CABG Remains the Best Therapy for Most Patients with LM Stenosis

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TCTAP 2022 Virtual Meeting

Mount Sinai Heart

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Disclosures:

- Royalties from coronary surgical instruments manufactured by Scanlan, Inc
- Consultant to Medtronic, MediStim, Vascular Graft Solutions, CryoLife
- I have devoted my career to complex coronary surgery and believe that we must continuously advance the field
- Gregg Stone is my friend and colleague (it’s ok that we don’t always agree on everything)

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EXCEL and NOBLE Prove that PCI Is Still Far From Being An Acceptable Alternative To CABG For Left Main Revascularization, With The Exception Of A Small Proportion of Patients!

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tct2017

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Study Design

2900 pts with unprotected left main disease

SYNTAX score ≤32
Consensus agreement of eligibility and equipoise by heart team

Yes
(N=1900)
Planned 2600

No
(N=1000)

Enrollment registry

Stratified by diabetes, SYNTAX score and center

R

PCI (Xience EES)
(N=950)

CABG
(N=950)

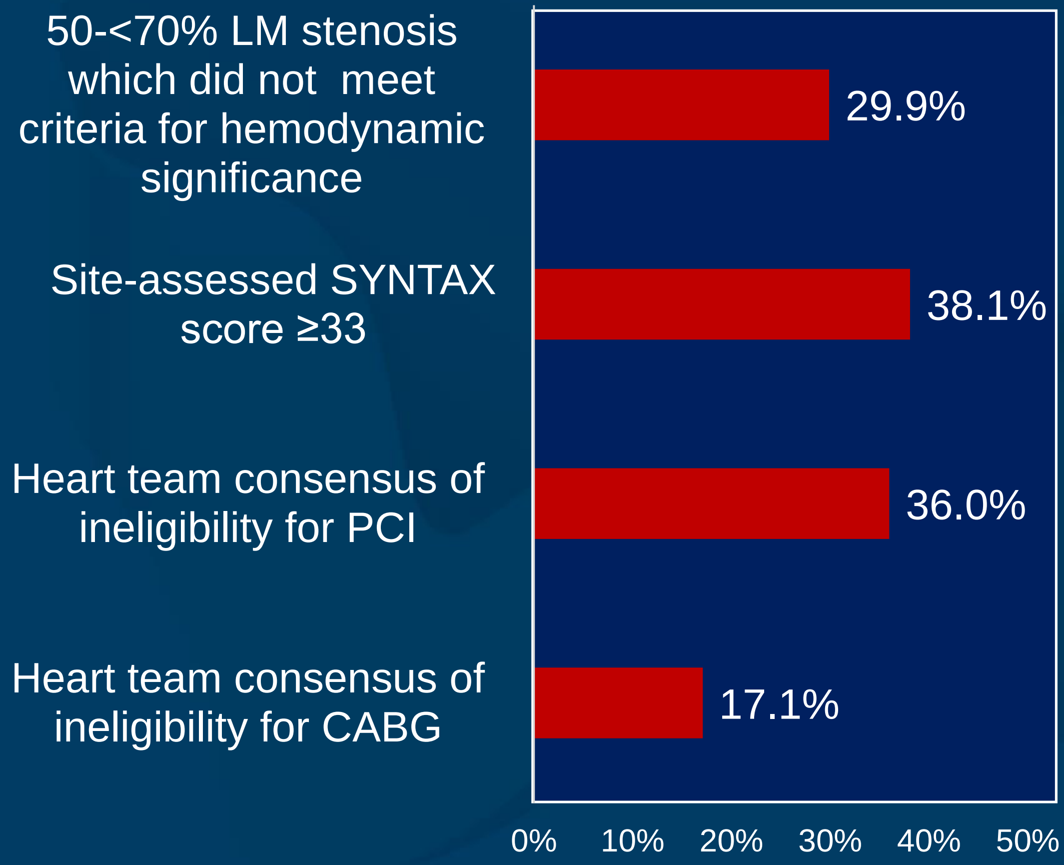
Way too short to see advantage of CABG over PCI!!

Follow-up: 1 month, 6 months, 1 year, annually through 5 years

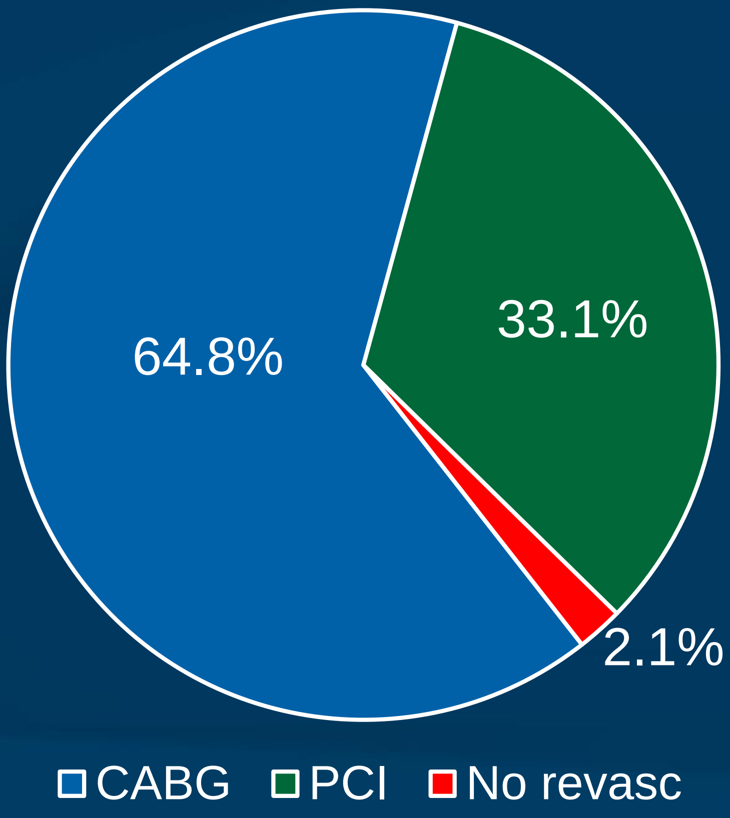
Primary endpoint: Measured at a median 3-yr FU, minimum 2-yr FU

Registry (n=1000)

Major reasons for exclusion from randomization



Treatment of registry patients



PCI Procedure

935 patients, 1021 planned procedures, 2287 stents

Planned staged procedures	9.1%
Arterial access site*	
- Femoral	72.9%
- Radial	26.9%
- Brachial	0.2%
IVUS guidance	77.2%
FFR assessment	9.0%
Hemodynamic support device*	5.2%
Contrast use* (cc)	256 ± 127
Fluoroscopy time* (min)	24 ± 16

# Vessels treated per pt*†	1.7 ± 0.8
- LM	100.0%**
- LAD	28.3%
- LCX	16.6%
- RCA	26.7%
# Lesions treated per pt*	1.9 ± 1.1
# Stents implanted per pt*	2.4 ± 1.5
- Total stent length (mm)*	49.1 ± 35.6
Type of stents implanted*	
- DES	99.8%
- EES	99.2%
- XIENCE	98.4%

*All procedures (index + planned staged); **Excludes pts with LM equivalent ds;
†Max 4 vessels, including LM as a separate vessel

EXCEL

CABG Procedure

923 patients and procedures

Off-pump CABG	29.4%
On-pump bypass duration (min)	83 ± 45
- Cross clamp duration (min)	55 ± 27
Epi-aortic ultrasound	13.1%
Transesophageal ultrasound	42.3%
Hemodynamic support device	3.5%

# Conduits per pt	2.6 ± 0.8
- Arterial conduits	1.4 ± 0.6
- Venous conduits	1.2 ± 0.9
Any IMA used	98.8%
Bilateral IMA used	28.8%
Any radial artery used	6.0%
Only arterial conduits used	24.8%
Vessels bypassed per pt	
- LAD	98.8%
- LCX	88.2%
- RCA	37.8%

EXCEL

Discharge Medications

	PCI (n=931)	CABG (n=911)	P-value
Aspirin	98.5%	98.0%	0.43
P2Y12 receptor inhibitor	97.6%	32.6%	<0.001
- Clopidogrel or ticlopidine	72.0%	32.1%	<0.001
- Prasugrel or ticagrelor	25.7%	0.5%	<0.001
Beta-blocker	83.4%	92.5%	<0.001
ACE inhibitors or receptor blocker	56.8%	42.2%	<0.001
Calcium channel blocker	5.9%	7.1%	0.29
Diuretic	3.6%	24.4%	<0.001
Aldosterone antagonist	0.1%	0.8%	0.04
Anti-arrhythmic agent	0.5%	11.6%	<0.001
Statin	96.7%	92.4%	<0.001
Chronic oral anticoagulant	1.3%	4.3%	<0.001

EXCEL

Adjudicated Outcomes at 3 Years (i)

	PCI (n=948)	CABG (n=957)	HR [95%CI]	P-value
Death, stroke or MI (1° endpoint)	15.4%	14.7%	1.00 [0.79, 1.26]	0.98
- Death	8.2%	5.9%	1.34 [0.94, 1.91]	0.11
- Definite cardiovascular	3.7%	3.4%	1.10 [0.67, 1.80]	0.71
- Definite non-cardiovascular	3.9%	2.3%	1.60 [0.91, 2.80]	0.10
- Undetermined cause	0.8%	0.3%	2.00 [0.50, 7.98]	0.32
- Stroke	2.3%	2.9%	0.77 [0.43, 1.37]	0.37
- MI	8.0%	8.3%	0.93 [0.67, 1.28]	0.64
- Peri-procedural	3.8%	6.0%	0.63 [0.42, 0.96]	0.03
- Spontaneous	4.3%	2.7%	1.60 [0.95, 2.70]	0.07
- STEMI	1.3%	2.8%	0.46 [0.23, 0.91]	0.02
- Non-STEMI	7.0%	5.9%	1.15 [0.80, 1.65]	0.46

