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Excel and Noble Trials : What Is the Impact on Clinical Practice Two Years Later

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Before EXCEL and NOBLE…

PCI vs CABG for LM Disease : 12 Meta-Analyses, 2009-2014

Author	Journal	Year	RCT	Non-RCT	Pts	FU

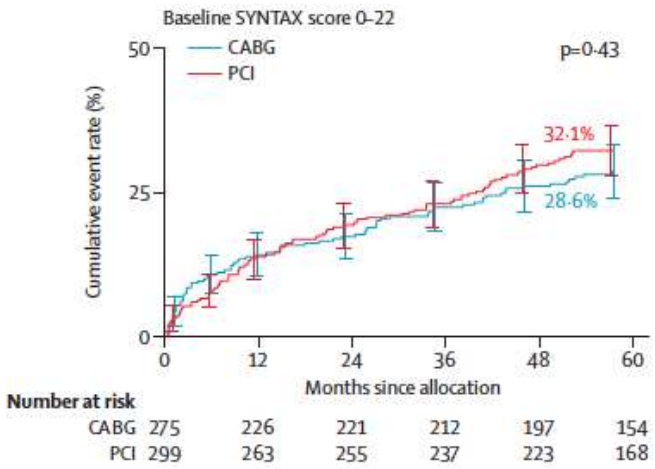
DES vs. CABG *for LM Disease*
Consensus from trials and meta-analysis

1.Stoke is Higher in CABG.
2.TVR is Higher in PCI.
3.Outcomes of PCI with DES is Comparable with CABG in low and intermediate risk patients
4. CABG is superior in patients with diffuse disease

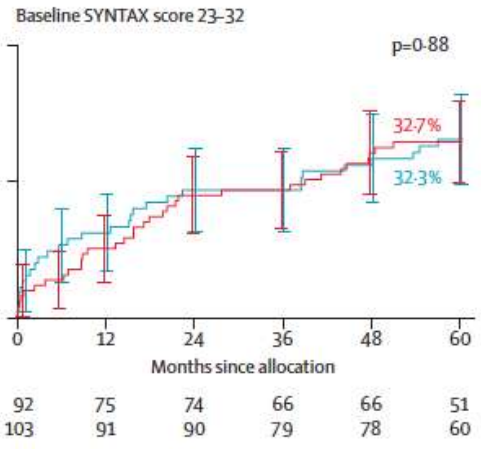
SYNTAX Trial : LM

5yrs Outcome

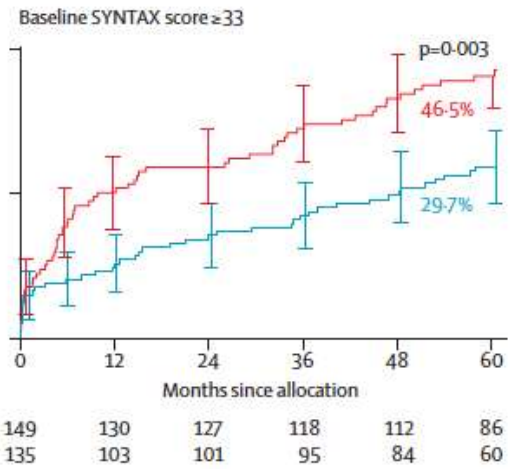
SYNTAX Score 0-22



SYNTAX Score 23-32



SYNTAX Score ≥ 33



Eur Heart J. 2014,35:2821-2830

The Trial That Changed our Practice …

European Heart Journal Advance Access published August 29, 2014

European Heart Journal
doi:10.1093/eurheartj/ehu278

ESC/EACTS GUIDELINES

2014 ESC/EACTS Guidelines on myocardial revascularization

The Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)

Recommendation for the type of revascularization (CABG or PCI) in patients with SCAD with suitable coronary anatomy for both procedures and low predicted surgical mortality

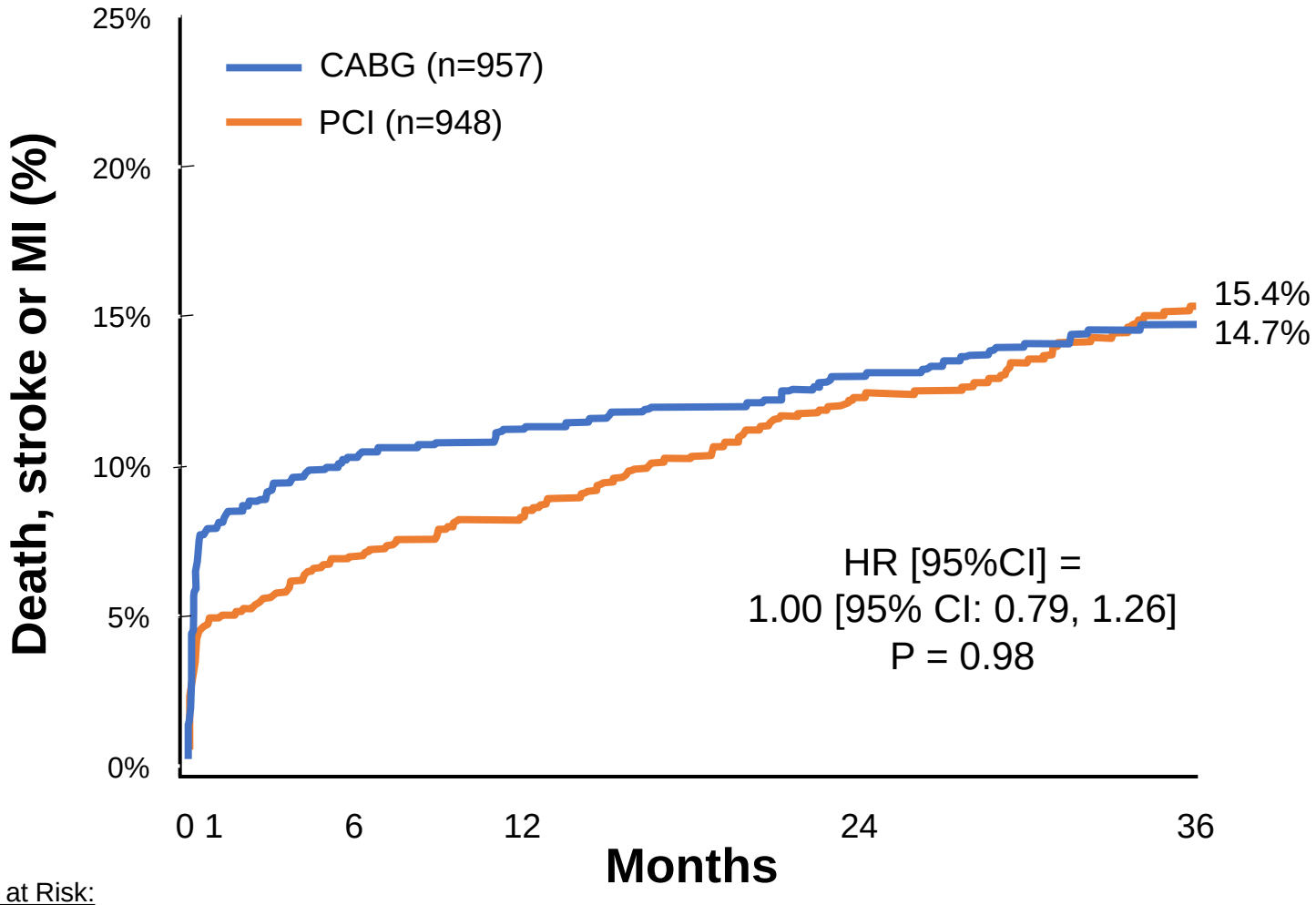
Yes We Can !

Left main disease with a SYNTAX score ≤ 22.	I	B	I	B	17,134,170
Left main disease with a SYNTAX score 23–32.	I	B	IIa	B	17

CABG = coronary artery bypass grafting; LAD = left anterior descending coronary artery; PCI = percutaneous coronary intervention; SCAD = stable coronary artery disease.
[a]Class of recommendation.
[b]Level of evidence.
[c]References.

Primary Endpoint

Death, Stroke or MI at 3 Years



No. at Risk:

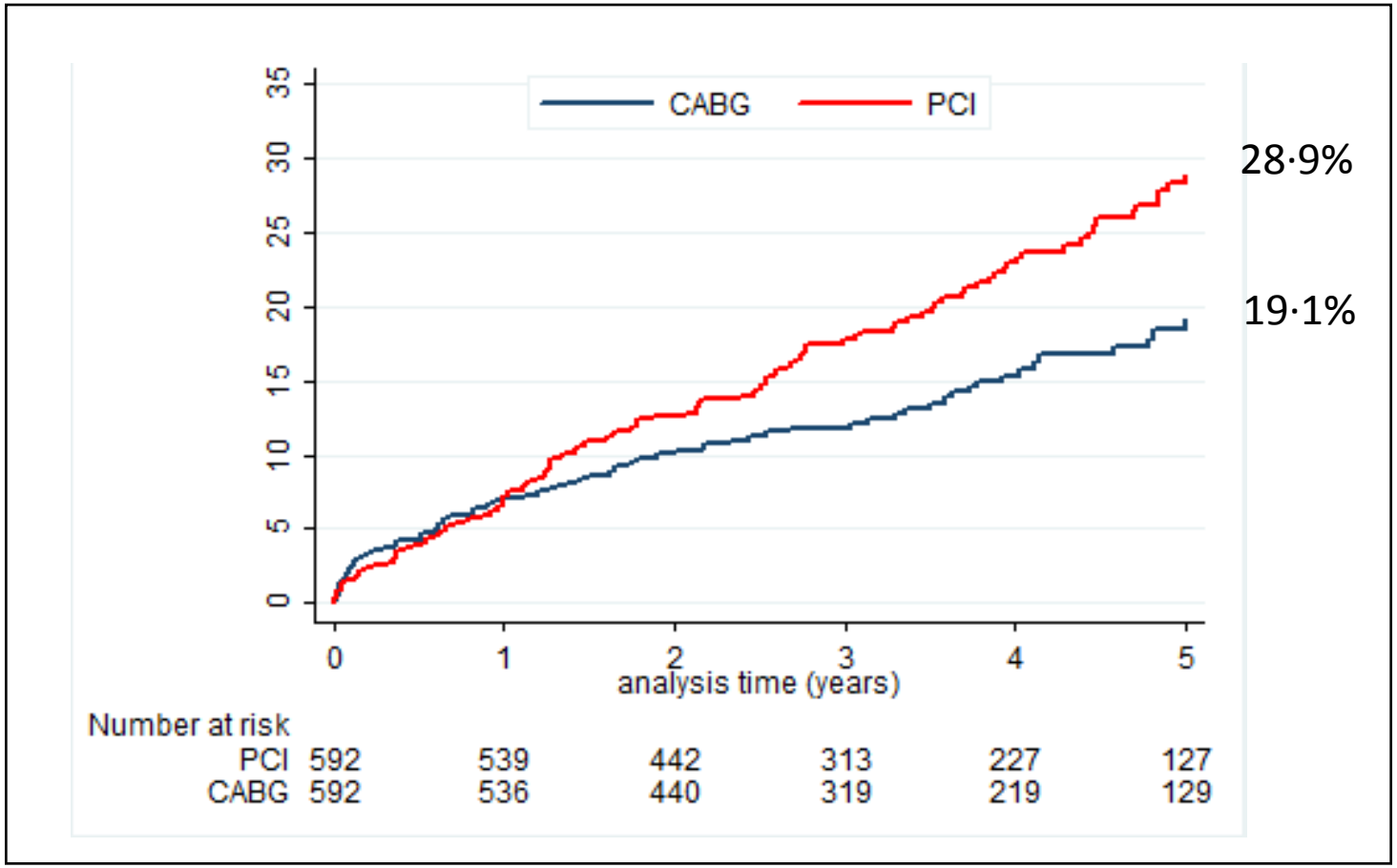
PCI	948	896	875	850	784	445
CABG	957	868	836	817	763	458

