

# EXCEL Trial

## Extended Long-term Results and Key Clinical Substudies

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Icahn School of Medicine at Mount Sinai, NY  
and the Cardiovascular Research Foundation

# General Disclosure Statement of Financial Interest

Speaker honoraria from Cook; Consultant to Valfix, TherOx, Robocath, HeartFlow, Ablative Solutions, Miracor, Neovasc, Abiomed, Ancora, Vectorious; Equity/options from Ancora, Qool Therapeutics, Cagent, Applied Therapeutics, Biostar family of funds, SpectraWave, Orchestra Biomed, Aria, Cardiac Success, Valfix

## Disclosure Statement of Financial Interest with Stent Manufacturers

**None**

# EXCEL: Study Design

2905 pts with unprotected left main disease

SYNTAX score  $\leq 32$

Consensus agreement of eligibility and equipoise by heart team

Yes

(N=1905)

No

(N=1000)

Enrollment  
registry

Stratified by diabetes, SYNTAX score and center

R

PCI (Xience EES)

(N=948)

CABG

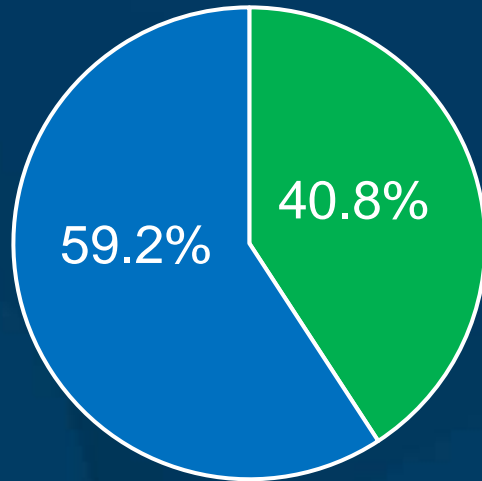
(N=957)

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

**Primary endpoint:** Death, MI or stroke measured at median 3-yr FU, min 2-yr FU

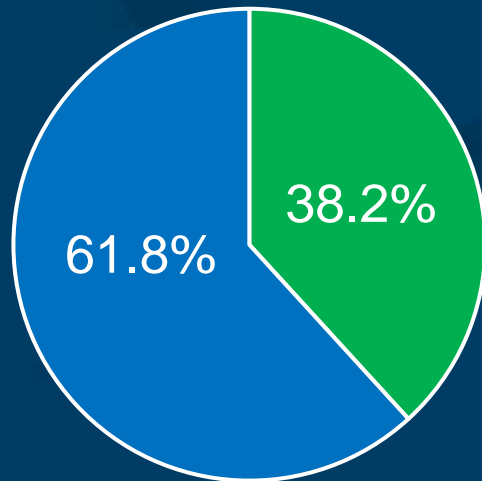
# SYNTAX Score

## Site Reported



Mean  $20.6 \pm 6.2$

P=0.52

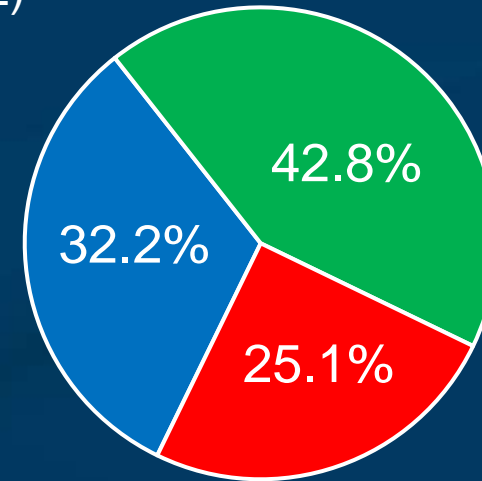


Mean  $20.5 \pm 6.1$

- Low ( $\leq 22$ )
- Intermediate (23-32)
- High ( $\geq 33$ )

