# 40 years of PCI and 20 years of LM PCI

## Insights From the MAIN-COMPARE and IRIS-MAIN Registries

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# Disclosure Statement of Financial Interest

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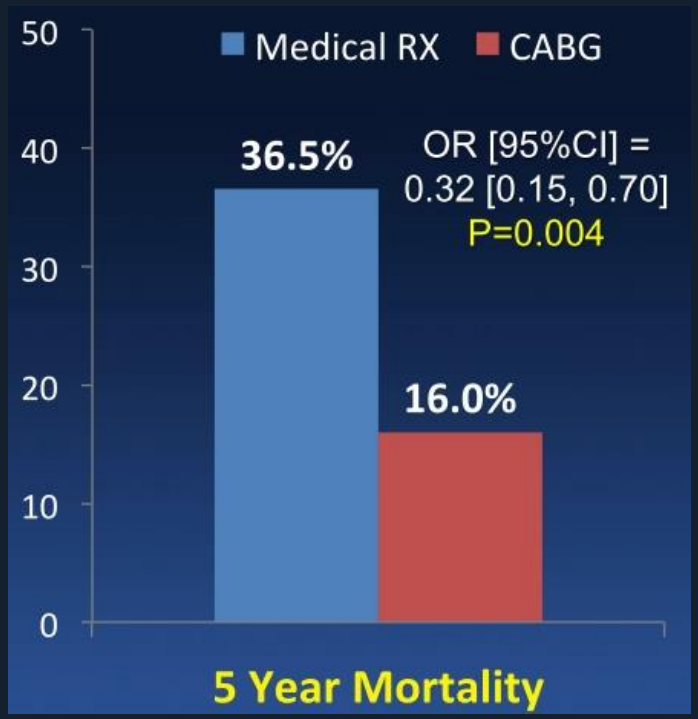
# Left Main Revascularization

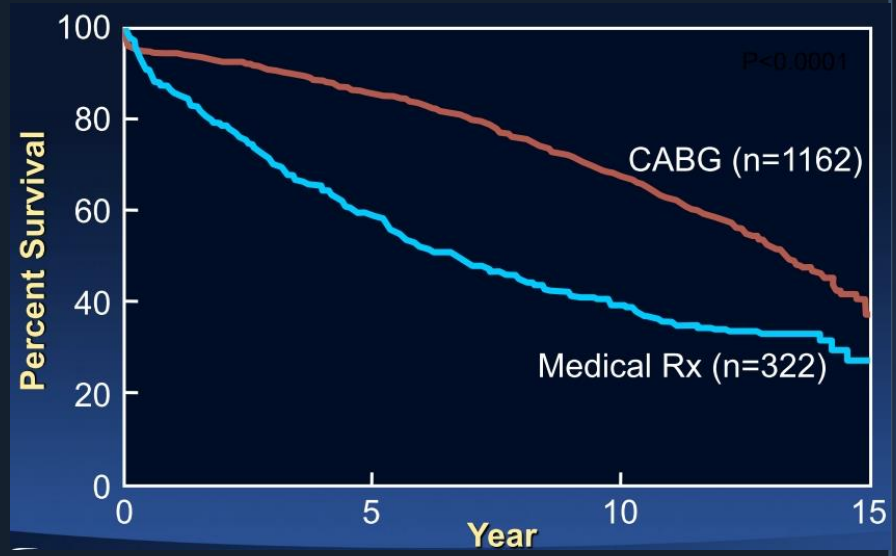
## *40 years ago*

CABG vs. Medical Rx
(150 pts, VA and EU RCT)




Yusuf S et al. Lancet 1994; 344: 563-70

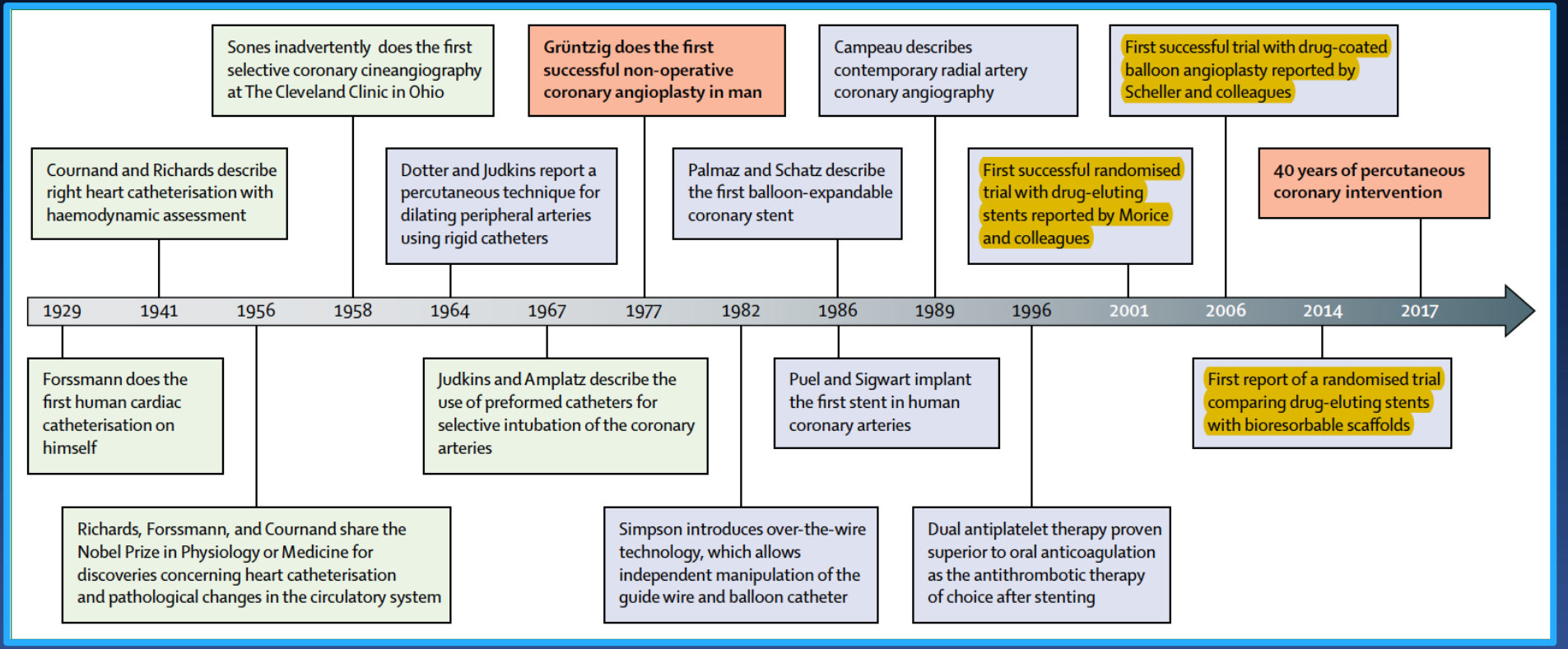
CABG vs. Medical Rx
(1484 pts, CASS Registry)




Yusuf S et al. Lancet 1994; 344: 563-70

PCI was not considered as an Tx option

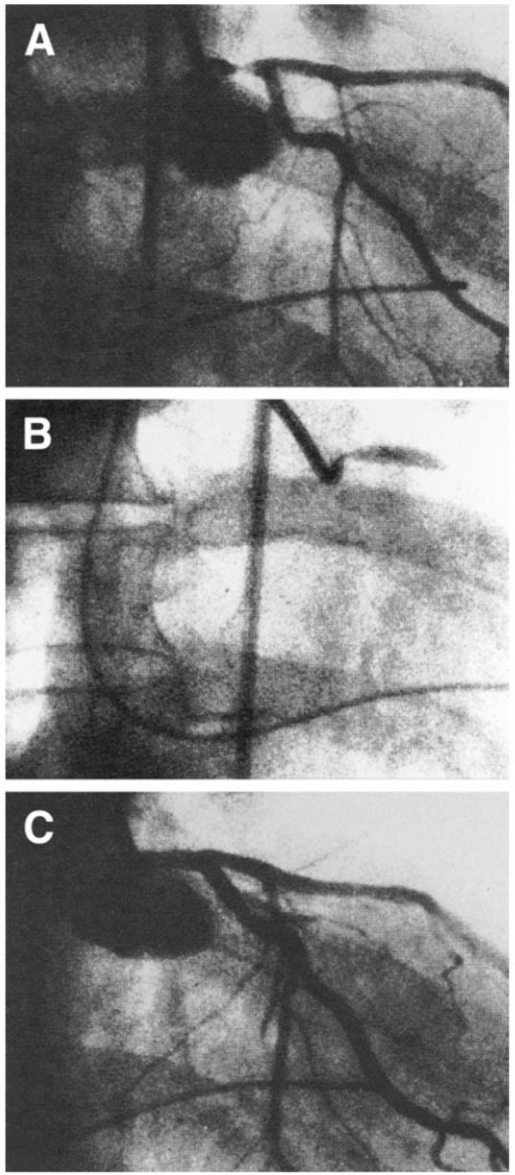
# 40-Years Long Journey of PCI




Robert A Byrne et al. Lancet 2017; 390: 781–92

**LETTER TO THE EDITOR**

# First Percutaneous Catheter Intervention for Left Main Coronary Artery Disease: 30 Years Ago




Gruntzig A. Lancet. 1978;1(8058):263. Transluminal dilatation of coronary-artery stenosis.

JACC Vol. 31, No. 1
January 1998:37–42



# Stenting of Unprotected Left Main Coronary Artery Stenoses: Immediate and Late Outcomes

SEUNG-JUNG PARK, MD, PHD, FACC, SEONG-WOOK PARK, MD, PHD, MYEONG-KI HONG, MD, SANG-SIG CHEONG, MD, CHEOL WHAN LEE, MD, JAE-JOONG KIM, MD, MUN K. HONG, MD, FACC,* GARY S. MINTZ, MD, FACC,* MARTIN B. LEON, MD, FACC*

*Seoul, Korea and Washington, D.C.*

*Objectives.* We examined the immediate and long-term outcomes after stenting of unprotected left main coronary artery (LMCA) stenoses in patients with normal left ventricular (LV) function.

*Background.* Left main coronary artery disease is regarded as an absolute contraindication for coronary angioplasty. Recently, several reports on protected or unprotected LMCA stenting, or both, suggested the possibility of percutaneous intervention for this prohibited area.

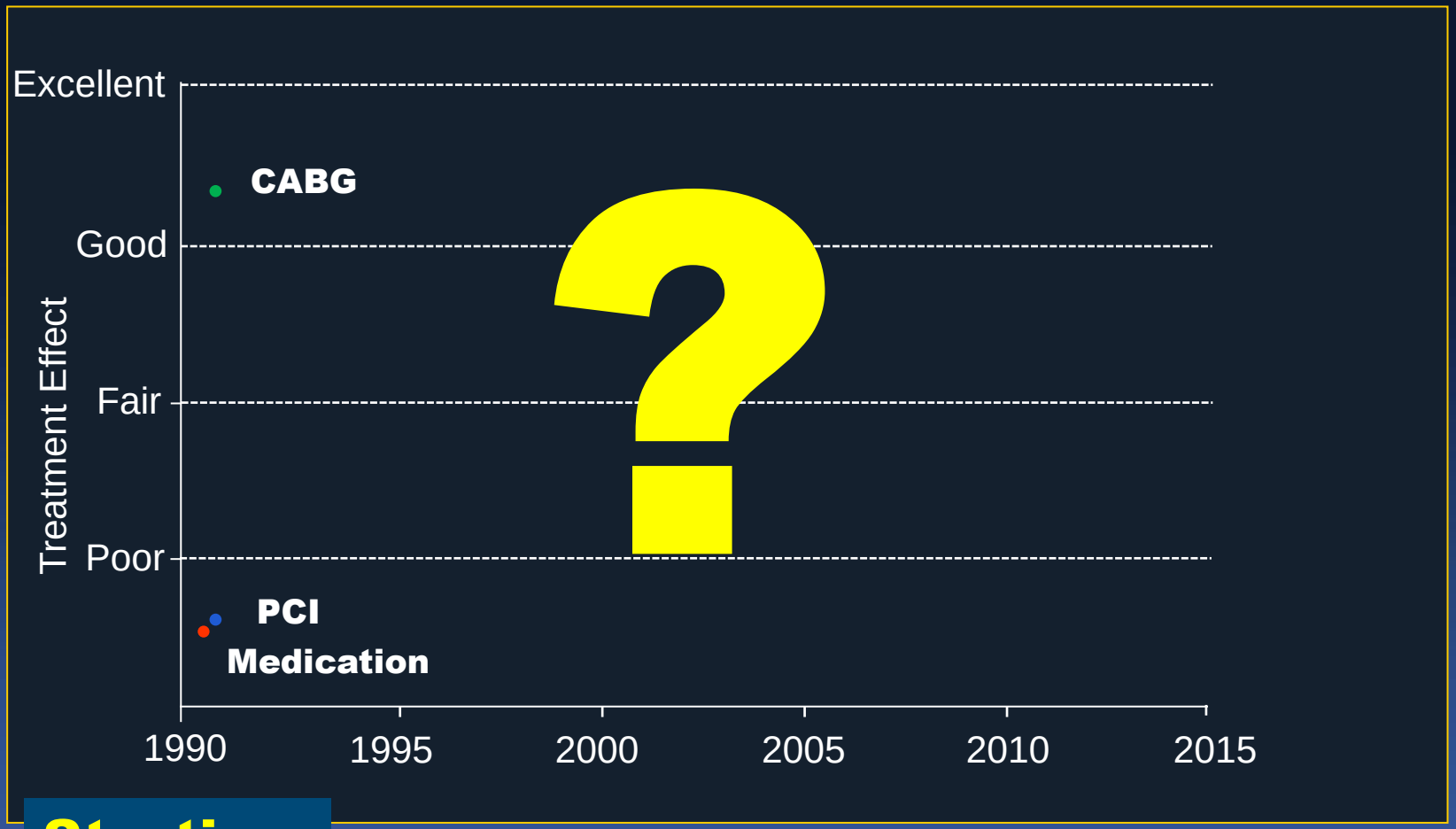
*Methods.* Forty-two consecutive patients with unprotected LMCA stenoses and normal LV function were treated with stents. The post-stent antithrombotic regimens were aspirin and ticlopidine; 14 patients also received warfarin. Patients were followed very closely with monthly telephone interviews and follow-up angiography at 6 months.

