# Left Main PCI vs. CABG:

## From the Final EXCEL Outcomes to Patient Recommendations


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Mount Sinai Heart

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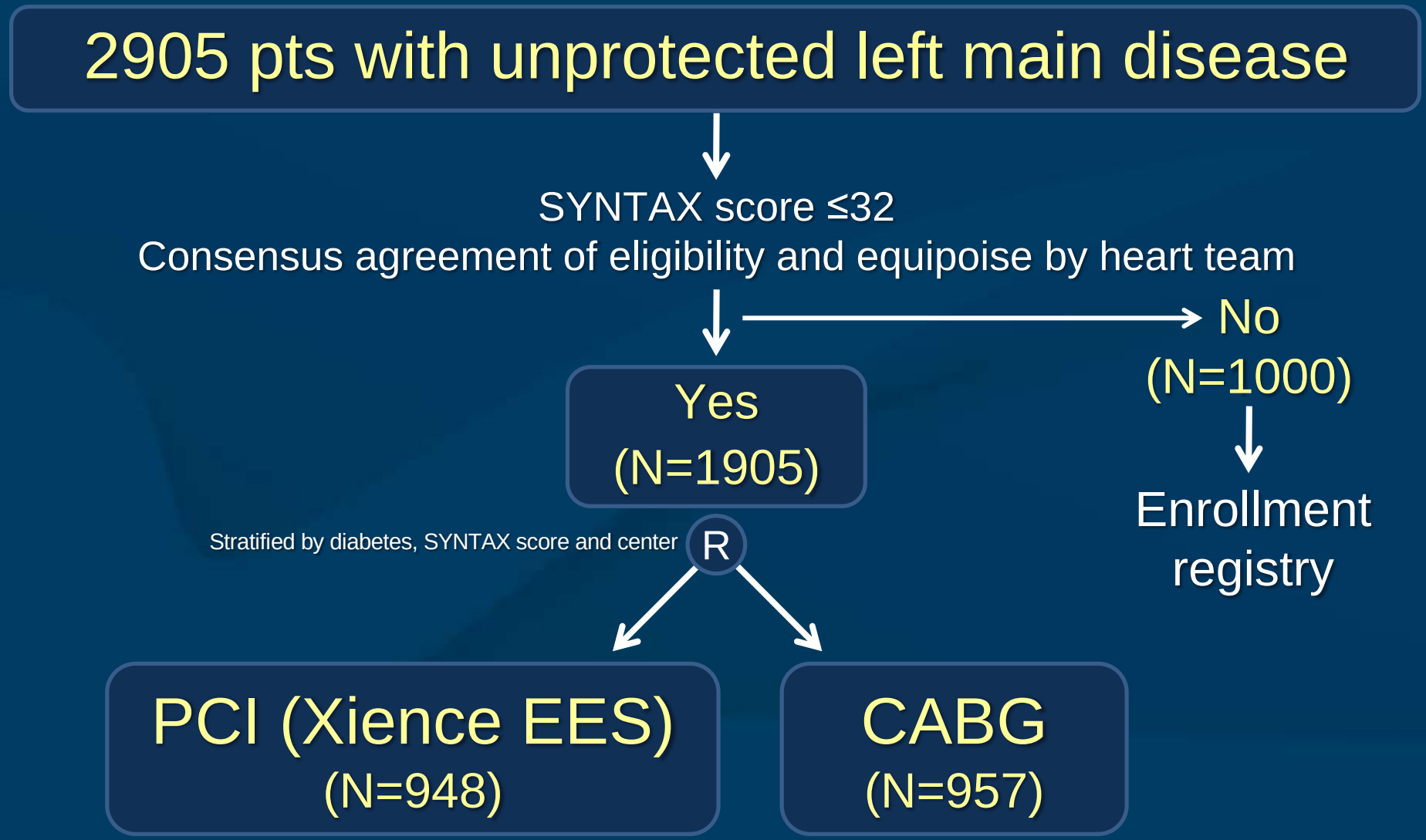
# Disclosure Statement of Financial Interest with Stent Manufacturers

**None**

# EXCEL: Study Design

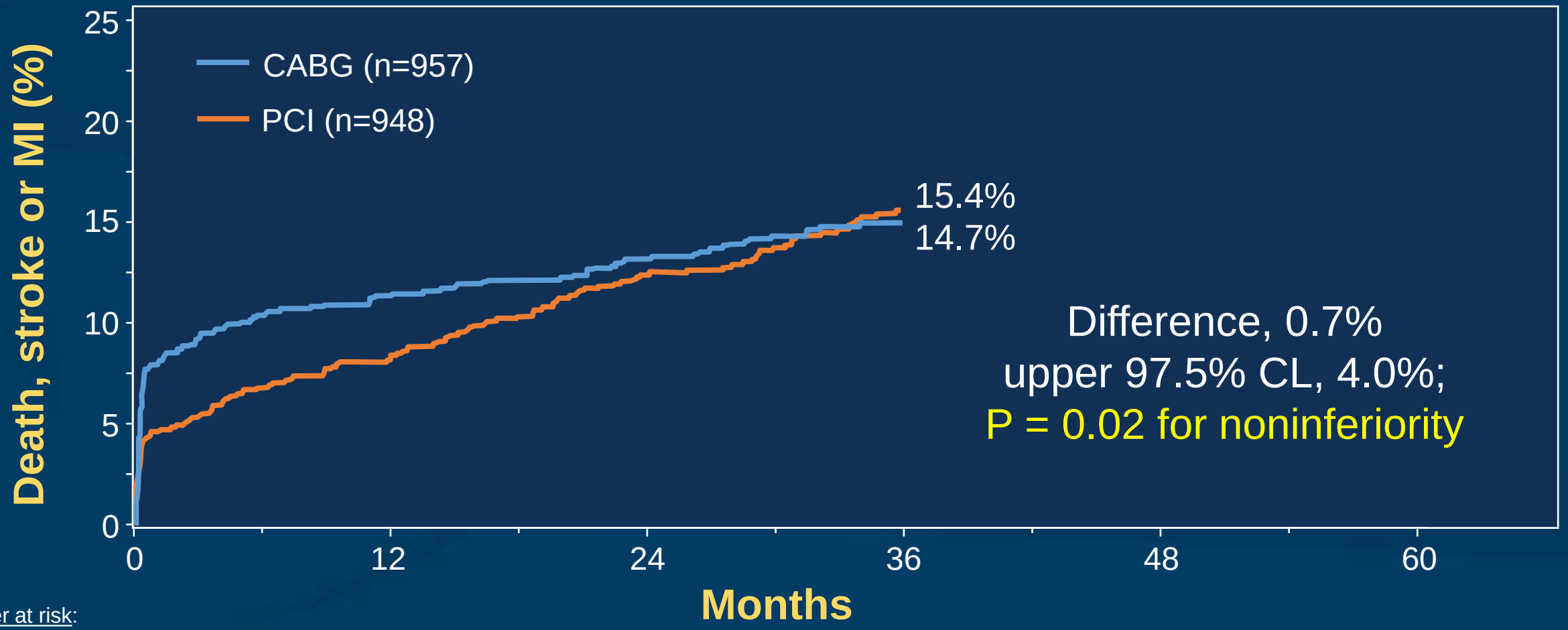



Follow-up: 1 month, 6 months, 1 year, annually through 5 years

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

# Primary Endpoint

## All-cause Death, Stroke or MI at Median 3 Years



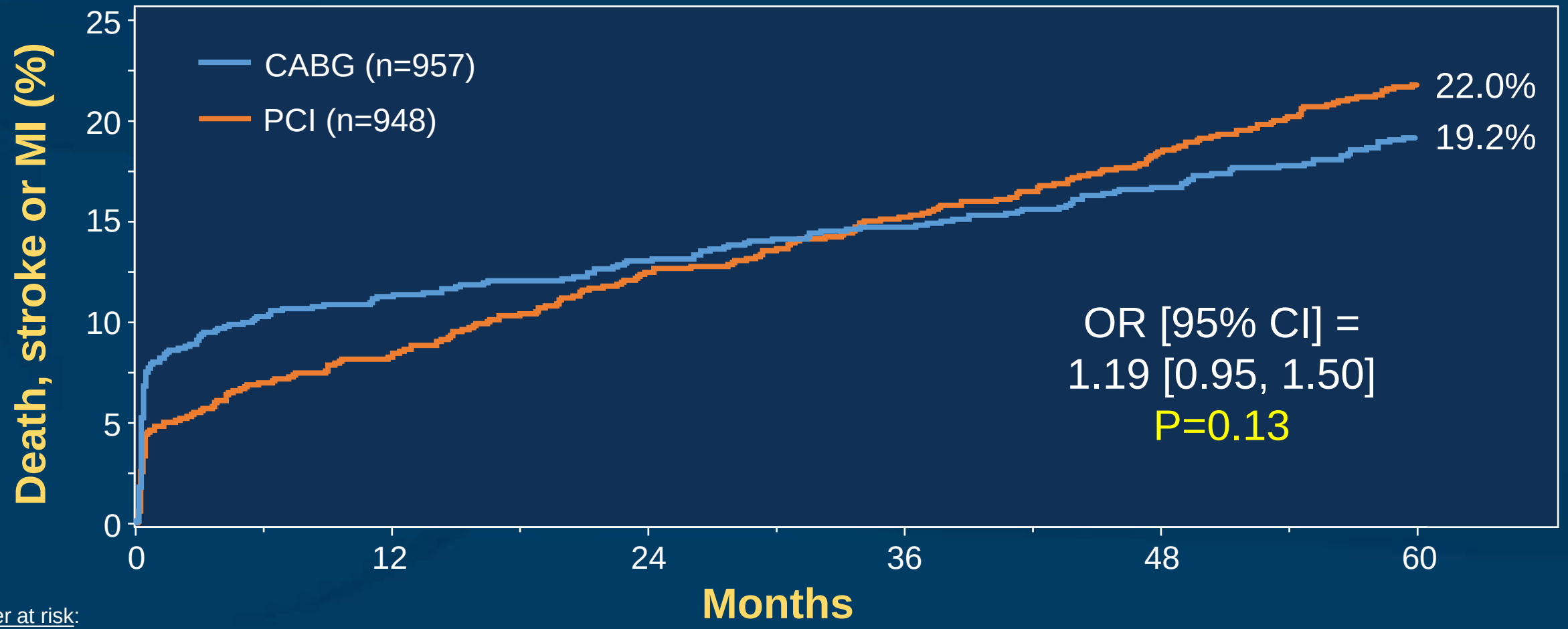

Number at risk:

