ΕΛΛΗΝΙΚΗ ΚΑΡΔΙΟΛΟΓΙΚΗ ΕΤΑΙΡΕΙΑ
HELLENIC CARDIOLOGICAL SOCIETY
ΕΛΛΗΝΙΚΗ ΕΤΑΙΡΕΙΑ ΧΕΙΡΟΥΡΓΩΝ ΘΩΡΑΚΟΣ - ΚΑΡΔΙΑΣ - ΑΓΓΕΙΩΝ

ICE 2017
Interventional Cardiovascular Education

Πανελλήνιο Συνέδριο Επεμβατικής Καρδιολογίας, Ηλεκτροφυσιολογίας και Καρδιοχειρουργικής
Panhellenic Congress of Interventional Cardiology, Electrophysiology and Cardiac Surgery

15-17 Δεκεμβρίου 2017
Ξενοδοχείο Atlantis, Ηράκλειο Κρήτης

CABG vs PCI σε νόσο στελέχους

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Θεραπευτηρίου ΄΄ΥΓΕΙΑ΄΄

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PCI vs CABG for left main disease

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Hygeia Hospital

ΕΘΝΙΚΟ & ΚΑΠΟΔΙΣΤΡΙΑΚΟ
ΠΑΝΕΠΙΣΤΗΜΙΟ ΑΘΗΝΩΝ
ΙΑΤΡΙΚΗ ΣΧΟΛΗ

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Δημήτριος Χρ Ηλιόπουλος

Διευθυντής Δ' Καρδιοχειρουργικής Κλινικής, Θεραπευτήριο «Υγεία», Αθήνα

Επικ. Καθηγητής Χειρουργικής,

Πανεπιστημίου Αθηνών

Συνέδριο;;;;

Σάββατο 16 Δεκεμβρίου 2017

Background

- Left main disease: ↑morbidity & mortality, ↑amount of myocardium at risk
- European and US guidelines recommend CABG
- Randomized non-inferiority trials examined the role of PCI

Historical Pros & Cons

CABG

- ✓ Angina relief
- ✓ Reduced re-intervention
- ✓ Complex anatomy
- ✓ Completed revascularization
- ✓ Mortality benefit in selected pts
- ✓ Potential high costs
- ✓ Invasive

PCI

- ✓ Initially cost effective
- ✓ Fast recovery
- ✓ Reduced acute complications
- ✓ Increased restenosis
- ✓ Repeat revascularization
- ✓ Least invasive

The NOBLE Trial

THELANCET-D-16-06724R2

S0140-6736(16)32052-9

Embargo: October 31, 2016—13:15 (GMT)

[redacted]

Percutaneous coronary angioplasty versus coronary artery bypass grafting in treatment of unprotected left main stenosis (NOBLE): a prospective, randomised, open-label, non-inferiority trial

*Timo Mäkikallio, Niels R Holm, Mitchell Lindsay, Mark S Spence, Andrejs Erglis, Ian B A Menown, Thor Trovik, Markku Eskola, Hannu Romppanen, Thomas Kellerth, Jan Ravkilde, Lisette O Jensen, Gintaras Kalinauskas, Rikard B A Linder, Markku Pentikainen, Anders Hervold, Adrian Banning, Azfar Zaman, Jamen Cotton, Erlend Eriksen, Sulev Margus, Henrik T Sørensen, Per H Nielsen, Matti Niemelä, Kari Kervinen, Jens F Lassen, Michael Maeng, Keith Oldroyd, Geoff Berg, Simon J Walsh, Colm G Hanratty, Indulis Kumsars, Peteris Stradins, Terje K Steigen, Ole Fröbert, Alastair N J Graham, Petter C Endresen, Matthias Corbascio, Olli Kajander, Uday Trivedi, Juha Hartikainen, Vesa Anttila, David Hildick-Smith, Leif Thuesen, Evald H Christiansen, for the NOBLE study investigators**

Hypothesis

PCI with drug-eluting stents produce non-inferior clinical results compared with CABG in revascularization of patients with unprotected left main coronary artery stenosis

Non-inferiority study

Inclusion criteria

- Stable angina, unstable angina, or acute coronary syndrome
- A significant left main lesion
  - Visually assessed stenosis diameter ≥50% or fractional flow reserve ≤0.80
  - Located in the ostium, mid-shaft, or bifurcation
- No more than three additional non-complex lesions
- Local interventional cardiologists and cardiac surgeons determined that equivalent revascularization could be achieved with CABG or PCI

