Long-Term and Updated Data from EXCEL and NOBLE

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The Cardiovascular Research Foundation

Disclosures

Gregg W. Stone

None

Study Design

2905 pts with unprotected left main disease

SYNTAX score ≤32

Consensus agreement of eligibility and equipoise by heart team

No (N=1000) → Enrollment registry

Yes (N=1905)

Stratified by diabetes, SYNTAX score and center → R

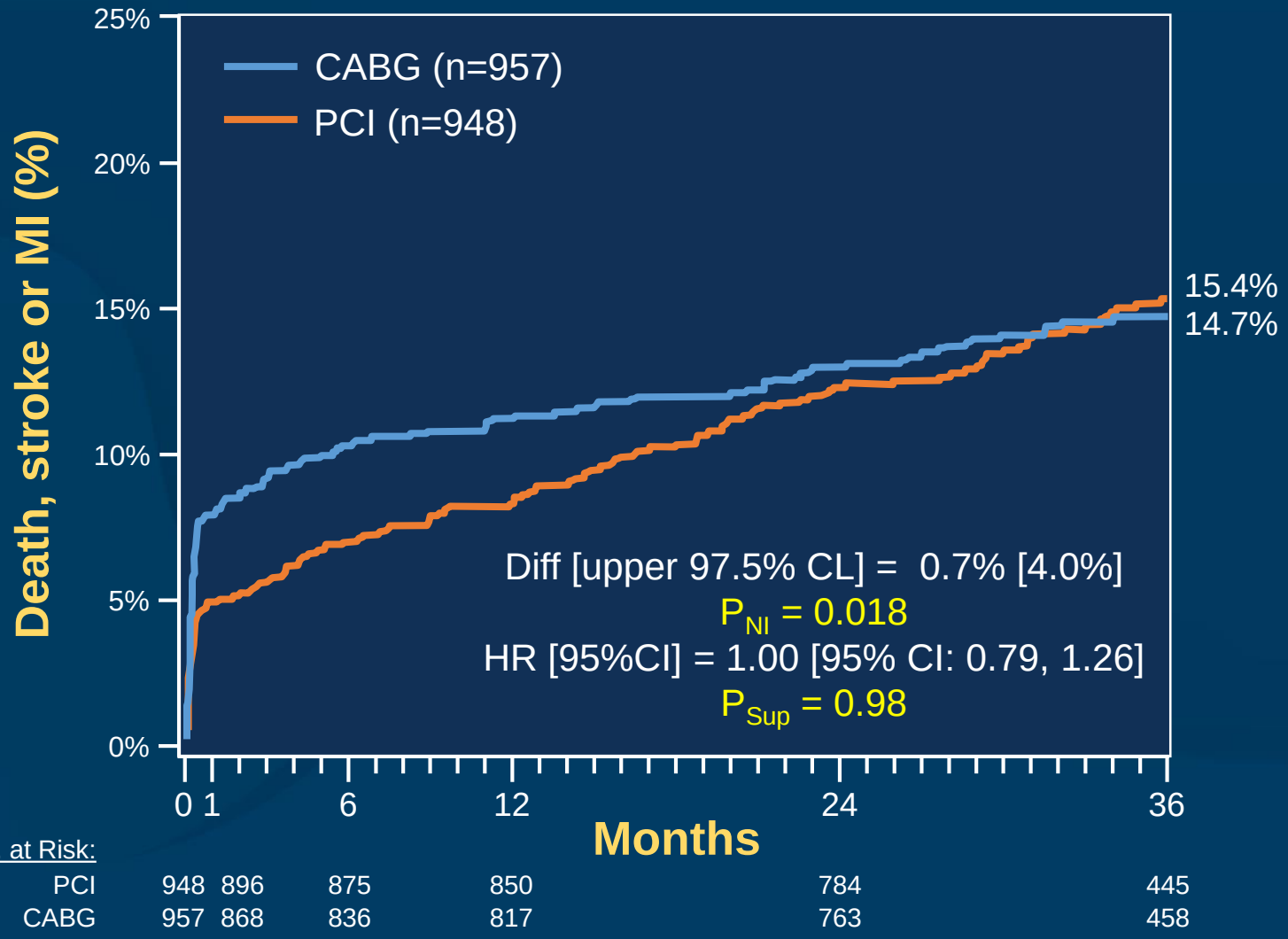
- PCI (Xience EES) (N=948)
- CABG (N=957)