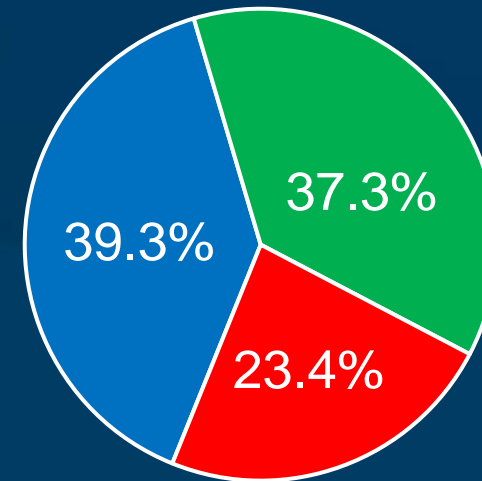
## PCI

## Core Lab



Mean  $26.9 \pm 8.8$

## CABG

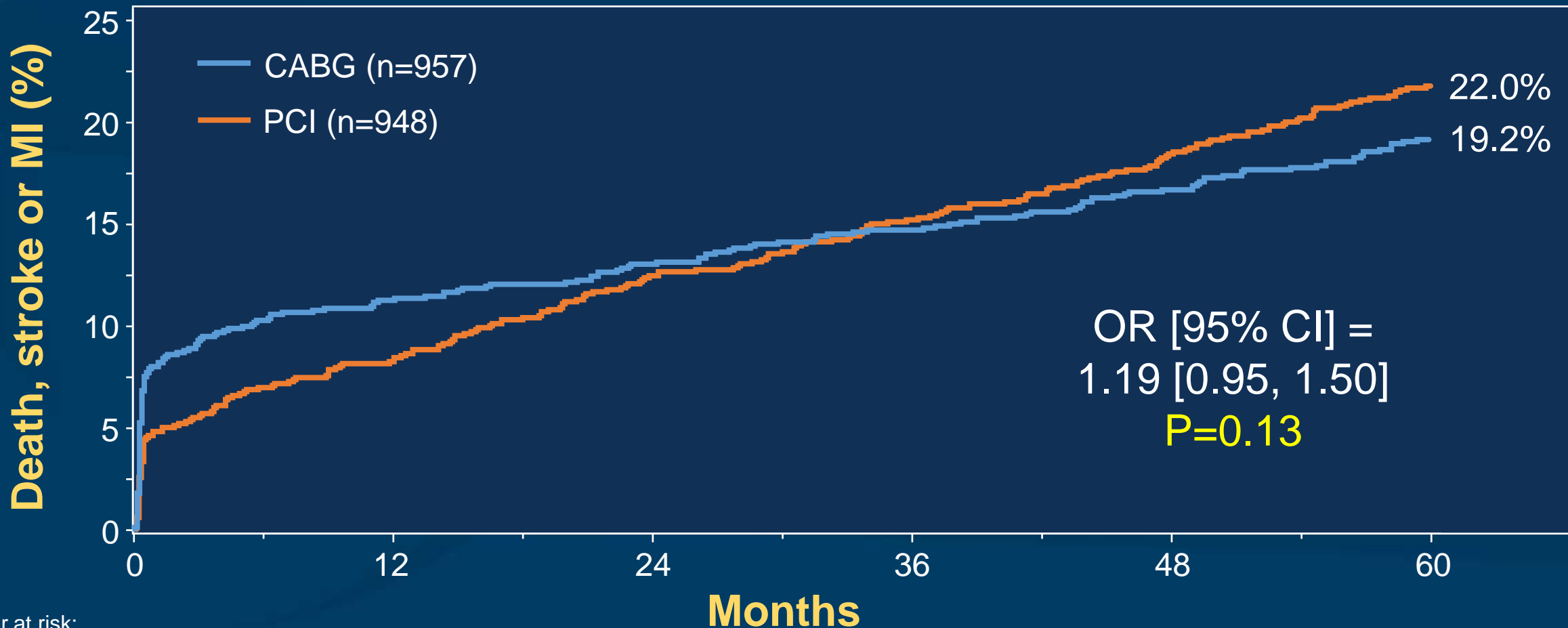


Mean  $26.0 \pm 9.8$

P=0.005

# Primary Endpoint

## All-cause Death, Stroke or MI at 5 Years



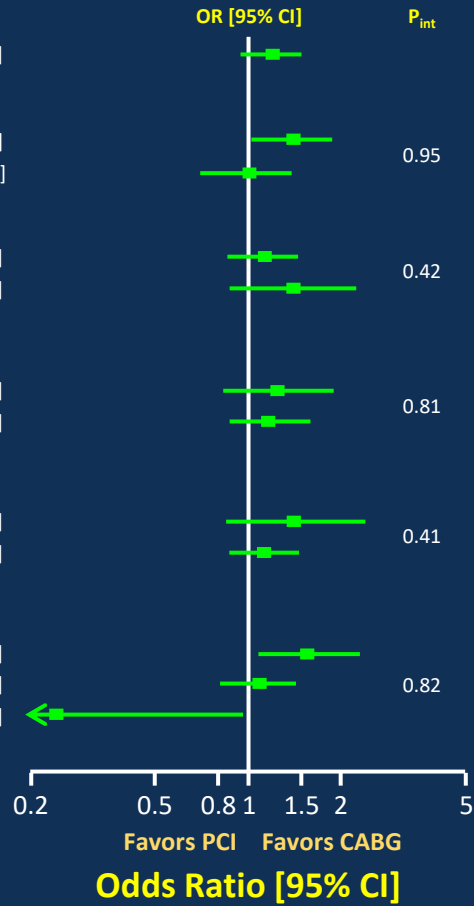
Number at risk:

PCI	948	854	809	778	738	486
CABG	957	818	789	763	734	532

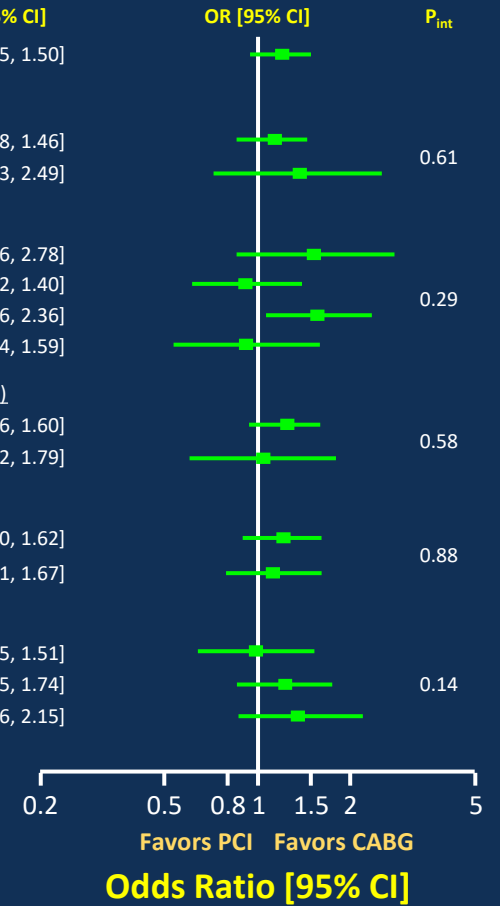
# Analysis of 10 pre-specified subgroups

## All-cause Death, Stroke or MI at 5 Years

Subgroup	PCI N=948	CABG N=957	OR [95% CI]	$P_{int}$
All patients	22.0% (203/948)	19.2% (176/957)	1.19 [0.95, 1.50]	
<u>Age (median cutoff)</u>				
- ≥67 years	27.2% (123/466)	21.8% (98/472)	1.39 [1.02, 1.89]	0.95
- <67 years	16.9% (80/482)	16.6% (78/485)	1.00 [0.71, 1.40]	
<u>Sex</u>				
- Male	20.6% (145/722)	18.7% (134/742)	1.12 [0.86, 1.46]	0.42
- Female	26.3% (58/226)	21.1% (42/215)	1.39 [0.88, 2.20]	
<u>Diabetes mellitus, medically treated</u>				
- Yes	29.0% (72/256)	25.5% (62/249)	1.24 [0.83, 1.86]	0.81
- No	19.4% (131/692)	16.9% (114/707)	1.17 [0.89, 1.55]	
<u>Chronic kidney disease</u>				
- eGFR ≤60 ml/min	34.0% (54/164)	27.6% (37/144)	1.44 [0.86, 2.39]	0.41
- eGFR >60 ml/min	19.5% (147/770)	17.6% (135/791)	1.13 [0.87, 1.47]	
<u>Geographic location</u>				
- North America	24.2% (89/381)	17.3% (61/371)	1.57 [1.09, 2.26]	0.82
- Europe	21.1% (111/534)	19.6% (102/541)	1.09 [0.81, 1.48]	
- Other	9.6% (3/33)	29.6% (13/45)	0.24 [0.06, 0.96]	



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All patients	22.0% (203/948)	19.2% (176/957)	1.19 [0.95, 1.50]	
<u>Left ventricular ejection fraction</u>				
- ≥50%	20.6% (158/782)	18.7% (144/796)	1.14 [0.88, 1.46]	0.61
- <50%	31.5% (33/111)	24.2% (26/115)	1.35 [0.73, 2.49]	
<u>Non-left main diseased coronary arteries (core lab assessment)</u>				
- 0	20.7% (33/163)	14.3% (23/167)	1.55 [0.86, 2.78]	0.29
- 1	21.2% (60/292)	21.9% (61/292)	0.94 [0.62, 1.40]	
- 2	25.0% (79/325)	17.8% (50/295)	1.58 [1.06, 2.36]	
- 3	19.2% (31/162)	20.7% (37/182)	0.93 [0.54, 1.59]	
<u>Left main bifurcation or trifurcation stenosis ≥50% (core lab assessment)</u>				
- Yes	22.7% (171/771)	19.0% (136/741)	1.24 [0.96, 1.60]	0.58
- No	19.2% (32/171)	18.9% (35/195)	1.05 [0.62, 1.79]	
<u>Syntax score (site reported)</u>				
- ≤22	21.9% (119/560)	18.7% (106/588)	1.21 [0.90, 1.62]	0.88
- 23 - 32	22.2% (84/386)	20.0% (70/366)	1.16 [0.81, 1.67]	
<u>Syntax score (core lab assessment)</u>				
- ≤22	17.2% (49/294)	16.7% (58/364)	0.99 [0.65, 1.51]	0.14
- 23 - 32	23.7% (91/392)	20.7% (69/346)	1.22 [0.85, 1.74]	
- ≥33	25.0% (56/228)	20.2% (42/216)	1.36 [0.86, 2.15]	



