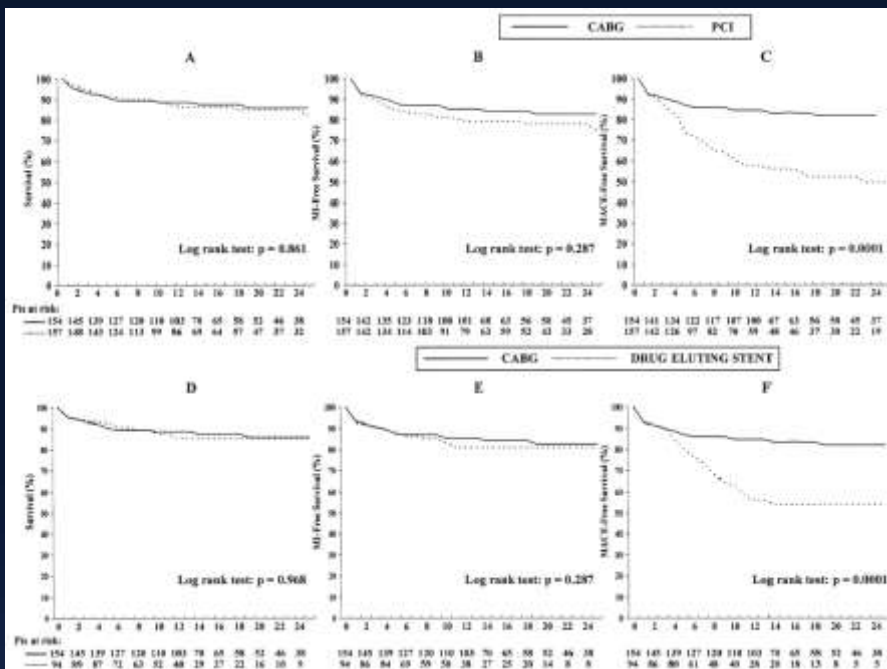


**Pre and Post EXCEL and NOBLE  
Era: what will Change in LM  
Treatment?**

**Tullio Palmerini  
University of Bologna  
Italy**

# Disclosure

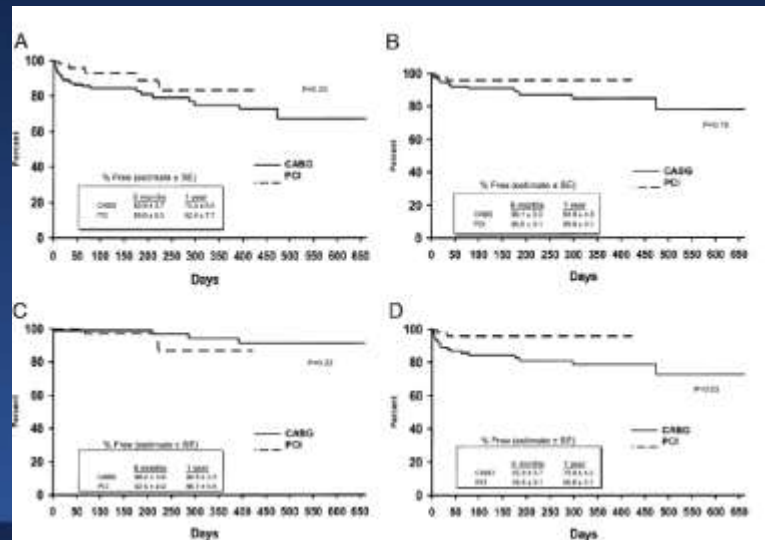
- **Speaker fee from Abbott**
- **Research grant from Eli Lilly**



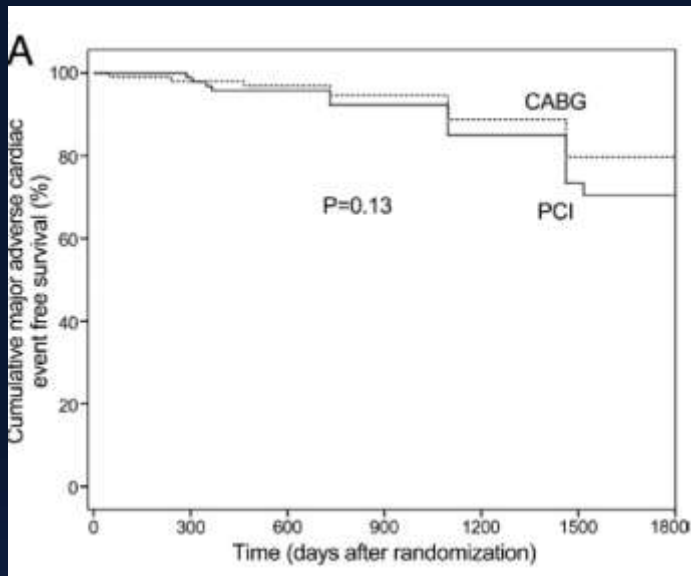
Palmerini et al; AJC 2006

	PCI-Treated Patients (n=107)	CABG-Treated Patients (n=142)	On Pump (n=86)	Off Pump (n=56)
<b>In hospital</b>				
Death	0	3 (2.1)	2 (2.3)	1 (1.7)
MI, n (%)	10 (9.3)	37 (26.05)	29 (33.7)	8 (14.3)
Q-wave MI, n	0	5	4	1
TLR, n (%)	0	3 (2.1)	1 (1.2)	2 (3.5)
TVR, n (%)	0	3 (2.1)	1 (1.2)	2 (3.5)
Cerebrovascular events, n (%)	0	2 (1.4)	1 (1.2)	1 (1.7)
<b>One-year follow-up</b>				
Death, n (%)	3 (2.8)	9 (6.4)	5 (5.9)	4 (7.2)
MI, n (%)	1 (0.9)	2 (1.4)	1 (1.2)	1 (1.8)
TLR, n (%)	17 (15.8)	5 (3.6)	2 (2.4)	3 (5.4)
TVR, n (%)	21 (19.6)	5 (3.6)	2 (2.4)	3 (5.4)
Clinically driven TVR, n	11	5	2	3
Cerebrovascular events, n (%)	1 (0.9)	1 (0.7)	1 (1.2)	0

