

ESC Clinical trial and Registry update
Munich 27th August 2012

Coronary Artery Revascularisation in Diabetes Trial

Presented by Roger Hall
On behalf of the CARDia Investigators

5 year follow up data



Dr Akhil Kapur (1964-2012)



Conflicts of interest

- None

Background



- Trial planned in early 2000s
- 1996: BARI diabetic subset (353 patients) showed that at 5 years PCI had double the mortality of CABG
- No randomised comparison of CABG and PCI in diabetics
- CARDia compared PCI with CABG in diabetics with multivessel (or complex LAD) disease.
- Plan to randomise 600 with sample size based on ARTS and EPI trial meta-analysis
- Non inferiority design

CARDia Investigators



- Chief Investigators: Akhil Kapur, Kevin Beatt, Roger Hall,
- Steering Committee: Roger Hall , Akhil Kapur, Kevin Beatt, Marcus Flather, Iqbal Malik, Petros Nihoyannopoulos, Keith Oldroyd, Andreas Baumbach, Gianni Angelini, Mark de Belder, Adam de Belder
- DSMB: Desmond Julian, Tom Treasure, Adrian Banning
- Coordinating Centre and Data management: Clinical Trials and Evaluation Unit, Royal Brompton Hospital, London
- Statisticians: Winston Banya and Michael Roughton
- CEC: Andrew Archbold, Doug Fraser, Iqbal Malik, Ayesha Qureshi, Kevin Fox, Mark Gunning, Marcus Flather, Simon Corbett, Simon Kennon, Roger Hall
- Funding: Supported by major grants from Hammersmith Hospitals special trustees, Eli Lilly, Cordis, BMS/Sanofi.
- Further support from Boston Scientific, Medtronic, Guidant and Jomed

CARDia: 24 Participating Centres



Centre	Principal Investigator	Patients
Hammersmith Hospital, London	Kevin Beatt, Punit Ramrakha, Roger Hall	84
St Mary's Hospital, London	Iqbal Malik	62
London Chest Hospital	Martin Rothman, Akhil Kapur, Anthony Mathur	52
St James Hospital, Dublin	Peter Crean	42
Royal Sussex County, Brighton	Steve Holmberg, Adam de Belder	34
Bristol Royal Infirmary	Andreas Baumbach, Gianni Angelini	33
James Cook University Hosp, Middlesboro	Mark de Belder	32
Western Infirmary, Glasgow	Keith Oldroyd	30
King's College Hospital	Martyn Thomas, Phillip McCarthy	27
Manchester Royal infirmary	Farzin Fath-Ordoubadi, Nick Curzen	19
Hairmyres Hospital	Keith Oldroyd, Barry Vallance	13
St Thomas' Hospital	Simon Redwood, Graham Venn	12

CARDia Participating Centres/ 2



Centre	Principal Investigator	Patients recruited
City Hospital, Birmingham	Teri Millane	12
Royal Victoria, Blackpool	David Roberts, Anoop Chauhan	11
Beaumont, Dublin	David Foley	11
St Bartholomew's Hospital, London	Richard Schilling, Akhil Kapur	10
Papworth Hospital, Cambridge	Peter Schofield	8
Royal Brompton Hospital	Carlo di Mario	4
North Staffs, Stoke	Mark Gunning	4
City Hospital, Nottingham	Kamran Baig, Rob Henderson	3
CTC, Liverpool	Rod Stables	3
Northern General, Sheffield	Ever Grech	2
Harefield Hospital	Charles Ilsley, Mark Mason	1
Mayday, Surrey	Kevin Beatt	1

Inclusion Criteria

- Age 18-80
- Significant coronary artery disease suitable for PCI or CABG
 - Proximal/Complex LAD
 - 2 or 3 Vessel disease
- Diabetes mellitus
- Stable angina or Non ST elevation-ACS

Main Exclusion Criteria

- Age >80 years
- Previous CABG or PCI
- Left main stem disease
- Cardiogenic shock
- Recent ST elevation myocardial infarction

Endpoints :