**No significant interactions**

# Analysis of 10 pre-specified subgroups

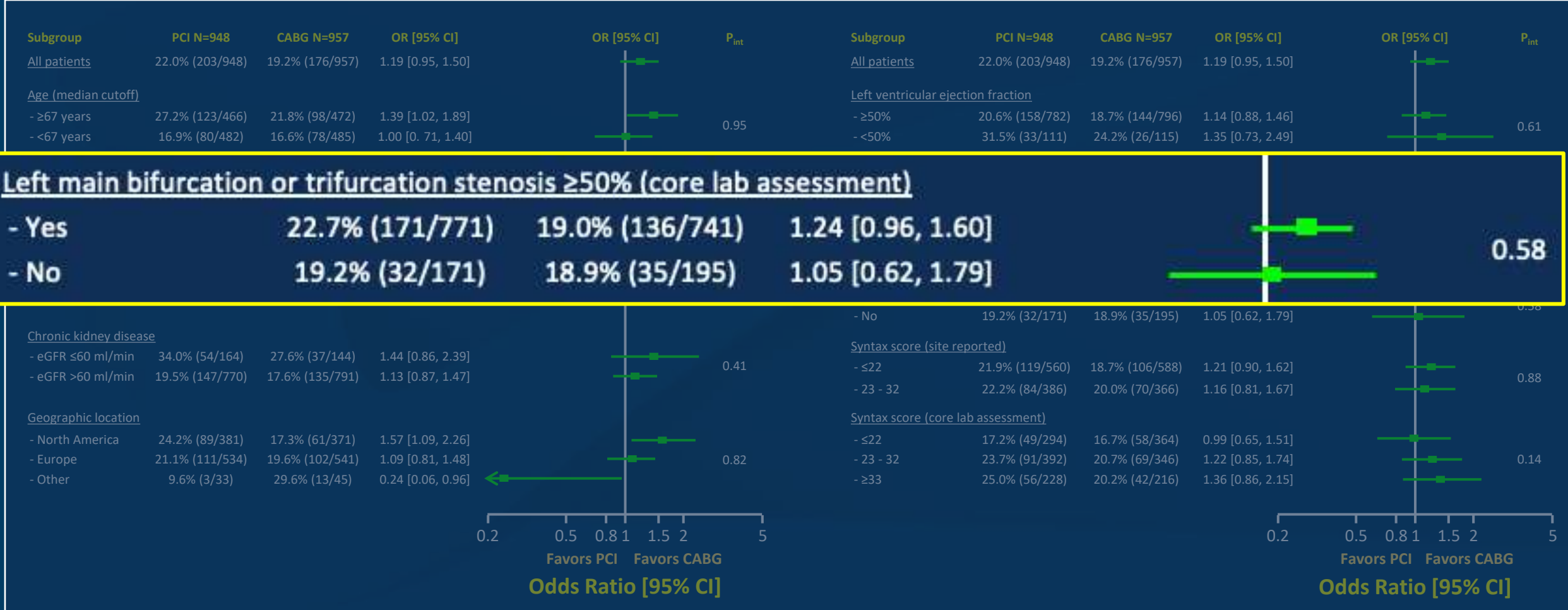
## All-cause Death, Stroke or MI at 5 Years



**No significant interactions**

# Analysis of 10 pre-specified subgroups

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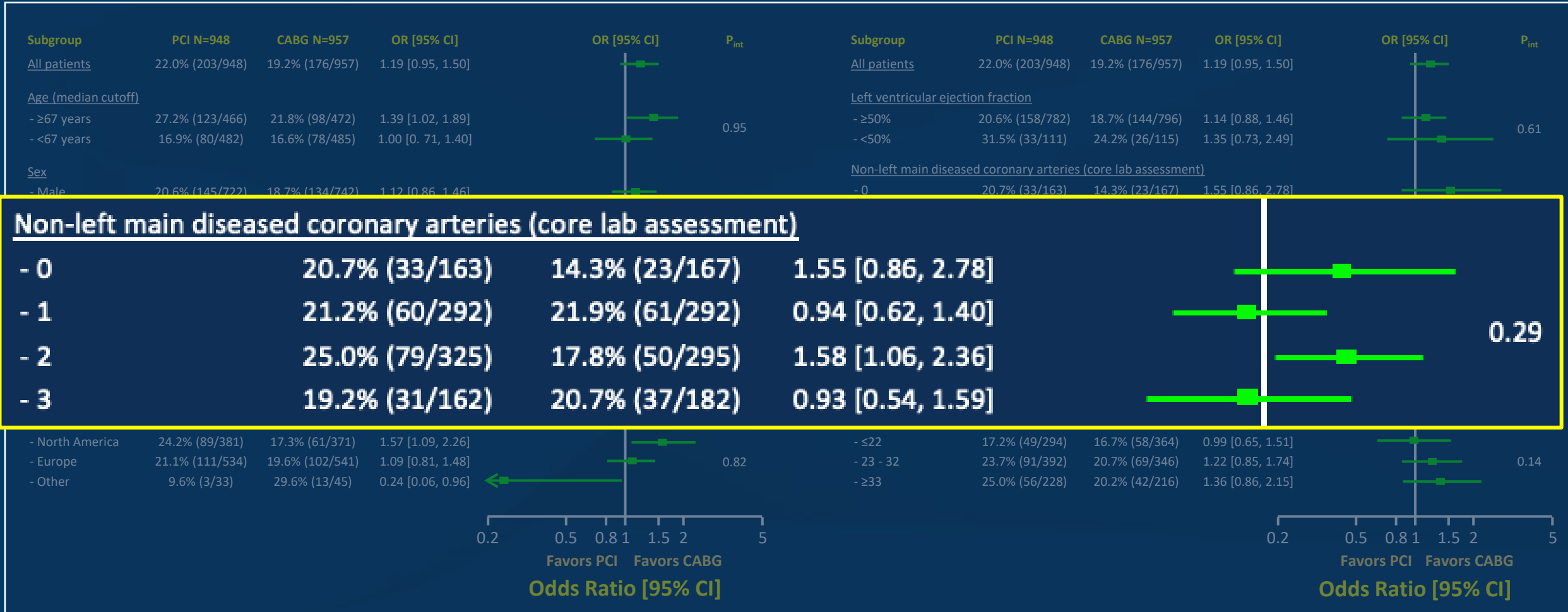