EXCEL

Adjudicated Outcomes at 3 Years (ii)

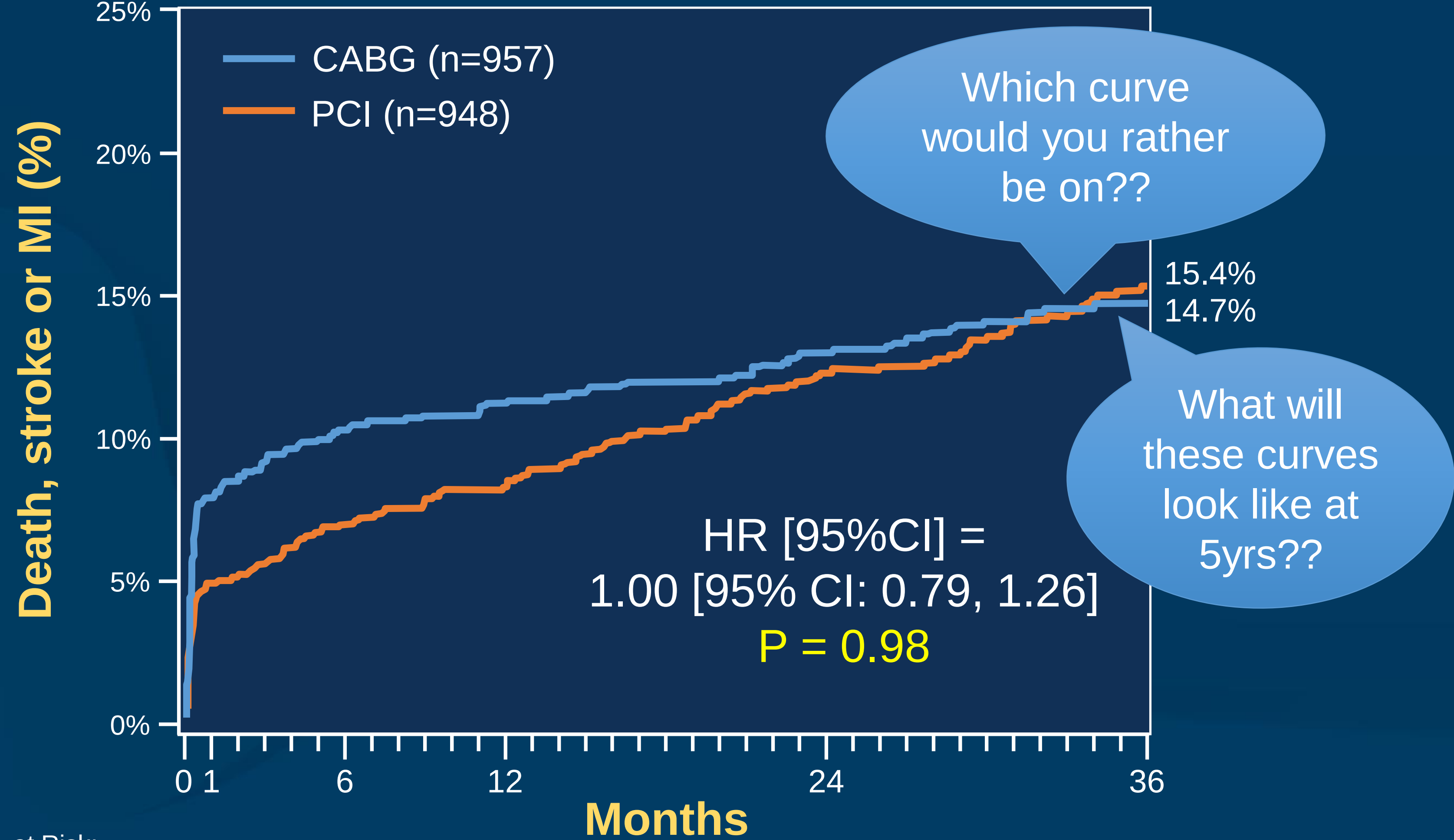
	PCI (n=948)	CABG (n=957)	HR [95%CI]	P-value
Death, stroke, MI or IDR	23.1%	19.1%	1.18 [0.97, 1.45]	0.10
- Ischemia-driven revasc (IDR)	12.6%	7.5%	1.72 [1.27, 2.33]	<0.001
- PCI	10.3%	6.8%	1.57 [1.13, 2.18]	0.006
- CABG	3.5%	0.8%	4.29 [1.88, 9.77]	<0.001
All revascularization	12.9%	7.6%	1.72 [1.27, 2.33]	<0.001
Stent thrombosis, def/prob	1.3%	0.0%	-	<0.001
- Definite	0.7%	0.0%	-	0.01
- Probable	0.7%	0.0%	-	0.01
- Early (0 - 30 days)	0.7%	0.0%	-	0.008
- Late (30 days – 1 year)	0.1%	0.0%	-	0.32
- Very late (1 year - 3 years)	0.5%	0.0%	-	0.05
Graft occlusion, symptomatic	0.0%	5.4%	-	<0.001
Definite stent thrombosis or symptomatic graft occlusion	0.7%	5.4%	0.12 [0.05, 0.28]	<0.001

Primary Endpoint
Landmark Analysis (post hoc)

	From randomization to 30 days				From 30 days to 3 years			
	PCI (n=948)	**CABG (n=957)**	**HR [95%CI]**	**P value**	**PCI (n=939)**	**CABG (n=947)**	**HR [95%CI]**	**P value**
Death, stroke or MI	4.9%	7.9%	0.61 [0.42, 0.88]	0.008	11.5%	7.9%	1.44 [1.06, 1.96]	0.02
- Death	1.0%	1.1%	0.90 [0.37, 2.22]	0.82	7.3%	4.9%	1.44 [0.98, 2.13]	0.06
- Stroke	0.6%	1.3%	0.50 [0.19, 1.33]	0.15	1.8%	1.8%	1.00 [0.49, 2.05]	1.00
- MI	3.9%	6.2%	0.63 [0.42, 0.95]	0.02	4.2%	2.5%	1.71 [1.00, 2.93]	0.05

Stroke and MI rates are non-hierarchical; i.e. include fatal and non-fatal events. The 30-day to 3-year landmark period includes all randomized pts at day 30 except those who died before day 30. Thus there may be some patients with a stroke or MI within 30 days who have a second event between 30 days and 3 years.

Primary Endpoint
Death, Stroke or MI at 3 Years

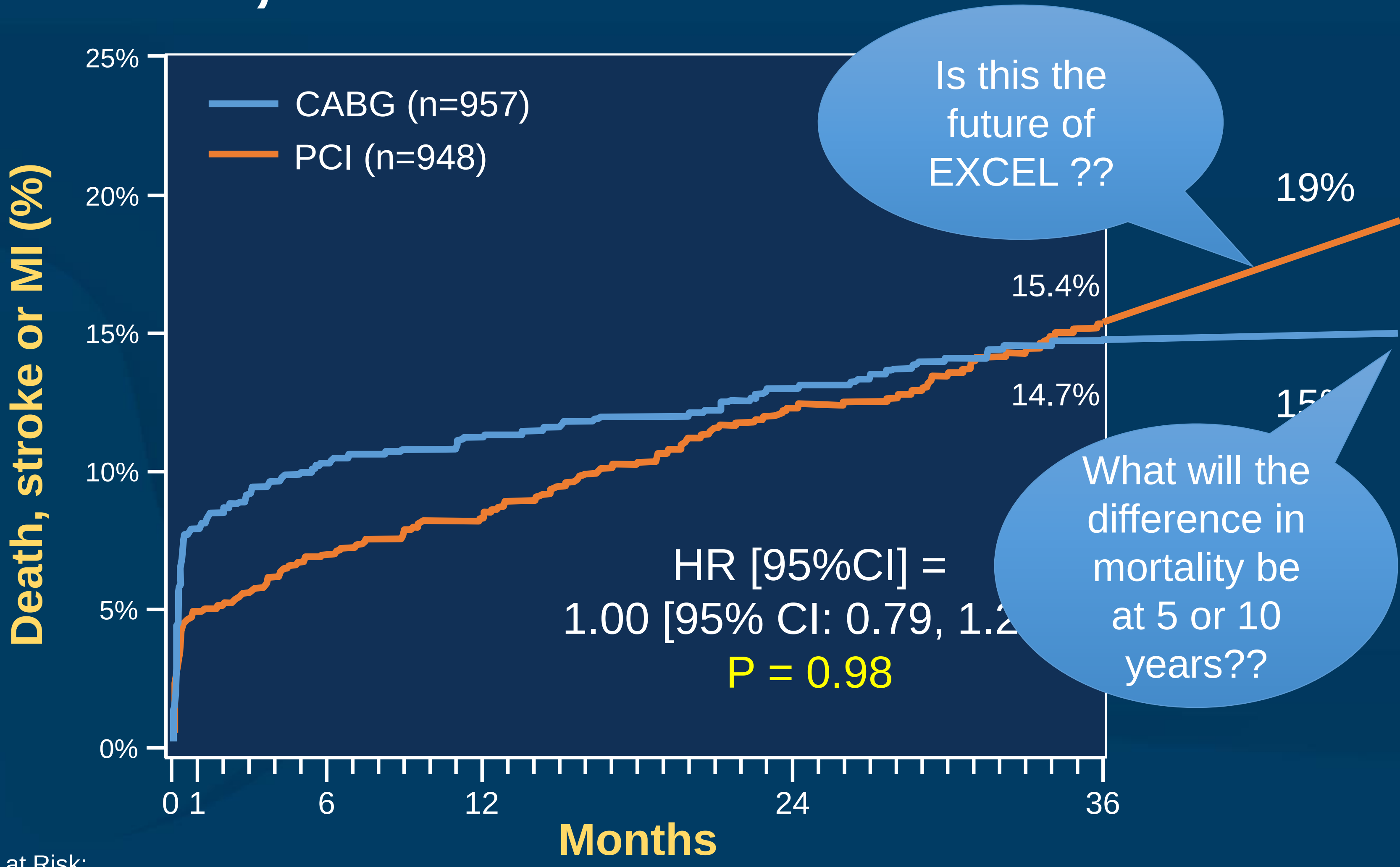


No. at Risk:

