



Morning Roundtable Forum - Antithrombotic Therapy: Finding the “Sweet-Spot”

PCI vs. CABG in LM PCI: Where are we in 2017?

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Disclosure Statement of Financial Interest

Within the past 12 months, I, **Davide Capodanno**, have had a financial interest/arrangement or affiliation with the organization(s) listed below.

Affiliation/Financial relationship

Company

- **Speakers' honoraria**

None

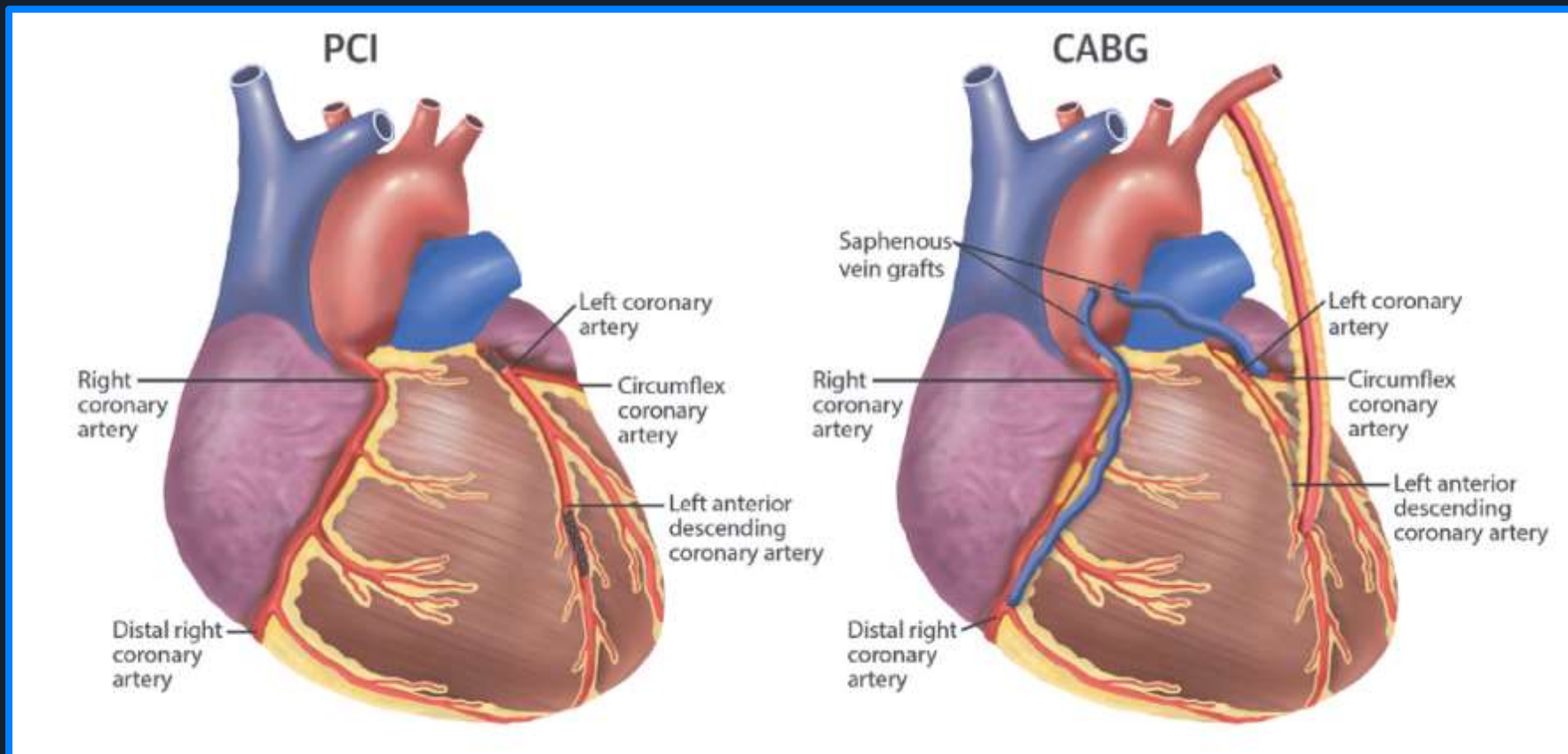
- **Consulting**

Abbott Vascular (VHD branch)

- **Advisory Board**

None

Decision-Making for Left Main Disease



PCI

Less invasive and shorter hospitalization
 Lower risk of periprocedural adverse events
 Long-term durability due to low risk of disease progression

