TCTAP 2023

Current Status of PCI vs CABG in LM disease

David P Taggart MD PhD FRCS FESC

Professor of Cardiovascular Surgery, University of Oxford

Conflicts of Interest:

(i) Clinical: Cardiac Surgeon (But Balanced Presentation of Available Data)
(ii) (Chairman of Surgical Ctte of EXCEL but withdrew from final NEJM publication)
(iii) Commercial: Consultant to Medistim, Medtronic, VGS

PCI vs CABG in Left Main Disease: A Warning !!

Drug Companies & Doctors: A Story of Corruption

Marcia Angell

January 15 2009

'**Conflicts of interest and biases exist in virtually every field of medicine, particularly those that rely heavily on drugs or devices. It is simply no longer possible to believe much of the clinical research that is published, or to rely on the judgment of trusted physicians or authoritative medical guidelines. I take no pleasure in this conclusion, which I reached slowly and reluctantly over my two decades as an editor of the New England Journal of Medicine.**'

Marcia Angell, Editor NEJM, January 2009

Evidence basis CABG vs PCI: 3 Key 'Rules' of Interpretation

(i) Are RCT patients typical of routine practice (CAD severity/ Syntax scores) ?

❌ No: usually very highly selected patients with less severe CAD

✔ **Underestimates the benefit of CABG in routine practice where MOST patients have more severe CAD than in RCT patients**

(ii) Duration of follow-up ?

❌ Must be a **minimum** of 5 years (ideally 10 years as in the ART)

✔ **Increasing length of follow-up = increasing benefit of CABG**

(iii) Use of Guideline Directed Medical Therapy (GDMT) ?

❌ Always **SIGNIFICANTLY** inferior in CABG vs PCI patients

✔ **CABG + GDMT: then even greater benefits over PCI**

ALWAYS EXAMINE THE ACTUAL DATA BEFORE READING TEXT WHICH OFTEN HAS A VERY PRO-PCI BIAS (eg EXCEL) !!

STATE-OF-THE-ART PAPER AND COMMENTARY

Revascularization for Unprotected Left Main Stem Coronary Artery Stenosis

Stenting or Surgery

- @ 90% LMS have multivessel CAD (CABG offers survival benefit)
- @ 90% LMS are distal/bifurcation (higher risk of restenosis)
- **(in EXCEL 81% distal LM)**
- **BUT EXCELLENT PCI OUTCOMES FOR ISOLATED OSTIAL/MID-SHAFT LESIONS (and possibly better than for CABG)**

Oxford, United Kingdom; Los Angeles, California; Buffalo, New York; Greenville and Durham, North Carolina; Atlanta, Georgia; Dallas, Texas; Leuven, Belgium; and Hamilton, Ontario, Canada

For coronary artery disease with unprotected left main stem (LMS) stenosis, coronary artery bypass grafting (CABG) is traditionally regarded as the "standard of care" because of its well-documented and durable survival advantage. There is now an increasing trend to use drug-eluting stents for LMS stenosis rather than CABG despite very little high-quality data to inform clinical practice. We herein: 1) evaluate the current evidence in support of the use of percutaneous revascularization for unprotected LMS; 2) assess the underlying justification for randomized controlled trials of stenting versus surgery for unprotected LMS; and 3) examine the optimum approach to informed consent. We conclude that CABG should indeed remain the preferred revascularization treatment in good surgical candidates with unprotected LMS stenosis.   (J Am Coll Cardiol 2008;51:885–92) © 2008 by the American College of Cardiology Foundation.

Stents versus Coronary-Artery Bypass Grafting for Left Main Coronary Artery Disease

Ki Bae Seung, M.D., Duk-Woo Park, M.D., Young-Hak Kim, M.D., Seung-Whan Lee, M.D., Cheol Whan Lee, M.D., Myeong-Ki Hong, M.D., Seong-Wook Park, M.D., Sung-Cheol Yun, Ph.D., Hyeon-Cheol Gwon, M.D., Myung-Ho Jeong, M.D., Yangsoo Jang, M.D., Hyo-Soo Kim, M.D., Pum Joon Kim, M.D., In-Whan Seong, M.D., Hun Sik Park, M.D., Taehoon Ahn, M.D., In-Ho Chae, M.D., Seung-Jea Tahk, M.D., Wook-Sung Chung, M.D., and Seung-Jung Park, M.D.

**MAIN-COMPARE Registry of LM disease in 2240 Patients:
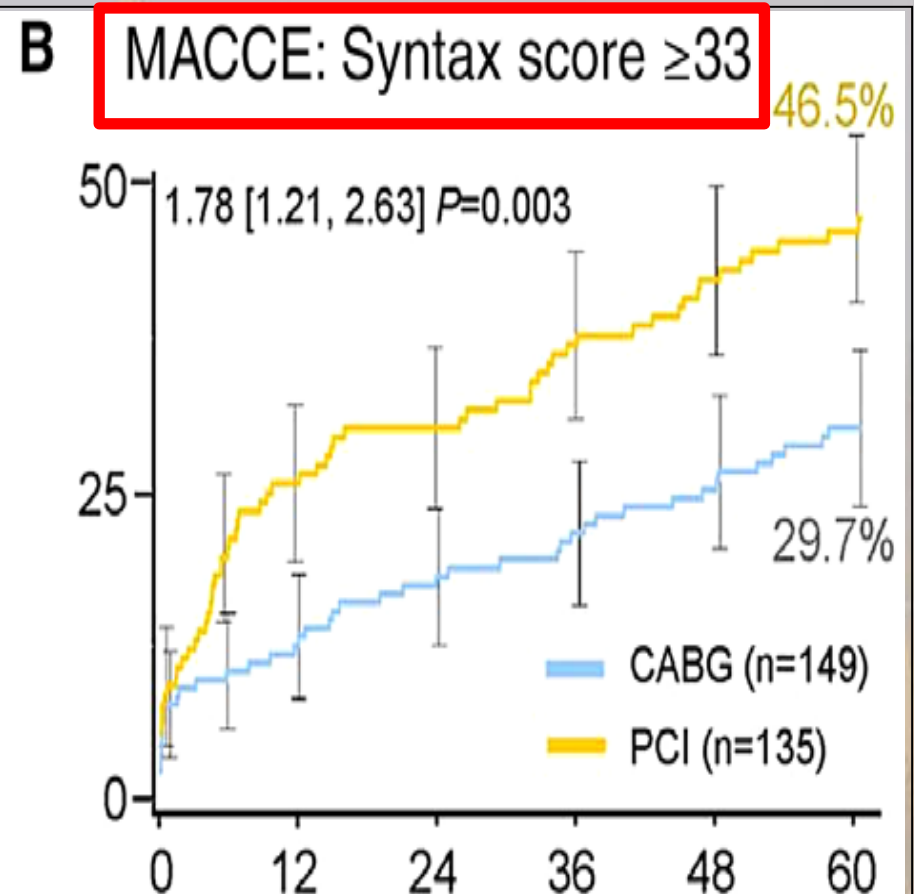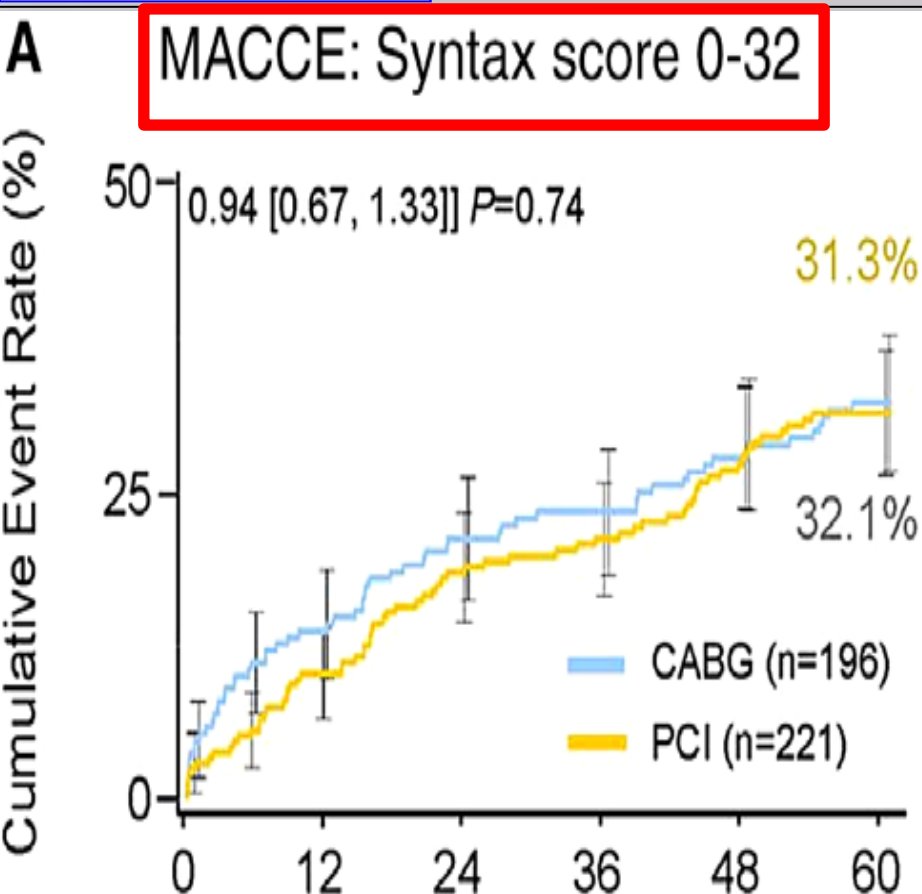1102 stents and 1138 CABG (more severe disease) followed for 3 years**

Table 3. Hazard Ratios for Clinical Outcomes after Stenting as Compared with after CABG among Propensity-Matched Patients.*

Outcome	Overall Cohort (N = 542 pairs)		Wave 1 (N = 207 pairs) BMS		Wave 2 (N = 396 p) DES	
	Hazard Ratio (95% CI)	P Value	Hazard Ratio (95% CI)	P Value	Hazard Ratio (95% CI)	P Value
Death	1.18 (0.77–1.80)	0.45	1.04 (0.59–1.83)	0.90	1.36 (0.80–2.30)	0.26
Composite outcome of death, Q-wave myocardial infarction, or stroke	1.10 (0.75–1.62)	0.61	0.86 (0.50–1.49)	0.59	1.40 (0.88–2.22)	0.15
Target-vessel revascularization	4.76 (2.80–8.11)	<0.001	10.70 (3.80–29.90)	<0.001	5.96 (2.51–14.10)	<0.001

In Propensity-Matched PCI vs CABG Patients: PCI with BMS or DES led to Non-significant Increased Hazard Ratio for Death, and Composite (Death/MI/Stroke) but Much Greater Target Vessel Revascularization (HR > 5; p<0.001)

Basis for PRECOMBAT Trial of 600 patients PCI vs CABG

A MACCE: Syntax score 0-32

0.94 [0.67, 1.33]] *P*=0.74

31.3%

32.1%

CABG (n=196)
PCI (n=221)

B MACCE: Syntax score ≥33

46.5%

1.78 [1.21, 2.63] *P*=0.003

29.7%

CABG (n=149)
PCI (n=135)

① Accelerating Divergence of Benefits in Favour of CABG in >32
② Used to define patients in the EXCEL trial (Syntax Scores <33)
③ CABG: Competitive flow if lower SYNTAX scores (ie less proximal CAD) ?

Five-Year Outcomes after PCI or CABG for Left Main Coronary Disease

G.W. Stone, A.P. Kappetein, J.F. Sabik, S.J. Pocock, M.-C. Morice, J. Puskas, D.E. Kandzari, D. Karmpaliotis, W.M. Brown III, N.J. Lembo, 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.E. Buszman, A. Bochenek, E. Schampaert, P. Pagé, R. Modolo, J. Gregson, C.A. Simonton, R. Mehran, I. Kosmidou, P. Généreux, A. Crowley, O. Dressler, and P.W. Serruys, for the EXCEL Trial Investigators*

*

- LARGEST, MOST DEFINITIVE TRIAL OF PCI vs CABG in LM
- SELECTED Patients: SYNTAX SCORES <33 (@ 1/3 of routine practice)
- 1905 (of 2600) patients randomized (but enrolment stopped early) !
- MEAN AGE 66: (life expectancy of 15-20 years)
- Primary Outcome: Composite of Death, MI, Stroke (NOT Revasc)
- Used new biochemical definition of MI (BUT did not include UDMI data)

Oxford Cardiologists and Surgeons 2nd largest recruiter worldwide to EXCEL trial
37 Authors (DT, chair of surgical committee, withdrew) *

CONCERN 1: Excess and Accelerating Mortality with PCI at 5 years

A **Death from Any Cause**

Odds ratio, 1.38 (95% CI, 1.03−1.85)

PCI — 13.0
CABG — 9.9
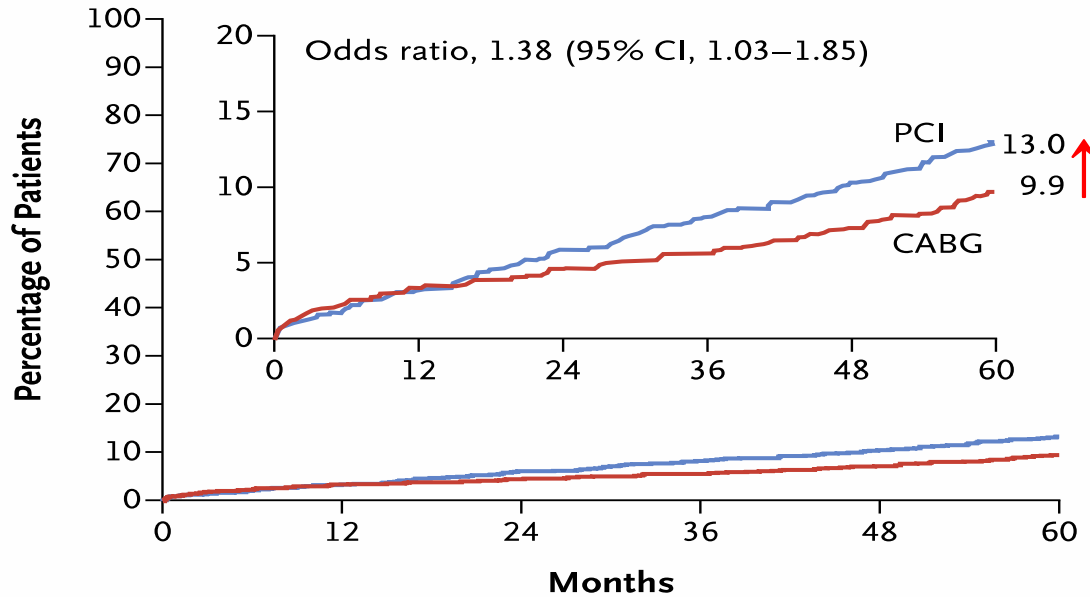
No. at Risk

PCI	948	902	868	841	810	545
CABG	957	889	865	844	815	596

Low-Risk Patients:

1) Mean age 66 yr,
2) Low/ intermediate severity LM disease (Syntax Scores < 33)

PCI at 5years:

- ↑ Death (38%),
- ↑ Non-procedural MI (ie real MI),
- ↑ Repeat Revasc,
- = Stroke:

NEJM Editor Initial Review: 'The finding of a higher mortality rate in one group than another in a clinical trial (unless the difference is clearly trivial) should receive central emphasis in the report of the results, and we would generally consider it important to include such information in the concluding statement in the final paragraph'.