GW Stone et al; N Engl J Med. 2016;375:2223–2235

NOBLE

Primary endpoint: MACCE

(All cuase-Mortality, Non-procedural MI, RR, Stroke)



T. Makikallio et al; Lancet. 2016;388:2743–2752

EXCEL and NOBLE Trials : Similarities and Diferences

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%

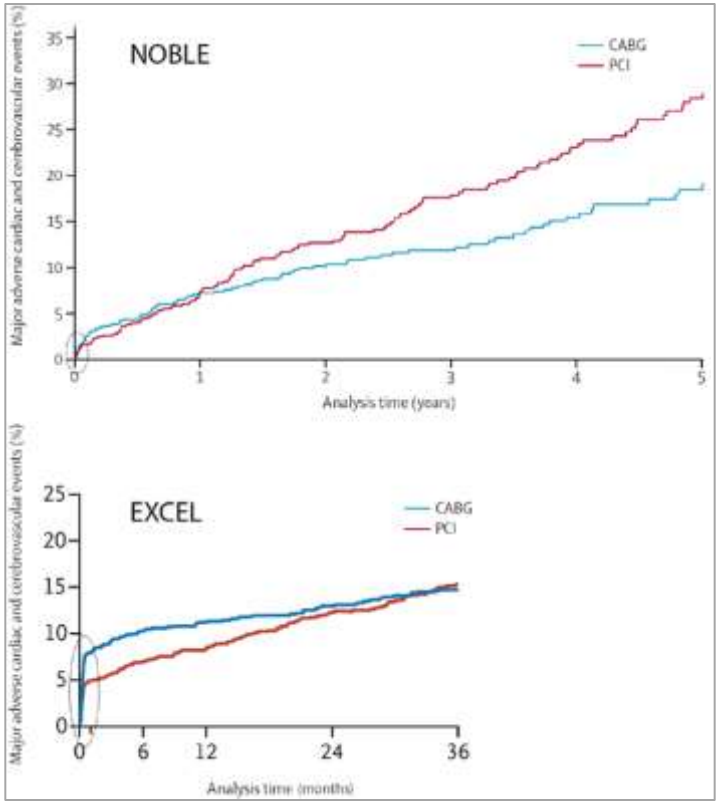
Holmes AA, Bangalore S. J Thorac Dis 2017;9(5):E451-E456.

EXCEL and NOBLE Trials : Similarities and Diferences

Variables	NOBLE trial	EXCEL trial
Trial design		
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%[‡]

Holmes AA, Bangalore S. J Thorac Dis 2017;9(5):E451-E456.

Primary end point event in NOBLE and EXCEL trials at 5 and 3 years of follow-up respectively.



Interpreting the results of EXCEL and NOBLE:

- **Study population : More 704 pts recruited in EXCEL** mean SYNTAX score of EXCEL was 20.6% versus 22.5 % in NOBLE (ns) but both had 81% of distal bifurcation disease. IVUS guidance was used in 77% of cases in EXCEL compared to 47% pre-stent and 77% post-stent in NOBLE. To underline the prevalence of distal LM bifurcation which might impact the outcome since it needs having an experienced heart team, familiar with current best practices and techniques for the management of these patients and to achieve optimal outcomes
- **All-cause-mortality or cardiac-death similar between PCI and CABG in both studies .**
- **Difference in rates of spontaneous MI and higher stent thrombosis** PCI may refflects the **different stents** used in the two trials. (meta-analysis has shown that the BES has an inferior safety profile compared to the EES).
- **In NOBLE, the higher rate of spontaneous MI and TLR** drove the primary composite endpoint in favor of CABG

October 2016 : Excel & Noble Trials at TCT

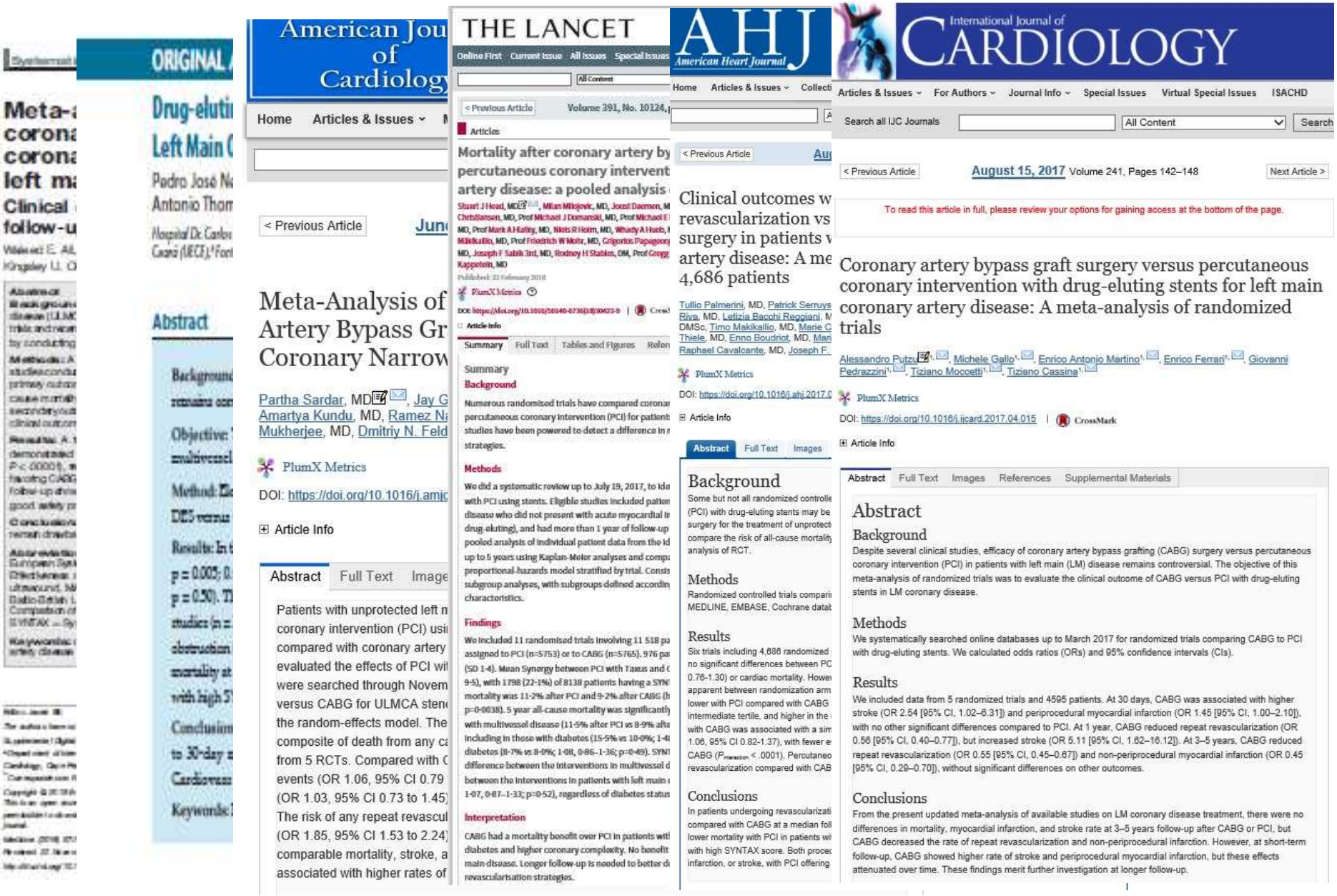
From October 2016 to Mrach 2018 : 269 pubblicaions !!

2 PCI vs CABG
5 Techniques
12 PCI outcomes
8 Intravsacular imaging
11 LM PCI in TAVR
17 Acute setting
25 PCI vs CABG meta-analysis or pooled analysis
…. Case Report and others

Summary of Major Clinical Trials Endpoints Evaluating PCI vs CABG for Management of Unprotected Left Main Coronary Artery Disease

- No difference in mortality between the two treatment strategies
- Meta-analysis including the SYNTAX, PRECOMBAT, Buodriot et al., NOBLE and EXCEL show no difference in safety endpoints.
- In patients with high-risk anatomy with LM and/or MV disease with CABG is clearly the better strategy with superior long-term outcomes.
- Patients with low or intermediate risk anatomy (SYNTAX score ≤32) either PCI or CABG are reasonable with PCI being associated with less morbidity, hospital stays and lower stroke rates in the periprocedural period but with higher over
- time despite use of II generation DES , intravscualr imaging , procedural techniques and medical therapy.

N. Borges, S.R Kapadia and SG Ellis: *Interventional Cardiology Review* 2017;12(2):92–6



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Pedro José N
Antonio Thom

Abstract

Objective:
Method:
Results:
Conclusion
Keywords:

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Meta-Analysis of
Artery Bypass Gr
Coronary Narrow

Partha Sardar, MD, Jay G
Amartya Kundu, MD, Ramez Na
Mukherjee, MD, Dmitriy N. Feld

PlumX Metrics

DOI: https://doi.org/10.1016/j.amjc

Article Info

Abstract Full Text Image

Patients with unprotected left m
coronary intervention (PCI) usi
compared with coronary artery
evaluated the effects of PCI wi
were searched through Novem
versus CABG for ULMCA sten
the random-effects model. The
composite of death from any ca
from 5 RCTs. Compared with
events (OR 1.06, 95% CI 0.79
(OR 1.03, 95% CI 0.73 to 1.45)
The risk of any repeat revascul
(OR 1.85, 95% CI 1.53 to 2.24)
comparable mortality, stroke, a
associated with higher rates of

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Articles

Mortality after coronary artery by
percutaneous coronary intervent
artery disease: a pooled analysis

Summary Full Text Tables and Figures

Summary

Background

Numerous randomised trials have compared coronar
percutaneous coronary intervention (PCI) for patient
studies have been powered to detect a difference in
strategies.