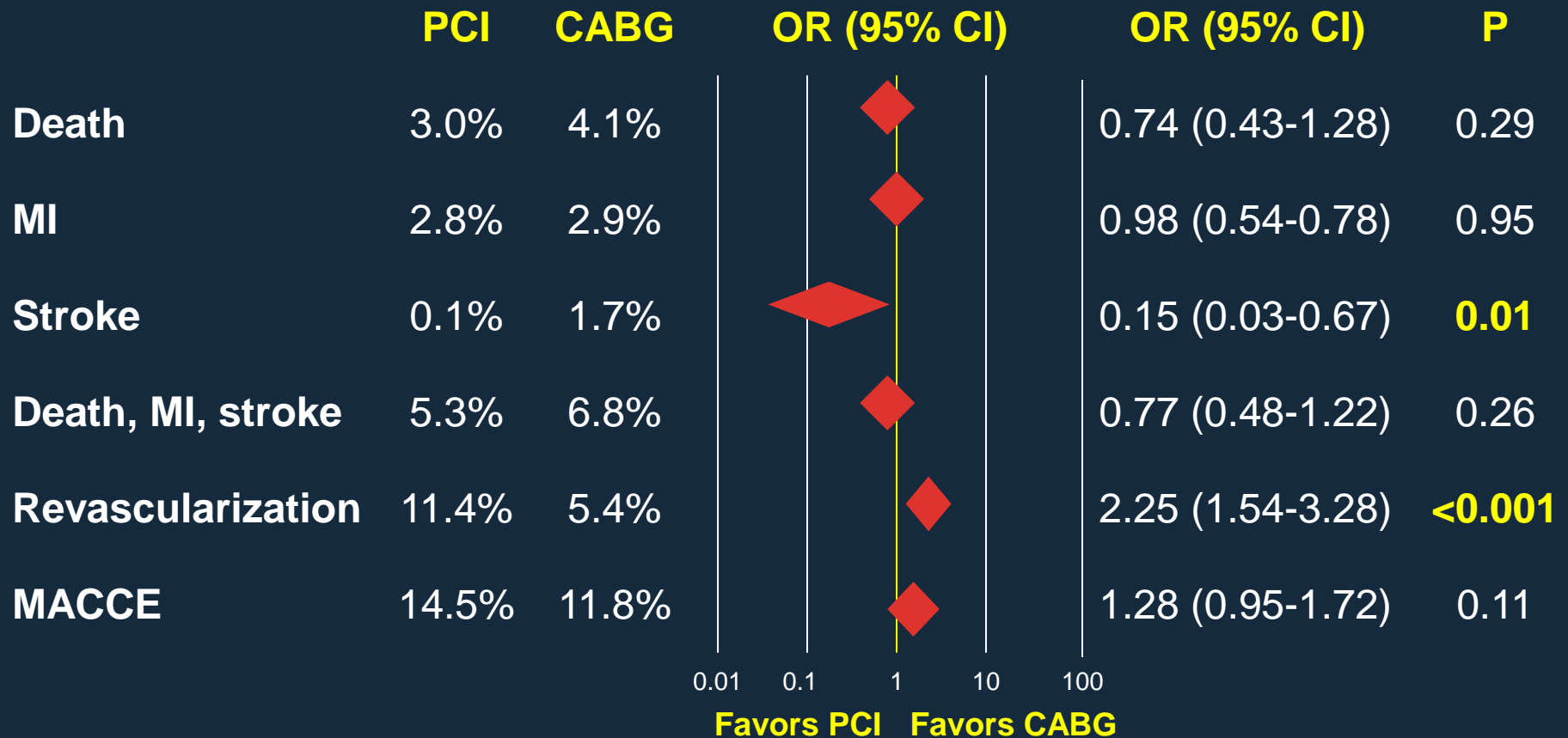
CABG

Lower risk of MACCE and repeat revascularization
 More complete revascularization
 Protection against events related to disease progression

PCI vs CABG for Left Main Disease

Study-level meta-analysis of 4 randomized trials (N=1,611)

1-Year Outcomes



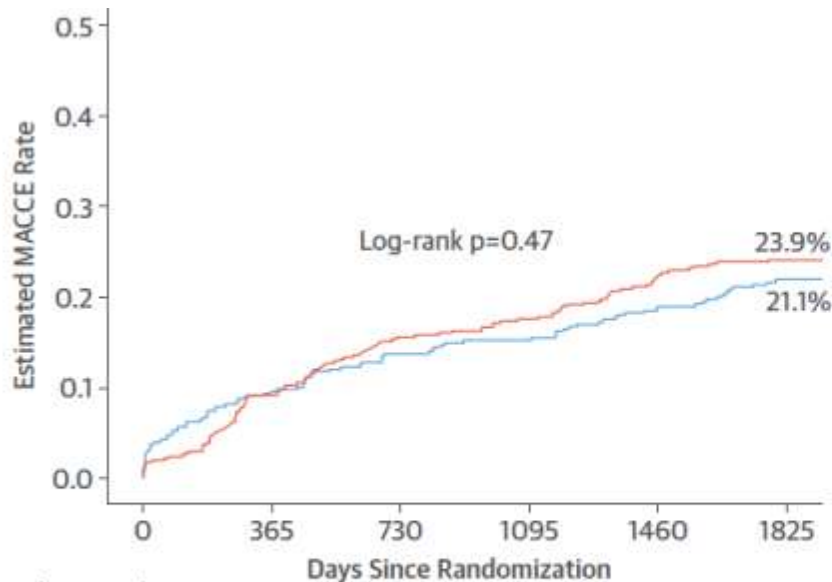
PCI vs CABG for Left Main Disease

Pooled analysis of SYNTAX LM and PRECOMBAT (N=1,305)

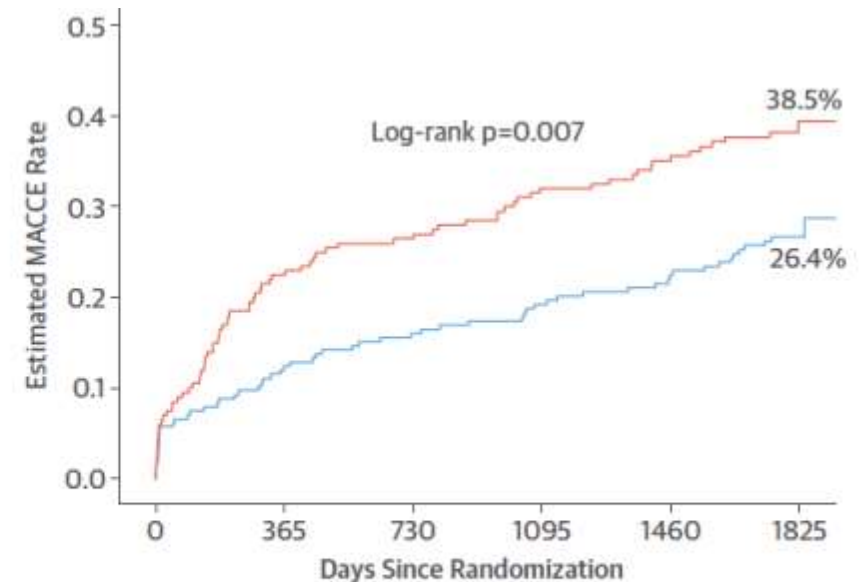
5-Year Outcomes

Low to Intermediate (0-32)
SYNTAX Scores

High (≥ 33)
SYNTAX Scores



Number at risk	0	365	730	1095	1460	1825
CABG	421	370	350	340	320	79
PCI	457	413	381	371	344	96



Number at risk	0	365	730	1095	1460	1825
CABG	227	195	185	175	167	61
PCI	200	155	146	134	127	38

Recommendations for LM Revascularization

United States



PCI

CABG

Low
SxScore 0-22

IIa B

I B

Intermediate
SxScore 23-32

IIb B

I B

High
SxScore >32

III B

I B

Europe



PCI

CABG

Low
SxScore 0-22

I B

I B

Intermediate
SxScore 23-32

IIa B

I B

High
SxScore >32

III B

I B

What Makes Current Guidelines Based on SYNTAX Outdated, Stimulating New Trials?