PCI	948	896	875	850	784	445
CABG	957	868	836	817	763	458

Primary Endpoint

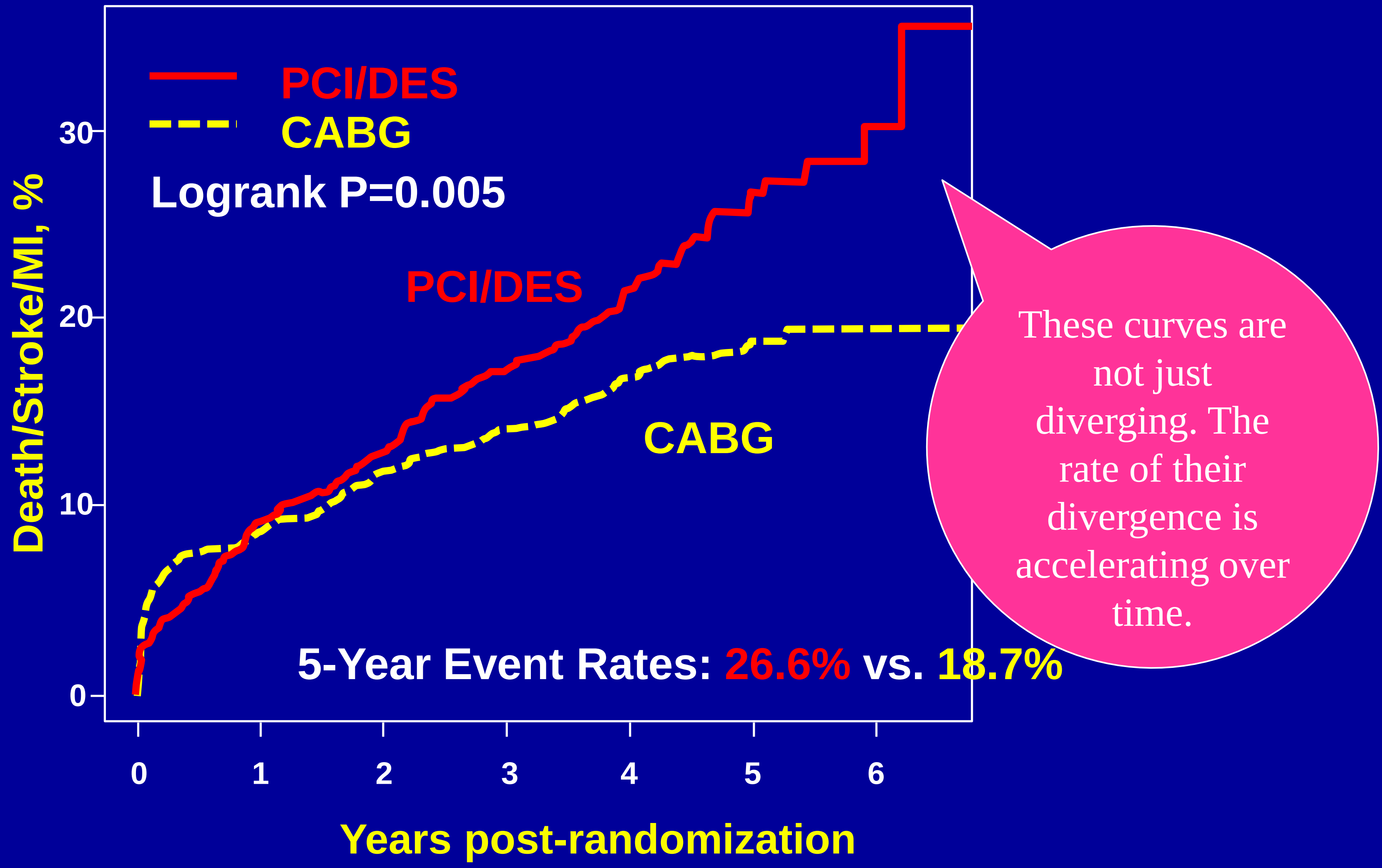
Death, Stroke or MI at 3 Years



No. at Risk:

PCI	948	896	875	850	784	445
CABG	957	868	836	817	763	458

PRIMARY OUTCOME – DEATH / STROKE / MI



PCI/DES N	953	848	788	625	416	219	40
CABG N	943	814	758	613	422	221	44

SYNTAX 1 and 5 Year Conclusions:

- "CABG remains the standard of care for patients with 3-vessel or LM CAD, since the use of CABG, as compared with PCI, resulted in lower rates of the combined end point of major adverse cardiac or cerebrovascular events at 1 year." Serruys et al, NEJM 2009;360:961-72
- "CABG should remain the standard of care for patients with complex lesions (high or intermediate SYNTAX scores). " Mohr et al, Lancet 2013;381:629-38.

SYNTAX 5 Yr FU Cause of Death

Milojevic et al, JACC 2016;67:42-55.

- Cumulative incidence of all-cause death was not significantly different between CABG and PCI (11.4% vs 13.9%; p=0.10).
- Note: SYNTAX was not powered for mortality alone!
- There were significant differences in terms of cardiovascular death (5.8% vs 9.6%; p=0.008) and cardiac death (5.3% vs 9.0%; p=0.003), in favor of CABG.
- These differences were caused primarily by a 10-fold reduction in MI-related death with CABG compared with PCI (0.4% vs 4.1%; p<0.0001).
- Treatment with PCI vs CABG was an independent predictor of cardiac death (HR 1.55; 95% CI 1.09 to 2.33; p=0.045).
- The difference in MI-related death was seen largely in patients with diabetes, 3-vessel disease, or high SYNTAX score.
- Conclusions: “During 5-year follow-up, CABG in comparison with PCI was associated with a significantly reduced rate of MI-related death, which was a leading cause of death after PCI.”

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

[NEJM November 7th 2019]

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 LEFT MAIN**
- **SELECTED** Patients: SYNTAX SCORES <33
- 1905 patients (2600 planned but trial stopped early)
- MEAN AGE 66: (life expectancy of 15-20 years)
- Primary Outcome: Composite of Death, MI, Stroke (NOT Revasc)

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Concerns About EXCEL 5-Year Analysis:

1) Interpretation/emphasis of the Mortality Data

2) Delay in Publishing Protocol Specified Periprocedural MI Data (8 months after 5 yr outcomes in NEJM July 16, 2020)

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

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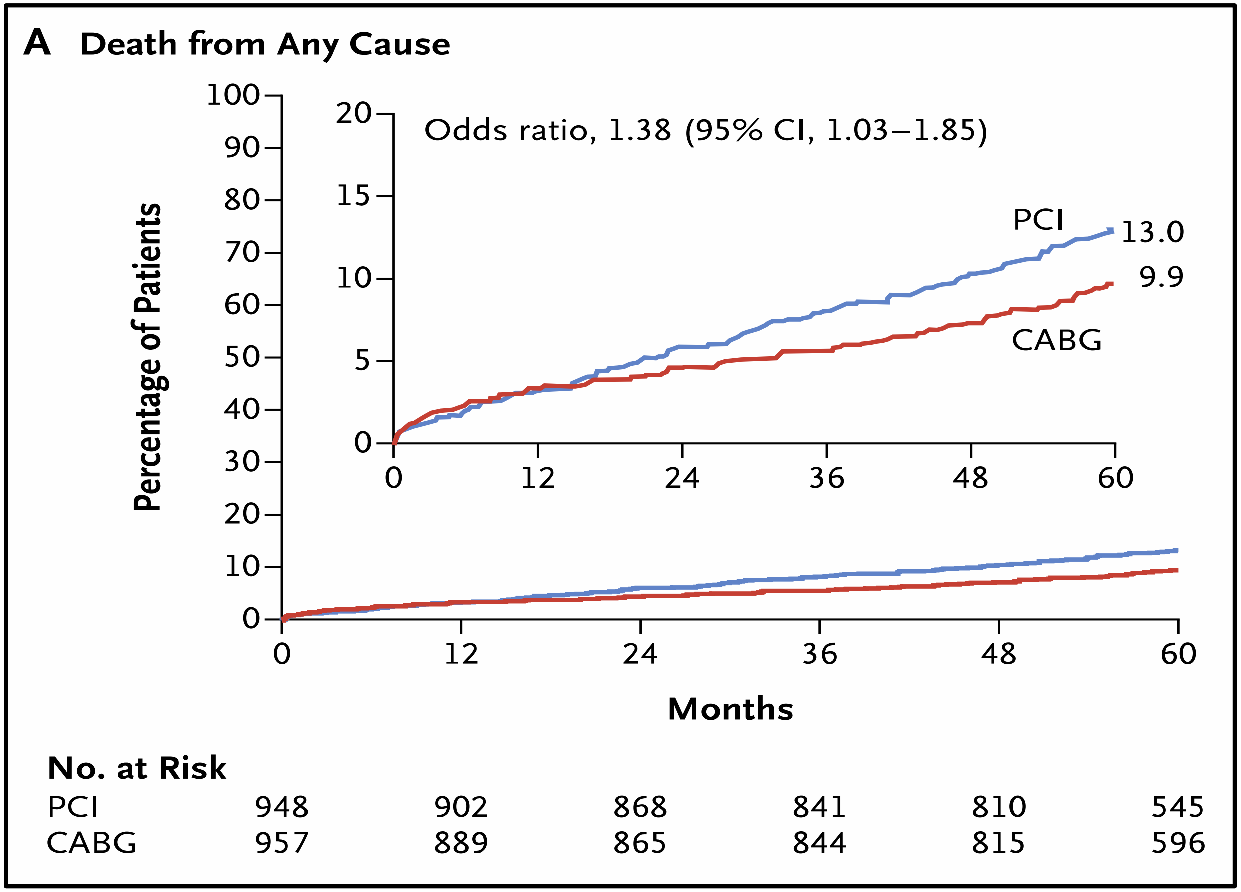
Excess and Accelerating Mortality with PCI at 5 years



