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# Impact of the SYNTAX score in patients with diabetes and left-main and/or multivessel coronary disease: a pooled analysis of individual patient level data from the SYNTAX, PRECOMBAT and BEST trials

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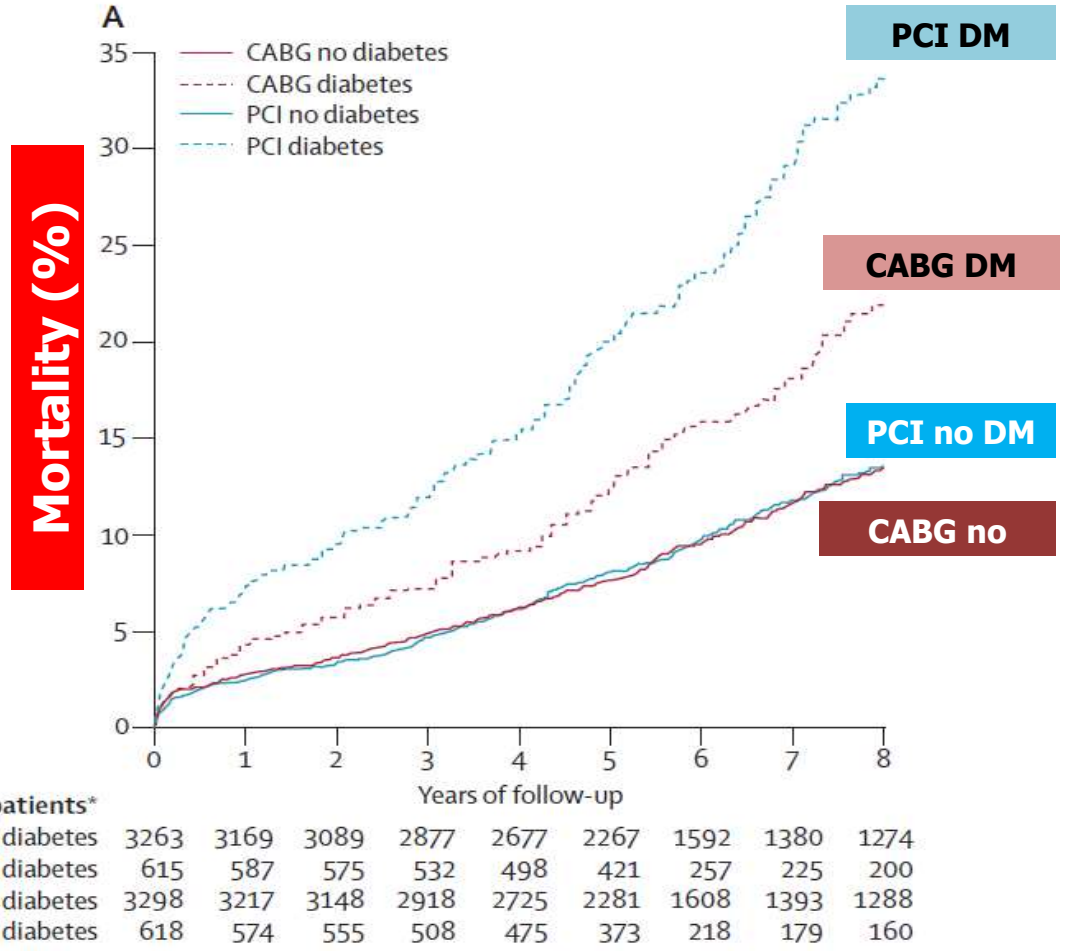
# Background 1: DM is associated with poor outcomes after CABG and PCI

**Coronary artery bypass surgery compared with percutaneous coronary interventions for multivessel disease: a collaborative analysis of individual patient data from ten randomized trials.** Hlatky et al. Lancet 2009

**10 randomized trials; ARTS(N=1205), BARI(N=1829), CABRI(N=1054), EAST(N=392), ERACI-II(N=450), GABI(N=323), MASS-II(N=408), RITA(N=1011), SoS(N=988), Toulouse10(N=152)**

↓

**6 Balloon trials**
**4 BMS trials**



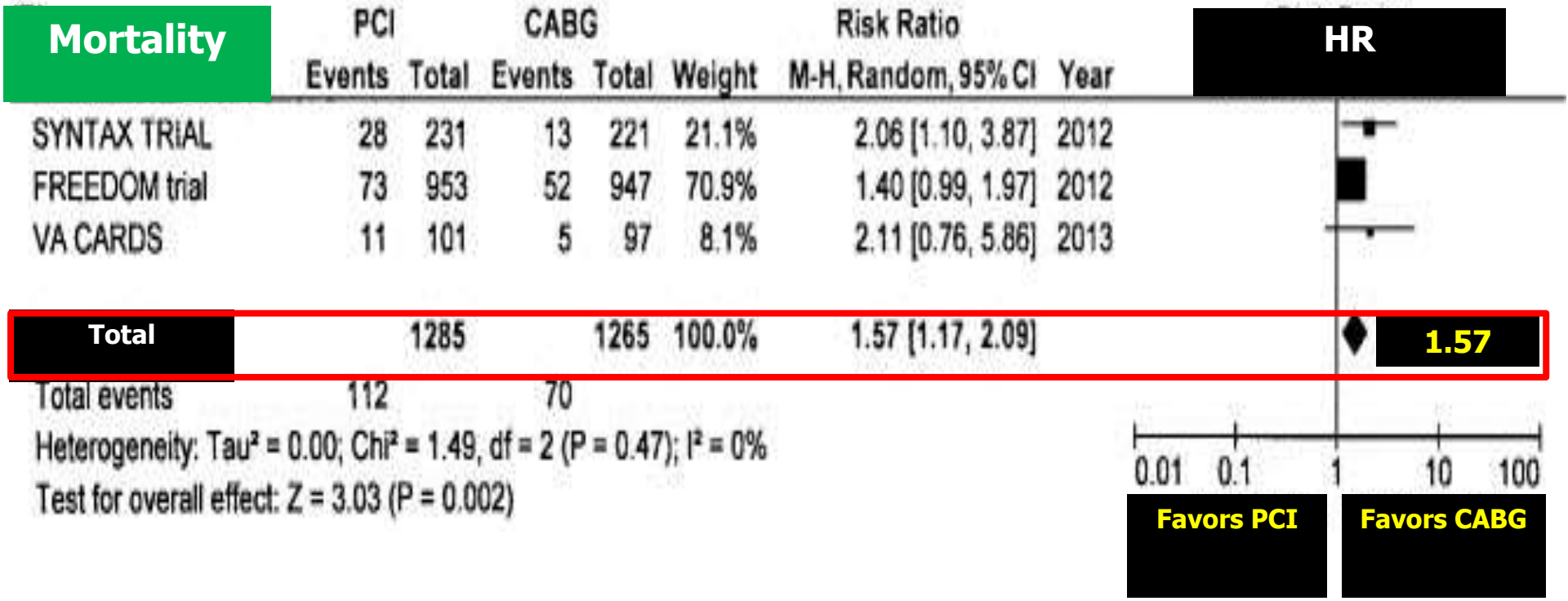
# Background 2: Previous meta-analysis of RCTs

| | SYNTAX Trial | CARDia Study | FREEDOM Trial | VA CARDS |
|---|---|---|---|---|
| Study type | Subgroup of RCT (noninferiority) | RCT (noninferiority) | RCT (superiority) | RCT |
| Study criteria | De novo LM and/or 3VD randomized to PCI or CABG | Diabetics with MVD or ostial/proximal LAD | Diabetics with MVD >70% in ≥2 major epicardial vessels | Diabetics with MVD including the LAD or isolated proximal LAD |
| Type of Stents | PES | BMS(31%), SES(69%) | SES/PES | SES/PES/ZES |
| Total No. of PCI patients | 231 | 256 | 953 | 101 |
| Total No. of CABG patients | 221 | 254 | 947 | 97 |
| Mean SYNTAX Score | 29±11.2 | N/A | 26.2±8.2 | 22.1±9.0 |
| Patients with 3VD | 71% | 65% | 83% | N/A |
| Patients with DES | 100% | 69% | 100% | 95.5% |
| Follow up | 5Y | 5.1Y | 3.8Y | 2Y |
| 1 Year death, MI, stroke,revascularization (PCI vs CABG) | 26.0 vs. 14.2% (p=0.003) | 19.3 vs. 11.3% (p=0.02) | 16.8 vs. 11.8% (p=0.004) | 17.5 vs. 17.1% (p=NS) |