*Results.* The procedural success rate was 100%, with no episodes of subacute thrombosis regardless of anticoagulation regimen. Six-month follow-up angiography was performed in 32 of 34 eligible patients. Angiographic restenosis occurred in seven patients (22%, 95% confidence interval 7% to 37%); five patients subsequently underwent elective coronary artery bypass graft surgery (CABG), and two patients were treated with rotational atherectomy plus adjunct balloon angioplasty. The only death occurred 2 days after elective CABG for treatment of in-stent restenosis. The other patients (without angiographic follow-up) remain asymptomatic.

*Conclusions.* Stenting of unprotected LMCA stenoses may be a safe and effective alternative to CABG in carefully selected patients with normal LV function. Further studies in larger patient populations are needed to assess late outcome.

(J Am Coll Cardiol 1998;31:37–42)

# How the treatments and clinical outcomes evolved over 2 decades




**Starting Point**

# 20 Years of Temporal Changes In PCI vs. CABG For LM Disease

## *Data from IRIS-MAIN Registry*

# Study Population

- **The IRIS MAIN registry** (clinicaltrials.gov number NCT 01341327) is a nonrandomized, multi-national, multicenter observational study to assess the practice and outcomes of LMCA disease.
- All-comers design, consecutive patients with LMCA disease treated with medical Rx, PCI, or CABG
- Between January 1995 and December 2013, a total of 5833 patients were enrolled from 50 academic and community hospitals in Asia (China, India, Indonesia, Japan, Malaysia, South Korea, Taiwan, and Thailand).

# Definition and Study Endpoint

***Three time periods***

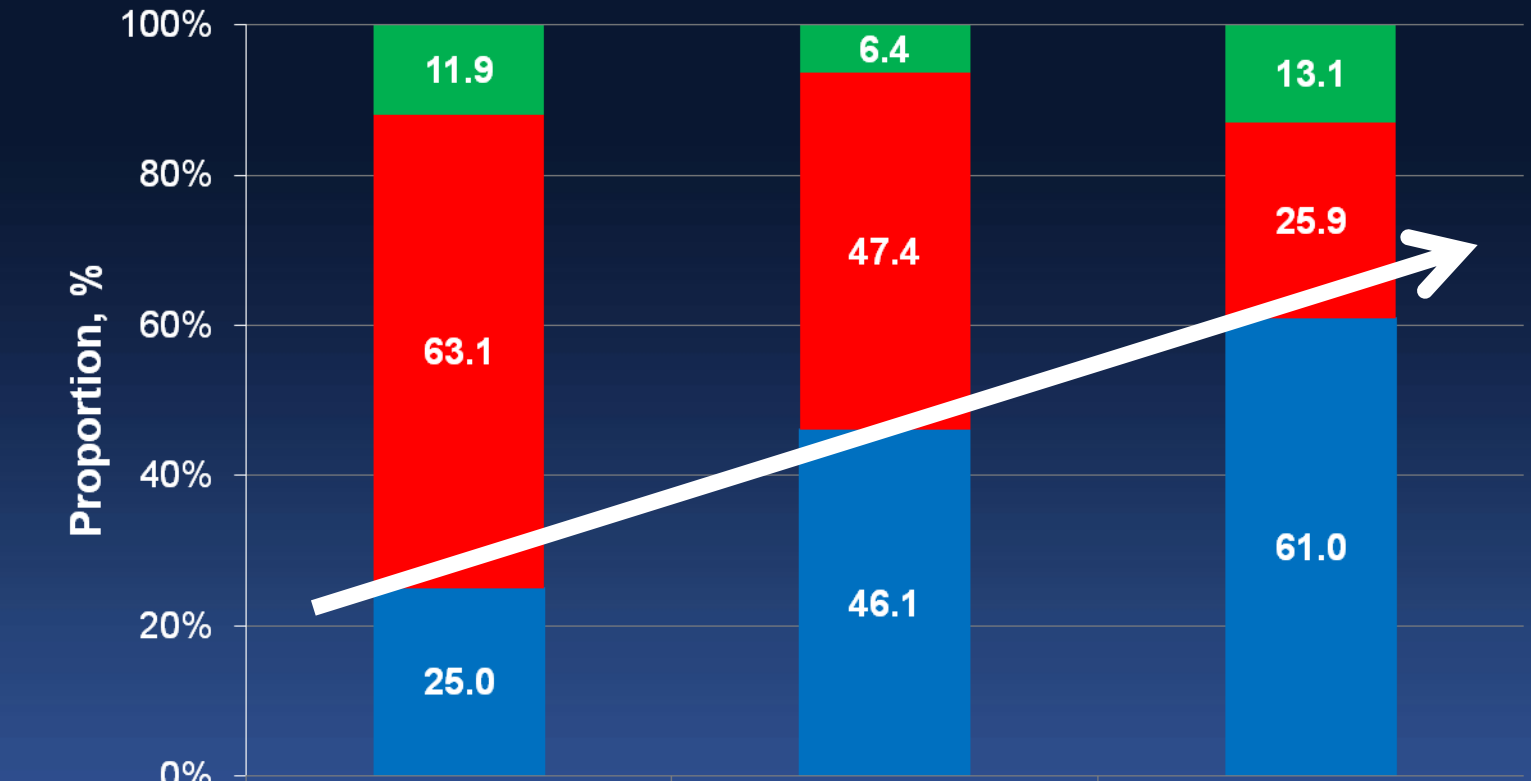
- Wave 1 (BMS) for 1995–2002
- Wave 2 (First G DES) for 2003–2006
- Wave 3 (Second G DES) for 2007–2013

***Study End Point***

- All-cause death
- Serious composite of death, MI, or stroke
- Repeat revascularization
- MACCE (death, MI, stroke, or RR)

# *Temporal Trends* of LM Revascularization,

*(IRIS LM Registry n=5,883)*



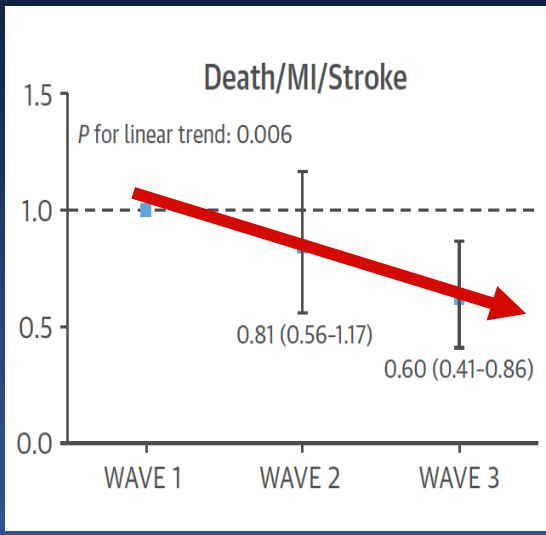

| | 1995-2002 | 2003-2006 | 2007-2013 |
|---|---|---|---|
| Medical Tx | 129 | 131 | 356 |
| CABG | 683 | 964 | 704 |
| PCI | 271 | 937 | 1658 |



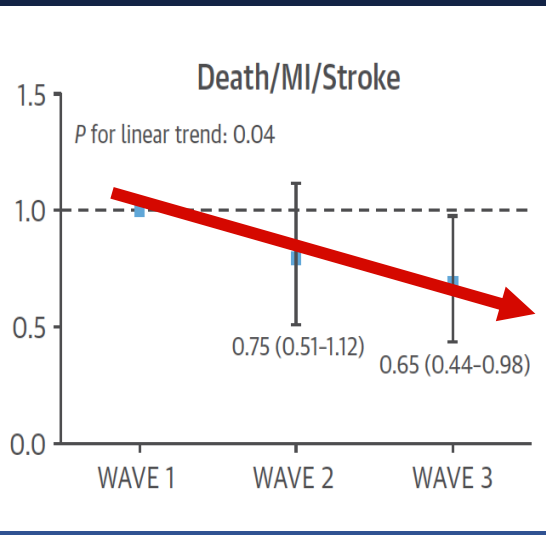
PH Lee, DW Park, SJ Park et al, JACC. 2016;68:1233-46.

# Secular Trend over 20 Years
# Adjusted Hazard Ratio

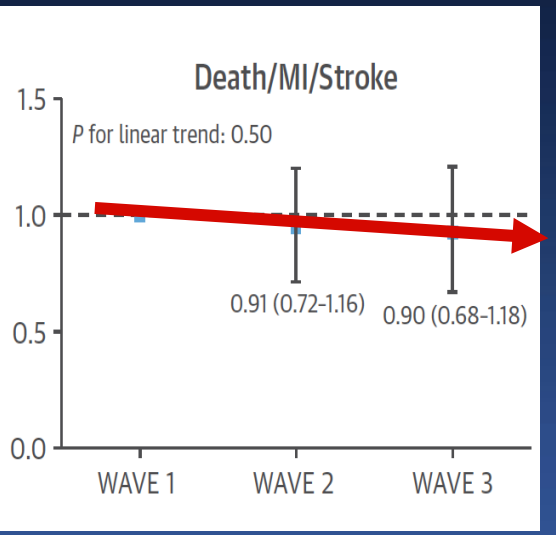
**Medication group**




**PCI group**



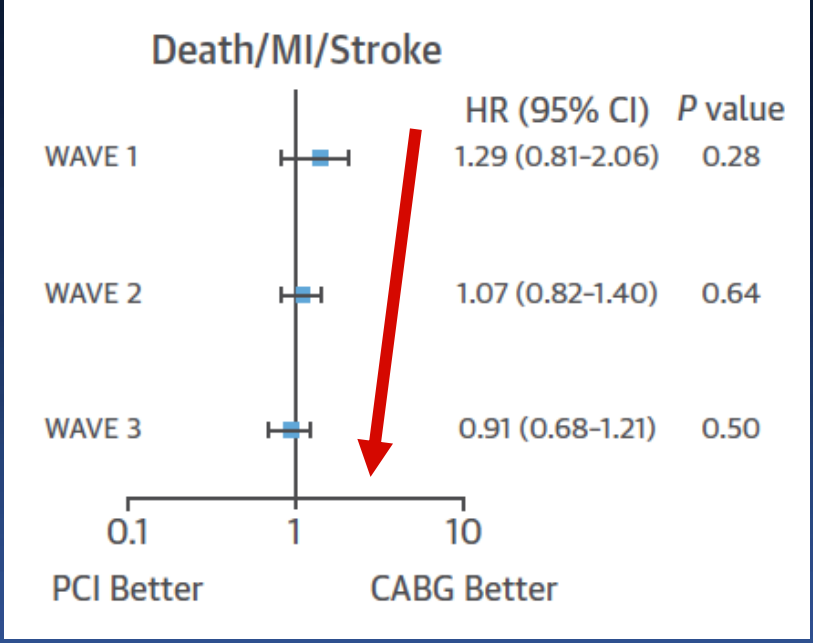

**CABG group**

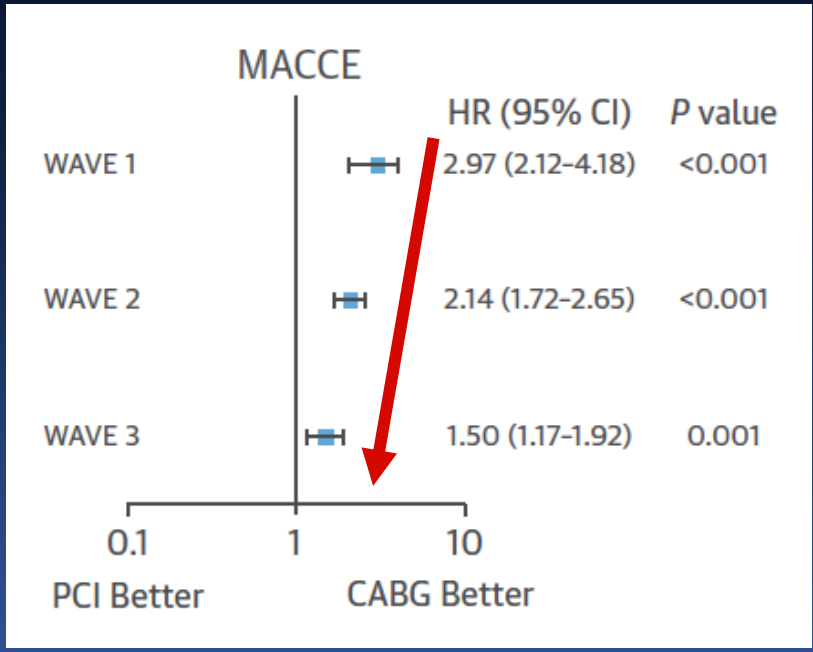





PH Lee, DW Park, SJ Park et al, JACC. 2016;68:1233-46.

