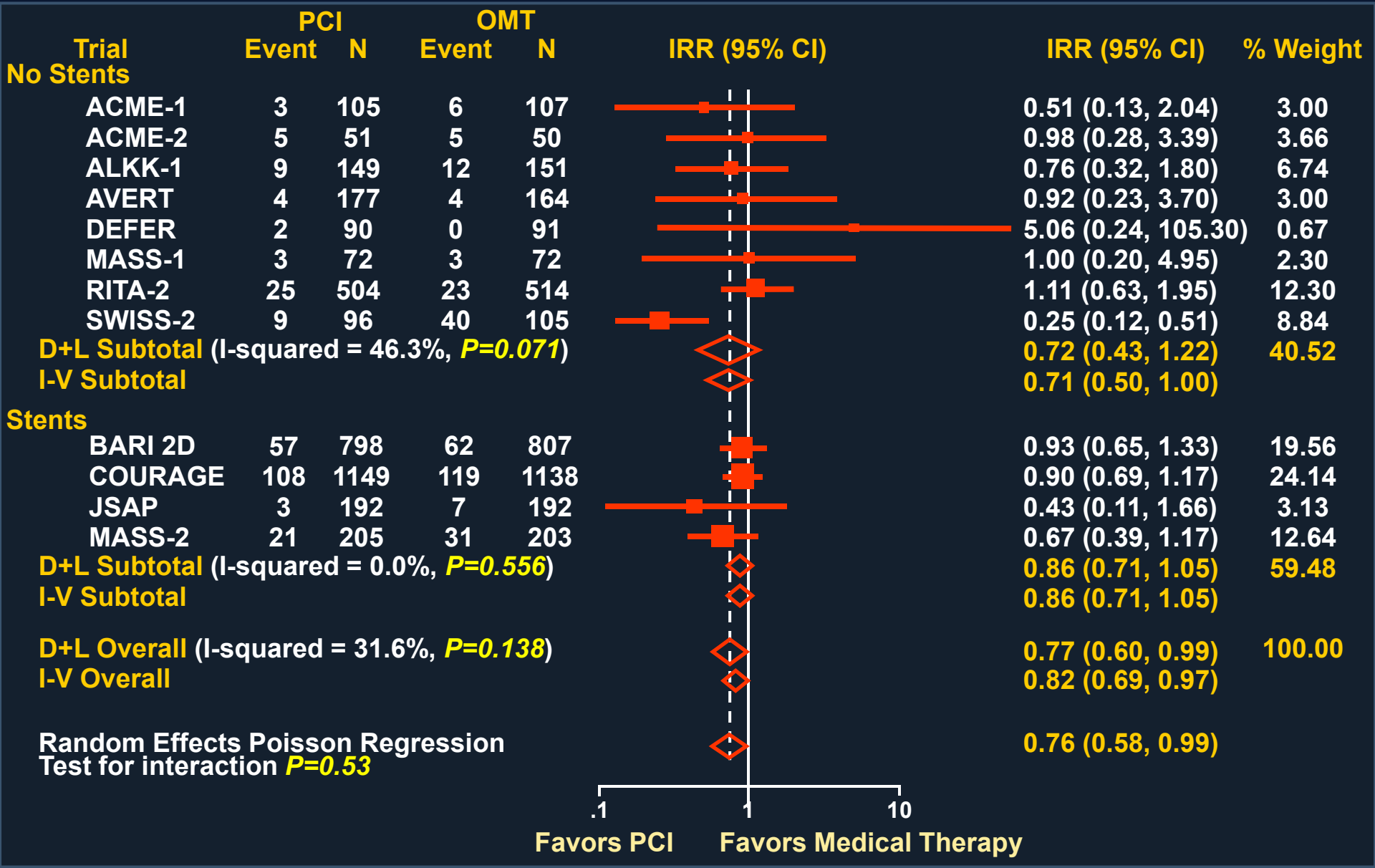
Choi et al, Ann Thorac Surg 2005;80:1353-6
Seoul, Korea

BARI-2D: Cumulative Incidence of New Angina in Initially Asymptomatic Patients

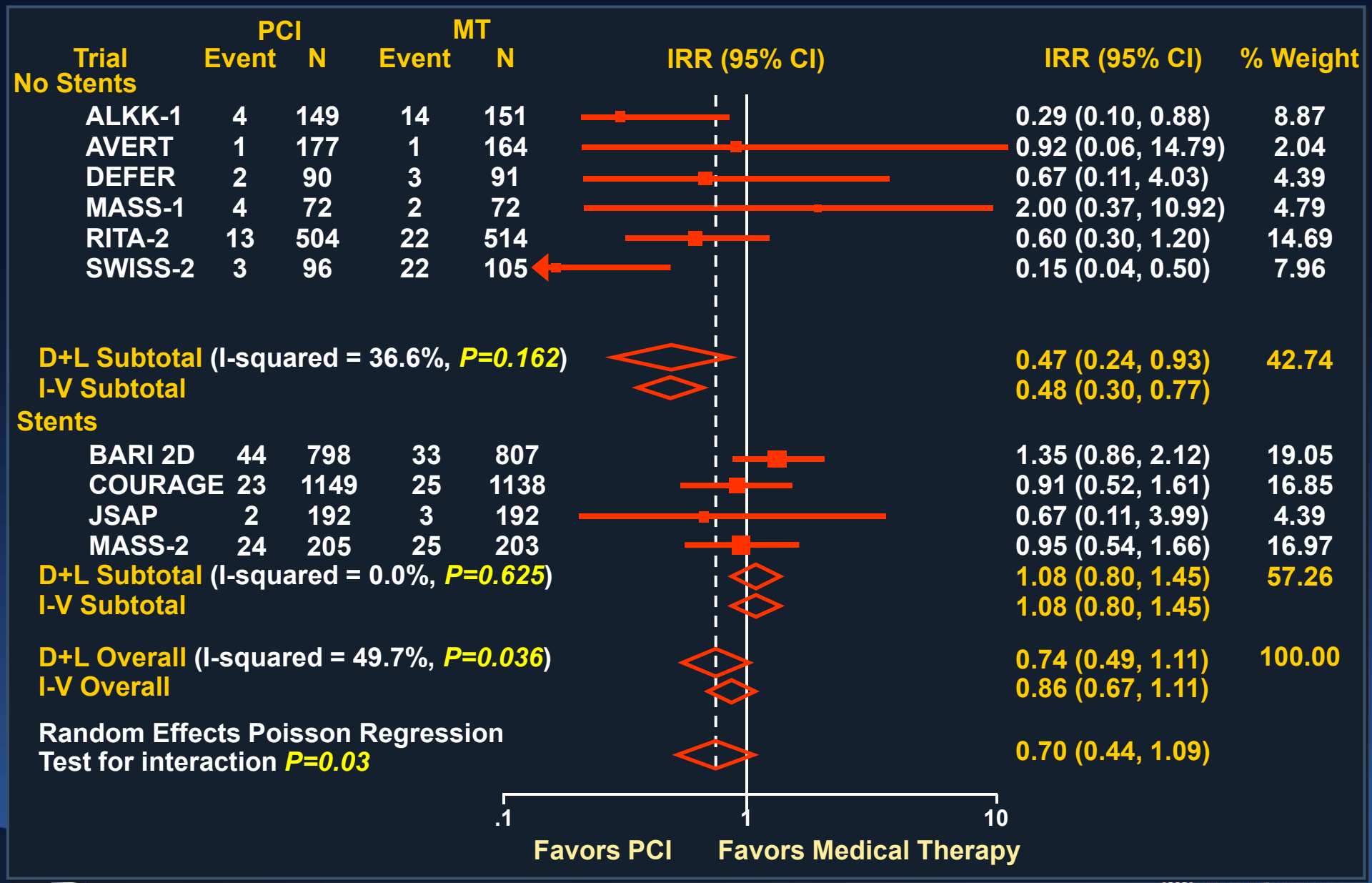


Dagenais et al, Circulation 2011

Spontaneous MI in Trials of PCI vs. OMT

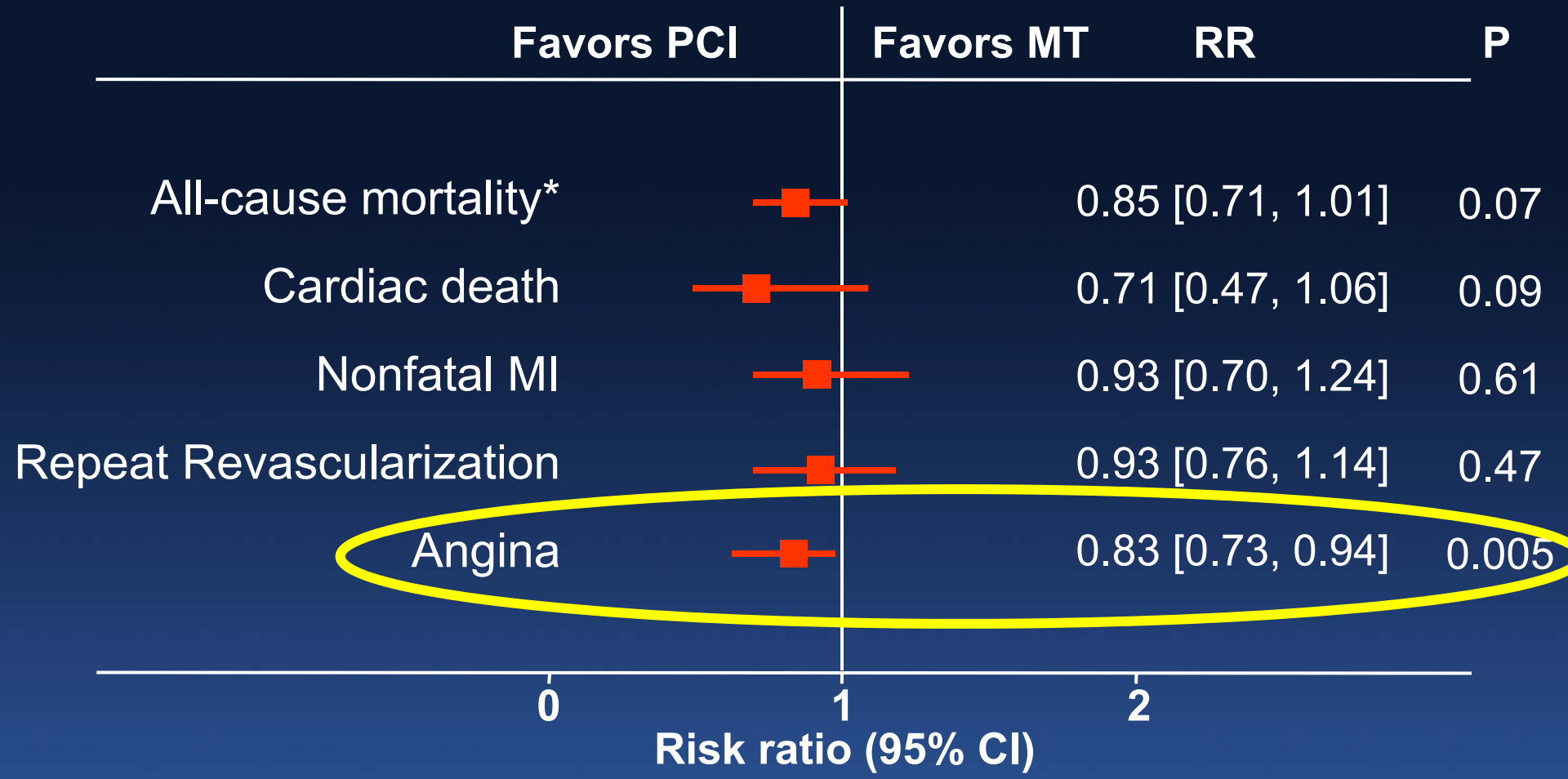


CV Mortality in Trials of PCI vs. OMT



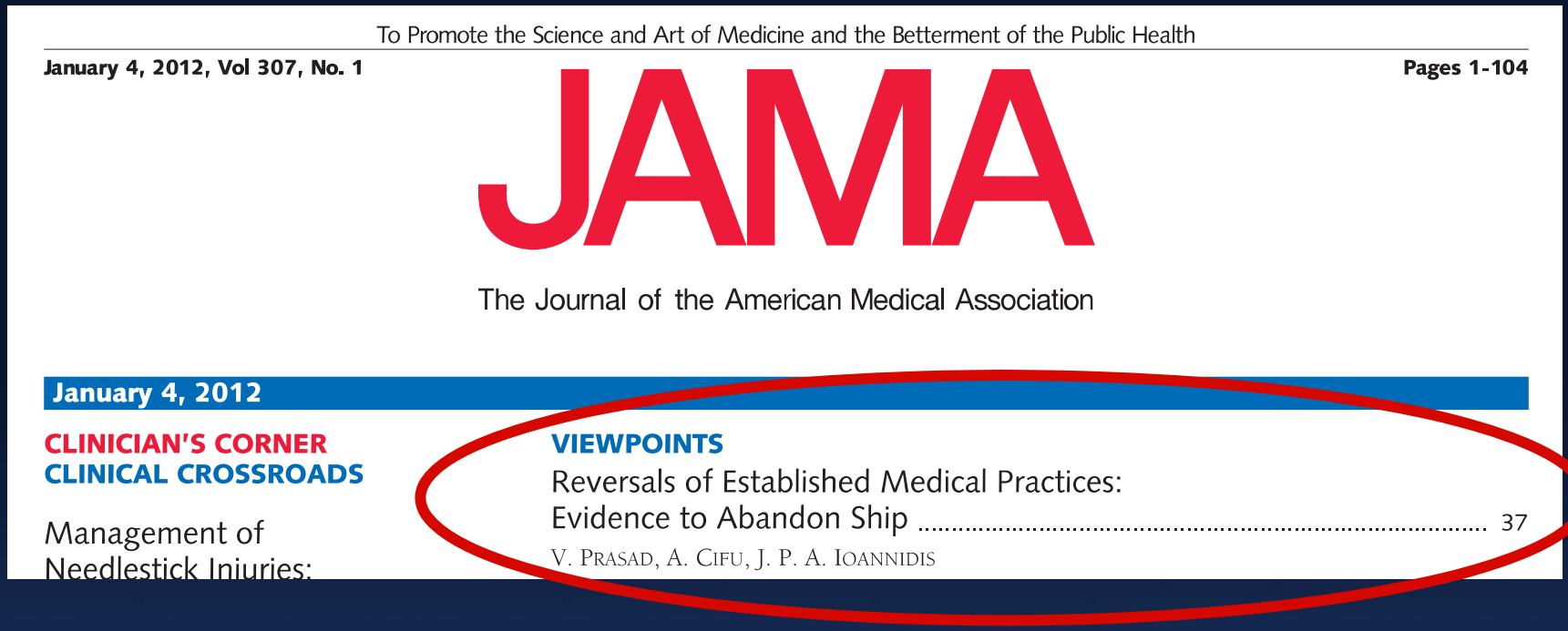
PCI vs. Medical Therapy for Stable CAD

12 RCTs enrolling 7182 participants



*All-cause mortality (in trials with >50% stent use) 0.93 [0.78, 1.11]

Pursnani et al, Circ CV Intv 2012



To Promote the Science and Art of Medicine and the Betterment of the Public Health

January 4, 2012, Vol 307, No. 1

Pages 1-104

JAMA

The Journal of the American Medical Association

January 4, 2012

CLINICIAN'S CORNER
CLINICAL CROSSROADS

Management of Needlestick Injuries:

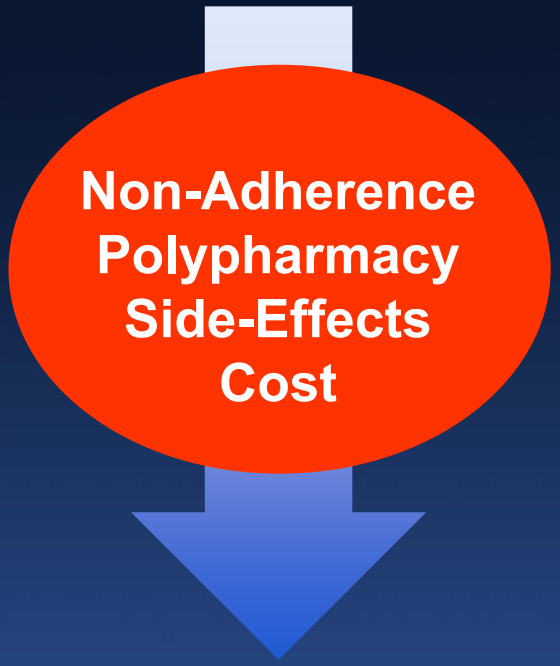
VIEWPOINTS

Reversals of Established Medical Practices: Evidence to Abandon Ship 37

V. Prasad, A. Cifu, J. P. A. Ioannidis

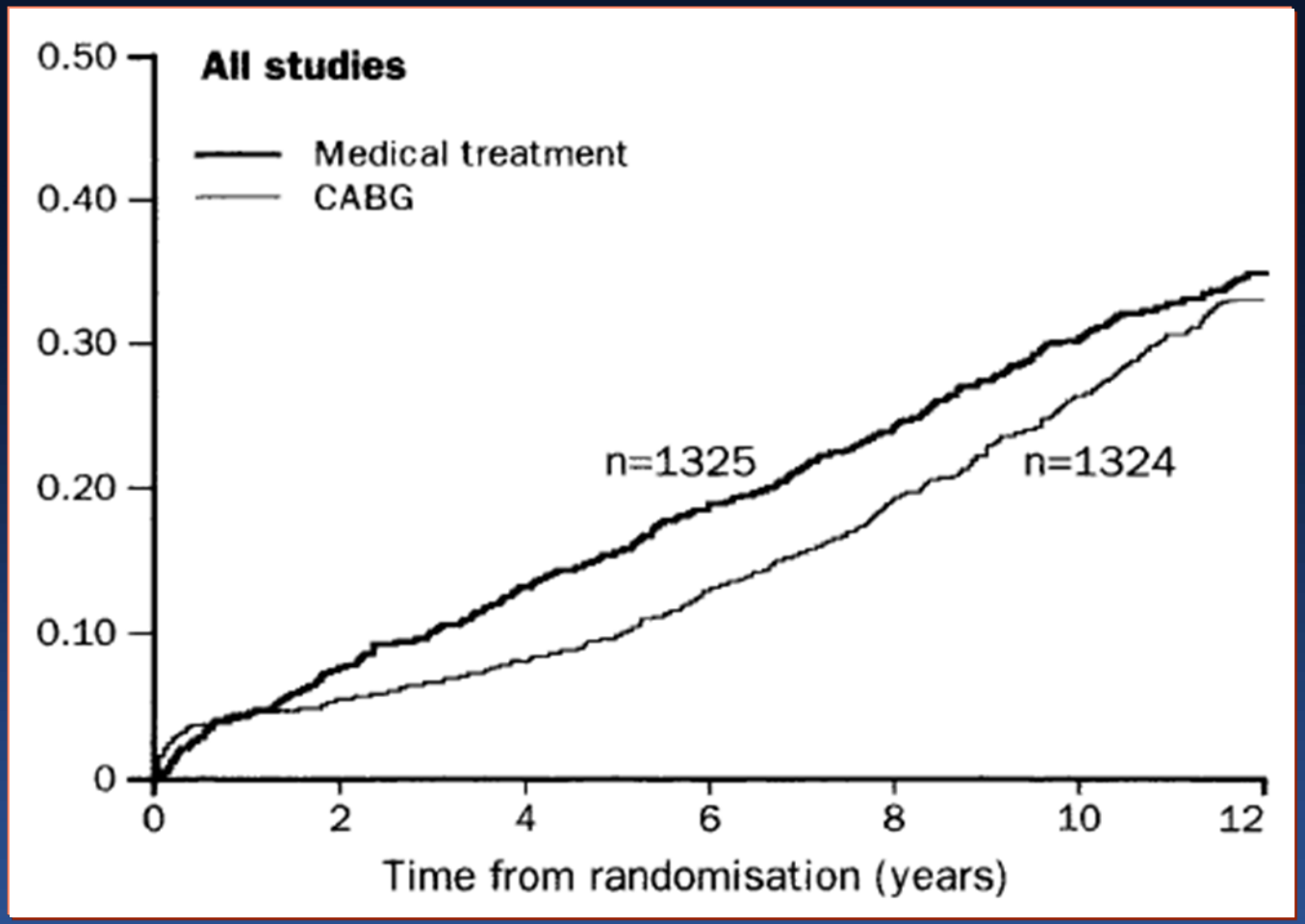
"As is the case with vertebroplasty, stenting performed in patients with stable disease is probably widely used as an expensive placebo for pain control."

How Do Our Patients Really Feel About Anti-Anginal Agents/OMT?



Agent	Issues for Patients
Beta-blockers	Sluggishness, fatigue
Nitrates	Really need to push for effect
Ca++ Channel Blockers	Reasonably tolerated
Ranolazine	COST!!! $200-$400/month

Multivessel CAD is Prognostically Important: Meta-Analysis of 7 RCTs



Yusuf S et al, Lancet 1994

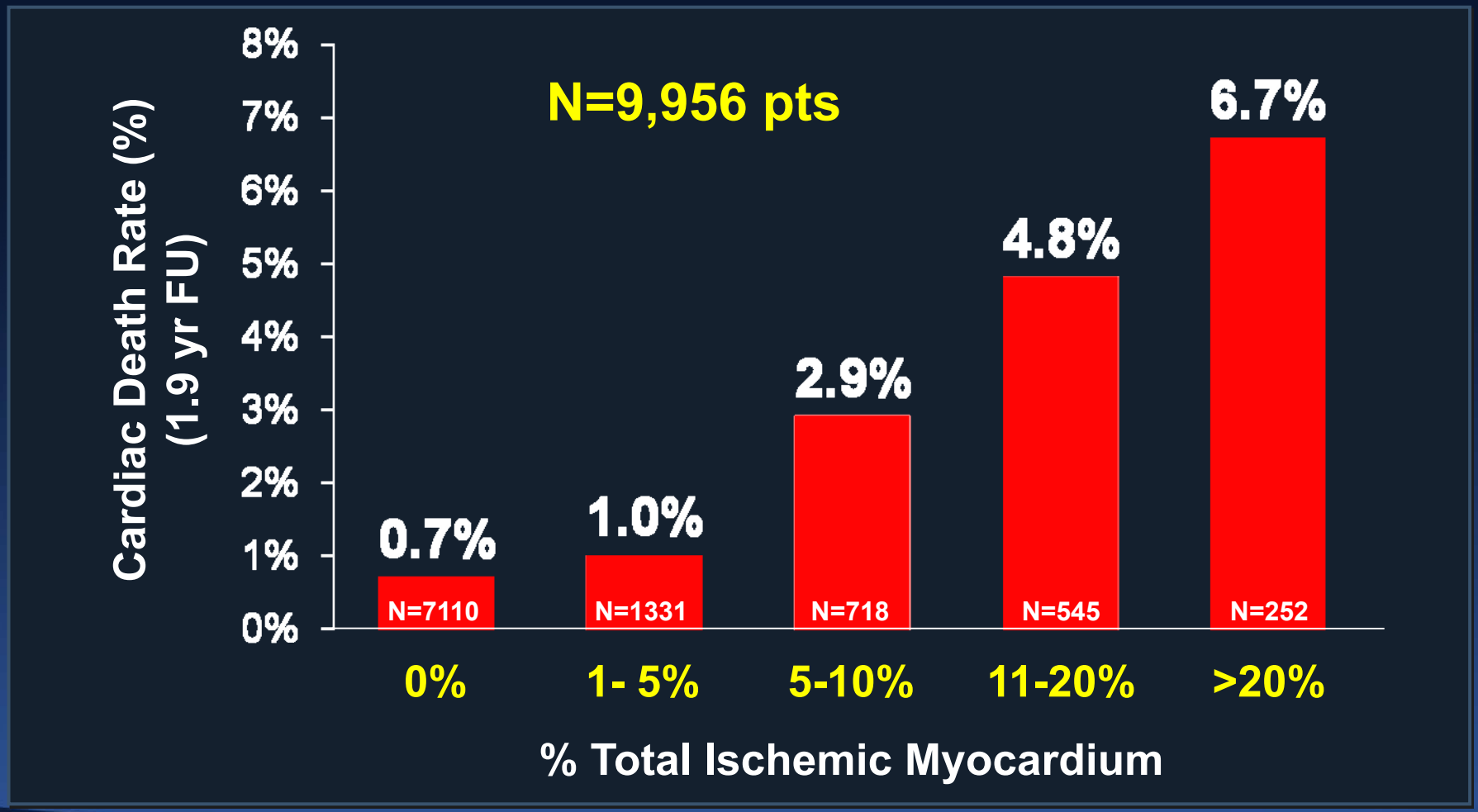
MASS II: 10-year Follow-up

	Medical n=203	PCI n=205	CABG n=203	p
Death/QWMI/Refractory Angina Req Revasc	59.1%	42.4%	33.0%	<0.001
Death	31.0%	24.1%	25.1%	0.089
Cardiac Death	20.7%	14.3%	10.8%	0.019
MI	20.7%	13.3%	10.3%	0.010
Additional Revasc	39.4%	41.9%	7.4%	0.001