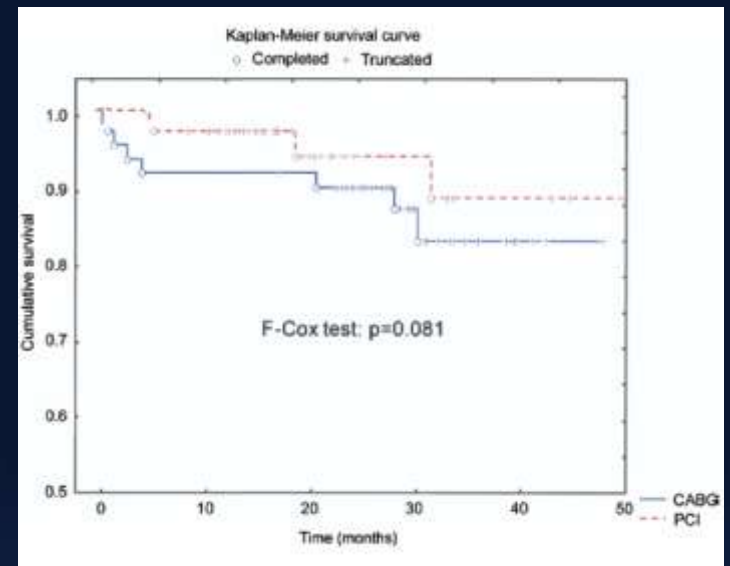
Chieffo et al; JACC 2006



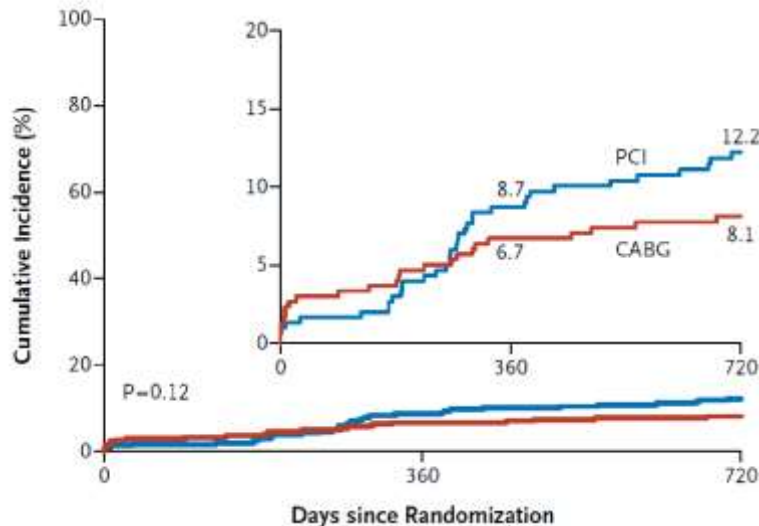
Lee et al; JACC 2006



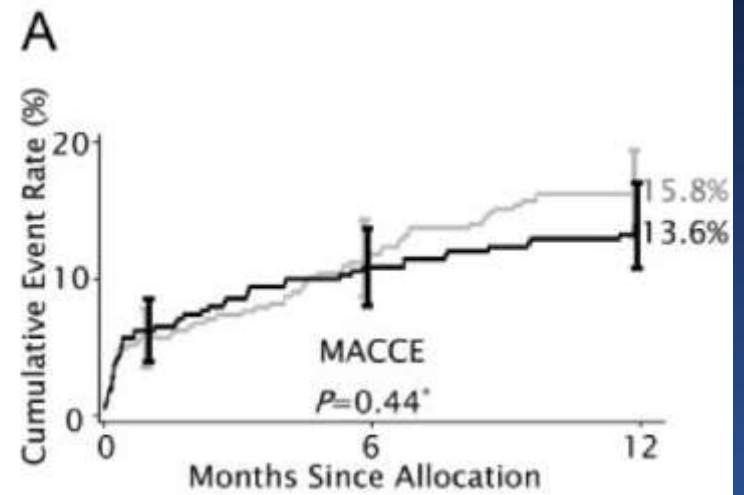
*Boudriot et al; JACC 2011*



*Buszman et al; JACC 2008*



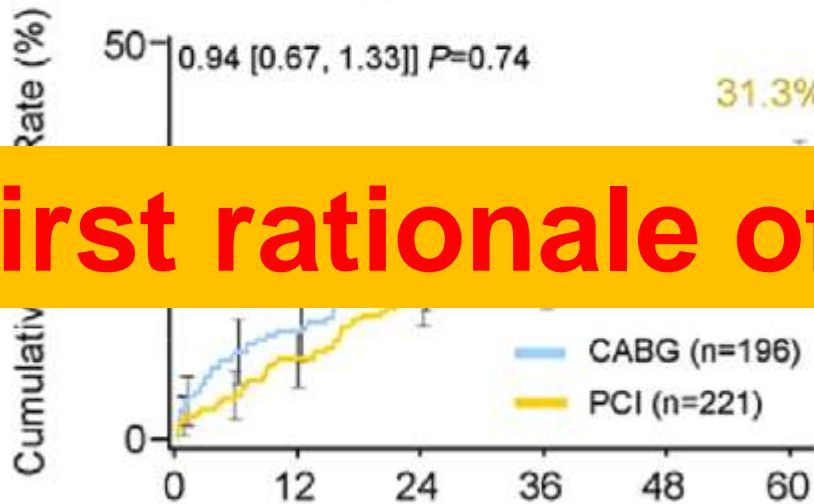
*Park et al; NEJM 2011*



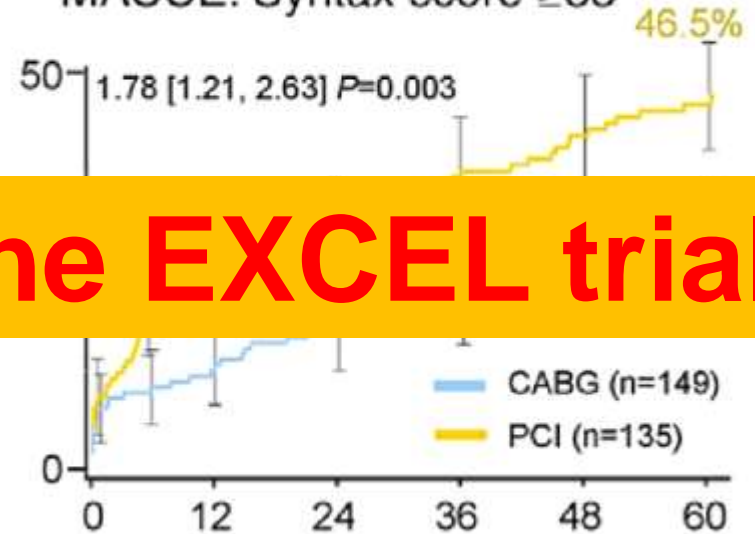
*Morice et al; Circulation 2010*

# SYNTAX LM outcomes stratified by the SYNTAX score

**A** MACCE: Syntax score 0-32



**B** MACCE: Syntax score  $\geq 33$



**First rationale of the EXCEL trial**

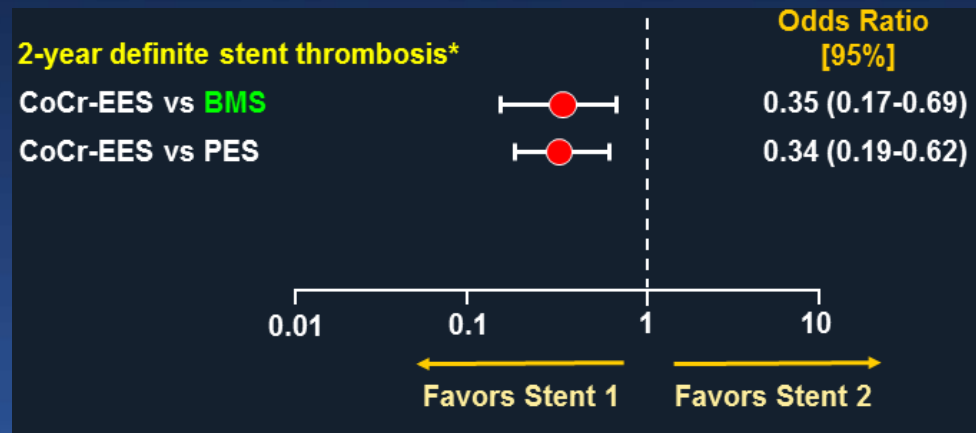
# Limits

- **Observational studies**
- **Relatively small RCTs**
- **Composite endpoint of death, MI, TVR**
- **Underpowered for clinically relevant endpoint such as death, MI or stroke**
- **First generation DES**

# Network meta-analysis: 49 RCTs and 50,844 pts



## Second rationale of the EXCEL trial



# Study design

2900 pts with unprotected left main disease

**Randomization stratified by**

- **Center**
- **Diabetes**
- **Syntax score**

PCI (Xience EES)  
(N=950)

CABG  
(N=950)