# PCI vs. CABG
# Adjusted Hazard Ratio

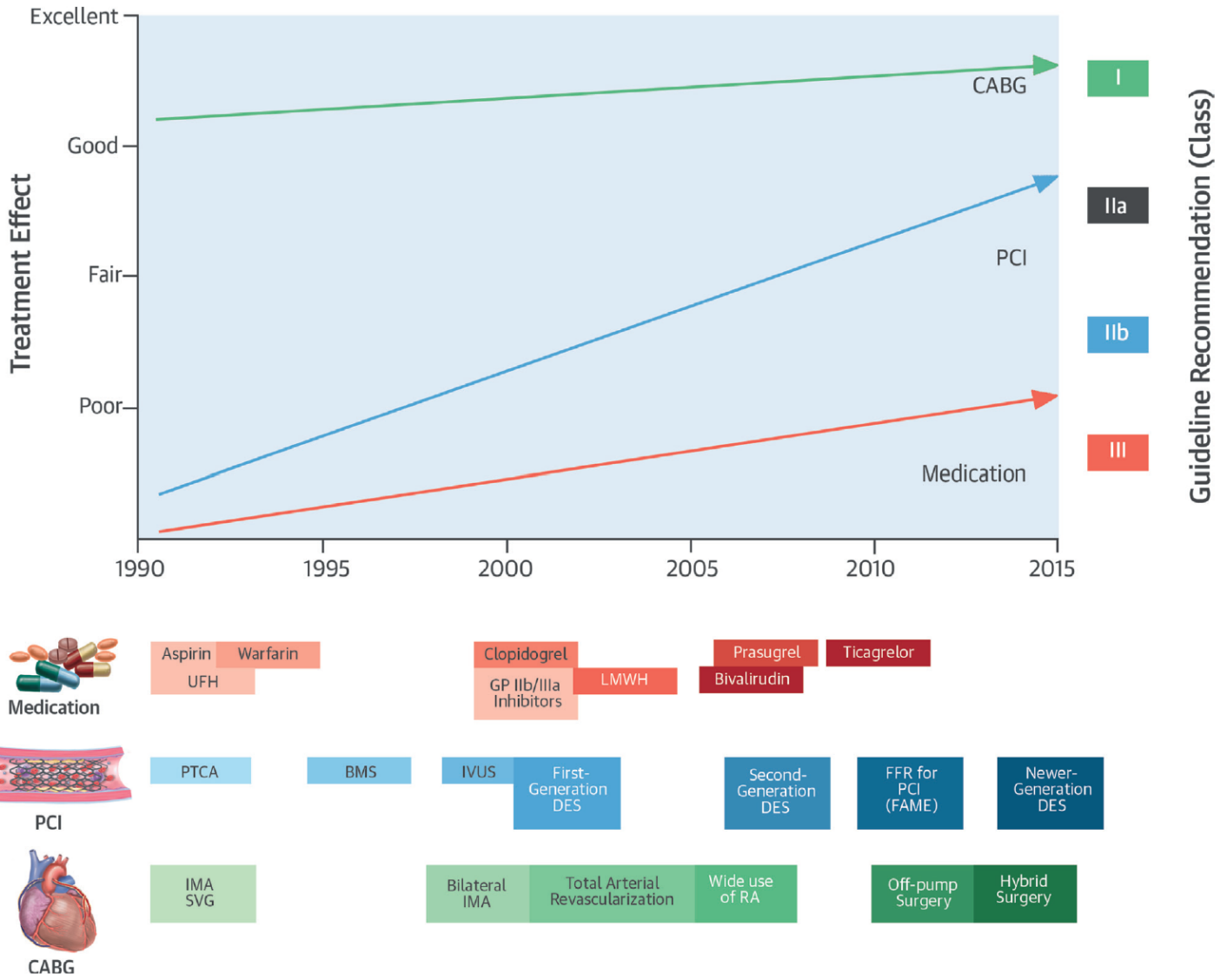




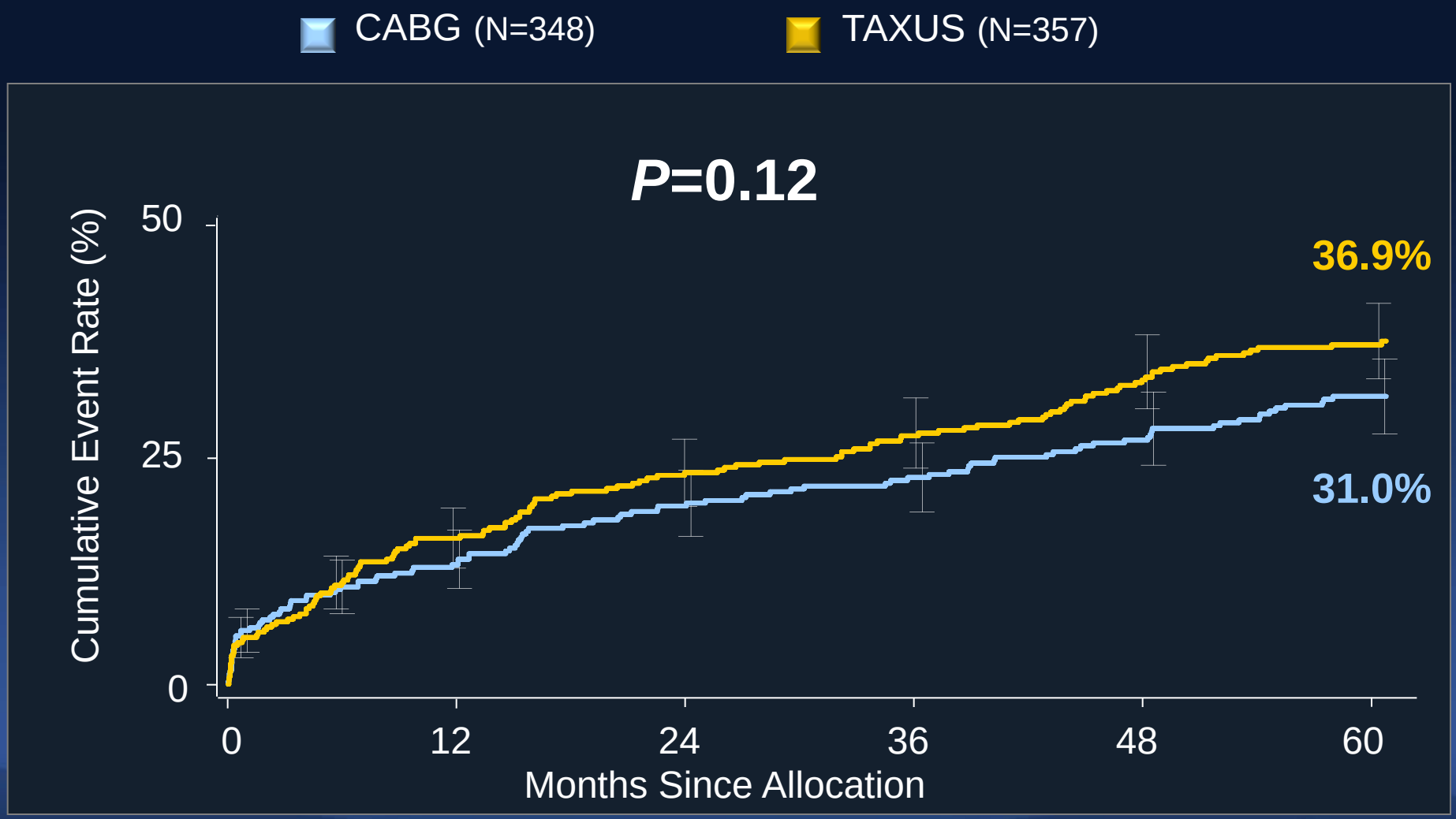

PH Lee, DW Park, SJ Park et al, JACC. 2016;68:1233-46.

**CENTRAL ILLUSTRATION** **Secular Changes of Treatment Effect and Guideline Recommendations in Relation to Medical Advances of Each Treatment Stratum for Left Main Coronary Artery Disease**




Lee, P.H. et al. J Am Coll Cardiol. 2016;68(11):1233-46.

# *SYNTAX (LM Subset), 1st-DES PES*
# Death /MI /Stroke /Repeat Revascularization

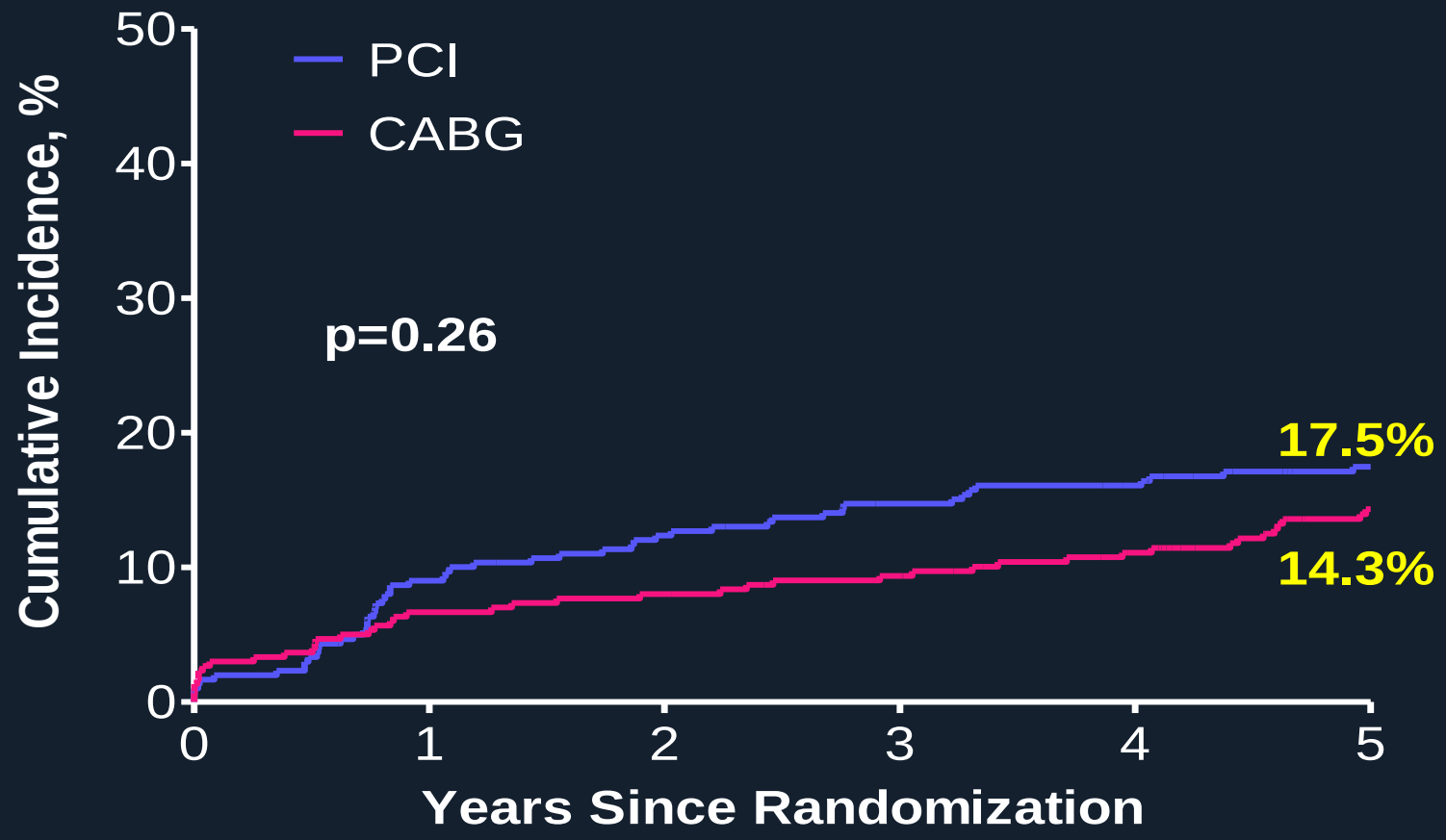



Cumulative KM Event Rate ± 1.5 SE; log-rank *P* value;*Binary rates

ITT population

# *PRECOMBAT, 1st-DES SES*

# Death. MI, Stoke or TVR




**Patient at risk**

| | | | | | | |
|---|---|---|---|---|---|---|
| **PCI** | 300 | 272 | 261 | 252 | 246 | 231 |
| **CABG** | 300 | 279 | 274 | 267 | 256 | 235 |



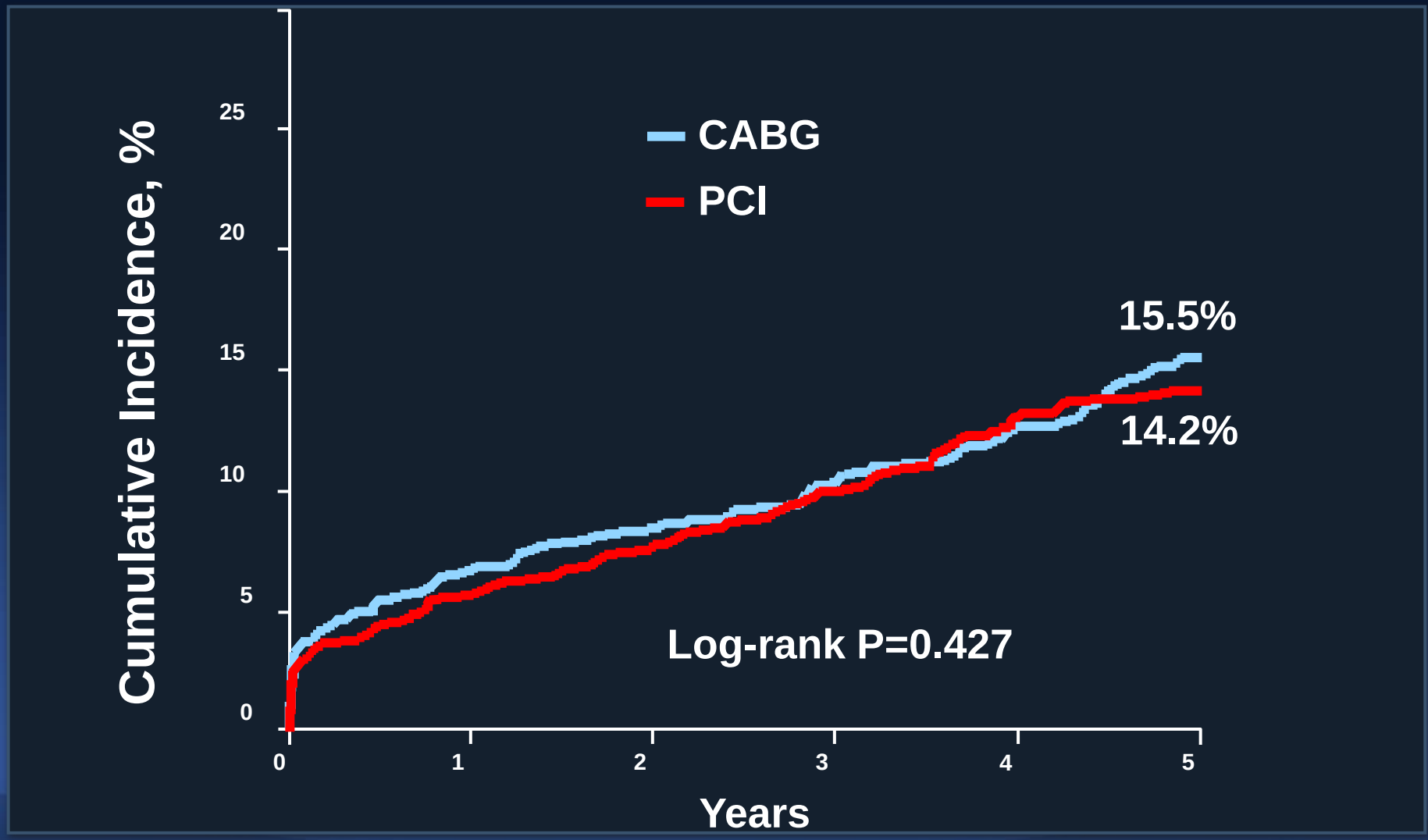
Ahn JM, Park DW, Park SJ et al, JACC. 2015 Mar 10.