'EXCEL CONCLUSIONS In patients with left main coronary artery disease of low or intermediate anatomical complexity, there was no significant difference between PCI and CABG with respect to the rate of the composite outcome of death, stroke, or myocardial infarction at 5 years.'

Prof DT : Final Conclusions Do NOT Reflect Real Mortality/MI Data (DT Resigned)

Implications of Alternative Definitions of Peri-Procedural Myocardial Infarction After Coronary Revascularization

[JACC Oct 6 2020]

John Gregson, PhD,[a] Gregg W. Stone, MD,[b,c] Ori Ben-Yehuda, MD,[c,d] Björn Redfors, MD, PhD,[c,d,e]

David E. Kandzari, MD,[f] Marie-Claude Morice, MD,[g] Martin B. Leon, MD,[c,d] Ioanna Kosmidou, MD, PhD,[c,d]

Nicholas J. Lembo, MD,[c,d] W. Morris Brown III, MD,[f] Dimitri Karmpaliotis, MD,[c,d] Adrian P. Banning, MD,[h]

Jose Pomar, MD,[i] Manel Sabaté, MD,[i] Charles A. Simonton, MD,[j] Ovidiu Dressler, MD,[c]

Arie Pieter Kappetein, MD, PhD,[k] Joseph F. Sabik III, MD,[l] Patrick W. Serruys, MD, PhD,[m,n] Stuart J. Pocock, PhD[a]

EXCEL
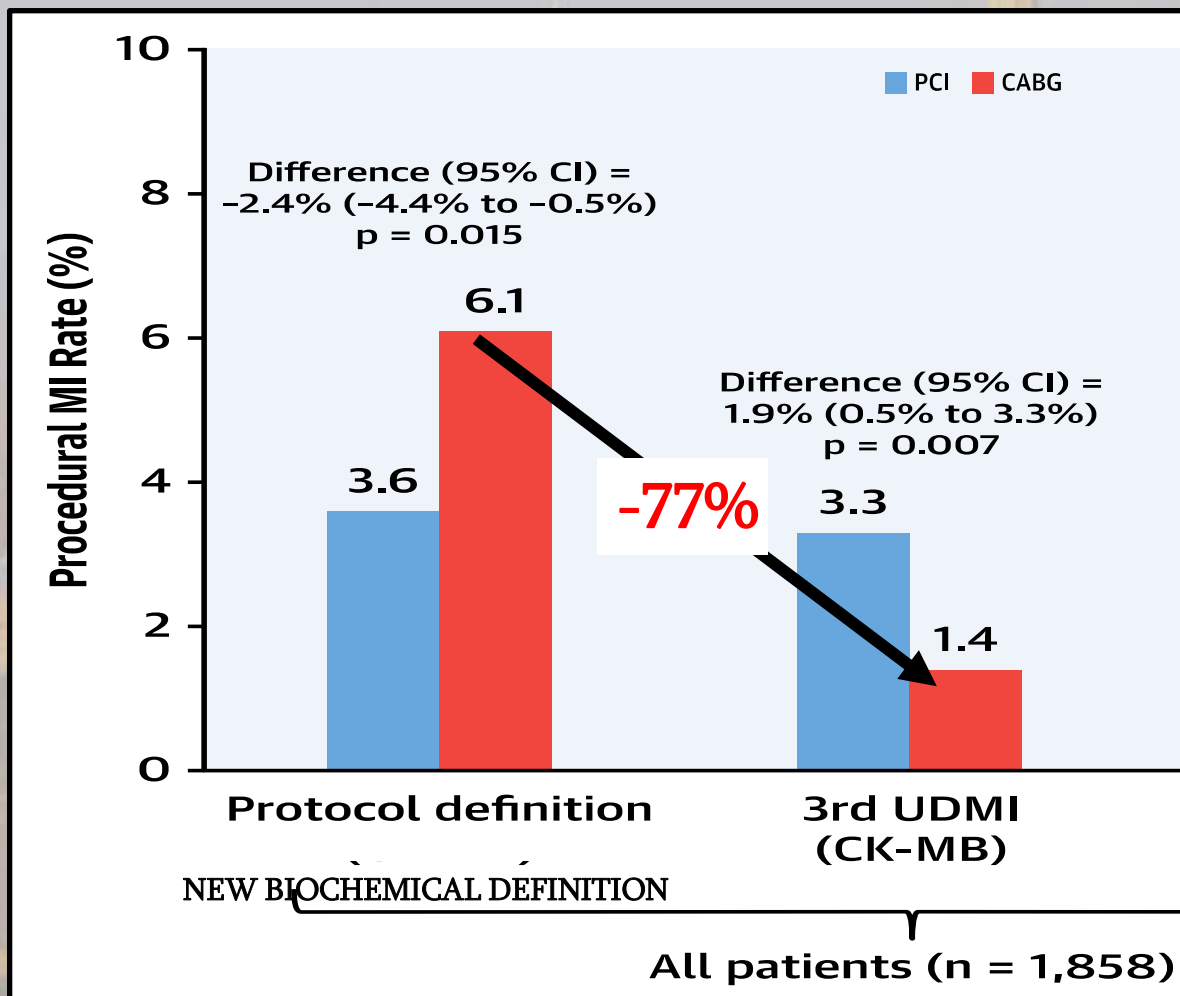
Left Main: The Continuing Debate: What to Believe ?

Mortality after drug-eluting stents vs. coronary artery bypass grafting for left main coronary artery disease: a meta-analysis of randomized controlled trials

[EHJ published online 2nd March 2020]

Yousif Ahmad [iD] [1,2]*, James P. Howard [iD] [2], Ahran D. Arnold [iD] [2], Christopher M. Cook[2], Megha Prasad[1], Ziad A. Ali[1,3], Manish A. Parikh[1], Ioanna Kosmidou [iD] [1,3], Darrel P. Francis[2], Jeffrey W. Moses[1,3], Martin B. Leon[1,3], Ajay J. Kirtane [iD] [1,3], Gregg W. Stone[3,4], and Dimitri Karmpaliotis[1]

[1]Center for Interventional Vascular Therapy, Columbia University Medical Center, NewYork—Presbyterian Hospital, 161 Fort Washington Avenue, New York, NY 10032, USA; [2]National Heart and Lung Institute, Imperial College London, Du Cane Road, London W12 0HS, UK; [3]The Cardiovascular Research Foundation, 1700 Broadway, New York, NY 10019, USA; and [4]Mount Sinai Hospital, Icahn School of Medicine at Mount Sinai, 1190 Fifth Avenue, New York, NY 10029, USA

Conclusion

5 RCTs
N=4,612

The totality of randomized clinical trial evidence demonstrated similar long-term mortality after PCI with DES compared with CABG in patients with LMCAD. Nor were there significant differences in cardiac death, stroke, or MI between PCI and CABG. Unplanned revascularization procedures were less common after CABG compared with PCI. These findings may inform clinical decision-making between cardiologists, surgeons, and patients with LMCAD.

Meta-analysis 'Magic' (i): 14 Authors (no surgeons)
- Dilute the Largest, Most Definitive LM Trial (EXCEL) with 4 older, smaller, weaker studies until mortality benefit of CABG disappears !
- No indication these were highly selected LM with relatively short follow-up

Meta-analysis 'Magic' (ii): A record speed of acceptance and publication ?
11 days from submission to review, revision, resubmission and final acceptance
1) Received 2/2/20
2) Revised 10/2/20
3) Accepted 13/2/20
4) Published 02/03/20

Left Main: The Continuing Debate: What to Believe ?

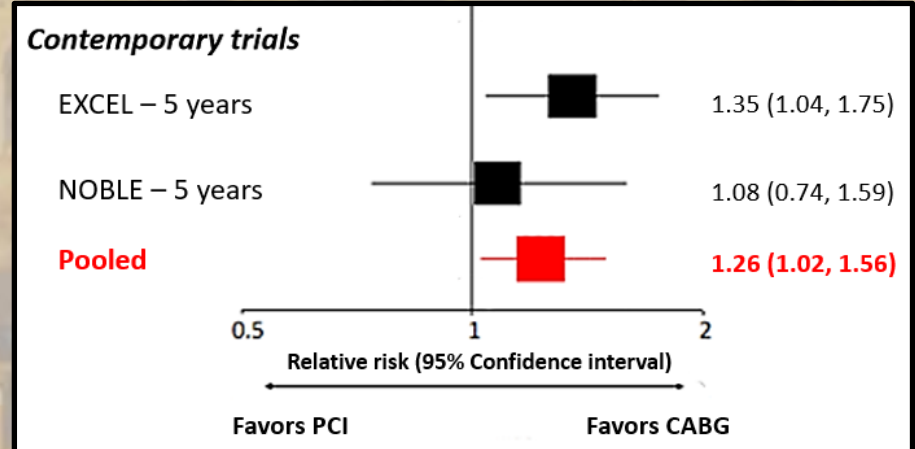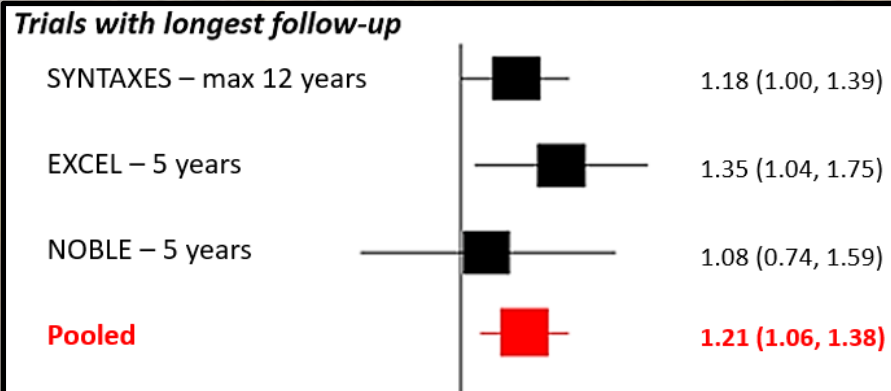## Bayesian Interpretation of the EXCEL Trial and Other Randomized Clinical Trials of Left Main Coronary Artery Revascularization

James M. Brophy, MD, PhD

CONCLUSIONS AND RELEVANCE Bayesian analysis assisted in RCT data interpretation and specifically suggested, whether based on EXCEL results alone or on the totality of available evidence, that PCI was associated with inferior long-term results for all events, including mortality, compared with CABG for patients with left main coronary artery disease.

Gaudino M, Freemantle N, Farkouh ME, JTCVS (2021)

Trials with longest follow-up

SYNTAXES – max 12 years	1.18 (1.00, 1.39)
EXCEL – 5 years	1.35 (1.04, 1.75)
NOBLE – 5 years	1.08 (0.74, 1.59)
Pooled	**1.21 (1.06, 1.38)**

Contemporary trials

EXCEL – 5 years	1.35 (1.04, 1.75)
NOBLE – 5 years	1.08 (0.74, 1.59)
Pooled	**1.26 (1.02, 1.56)**

Relative risk (95% Confidence interval)

Favors PCI   Favors CABG

Patients with SYNTAX scores <33

Percutaneous coronary intervention with drug-eluting stents versus coronary artery bypass grafting in left main coronary artery disease: an individual patient data meta-analysis [Lancet 2021]

Marc S Sabatine*, Brian A Bergmark*, Sabina A Murphy, Patrick T O'Gara, Peter K Smith, Patrick W Serruys, A Pieter Kappetein, Seung-Jung Park, Duk-Woo Park, Evald H Christiansen, Niels R Holm, Per H Nielsen, Gregg W Stone, Joseph F Sabik, Eugene Braunwald

- 4 RCT (4394 patients): SYNTAX, PRECOMBAT, NOBLE, EXCEL
- Median age 66 (expected life expectancy 15-20 years)
- Median SYNTAX score of 25 (75% <32): 'real life' 66%> 32
- 25% DM

5 years	PCI (2197)	CABG (2197)	P	5 years
Death	11.2%	10.2%	0.33	↑
Spontaneous MI	6.2%	2.6%	**<0.0001**	↑↑↑
Repeat Revasc	18.3%	10.7%	**<0.0001**	↑↑↑
Stroke	2.7%	3.1%	**0.36**	**=**