Primary outcome: **Composite of death, myocardial infarction, stroke(time to first event)**

Secondary outcome: **rate of repeat revascularisation**

Definitions:

- **Death:** All cause mortality
- **Myocardial infarction:**
 - First 7 days post revascularisation one or more of following –
 - CK or CKMB >3x ULN, Tn (T or I) >1, ECG new Q waves
 - After first 7 days need at least 2 of i) raised enzymes (CK/CKMB >x2 ULN or Troponin T or I >1), ii) new Q waves on ECG, iii) ischaemic symptoms
- **Stroke:** Neurological signs/symptoms that persist for more than 24 hrs with a neurological imaging study that does not indicate a different aetiology

Analysis: Non inferiority, upper bound of 95% CI not to exceed 12% (~80% power with 500 patients and 27% event rate)

CARDia Patient flow Chart



510 Pts randomised

CABG

254 patients

6 withdrew consent (no further data) *
14 crossed over to PCI

5 yr follow up
248 records available
204 *alive, included and followed up*
33 *deaths*
7 *lost to follow up*
4 *further withdrawals*

PCI

256 patients

2 withdrew consent (no further data)*
1 crossed over to CABG
31% BMS, 69% DES

5 year follow
254 records available
198 *alive, included and followed up*
41 *deaths*
11 *lost to follow up*
4 *further withdrawals*

