



SYNTAX Five-year Results: Left Main Cohort

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Background

- **The SYNTAX trial assessed the optimum revascularisation treatment for patients with de-novo LM or 3VD (or both), by randomly assigning patients to either PCI with a first-generation PES or CABG.**
- **For the primary endpoint of MACCE at 1 year, PCI did not meet the goal of non-inferiority compared with CABG.**
- **In the observational hypothesis-generating analysis of patients with LM disease, PCI had safety and efficacy outcomes comparable to CABG at 1 year.**



SYNTAX Trial Design



 62 EU Sites +  23 US Sites

Heart Team (surgeon & interventional cardiologist)

Amenable for both treatment options

Amenable for only one treatment approach

Stratification:
LM and Diabetes

Randomized Arms
N=1800

Two Registry Arms
N=1275

CABG
n=897

vs

TAXUS*
n=903

CABG
n=1077

PCI
n=198

3VD
n=549
(66.3%)

LM
n=348
(33.7%)

3VD
n=546
(65.4%)

LM
n=357
(34.6%)

*TAXUS Express

Beware of All-Comers trials!

Evaluating the 'all-comers' design: a comparison of participants in two 'all-comers' PCI trials with non-participants

Sanneke P.M. de Boer, Mattie J. Lenzen, Rohit M. Oemrawsingh, Cihan Simsek, Henricus J. Duckers, Willem J. van der Giessen, Patrick W. Serruys, and Eric Boersma*

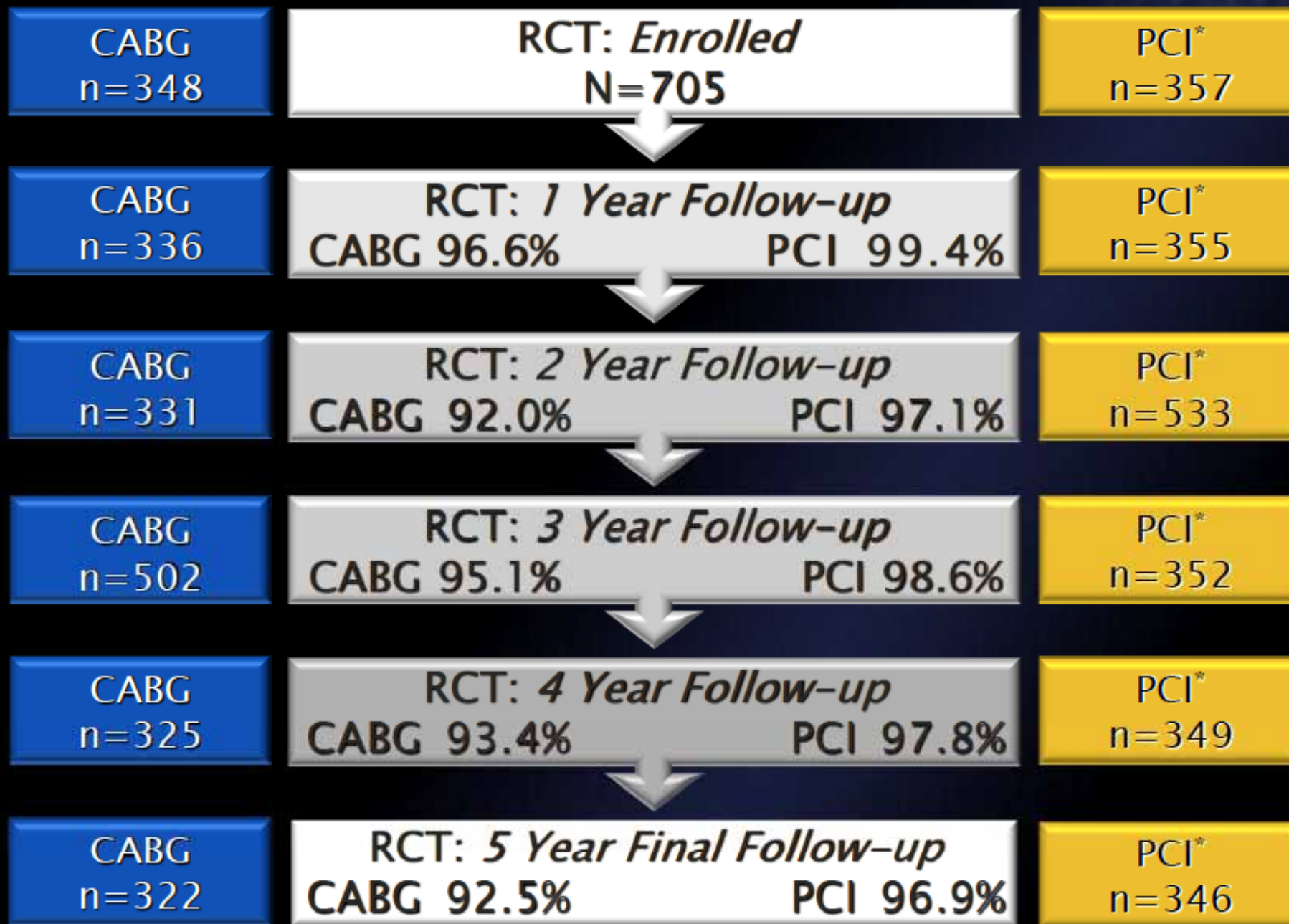
Conclusions

- Applying the all-comers design did not result in inclusion of all consecutive patients, as only half of the target population was enrolled.
- This design included more patients than observed in classical RCTs.
- AC-RCT participants and non-participants were different in terms of baseline characteristics and outcome.