1. In SYNTAX, left main disease was just a subgroup
2. Patients where CABG has established benefits (ie, MVD, high SYNTAX score) were included
3. One year follow-up proved to be an insufficient timeframe to capture the true benefit accrual of CABG
4. First-generation drug-eluting stents were used
5. IVUS/FFR guidance was uncommon
6. Discretionary angiographic follow up overly inflated the number of events in the PCI arm
7. Best standards of CABG were also underused

EXCEL and NOBLE in Perspective

	SYNTAX	EXCEL	NOBLE
All-comers	Yes	No	No
Patient population	LM/3VD	LM	LM
SYNTAX score	Any	≤ 32	Low
Primary endpoint*	Death/MI/CVA/TVR	Death/MI/CVA	Death/MI/CVA/TVR
Follow up	1 year	3 year (median)	3 year (median)
IVUS	Infrequent	Recommended	Recommended
FFR guidance	Infrequent	Recommended	Recommended
Stent	PES	EES	BES recommended
Angio FU	At discretion	Not recommended	Not recommended

*The definition of MI in EXCEL included large periprocedural MI. NOBLE did not include periprocedural MI in the primary endpoint

EXCEL and NOBLE – A Closer Look

	EXCEL	NOBLE
Randomized pts, centers, countries, geographies	1,905 pts at 126 sites in 17 countries (US, EU)	1,201 pts at 36 sites in 9 countries (EU)
Recruitment period	2010-2014	2008-2015
Age*	66 years (mean)	66 years (mean)
Diabetes mellitus*	30%	15%
LVEF*	57% (mean)	60% (mean)
Acute coronary syndrome*	24%	18%
SYNTAX score* (Core-lab)	27 (mean)	23 (mean)
Distal location*	82%	81%
IVUS use*	77%	74%
Off-Pump CABG	29%	16%
Arterial conduits used	99%	95%
Only arterial conduits used	25%	14%

*Data are shown for the PCI cohort



EXCEL: 3 Years Outcomes

	PCI (n=948)	CABG (n=957)	Diff [upper confidence limit]	P _{NI}	HR [95%CI]	P _{Sup}
Primary endpoint						
Death, stroke or MI at 3 years	15.4%	14.7%	0.7% [4.0%] [†]	0.018	-	-
Secondary endpoints						
Death, stroke or MI at 30 days	4.9%	7.9%	-3.1% [-1.2%]	<0.001	-	-
Death, stroke, MI or ischemia-driven revasc at 3 years	23.1%	19.1%	4.0% [7.2%]	0.01	-	-
Death, stroke or MI at 3 years	15.4%	14.7%	-	-	1.00 [0.79, 1.26]	0.98

EXCEL: Landmark Analysis

	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

NOBLE: 5-Year Outcomes

	PCI* (n=592)	CABG* (n=592)	HR [95%CI]	P _{Sup}
MACCE	29%	19%	1.48 (1.11-1.96)	0.007
Death	12%	9%	1.07 (0.67-1.72)	0.77
Non-procedural MI	7%	2%	2.88 (1.40-5.90)	0.004
Stroke	5%	2%	2.25 (0.93-5.48)	0.07
Repeat revascularization	16%	10%	1.50 (1.04-2.17)	0.032

*Data are shown as 5-year K-M estimates

EXCEL and NOBLE - Interpretation

EXCEL



In patients with left main coronary artery disease and low or intermediate SYNTAX scores by site assessment, **PCI with everolimus-eluting stents was noninferior to CABG** with respect to the rate of the composite end point of death, stroke, or myocardial infarction at 3 years.