Low-Risk Patients

1) Mean age 66 yr,
2) Low/ intermediate severity LM disease)

PCI at 5years:

- ↑ **Death (38%)**
- ↑ Non-procedural MI (ie real MI),
- ↑ Repeat Revasc
- Stroke: No difference

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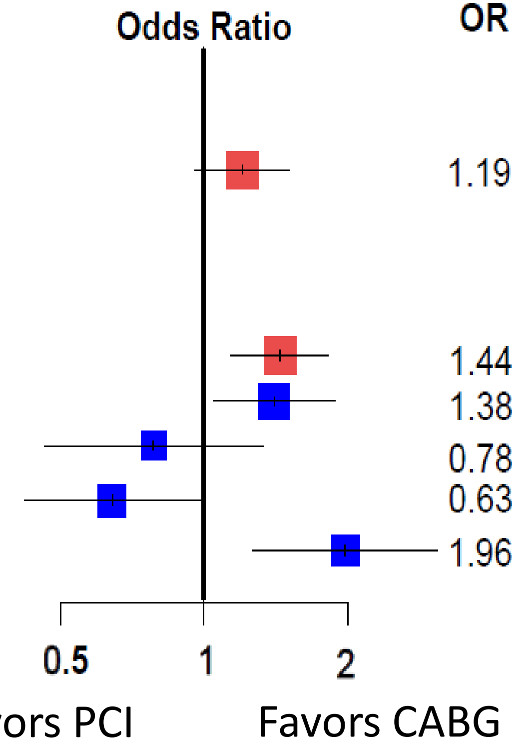
EXCEL EXCLUDING PERI-PROCEDURAL MI (like NOBLE)

(M Gaudino et al JTCVS 2020)

Endpoint	PCI Events	PCI Total	CABG Events	CABG Total	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) and Repeat Revascularization

GW Stone, PW Serruys, J Sabik et al. NEJM July 16 2020

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 PCI vs CABG: 2.4

(ii) HR for All MI PCI vs CABG: 2.0

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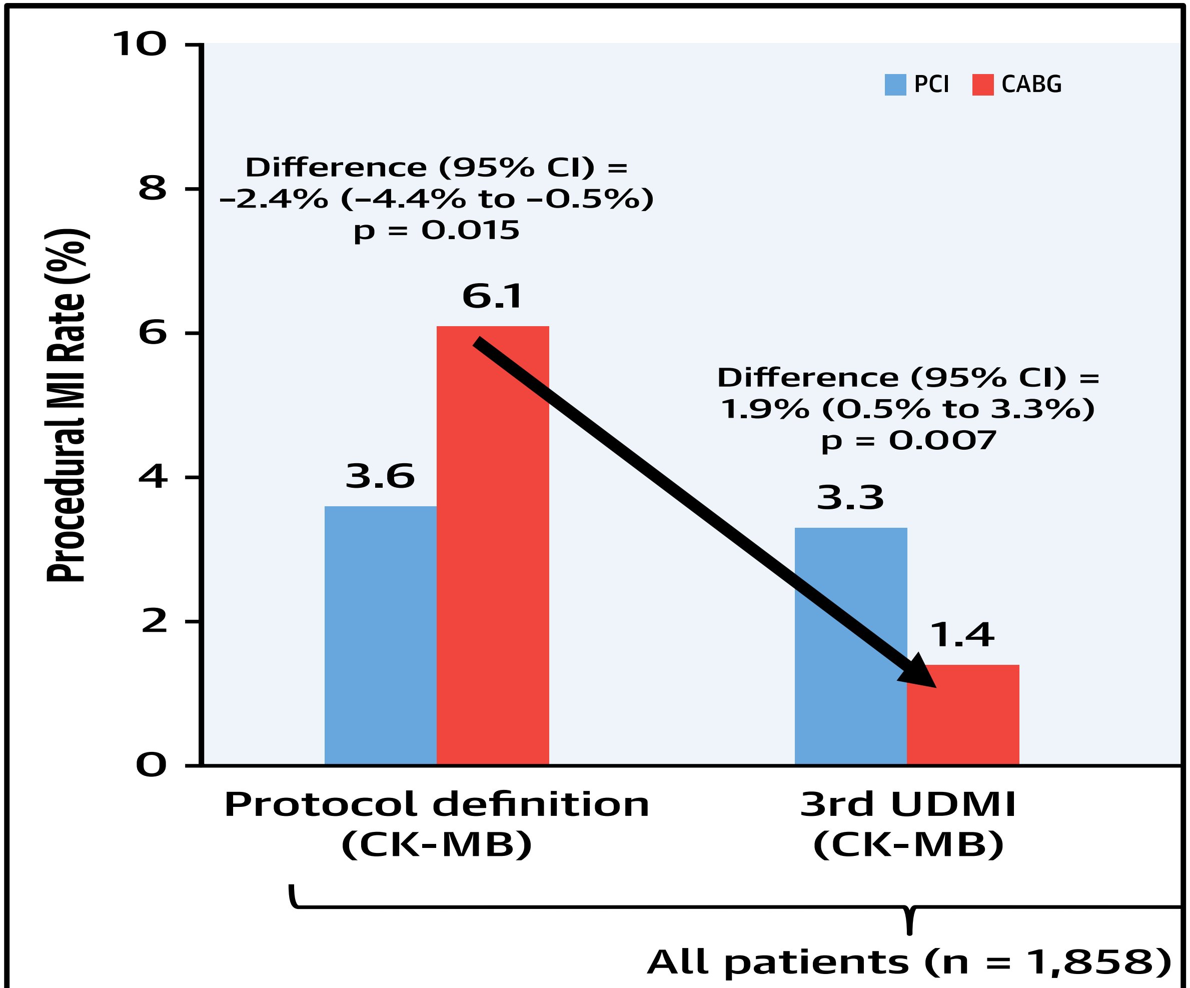
Implications of Alternative Definitions of Peri-Procedural Myocardial Infarction After Coronary Revascularization

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]

[JACC Oct 6 2020]



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THE PRESENT AND FUTURE

STATE-OF-THE-ART REVIEW

Design of Major Randomized Trials

Part 3 of a 4-Part Series on Statistics for Clinical Trials

Stuart J. Pocock, PhD,* Tim C. Clayton, MSc,* Gregg W. Stone, MD†

Choice of outcomes

- Define the primary efficacy endpoint
- Take care in selecting components of composite primary endpoint
- List secondary endpoints
- Incorporate pre-defined safety concerns into overall outcome priorities

What events should contribute to a composite primary endpoint?..... the usual composite is CV death, MI, and stroke. Some are tempted to add in extra components .... this boosts the numbers of events but dilutes the effect and meaning of the composite. For instance, the most frequent (and often least clinically relevant) component tends to be the driver of event rates (**e.g., enzymatic MIs**)

THAT IS EXACTLY WHAT HAPPENED IN EXCEL !

EXCEL: Statistics

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*

Primary outcome at 3 years: **Non-Inferiority** upper margin 4.2%

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*

Primary outcome at 5 years: '**Superiority**': 2.8%: 95% CI -0.9% to 6.5%: p=0.13

NOBLE: PCI vs CABG in Unprotected LM Stenosis

Evald Hoj Christiansen et al, Lancet 2016.

- **Primary endpoint: MACCE including death, stroke, non-procedural MI or repeat revascularization**

NOBLE: PCI vs CABG in Unprotected LM Stenosis

NOBLE

Randomized (n= 1201)

Allocated to PCI (n=598)
- Received PCI (n=585)
- Did not receive PCI (n=13)
  - Died before PCI (n=1)
  - Patient refused PCI (n=4)
  - PCI Operator refused (n=4)
  - LMCA lesion not significant (n=4)
- Received CABG as index treat. (n=6)
- No index treatment (n=7)

Lost to follow-up (n=6)
- Emigration (n=1)
- Contact lost (n=2)
- Withdrawal (n=3)

Patients allocated to PCI in analysis (n=592)

Allocated to CABG (n=603)
- Received CABG (n=570)
- Did not receive CABG (n=33)
  - Died before CABG (n=1)
  - Patient refused CABG (n=15)
  - Not eligible for CABG (n=15)
  - Cross over by mistake (n=2)
- Received PCI as index treat. (n=26)
- No index treatment (n=7)

Lost to follow-up (n=11)
- Emigration (n=0)
- Contact lost (n=0)
- Withdrawal (n=11)

Patients allocated to CABG in analysis (n=592)

