LM Revascularization 2022:
Guidelines and Concept Change

Duk-Woo Park, MD
Professor, Heart Institute, Asan Medical Center,
University of Ulsan College of Medicine, Seoul, Korea

Disclosure

- Dr D.-W. Park reports grants from Daiichi-Sankyo, ChongKunDang Pharm, and Daewoong Pharm; personal fees from Edwards and Medtronic; and grants and personal fees from Abbott Vascular

Interventional Cardiologist Dilemma in Contemporary ISCHEMIA Trial Era

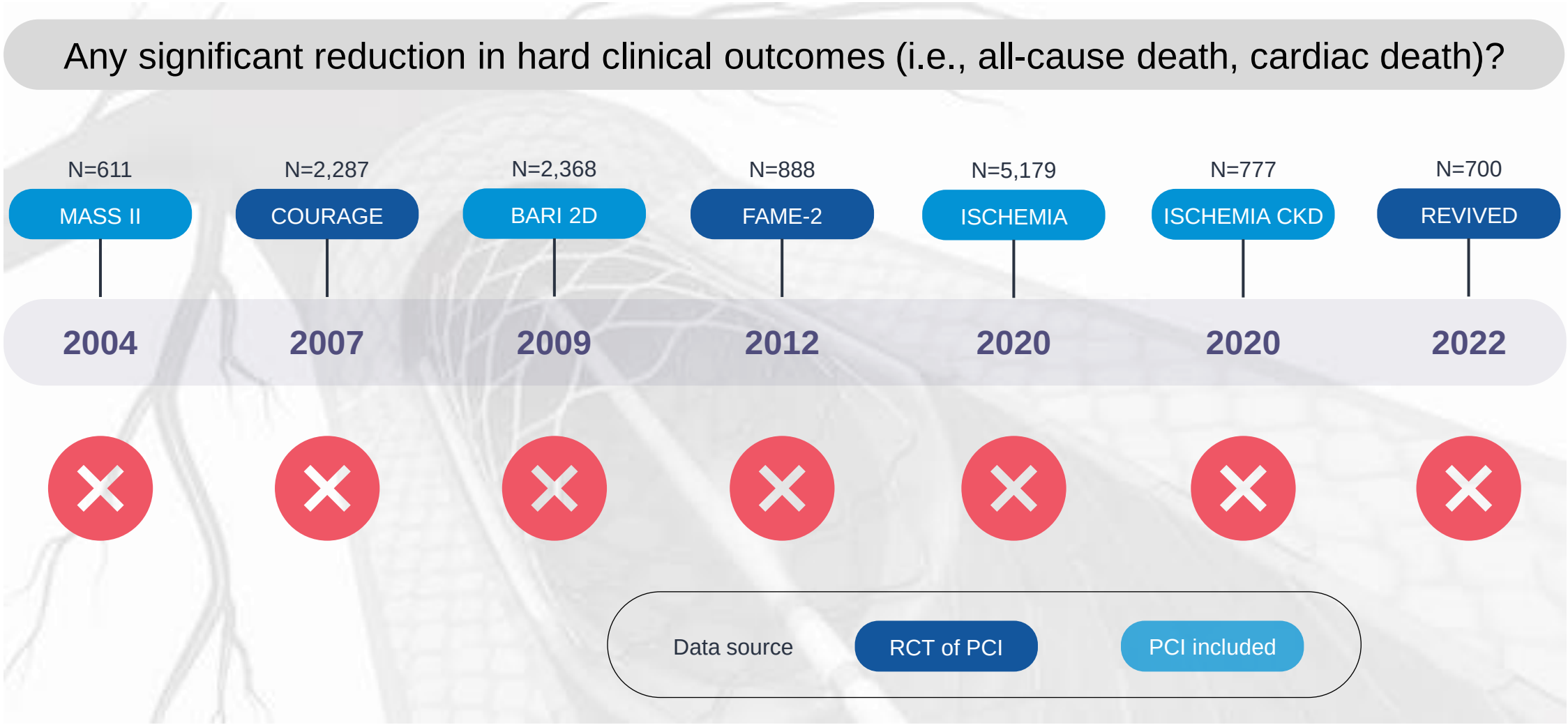
- Each time, new series of PCI trials goes **neutral or worse** vs. OMT or CABG, some in the interventional cardiology community call for another new RCTs with “different patients”, “better stents”, “more IVUS”, “more FFR”, “more follow-up”, “another trial endpoints”.
  - I’m an interventional cardiologist but, with the evidence generated so far, I believe we can safely conclude that PCI does not improve survival in patients with SIHD.
  - However, PCI maintains a key role in ACS, and for the improvement of patient-oriented outcome measures in patients with angina unresponsive to medical therapy or unwilling to take too many anti-anginal medications or unwilling to receive invasive CABG.

@dukwoo_park

dwpark@amc.seoul.kr

PCI vs. OMT for SIHD

Any significant reduction in hard clinical outcomes (i.e., all-cause death, cardiac death)?



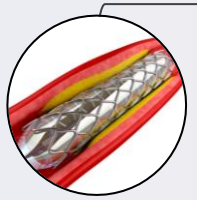
REVIVED

Percutaneous revascularization for ischemic left ventricular dysfunction

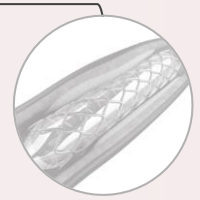
MULTICENTER, RANDOMIZED, OPEN LABEL

700

Patients with a LVEF of 35% or less, extensive CAD amenable to PCI, and demonstrable myocardial viability, **most with little or no angina**



PCI
+ OMT



No PCI
OMT only

↓ KCCQ and EQ-5D-5L scores at 6 and 12 months; no difference at 24 months

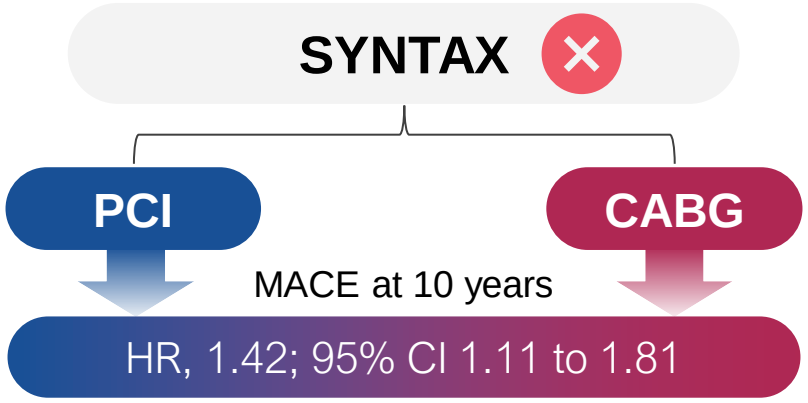
41 months (median)

37.2% — Death or hospitalization for heart failure — **38.0%**

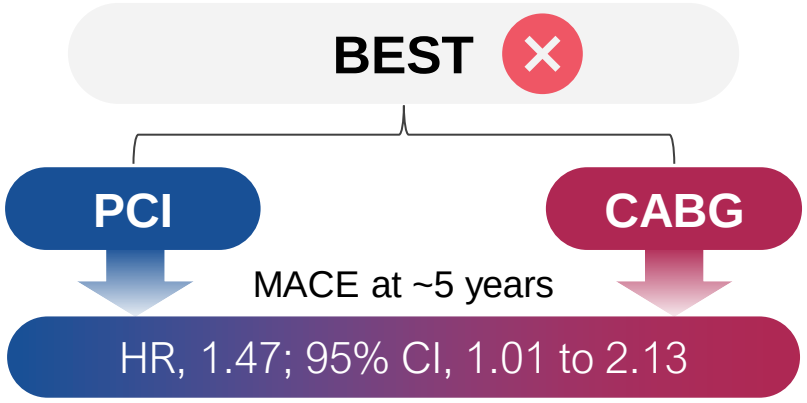
HR, 0.99; 95% CI, 0.78 to 1.27; P=0.96

Perera D, et al. N Engl J Med 2022; DOI: 10.1056/NEJMoa2206606

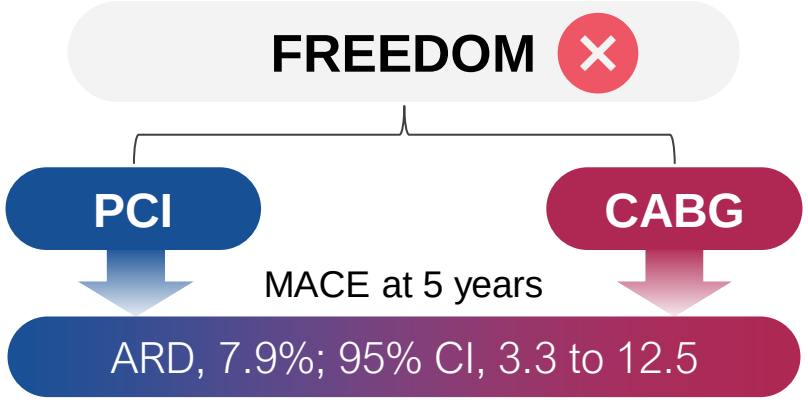
PCI or CABG for multivessel disease



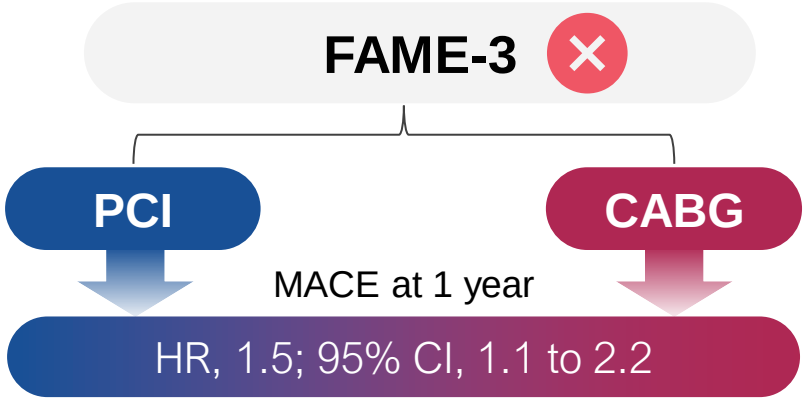
Lancet 2019;394;1325-1334



N Engl J Med 2015;372:1204-1212



N Engl J Med 2012;367:2375-2384



N Engl J Med 2022;386:128-137

Class I recommendations for **prognosis**

American College of Cardiology
American Heart Association
Coronary artery revascularization 2021

Recommendations for revascularization	Class	Level
In patients with SIHD and multivessel CAD appropriate for CABG with severe left ventricular systolic dysfunction (left ventricular ejection fraction <35%), CABG is recommended to improve survival (Based on STICH 10-Year FU) (Issued before REVIVED)	1	A