90% proximal LAD involvement; 58% 3VD

Hueb W et al, Circulation 2010

Non-Invasive Risk-Stratification in Stable CAD



Hachamovitch et al, *Circulation* 2003;107:2900-07

Look AHEAD Stopped for Futility

The New York Times

October 19, 2012

Diabetes Study Ends Early With a Surprising Result

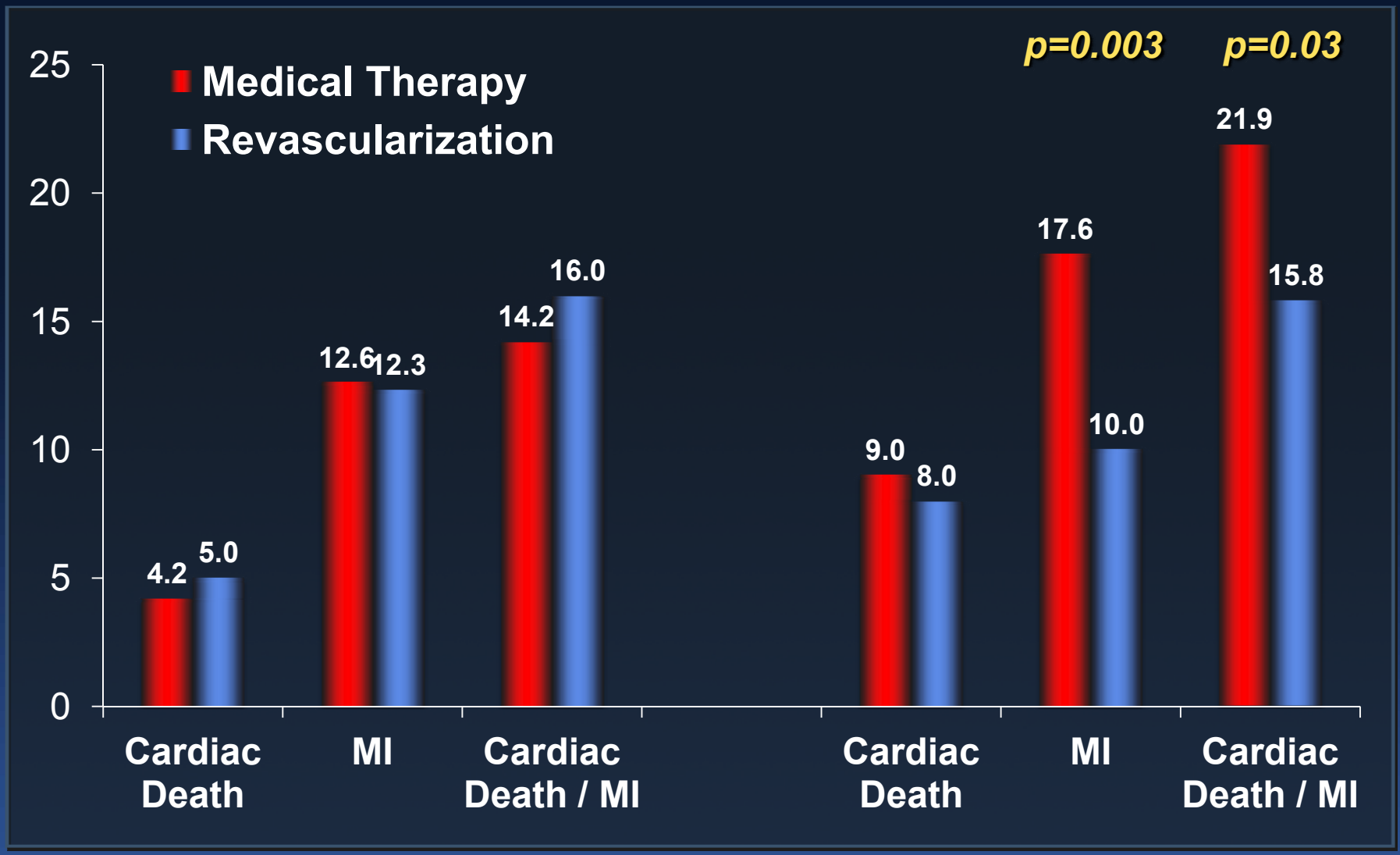
By GINA KOLATA

A large federal study of whether diet and weight loss can prevent heart attacks and strokes in overweight and obese people with Type 2 diabetes has ended two years ahead of schedule because the intensive program did not help.

"That may be the choice we are highlighting. You can take more medications - and more, I should say, expensive medications - or you can chose a lifestyle intervention and use fewer drugs and come to the same cardiovascular disease risk"

D. Nathan, NY Times 10/19/12

BARI-2D Endpoints by Stratum



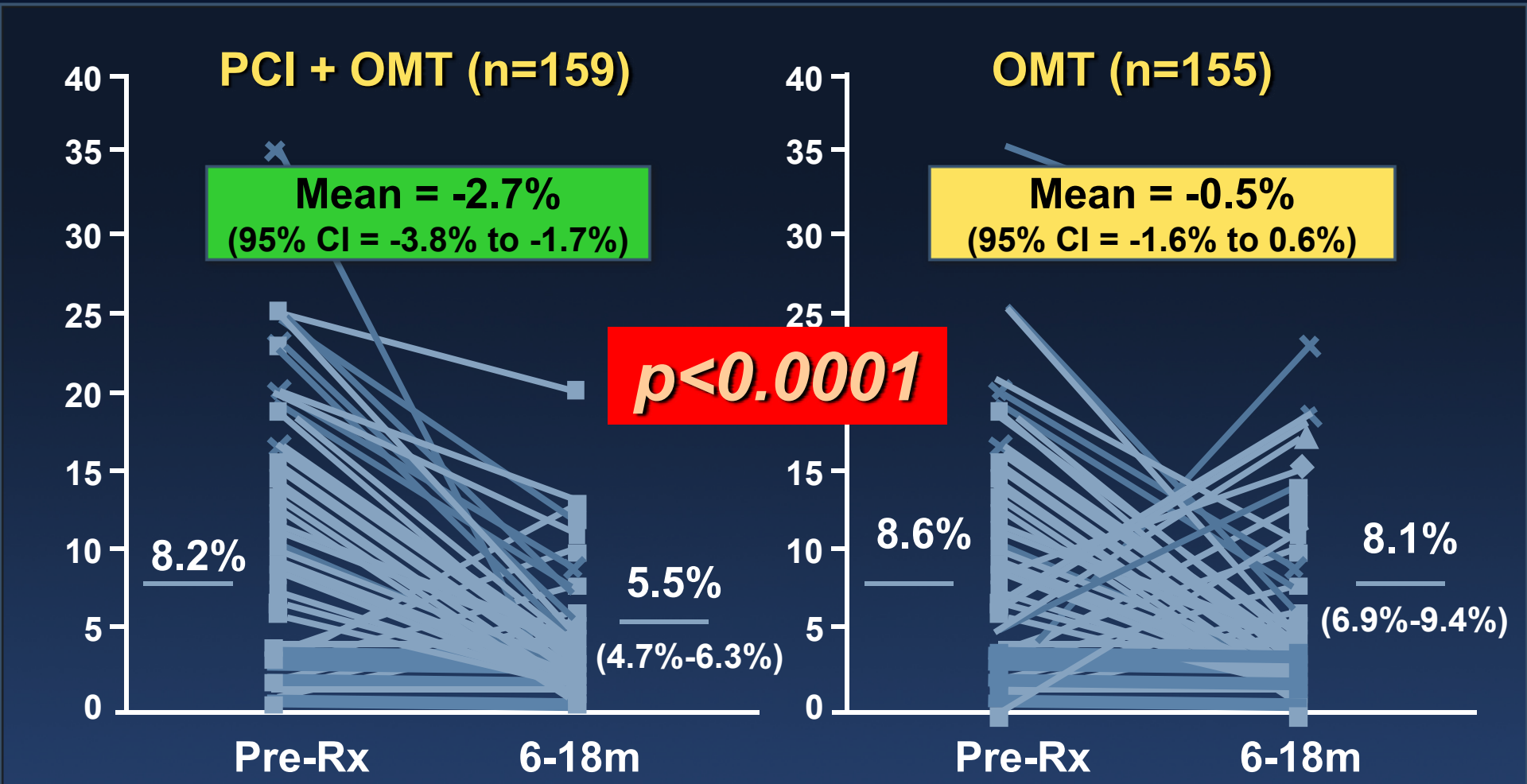
Chaitman et al, Circulation 2009

BARI 2D: Who got Revascularized?

	PCI Stratum	CABG Stratum	*p*
	N=1176	N=1192	
USA	73.7%	41.4%	<0.0001
Prior MI	30.1%	36.0%	<0.05
Proximal LAD disease	10.3%	19.4%	<0.05
Pts without prior procedures			
N lesions ≥50% DS, mean	2.1 ± 1.5	3.6 ± 1.7	<0.0001
N lesions ≥70% DS, mean	0.8 ± 1.0	1.7 ± 1.3	<0.0001
N of diseased vessels			<0.0001
- 0	4%	1%	
- 1	41%	9%	
- 2	36%	37%	
- 3	19%	53%	
Any total occlusions	7%	14%	<0.0001
Jeopardy index, %	38 ± 22	61 ± 21	<0.0001

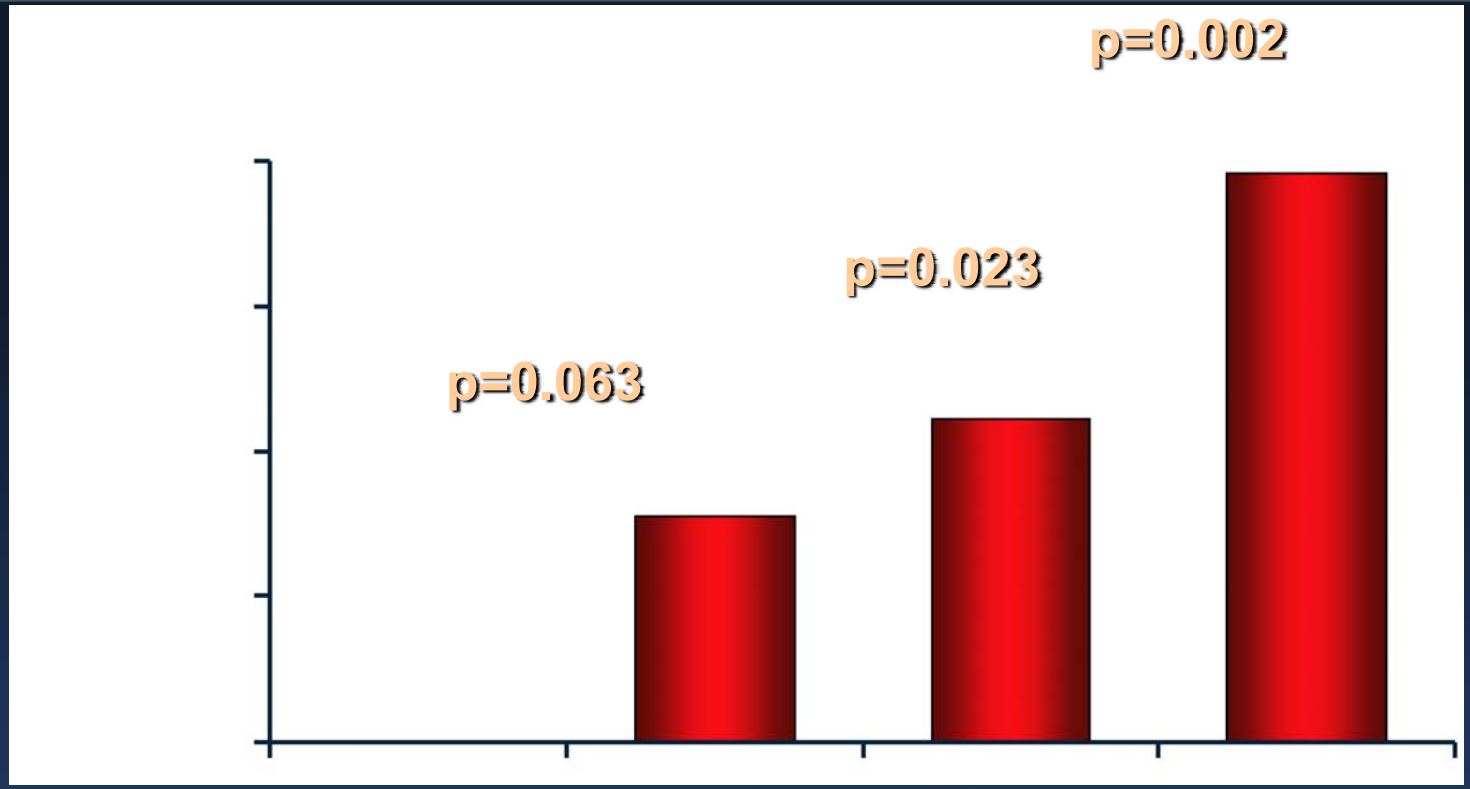
The BARI 2D Study Group. *NEJM* 2009;360:2503-15
Schwartz L et al. *AJC* 2009;103:632–638

MPS % Ischemic Myocardium (95% CI) Pre-Rx & 6-18 Months



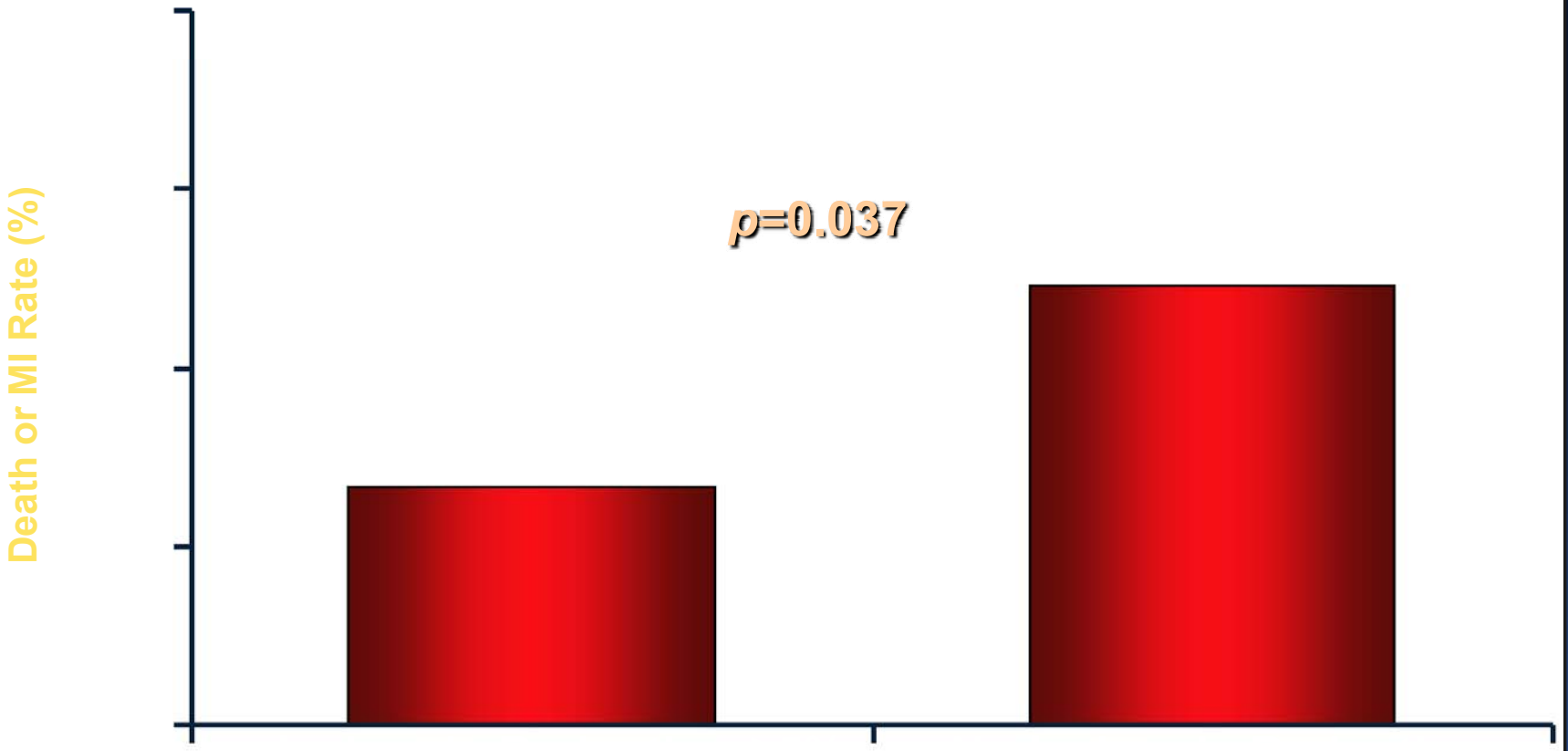
Shaw, et al, AHA 2007 and *Circulation* 2008

Rates of Death or MI by Residual Ischemia on 6-18m MPS



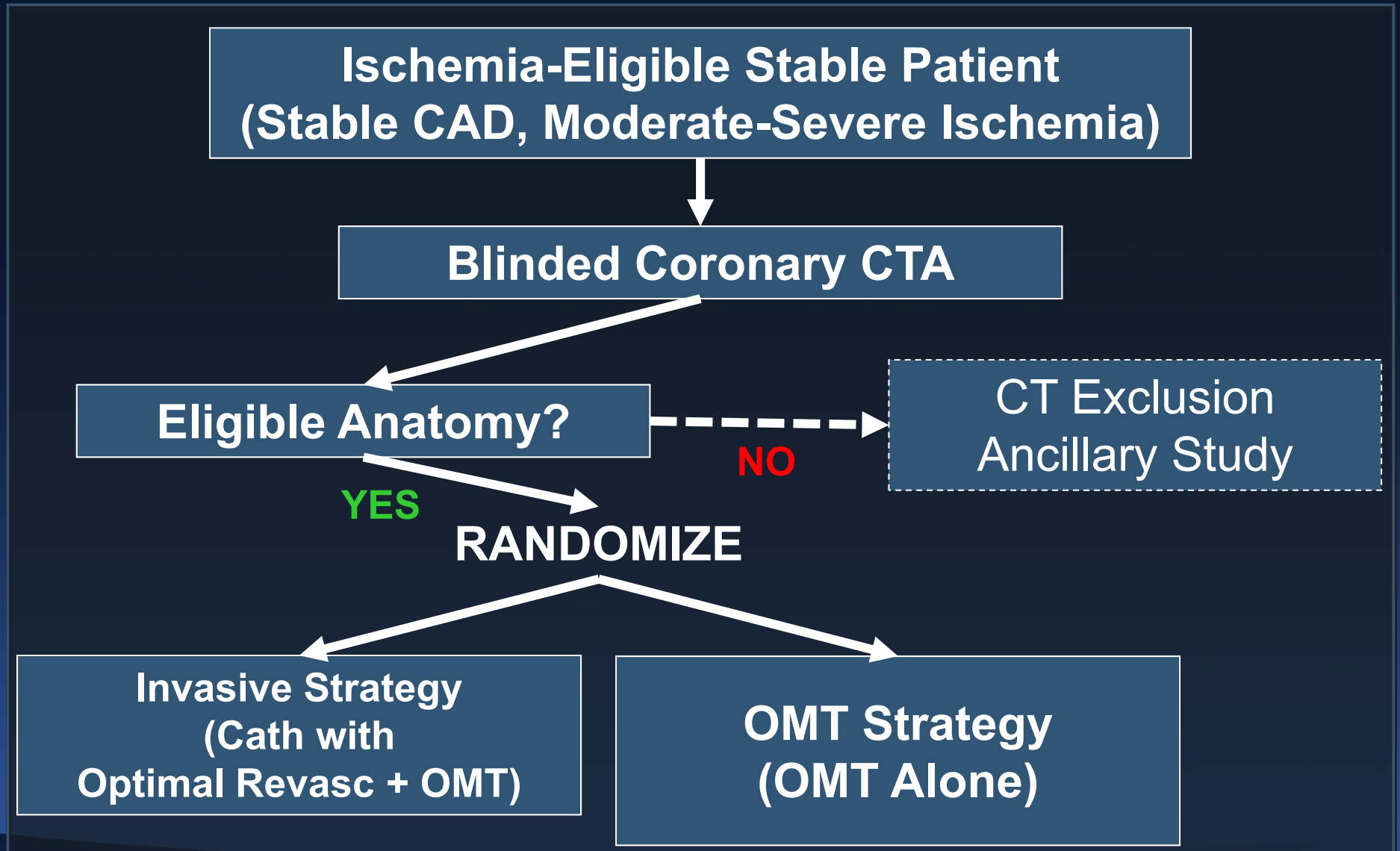
Shaw, et al, AHA 2007 and *Circulation* 2008

Rates of Death or MI by Ischemia Reduction



Shaw, et al, AHA 2007 and *Circulation* 2008

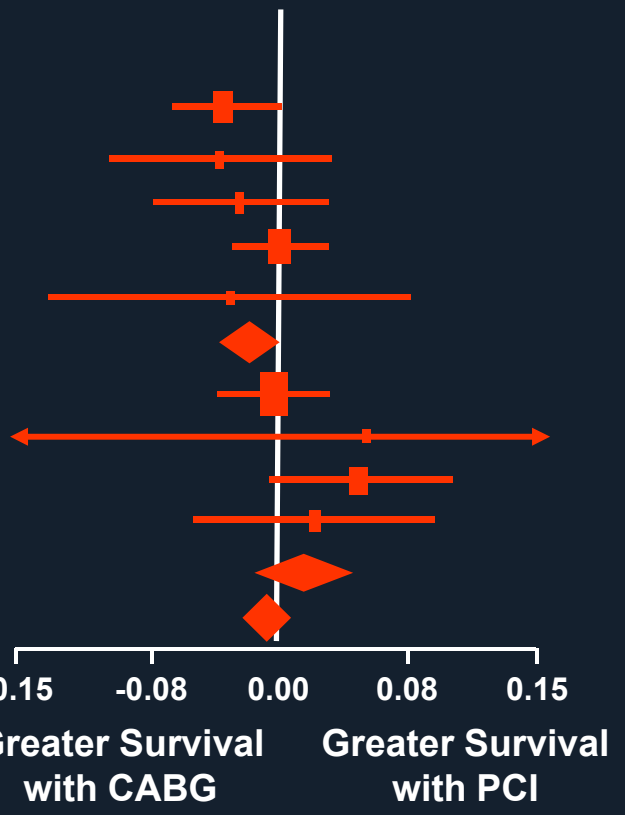
ISCHEMIA Trial Proposed Design



J. Hochman, TCT 2010

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

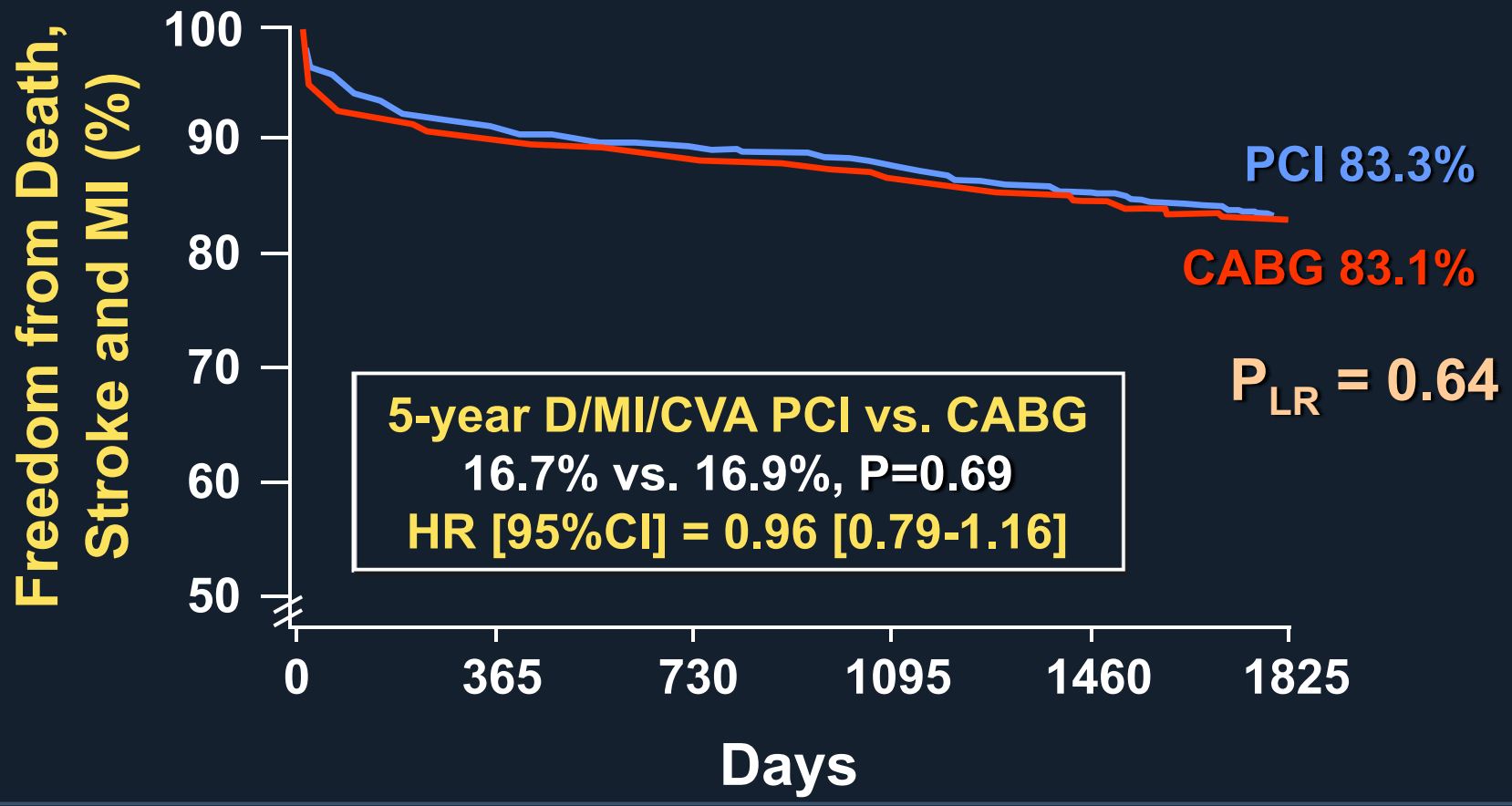
Study, Year (Reference)	Surviving Patients/All Patients, n/n	
	PCI	CABG
BARI, 1996 (64)	790/915	816/914
EAST, 2000 (80)	153/174	161/177
GABI, 2005 (88)*	164/177	157/165
RITA, 1998 (110)	483/510	474/501
French Monocentric Study, 1997 (126)	66/76	68/76
Balloon overall	1656/1852	1676/1833
ARTS, 2005 (23)	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