Huang et al. CARDIOLOGY 2014, Harskamp et al. Cardior Ther. 2013

# Background 2: Previous meta-analysis of RCTs

**Effectiveness of Percutaneous Coronary Intervention With Drug-Eluting Stents Compared With Bypass Surgery in Diabetics With Multivessel Coronary Disease: Comprehensive Systematic Review and Meta-analysis of Randomized Clinical Data**




Hakeem et al. JAHA 2014

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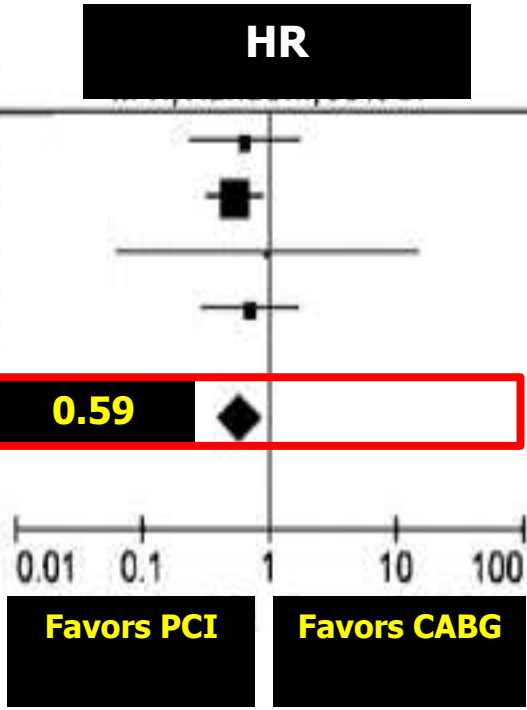
**Effectiveness of Percutaneous Coronary Intervention With Drug-Eluting Stents Compared With Bypass Surgery in Diabetics With Multivessel Coronary Disease: Comprehensive Systematic Review and Meta-analysis of Randomized Clinical Data**

**Stroke**

| | PCI | | CABG | | | Risk Ratio | |
|---|---|---|---|---|---|---|---|
| | Events | Total | Events | Total | Weight | M-H, Random, 95% CI | Year |
| SYNTAX TRIAL | 6 | 231 | 9 | 221 | 16.6% | 0.64 [0.23, 1.76] | 2012 |
| FREEDOM trial | 20 | 953 | 37 | 947 | 59.6% | 0.54 [0.31, 0.92] | 2012 |
| VA CARDS | 1 | 101 | 1 | 97 | 2.3% | 0.96 [0.06, 15.14] | 2013 |
| CARDIA Study | 8 | 254 | 11 | 248 | 21.5% | 0.71 [0.29, 1.74] | 2013 |
| **Total** | | 1539 | | 1513 | 100.0% | 0.59 [0.39, 0.90] | |
| Total events | 35 | | 58 | | | | |

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.42$, $df = 3$ ($P = 0.94$); $I^2 = 0\%$

Test for overall effect: $Z = 2.46$ ($P = 0.01$)




Hakeem et al. JAHA 2014

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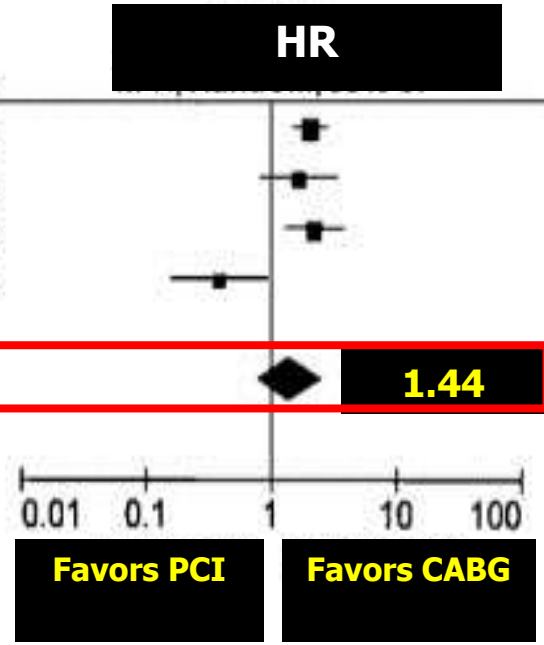
**Effectiveness of Percutaneous Coronary Intervention With Drug-Eluting Stents Compared With Bypass Surgery in Diabetics With Multivessel Coronary Disease: Comprehensive Systematic Review and Meta-analysis of Randomized Clinical Data**

**Myocardial infarction**

| | PCI | | CABG | | | Risk Ratio | |
|---|---|---|---|---|---|---|---|
| | Events | Total | Events | Total | Weight | M-H, Random, 95% CI | Year |
| FREEDOM trial | 98 | 953 | 48 | 947 | 31.3% | 2.03 [1.45, 2.83] | 2012 |
| SYNTAX TRIAL | 19 | 231 | 11 | 221 | 23.0% | 1.65 [0.80, 3.39] | 2012 |
| CARDIA Study | 36 | 254 | 16 | 248 | 26.5% | 2.20 [1.25, 3.85] | 2013 |
| VA CARDS | 6 | 101 | 15 | 97 | 19.2% | 0.38 [0.16, 0.95] | 2013 |
| **Total** | | 1539 | | 1513 | 100.0% | 1.44 [0.79, 2.60] | |
| Total events | 159 | | 90 | | | | |

Heterogeneity: $Tau^2 = 0.27$; $Chi^2 = 12.21$, $df = 3$ ($P = 0.007$); $I^2 = 75\%$

Test for overall effect: $Z = 1.19$ ($P = 0.23$)