| | | | | |
|---|---|---|---|---|
| PCI | 948 | 850 | 784 | 445 |
| CABG | 957 | 817 | 763 | 458 |

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

# 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 |

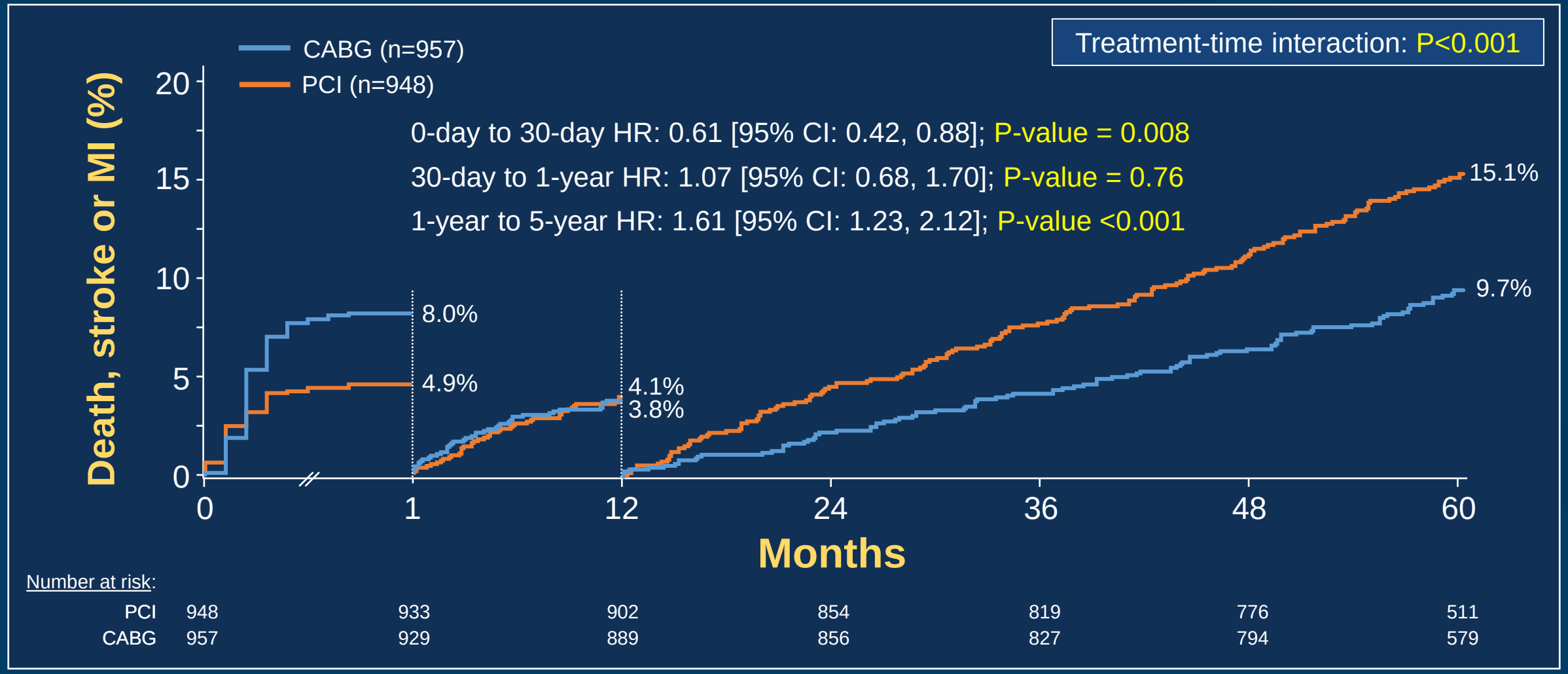
Stone GW et al. NEJM 2019;381:1820-30

EXCEL

# Piecewise Hazards

# All-cause Death, Stroke or MI

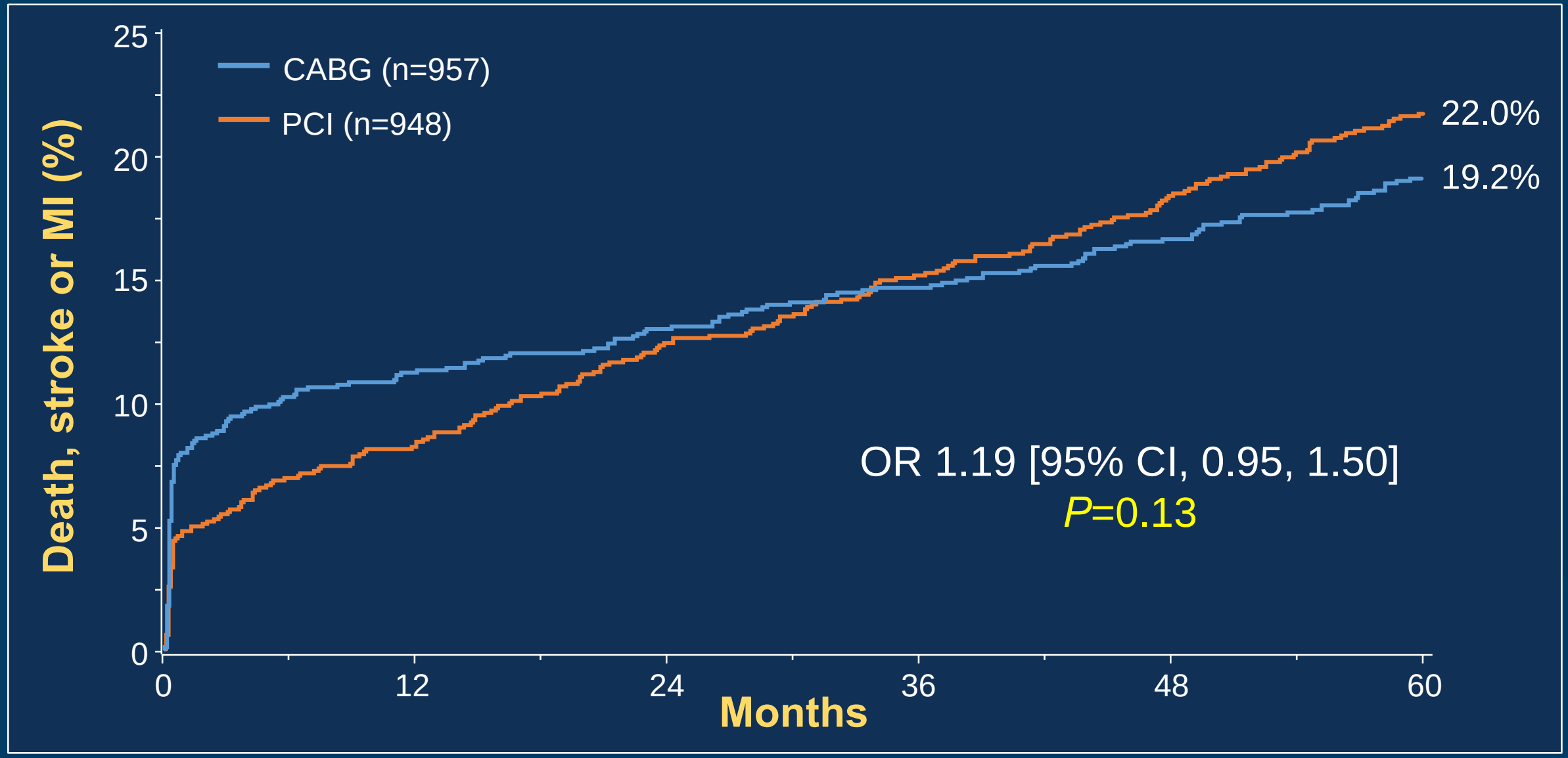
## Three distinct periods of varying relative risk