# IPD Meta-Analysis (n=3,280)

Database Pooling of
SYNTAX (n=1800, PES),
BEST (n=880, EES), and
PRECOMBAT (n=600, SES) trials.

*Patient-Level Meta-Analysis (n=1,293)*

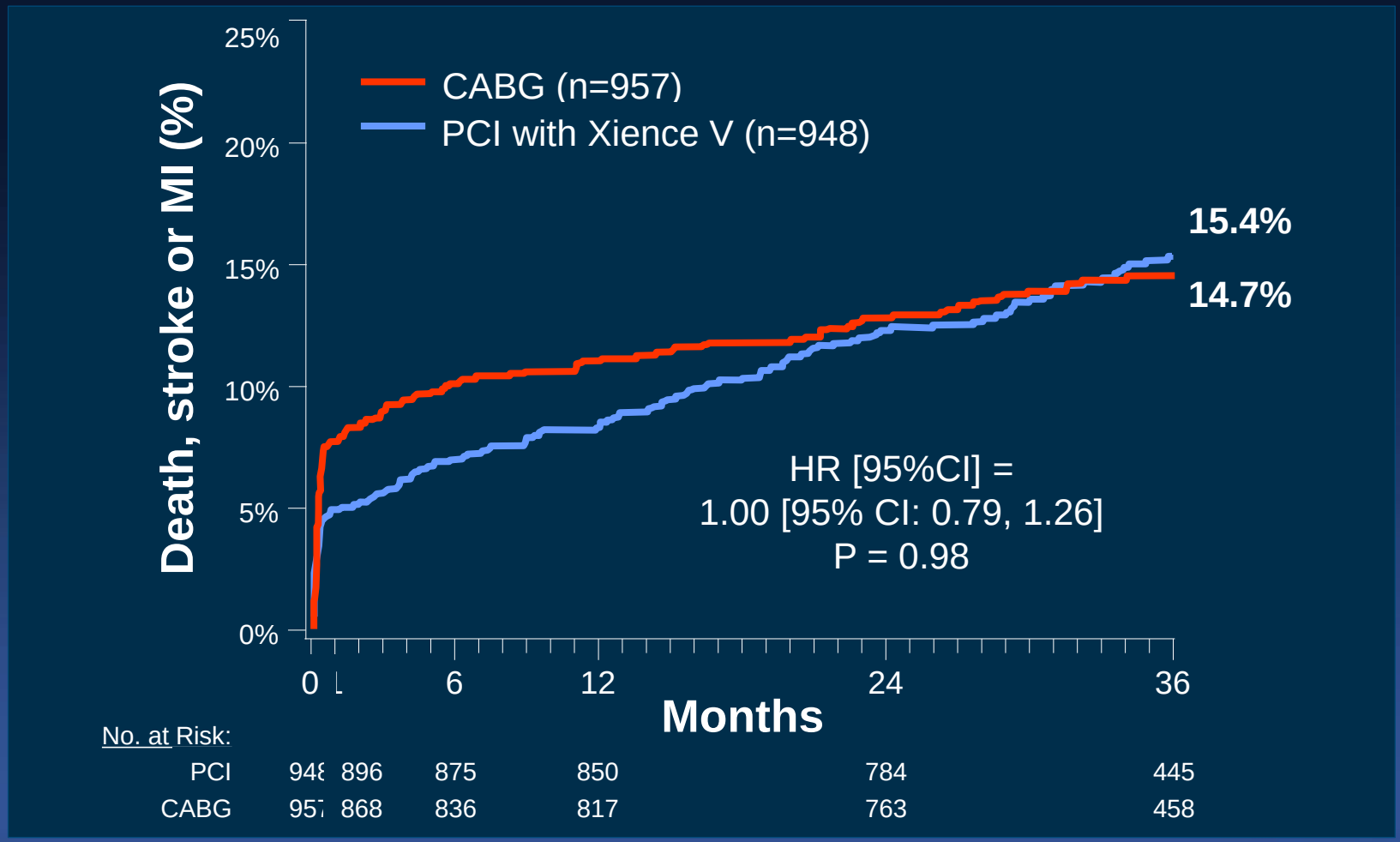
# *LM Subset /* Death, MI or Stroke




Lee CW, Par DW, Park SJ et al, JACC 2015

EXCEL

# Primary Endpoint
## Death, Stroke or MI at 3 Years

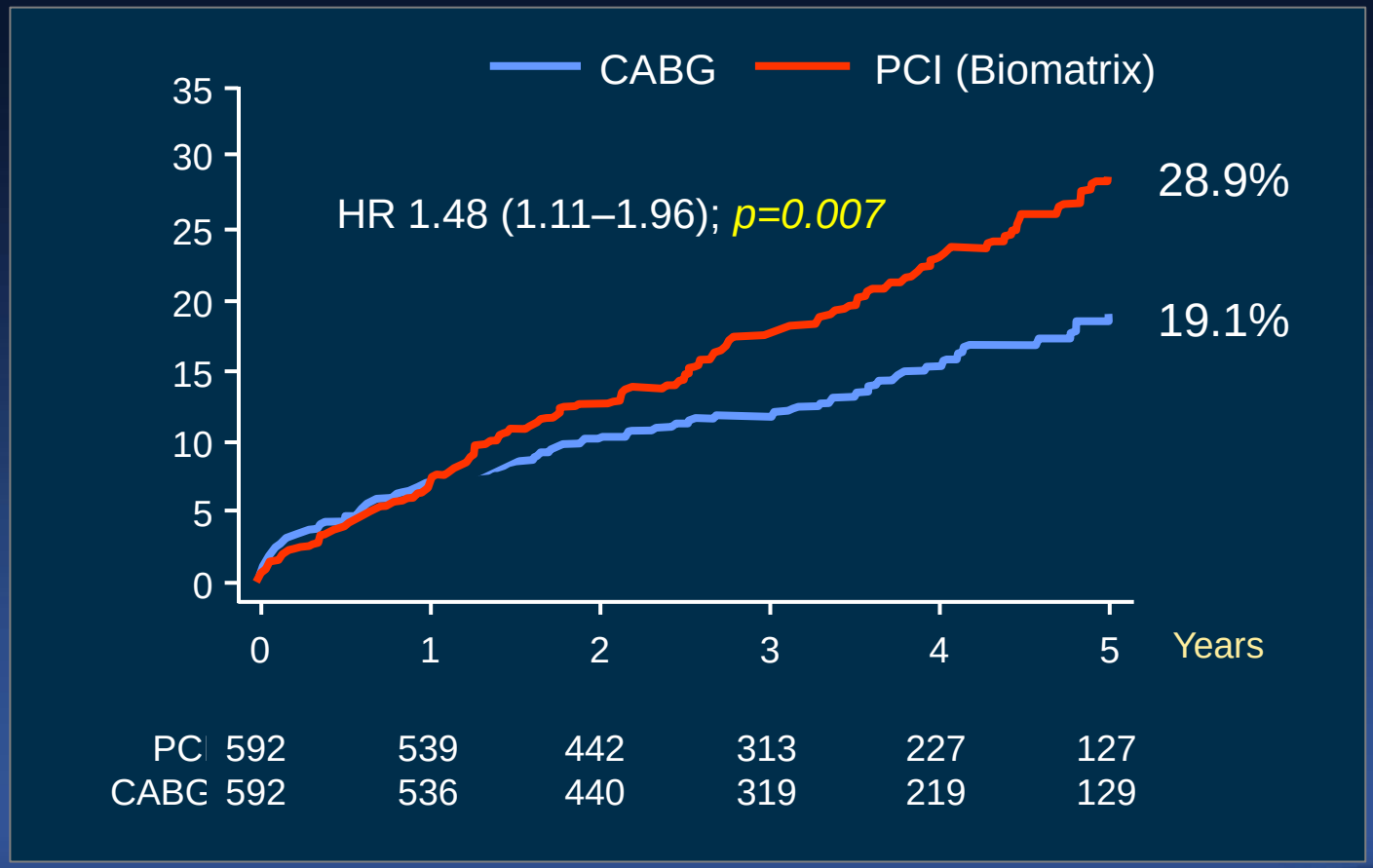





Gregg W.Stone, NEJM 2016;375:2223-2235

NOBLE

# Primary Endpoint
## Death, non-procedural MI, repeat Revascularization and Stroke at 3 Years






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

# IPD Meta-Analysis 2018: PCI vs. CABG for MVD or LM

## Mortality after coronary artery bypass grafting versus percutaneous coronary intervention with stenting for coronary artery disease: a pooled analysis of individual patient data

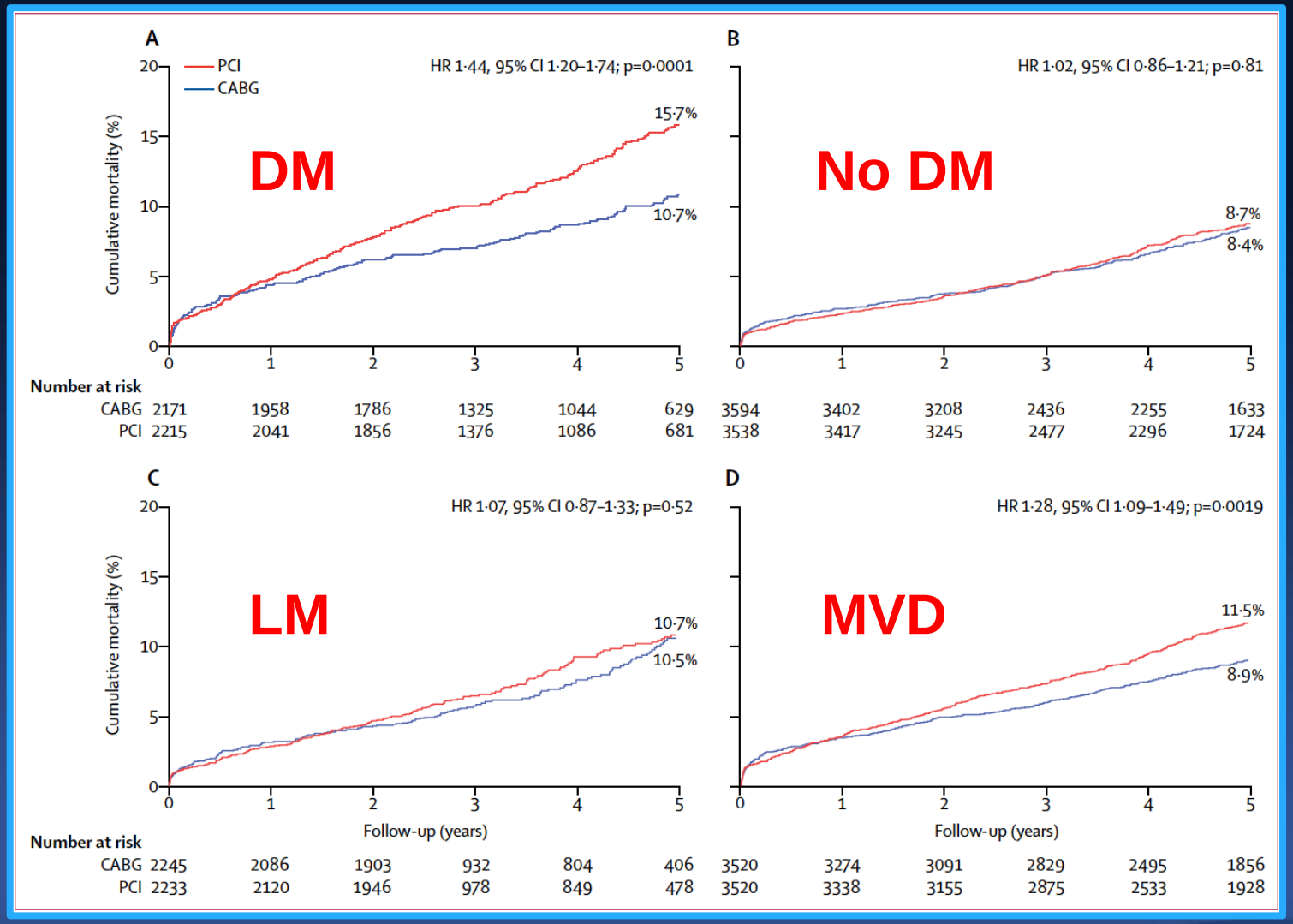
*Stuart J Head, Milan Milojevic, Joost Daemen, Jung-Min Ahn, Eric Boersma, Evald H Christiansen, Michael J Domanski, Michael E Farkouh, Marcus Flather, Valentin Fuster, Mark A Hlatky, Niels R Holm, Whady A Hueb, Masoor Kamalesh, Young-Hak Kim, Timo Mäkikallio, Friedrich W Mohr, Grigorios Papageorgiou, Seung-Jung Park, Alfredo E Rodriguez, Joseph F Sabik 3rd, Rodney H Stables, Gregg W Stone, Patrick W Serruys, Arie Pieter Kappetein*

