

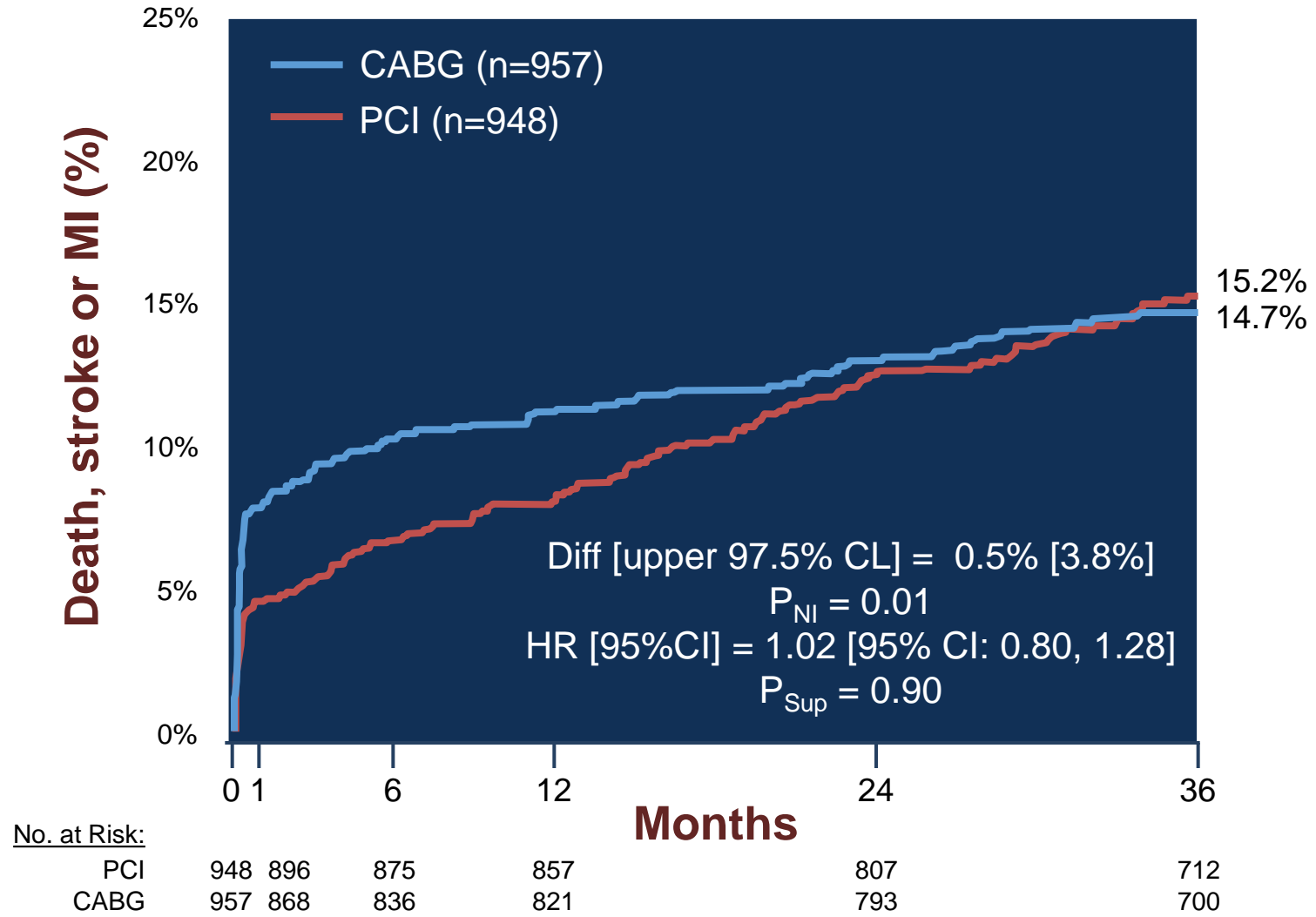
Disclosure

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below

<u>Affiliation/Financial Relationship</u>	<u>Company</u>
Institutional Grant/Research Support	Biotronik, Boston Scientific, Medtronic CardioVascular, Medinol, Orbus Neich
Consulting Fees/Honoraria	Biotronik, Boston Scientific Corporation, Medtronic CardioVascular, Cardinal Health
Major Stock Shareholder/Equity	None
Royalty Income	None
Ownership/Founder	None
Intellectual Property Rights	None
Other Financial Benefit	None

EXCEL Complete 3 Year Follow-up

Death, Stroke or MI at 3 Years



EXCEL Complete 3 Year Follow-up

Outcomes at 3 Years

	PCI (n=948)	CABG (n=957)	HR [95%CI]	P value
Death, stroke or MI (1° endpoint)	15.2%	14.7%	1.02 [0.80, 1.28]	0.90
- Death	8.0%	5.8%	1.36 [0.96, 1.93]	0.08
- Definite cardiovascular	3.7%	3.3%	1.13 [0.69, 1.84]	0.64
- Definite non-cardiovascular	3.8%	2.2%	1.68 [0.97, 2.93]	0.06
- Undetermined cause	0.7%	0.5%	1.48 [0.42, 5.26]	0.54
- Stroke	2.3%	3.1%	0.74 [0.42, 1.31]	0.30
- MI	8.0%	8.4%	0.94 [0.68, 1.29]	0.69
Death, stroke, MI or IDR	22.8%	18.9%	1.20 [0.98, 1.46]	0.08
- Ischemia-driven revasc (IDR)	12.5%	7.4%	1.72 [1.27, 2.32]	<0.001
Definite stent thrombosis or symptomatic graft occlusion	0.8%	5.3%	0.14 [0.06, 0.31]	<0.001

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30-Day Major Adverse Events

	PCI (n=948)	CABG (n=957)	RR [95%CI]	P value
Peri-procedural MAE, any	8.1%	23.0%	0.35 [0.28, 0.45]	<0.001
- Death*	0.9%	1.0%	0.91 [0.39, 2.23]	0.83
- Stroke*	0.6%	1.3%	0.50 [0.19, 1.34]	0.16
- Myocardial infarction*	3.9%	6.2%	0.63 [0.42, 0.95]	0.02
- Ischemia-driven revascularization*	0.6%	1.4%	0.47 [0.18, 1.22]	0.11
- TIMI major/minor bleeding	3.7%	8.9%	0.42 [0.28, 0.61]	<0.001
- Transfusion ≥2 units	4.0%	17.0%	0.24 [0.17, 0.33]	<0.001
- Major arrhythmia**	2.1%	16.1%	0.13 [0.08, 0.21]	<0.001
- Surgery/radiologic procedure	1.3%	4.1%	0.31 [0.16, 0.59]	<0.001
- Renal failure†	0.6%	2.5%	0.25 [0.10, 0.61]	<0.001
- Sternal wound dehiscence	0.0%	2.0%	0.03 [0.00, 0.43]	<0.001
- Infection requiring antibiotics	2.5%	13.6%	0.18 [0.12, 0.28]	<0.001
- Prolonged intubation (>48 hours)	0.4%	2.9%	0.14 [0.05, 0.41]	<0.001
- Post-pericardiotomy syndrome	0.0%	0.4%	0.11 [0.01, 2.08]	0.12

*Adjudicated events; others are site-reported. **SVT requiring cardioversion, VT or VF requiring treatment, or bradyarrhythmia requiring temp or perm PM. †Scr increased by ≥5 mg/dL from baseline or need for dialysis.