EXCEL

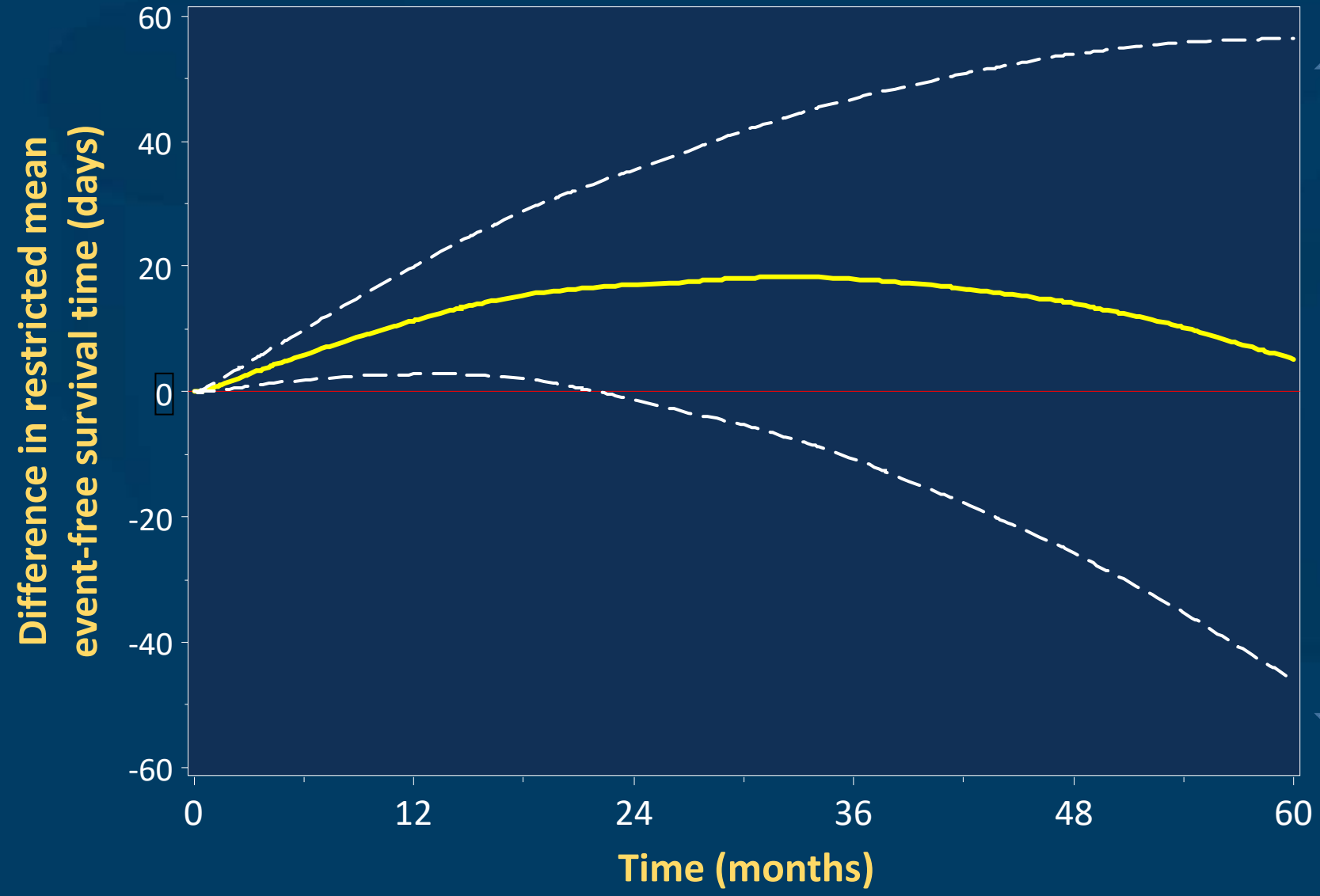
# Restricted Mean Survival Time Analysis

## 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

Stone GW et al. NEJM 2019;381:1820-30

# The Purpose of the Heart Team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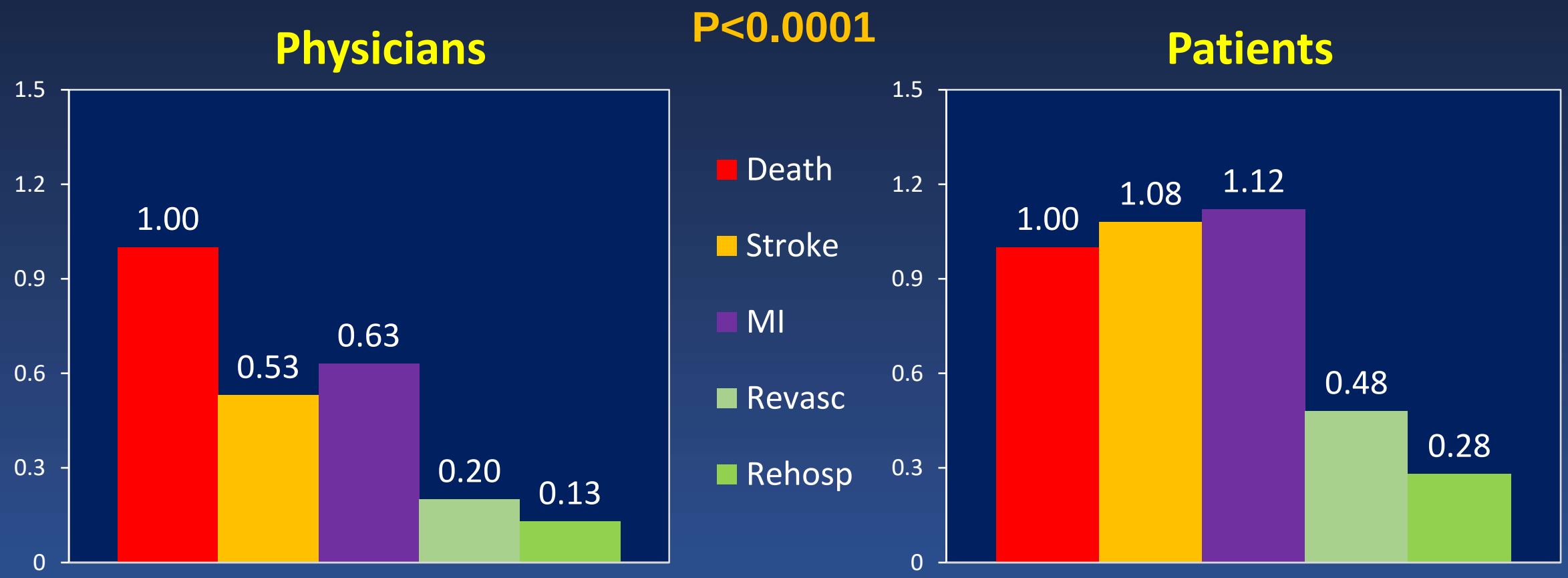
# What Outcomes Matter Most to Doctors and Patients?

164 clinical trialists and 785 CV pts weighted the relative importance of death, stroke, MI coronary revasc (PCI or CABG), and hosp for angina

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Stolker JM et al. Circulation. 2014;130:1254-61

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# LM PCI vs CABG Controversies

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

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

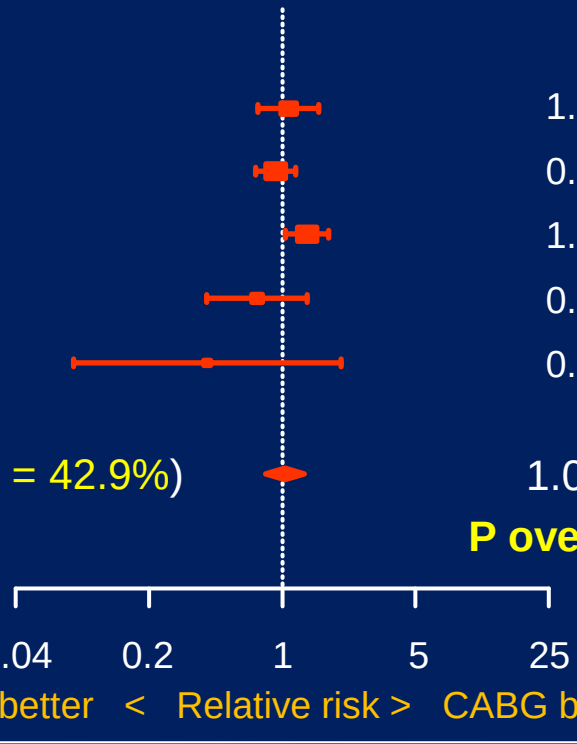
## Including long-term EXCEL, NOBLE and SYNTAX data

## All-cause Death

| Study and Year | PCI Events | PCI N | CABG Events | CABG N | Weight (%) | Relative risk [95% CI] |
|---|---|---|---|---|---|---|
| Risk of death | | | | | | |
| NOBLE – 5 year, 2019 | 54 | 592 | 50 | 592 | 22.4 | 1.08 [0.75, 1.56] |
| SYNTAX – 10 year, 2019 | 93 | 357 | 98 | 348 | 32.9 | 0.93 [0.73, 1.18] |
| EXCEL – 5 year, 2019 | 119 | 948 | 89 | 957 | 31.3 | 1.35 [1.04, 1.75] |
| PRECOMBAT – 5 year, 2015 | 17 | 300 | 23 | 300 | 11.4 | 0.74 [0.40, 1.36] |
| Boudriot – 1 year 2011 | 2 | 100 | 5 | 101 | 2.0 | 0.40 [0.08, 2.03] |
| REML model for all studies (Q=7.28, df=4, p for heterogeneity=0.12; $I^2$ = 42.9%) | | | | | | 1.03 [0.82, 1.30] |

**P overall effect = 0.78**

Moderate heterogeneity due to EXCEL. If EXCEL removed:
RR 0.93, 95% CI 0.77–1.13; P= 0.47; $I^2$ = 0.0%

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Ahmad Y et al. EHJ 2020;41:3228-35