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

Primary endpoint: D/MI/CVA at median 3-yr FU, minimum 2-yr FU

Primary Endpoint

Death, Stroke or MI at 3 Years



Stone GW et al. N Engl J Med 2016;375:2223-35

Adjudicated Outcomes at 30 Days

	PCI (n=948)	CABG (n=957)	HR [95%CI]	P-value
Death, stroke or MI	4.9%	7.9%	0.61 [0.42, 0.88]	0.008
- Death	1.0%	1.1%	0.90 [0.37, 2.22]	0.82
- Stroke	0.6%	1.3%	0.50 [0.19, 1.33]	0.15
- MI	3.9%	6.2%	0.63 [0.42, 0.95]	0.02
- Peri-procedural	3.6%	5.9%	0.61 [0.40, 0.93]	0.02
- Spontaneous	0.3%	0.3%	1.00 [0.20, 4.95]	1.00
- STEMI	0.7%	2.3%	0.32 [0.14, 0.74]	0.005
- Non-STEMI	3.2%	3.9%	0.82 [0.50, 1.32]	0.41
Death, stroke, MI or IDR	4.9%	8.4%	0.57 [0.40, 0.82]	0.002
- Ischemia-driven revasc (IDR)	0.6%	1.4%	0.46 [0.18, 1.21]	0.11
Stent thrombosis, def/prob	0.6%	0.0%	-	0.01
Graft occlusion, symptomatic	0.0%	1.2%	-	<0.001
Definite stent thrombosis or symptomatic graft occlusion	0.3%	1.2%	0.27 [0.08, 0.97]	0.03

Major Adverse Events Within 30 Days

	PCI (n=948)	CABG (n=957)	RR [95%CI]	P-value
Peri-procedural MAE, any	12.4%	44.0%	0.28 [0.24, 0.34]	<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 ≥0.5 mg/dL from baseline or need for dialysis.

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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