11518 Patients with 11 RCT with BMS or DES: ERACI II (n=450), ARTS (n=1205), MASS-II (n=408), SoS (n=988), SYNTAX (n=1800), PRECOMBAT (n=600), FREEDOM (n=1900), VA CARDS (n=198), BEST (n=880), NOBLE (n=1184), and EXCEL (n=1905)



Head SJ et al. Lancet February 22, 2018

# IPD Meta-Analysis 2018: PCI vs. CABG




Head SJ et al. Lancet February 22, 2018

# 2018 Updated ESC/EACTS Guideline : PCI vs. CABG for Left Main

**Recommendations on criteria for the choice between coronary artery bypass grafting and percutaneous coronary intervention**

| Recommendations | Class[a] | Level[b] |
|---|---|---|
| **Assessment of CAD complexity** | | |
| In patients with LM or multivessel disease, it is recommended that the SYNTAX score is calculated to assess the anatomical complexity of CAD and the long-term risk of mortality and morbidity after PCI.[117–124] | I | B |
| When considering the decision between CABG and PCI, completeness of revascularization should be prioritized.[131,132,134–136] | IIa | B |



| Left main CAD | | | | |
|---|---|---|---|---|
| Left main disease with low SYNTAX score (0 - 22).[69,121,122,124,145–148] | I | A | I | A |
| Left main disease with intermediate SYNTAX score (23 - 32).[69,121,122,124,145–148] | I | A | IIa | A |
| Left main disease with high SYNTAX score (≥33).[c] [69,121,122,124,146–148] | I | A | III | B |

Eur Heart J. 2018 Aug 25. doi: 10.1093/eurheartj/ehy394

# PCI vs. CABG in LM Disease, *2018*

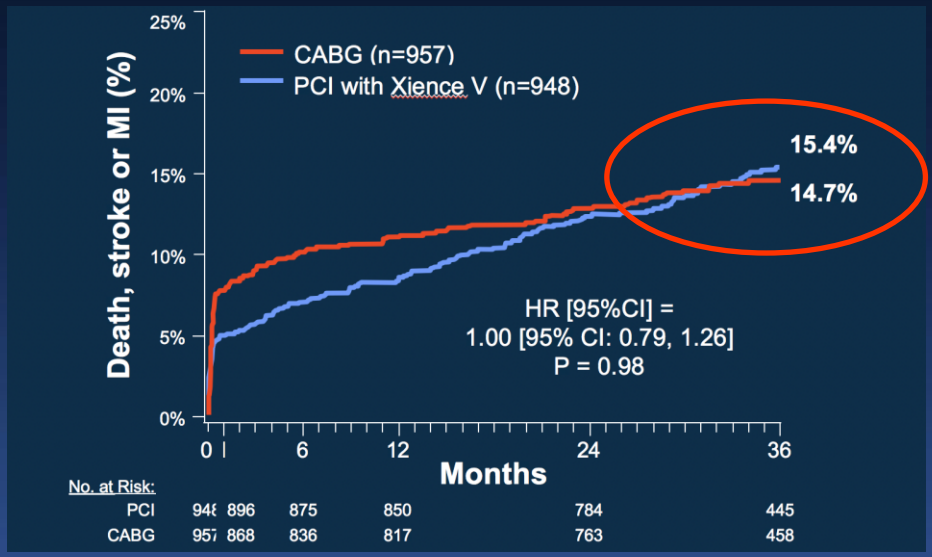
***However, The Game Is Just Begun !***

**One Important Remaining Point:**
**We Are Demanding Very Long-Term (ie,10-Year) Results of PCI and CABG for LM disease**

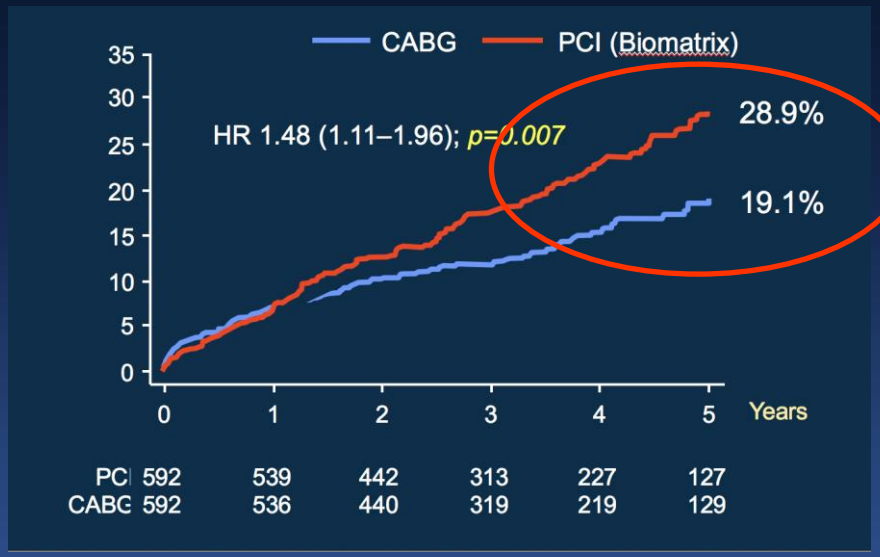
# Why We Need Very Long-Term Comparative Outcomes of PCI vs. CABG in LM Disease?

## There Is Some Signals...

### EXCEL




### NOBLE




Longer-term follow-up (beyond 5 years) is necessary to examine additional differences between PCI and CABG over time.

# Ten-Year Outcomes of Stenting versus Coronary-Artery Bypass Grafting for Unprotected Left Main Coronary Artery Disease

## : 10-Year Final Report From the MAIN-COMPARE Registry

**Seung-Jung Park, MD, PhD**

**Presented at 2018 TCT Late-Breaking Trial Session**

# MAIN-COMPARE Registry

Wave 1 (BMS era)

LM disease treated with BMS (n=318) and concurrent CABG (n=448) btw 2000~2003

Wave 2 (DES era)

LM disease treated with DES (n=784) and concurrent CABG (n=690) btw 2003~2006

From January 2000 through June 2006

Total 2240

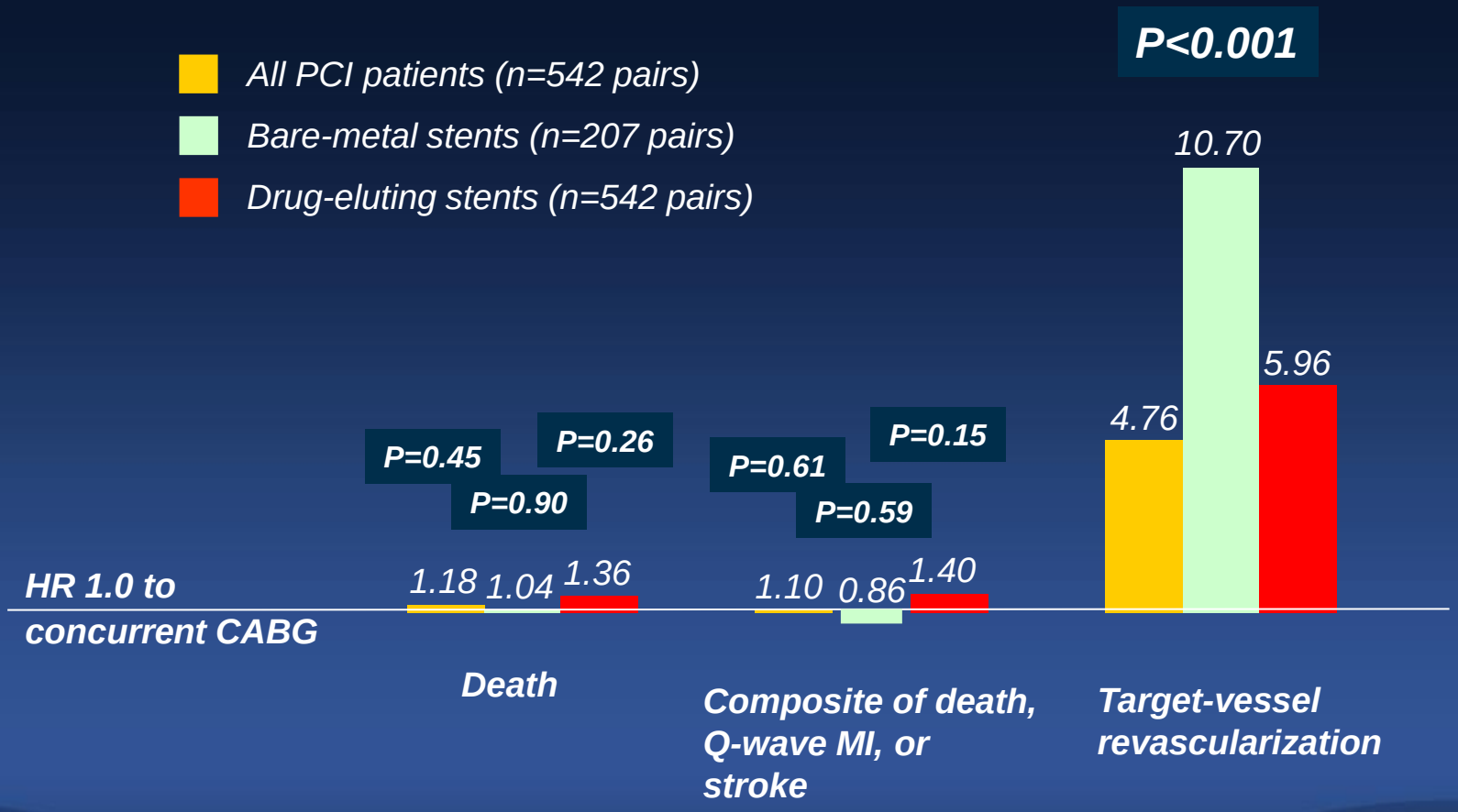
Stent (N=1102)

CABG (N=1138)


Clinical follow-up every 12 months
Death, Composite of Death/MI/Stoke, TVR

# MAIN COMPARE Registry, 3-Year

## Adjusted HR by Use of PS Matching

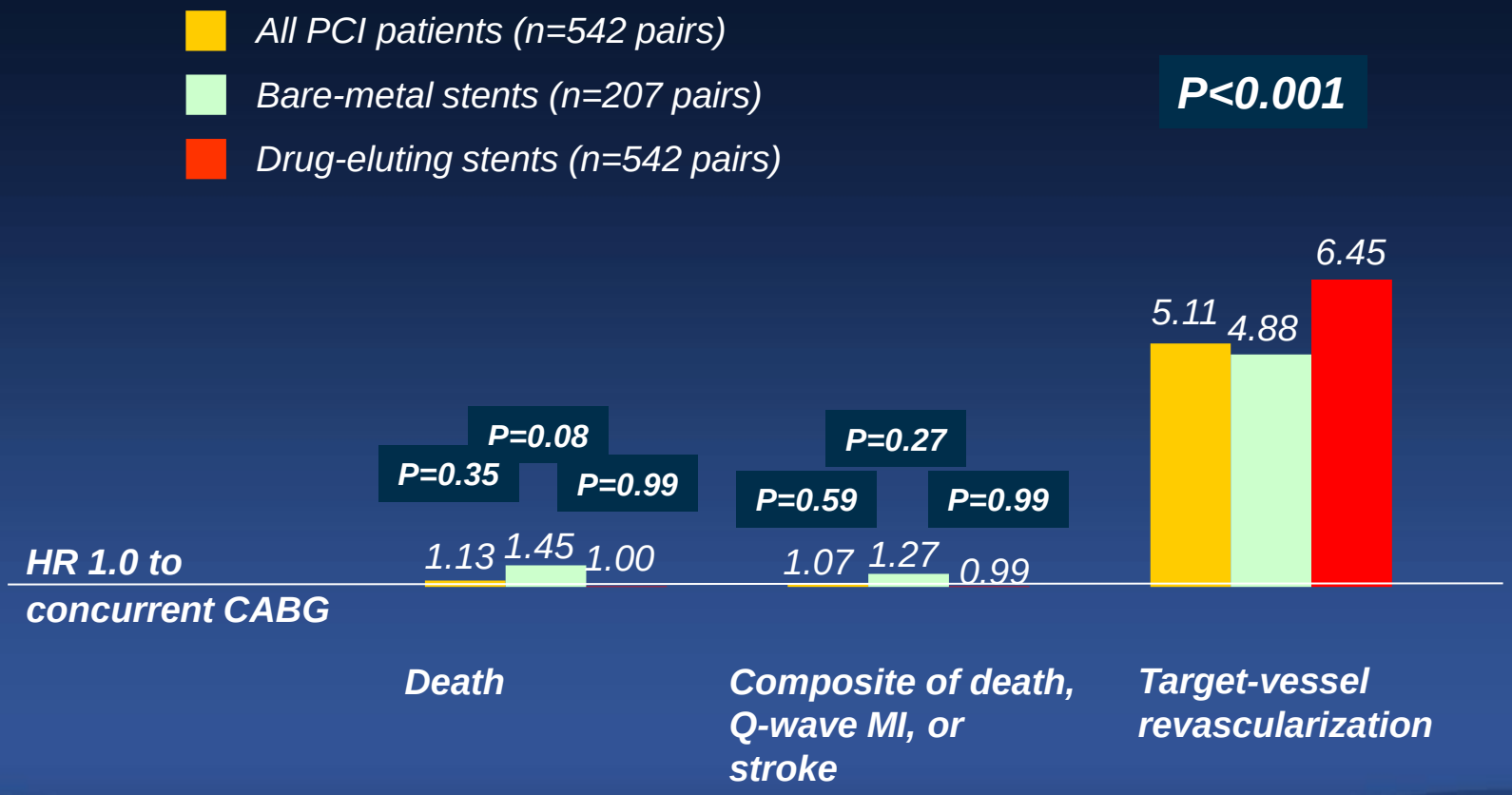





Seung KB, Park DW, Park SJ, et al. N Engl J Med 2008;358:1781-92

# MAIN COMPARE Registry, 5-Year

## Adjusted HR by Use of IPTW Method






Park DW, Park SJ, et al. J Am Coll Cardiol. 2010;56:117-24.