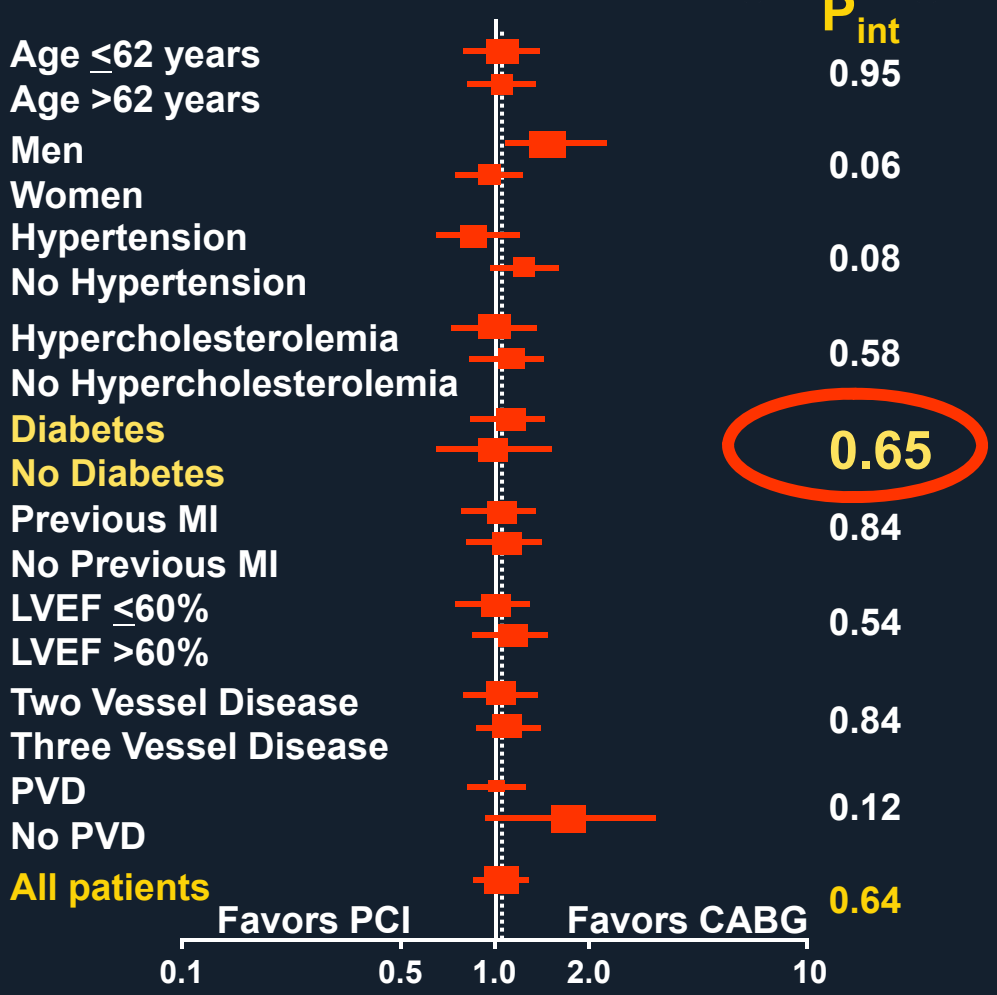
4 randomized trials, 3,051 randomized pts,
5-year follow-up (patient level pooled analysis)



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

Bare Metal Stents vs. CABG

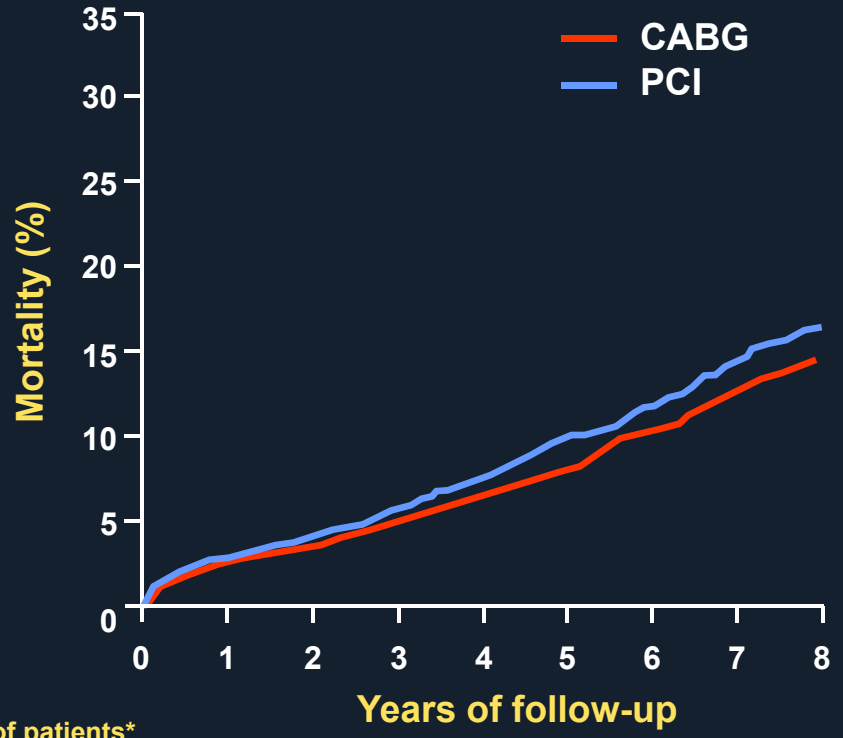
4 randomized trials, 3,051 randomized pts, 5-year follow-up

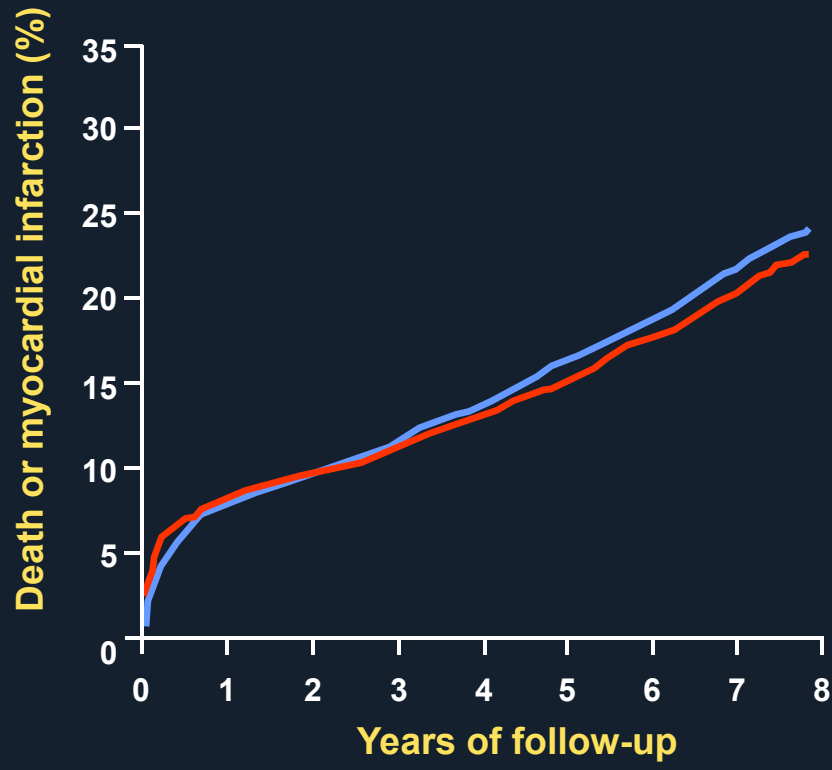


Adjusted HR [95%CI] for death, stroke or MI

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

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





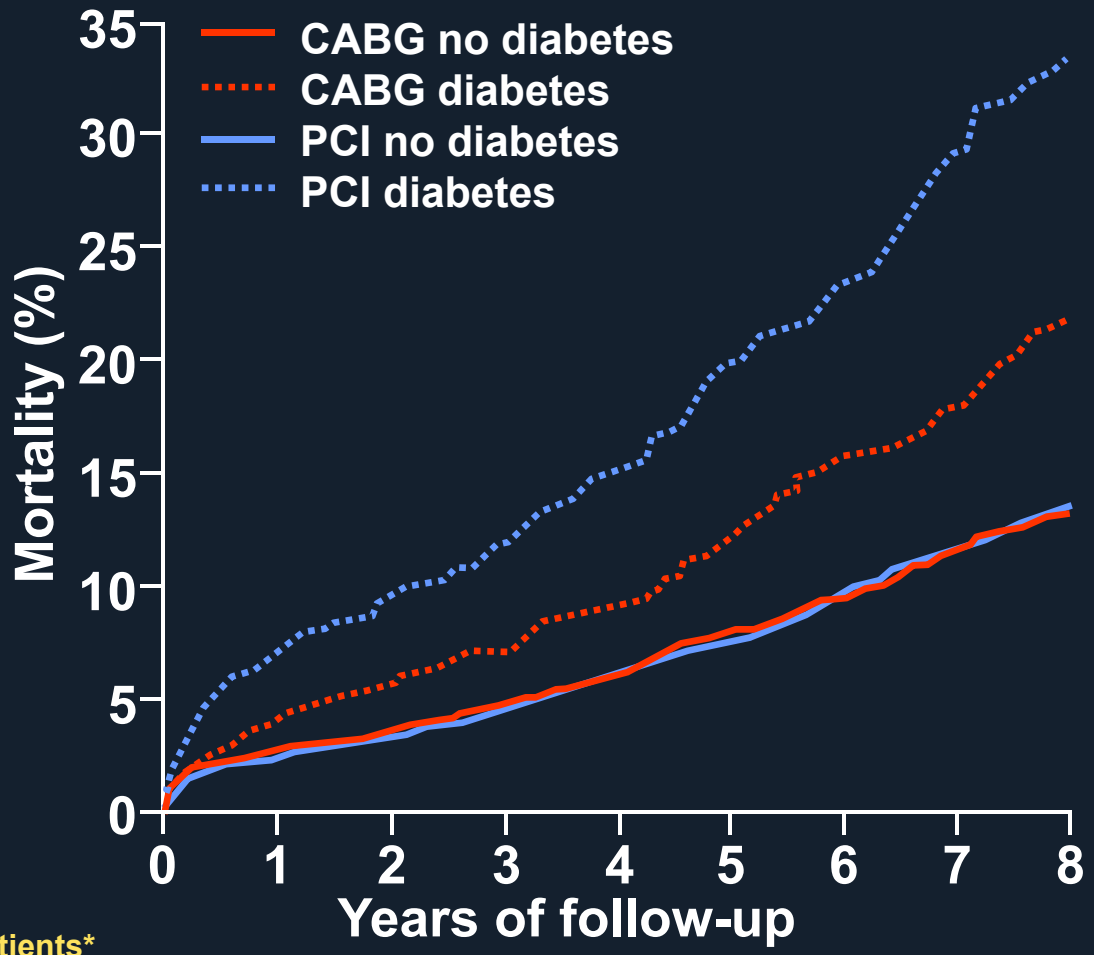
No. of patients*

CABG	3889	3767	3675	3415	3180	2693	1853	1609	1477
PCI	3923	3798	3709	3431	3205	2658	1828	1576	1452

CABG	3695	3369	3269	3001	2763	2294	1501	1269	1161
PCI	3725	3419	3310	3023	2797	2267	1491	1253	1150

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

CABG vs PCI :Death and Diabetic Status



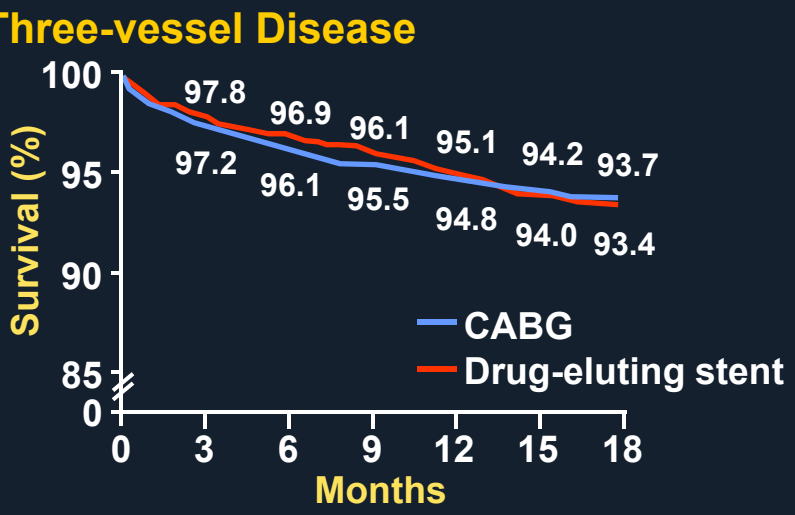
Number of patients*									
CABG no diabetes	3263	3169	3089	2877	2677	2267	1592	1380	1274
CABG diabetes	615	587	575	532	498	421	257	225	200
PCI no diabetes	3298	3217	3148	2918	2725	2281	1608	1393	1288
PCI diabetes	618	574	555	508	475	373	218	179	160

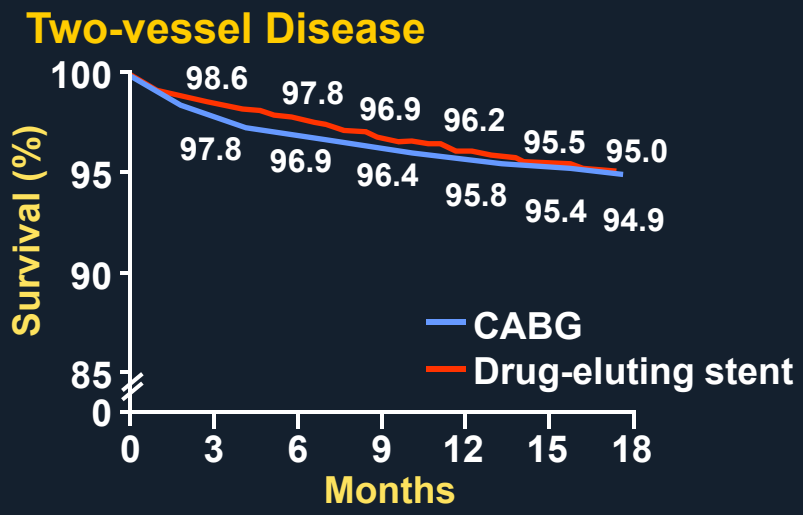
Hlatky et al, *The Lancet* 2009;373:1190-1197