Methods

We did a systematic review up to July 19, 2017, to ide
with PCI using stents. Eligible studies included patien
disease who did not present with acute myocardial in
drug-eluting), and had more than 1 year of follow-up
pooled analysis of individual patient data from the id
up to 5 years using Kaplan-Meier analyses and compa
proportional-hazards model stratified by trial. Consis
subgroup analyses, with subgroups defined accordin
characteristics.

Findings

We included 11 randomised trials involving 11 518 pa
assigned to PCI (n=5753) or to CABG (n=5765). 976 pa
(SD 1·4). Mean Synergy between PCI with Taxus and
9·5), with 1798 (22·1%) of 8138 patients having a SYN
mortality was 11·2% after PCI and 9·2% after CABG (h
p=0·0038). 5 year all-cause mortality was significantly
with multivessel disease (11·5% after PCI vs 8·9% afte
including in those with diabetes (15·5% vs 10·0%; 1·4
diabetes (8·7% vs 8·9%; 1·08, 0·86–1·36; p=0·49). SYNT
difference between the interventions in multivessel d
between the interventions in patients with left main
1·07, 0·87–1·33; p=0·52), regardless of diabetes status

Interpretation

CABG had a mortality benefit over PCI in patients wit
diabetes and higher coronary complexity. No benefit
main disease. Longer follow-up is needed to better d
revascularisation strategies.

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American Heart Journal

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Clinical outcomes w
revascularization vs
surgery in patients
artery disease: A me
4,686 patients

Tullio Palmerini, MD, Patrick Serruys
Riva, MD, Letizia Bacchi Reggiani,
DMSc, Timo Makikallio, MD, Marie C
Thiele, MD, Enno Boudriot, MD, Mari
Raphael Cavalcante, MD, Joseph F.

PlumX Metrics

DOI: https://doi.org/10.1016/j.ahj.2017.0

Article Info

Abstract Full Text Images

Background

Some but not all randomized controlle
(PCI) with drug-eluting stents may be
surgery for the treatment of unprotect
compare the risk of all-cause mortalit
analysis of RCT.

Methods

Randomized controlled trials compari
MEDLINE, EMBASE, Cochrane datab

Results

Six trials including 4,686 randomized
no significant differences between PC
0.76-1.30) or cardiac mortality. Howe
apparent between randomization arm
lower with PCI compared with CABG
intermediate tertile, and higher in the
with CABG was associated with a sim
1.06, 95% CI 0.82-1.37), with fewer e
CABG ($P_{interaction}$ < .0001). Percutaneo
revascularization compared with CAB

Conclusions

In patients undergoing revascularizati
compared with CABG at a median foll
lower mortality with PCI in patients wi
with high SYNTAX score. Both proce
infarction, or stroke, with PCI offering

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CARDIOLOGY

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Coronary artery bypass graft surgery versus percutaneous coronary intervention with drug-eluting stents for left main coronary artery disease: A meta-analysis of randomized trials

Alessandro Putzu, Michele Gallo, Enrico Antonio Martino, Enrico Ferrari, Giovanni Pedrazzini, Tiziano Moccetti, Tiziano Cassina

PlumX Metrics

DOI: https://doi.org/10.1016/j.ijcard.2017.04.015 | CrossMark

Article Info

Abstract Full Text Images References Supplemental Materials

Abstract

Background

Despite several clinical studies, efficacy of coronary artery bypass grafting (CABG) surgery versus percutaneous coronary intervention (PCI) in patients with left main (LM) disease remains controversial. The objective of this meta-analysis of randomized trials was to evaluate the clinical outcome of CABG versus PCI with drug-eluting stents in LM coronary disease.

Methods

We systematically searched online databases up to March 2017 for randomized trials comparing CABG to PCI with drug-eluting stents. We calculated odds ratios (ORs) and 95% confidence intervals (CIs).

Results

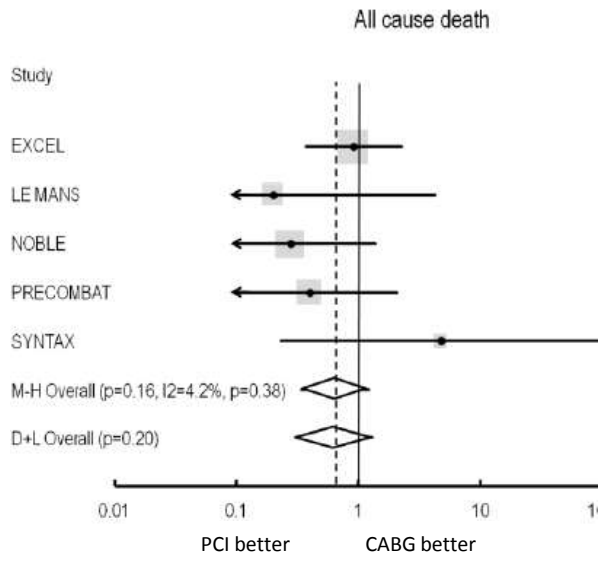
We included data from 5 randomized trials and 4595 patients. At 30 days, CABG was associated with higher stroke (OR 2.54 [95% CI, 1.02–6.31]) and periprocedural myocardial infarction (OR 1.45 [95% CI, 1.00–2.10]), with no other significant differences compared to PCI. At 1 year, CABG reduced repeat revascularization (OR 0.56 [95% CI, 0.40–0.77]), but increased stroke (OR 5.11 [95% CI, 1.62–16.12]). At 3–5 years, CABG reduced repeat revascularization (OR 0.55 [95% CI, 0.45–0.67]) and non-periprocedural myocardial infarction (OR 0.45 [95% CI, 0.29–0.70]), without significant differences on other outcomes.

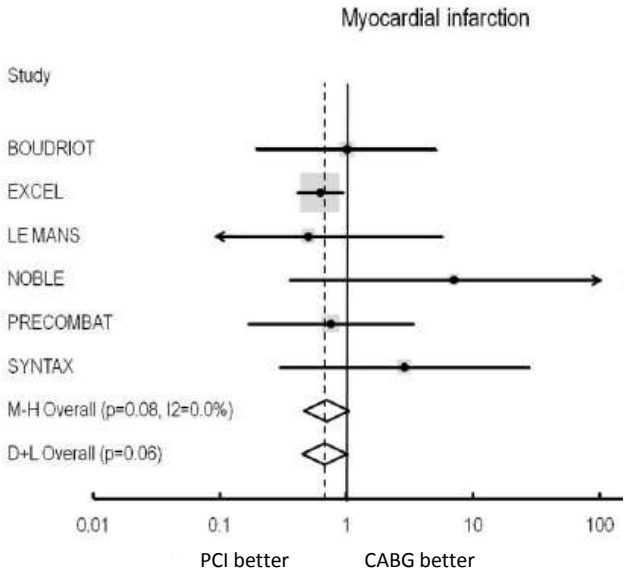
Conclusions

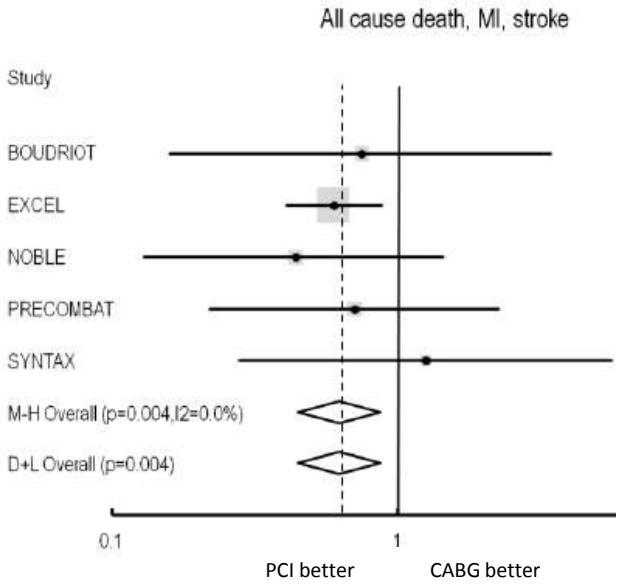
From the present updated meta-analysis of available studies on LM coronary disease treatment, there were no differences in mortality, myocardial infarction, and stroke rate at 3–5 years follow-up after CABG or PCI, but CABG decreased the rate of repeat revascularization and non-periprocedural infarction. However, at short-term follow-up, CABG showed higher rate of stroke and periprocedural myocardial infarction, but these effects attenuated over time. These findings merit further investigation at longer follow-up.

