Revascularization Choices in Patients with Diabetes

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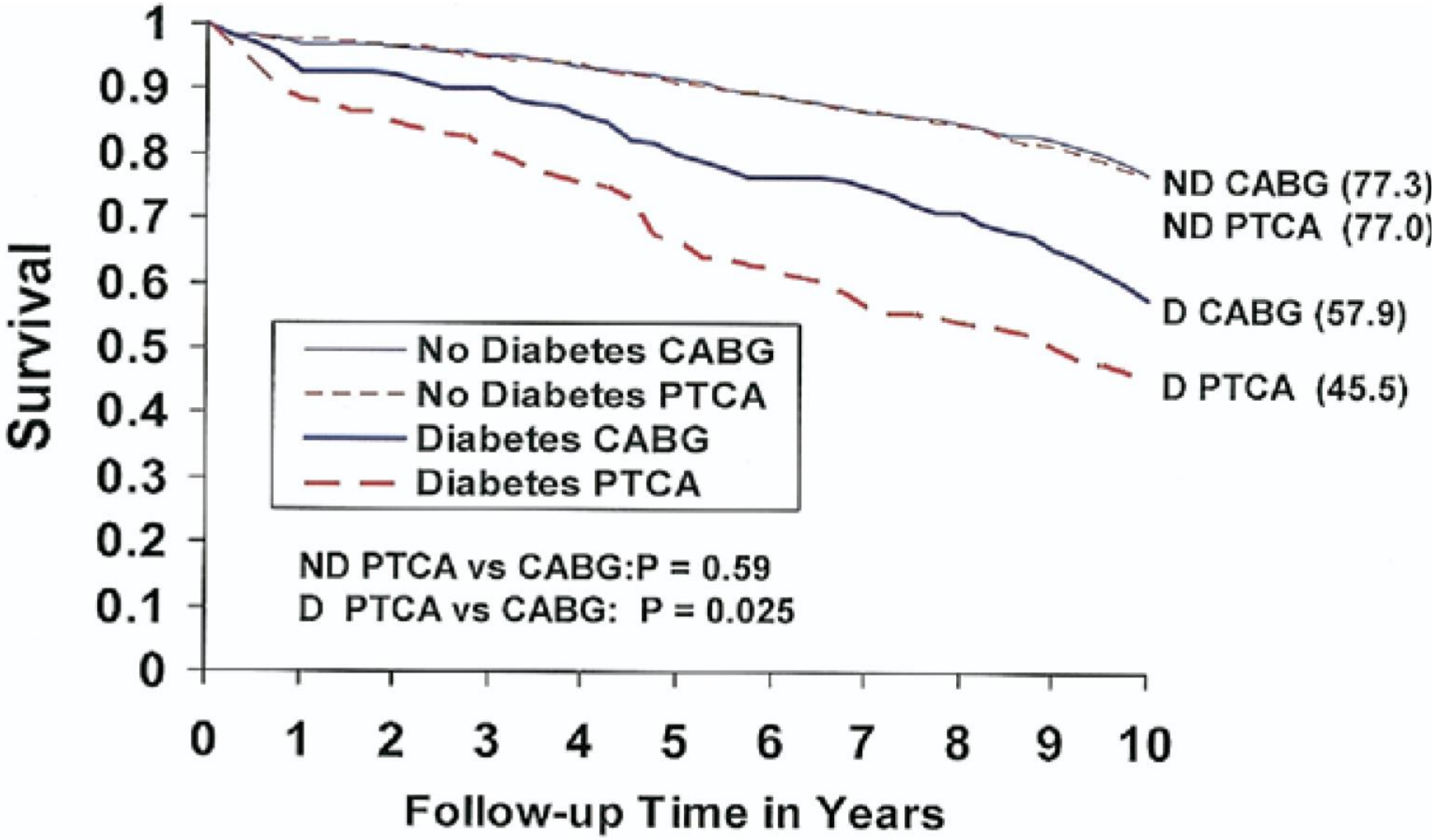
Outline

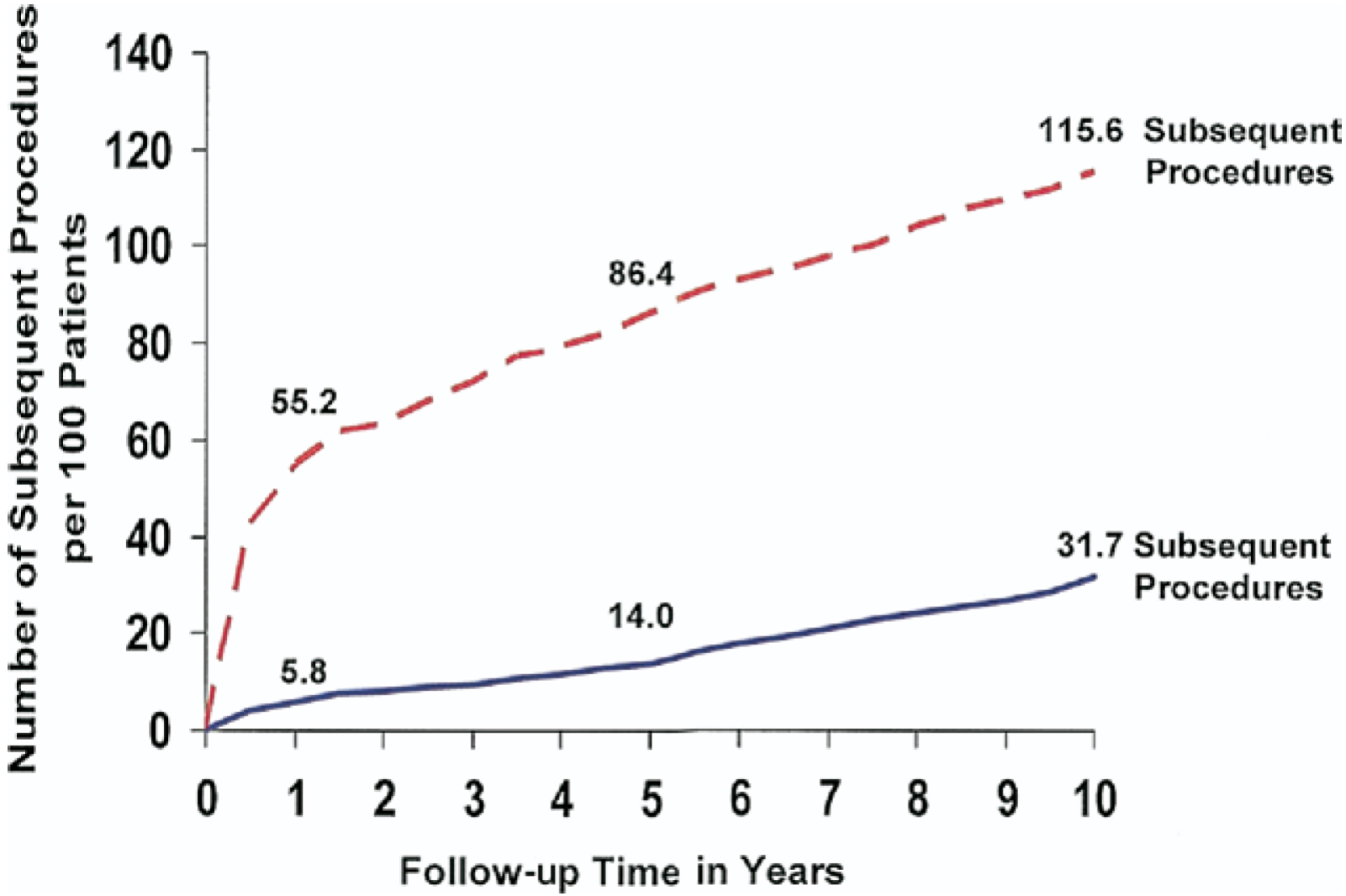
- Revascularization vs. medical therapy
- Choice of revascularization method
- Stent selection
- Graft selection and patency