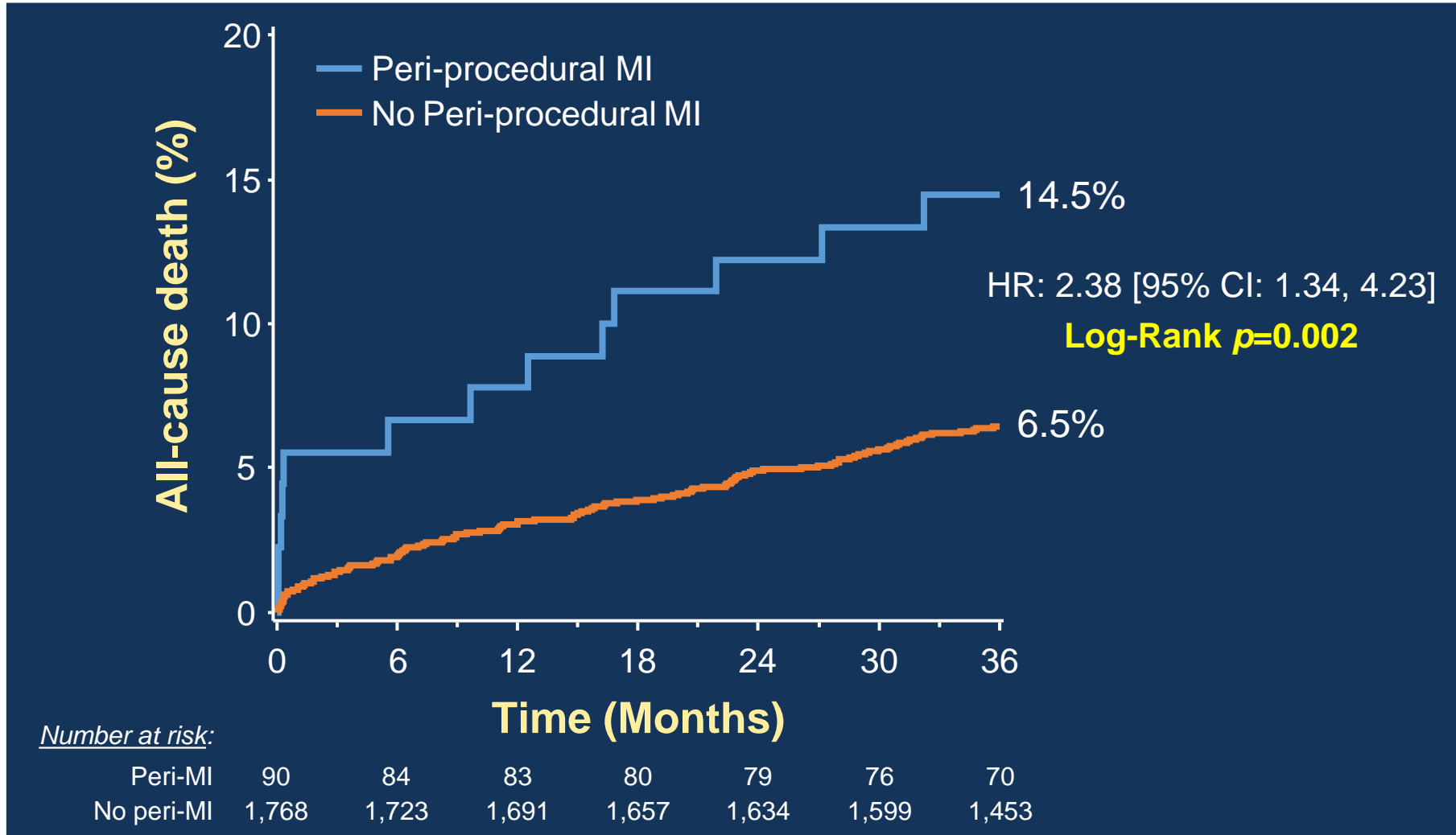
Periprocedural Myocardial Infarction

- Peri-procedural MI was defined using an identical threshold for PCI and CABG to minimize ascertainment bias:
 - >10 times URL peak CK-MB elevation within 72 hours
 - OR
 - >5 times URL PLUS at least one of the following:
 - New pathological Q waves in at least 2 contiguous leads or new persistent non-rate related LBBB
 - Angiographically documented graft or native coronary artery occlusion or new severe stenosis with thrombosis and/or diminished epicardial flow
 - Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality

Treated as
randomized

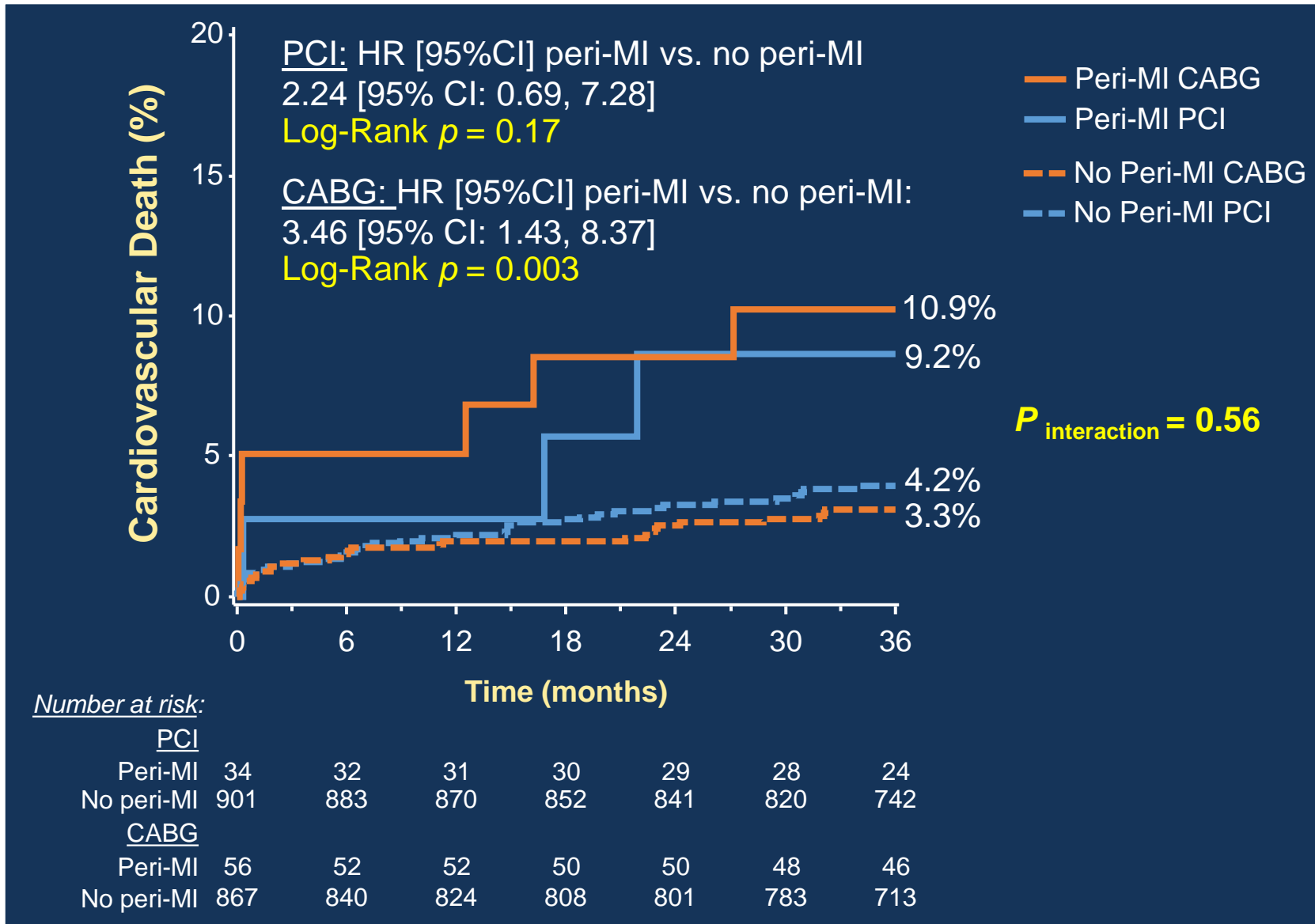
	Periprocedural MI	P value
PCI	3.6% (34/935)	0.01
CABG	6.1% (56/923)	

Periprocedural Myocardial Infarction, 3-Year All-Cause Mortality



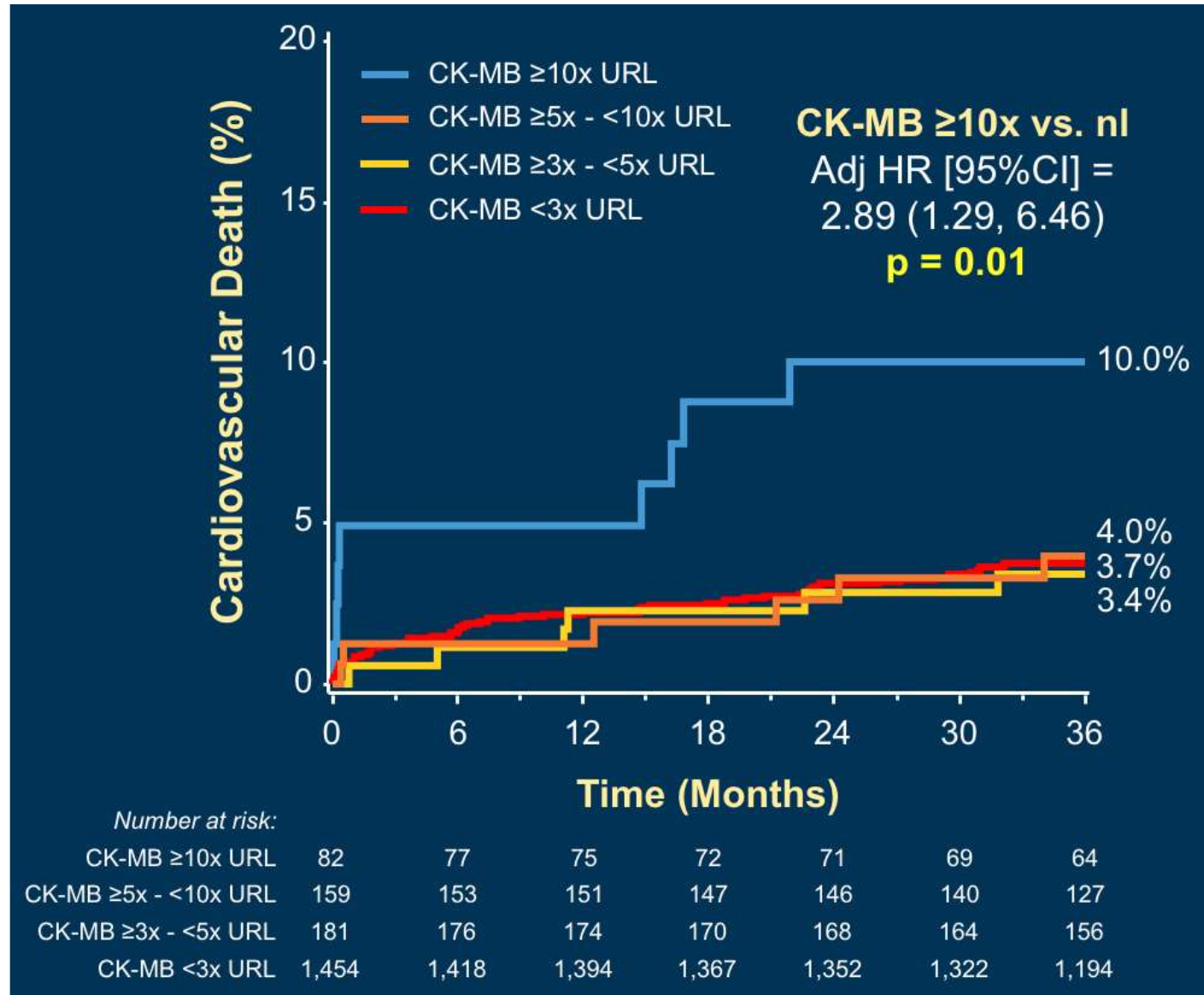
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Periprocedural Myocardial Infarction, 3-Year Cardiovascular Death