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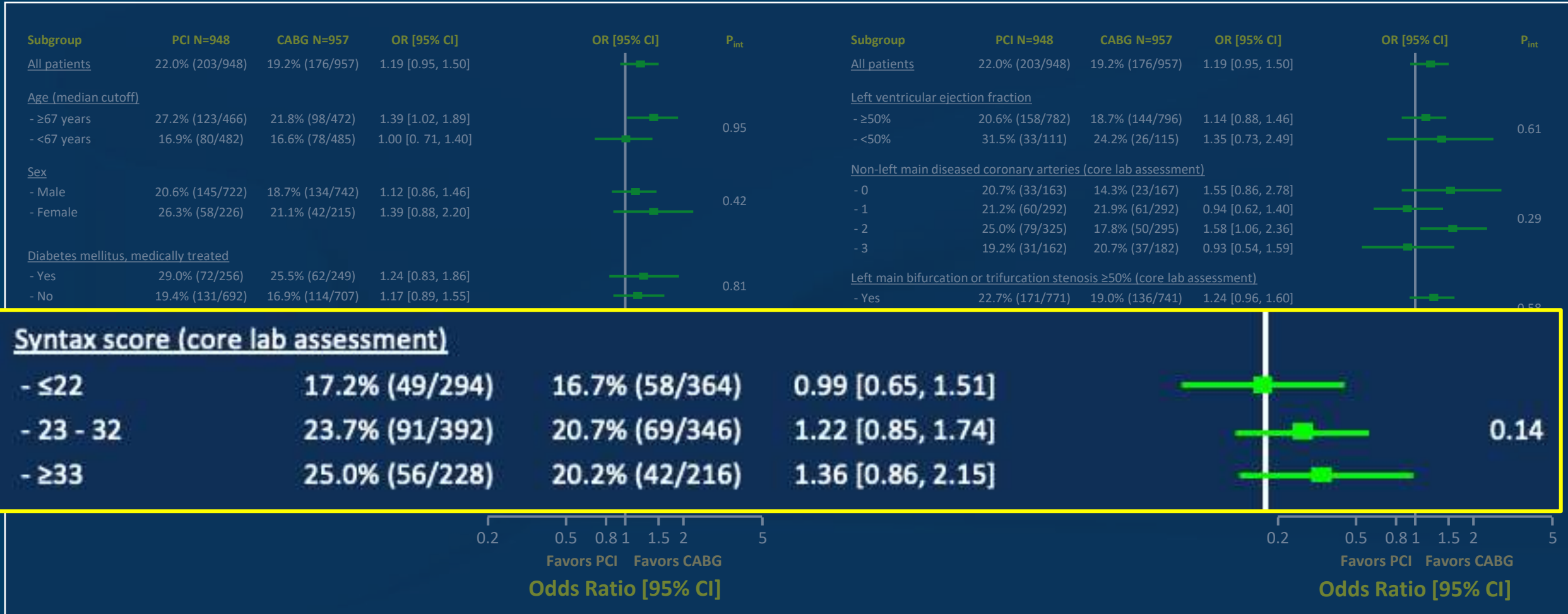
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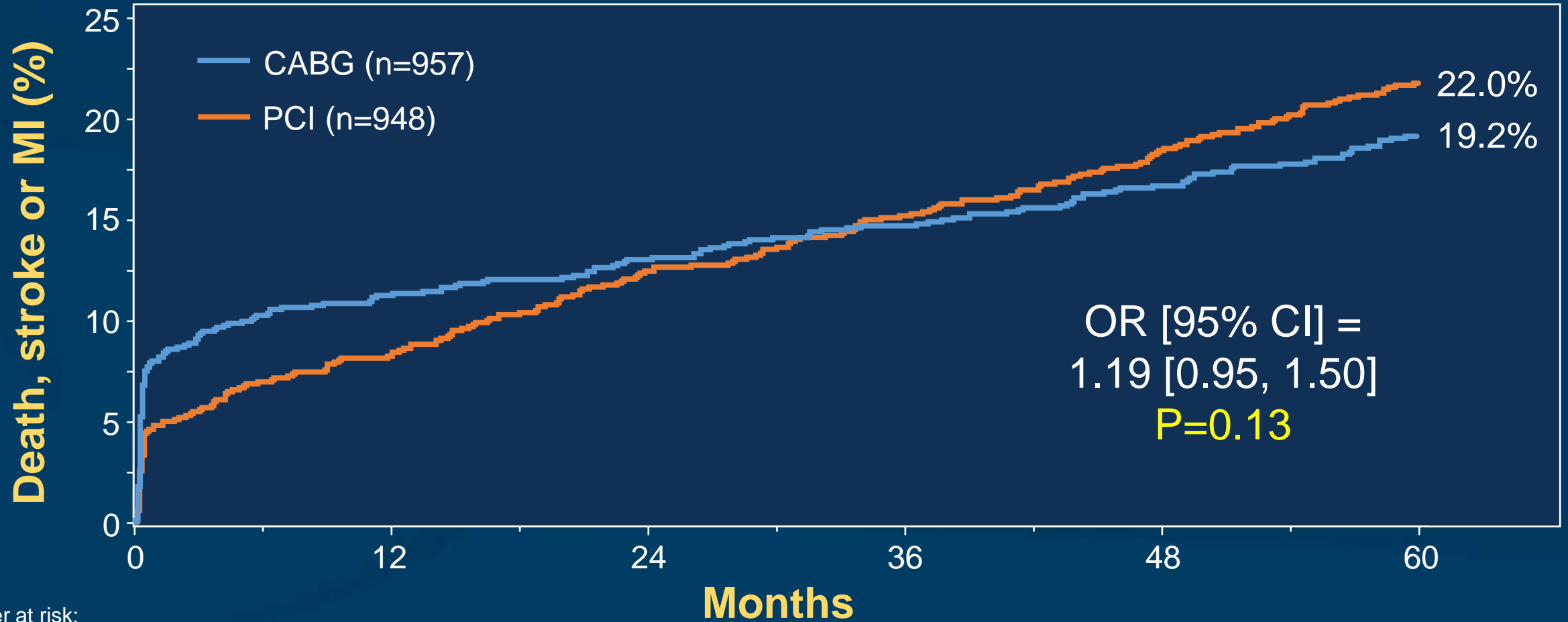
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# Primary Endpoint