Lawton J, et al. J Am Coll Cardiol. 2022;79:e21-e129

European Society of Cardiology
European Association for Cardiothoracic Surgery
Myocardial revascularization 2018

Recommendations for revascularization	Class	Level
Two- or three-vessel disease with stenosis >50% with impaired LV function (LVEF ≤35%) (Issued before REVIVED)	I	A
Large area of ischaemia detected by functional testing (>10% LV) or abnormal invasive FFR (Issued before ISCHEMIA)	I	B

Neumann FJ, et al. Eur Heart J. 2019;40:87-165

Class I recommendations for **symptoms**

American College of Cardiology
American Heart Association
Coronary artery revascularization 2021

Recommendations for revascularization	Class	Level
In patients with refractory angina despite medical therapy and with significant coronary artery stenoses amenable to revascularization, revascularization is recommended to improve symptoms	1	A

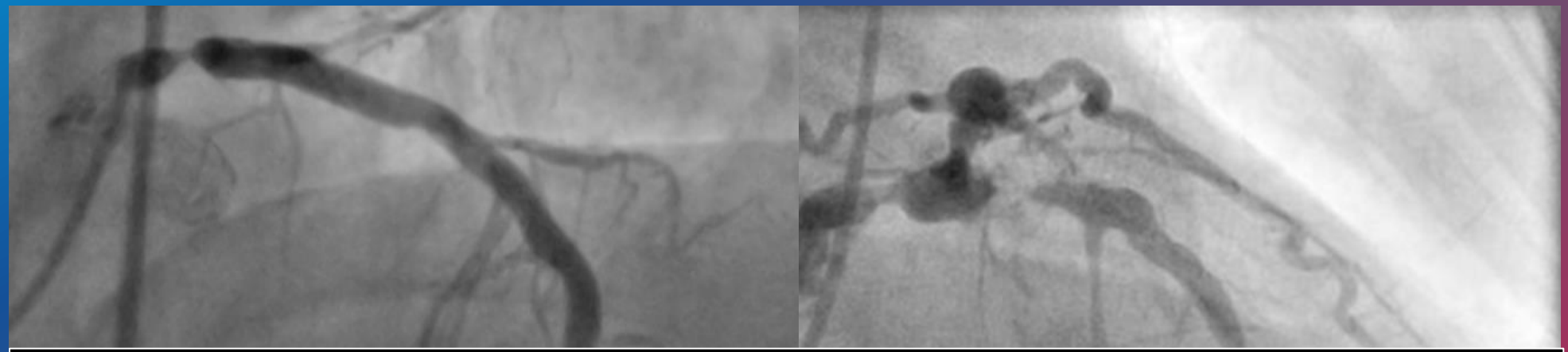
Lawton J, et al. J Am Coll Cardiol. 2022;79:e21-e129

European Society of Cardiology
European Association for Cardiothoracic Surgery
Myocardial revascularization 2018

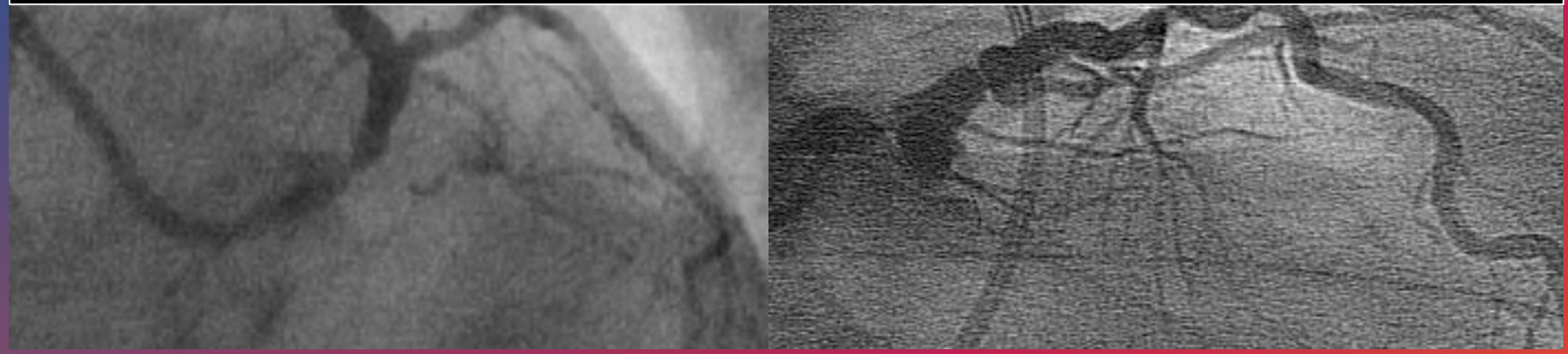
Recommendations for revascularization	Class	Level
Haemodynamically significant coronary stenosis in the presence of limiting angina or angina equivalent, with insufficient response to optimized medical therapy* * in consideration of patient compliance and wishes in relation to the intensity of anti-anginal therapy	I	A

Neumann FJ, et al. Eur Heart J. 2019;40:87-165

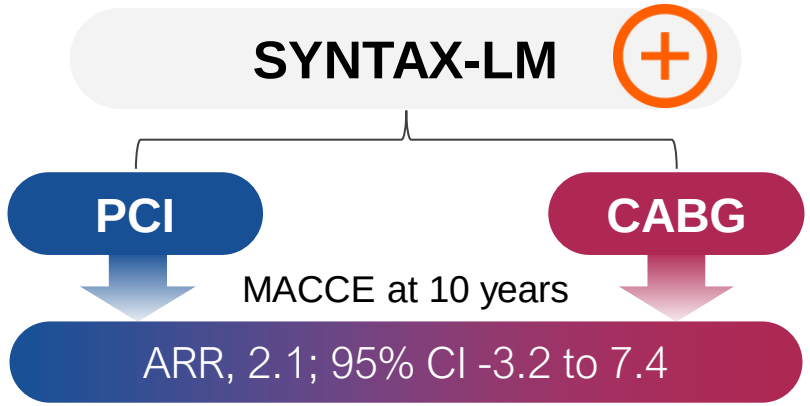
Diverse Spectrum of Left Main Disease



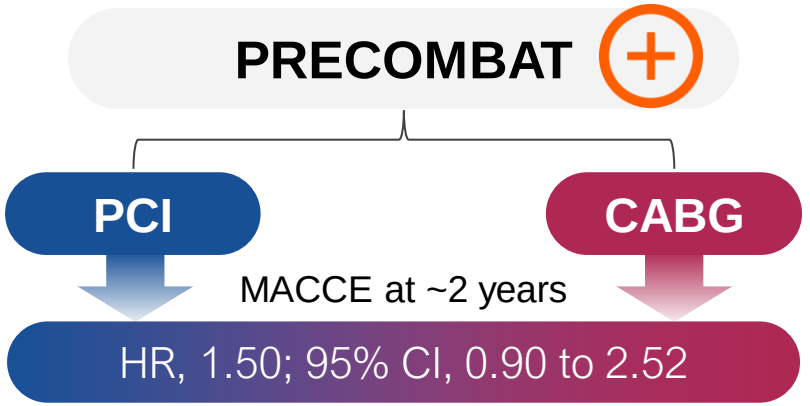
Until recently, CABG was the gold standard treatment for LMCAD