* Not included in subsequent analysis

Main Baseline Characteristics

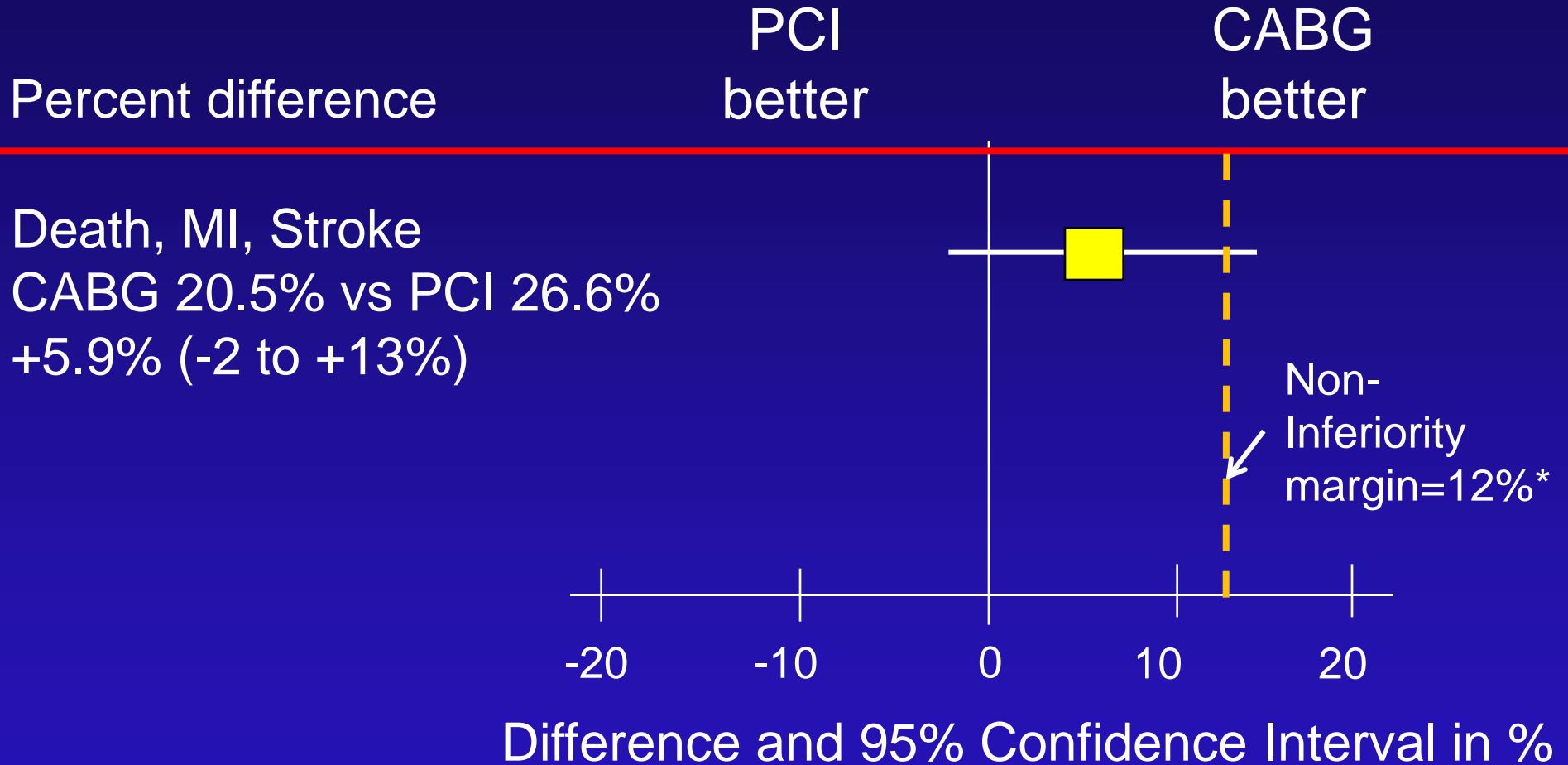


Variable	Units	CABG	PCI
Number in group		254	256
Age	Years	63.6	64.3
Male	%	77.9	70.7
Years with diabetes	Years	10.4	10.1
Type 1	%	5.3	2.8
Hba1c	%	7.9	7.9
BMI	kg/m ²	29.4	29.2
Creatinine	μmol/l	107.0	104.2
Ethnicity White	%	72.4	67.1
South Asian		20.1	25.9
Acute admission	%	23.6	21.5
3 vessel disease	%	58.7	64.8

Results

- 510 patients enrolled (1st patient enrolled Jan 2002, final Follow up April 2012)
- Median follow up 5.1 years inter-quartile range 3.8 to 5.4 years
- Mean vessels/ patient revascularised in CABG group = 2.9 (94% received LIMA grafts)
- Mean number of stents/ patient in PCI group = 3.6 (69% drug eluting stents)