BARI: Overall Survival by Randomized Treatment Stratified by Diabetes Status



J Am Coll Cardiol 2007;49:1600-6

Cumulative Number of Subsequent Revascularization Procedures per 100 Patients

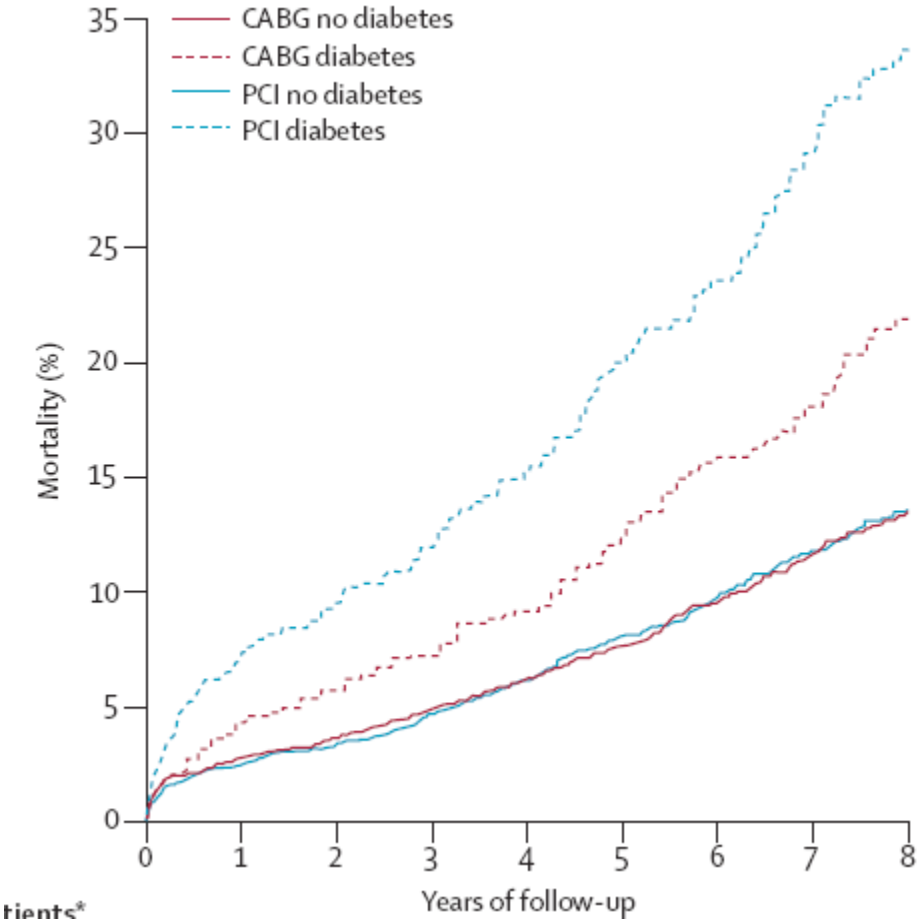


J Am Coll Cardiol 2007;49:1600-6

Pooled individual patient data from 10 randomized trials comparing the effectiveness of CABG with PCI (n=7812)

- During a median follow-up of 5.9 years, mortality in patients with diabetes (CABG, n=615; PCI, n=618) was 30% lower in the CABG group than in the PCI group

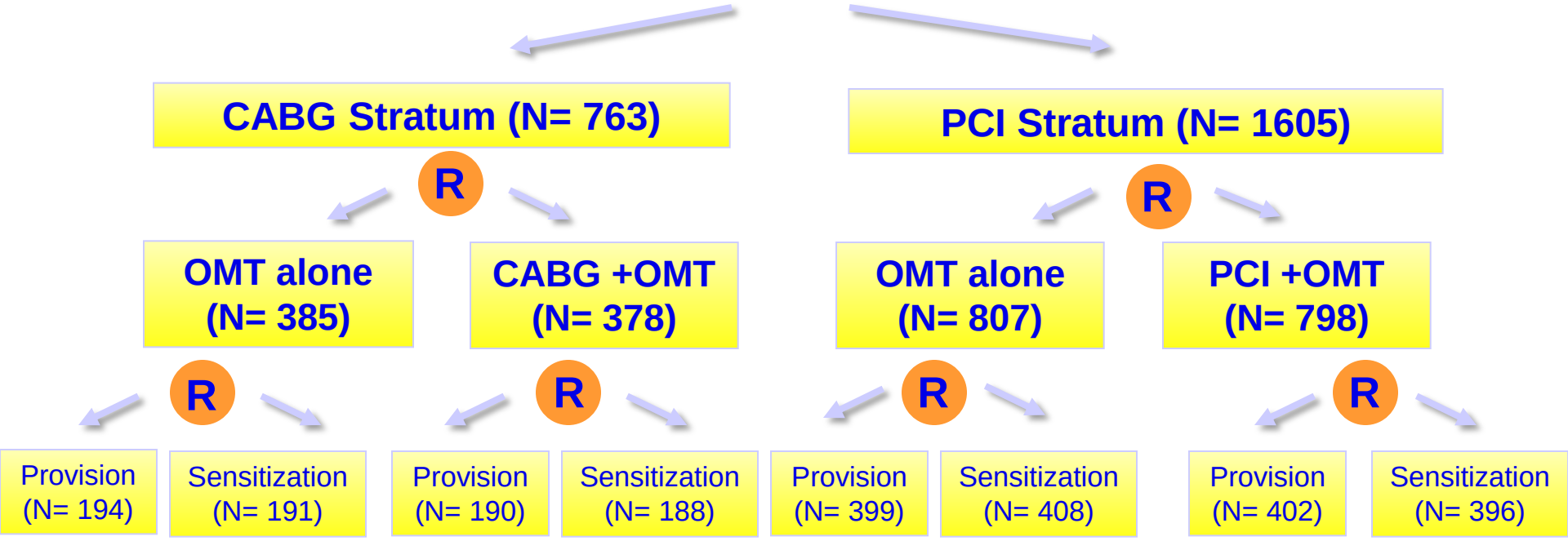
- The beneficial effect of CABG compared with PCI on survival did not differ between balloon angioplasty (n=6) and bare-metal stent (n=4) trials



Lancet 2009; 373: 1190–97

BARI 2D Trial: Study Design

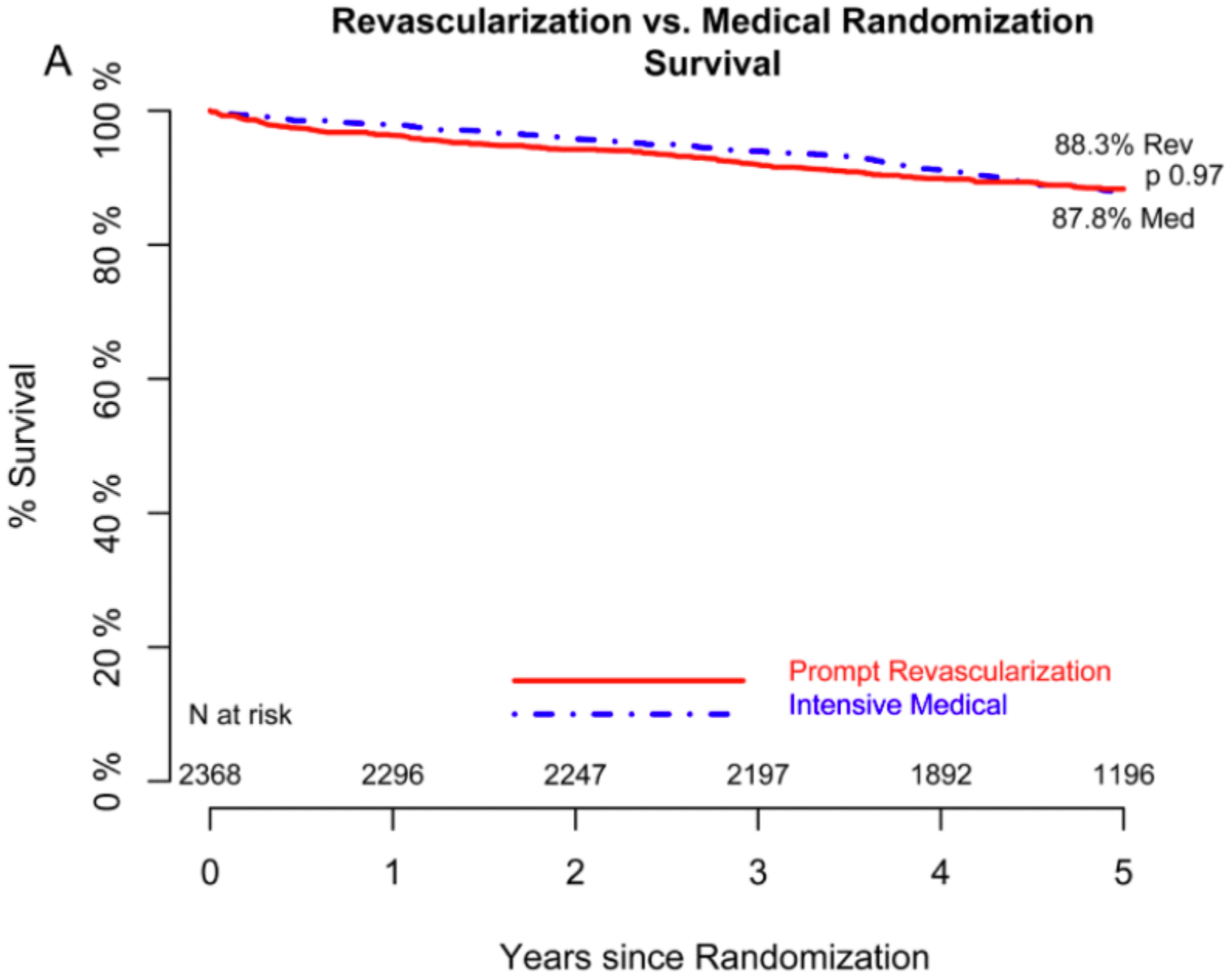
2368 patients with mild to moderate CAD and Type 2 diabetes prior to randomization. Prospective. Randomized. Mean follow-up 5.3 years



