TCTAP
Seoul 2013

CABG in Diabetic Patients: No Doubt, Surgery is Clearly the Winner !

David P Taggart MD PhD FRCS
Professor of Cardiovascular Surgery, University of Oxford

Conflicts of Interest:
(i) Clinical: Cardiac Surgeon
(ii) Commercial: Consultant to Medtronic, Abbott, AstraZeneca, Novadaq, VGS, Cardioguard

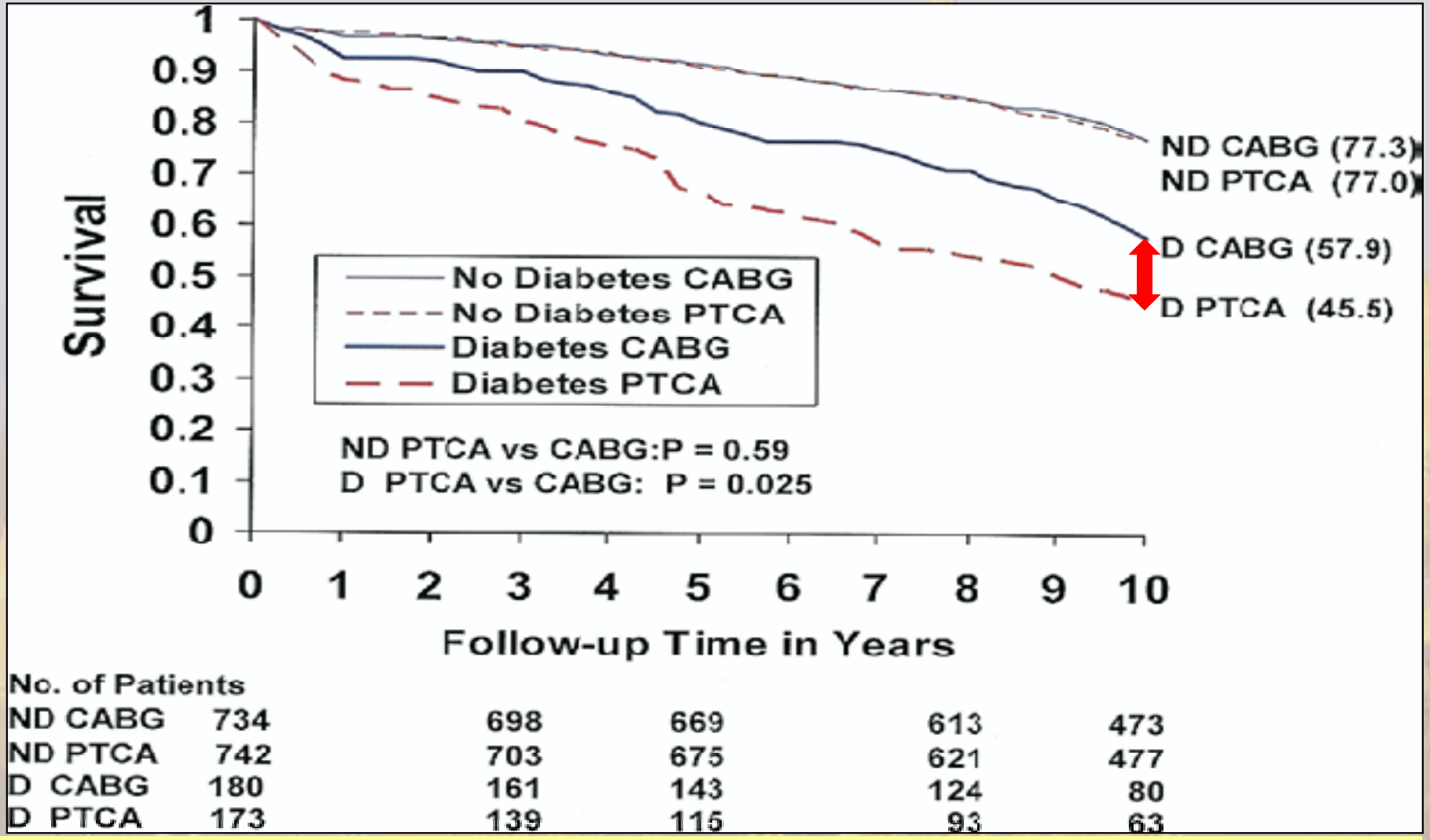
Diabetes Mellitus (DM): A Growing Epidemic

- 24 million DM in USA, > 170 million worldwide
- WHO estimate DM will double by 2030
- 4-6 fold increase in adverse cardiovascular events
- DM present in >25% CABG and >30% ACS patients
- In DM 75% of deaths, 80% hospital admissions are CVS

The Final 10-Year Follow-Up: Results From the BARI Randomized Trial

The BARI Investigators* [J Am Coll Cardiol 2007;49:1600–6]

- 1829 patients: (12% of potentially eligible population)
- 353 diabetic patients: (19% of All BARI patients)
- Low Severity CAD: 41% 3vCAD; 31% proximal LAD; normal LV function



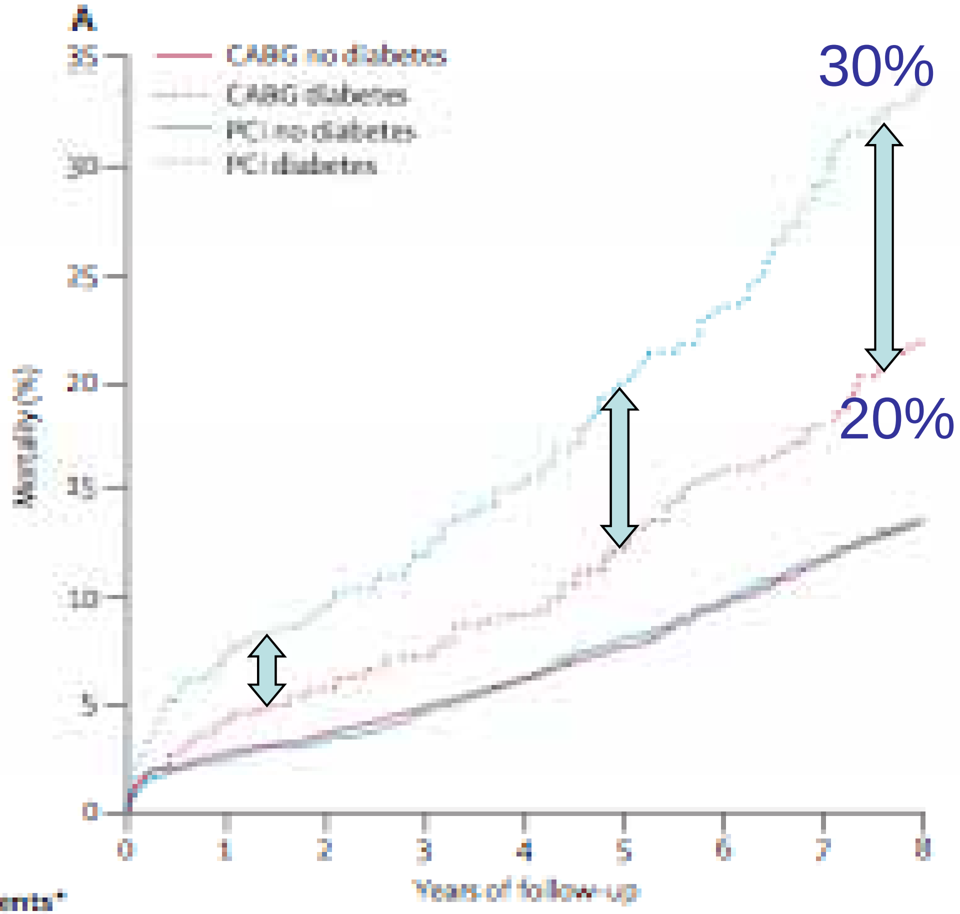
Increase in repeat revasc x4 in PCI (58% of PCI received CABG)
On ITT analyses this 'reduces' the real survival benefit of CABG