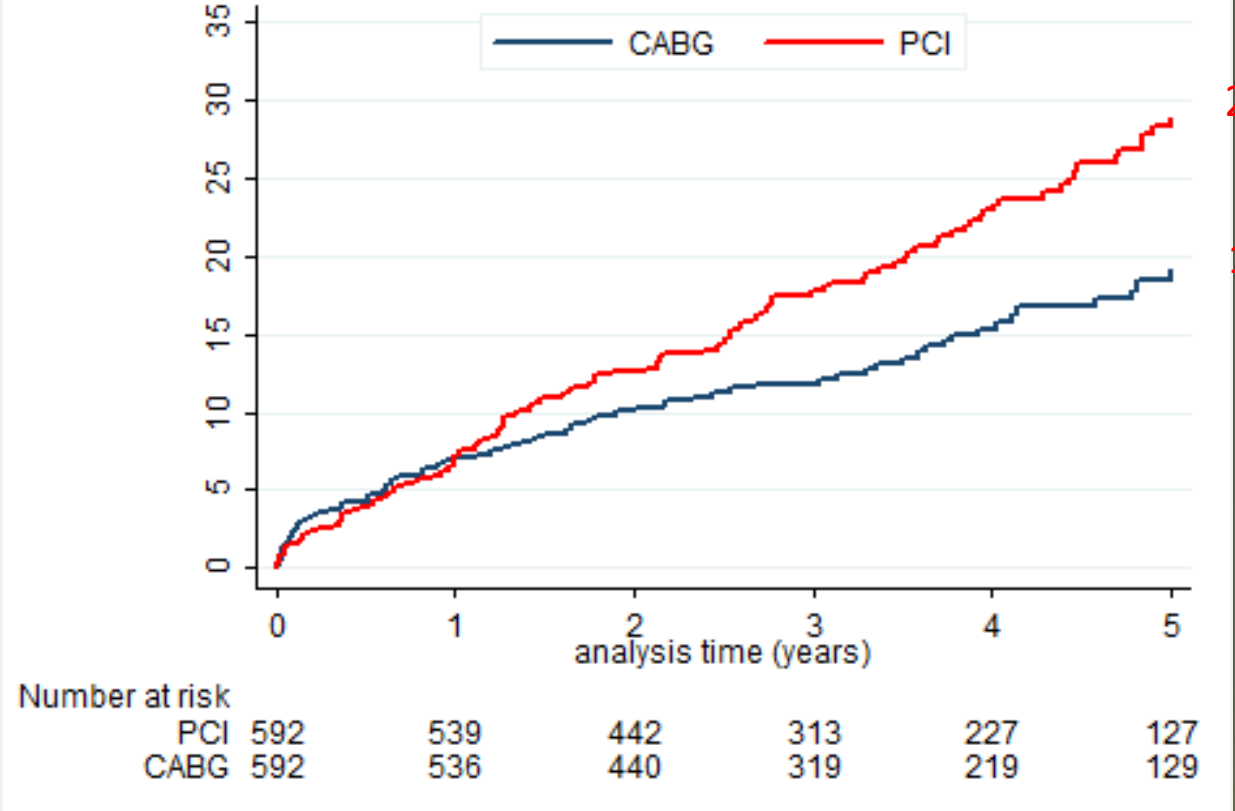
Primary endpoint

A composite of major adverse cardiac and cerebrovascular events (*MACCE*)

in 5 years

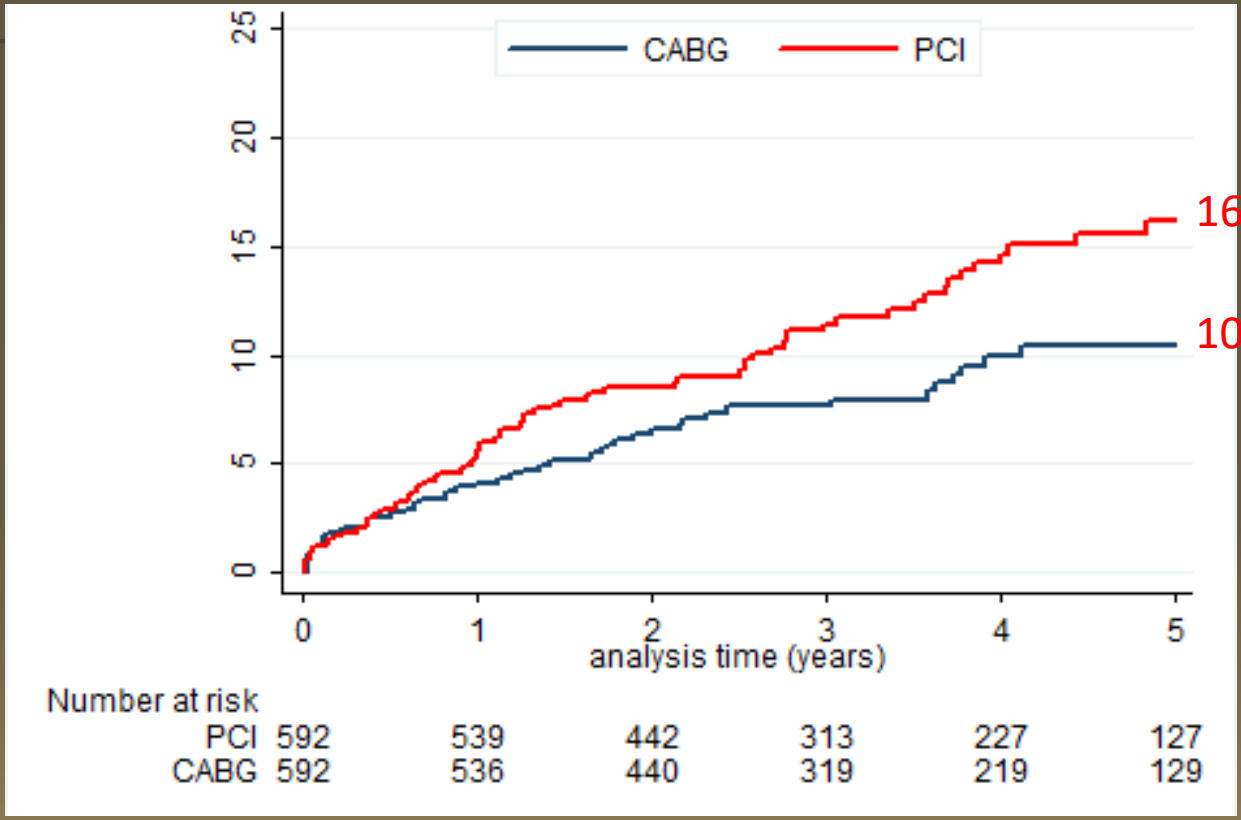
- Death from any cause
- Non-procedural myocardial infarction
- Repeat revascularization
- Stroke