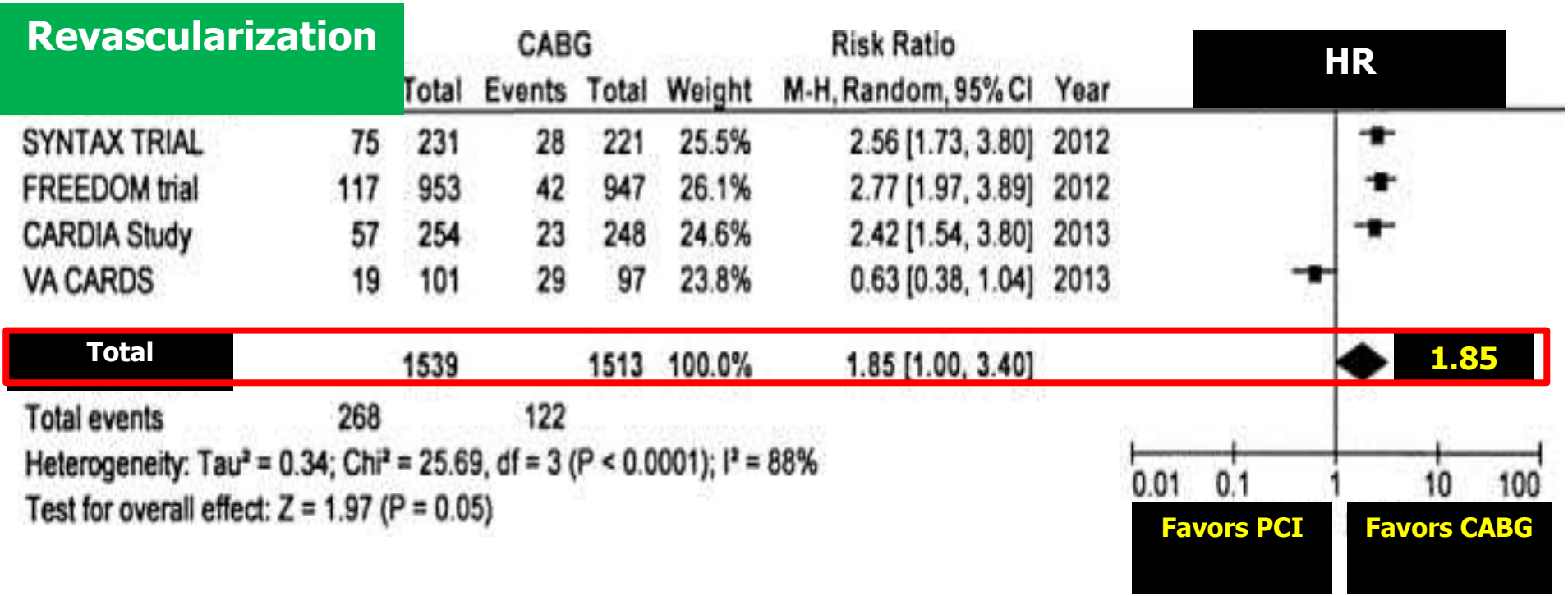



Hakeem et al. JAHA 2014

# Background 2: Previous meta-analysis of RCTs

**Effectiveness of Percutaneous Coronary Intervention With Drug-Eluting Stents Compared With Bypass Surgery in Diabetics With Multivessel Coronary Disease: Comprehensive Systematic Review and Meta-analysis of Randomized Clinical Data**

**Revascularization**




Hakeem et al. JAHA 2014

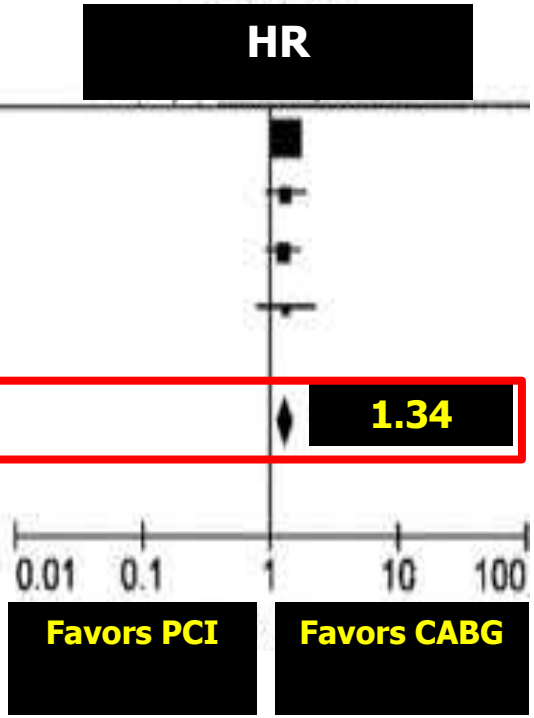
# Background 2: Previous meta-analysis of RCTs

**Effectiveness of Percutaneous Coronary Intervention With Drug-Eluting Stents Compared With Bypass Surgery in Diabetics With Multivessel Coronary Disease: Comprehensive Systematic Review and Meta-analysis of Randomized Clinical Data**

| MACE | PCI Events | PCI Total | CABG Events | CABG Total | Weight | Risk Ratio M-H, Random, 95% CI | Year |
|---|---|---|---|---|---|---|---|
| FREEDOM trial | 200 | 953 | 146 | 947 | 56.2% | 1.36 [1.12, 1.65] | 2012 |
| SYNTAX TRIAL | 54 | 231 | 39 | 221 | 15.5% | 1.32 [0.92, 1.91] | 2012 |
| CARDIA Study | 68 | 254 | 52 | 248 | 21.1% | 1.28 [0.93, 1.75] | 2013 |
| VA CARDS | 25 | 101 | 18 | 97 | 7.3% | 1.33 [0.78, 2.28] | 2013 |
| **Total** | | 1539 | | 1513 | 100.0% | 1.34 [1.16, 1.54] | |
| Total events | 347 | | 255 | | | | |

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.12$, df = 3 ($P = 0.99$); $I^2 = 0\%$

Test for overall effect: $Z = 3.91$ ($P < 0.0001$)