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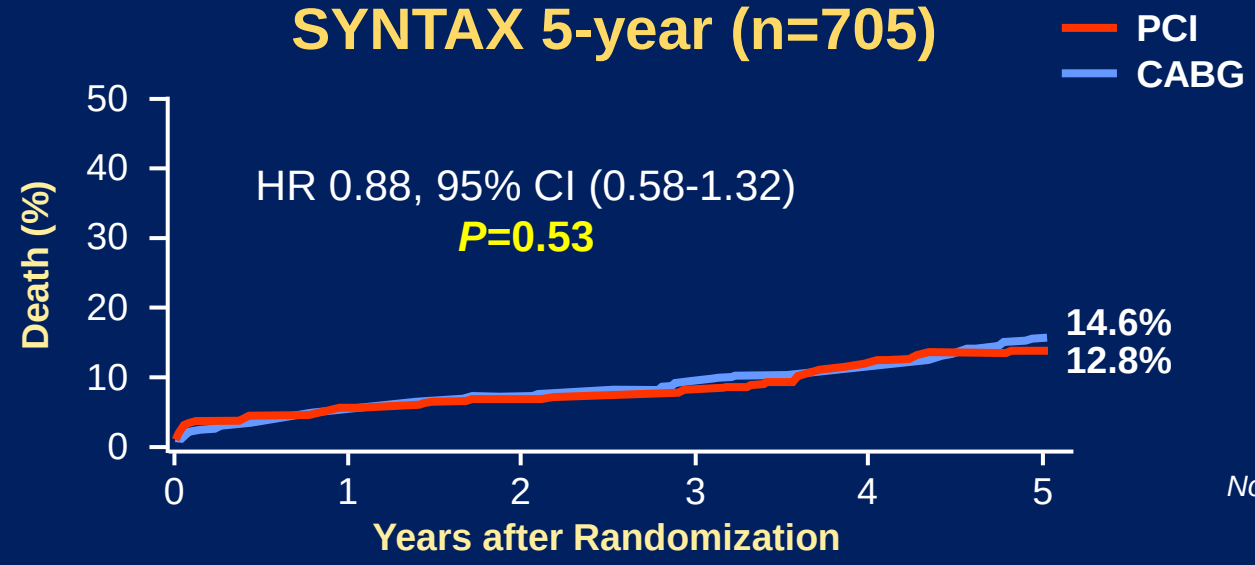
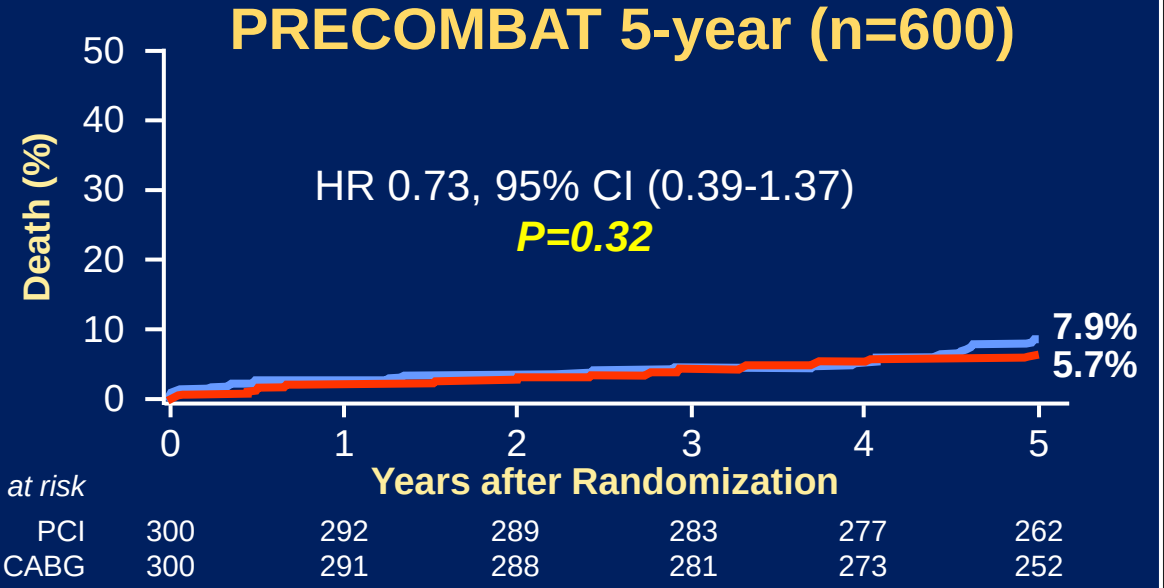
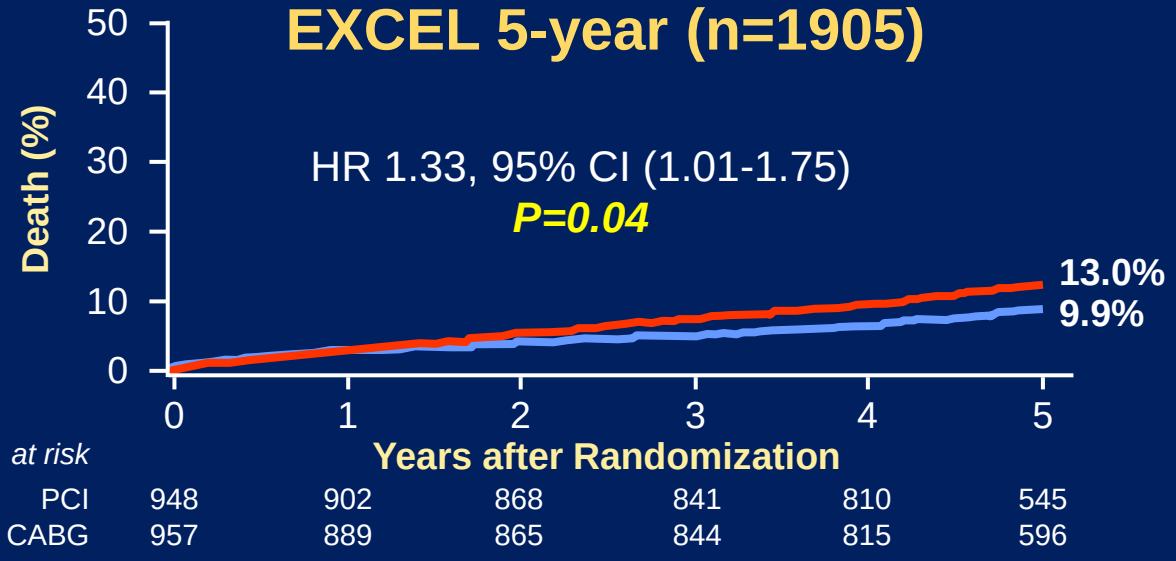
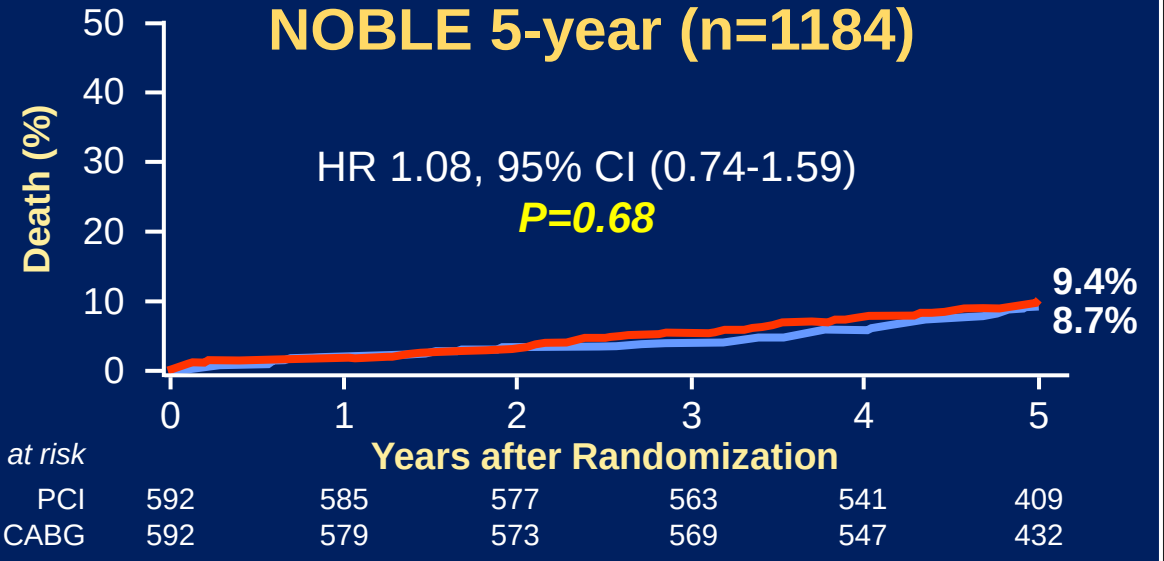
# Long-term Mortality after LM DES vs CABG (n=4,394)

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Morice MC et al. *Circulation* 2014;129:2388-94; Ahn JM et al. *JACC* 2015;65:2198–206
Stone GW et al. *NEJM* 2019:381:1820-30; Holm NR et al. Lancet 2019:on-line