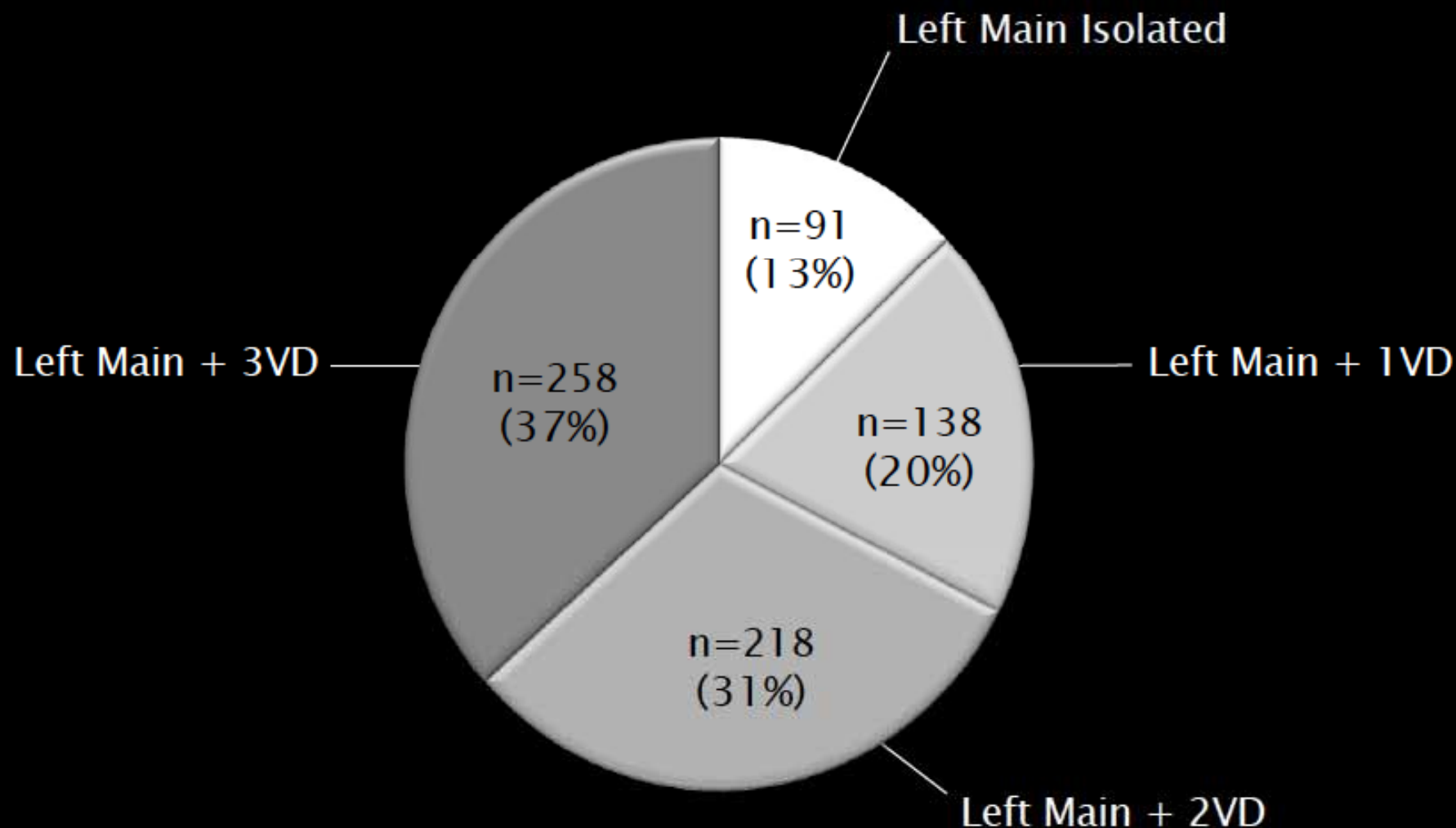


Patient Disposition to 5 Years

LM Subset Intent-to-Treat



Heterogeneity in the Left Main Group



Patient Characteristics

LM Subset



	CABG N=348	TAXUS N=357	<i>P</i> value
Age*, mean \pm SD (y)	65.6 \pm 10.1	65.4 \pm 9.8	0.78
Medically treated diabetes*, %	22.4	21.8	0.86
BMI, mean \pm SD	27.7 \pm 5.0	28.2 \pm 4.9	0.24
Additive euroSCORE*, mean \pm SD	3.9 \pm 2.9	3.9 \pm 2.8	0.91
Total Parsonnet score*, mean \pm SD	9.1 \pm 7.4	8.9 \pm 7.8	0.77
Total SYNTAX Score, mean \pm SD	26.7 \pm 11.5	28.1 \pm 12.4	0.13
No. lesions, mean \pm SD	3.2 \pm 1.9	3.3 \pm 1.8	0.89

Core laboratory reported unless *Site-reported

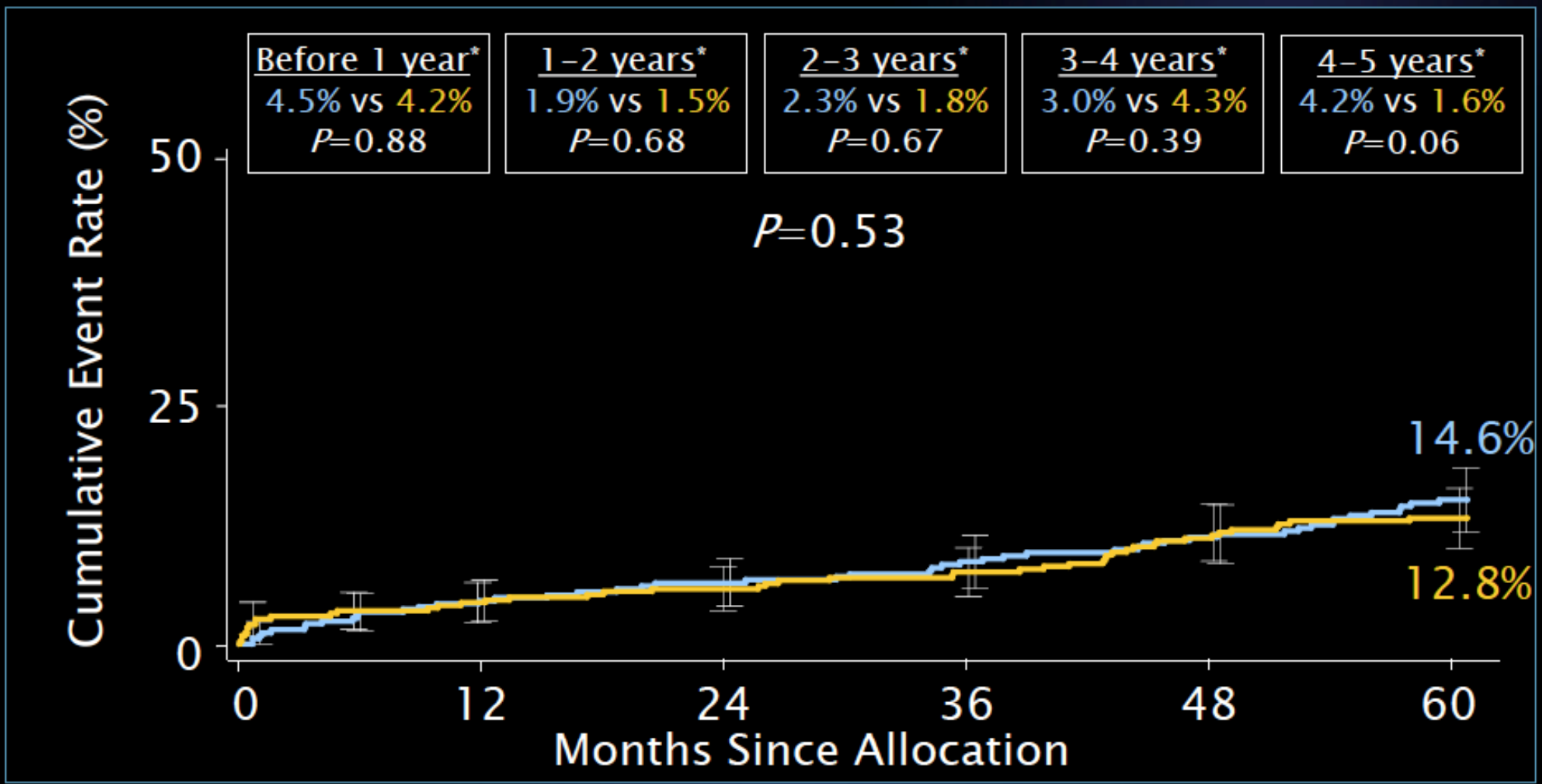
All-Cause Death to 5 Years

Left Main Subset



■ CABG (N=348)

■ TAXUS (N=357)