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

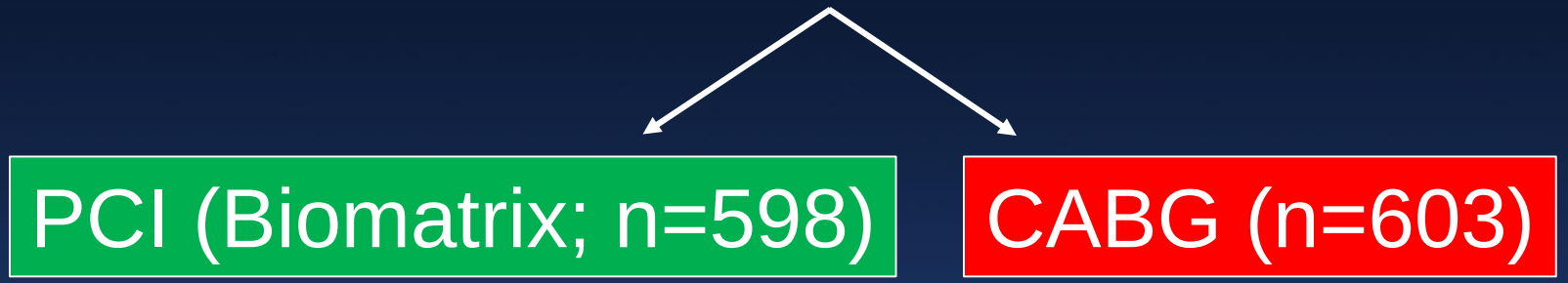
NOBLE Trial

LM disease + ≤3 additional non-complex lesions

Clinical equipoise for PCI vs. CABG

Excluded: CTO, 2-stent bif, severe calc/tortuous