Primary endpoint: MACCE



Superiority of CABG vs PCI (p<0.001)

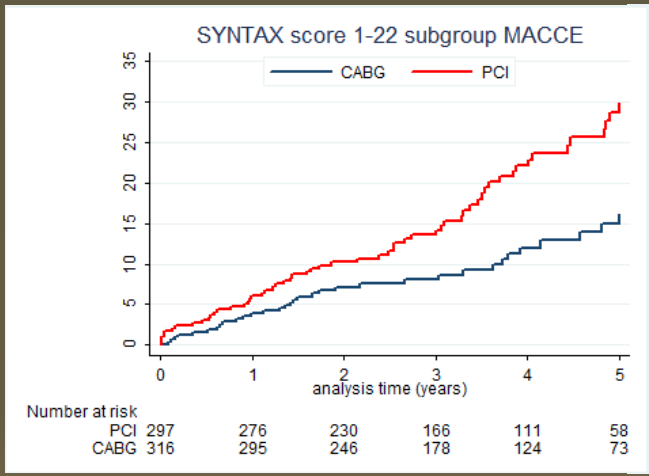
The NOBLE Trial



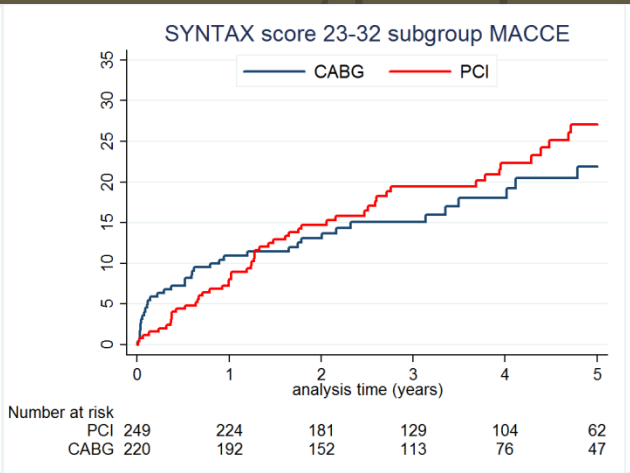
The NOBLE Trial

K-M estimates

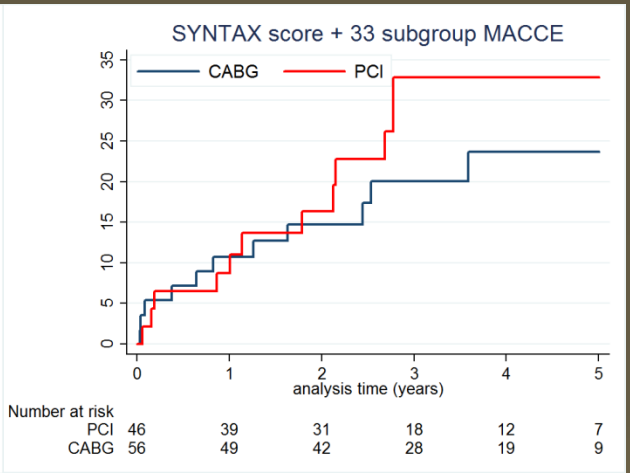
SYNTAX score subgroups



HR 1·88 (1·23–2·89); p=0·0031



HR 1·16 (0·76–1·78); p=0·48



HR 1·41 (0·62–3·20); p=0·41

SYNTAX score assessed by independent corelab (CERC)

Outline of the results

- *PCI did not meet non-inferiority* for the primary endpoint of 5-year MACCE compared to CABG
- **CABG was superior to PCI**
- PCI resulted in higher rates of non-procedural myocardial infarctions
- Repeat revascularization was higher after PCI, primarily due to de novo lesions and non LMCA target lesion revascularization
- All-cause mortality was similar for PCI and CABG

The EXCEL Trial

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 DECEMBER 8, 2016 VOL. 375 NO. 23

Everolimus-Eluting Stents or Bypass Surgery for Left Main Coronary Artery Disease

G.W. Stone, J.F. Sabik, P.W. Serruys, C.A. Simonton, P. Généreux, J. Puskas, D.E. Kandzari, M.-C. Morice, N. Lembo, W.M. Brown III, D.P. Taggart, A. Banning, B. Merkely, F. Horkay, P.W. Boonstra, A.J. van Boven, I. Ungi, G. Bogáts, S. Mansour, N. Noiseux, M. Sabaté, J. Pomar, M. Hickey, A. Gershlick, P. Buszman, A. Bochenek, E. Schampaert, P. Pagé, O. Dressler, I. Kosmidou, R. Mehran, S.J. Pocock, and A.P. Kappetein, for the EXCEL Trial Investigators*