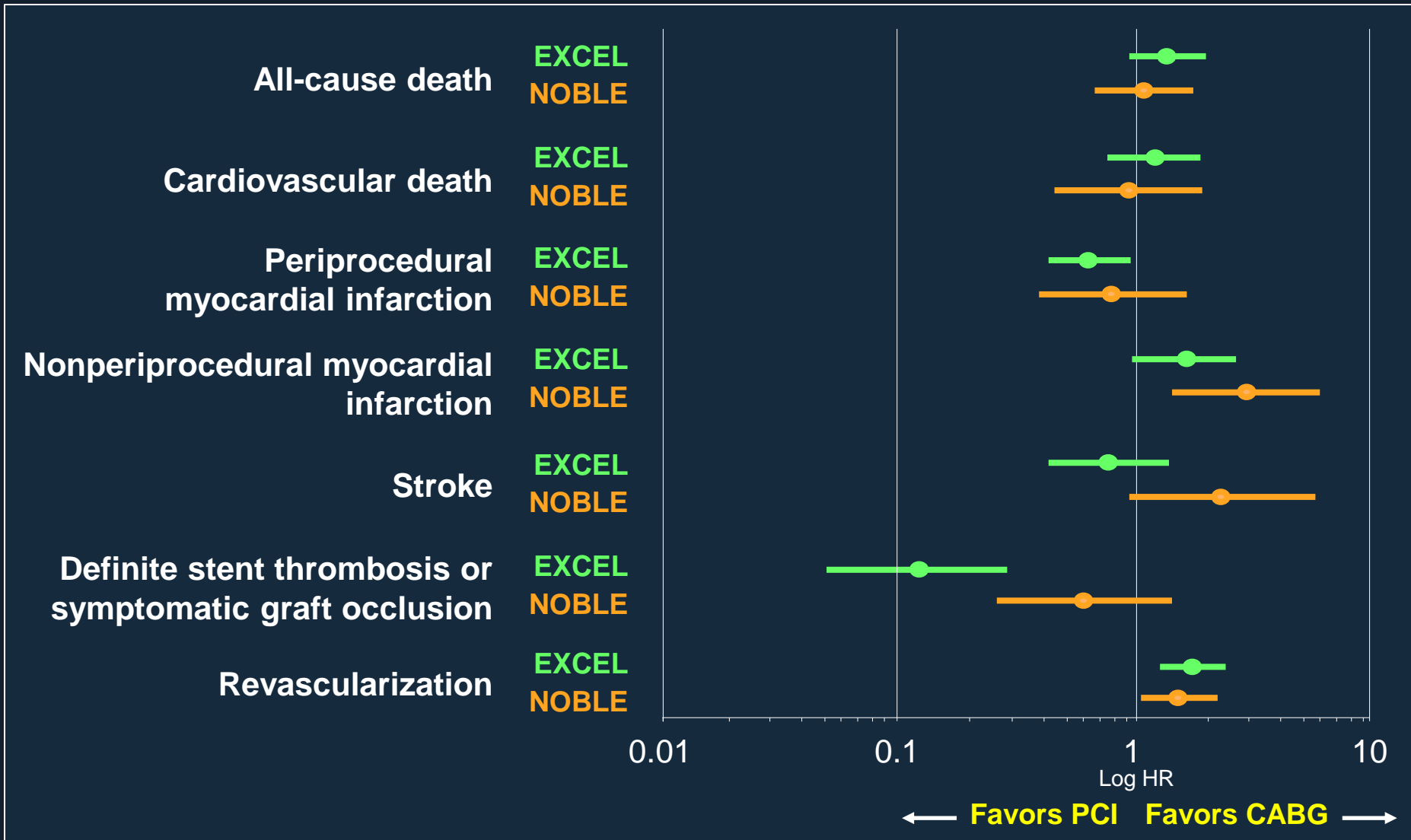
NOBLE



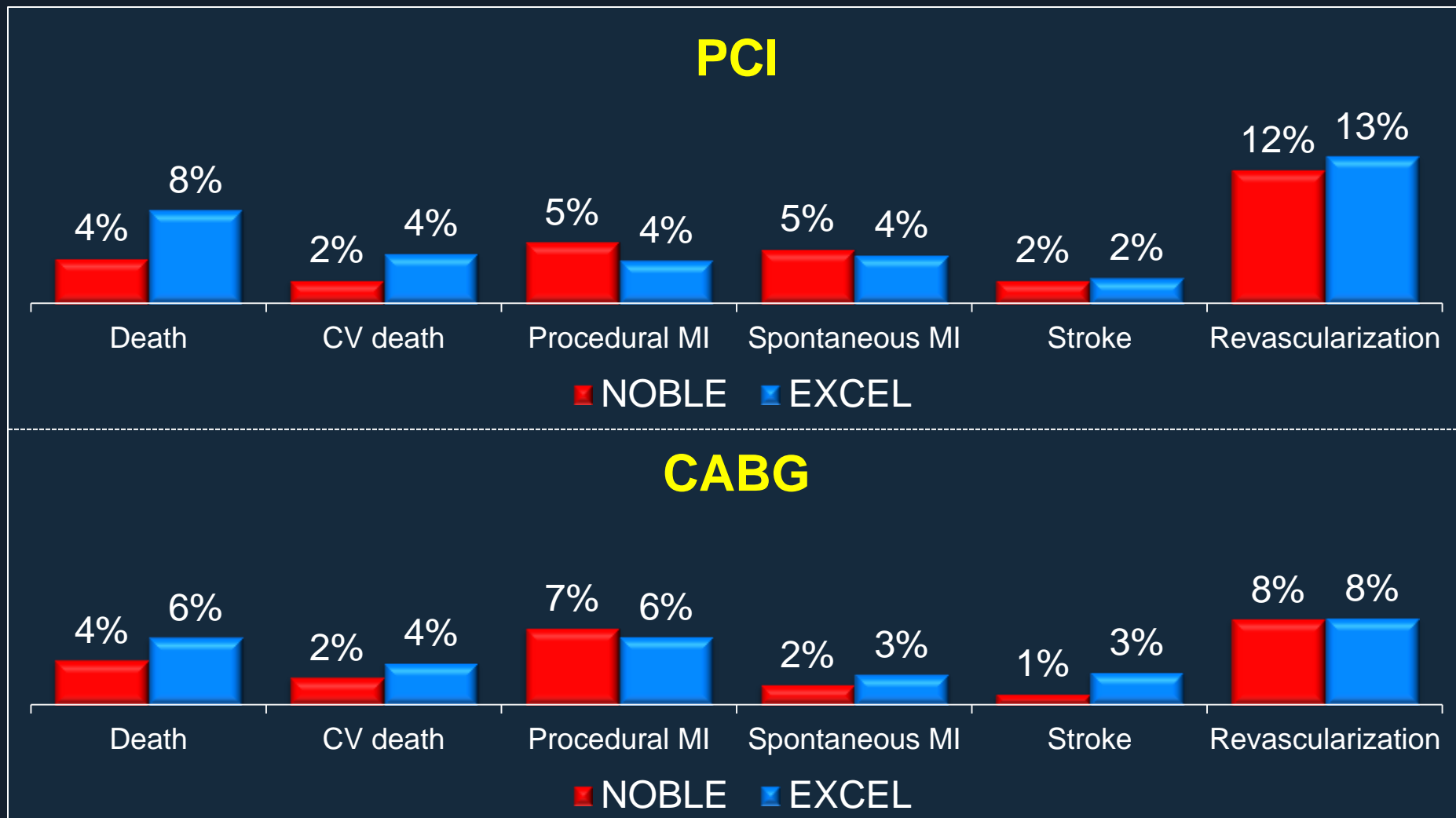
The findings of this study suggest that **CABG might be better than PCI** for treatment of left main stem coronary artery disease.

Stone GW, et al. N Engl J Med. 2016;375:2223-2235
Mäkikallio T, et al. Lancet. 2016;388:2743-2752

More Alike Than Different?