Coronary artery bypass surgery compared with percutaneous coronary interventions for multivessel disease: a collaborative analysis of individual patient data from ten randomised trials **Lancet 2009**

24 Authors: NO Surgeons!!!

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

- OVERALL
- 7812 patients
- Median follow up 6 years
- 65%: 1 or 2 VD; all normal LV
- HR CABG: 0.91: p=0.12



Number of patients*	0	1	2	3	4	5	6	7	8
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

- 1233 patients with DM
- HR for CABG vs PCI in DM 0.70; p=0.01
- Survival benefit of CABG increases with time

ORIGINAL ARTICLE

Long-Term Outcomes of Coronary-Artery Bypass Grafting versus Stent Implantation

Edward L. Hannan, Ph.D., Michael J. Racz, Ph.D., Gary Walford, M.D., Robert H. Jones, M.D., Thomas J. Ryan, M.D., Edward Bennett, M.D., Alfred T. Culliford, M.D., O. Wayne Isom, M.D., Jeffrey P. Gold, M.D., and Eric A. Rose, M.D.

NEJM 2005

HR for DEATH with DM at Median 3 Years Follow-up: CABG vs stents

		DM (18029)		
	LAD disease	PCI	CABG	HR
2VD (7780)	None	1352	423	0.69 (0.46-1.03)
	Non proximal	1485	610	0.59 (0.40-0.87)
	Proximal	1438	2472	0.71 (0.57-0.88)
3VD (10249)	Non proximal	666	1824	0.65 (0.49-0.85)
	Proximal	644	7115	0.69 (0.55-0.86)

Routine clinical practice in DM: PCI vs CABG

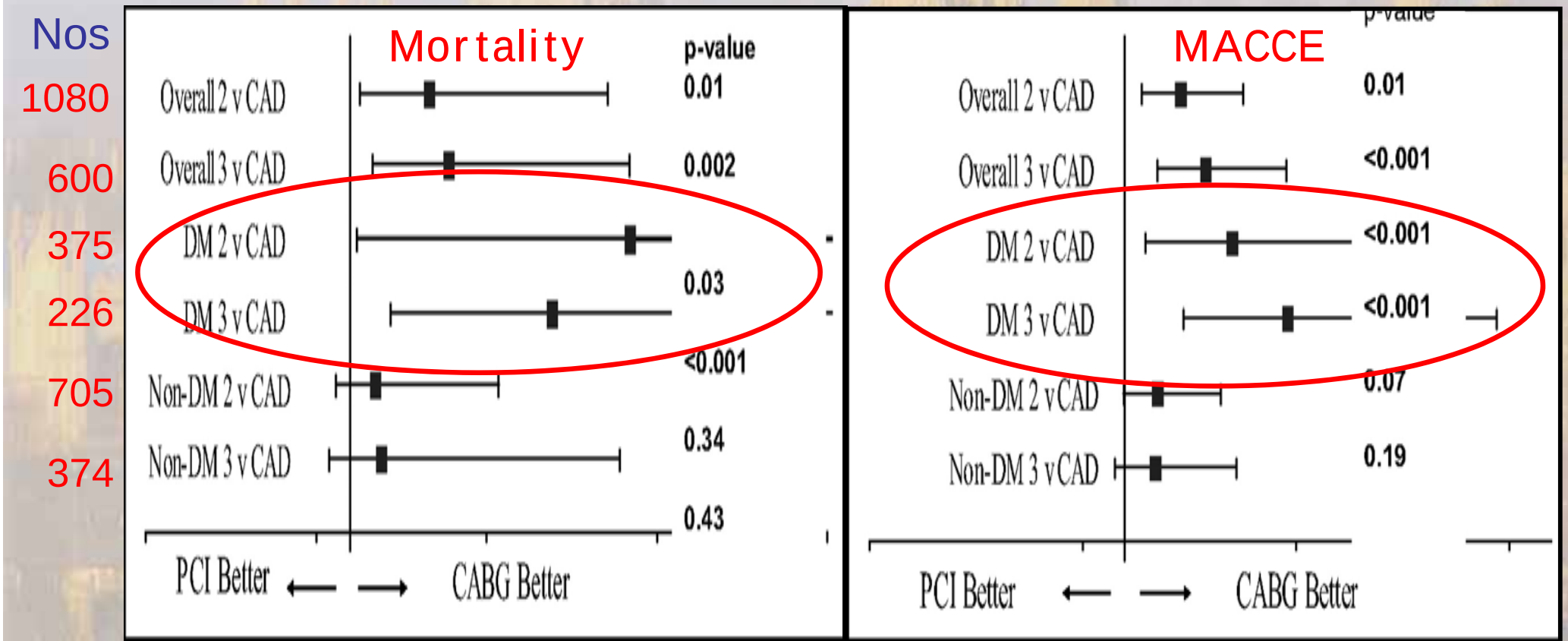
Survival of Patients With Diabetes and Multivessel Coronary Artery Disease After Surgical or Percutaneous Coronary Revascularization: Results of a Large Regional Prospective Study

Nathaniel W. Niles, MD,* Paul D. McGrath, MD, FACC,† David Malenka, MD, FACC,*

JACC 2001

- **2766 risk matched DIABETICS: PCI ↑ 5 yr mortality x 2 – 4**

Javaid et al. [Circ 2007] 1680 patients DES vs CABG 1 year follow up



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JANUARY 24, 2008 VOL. 358 NO. 4