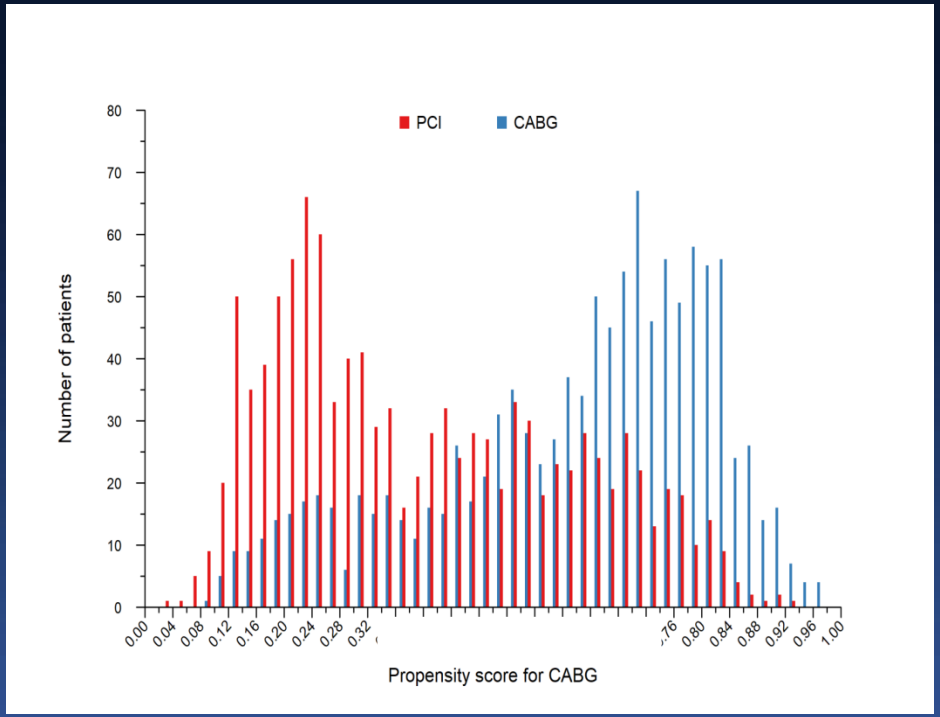
# Follow-up and National DB Linkage

- In this report, the follow-up period was extended through December 31, 2016, to ensure that all patients had the opportunity for at least 10-year follow-up evaluation.
- For validation of complete follow-up data on mortality, information about vital status was obtained from the National Population Registry of the Korea National Statistical Office with the use of a unique personal identification number up to December, 31, 2016.
- The median duration of follow-up among all patients was 12.0 years (IQR, 10.7 to 13.5); the maximum follow-up was 17.6 years.

# Baseline Characteristics

| | Unadjusted Data | | |
|---|---|---|---|
| | PCI (N = 1102) | CABG (N = 1138) | P Value |
| Age (yr) | 61.3±11.7 | 62.9±9.4 | <0.001 |
| Male gender | 779 (70.7) | 830 (72.9) | 0.24 |
| Diabetes mellitus | | | |
| Any diabetes | 327 (29.7) | 395 (34.7) | 0.01 |
| Requiring insulin | 75 (6.8) | 93 (8.2) | 0.22 |
| Hypertension | 546 (49.5) | 562 (49.4) | 0.94 |
| Hyperlipidemia | 315 (28.6) | 371 (32.6) | 0.04 |
| Current smoker | 282 (25.6) | 339 (29.8) | 0.03 |
| Previous PCI | 200 (18.1) | 125 (11.0) | <0.001 |
| Previous MI | 89 (8.1) | 132 (11.6) | 0.005 |
| Previous CHF | 27 (2.5) | 38 (3.3) | 0.21 |
| Chronic lung disease | 22 (2.0) | 23 (2.0) | 0.97 |
| Cerebrovascular disease | 78 (7.1) | 83 (7.3) | 0.84 |
| PVD | 16 (1.5) | 62 (5.4) | <0.001 |
| Renal failure | 30 (2.7) | 34 (3.0) | 0.71 |
| Ejection fraction (%) | 60.6±10.8 | 57.2±11.9 | <0.001 |

*Distribution of Propensity-Score*



# Baseline Characteristics

| | Unadjusted Data | | | Data Adjusted with IPTW | | | After Propensity Matching | |
|---|---|---|---|---|---|---|---|---|
| | PCI (N = 1102) | CABG (N = 1138) | P Value | PCI (N = 1102) | CABG (N = 1138) | P Value | PCI (N=659) | CABG (N=659) |
| Age (yr) | 61.3±11.7 | 62.9±9.4 | <0.001 | 62.1±11.0 | 62.1±10.1 | 0.89 | 62.6±11.2 | 63.2±9.7 |
| Male gender | 779 (70.7) | 830 (72.9) | 0.24 | 797 (72.3) | 820 (72.1) | 0.90 | 472 (71.6) | 457 (69.4) |
| Diabetes mellitus | | | | | | | | |
| Any diabetes | 327 (29.7) | 395 (34.7) | 0.01 | 338 (30.6) | 356 (31.3) | 0.73 | 338 (30.6) | 197 (29.9) |
| Requiring insulin | 75 (6.8) | 93 (8.2) | 0.22 | 84 (7.6) | 89 (7.9) | 0.82 | 84 (7.6) | 44 (6.7) |
| Hypertension | 546 (49.5) | 562 (49.4) | 0.94 | 525 (47.7) | 551 (48.4) | 0.71 | 525 (47.7) | 335 (50.8) |
| Hyperlipidemia | 315 (28.6) | 371 (32.6) | 0.04 | 340 (30.8) | 339 (29.8) | 0.60 | 340 (30.8) | 201 (30.5) |
| Current smoker | 282 (25.6) | 339 (29.8) | 0.03 | 313 (28.4) | 330 (29.0) | 0.76 | 313 (28.4) | 188 (28.5) |
| Previous PCI | 200 (18.1) | 125 (11.0) | <0.001 | 165 (15.0) | 172 (15.1) | 0.93 | 165 (15.0) | 99 (15.0) |
| Previous MI | 89 (8.1) | 132 (11.6) | 0.005 | 99 (9.0) | 111 (9.8) | 0.54 | 99 (9.0) | 67 (10.2) |
| Previous CHF | 27 (2.5) | 38 (3.3) | 0.21 | 32 (2.9) | 33 (2.9) | 0.95 | 32 (2.9) | 17 (2.6) |
| Chronic lung disease | 22 (2.0) | 23 (2.0) | 0.97 | 25 (2.3) | 20 (1.7) | 0.36 | 8 (1.2) | 10 (1.5) |
| Cerebrovascular disease | 78 (7.1) | 83 (7.3) | 0.84 | 71 (6.5) | 74 (6.5) | 0.96 | 48 (7.3) | 48 (7.3) |
| PVD | 16 (1.5) | 62 (5.4) | <0.001 | 46 (4.2) | 43 (3.9) | 0.66 | 15 (2.3) | 10 (1.5) |
| Renal failure | 30 (2.7) | 34 (3.0) | 0.71 | 34 (3.1) | 35 (3.1) | 0.98 | 16 (2.4) | 21 (3.2) |
| Ejection fraction (%) | 60.6±10.8 | 57.2±11.9 | <0.001 | 59.8±11.0 | 59.0±11.2 | 0.12 | 59.7±11.1 | 59.4±11.5 |

# Baseline Characteristics

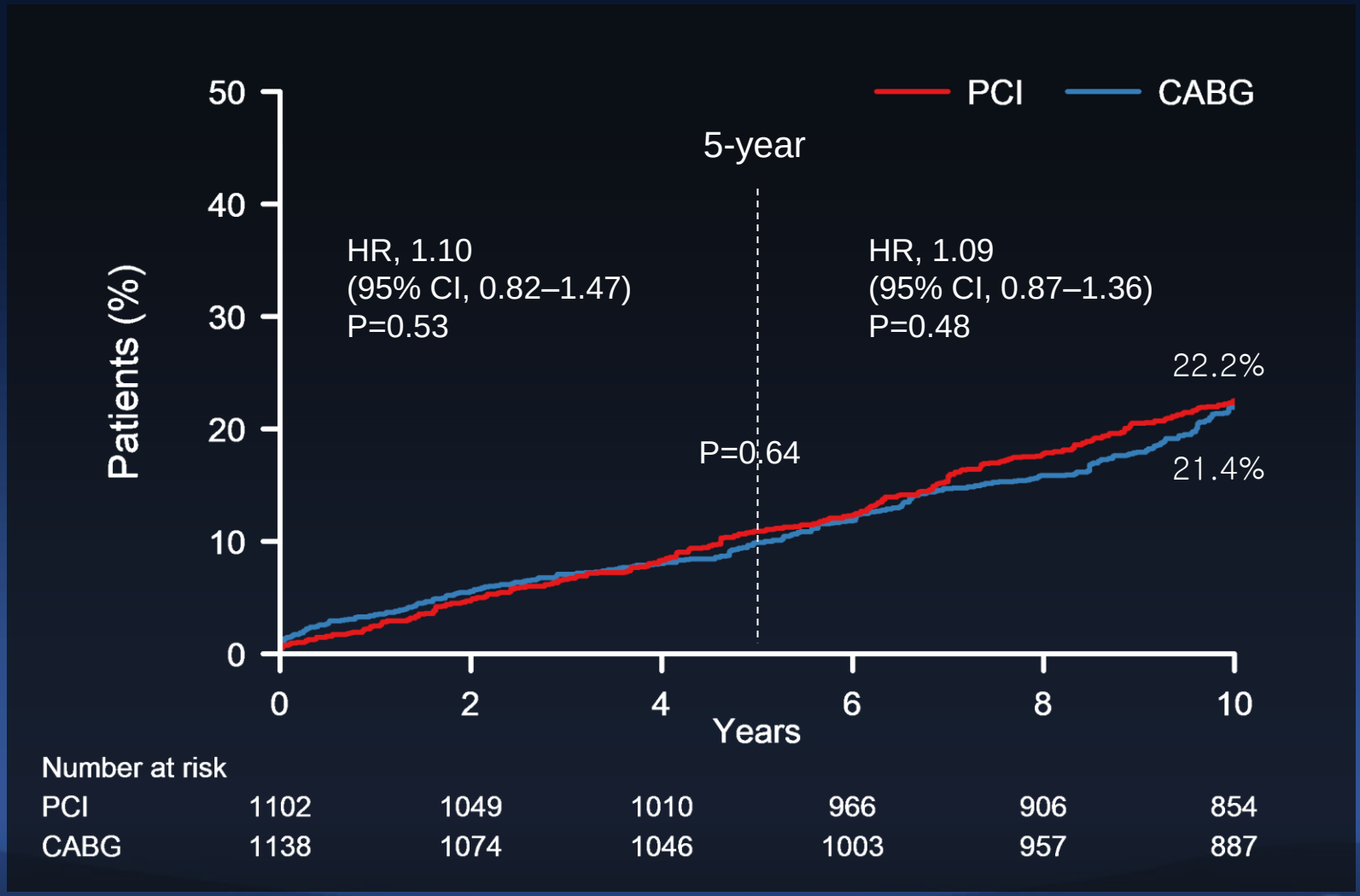
| | Unadjusted Data | | | Data Adjusted with IPTW | | | After Propensity Matching | |
|---|---|---|---|---|---|---|---|---|
| | PCI (N = 1102) | CABG (N = 1138) | P Value | PCI (N = 1102) | CABG (N = 1138) | P Value | PCI (N=659) | CABG (N=659) |
| ECG findings | | | 0.53 | | | 0.92 | | |
| Sinus rhythm | 1078 (97.8) | 1105 (97.1) | | 1076 (97.7) | 1109 (97.4) | | 644 (97.7) | 641 (92.3) |
| Atrial fibrillation | 22 (2.0) | 31 (2.7) | | 24 (2.2) | 28 (2.5) | | 15 (2.3) | 17 (2.6) |
| Other | 2 (0.2) | 2 (0.2) | | 1 (0.1) | 1 (0.1) | | 0 (0.0) | 1 (0.2) |
| Clinical indication | | | <0.001 | | | 0.96 | | |
| Silent ischemia | 33 (3.0) | 25 (2.2) | | 30 (2.7) | 32 (2.8) | | 23 (3.5) | 19 (2.9) |
| Chronic stable angina | 353 (32.0) | 226 (19.9) | | 289 (26.1) | 296 (26.0) | | 166 (25.2) | 173 (26.3) |
| Unstable angina | 608 (55.2) | 775 (68.1) | | 677 (61.4) | 692 (60.1) | | 401 (60.9) | 402 (61.0) |
| NSTEMI | 108 (9.8) | 112 (9.8) | | 107 (9.7) | 118 (10.4) | | 69 (10.5) | 65 (9.9) |
| LM disease location | | | 0.04 | | | 0.87 | | |
| Ostium or shaft | 557 (50.6) | 526 (46.2) | | 522 (47.3) | 543 (47.7) | | 316 (48.0) | 321 (48.7) |
| Distal bifurcation | 545 (49.5) | 612 (53.8) | | 580 (52.7) | 595 (52.3) | | 343 (52.0) | 338 (51.3) |
| Extent of disease | | | <0.001 | | | 0.98 | | |
| LM only | 278 (25.2) | 71 (6.2) | | 175 (15.9) | 186 (16.4) | | 81 (12.3) | 71 (10.8) |
| LM plus 1-VD | 264 (24.0) | 119 (10.5) | | 192 (17.4) | 201 (17.6) | | 114 (17.3) | 112 (17.0) |
| LM plus 2-VD | 287 (26.0) | 299 (26.3) | | 288 (26.1) | 291 (25.6) | | 212 (32.2) | 223 (33.8) |
| LM plus 3-VD | 273 (24.8) | 649 (57.0) | | 448 (40.1) | 460 (40.4) | | 252 (38.2) | 253 (38.4) |
| RCA disease | 396 (35.9) | 804 (70.7) | <0.001 | 584 (53.0) | 597 (52.5) | 0.81 | 350 (53.1) | 353 (53.6) |
| Restenotic lesion | 32 (2.9) | 14 (1.2) | 0.005 | 22 (2.0) | 22 (1.9) | 0.88 | 17 (2.6) | 12 (1.8) |