## Non-proportional Hazards



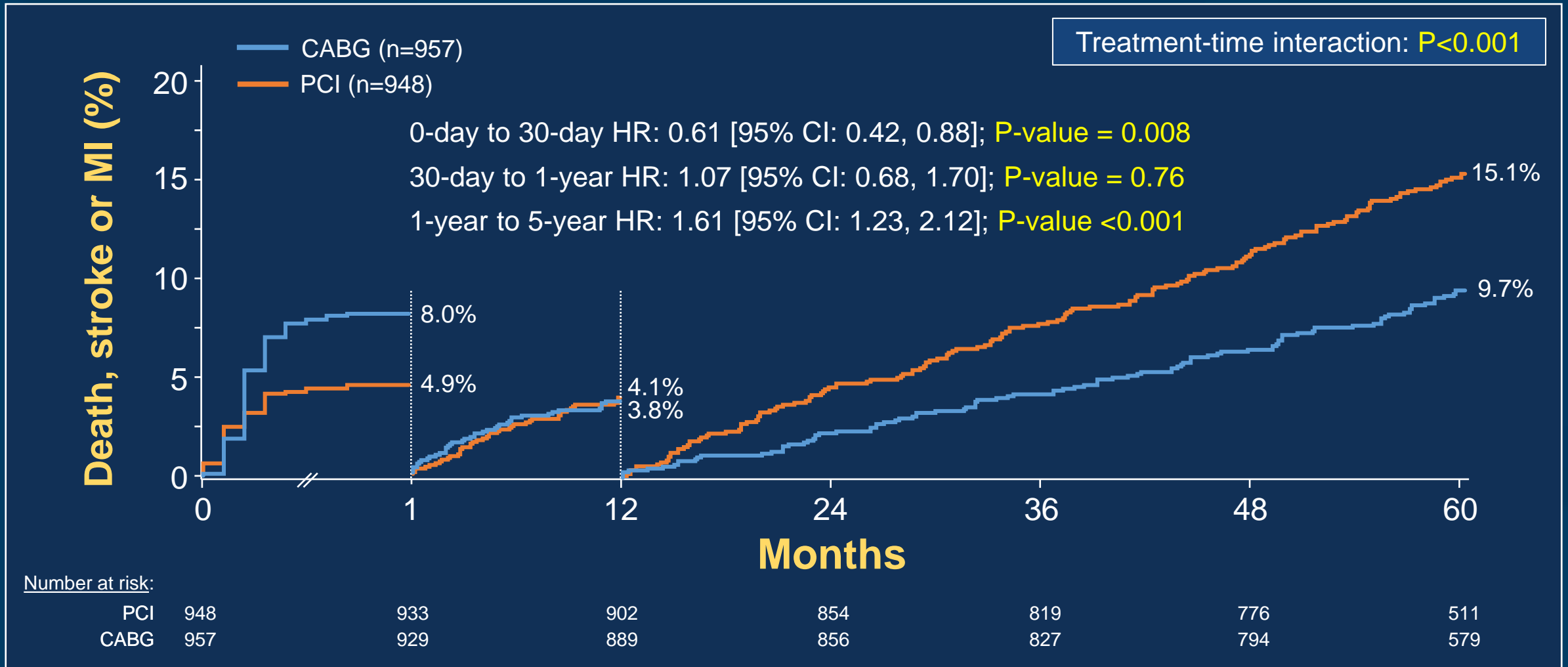
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# Piecewise Hazards