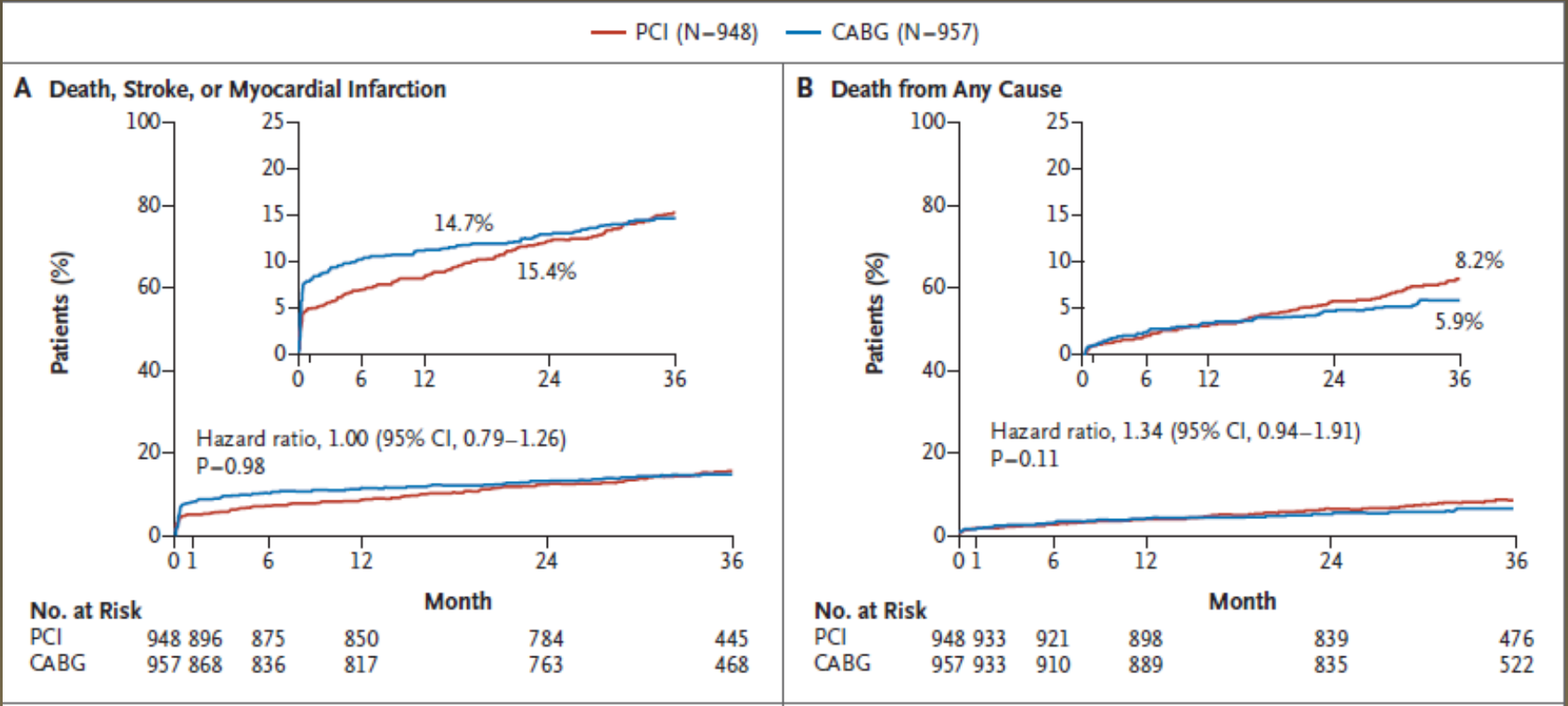


Figure 1. Time-to-Event Curves for the Primary Composite End Point and its Components.

Panel A shows the results of the analysis of the primary composite end point of death, stroke, or myocardial infarction at 3 years. Results of analyses of the components of the primary end point are shown in Panel B (death from any cause), Panel C (stroke), and Panel D (myocardial infarction). Event rates were based on Kaplan–Meier estimates in time-to-first-event analyses. Hazard ratios are for the patients who underwent percutaneous coronary intervention (PCI) with everolimus-eluting stents. The rates of stroke and myocardial infarction are nonhierarchical (i.e., fatal and nonfatal events were included). In each panel, the inset shows the same data on an enlarged y axis. CABG denotes coronary-artery bypass grafting.