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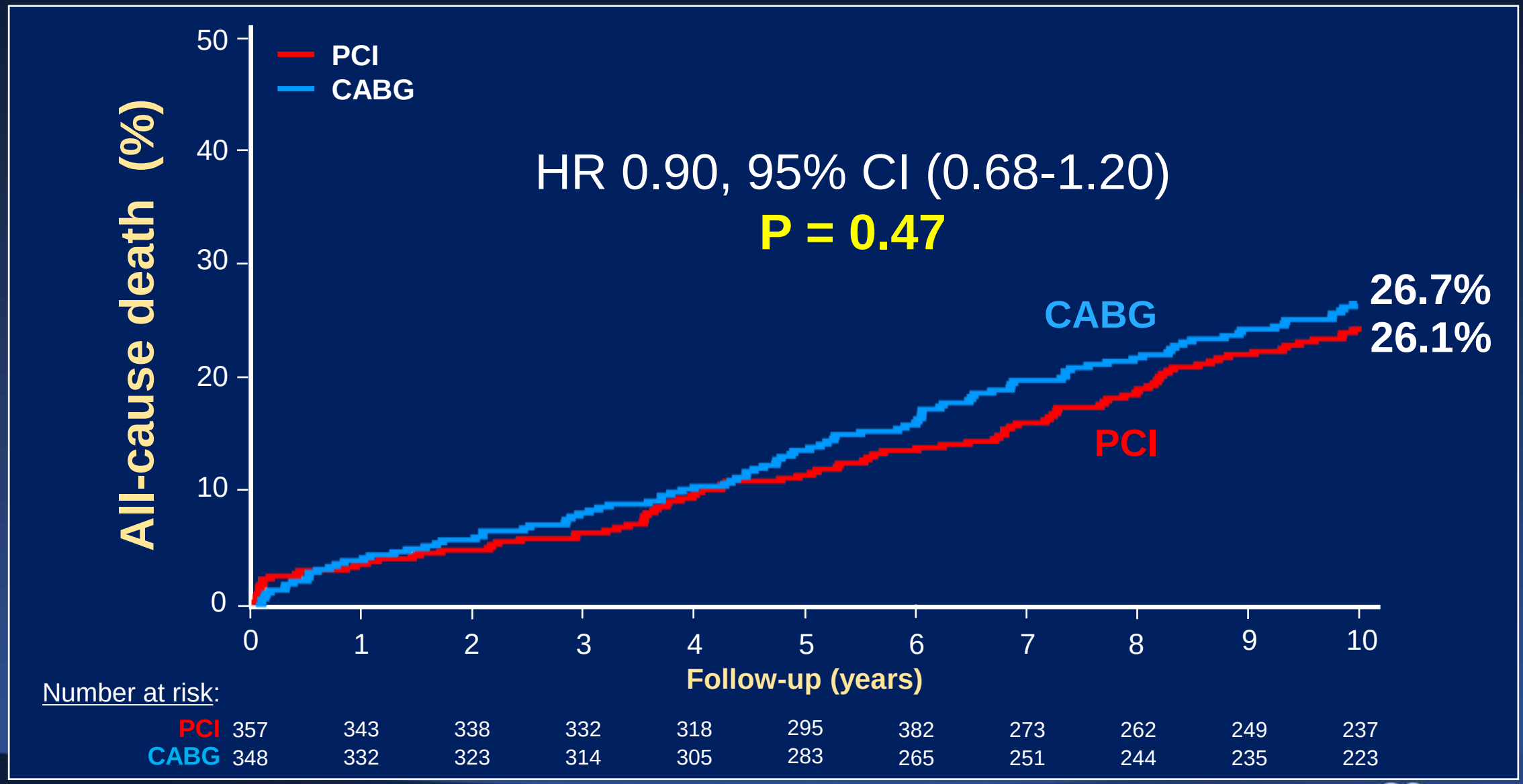
# SYNTAX Left Main at 10 Years: Mortality

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Thuijs DJFM et al. Lancet. 2019;394(10206):1325-34

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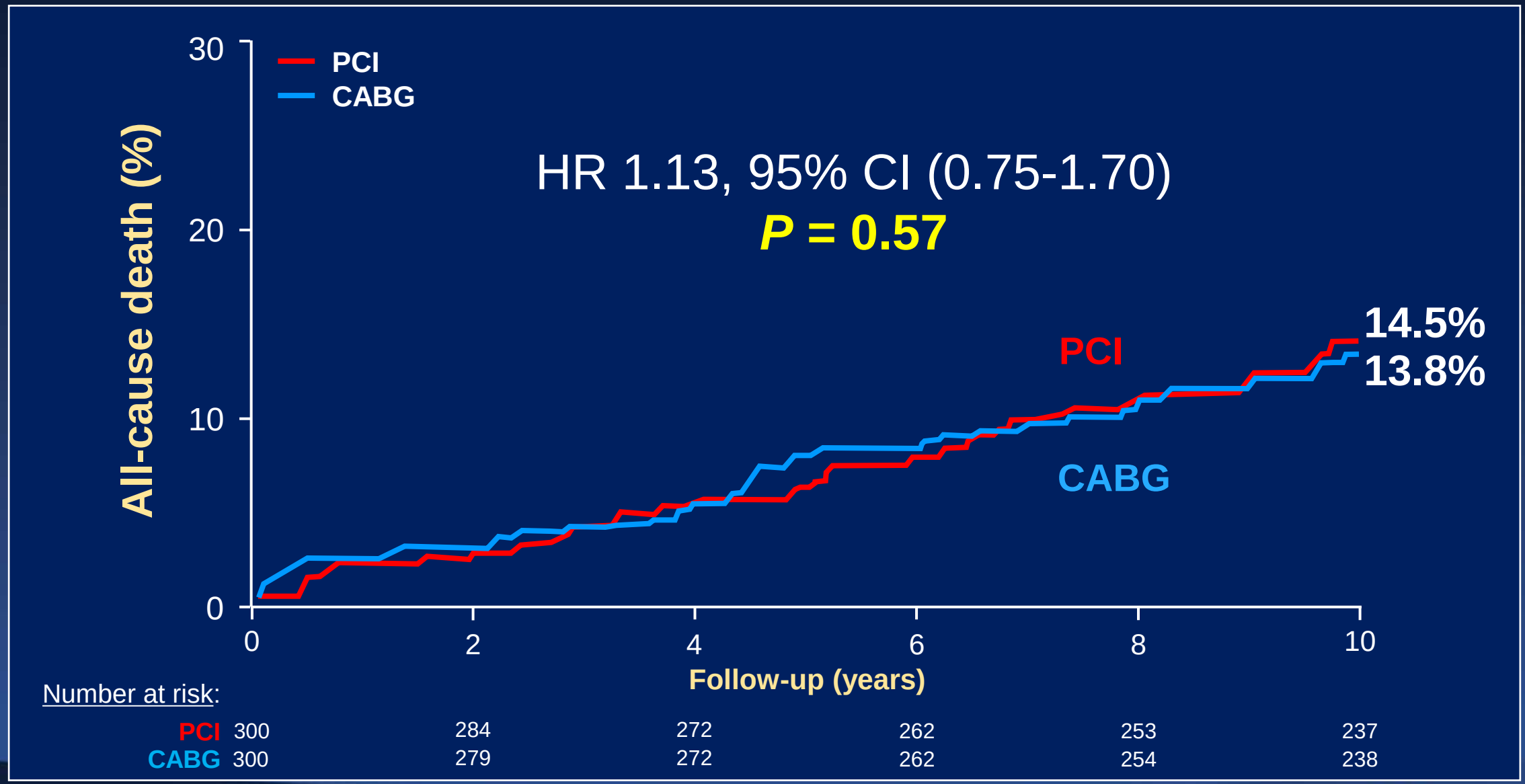
# PRECOMBAT Left Main at 10 Years: Mortality

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Park DW et al. *Circulation*. 2020;141:1437–46

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# LM PCI vs CABG Controversies

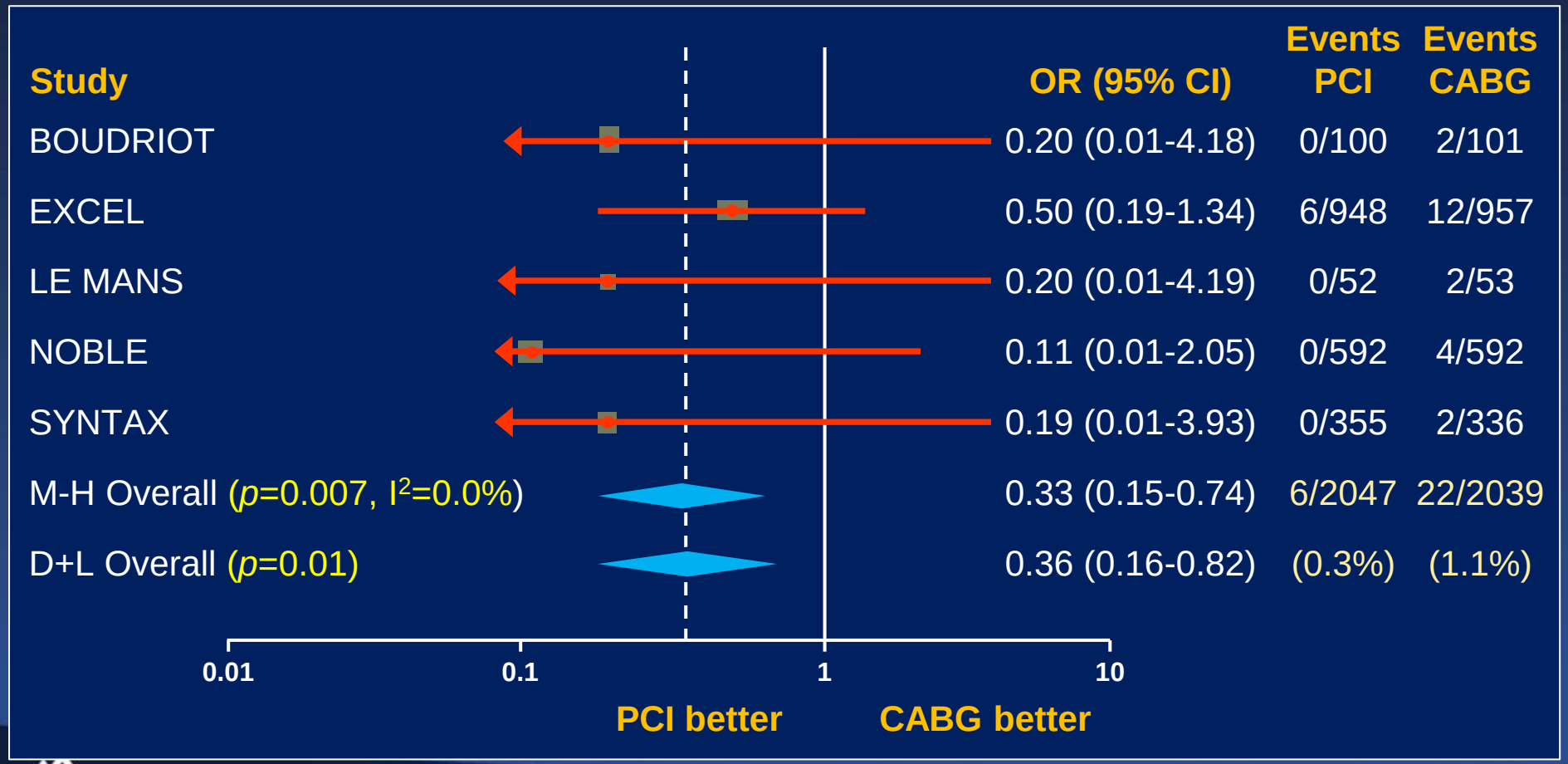
## Are Stroke Rates Different?