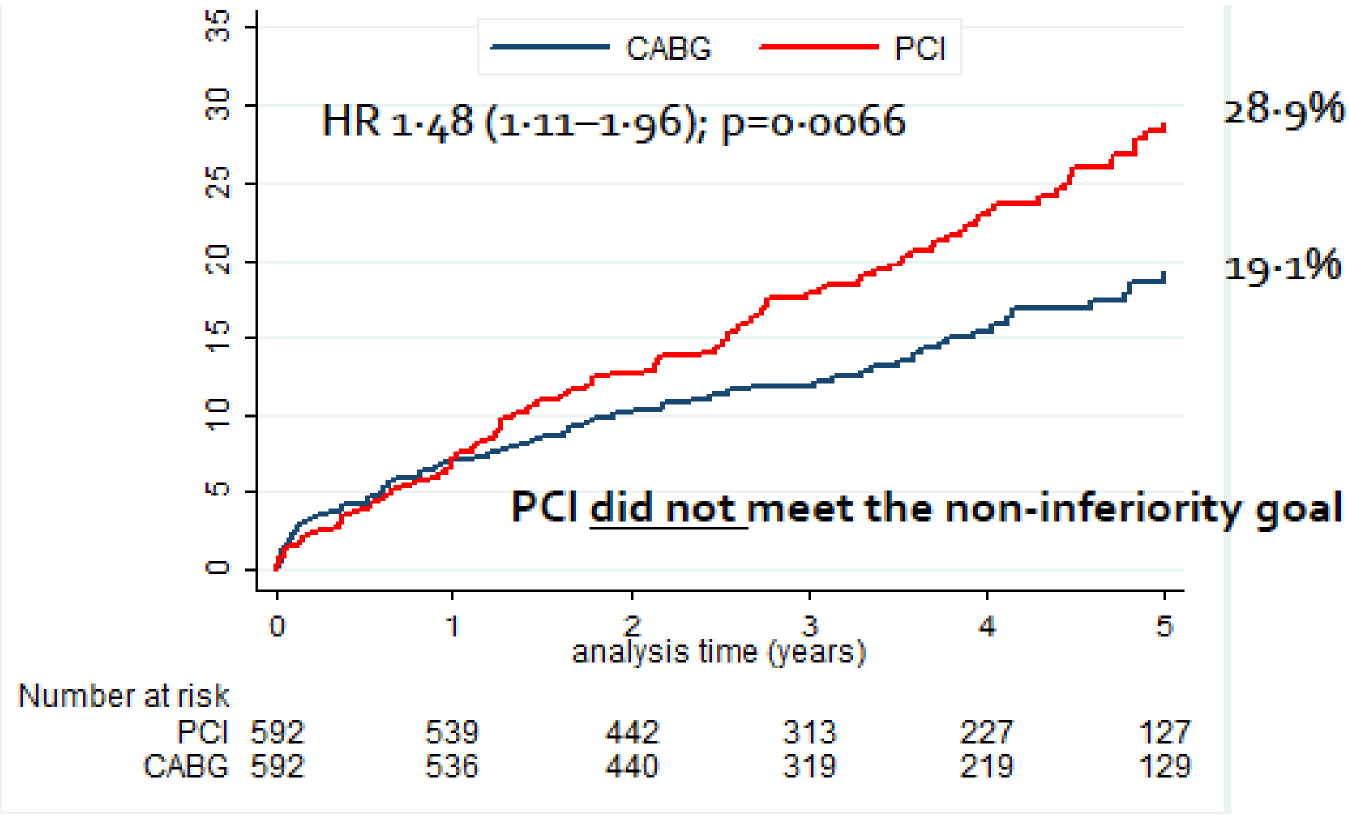
NOBLE

Treatment CABG

Off–pump technique		88 (15·6%)
Arterial graft		532 (94·5%)
Arterial graft to LAD		526 (93·4%)
LIMA + RIMA grafts		44 (7·9%)
LIMA + venous graft		480 (85·7%)
Radial artery graft		26 (4·8%)
Venous grafts only		27 (5·0%)
Grafts per patient	1	23 (4·1%)
	2	294 (52·0%)
	3	220 (39·0%)
	4	25 (4·4%)
	5	3 (0·6%)