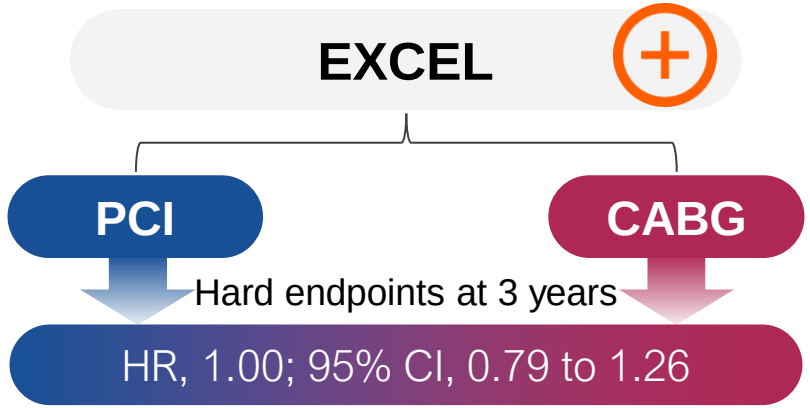
PCI vs. CABG for left main disease



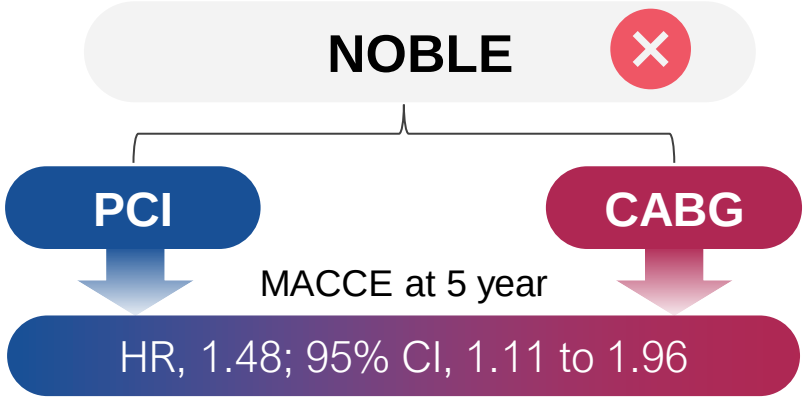
Circulation. 2010;121:2645-2653



N Engl J Med 2011;364:1718-27



N Engl J Med 2016;375:2223-2235



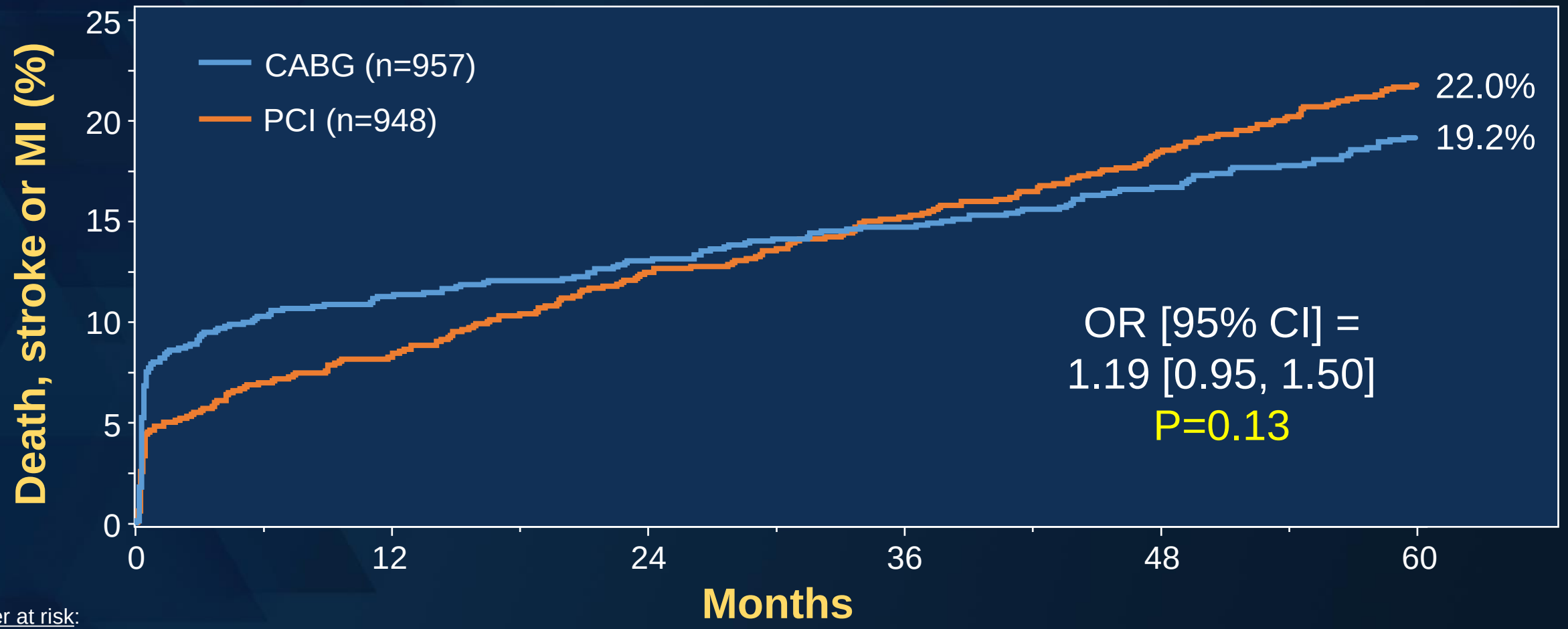
Lancet 2016; 388):2743-2752

LM PCI vs CABG Controversy
= EXCEL Controversy

Is Mortality Different?

Primary Endpoint

All-cause Death, Stroke or MI at 5 Years

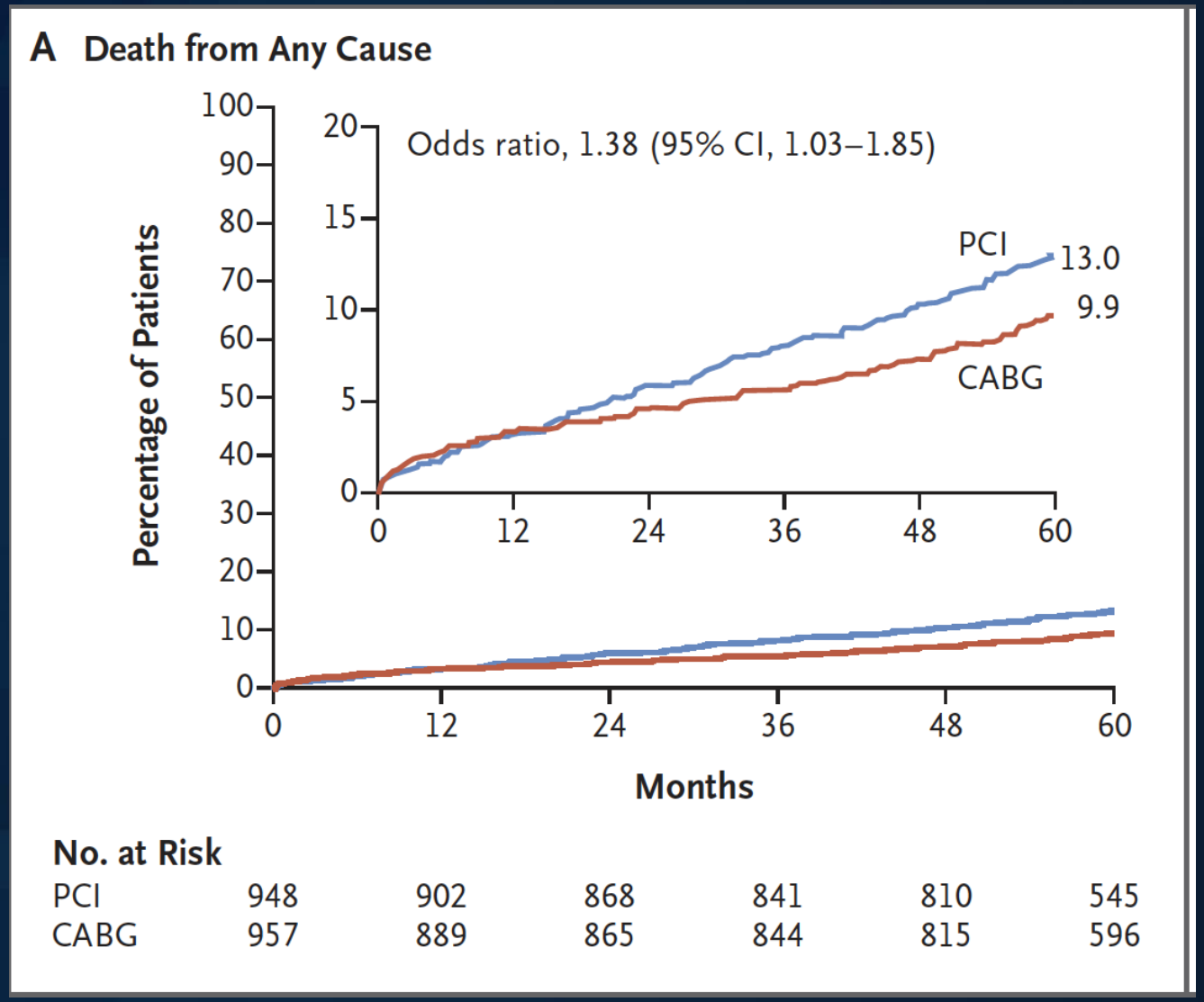


Number at risk:

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

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

Secondary Endpoint
All-cause Mortality at 5 Years

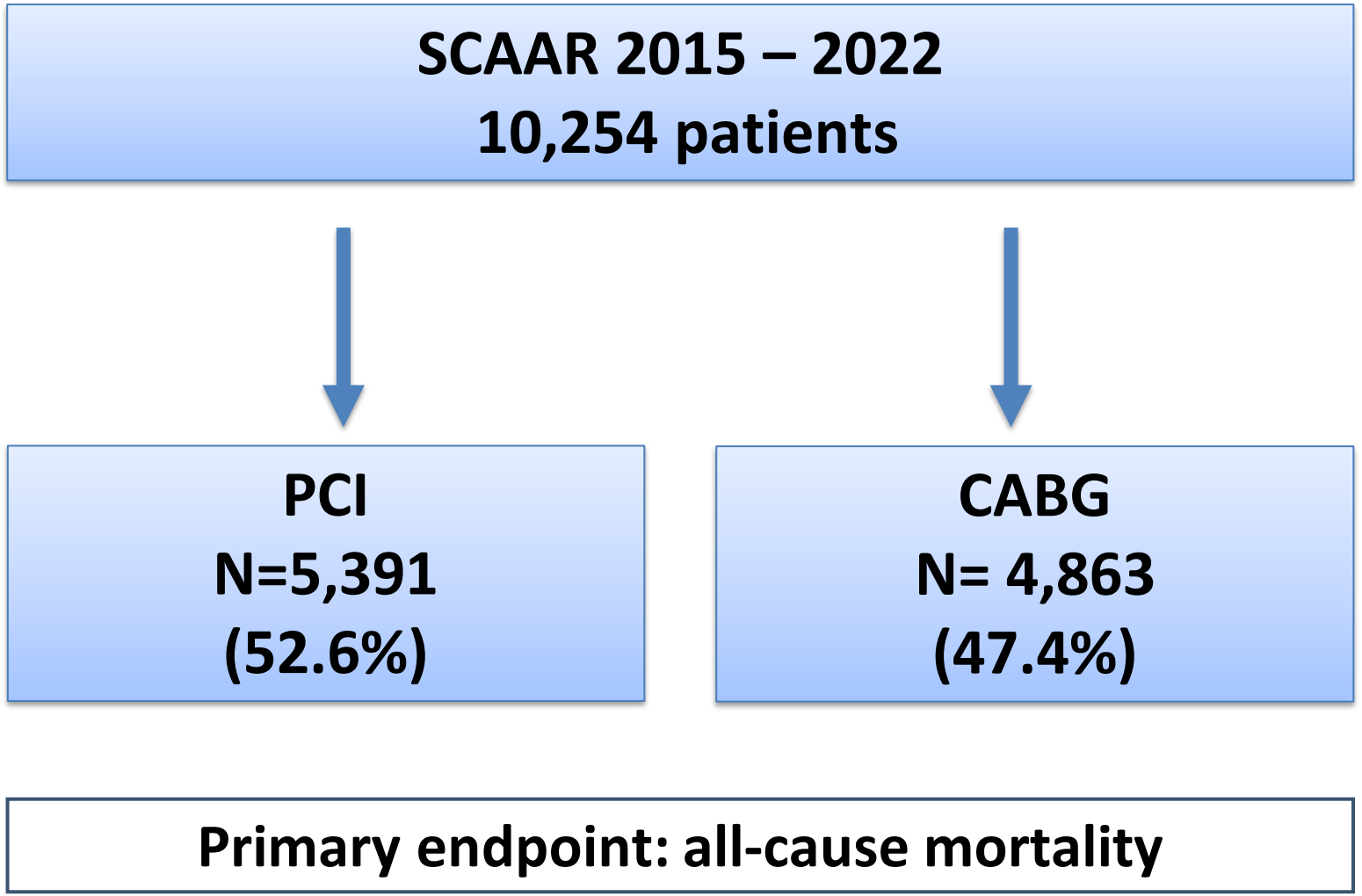


Survival after PCI or CABG for Left Main Coronary Disease: A report from the Swedish Coronary Angiography and Angioplasty Registry