# Updated Meta-analysis of LM DES Trials

## 6 RCTs, 4,686 pts, longest FU (median 39 mos)

(EXCEL, NOBLE, SYNTAX, PRECOMBAT, Boudriot et al, Le MANS)

## 30-day Stroke




1-year Stroke
RR 0.38, 95% CI 0.19–0.77;
P=0.008, $I^2$=7.3%

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Palmerini T et al. Am Heart J 2017;190:54-63
Ahmad Y et al. EHJ 2020;41:3228-35


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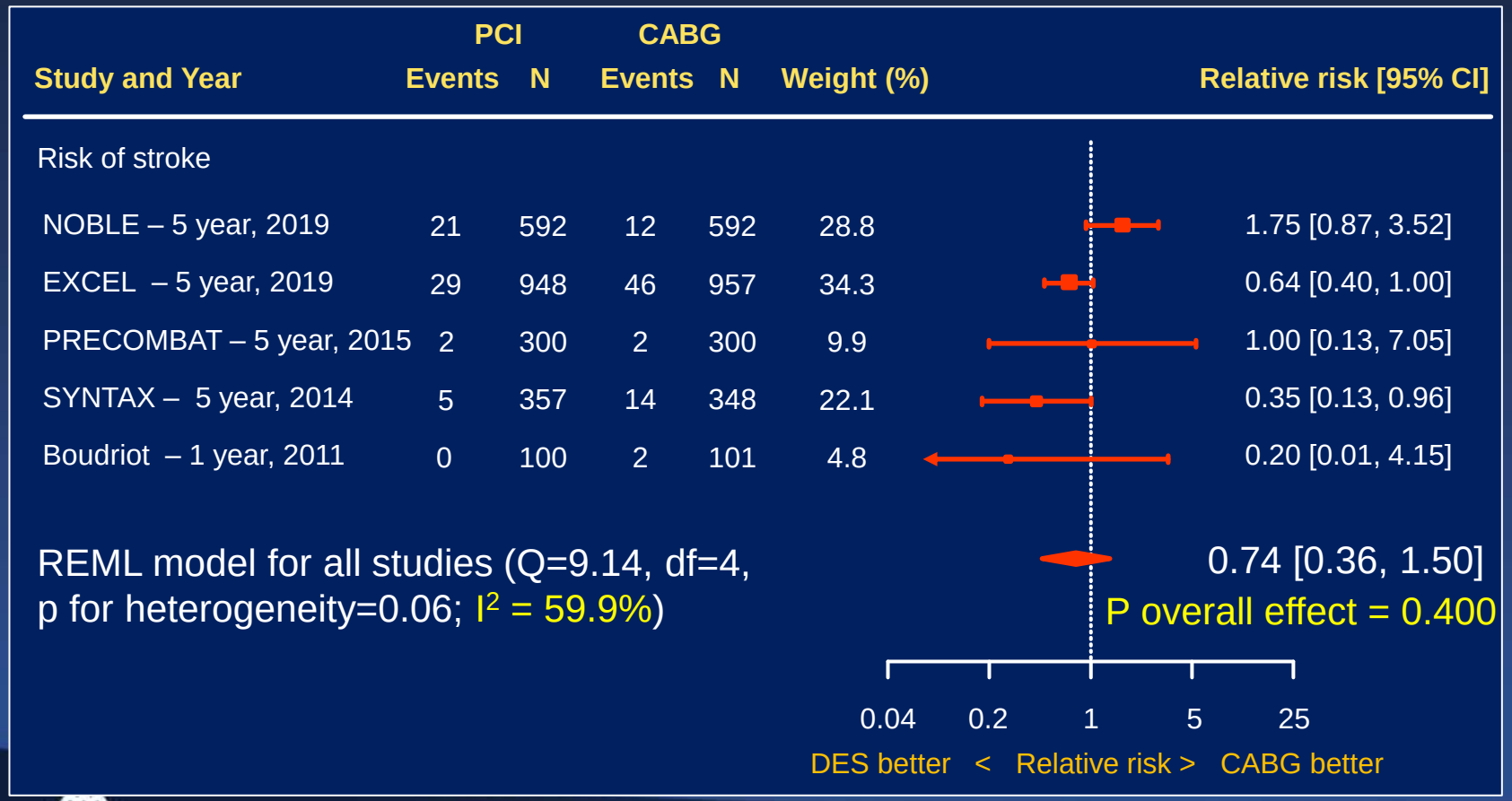
# Updated Meta-analysis of LM DES vs. CABG Trials

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

## Including long-term EXCEL, NOBLE and SYNTAX data

## Stroke




High 5-year heterogeneity due to high rates of stroke b/t 1 and 5 years in NOBLE

If NOBLE removed: RR 0.58, 95% CI 0.39–0.86, P=0.008; $I^2$ = 0.0%;

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Ahmad Y et al. EHJ 2020;41:3228-35

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# LM PCI vs CABG Controversies

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

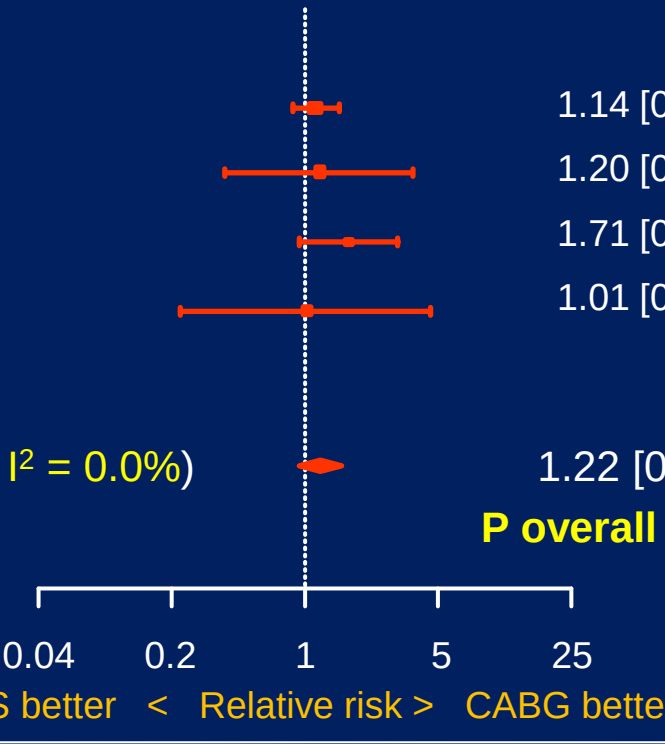
## 5 RCTs, 4,612 pts, mean 5.6-year FU

## Including long-term EXCEL, NOBLE and SYNTAX data

## **All MI** (procedural + non-procedural)

| Study and Year | PCI Events | PCI N | CABG Events | CABG N | Weight (%) | Relative risk [95% CI] |
|---|---|---|---|---|---|---|
| Risk of MI | | | | | | |
| EXCEL – 5 year, 2019 | 95 | 948 | 84 | 957 | 76.5 | 1.14 [0.86, 1.51] |
| PRECOMBAT – 5 year, 2015 | 6 | 300 | 5 | 300 | 4.3 | 1.20 [0.37, 3.89] |
| SYNTAX – 5 year, 2014 | 28 | 357 | 16 | 348 | 16.8 | 1.71 [0.94, 3.10] |
| Boudriot – 1 year, 2011 | 3 | 100 | 3 | 101 | 2.4 | 1.01 [0.21, 4.89] |
| REML model for all studies (Q=1.49, df=3, p for heterogeneity=0.69; $I^2$ = 0.0%) | | | | | | 1.22 [0.96, 1.56] |

**P overall effect = 0.11**

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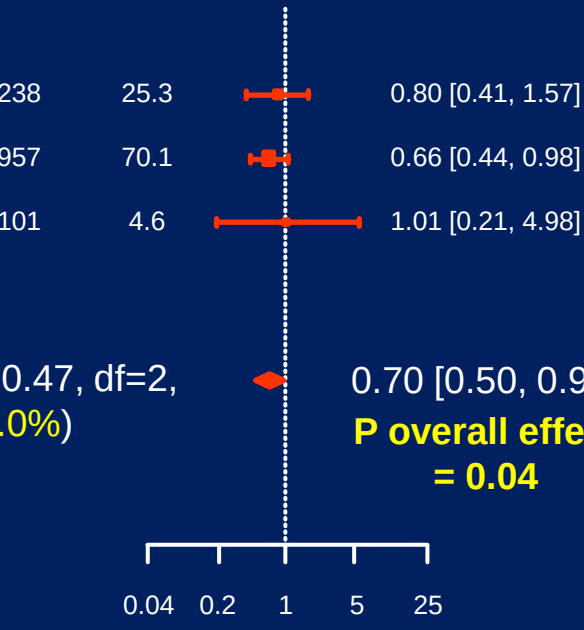
# Updated Meta-analysis of LM DES vs. CABG Trials