Manuscript Title gives no indication that results applicable to @ 1/3 of LM
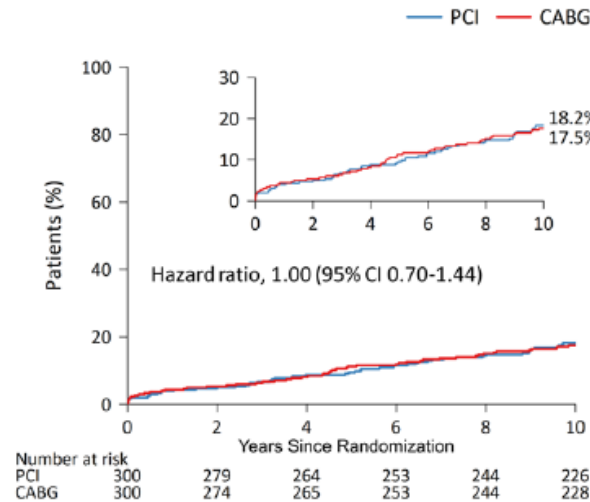
Ten-Year Outcomes After Drug-Eluting Stents Versus Coronary Artery Bypass Grafting for Left Main Coronary Disease
Extended Follow-Up of the PRECOMBAT Trial

[Circ 2020]

A Primary Composite Outcome — PCI — CABG; 29.8%, 24.7%; Hazard Ratio, 1.25 (95% CI 0.93–1.69)
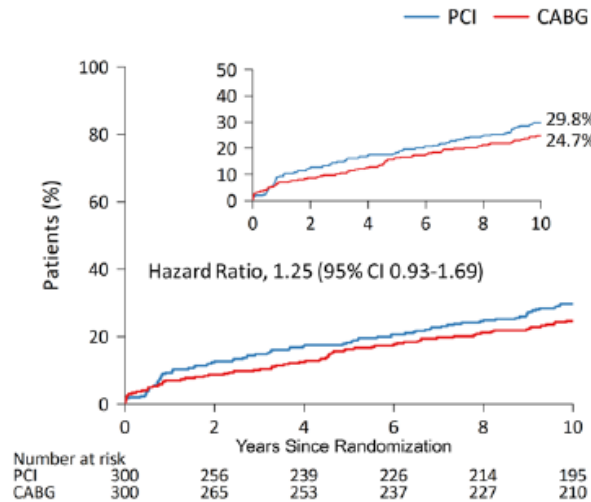
B Composite of Death, Myocardial Infarction, or Stroke — PCI — CABG; 18.2%, 17.5%; Hazard ratio, 1.00 (95% CI 0.70–1.44)

C Death from Any Cause — PCI — CABG; 14.5%, 13.8%; Hazard ratio, 1.13 (95% CI 0.75–1.70)
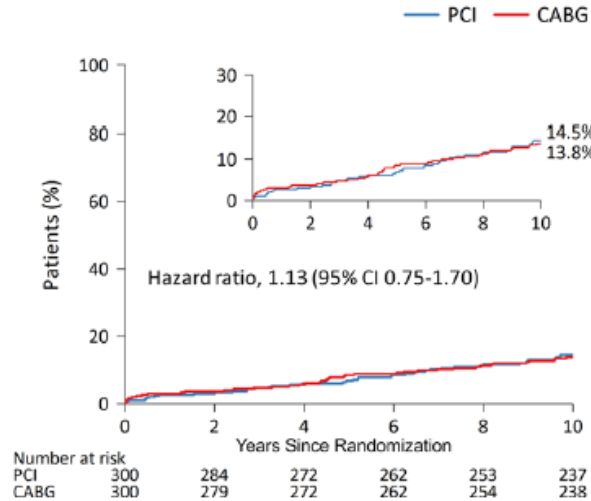
D Ischemia-Driven Target-Vessel Revascularization — PCI — CABG; 16.1%, 8.0%; Hazard ratio, 1.98 (95% CI 1.21–3.21)
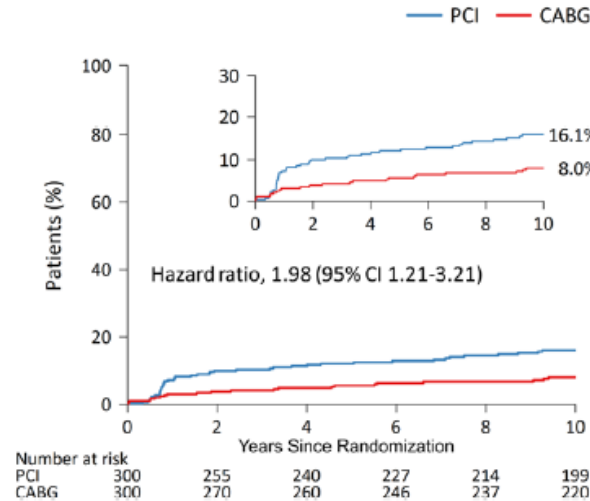
PRECOMBAT

N=600

Highly Selected

Low Syntax Scores

10 yr: ≈ Survival

⬇ Revasc with CABG

10-Year Outcomes of Stents Versus Coronary Artery Bypass Grafting for Left Main Coronary Artery Disease

JACC DEC 2018

Duk-Woo Park, MD,[a,*] Jung-Min Ahn, MD,[a,*] Sung-Cheol Yun, PhD,[b] Yong-Hoon Yoon, MD,[a] Do-Yoon Kang, MD,[a] Pil Hyung Lee, MD,[a] Seung-Whan Lee, MD,[a] Seong-Wook Park, MD,[a] Ki Bae S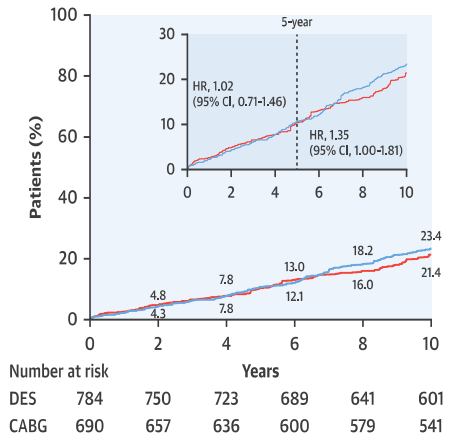eung, MD,[c] Hyeon-Cheol Gwon, MD,[d] Myung-Ho Jeong, MD,[e] Yangsoo Jang, MD,[f] Hyo-Soo Kim, MD,[g] In-Whan Seong, MD,[h] Hun Sik Park, MD,[i] Taehoon Ahn, MD,[j] In-Ho Chae, MD,[k] Seung-Jea Tahk, MD,[l] Seung-Jung Park, MD[a]

CENTRAL ILLUSTRATION Long-Term Outcomes of Drug-Eluting Stents Versus Coronary Artery Bypass Grafting for Left Main Disease

N=1474

Significant increase in mortality with DES vs CABG between 5 and 10 years
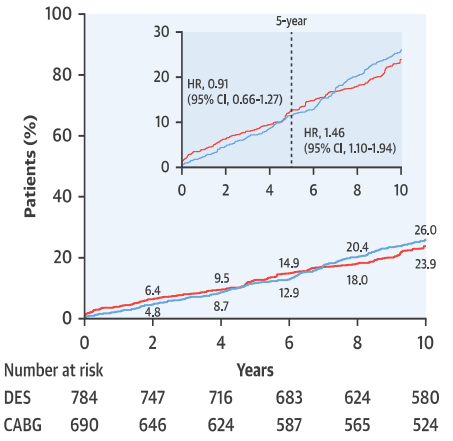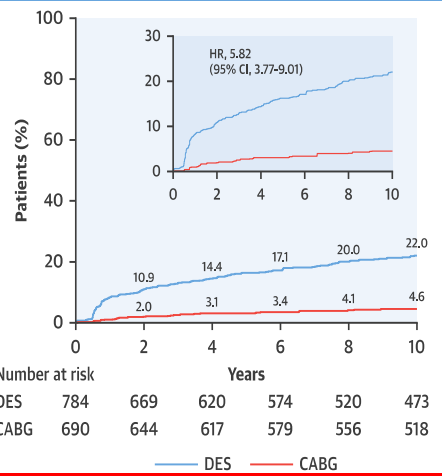
Propensity Matching
- 'Real Life' Patients
- (Still Lower Severity
- Disease !)
- CABG Cohort More Severe CAD

- AGE: 62
- DM: 30%
- EF: 60%
- LM Ostium/Shaft: 48%

LM only: 12%
+1 VD: 17%
+ 2VD: 32%
+ 3VD: 38%

Long-Term Outcomes After PCI or CABG for Left Main Coronary Artery Disease According to Lesion Location

[JACCCI 2020]

Junho Hyun, MD, Ju Hyeon Kim, MD, Yeongjin Jeong, MD, KyungJin Choe, MD, Junghoon Lee, MD, Yujin Yang, MD, Tae Oh Kim, MD, Hanbit Park, MD, Sang-Cheol Cho, MD, Euihong Ko, MD, Do-Yoon Kang, MD, Pil Hyung Lee, MD, Jung-Min Ahn, MD, Seung-Jung Park, MD, Duk-Woo Park, MD, on behalf of the MAIN-COMPARE Registry
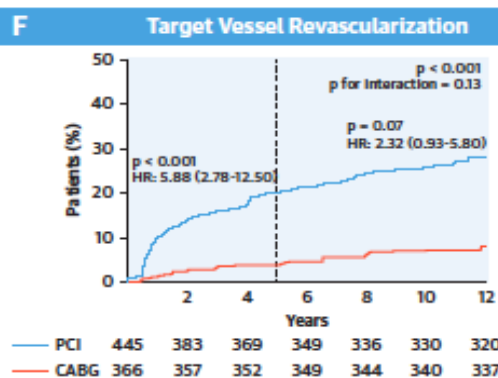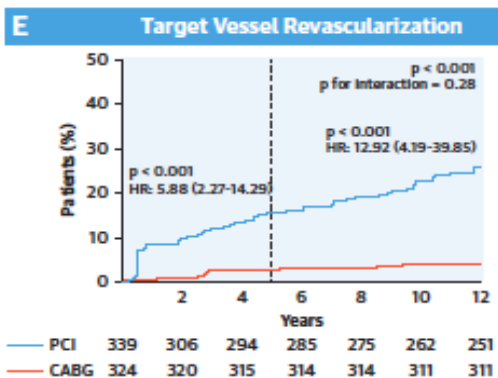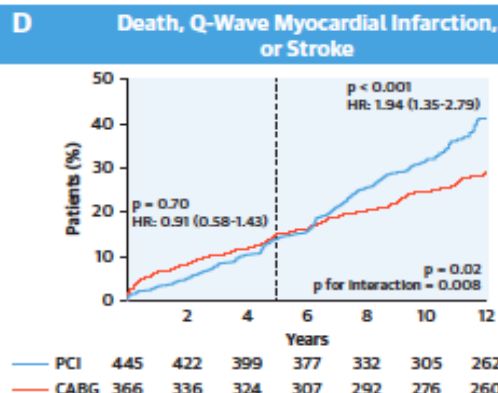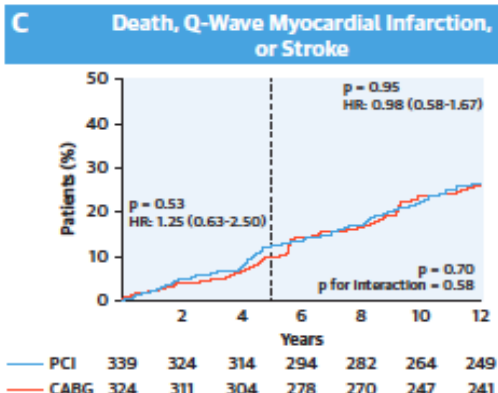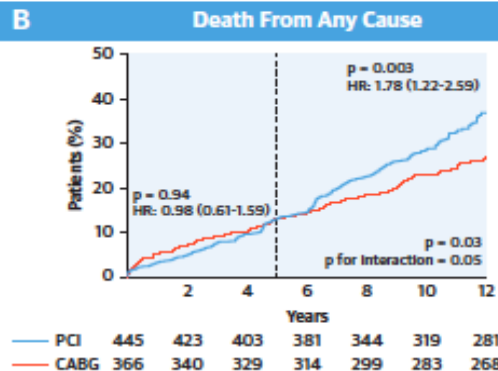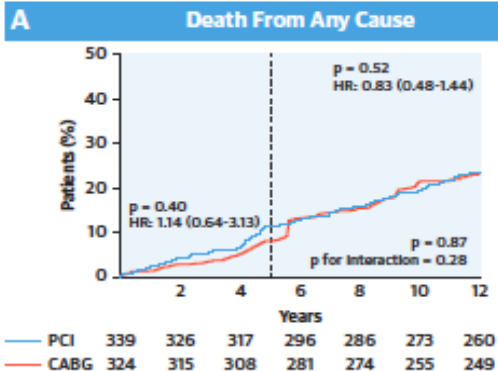
LESION LOCATION

MAIN-COMPARE REGISTRY

549 patients @ 12 years

Distal/Bifurcation LM:

1) ↑ Mortality

2) ↑ MACE

3) ↑ Revasc

2018 ESC/EACTS Guidelines on myocardial revascularization

Recommendations according to extent of CAD	CABG		PCI	
	Class[a]	Level[b]	Class[a]	Level[b]
One-vessel CAD				
Without proximal LAD stenosis.	IIb	C	I	C
With proximal LAD stenosis.[68,101,139–144]	I	A	I	A
Two-vessel CAD				
Without proximal LAD stenosis.	IIb	C	I	C
With proximal LAD stenosis.[68,70,73]	I	B	I	C
Left main CAD				
Left main disease with low SYNTAX score (0 - 22).[69,121,122,124,145–148]	I	A	I	A
Left main disease with intermediate SYNTAX score (23 - 32).[69,121,122,124,145–148]	I	A	IIa ?	A
Left main disease with high SYNTAX score (≥33).[c 69,121,122,124,146–148] 66%	I	A	III	B
Three-vessel CAD without diabetes mellitus				
Three-vessel disease with low SYNTAX score (0 - 22).[102,105,121,123,124,135,149]	I	A	I	A
Three-vessel disease with intermediate or high SYNTAX score (>22).[c 102,105,121,123,124,135,149] 79%	I	A	III	A
Three-vessel CAD with diabetes mellitus				
Three-vessel disease with low SYNTAX score 0–22.[102,105,121,123,124,135,150–157]	I	A	IIb ?	A
Three-vessel disease with intermediate or high SYNTAX score (>22).[c 102,105,121,123,124,135,150–157]	I	A	III	A

CABG would be better if more arterial grafts and greater use of medical therapy !!