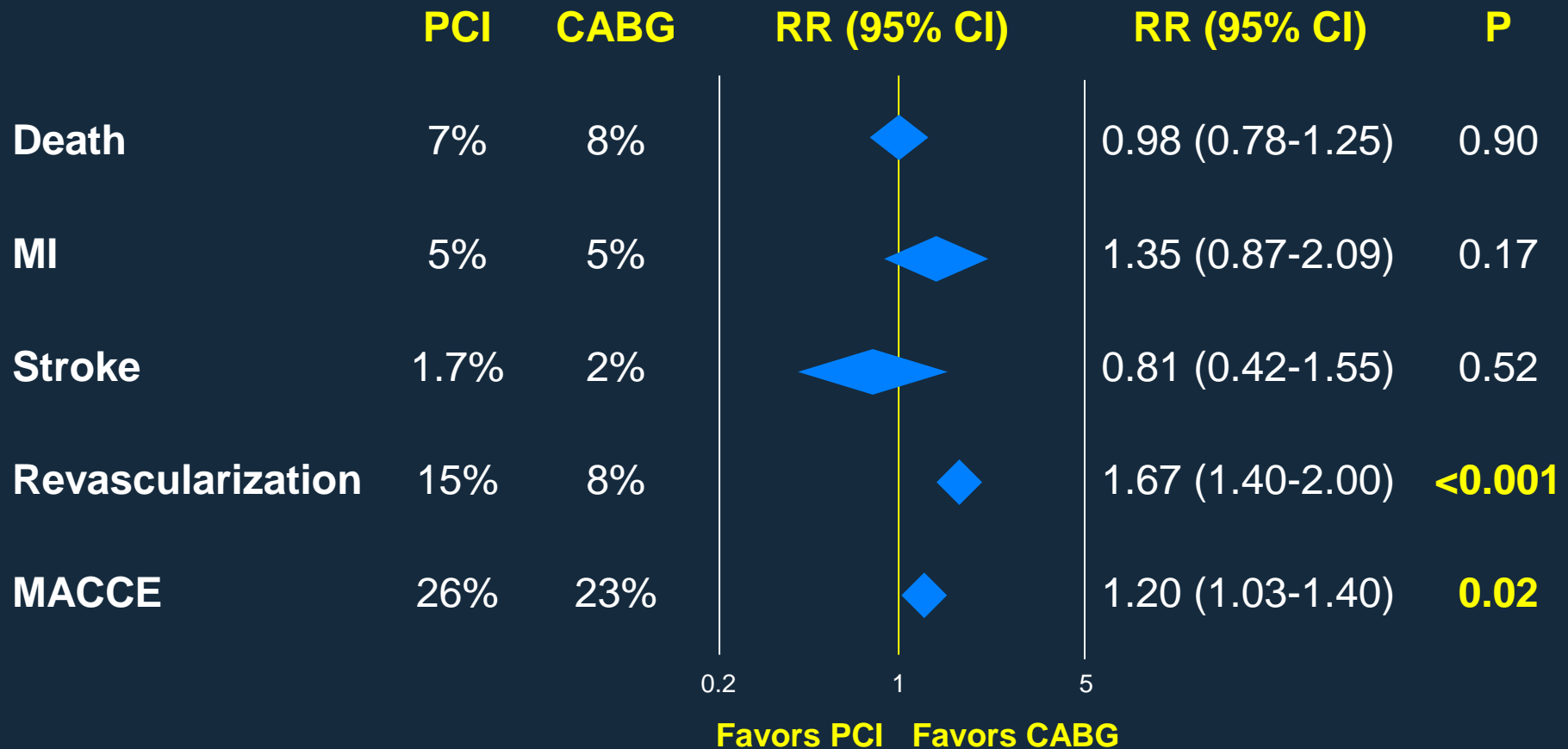
Aligning Outcome Rates of EXCEL and NOBLE at Three Years



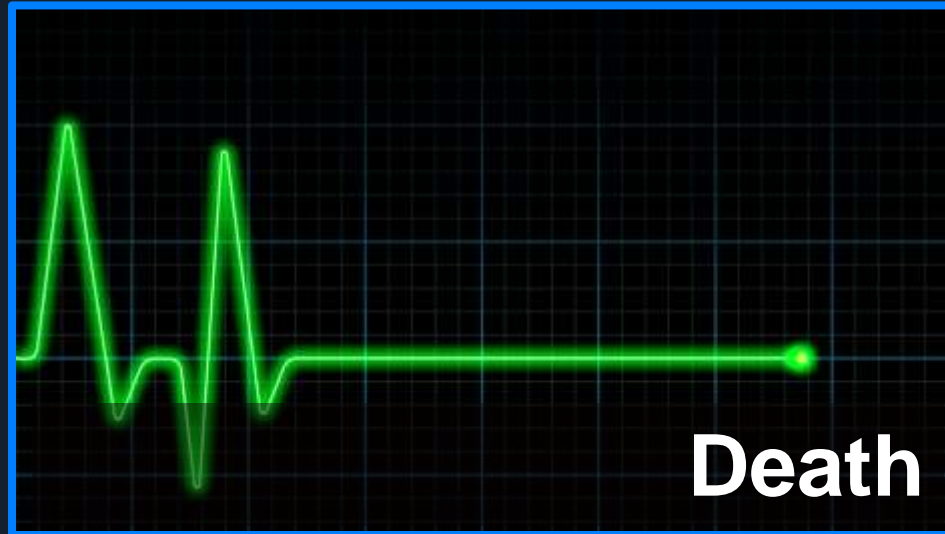
PCI vs CABG for Left Main Disease

Study-level meta-analysis of 6 randomized trials (N=4,700)

Longest Follow-up Outcomes

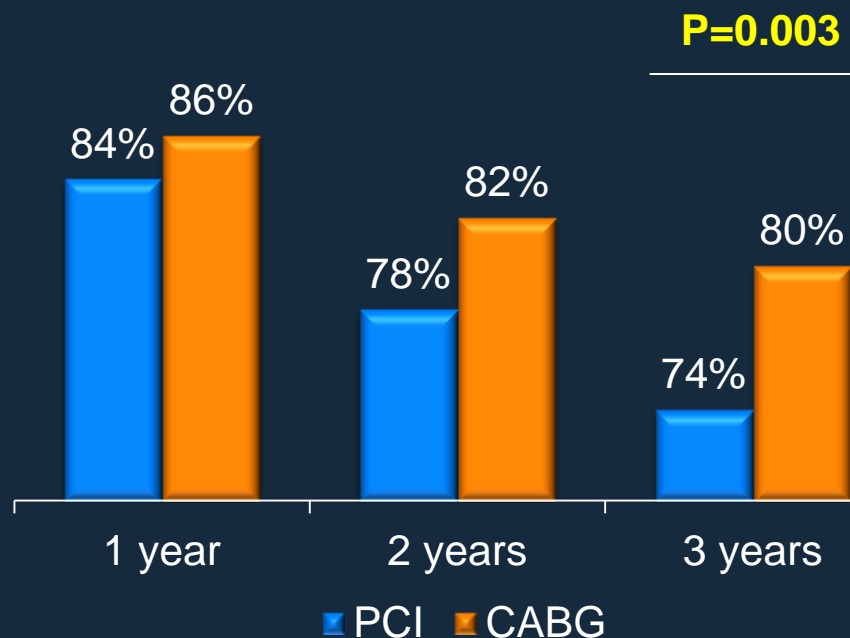


Are All Endpoints Created Equal?