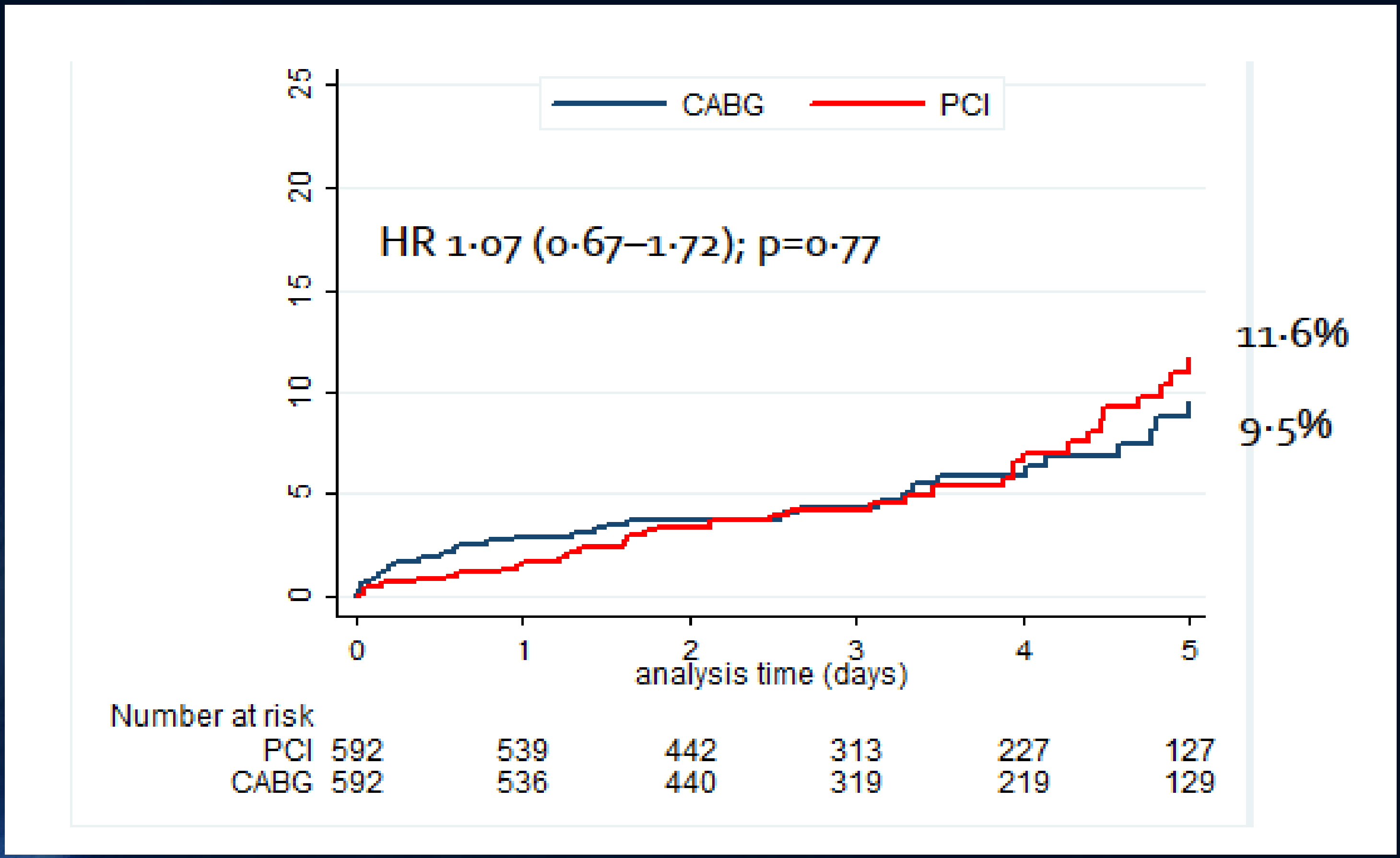
NOBLE

Results
Primary endpoint: MACCE



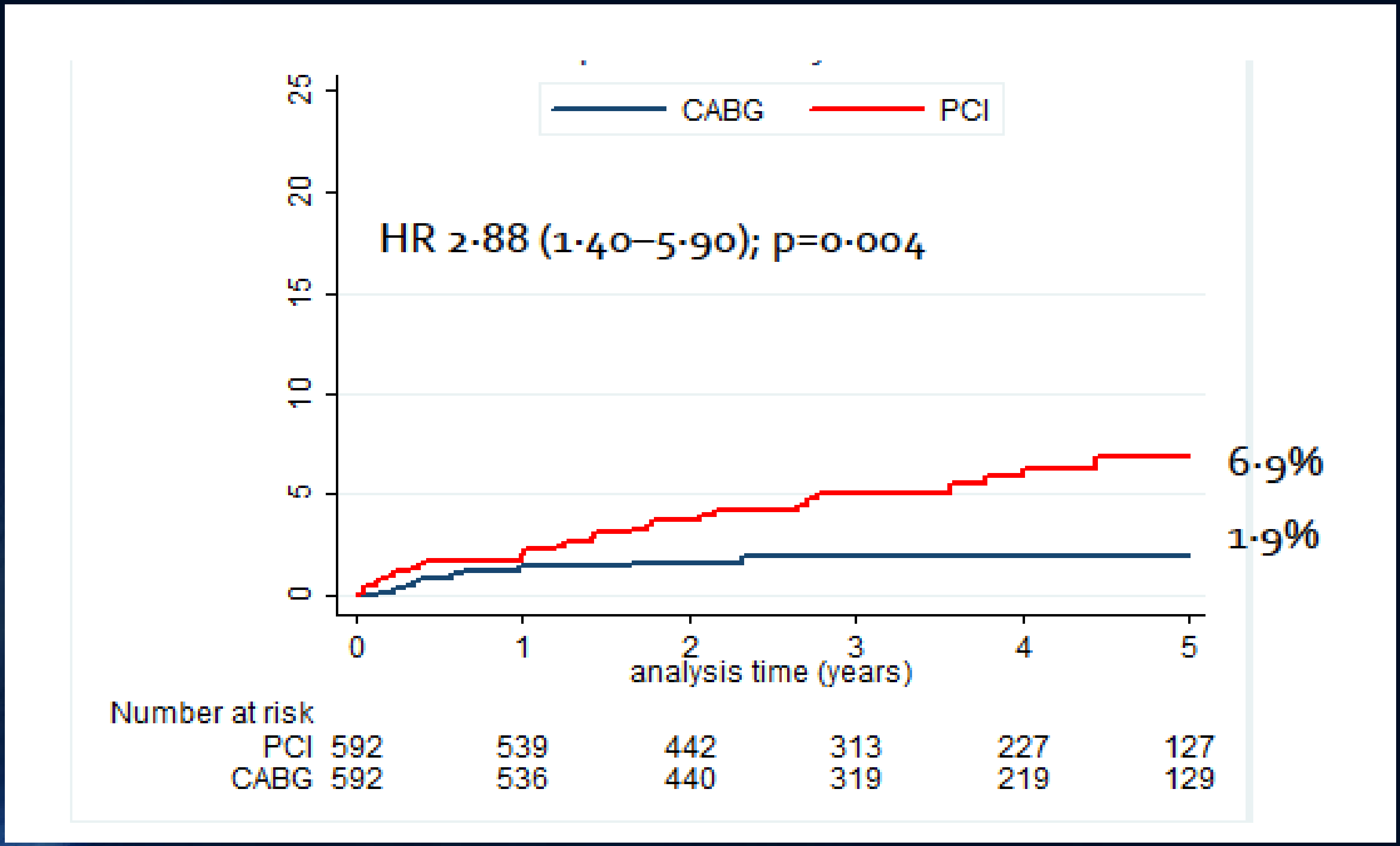
NOBLE

Results
All-cause mortality



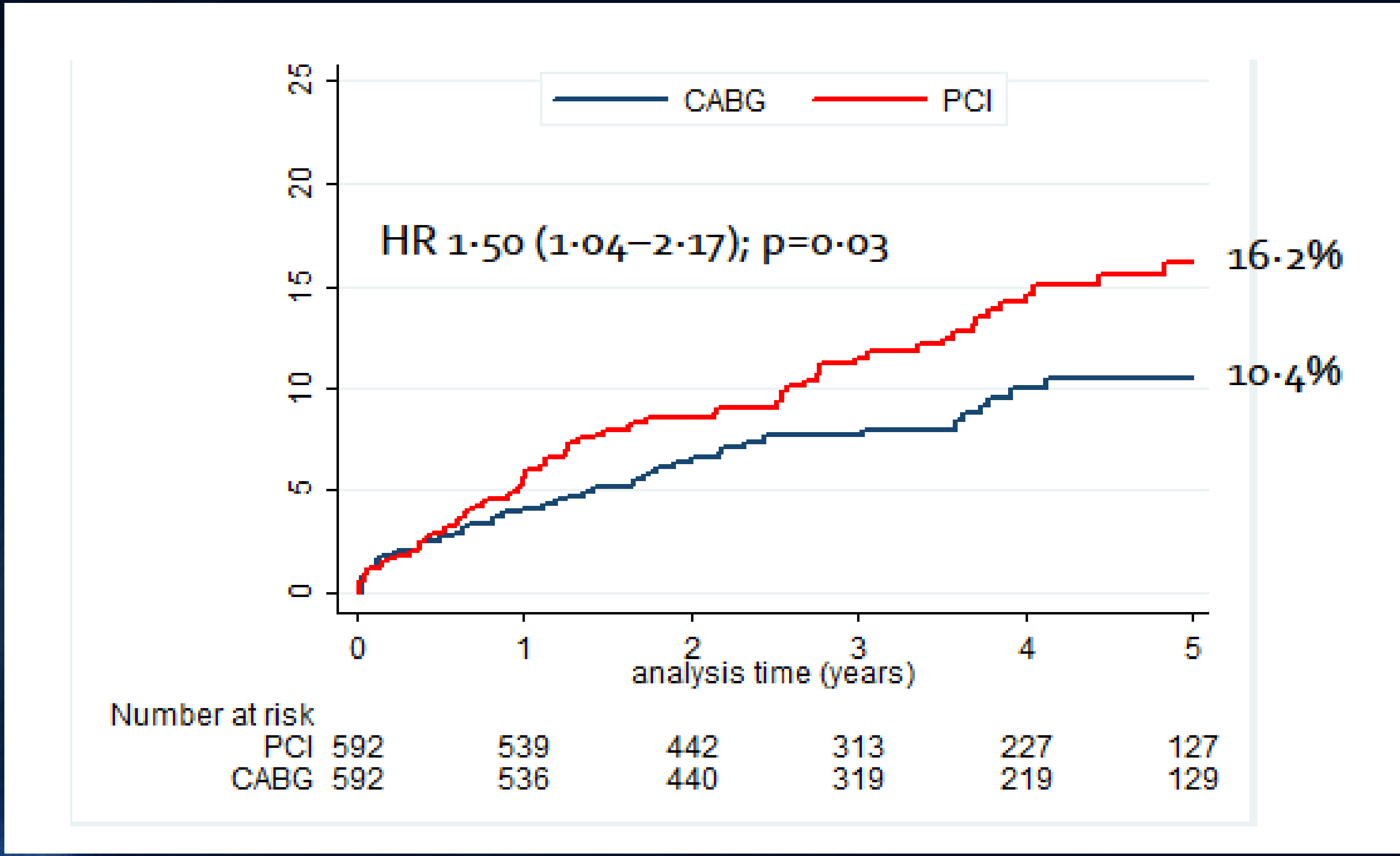
NOBLE

Results
Non-procedural myocardial infarction

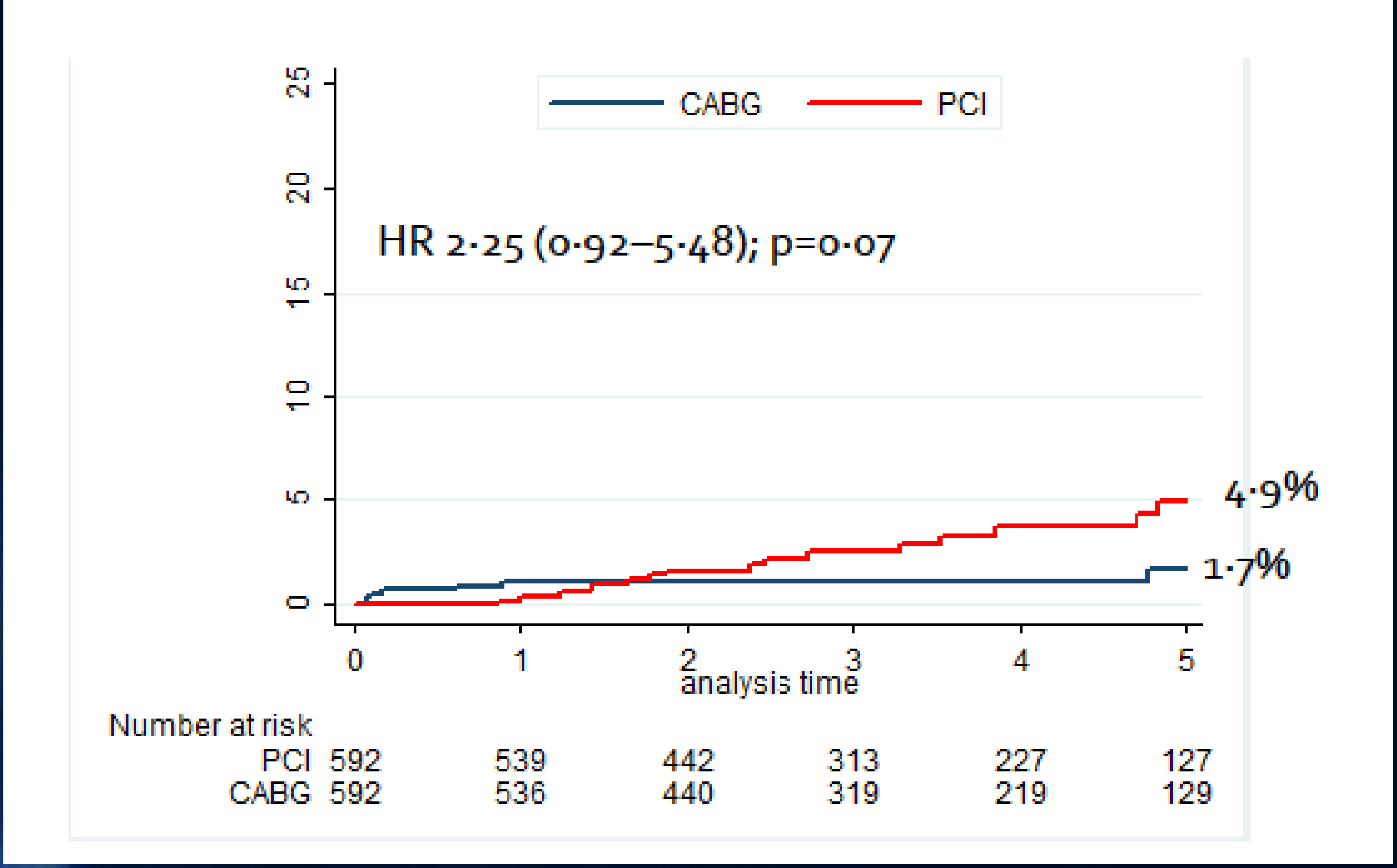


NOBLE

Results
Total repeat revascularization



Results
Stroke

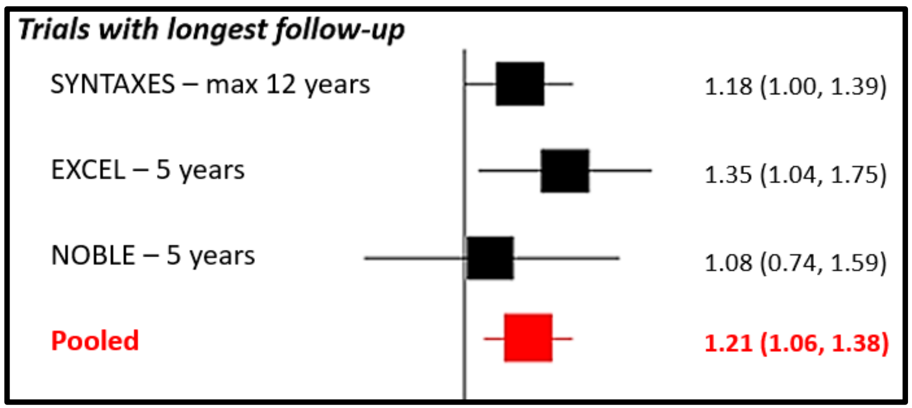


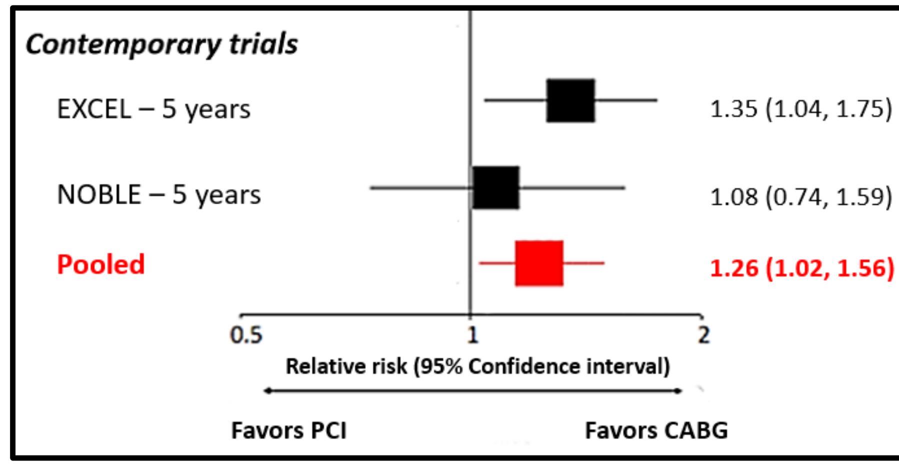
NOBLE

Conclusions

- PCI did not meet non-inferiority for the primary endpoint of 5-year MACCE compared to CABG for treatment of left main stenosis
- PCI resulted in higher rates of non-procedural myocardial infarctions and any revascularization
- All-cause mortality was similar for PCI and CABG