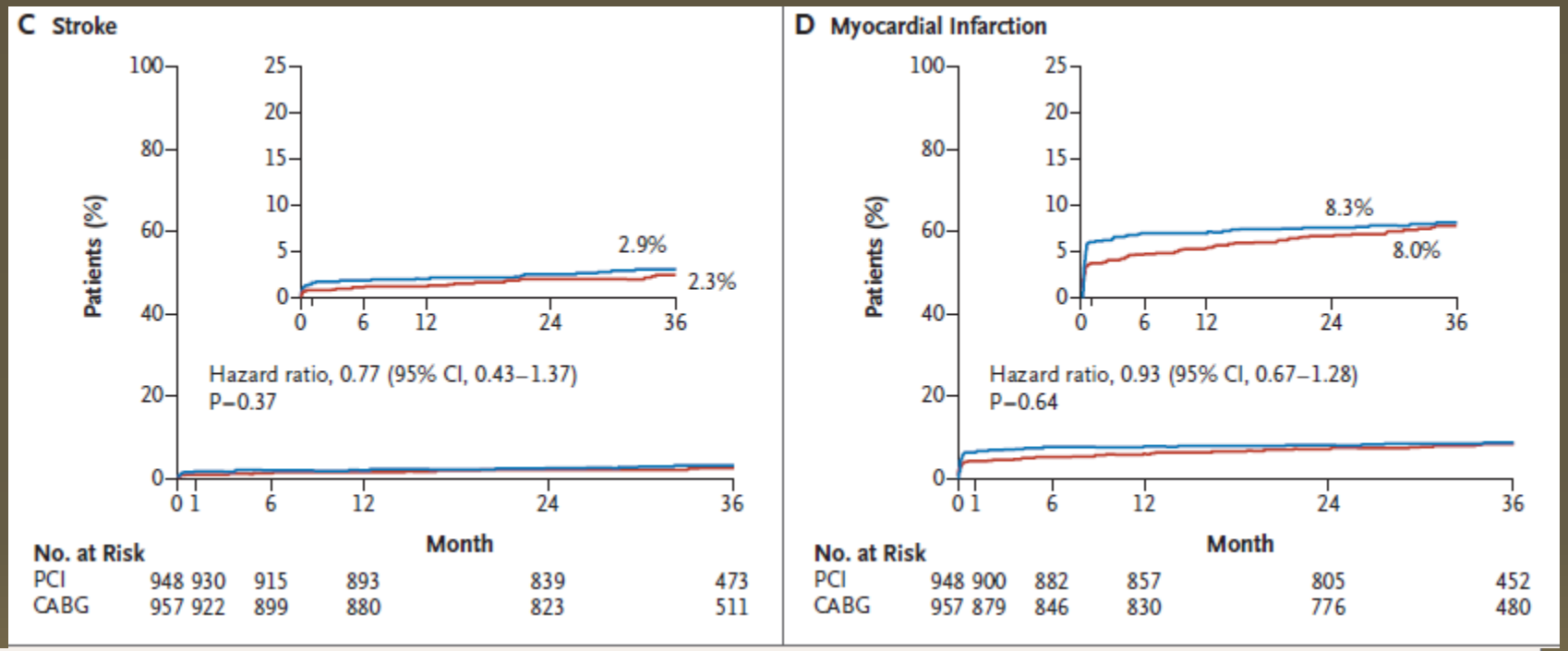


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Table 3. Additional Secondary Clinical End Points.*

Variable	PCI (N=948)		CABG (N=957)		Hazard Ratio (95% CI)	P Value
	Events	Event Rate†	Events	Event Rate†		
	no.	%	*no.*	%		
Clinical end points at 30 days						
Death, stroke, or myocardial infarction	46	4.9	75	7.9	0.61 (0.42–0.88)	0.008
Death	9	1.0	10	1.1	0.90 (0.37–2.22)	0.82
Stroke	6	0.6	12	1.3	0.50 (0.19–1.33)	0.15
Myocardial infarction	37	3.9	59	6.2	0.63 (0.42–0.95)	0.02
Periprocedural	34	3.6	56	5.9	0.61 (0.40–0.93)	0.02
Spontaneous	3	0.3	3	0.3	1.00 (0.20–4.95)	1.00
STEMI	7	0.7	22	2.3	0.32 (0.14–0.74)	0.005
Non-STEMI	30	3.2	37	3.9	0.82 (0.50–1.32)	0.41
Q-wave	7	0.7	14	1.5	0.50 (0.20–1.24)	0.13
Non–Q-wave	30	3.2	43	4.5	0.70 (0.44–1.12)	0.13
Death, stroke, myocardial infarction, or ischemia-driven revascularization	46	4.9	80	8.4	0.57 (0.40–0.82)	0.002
Revascularization						
Ischemia-driven revascularization	6	0.6	13	1.4	0.46 (0.18–1.21)	0.11
All revascularization	7	0.7	13	1.4	0.54 (0.21–1.35)	0.18
Stent thrombosis, definite or probable‡	6	0.6	0	0	—	0.01
Graft occlusion, symptomatic	0	0	11	1.2	—	<0.001
Definite stent thrombosis or symptomatic graft occlusion‡	3	0.3	11	1.2	0.27 (0.08–0.97)	0.03
Bleeding according to BARC criteria§[15]						
Any	69	7.3	123	13.0	0.55 (0.41–0.74)	<0.001
Type 2–5	51	5.4	111	11.7	0.45 (0.32–0.63)	<0.001
Type 3–5	23	2.4	82	8.7	0.27 (0.17–0.43)	<0.001
Bleeding according to TIMI criteria[15]						
Major or minor	35	3.7	85	9.0	0.41 (0.27–0.60)	<0.001
Major	11	1.2	37	3.9	0.29 (0.15–0.58)	<0.001
Minor	24	2.5	49	5.2	0.49 (0.30–0.79)	0.003
Blood transfusion	30	3.2	120	12.7	0.24 (0.16–0.36)	<0.001

30-day data

3-year data

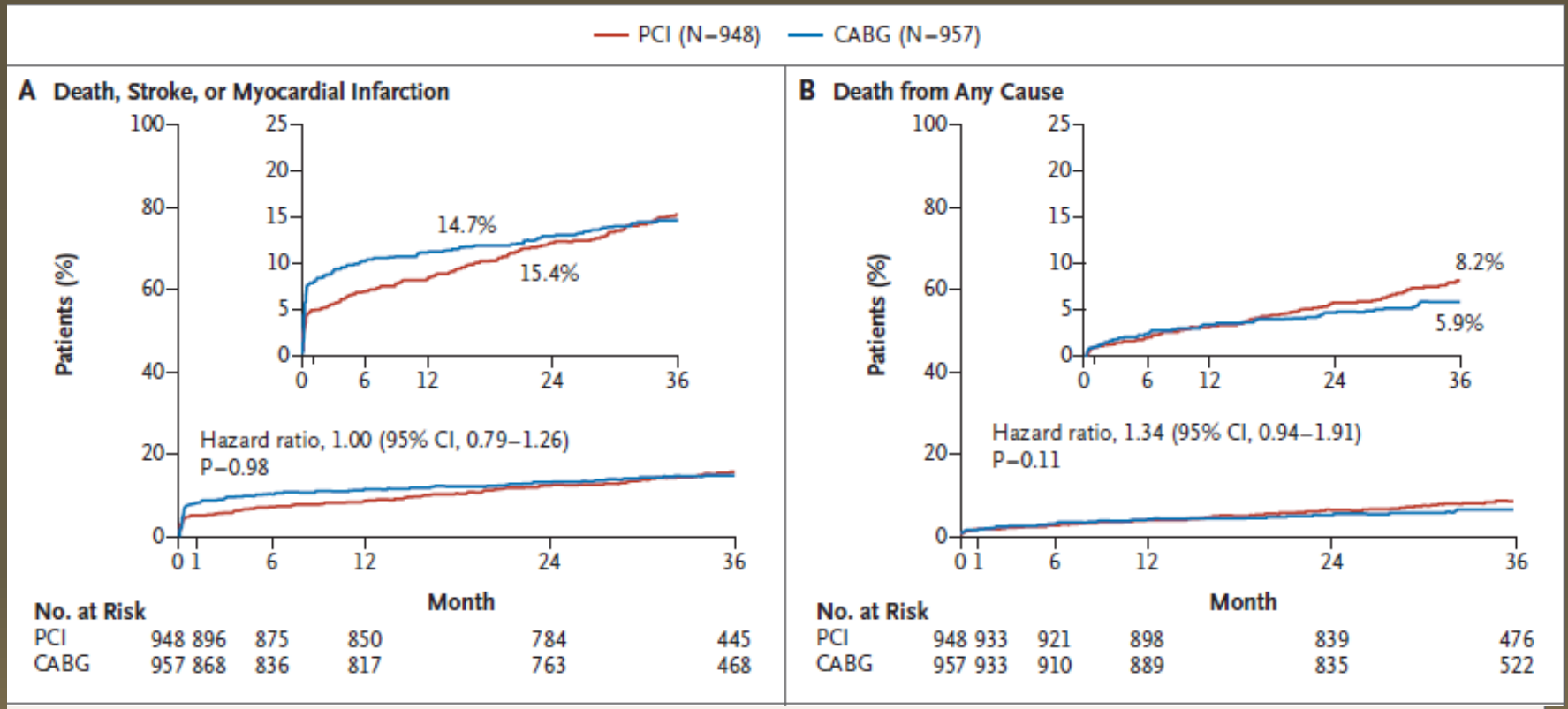
Table 3. Additional Secondary Clinical End Points.*