# Procedural Characteristics

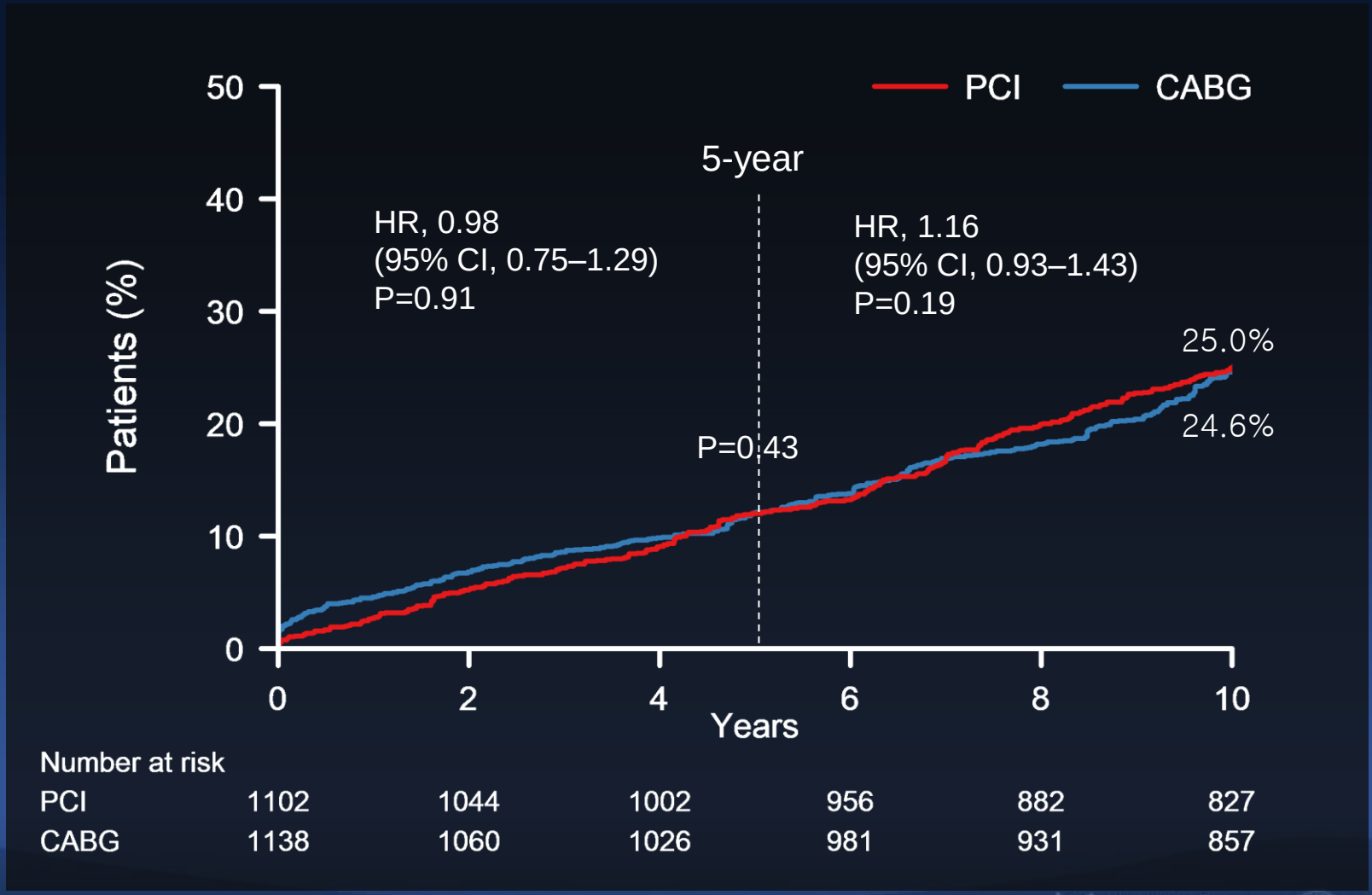
| | CABG (n = 1138) | PCI (n = 1102) |
|---|---|---|
| **CABG Group** | | |
| Off-pump surgery (%) | 42 | - |
| At least one arterial conduit (%) | 98 | - |
| IMA to LAD Graft (%) in patients with arterial conduits | 98 | - |
| Grafts / Patients (Mean ± SD) | 2.9±1.0 | - |
| **PCI Group** | | |
| Bare-metal stents(%) | - | 29 |
| Drug-eluting stents (%) | | 71 |
| Sirolimus stents of DES (%) | | 77 |
| Paclitaxel stents of DES (%) | | 23 |
| Number of stents at LMCA lesions | - | 1.2±0.5 |
| Total length of stents at LMCA (mm) | - | 28±21 |
| Average stent diameter at LM site | - | 3.5±0.4 |
| Number of stents per patients | - | 1.9±1.1 |

# Adjusted Curves with the Use of IPTW Method

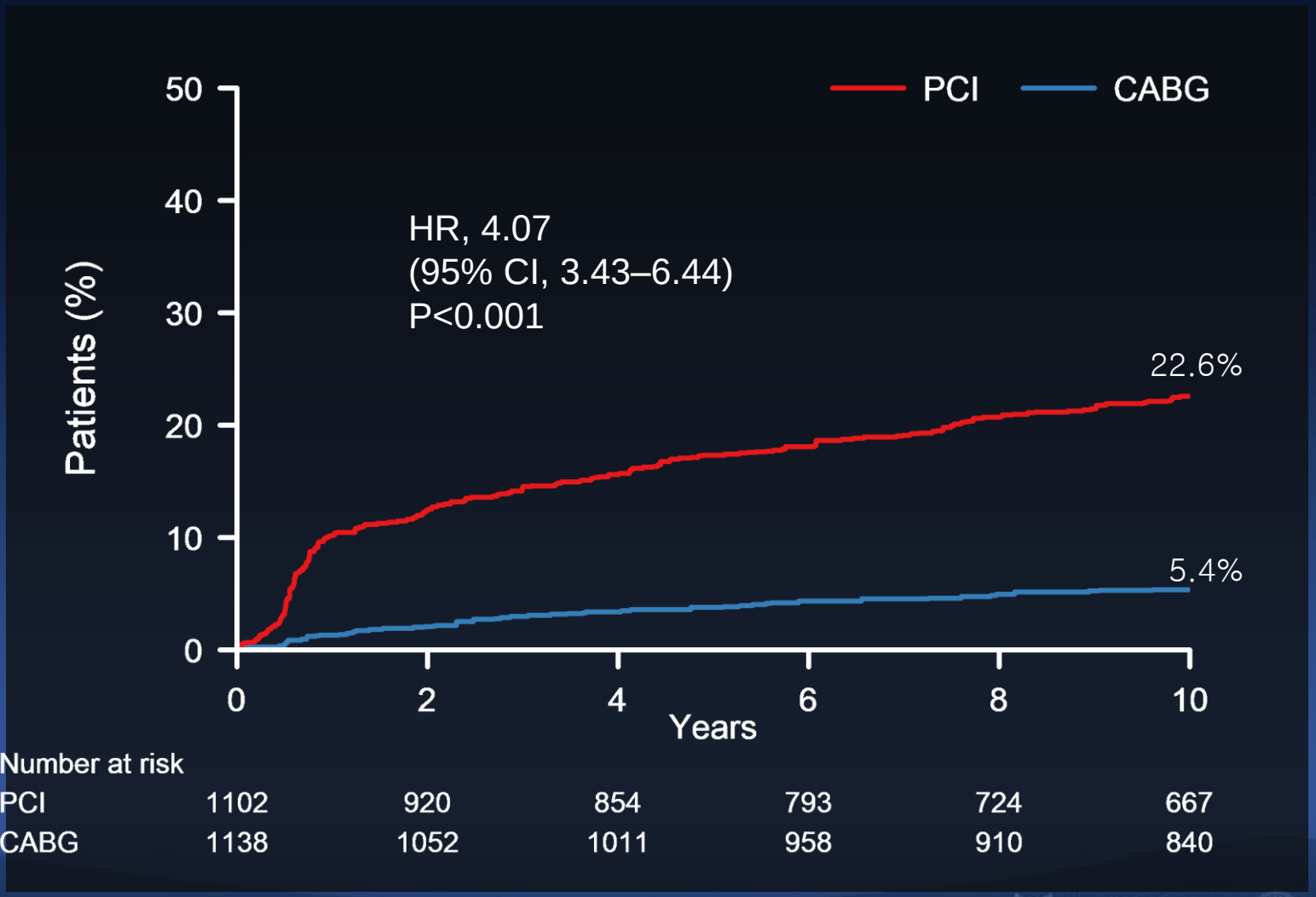
# Overall Cohort
## Death



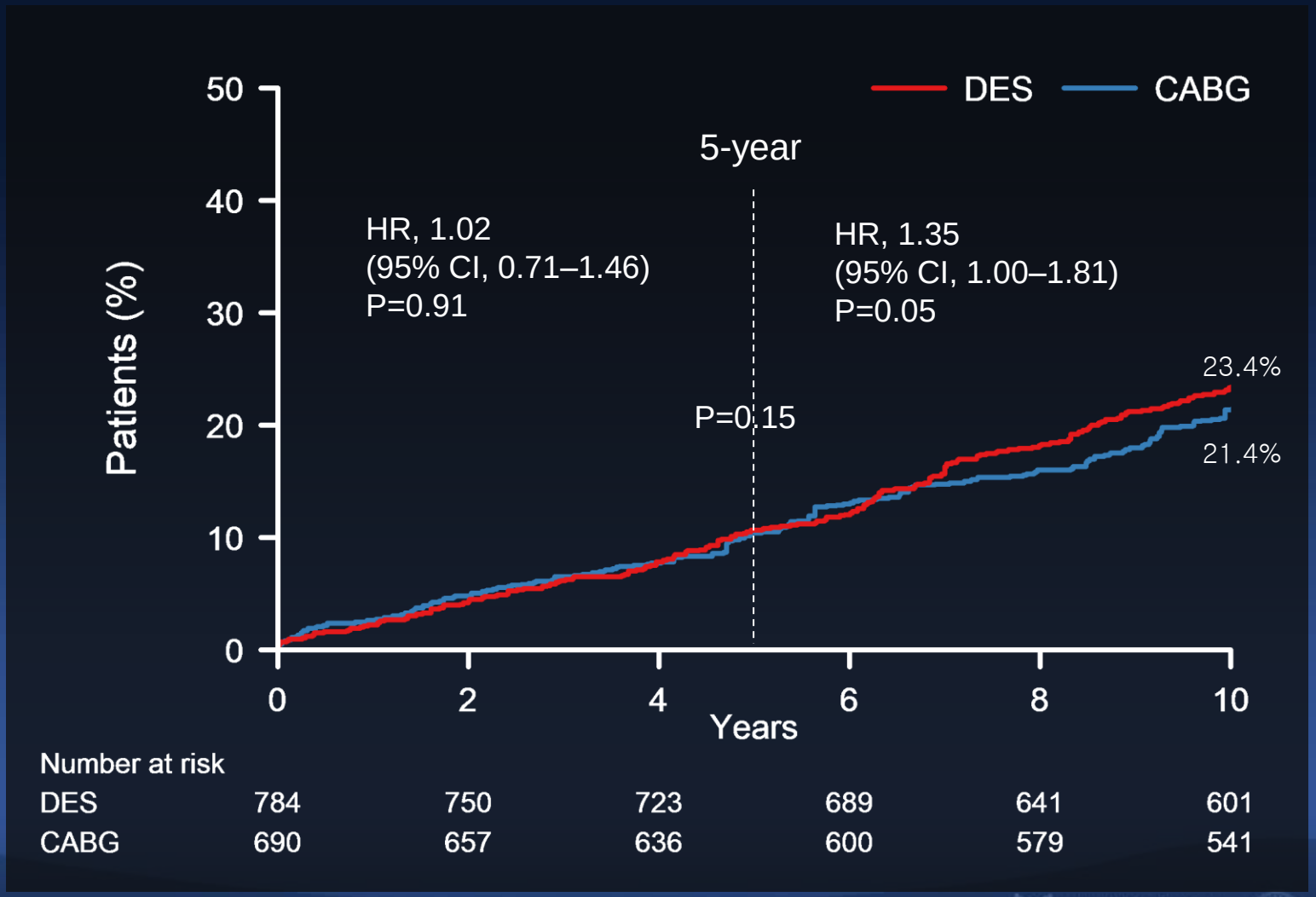
# Overall Cohort
# Death, Q-MI, or Stroke