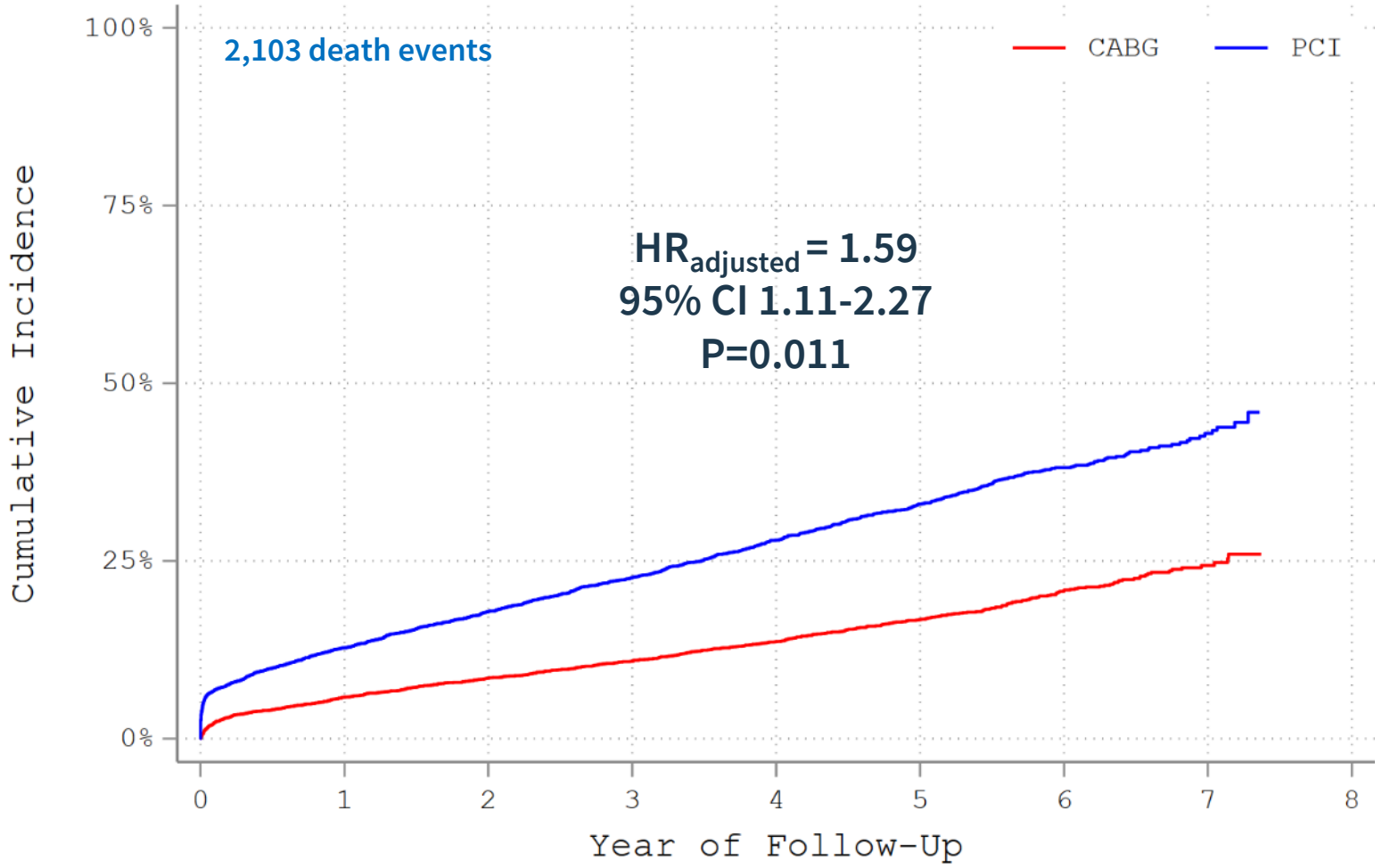
Elmir Omerovic
MD, PhD, FESC, Professor of Cardiology
Department of Cardiology, Sahlgrenska University Hospital,
Institute of Medicine, Gothenburg University
Gothenburg, Sweden

Truls Råmunddal, Björn Redfors, Pétur Petursson, Oskar Angerås, Araz Rawshani, Moman Mohammad, Jonas Persson, Tomas Jernberg, Göran Dellgren, Ole Fröbert, Nils Witt, Stefan James, Rickard Linder, David Erlinge, Anders Jeppsson, Elmir Omerovic

Methods


SCAAR 2015 – 2022
10,254 patients
PCI
N=5,391
(52.6%)
CABG
N= 4,863
(47.4%)
Primary endpoint: all-cause mortality

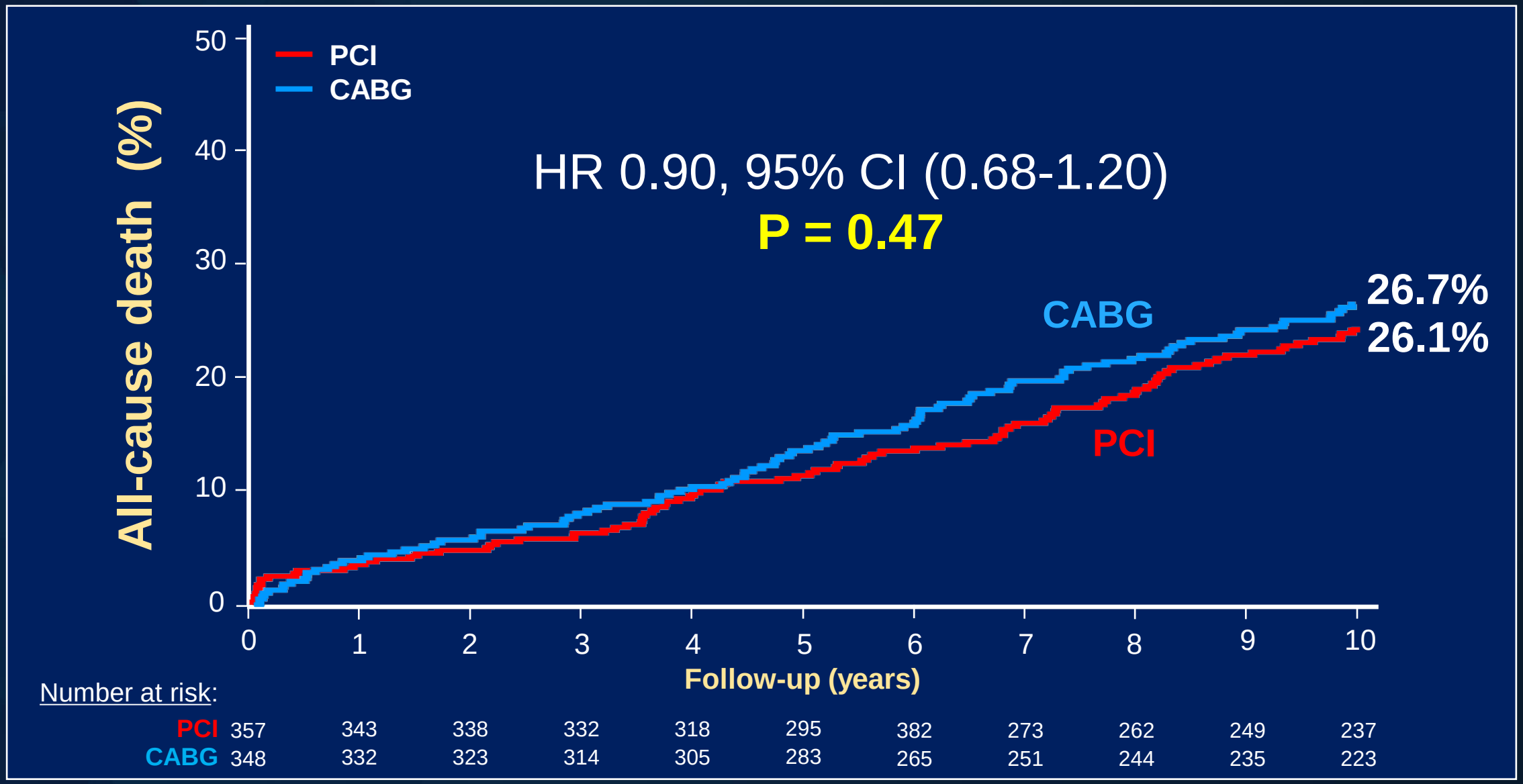
All-Cause Mortality



Number at risk

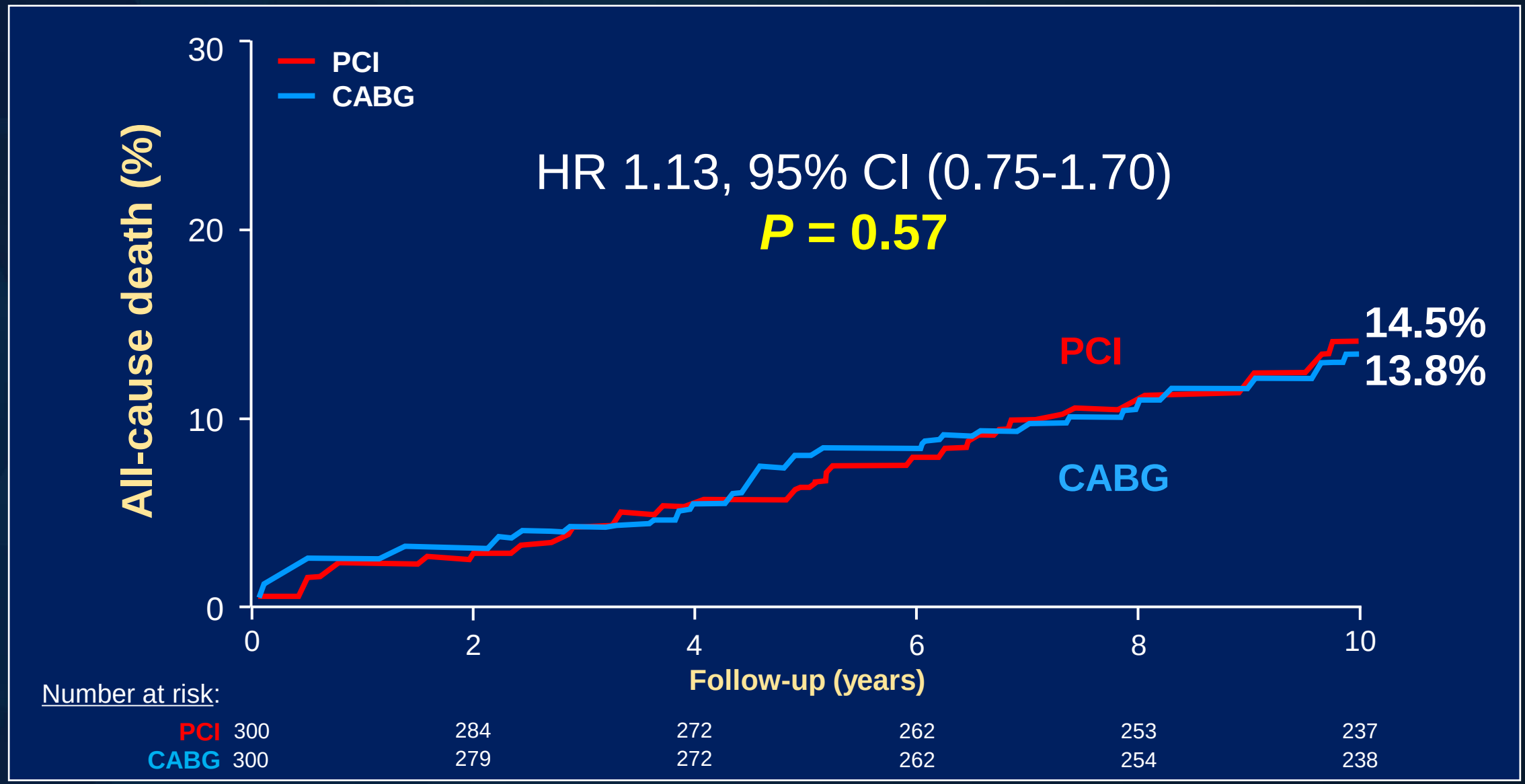
CABG	4863	4054	3435	2808	2116	1442	810	209	0
PCI	5391	4055	3308	2501	1795	1147	587	146	0

SYNTAX Left Main at 10 Years: Mortality



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

PRECOMBAT Left Main at 10 Years: Mortality



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

Individual Outcomes at 5 Years

EXCEL was not powered for these outcomes

- Prone to type II error (false negatives)

Not adjusted for multiplicity

- Prone to type I error (false positives)

Not designed for hypothesis testing

- No P-values

IPD Meta-analysis!