Variable	PCI (N=948)		CABG (N=957)		Hazard Ratio (95% CI)	P Value
	Events	Event Rate†	Events	Event Rate†		
	no.	%	*no.*	%		
Clinical end points at 3 yr						
Death, stroke, or myocardial infarction: primary end point	137	15.4	135	14.7	1.00 (0.79–1.26)	0.98
Death	71	8.2	53	5.9	1.34 (0.94–1.91)	0.11
Cardiovascular	39	4.4	33	3.7	1.18 (0.74–1.87)	0.48
Definite	33	3.7	30	3.4	1.10 (0.67–1.80)	0.71
Undetermined cause	6	0.8	3	0.3	2.00 (0.50–7.98)	0.32
Noncardiovascular	32	3.9	20	2.3	1.60 (0.91–2.80)	0.10
Stroke	20	2.3	26	2.9	0.77 (0.43–1.37)	0.37
Myocardial infarction	72	8.0	77	8.3	0.93 (0.67–1.28)	0.64

Reviewing the results

Scissors diagram

The gap is expanding



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NOBLE

EXCEL

Variables	NOBLE trial	EXCEL trial
Trial design		
Patient characteristics	STEMI within 24 h excluded	All ACS eligible
Anatomic characteristics	ULMCAD stenosis >50% or FFR<0.80; no more than 3 additional lesion or complex addition lesion	ULMCAD stenosis >70% or if 50–70% then FFR<0.80; SYNTAX <32
Primary endpoint	Death, spontaneous MI, stroke or revascularization	Death, any MI or stroke
Geographic region	100% Europe	56% Europe, 40% North America, 4% Other*
Sample size	1,201	1,905
Median follow-up time	3.1 years	3.0 years
Study population		
SYNTAX score	22.5±7.5	20.6±6.2
ACS	18%	15% (1.4% STEMI)
LVEF	60% (IQR 55–65%)	57%±10%
Diabetes	PCI group: 15%; CABG group: 15%	PCI group: 32.2%; CABG group: 28.0%
Procedural characteristics		
Stent used	89% biolimus-eluting stent (BIOMATRIX™), 11% 1st Gen DES	100% everolimus-eluting stent (XIENCE™)
Distal/bifurcation disease	81%	81%
IVUS guidance	Pre-stent evaluation: 47%; post-stent evaluation: 77%	IVUS guidance: 77%
2-stents used	37%	NR
2-stent technique	Culotte: 24%; crush: 4%; other: 9%	NR
LIMA to LAD	96%	98.8%
Only arterial grafts used	14.3%	24.8%
Results: PCI *vs.* CABG		
Primary endpoint	Favors CABG	No difference
All-cause-mortality	No difference	No difference
Cardiac mortality	No difference	No difference
Total MI	NR	No difference
Spontaneous MI	Favors CABG	No difference
Stroke	No difference	No difference
Total revascularization	Favors CABG	Favors CABG
Target-lesion revascularization	No difference	No difference
LMCA revascularization	No difference	NR
Stent thrombosis	2%†, 0.8% (BIOMATRIX™ DES only)†	0.7%‡

PLOS ONE

RESEARCH ARTICLE

Unprotected left main revascularization: Percutaneous coronary intervention versus coronary artery bypass. An updated systematic review and meta-analysis of randomised controlled trials

Luca Testa[1]*, Azeem Latib[2], Mario Bollati[1], Rocco Antonio Montone[1], Antonio Colombo[2], Filippo Crea[3], Francesco Bedogni[1]

1 Dept. of Cardiology, IRCCS Pol S. Donato, Milan, Italy, **2** Interventional Cardiology Unit, San Raffaele Scientific Institute; EMO GVM Centro Cuore Columbus Milan, Italy, **3** Dept of Cardiology, Catholic Univ. of the Sacred Heart, Rome, Italy

Study design

Table 1. Features of included studies. CABG: Coronary artery bypass graft; CVA; cerebrovascular accident; DES: drug eluting stent; LAD: left anterior descending; MI: myocardial infarction; PCI: percutaneous coronary intervention; RCT: randomised controlled trial.