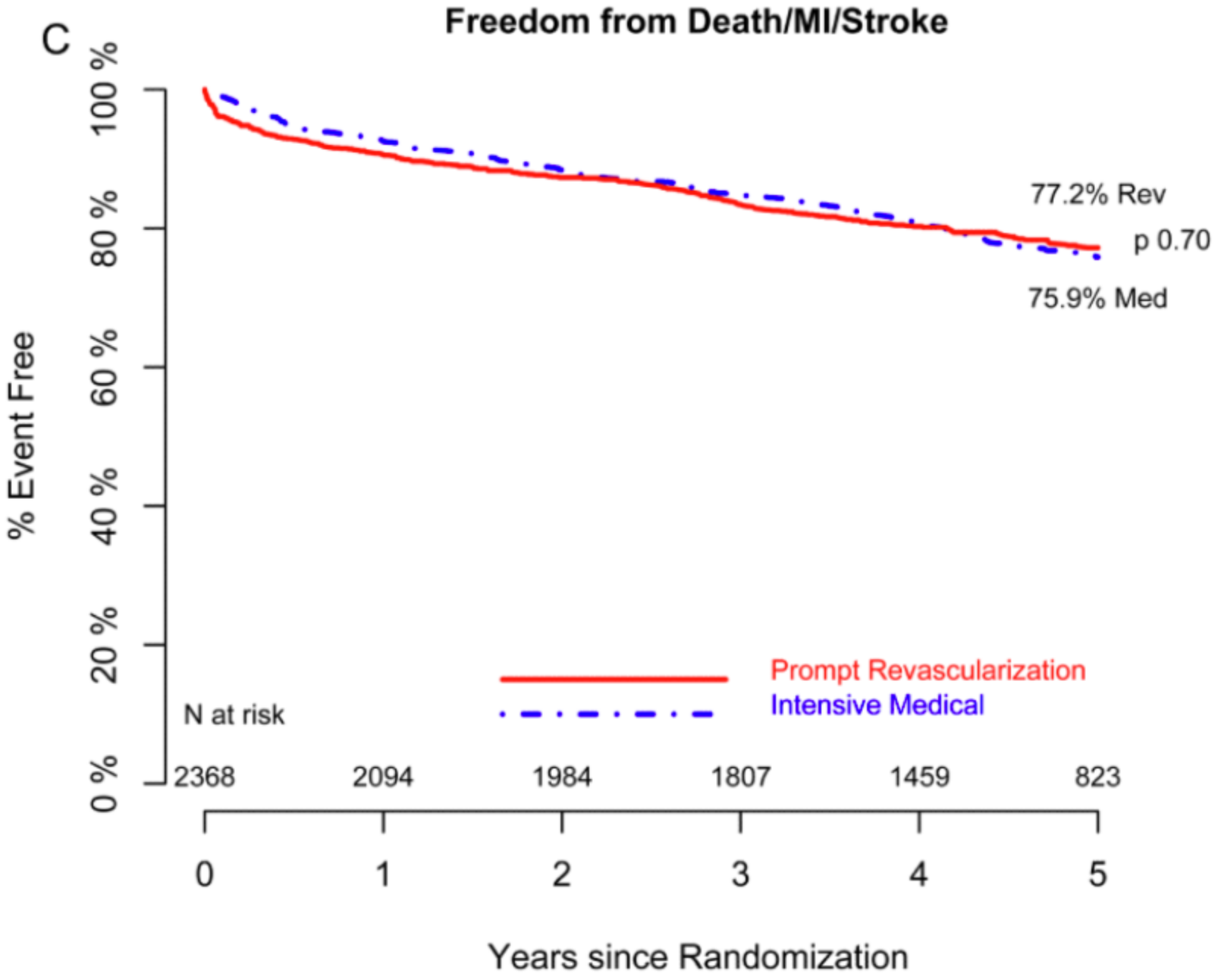
- **Primary Endpoint: Death (from any cause)**
- **Secondary Endpoint: Composite of Death, MI, or Stroke**