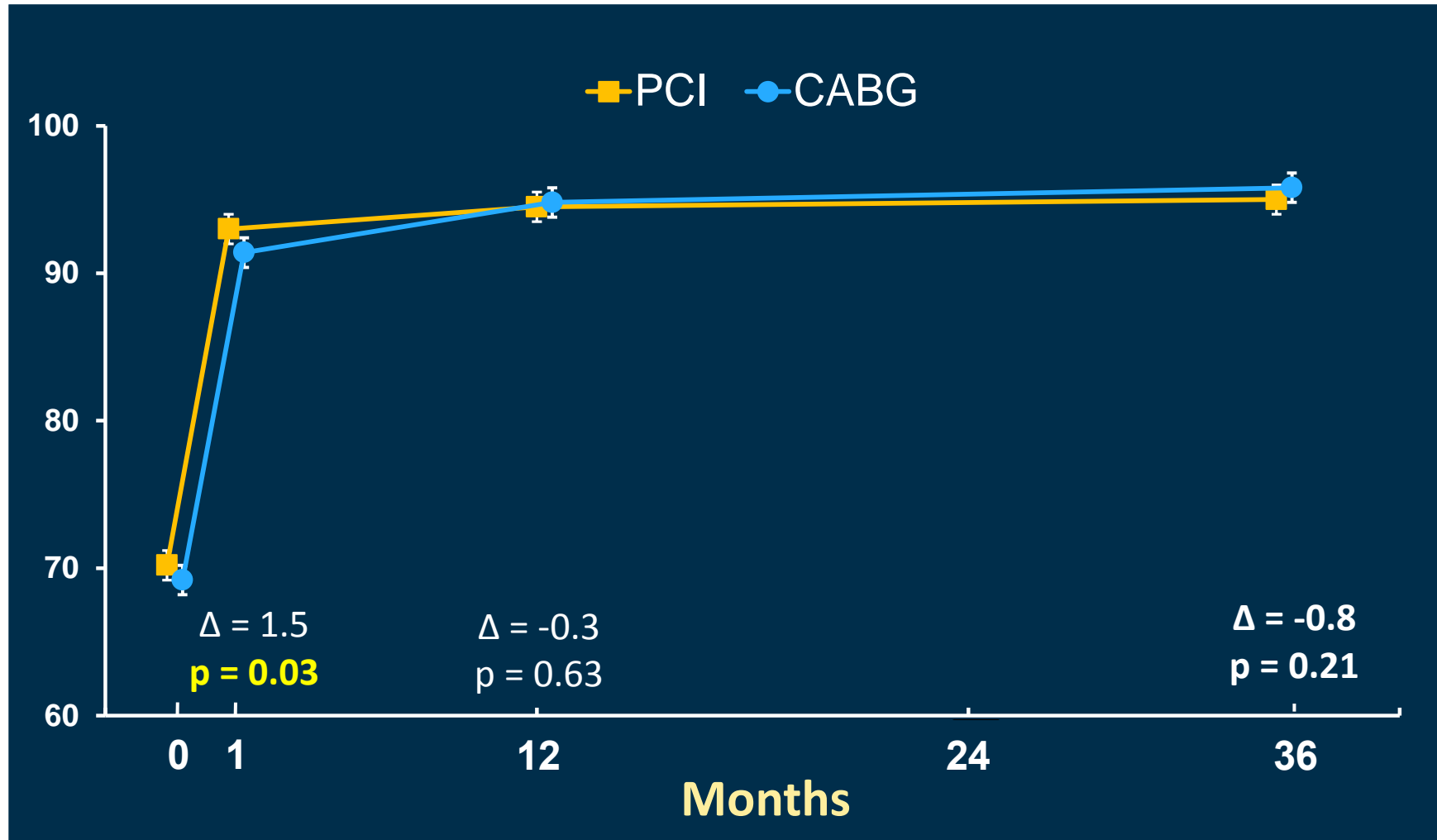
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Periprocedural Myocardial Infarction, 3-Year Cardiovascular Death



EXCEL

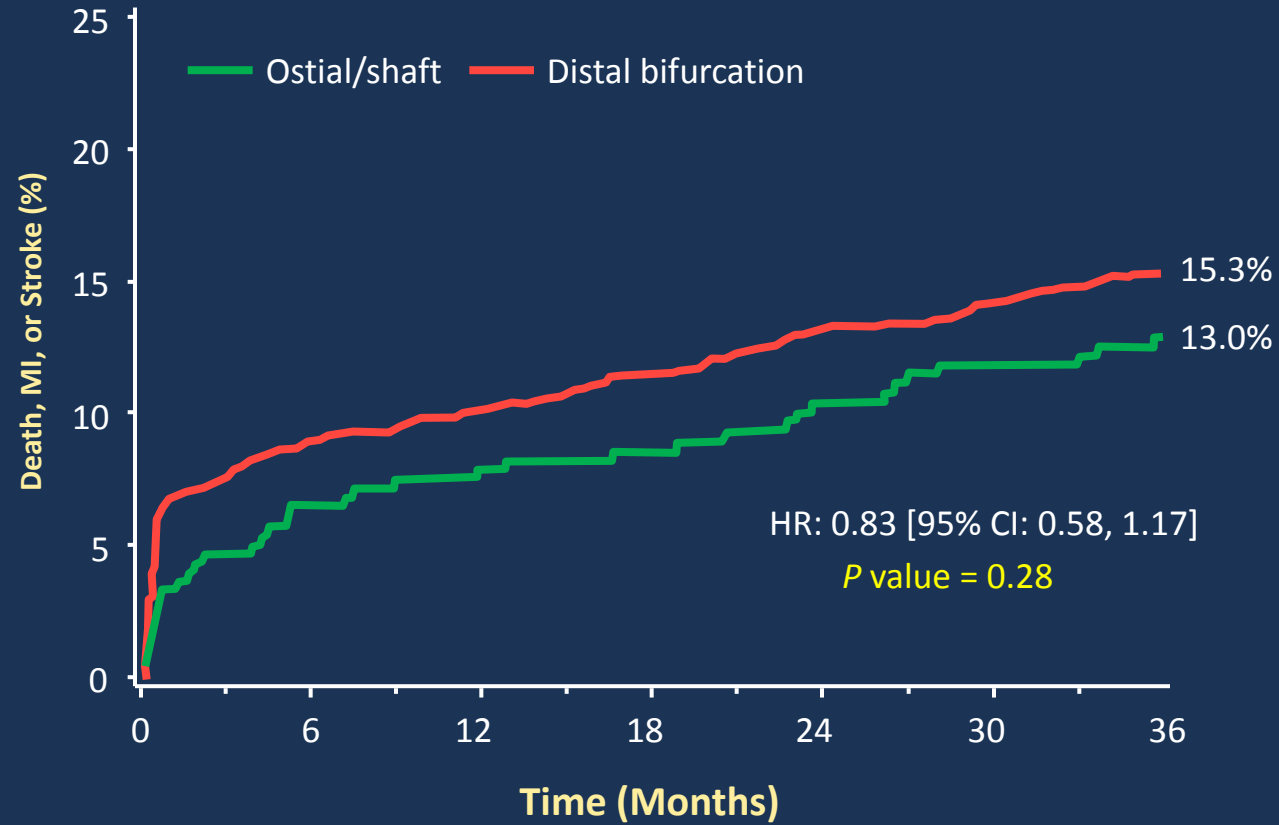
Self-Reported Health Status: SAQ Angina Frequency