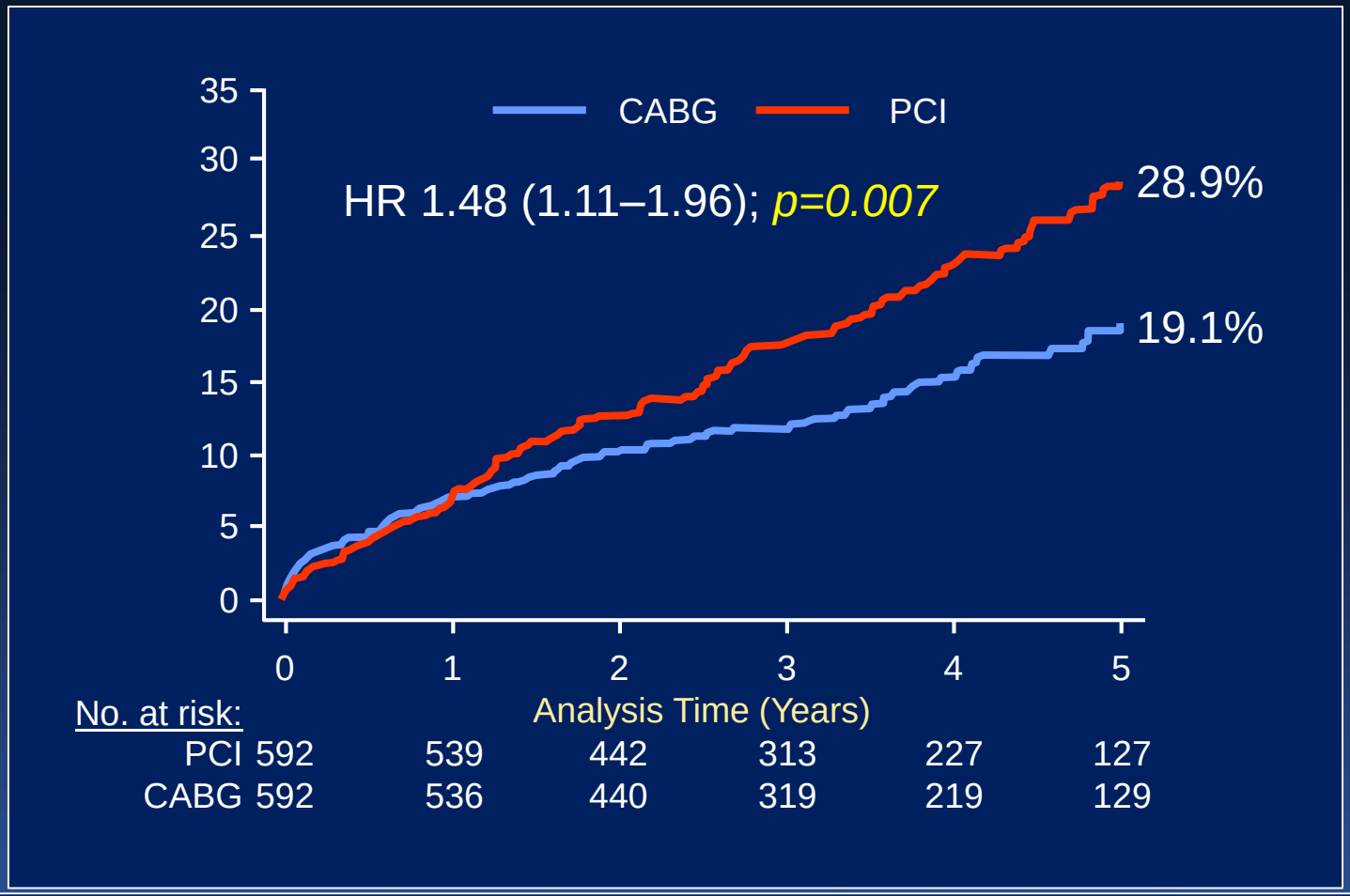
N=1201



Primary endpoint

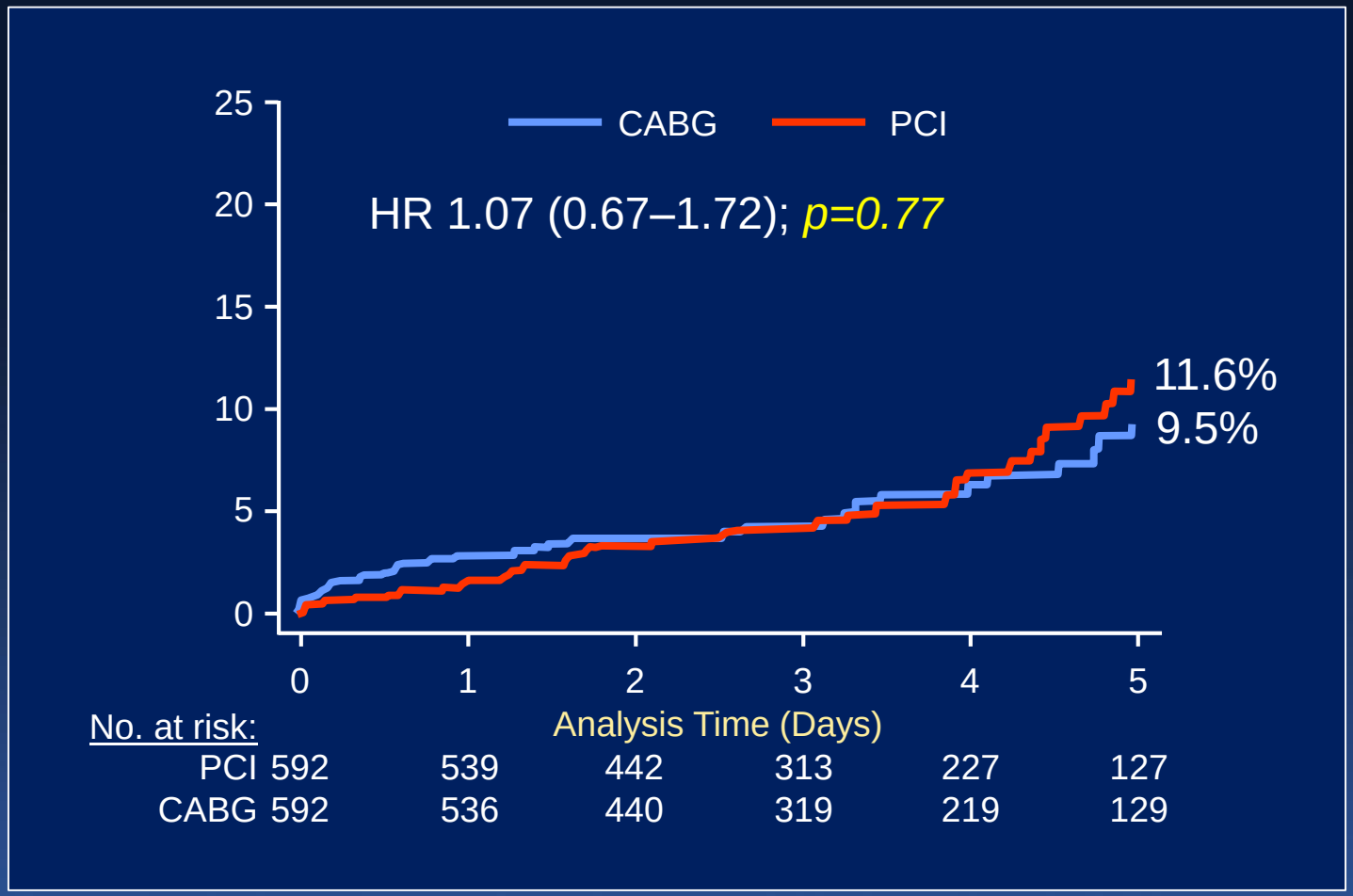
MACCE: death, non-procedural MI, repeat revasc, stroke at median 3 years (with FU up to 5 years)