Primary analysis for non inferiority



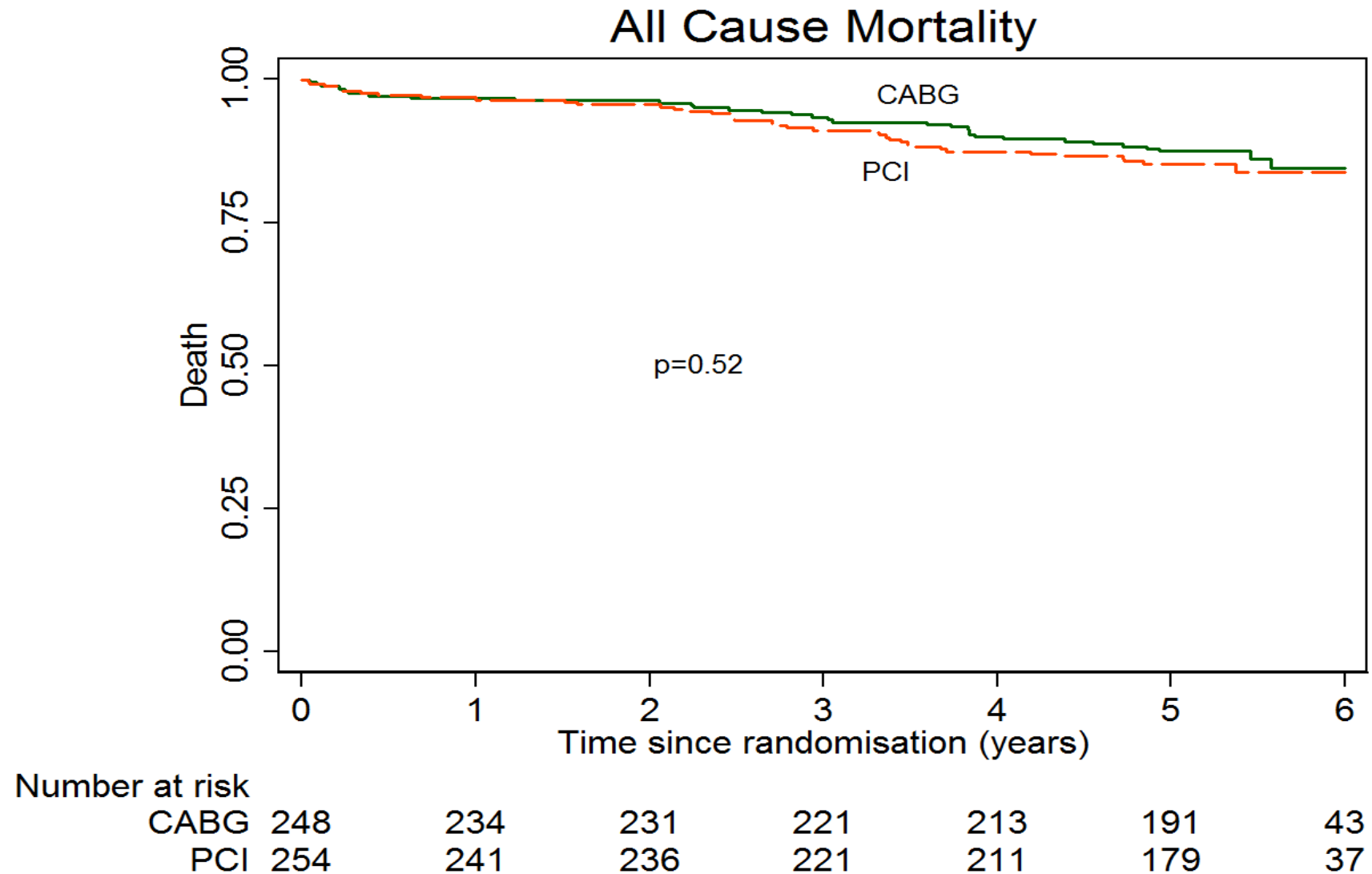
*Non inferiority method based on PARTNER Trial NEJM 2011;364:2187-98.

