Left Main PCI in 2017: Ready to EXCEL?

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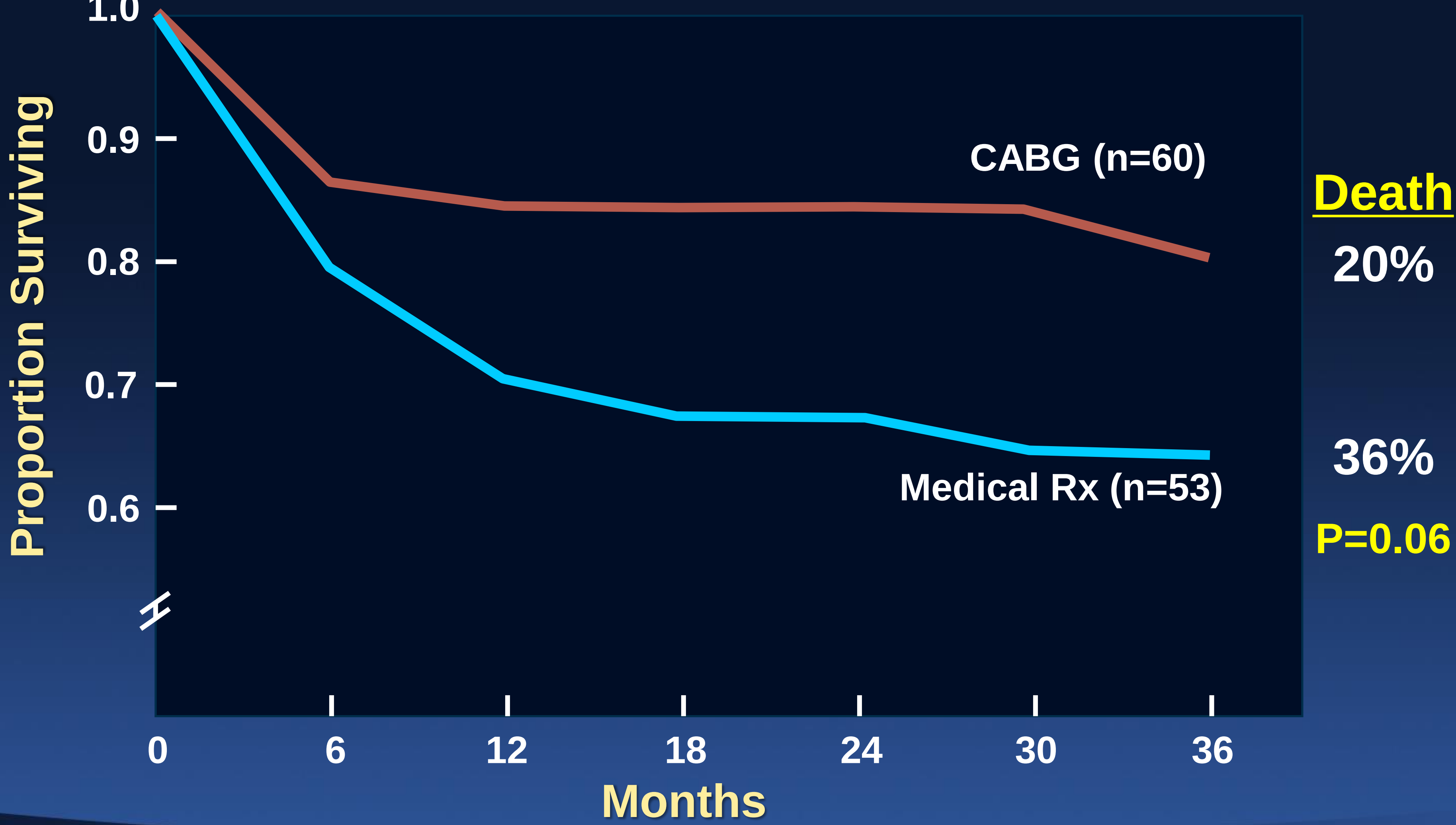
Disclosure Statement of Financial Interest

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

None

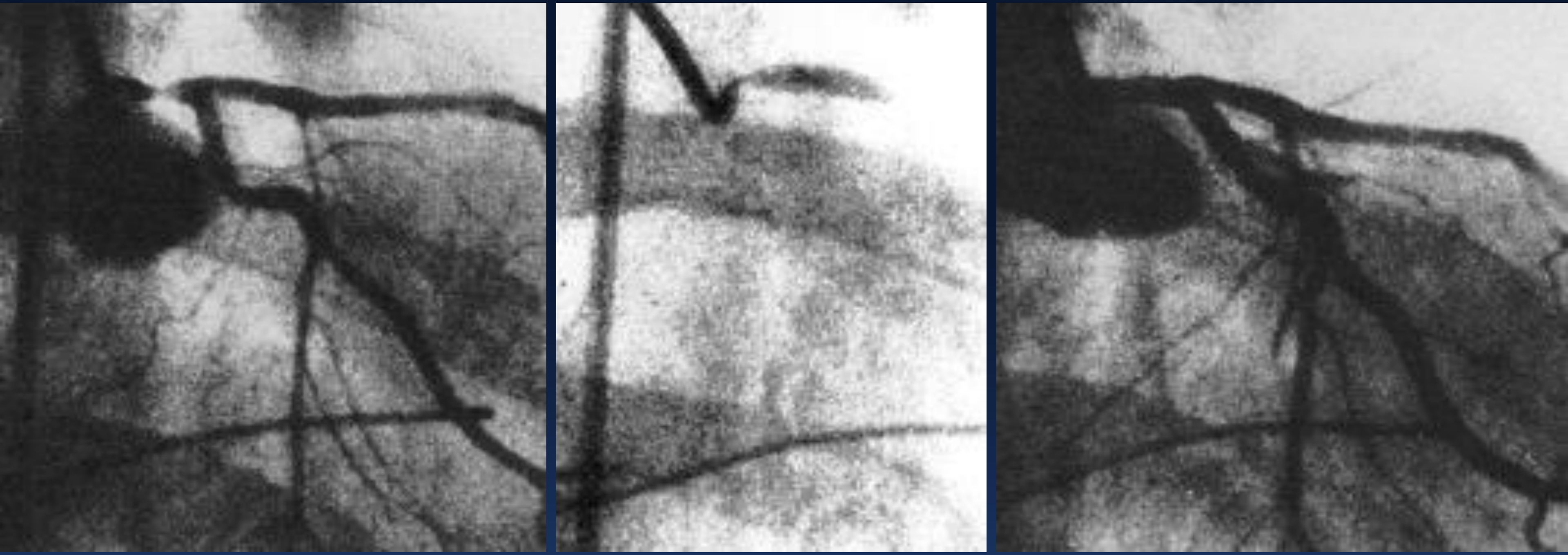
VA Randomized Trial (n=113)