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

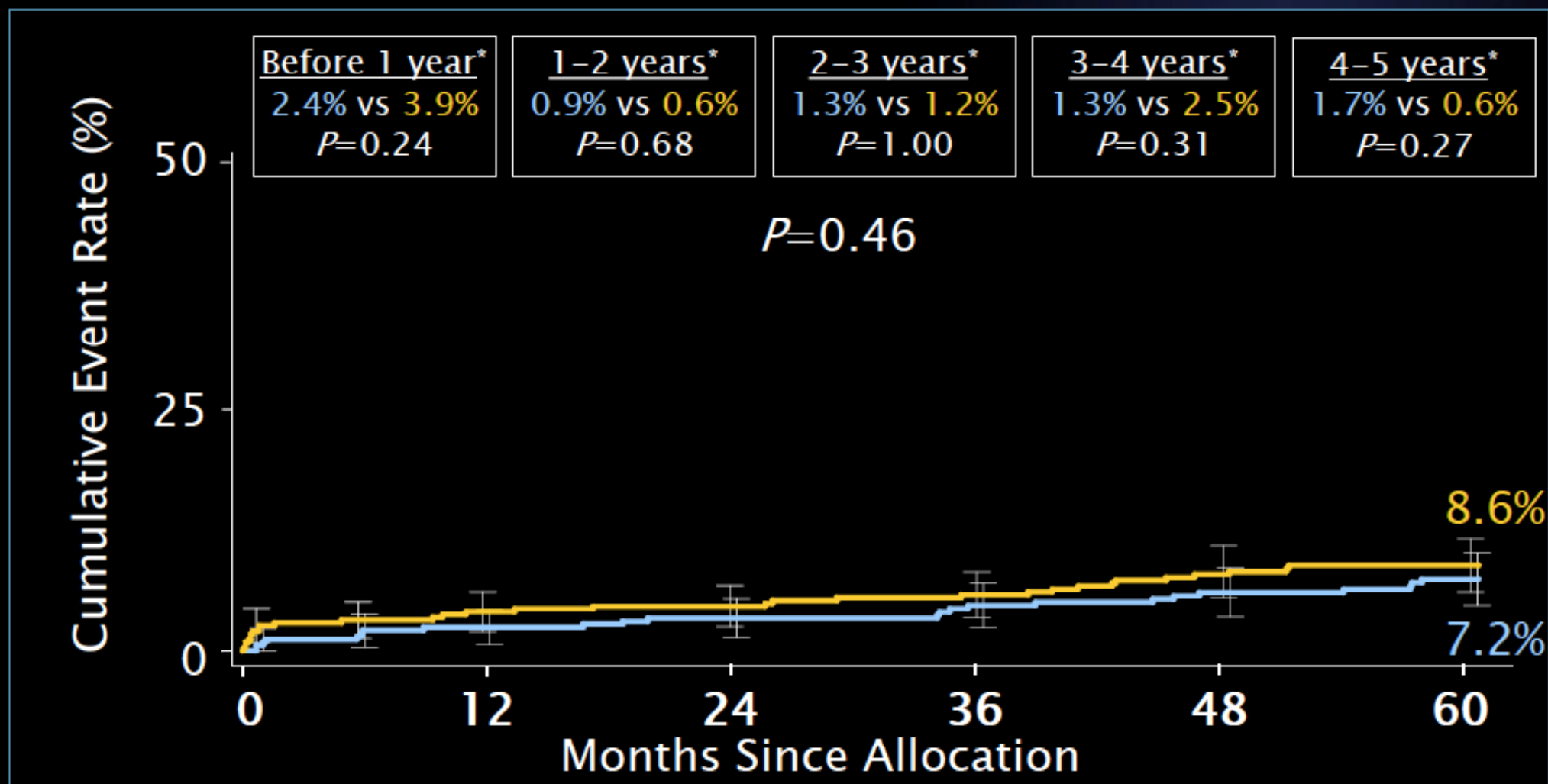
ITT population

Cardiac Death to 5 Years *Left Main Subset*



■ CABG (N=348)

■ TAXUS (N=357)



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

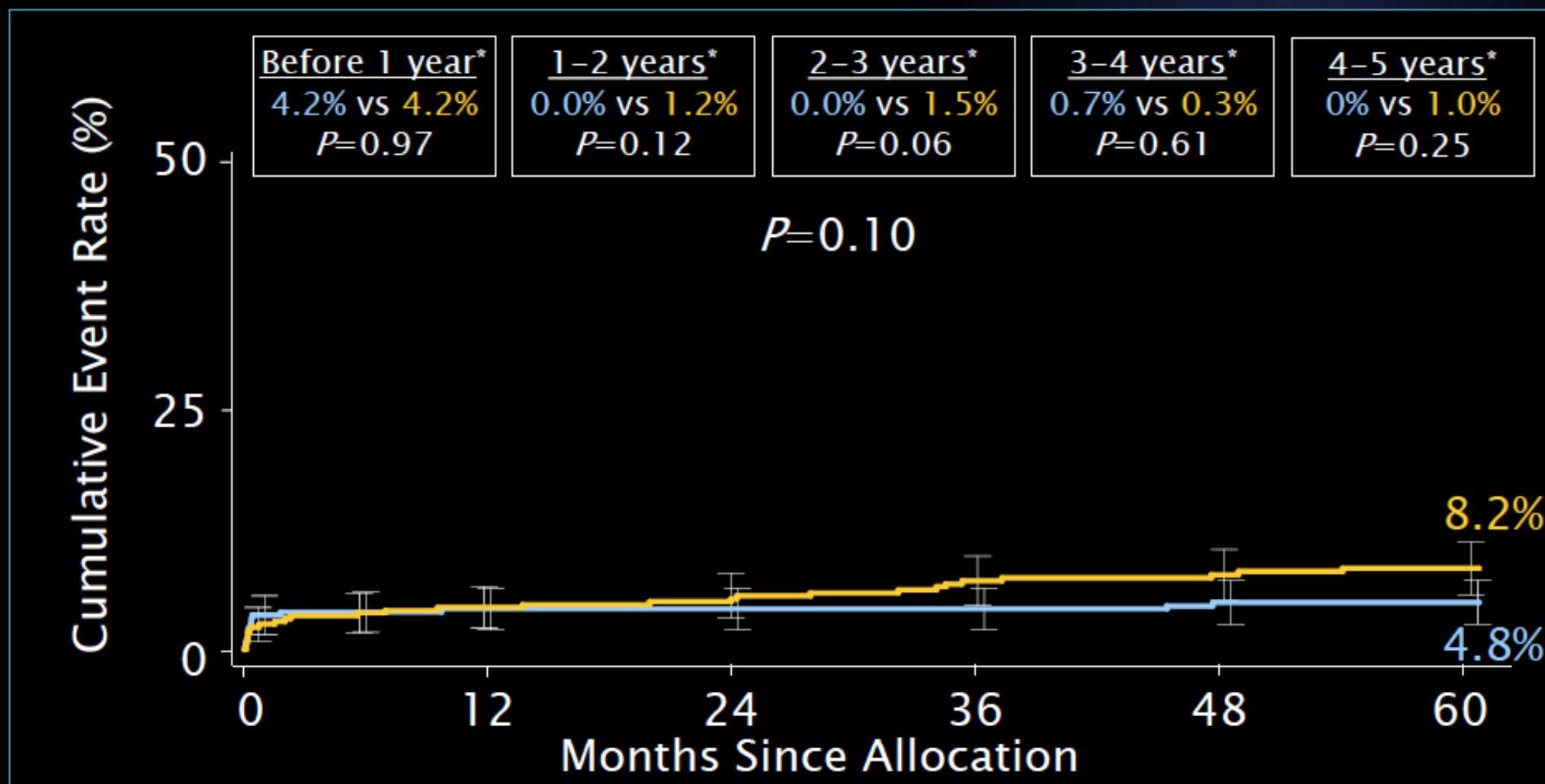
ITT population

Myocardial Infarction to 5 Years *Left Main Subset*



■ CABG (N=348)