Frye et al. N Engl J Med 2009;360:2503-15

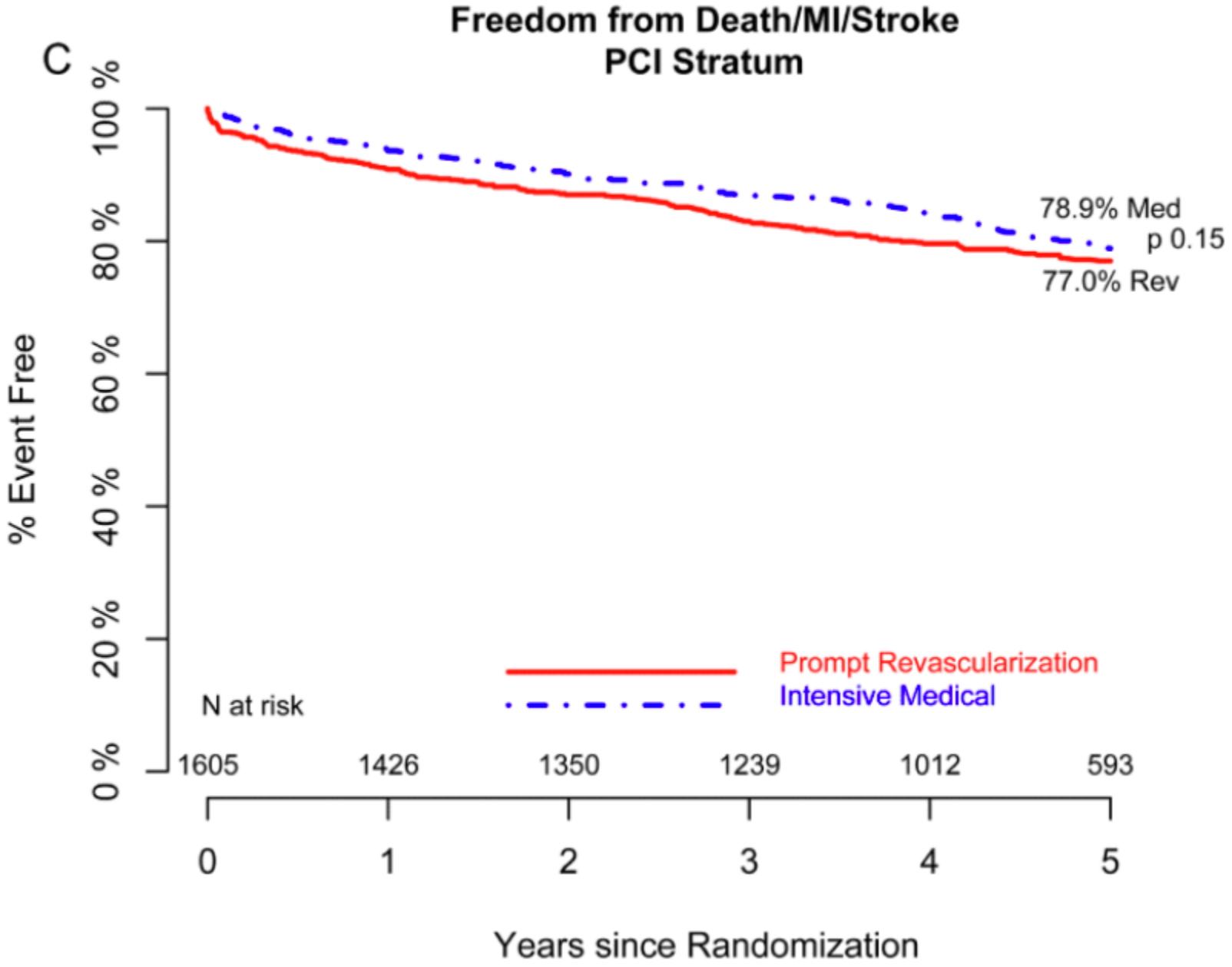
BARI 2D


A
Revascularization vs. Medical Randomization
Survival
% Survival
100 %
80 %
60 %
40 %
20 %
0 %
88.3% Rev
p 0.97
87.8% Med
Prompt Revascularization
Intensive Medical
N at risk
2368
2296
2247
2197
1892
1196
0
1
2
3
4
5
Years since Randomization

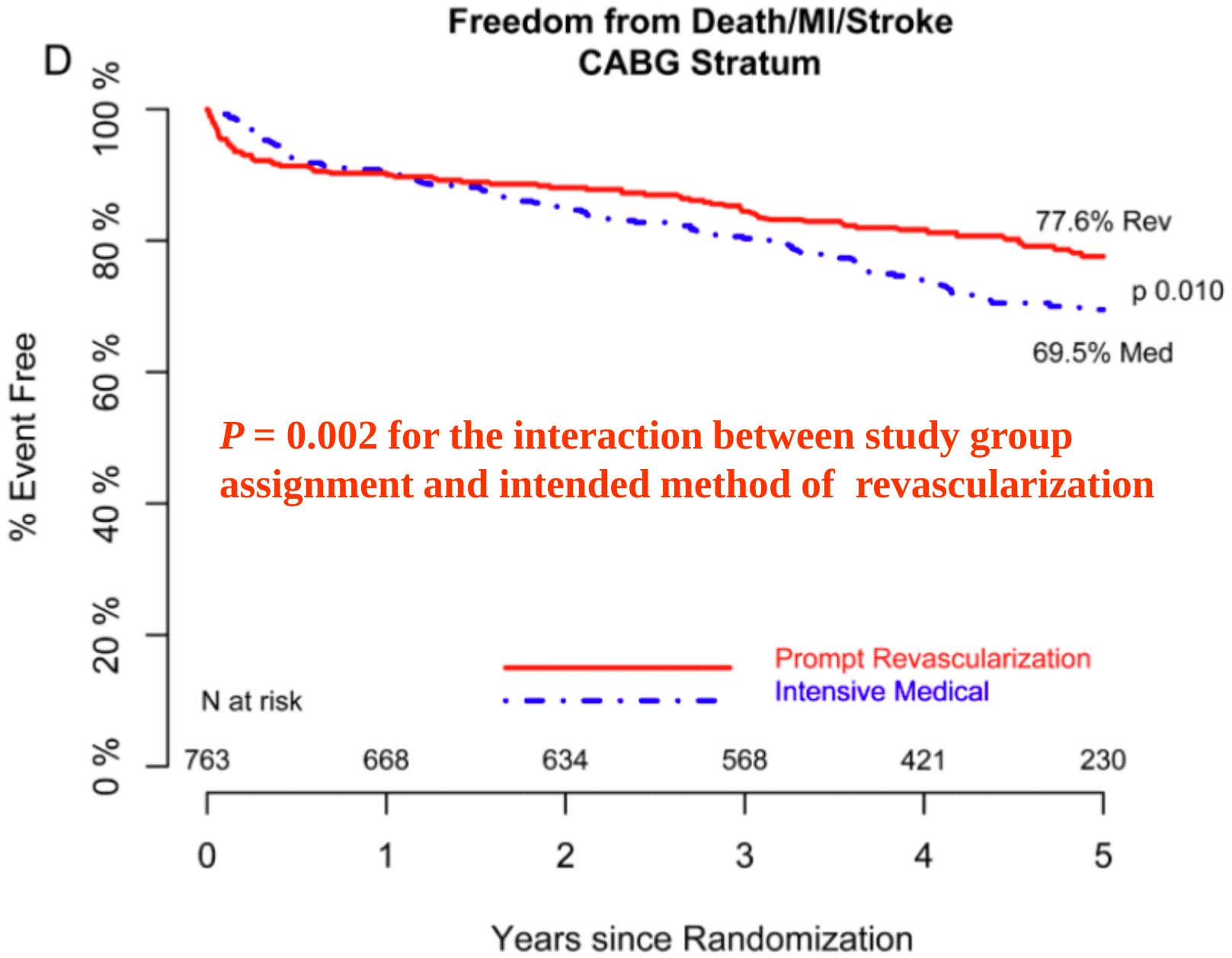
BARI 2D


C
Freedom from Death/MI/Stroke
100 %
80 %
60 %
40 %
20 %
0 %
% Event Free
77.2% Rev
p 0.70
75.9% Med
Prompt Revascularization
Intensive Medical
N at risk
2368
2094
1984
1807
1459
823
0
1
2
3
4
5
Years since Randomization