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

Percutaneous coronary intervention with drug-eluting stents versus coronary artery bypass grafting in left main coronary artery disease: an individual patient data meta-analysis

Marc S Sabatine, Brian A Bergmark*, Sabina A Murphy, Patrick T O'Gara, Peter K Smith, Patrick W Serruys, A Pieter Kappetein, Seung-Jung Park, Duk-Woo Park, Evald H Christiansen, Niels R Holm, Per H Nielsen, Gregg W Stone, Joseph F Sabik, Eugene Braunwald*

Summary

Background The optimal revascularisation strategy for patients with left main coronary artery disease is uncertain. We therefore aimed to evaluate long-term outcomes for patients treated with percutaneous coronary intervention (PCI) with drug-eluting stents versus coronary artery bypass grafting (CABG).

Methods In this individual patient data meta-analysis, we searched MEDLINE, Embase, and the Cochrane database using the search terms "left main", "percutaneous coronary intervention" or "stent", and "coronary artery bypass graft*" to identify randomised controlled trials (RCTs) published in English between database inception and Aug 31, 2021, comparing PCI with drug-eluting stents with CABG in patients with left main coronary artery disease that had at least 5 years of patient follow-up for all-cause mortality. Two authors (MSS and BAB) identified studies meeting the criteria. The primary endpoint was 5-year all-cause mortality. Secondary endpoints were cardiovascular death, spontaneous myocardial infarction, procedural myocardial infarction, stroke, and repeat revascularisation. We used a one-stage approach; event rates were calculated by use of the Kaplan-Meier method and treatment group comparisons were made by use of a Cox frailty model, with trial as a random effect. In Bayesian analyses, the probabilities of absolute risk differences in the primary endpoint between PCI and CABG being more than 0·0%, and at least 1·0%, 2·5%, or 5·0%, were calculated.

Published Online
November 15, 2021
https://doi.org/10.1016/S0140-6736(21)02334-5

See Online/Comment
https://doi.org/10.1016/S0140-6736(21)02491-0

*Contributed equally

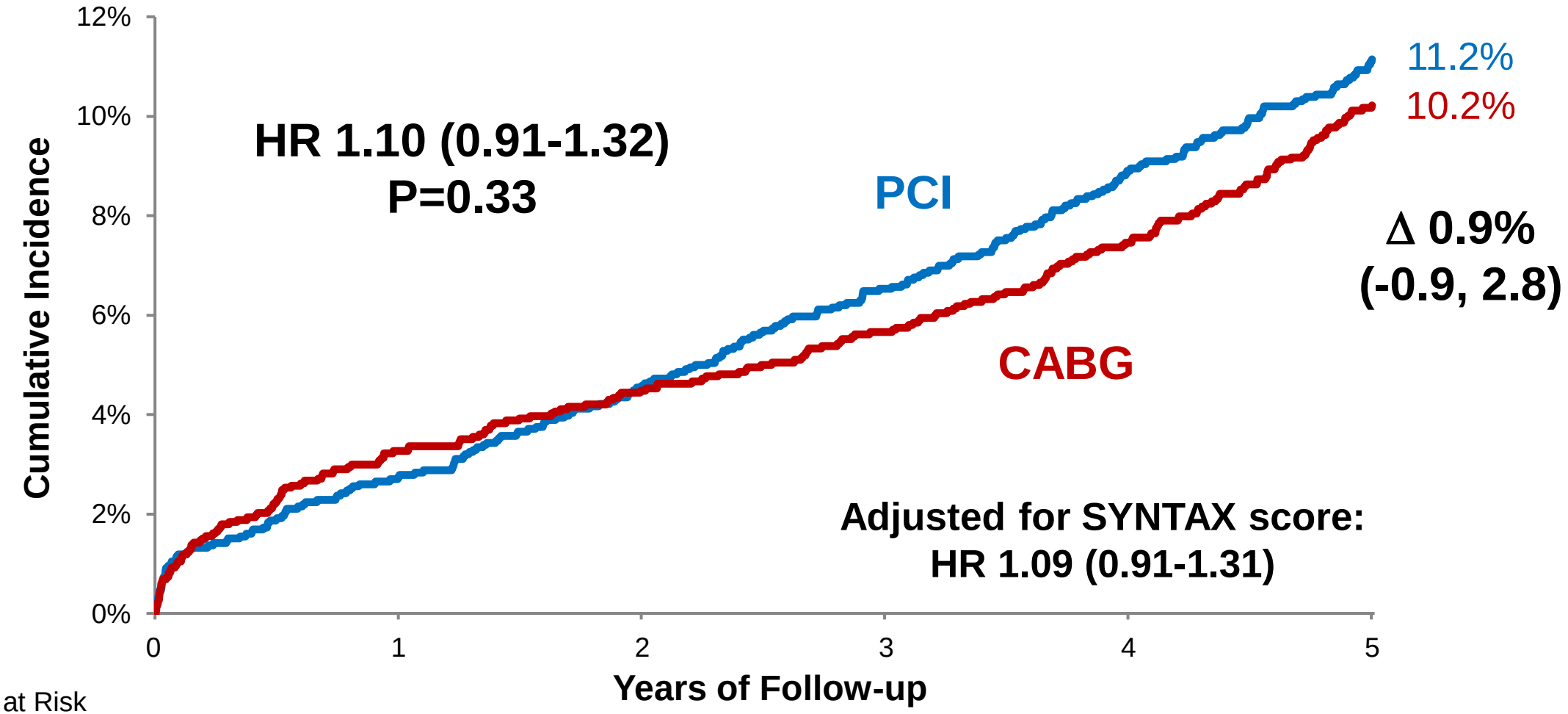
Thrombolysis in Myocardial Infarction Study Group (Prof M S Sabatine MD, B A Bergmark MD, S A Murphy MPH, Prof E Braunwald MD) **and Division of Cardiovascular Medicine** (Prof M S Sabatine, B A Bergmark, S A Murphy, Prof P T O'Gara MD,

Trial Summaries

	SYNTAX (LM)	PRECOMBAT	NOBLE	EXCEL
N	705	600	1201	1905
Yrs enrol.	2005-2007	2004-2009	2008-2015	2010-2014
Regions	Europe/NA	Asia/Pacific	Europe	Europe/NA/SA/Asia/Pacific
PEP	Death, stroke, MI, or repeat revasc	Death, stroke, MI or ID-TVR	Death, stroke, non-procedural MI, or repeat revasc	Death, stroke, or MI
Key Inclusion	• LMCA ≥50% • Stable or unstable angina or silent isch.	• LMCA ≥50% • Silent isch. stable angina, UA, or MI >1wk	• LMCA ≥50% or FFR ≤0.80 • ≤3 other complex lesions • Stable angina, NSTEACS, STEMI >24h	• LMCA ≥70% or 50-70% plus invasive[1] or non-invasive assessment • Local SYNTAX ≤32
Key Exclusion	• Prior PCI/CABG • Acute MI	• Prior CABG or LM PCI • Prior PCI w/in 12 mo • AMI w/in 1 week • Plan to treat >1 CTO • LVEF <30%	• STEMI <24 hrs	• Prior CABG or LM PCI • Prior PCI w/in 12mo • CK-MB >ULN