■ TAXUS (N=357)



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

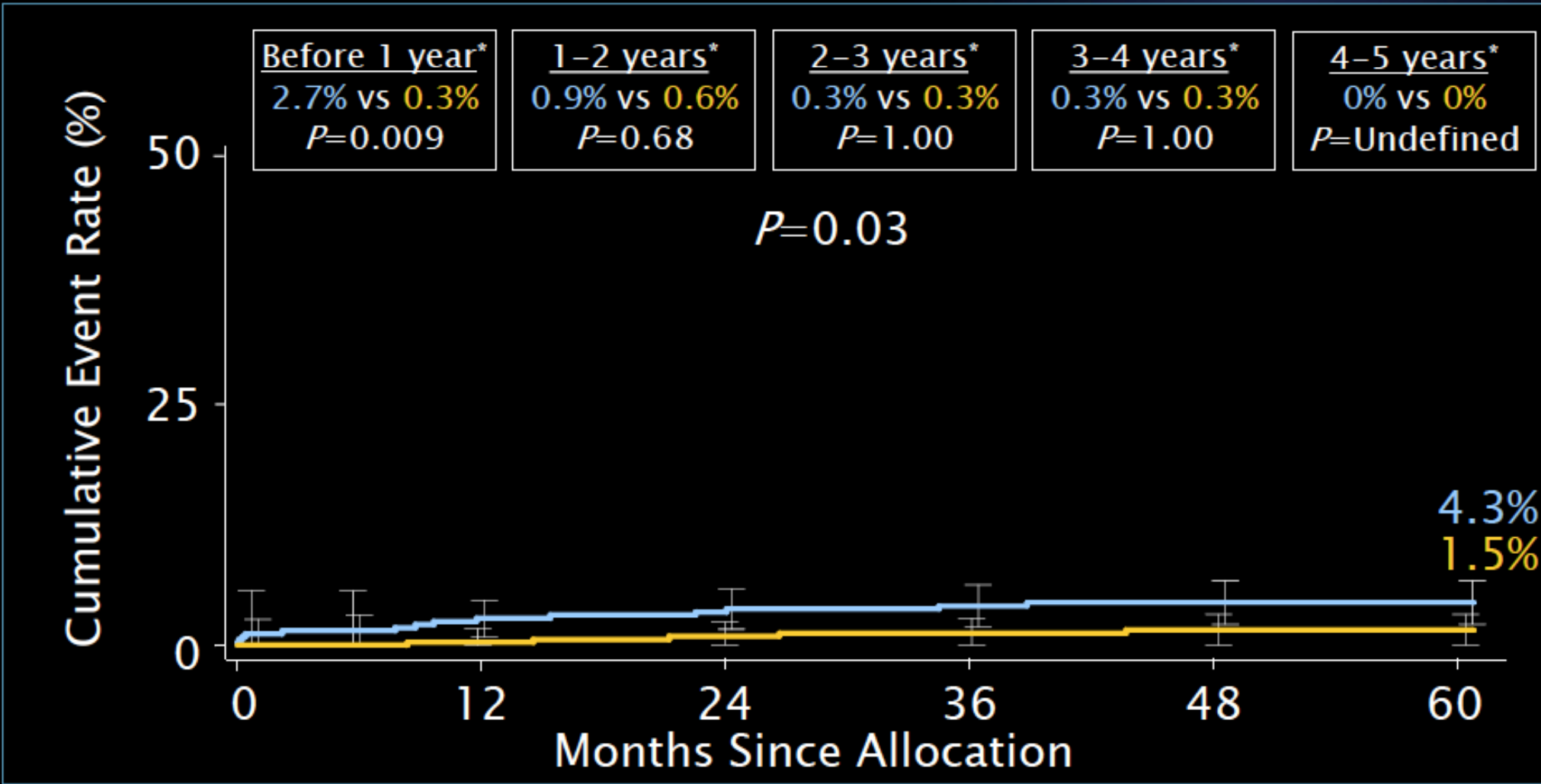
ITT population

CVA to 5 Years Left Main Subset



■ CABG (N=348)

■ TAXUS (N=357)