PCI vs CABG for LM – a Meta-Analysis of Six Randomized Trials and 4,686 pts

30-day outcomes



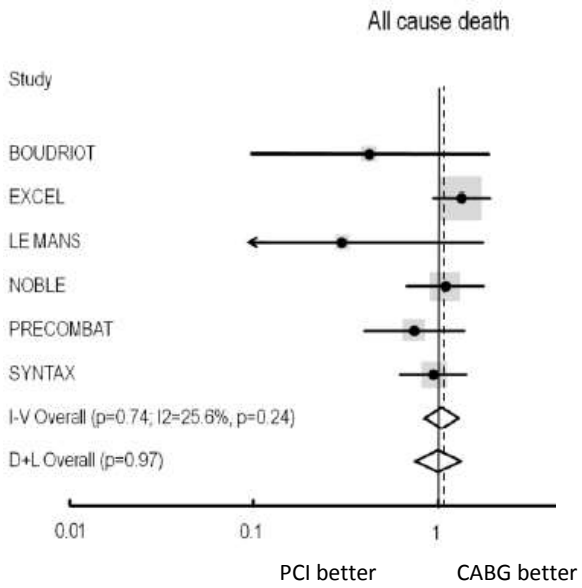


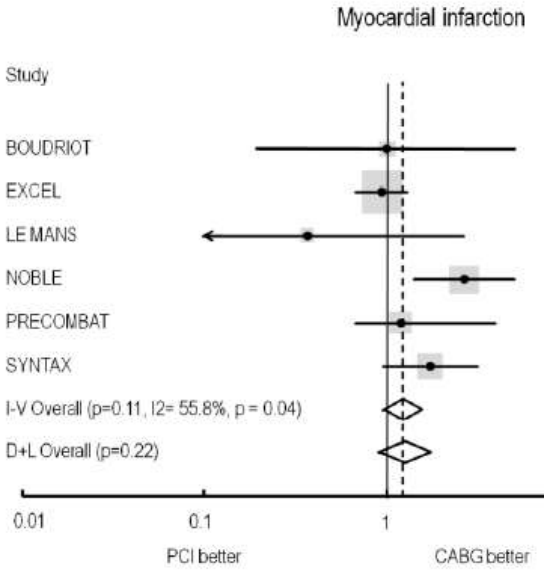


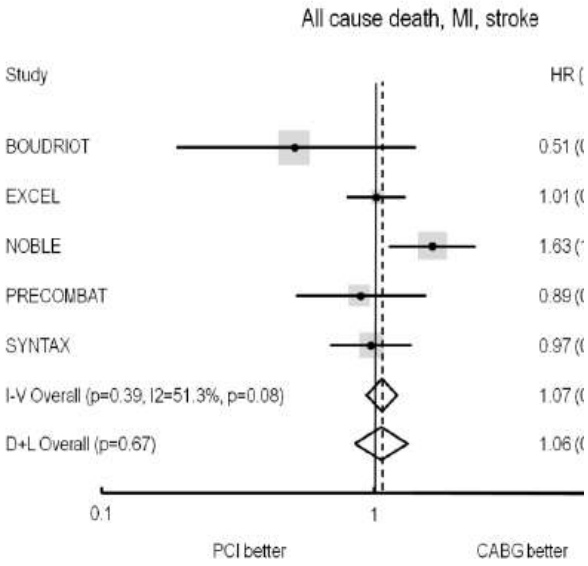
Palmerini T et al. *Am Heart J* 2017

PCI vs CABG for LM – a Meta-Analysis of Six Randomized Trials and 4,686 pts

Long Term outcomes

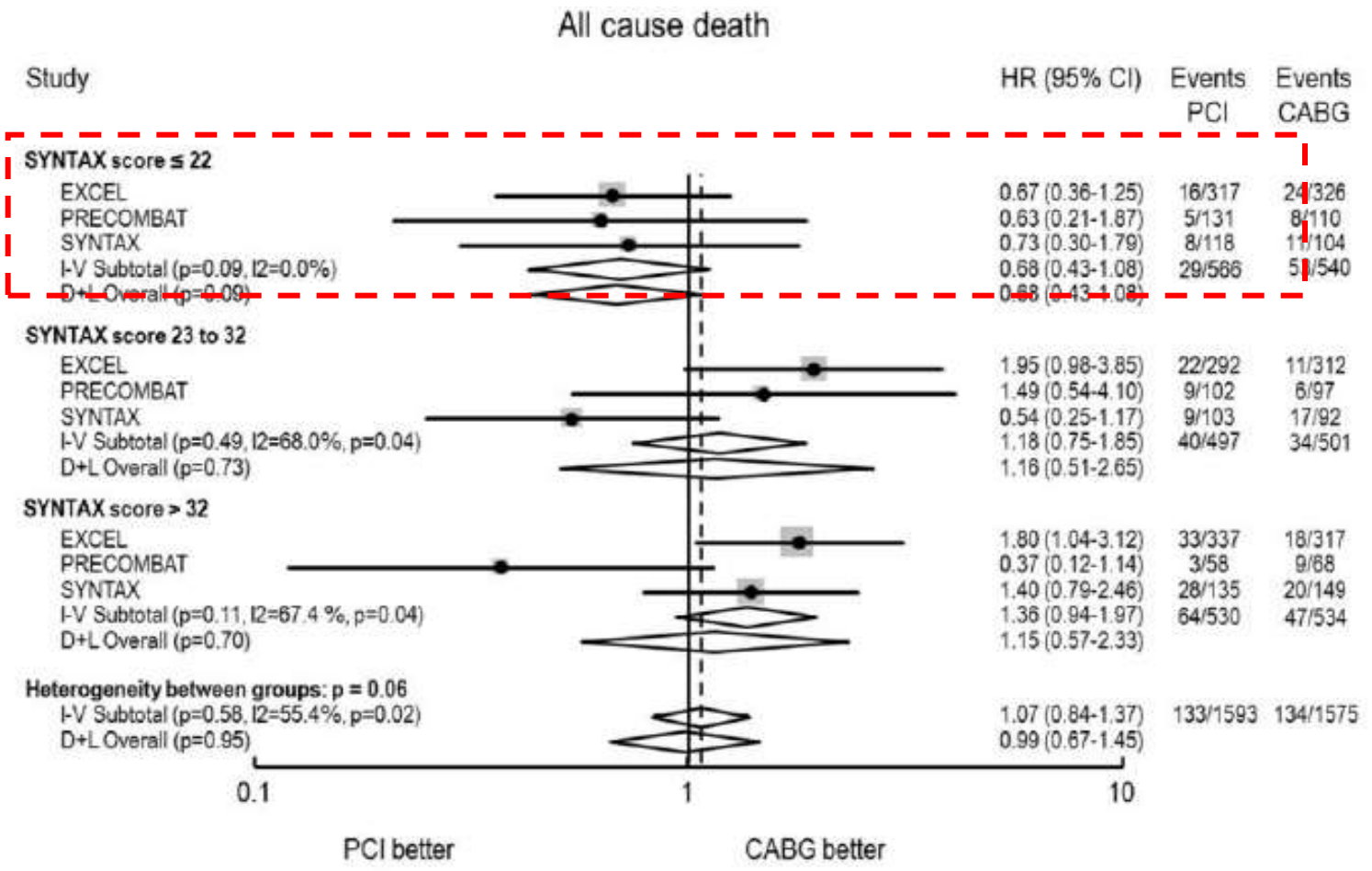






Palmerini T et al. *Am Heart J* 2017

PCI vs CABG for LM – a Meta-Analysis of Six Randomized Trials and 4,686 pts



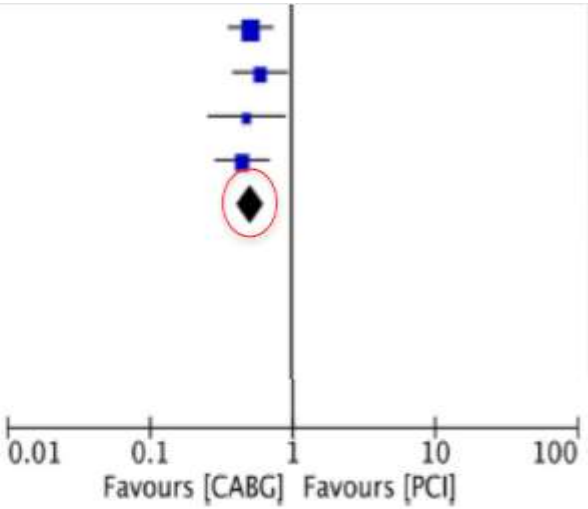
Palmerini T et al. *Am Heart J* 2017

Repeat Revascularization

EXCEL	67	957	114	948	37.6%	0.55 [0.40, 0.76]
NOBLE	47	592	71	592	23.1%	0.63 [0.43, 0.93]
PRECOMBAT	21	300	38	300	12.5%	0.52 [0.30, 0.91]
SYNTAX	49	348	90	357	26.9%	0.49 [0.33, 0.71]
Subtotal (95% CI)		**2197**		**2197**	**100.0%**	**0.55 [0.45, 0.67]**
Total events	184		313			

Heterogeneity: $Chi^2 = 0.94$, $df = 3$ ($P = 0.82$); $I^2 = 0\%$

Test for overall effect: $Z = 6.08$ ($P < 0.00001$)



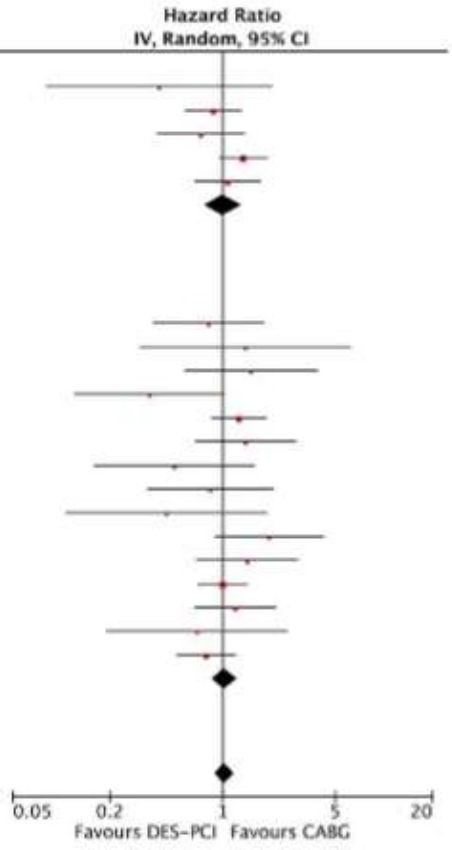
Putzu A, et al. *International J Cardiol* 2017

Drug-eluting stents versus coronary artery bypass grafting for left-main coronary artery disease

Hisato Takagi, MD, PhD[1] | Tomo Ando, MD[2] | Takuya Umemoto, MD, PhD[1] |
for the ALICE (All-Literature Investigation of Cardiovascular Evidence) Group

Death at follow-up

Study or Subgroup	Weight	Hazard Ratio IV, Random, 95% CI
1.1.1 Randomized controlled trials		
Boudriot 2011	0.7%	0.40 [0.08, 2.03]
SYNTAX 2014	10.2%	0.88 [0.58, 1.32]
PRECOMBAT 2015	4.7%	0.73 [0.39, 1.37]
EXCEL 2016	13.2%	1.34 [0.94, 1.91]
NOBLE 2016	8.0%	1.07 [0.67, 1.72]
Subtotal (95% CI)	**37.0%**	**1.01 [0.78, 1.31]**
Heterogeneity: $Tau^2 = 0.02$; $Chi^2 = 5.18$, df = 4 (P = 0.27); $I^2 = 23\%$		
Test for overall effect: Z = 0.07 (P = 0.94)		
1.1.2 Observational studies with propensity-score analysis		
Palmerini 2007	3.0%	0.82 [0.37, 1.81]
Wu 2008	0.9%	1.38 [0.30, 6.25]
White 2008	2.1%	1.50 [0.58, 3.89]
Wu 2010	1.7%	0.35 [0.12, 1.03]
MAIN-COMPARE 2010	11.0%	1.26 [0.85, 1.87]
Kang 2010	3.6%	1.39 [0.68, 2.86]
Chieffo 2010	1.5%	0.50 [0.16, 1.58]
ASAN-MAIN 2010	2.3%	0.84 [0.34, 2.07]
Rittger 2011	0.9%	0.45 [0.11, 1.89]
Yi 2012	3.1%	1.94 [0.89, 4.25]
Watanabe 2012	3.6%	1.42 [0.69, 2.93]
DELTA 2012	13.1%	1.00 [0.70, 1.43]
Chang 2012	5.5%	1.20 [0.67, 2.14]
Gao 2016	1.2%	0.69 [0.19, 2.54]
Yu 2016	9.6%	0.79 [0.52, 1.21]
Subtotal (95% CI)	**63.0%**	**1.03 [0.86, 1.24]**
Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 14.98$, df = 14 (P = 0.38); $I^2 = 7\%$		
Test for overall effect: Z = 0.34 (P = 0.73)		
Total (95% CI)	**100.0%**	**1.03 [0.90, 1.18]**
Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 20.16$, df = 19 (P = 0.38); $I^2 = 6\%$		
Test for overall effect: Z = 0.41 (P = 0.68)		
Test for subgroup differences: $Chi^2 = 0.02$, df = 1 (P = 0.89), $I^2 = 0\%$		