Summary and Conclusions: LM CABG vs PCI

Multi-Vessel Disease (No Left Main):

1) CABG: Clearly superior for All SYNTAX scores and Especially in DM

Left Main Disease (of whom up to 90% also have Multi-Vessel CAD):

1) CABG: Clearly Superior For Severe Disease (Syntax scores >32)

2) The two largest, definitive trials of PCI vs CABG in patients with Low/Intermediate Severity LM Disease (SYNTAX scores < 33) show CABG to be superior for Mortality (EXCEL) and Non-procedural MI and Repeat Revascularization (EXCEL and NOBLE)

3) Most LM long-term (5 - 10 years) mortality data show superior survival for CABG in patients with low/intermediate SYNTAX Scores (none show PCI to be superior to CABG) and always for repeat revascularization

4) LM Location (ostial/mid shaft vs bifurcation) is vital to subsequent outcomes and CABG appears superior for distal/bifurcation lesions while PCI may offer equal outcomes in non-bifurcation lesions, and especially in the absence of significant additional proximal CAD (but still a much higher need for repeat revasc)

5) Repeat revascularization predicts increased mortality

Personal View: Current data still suggests a cautious approach to the use of stents in patients with Low/Intermediate severity Left Main Disease **and especially in distal/ bifurcation lesions and in younger patients with anticipated long-life expectancy.**

LM: SYNTAXES at 10 years: [Thuijs et al Lancet 2019]

B   **Left main coronary artery disease**

PCI group
CABG group

N=705
Mean Syntax Score 29

HR 0·90 (95% CI 0·68–1·20)
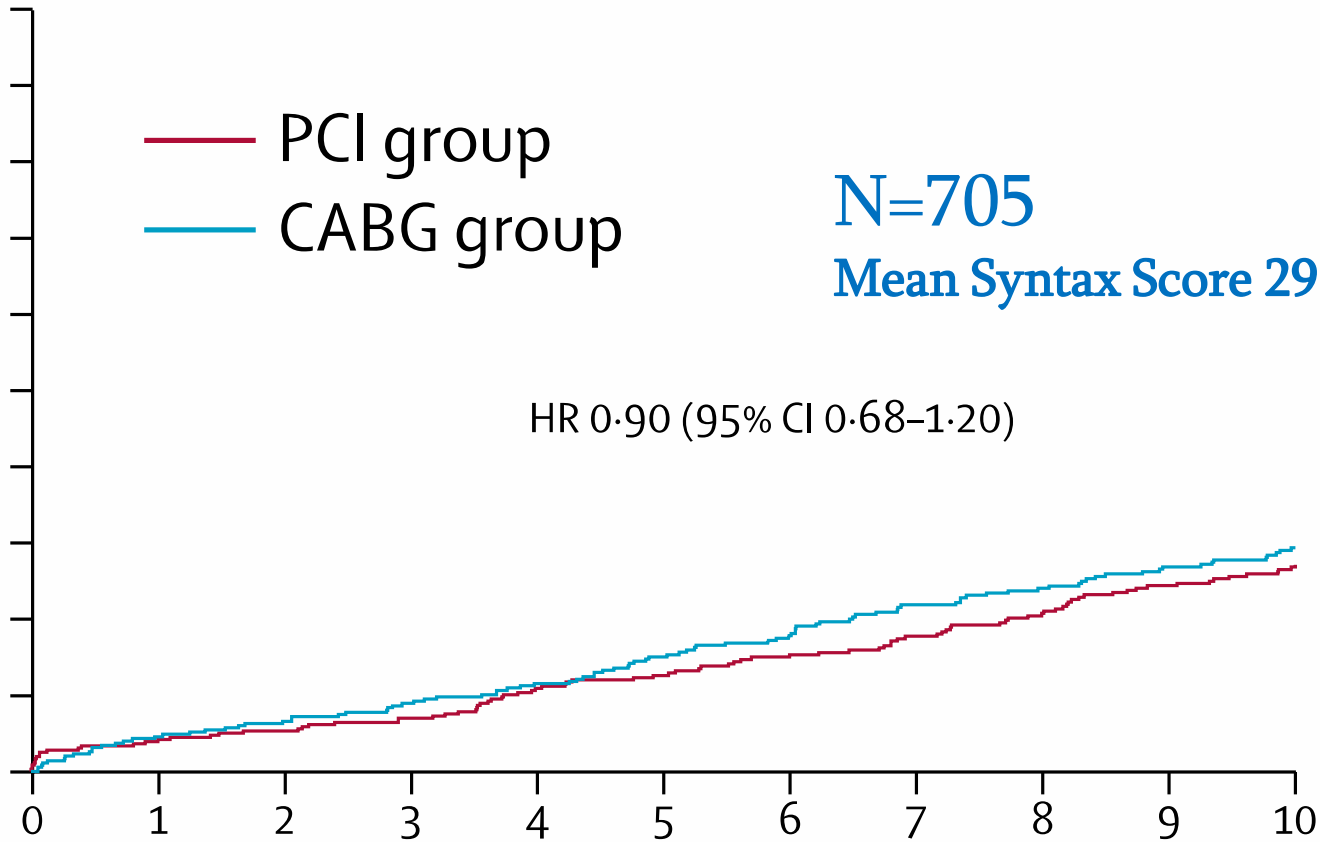
0	1	2	3	4	5	6	7	8	9	10
357	343	338	332	318	295	282	273	262	249	237
348	332	323	314	305	283	265	251	244	235	223

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,

LM: NOBLE RCT
1201 Patients
No Registry Patients
Lancet 2016

Mean Age: 66 vs EXCEL 66
Mean SYNTAX Score: 22 vs EXCEL 26)
Diabetes:15% vs EXCEL 30%

HR 1·46, 1·10–1·95, p=0·01

Number at risk

PCI	592	539	442	313	227	127
CABG	592	536	440	319	219	129

HR 1·04, 0·65–1·67; p=0·86

Mortality
12%   9%

Number at risk

PCI	592	539	442	313	227	127
CABG	592	536	440	319	219	129

HR 2·88, 1·40–5·90; p=0·004

MI
7%   2%

592	539	442	313	227	127
592	536	440	319	219	129

HR 1·50, 1·04–2·17, p=0·03

REVASC
16%   10%

Number at risk

PCI	592	539	442	313	227	127
CABG	592	536	440	319	219	129

HR 2·25, 0·92–5·48, p=0·07

STROKE
5%   2%
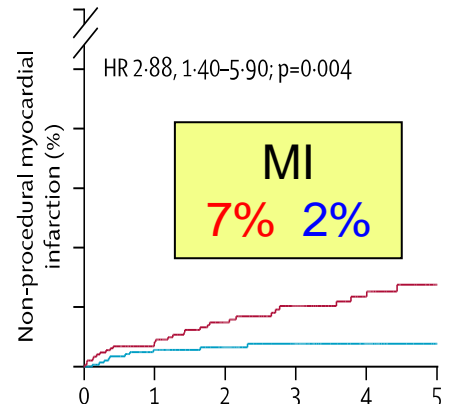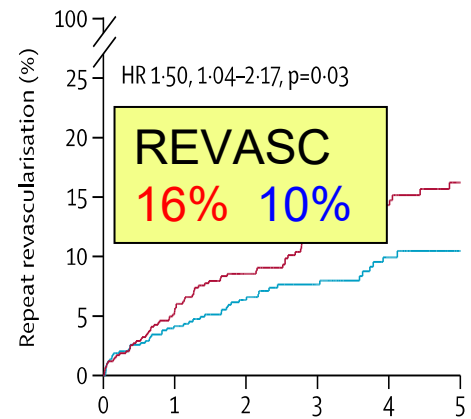
592	539	442	313	227	127
592	536	440	319	219	129

Left Main (LM): PCI vs CABG

1) Key Issues in Data Interpretation

2) PCI vs CABG in Multi-vessel CAD (No Left Main)

3) Changing Perspective of PCI in LM Disease Over Last Decade

4) The Most Recent LM RCTs (ISCHEMIA trial excluded LM disease)

5) Survival Data at 5-10 years

6) Impact of SYNTAX Scores

7) Impact of Diabetes

8) Impact of LM Location (Ostial/Shaft vs Distal/Bifurcation)

9) Impact of Repeat Revascularization

CABG vs PCI: Multi-Vessel Disease (No Left Main)

1) CABG: ↑ Survival

2) CABG: ↓ Myocardial Infarction

3) CABG: ↓ Repeat Revascularization

4) CABG: Benefits ↑ Diabetes

5) CABG Benefits ↑ Impaired Left Ventricular Function

6) Possible Small (1-2% Increase in Risk of Stroke Over 5 years)

What Is The Situation For Left Main Disease ?

EXCEL: The Controversy

Four Major Concerns in EXCEL 5-Year Analysis:

1) Interpretation of the Mortality Data
   ('one of 20 underpowered secondary endpoints')

2) Persistent Failure to Publish Protocol Specified UDMI Data
   (eventually 8 months later at insistence of NEJM editors)

3) Changed Statistical Analysis: Non-Inferiority (3 yrs) to
   Superiority (5 yrs)

4) Failure to Share Trial Data (Unusual for Legitimate Request)

Controversy Extended to both the Medical Domain/Literature (EACTS, ESC, AATS, STS) and Public Domain (BBC Dec 2019, March 2020)

1 **Correspondence**

2 PCI or CABG for Left Main Coronary Artery Disease

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DE: jjarcho
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10 To the Editor: In the {sa1q1}EXCEL (Evaluation of XIENCE versus Coronary
11 Artery Bypass Surgery for Effectiveness of Left Main Revascularization) trial
12 (Nov. 7 issue),[1] Stone et al. report no significant difference in the 5-year
13 composite outcome of death, stroke, or myocardial infarction among patients
14 with stable left main coronary artery disease who underwent either percutaneous
15 coronary intervention (PCI) with drug-eluting stents or coronary-artery bypass
16 grafting (CABG). We have three fundamental concerns regarding these findings.
17   First, the incidence of death from any cause {sa1q2}was 13.0% in the PCI
18 group and 9.0% in the CABG group (odds ratio, 1.38; 95% confidence interval
19 [CI], 1.03 to 1.85). Although the difference was not adjusted for multiple
20 comparisons, the increased risk is unequivocally the most important outcome
21 in a relatively young population (average age, 66 years), particularly since
22 the between-group difference continued to diverge over time. Second, the
23 cause of death was adjudicated ({sa1q3}as definite cardiovascular, definite
24 noncardiovascular, or undetermined, with undetermined causes classified as
25 cardiovascular), even though such adjudication is notoriously susceptible to bias,
26 especially in an open-label trial. Third, the investigators used a new, untested
27 definition of periprocedural myocardial infarction that clearly penalizes surgery
28 and that is the key driver of the composite outcome that claims no difference
29 in the two treatment strategies. The EXCEL protocol repeatedly stated that the
30 Universal Definition of Myocardial Infarction would also be used, but such
31 data were not provided. Consequently, the first author of this letter withdrew
32 authorship from the manuscript.

Conflict
33   No potential conflict of interest relevant to this letter was reported.

Reference
1.   Stone GW, Kappetein AP, Sabik JF, et al. Five-year outcomes after PCI or CABG for left main
coronary disease. N Engl J Med 2019;381:1820-30. [PMID: 31562798]

EXCEL published
NEJM 7th November 2019

DT/MG Letter submitted
14th November 2019:
'3 fundamental concerns'

(i) Differential and Accelerating Death Rates in the PCI group
(ii) 'Adjudicated' Death
(iii) New untested definition of MI + failure to provide protocol specified UDMI data

Proofs of letter received
20 March 2020

Letter finally published
16 July 2020

8 months after the trial !!

EXCEL EXCLUDING NEW PERI-PROCEDURAL MI DEFINITION (M Gaudino, NY)

Endpoint	PCI Events	PCI Total	CABG Events	CABG Total	Odds Ratio	OR	95%CI
Original analysis							
Death, stroke or MI	203	948	176	957		1.19	[0.95; 1.50]
Alternate analysis							
Death, stroke, non-peri-procedural MI	204	948	153	957		1.44	[1.14; 1.82]
Death	119	948	89	957		1.38	[1.03; 1.85]
Stroke	26	948	33	957		0.78	[0.46; 1.31]
Peri-procedural MI	37	948	57	957		0.63	[0.41; 0.96]
Non-peri-procedural MI	59	948	31	957		1.96	[1.25; 3.06]

CABG a 'CLEAR WINNER' for
(i)   the Composite End-Point and
(ii)   the Individual Components of: Death, Non-Procedural (ie 'Real' MI)
(iii) (and Repeat Revascularization)

Ten-year Outcomes After Drug-Eluting Stents or Bypass Surgery for Left Main Coronary Disease in Patients With and Without Diabetes Mellitus: The PRECOMBAT Extended Follow-Up Study

[JAHA 2021]