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

### Including long-term EXCEL, NOBLE and SYNTAX data

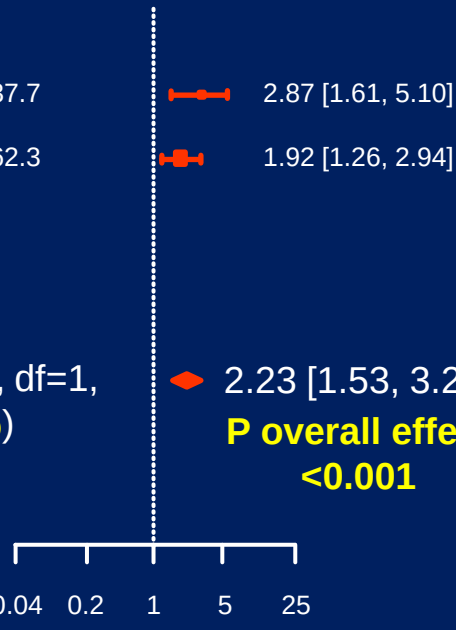
## Procedural MI

| Study and Year | PCI Events | PCI N | CABG Events | CABG N | Weight (%) | Relative risk [95% CI] |
|---|---|---|---|---|---|---|
| Risk of peri-procedural MI | | | | | | |
| NOBLE – 5 year, 2019 | 16 | 296 | 16 | 238 | 25.3 | 0.80 [0.41, 1.57] |
| EXCEL – 5 year, 2019 | 37 | 948 | 57 | 957 | 70.1 | 0.66 [0.44, 0.98] |
| Boudriot – 1 year, 2011 | 3 | 100 | 3 | 101 | 4.6 | 1.01 [0.21, 4.98] |
| REML model for all studies (Q=0.47, df=2, p for heterogeneity=0.79; $I^2$ = 0.0%) | | | | | | 0.70 [0.50, 0.99] **P overall effect = 0.04** |




## Non-procedural MI

| Study and Year | PCI Events | PCI N | CABG Events | CABG N | Weight (%) | Relative risk [95% CI] |
|---|---|---|---|---|---|---|
| Risk of spontaneous MI | | | | | | |
| NOBLE – 5 year, 2019 | 43 | 592 | 15 | 592 | 37.7 | 2.87 [1.61, 5.10] |
| EXCEL – 5 year, 2019 | 59 | 948 | 31 | 957 | 62.3 | 1.92 [1.26, 2.94] |
| REML model for all studies (Q=1.20, df=1, p for heterogeneity=0.27; $I^2$ = 16.5%) | | | | | | 2.23 [1.53, 3.27] **P overall effect <0.001** |

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Ahmad Y et al. EHJ 2020;41:3228-35

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# LM PCI vs CABG Controversies

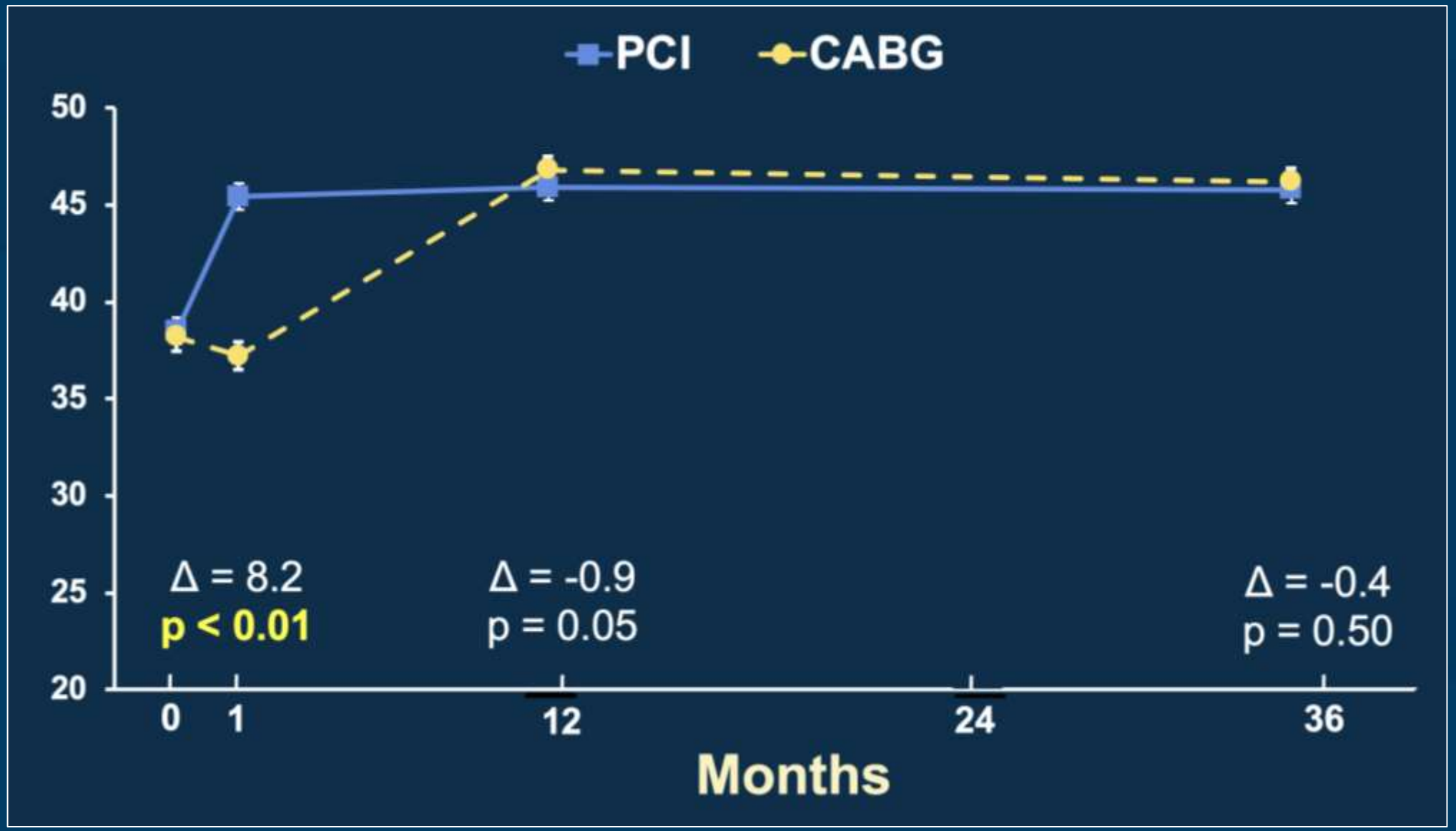
# Major Adverse Events Within 30 Days

| | 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.

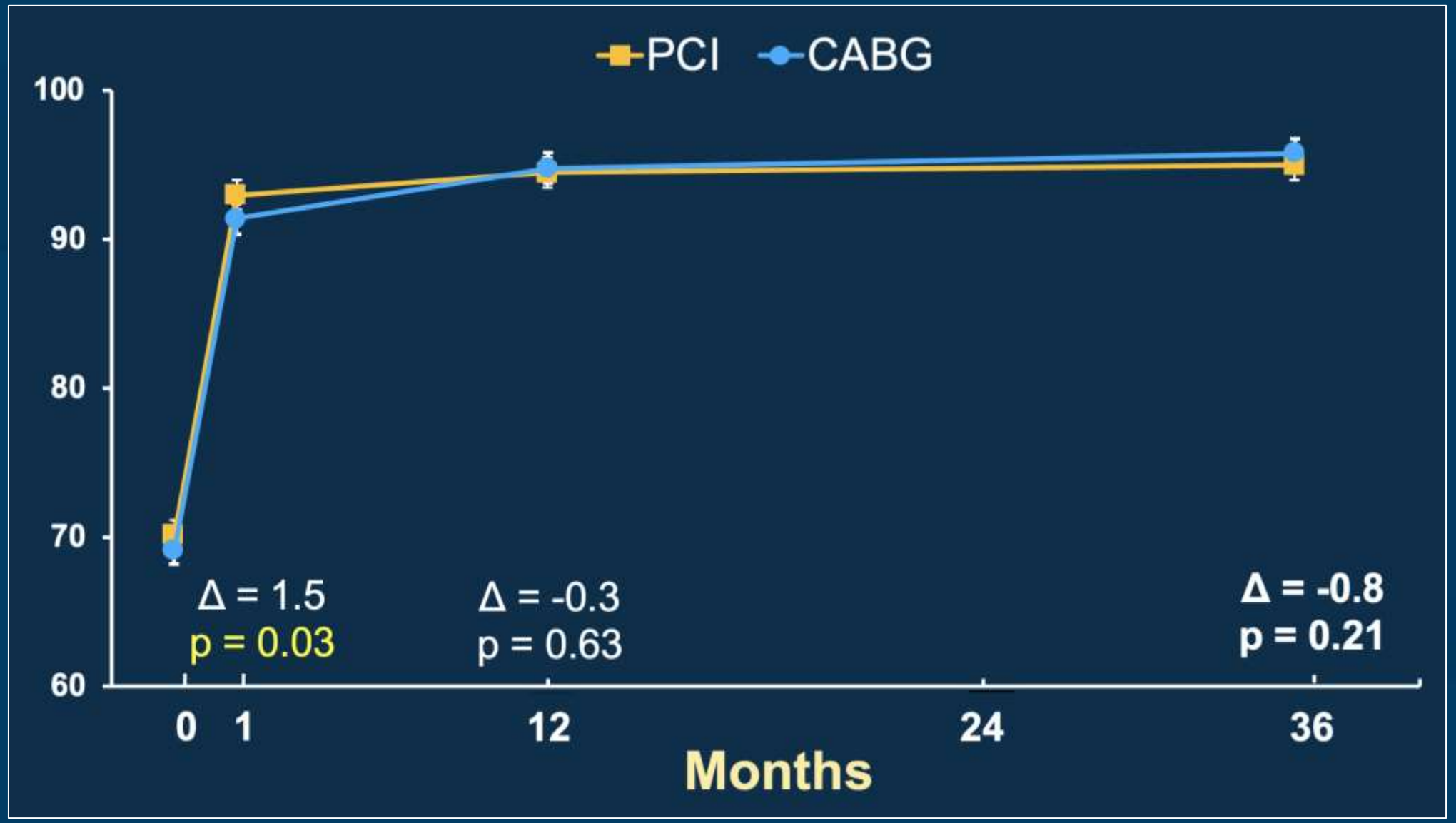
**Stone GW et al. N Engl J Med 2016;375:2223-35**