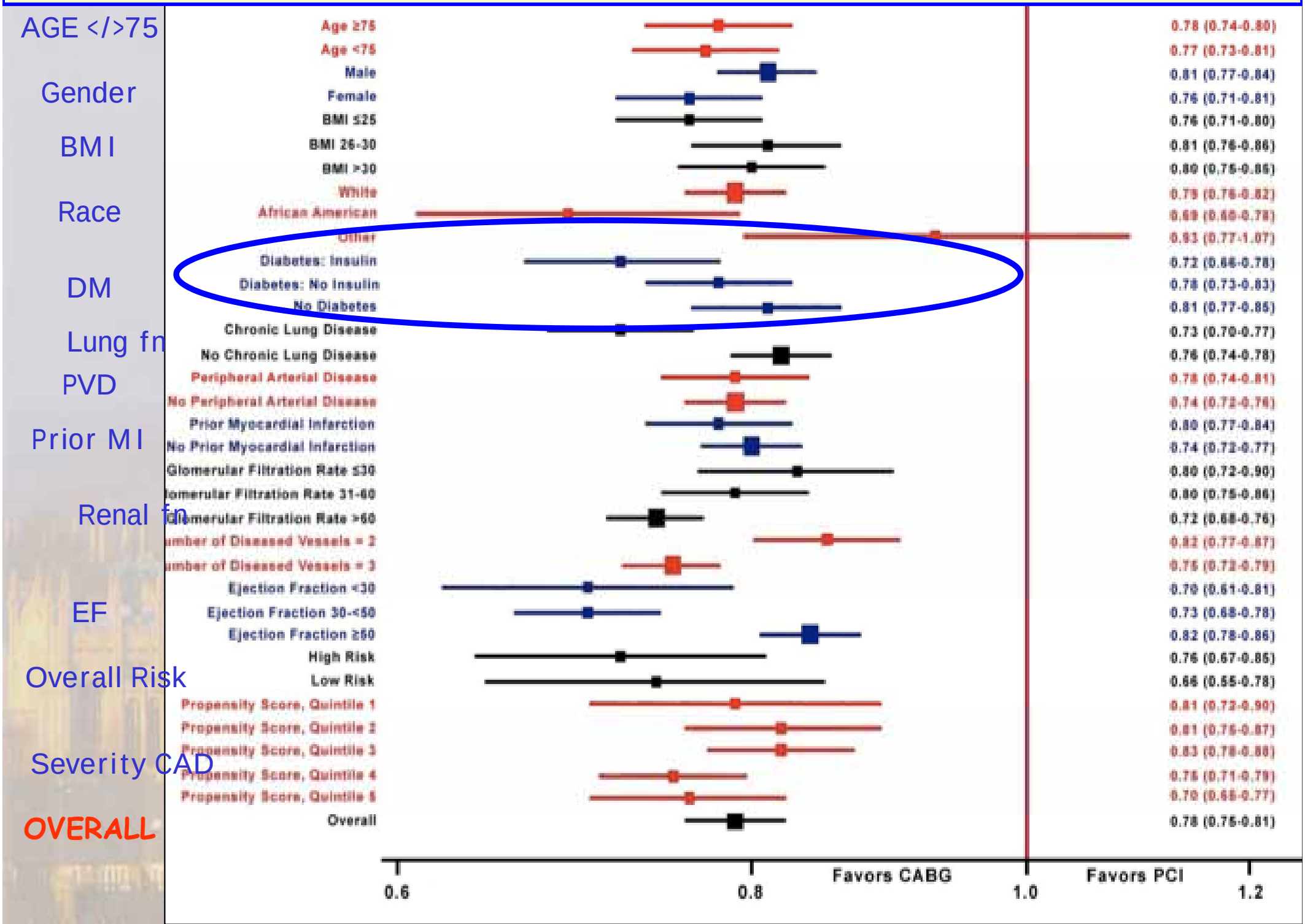
Drug-Eluting Stents vs. Coronary-Artery Bypass Grafting in Multivessel Coronary Disease

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.

Table 3. Hazard Ratios for Death and for Death or Myocardial Infarction after CABG and after Treatment with a Drug-Eluting Stent, According to Selected Subgroups of Patients.*

Variable	No. of Patients	Mean Follow-up	Death			Death or Myocardial Infarction		
			No. of Events	Adjusted Hazard Ratio (95% CI)†	P Value	No. of Events	Adjusted Hazard Ratio (95% CI)†	P Value
		mo						
Diabetes								
CABG	2844	18.9	242	0.97 (0.77–1.20)	0.75	304	0.84 (0.69–1.01)	0.07
Stent	3256	18.5	224	Reference		343	Reference	
Ejection fraction <40%								
CABG	1614	18.6	181	0.77 (0.59–1.00)	0.05	213	0.67 (0.53–0.84)	<0.001
Stent	1059	17.8	144	Reference		183	Reference	
Age ≥80 yr								
CABG	760	18.0	107	0.74 (0.55–1.00)	0.05	125	0.74 (0.56–0.96)	0.03
Stent	1266	17.8	175	Reference		216	Reference	

189,793 PPM patients from ACC (PCI) and STS (CABG) databases: NEJM 2012



BARI 2D: [NEJM 2009]

(i) optimal medical therapy vs prompt revascularization (prespecified to PCI/CABG)
(ii) Insulin vs oral hypoglycaemics

2368 patients (2001-05)	PCI (1605)	CABG (763)
Age (sd) [% male]	62 (9); [68%]	63 (8); [76%]
DM (years); [% insulin]	10(9); [31%]	11(8); [22%]
Unstable; prior revasc	11% 29%	7%; 13%
3 vessel disease	20%	52%
Significant LAD disease	10%	19%
Ejection Fraction	57 (11)	57 (11)

	Medical	PCI	Medical	CABG
	807	798	385	378
5 years Death	11.9%	12.8%	16.9%	14%
5 years MI	10.2%	11.3%	14.6%	7.4%*
5 years Stroke	2.9%	2.9%	2.6%	1.9%
5 years Death,MI,Stroke	20.8%	23.4%	29.9%	20.9%*

By 5 years 42% of medical group required revascularization (ITT analyses !)

- Overall Low severity CAD (NO Registry Data: what % of all DM enrolled ?)
- PCI had no benefit over medical treatment but CABG (prespecified) did
- High risk of subsequent revascularization in medical group (42%)

Randomized Comparison of PCI with CABG in Diabetic Patients: 1 Year Results of the CARDia Trial. JACC 2010

- 510 of 600 patients recruited over 5 years: 'early termination due to slow recruitment'

	PCI (256)	CABG (254)
Age (% male)	64 (71%)	64 (78%)
urgent	22%	24%
Insulin dependent	31% (10 years)	31% (10 years)
3vd	65%	58%
EF	59%	60%

Death	3.2%	3.3%
MI	8.4%	5.7% (Δ -32%)
CVA	0.4%	2.5%
1 year death/MI/CVA	11.6%	10.2%
Revascularization	12%	2%
Composite	18%	11%

- No Registry Data (what % of diabetic patients enrolled ?)
  - Approx 26000 DM had CABG in same period in UK ie <0.5% enrolled

Treatment of Complex Coronary Artery Disease in Patients with Diabetes: 5-Year Results Comparing Outcomes of Bypass Surgery and Percutaneous Coronary Intervention in the SYNTAX Trial

EJCTS 2013

A. Pieter Kappetein[1], Stuart J. Head[1], Marie-Claude Morice[2], Adrian P. Banning[3], Patrick W. Serruys[4], Friedrich-Wilhelm Mohr[5], Keith D. Dawkins[6], Michael J. Mack[7], on behalf of the SYNTAX Investigators.