NOBLE
Primary Endpoint: MACCE (w/o proc MI)



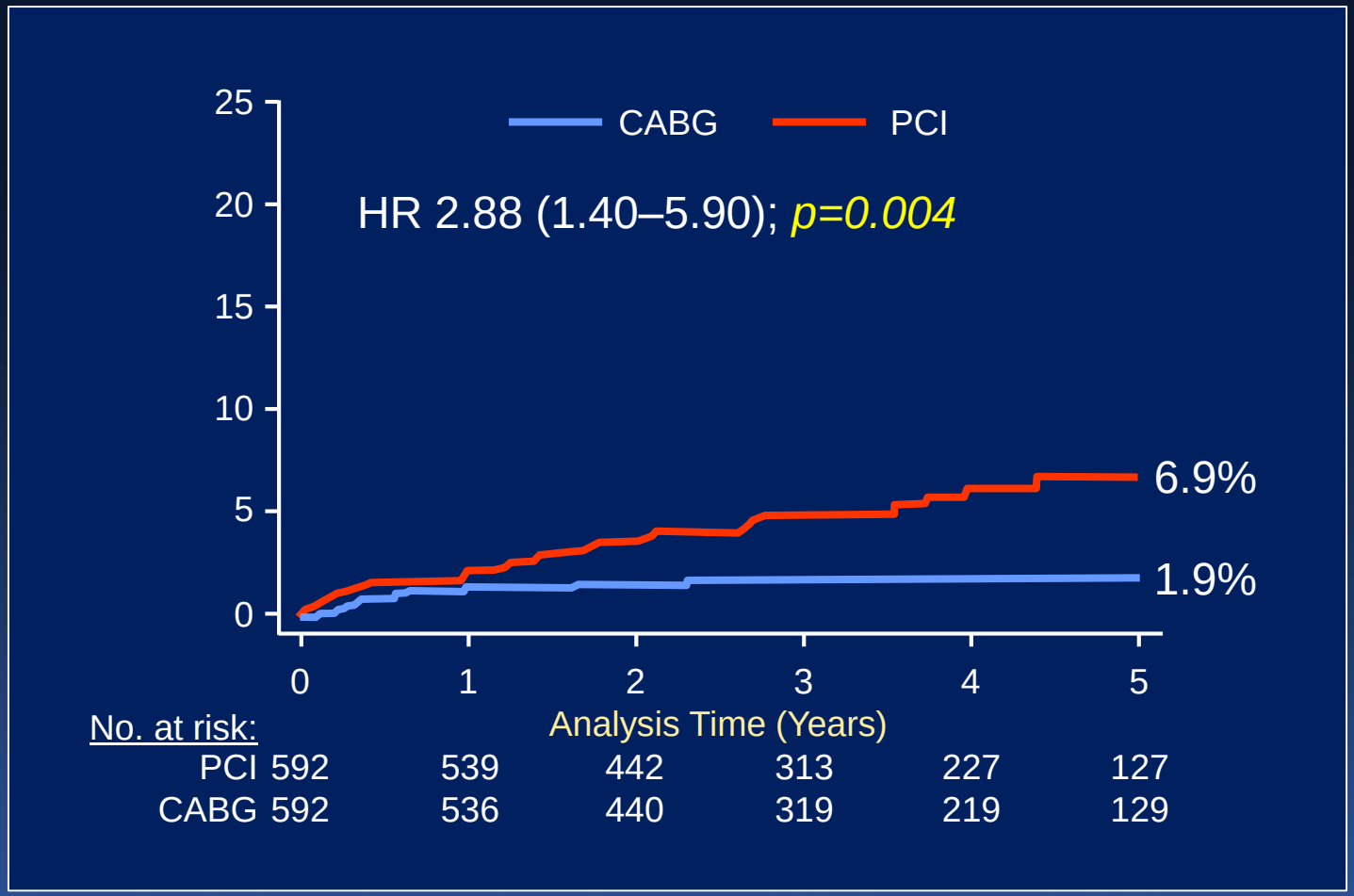
PCI did not show non-inferiority and CABG was superior to PCI