LM Stenosis



Takaro T et al: Circulation 1976;54(6 Suppl):III107-17.

Gruntzig's 3rd PTCA



"Third PCI patient ever treated. Forty-three year old man with severe angina pectoris since September, 1977. First angiogram (November 11) revealed severe stenosis of the main L.C.A. . ."

Note: The patient expired suddenly about 4 months after this procedure.

Gruntzig A. Lancet 1978;1:263.

The Rocky Road to PCI of LM Ds.
- Balloon angioplasty -

127 pts at MAHI: elective protected (n=84), elective unprotected (n=33; 18 surgical contraindications; 15 surgical candidates), AMI (n=10)

	Elective protected (n=84)	Elective unprotected (n=33)	AMI unprotected (n=10)
Procedural success	94%		90%
Mortality			
- In-hospital	2.4%	9.1%	50%
- Mean 2-year	10.7%	60.6%	70%
Post d/c MI	5.9%	8.0%	20%
Post d/c revasc	37.3%	42.3%	60%

O'Keefe JH, Hartzler GO, et al. Am J Cardiol. 1998;64:144-7

The Rocky Road to PCI of LM Ds.
- Atherectomy and bare metal stents -

107 pts from 25 centers (all unprotected): elective (n=91; 47 absolute or relative surgical contraindications; 44 surgical candidates), AMI (n=16). BMS in 50% (remainder atherectomy or PTCA)

	Elective (n=91)	AMI (n=16)
Procedural success	96.2%	
Mortality, in-hospital	12.1%	68.8%
Mortality, 9-months	34.0%	75.0%
- Stent	29.5%	
- CABG candidate	15.7%	
- Not CABG cand.	70.5%	
Restenosis >4 mos	22.0%	

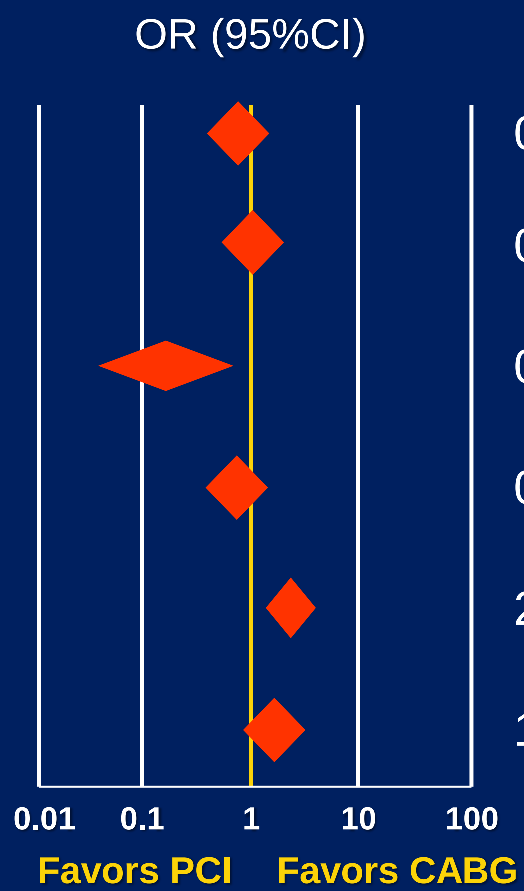
Ellis SG et al. Circulation 1997;96:3867–72

PCI (1st gen DES) vs. CABG for Left Main Ds.