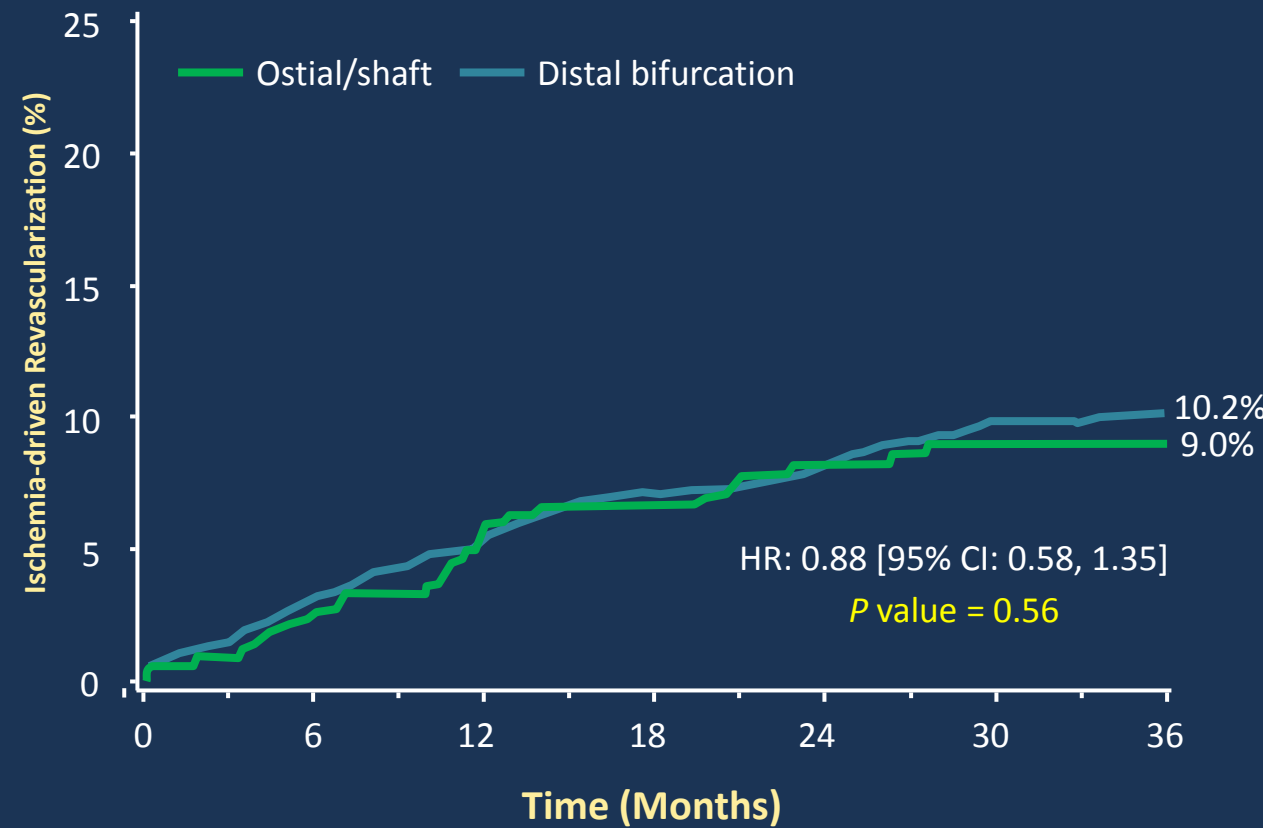
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Outcomes According to LM Disease Location

Three Year Primary Outcome: Death, MI or Stroke



Three Year Ischemia-Driven Revascularization



Number at risk:

Ostial/shaft	293	269	262	258	253	244	293	219	275	261	254	249	239	216
Distal bifurcation	1,559	1,401	1,373	1,335	1,307	1,277	1,559	1,157	1,462	1,407	1,351	1,321	1,274	1,162

Outcomes According to LM Disease Location

PCI vs CABG Outcomes According to LM Location

	Ostial or Shaft only (15.8%)				Distal Bifurcation (84.2%)				P value for interaction
	PCI (N=141)	CABG (N=152)	HR [95%CI]	P-value	PCI (N=789)	CABG (N=770)	HR [95%CI]	P value	
Death, MI or stroke	12.4%	13.5%	0.87 [0.46,1.66]	0.67	15.6%	14.9%	1.03 [0.80,1.34]	0.80	0.64
- Death	8.8%	6.1%	1.40 [0.60,3.38]	0.42	7.8%	5.9%	1.30 [0.90,1.95]	0.15	0.88
- MI	3.7%	6.8%	0.52 [0.18,1.53]	0.23	8.7%	8.4%	1.02 [0.72,1.44]	0.91	0.25
- Stroke	2.3%	4.1%	0.52 [0.13,2.09]	0.35	2.4%	2.9%	0.82 [0.44,1.54]	0.53	0.57
IDR	9.7%	8.4%	1.16 [0.53,2.54]	0.71	13.0%	7.2%	1.86 [1.33,2.60]	0.0002	0.28
Death, MI, stroke or IDR	18.2%	18.3%	0.95 [0.5,1.64]	0.85	23.6%	19.0%	1.23 [0.99,1.54]	0.058	0.39

Outcomes According to LM Disease Location

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Stent Strategy for Distal Bifurcation Disease

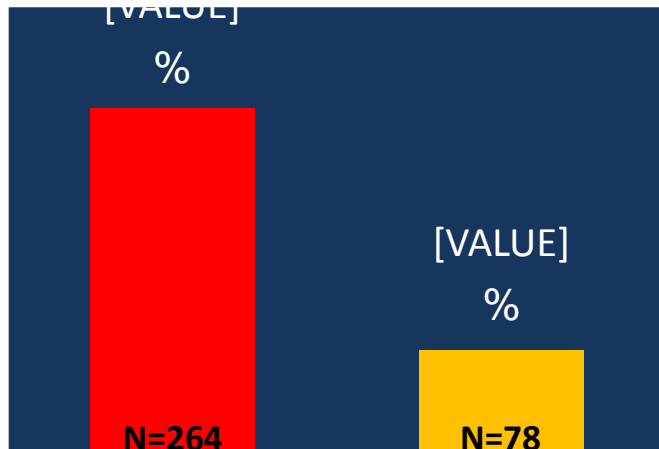
Provisional 1-Stent vs. Planned 2-Stents
For LM Distal Bifurcation Disease (n=529)