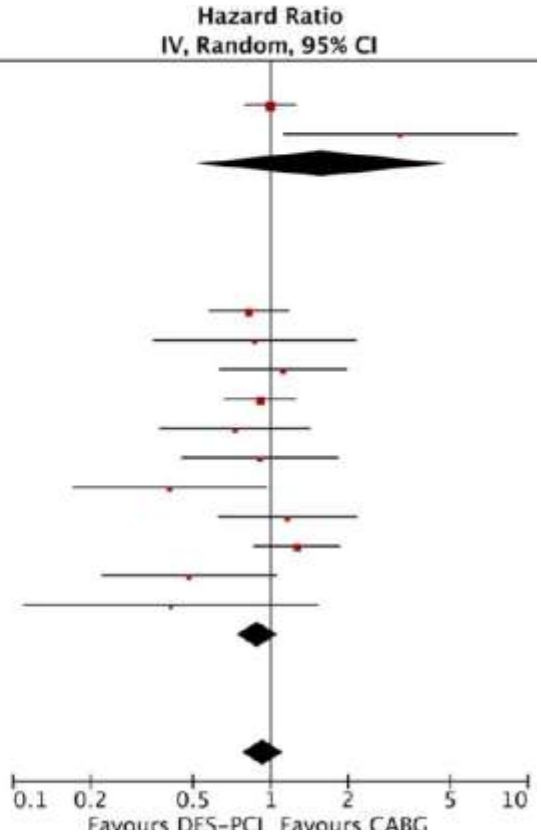
Catheter Cardiovasc Interv. 2018;91:697–709.

Drug-eluting stents versus coronary artery bypass grafting for left-main coronary artery disease

Hisato Takagi, MD, PhD[1] | Tomo Ando, MD[2] | Takuya Umemoto, MD, PhD[1] |
for the ALICE (All-Literature Investigation of Cardiovascular Evidence) Group

Composite of death / MI at follow-up

Study or Subgroup	Weight	Hazard Ratio IV, Random, 95% CI
1.8.1 Randomized controlled trials		
EXCEL 2016	19.1%	1.00 [0.79, 1.26]
Boudriot 2011	2.7%	3.19 [1.12, 9.09]
Subtotal (95% CI)	**21.8%**	**1.59 [0.52, 4.84]**
Heterogeneity: $Tau^2 = 0.53$; $Chi^2 = 4.51$, df = 1 (P = 0.03); $I^2 = 78\%$		
Test for overall effect: Z = 0.81 (P = 0.42)		
1.8.2 Observational studies with propensity-score analysis		
Yu 2016	13.3%	0.83 [0.58, 1.18]
Gao 2016	3.5%	0.87 [0.35, 2.15]
Chang 2012	7.3%	1.12 [0.63, 1.99]
DELTA 2012	14.7%	0.91 [0.66, 1.26]
CUSTOMIZE 2011	5.7%	0.73 [0.37, 1.43]
ASAN-MAIN 2010	5.3%	0.91 [0.45, 1.83]
Chieffo 2010	3.7%	0.41 [0.17, 0.97]
Kang 2010	6.4%	1.17 [0.63, 2.17]
MAIN-COMPARE 2010	12.2%	1.27 [0.86, 1.87]
Wu 2008	4.4%	0.48 [0.22, 1.06]
Ghenim 2009	1.8%	0.41 [0.11, 1.53]
Subtotal (95% CI)	**78.2%**	**0.89 [0.74, 1.07]**
Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 11.81$, df = 10 (P = 0.30); $I^2 = 15\%$		
Test for overall effect: Z = 1.25 (P = 0.21)		
Total (95% CI)	**100.0%**	**0.93 [0.78, 1.12]**
Heterogeneity: $Tau^2 = 0.03$; $Chi^2 = 17.53$, df = 12 (P = 0.13); $I^2 = 32\%$		
Test for overall effect: Z = 0.77 (P = 0.44)		



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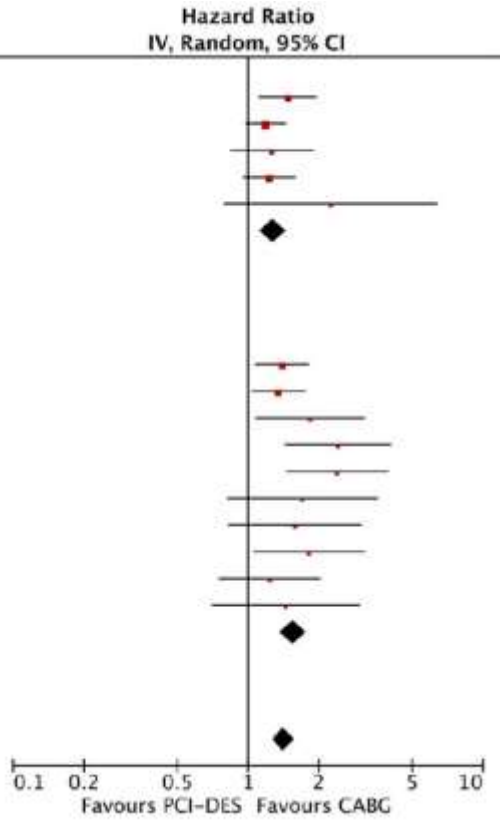
Drug-eluting stents versus coronary artery bypass grafting for left-main coronary artery disease

Hisato Takagi, MD, PhD[1] | Tomo Ando, MD[2] | Takuya Umemoto, MD, PhD[1] |
for the ALICE (All-Literature Investigation of Cardiovascular Evidence) Group

Composite of death / MI, and TLR at follow-up

Study or Subgroup	Weight	Hazard Ratio IV, Random, 95% CI
1.9.1 Randomized controlled trials		
NOBLE 2016	11.1%	1.48 [1.11, 1.96]
EXCEL 2016	18.7%	1.19 [0.97, 1.45]
PRECOMBAT 2015	6.0%	1.26 [0.84, 1.90]
SYNTAX 2014	13.0%	1.23 [0.95, 1.59]
Boudriot 2011	1.0%	2.25 [0.79, 6.40]
Subtotal (95% CI)	**49.8%**	**1.27 [1.12, 1.45]**
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 2.72$, df = 4 (P = 0.61); $I^2 = 0\%$		
Test for overall effect: Z = 3.64 (P = 0.0003)		
1.9.2 Observational studies with propensity-score analysis		
Yu 2016	12.4%	1.39 [1.07, 1.82]
DELTA 2012	12.2%	1.35 [1.03, 1.76]
Watanabe 2012	3.6%	1.83 [1.07, 3.13]
Yi 2012	3.8%	2.41 [1.43, 4.07]
CUSTOMIZE 2011	4.1%	2.39 [1.45, 3.94]
Rittger 2011	2.0%	1.70 [0.81, 3.57]
Chieffo 2010	2.5%	1.58 [0.82, 3.05]
Kang 2010	3.5%	1.81 [1.05, 3.13]
Wu 2010	4.1%	1.24 [0.75, 2.04]
White 2008	2.0%	1.45 [0.70, 3.00]
Subtotal (95% CI)	**50.2%**	**1.56 [1.36, 1.78]**
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 8.86$, df = 9 (P = 0.45); $I^2 = 0\%$		
Test for overall effect: Z = 6.28 (P < 0.00001)		
Total (95% CI)	**100.0%**	**1.42 [1.28, 1.58]**
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 15.86$, df = 14 (P = 0.32); $I^2 = 12\%$		
Test for overall effect: Z = 6.55 (P < 0.00001)		
Test for subgroup differences: $Chi^2 = 4.28$, df = 1 (P = 0.04), $I^2 = 76.6\%$		



Catheter Cardiovasc Interv. 2018;91:697–709.

PLOS ONE

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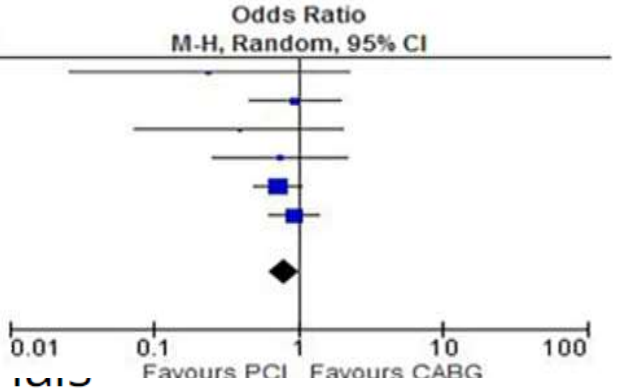
Death

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
LEMANS	1	52	4	53	1.2%	0.24 [0.03, 2.23]	2008
SYNTAX LM	15	355	15	336	11.1%	0.94 [0.45, 1.96]	2009
Boudriot et al	2	100	5	101	2.2%	0.39 [0.07, 2.07]	2010
PRECOMBAT	6	300	8	300	5.2%	0.74 [0.26, 2.17]	2011
EXCEL	50	948	68	957	42.0%	0.73 [0.50, 1.06]	2016
NOBLE	53	592	56	592	38.3%	0.94 [0.63, 1.40]	2016
Total (95% CI)		**2347**		**2339**	**100.0%**	**0.81 [0.63, 1.03]**	
Total events	127		156				

Heterogeneity: Tau² = 0.00; Chi² = 2.94, df = 5 (P = 0.71); I² = 0%

Test for overall effect: Z = 1.73 (P = 0.08)