Meta-analysis of 4 RCTs, 1,611 Patients

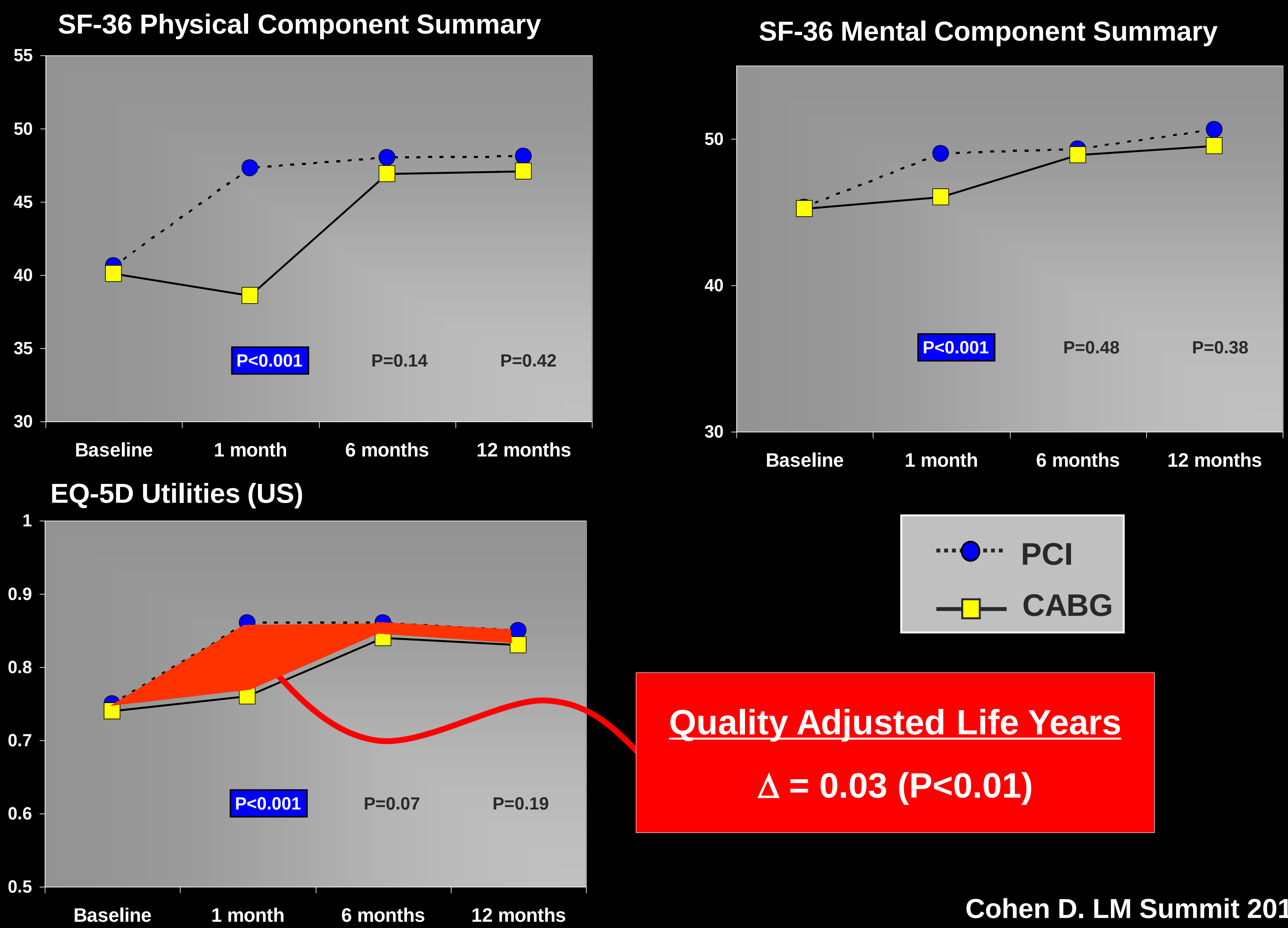
1-Year Outcomes

	PCI	CABG	OR (95%CI)	*p*-Value
Death	3.0% (24/807)	4.1% (32/790)	0.74 (0.43-1.28)	0.29
MI	2.8% (23/807)	2.9% (23/790)	0.98 (0.54-1.78)	0.95
Stroke	0.1% (1/707)	1.7% (12/689)	0.15 (0.03-0.67)	0.01
Death, MI, or stroke	5.3% (35/655)	6.8% (43/636)	0.77 (0.48-1.22)	0.26
Repeat Revasc	11.4% (92/807)	5.4% (43/790)	2.25 (1.54-3.28)	<0.001
MACCE	14.5% (117/807)	11.8% (93/790)	1.28 (0.95-1.72)	0.11



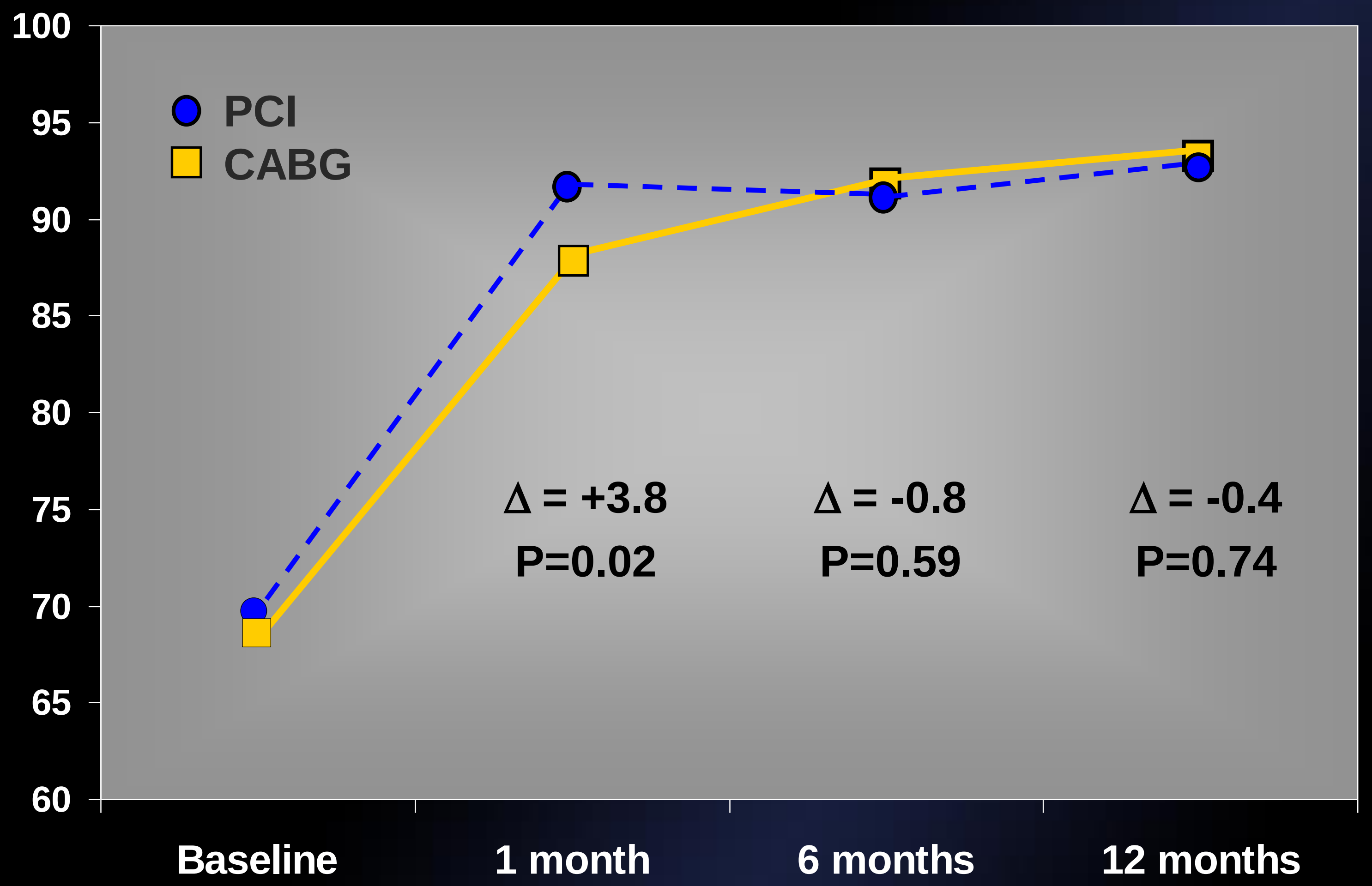
Capodanno D et al. *JACC* 2011;58:1426-32