Yeong Jin Jeong (ID), MD*; Jung-Min Ahn (ID), MD*; Junho Hyun (ID), MD; Junghoon Lee (ID), MD; Ju Hyeon Kim, MD; Yujin Yang, MD; Kyungjin Choe, MD; Hanbit Park, MD; Do-Yoon Kang, MD; Pil Hyung Lee, MD; Soo-Jin Kang, MD; Seung-Whan Lee (ID), MD; Young-Hak Kim, MD; Cheol Whan Lee, MD; Seong-Wook Park, MD; Seung-Jung Park (ID), MD; Duk-Woo Park (ID), MD, PhD
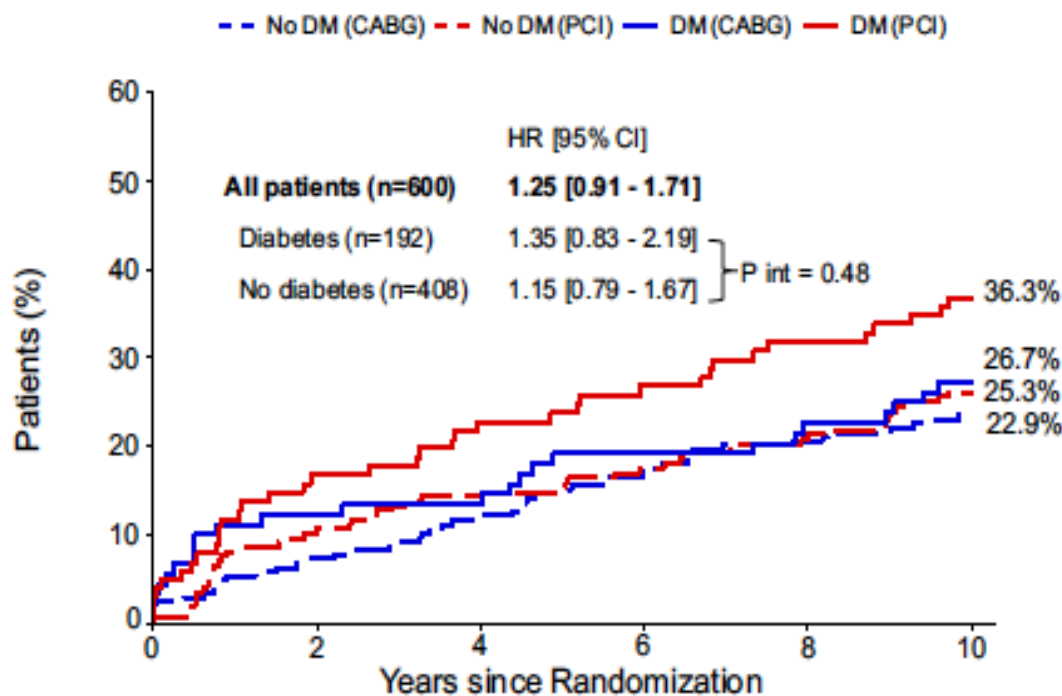
DIABETES (n=192)

PRECOMBAT: n=600 (low severity CAD)

PCI vs CABG:

MACCE: 36% vs 27% (-9%) (p=0.2)

DEATH: 18% vs 13% (-5%) (p=0.2) (supplement)

Mortality After Repeat Revascularization Following PCI or CABG for Left Main Disease

The EXCEL Trial

Gennaro Giustino, MD,[a] Patrick W. Serruys, MD, PhD,[b] Joseph F. Sabik III, MD,[c] Roxana Mehran, MD,[a,d] Akiko Maehara, MD,[d,e] John D. Puskas, MD,[f] Charles A. Simonton, MD,[g] Nicholas J. Lembo, MD,[d,e] David E. Kandzari, MD,[h] Marie-Claude Morice, MD,[i] David P. Taggart, MD, PhD,[j] Anthony H. Gershlick, MD,[k] Michael Ragosta III, MD,[l] Irving L. Kron, MD,[l] Yangbo Liu, MS,[d] Zixuan Zhang, MS,[d] Thomas McAndrew, PhD,[d] Ovidiu Dressler, MD,[d] Philippe Généreux, MD,[d,m,n] Ori Ben-Yehuda, MD,[d,e] Stuart J. Pocock, PhD,[o] Arie Pieter Kappetein, MD, PhD,[p] Gregg W. Stone, MD[d,e]

FIGURE 2 Early and Late Risk for Mortality After Any Repeat Revascularization in the Overall Population

All-Cause Mortality

Cardiovascular Mortality
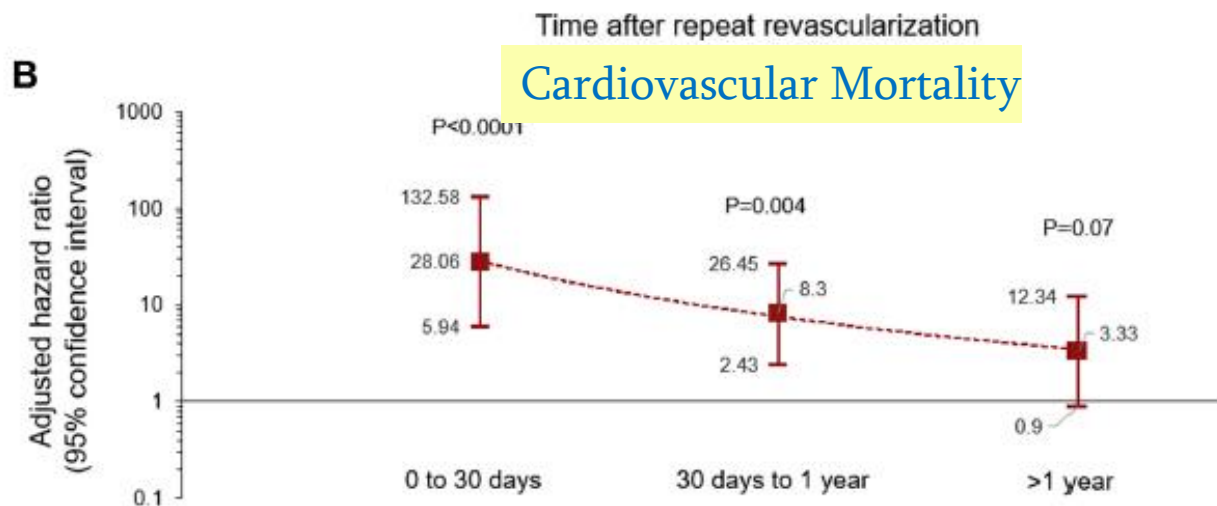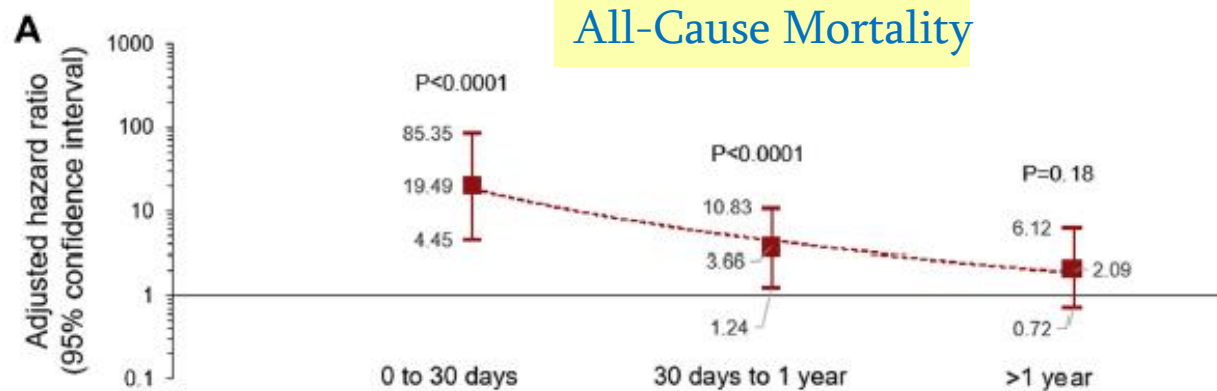
Repeat Revascularization is a Strong Predictor of Increased Mortality

3 REASONS WHY CABG HAS A SURVIVAL BENEFIT OVER PCI

1 **Anatomically, atheroma is mainly located in the proximal coronary arteries**
Placing bypass grafts to the **MID CORONARY VESSEL** has **TWO** effects
(i) Complexity of proximal '**CULPRIT**' lesion is irrelevant
(ii) Over the long term offers prophylaxis against **FUTURE** proximal 'culprit' lesions
In contrast, PCI only treats '**SUITABLE**' localised proximal 'culprit' lesions but has **NO PROPHYLACTIC BENEFIT** against new proximal disease

2 THE NEW ENGLAND JOURNAL OF MEDICINE   Aug. 25, 1988

IMA elutes NO into coronary circulation reducing risk of further disease
DIFFERENCE BETWEEN ENDOTHELIUM-DEPENDENT RELAXATION IN ARTERIAL AND IN VENOUS CORONARY BYPASS GRAFTS

THOMAS F. LÜSCHER, M.D., DENNIS DIEDERICH, M.D., ROBERT SIEBENMANN, M.D., KURT LEHMANN, M.D.,

Drug-Eluting Stent and Coronary Thrombosis
Biological Mechanisms and Clinical Implications [CIRC 2007]

Thomas F. Lüscher, MD; Jan Steffel, MD; Franz R. Eberli, MD; Michael Joner, MD;

impairs re-endothelialization, downstream endothelial function and creates pro-thrombotic milieu

3 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)
Residual SYNTAX score >8 increases mortality and MACCE (Farooq, Serruys CIRC 2013)

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

EXCEL: 5 YEARS 'Clinical Reality' [NEJM 2019]

A Death from Any Cause

Odds ratio, 1.38 (95% CI, 1.03–1.85)

PCI 13.0
CABG 9.9

Percentage of Patients

Months
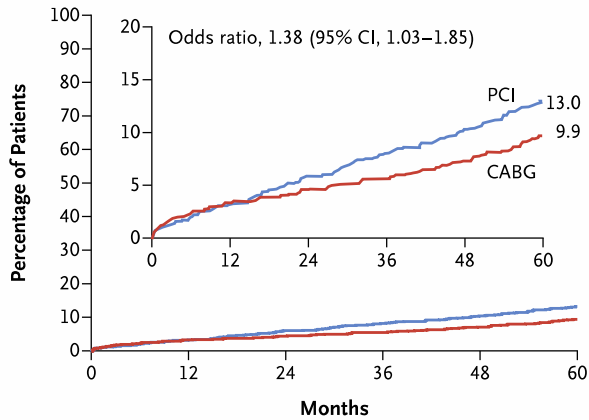
No. at Risk
PCI	948	902	868	841	810	545
CABG	957	889	865	844	815	596

B Stroke

Odds ratio, 0.78 (95% CI, 0.46–1.31)

CABG 3.7
PCI 2.9

Percentage of Patients

Months
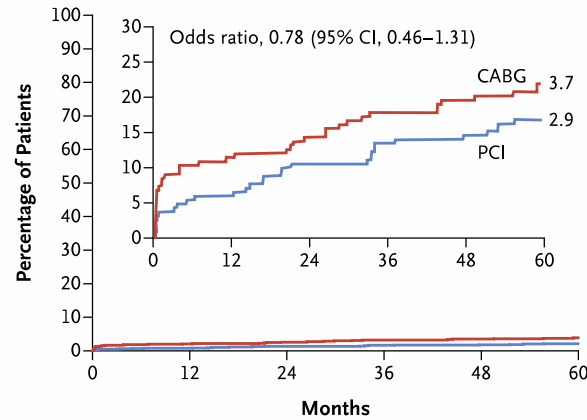
No. at Risk
PCI	948	896	858	831	799	534
CABG	957	879	851	828	799	583

C Myocardial Infarction

Odds ratio, 1.14 (95% CI, 0.84–1.55)

PCI 10.6
CABG 9.1

Percentage of Patients

Months
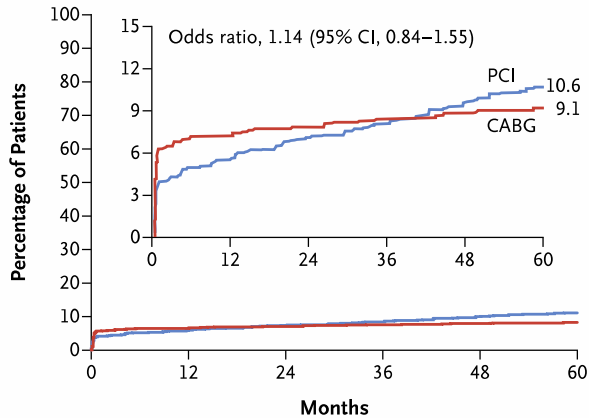
No. at Risk
PCI	948	860	819	788	750	496
CABG	957	827	801	778	749	543

D Ischemia-Driven Revascularization

Odds ratio, 1.84 (95% CI, 1.39–2.44)
P<0.001

PCI 16.9
CABG 10.0

Percentage of Patients

Months
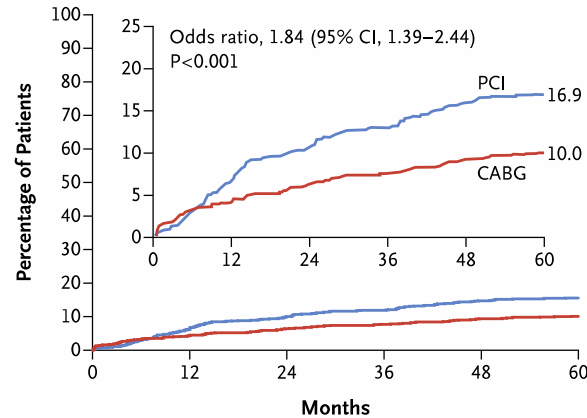
No. at Risk
PCI	948	847	781	741	690	457
CABG	957	853	814	785	744	542

Low-Risk Left Main:

1) Mean age 66 yr,
2) Low/ intermediate severity LM disease (Syntax Scores < 33)

PCI at 5years:

- ↑ Death (38%) (Accelerating in PCI group !!!)
- ↑ Non-procedural MI (ie real MI),
- ↑ Repeat Revasc
- = Stroke:

CONCLUSIONS In patients with left main coronary artery disease of low or intermediate anatomical complexity, there was no significant difference between PCI and CABG with respect to the rate of the composite outcome of death, stroke, or myocardial infarction at 5 years. (Funded by Abbott Vascular)

CORRESPONDENCE

Table 1. Cumulative Incidence of Myocardial Infarction at 5 Years, According to Two Definitions.*

Outcome	PCI (N = 948)		CABG (N = 957)		Difference (95% CI)†
	Patients	Event Rate	Patients	Event Rate	
	no.	*%*	*no.*	*%*	*percentage points*
Protocol definition					
Procedural myocardial infarction	37	3.9	57	6.0	−2.1 (−4.1 to −0.2)
All myocardial infarction	95	10.2	84	9.0	1.2 (−1.5 to 3.9)
Third universal definition					
Procedural myocardial infarction	31	3.3	13	1.4	1.9 (0.5 to 3.3)
All myocardial infarction	89	9.6	43	4.7	4.9 (2.6 to 7.2)

* Listed are cumulative incidences of myocardial infarction in the EXCEL trial, so the data vary slightly from the Kaplan–Meier rates reported in the original article; the cumulative incidences are not calculated as the ratio of the numerator to the denominator of patients. Procedural myocardial infarction was defined according to the prespecified protocol definition used in the primary outcome analysis and according to the Third Universal Definition of Myocardial Infarction; the latter definition was a secondary outcome measure in the trial. CABG denotes coronary-artery bypass grafting, CI confidence interval, and PCI percutaneous coronary intervention.
† The between-group difference was calculated by subtracting the percentage in the CABG group from that in the PCI group.