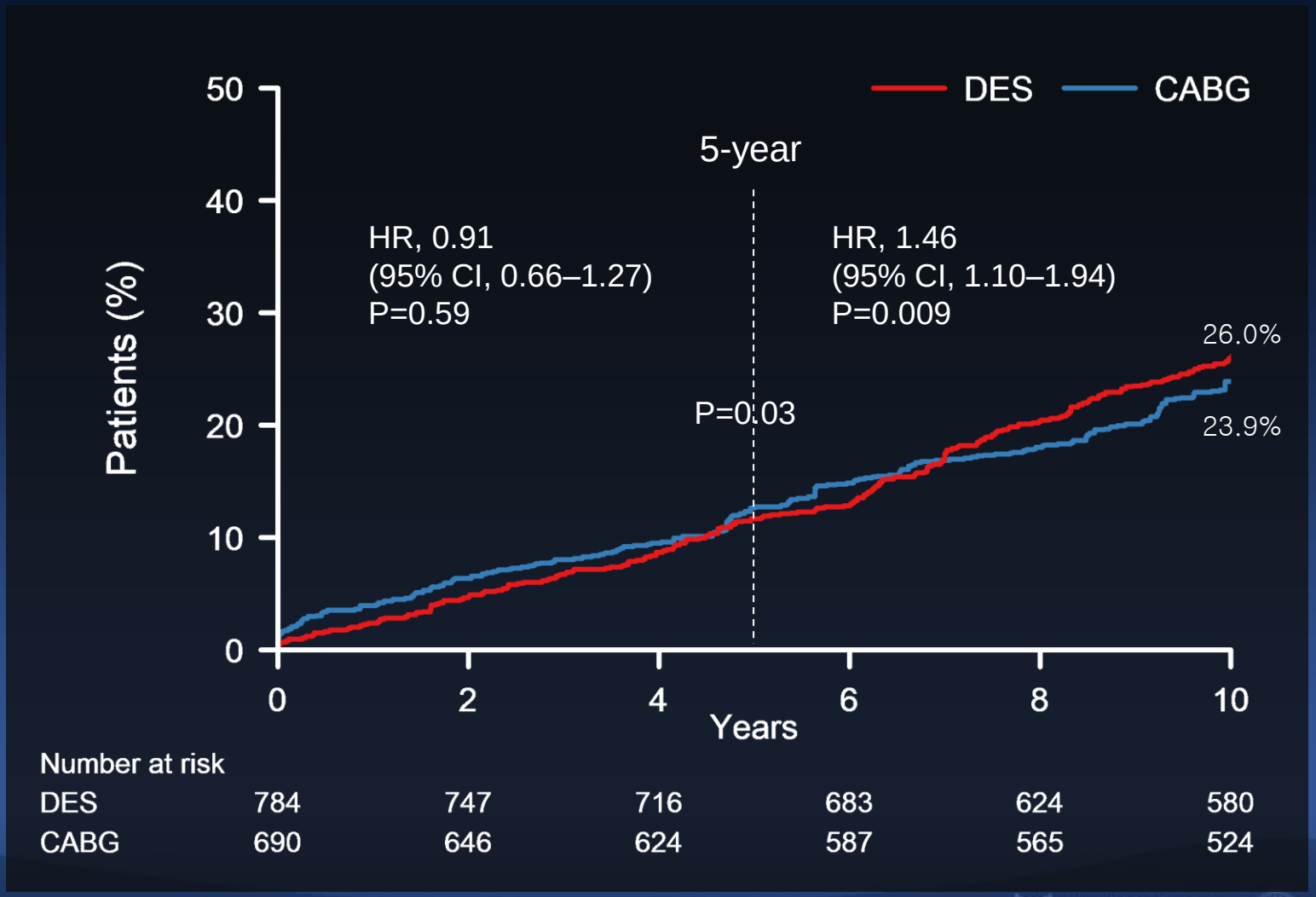
# Overall Cohort
# TVR



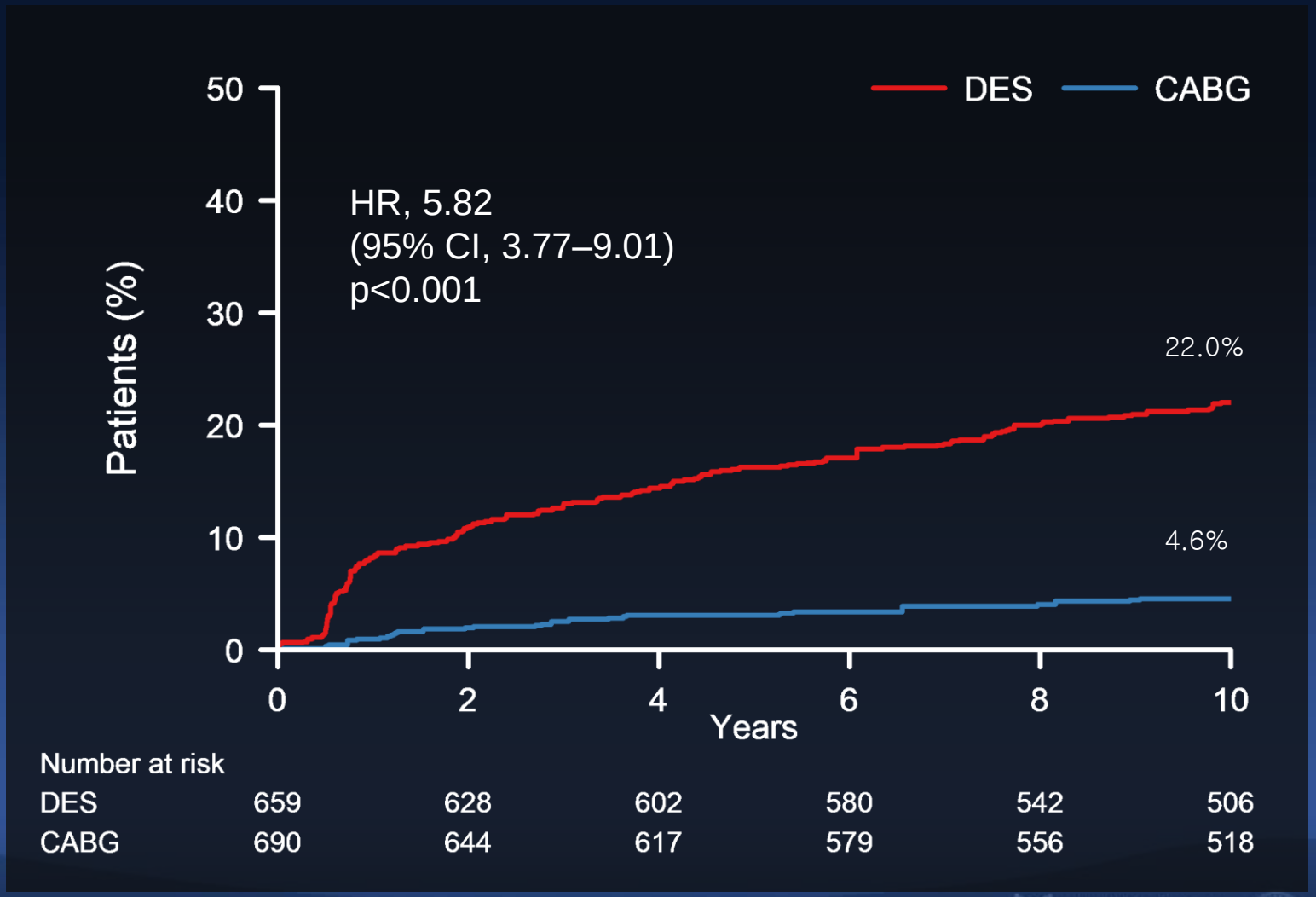
# Wave 2 (DES vs, CABG)
## Death



# Wave 2 (DES vs. CABG)
## Death, Q-MI, or Stroke



# Wave 2 (DES vs. CABG)
## TVR



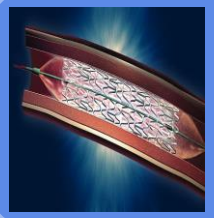
# Conclusions

- In this large-scale, multi-center cohort of patients with LMCA disease, there was no significant difference in the rates of death and a composite end point of death, Q-wave MI, or stroke between the PCI and the CABG groups up to 10 years.
- However, in the cohort comparing DES and concurrent CABG, DES was associated with higher risks of death and serious composite outcomes compared to CABG after 5 years: the treatment benefit of CABG has diverged over time during continued follow-up.
- The rate of target-vessel failure was consistently higher in the PCI group.

# DES vs. CABG
# *for LM Disease 2018*

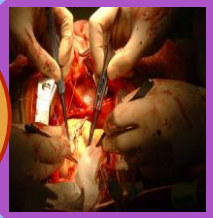
1. Mortality of PCI with DES is Comparable with CABG
2. More protective for MI in CABG
3. Higher Stroke in CABG
4. Higher Revascularization in PCI
5. 10-Year report of the MAIN-COMPARE registry showed higher risks of death and serious composite outcomes after DES than after CABG.
6. Long-term (10 year) comparative outcomes should be confirmed or refuted via extended FU of RCTs (EXCEL and NOBLE).

# Contemporary Heart Team for Decision-Making



**PCI**
- Less invasive and early recovery
- Early safety advantage
(less MI, less stroke, or less major periprocedural adverse events)
- Similar mortality

**Heart Team Approach**



**CABG**
- Long-term durability
- Less revascularization
- Less spontaneous MI
- Similar mortality

Favor for PCI ← **Recommendation** → Favor for CABG

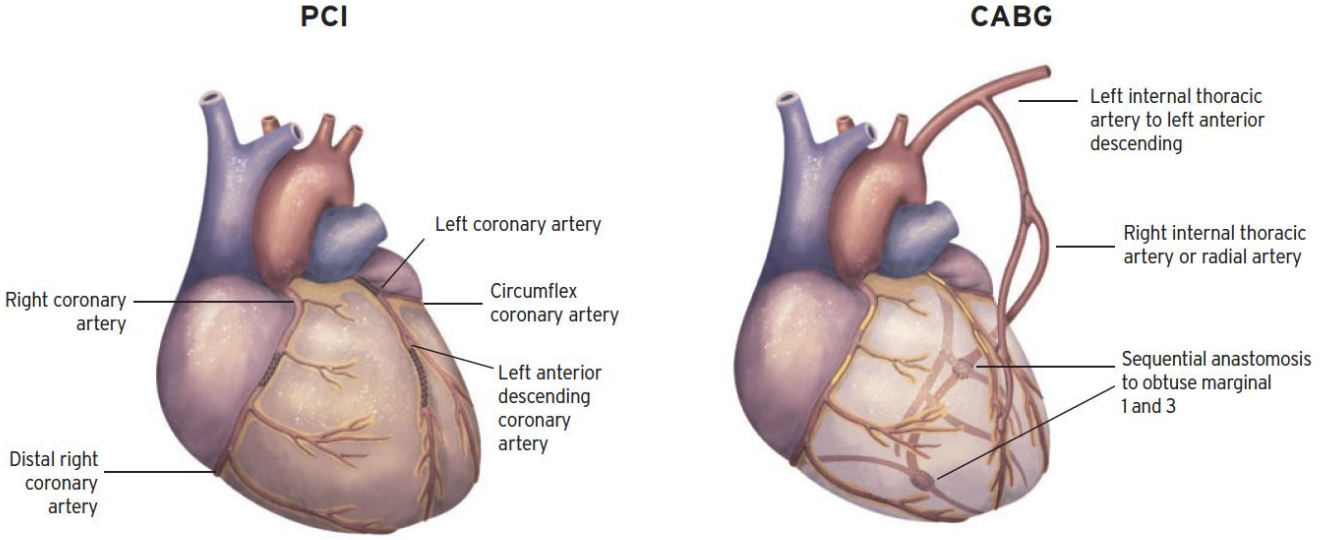
| | | | |
|---|---|---|---|
| **Clinical Factors** | - Urgent revascularization<br>- Serious comorbidity and high surgical risk (i.e., chronic lung disease, advanced age, disability from prior stroke, prior bypass surgery, or poor general performance) | - Clinical equipose | - Low ejection fraction<br>- Longstanding diabetes<br>- Need for any concomitant cardiac surgery<br>- High-bleeding risk unable to comply with DAPT |
| **Anatomical Factors** | - Ostial or trunk LM disease<br>- Isolate LM disease (non-bifurcational or bifurcational)<br>- LM plus additional 1-vessel disease | - LM plus additional 2-vessel disease | - LM plus additional 3-vessel disease<br>- Combined complex anatomy not suitable for PCI (i.e., severe calcification or tortuosity, CTO, multiple/diffuse long lesions, or complex in-stent restenosis) |

Each patient's individual circumstances and preferences



Par DW, Park SJ. Circ Cardiovasc Interv. 2017 Jun;10(6)

# Contemporary Heart Team for Decision-Making




## FAVOURS PCI

**Clinical characteristics**

Presence of severe co-morbidity (not adequately reflected by scores)

Advanced age/frailty/reduced life expectancy

Restricted mobility and conditions that affect the rehabilitation process

**Anatomical and technical aspects**

MVD with SYNTAX score 0–22

Anatomy likely resulting in incomplete revascularization with CABG due to poor quality or missing conduits

Severe chest deformation or scoliosis

Sequelae of chest radiation

Porcelain aorta[a]

## FAVOURS CABG

**Clinical characteristics**

Diabetes

Reduced LV function (EF ≤35%)

Contraindication to DAPT

Recurrent diffuse in-stent restenosis

**Anatomical and technical aspects**

MVD with SYNTAX score ≥23

Anatomy likely resulting in incomplete revascularization with PCI

Severely calcified coronary artery lesions limiting lesion expansion

**Need for concomitant interventions**

Ascending aortic pathology with indication for surgery

Concomitant cardiac surgery

Neumann FJ et al. 2018 ESC/EACTS Guidelines