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

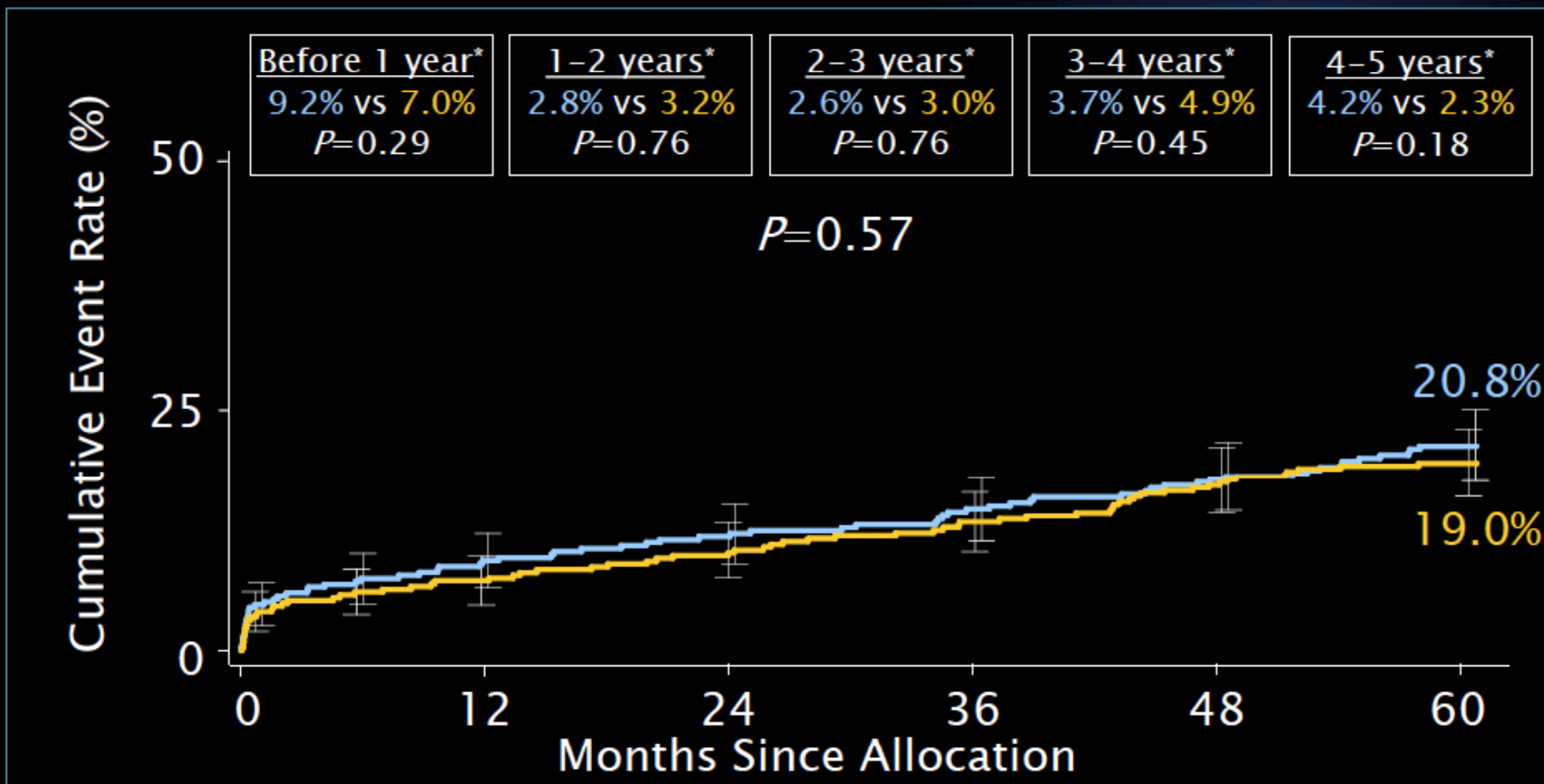
ITT population

All-Cause Death/CVA/MI to 5 Years *Left Main Subset*



■ CABG (N=348)

■ TAXUS (N=357)



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

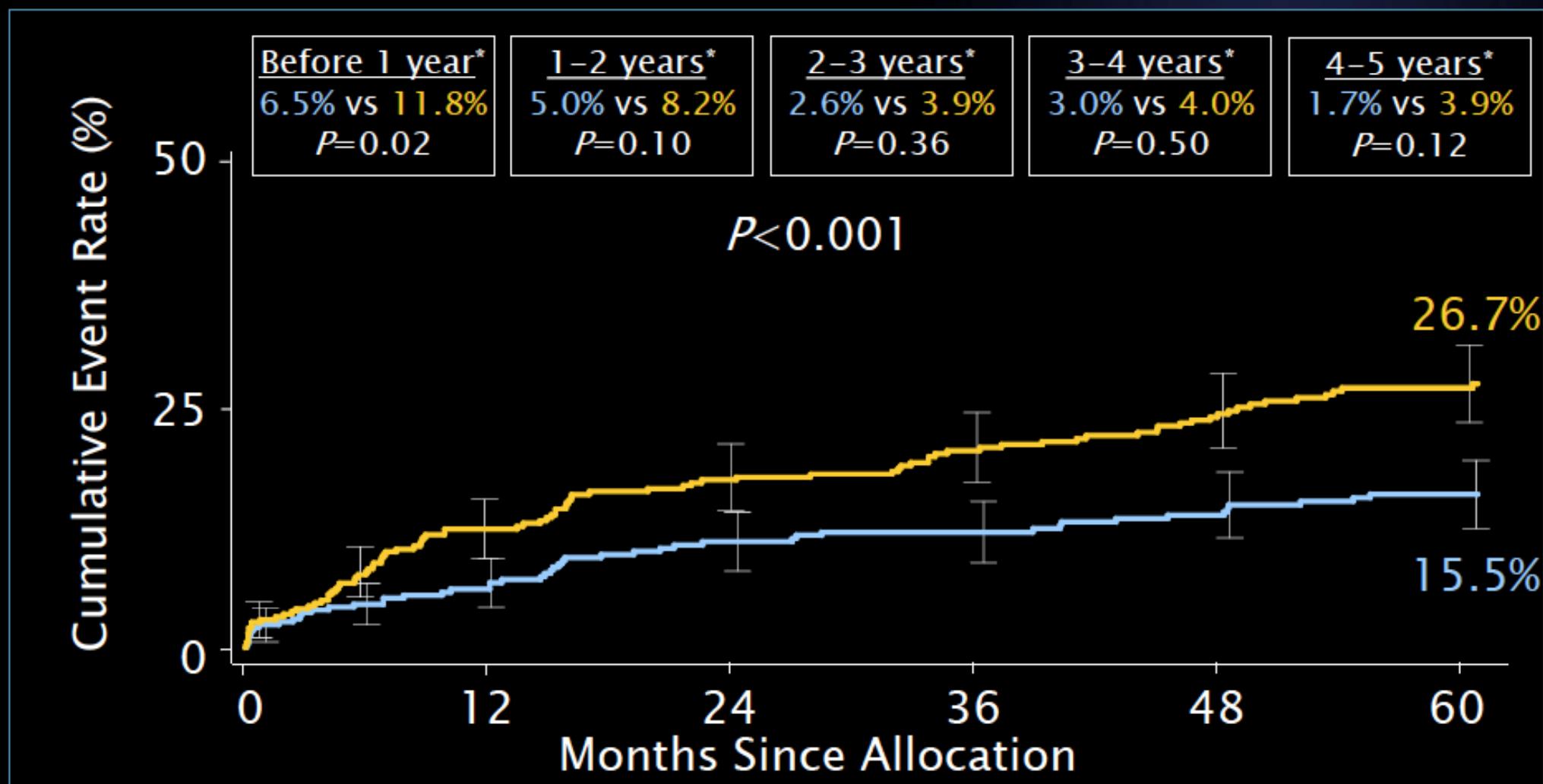
ITT population

Repeat Revascularization to 5 Years *Left Main Subset*



■ CABG (N=348)

■ TAXUS (N=357)