*Stone; nejm 2016*

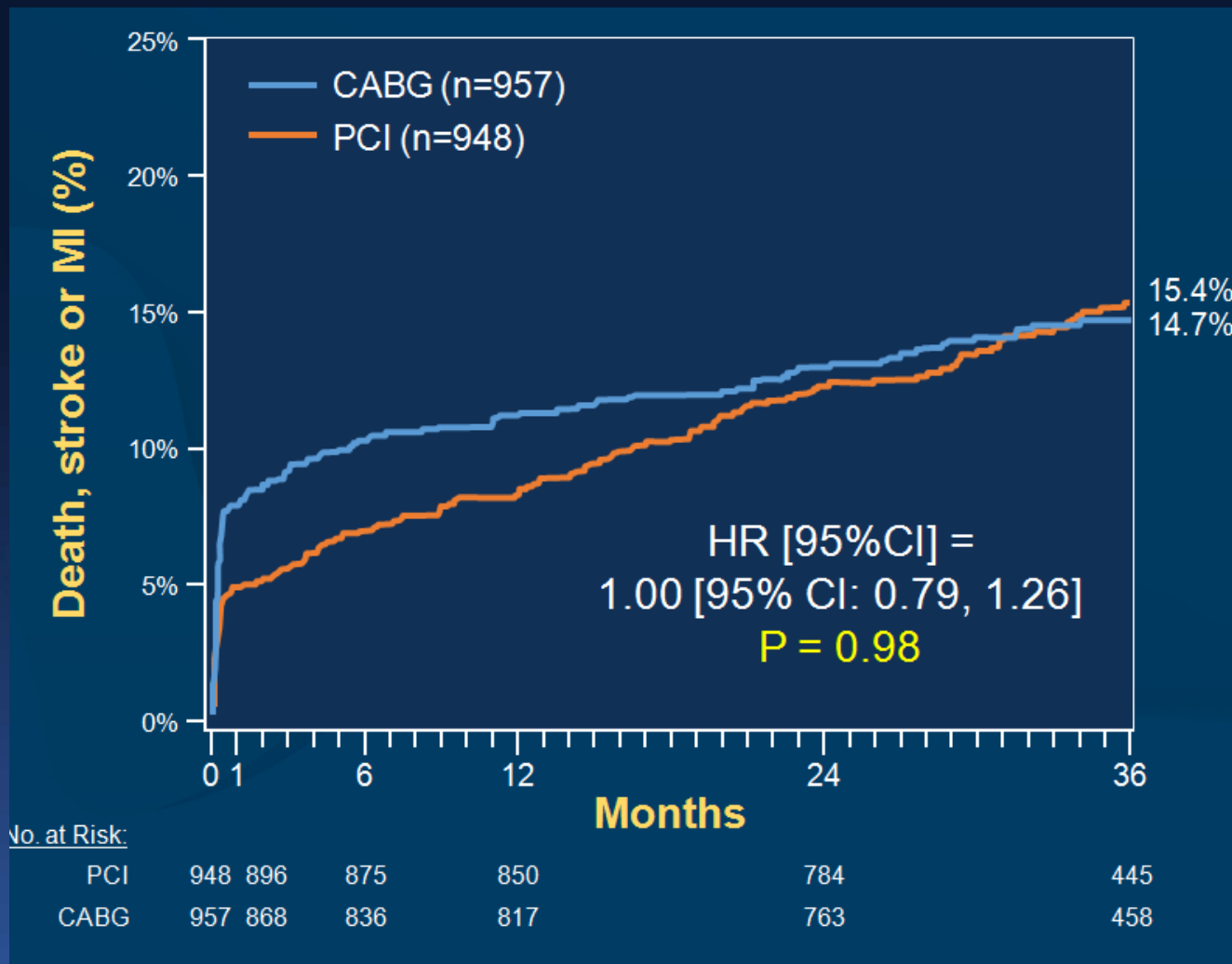


# Primary and Secondary Endpoints

Tested hierarchically to preserve alpha

Endpoint	Timing of follow-up	Powered for
Primary endpoint: Death, stroke or MI	Median 3 years, minimum 2 years	Non-inferiority
Secondary endpoint #1: Death, stroke or MI	30 days	Non-inferiority
Secondary endpoint #2a: Death, stroke, MI or IDR	Median 3 years, minimum 2 years	Non-inferiority
Secondary endpoint #2b: Death, stroke or MI	Median 3 years, minimum 2 years	Superiority