Site-assessed distal LM bifurcation disease with QCA

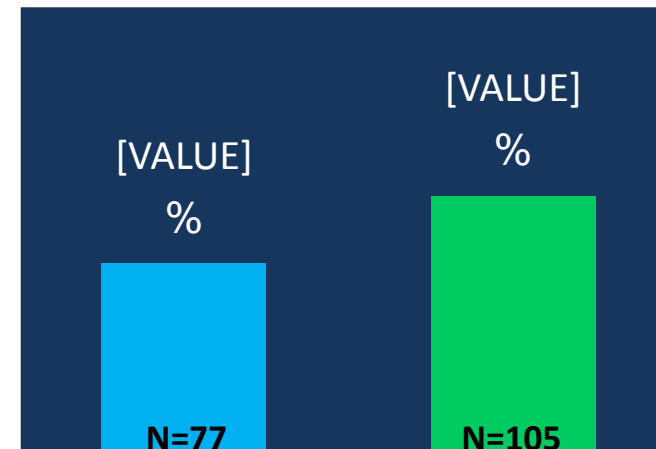
N=524

0 or 1 side branches
with DS \geq 50% by QCA
N=342 (65.3%)

2 side branches
with DS \geq 50% by QCA
N=182 (34.7%)



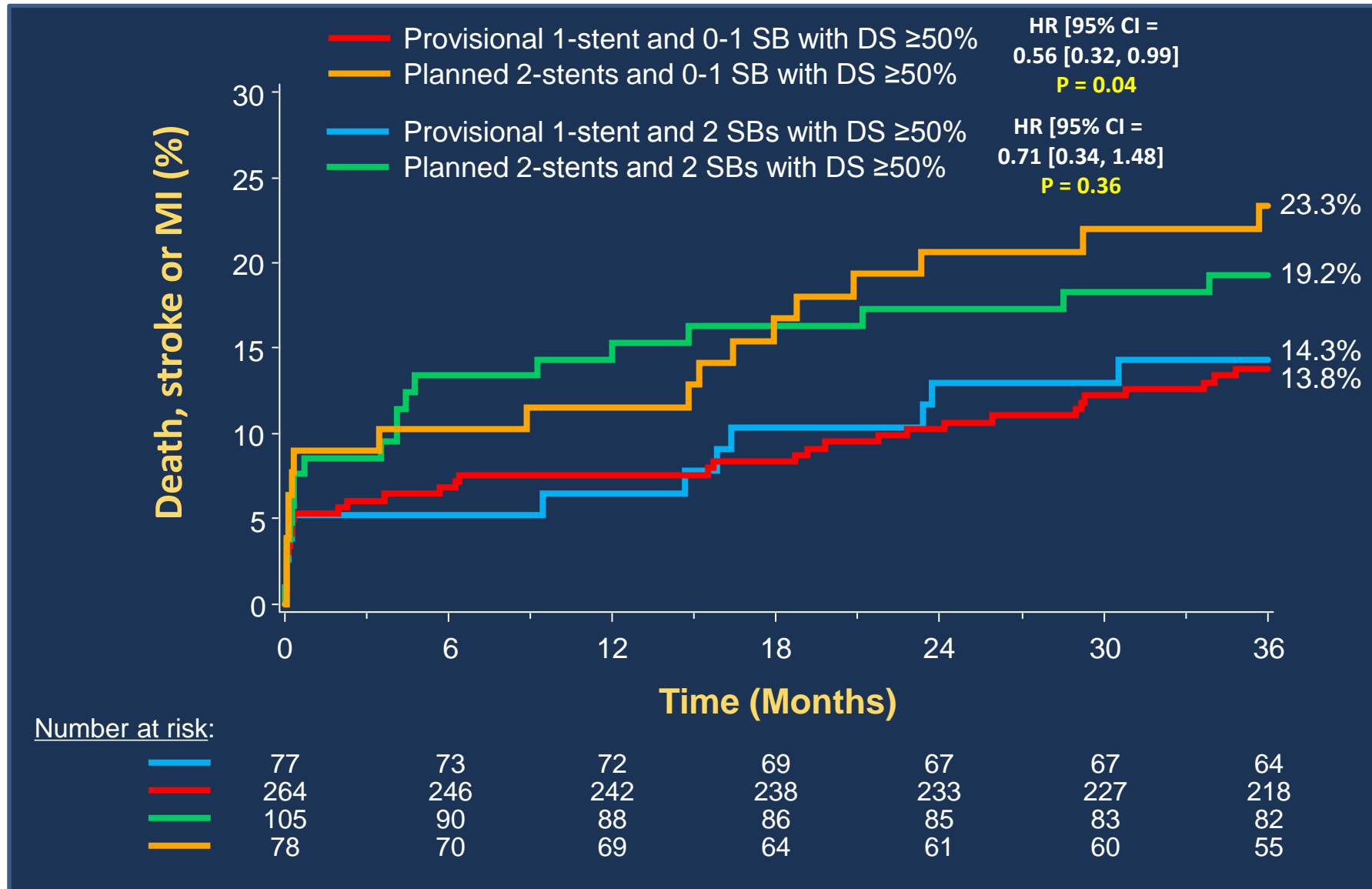
Provisional 1-stent Planned 2-stent



Provisional 1-stent Planned 2-stent

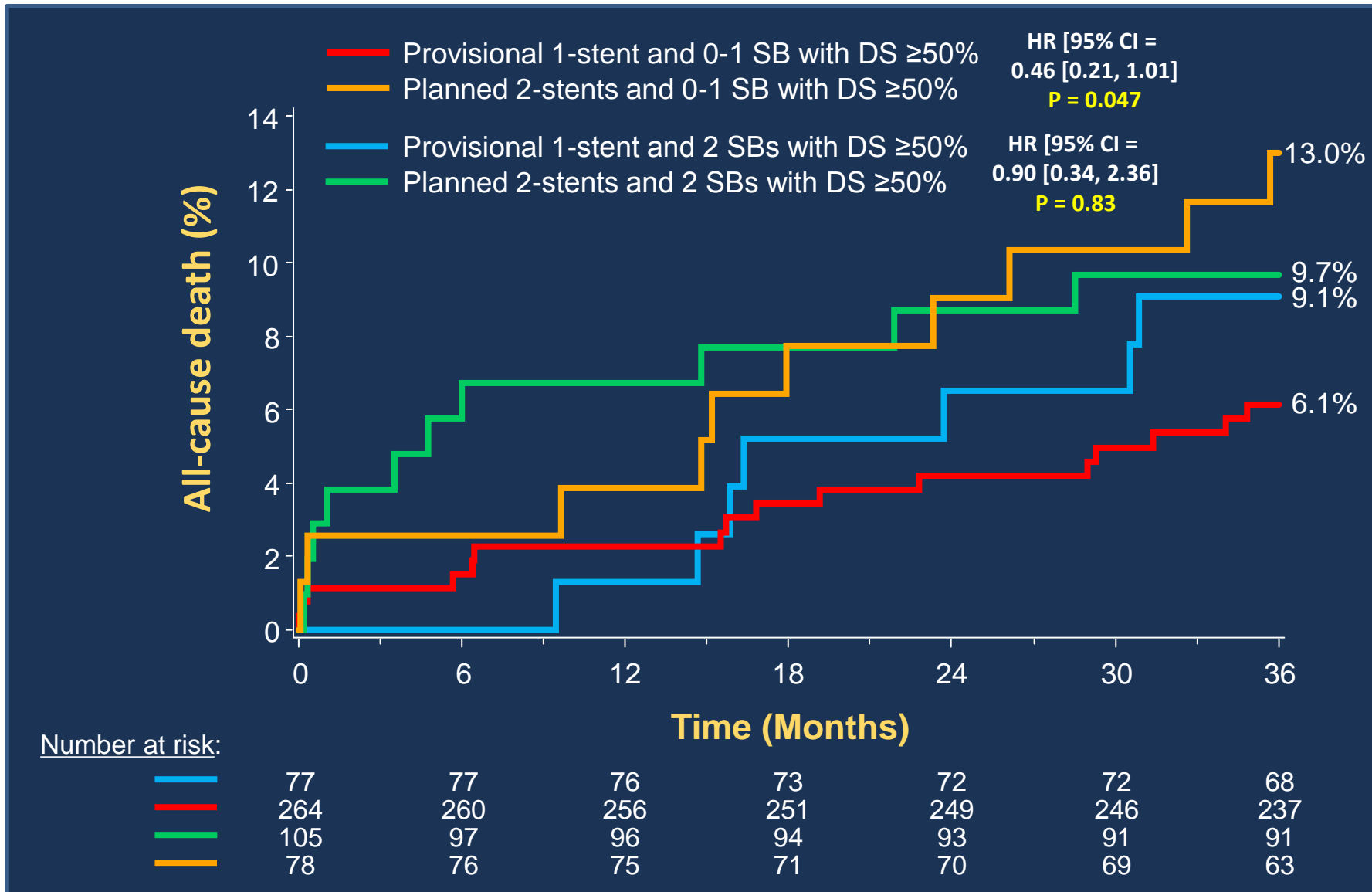
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Provisional 1-Stent vs. Planned 2-Stents For LM Distal Bifurcation Disease (n=529)



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Provisional 1-Stent vs. Planned 2-Stents For LM Distal Bifurcation Disease (n=529)



Death, MI, or Stroke at 3 Years

Variable	Hazard Ratio, 95% CI	P Value
Planned provisional vs 2 stents	0.55 [0.35 - 0.87]	0.005
Age (per year)	1.04 [1.01 - 1.07]	0.006
Male	0.61 [0.37 - 1.01]	0.056

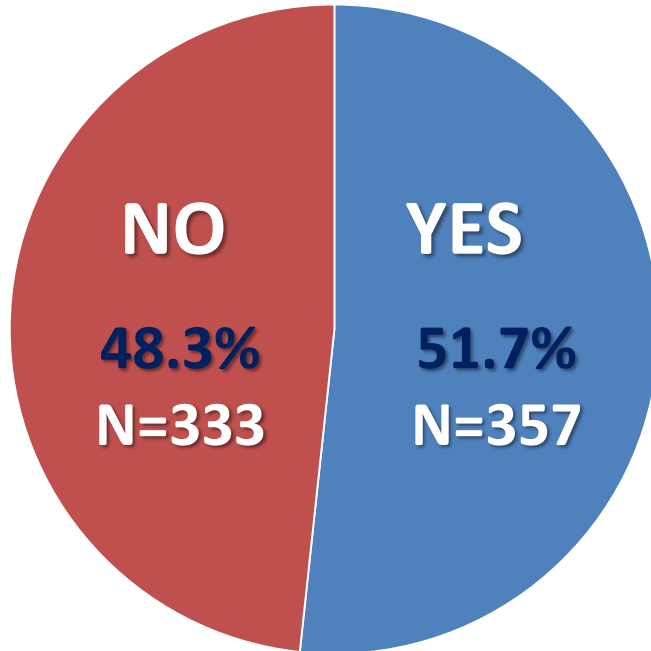
Death, MI, Stroke, or IDR at 3 Years

Variable	Hazard Ratio, 95% CI	P Value
Planned provisional vs 2 stents	0.65 [0.44 - 0.96]	0.03
Age (per year)	1.02 [1.00 - 1.04]	0.06
Male	0.66 [0.43 - 1.01]	0.053