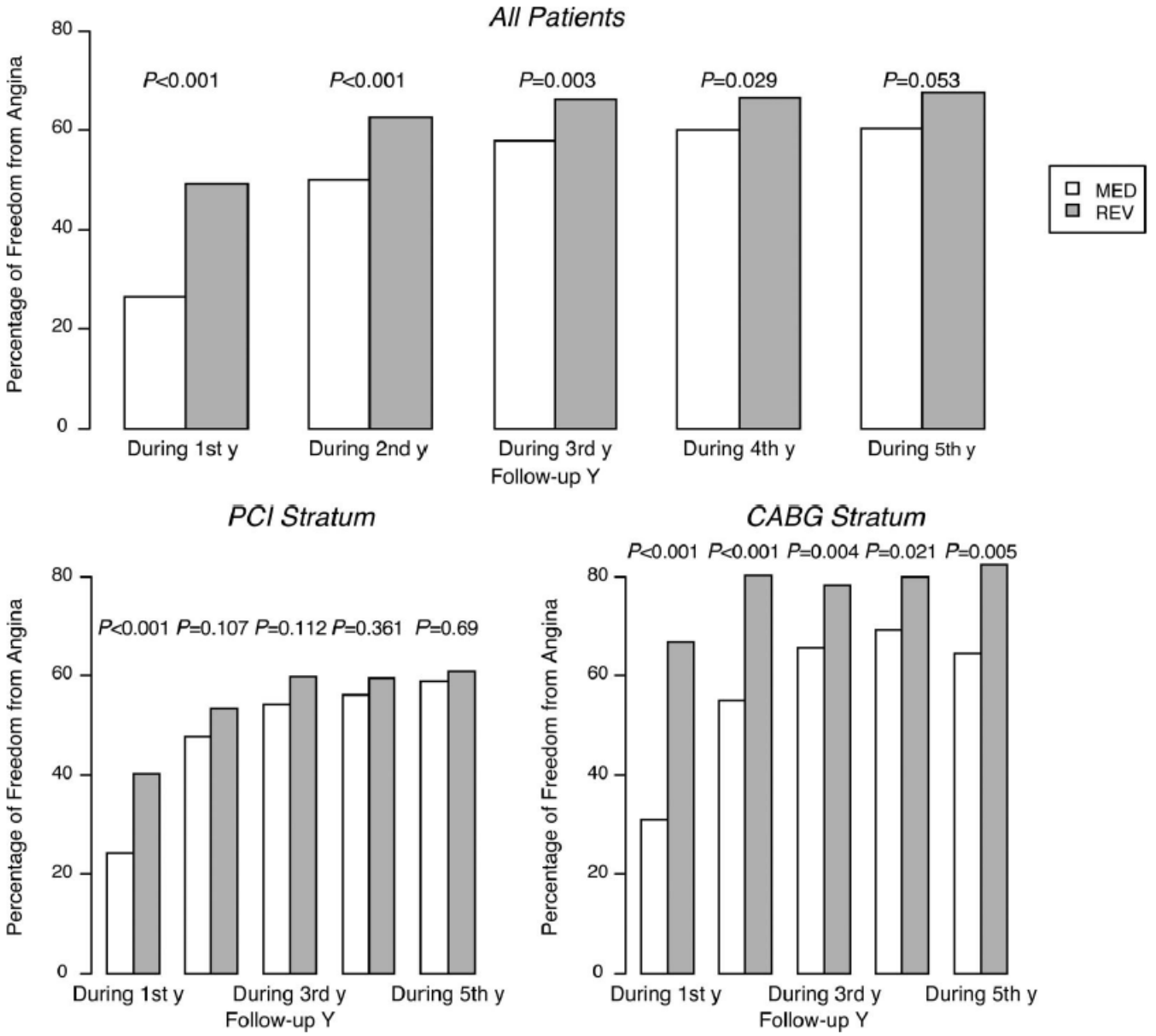
BARI 2D


Freedom from Death/MI/Stroke
PCI Stratum
C
100 %
80 %
60 %
40 %
20 %
0 %
% Event Free
78.9% Med
p 0.15
77.0% Rev
Prompt Revascularization
Intensive Medical
N at risk
1605
1426
1350
1239
1012
593
0
1
2
3
4
5
Years since Randomization

BARI 2D

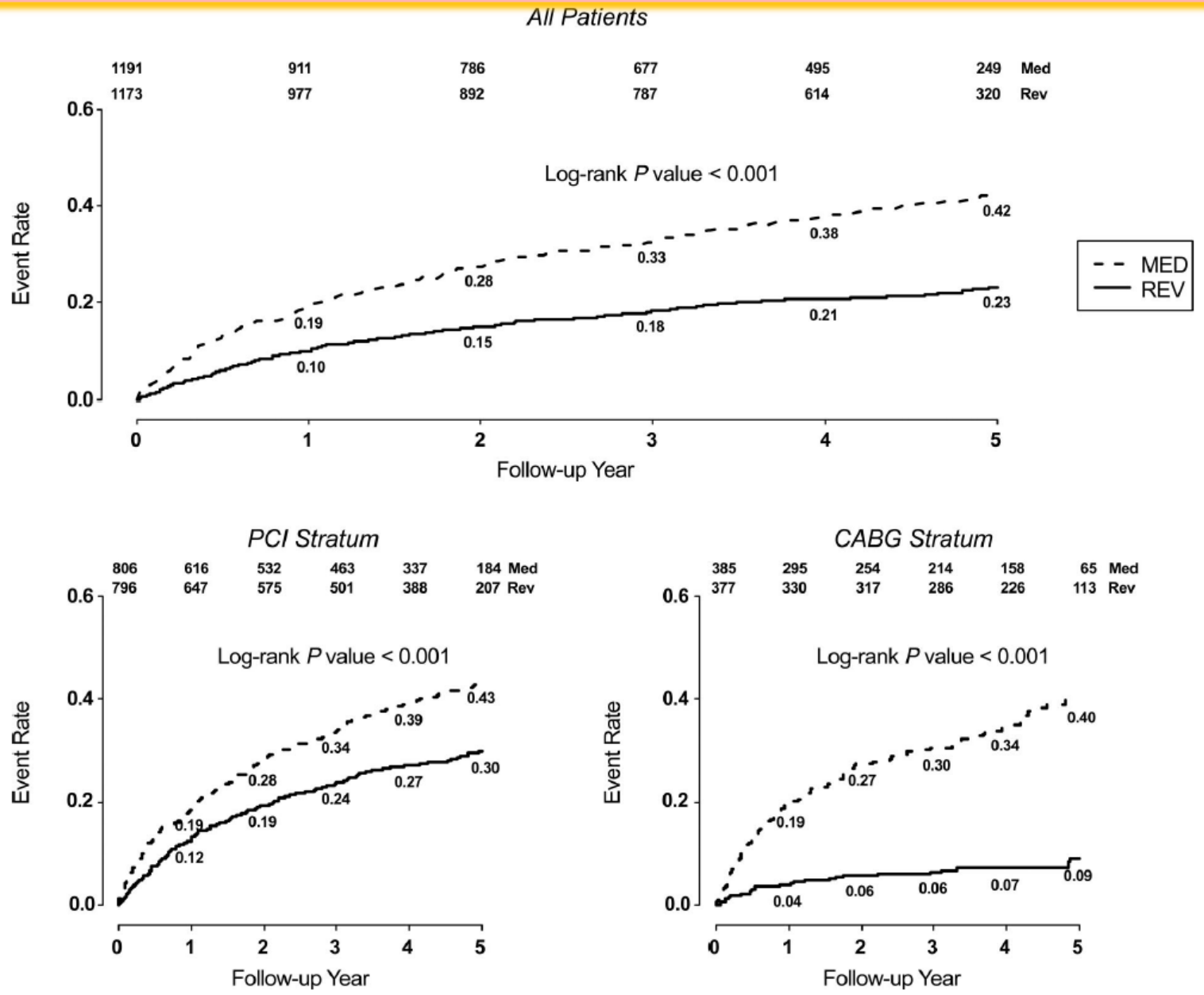

D
Freedom from Death/MI/Stroke
CABG Stratum
% Event Free
100 %
80 %
60 %
40 %
20 %
0 %
77.6% Rev
p 0.010
69.5% Med
P = 0.002 for the interaction between study group assignment and intended method of revascularization
Prompt Revascularization
Intensive Medical
N at risk
763
668
634
568
421
230
0
1
2
3
4
5
Years since Randomization

Freedom from angina for patients with angina at entry



Dagenais, *Circulation.* 2011;123:1492-500

Cumulative rate of the first revascularizations in BARI-2D



Dagenais, *Circulation.* 2011;123:1492-500

Conclusions from BARI-2D

- **The BARI 2D trial demonstrated that for many patients with DM and mild or moderate CAD, optimal medical therapy rather than any intervention is an excellent first-line strategy**

- **Revascularization can be applied later if drug therapy does not adequately control symptoms without incurring an increased risk of MI or cardiac death**

SYNTAX (SYNergy Between PCI With TAXus and Cardiac Surgery)

- The SYNTAX study was the first to compare CABG and the TAXUS Express PES in patients with and without diabetes and with complex left main and/or 3-vessel disease (452 with medically treated DM; 71% were treated for 3-vessel disease and 29% for left main disease)

- In patients with diabetes, the 1-year composite MACCE rate was significantly higher after PES treatment compared with CABG treatment (RR 1.83, 95% CI 1.22–2.73; P=0.003)

- The relative risk of repeat revascularization of PES over CABG was 3.18 in patients with diabetes compared with 1.94 in patients without diabetes

Banning et al. J Am Coll Cardiol 2010;55:1067-75

SYNTAX (SYNergy Between PCI With TAXus and Cardiac Surgery)

- Compared with CABG, mortality was higher after PES use for patients with diabetes with highly complex lesions (4.1% vs. 13.5%; $P = 0.04$).