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

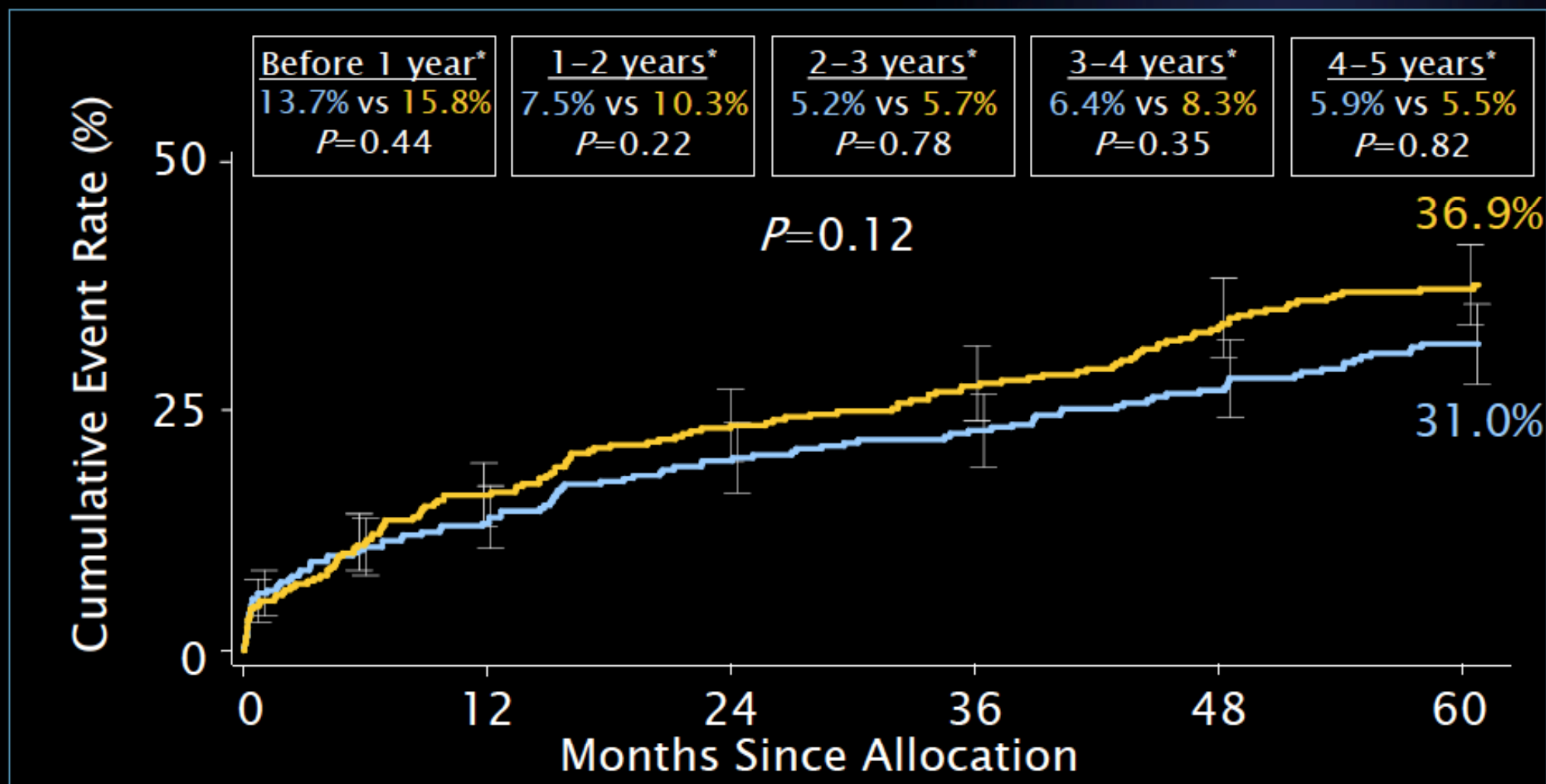
ITT population

MACCE to 5 Years *Left Main Subset*



■ CABG (N=348)

■ TAXUS (N=357)




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


ITT population

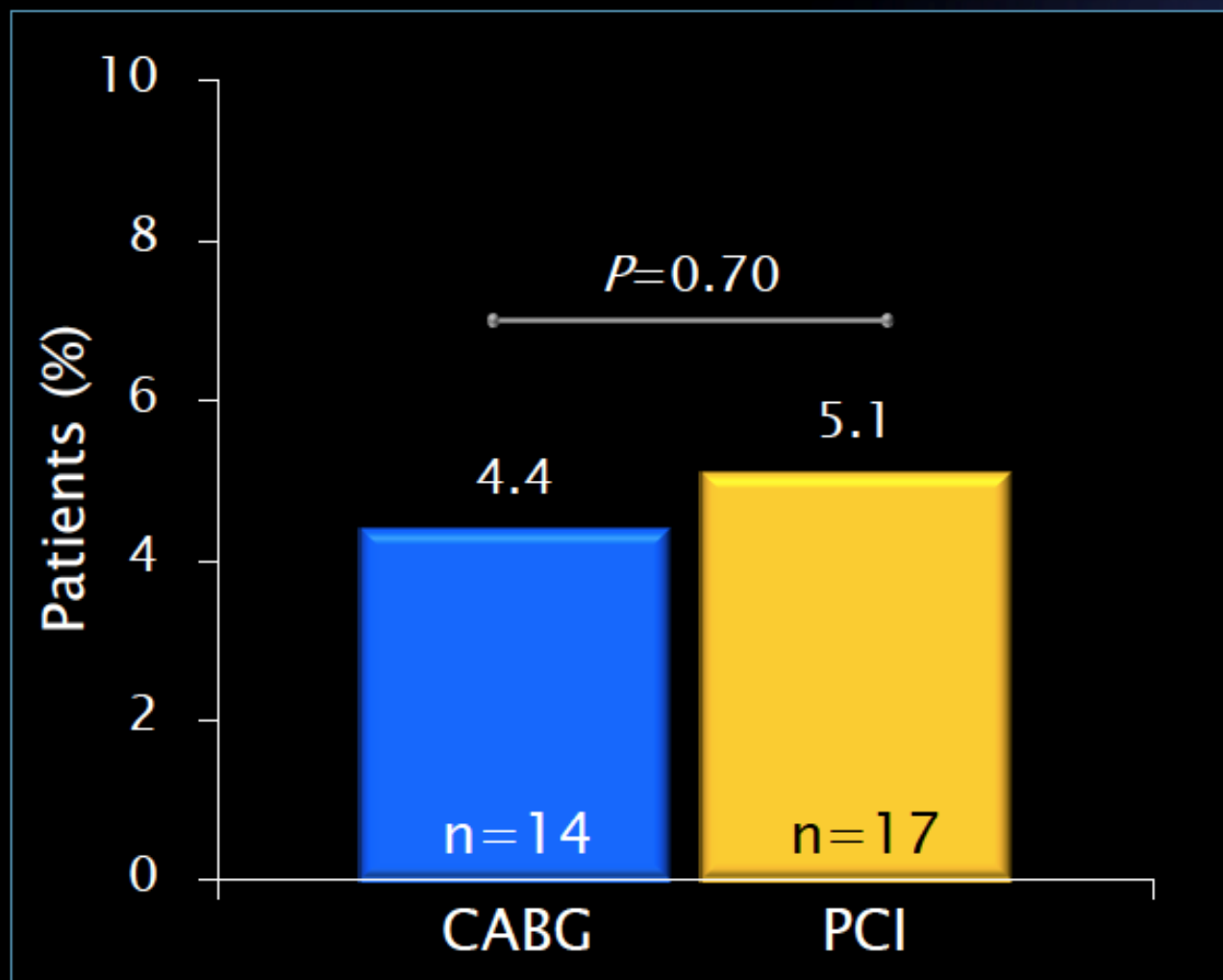
Symptomatic Graft Occlusion & Stent Thrombosis to 5 Years