[1] IVUS ≤6.0mm^2 and/or FFR ≤0.80

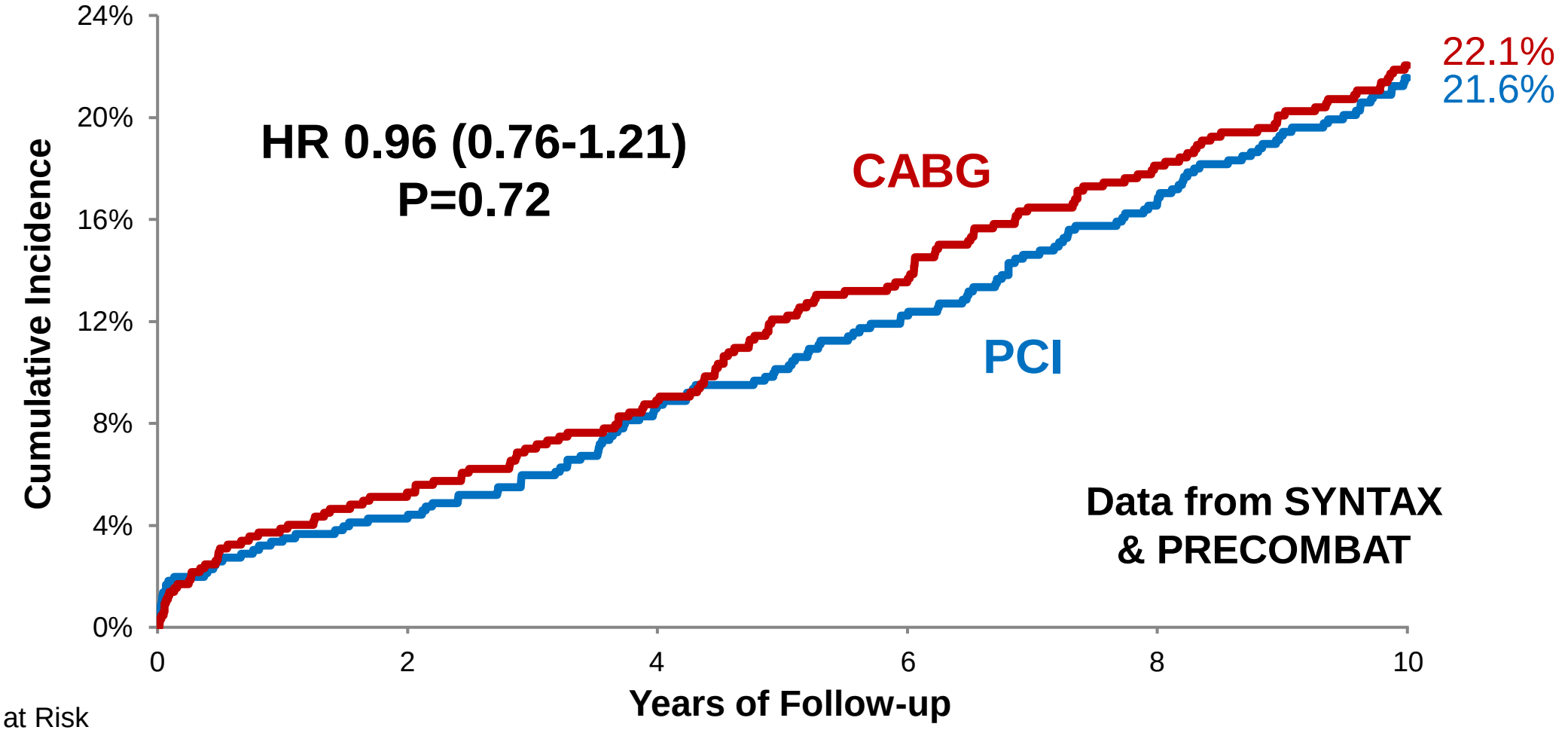
Mortality



Number at Risk

CABG	2197	2085	2042	2002	1939	1585
PCI	2197	2120	2068	2015	1942	1539

Two Trials with 10-Year Mortality Data

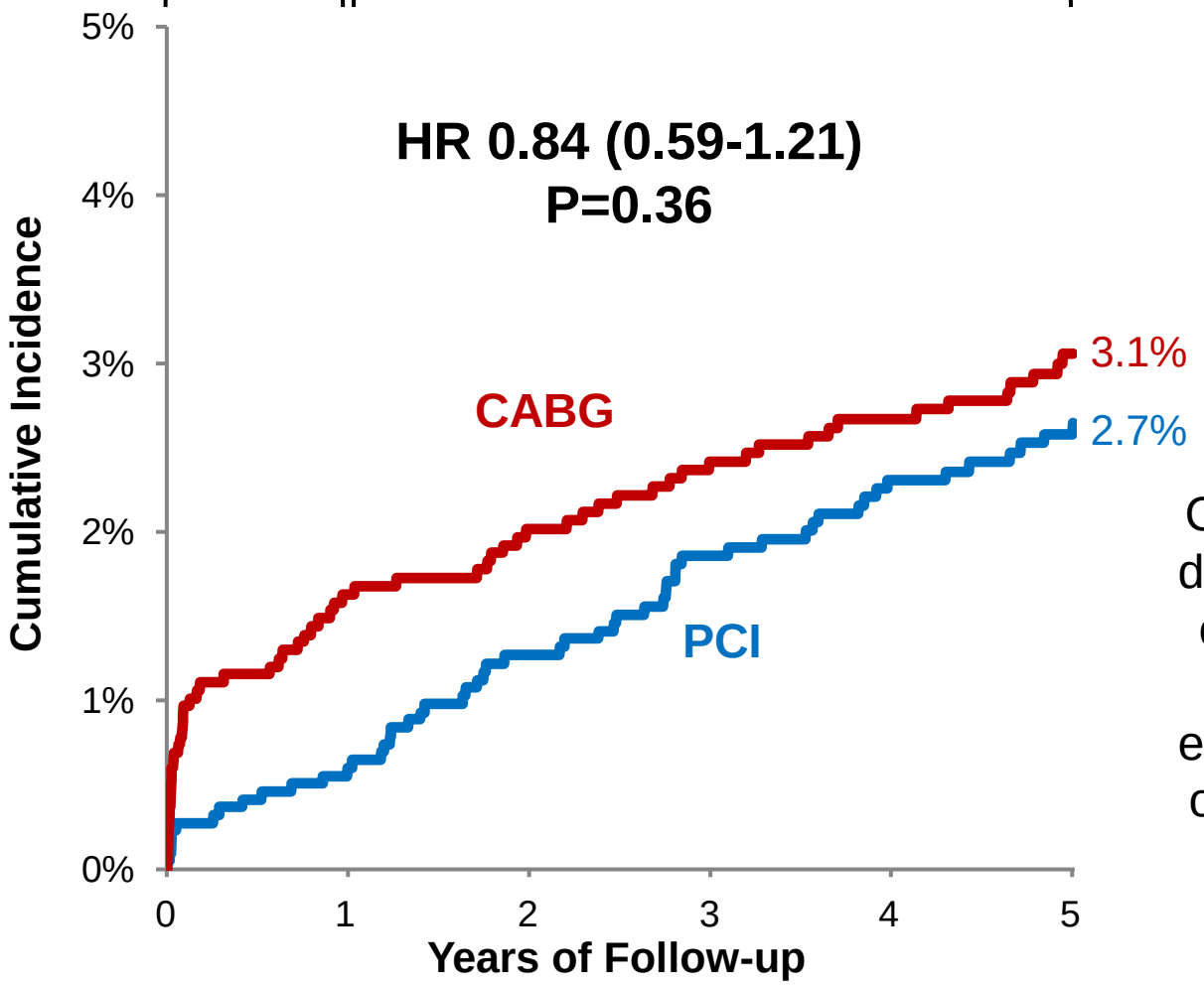


Number at Risk

CABG	648	604	577	531	500	463
PCI	657	623	591	547	519	475

Stroke

1st Year
13 vs. 35 events
HR 0.37 (0.19-0.69)
P=0.002
Absolute Δ 1.0%



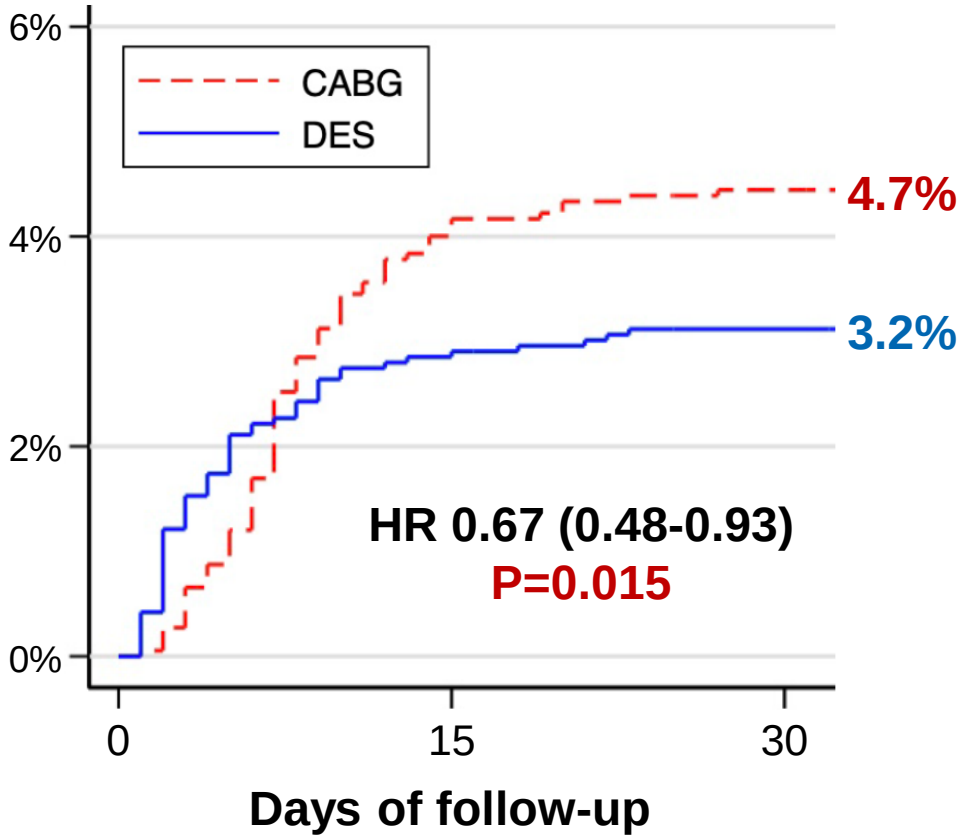
Beyond 1st Year
42 vs. 28 events
HR 1.49 (0.93-2.41)

Convergence of the curves was driven by a markedly higher rate of late (>1-year) stroke in PCI-treated pts in NOBLE, with no evidence of increased risk in the other 3 trials or any prior trial of PCI vs. CABG.

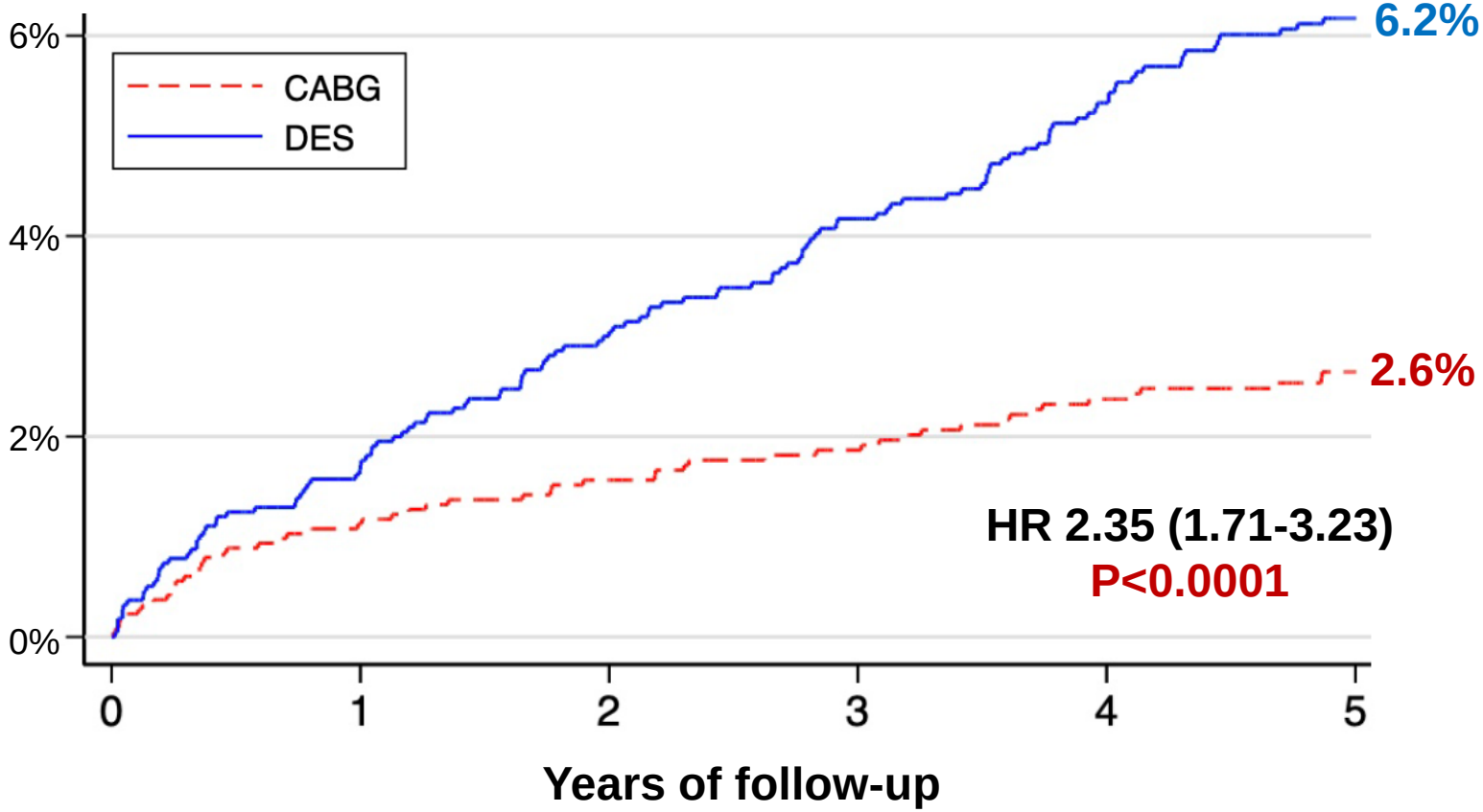
Sabatine MS et al. Lancet 2021;https://doi.org/10.1016/S0140-6736(21)02334-5