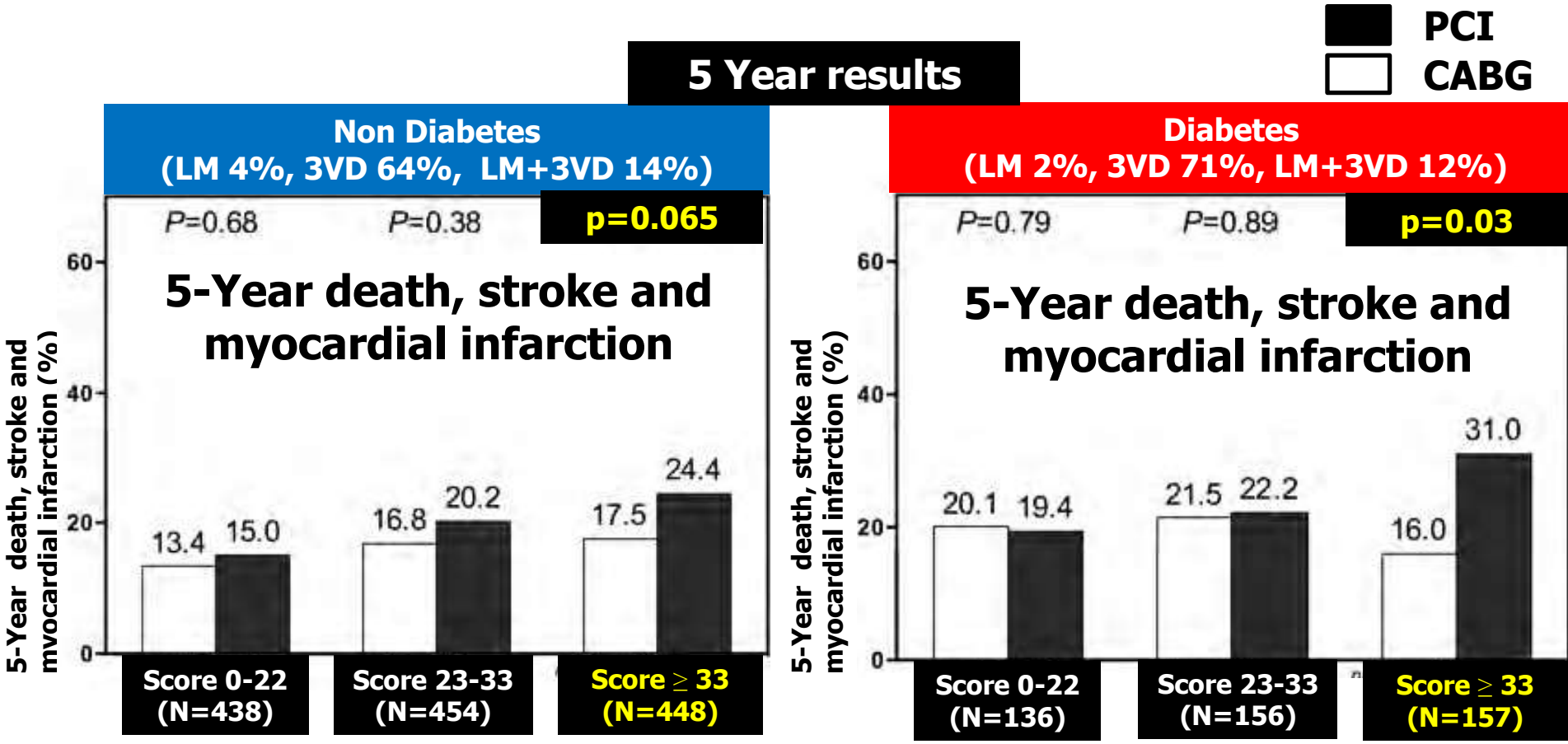



Hakeem et al. JAHA 2014

# Background 3: Syntax

**In the Syntax trial, interaction between Syntax Score and outcomes in Diabetic population were suggested.**

## Non Diabetes (1348pts) versus Diabetes (452pts)




Kappetein et al. EJCTS 2013

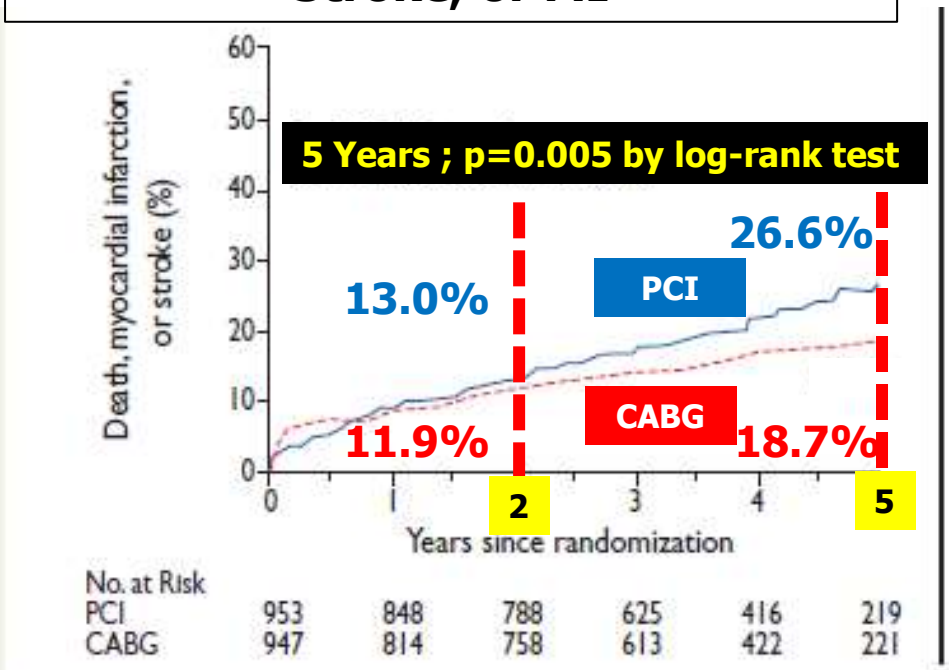
# Background 4: Freedom study

## SES/PES vs. CABG

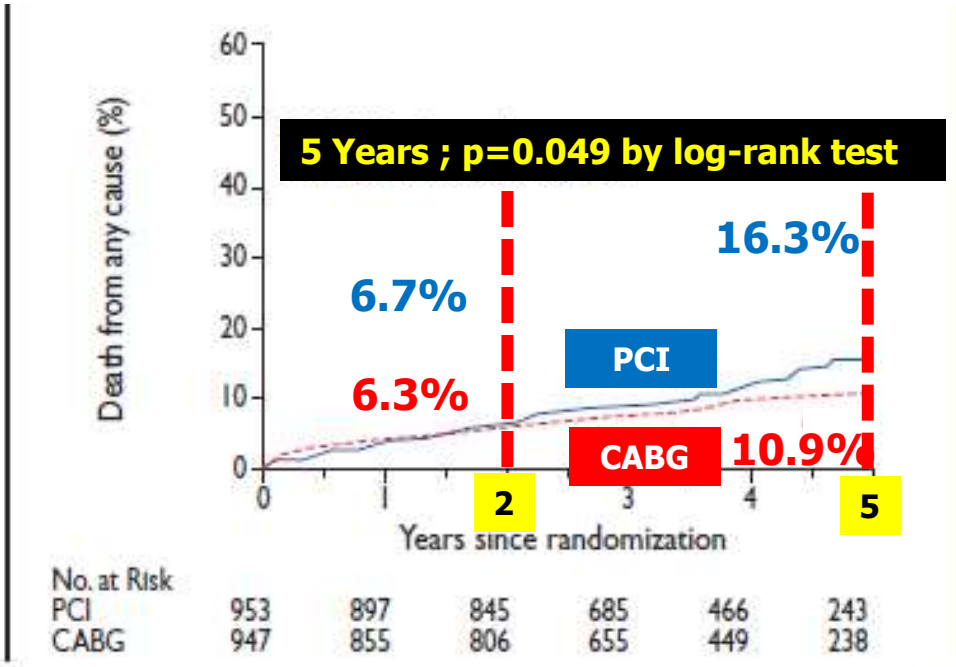
**Strategies for multivessel revascularization in patients with diabetes.**

**5 Year results**

**A composite end point of death, Stroke, or MI**




**Death from any cause**




**In the Freedom trial, CABG had better outcomes compared to PCI. Interaction between Syntax Score and outcomes were not yet analyzed…**

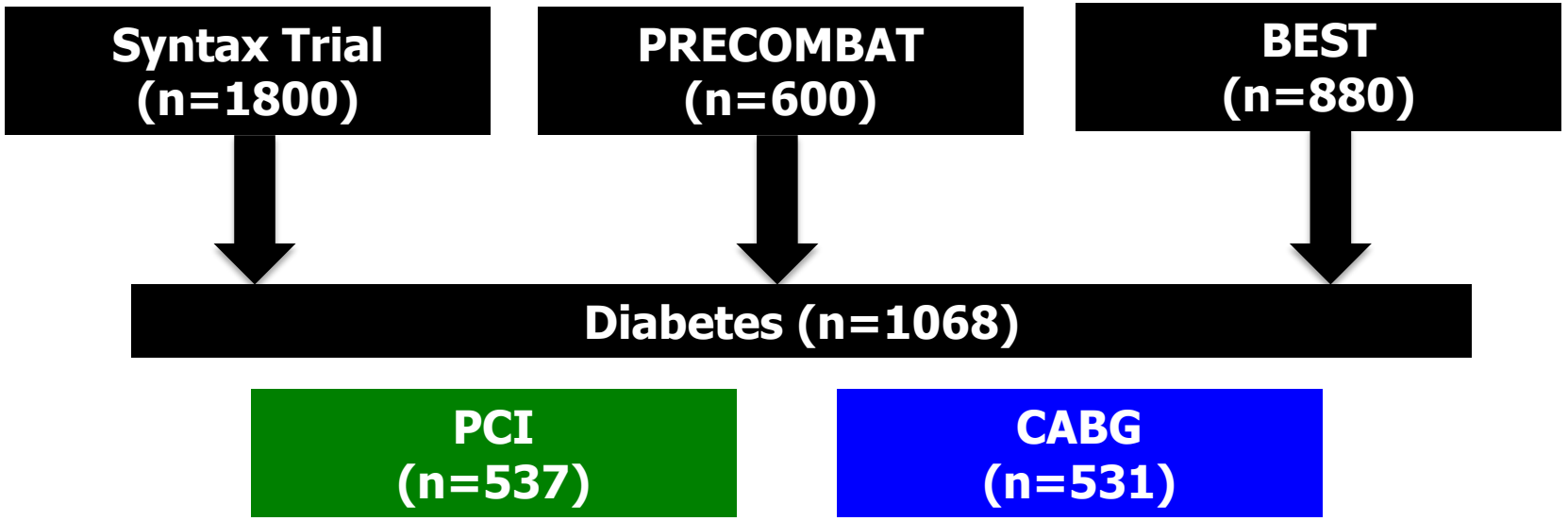
**Farkouh et al. NEJM 2012**

# The Aims

- **To assess long-term (5-year) outcomes in diabetic patients with both left-main and/or multivessel disease who were treated with first or second generation drug-eluting stent, using a patient-level pooled database of 3 large randomized controlled trials comparing CABG and PCI (Syntax, PRECOMBAT and BEST trials).**