Non inferiority intention to treat analysis

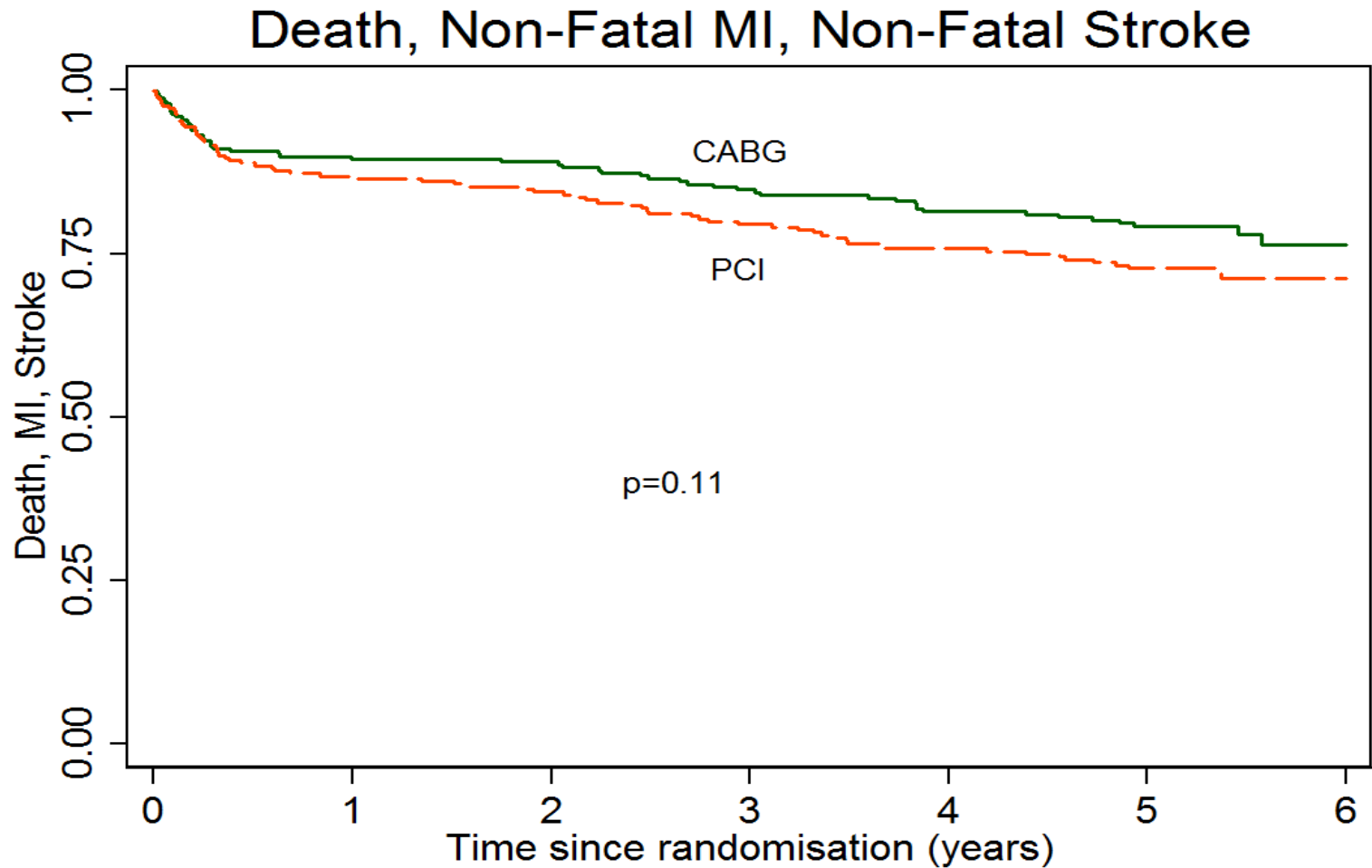


Adjudicated events post randomisation	CABG (248)	PCI (254)	p value	HR and 95% CI
Death, MI, stroke (primary outcome) (n)	20.5% (52)	26.6% (68)	0.11	1.34 (0.94,1.93)
Death	12.6 % (32)	14% (37)	0.53	1.17 (0.73,1.87)
Non fatal MI	6.3% (16)	14% (36)	0.007	2.26 (1.25,4.08)
Non fatal stroke	4.3% (11)	3.1% (8)	0.48	0.72 (0.29,1.79)
Repeat revascularisation	8.3% (23)	21.9% (57)	<0.001	2.87 (1.74, 4.74)
Death, MI, stroke, repeat revasc	26% (66)	37.5% (96)	0.005	1.56 (1.14, 2.14)