- Revascularization with PES resulted in higher repeat revascularization for both patients without diabetes (5.7% vs. 11.1%) and patients with diabetes (6.4% vs. 20.3%)

Banning et al. Am Coll Cardiol 2010;55:1067-75

FREEDOM Design

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

Randomized 1:1

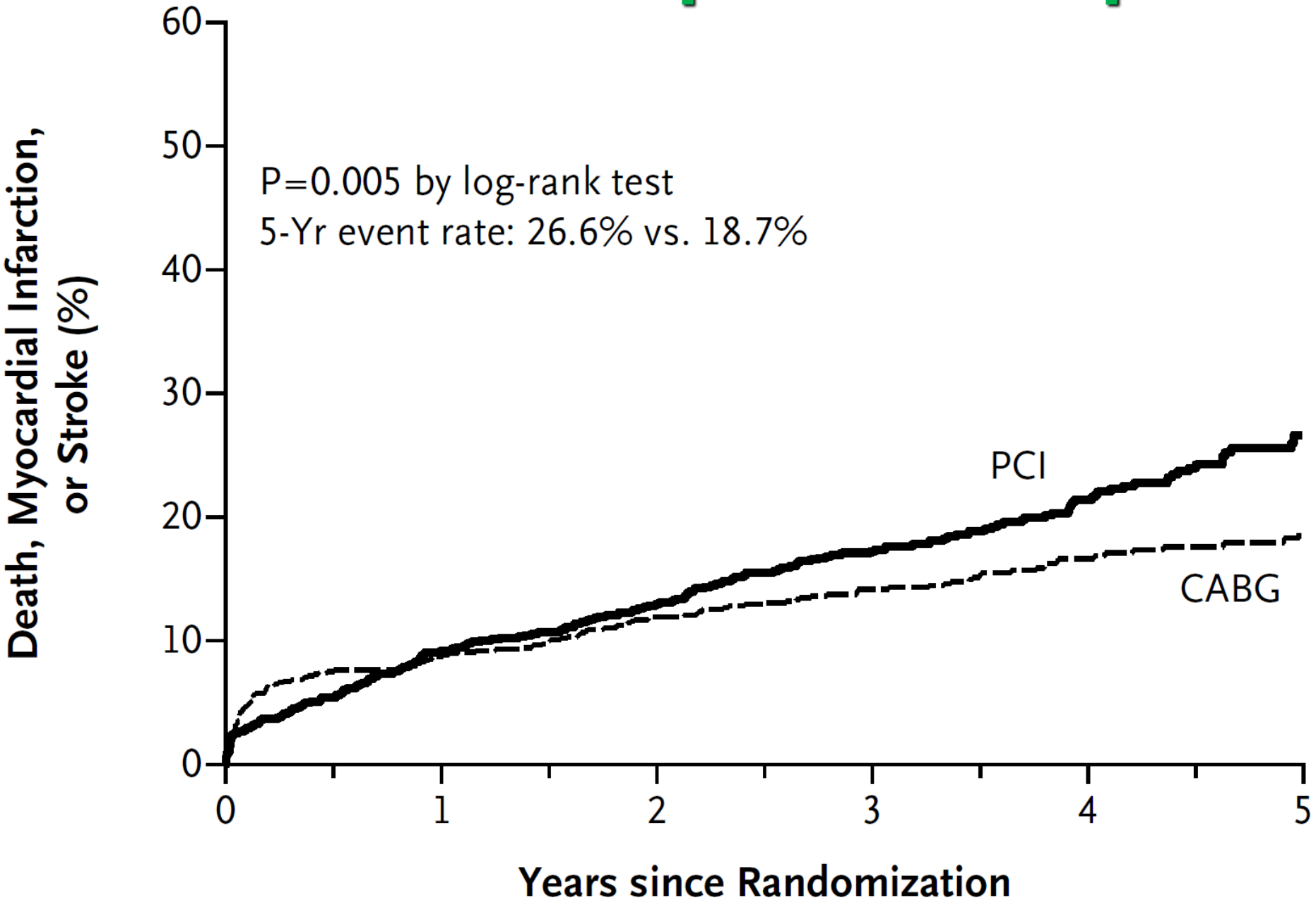
MV-Stenting
With Drug-eluting

CABG
With or Without CPB

All concomitant Meds shown to be beneficial were encouraged

Farkouh et al. N Engl J Med 2012;367:2375-84

FREEDOM - Composite Endpoint



Kaplan–Meier Estimates of Key Outcomes at 2 Years and 5 Years after Randomization

Table 2. Kaplan–Meier Estimates of Key Outcomes at 2 Years and 5 Years after Randomization.

Outcome	2 Years after Randomization		5 Years after Randomization		Patients with Event		P Value*
	PCI	CABG	PCI	CABG	PCI	CABG	
	number (percent)				*number*		
Primary composite†	121 (13.0)	108 (11.9)	200 (26.6)	146 (18.7)	205	147	0.005‡
Death from any cause	62 (6.7)	57 (6.3)	114 (16.3)	83 (10.9)	118	86	0.049
Myocardial infarction	62 (6.7)	42 (4.7)	98 (13.9)	48 (6.0)	99	48	<0.001
Stroke	14 (1.5)	24 (2.7)	20 (2.4)	37 (5.2)	22	37	0.03§
Cardiovascular death	9 (0.9)	12 (1.3)	73 (10.9)	52 (6.8)	75	55	0.12

Farkouh et al. N Engl J Med 2012;367:2375-84

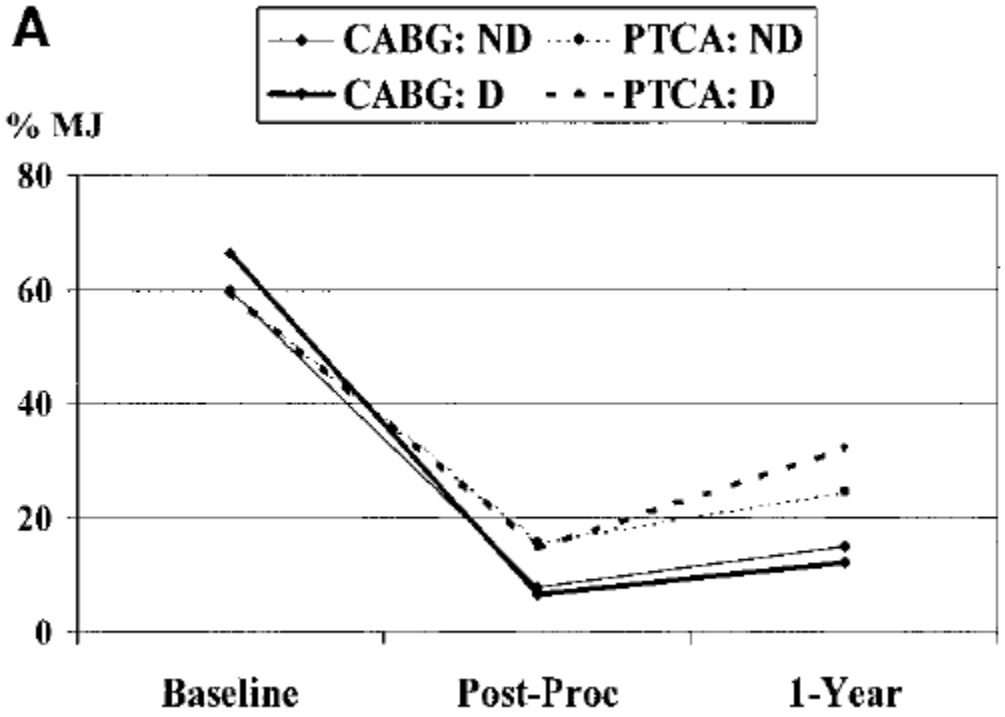
Explaining the mortality benefit of CABG
1. Complete Revascularization

- In the BARI study population, 3.1 grafts were placed per patient undergoing CABG, whereas the mean number of successfully treated lesions in the PTCA group was 2.0

- The amount of jeopardized myocardium decreases initially following revascularization and increases subsequently with target lesion restenosis, graft failure, or the development of new narrowings in native vessels

- The total percentage of jeopardized myocardium can be calculated as the overall percentage of the coronary perfusion territory compromised by stenoses ≥50%

Percentage of jeopardized myocardium by diabetes status and initial revascularization (1-year protocol angiography)



Kip et al. Circulation 2002;105:1914-20

Explaining the mortality benefit of CABG

2. Disease Progression

- The lower rate of nonfatal myocardial infarction with surgical revascularization observed in BARI-2D is consistent with the hypothesis that, bypass grafts to the mid-coronary vessel treat the culprit lesion and prophylaxes against new proximal disease – either progression of proximal narrowing or plaque rupture occurring proximal to a patent graft insertion