NOBLE
All-cause Mortality

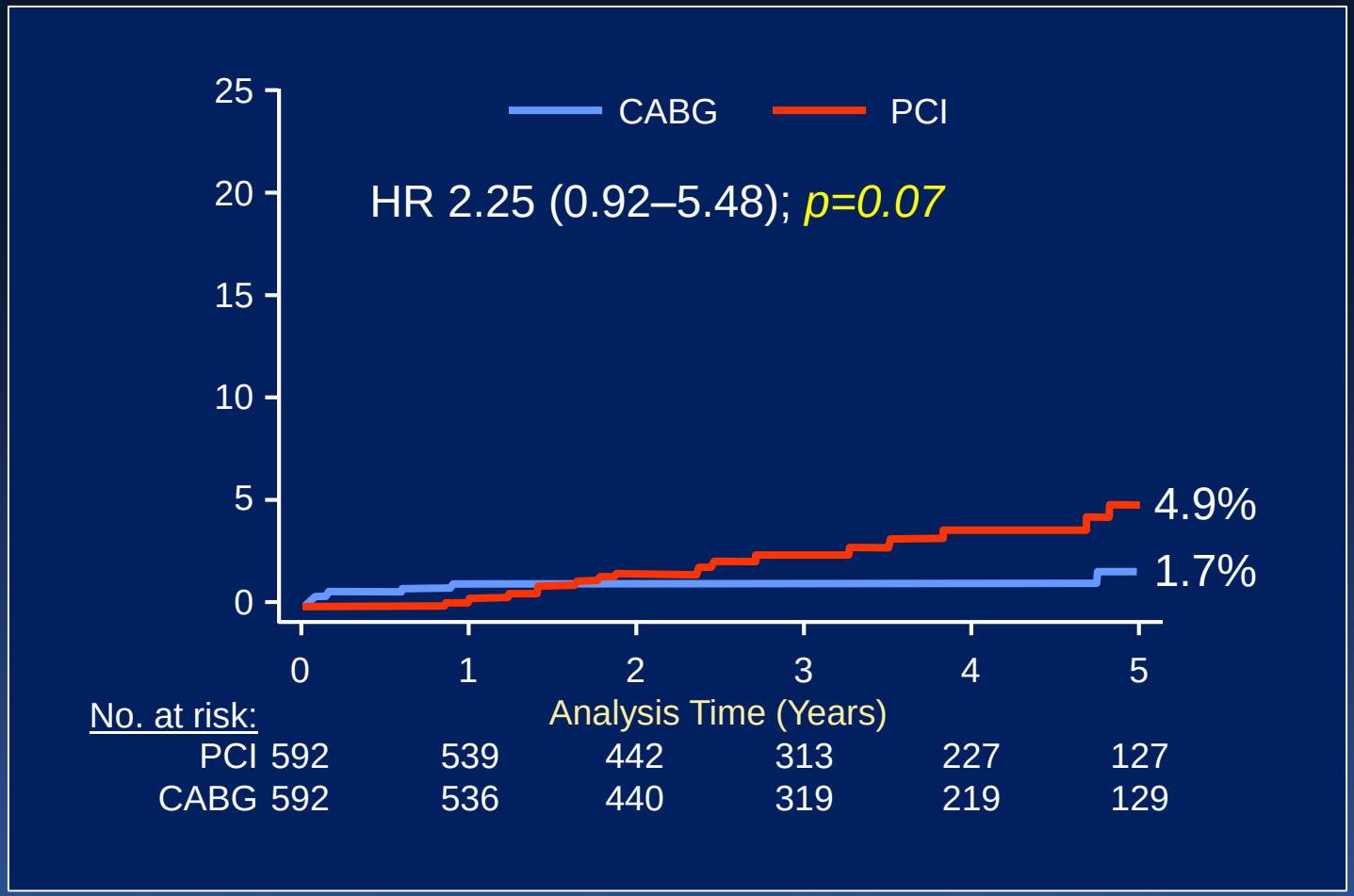


Makikallio T et al. Lancet 2016;388:2743–52

NOBLE
Non-procedural Myocardial Infarction



NOBLE
Stroke



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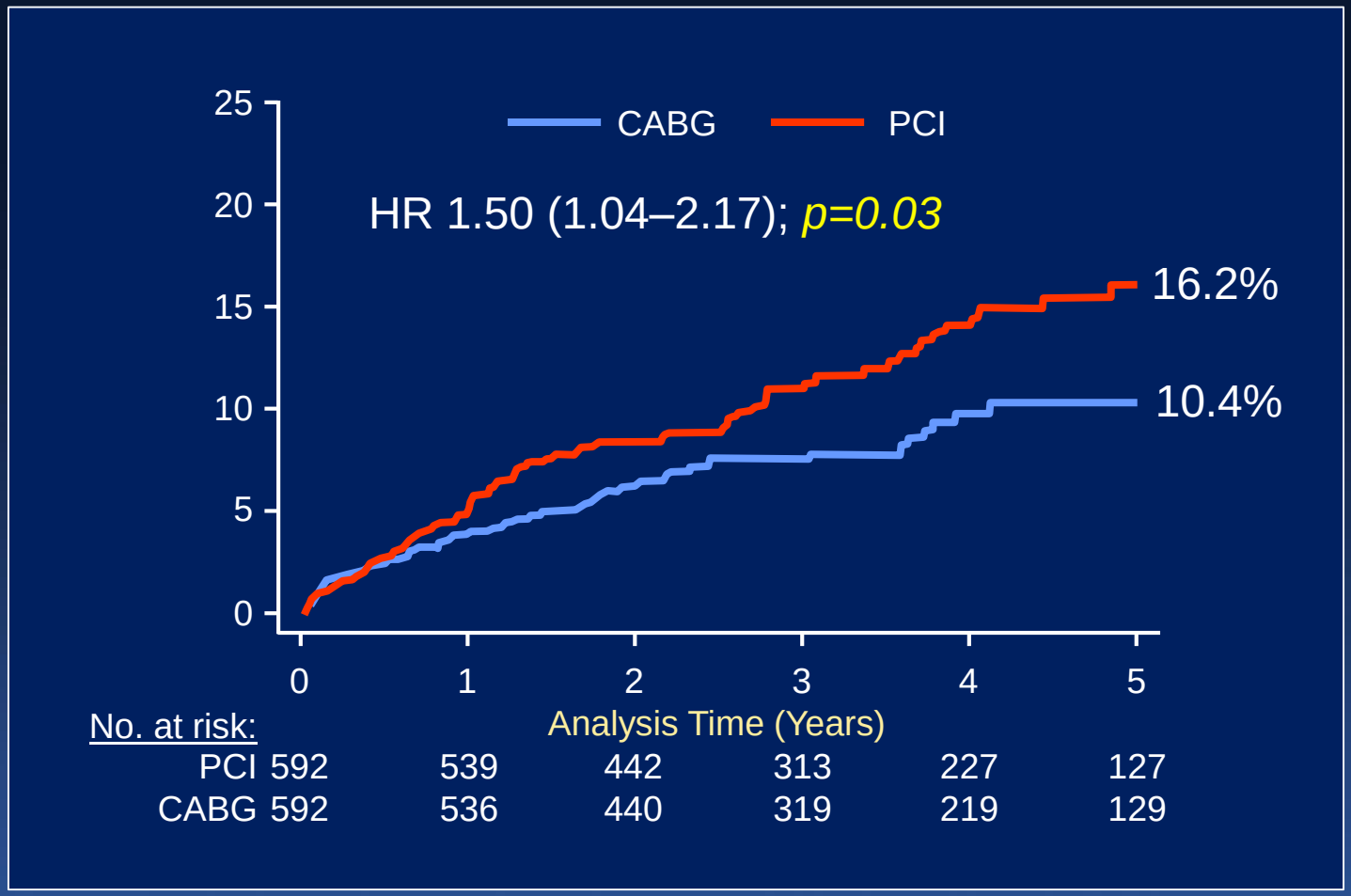
NOBLE
Total Repeat Revascularization



NOBLE
Secondary Endpoints

	PCI	CABG	*P* value
Definite ST or symptomatic graft occlusion*	3% (9)	4% (15)	0.22
Procedural myocardial infarction (post hoc)	5% (16/296)	7% (16/238)	0.52