All cause mortality up to 6 yrs



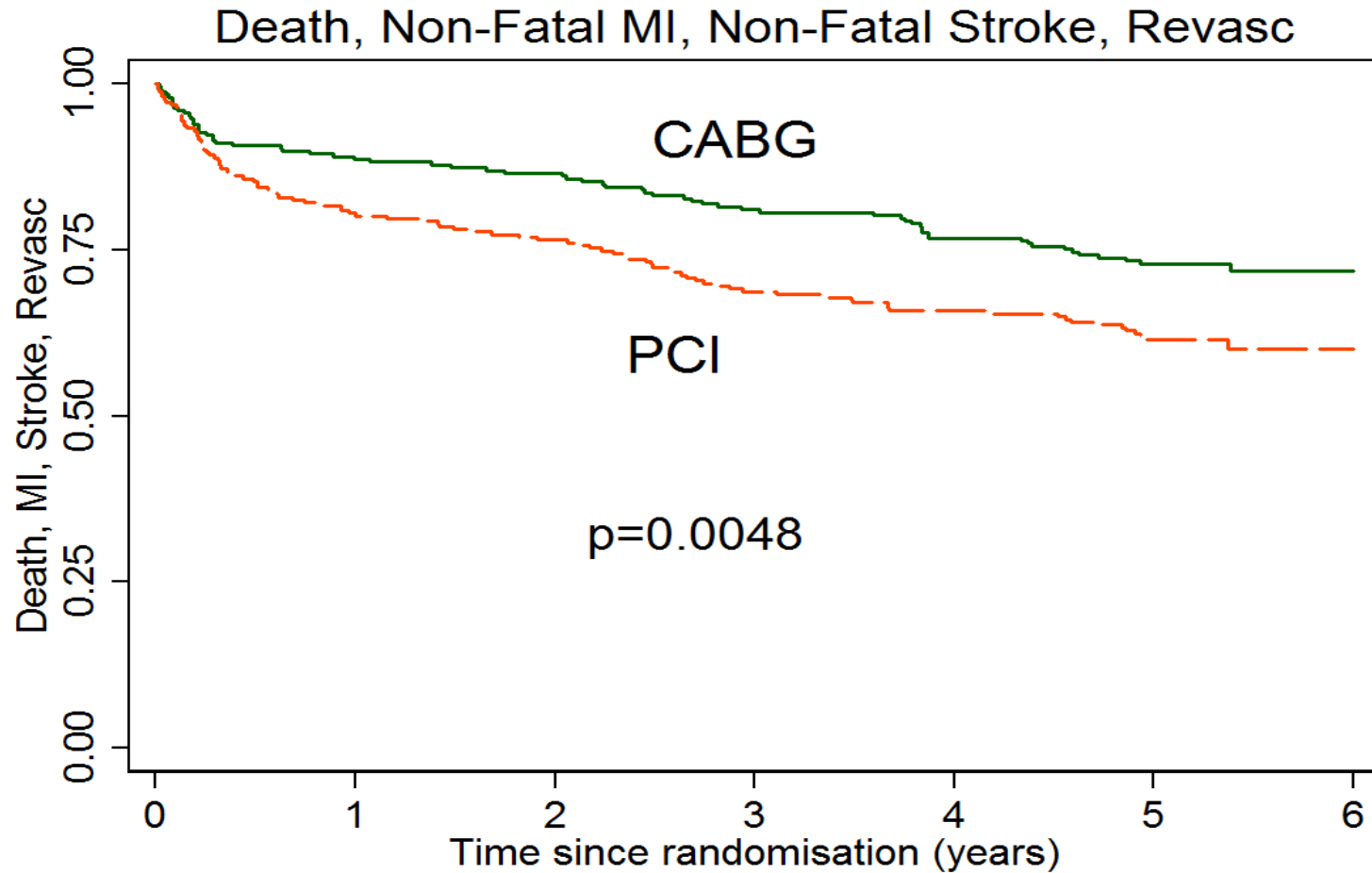
Primary endpoint up to 6 yrs



Number at risk

CABG	248	216	213	200	192	174	38
PCI	254	216	208	192	182	148	28

Primary composite endpoint *plus repeat revascularisation to 6 yrs*



Number at risk

CABG	248	214	207	191	181	159	36
PCI	254	201	189	167	159	124	26

CARDia 5 yr FU

Summary and Conclusions 1

- Primary outcome does not demonstrate non-inferiority of PCI compared to CABG
- Conventional analysis does not show a statistical difference in primary outcome but study underpowered for this comparison
- Higher rates of MI and repeat revascularisation in PCI group
- No clear evidence to support routine PCI in patients with diabetes and multivessel disease

CARDia 5 yr FU

Summary and Conclusions 2



- Previous reports of much higher mortality for PCI at 5 yrs not confirmed and mortality very similar for two treatments
- *Clinical message*
 - *CABG remains the preferred method of revascularisation unless there are clinical features that make PCI clearly preferable.*
 - *In **such a patient** it is reasonable for PCI to be performed after appropriate consultation with colleagues (including surgeons) and also the patient*