Procedural and Spontaneous MI

Procedural MI
(protocol definition)



Spontaneous MI



Sabatine MS et al. Lancet 2021;https://doi.org/10.1016/S0140-6736(21)02334-5

Summary

Comparing PCI w/ DES vs. CABG in Pts w/ LM CAD, median SYNTAX score of 25, and deemed equally suitable candidates for either revascularization approach:

No statistically significant difference in survival at 5 yrs (and 10 yrs)

PCI

↓ early stroke

CABG

↓ spontaneous MI
↓ repeat revascularization

Differences in risk of procedural MI depended on the definition used

Contemporary Left Main Guidelines

2021 ACC/AHA/SCAI

Left main CAD

1	B-R	3. In patients with SIHD and significant left main stenosis, CABG is recommended to improve survival (9-12).
2a	B-NR	4. In selected patients with SIHD and significant left main stenosis for whom PCI can provide equivalent revascularization to that possible with CABG, PCI is reasonable to improve survival (9).

(Issued after EXCEL)

2018 ESC

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

(Issued before EXCEL)

Left Main PCI

There Are Still
Unmet Needs

JACC: ASIA VOL. 2, NO. 2, 2022

STATE-OF-THE-ART REVIEW

Percutaneous Coronary Intervention for Left Main Coronary Artery Disease

Present Status and Future Perspectives

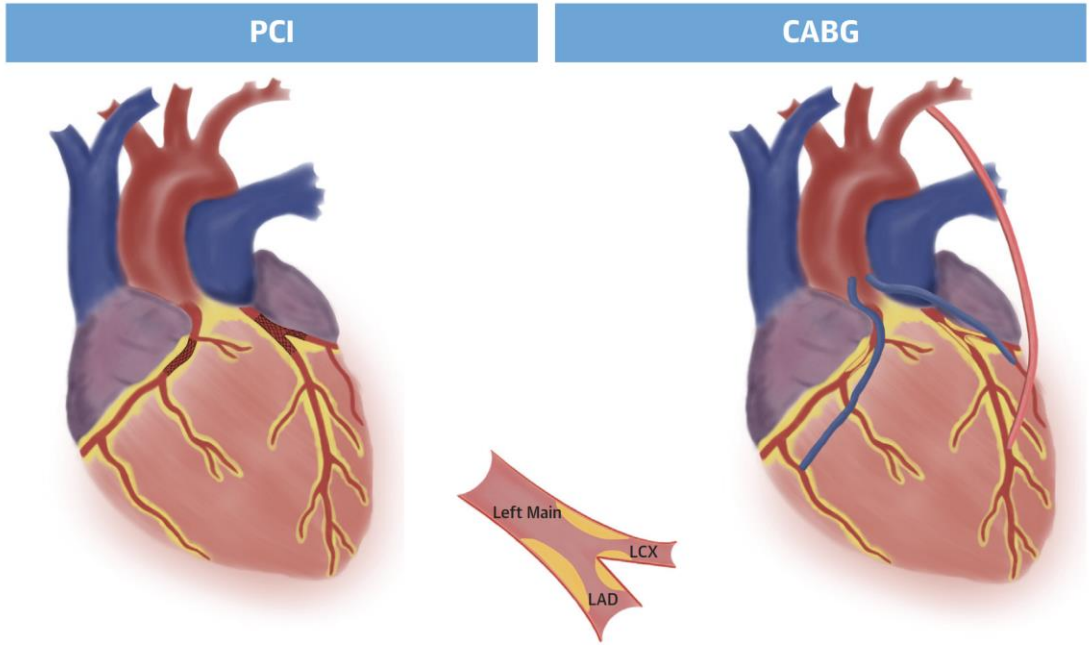
Sangwoo Park, MD,[a] Seung-Jung Park, MD, PhD,[b] Duk-Woo Park, MD, PhD[b]

ABSTRACT

For several decades, coronary artery bypass grafting has been regarded as the standard choice of revascularization for significant left main coronary artery (LMCA) disease. However, in conjunction with remarkable advancement of device technology and adjunctive pharmacology, percutaneous coronary intervention (PCI) offers a more expeditious approach with rapid recovery and is a safe and effective alternative in appropriately selected patients with LMCA disease. Several landmark randomized clinical trials showed that PCI with drug-eluting stents for LMCA disease is a safe option with similar long-term survival rates to coronary artery bypass grafting surgery, especially in those with low and intermediate anatomic risk. Although it is expected that the updated evidence from recent randomized clinical trials will determine the next guidelines for the foreseeable future, there are still unresolved and unmet issues of LMCA revascularization and PCI strategy. This paper provides a comprehensive review on the evolution and an update on the management of LMCA disease. (JACC: Asia 2022;2:119-138) © 2022 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

JACC: Asia 2022;2:119–138

CENTRAL ILLUSTRATION Key Summary of Issues for Left Main Revascularization



Left Main Revascularization

What is Known?

PCI versus CABG

- Have comparable risks for overall mortality and the composite of death, MI, or stroke in patients with low to intermediate anatomical complexity

Advantage of CABG

- Lower risk of repeat revascularization
- More CR especially in high anatomical complexity
- Less spontaneous MI

Advantage of PCI

- Less invasive and shorter hospitalization
- Early mental and physical recovery
- Lower risk of short-term morbidity

What is Unknown?

PCI versus CABG

- Long-term treatment effect of CABG vs. state-of-the-art PCI
- Long-term comparative clinical outcomes between CABG and PCI in a specific population (patient with diabetes, HFrEF, distal LMCA bifurcation disease)
- Threshold for reasonable IR

Left main PCI

- Optimal stent strategy for distal LMCA bifurcation disease
- Optimal antithrombotic strategy following complex PCI, especially in Asian patients

Park S, et al. JACC: Asia. 2022;2(2):119-138.

ESC European Society of Cardiology

European Heart Journal (2022) **43**, 4635–4643
https://doi.org/10.1093/eurheartj/ehac542

STATE OF THE ART REVIEW
Acute cardiovascular care

Left main coronary disease: evolving management concepts

Paul W. Armstrong [1,2]*, Eric R. Bates [3], and Mario Gaudino [4]

[1]Canadian VIGOUR Centre, University of Alberta, 4-120 Katz Group Centre for Pharmacy and Health Research, Edmonton, AB T6G 2E1, Canada; [2]Division of Cardiology, Department of Medicine, University of Alberta, 2C2 Cardiology Walter MacKenzie Center, University of Alberta Hospital, 8440-111 St., Edmonton, AB T6G 2B7, Canada; [3]Division of Cardiovascular Medicine, Department of Internal Medicine, University of Michigan, 1500 E. Medical Center Drive 2139 Cardiovascular Center, Ann Arbor, MI 48109, USA; and [4]Department of Cardiothoracic Surgery, Weill Cornell Medicine, 525 East 68th St, Box 110, New York, NY 10065, USA

Received 1 March 2022; revised 25 July 2022; accepted 16 September 2022; online publish-ahead-of-print 29 September 2022