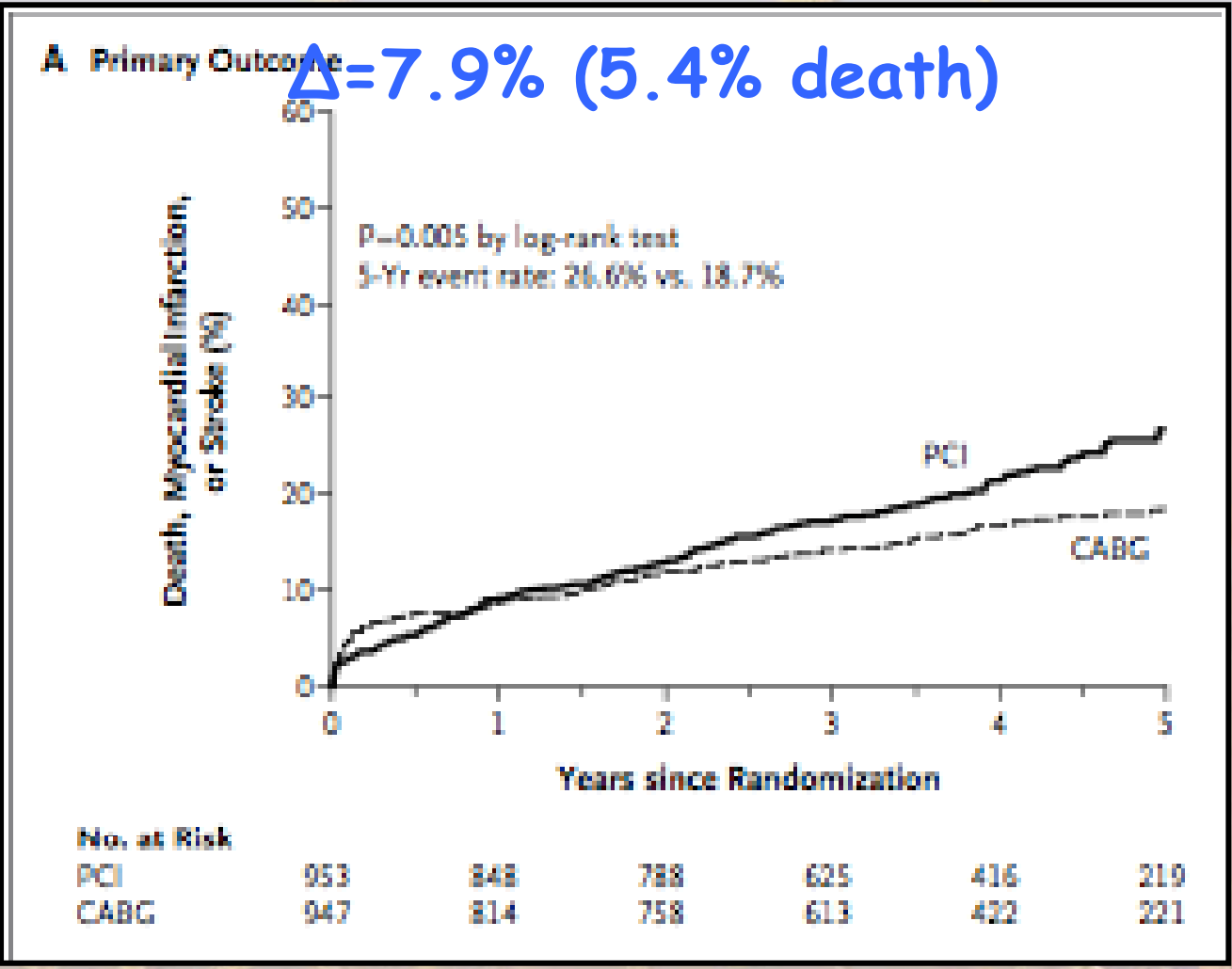
	DM=452		
	CABG=221	PCI=231	
MACCE %	29	47	<0.001
All cause death/stroke/MI %	19	24	0.26
All death %	13	20	0.06
Cardiac death %	6.5	13	0.03
Stroke %	4.7	3	0.34
MI %	5.4	9	0.20
Repeat Revascularization %	15	35	<0.001
Repeat PCI %	13	29	<0.001
Repeat CABG %	1.9	8.7	0.004
Graft Occlusion/stent thrombosis %	4.3	5.3	0.61

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Strategies for Multivessel Revascularization in Patients with Diabetes

Δ=7.9% (5.4% death)



Fundamental Question

WHY DOES CABG HAVE SUCH A SURVIVAL BENEFIT OVER PCI ?

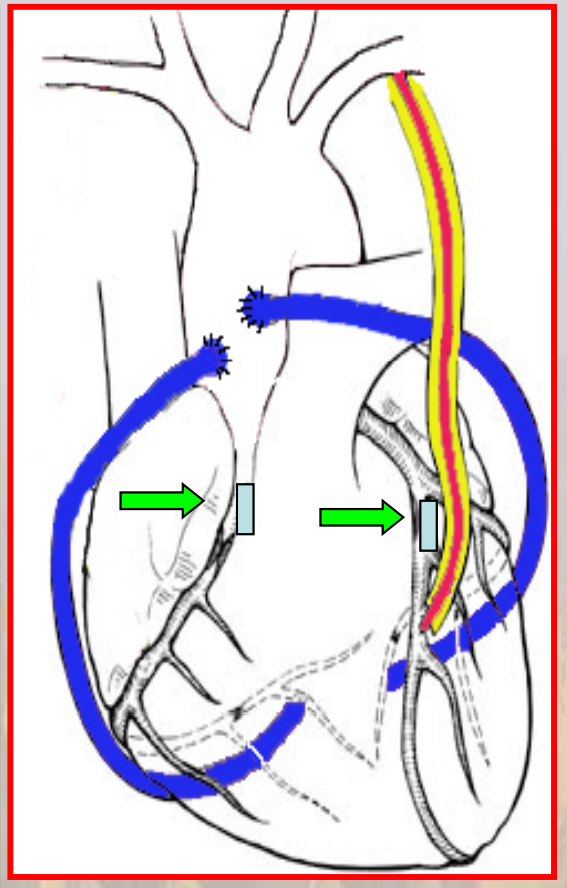
Anatomically, atheroma is mainly located in the proximal coronary arteries

During CABG placing bypass grafts to the **MID CORONARY VESSEL** has **TWO** effects

(i) Complexity of 'CULPRIT' lesion irrelevant

(ii) over the long term, CABG offers prophylaxis against FUTURE 'culprit' lesions by protecting whole zones of vulnerable proximal myocardium in diffusely unstable coronary endothelium

- In contrast, PCI with stents ( ) only treats **'SUITABLE'** localised proximal 'culprit' lesions but has **NO PROPHYLACTIC BENEFIT** against new disease (proximal to, within or distal to the stent) which nullifies the benefit of the stent