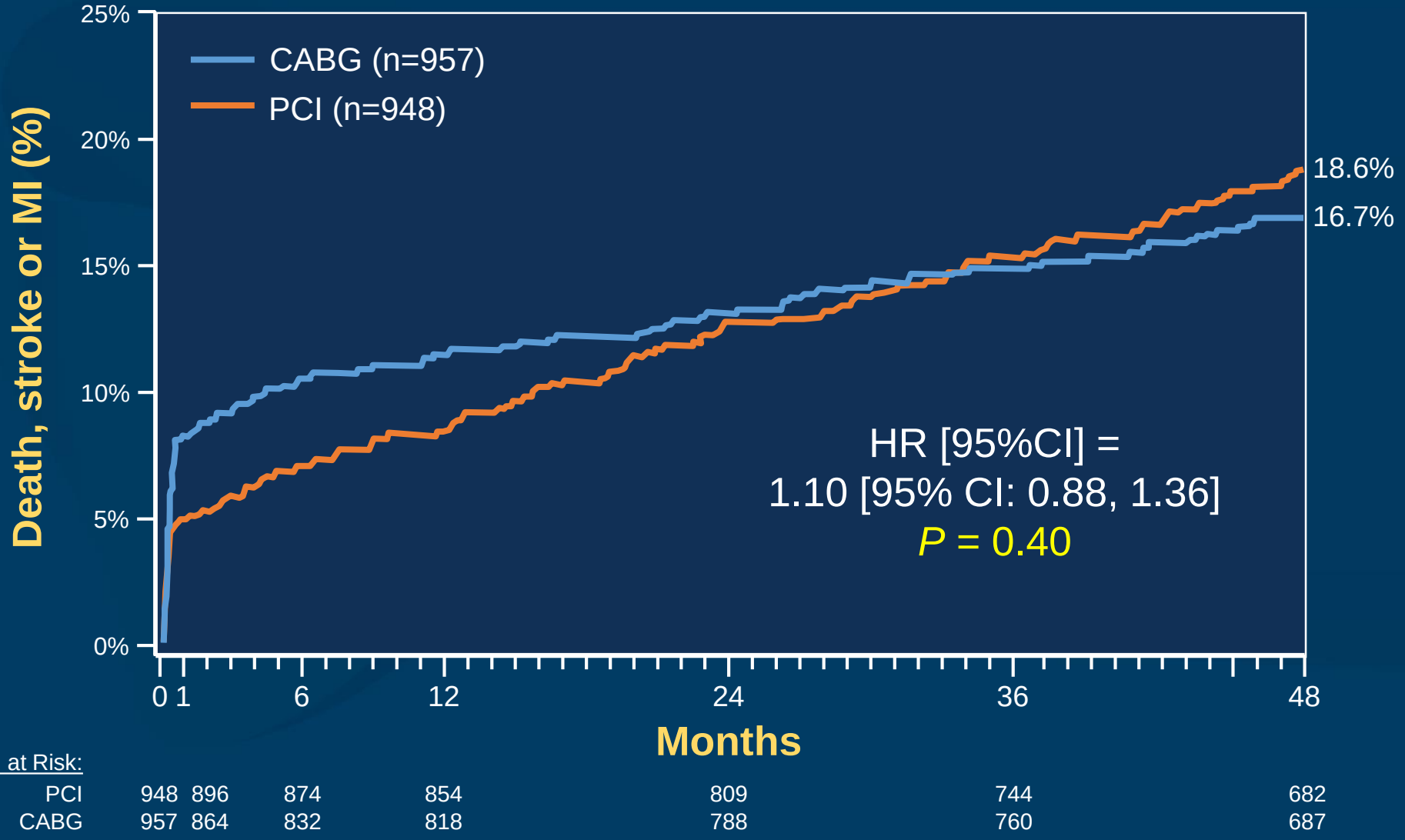
* Kaplan-Meier 5-year estimates by intention-to-treat

EXCEL vs 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
Primary endpoint	D, MI or stroke	D, MI, stroke or revasc
- Included peri-procedural MI	Yes	No
Stent	Xience	Biomatrix
- 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 with higher SYNTAX score	Yes	No!

Primary Endpoint

Death, Stroke or MI at 4 Years



No. at Risk:

PCI	948	896	874	854	809	744	682
CABG	957	864	832	818	788	760	687

Stone GW et al. TCT 2018

Primary Endpoint Landmark Analysis (post hoc)