LM Subset

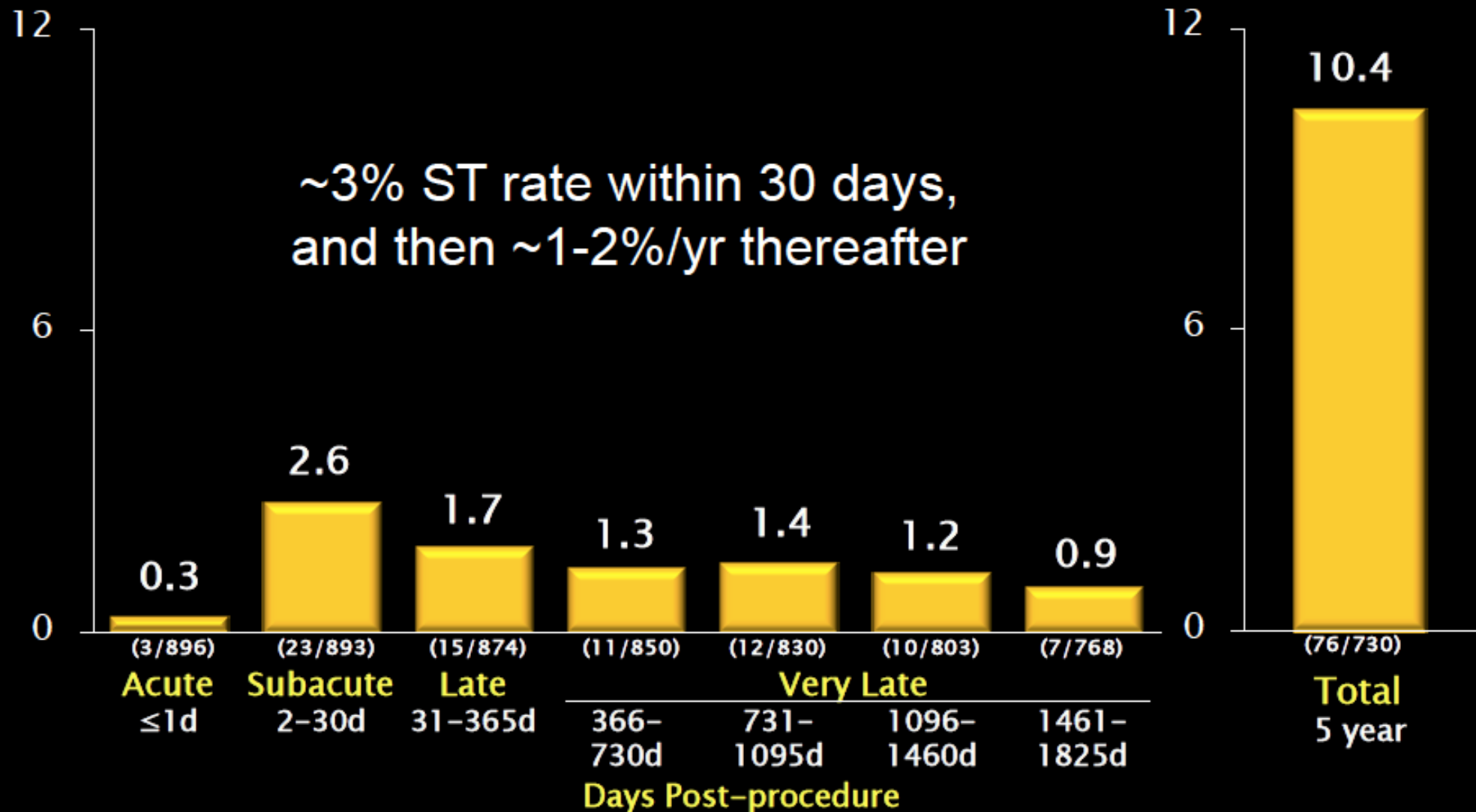
 CABG (n=348)

 TAXUS (n=357)



Post-procedure; ITT population

SYNTAX: Definite/Probable ARC Stent Thrombosis to 5 Years *(Per Patient)*

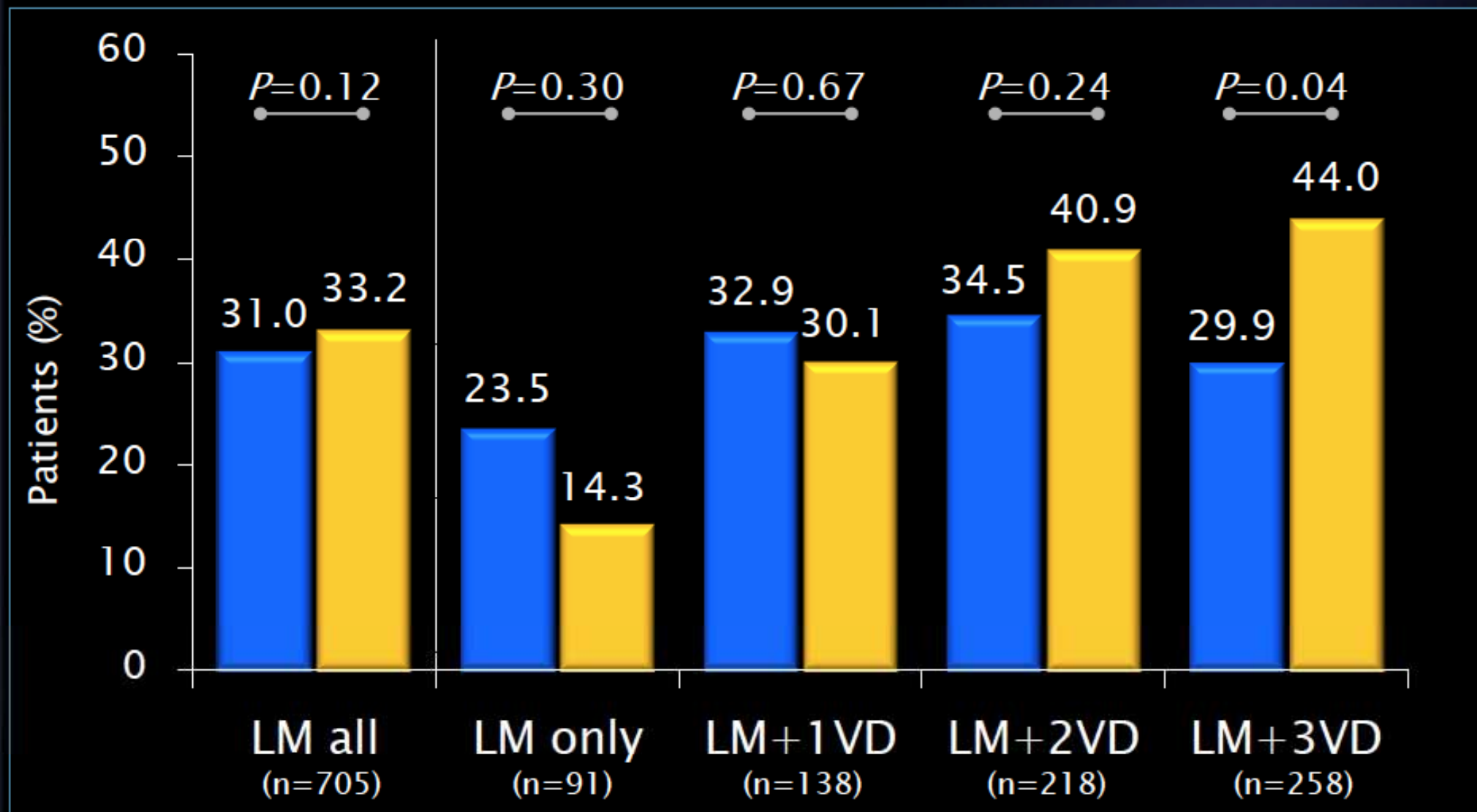


Rate was ~ same in the LM and 3VD cohorts, and roughly independent of Syntax Score