# Death, stroke or MI at 3 years



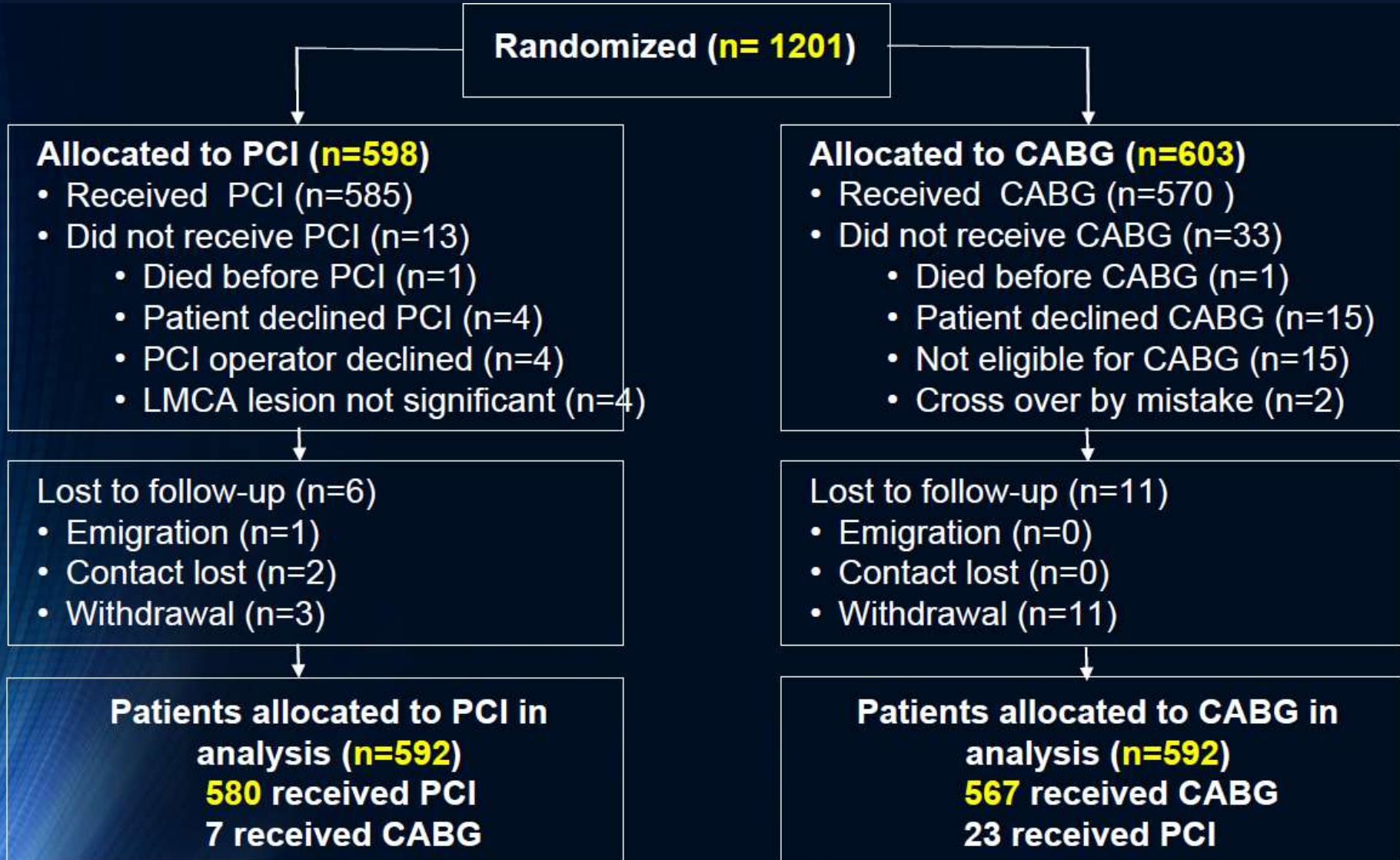
Stone; nejm 2016

# Adjudicated outcomes at 3 years

	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

**Stone; TCT 2016**

# NOBLE trial

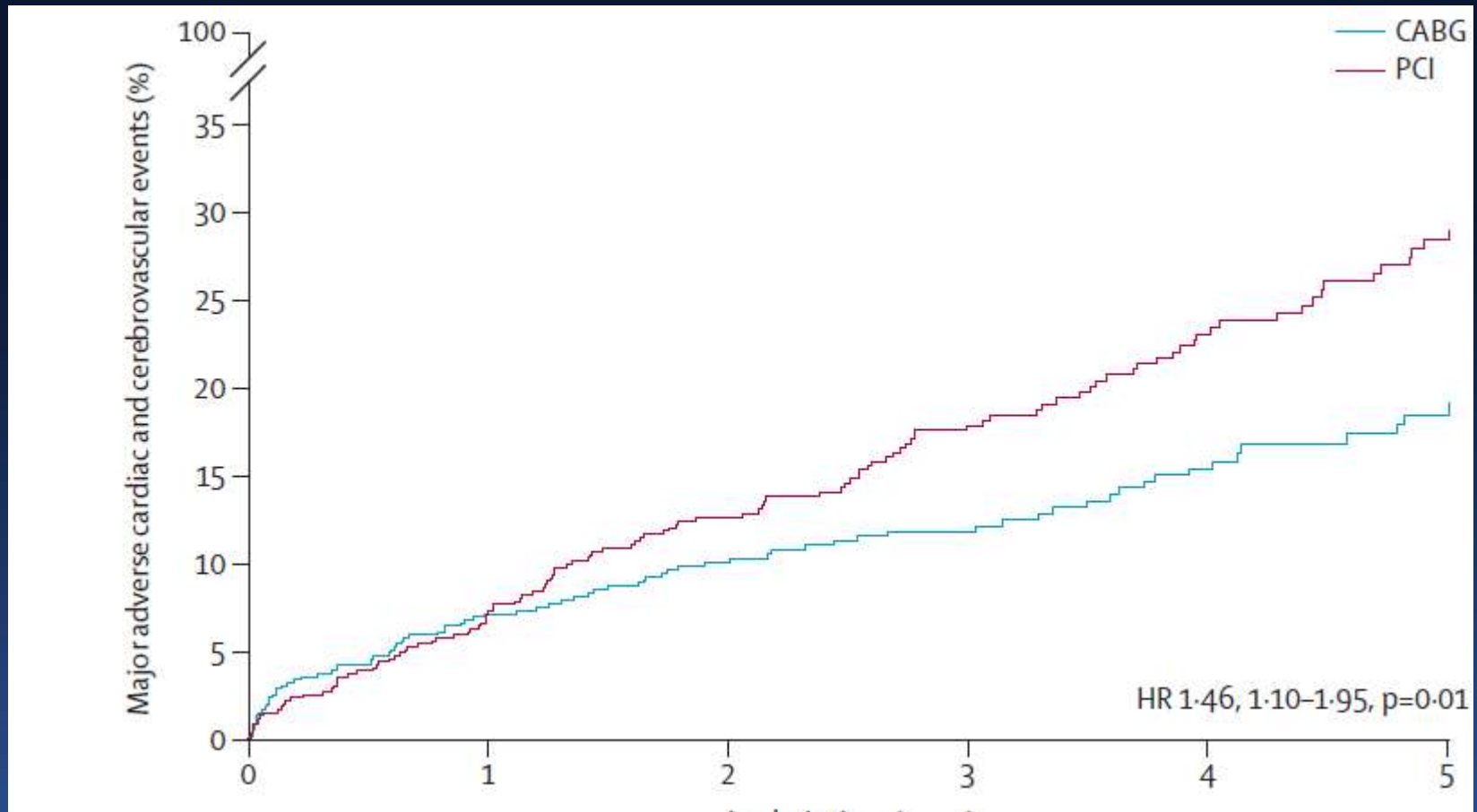


# Inclusion criteria

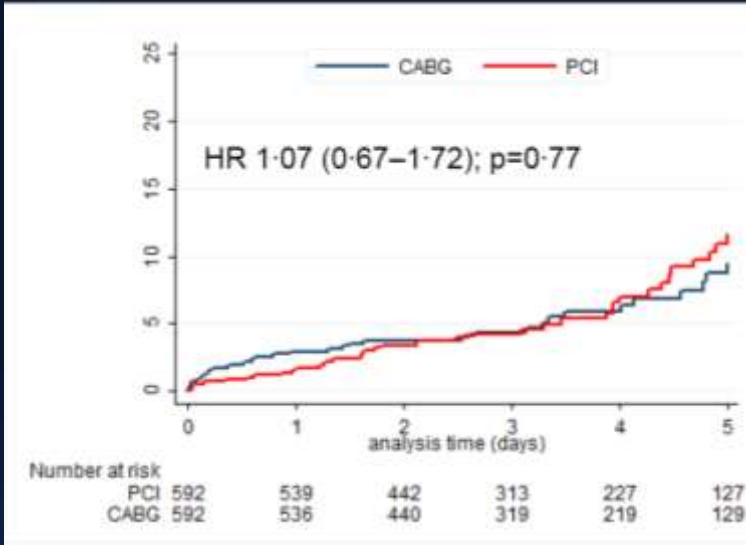
- Stable angina, unstable angina, or acute coronary syndrome
- A significant left main lesion
  - Visually assessed stenosis diameter  $\geq 50\%$  or fractional flow reserve  $\leq 0.80$
  - Located in the ostium, mid-shaft, or bifurcation
- No more than three additional non-complex lesions
- Local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



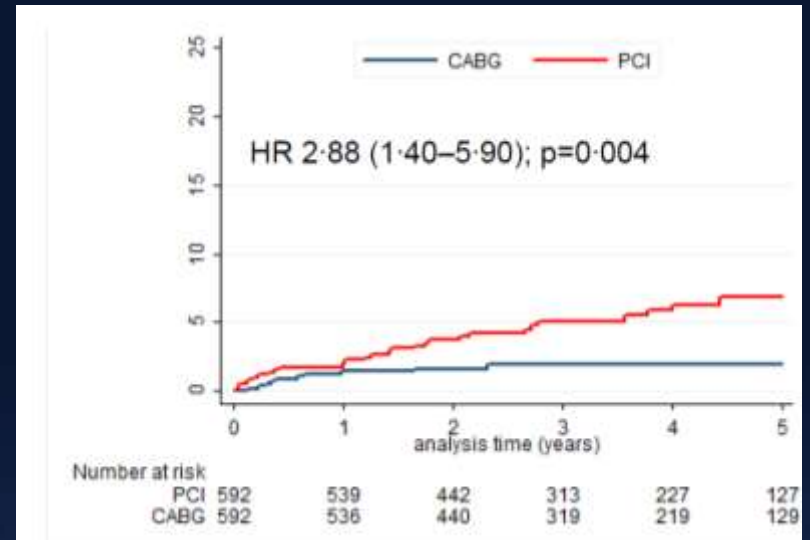
# Primary endpoint: Death, MI, RR, and Stroke