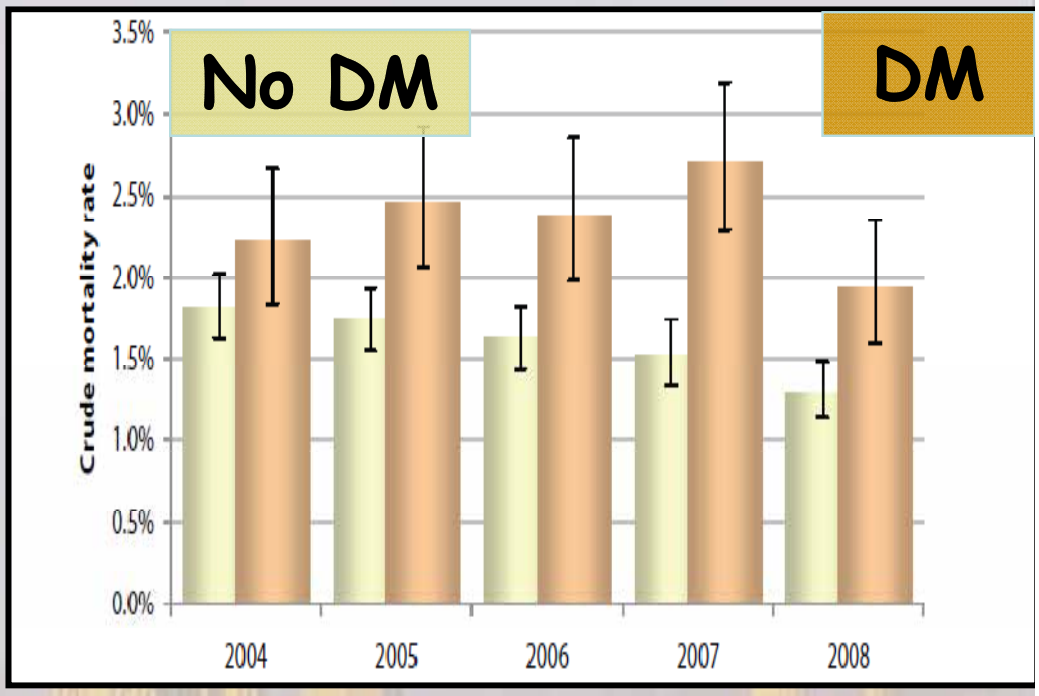
2. PCI means incomplete revascularization (Hannan Circ 2006)

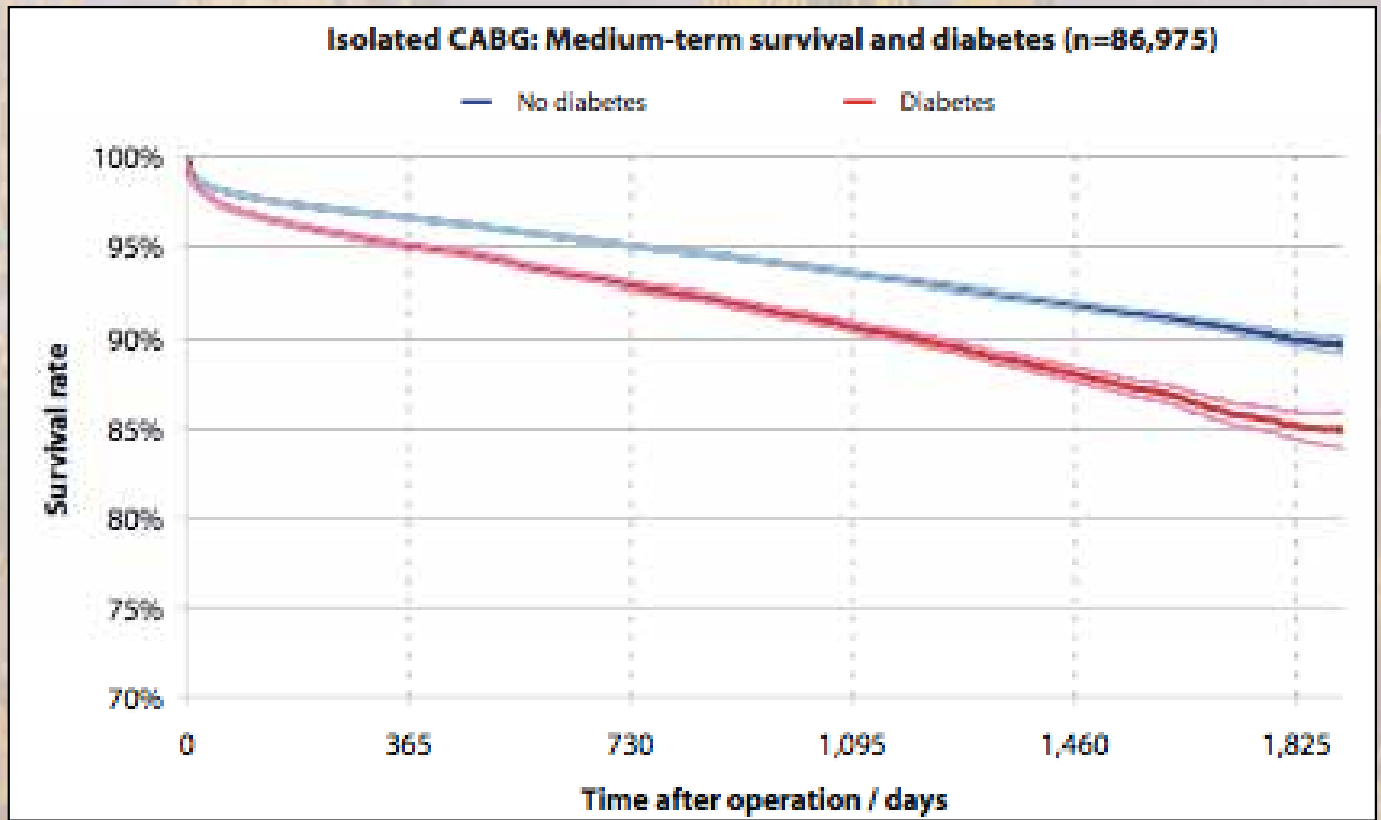
- Of 22,000 PCI 69% had incomplete revascularization
- >2 vessels (+/- CTO) HR for mortality 1.4 (95% CI = 1.1-1.7)

PCI will 'never' match the results of CABG for LM/MVD (POBA;BMS;DES)

6th UK and Ireland SCTS Database (2009)

		MORTALITY	
	5 yr: 2004-08	All	Elective
Total	114300	1.8%	1.1%
NonDM	88280 (77%)	1.6%	1.0%
DM	26020 (23%)	2.6%	1.6%





Summary and Conclusions: CABG vs PCI in DM

- All evidence from RCTs and Propensity Matched Registries consistently confirm that CABG vs PCI results in
- ✓ better survival (by at least 5% at 5 years)
- ✓ reduced MI (by at least 50% at 5 years)
- ✓ reduced repeat revascularization (by at least 50% at 5 years)

Summary and Conclusions

- All evidence from RCTs and Propensity Matched Registries confirm that CABG results in better survival and reduced MI and repeat revasc vs PCI
- Strongest RCT evidence from Hlatky collaborative analyses
  - Significant survival benefit for DM with CABG at 6 years (HR 0.7)
- Propensity Matched Registry Data (reflecting real clinical practice) consistently show survival benefit of CABG over PCI in DM
- BARI 2D (low severity of CAD)
  - No benefit of PCI vs OMT
  - CABG reduced risk of MI (and also reduced absolute mortality by3%)
- SYNTAX trial showed that at 5 years DM patients have better survival, reduced MI and repeat revasc with CABG vs PCI
- FREEDOM trial confirms 5% survival benefit of CABG
- In ALL 78,000 elective CABG patients in UK (2004-08) 1.1% mortality
- Survival benefit of CABG vs stents accrues with time