European Heart Journal (2022) **43**, 4635–4643

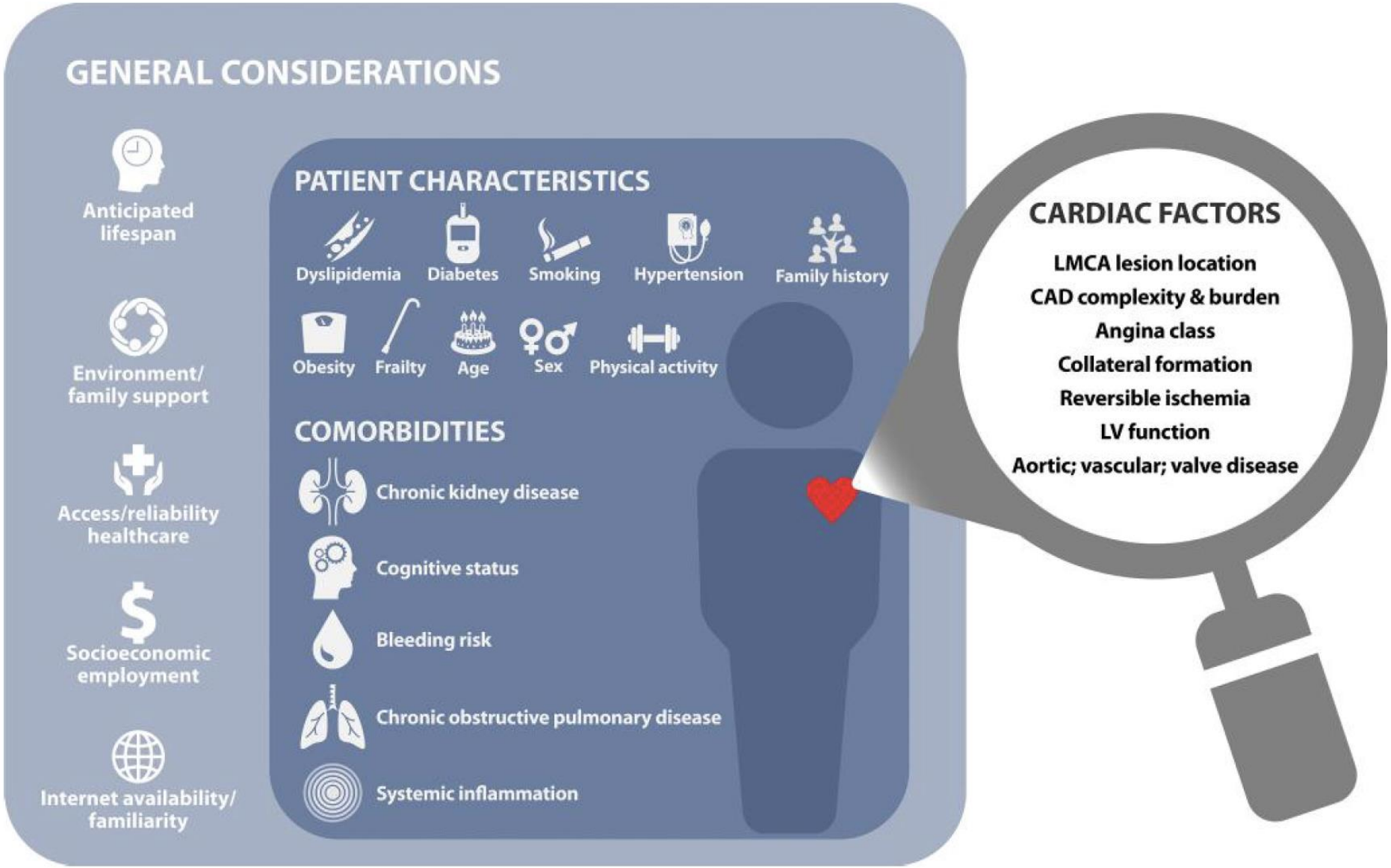


Figure 1 Profiling risk in patients with stable ischaemia and left main coronary disease. General considerations provide context for individual patient characteristics and comorbidities which then converge into the LMCA and cardiac-specific modulating factors. LMCA, left main coronary artery; CAD, coronary artery disease; LV, left ventricular.

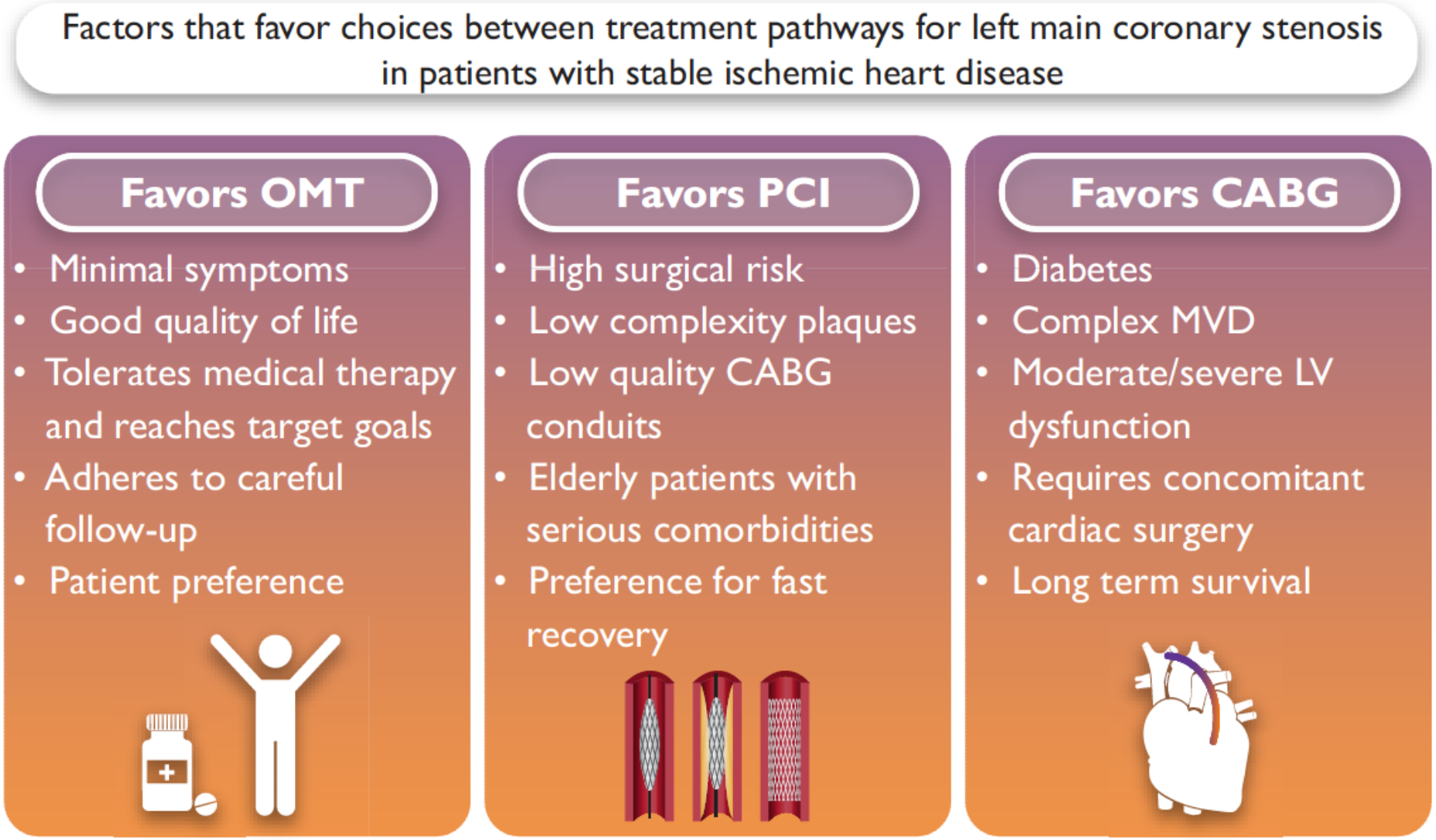
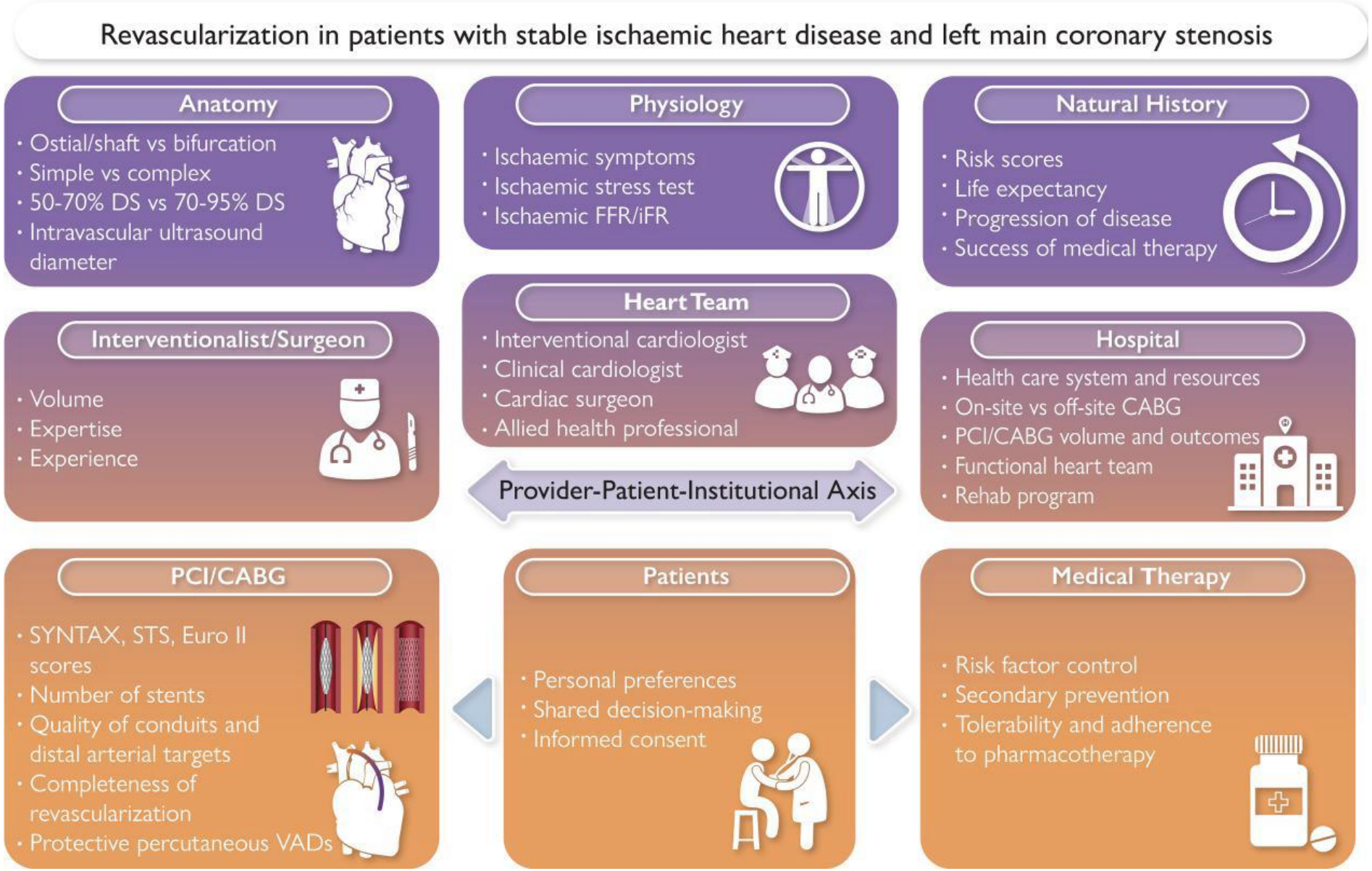


Figure 2 Factors that favour choices between treatment pathways for left main coronary stenosis in patients with stable ischaemic heart disease. CABG, coronary artery bypass graft; LV, left ventricular; MVD, multivessel disease; OMT, optimal medical therapy; PCI, percutaneous coronary intervention.

Graphical Abstract: Comprehensive Approach for Left Main Disease



Conclusion:

Guideline and Concept Change 2023 for Left Main PCI

- Contemporary evidences demonstrated that PCI was comparable to CABG in mortality and hard clinical endpoints for left main disease.
- PCI and CABG are different interventions that are performed in different patients by different physicians with different aims: two interventions are complementary, not antagonists.
- The patient occupies the center of the decision-making process along with the Heart Team. These two central elements are joined across an axis that integrates the individual's interventional/surgical expertise and their host institution's resources and characteristics.
- Ultimately, through shared decision-making, these comprehensive factors inform the optimal individual patient choice for treatment of left main disease.