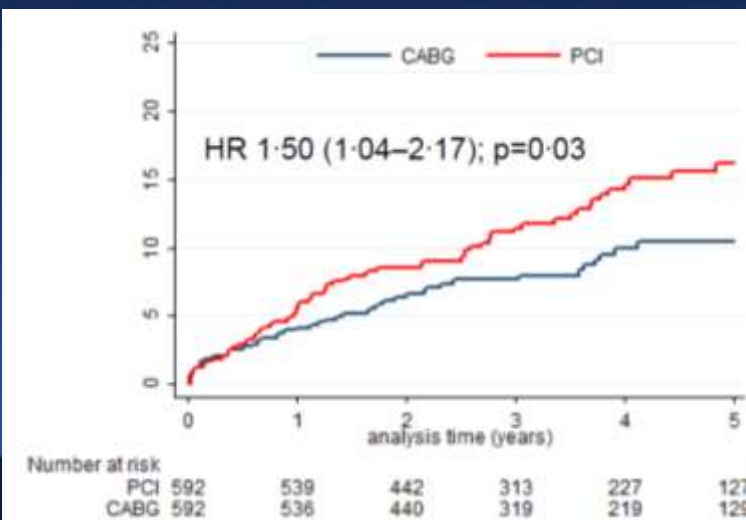
## All cause mortality



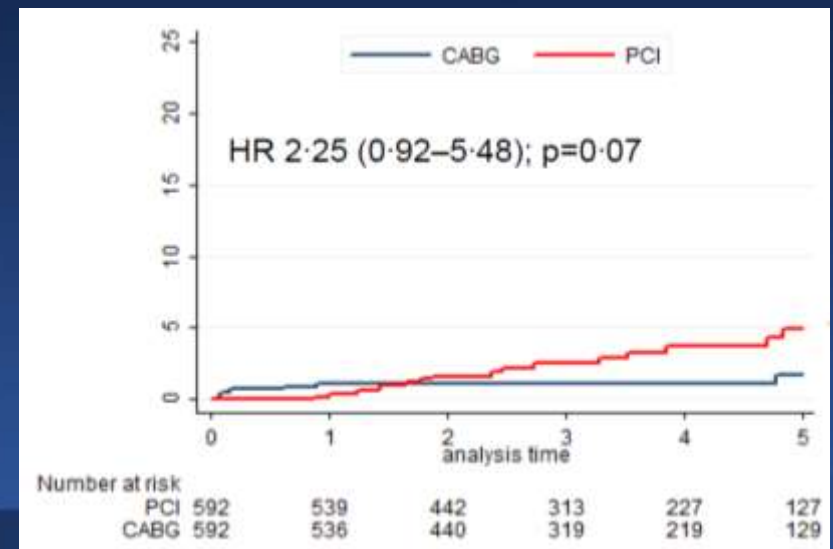
## Non-procedural myocardial infarction



## Repeat revascularization



## Stroke



# EXCEL vs NOBLE

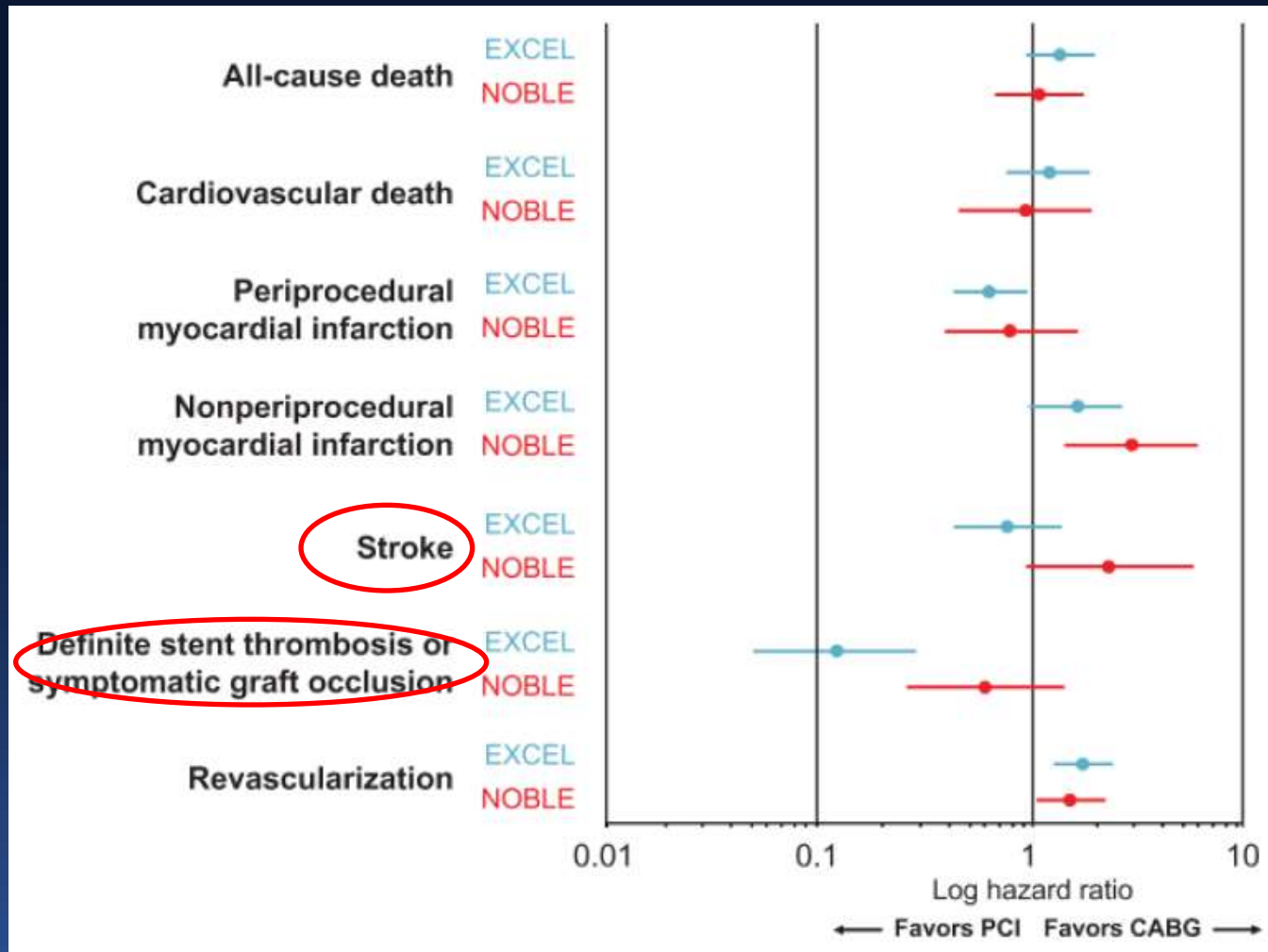
	<b>Excel</b>	<b>Noble</b>
All comers	No	No
Patient population	ULMCA	ULMCA
SYNTAX score	$\leq 32$	Low
<b>Primary EP</b>	Death/MI/stroke	Death/MI/Str/Rev
Follow-up	3 y (median)	3 y (median)
IVUS	Recomm.	Recomm.
FFR guidance	Recomm.	Recomm.
<b>Stent</b>	EES	SES/BES
Angio follow-up	Not recomm.	Not recomm.



# EXCEL vs NOBLE

	<b>EXCEL</b>	<b>NOBLE</b>
<b>Age</b>	<b>66 y (mean)</b>	<b>66 y (mean)</b>
<b>Diabetes mellitus</b>	<b>30%</b>	<b>15%</b>
<b>LVEF</b>	<b>57% (mean)</b>	<b>60% (mean)</b>
<b>ACS</b>	<b>24%</b>	<b>18%</b>
<b>SYNTAX score</b>	<b>27 (mean)</b>	<b>23 (mean)</b>
<b>Distal location</b>	<b>82%</b>	<b>81%</b>
<b>IVUS use</b>	<b>77%</b>	<b>74%</b>
<b>Off-pump CABG</b>	<b>29%</b>	<b>16%</b>
<b>Arterial conduits</b>	<b>99%</b>	<b>95%</b>