SYNTAX Generic QOL and Utilities: LM Subgroup



Cohen D. LM Summit 2010

Primary QOL Endpoint (LM Subgroup): SAQ-Angina Frequency



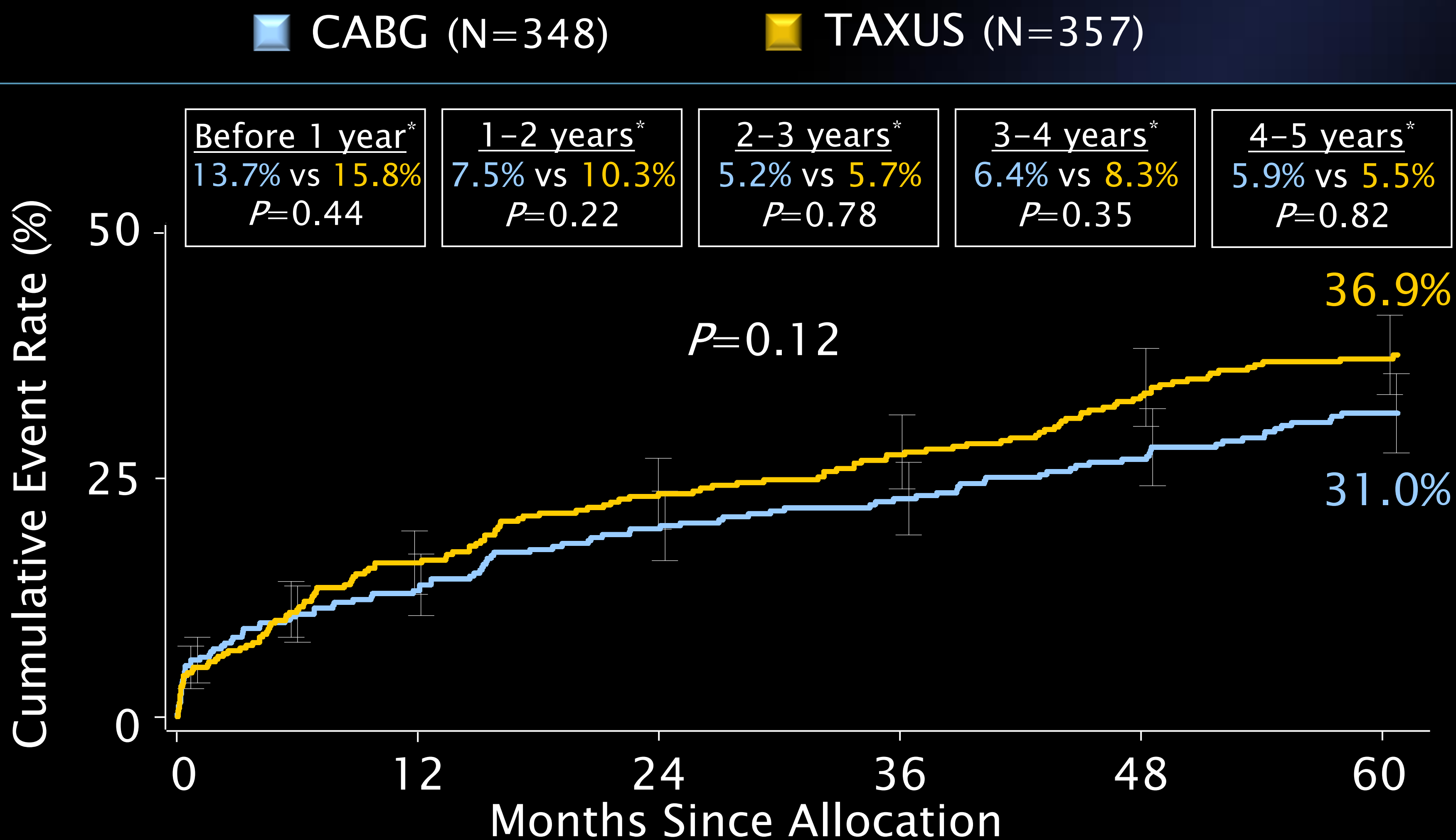
Cohen D. LM Summit 2010

Total 1-Year Costs: LM Subgroup

Left Main SYNTAX