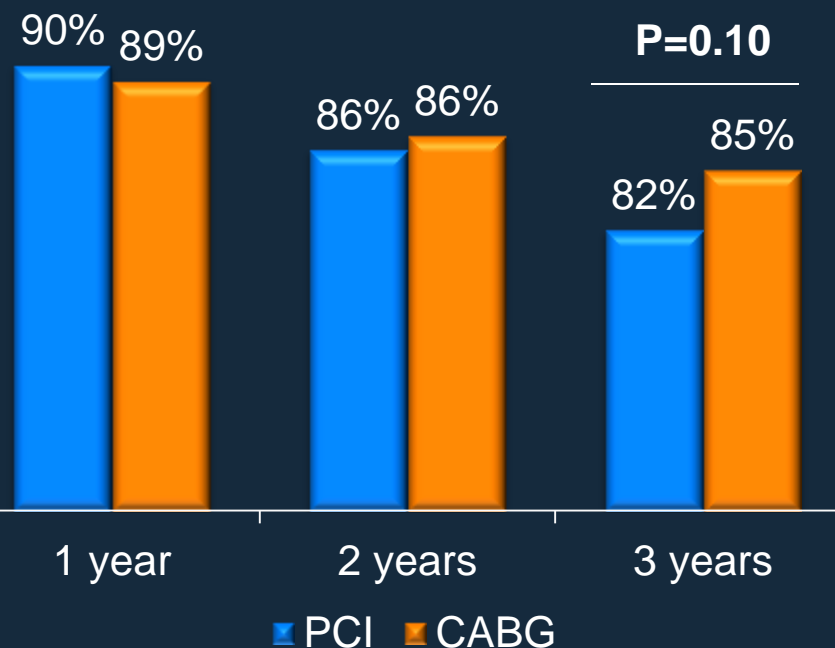


Repeat Revascularization: The Case for Weighting 1,204 matched PCI and CABG patients from DELTA

Time-To-Event Analysis MACCE-Free K-M Estimates



Weighted Composite Endpoint* MACCE-Free K-M Estimates



*Using weights of 1.00, 0.47, 0.38 and 0.25 for Death, CVA, MI and TVR, respectively.

Risk Stratification for LM Revascularization



SYNTAX score

Assessment of the location, extent and complexity of coronary artery disease

Functional SXscore

As SYNTAX score but based on functionally significant lesions

Residual SxScore CABG SXScore

Marker of complete revascularization

Global Risk, CSS, Log CSS

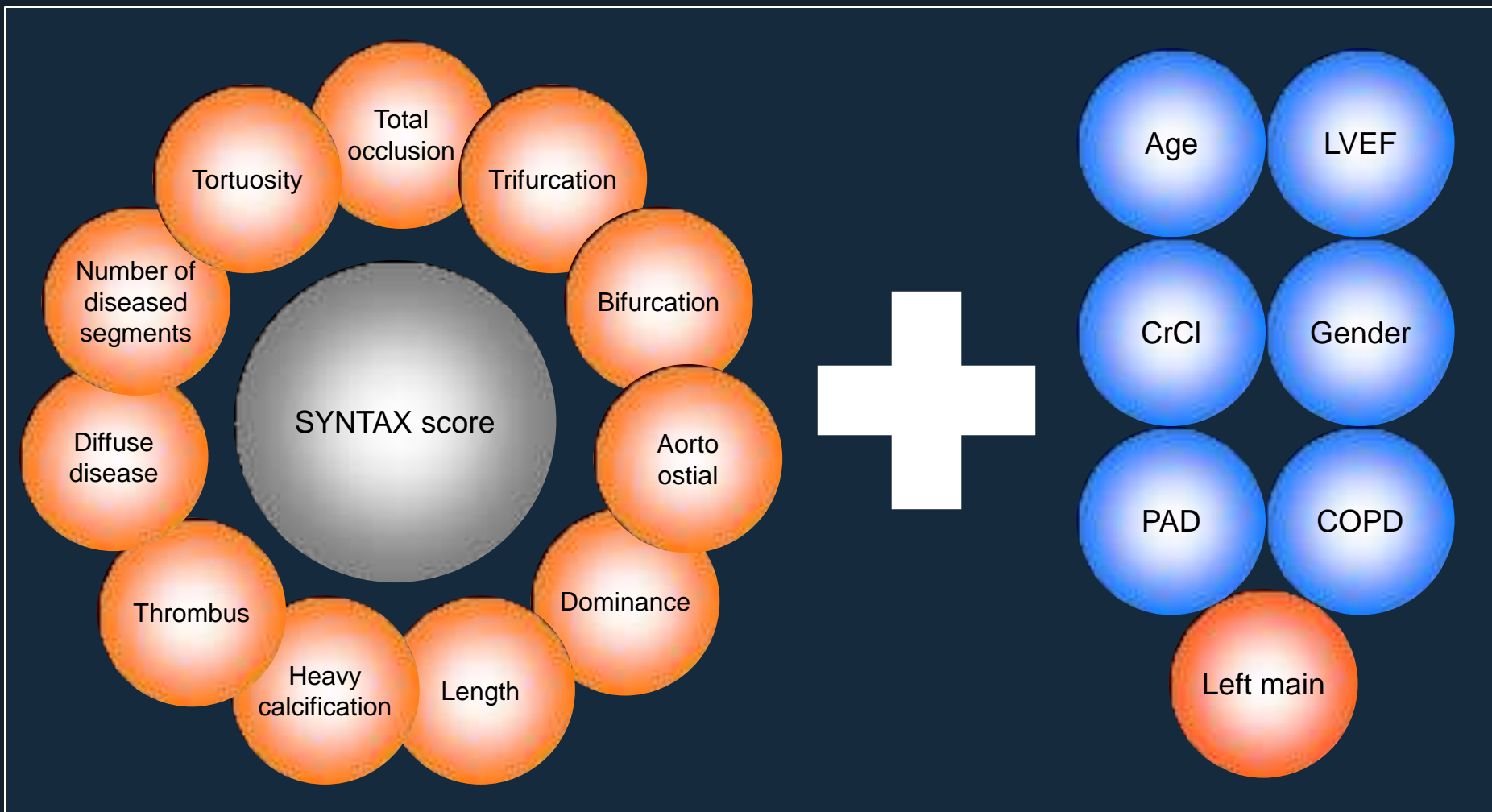
To improve the predictive power of the SYNTAX score

SYNTAX score II

Individual decision making for PCI vs. CABG

SYNTAX Score II: What Makes It Different?