# EXCEL vs NOBLE



# Definite or probable stent thrombosis

---

**Excel**

**Noble**

---

**Definite stent thrombosis**

**0.7%**

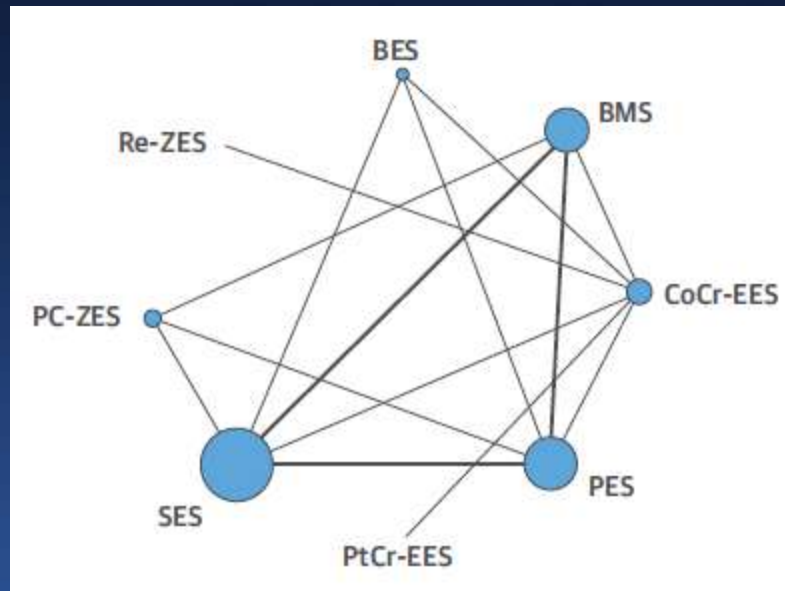
**3.0%**

# Long-Term Safety of Drug-Eluting and Bare-Metal Stents

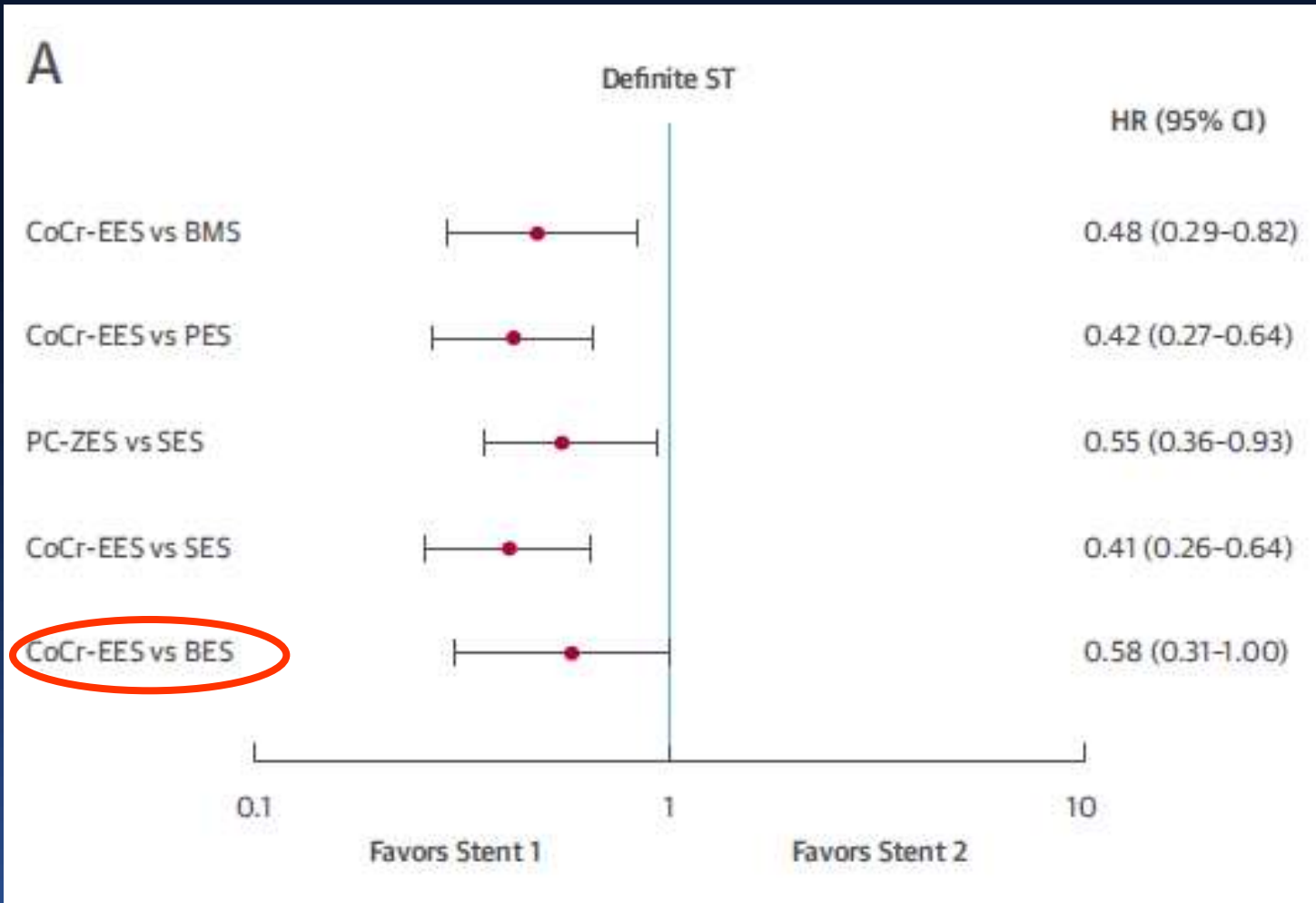


## Evidence From a Comprehensive Network Meta-Analysis

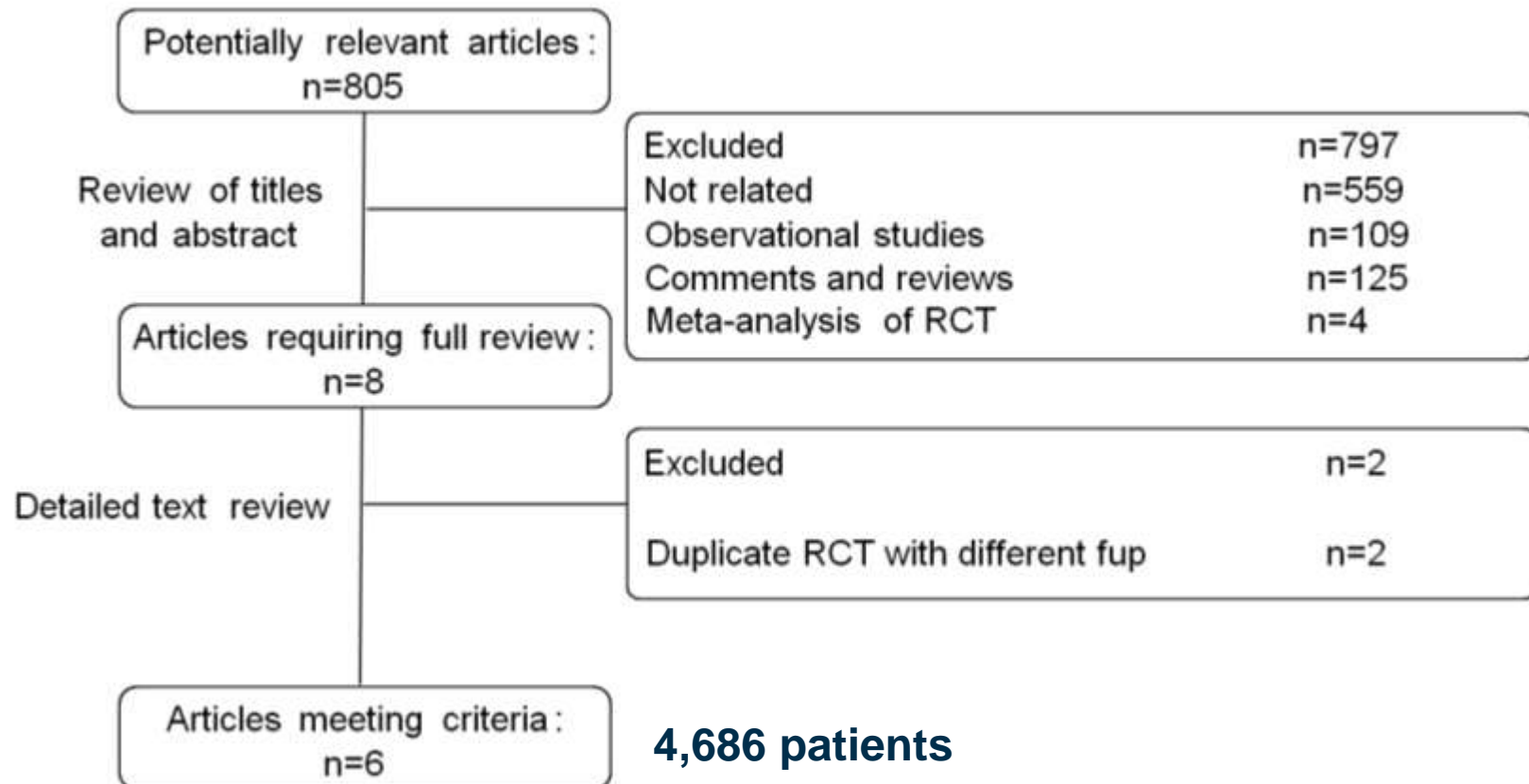
Tullio Palmerini, MD,\* Umberto Benedetto, MD,† Giuseppe Biondi-Zoccai, MD,‡ Diego Della Riva, MD,\*  
Letizia Bacchi-Reggiani, MSTAT,\* Pieter C. Smits, MD, PhD,§ Georgios J. Vlachojannis, MD, PhD,§  
Lisette Okkels Jensen, MD,|| Evald H. Christiansen, MD, PhD,¶ Klára Berencsi, MSTAT,|| Marco Valgimigli, MD,#  
Carlotta Orlandi, MD,\* Mario Petrou, MD,† Claudio Rapezzi, MD,\* Gregg W. Stone, MD\*\*