The NEW ENGLAND JOURNAL of MEDICINE

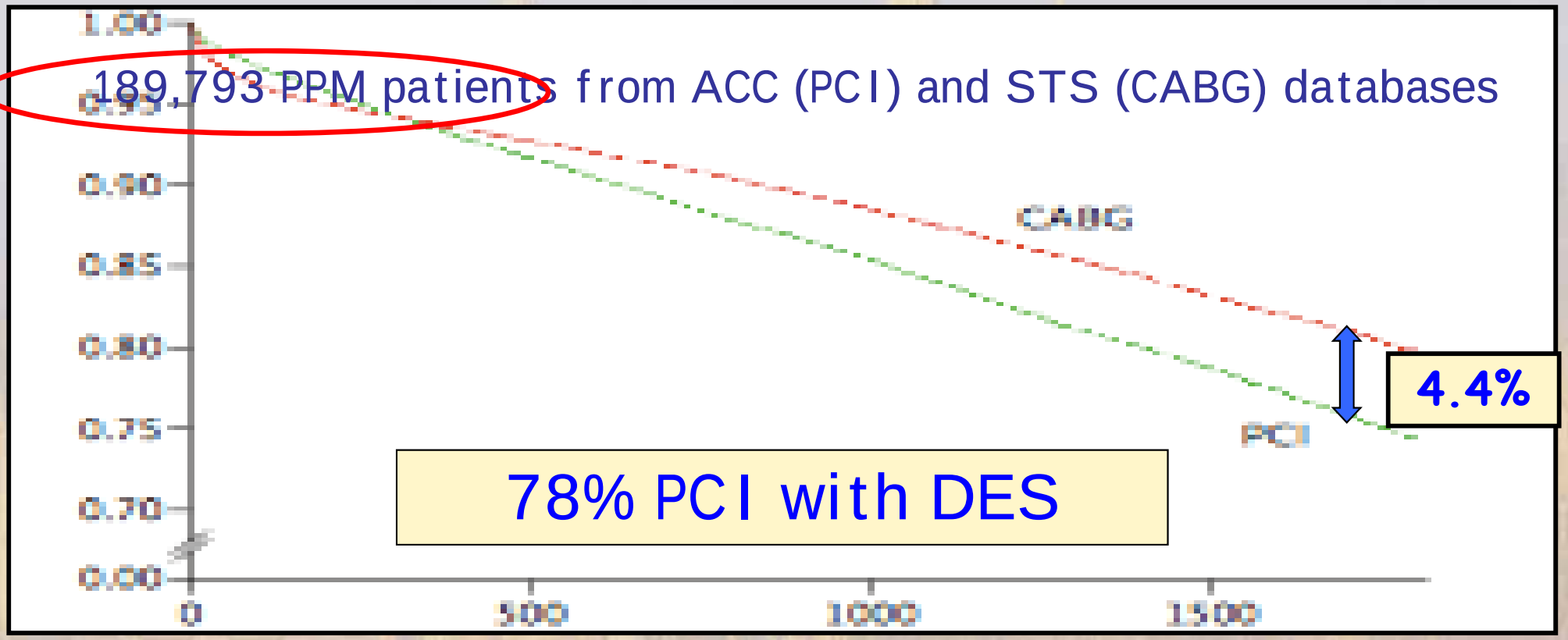
NEJM 2012

ORIGINAL ARTICLE

Comparative Effectiveness of Revascularization Strategies

William S. Weintraub, M.D., Maria V. Grau-Sepulveda, M.D., M.P.H.,

189,793 PPM patients from ACC (PCI) and STS (CABG) databases



78% PCI with DES

- ✓At 4 years CABG increases survival by 4.4%: HR 0.79 (0.76-0.82)
- ✓Survival benefit of CABG increases with time

THE SYNTAX TRIAL

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MARCH 5, 2009 VOL. 360 NO. 10

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

Patrick W. Serruys, M.D., Ph.D., Marie-Claude Morice, M.D., A. Pieter Kappetein, M.D., Ph.D.,

Landmark trial (of 5 year outcomes of PCI vs CABG)
'All comer' trial (vs highly select patients in all previous RCTs)Nested Parallel Registry (35% of patients straight to CABG !!)

Comparison of coronary bypass surgery with drug-eluting stenting for the treatment of left main and/or three-vessel disease: 3-year follow-up of the SYNTAX trial

Arie Pieter Kappetein[1*], Ted E. Feldman[2], Michael J. Mack[3], Marie-Claude Morice[4],

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JUNE 11, 2009 VOL. 360 NO. 24

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

The BARI 2D Study Group*

The NEW ENGLAND JOURNAL of MEDICINE

EDITORIALS

Diabetes with Coronary Disease — A Moving Target amid Evolving Therapies?

William E. Boden, M.D., and David P. Taggart, M.D., Ph.D.

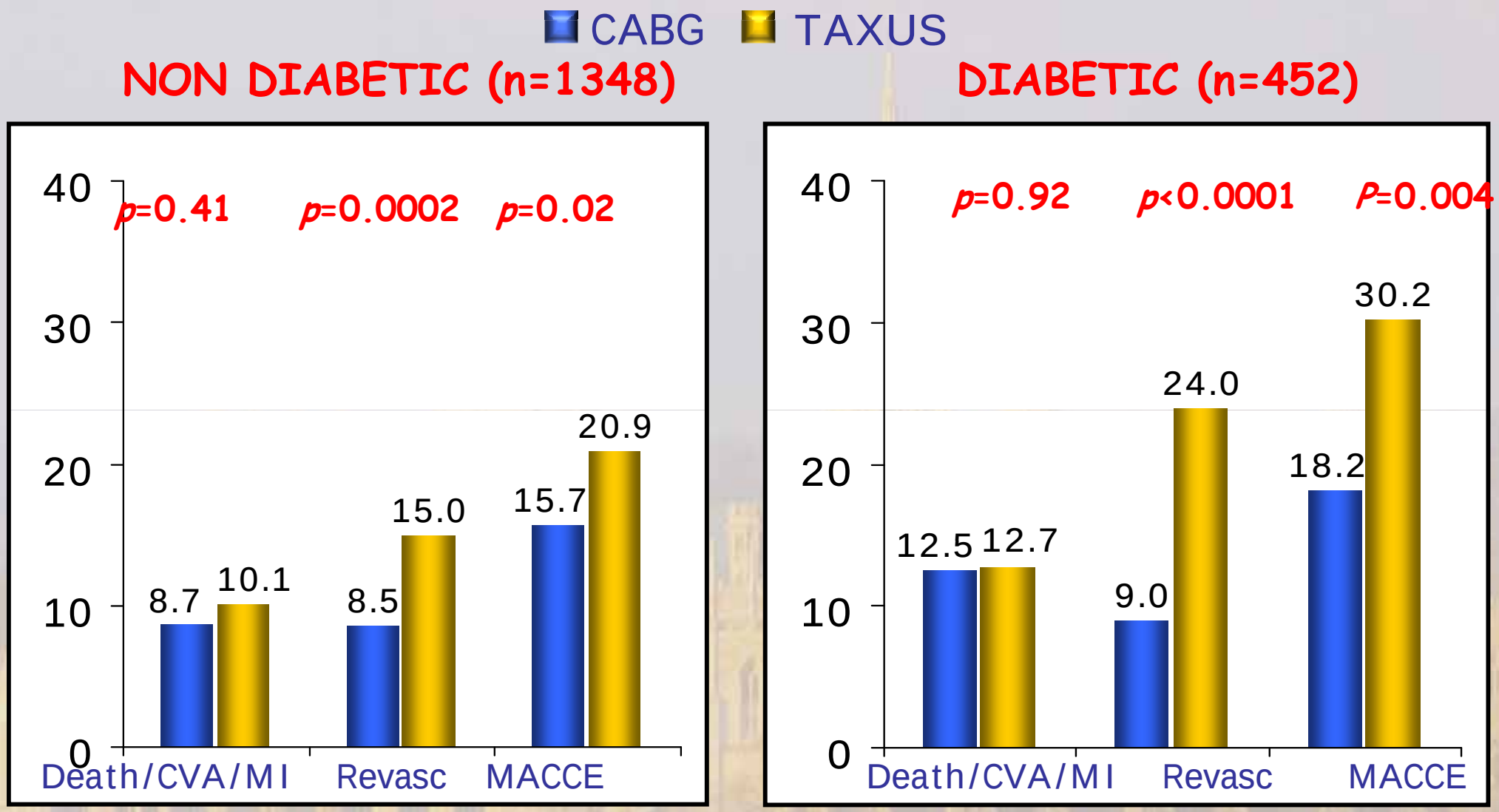
9.1.2 Type of intervention: coronary artery bypass grafting vs. percutaneous coronary intervention