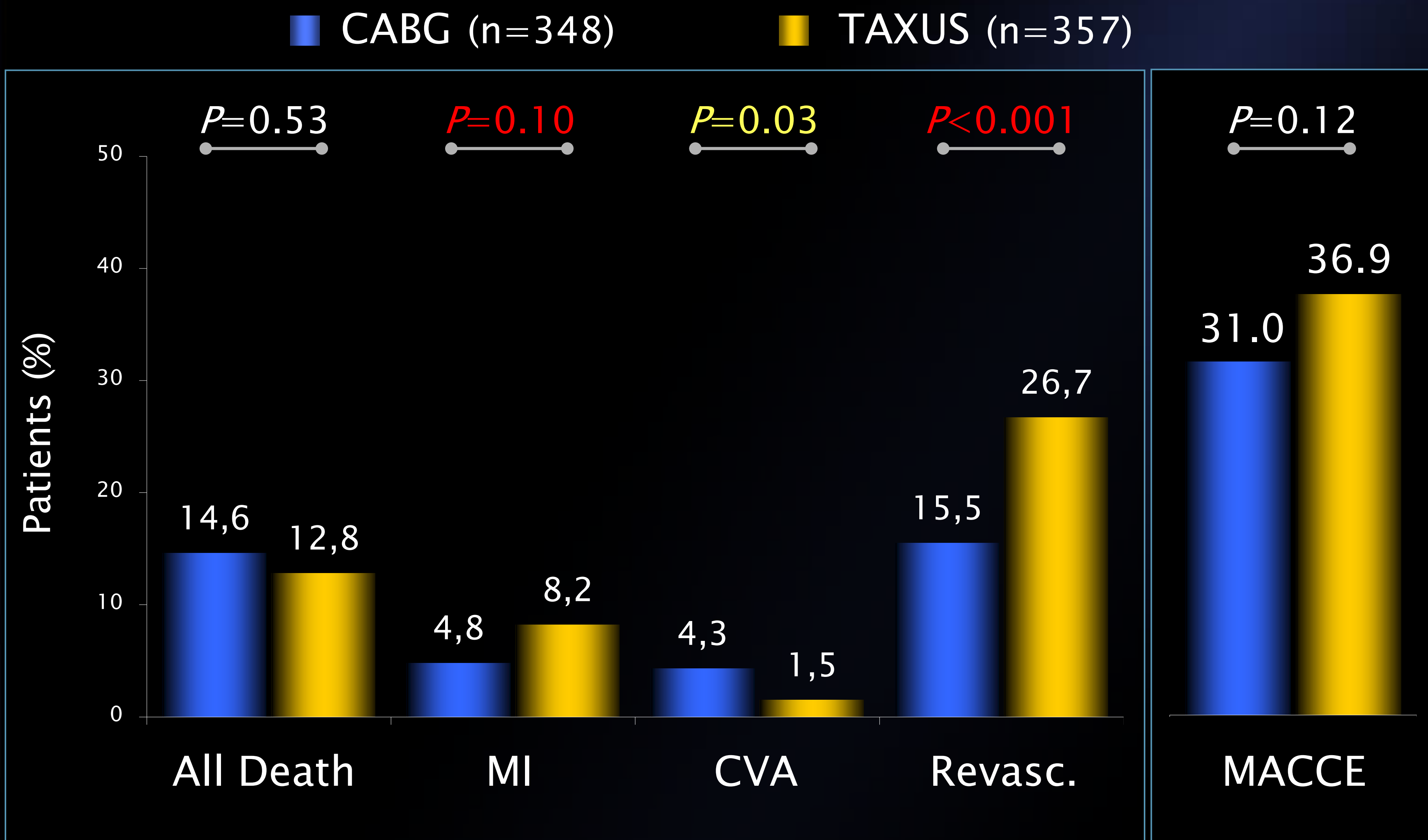
Cohen D. LM Summit 2010

SYNTAX: MACCE to 5 Years
Left Main Subset



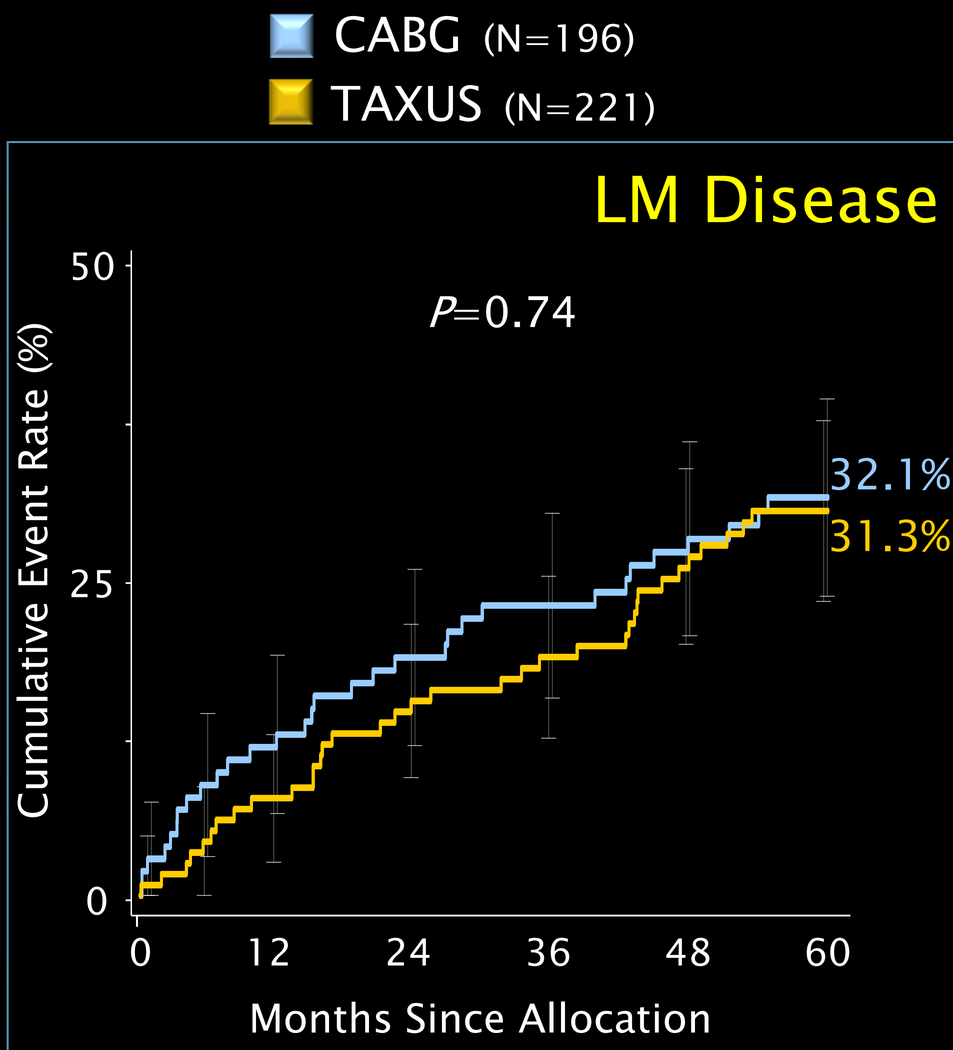
Morice MC et al. Circulation. 2014;129:2388–94

Left Main Disease
5-year Outcomes (N=705)



Morice MC et al. Circulation. 2014;129:2388-94