(In contrast to the new biochemical definition of MI which was higher in CABG)
3rd UDMI DATA showed that with PCI
(i)   HR for Procedural MI was 2.4
(ii) HR for All MI was 2.0

BUT
(i) Not presented to ESC/EACTS Guideline Taskforce on Myocardial Revascularization
(ii) Not presented in 2016 and 2019 NEJM publications

Left Main: Head et al Lancet 2018:

C

Cumulative mortality (%)

HR 1·07, 95% CI 0·87–1·33; p=0·52

N= 4478 (11 RCT)
Pooled Individual Patient Data
Mean Syntax Score 26

— PCI group
— CABG group

10·7%
10·5%

Follow-up (years)

Number at risk

	0	1	2	3	4	5
CABG	2245	2086	1903	932	804	406
PCI	2233	2120	1946	978	849	478
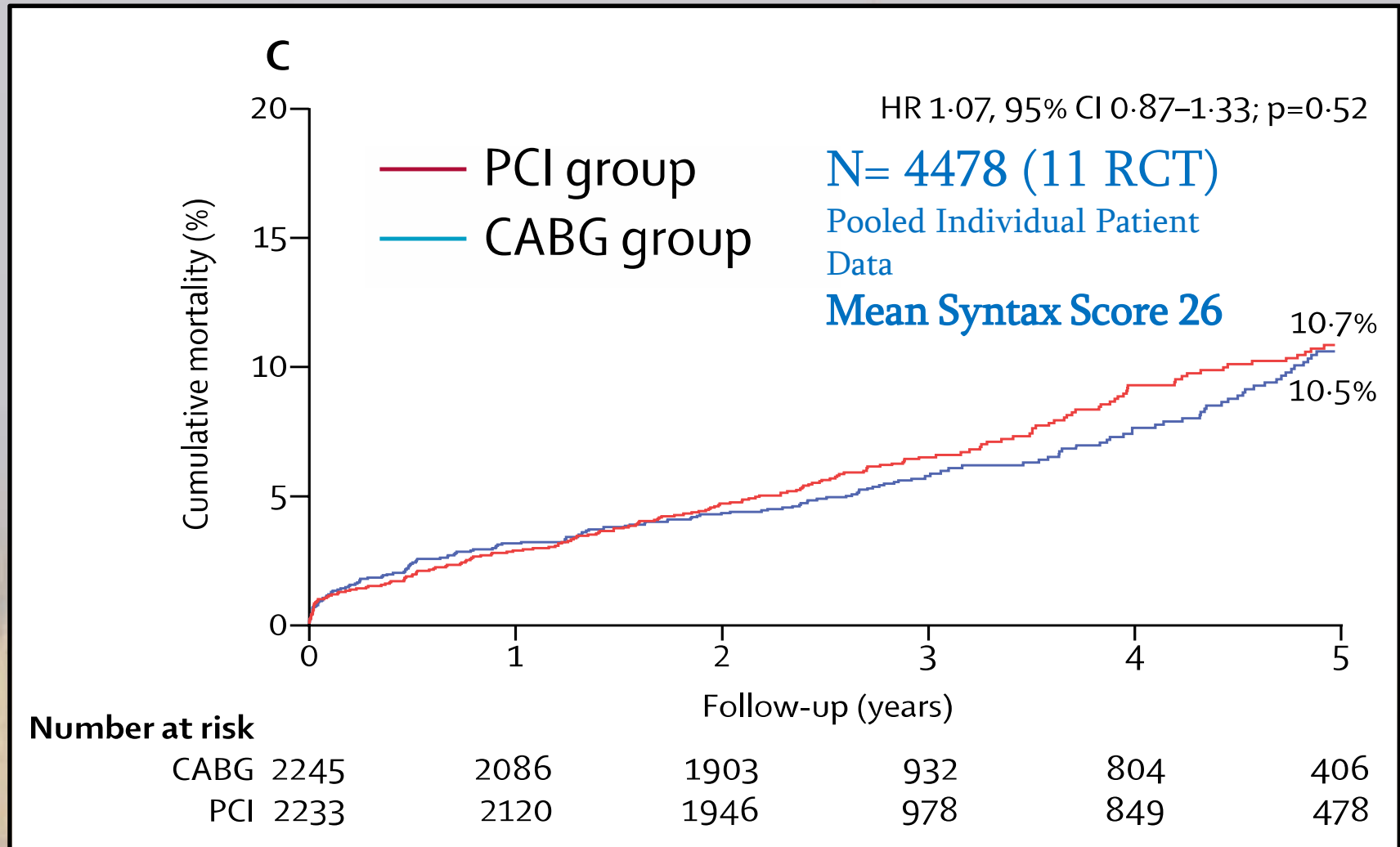
25% Diabetes (1120): MORTALITY CABG 13.4% vs 16.5% PCI: p=0.054

Ten-Year Outcomes After Drug-Eluting Stents Versus Coronary Artery Bypass Grafting for Left Main Coronary Disease

Extended Follow-Up of the PRECOMBAT Trial

Duk-Woo Park, MD*
Jung-Min Ahn, MD*
Hanbit Park, MD
Sung-Cheol Yun, PhD
Do-Yoon Kang, MD
Pil Hyung Lee, MD
Young-Hak Kim, MD
Do-Sun Lim, MD
Seung-Woon Rha, MD
Gyung-Min Park, MD
Hyeon-Cheol Gwon, MD
Hyo-Soo Kim, MD
In-Ho Chae, MD
Yangsoo Jang, MD
Myung-Ho Jeong, MD
Seung-Jea Tahk, MD
Ki Bae Seung, MD
Seung-Jung Park◉, MD
On behalf of the
PRECOMBAT
Investigators

PRECOMBAT: N = 600: Mean SYNTAX SCORE 25

C Death from Any Cause

Hazard ratio, 1.13 (95% CI 0.75-1.70)

14.5%
13.8%

Number at risk

PCI	300	284	272	262	253	237
CABG	300	279	272	262	254	238

A Primary Composite Outcome

Hazard Ratio, 1.25 (95% CI 0.93-1.69)

29.8%
24.7%

Number at risk

PCI	300	256	239	226	214	195
CABG	300	265	253	237	227	210
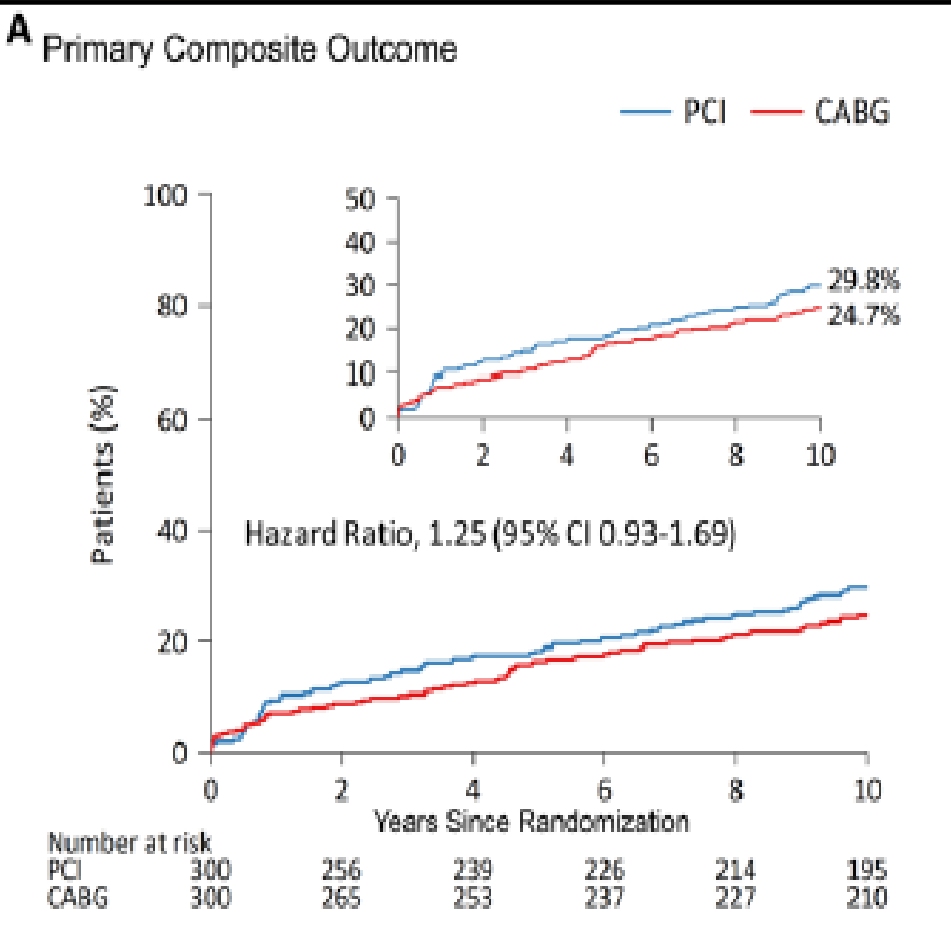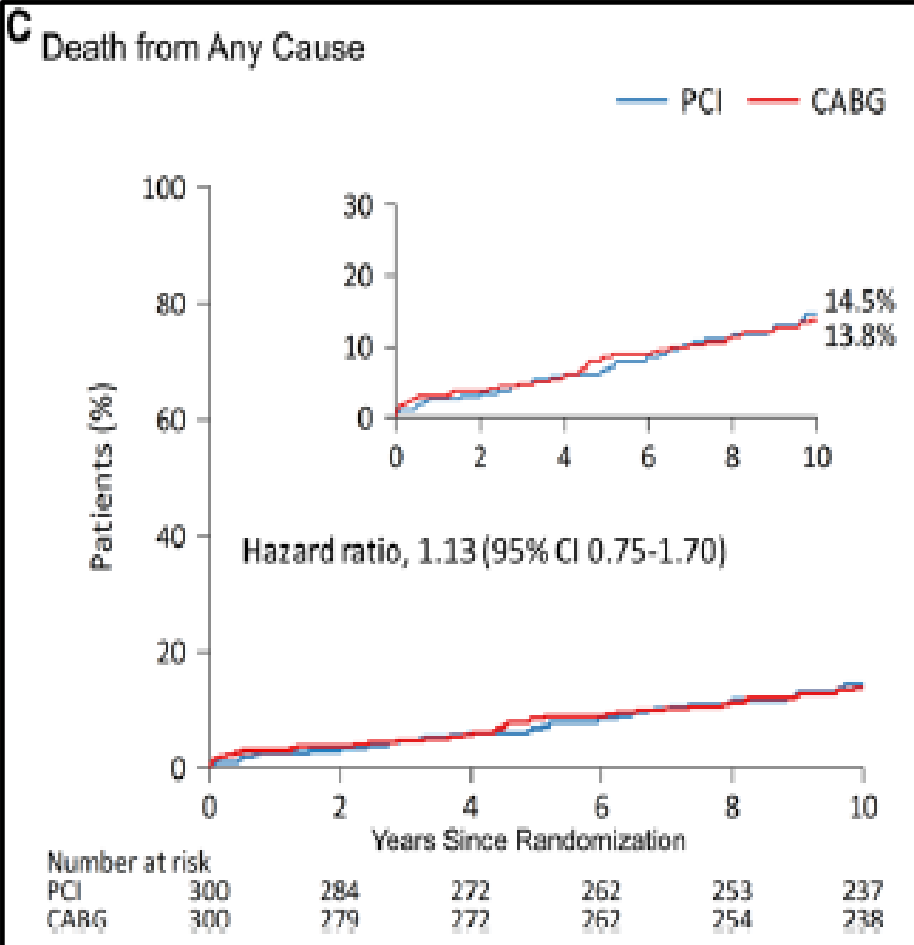
CAVG vs PCI Death, MI, Stroke Similar but REVASC 8% CABG vs 16% PCI

Impact of SYNTAX Score on 10-Year Outcomes After Revascularization for Left Main Coronary Artery Disease

Yong-Hoon Yoon, MD,[a] Jung-Min Ahn, MD,[b] Do-Yoon Kang, MD,[b] Hanbit Park, MD,[b] Sang-Cheol Cho, MD,[b] Pil Hyung Lee, MD,[b] Seung-Whan Lee, MD,[b] Seong-Wook Park, MD,[b] Duk-Woo Park, MD,[b] Seung-Jung Park, MD[b]