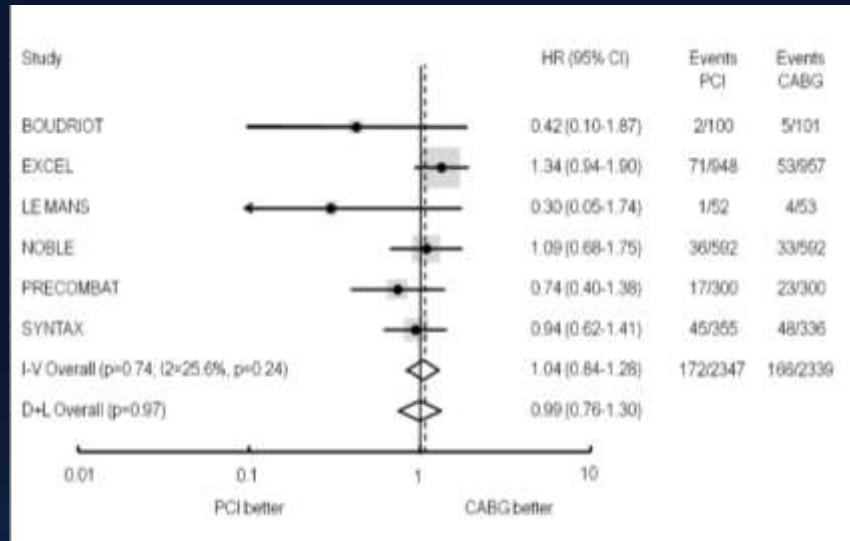
***RCT with at least 3-year fup  
51 RCTs with 52,158 patients  
Mean follow up 4 years***



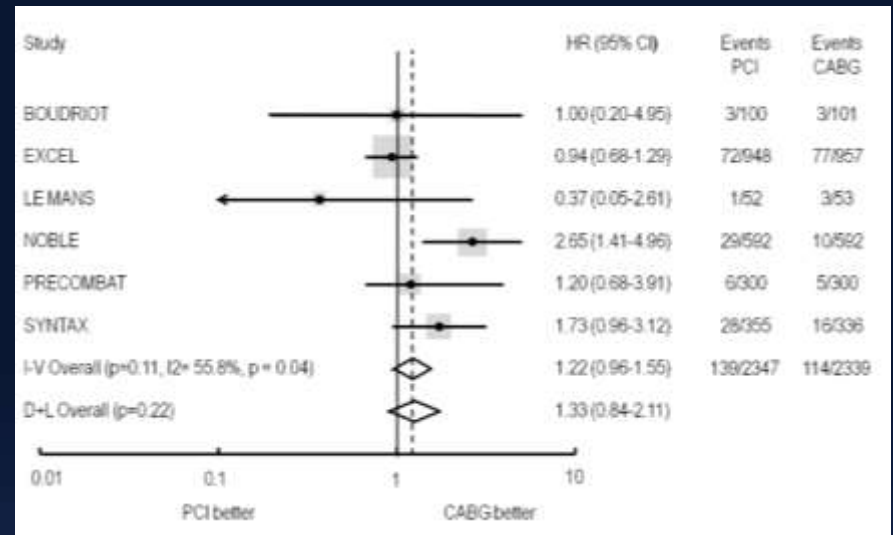
# Flow diagram



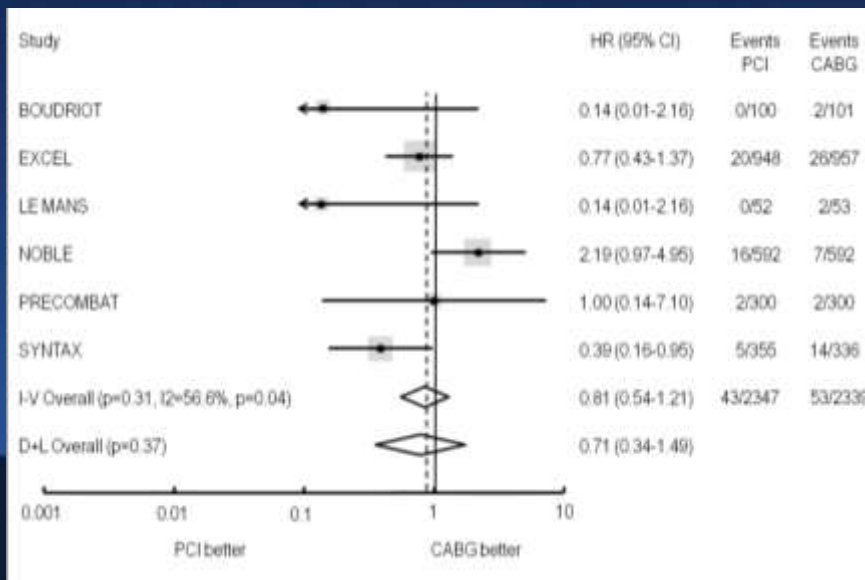
## All cause mortality



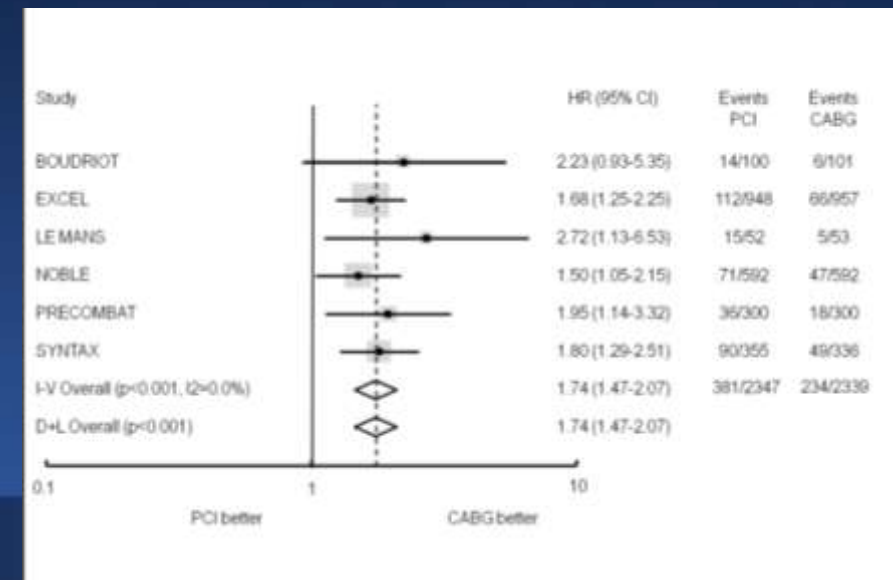
## Myocardial infarction



## Stroke



## Repeat revascularization









# European Guidelines

Recommendations according to extent of CAD	CABG		PCI		Ref <sup>c</sup>
	Class <sup>a</sup>	Level <sup>b</sup>	Class <sup>a</sup>	Level <sup>b</sup>	
One or two-vessel disease without proximal LAD stenosis.	IIb	C	I	C	
One-vessel disease with proximal LAD stenosis.	I	A	I	A	107,108,160, 161,178,179
Two-vessel disease with proximal LAD stenosis.	I	B	I	C	108,135,137
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
Left main disease with a SYNTAX score >32.	I	B	III	B	17
Three-vessel disease with a SYNTAX score ≤ 22.	I	A	I	B	17,157,175,176
Three-vessel disease with a SYNTAX score 23–32.	I	A	III	B	17,157,175,176
Three-vessel disease with a SYNTAX score >32.	I	A	III	B	17,157,175,176

# 2014 ACC/AHA Guidelines

	Class Of Recommendation	LOE
<b>CABG</b>	<b>I</b>	<b>B</b>
<b>PCI</b>	IIa—For SIHD when low risk of PCI complications and high likelihood of good long-term outcome (e.g., <u>SYNTAX score of <math>\leq 22</math></u> , ostial or trunk left main CAD), <b>and</b> a significantly increased CABG risk (e.g., STS-predicted risk of <u>operative mortality <math>\geq 5\%</math></u> )	<b>B</b>
	IIb—For SIHD when low to intermediate risk of PCI complications and intermediate to high likelihood of good long-term outcome (e.g., SYNTAX score of $< 33$ , bifurcation left main CAD) <b>and</b> increased CABG risk (e.g., moderate-severe COPD, disability from prior stroke, prior cardiac surgery, STS-predicted operative mortality $> 2\%$ )	<b>B</b>
	III: Harm—For SIHD in patients (versus performing CABG) with unfavorable anatomy for PCI and who are good candidates for CABG	<b>B</b>



Helping Cardiovascular Professionals  
Learn. Advance. Heal.