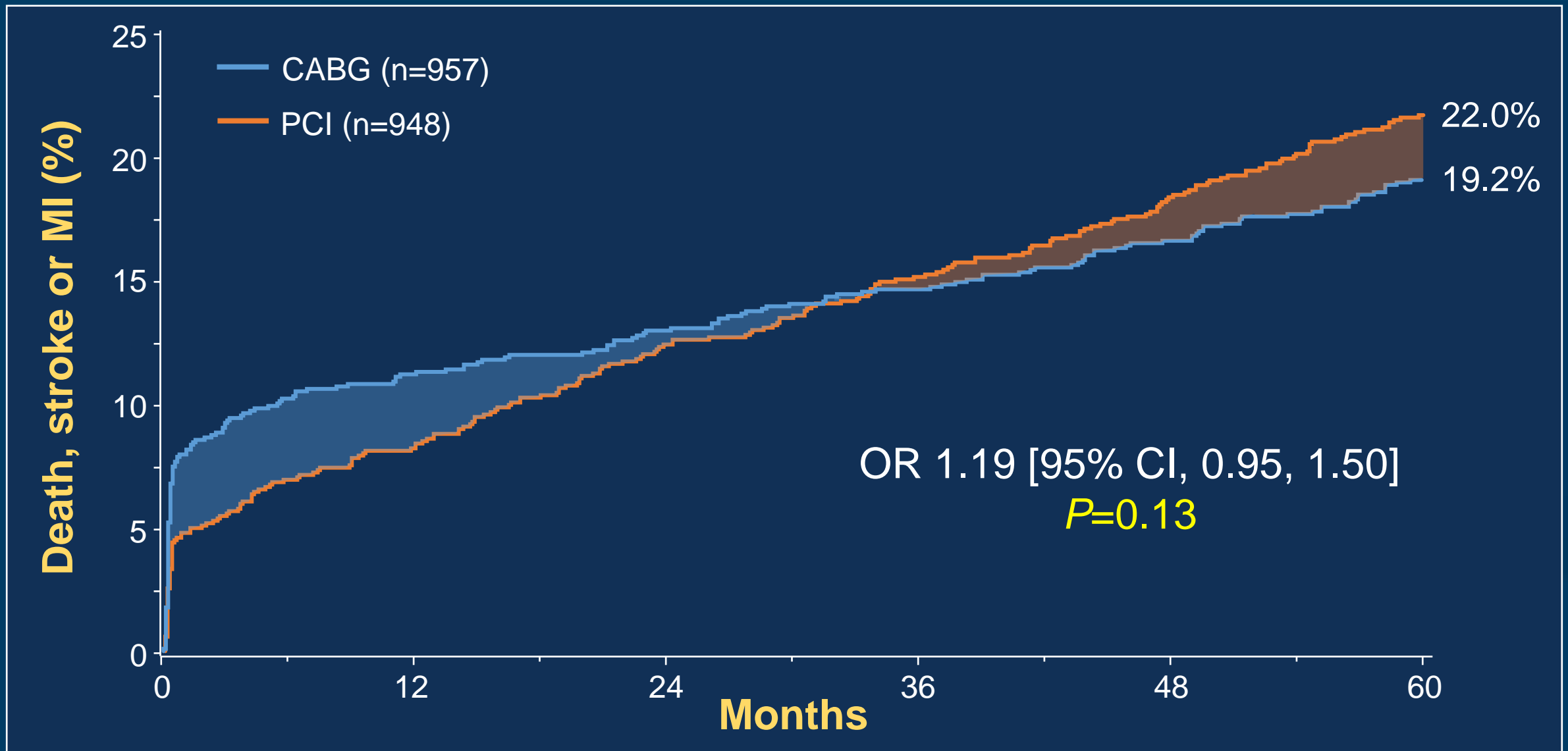
## All-cause Death, Stroke or MI

Three distinct periods of varying relative risk



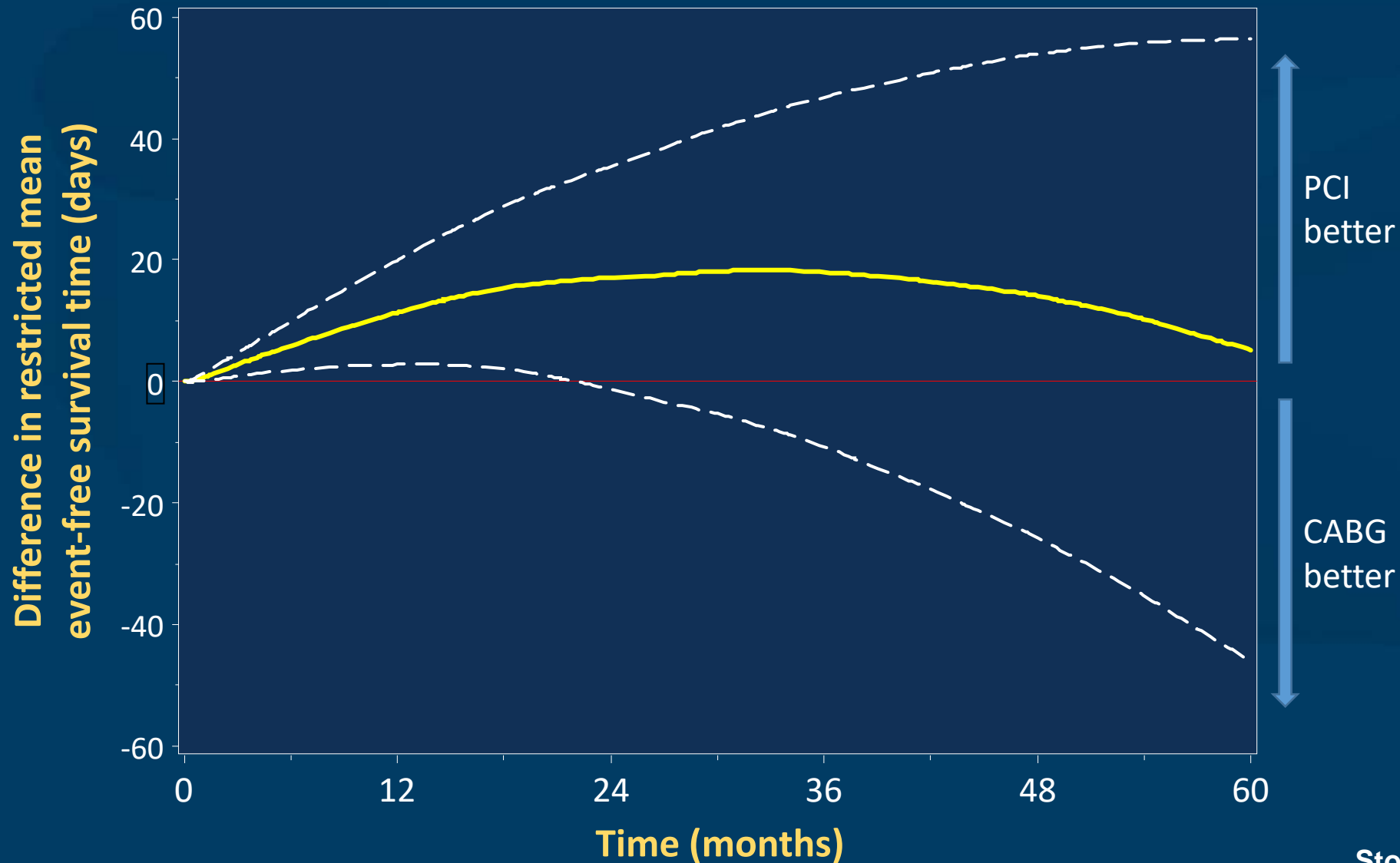
# Restricted Mean Survival Time Analysis

## All-cause Death, Stroke or MI



# Restricted Mean Survival Time Analysis

## All-cause Death, Stroke or MI



At the end of the 5-year follow-up period, event-free survival time was **5.2 days** (95% CI -46.1 to 56.5 days) longer after PCI compared with CABG

# 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]	<b>0.008</b>
- 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]	<b>0.02</b>
- Peri-procedural	3.6%	5.9%	0.61 [0.40, 0.93]	<b>0.02</b>
- Spontaneous	0.3%	0.3%	1.00 [0.20, 4.95]	1.00
- STEMI	0.7%	2.3%	0.32 [0.14, 0.74]	<b>0.005</b>
- 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]	<b>0.002</b>
- Ischemia-driven revasc (IDR)	0.6%	1.4%	0.46 [0.18, 1.21]	0.11
Stent thrombosis, def/prob	0.6%	0.0%	-	<b>0.01</b>
Graft occlusion, symptomatic	0.0%	1.2%	-	<b>&lt;0.001</b>
Definite stent thrombosis or symptomatic graft occlusion	0.3%	1.2%	0.27 [0.08, 0.97]	<b>0.03</b>

# 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.



# Primary Endpoint at 5 Years

	PCI (N=948)	CABG (N=957)	Difference [95% CI]	Odds ratio [95% CI]
<b>Death, stroke or MI</b>	22.0% (203)	19.2% (176)	2.8% [-0.9%, 6.5%]	1.19 [0.95, 1.50]
Death, all-cause	13.0% (119)	9.9% (89)	3.1% [0.2%, 6.1%]	1.38 [1.03, 1.85]
- Cardiovascular	6.8% (61)	5.5% (49)	1.3% [-0.9%, 3.6%]	1.26 [0.85, 1.85]
- Definite cardiovascular	5.0% (45)	4.5% (40)	0.5% [-1.4%, 2.5%]	1.13 [0.73, 1.74]
- Undetermined cause	1.9% (16)	1.1% (9)	0.9% [-0.3%, 2.0%]	1.78 [0.78, 4.06]
- Non-cardiovascular	6.6% (58)	4.6% (40)	2.0% [-0.2%, 4.2%]	1.47 [0.97, 2.23]
Cerebrovascular events	3.3% (29)	5.2% (46)	-1.9% [-3.8%, 0.0%]	0.61 [0.38, 0.99]
- Stroke	2.9% (26)	3.7% (33)	-0.8% [-2.4%, 0.9%]	0.78 [0.46, 1.31]
- Transient ischemic attack	0.3% (3)	1.6% (14)	-1.3% [-2.2%, -0.4%]	0.21 [0.06, 0.74]
Myocardial infarction	10.6% (95)	9.1% (84)	1.4% [-1.3%, 4.2%]	1.14 [0.84, 1.55]
- Peri-procedural	3.9% (37)	6.1% (57)	-2.1% [-4.1%, -0.1%]	0.63 [0.41, 0.96]
- Non-peri-procedural	6.8% (59)	3.5% (31)	3.2% [1.2%, 5.3%]	1.96 [1.25, 3.06]
ID-revascularization	16.9% (150)	10.0% (88)	6.9% [3.7%, 10.0%]	1.84 [1.39, 2.44]

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# Adjudicated Non-Cardiovascular Causes of Death