FIGURE 3 10-Year Kaplan-Meier Curves for Clinical Events Stratified by SYNTAX Score Category in CABG and PCI Groups
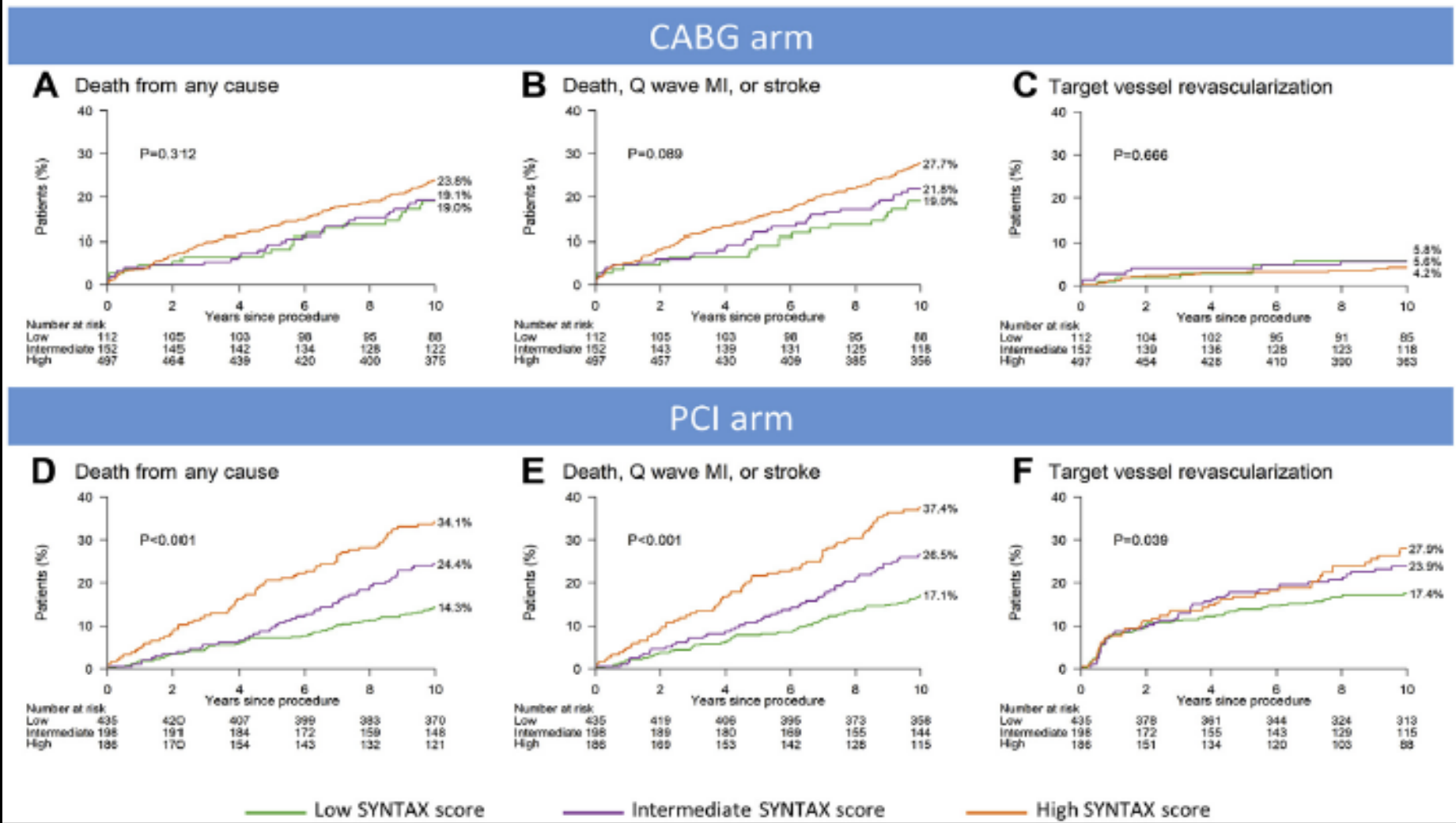
(i) Clear Benefit of CABG in High SS (ii) SS discriminative for PCI but not

2018 ESC/EACTS Guidelines on myocardial revascularization

Left main CAD	CABG		PCI			
Left main disease with low SYNTAX score (0 - 22).[69,121,122,124,145–148]	I	A	I		**?**	A
Left main disease with intermediate SYNTAX score (23 - 32).[69,121,122,124,145–148]	I	A	IIa			A
Left main disease with high SYNTAX score (≥33).[c 69,121,122,124,146–148]	I	A	III			B

Stable Multi-vessel or Left Main Coronary Artery Disease With Suitable Anatomy for PCI and CABG and Clinical Eligibility for either PCI or CABG

EHJ 2019

Three-vessel CAD

Left main CAD

Syntax Score 0-22

SYNTAX Score > 22

SYNTAX Score 0-22

SYNTAX 23-32

SYNTAX Score >32

No Diabetes

Diabetes

PCI IA
CABG IA

PCI IIb A
CABG IA

PCI IIIA
CABG IA

PCI IA
CABG IA

PCI IIa A
CABG IA

PCI IIIB
CABG IA
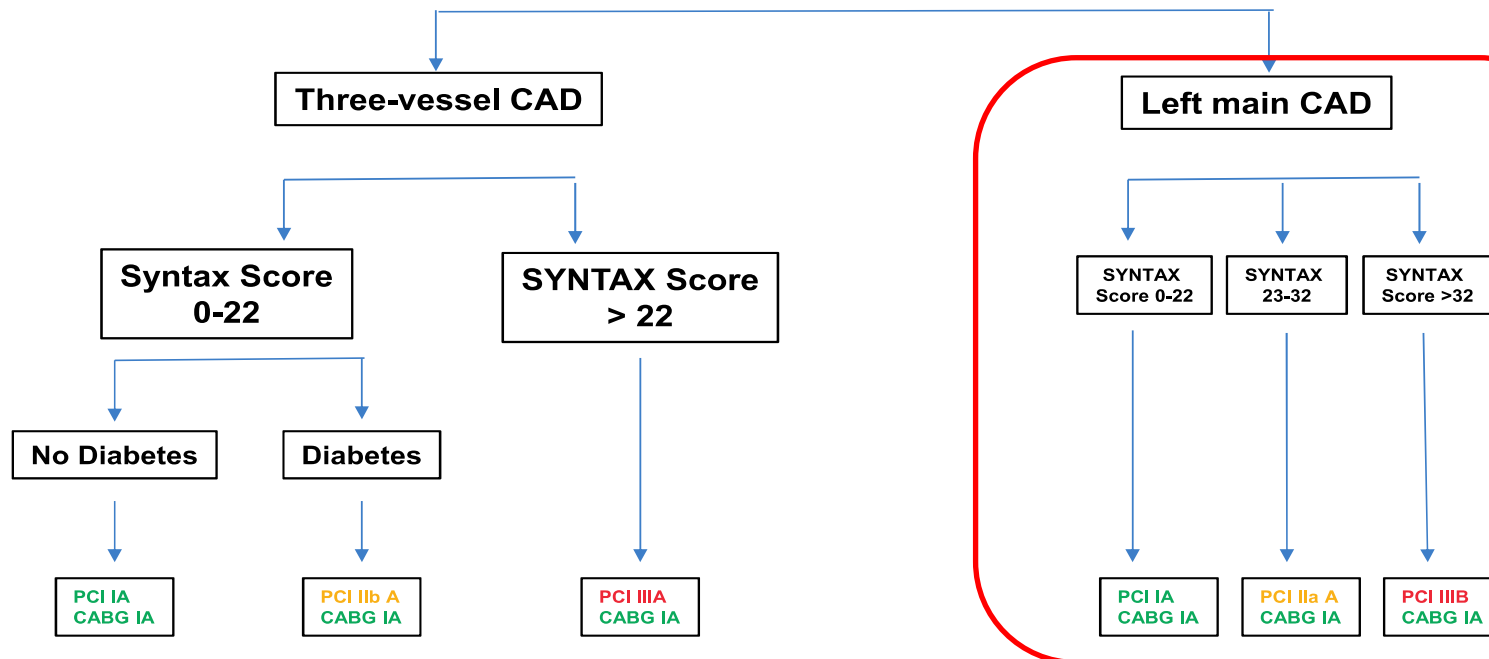
Take home figure Algorithm to guide the choice of revascularization procedure across major categories in patients with multivessel or left main coronary artery disease. Class recommendations correspond to the 2018 ESC/EACTS Guidelines on myocardial revascularization. CABG, coronary artery bypass grafting; CAD, coronary artery disease; LAD, left anterior descending artery; PCI, percutaneous coronary intervention.

Subgroup	PCI (N=948)		CABG (N=957)		Odds Ratio (95% CI)	
	Events/total patients no.	Event rate %	Events/total patients no.	Event rate %		
All patients	203/948	22.0	176/957	19.2		1.19 (0.95–1.50)
Age (median cutoff)						
≥67 yr	123/466	27.2	98/472	21.8		1.39 (1.02–1.89)
<67 yr	80/482	16.9	78/485	16.6		1.00 (0.71–1.40)
Sex						
Male	145/722	20.6	134/742	18.7		1.12 (0.86–1.46)
Female	58/226	26.3	42/215	21.1		1.39 (0.88–2.20)
Diabetes mellitus, medically treated						
Yes	72/256	29.0	62/249	25.5		1.24 (0.83–1.86)
No	131/692	19.4	114/707	16.9		1.17 (0.89–1.55)
Chronic kidney disease						
Estimated GFR ≤60 ml/min	54/164	34.0	37/144	27.6		1.44 (0.86–2.39)
Estimated GFR >60 ml/min	147/770	19.5	135/791	17.6		1.13 (0.87–1.47)
Left ventricular ejection fraction						
≥50%	158/782	20.6	144/796	18.7		1.14 (0.88–1.46)
<50%	33/111	31.5	26/115	24.2		1.35 (0.73–2.49)
Geographic region						
North America	89/381	24.2	61/371	17.3		1.57 (1.09–2.26)
Europe	111/534	21.1	102/541	19.6		1.09 (0.81–1.48)
Other	3/33	9.6	13/45	29.6		0.24 (0.06–0.96)
Non–left main diseased coronary arteries (core laboratory assessment)						
0	33/163	20.7	23/167	14.3		1.55 (0.86–2.78)
1	60/292	21.2	61/292	21.9		0.94 (0.62–1.40)
2	79/325	25.0	50/295	17.8		1.58 (1.06–2.36)
3	31/162	19.2	37/182	20.7		0.93 (0.54–1.59)
Left main bifurcation or trifurcation stenosis ≥50% (core laboratory assessment)						
Yes	171/771	22.7	136/741	19.0		1.24 (0.96–1.60)
No	32/171	19.2	35/195	18.9		1.05 (0.62–1.79)
SYNTAX score (site reported)						
≤22	119/560	21.9	106/588	18.7		1.21 (0.90–1.62)
23–32	84/386	22.2	70/366	20.0		1.16 (0.81–1.67)
SYNTAX score (core laboratory assessment)						
≤22	49/294	17.2	58/364	16.7		0.99 (0.65–1.51)
23–32	91/392	23.7	69/346	20.7		1.22 (0.85–1.74)
≥33	56/228	25.0	42/216	20.0		1.36 (0.86–2.15)

0.2 0.5 1.0 1.5 2.0 5.0

← PCI Better   CABG Better →

2018 ESC/EACTS Guidelines on myocardial revascularization

Recommendations according to extent of CAD	CABG		PCI	
	Class[a]	Level[b]	Class[a]	Level[b]
One-vessel CAD				
Without proximal LAD stenosis.	IIb	C	I	C
With proximal LAD stenosis.[68,101,139−144]	I	A	I	A
Two-vessel CAD				
Without proximal LAD stenosis.	IIb	C	I	C
With proximal LAD stenosis.[68,70,73]	I	B	I	C
Left main CAD				
Left main disease with low SYNTAX score (0 - 22).[69,121,122,124,145−148]	I	A	I	A
Left main disease with intermediate SYNTAX score (23 - 32).[69,121,122,124,145−148]	I	A	IIa **?**	A
Left main disease with high SYNTAX score (≥33).[c 69,121,122,124,146−148] **66%**	I	A	III	B
Three-vessel CAD without diabetes mellitus				
Three-vessel disease with low SYNTAX score (0 - 22).[102,105,121,123,124,135,149]	I	A	I	A
Three-vessel disease with intermediate or high SYNTAX score (>22).[c 102,105,121,123,124,135,149] **79%**	I	A	III	A
Three-vessel CAD with diabetes mellitus				
Three-vessel disease with low SYNTAX score 0−22.[102,105,121,123,124,135,150−157]	I	A	IIb **?**	A
Three-vessel disease with intermediate or high SYNTAX score (>22).[c 102,105,121,123,124,135,150−157]	I	A	III	A

CABG would be better if more arterial grafts and greater use of medical therapy !!

Table 2. Primary and Secondary Outcomes over Three Periods.*

Variable	PCI		CABG		Hazard Ratio (95% CI)
	Events	Event Rate	Events	Event Rate	
	no./no. of patients	%	no./no. of patients	%	
Outcomes at 30 days					
Death, stroke, or myocardial infarction	46/948	4.9	75/957	8.0	0.61 (0.42–0.88)
Death	9/948 *	1.0	10/957	1.1	0.90 (0.37–2.21)
Stroke	6/948	0.6	12/957	1.3	0.50 (0.19–1.32)
Myocardial infarction	37/948	3.9	59/957	6.3	0.63 (0.42–0.94)
Death, stroke, myocardial infarction, or ischemia-driven revascularization	46/948	4.9	80/957	8.5	0.57 (0.40–0.82)
Ischemia-driven revascularization	6/948	0.6	13/957	1.4	0.46 (0.17–1.21)
Definite stent thrombosis or symptomatic graft stenosis or occlusion	3/948	0.3	11/957	1.2	0.27 (0.08–0.97)
Outcomes from 30 days to 1 yr					
Death, stroke, or myocardial infarction	38/948	4.1	35/957	3.8	1.07 (0.68–1.70)
Death	22/948	2.4	23/957	2.5	0.94 (0.53–1.69)
Stroke	5/948	0.5	7/957	0.8	0.71 (0.22–2.23)
Myocardial infarction	16/948	1.7	10/957	1.1	1.58 (0.72–3.48)
Death, stroke, myocardial infarction, or ischemia-driven revascularization	83/948	8.9	56/957	6.1	1.48 (1.05–2.07)
Ischemia-driven revascularization	59/948	6.4	28/957	3.1	2.10 (1.34– 3.30)
Definite stent thrombosis or symptomatic graft stenosis or occlusion	0/948	0	22/957	2.4	—
Outcomes from 1 yr to 5 yr					
Death, stroke, or myocardial infarction	133/933	15.1	83/929	9.7	1.61 (1.23–2.12)
Death	88/933	10.0	56/929	6.6	1.57 (1.12–2.19)
Stroke	16/933	1.9	15/929	1.8	1.06 (0.52–2.15)
Myocardial infarction	43/933	5.1	20/929	2.4	2.16 (1.27–3.67)
Death, stroke, myocardial infarction, or ischemia-driven revascularization	198/933	22.4	118/929	13.8	1.74 (1.38–2.18)
Ischemia-driven revascularization	100/933	11.6	49/929	5.8	2.10 (1.49–2.95)
Definite stent thrombosis or symptomatic graft stenosis or occlusion	7/933	0.8	25/929	3.0	0.28 (0.12–0.64)

Primary and Secondary Outcomes over 3 periods

0-30 DAYS
No difference:
Death, Stroke, Revasc
but higher MI in CABG using new definition

30 DAYS-1Year
No difference:
Death, Stroke, MI,
but higher revasc in PCI group

1-5 Years
PCI Large Increase:
Death, MI, Revasc
(no difference in stroke)

CONCLUSION: 'No Difference' ?????