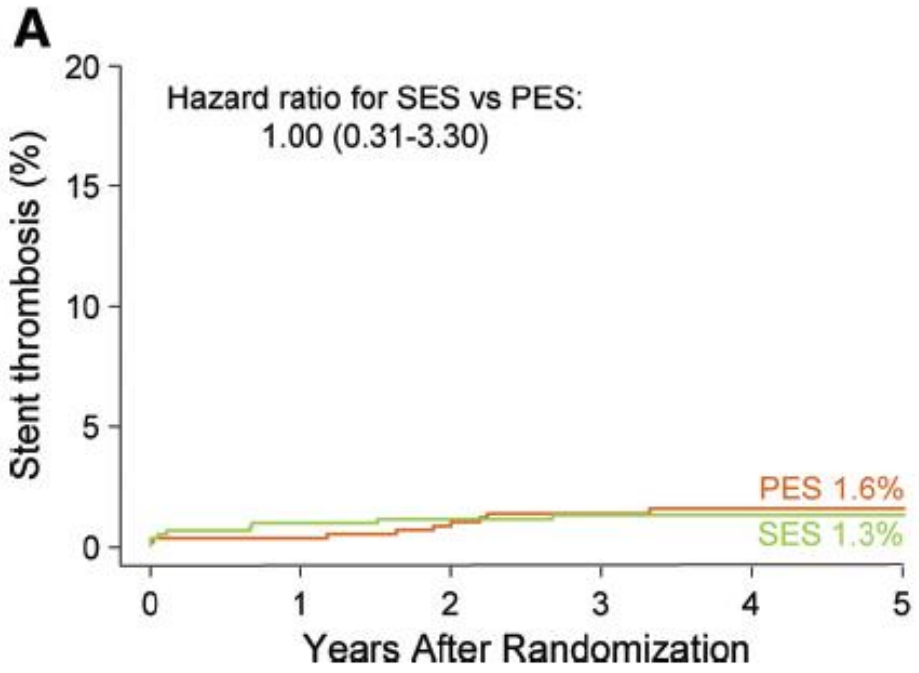
- Proximal coronary arterial bare metal and drug-eluting, cannot protect against new disease – plaque rupture or stable occlusive lesions

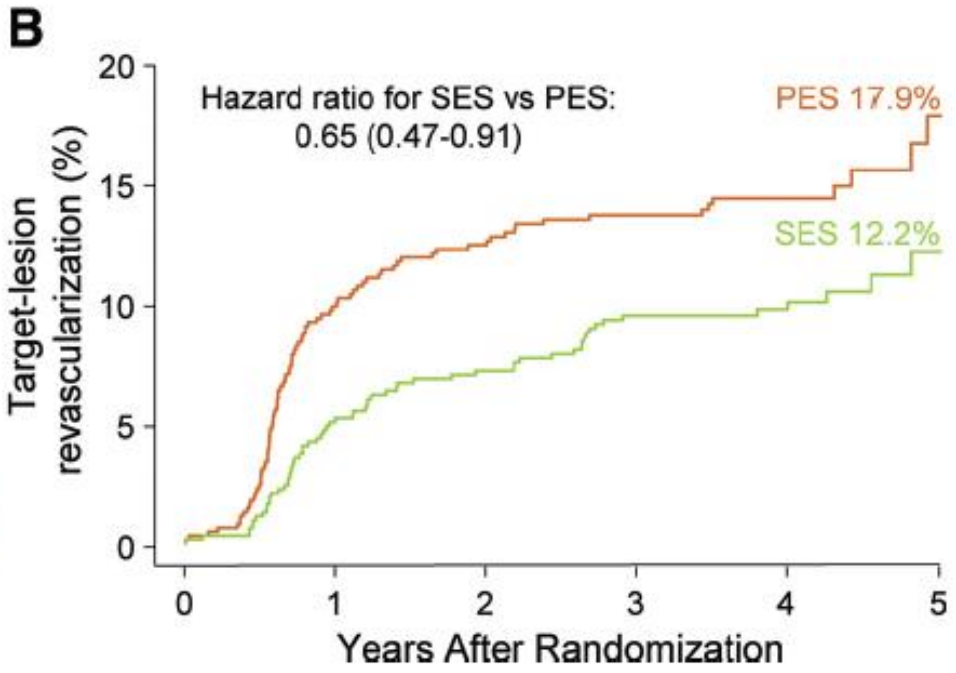
PCI vs. CABG – Summary

- The effectiveness of PCI for treated patients with diabetes with asymptomatic ischemia or CCS class I or II angina who have 2- or 3-vessel CAD with significant proximal LAD who are otherwise eligible for CABG is not well established

- CABG is superior in terms of survival, recurrent infarctions and freedom from reintervention for patients with treated DM with moderate to severe symptoms and multivessel CAD in the setting of significant proximal left anterior descending artery involvement, and diabetic patients with a significant LM stenosis

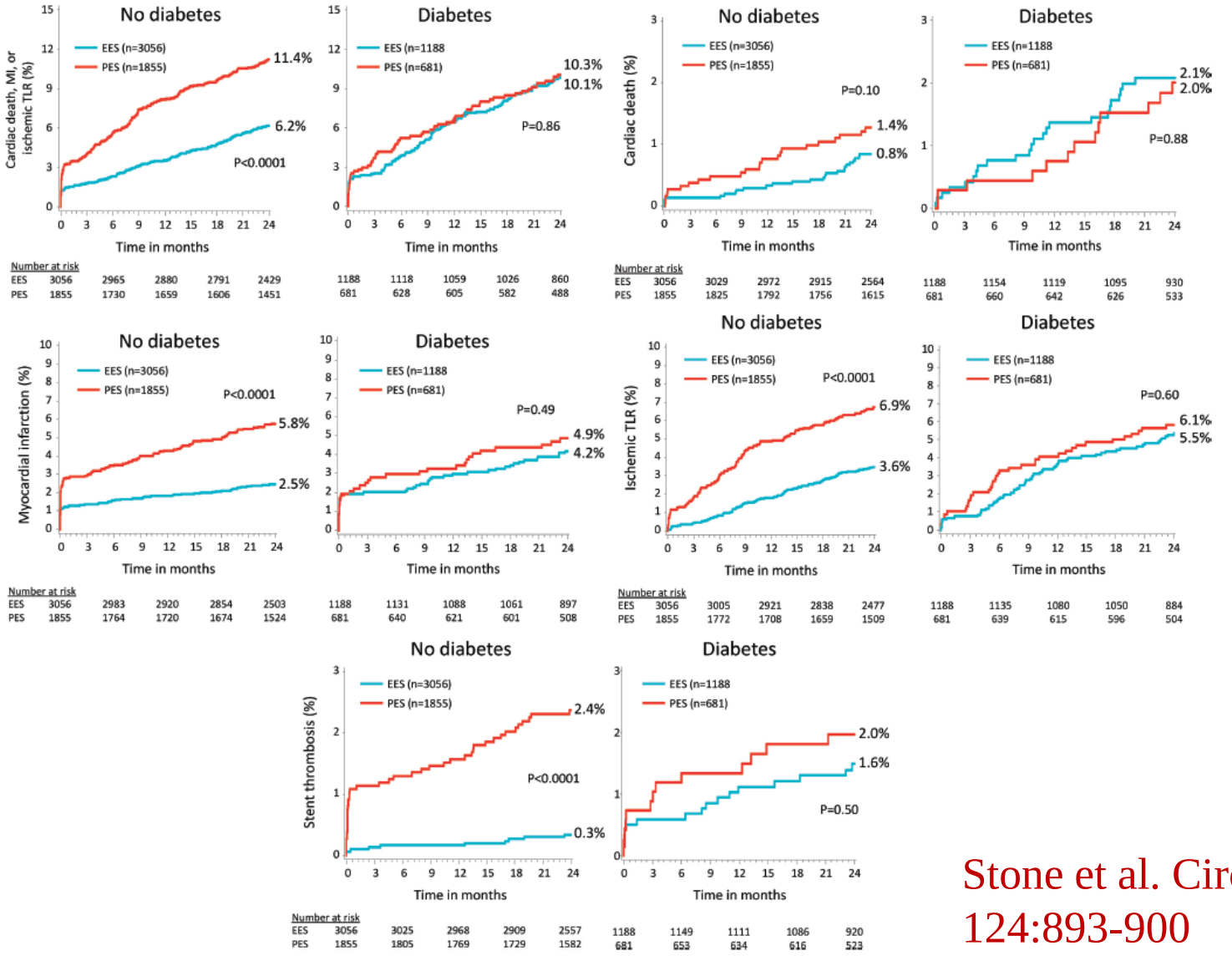
SES vs. PES: Pooling individual-patient data of 6 randomized trials specifically designed for diabetic patients