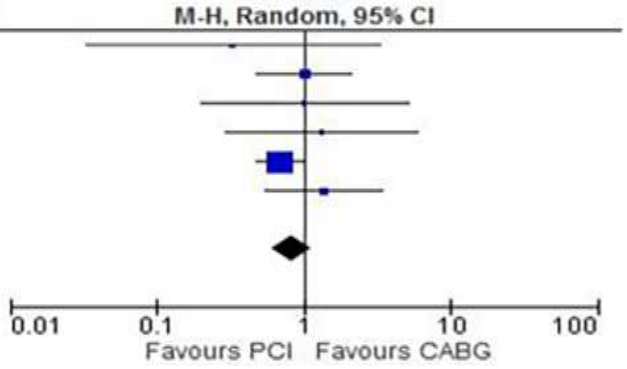
randomised controlled trials

MI

Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	Year
LEMANS	1	52	3	53	1.8%	0.33 [0.03, 3.25]	2008
SYNTAX LM	15	355	14	336	16.8%	1.01 [0.48, 2.14]	2009
Boudriot et al	3	100	3	101	3.5%	1.01 [0.20, 5.13]	2010
PRECOMBAT	4	300	3	300	4.1%	1.34 [0.30, 6.03]	2011
EXCEL	47	948	67	957	62.9%	0.69 [0.47, 1.02]	2016
NOBLE	11	592	8	592	11.0%	1.38 [0.55, 3.46]	2016
Total (95% CI)		**2347**		**2339**	**100.0%**	**0.82 [0.60, 1.11]**	
Total events	81		98				

Heterogeneity: Tau² = 0.00; Chi² = 3.38, df = 5 (P = 0.64); I² = 0%

Test for overall effect: Z = 1.29 (P = 0.20)

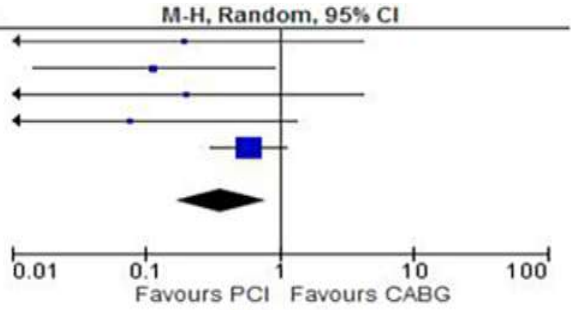


Stroke

Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	Year
LEMANS	0	52	2	53	6.1%	0.20 [0.01, 4.19]	2008
SYNTAX LM	1	355	8	336	12.6%	0.12 [0.01, 0.93]	2009
PRECOMBAT	0	300	2	300	6.2%	0.20 [0.01, 4.16]	2011
NOBLE	0	592	6	592	6.9%	0.08 [0.00, 1.35]	2016
EXCEL	14	948	24	957	68.1%	0.58 [0.30, 1.13]	2016
Total (95% CI)		**2247**		**2238**	**100.0%**	**0.36 [0.17, 0.79]**	
Total events	15		42				

Heterogeneity: Tau² = 0.11; Chi² = 4.44, df = 4 (P = 0.35); I² = 10%

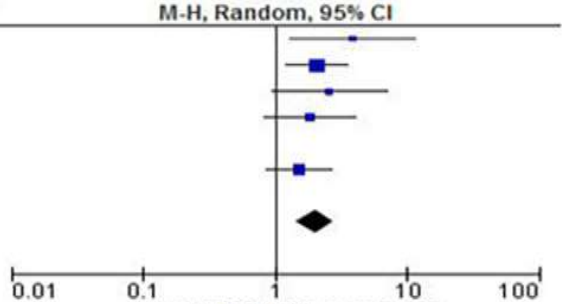
Test for overall effect: Z = 2.57 (P = 0.01)



TVR

Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	Year
LEMANS	15	52	5	53	8.3%	3.89 [1.30, 11.68]	2008
SYNTAX LM	45	355	22	336	35.3%	2.07 [1.22, 3.53]	2009
Boudriot et al	14	100	6	101	10.1%	2.58 [0.95, 7.01]	2010
PRECOMBAT	18	300	10	300	16.1%	1.85 [0.84, 4.08]	2011
EXCEL	0	0	0	0		Not estimable	2016
NOBLE	30	592	20	592	30.2%	1.53 [0.86, 2.72]	2016
Total (95% CI)		**1399**		**1382**	**100.0%**	**2.00 [1.46, 2.75]**	
Total events	122		63				

Heterogeneity: Tau² = 0.00; Chi² = 2.55, df = 4 (P = 0.64); I² = 0%

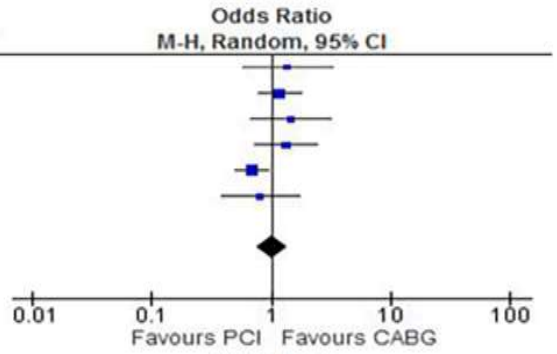


MACE

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
LEMANS	16	52	13	53	9.1%	1.37 [0.58, 3.23]	2008
SYNTAX LM	56	355	46	336	23.3%	1.18 [0.77, 1.80]	2009
Boudriot et al	19	100	14	101	11.2%	1.46 [0.69, 3.10]	2010
PRECOMBAT	26	300	20	300	15.3%	1.33 [0.72, 2.44]	2011
EXCEL	71	948	100	957	29.7%	0.69 [0.50, 0.95]	2016
NOBLE	13	592	16	592	11.5%	0.81 [0.39, 1.70]	2016
Total (95% CI)		**2347**		**2339**	**100.0%**	**1.02 [0.76, 1.36]**	
Total events	201		209				

Heterogeneity: Tau² = 0.05; Chi² = 8.05, df = 5 (P = 0.15); I² = 38%

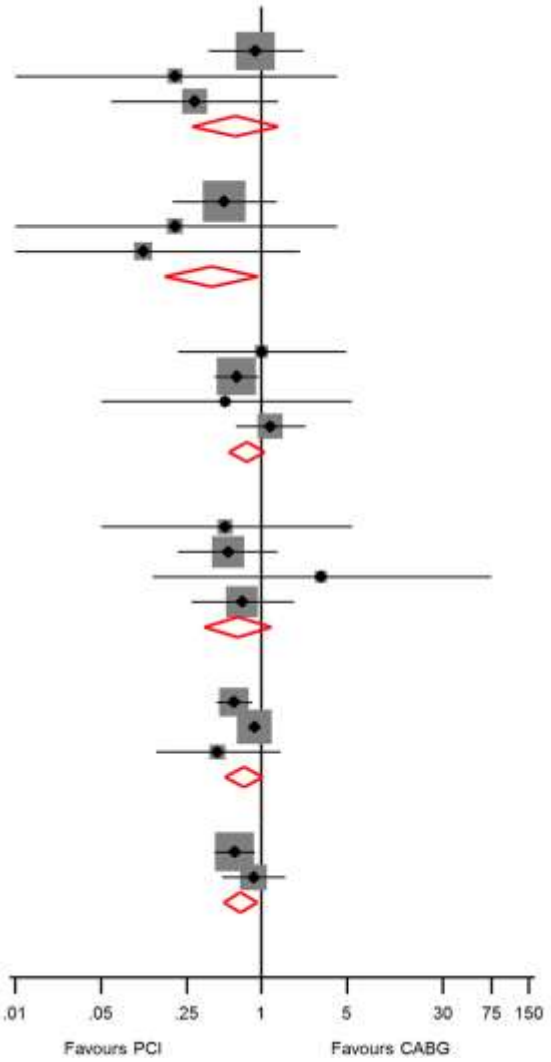
Test for overall effect: Z = 0.13 (P = 0.89)



L Test et al 2017

Effect of PCI on 30-day risk of all-cause mortality and major cardiovascular outcomes

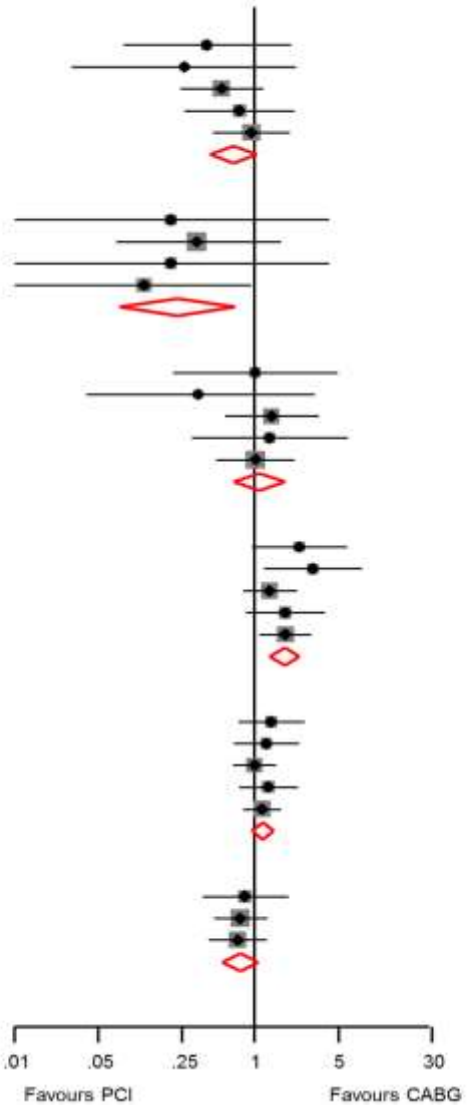
Outcome / Study	PCI Events / Participants	CABG Events / Participants	HR (95% CI)
All-cause death			
EXCEL	9 / 948	10 / 957	0.90 (0.37, 2.22)
LE MANS	0 / 52	2 // 53	0.20 (0.01, 4.15)
NOBLE	2 / 592	7 / 592	0.29 (0.06, 1.37)
Subtotal			0.61 (0.27, 1.36)
Stroke			
EXCEL	6 / 948	12 / 957	0.50 (0.19, 1.33)
LE MANS	0 / 52	2 / 53	0.20 (0.01, 4.15)
NOBLE	0 / 592	4 / 592	0.11 (0.01, 2.06)
Subtotal			0.39 (0.16, 0.94)
Myocardial Infarction			
Boudriot et al	3 / 100	3 / 101	1.01 (0.21, 4.89)
EXCEL	37 / 948	59 / 957	0.63 (0.42, 0.95)
LE MANS	1 //52	2 / 53	0.51 (0.05, 5.45)
NOBLE	19 / 592	16 / 592	1.19 (0.62, 2.29)
Subtotal			0.76 (0.54, 1.06)
Repeat revascularization			
Boudriot et al	1 / 100	2 / 101	0.51 (0.05, 5.48)
EXCEL	7 / 948	13 / 957	0.54 (0.21, 1.35)
LE MANS	1 // 52	0 / 53	3.06 (0.13, 73.36)
NOBLE	7 / 592	10 / 592	0.70 (0.27, 1.83)
Subtotal			0.64 (0.34, 1.21)
MACCE			
EXCEL	53 / 948	88 / 957	0.60 (0.43, 0.85)
LE MANS	1 // 52	7 / 53	0.88 (0.79, 0.99)
PRECOMBAT	4 / 300	9 / 300	0.44 (0.14, 1.43)
Subtotal			0.72 (0.51, 1.03)
Death, stroke, or MI			
EXCEL	46 / 948	75 / 957	0.61 (0.42, 0.88)
NOBLE	21 / 592	27 / 592	0.87 (0.48, 1.56)
Subtotal			0.67 (0.49, 0.92)