MACCE to 5 Years by SYNTAX Score Tercile *Low to Intermediate Scores (0-32)*

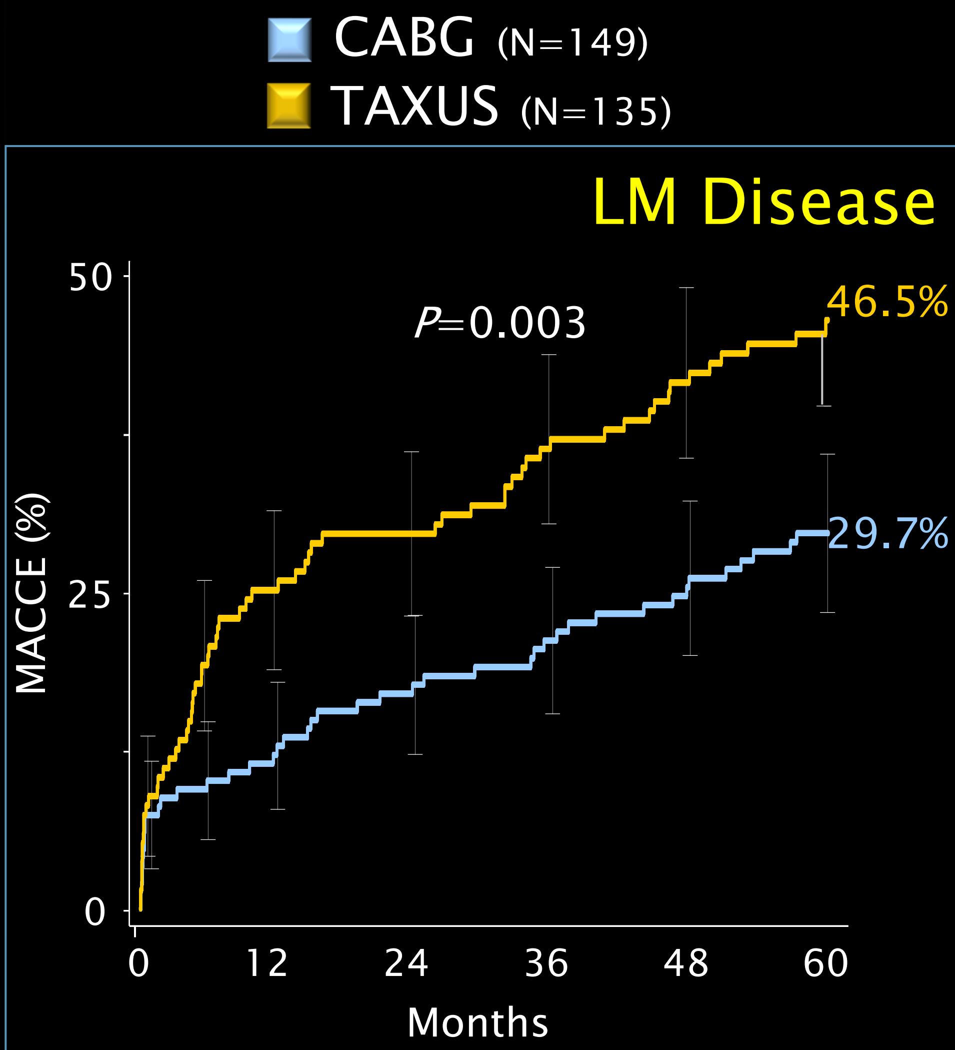


	CABG	PCI	*P* value
Death	15.1%	7.9%	0.02
CVA	3.9%	1.4%	0.11
MI	3.8%	6.1%	0.33
Death, CVA or MI	19.8%	14.8%	0.16
Revasc.	18.6%	22.6%	0.36