All RCTs have shown higher rates of repeat revascularization procedures after PCI, compared with CABG, in diabetic patients.[29] A recent meta-analysis on individual data from 10 RCTs of elective myocardial revascularization[29] confirms a distinct survival advantage for CABG over PCI in diabetic patients. Five-year mortality was 20% with PCI, compared with 12.3% with CABG (OR 0.70, 95% CI 0.56–0.87), whereas no difference was found for non-diabetic patients; the interaction between diabetic status and type of revascularization was significant. The AWESOME trial[113] randomized high-risk patients

Table 16 Specific recommendations for diabetic patients

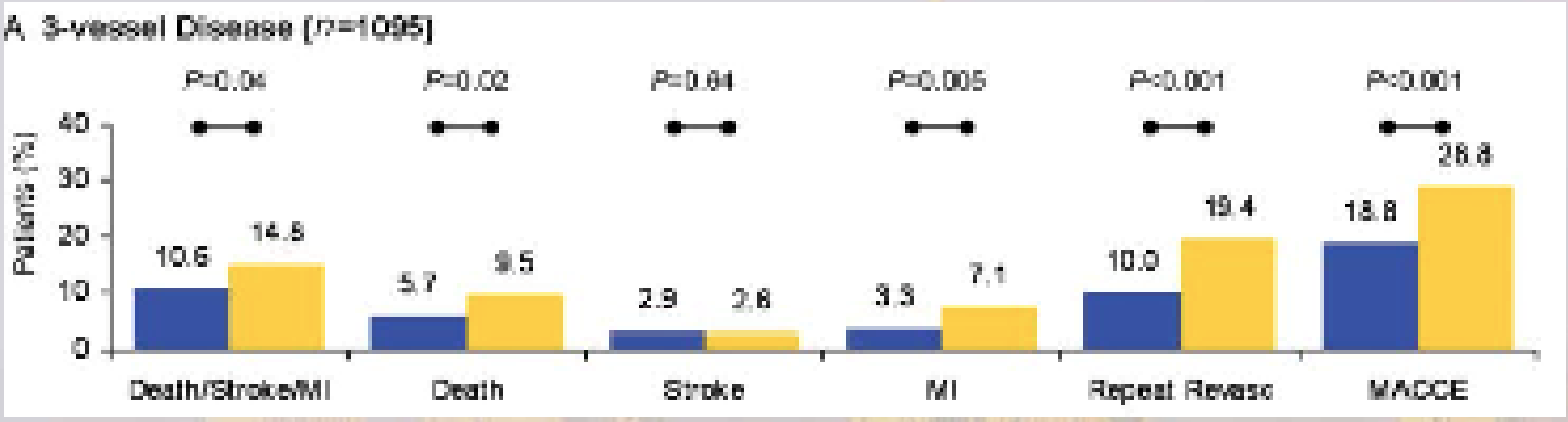
CABG should be considered, rather than PCI, when the extent of the CAD justifies a surgical approach (especially MVD), and the patient's risk profile is acceptable.	IIa	B	29, 34, 113, 116

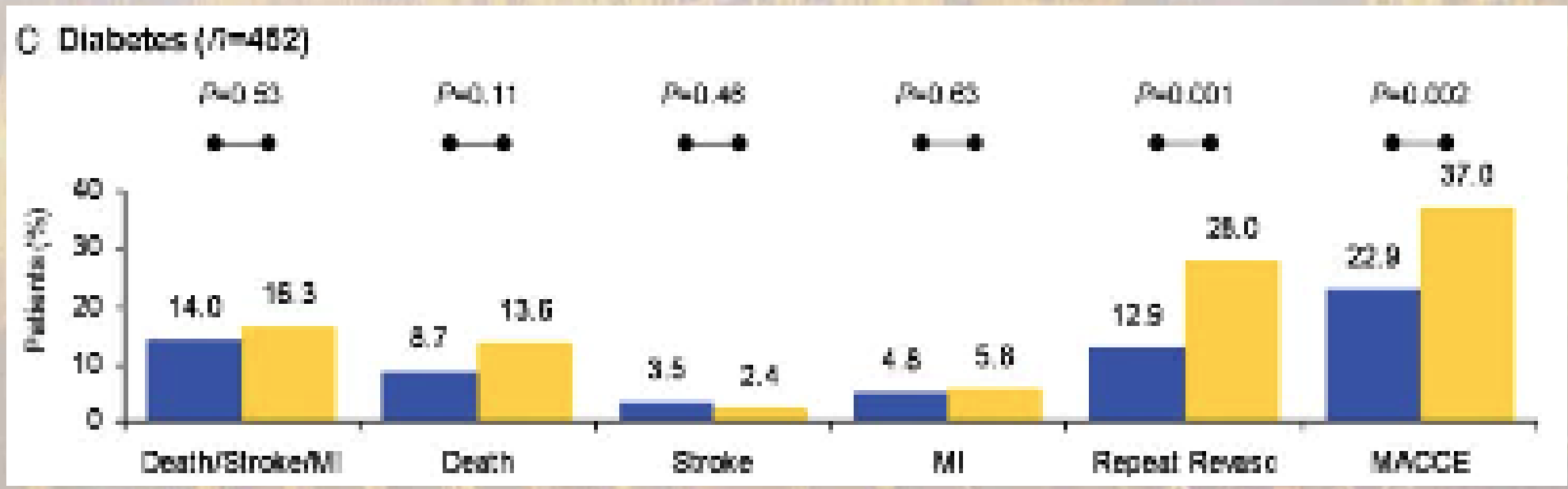
SYNTAX: 2 year outcome DIABETES vs NO DIABETES



- DM do worse on all outcomes
- Revasc and MACCE higher for PCI in both nonDM and even> in DM

SYNTAX 3 YRS


A 3-vessel Disease (n=1095)
P=0.04
P=0.02
P=0.64
P=0.005
P<0.001
P<0.001
Patients (%)
40
30
20
10
0
10.6
14.5
5.7
9.5
2.9
2.6
3.5
7.1
10.0
19.4
18.8
28.8
Death/Stroke/MI
Death
Stroke
MI
Repeat Revasc
MACCE


C Diabetes (n=452)
P=0.53
P=0.11
P=0.46
P=0.65
P=0.001
P=0.002
Patients (%)
40
30
20
10
0
14.0
15.3
8.7
13.6
3.5
2.4
4.6
5.8
12.9
26.0
22.9
37.0
Death/Stroke/MI
Death
Stroke
MI
Repeat Revasc
MACCE