Gaudino M, Freemantle N, Farkouh ME, JTCVS 2020





Patients with SYNTAX scores <33

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JAMA Intern Med. 2020;180(7):986-992. doi:10.1001/jamainternmed.2020.1647
Published online June 1, 2020.

JAMA Internal Medicine | **Original Investigation**

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

James M. Brophy, MD, PhD

RESULTS When EXCEL data were analyzed using the originally stated noninferiority design, the 5-year primary outcome difference reported (2.8%; 95% CI, −0.9% to 6.5%) exceeded the predefined 4.2% noninferiority margin; thus, the null hypothesis of PCI inferiority could not be rejected. By contrast, the present bayesian analysis of the EXCEL primary outcome estimated 95% probability that the 5-year primary outcome difference was increased with PCI compared with CABG and 87% probability that this difference was greater than 1 extra

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.

Sanjay Kaul MD, Cardiologist from Cedars-Sinai, strongly supported this (re-)analysis and interpretation in the Invited Commentary that accompanied the Brophy paper.

Routine LM Stenting Instead of CABG??

Can ≠ Should

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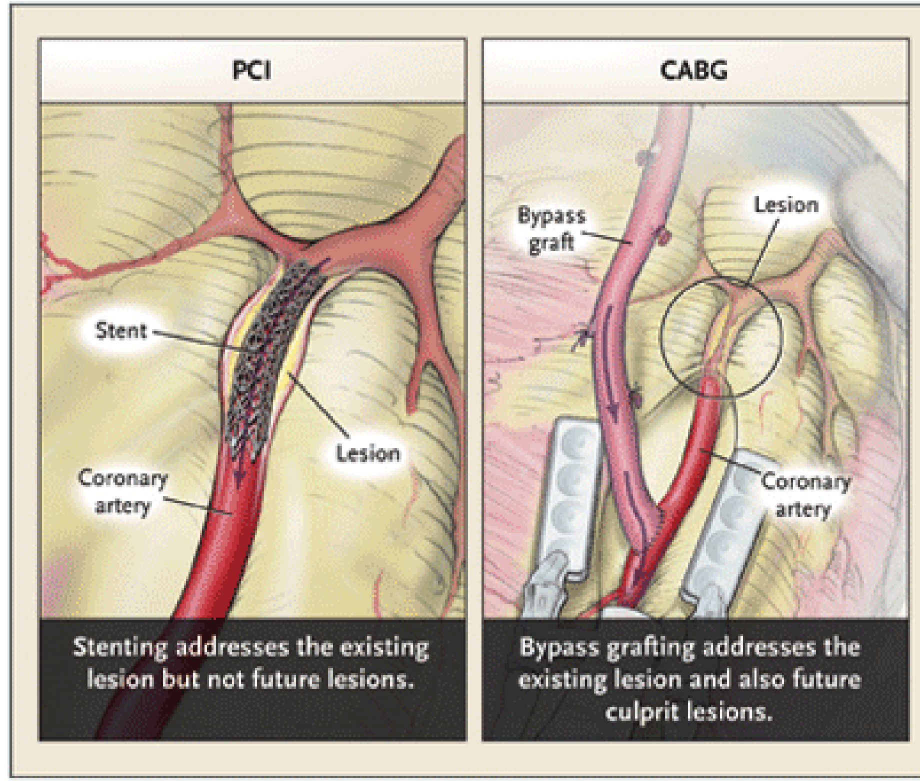
Why is CABG better than PCI?

- PCI treats an isolated flow-limiting lesion in the proximal vessel.
- CABG bypasses the proximal 2/3 of the vessel, where the current lesion(s) *and future threatening lesions* occur.
- <u>Especially with LM CAD, the region of vessel(s) in which future lesions may occur is LARGE</u>.
- *This advantage of CABG will persist, even if Stent restenosis is ZERO.*



<u>NEJM , May 2005</u>

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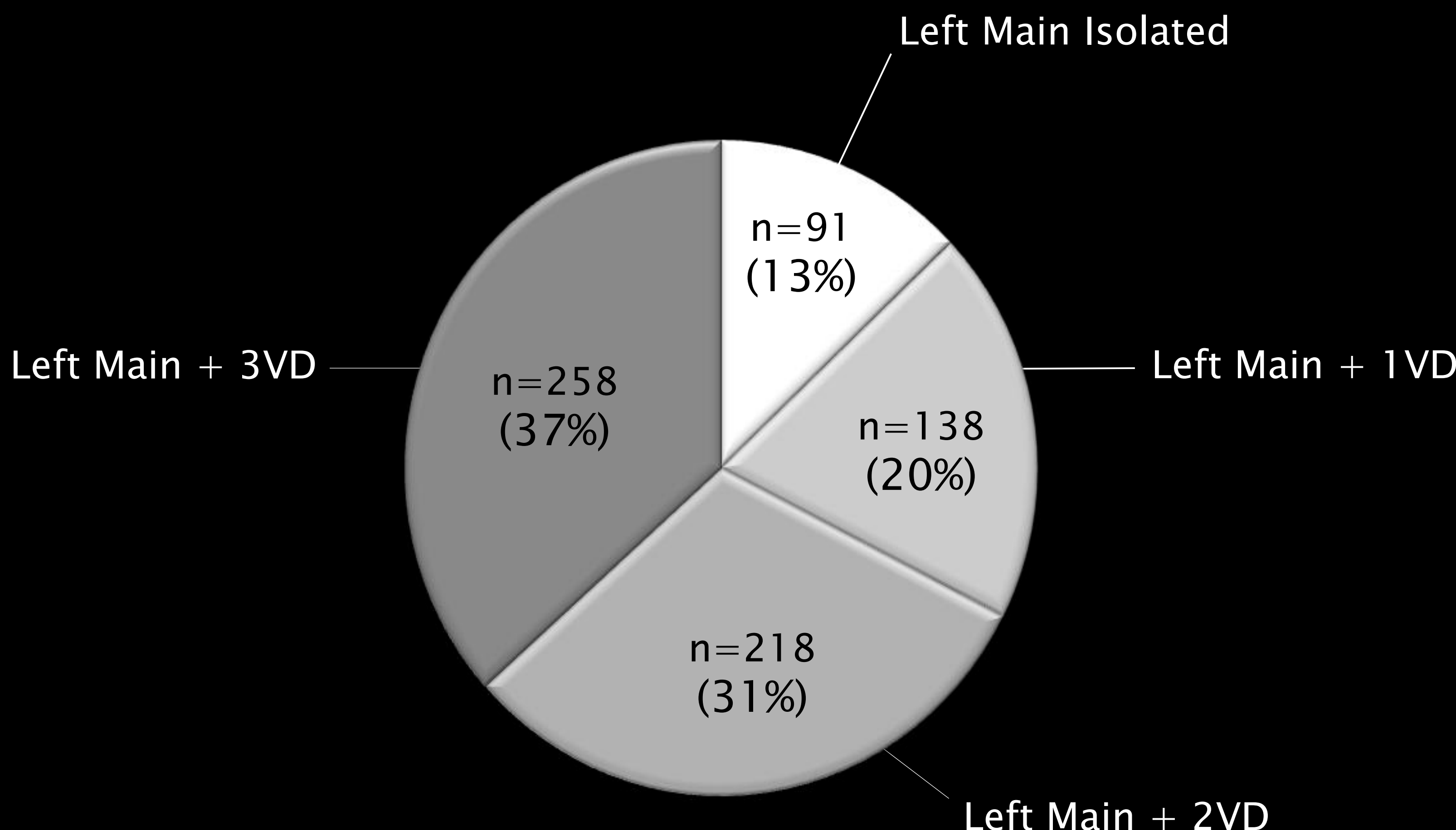
Heterogeneity in the Left Main Group