NY State Registries: DES vs CABG
Unadjusted and Adjusted Mortality

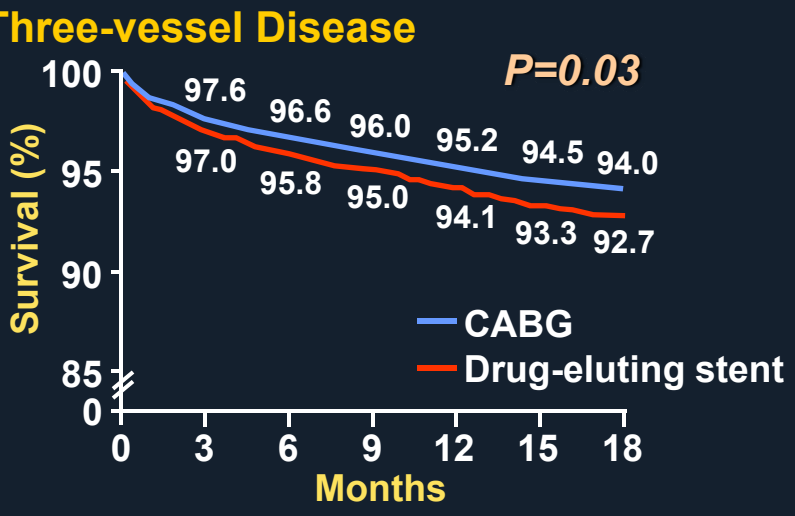
CABG=9963 DES=7437

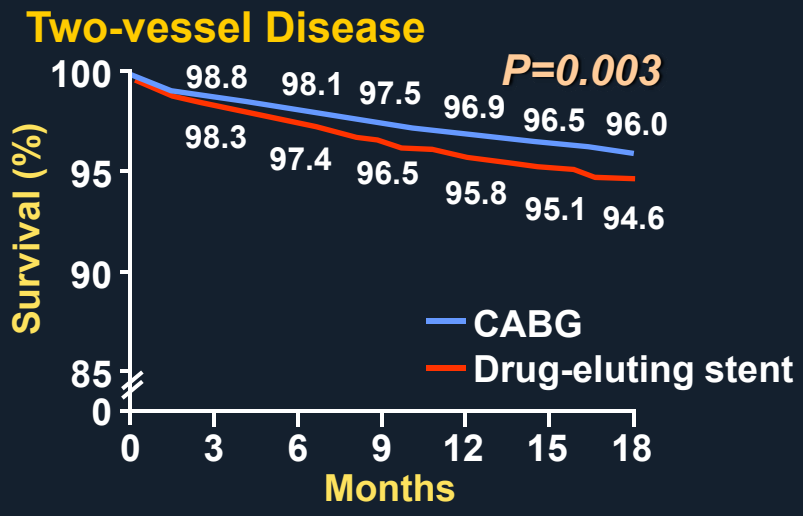
Unadjusted





Adjusted

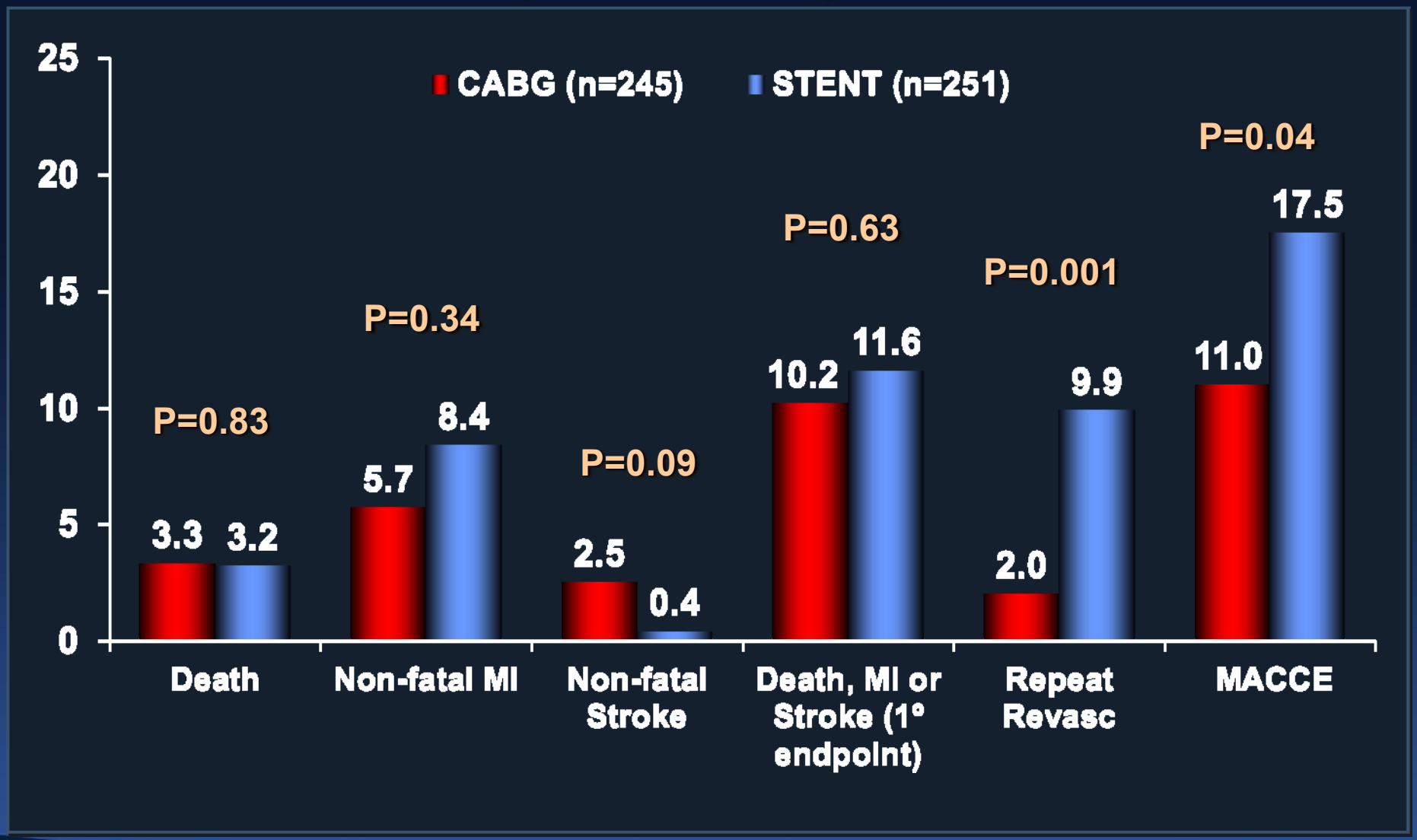




Hannan et al, *N Engl J Med* 2008;358:331-334

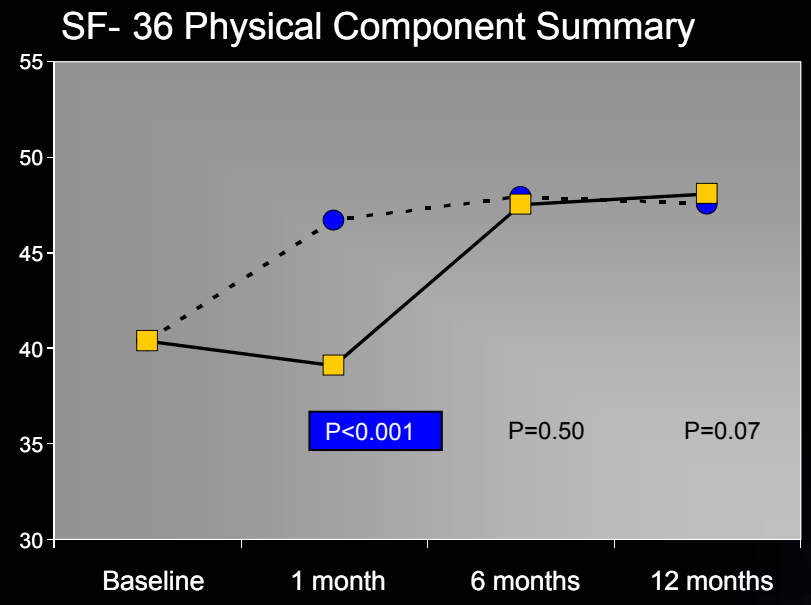
CARDia: 1-Year MACCE

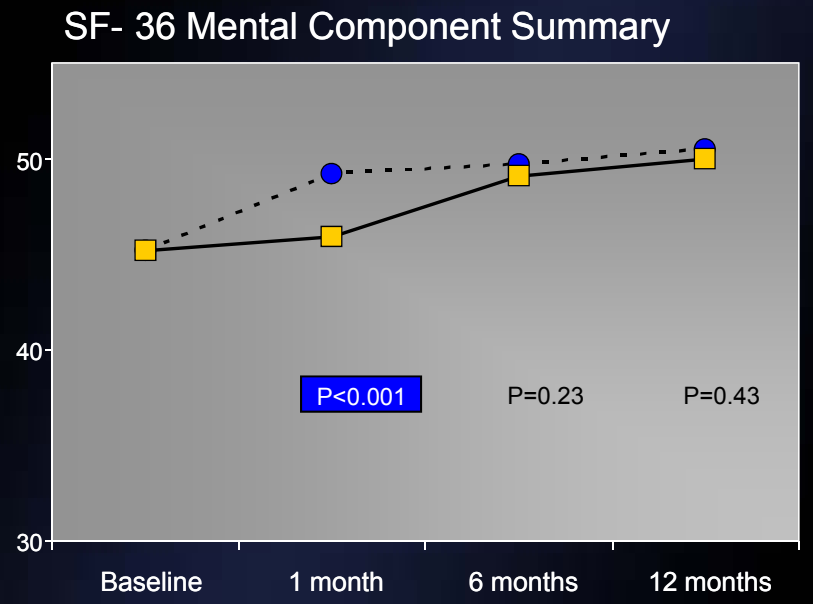
61% 3VD (LM excluded) 31% IDDM

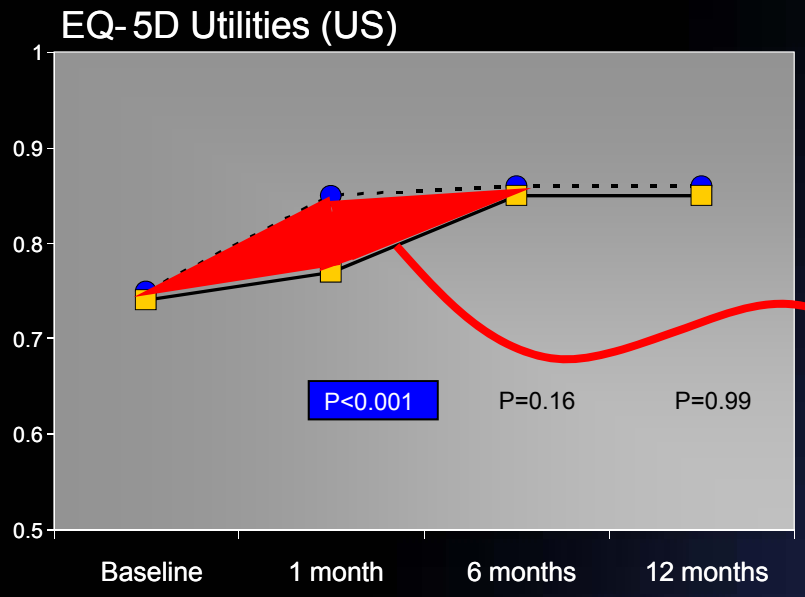


Akhil Kapur, ESC 2008

SYNTAX: Generic QOL and Utilities







PCI

CABG

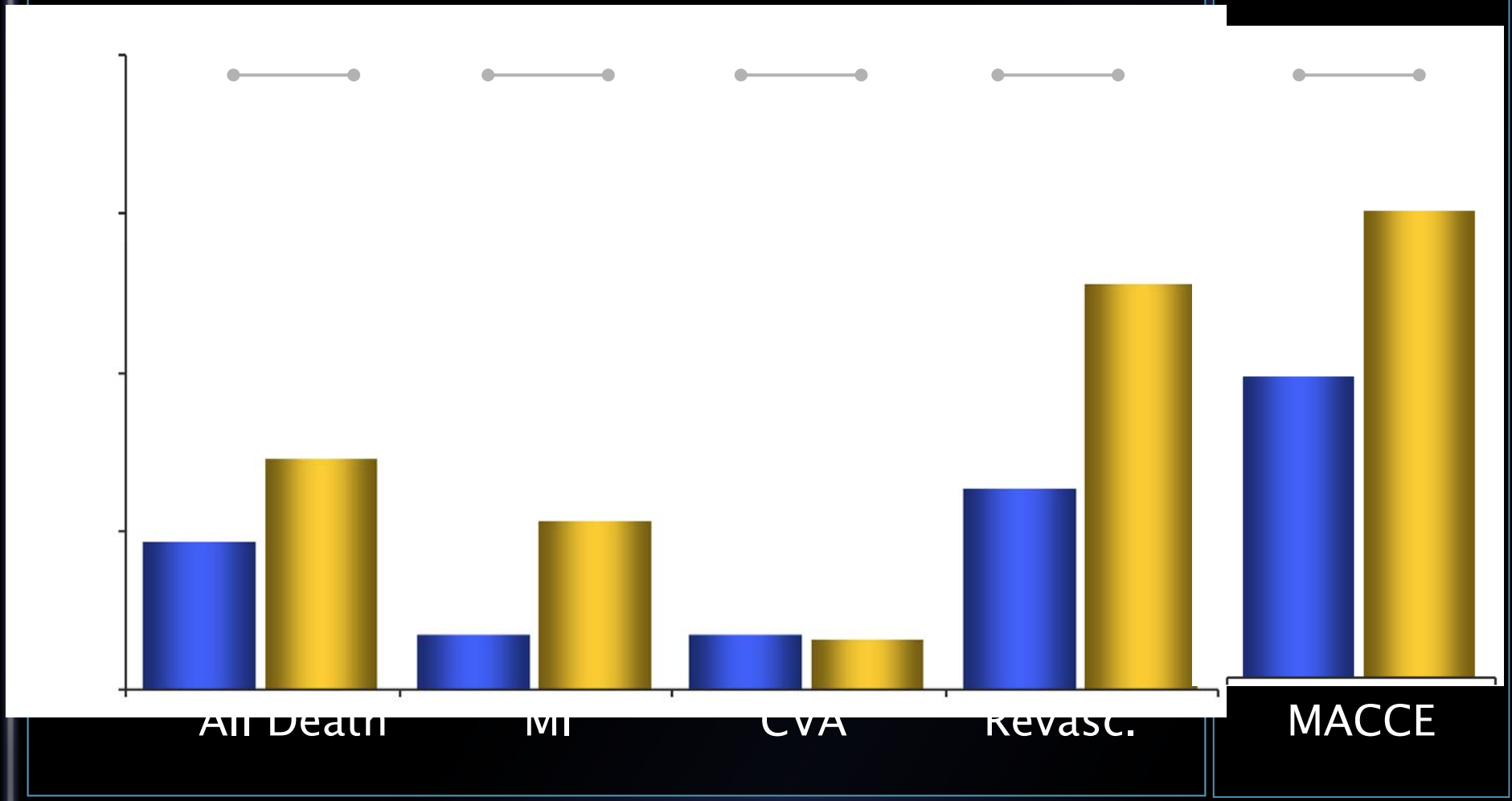
Quality Adjusted Life Years

Δ = 0.02 (P<0.01)

Cohen DJ et al. NEJM 2011;364:1016-26.

3VD Disease
5-year Outcomes (N=1095)

CABG (n=549) TAXUS (n=546)



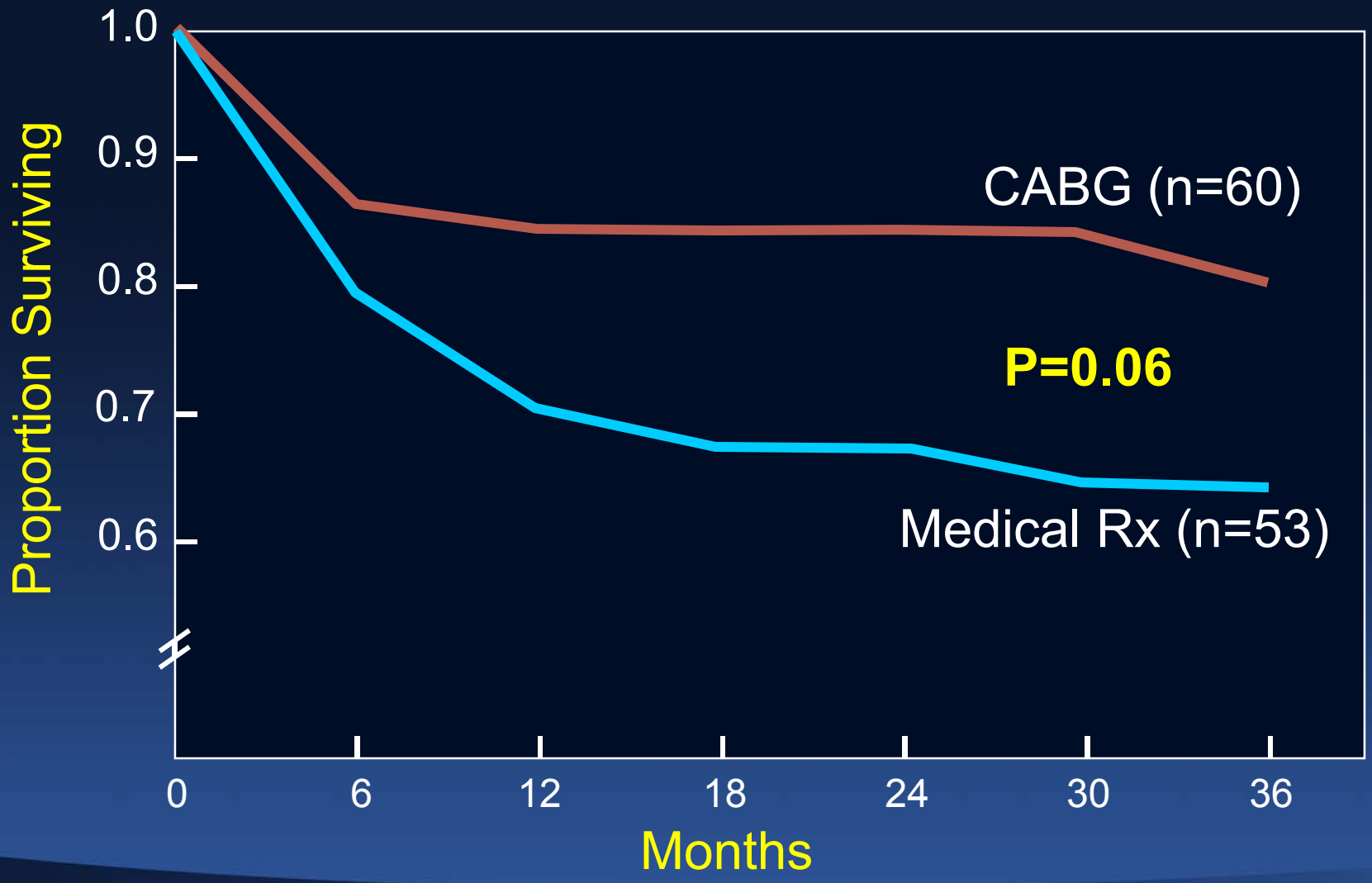
Cumulative KM Event Rate; log-rank *P* value

ITT population

Summary

- In randomized 3VD patients at 5 years:
  - Significantly higher rate of revascularization in the PCI group (12.6% CABG vs 26.4% PCI)
  - Overall MACCE in the PCI group was significantly higher than in CABG patients (24.2% CABG vs 37.5% PCI)
  - Overall safety outcomes (Death/CVA/MI) were significantly increased in PCI patients (14.0% CABG vs 22.0% PCI)
- Results notably affected by baseline lesion complexity
  - In low SYNTAX Scores (0-22), MACCE, all-cause death, and MI rates are comparable between treatment groups
  - Most importantly, in patients with intermediate (23-32) or high SYNTAX Scores (≥33), MACCE, mortality and MI are significantly higher compared to CABG at 5 years
- In contrast to PCI, surgical results at 5 years remain excellent and unaffected by baseline lesion complexity

VA Randomized Trial (n=113)
LM Stenosis



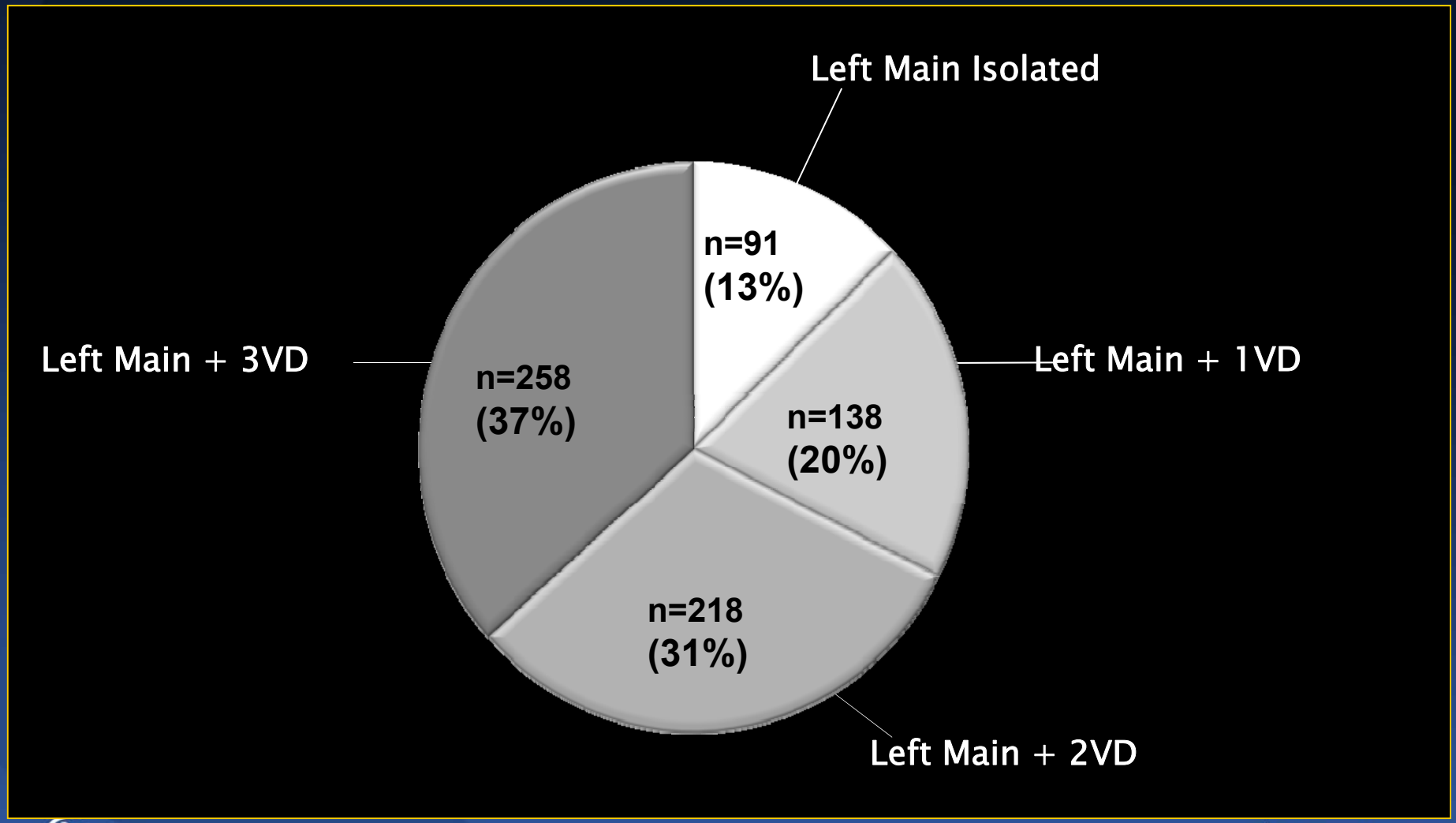
Death

20%

36%

Takaro T et al: Circulation 1976;54(6 Suppl):III107-17.

Heterogeneity in the Left Main Group



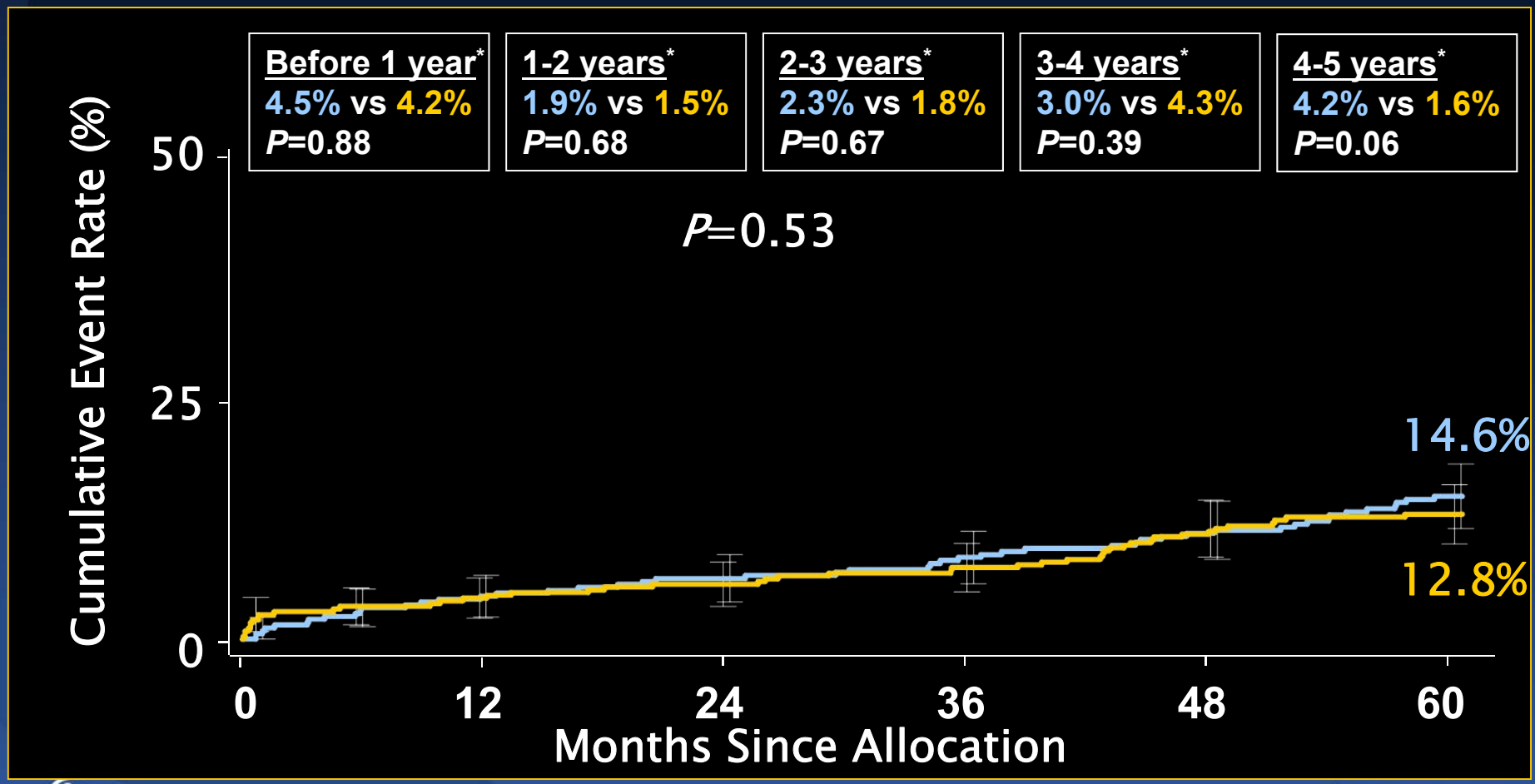
Site-reported data

Patient Characteristics
LM Subset

	CABG N=348	TAXUS N=357	*P* value
Age*, mean ± SD (y)	65.6 ± 10.1	65.4 ± 9.8	0.78
Medically treated diabetes*, %	22.4	21.8	0.86
BMI, mean ± SD	27.7 ± 5.0	28.2 ± 4.9	0.24
Additive euroSCORE*, mean ± SD	3.9 ± 2.9	3.9 ± 2.8	0.91
Total Parsonnet score*, mean ± SD	9.1 ± 7.4	8.9 ± 7.8	0.77
Total SYNTAX Score, mean ± SD	26.7 ± 11.5	28.1 ± 12.4	0.13
No. lesions, mean ± SD	3.2 ± 1.9	3.3 ± 1.8	0.89

Core laboratory reported unless *Site-reported

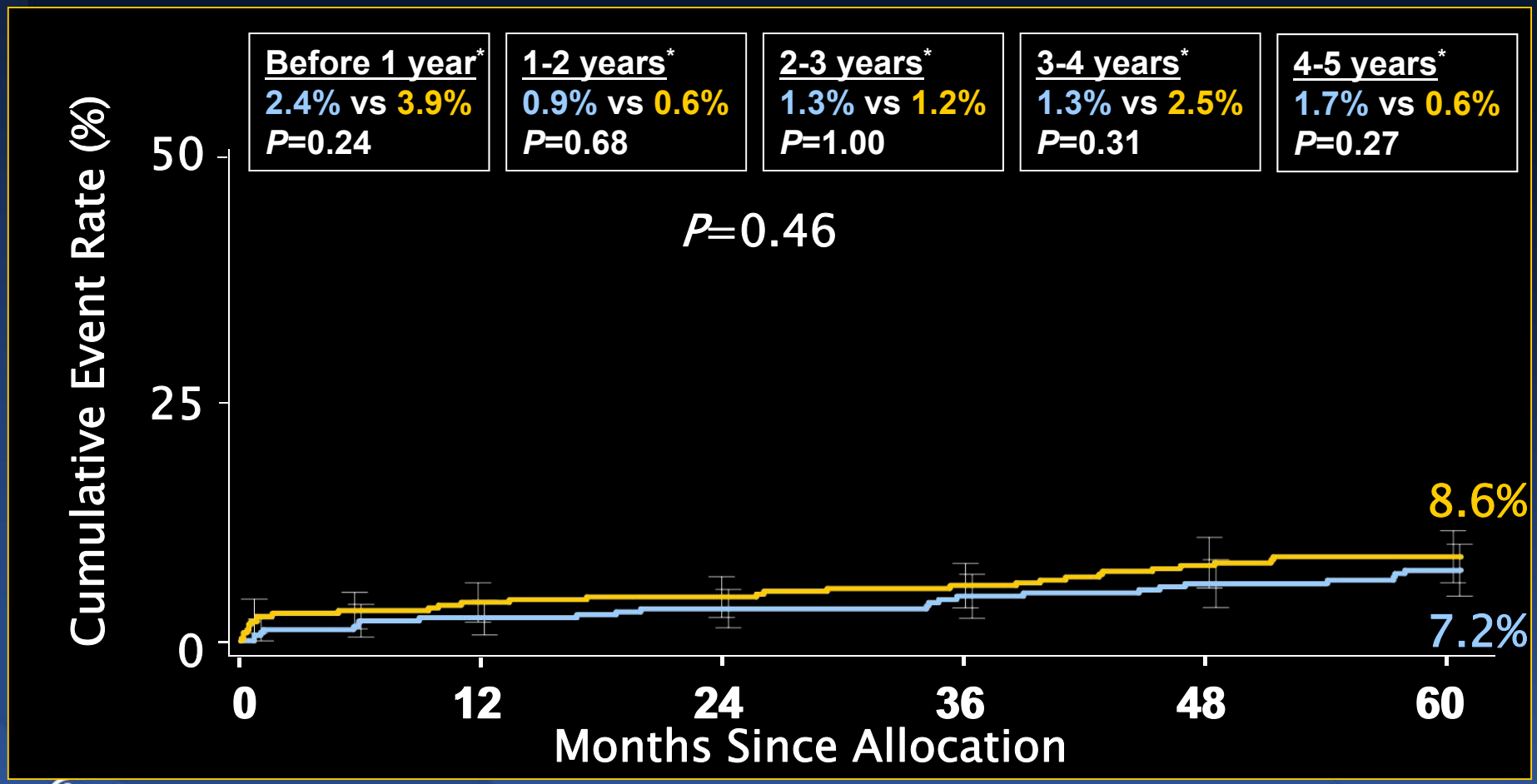
All-Cause Death to 5 Years
Left Main Subset