Candidate variables in models: planned provisional 1 stent vs 2 stents, age, male, recent MI (<7 days), current smoker, diabetes, creatinine clearance <60 ml/min, SYNTAX score (core lab), LM ostial or shaft DS >50% (core lab), worst LM %DS (core lab), ostial LAD %DS (core lab), ostial LCX %DS (core lab), TIMI flow <3 in LCX or LAD, LVEF%

IVUS-guided PCI was
performed in 690/935 pts (74%)

Change in LM stenting by IVUS



- Used larger balloon: 30% (107)
- Post-dilated: 29% (102)
- Used higher pressure: 17% (62)
- Treated stent under-expansion: 16% (57)
- Led to provisional 1 stent strategy rather than planned 2 stents: 11% (41)
- Led to planned 2 stent strategy rather than provisional 1 stent: 9% (33)

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3-Year Outcomes According to LM MSA

IVUS MSA tertiles (range)	Low: 4.4-8.7 (n=172)	Intermediate: 8.8-10.9 (n=169)	High: 11.0-17.8 (n=163)	<i>P</i> L vs I	<i>P</i> L vs H
Death/MI/stroke	19.4% (32)	16.1% (26)	9.6% (15)	0.45	0.01
Death/MI/stroke/IDR*	26.6% (44)	23.8% (39)	18.3% (29)	0.66	0.08
All-cause death	13.8% (22)	10.0% (16)	5.2% (8)	0.34	0.01
Cardiovascular death	7.4% (12)	4.8% (8)	4.0% (6)	0.39	0.16
MI	10.5% (17)	8.2% (13)	3.7% (6)	0.49	0.02
Stroke	1.8% (3)	1.2% (2)	2.1% (3)	0.66	0.98
Stent thrombosis (D/P)	3.1% (5)	1.2% (2)	0.0% (0)	0.26	0.03
Left main IDR	12.0% (19)	8.3% (13)	8.8% (14)	0.30	0.41
Non-TV IDR	1.9% (3)	3.3% (5)	1.3% (2)	0.48	0.65