Study	Design	PCI (N)	DES, %	CABG (N)	Arterial graft to LAD, %	Primary end point
LEMANS[3,9]	RCT	52	35	53	81	Cardiac death, MI, CVA, repeat revascularization, and/or acute/subacute ST
SYNTAX Left Main[4,10]	Pre-specified subanalysis from a RCT	357	100	348	97	All-cause death, CVA, MI, and repeat revascularization
Boudriot et al[5]	RCT	100	100	101	99	All-cause death, MI, and repeat revascularization
PRECOMBAT[6,11]	RCT	300	100	300	94	All-cause death, CVA, MI, and repeat revascularization
EXCEL[7]	RCT	948	100	957	99	Death, stroke, or myocardial infarction
NOBLE[8]	RCT	598	100	603	93	Death from any cause, non-procedural myocardial infarction, repeat revascularisation, or stroke

Patient characteristics

Table 2. Patients and procedural features of included studies.

Study	Age	Diabetes	Distal LM	No of Diseased vessel 0/1/2/3%	Syntax Score	Complete Revascularization (overall,PCI, CABG)
LEMANS[3,9]	61	18	58	0/9/23/68	23	84/79/89
SYNTAX Left Main[4,10]	65	25	61	13/20/31/36	30	68/65/73
Boudriot et al [5]	68	36	71	29/31/27/14	24	98/98/97
PRECOMBAT[6,11]	62	32	65	10/17/32/41	25	69/68/70
EXCEL[7]	66	29	80	163/292/325/162	20	NA
NOBLE[8]	66	15	81	NA	22	92 (PCI only)