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

T population

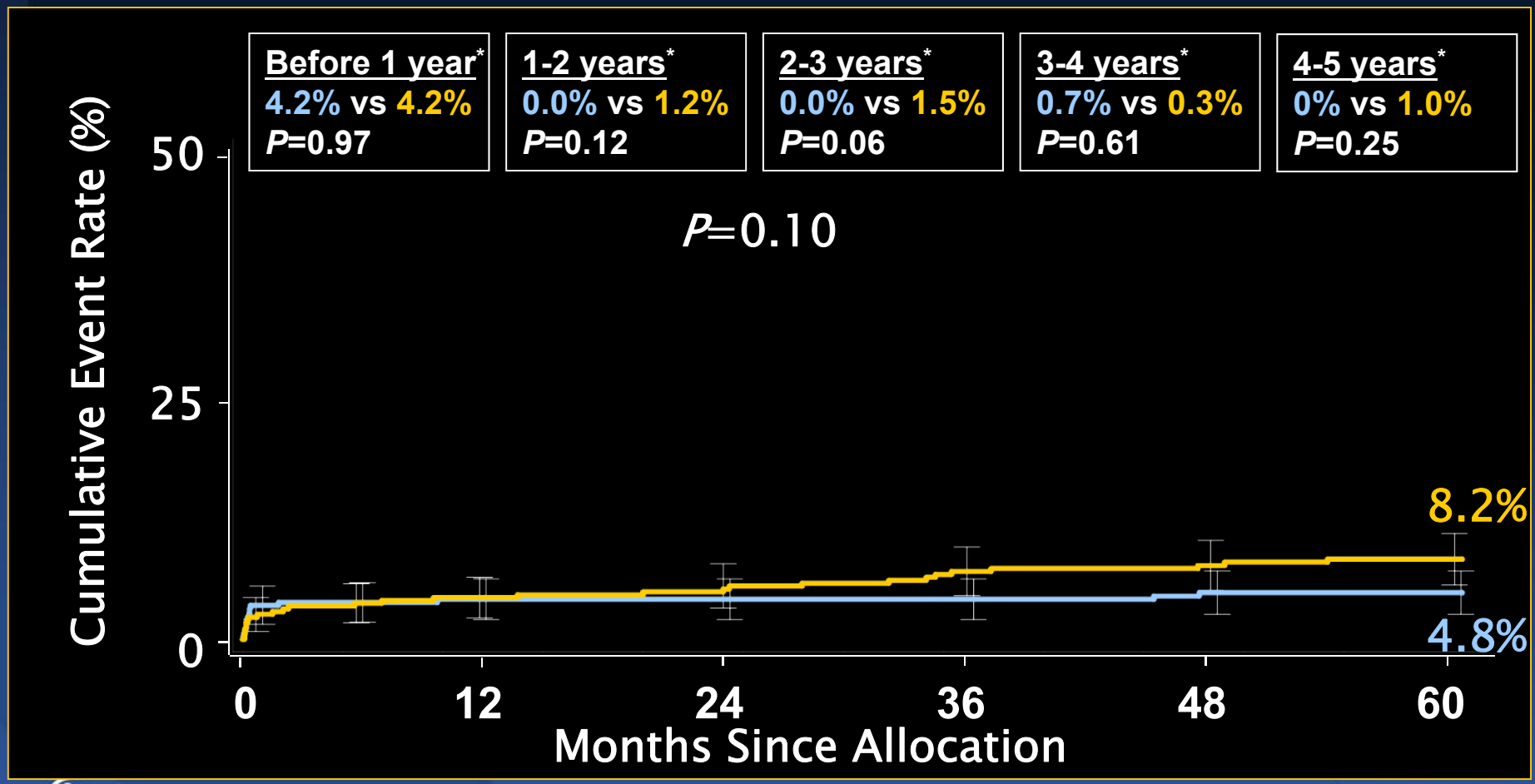
Cardiac Death to 5 Years
Left Main Subset



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

ITT population

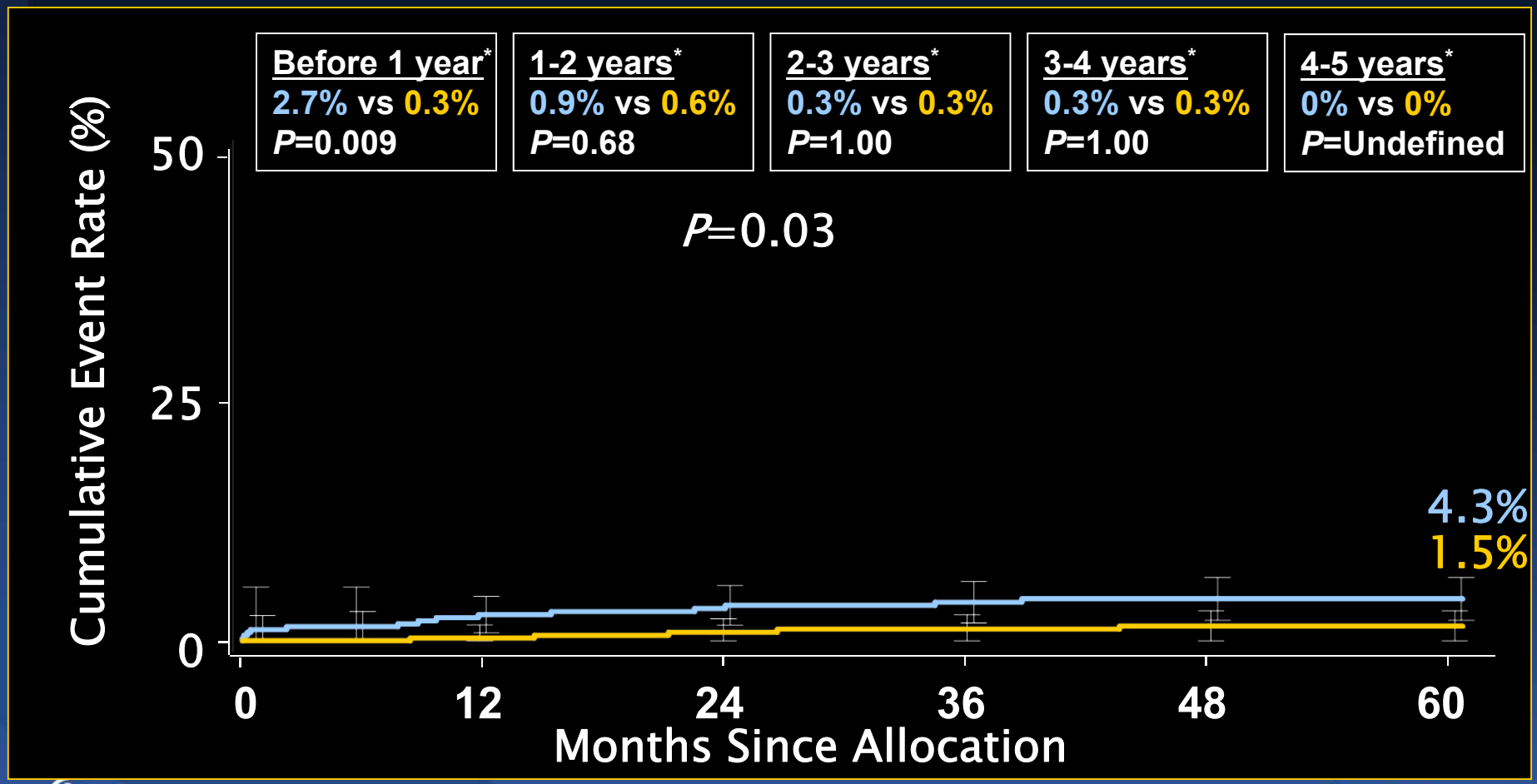
Myocardial Infarction to 5 Years
Left Main Subset



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

T population

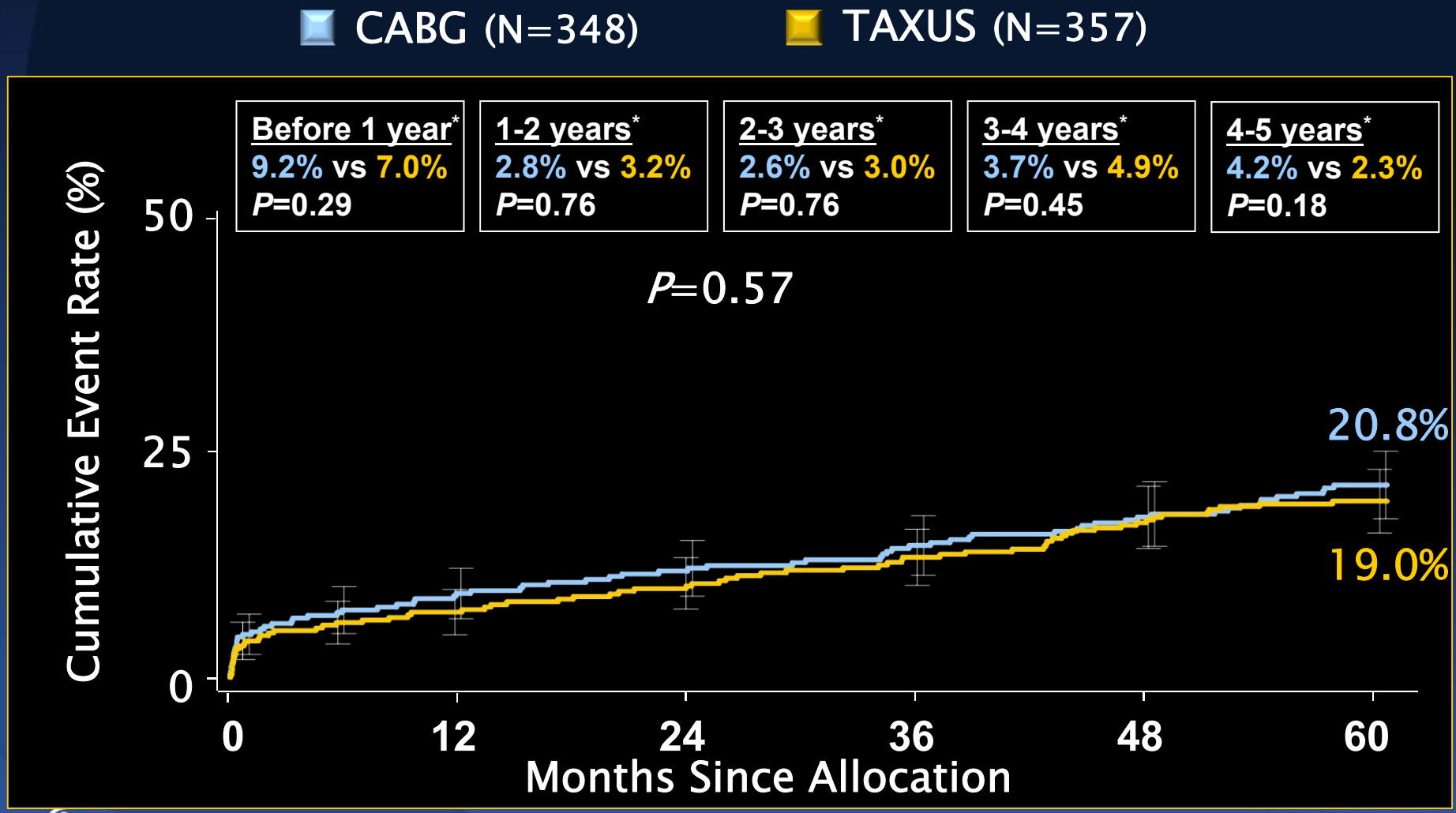
CVA to 5 Years
Left Main Subset



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

ITT population

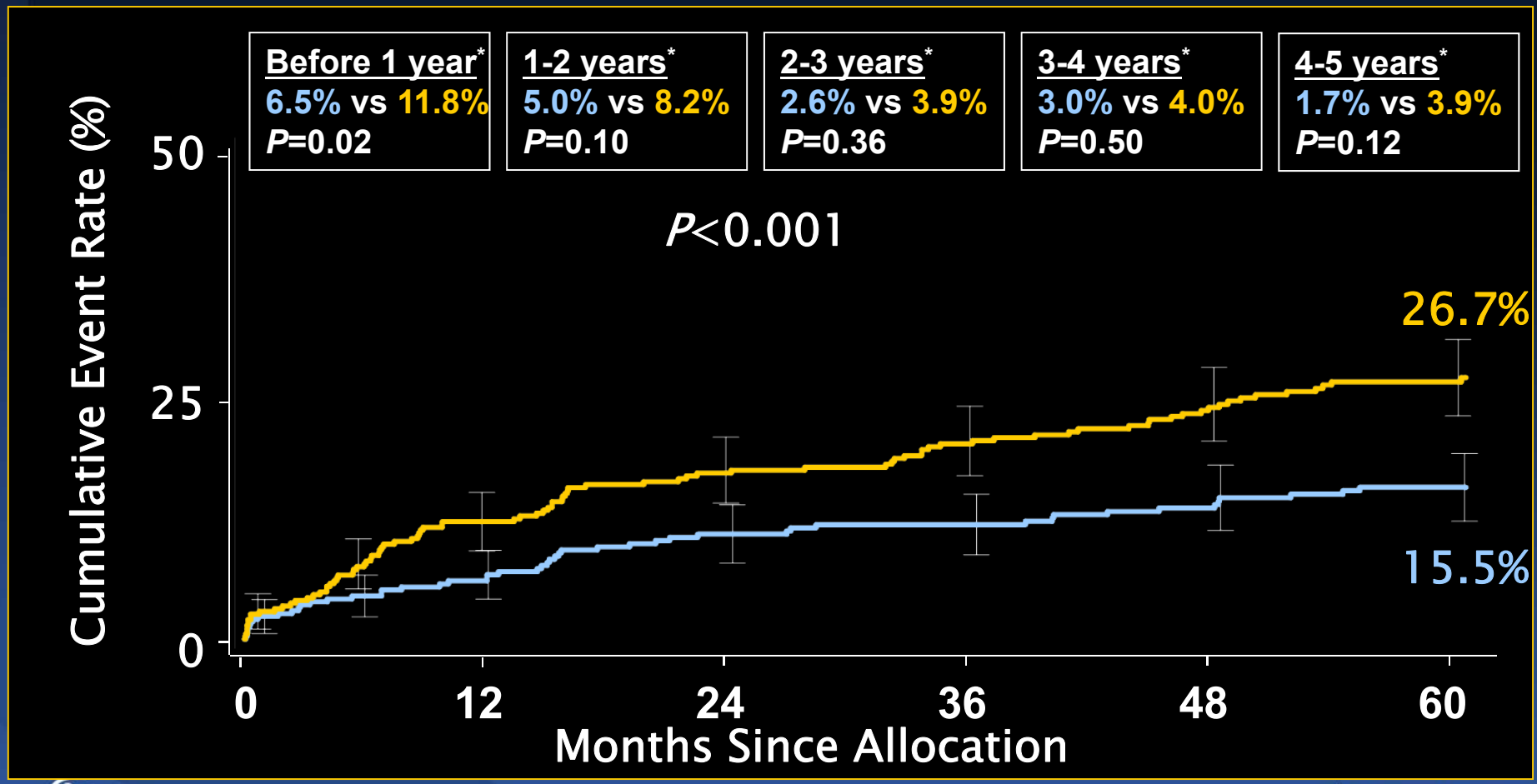
All-Cause Death/CVA/MI to 5 Years
Left Main Subset



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

T population

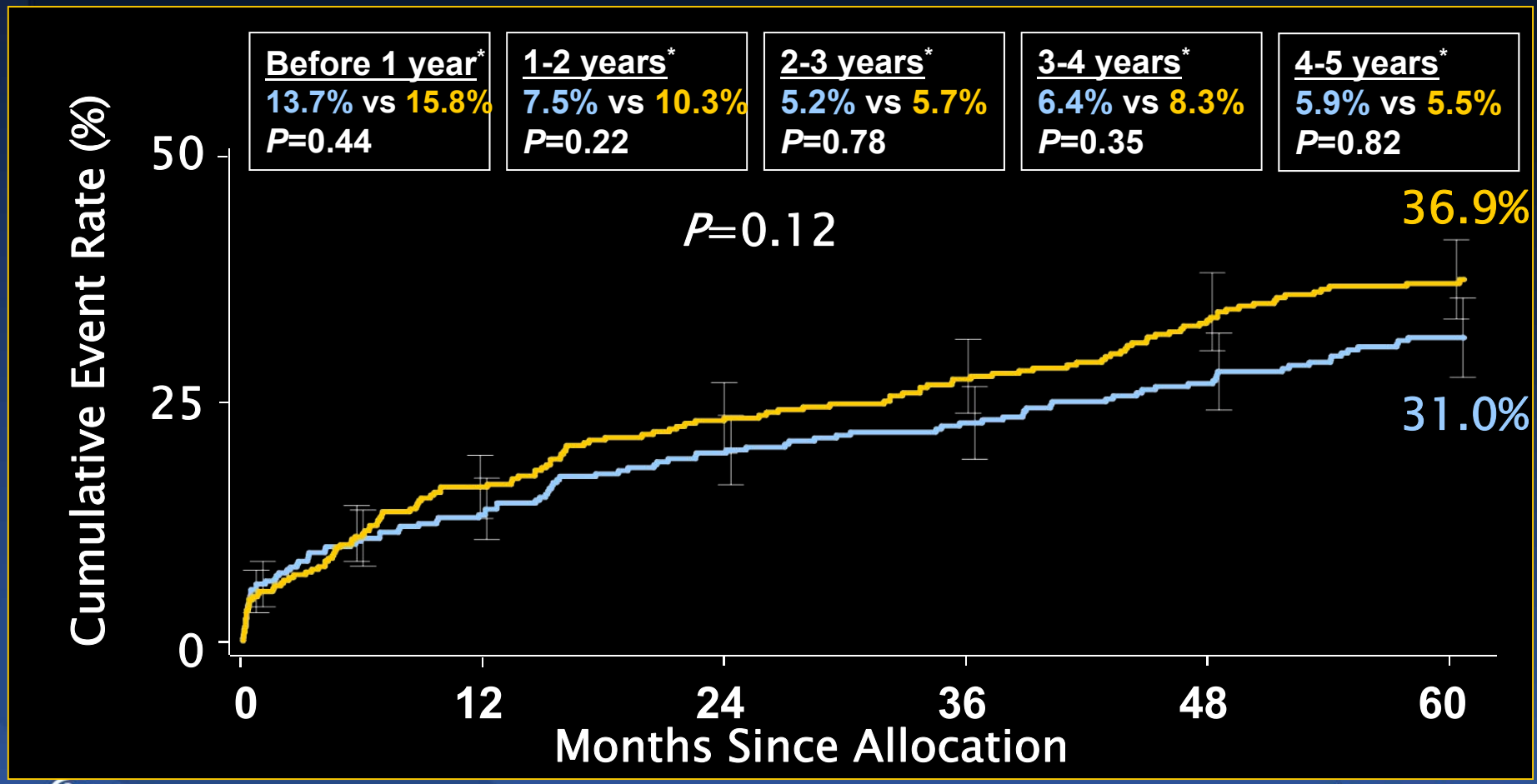
Repeat Revascularization to 5 Years
Left Main Subset



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

T population

MACCE to 5 Years
Left Main Subset

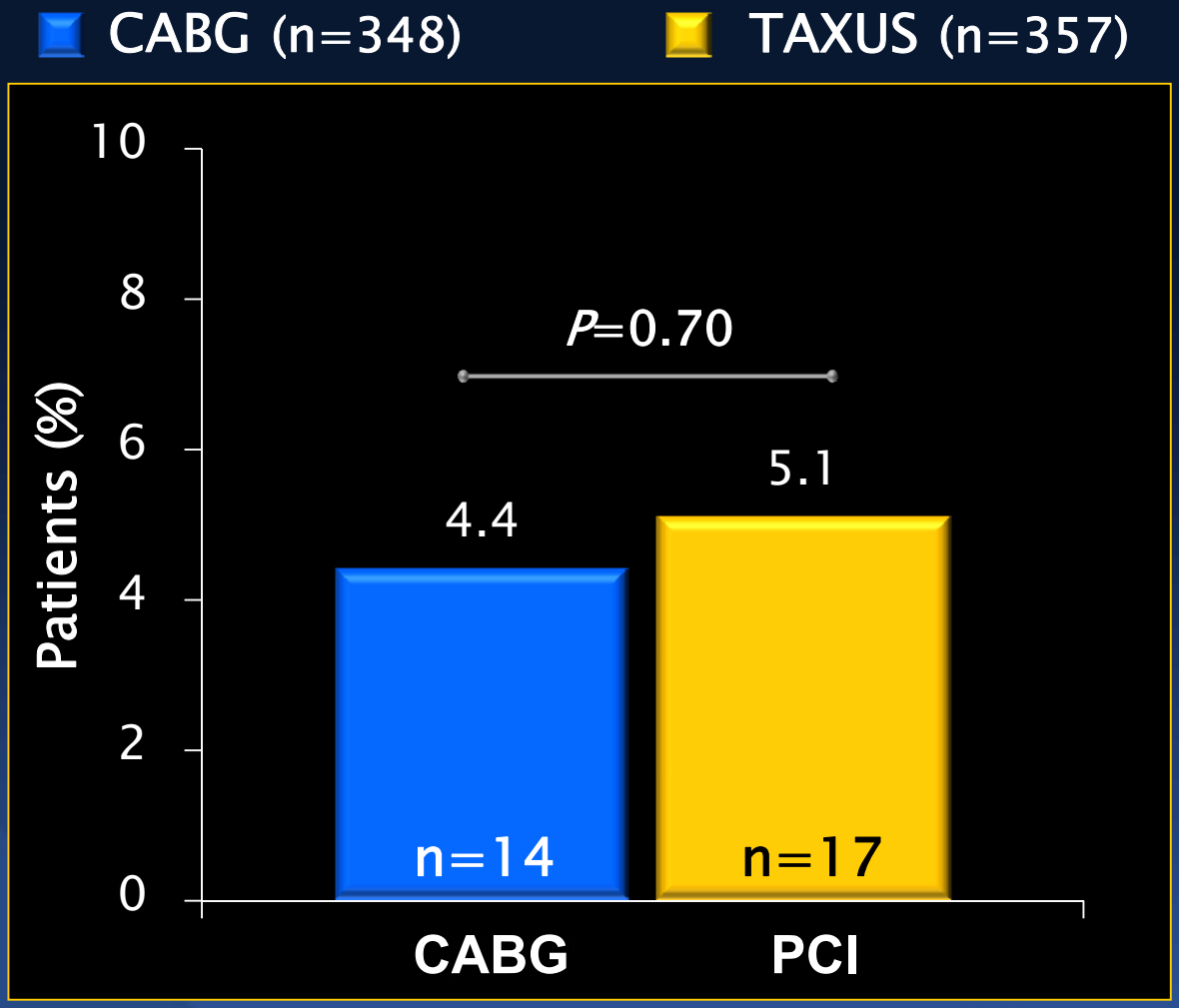


Cumulative KM Event Rate ± 1.5 SE; log-rank *P* value;*Binary rates

ITT population

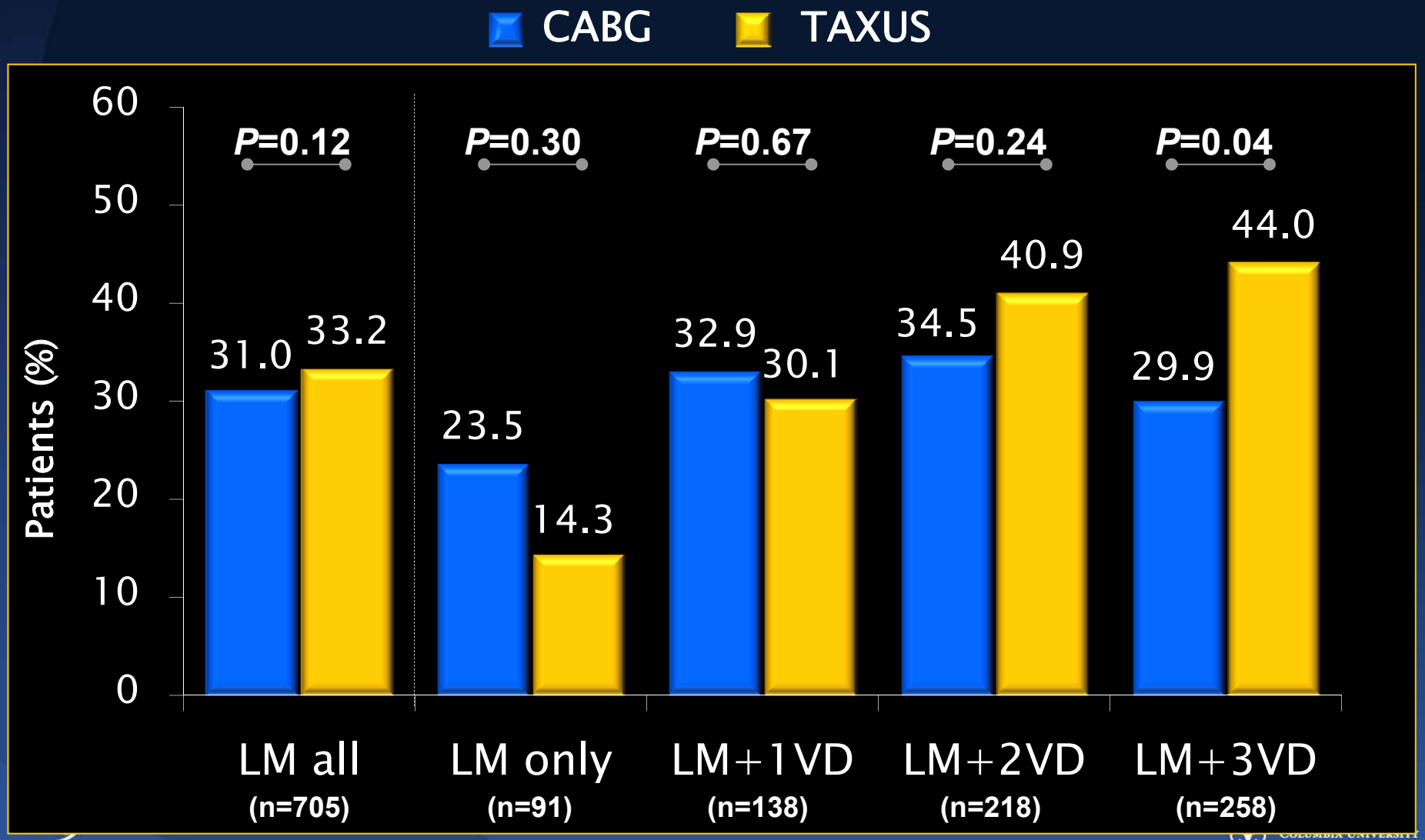
Symptomatic Graft Occlusion & Stent Thrombosis to 5 Years