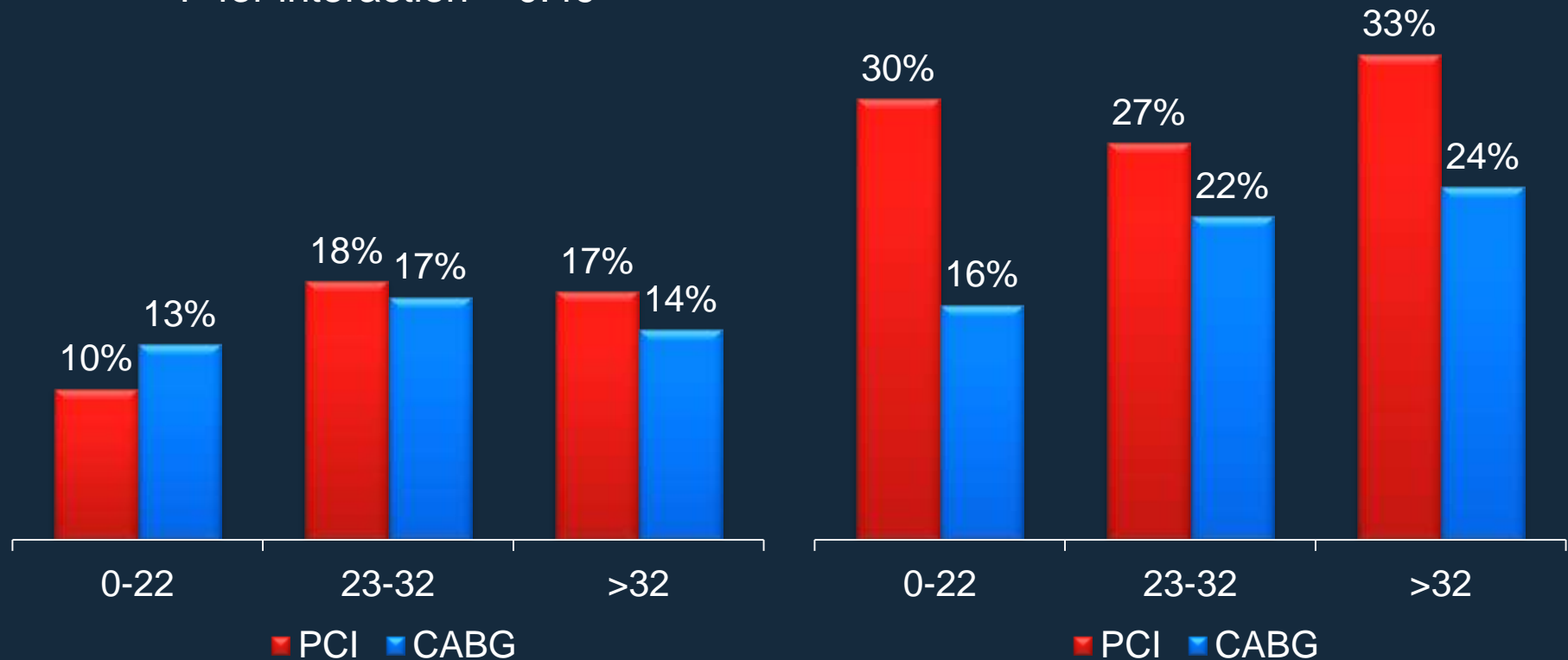
12 Angiographic and 6 Clinical Variables



Can We Trust the SYNTAX score Anymore?

EXCEL

P for interaction = 0.49



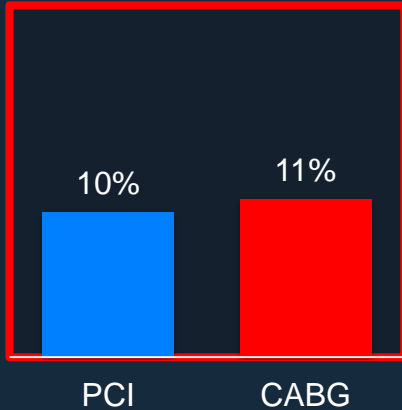
*Percentages K-M estimates at 3 years (EXCEL) or 5 years (NOBLE)



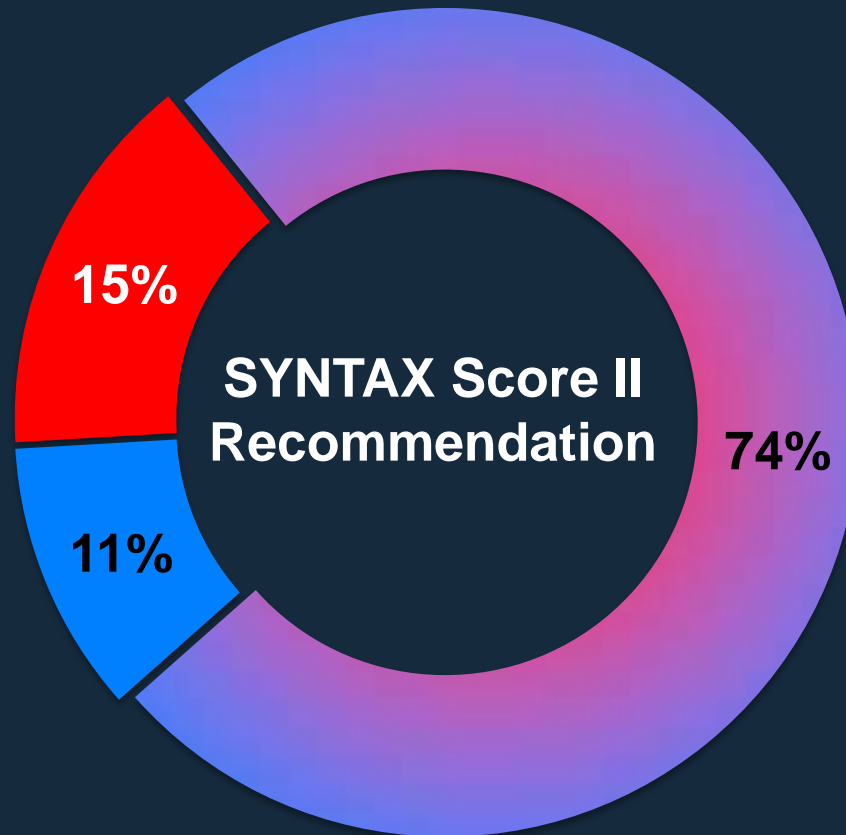
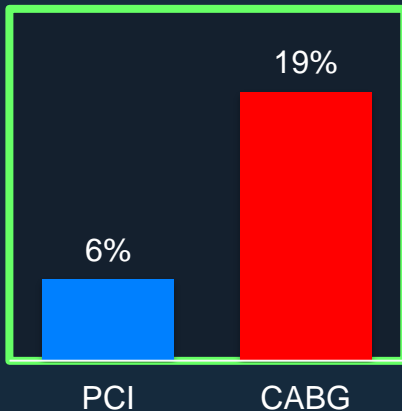
SYNTAX Score II in Left Main PCI or CABG