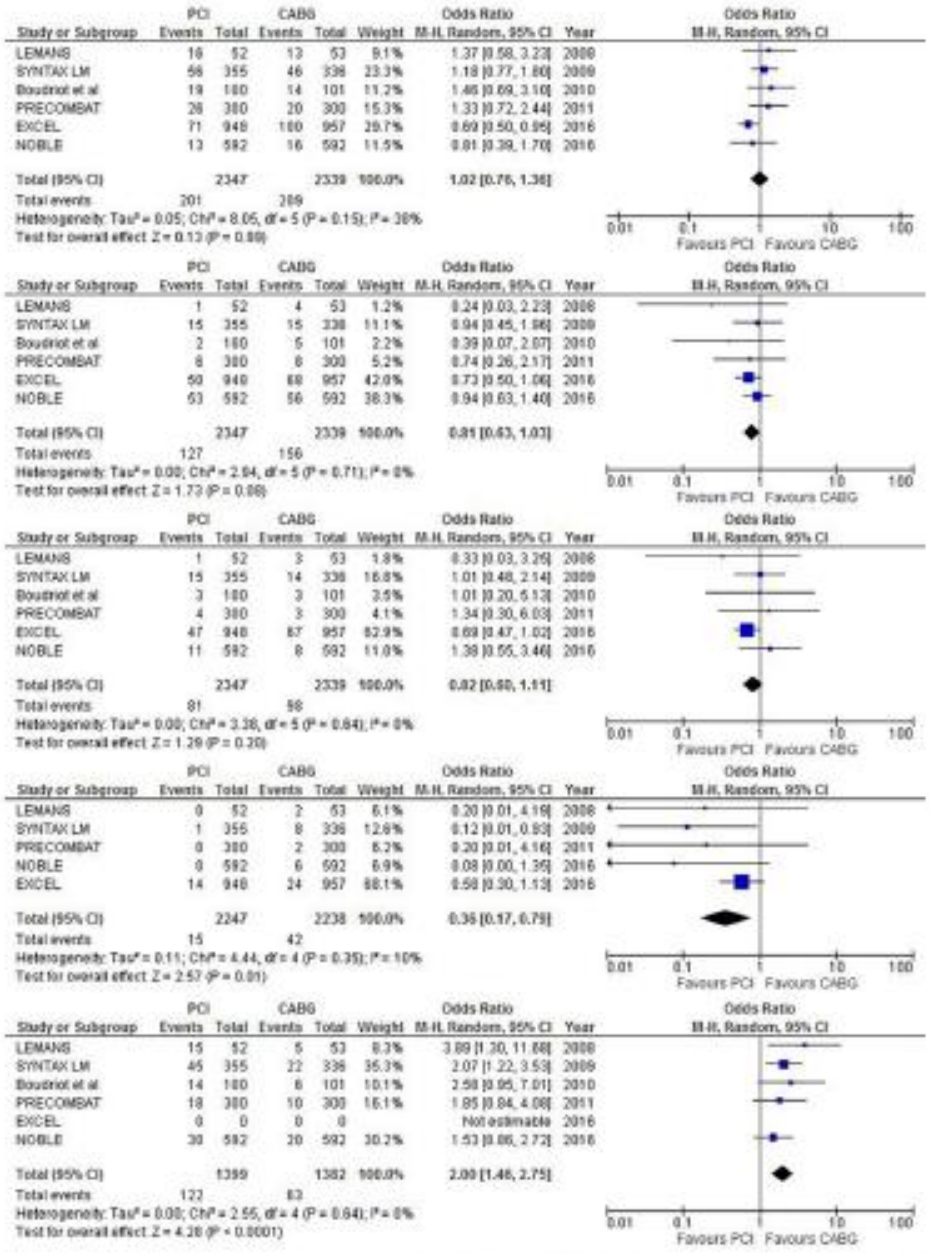
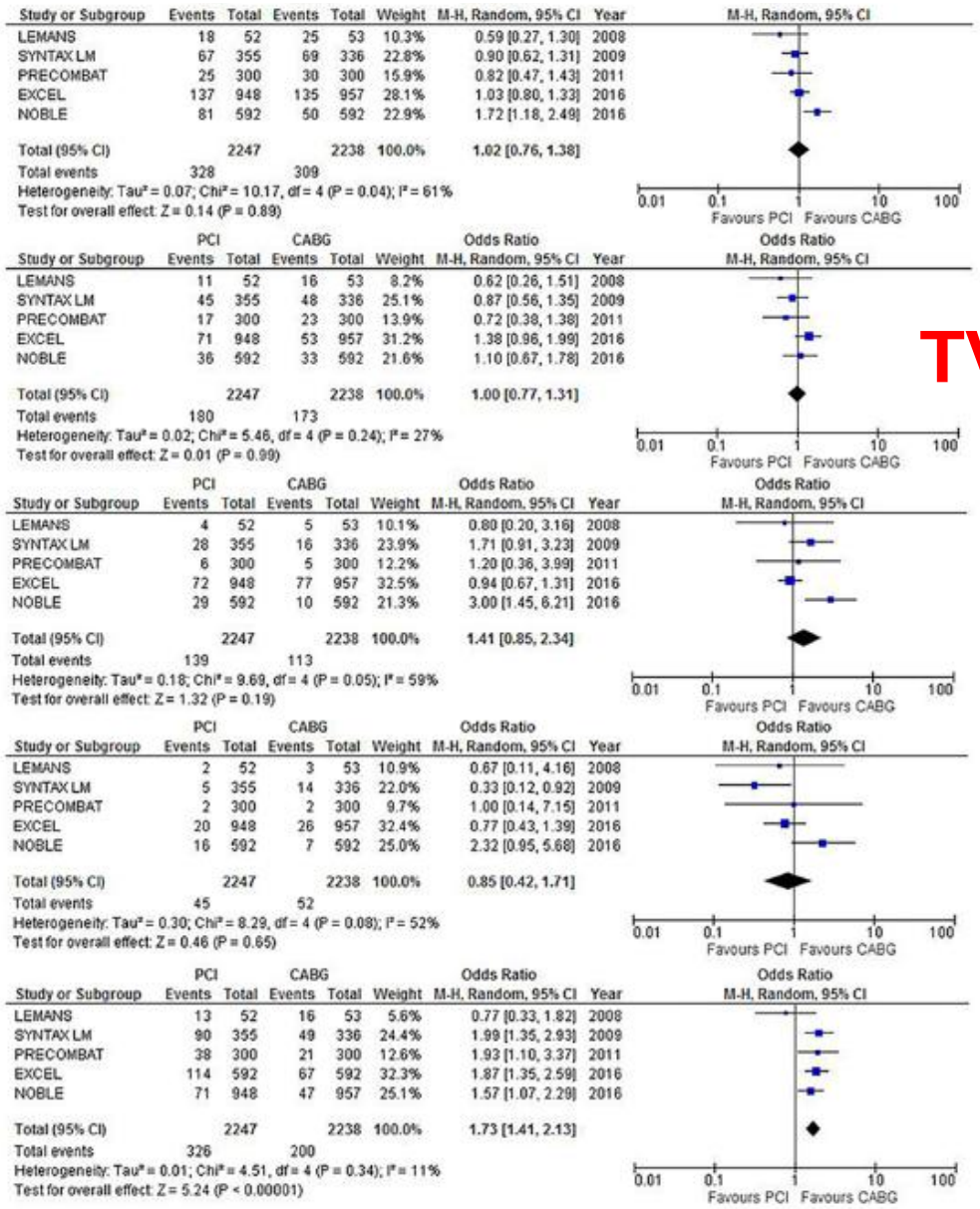


Fig 2. Major adverse cardiovascular events at 1 year (from top to bottom, MACE, Death, MI, Stroke, TVR)

✓ Stroke favors PCI

✓ TVR favors CABG



TVR favors CAB

Fig 3. Major adverse cardiovascular events at a median FU of 5 years, mean 5.6 years (from top to bottom, MACE, Death, MI, Stroke, TVR)

Main findings: *Equivalence*

Main findings can be featured as follows:

- At 1 year follow-up PCI and CABG achieve substantial equivalence with respect to the cumulative end point of MACE (overall death, MI and stroke), while CABG is associated with a higher risk of stroke and PCI is associated with a higher risk of TVR
- At long term follow up, PCI and CABG are equivalent with respect to MACE, mortality, MI and risk of stroke, while PCI is associated with a higher risk of TVR.

European Heart Journal
doi:10.1093/eurheartj/ehu278b

ESC/EACTS GUIDELINES

European guidelines for unprotected Left Main disease

- **CABG: IB (regardless of SYNTAX score)**
- PCI: IB (SYNTAX score <22)
- PCI: IIA (SYNTAX score 23-32)
- PCI: IIIB (SYNTAX score >32)

PCI ≤ CABG

Comments on the debate

- " Surgery solves the problem **long-term**."
- "Some eligible patients will prefer surgery, and some eligible patients will prefer PCI."
- "In the EXCEL trial, by the time you get out **over 3 years**, death is beginning to split in favor of surgery."
- "Since the results, on their surface, are somewhat discordant with each other, it's probably **not** going to be **enough** to change the guidelines."
- The "*devil is in the details*."

Take home message

CABG remains the preferred method

while the long-term outcomes of NOBLE

and EXCEL trials are anticipated

Thank you !