LM Subset



Post-procedure, ITT population

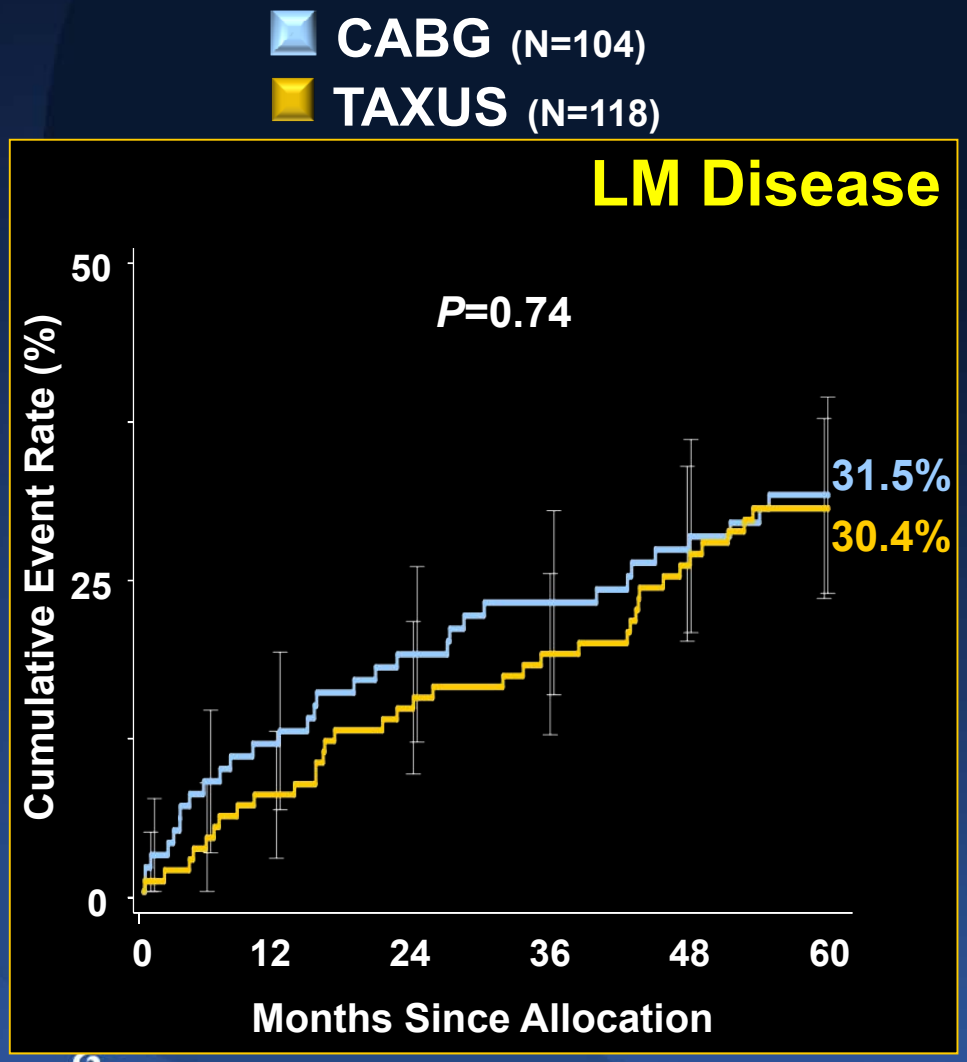
MACCE to 5 Years
Left Main Subsets



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

ITT population

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

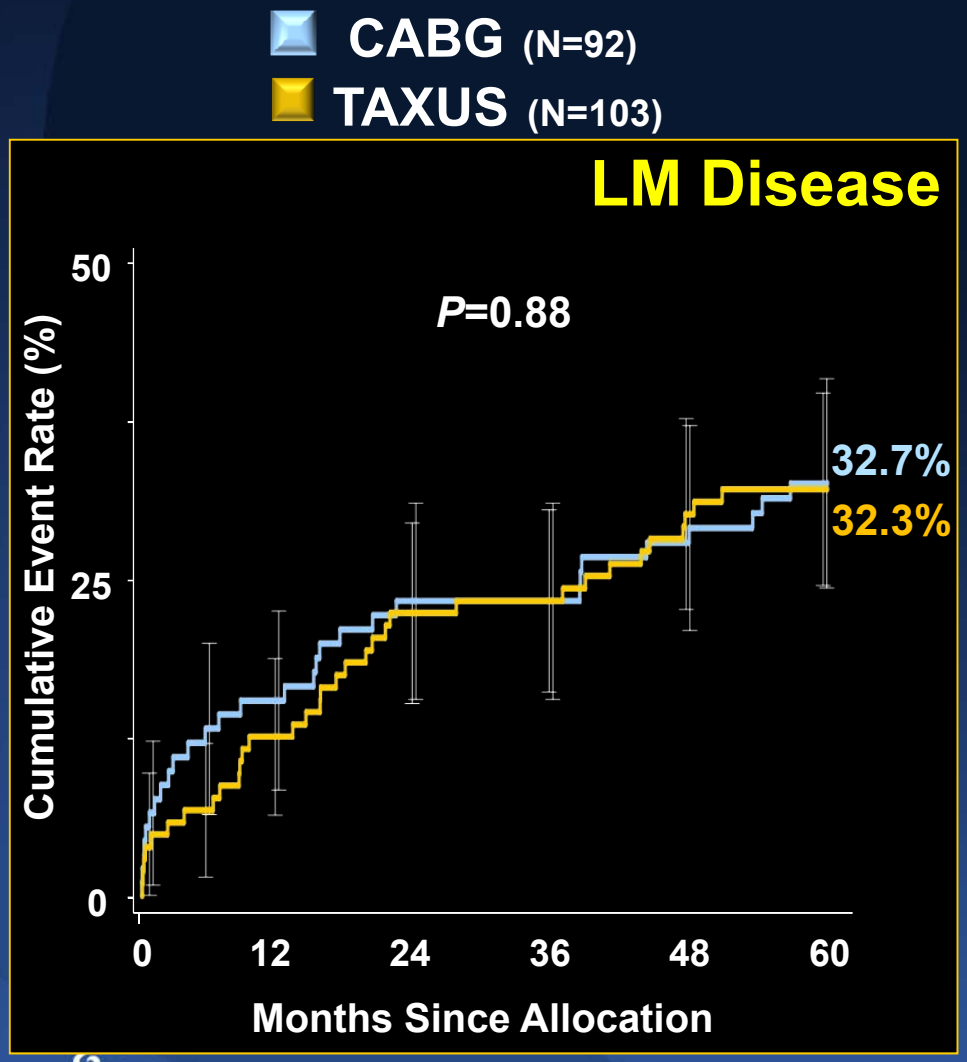


	CABG	PCI	*P* value
Death	11.3%	7.0%	0.28
CVA	4.1%	1.8%	0.28
MI	3.1%	6.2%	0.32
Death, CVA or MI	15.2%	13.9%	0.71
Revasc.	20.3%	23.0%	0.65

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

Site-reported Data; ITT population

MACCE to 5 Years by SYNTAX Score Tercile
LM Subset Intermediate Scores 23-32



	CABG	PCI	*P* value
Death	19.3%	8.9%	0.04
CVA	3.6%	1.0%	0.23
MI	4.6%	6.0%	0.71
Death, CVA or MI	24.9%	15.7%	0.11
Revasc.	16.6%	22.2%	0.40

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

Site-reported Data; ITT population

Summary

Left Main Subset

- At 5 years, overall MACCE in the PCI group was comparable with CABG (31.0% CABG vs 36.9% PCI)
- Similar overall safety outcomes (Death/CVA/MI) between CABG and PCI at 5 years (20.8% CABG vs 19.0% PCI)
- There was a higher rate of revascularization in the PCI group (15.5% CABG vs 26.7% PCI), driven primarily by patients with high baseline SYNTAX scores
- A higher rate of CVA in the CABG group (4.3% CABG vs 1.5% PCI) was driven mostly by periprocedural events, with no difference between groups after 1 year
- PCI outcomes are excellent relative to CABG in LM isolated and LM+1VD

Conclusions

For patients with left main disease

- Revascularization with PCI has comparable safety and efficacy outcomes to CABG
- PCI is therefore a reasonable treatment alternative in this patient population, in particular, when the SYNTAX Score is low (≤22) or intermediate (23–32)

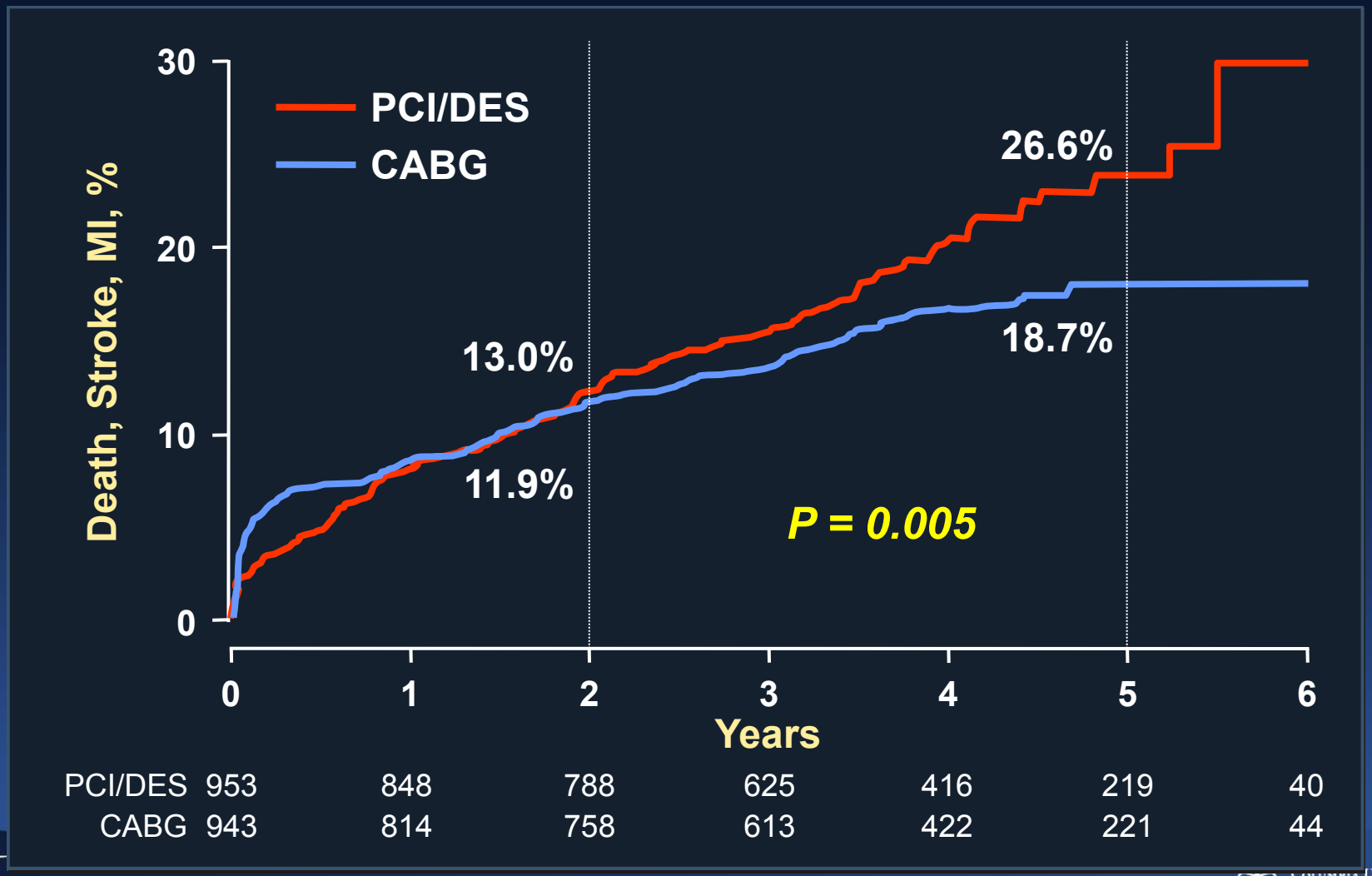
Backups

PCI and CABG Post-SYNTAX

- Each strategy can have great outcomes in appropriately selected patients
- What outcomes are important?
  - Repeat procedures with PCI
  - Increased morbidity with CABG
- Site-specific differences
- Anatomic and patient factors
- Patient preferences

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

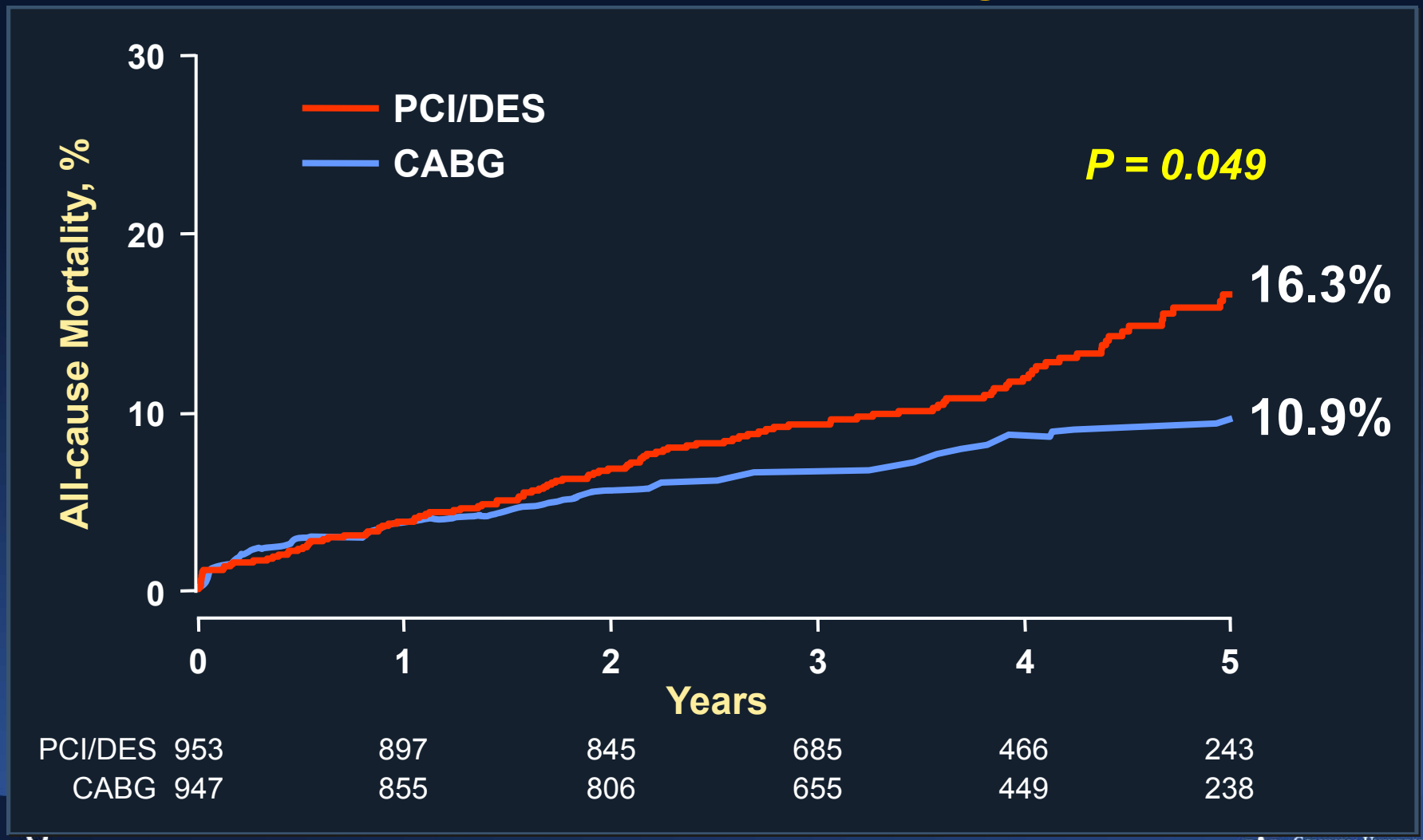
1° Endpoint: Death, Stroke, or MI



Farkouh ME et al. NEJM 2012

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

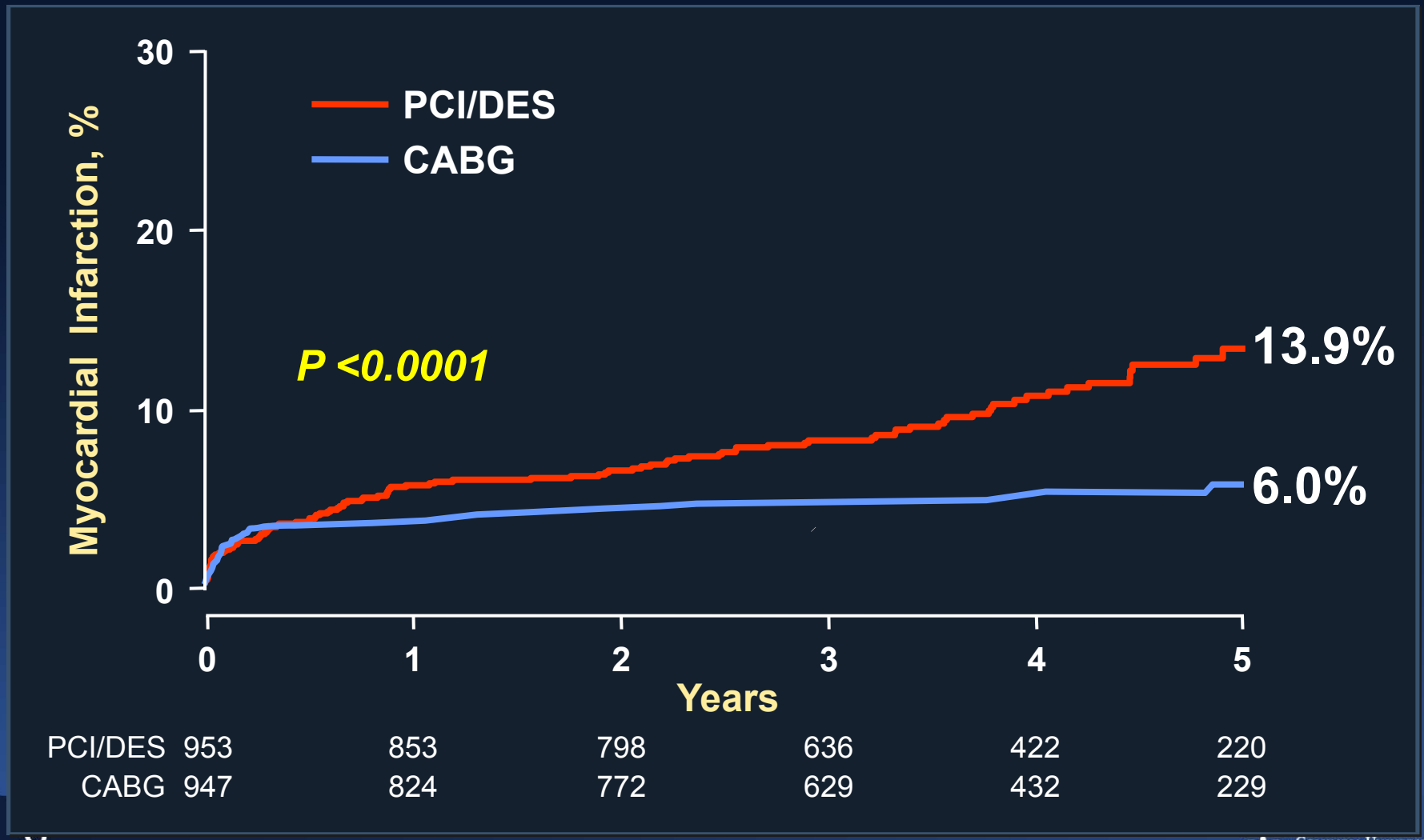
All-cause Mortality



Farkouh ME et al. NEJM 2012

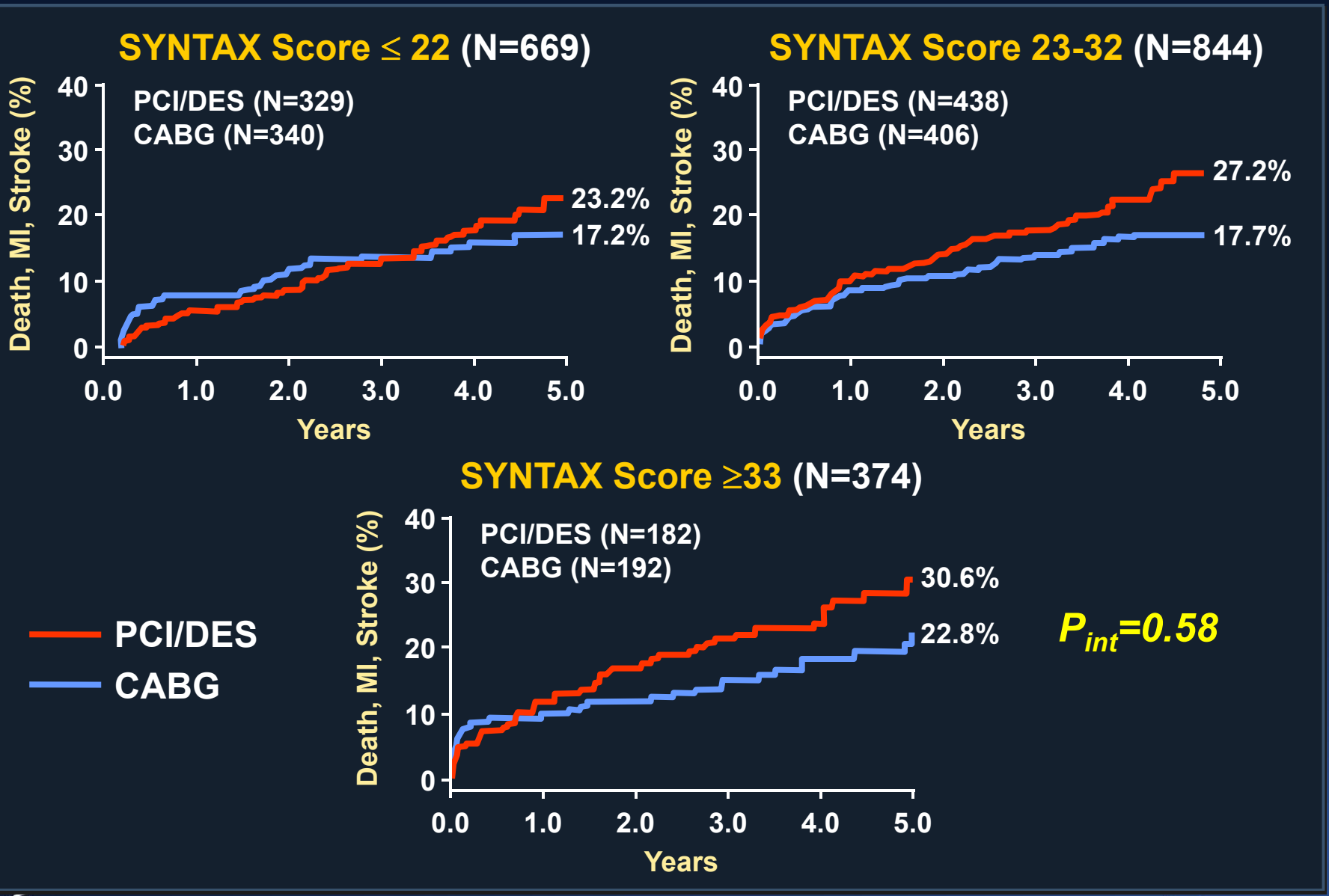
FREEDOM: 1900 pts with diabetes +MVD randomized to SES/PES vs. CABG