Laukkanen JA, *et al. Open Heart* 2017;4:e000638. doi:10.1136/openhrt-2017-000638

Effect of PCI on one year risk of all-cause mortality and major cardiovascular outcomes

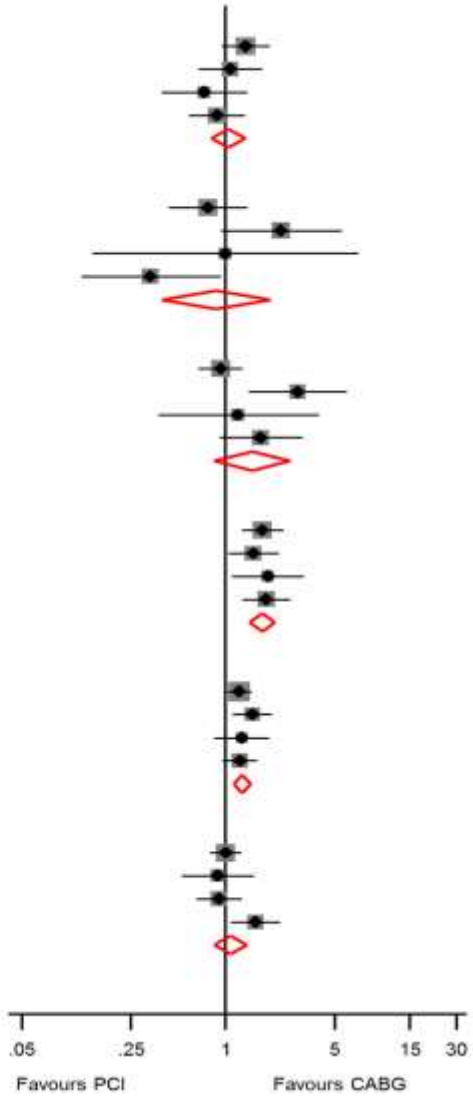
Outcome / Study	PCI Events / Participants	CABG Events / Participants	HR (95% CI)
All-cause death			
Boudriot et al	2 / 100	5 / 101	0.40 (0.08, 2.03)
LE MANS	1 // 52	4 // 53	0.26 (0.03, 2.20)
NOBLE	9 / 592	17 / 592	0.53 (0.24, 1.18)
PRECOMBAT	6 / 300	8 / 300	0.75 (0.26, 2.14)
SYNTAX	15 / 355	15 / 336	0.94 (0.45, 1.96)
Subtotal			0.66 (0.42, 1.04)
Stroke			
LE MANS	0 / 52	2 // 53	0.20 (0.01, 4.15)
NOBLE	2 / 592	6 / 592	0.33 (0.07, 1.65)
PRECOMBAT	0 / 300	2 / 300	0.20 (0.01, 4.15)
SYNTAX	1 / 355	8 / 336	0.12 (0.01, 0.93)
Subtotal			0.23 (0.07, 0.69)
Myocardial Infarction			
Boudriot et al	3 / 100	3 / 101	1.01 (0.21, 4.89)
LE MANS	1 // 52	3 // 53	0.34 (0.04, 3.16)
NOBLE	11 / 592	8 / 592	1.38 (0.56, 3.39)
PRECOMBAT	4 / 300	3 / 300	1.33 (0.30, 5.91)
SYNTAX	15 / 355	14 / 336	1.02 (0.48, 2.14)
Subtotal			1.09 (0.66, 1.78)
Repeat revascularization			
Boudriot et al	14 / 100	6 / 101	2.36 (0.94, 5.89)
LE MANS	15 / 52	5 // 53	3.06 (1.20, 7.80)
NOBLE	32 / 592	24 / 592	1.33 (0.80, 2.24)
PRECOMBAT	18 / 300	10 / 300	1.80 (0.85, 3.84)
SYNTAX	42 / 355	22 / 336	1.81 (1.10, 2.96)
Subtotal			1.77 (1.33, 2.37)
MACCE			
Boudriot et al	19 / 100	14 / 101	1.37 (0.73, 2.58)
LE MANS	16 / 52	13 / 53	1.25 (0.67, 2.34)
NOBLE	42 / 592	42 / 592	1.00 (0.66, 1.51)
PRECOMBAT	26 / 300	20 / 300	1.30 (0.74, 2.28)
SYNTAX	56 / 355	46 / 336	1.15 (0.80, 1.65)
Subtotal			1.16 (0.94, 1.44)
Death, stroke, or MI			
PRECOMBAT	10 / 300	12 / 300	0.83 (0.37, 1.90)
SYNTAX	25 / 355	31 / 336	0.76 (0.46, 1.27)
NOBLE	22 / 592	31 / 592	0.72 (0.41, 1.26)
Subtotal			0.76 (0.54, 1.06)



Laukkanen JA, *et al. Open Heart* 2017;4:e000638. doi:10.1136/openhrt-2017-000638

Effect of PCI on 3 to 5-year risk of all-cause mortality and major cardiovascular outcomes

Outcome / Study	PCI Events / Participants	CABG Events / Participants	HR (95% CI)
All-cause death			
EXCEL	71 / 948	53 / 957	1.34 (0.94, 1.91)
NOBLE	36 / 592	33 / 592	1.07 (0.67, 1.72)
PRECOMBAT	17 / 300	23 / 300	0.73 (0.39, 1.37)
SYNTAX	45 / 357	48 / 348	0.88 (0.58, 1.32)
Subtotal			1.04 (0.81, 1.33)
Stroke			
EXCEL	20 / 948	26 / 957	0.77 (0.43, 1.37)
NOBLE	16 / 592	7 / 592	2.25 (0.93, 5.48)
PRECOMBAT	2 / 300	2 / 300	0.99 (0.14, 7.02)
SYNTAX	5 / 357	14 / 348	0.33 (0.12, 0.93)
Subtotal			0.87 (0.39, 1.93)
Myocardial Infarction			
EXCEL	72 / 948	77 / 957	0.93 (0.67, 1.28)
NOBLE	29 / 592	10 / 592	2.88 (1.40, 5.90)
PRECOMBAT	6 / 300	5 / 300	1.20 (0.37, 3.93)
SYNTAX	28 / 357	16 / 348	1.67 (0.91, 3.10)
Subtotal			1.48 (0.85, 2.58)
Repeat revascularization			
EXCEL	114 / 948	67 / 957	1.72 (1.27, 2.33)
NOBLE	71 / 592	47 / 592	1.50 (1.04, 2.17)
PRECOMBAT	38 / 300	21 / 300	1.86 (1.09, 3.17)
SYNTAX	90 / 357	49 / 348	1.82 (1.28, 2.57)
Subtotal			1.70 (1.42, 2.05)
MACCE			
EXCEL	251 / 948	202 / 957	1.22 (1.02, 1.47)
NOBLE	121 / 592	81 / 592	1.48 (1.11, 1.96)
PRECOMBAT	52 / 300	42 / 300	1.27 (0.84, 1.90)
SYNTAX	130 / 357	103 / 348	1.23 (0.95, 1.59)
Subtotal			1.27 (1.12, 1.44)
Death, stroke, or MI			
EXCEL	137 / 948	135 / 957	1.00 (0.79, 1.26)
PRECOMBAT	25 / 300	28 / 300	0.89 (0.52, 1.52)
SYNTAX	67 / 357	69 / 348	0.91 (0.65, 1.27)
NOBLE	81 / 592	50/ 592	1.55 (1.08, 2.22)
Subtotal			1.07 (0.84, 1.35)



Laukkanen JA, *et al. Open Heart* 2017;4:e000638. doi:10.1136/openhrt-2017-000638

Generalizability of EXCEL and NOBLE results to a large registry population with unprotected left main coronary artery disease

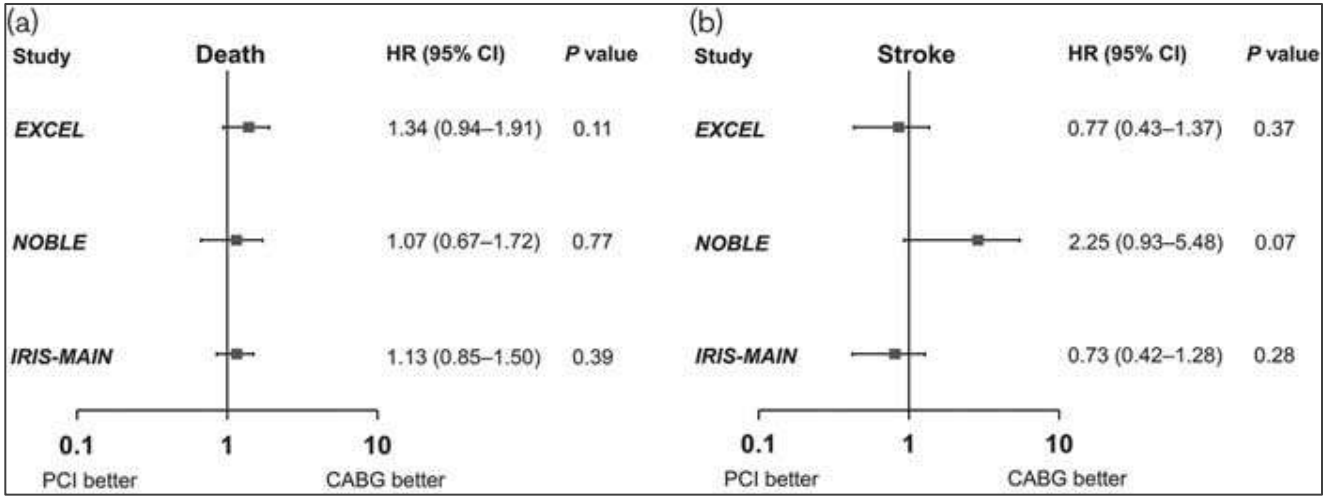
Table 1 Key features of each clinical study