- **In all 3 trials, the independent corelabs assessed angiographic SYNTAX scores.**

# Methods - population




- **1068 diabetic patients with multivessel CAD and/or left-main involvement randomized in the SYNTAX, PRECOMBAT and BEST trials were included.**

- **Treatment for diabetes included diet only, oral medication and/or insulin therapy, at variance of the previous SYNTAX trial reports on diabetic patients where those treated with diet only (n=59) were excluded.**

- **In the present study, we performed a merging of the individual patient-level data of the three trials.**

# Baseline Characteristics

| | PCI (n=537) | CABG (n=531) | p value |
|---|---|---|---|
| Age (years) | 64.3 ± 8.8 | 65.2 ± 8.9 | 0.11 |
| Male gender | 70.0% | 73.4% | 0.21 |
| Insulin use | 22.2% | 22.6% | 0.86 |
| Current smoking | 20.7% | 20.1% | 0.81 |
| Dyslipidemia | 66.2% | 63.4% | 0.35 |
| Previous MI | 18.0% | 18.3% | 0.89 |
| Previous stroke | 5.8% | 7.8% | 0.25 |
| Peripheral Vascular Disease | 9.3% | 8.7% | 0.71 |
| COPD | 5.8% | 5.6% | 0.93 |

# Baseline Characteristics

| | PCI (n=537) | CABG (n=531) | p value |
|---|---|---|---|
| SYNTAX Score | 27.3 ± 9.8 | 27.6 ± 10.3 | 0.68 |
| EuroSCORE | 3.4 ± 2.4 | 3.4 ± 2.4 | 0.79 |
| LVEF (%) | 57.5 ± 12.8 | 59.0 ± 10.6 | 0.07 |
| CrCl (ml/min) | 78.6 ± 33.1 | 79.1 ± 30.3 | 0.81 |
| Acute clinical presentation | 35.4% | 34.2% | 0.67 |
| Disease extent | | | 0.7 |
| Left-main disease | 34.8% | 33.7% | |
| 3-vessel disease | 65.2% | 66.3% | |

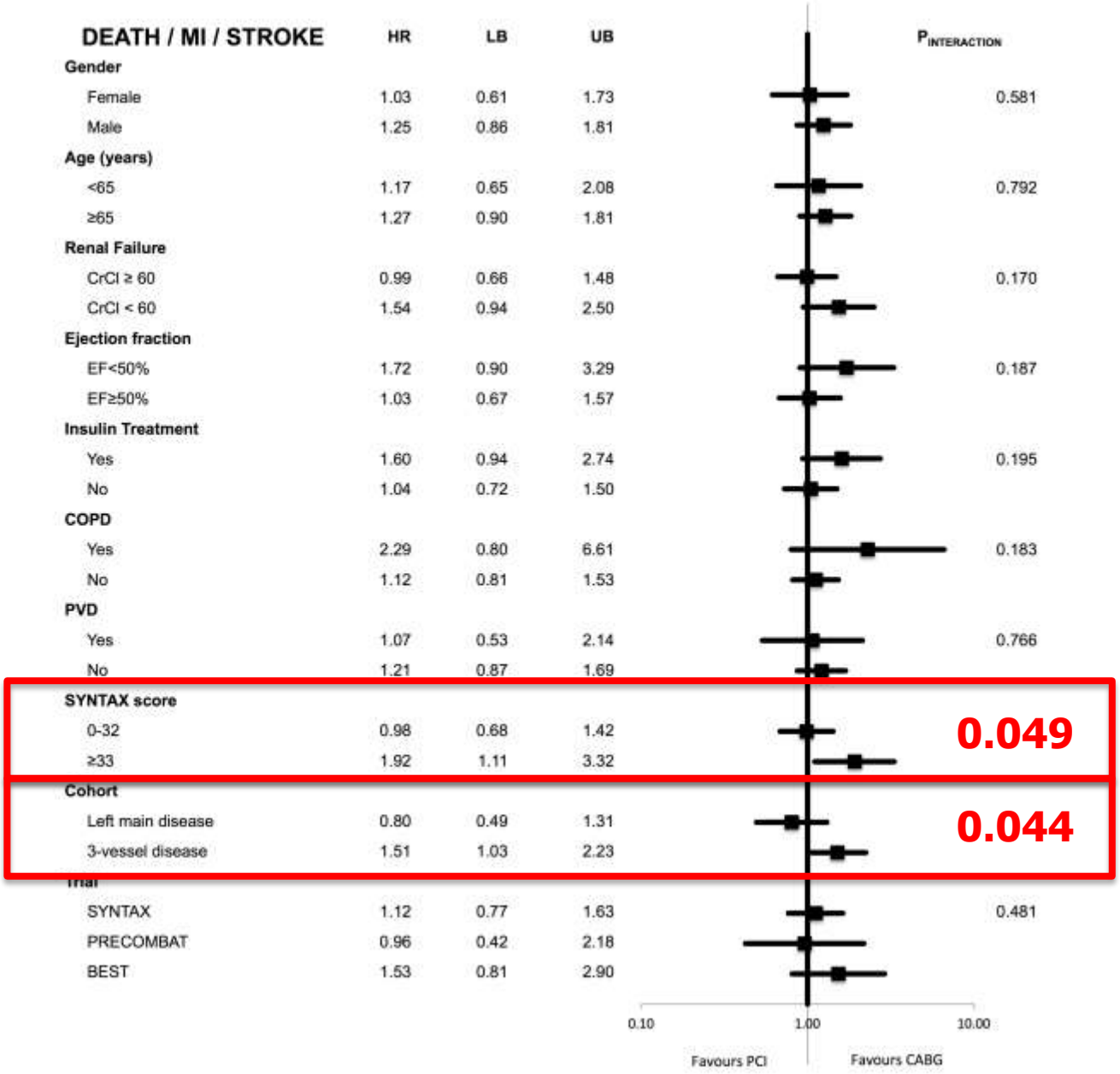
# Baseline Characteristics

| | PCI (n=537) | CABG (n=531) |
|---|---|---|
| Number of stents | 4.0 ± 2.1 | - |
| Total stent length (mm) | 86.7 ± 45.4 | - |
| Stent type per patient | | |
| Paclitaxel | 47.5% | - |
| Sirolimus | 19.0% | - |
| Everolimus | 33.5% | - |
| Off-pump CABG | - | 40.3% |
| LIMA use | - | 90.8% |
| Number of total conduits | - | 2.9 ± 0.8 |
| Number of arterial conduits | - | 1.7 ± 0.9 |
| Number of venous conduits | - | 1.2 ± 0.9 |