Morice MC et al. Circulation. 2014;129:2388-94

MACCE to 5 Years by SYNTAX Score Tercile *High Scores ≥33*

SYNTAX



	CABG	PCI	*P* value
Death	14.1%	20.9%	0.11
CVA	4.9%	1.6%	0.13
MI	6.1%	11.7%	0.13
Death, CVA or MI	22.1%	26.1%	0.40
Revasc.	11.6%	34.1%	<0.001

Morice MC et al. Circulation. 2014;129:2388-94

2012 ACC/AHA Guidelines

Left main revascularization to improve survival (pre-EXCEL and NOBLE)

CABG	I	B
PCI	IIa—For SIHD when *both* of the following are present: ■ Anatomic conditions associated with a low risk of PCI procedural complications and a high likelihood of good long-term outcome (e.g., a low SYNTAX score of ≤22, ostial or trunk left main CAD) ■ Clinical characteristics that predict a significantly increased risk of adverse surgical outcomes (e.g., STS-predicted risk of operative mortality ≥5%)	B
	IIa—For UA/NSTEMI if not a CABG candidate	B
	IIa—For STEMI when distal coronary flow is TIMI flow grade <3 and PCI can be performed more rapidly and safely than CABG	C
	IIb—For SIHD when *both* of the following are present: ■ Anatomic conditions associated with a low to intermediate risk of PCI procedural complications and an intermediate to high likelihood of good long-term outcome (e.g., low-intermediate SYNTAX score of <33, bifurcation left main CAD) ■ Clinical characteristics that predict an increased risk of adverse surgical outcomes (e.g., moderate–severe COPD, disability from prior stroke, or prior cardiac surgery; STS-predicted operative mortality >2%)	B
	III: Harm—For SIHD in patients (versus performing CABG) with unfavorable anatomy for PCI and who are good candidates for CABG	B

Patel MR et al. JACC 2017:on-line
Adapted from Finn SD et al. JACC 2012;60:e44–164

2014 ESC/EACTS Guidelines on Myocardial Revascularization: Left Main PCI

(pre-EXCEL and NOBLE)

Class	Level of evidence	Recommendation
I	B	With a SYNTAX score ≤22
IIa	B	With a SYNTAX score 22 - 32
III	B	With a SYNTAX score >32

EXCEL

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)

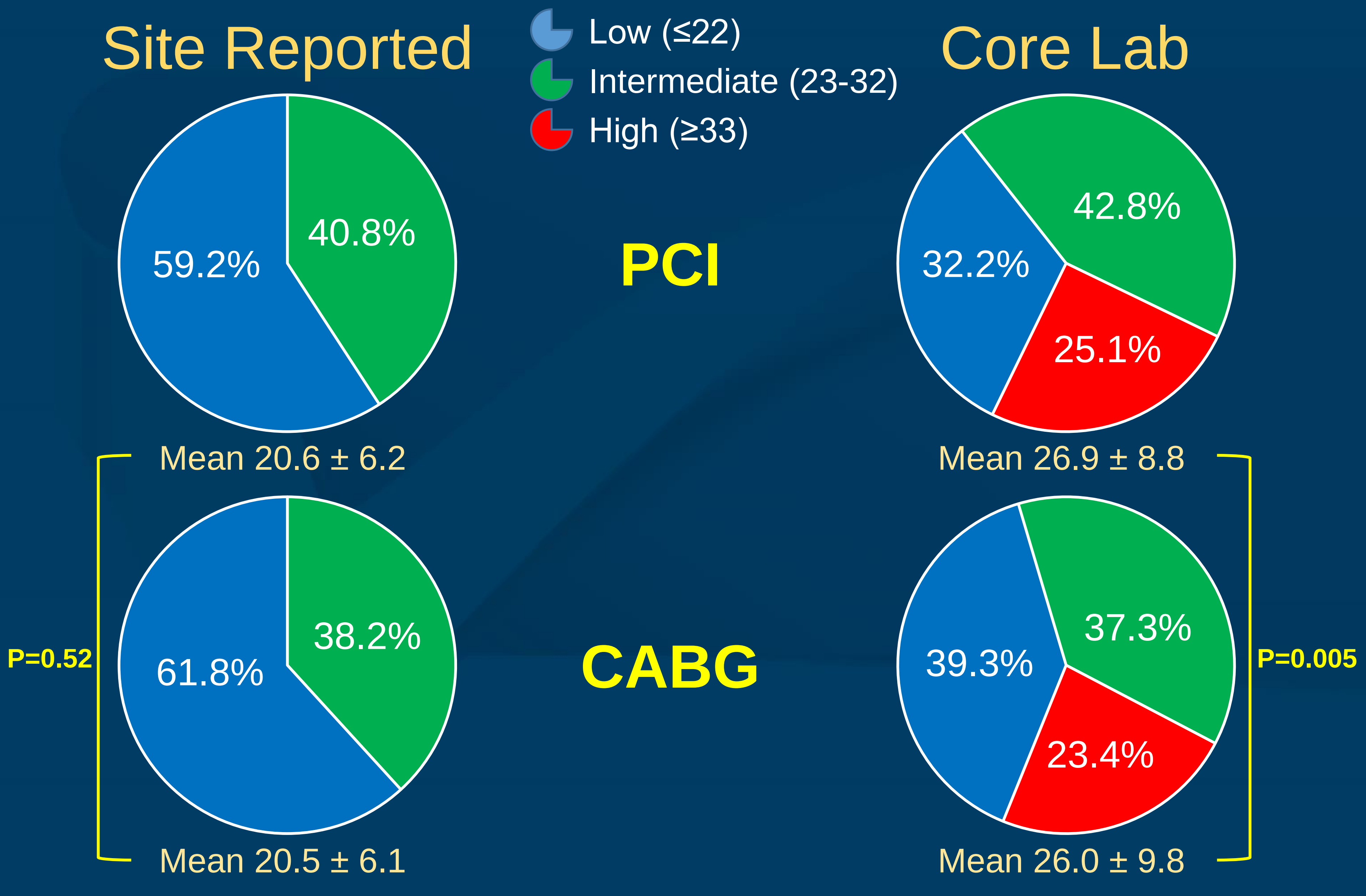
CABG

(N=957)