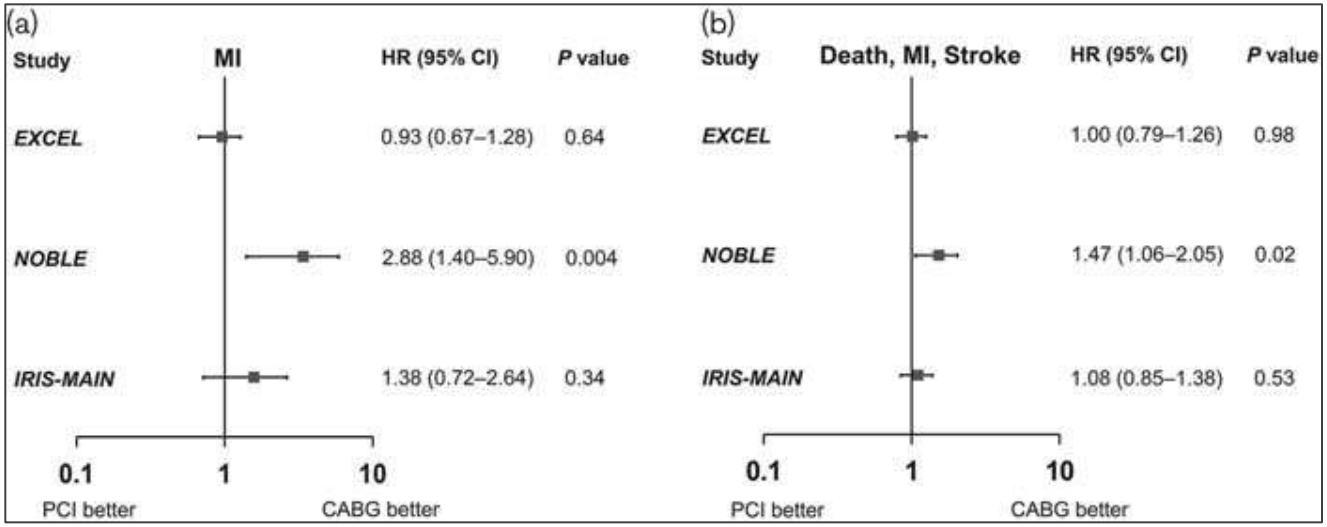
Designs	EXCEL trial	NOBLE trial	IRIS–MAIN registry
Study type	Multicenter (126 sites in North/South America, Europe, Asia Pacific), prospective, open-label, randomized, noninferiority design trial comparing PCI and CABG	Multicenter (36 sites in northern Europe), prospective, open-label, randomized, noninferiority design trial comparing PCI and CABG	Multicenter (50 sites in Asia), prospective, nonrandomized observational registry including PCI, CABG, or medication alone
Main inclusion criteria	Unprotected LMCA disease with angiographic DS > 70%, as estimated visually, or 50% ≤ DS <70% with at least one of following: (a) noninvasive evidence of ischemia referable to LMCA lesion; (b) IVUS MLA ≤ 6.0 mm^2; or (c) FFR ≤ 0.80	Unprotected LMCA disease with angiographic DS > 50%, as estimated visually, or FFR <0.8	Unprotected LMCA disease with angiographic DS > 50%, as estimated visually
Key exclusion criteria	SYNTAX score ≥ 33, prior PCI at left main (any time) or any other coronary artery (within 1 year), prior CABG, concomitant valvular or aortic surgery, CK-MB more than normal or recent MI with CK-MB still elevated, left main reference vessel diameter <2.25 or > 4.25 mm	STEMI within 24 h, > 3 or complex additional coronary lesions (length > 25 mm, chronic total occlusion, two-stent bifurcation, calcified or tortuous vessel morphology), patient is too high risk for CABG or PCI, expected survival <1 year	Minimal exclusion criteria (prior CABG, concomitant valvular or aortic surgery)
Primary endpoint	Composite of all-cause death, MI, or stroke	Composite rate of all-cause death, nonprocedural MI, repeat revascularization, or stroke	Outcomes of interest were death, MI, stroke, repeat revascularization, and its composite outcome
Recruitment period	September 2010–March 2014	December 2008–January 2015	November 2006–December 2013
Follow-up period (median) (years)	3.0 (2.4–3.0)	3.1 (2.0–5.0)	3.0 (2.0–4.1)
Number of CABG patients	957	592	774
Number of PCI patients	948	592	1707
Stent type used for PCI	XIENCE cobalt–chromium everolimus-eluting stent	BioMatrix biolimus-eluting stent recommended since March 2010, but other CE-marked DES allowed	Any second generation DES available in each participating center

CABG, coronary artery bypass grafting; CK-MB, creatine kinase-myocardial band; DES, drug-eluting stent; DS, diameter stenosis; EXCEL, Evaluation of XIENCE Everolimus-Eluting Stent Versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization; FFR, fractional flow reserve; IRIS–MAIN, Interventional Research Incorporation Society–Left MAIN Revascularization; IVUS, intravascular ultrasound; LMCA, left main coronary artery; MI, myocardial infarction; MLA, minimal lumen area; NOBLE, Nordic–Baltic–British Left Main Revascularization Study; PCI, percutaneous coronary intervention; STEMI, ST-segment elevation myocardial infarction; SYNTAX, Synergy Between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery.

P H Lee et al , Coronary Artery Disease 2017, 28:675–682

Generalizability of EXCEL and NOBLE results to a large registry population with unprotected left main coronary artery disease



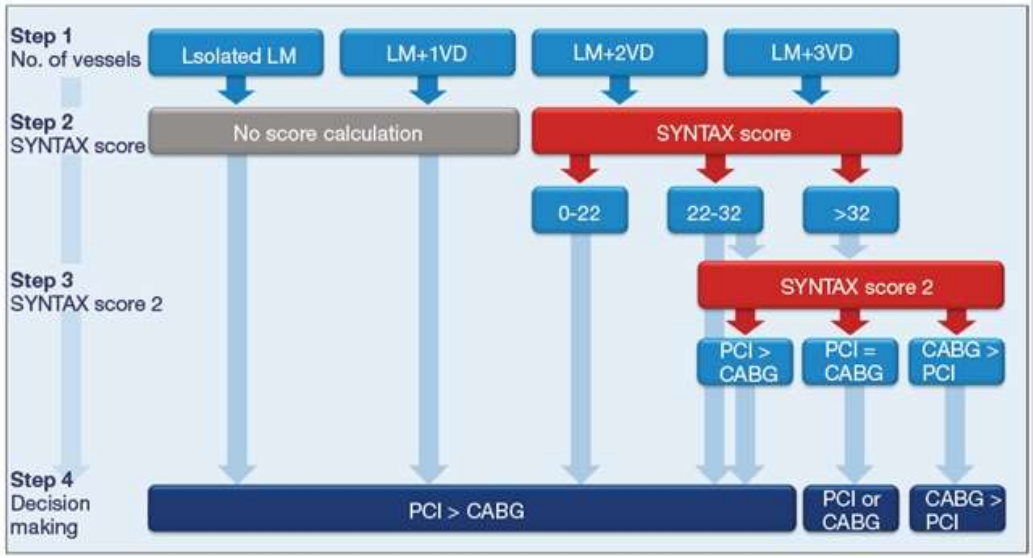


P H Lee et al , Coronary Artery Disease 2017, 28:675–682

European Proposal : Algorithm for Management of Unprotected Left Main Coronary Artery Disease

by D Capodanno

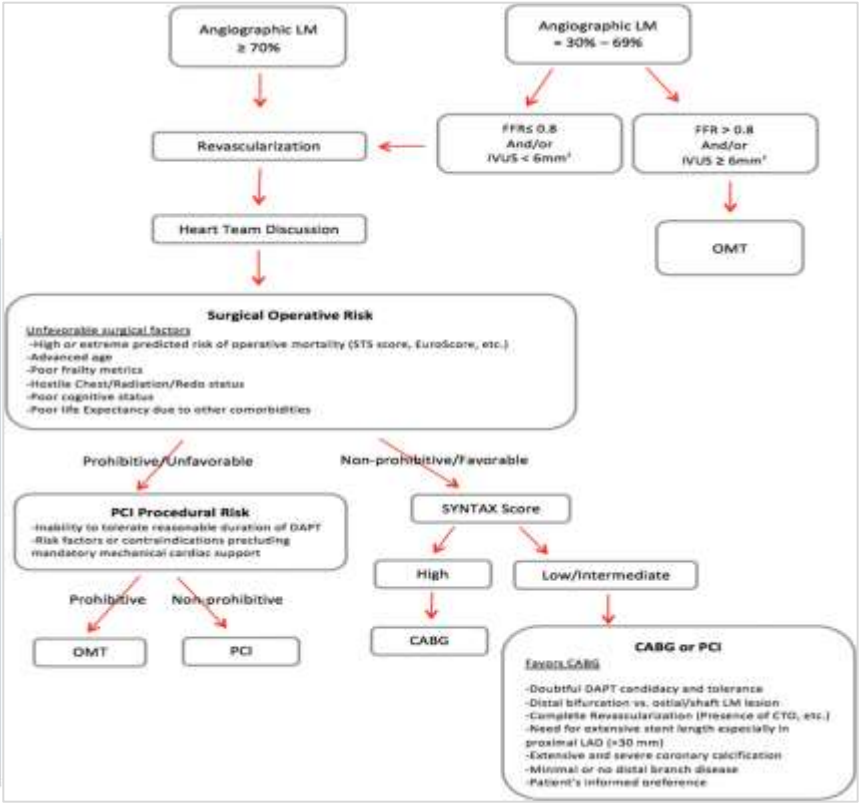
J Thorac Dis 2017;9(9):2766-2770



Management of Left Main Coronary Artery Disease

R Ramadan, W.E. Boden, S Kinlay,

J Am Heart Assoc. 2018;7:e008151. DOI: 10.1161/JAHA.117.008151



European Heart Journal Advance Access published August 29, 2014

European Heart Journal
doi:10.1093/eurheartj/ehu278

ESC/EACTS GUIDELINES

2014 ESC/EACTS Guidelines on myocardial revascularization

The Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)

Recommendation for the type of revascularization (CABG or PCI) in patients with SCAD with suitable coronary anatomy for both procedures and low predicted surgical mortality

Left main disease with a SYNTAX score ≤ 22.	I	B	I	B	17,134,170
Left main disease with a SYNTAX score 23–32.	I	B	IIa	B	17

Yes We Can… but we should continue to improve doing it improving outcomes in both PCI and CABG , waiting for longer follow-up data (10 yrs ?)

- **Benefit of CABG is often seen after extended follow-up (median follow-up duration of 3.1 years, which is relatively short in both studies).Longer-term follow-up data from both trials provide insights into the durability of the results for both PCI and CABG.**

- **The decision between PCI and CABG for ULMCAD still being based on weighing the benefits and risks of PCI versus CABG and taking patient preference into consideration.**

Thank You for Your Attention!