# Overall clinical outcomes at 5 years

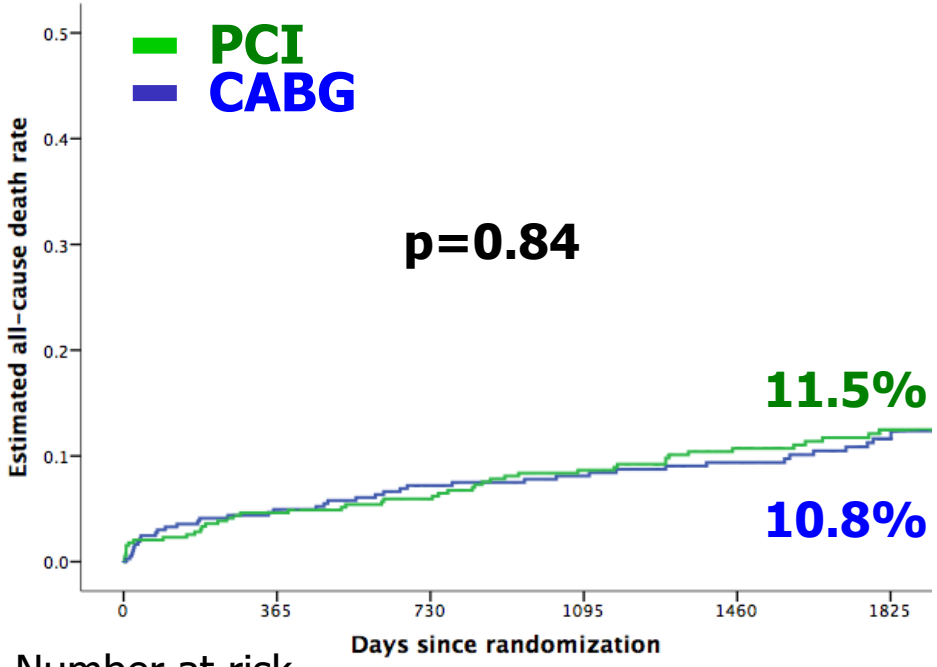
| | PCI (n=537) | CABG (n=531) | HR (95% CI) | p value |
|---|---|---|---|---|
| **All-cause Death** | 13.6% | 10.2% | 1.33 (0.93-1.89) | 0.12 |
| **Cardiac death** | 8.9% | 6.0% | 1.48 (0.94-2.31) | 0.09 |

# Subgroup analysis – Death/MI/Stroke

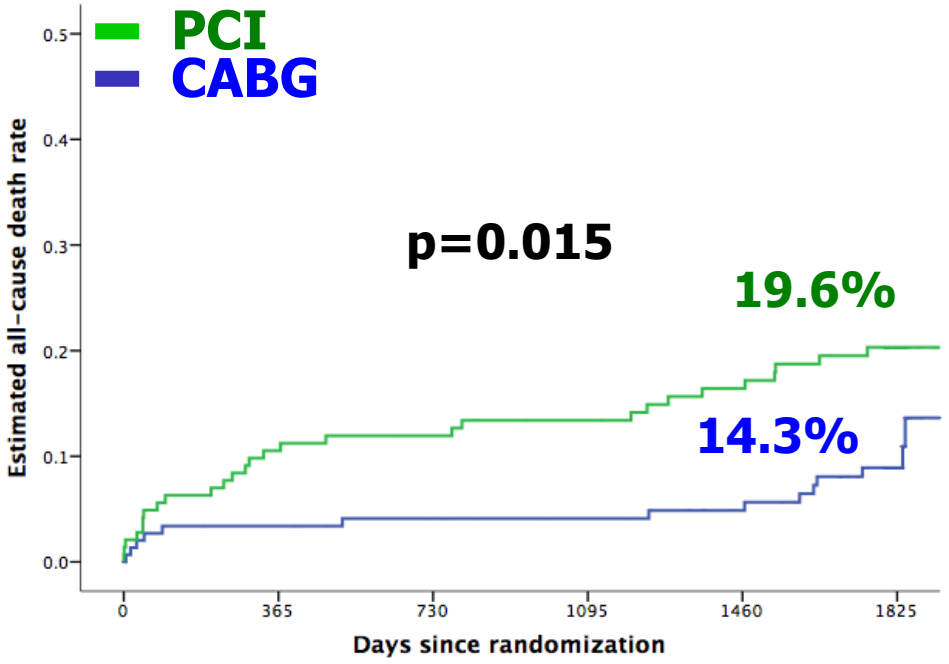


# All-cause death in Low vs High Syntax Score Diabetic population

## Low Syntax scores (0-32)




## High Syntax scores (≥33)

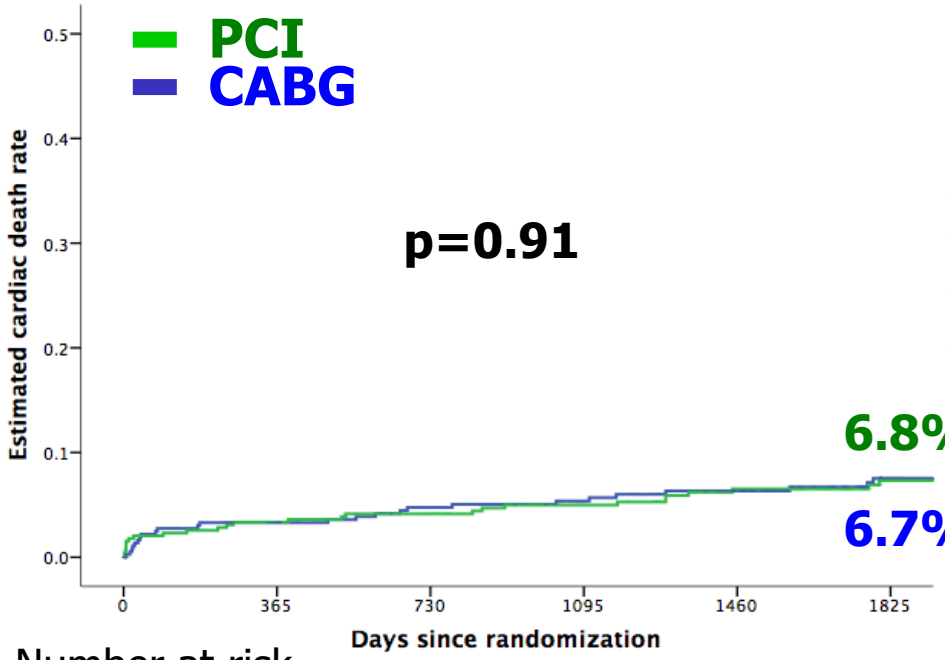



Number at risk

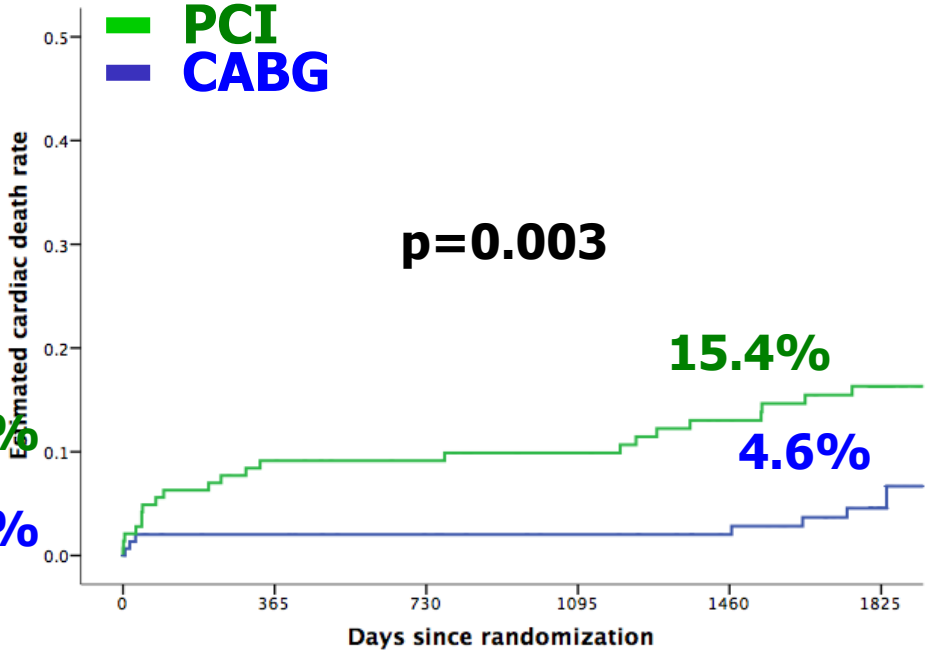
| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| CABG | 369 | 341 | 319 | 297 | 268 | 121 | 151 | 138 | 133 | 128 | 121 | 58 |
| PCI | 390 | 370 | 353 | 325 | 291 | 137 | 143 | 127 | 122 | 116 | 108 | 50 |