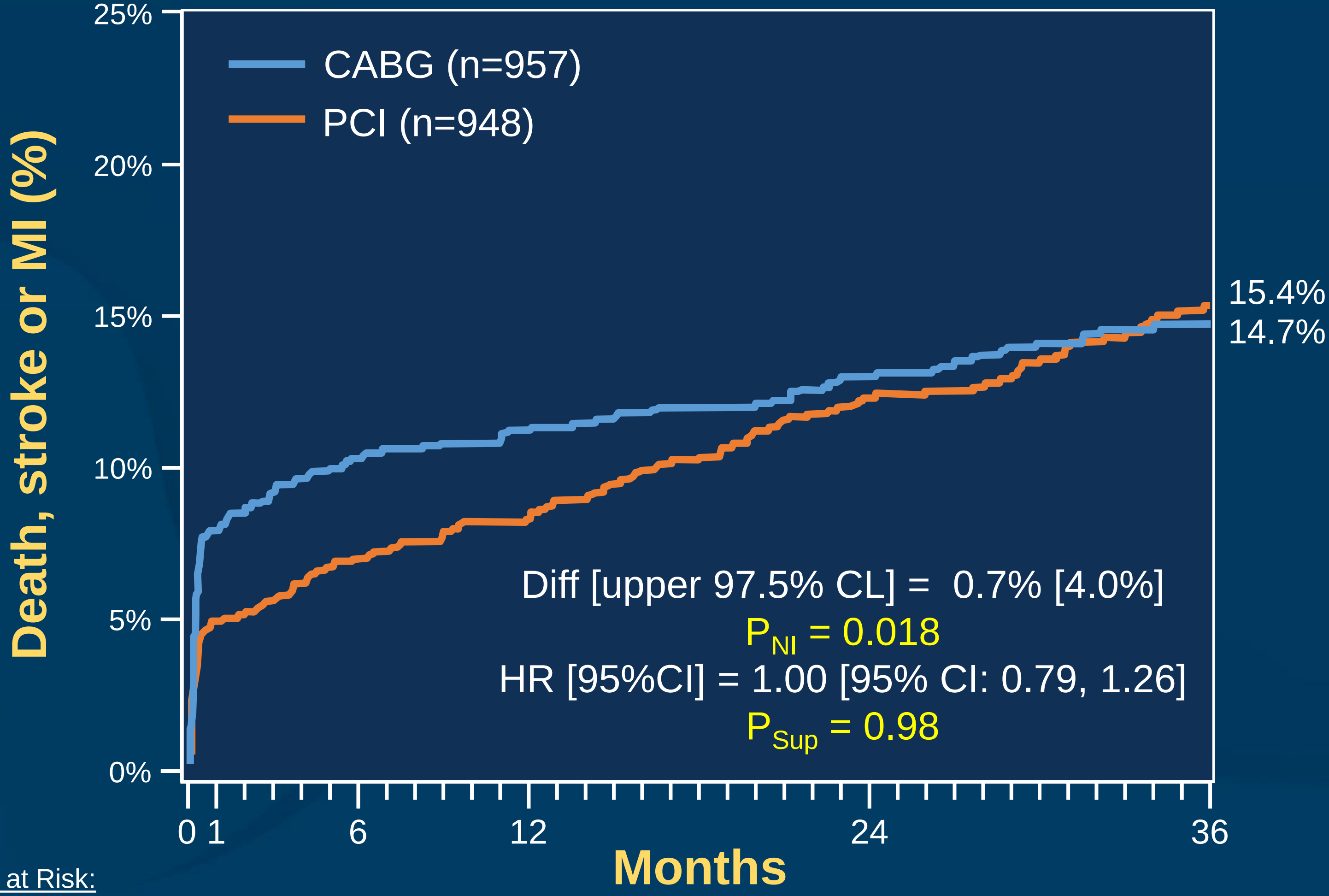
Follow-up: 1 month, 6 months, 1 year, annually through 5 years

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

SYNTAX Score



Primary Endpoint
Death, Stroke or MI at 3 Years



No. at Risk:	0	1	6	12	24	36
PCI	948	896	875	850	784	445
CABG	957	868	836	817	763	458

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

EXCEL

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

EXCEL

Major Adverse Events Within 30 Days

	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 temporary or permanent pacemaker.
[†]Serum creatinine increased by ≥0.5 mg/dL from baseline or need for dialysis.

EXCEL

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

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!

LM Revascularization with Low/Int SS

CABG vs. PCI with Contemporary DES

- **Mortality:** Similar with PCI and CABG
- **MI:** Lower with PCI in the peri-procedural period; higher with PCI during long-term FU – similar through 5 years
- **Stroke:** Not a major reason to prefer PCI over CABG
- **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 – and yes, I do think PCI should be class I

EXCEL at TCT 2017

Extraordinary new data from EXCEL

- Complete 3-year data
- Quality of life (late breaking trial)
- 30 abstracts submitted!
  - Distal LM bifurcation treatment and outcomes
  - Implications of peri-procedural and late MI
  - Geographic differences
  - Outcomes according to STS risk score
  - …and much more!

The End (Result)