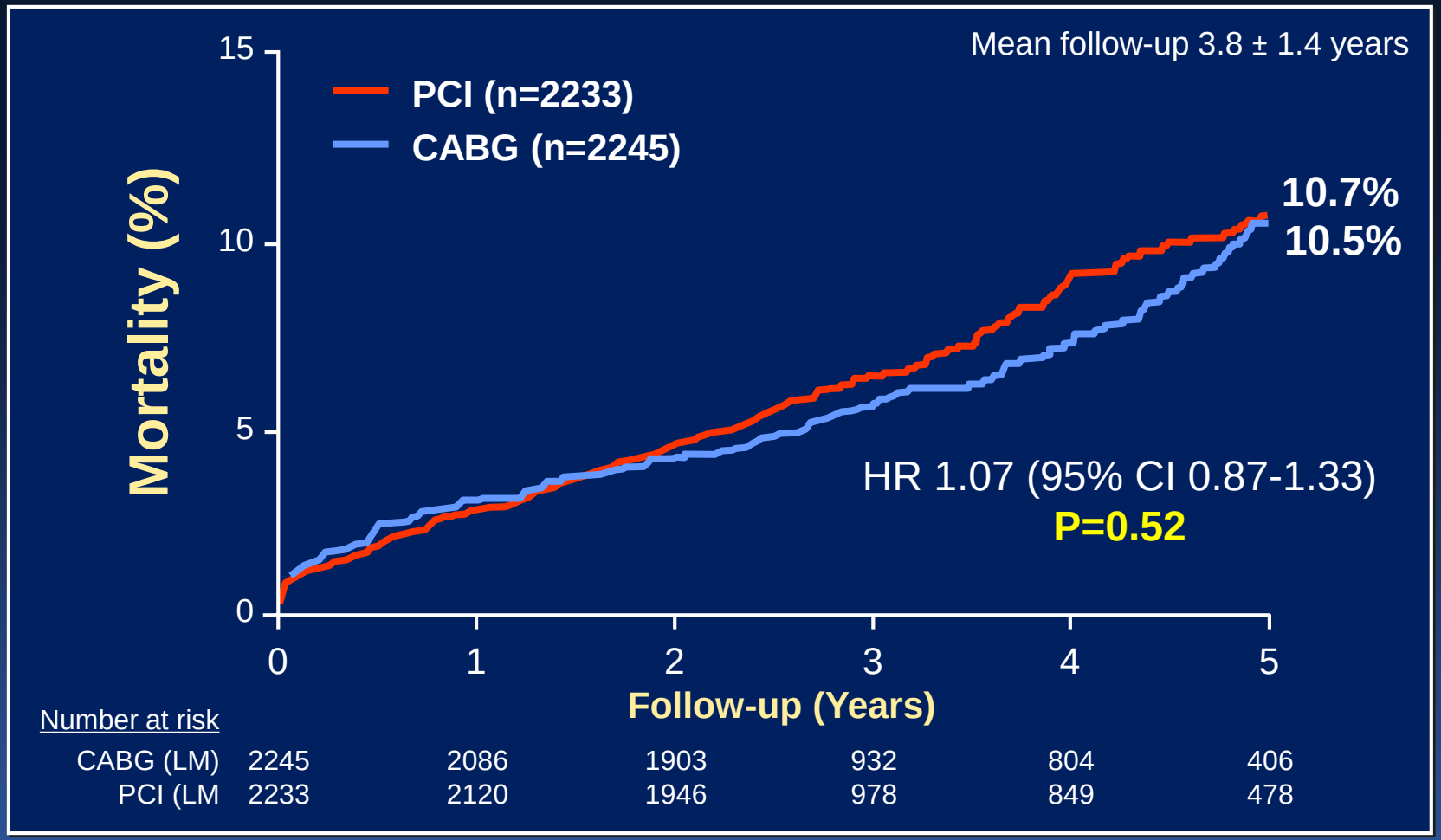
	From randomization to 30 days				From 30 days to 4 years			
	PCI (n=948)	CABG (n=957)	HR [95%CI]	P value	PCI (n=933)	CABG (n=929)	HR [95%CI]	P value
Death, stroke or MI	4.9%	7.9%	0.61 [0.42, 0.88]	0.008	14.8%	10.1%	1.48 [1.14, 1.93]	0.003
- Death	1.0%	1.1%	0.90 [0.37, 2.22]	0.82	9.4%	6.5%	1.47 [1.05, 2.05]	0.02
- Stroke	0.6%	1.3%	0.50 [0.19, 1.33]	0.15	2.0%	2.2%	0.94 [0.49, 1.79]	0.85
- MI	3.9%	6.2%	0.63 [0.42, 0.95]	0.02	5.7%	3.0%	1.92 [1.19, 3.08]	0.006

Stroke and MI rates are non-hierarchical; i.e. include fatal and non-fatal events. The 30-day to 4-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 4 years.

Individual-patient-data Analysis from 11 PCI vs. CABG Trials

11,518 randomized pts; 4,478 (38.9%) with left main ds.

All-cause Mortality (Left Main)



LM Revascularization with Low/Int SS
CABG vs. PCI with Contemporary DES

- **Mortality:** Similar with PCI and CABG
- **Stroke:** Lower after PCI compared with CABG
- **MI:** Lower with PCI in the peri-procedural period; higher with PCI during long-term FU – similar through 5 years
- **Short-term morbidity:** Substantially less with PCI
- **Revascularization:** Less with CABG than PCI (~5%)

PCI with contemporary DES (especially Xience, as proven in EXCEL) may be considered an acceptable or even preferred revascularization modality for selected pts with LMCAD, a decision which should be made after heart team discussion, taking into account each patient's individual circumstances and preferences

LM Revascularization with Low/Int SS

CABG vs. PCI with Contemporary DES

5-year EXCEL follow-up – final report!