# Cardiac death in Low vs High Syntax Score Diabetic population

## Low Syntax scores (0-32)




## High Syntax scores (≥33)

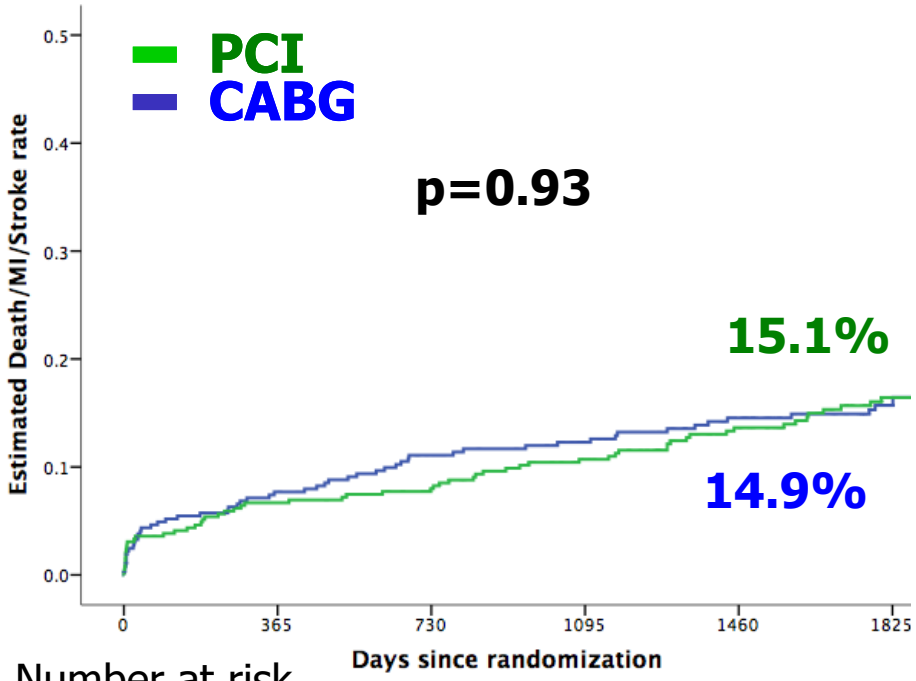



Number at risk

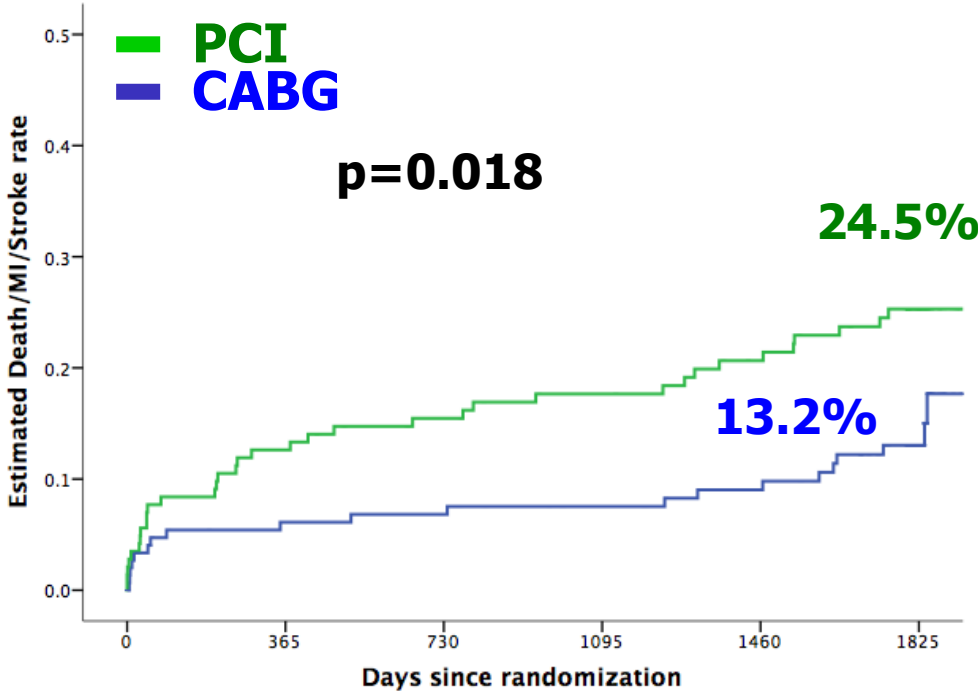
| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| CABG | 369 | 341 | 319 | 297 | 268 | 121 | 151 | 138 | 133 | 128 | 121 | 58 |
| PCI | 390 | 370 | 353 | 325 | 291 | 137 | 143 | 127 | 122 | 116 | 108 | 50 |