# SF-12 Physical Summary Scale



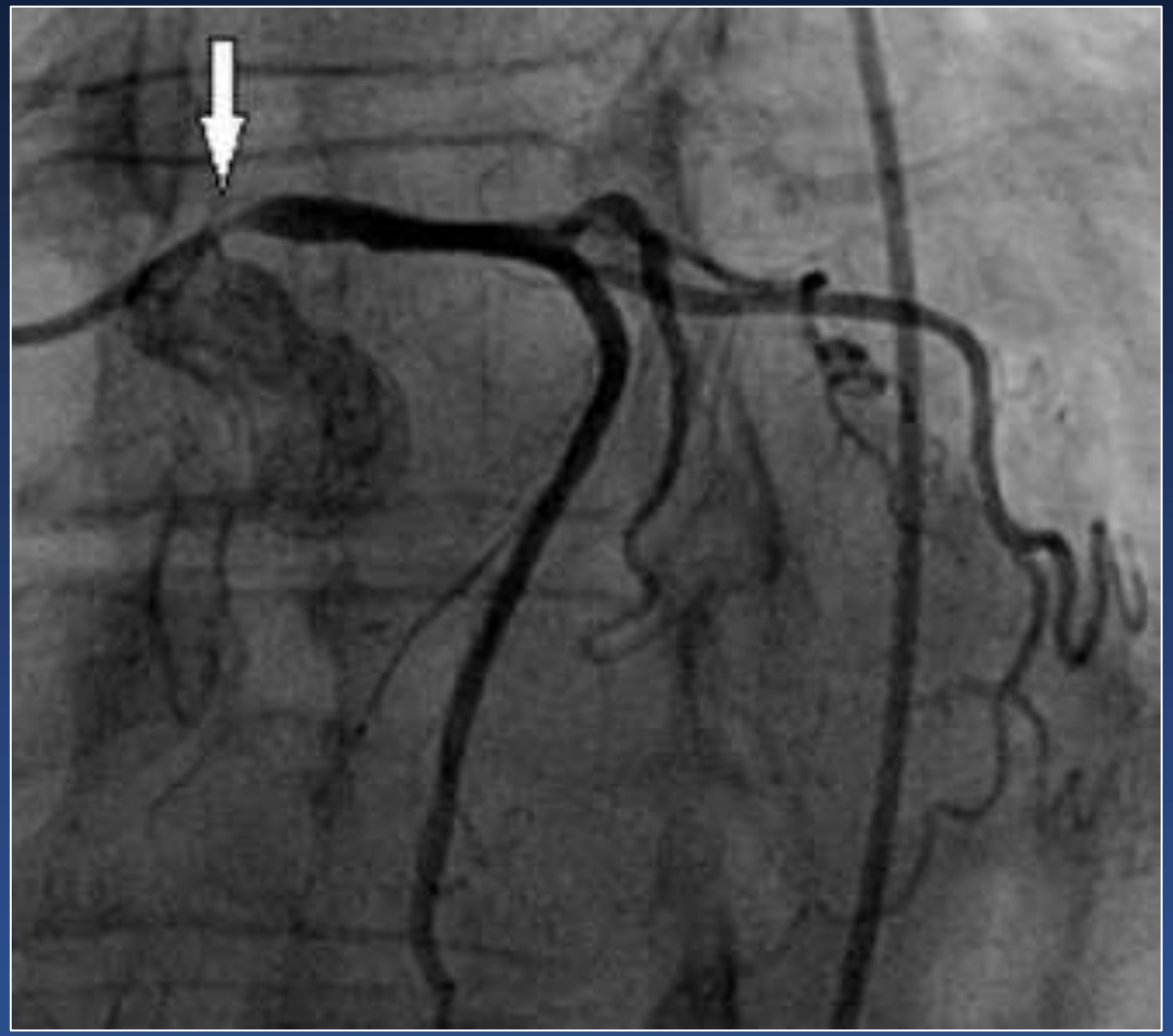

Baron SJ et al. JACC 2017;70:3113-22

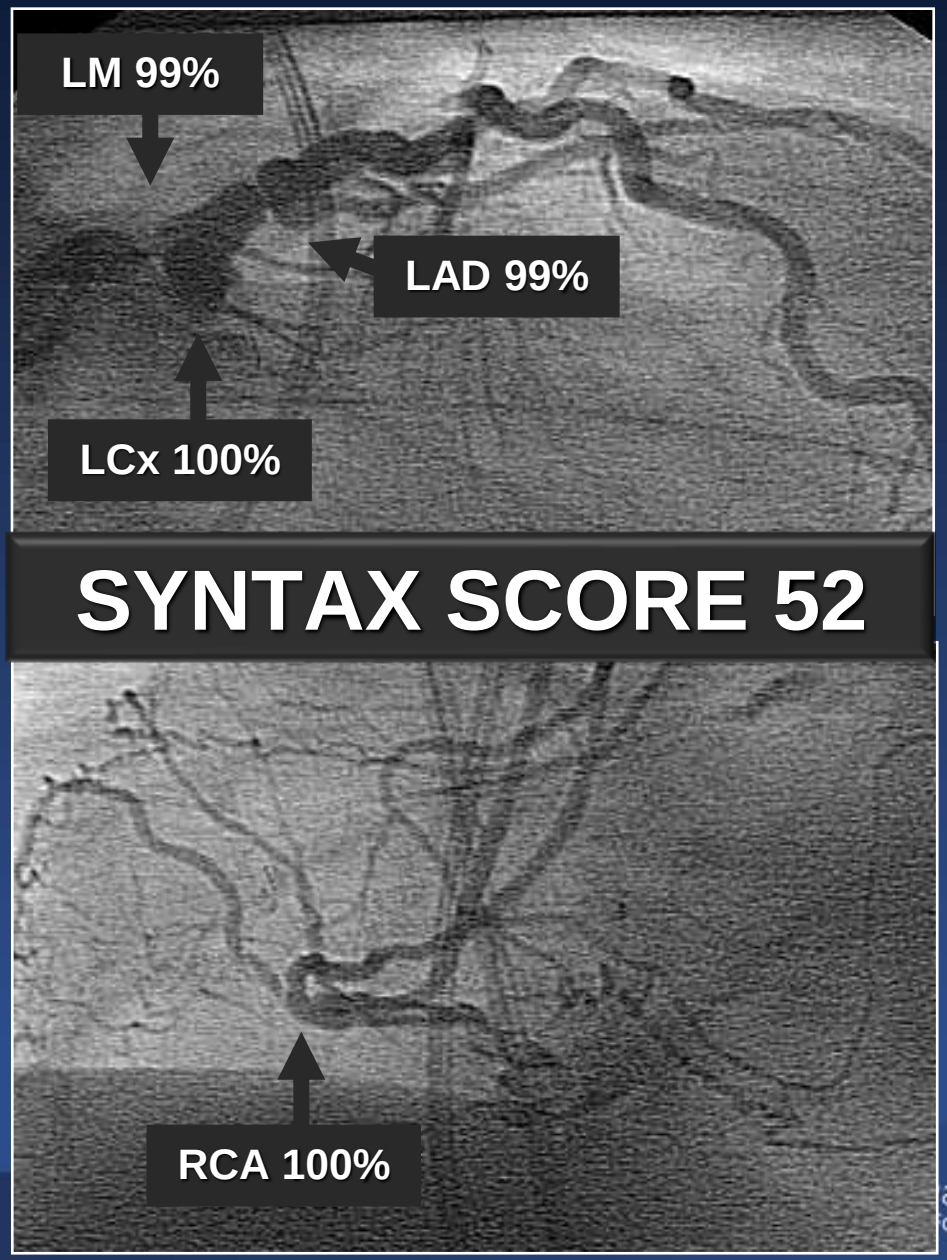
# SAQ-Angina Frequency




Baron SJ et al. JACC 2017;70:3113-22

# Obvious Choices vs. Equipoise



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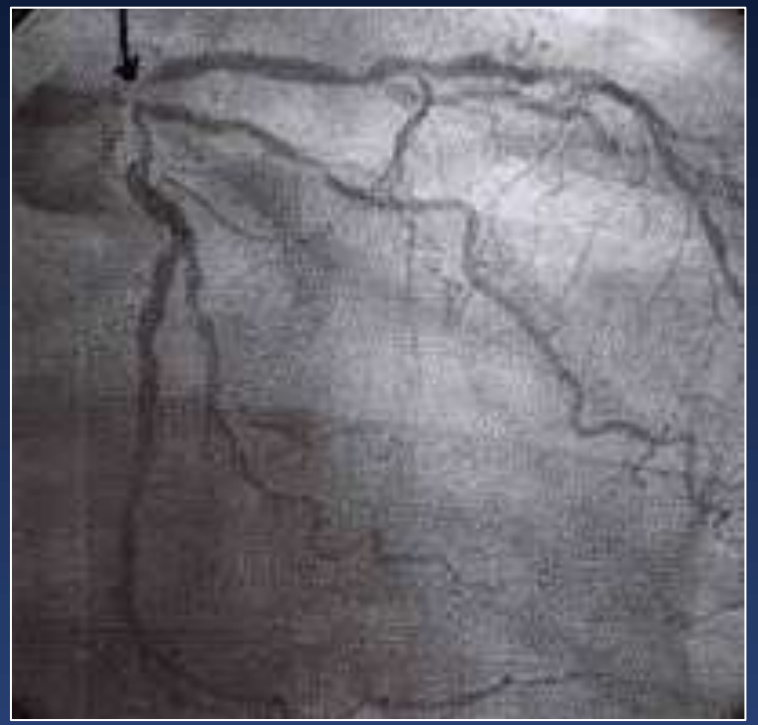
# Obvious Choices vs. Equipoise



# Left Main PCI vs. CABG Heart Team Discussions:

## Two very different procedures

### PCI

<u>Early advantages</u>

- 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

<u>Late advantages</u>

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

### PCI and CABG

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