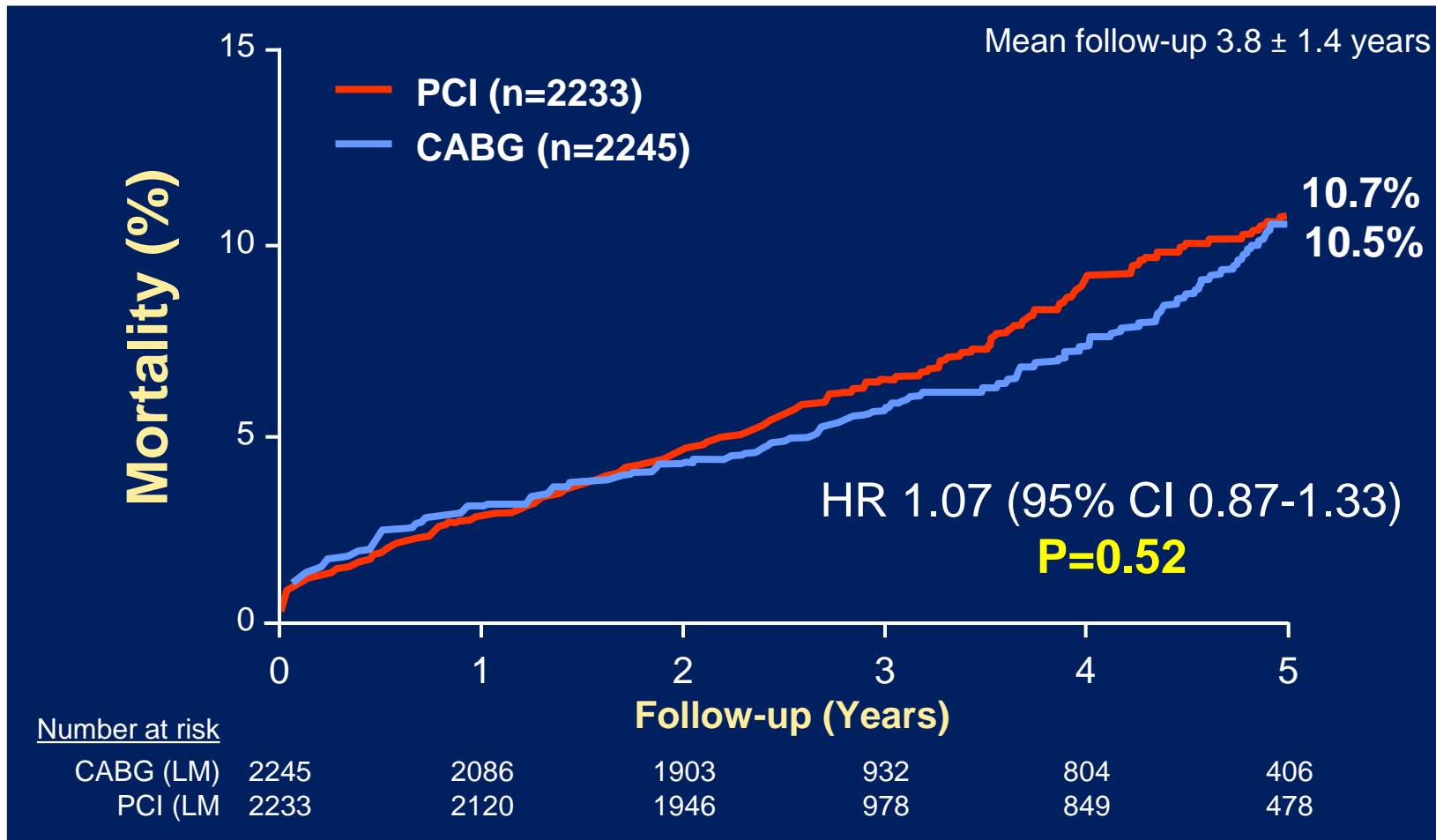
*IDR: ischemia driven revascularization

EXCEL and NOBLE

	EXCEL	NOBLE
Number of patients	1905	1201
Number of centers	126	36
Number of countries	17 (US, EU, SA, Asia Pacific, Middle East)	7 (UK, Scandinavia)
SYNTAX score inclusion	≤32	No restriction
Diabetes mellitus	30%	15%
Primary endpoint	D, MI or stroke	D, MI, stroke or revasc
- Included peri-procedural MI	Yes	No
Stent	Xience	Biomatrix, Other
- 3-year definite ST rate	0.7%	3%
- Def ST < symptomatic graft occlusion	Yes	No
Stroke: PCI vs CABG	Less with PCI	More with PCI!
Worse PCI prognosis w/ higher SYNTAX score	Yes/No	No!

Left Main Trials Systematic Overview

Individual-patient-data Analysis from 11 PCI vs. CABG Trials
11,518 randomized pts; 4,478 (38.9%) with left main disease



Left Main Trials Systematic Overview

Individual-patient-data Analysis from 11 PCI vs. CABG Trials
11,518 randomized pts; 4,478 (38.9%) with left main disease

	PCI (n=2,233)	CABG (n=2,245)	HR (95%CI]	P value	P _{int}
Overall mortality	10.7% (174)	10.5% (158)	1.07 [0.87, 1.33]	0.52	
Diabetes	16.5% (71)	13.4% (51)	1.34 [0.93, 1.91]	0.11	0.13
No diabetes	8.8% (104)	9.6% (107)	0.94 [0.72, 1.23]	0.65	
SYNTAX score 0-22	8.1% (45)	8.3% (49)	0.91 [0.60, 1.36]	0.64	
SYNTAX score 23-32	10.8% (67)	12.7% (63)	0.92 [0.65, 1.30]	0.65	0.38
SYNTAX score ≥33	15.0% (56)	12.4% (45)	1.39 [0.94, 2.06]	0.10	

Unprotected Left Main Revascularization

Standards of Care in Evolution

- PCI with contemporary DES and technique may be considered an acceptable or even preferred revascularization method for selected patients with LM disease
 - **Mortality:** Similar between PCI and CABG
 - **MI:** Lower with PCI in the peri-procedural period; higher with PCI during long-term FU – similar through 5 years
 - **Stroke:** Overall not an driving factor for PCI over CABG but generally higher with CABG
 - **Periprocedural morbidity:** Considerably higher with CABG
 - **Revascularization:** Higher with PCI (absolute difference ~5%)
- As emerging evidence demonstrates equipoise between revascularization strategies, attention turns to important details of technique, imaging, stent selection, pharmacology, clinical surveillance...