# Death/MI/Stroke in Low vs High Syntax Score Diabetic population

## Low Syntax scores (0-32)




## High Syntax scores (≥33)

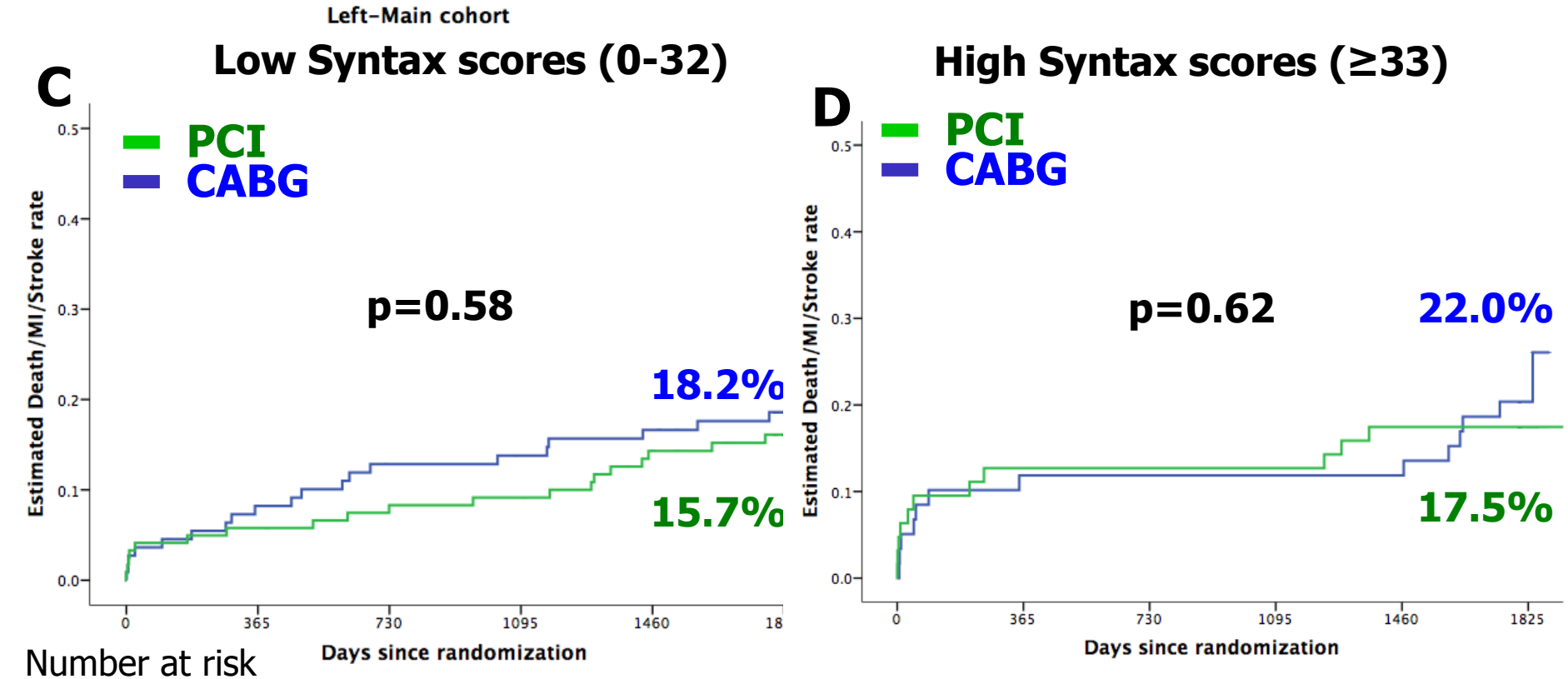



Number at risk

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| CABG | 369 | 331 | 305 | 282 | 252 | 113 | 151 | 134 | 131 | 125 | 117 | 57 |
| PCI | 390 | 362 | 346 | 319 | 282 | 130 | 143 | 124 | 117 | 111 | 104 | 46 |

# Death/MI/Stroke in Low vs High Syntax Score

## LM subset

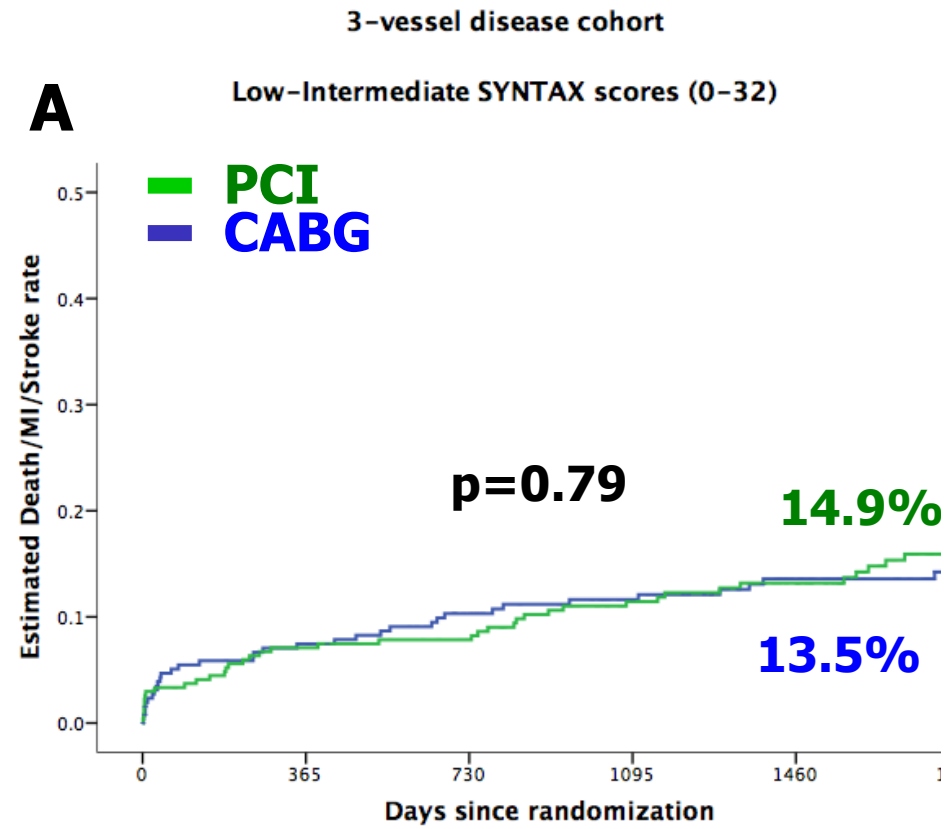


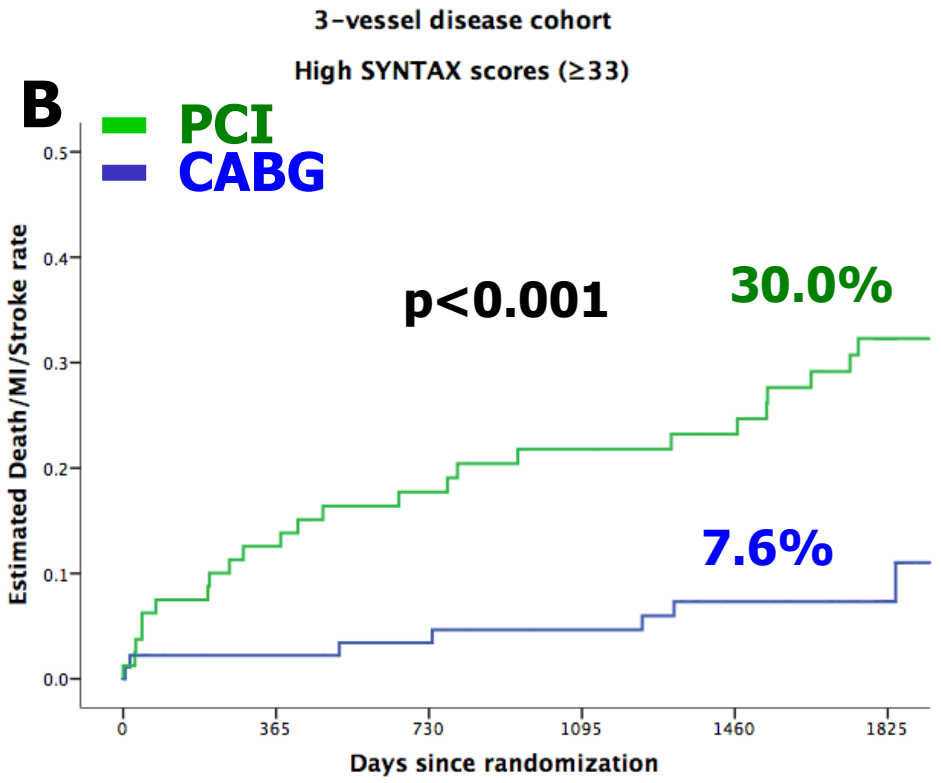

Number at risk

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| CABG | 109 | 99 | 93 | 91 | 88 | 18 | 59 | 52 | 52 | 52 | 52 | 20 |
| PCI | 120 | 114 | 109 | 107 | 98 | 24 | 62 | 55 | 55 | 55 | 52 | 18 |

# Death/MI/Stroke in Low vs High Syntax Score

## 3VD subset




| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| CABG | 259 | 232 | 212 | 191 | 164 | 95 | 91 | 82 | 79 | 73 | 65 | 37 |
| PCI | 269 | 248 | 237 | 212 | 184 | 106 | 79 | 69 | 62 | 56 | 52 | 28 |

# Summary and Conclusion

1) **Overall, PCI and CABG had similar rates of the safety endpoint of death, MI or stroke at 5 years of follow-up**

2) **In patients with low-intermediate (0-32) SYNTAX scores, PCI and CABG showed superimposed Kaplan-Meier curves of all-cause death, cardiac death and the composite of death, MI and stroke throughout the entire 5 years of follow-up**

1) **In patients with high (≥33) SYNTAX scores, PCI had significantly higher rates of all-cause death, cardiac death and the composite of death, MI or stroke at 5 years**

2) **SYNTAX score and anatomic subset (left-main / 3-vessel disease) showed significant interaction with treatment effect; In the 3-vessel disease cohort, results were consistent with the overall population.**

1) **In this large pooled population of diabetic patients with left-main and/or 3-vessel CAD, CABG and PCI had similar rates of the composite of death, MI or stroke in patients with low-intermediate SYNTAX score. In patients with high SYNTAX scores, CABG was safer than PCI.**