Myocardial Infarction



Farkouh ME et al. NEJM 2012

Death, Stroke, MI by Syntax Score



Farkouh ME et al. *NEJM* 2012

Other notes about FREEDOM

- 3VD: 86%
- Mean 5.7 lesions per pt
- Mean 3.5 lesions per pt stented
- CTOs: only 6% of pts
- Prior stroke: only 3% of pts

What is Great about CABG (The Gold Standard for Multivessel Disease)

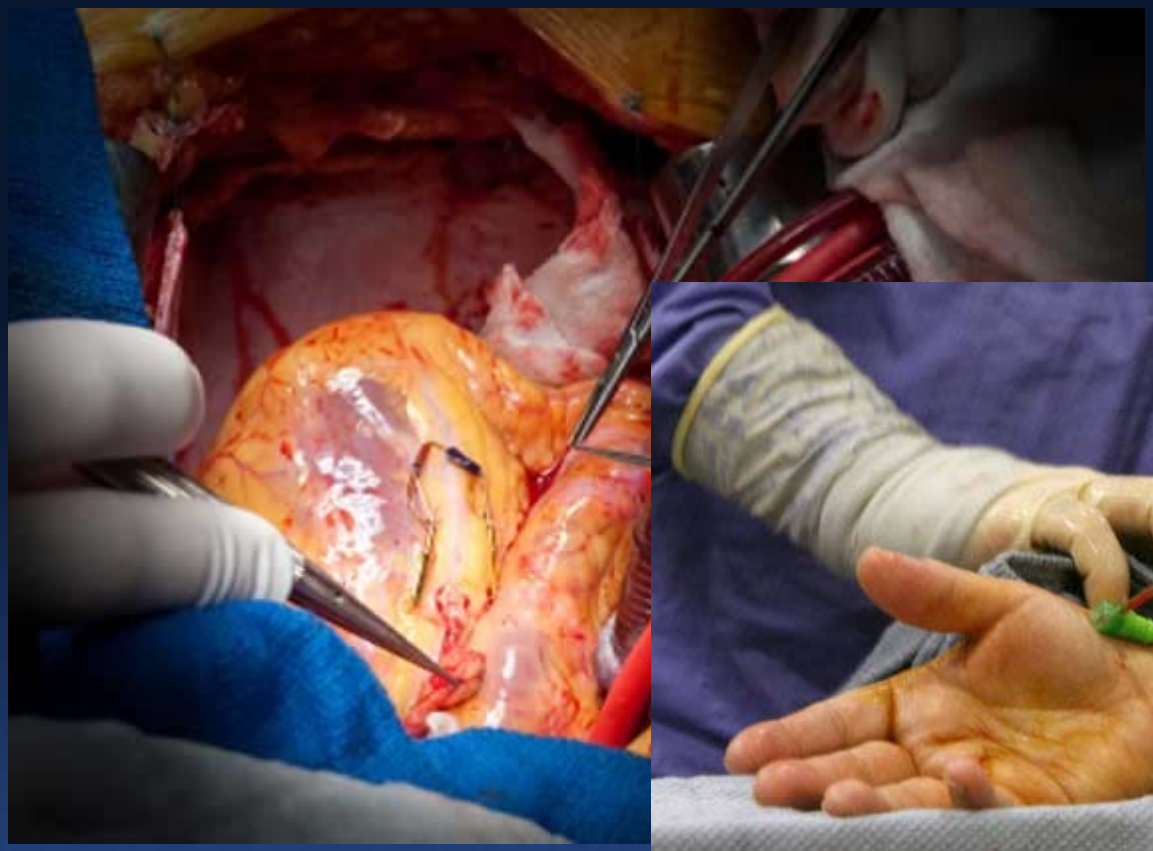
- One-stop shopping with a lasting procedure and data (both vs. PCI AND vs. OMT) in its favor!
- Complete / Difficult revascularization is more easily achievable
- Compliance/adherence less of an issue
- Provided the patient isn't frail, I generally feel confident with surgical risk assessment

So why do many patients and physicians still favor PCI?
Answer: (It's not all referral bias!)

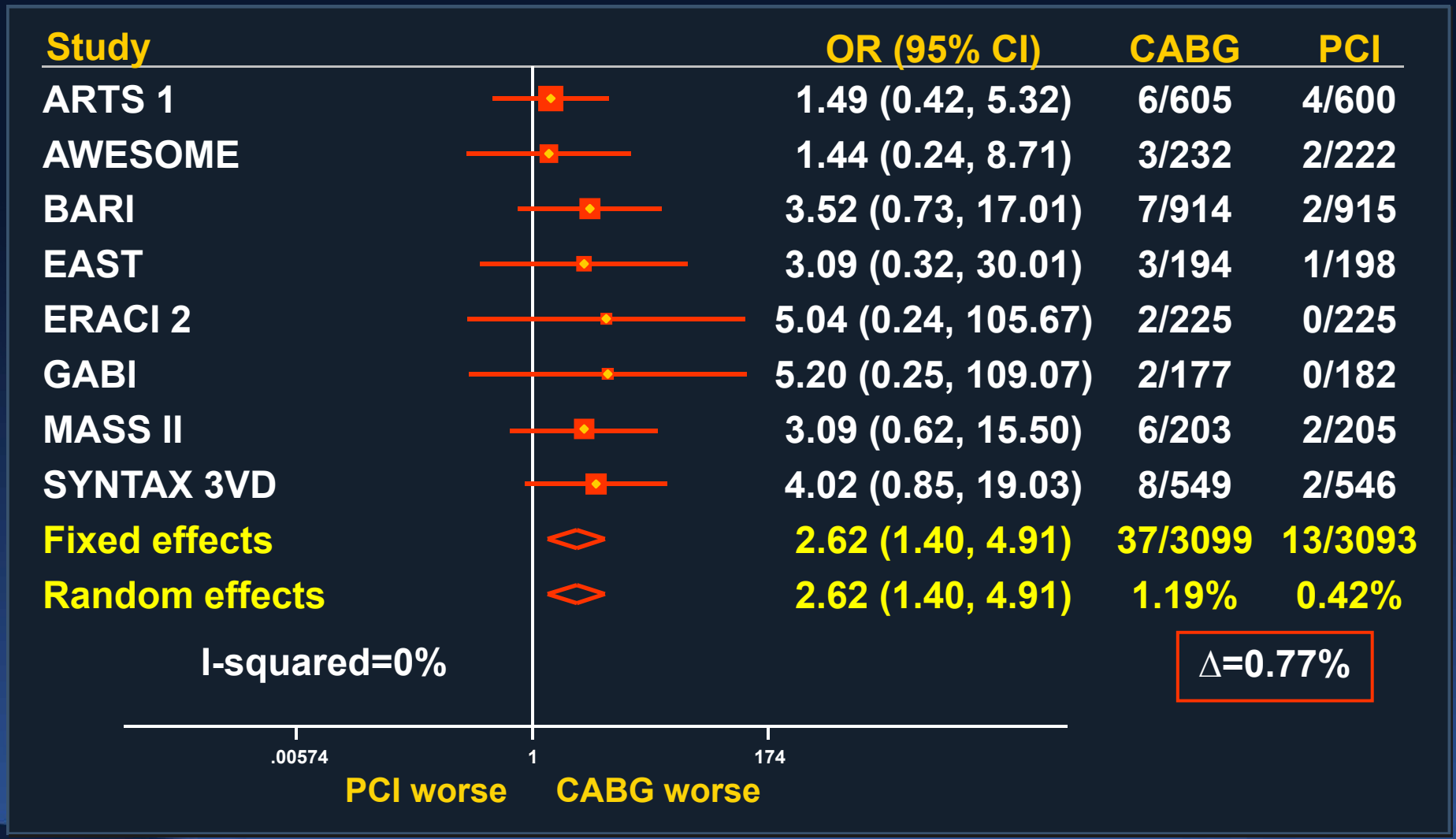
Why Patients (and Physicians) Still Often Prefer PCI…

- Referral Bias
- It's LESS INVASIVE!
- Other issues with CABG including neurocognitive issues, stroke
- The SYNTAX and FREEDOM data doesn't apply to current practice
- Non-randomized data are poorly informative
  - Selection bias is rampant

Two Very Different Procedures…



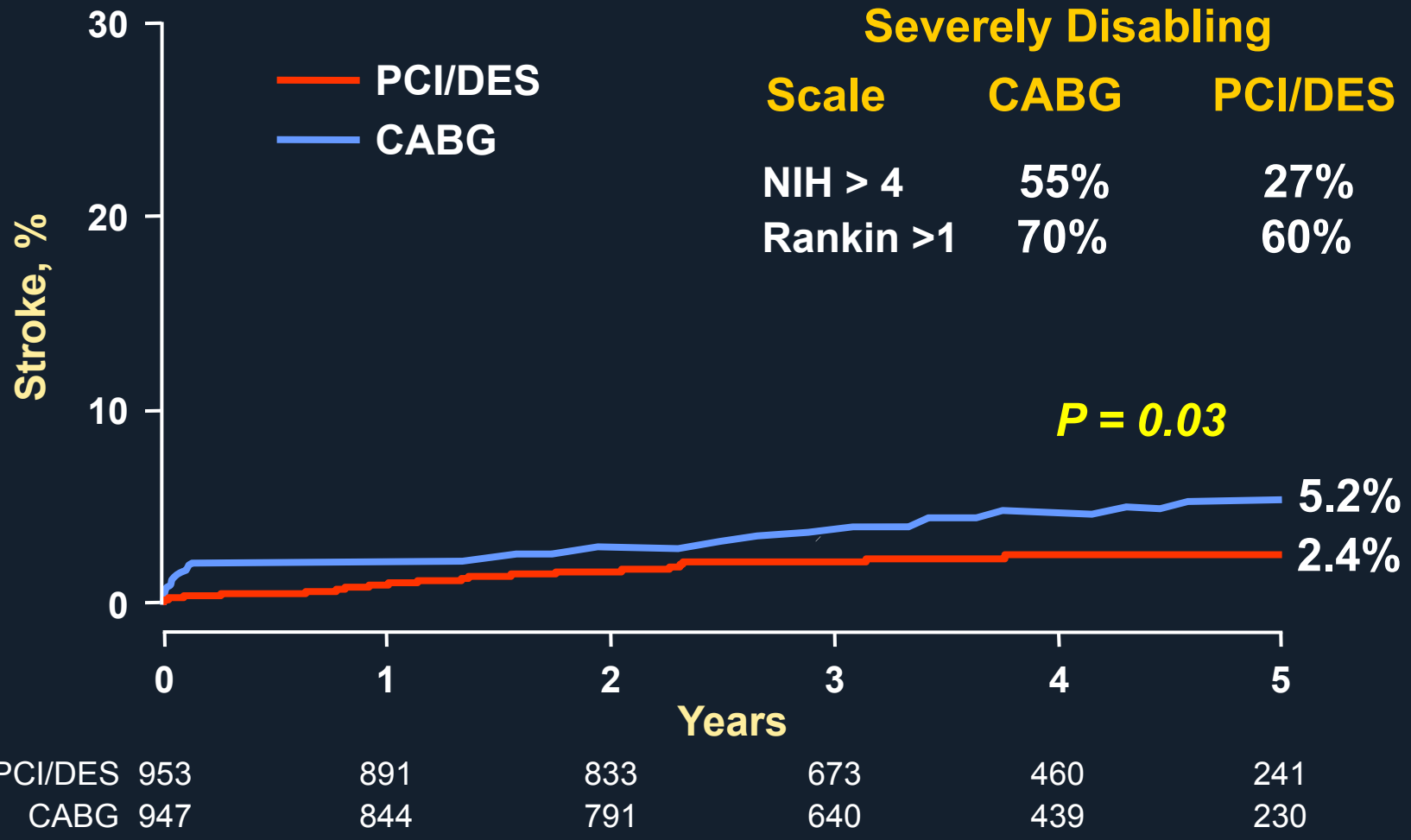
Risk of Stroke with CABG vs PCI: Meta-analysis of 8 RCTs: 30-day Follow-up



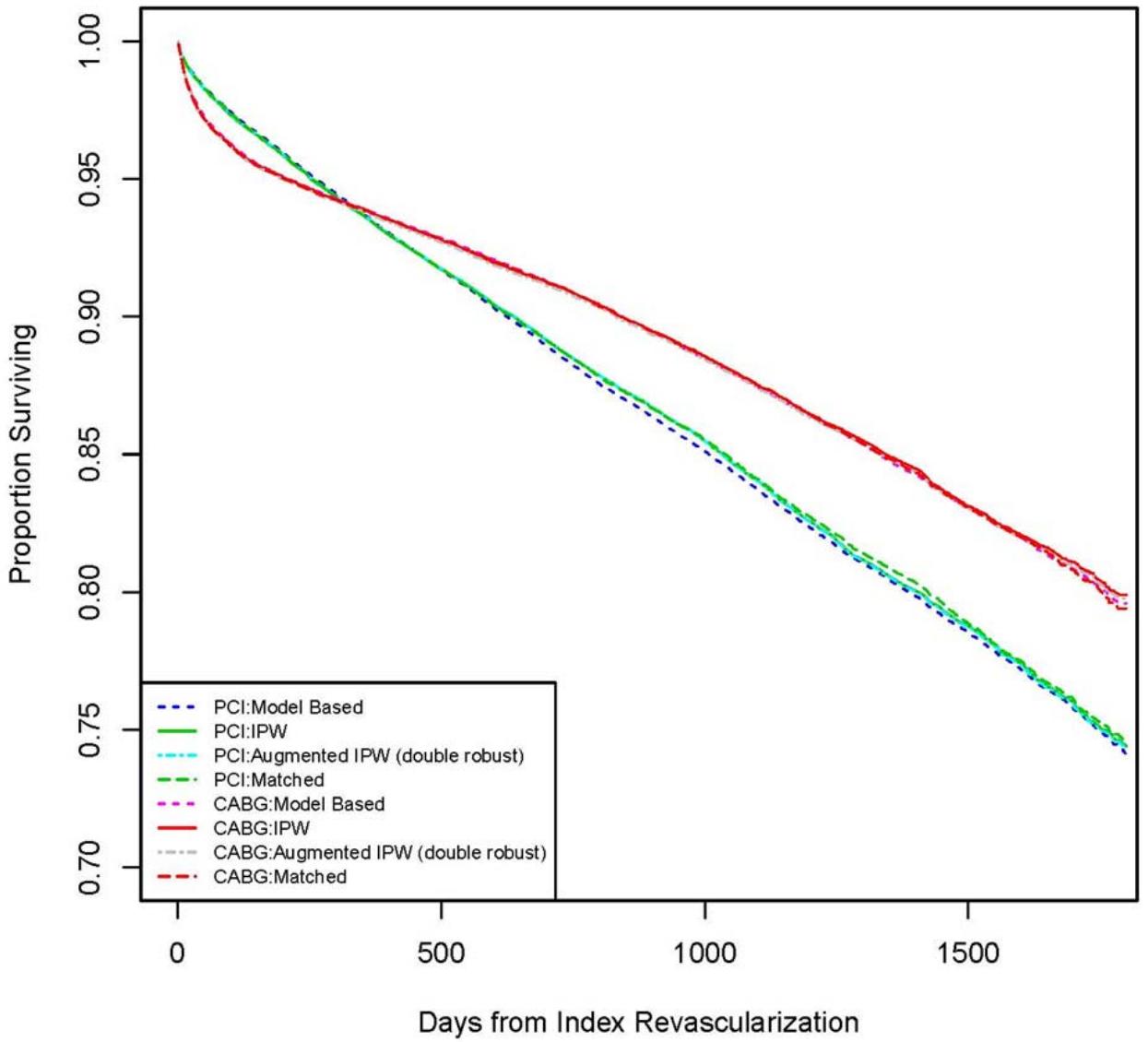
Palmerini et al. JACC 2012;60:798-805

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

Stroke



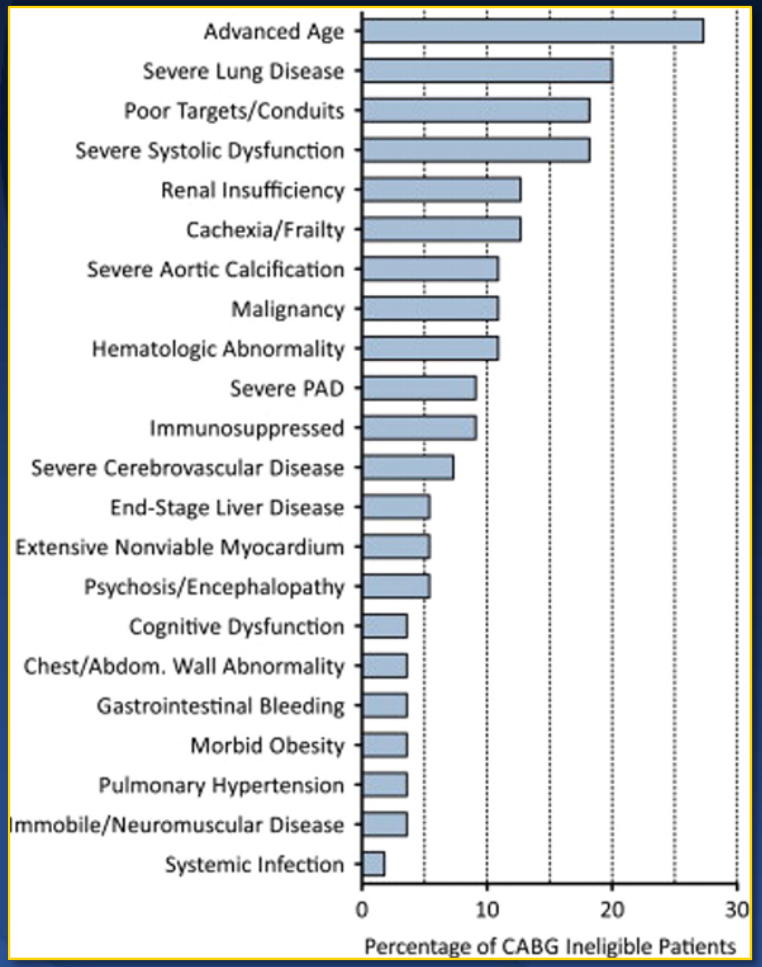
Farkouh ME et al. NEJM 2012


Comparison of Risk Adjusted Survival Methods
Proportion Surviving
1.00
0.95
0.90
0.85
0.80
0.75
0.70
0
500
1000
1500
Days from Index Revascularization
PCI:Model Based
PCI:IPW
PCI:Augmented IPW (double robust)
PCI:Matched
CABG:Model Based
CABG:IPW
CABG:Augmented IPW (double robust)
CABG:Matched

Baseline Data

	Unadjusted			IPW Adjusted		
	CABG (n=86,244)	PCI (n=103,549)	P Value	CABG (n=86,244)	PCI (n=103,549)	P Value
Age	73.1 ± 5.6	74.7 ± 6.5	<0.0001	74.0 ± 9.2	74.0 ± 8.3	0.49
Male	68.6	57.8	<0.0001	62.3	62.8	0.17
History of CHF	11.5	10.2	<0.0001	11.2	10.8	0.067
History of MI	25.3	24.6	0.0001	24.5	24.7	0.51
Diabetes	38.6	34.4	<0.0001	35.8	35.8	0.97
Insulin Requiring	10.2	9.8	0.0069	9.7	9.9	0.35
Hypertension	84.8	83.4	<0.0001	83.9	83.8	0.58
Renal Failure	6.1	6.2	0.57	6.1	6.1	0.80
CKD	20.7	18.9	<0.0001	19.4	19.6	0.50
CVD	17.6	15.8	<0.0001	16.6	16.6	0.86
PAD	17.9	15.3	<0.0001	16.4	16.4	0.97
BMI	28.7 ± 5.8	28.7 ± 5.9	0.78	28.8 ± 8.6	28.7 ± 7.9	0.97
Former Smoker	44.0	42.5	<0.0001	43.0	43.3	0.45
Current Smoker	12.9	11.6	<0.0001	11.9	12.0	0.74
No Angina	21.8	30.8	<0.0001	26.4	26.8	0.23
Stable Angina	49.6	22.6	<0.0001	34.6	34.9	0.46
Unstable Angina	28.6	46.6	<0.0001	39.0	38.3	0.066
Ejection Fraction	52.9± 12.2	55.5 ± 11.4	<0.0001	54.4 ± 17.6	54.4 ± 16.2	0.58
3 Vessel Disease	80.3	32.1	<0.0001	53.2	53.8	0.043
Status Urgent	68.6	57.8	<0.0001	62.3	62.8	0.17

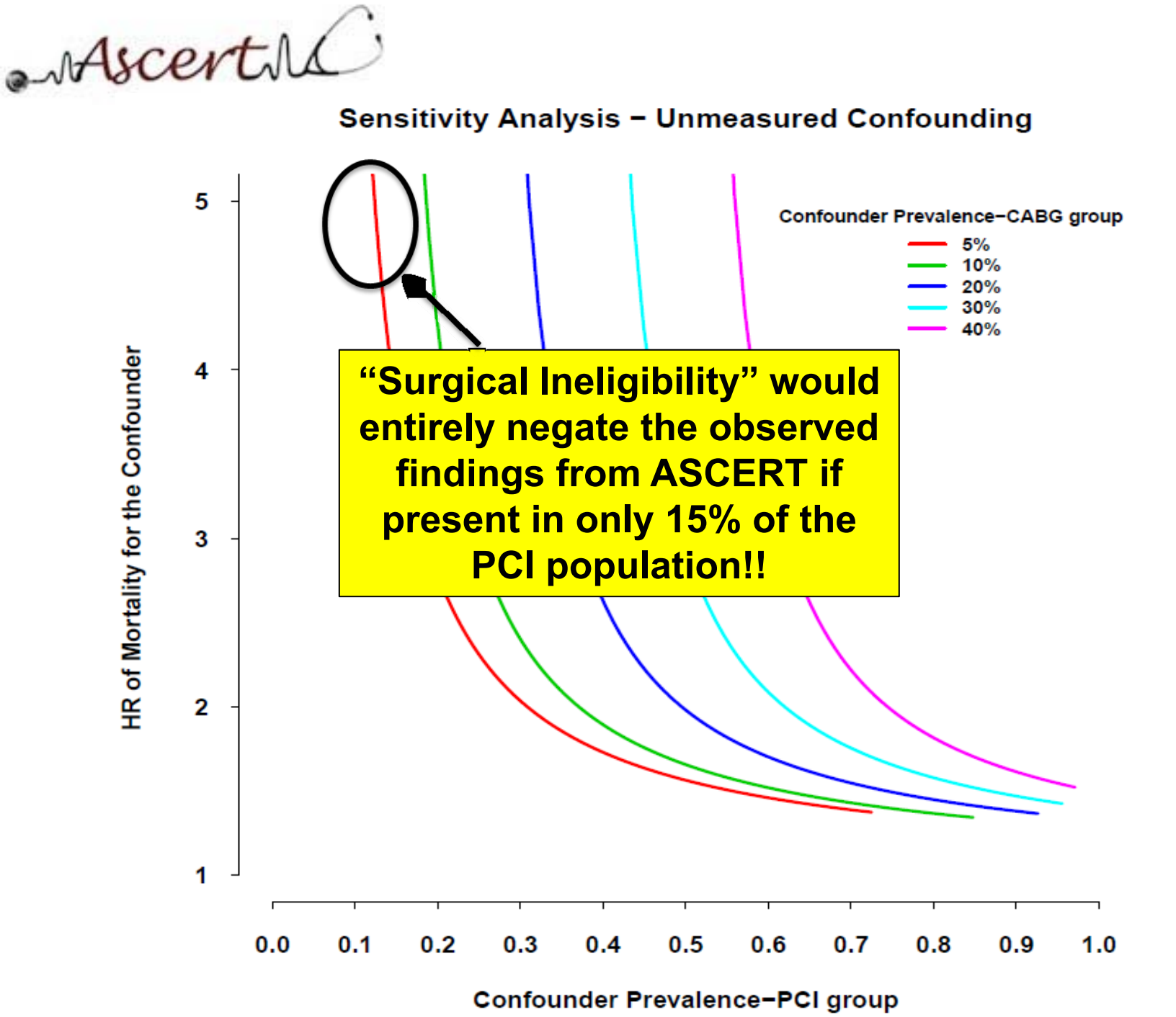
Surgical Candidacy and Selection Bias in National Observational Registries: Case Study Using LMCA PCI



"Surgical ineligibility" independently conferred a 5-fold higher risk of mortality not accounted for by:

- ***NCDR risk score***
- ***STS risk score***
- ***Euroscore***

McNulty et al. JACC CV Intv 2011


Sensitivity Analysis – Unmeasured Confounding
Confounder Prevalence–CABG group
5%
10%
20%
30%
40%
"Surgical Ineligibility" would entirely negate the observed findings from ASCERT if present in only 15% of the PCI population!!
HR of Mortality for the Confounder
1
2
3
4
5
0.0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1.0
Confounder Prevalence–PCI group

When does “comparative effectiveness” in fact represent “ineffective comparativeness”??