Pooled analysis of SYNTAX LM and PRECOMBAT (N=1,299)

CABG recommended

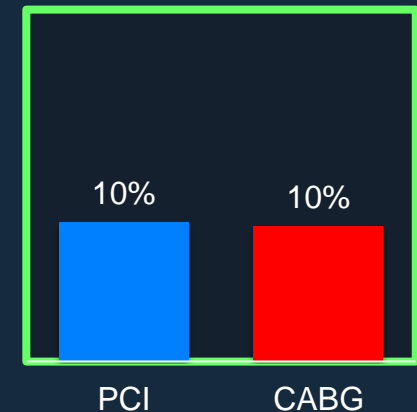


PCI recommended

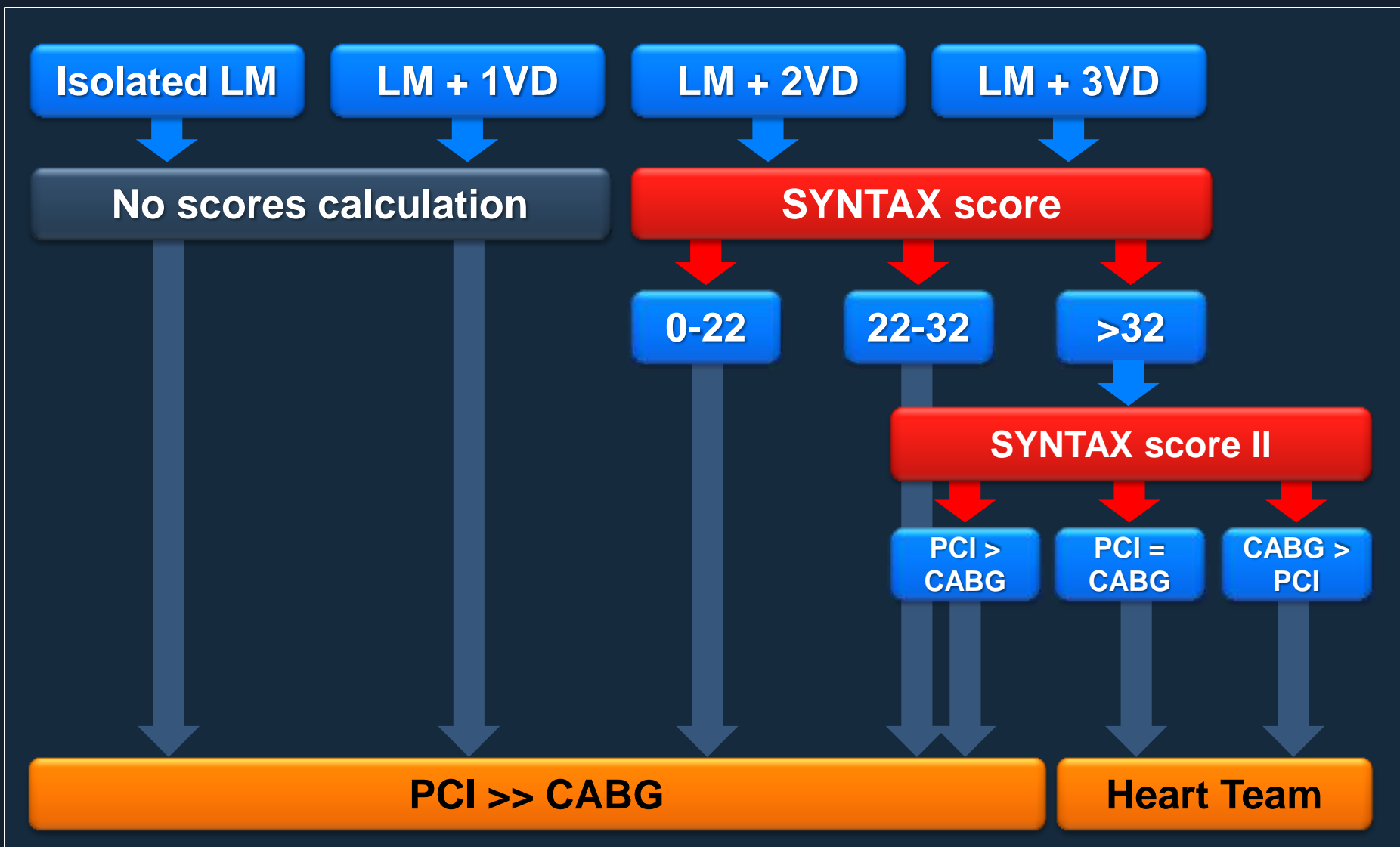


5-Year Death

Equipose



Risk Scores In Everyday Clinical Practice



After EXCEL and NOBLE

Implications for Next Guidelines

- ① After EXCEL and NOBLE, the SYNTAX score-based approach for left main disease recommendations should be revisited. At the very least, based on EXCEL, the low and intermediate categories should be collapsed
- ② Recommendations could become class I for PCI being no longer an “alternative” to CABG, but an “acceptable” or even “preferred” choice in selected patients
- ③ With two more randomized trials, the current B level of evidence for left main revascularization by PCI or CABG should be upgraded to A
- ④ In general, I expect new left main recommendations to be more patient-centered based on the early- and long-term trade-offs of each procedure, focused on ways to improve outcomes for PCI and CABG patients alike by optimizing background medical therapy

Closing Remarks: “My practice in 2017”

- 1. Isolated left main disease** with lower anatomical complexity (i.e. ostium or shaft only, simple distal left main bifurcation) is the ideal candidate for **ad hoc PCI**
- 2. Complex left main disease** involving the bifurcation or left main in the context of multivessel disease requires Heart Team consensus. The **SYNTAX scores I and II** are useful but imperfect companions for decision-making (ie, after NOBLE and EXCEL I’m not sure about SYNTAX score I in general, and also about patients recommended for CABG by the SYNTAX score II...)
 - ❖ Low risk patients with complete revascularization achievable, high risk surgical candidates, or patient preference after discussion of pros and cons: **Elective PCI**
 - ❖ Complete revascularization achievable with PCI at the price of complex interventions and too many stents implanted: **CABG**