Kufner at al. *Am Heart J* 2011;162:740-747

Differential Clinical Responses to Everolimus-Eluting and Paclitaxel-Eluting Stents in Patients With and Without Diabetes Mellitus



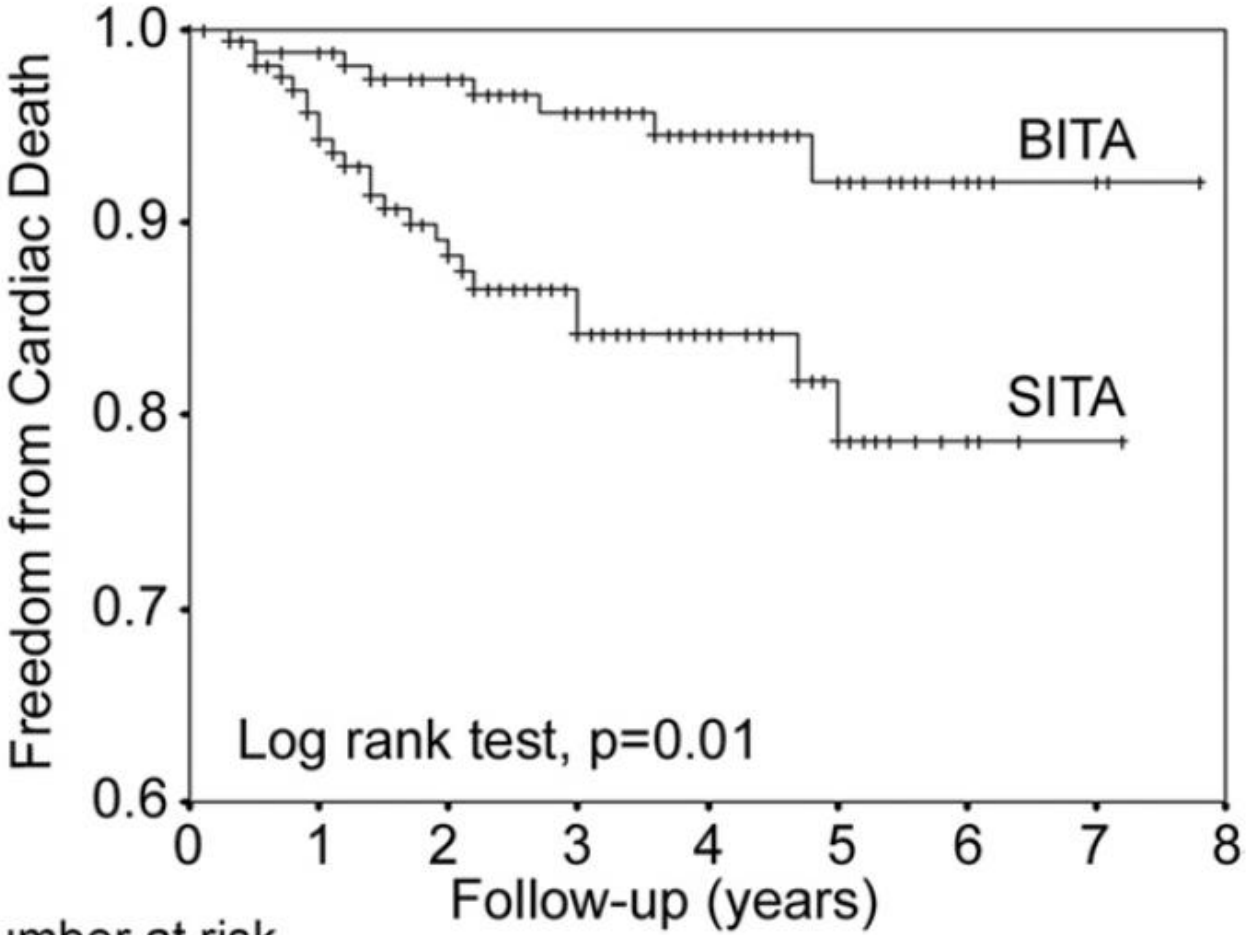
Stone et al. Circulation 2011; 124:893-900

Graft selection and patency

- DM does not appear to adversely affect patency of internal thoracic artery (ITA) grafts
- Nonrandomized analyses indicate that bilateral internal thoracic artery (BITA) grafting appears to be particularly important in the diabetic population
- However, the use of BITA results in greater sternal wound complications in patients with DM (especially insulin-treated)
- Harvesting skeletonized ITA may reduce the risk of sternal wound complications associated with BITA by minimizing the risk of devascularization of the sternum (as compared with removal with an attached muscle pedicle)

Schwartz et al. Circulation 2002;106:2652-8
Pevni et al. Circulation 2008;118:705-12

BITA vs. SITA in Patients with Diabetes



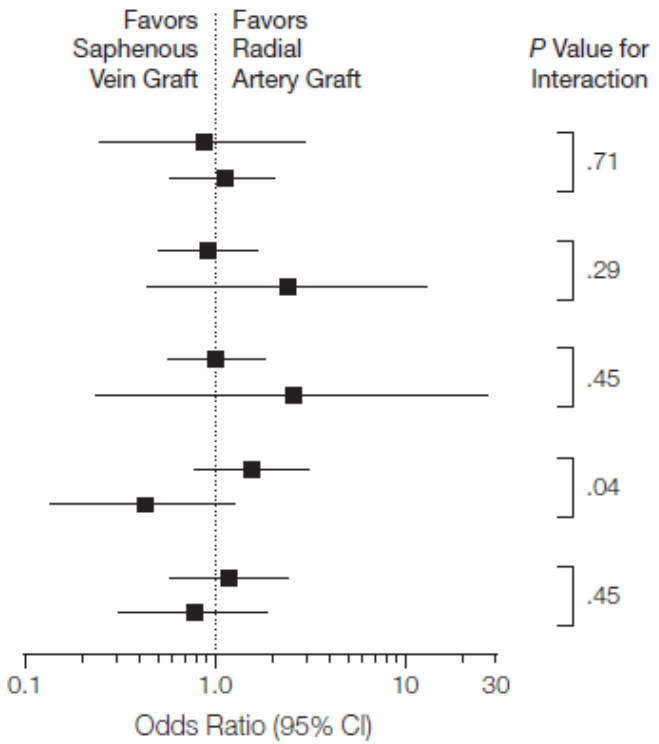
Number at risk

SITA	170	148	110	75	47	25	9	2
BITA	170	159	138	103	68	38	12	2

Kinoshita et al. *Ann Thorac Surg* 2010;90:1173-1179

Radial Artery Grafts vs Saphenous Vein Grafts: Patency at 1 Year After Surgery

	Saphenous Vein Grafts		Radial Artery Grafts		
	No. of Patent Grafts	Total No. of Grafts	No. of Patent Grafts	Total No. of Grafts	*P* Value for Interaction
Vessel to be bypassed					
LAD	35	41	30	36	.71
Other	204	228	208	230	
On/off pump					
On pump	214	237	221	247	.29
Off pump	25	32	17	19	
Target vessel size					
≤2 mm	216	243	217	244	.45
>2 mm	20	23	17	18	
Diabetes					
No	139	164	138	154	.04
Yes	99	104	100	112	
Smoking history					
Current smoker	172	190	192	209	.45
Ex-smoker or never	66	78	46	57	



- Radial artery (RA) conduits obtained from patients with DM has greater tendency to spasm compared with RAs from patients without DM, and exhibit impaired endothelial function

Goldman et al. JAMA 2011;305:167-74

THANK YOU FOR YOUR ATTENTION !