EXCEL: The Controversy

Four Major Concerns in EXCEL 5-Year Analysis:

1) Interpretation of the Mortality Data
   ('one of 20 underpowered secondary endpoints')

2) Persistent Failure to Publish Protocol Specified MI Data
   (eventually 8 months later at insistence of NEJM editors)

3) Changed Statistical Analysis: Non-Inferiority (3 yrs) to Superiority (5 yrs)

4) Failure to Share Trial Data

Controversy Extended to both the Medical Domain (EACTS, ESC, AATS, STS) and Public Domain (BBC Dec 2019, March 2020)

Excel: The Facts vs The Fiction

1. The largest and most definitive trial of PCI vs CABG in LM disease
   (4 PI, investigators, patients deserve enormous credit for driving this pivotal trial)

2. Academic: I was Chairman of the Surgical Committee of the EXCEL Trial during the design and recruitment phase

3. Oxford: 2nd largest recruiter of EXCEL patients worldwide (n=100), (demonstrating sincere commitment of Oxford Cardiologist/Surgeons !)

4. I withdrew my authorship from the final NEJM manuscript (2019) over INTERPRETATION of the data

5. **There was NO attempt in the EXCEL trial to manipulate/distort the data that was actually presented**

6. **BUT, by failing to present vital MI protocol specified data,there was, by omission, manipulation/distortion of the 'true' interpretation of the trial**

WHITE PAPER

Myocardial Revascularization Trials
Beyond the Printed Word

ABSTRACT: This article reviews the context and evidence of recent myocardial revascularization trials that compared percutaneous coronary intervention with coronary artery bypass grafting for the treatment of left main and multivessel coronary artery disease. We develop the rationale that some of the knowledge synthesis resulting from these trials, particularly with regard to the claimed noninferiority of percutaneous coronary intervention beyond nondiabetic patients with low anatomic complexity, may have been affected by trial design, patient selection based on suitability for percutaneous coronary intervention, and end point

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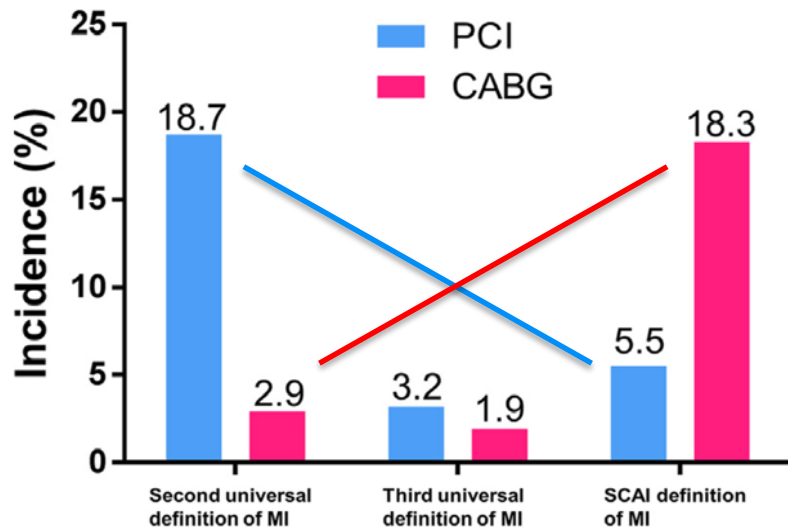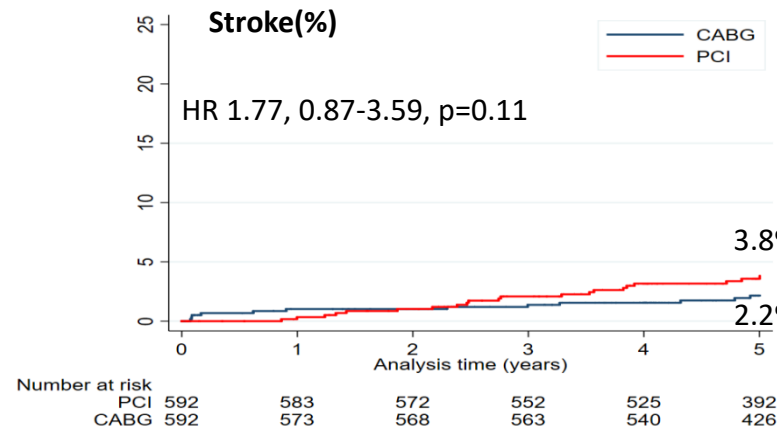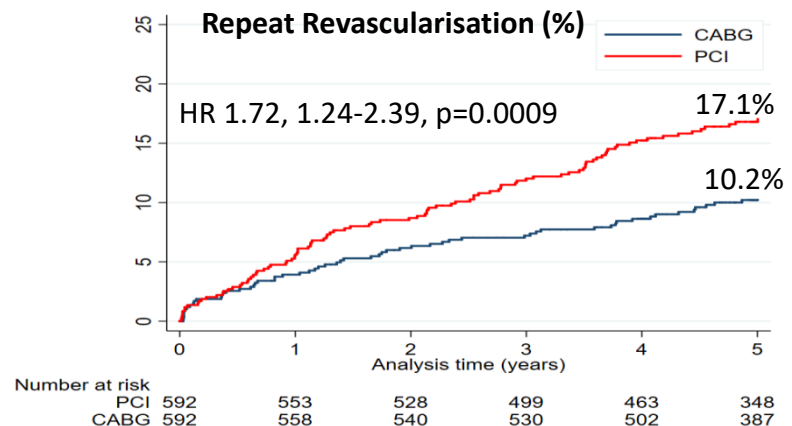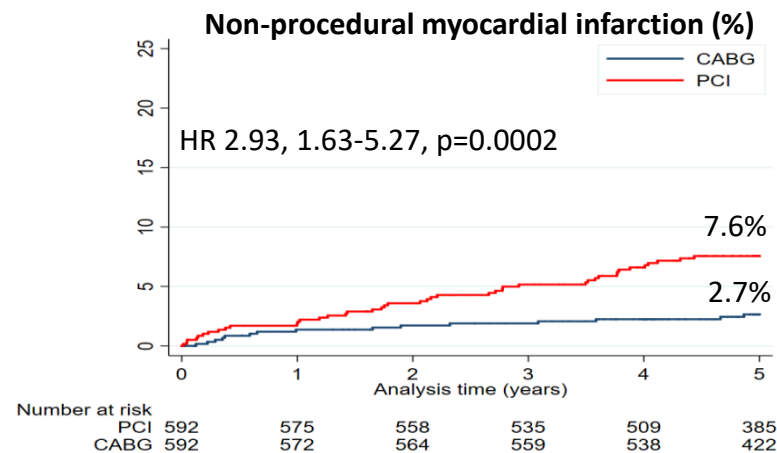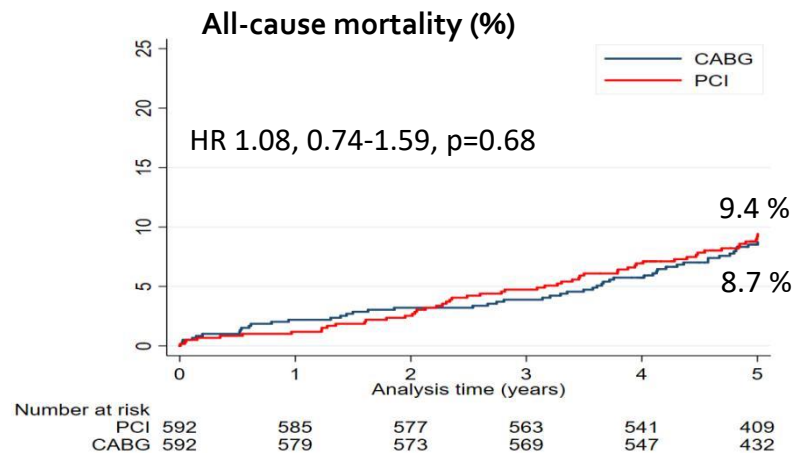Duke E. Cameron, MD
David P. Taggart, MD

Figure 1. Rates of periprocedural myocardial infarction (MI) according to various definitions in 7697 patients who received percutaneous coronary intervention (PCI; n=4514) or coronary artery bypass grafting (CABG; n=3183) between 2003 and 2013 and for whom serial measurements of creatine kinase-MB were available.

SCAI indicates Society for Cardiovascular Angiography and Interventions. Reproduced from Cho et al[15] with permission. Copyright © 2017, Elsevier.

'Hence a change in the definition of Periprocedural MI, from the original EXCEL trial protocol, contemporary with the 2nd Universal Definition, to the SCAI definition used in the analyses, affected the composite primary end point and the non-inferiority result of the EXCEL study. Without this modification it is plausible that the composite primary end point of MACCE, which included periprocedural MI in the first 30 days, would have changed in favor of CABG.'

All-cause mortality (%)

HR 1.08, 0.74-1.59, p=0.68

9.4 %
8.7 %

Number at risk
PCI 592 585 577 563 541 409
CABG 592 579 573 569 547 432

Non-procedural myocardial infarction (%)

HR 2.93, 1.63-5.27, p=0.0002

7.6%
2.7%

Number at risk
PCI 592 575 558 535 509 385
CABG 592 572 564 559 538 422

Repeat Revascularisation (%)

HR 1.72, 1.24-2.39, p=0.0009

17.1%
10.2%

Number at risk
PCI 592 553 528 499 463 348
CABG 592 558 540 530 502 387

Stroke(%)

HR 1.77, 0.87-3.59, p=0.11

3.8%
2.2%

Number at risk
PCI 592 583 572 552 525 392
CABG 592 573 568 563 540 426

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Two Definitions of MI in EXCEL Protocol (Appendix A NEJM 2019)

EXCEL Clinical Trial Protocol Version 4.0: 22nd July 2011 [NEJM 2019]
'Protocol Defined MI: MI Adjudicated per Universal Definition'
'All MI (periprocedural, spontaneous, Q-wave and non Q-wave) including large and small' (And repeated in the protocol)

Expert Consensus Document

Universal Definition of Myocardial Infarction

Kristian Thygesen; Joseph S. Alpert; Harvey D. White;
on behalf of the Joint ESC/ACCF/AHA/WHF Task Force
for the Redefinition of Myocardial Infarction   [CIRC 2007]

'If troponin assays are not available, the best alternative is CKMB'

EXCEL PROTOCOL: Definition of Myocardial Infarction [16.1.2.,p 92]
Different criteria for spontaneous and peri-procedural MI will be utilized.
New biochemical definition (SCAI definition eventually published in JACC 2013)

NEJM 2019: 'Third, a specific bio-marker-based definition of large periprocedural myocardial infarction was used in the present trial; this definition differs from the criteria used in the 3rd UDMI (which was developed while the current trial was ongoing)'.
(Genuine Confusion and Misunderstanding of which UDMI !!)

BUT: EXCEL Protocol **SPECIFIED** reporting of **BOTH** the standard (UDMI) and new (SCAI) definition of procedural MI. (To allow comparison of these definitions (i) within EXCEL and (ii) with other studies); only the new definition, that drove the composite end point was reported

Conclusions:
NOBLE 5-year follow-up

- The NOBLE trial has reached the predefined number of endpoints and is conclusive

- PCI remained inferior to CABG in 5-year MACCE

- CABG was superior to PCI – also in the group with SYNTAX score <23

- All-cause mortality was similar for PCI and CABG

- PCI resulted in higher rates of non-procedural myocardial infarctions and repeat revascularization

TCT 2019

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CORRESPONDENCE

Table 1. Cumulative Incidence of Myocardial Infarction at 5 Years, According to Two Definitions.*

Outcome	PCI (N = 948)		CABG (N = 957)		Difference (95% CI)†
	Patients	Event Rate	Patients	Event Rate	
	no.	*%*	*no.*	*%*	*percentage points*
Protocol definition					
Procedural myocardial infarction	37	3.9	57	6.0	−2.1 (−4.1 to −0.2)
All myocardial infarction	95	10.2	84	9.0	1.2 (−1.5 to 3.9)
Third universal definition					
Procedural myocardial infarction	31	3.3	13	1.4	1.9 (0.5 to 3.3)
All myocardial infarction	89	9.6	43	4.7	4.9 (2.6 to 7.2)

* Listed are cumulative incidences of myocardial infarction in the EXCEL trial, so the data vary slightly from the Kaplan–Meier rates reported in the original article; the cumulative incidences are not calculated as the ratio of the numerator to the denominator of patients. Procedural myocardial infarction was defined according to the prespecified protocol definition used in the primary outcome analysis and according to the Third Universal Definition of Myocardial Infarction; the latter definition was a secondary outcome measure in the trial. CABG denotes coronary-artery bypass grafting, CI confidence interval, and PCI percutaneous coronary intervention.
† The between-group difference was calculated by subtracting the percentage in the CABG group from that in the PCI group.

3rd UDMI DATA:
(i) HR for Procedural MI with PCI: 2.4 (higher than that reported by the BBC)
(ii) HR for All MI: 2.0
BUT
(i) Data PIs repeatedly said did not exist (and called the BBC 'fake information' in BMJ)
(ii) Not presented to ESC/EACTS Guideline Taskforce on Myocardial Revascularization
(iii) Not presented in 2016 and 2019 NEJM publications
(iv) No explanation or clarification of repeated misrepresentation

Lessons for all RCTs, Journal Publications (NEJM !), Guidelines, Patients: TRUST