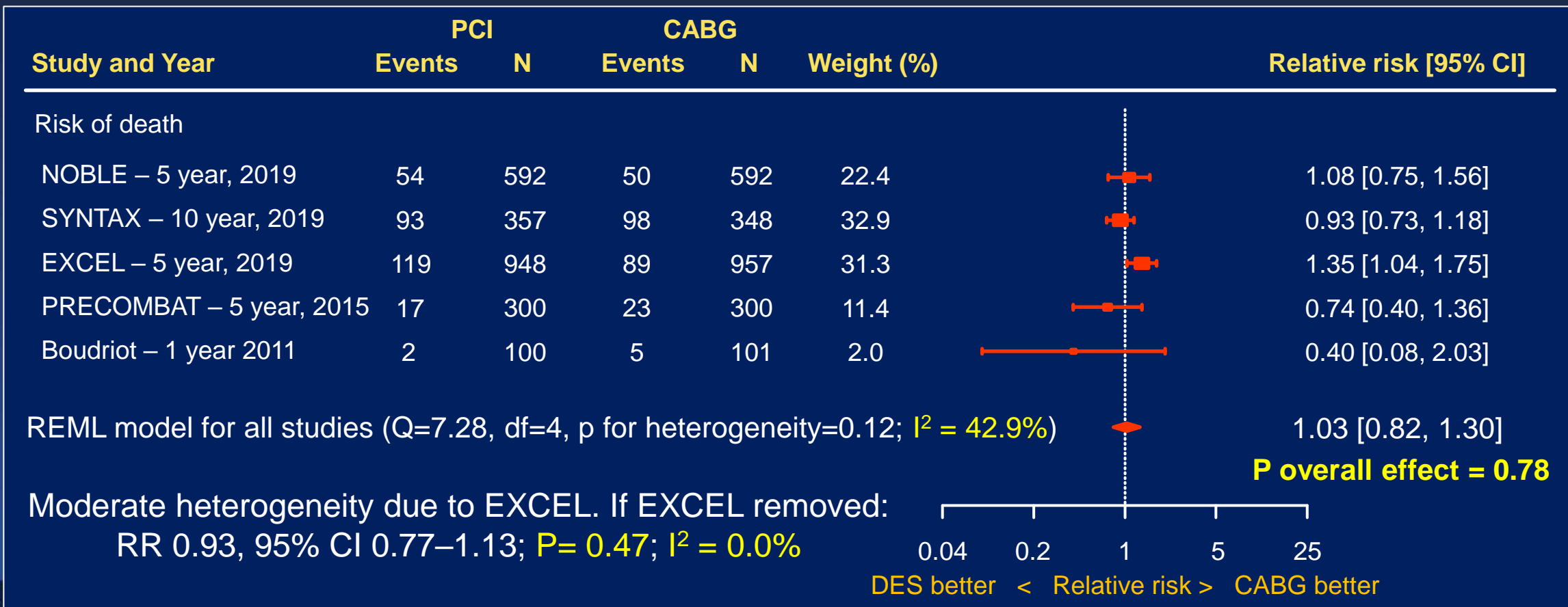
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Definite non-cardiovascular	6.6% (58)	4.6% (40)	2.0% [-0.2%, 4.2%]
Pulmonary	1.0% (8)	0.6% (5)	0.4% [-0.5%, 1.2%]
Infection (includes sepsis)	1.6% (14)	0.8% (7)	0.8% [-0.2%, 1.8%]
Gastrointestinal	0.1% (1)	0.2% (2)	-0.1% [-0.5%, 0.3%]
Malignancy	3.4% (29)	2.7% (23)	0.7% [-1.0%, 2.3%]
Accident/trauma	0.3% (3)	0.2% (2)	0.1% [-0.4%, 0.6%]
Non-cardiovascular organ failure	0.2% (2)	0.0% (0)	0.2% [-, -]
Other non-cardiovascular cause	0.0% (0)	0.2% (2)	-0.2% [-, -]

# Updated Meta-analysis of LM DES vs. CABG Trials

5 RCTs, 4,612 pts, mean 5.6-year FU

Including long-term EXCEL, NOBLE and SYNTAX data

## All-cause Death



# Primary Endpoint at 5 Years

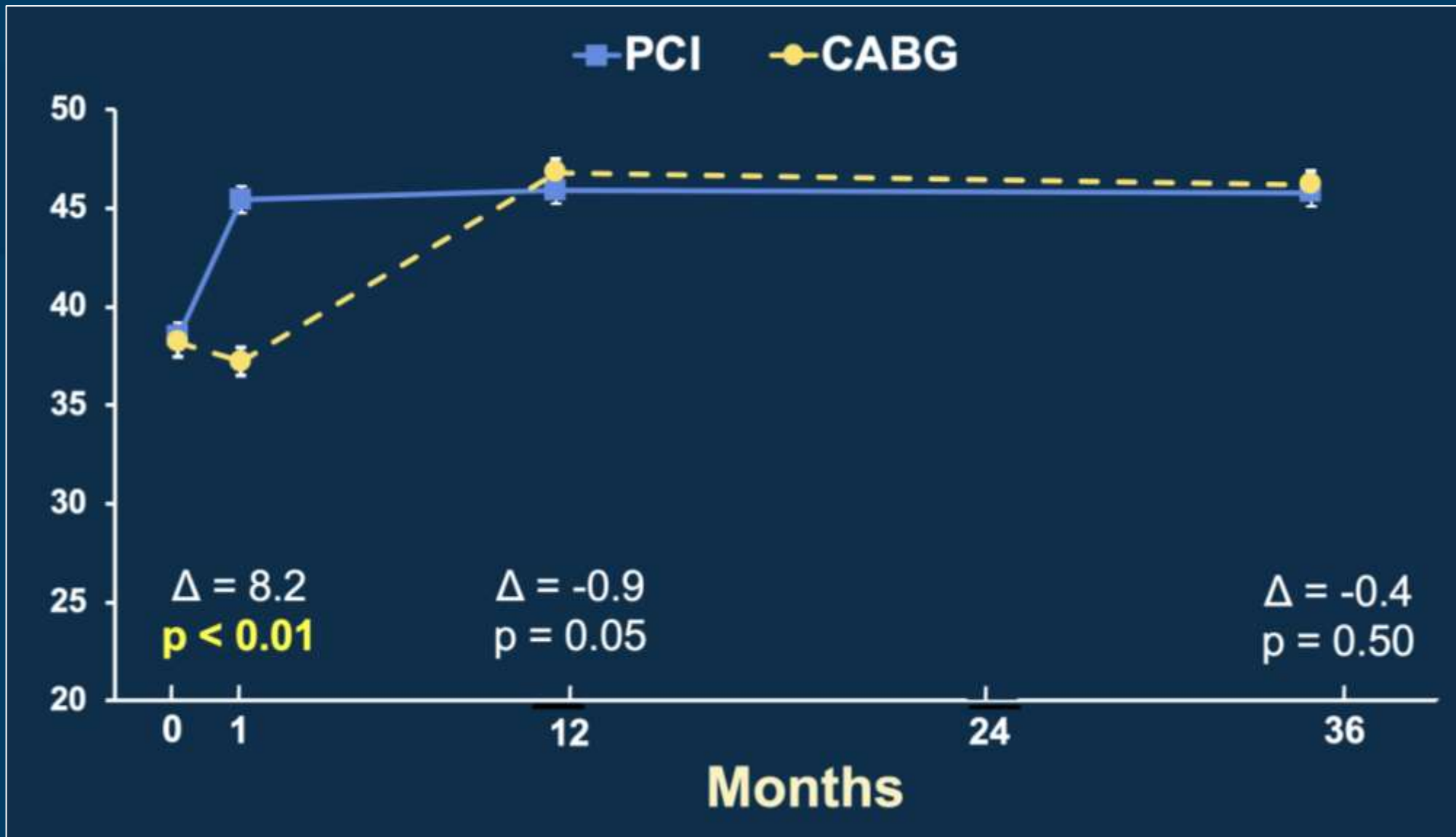
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- Cardiovascular	6.8% (61)	5.5% (49)	1.3% [-0.9%, 3.6%]	1.26 [0.85, 1.85]
- Definite cardiovascular	5.0% (45)	4.5% (40)	0.5% [-1.4%, 2.5%]	1.13 [0.73, 1.74]
- Undetermined cause	1.9% (16)	1.1% (9)	0.9% [-0.3%, 2.0%]	1.78 [0.78, 4.06]
- Non-cardiovascular	6.6% (58)	4.6% (40)	2.0% [-0.2%, 4.2%]	1.47 [0.97, 2.23]
Cerebrovascular events	3.3% (29)	5.2% (46)	<b>-1.9% [-3.8%, 0.0%]</b>	0.61 [0.38, 0.99]
- Stroke	2.9% (26)	3.7% (33)	-0.8% [-2.4%, 0.9%]	0.78 [0.46, 1.31]
- Transient ischemic attack	0.3% (3)	1.6% (14)	-1.3% [-2.2%, -0.4%]	0.21 [0.06, 0.74]
Myocardial infarction	10.6% (95)	9.1% (84)	1.4% [-1.3%, 4.2%]	1.14 [0.84, 1.55]
- Peri-procedural	3.9% (37)	6.1% (57)	-2.1% [-4.1%, -0.1%]	0.63 [0.41, 0.96]
- Non-peri-procedural	6.8% (59)	3.5% (31)	3.2% [1.2%, 5.3%]	1.96 [1.25, 3.06]
ID-revascularization	16.9% (150)	10.0% (88)	6.9% [3.7%, 10.0%]	1.84 [1.39, 2.44]