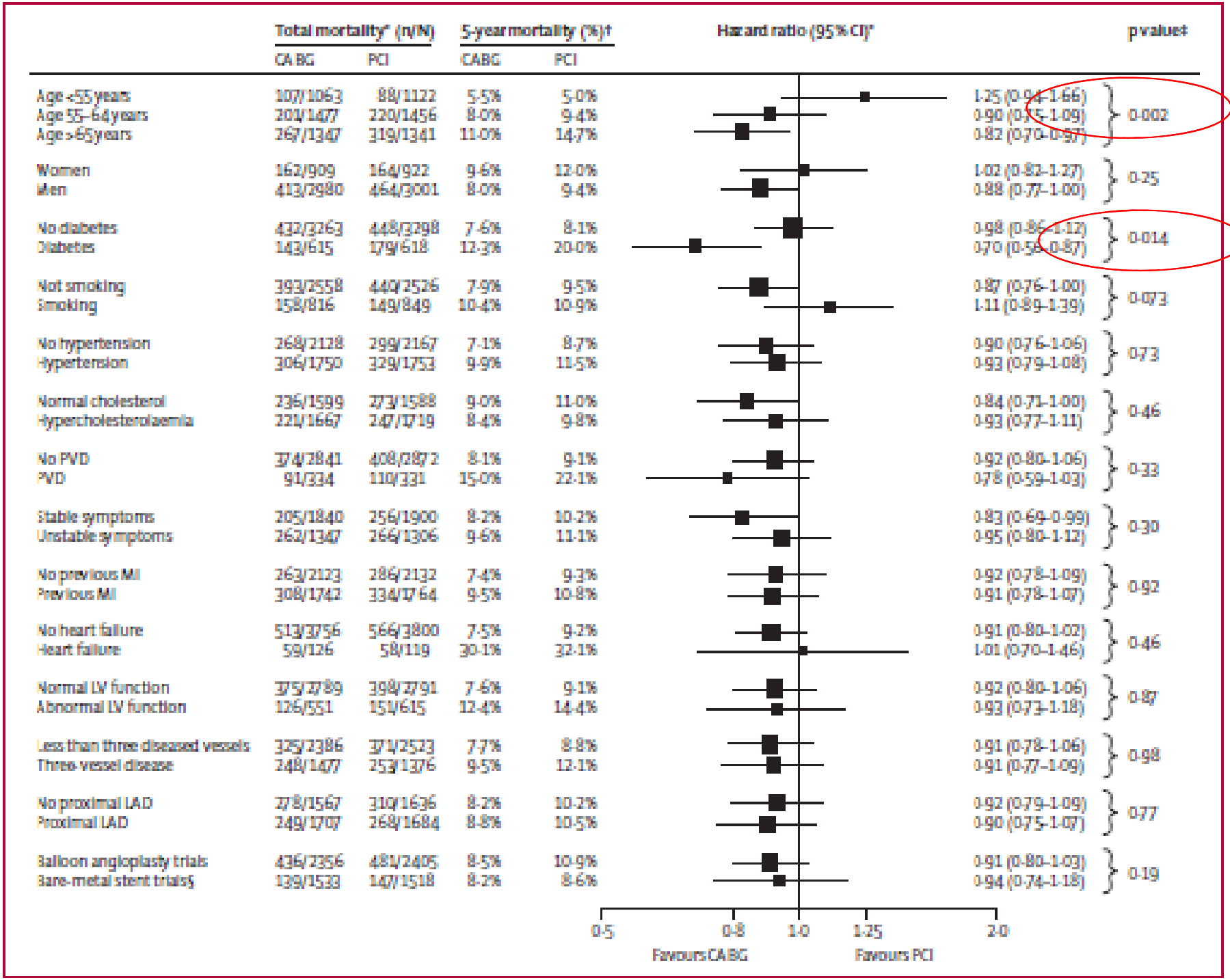

Total mortality* (n/N)
5-year mortality (%)†
Hazard ratio (95% CI)*
p value‡
CABG
PCI
CABG
PCI
Age <55 years 107/1063 88/1122 5·5% 5·0% 1·25 (0·94–1·66)
Age 55–64 years 201/1477 220/1456 8·0% 9·4% 0·90 (0·75–1·09)
Age >65 years 267/1347 319/1341 11·0% 14·7% 0·82 (0·70–0·97)
0·002
Women 162/909 164/922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

Table 2. Hazard Ratios for Death after CABG as Compared with after Stenting in Various Subgroups.*

Subgroup	All Patients	Patients with Diabetes	Patients with Ejection Fraction <40%	Patients with Ejection Fraction ≥40%†
Two-vessel disease				
No disease of LAD artery				
No. of patients				
Stenting group	5,847	1352	451	5,396
CABG group	1,309	423	212	1,097
Unadjusted hazard ratio (95% CI)	1.29 (1.02–1.62)	0.95 (0.65–1.37)	1.09 (0.70–1.72)	1.18 (0.90–1.56)
Adjusted hazard ratio (95% CI)	0.75 (0.58–0.98)	0.69 (0.46–1.03)	0.95 (0.59–1.52)	0.69 (0.51–0.93)
Disease of nonproximal LAD artery				
No. of patients				
Stenting group	5,891	1485	610	5,281
CABG group	1,690	513	278	1,412
Unadjusted hazard ratio (95% CI)	1.05 (0.84–1.31)	0.70 (0.48–1.02)	1.15 (0.78–1.69)	0.89 (0.68–1.18)
Adjusted hazard ratio (95% CI)	0.76 (0.60–0.96)	0.59 (0.40–0.87)	1.01 (0.67–1.55)	0.67 (0.50–0.89)
Disease of proximal LAD artery				
No. of patients				
Stenting group	6,033	1438	803	5,230
CABG group	8,410	2472	1615	6,795
Unadjusted hazard ratio (95% CI)	0.97 (0.85–1.10)	0.87 (0.71–1.07)	0.70 (0.56–0.87)	1.00 (0.86–1.18)
Adjusted hazard ratio (95% CI)	0.75 (0.66–0.86)	0.71 (0.57–0.88)	0.64 (0.51–0.81)	0.82 (0.69–0.97)
Three-vessel disease				
Disease of nonproximal LAD artery				
No. of patients				
Stenting group	2,166	666	342	1,824
CABG group	4,946	1824	1196	3,750
Unadjusted hazard ratio (95% CI)	0.89 (0.74–1.06)	0.77 (0.59–0.99)	0.61 (0.46–0.81)	0.94 (0.75–1.17)
Adjusted hazard ratio (95% CI)	0.74 (0.62–0.90)	0.65 (0.49–0.85)	0.64 (0.48–0.87)	0.76 (0.60–0.96)
Disease of proximal LAD artery				
No. of patients				
Stenting group	2,165	644	399	1,766
CABG group	20,857	7115	5597	15,260
Unadjusted hazard ratio (95% CI)	0.67 (0.59–0.77)	0.66 (0.53–0.81)	0.55 (0.44–0.69)	0.64 (0.53–0.76)
Adjusted hazard ratio (95% CI)	0.64 (0.56–0.74)	0.69 (0.55–0.86)	0.68 (0.54–0.85)	0.60 (0.50–0.72)