CABG vs. PCI

Same age and predicted risk!

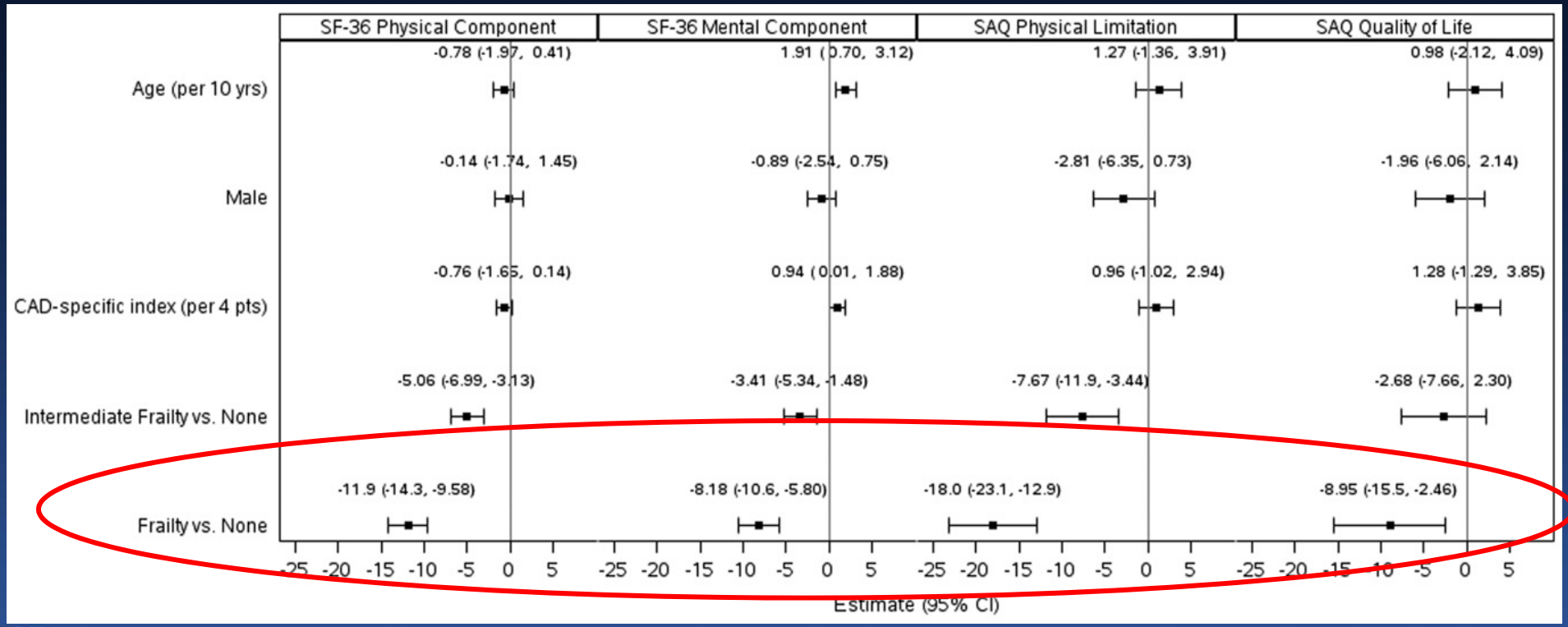
Images c/o M. Mack

Impact of Frailty on Health Status of Elderly Patients Undergoing PCI

629 patients ≥65 yrs old who underwent PCI at Mayo Clinic

~1/5 were "frail" and nearly 1/2 were "intermediate"

Frail pts had more CAD and more comorbidities

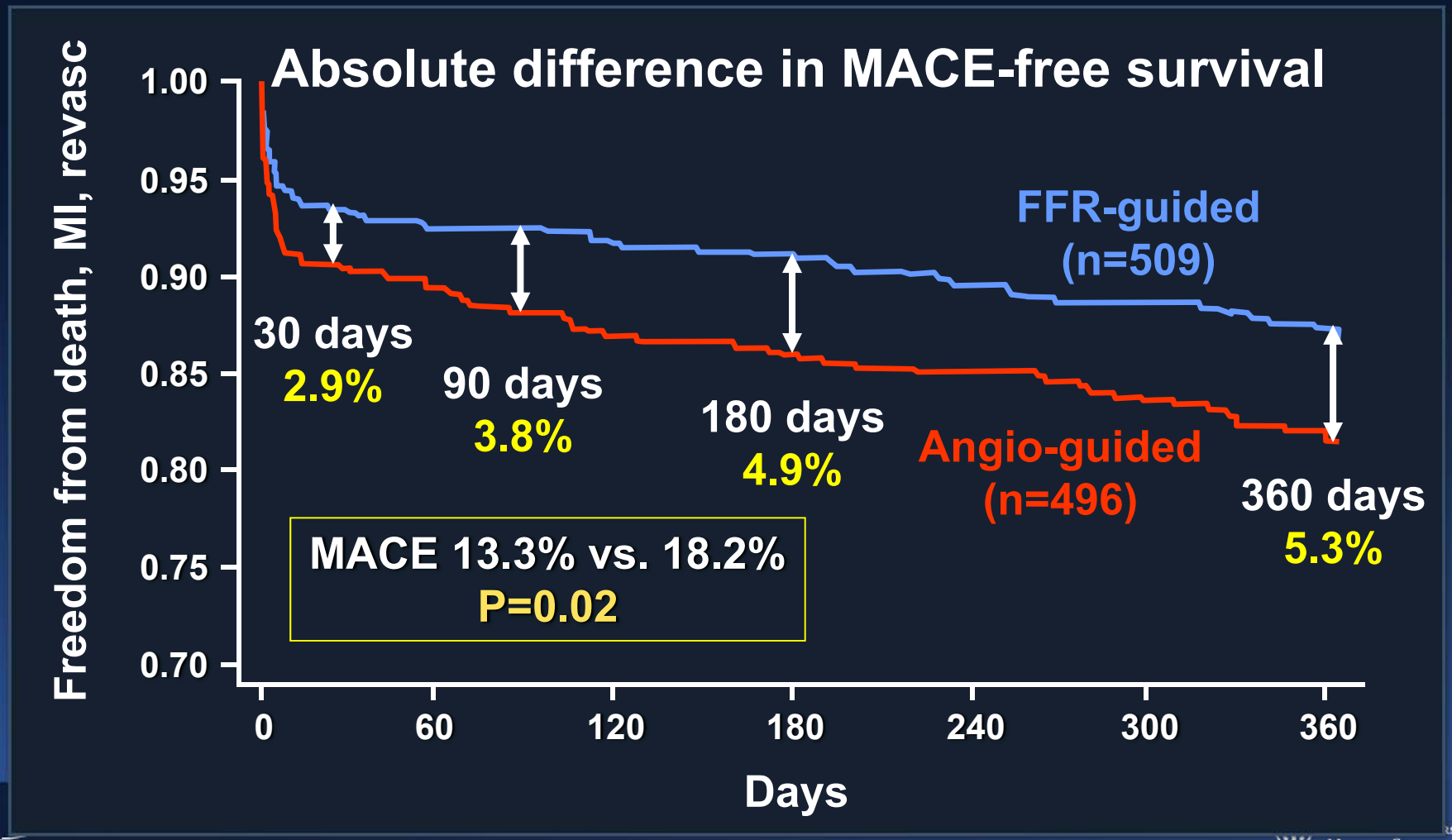


Gharacholou et al, AJC 2012

PCI is Better Now than it Was in SYNTAX and FREEDOM!

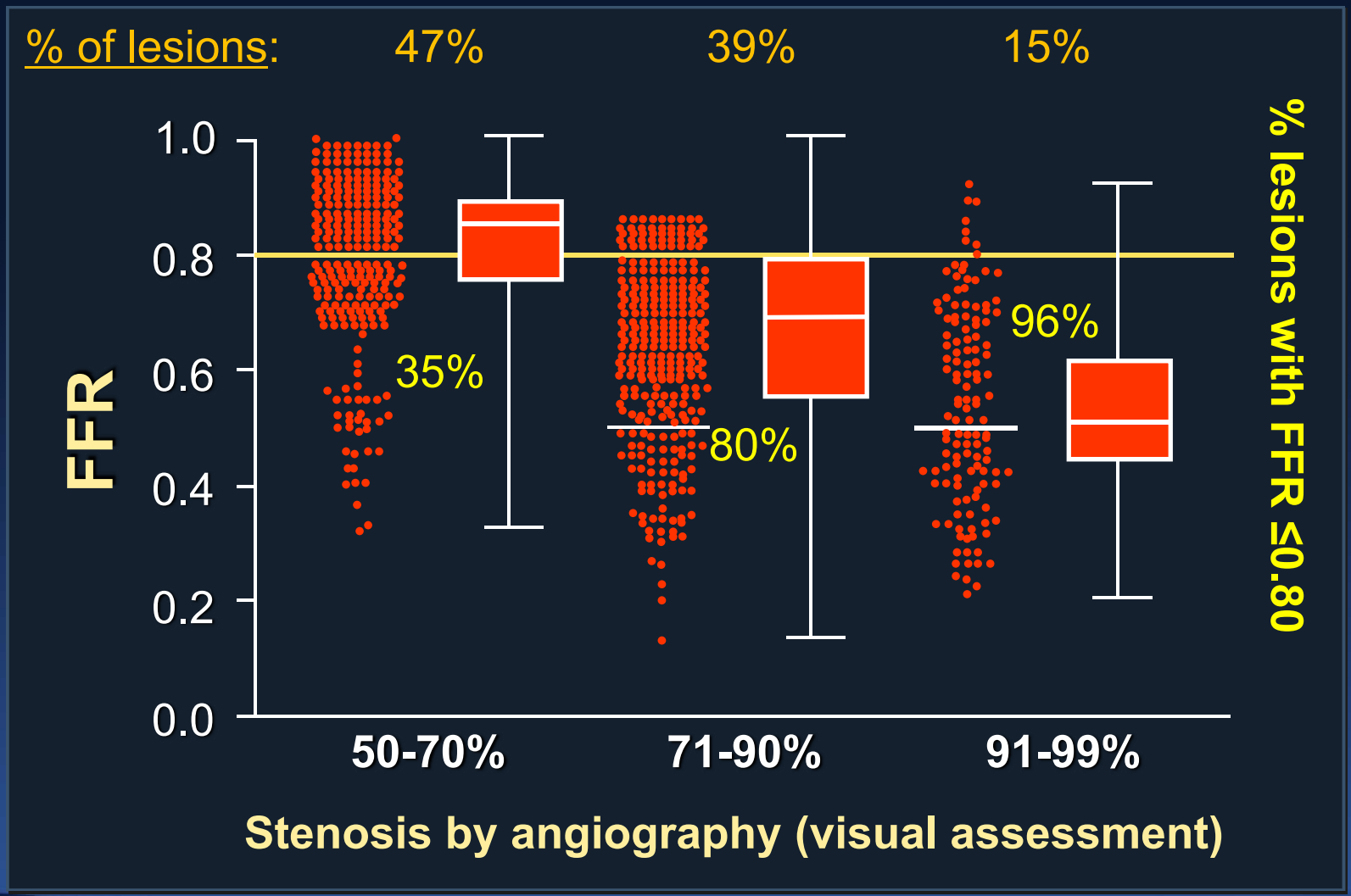
FAME: Optimizing Complete Revascularization

1005 pts with MVD undergoing PCI with DES were randomized to FFR-guided vs. angio-guided intervention



Tonino PAL et al. *NEJM* 2009;360:213–24

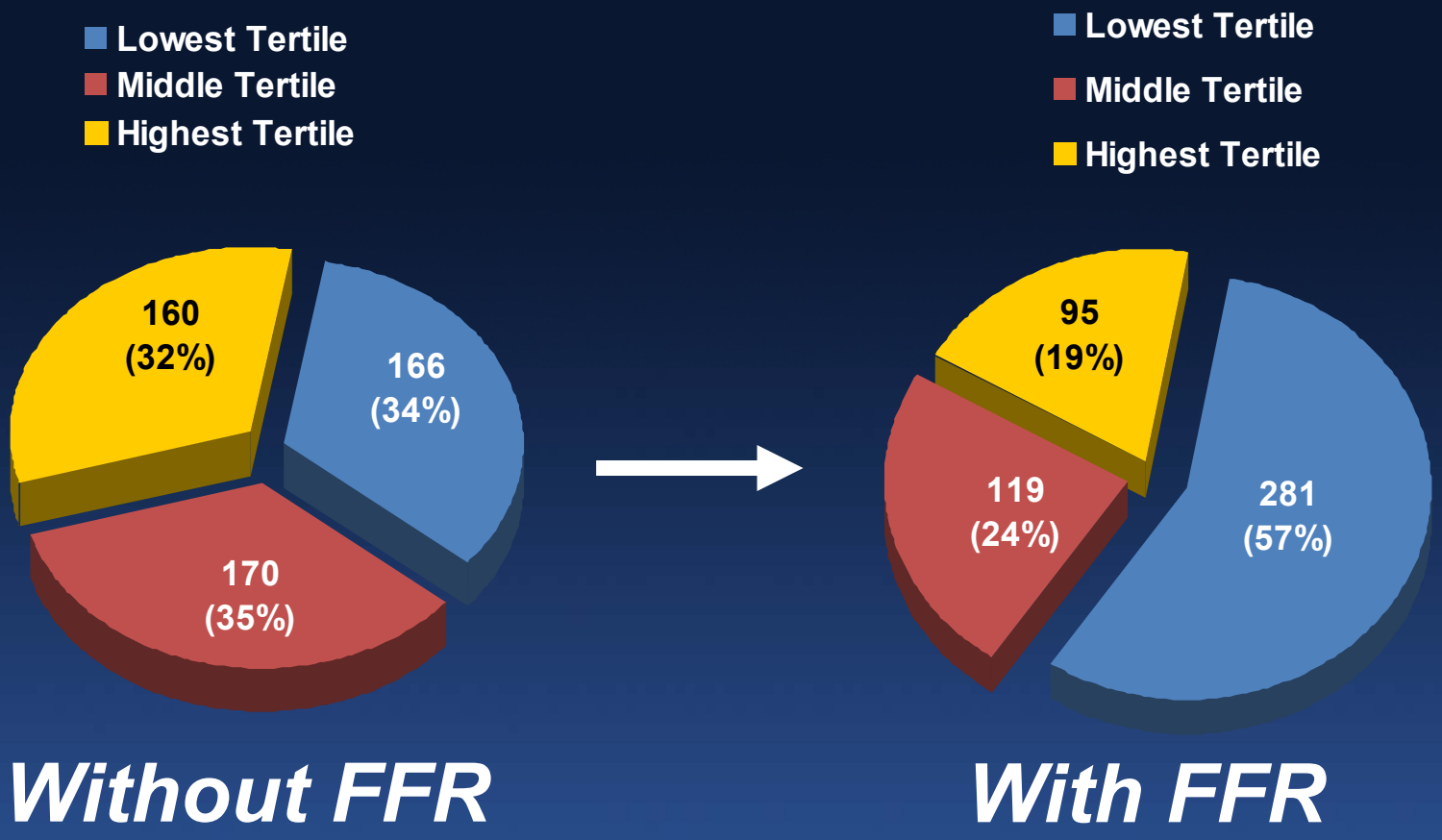
Relationship Between Visual Angiographic %DS and FFR (n=1,329)



Tonino PAL et al. JACC 2010;55;2816-2821

Change in SYNTAX Score after FFR

SYNTAX score ~500 FAME patients after FFR

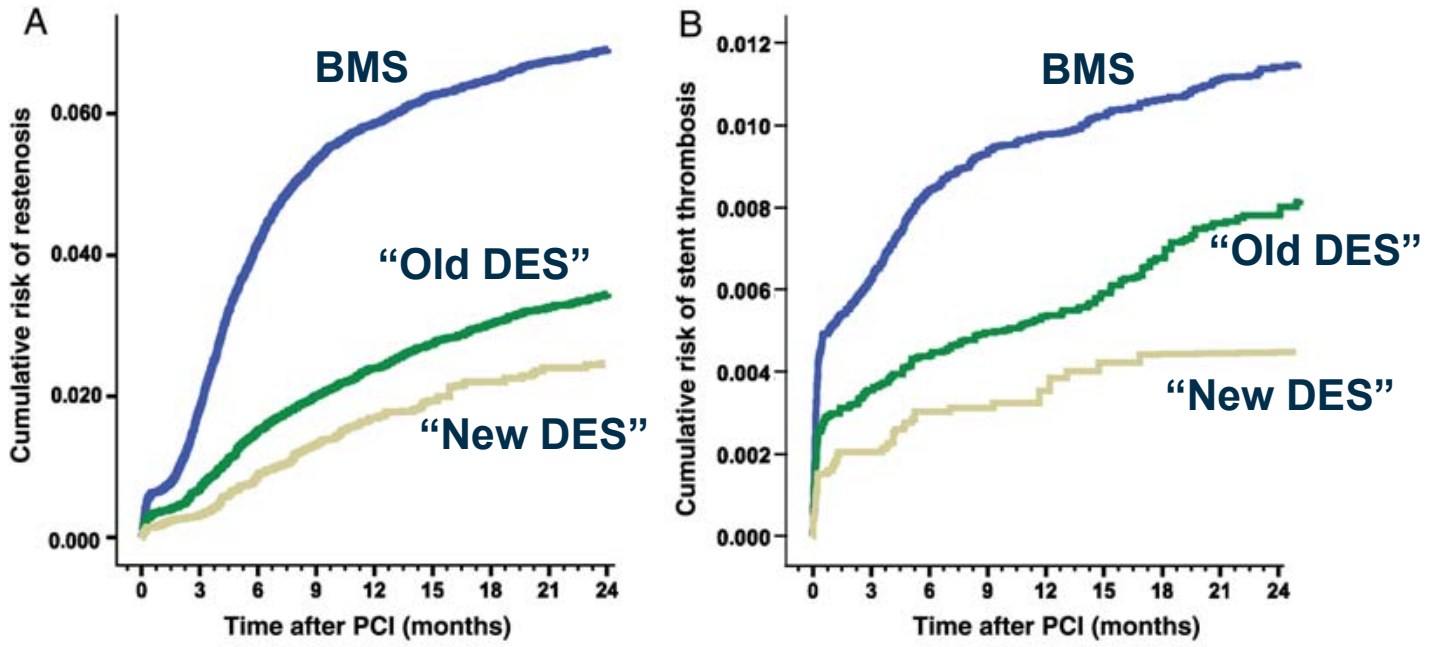


Without FFR ***With FFR***

CW Nam (preliminary data); presented TCT 2010

SCAAR Registry (94,384 pts)
Adjusted Risks of Adverse Events at 2 yrs

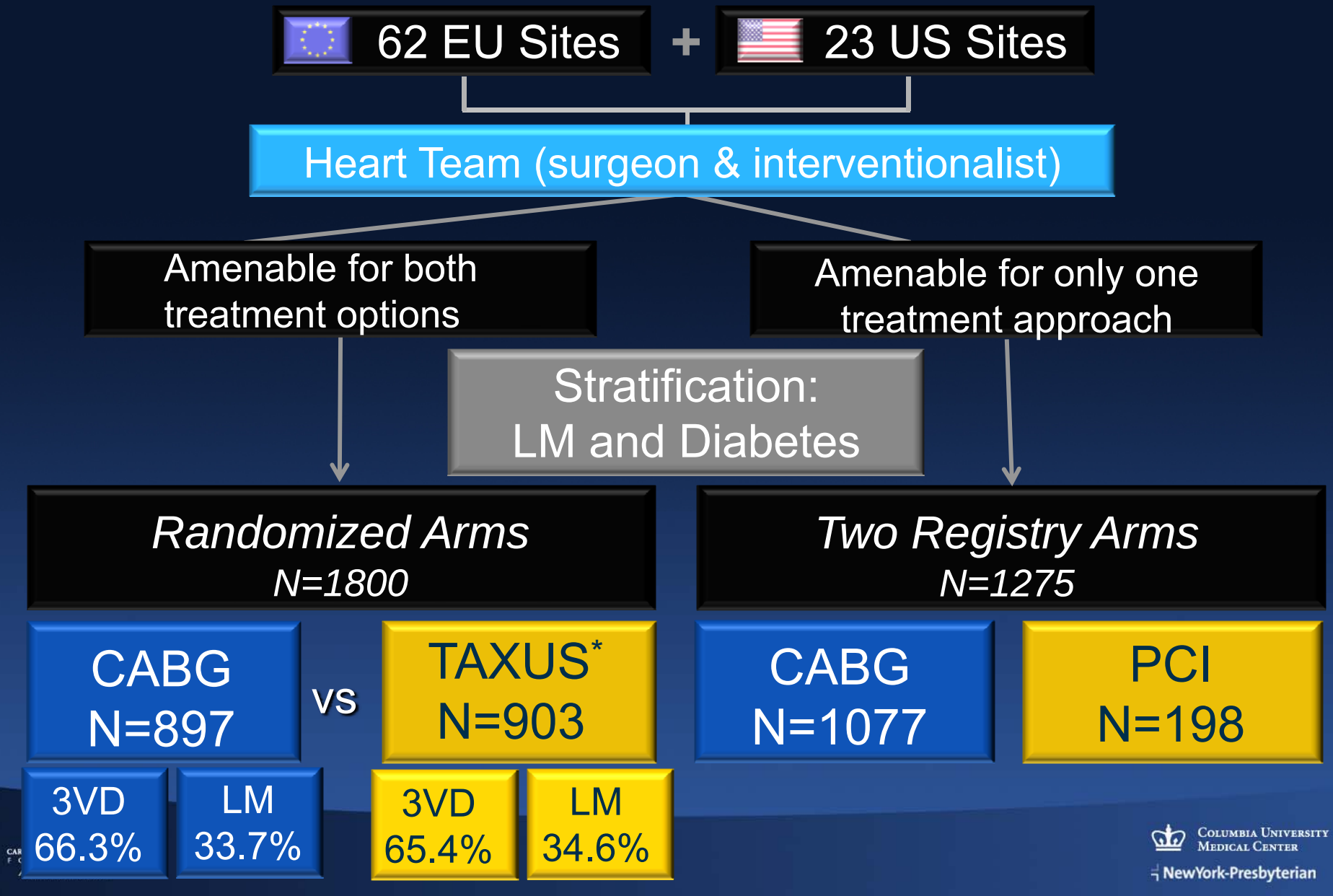
Restenosis | **Definite ST**



n at risk	0 months	6 months	12 months	18 months	24 months
BMS	64 631	56 070	47 968	40 539	32 698
o-DES	19 202	17 862	16 014	13 517	10 533
n-DES	10 551	8092	4188	2005	847

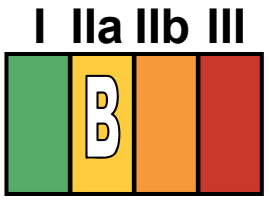
Sarno et al, Eur Heart J 2012

SYNTAX Trial Design



ACC/AHA/SCAI PCI Guidelines: Heart Team Approach to Revascularization Decisions

A Heart Team approach to revascularization is recommended in patients with unprotected left main or complex CAD.



Calculation of the STS and SYNTAX scores is reasonable in patients with unprotected left main and complex CAD.

Conclusions
PCI and CABG for MVD in 2013

- Multivessel disease is a high-risk and prognostically important patient scenario
  - "Least stable" subtype of "stable ischemic heart disease (SIHD)"
- (Regional) functional assessments trump angiography
- For true MVD, take patients off of the table to objectively assess all options
- Honest patient selection attuned to objective patient preference will generally dictate the best/most appropriate care!