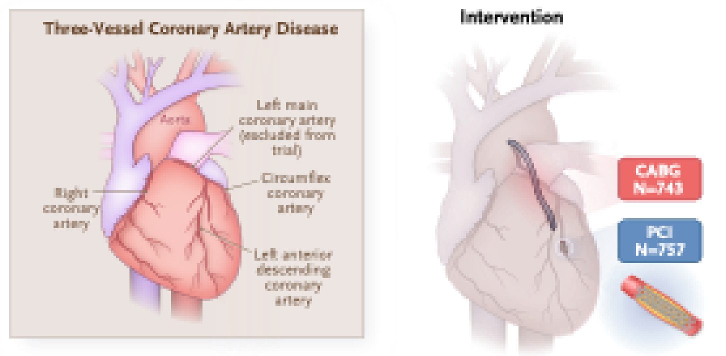
Site-reported data

Fractional Flow Reserve–Guided PCI as Compared with Coronary Bypass Surgery

Fearon WF et al. DOI: 10.1056/NEJMoa2112299

CLINICAL PROBLEM

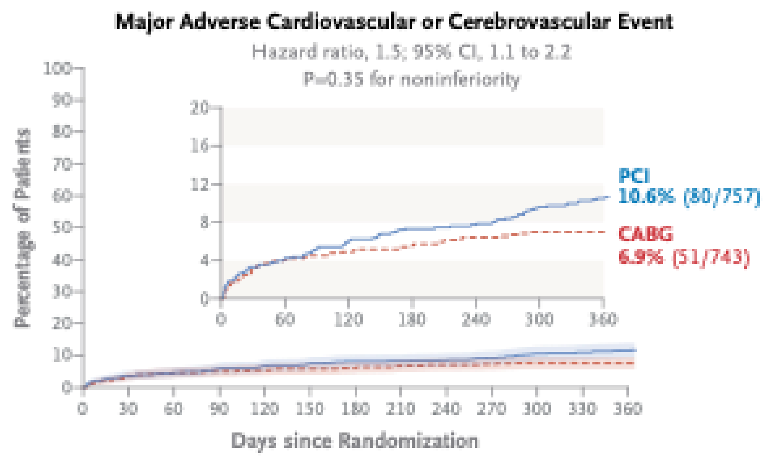
In patients with three-vessel coronary artery disease, coronary-artery bypass grafting (CABG) has shown better outcomes than revascularization with percutaneous coronary intervention (PCI) in large, randomized trials. However, since those trials were conducted, some studies have shown improvements in outcomes with PCI when guided by measurement of fractional flow reserve (FFR).



CLINICAL TRIAL

Design: A multicenter randomized, controlled trial examined whether PCI using current-generation drug-eluting stents and guided by FFR is noninferior to CABG with respect to outcomes at 1 year in patients with three-vessel coronary artery disease.

Intervention: 1500 patients with angiographically identified three-vessel coronary artery disease not involving the left main coronary artery were randomly assigned to undergo FFR-guided PCI or CABG. The primary end point was occurrence within 1 year of a major adverse cardiac or cerebrovascular event, defined as death from any cause, myocardial infarction, stroke, or repeat revascularization.



CONCLUSIONS

In patients with three-vessel coronary artery disease, FFR-guided PCI was not found to be noninferior to CABG with respect to the incidence of a composite of death, myocardial infarction, stroke, or repeat revascularization at 1 year. (Funded by Medtronic and Abbott Vascular; FAME 3 ClinicalTrials.gov number, NCT02100722.)

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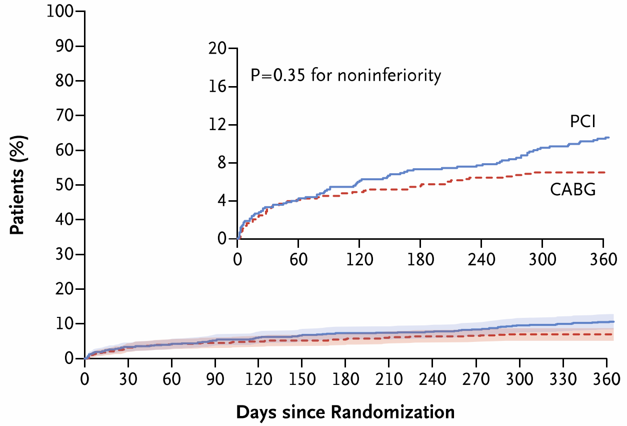

No. at Risk

PCI	757	728	721	713	707	702	697	696	693	687	678	674	670
CABG	743	709	701	698	695	693	691	686	683	682	679	679	679

Figure 1. Kaplan–Meier Curves for the Primary End Point.
The primary end point was the occurrence within 1 year of a major adverse cardiac or cerebrovascular event, defined as death from any cause, myocardial infarction, stroke, or repeat revascularization. The inset shows the same data on an enlarged y axis. CABG denotes coronary-artery bypass grafting, and PCI percutaneous coronary intervention.

FAME 3 Trial NEJM 2022

Subgroup	PCI (total no.)	CABG (total no.)	PCI (1-yr incidence (%))	CABG (1-yr incidence (%))
All patients	757	743	10.6	6.9
Age				
≥65 yr	434	409	9.4	8.1
<65 yr	323	334	12.1	5.4
Sex				
Female	141	124	11.3	13.7
Male	616	619	10.4	5.5
Diabetes				
No	543	529	9.4	7.0
Yes	214	214	13.6	6.5
NSTE-ACS				
No	456	454	10.1	5.9
Yes	300	287	11.3	8.4
LVEF				
>50%	616	610	10.4	6.6
30–50%	137	130	10.9	8.5
Previous PCI				
No	658	637	9.3	6.8
Yes	98	104	19.4	7.7
SYNTAX score				
0–22	237	245	5.5	8.6
23–32	365	343	13.7	6.1
≥33	132	122	12.1	6.6

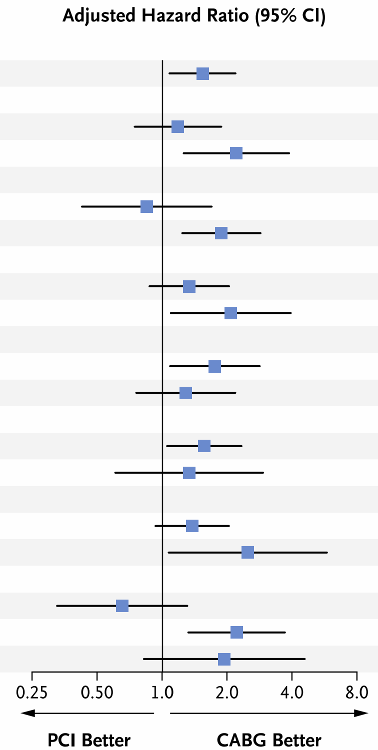

Figure 2. Subgroup Analyses of the Primary End Point.
The Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery (SYNTAX) score is an angiography-based score evaluating the severity of coronary artery disease; lower scores indicate less complexity of coronary artery disease and predict a better outcome with PCI (the lowest score is 0, and there is no upper limit). Scores were calculated by the core laboratory. CI denotes confidence interval, LVEF left ventricular ejection fraction, and NSTE-ACS non–ST-segment elevation acute coronary syndrome.

CONCLUSIONS

In patients with three-vessel coronary artery disease, FFR-guided PCI was not found to be noninferior to CABG with respect to the incidence of a composite of death, myocardial infarction, stroke, or repeat revascularization at 1 year. (Funded by Medtronic and Abbott Vascular; FAME 3 ClinicalTrials.gov number, NCT02100722.)

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Table 3. **End Points at 1 Year.**

End Point	PCI (N=757)	CABG (N=743)	Hazard Ratio (95% CI)	P Value
	*no. of patients (%)**			
Primary end point				
Death from any cause, myocardial infarction, stroke, or repeat revascularization	80 (10.6)	51 (6.9)	1.5 (1.1–2.2)	0.35†
Secondary end points‡				
Death	12 (1.6)	7 (0.9)	1.7 (0.7–4.3)	
Death from cardiac causes	6 (0.8)	4 (0.5)		
Myocardial infarction	39 (5.2)	26 (3.5)	1.5 (0.9–2.5)	
Spontaneous	25 (3.3)	17 (2.3)		
Procedural	13 (1.7)	9 (1.2)		
Stroke	7 (0.9)	8 (1.1)	0.9 (0.3–2.4)	
Death, myocardial infarction, or stroke	55 (7.3)	39 (5.2)	1.4 (0.9–2.1)	
Repeat revascularization	45 (5.9)	29 (3.9)	1.5 (0.9–2.3)	
PCI	39 (5.2)	26 (3.5)		
CABG	6 (0.8)	3 (0.4)		
Safety end points§				
BARC type 3–5 bleeding¶	12 (1.6)	28 (3.8)		0.009
Acute kidney injury‖	1 (0.1)	7 (0.9)		0.04
Atrial fibrillation or clinically significant arrhythmia	18 (2.4)	105 (14.1)		<0.001
Definite stent thrombosis	6 (0.8)	NA		
Definite symptomatic graft occlusion	NA	10 (1.3)		
Rehospitalization within 30 days	42 (5.5)	76 (10.2)		<0.001

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In patients with three-vessel coronary artery disease, FFR-guided PCI was not found to be noninferior to CABG with respect to the incidence of a composite of death, myocardial infarction, stroke, or repeat revascularization at 1 year. (Funded by Medtronic and Abbott Vascular; FAME 3 ClinicalTrials.gov number, NCT02100722.)

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CABG versus PCI – End of the Debate?

Frederick G.P. Welt, MD (Cardiologist)
Invited Commentary on FAME 3 Trial, NEJM 2022

- "The totality of the data to date supports CABG as the standard of care for patients with stable multivessel coronary disease when the overall surgical risk is not high, when the complexity and burden of angiographic disease is high and when diabetes is present."
- "FFR-guided PCI does not result in outcomes as good as those of CABG in patients with angiographically defined multivessel coronary disease."

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Conclusions: PCI vs CABG for LM CAD

- Risk of CABG is related to patient related factors
- Risk of PCI is related to CAD complexity
- The majority of LM disease (60-75%) - high CAD complexity - best treated with surgery
- PCI for LM CAD is most appropriate for patients with isolated LM disease, and those with limited life expectancy and/or elevated risk factors for CABG.

Hybrid Coronary Revascularization Versus Off-Pump Coronary Artery Bypass for the Treatment of Left Main Coronary Stenosis

Michael E. Halkos, MD, S. Tanveer Rab, MD, Thomas A. Vassiliades, MD, MBA, Douglas C. Morris, MD, John S. Douglas, MD, Patrick D. Kilgo, MS, Henry A. Liberman, MD, Robert A. Guyton, MD, Vinod H. Thourani, MD, and John D. Puskas, MD

(Ann Thorac Surg 2011;92:2155–60)

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