# Primary Endpoint at 5 Years

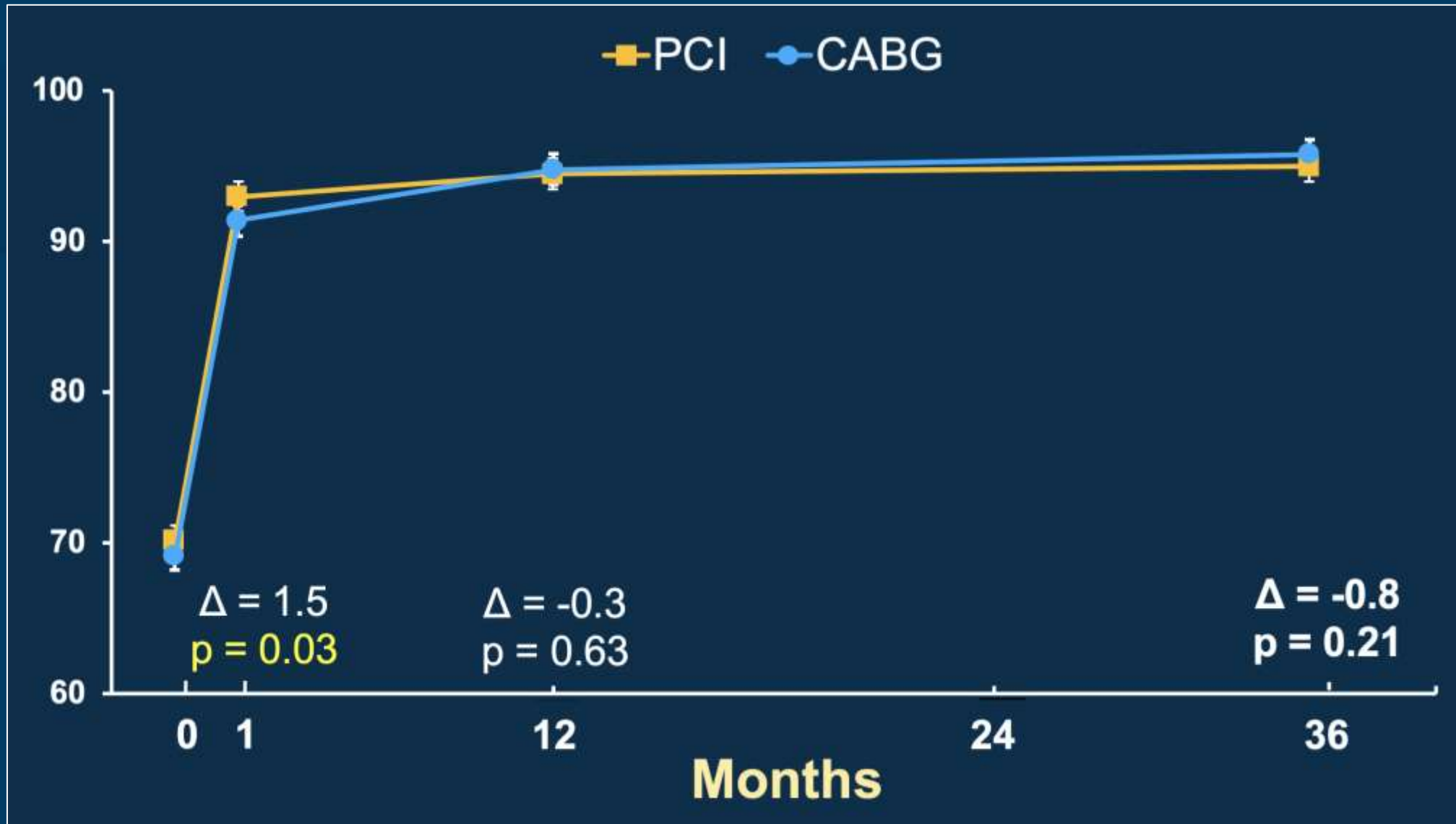
	PCI (N=948)	CABG (N=957)	Difference [95% CI]	Odds ratio [95% CI]
<b>Death, stroke or MI</b>	22.0% (203)	19.2% (176)	2.8% [-0.9%, 6.5%]	1.19 [0.95, 1.50]
Death, all-cause	13.0% (119)	9.9% (89)	3.1% [0.2%, 6.1%]	1.38 [1.03, 1.85]
- Cardiovascular	6.8% (61)	5.5% (49)	1.3% [-0.9%, 3.6%]	1.26 [0.85, 1.85]
- Definite cardiovascular	5.0% (45)	4.5% (40)	0.5% [-1.4%, 2.5%]	1.13 [0.73, 1.74]
- Undetermined cause	1.9% (16)	1.1% (9)	0.9% [-0.3%, 2.0%]	1.78 [0.78, 4.06]
- Non-cardiovascular	6.6% (58)	4.6% (40)	2.0% [-0.2%, 4.2%]	1.47 [0.97, 2.23]
Cerebrovascular events	3.3% (29)	5.2% (46)	-1.9% [-3.8%, 0.0%]	0.61 [0.38, 0.99]
- Stroke	2.9% (26)	3.7% (33)	-0.8% [-2.4%, 0.9%]	0.78 [0.46, 1.31]
- Transient ischemic attack	0.3% (3)	1.6% (14)	-1.3% [-2.2%, -0.4%]	0.21 [0.06, 0.74]
Myocardial infarction	10.6% (95)	9.1% (84)	1.4% [-1.3%, 4.2%]	1.14 [0.84, 1.55]
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- Non-peri-procedural	6.8% (59)	3.5% (31)	3.2% [1.2%, 5.3%]	1.96 [1.25, 3.06]
ID-revascularization	16.9% (150)	10.0% (88)	<b>6.9% [3.7%, 10.0%]</b>	1.84 [1.39, 2.44]



# SF-12 Physical Summary Scale



# SAQ-Angina Frequency



# Left Main PCI vs. CABG Heart Team Discussions:

## Two very different procedures

### PCI

#### Early advantages

- Less invasive
- Fewer peri-procedural complications (stroke, MI, Afib, bleeding, AKI, etc.)
- Lower 30-day MACE
- More rapid recovery with better early QoL and earlier angina relief



### CABG

#### Late advantages

- More durable
- Fewer adverse events beyond 1 year – particularly MI and repeat revascularization procedures

### PCI and CABG

No significant major differences in long-term survival, MACE (death, MI or stroke) or QoL