# ACC/AHA appropriate use criteria for coronary revascularization

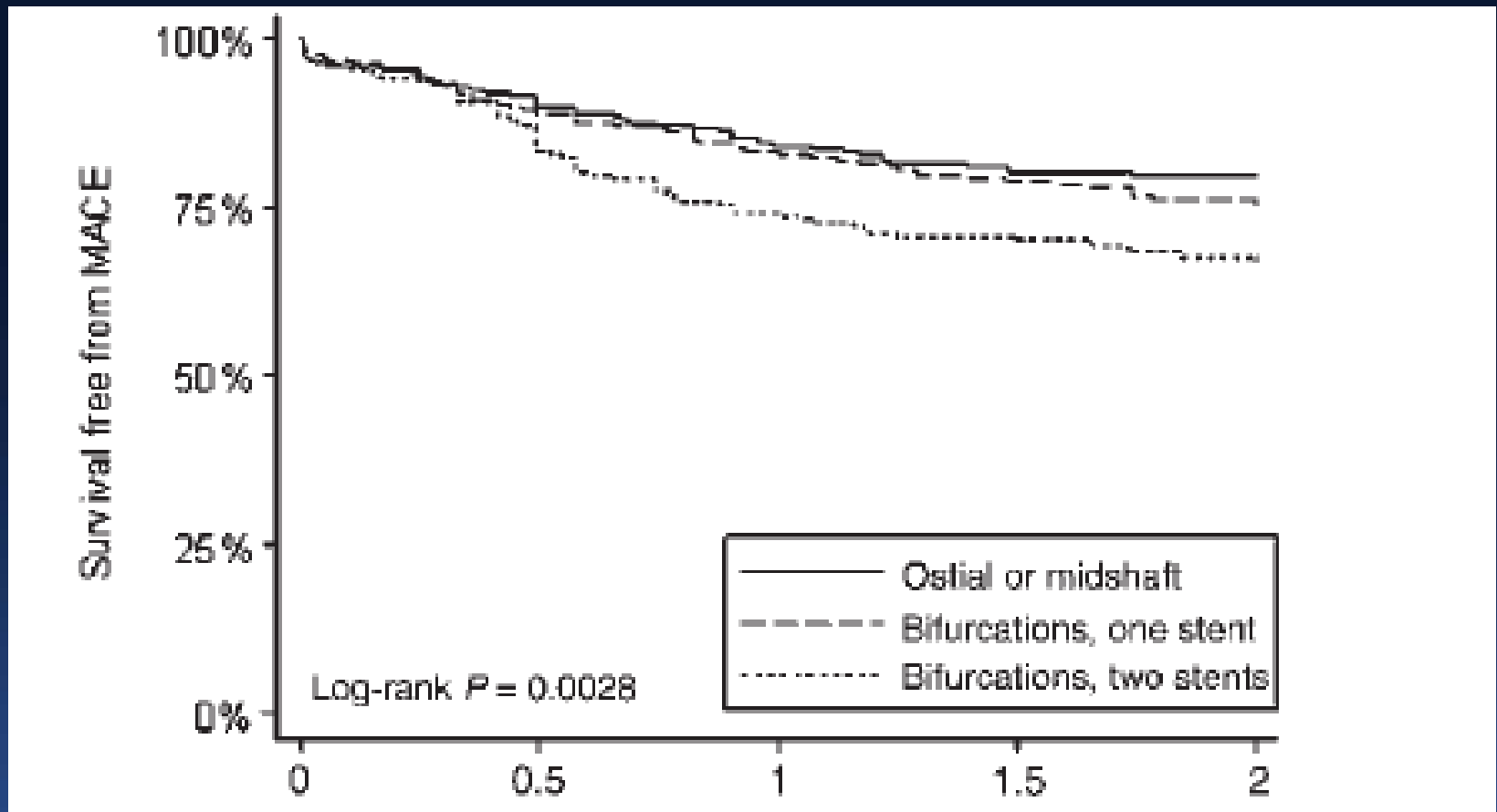
Indication	Asymptomatic				Ischemic Symptoms			
	Not on AA Therapy or With AA Therapy		Not on AA Therapy		On 1 AA Drug (BB Preferred)		On ≥2 AA Drugs	
	PCI	CABG	PCI	CABG	PCI	CABG	PCI	CABG
24. <ul style="list-style-type: none"> <li>Isolated LMCA disease</li> <li>Ostial or midshaft stenosis</li> </ul>	M (6)	A (8)	A (7)	A (8)	A (7)	A (9)	A (7)	A (9)
25. <ul style="list-style-type: none"> <li>Isolated LMCA disease</li> <li>Bifurcation involvement</li> </ul>	M (5)	A (8)	M (5)	A (8)	M (5)	A (9)	M (6)	A (9)
26. <ul style="list-style-type: none"> <li>LMCA disease</li> <li>Ostial or midshaft stenosis</li> <li>Concurrent multivessel disease</li> <li>Low disease burden (e.g., 1-2 additional focal stenoses, SYNTAX score ≤22)</li> </ul>	M (6)	A (8)	M (6)	A (9)	A (7)	A (9)	A (7)	A (9)
27. <ul style="list-style-type: none"> <li>Ostial or midshaft stenosis</li> <li>Concurrent multivessel disease</li> <li>Intermediate or high disease burden (e.g., 1-2 additional bifurcation stenosis, long stenoses, SYNTAX score &gt;22)</li> </ul>	M (4)	A (9)	M (4)	A (9)	M (4)	A (9)	M (4)	A (9)
28. <ul style="list-style-type: none"> <li>LMCA disease</li> <li>Bifurcation involvement</li> <li>Low disease burden in other vessels (e.g., 1-2 additional focal stenosis, SYNTAX score ≤22)</li> </ul>	M (4)	A (8)	M (5)	A (8)	M (5)	A (9)	M (6)	A (9)
29. <ul style="list-style-type: none"> <li>LMCA disease</li> <li>Bifurcation involvement</li> <li>Intermediate or high disease burden in other vessels (e.g., 1-2 additional bifurcation stenosis, long stenoses, SYNTAX score &gt;22)</li> </ul>	R (3)	A (8)	R (3)	A (9)	R (3)	A (9)	R (3)	A (9)



# Ostial and midshaft lesions vs. bifurcation lesions in 1111 patients with unprotected left main coronary artery stenosis treated with drug-eluting stents: results of the survey from the Italian Society of Invasive Cardiology

Tullio Palmerini<sup>1\*</sup>, Diego Sangiorgi<sup>1</sup>, Antonio Marzocchi<sup>1</sup>, Corrado Tamburino<sup>2</sup>, Imad Sheiban<sup>3</sup>, Massimo Margheri<sup>4</sup>, Giuseppe Vecchi<sup>5</sup>, Giuseppe Sangiorgi<sup>6</sup>, Michele Ruffini<sup>7</sup>, Antonio L. Bartorelli<sup>8</sup>, Carlo Briguori<sup>9</sup>, Luigi Vignali<sup>10</sup>, Francesco Di Pede<sup>11</sup>, Angelo Ramondo<sup>12</sup>, Luigi Inglese<sup>13</sup>, Marco De Carlo<sup>14</sup>, Leonardo Bolognese<sup>15</sup>, Alberto Benassi<sup>16</sup>, Cataldo Palmieri<sup>17</sup>, Vincenzo Filippone<sup>18</sup>, Fabio Barlocco<sup>19</sup>, Giulia Lauria<sup>1</sup>, and Stefano De Servi<sup>19</sup>

# Ostial vs bifurcation lesions



# Conclusions

- **Across all RCTs performed so far, PCI was associated with similar rates of death, MI or stroke, but higher rates of TVR.**
- **PCI can thus be considered an acceptable strategy of revascularization in selected patients with ULMCA stenosis as an alternative to CABG.**
- **Heart team discussion remains a fundamental step for the decision making of the optimal strategy of revascularization in this subset of patients.**