MACCE to 5 Years *Left Main Subsets*



CABG **TAXUS**



Cumulative KM Event Rate; log-rank Pvalue

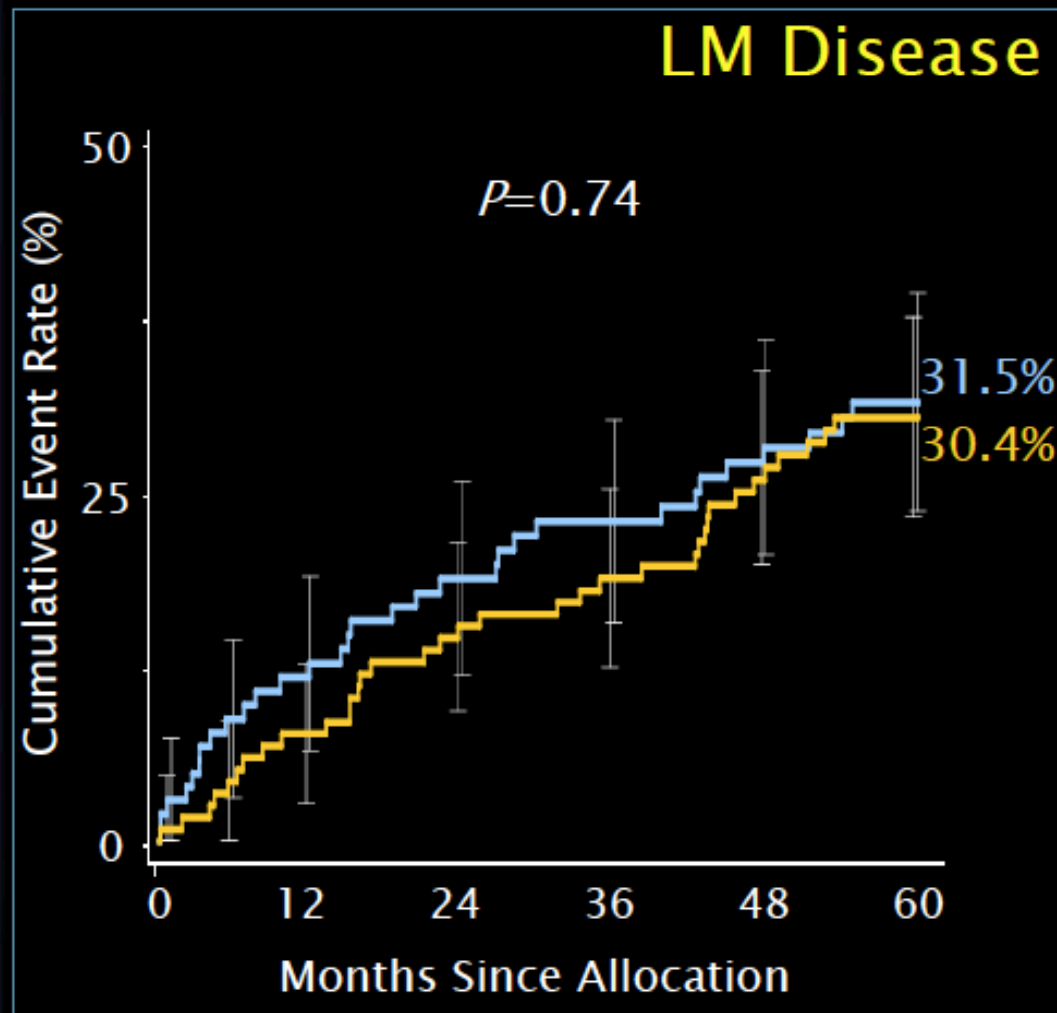
ITT population

MACCE to 5 Years by SYNTAX Score Tercile

LM Subset *Low Scores 0-22*



■ CABG (N=104)
 ■ TAXUS (N=118)



	CABG	PCI	P value
Death	11.3%	7.0%	0.28
CVA	4.1%	1.8%	0.28
MI	3.1%	6.2%	0.32
Death, CVA or MI	15.2%	13.9%	0.71
Revasc.	20.3%	23.0%	0.65

Cumulative KM Event Rate \pm 1.5 SE; log-rank P value

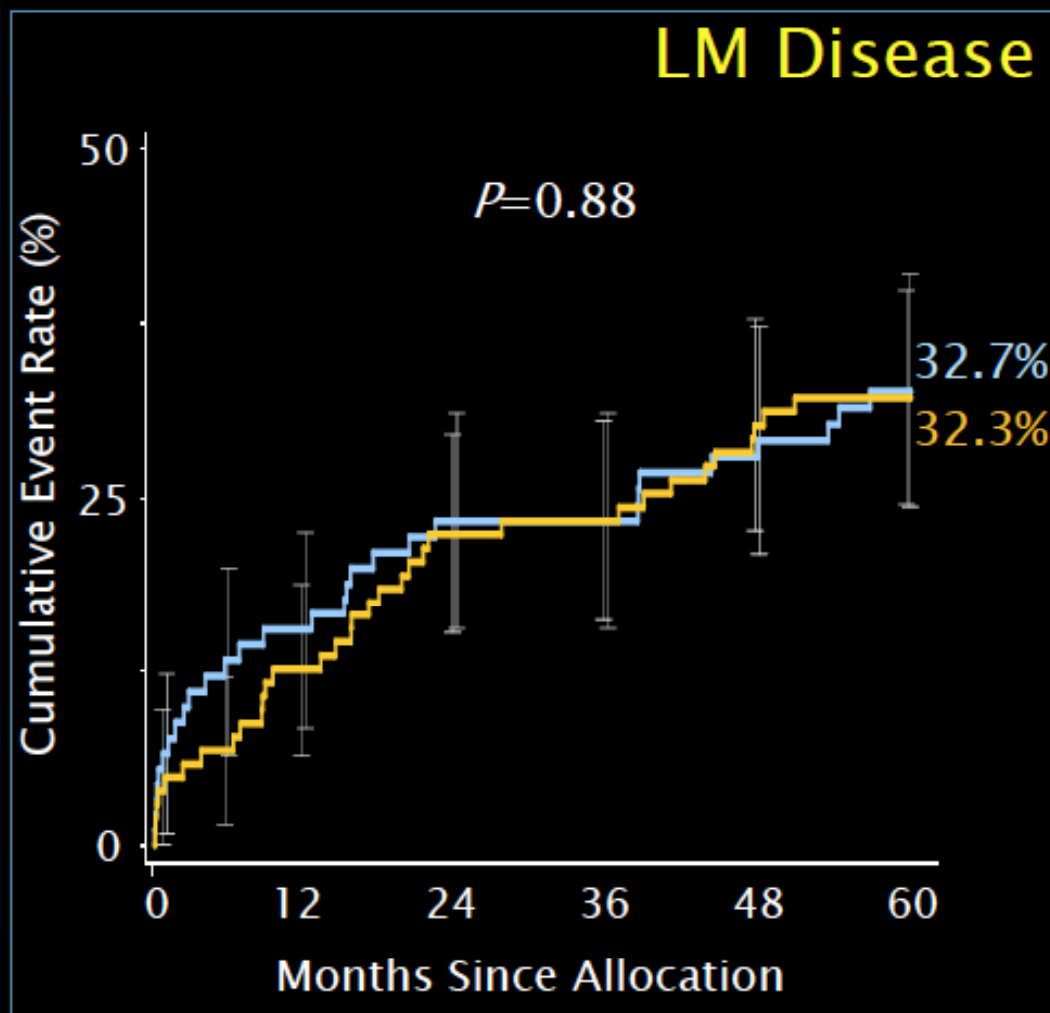
Site-reported Data; ITT population

MACCE to 5 Years by SYNTAX Score Tercile

LM Subset Intermediate Scores 23–32



- CABG (N=92)
- TAXUS (N=103)



	CABG	PCI	P value
Death	19.3%	8.9%	0.04
CVA	3.6%	1.0%	0.23
MI	4.6%	6.0%	0.71
Death, CVA or MI	24.9%	15.7%	0.11
Revasc.	16.6%	22.2%	0.40

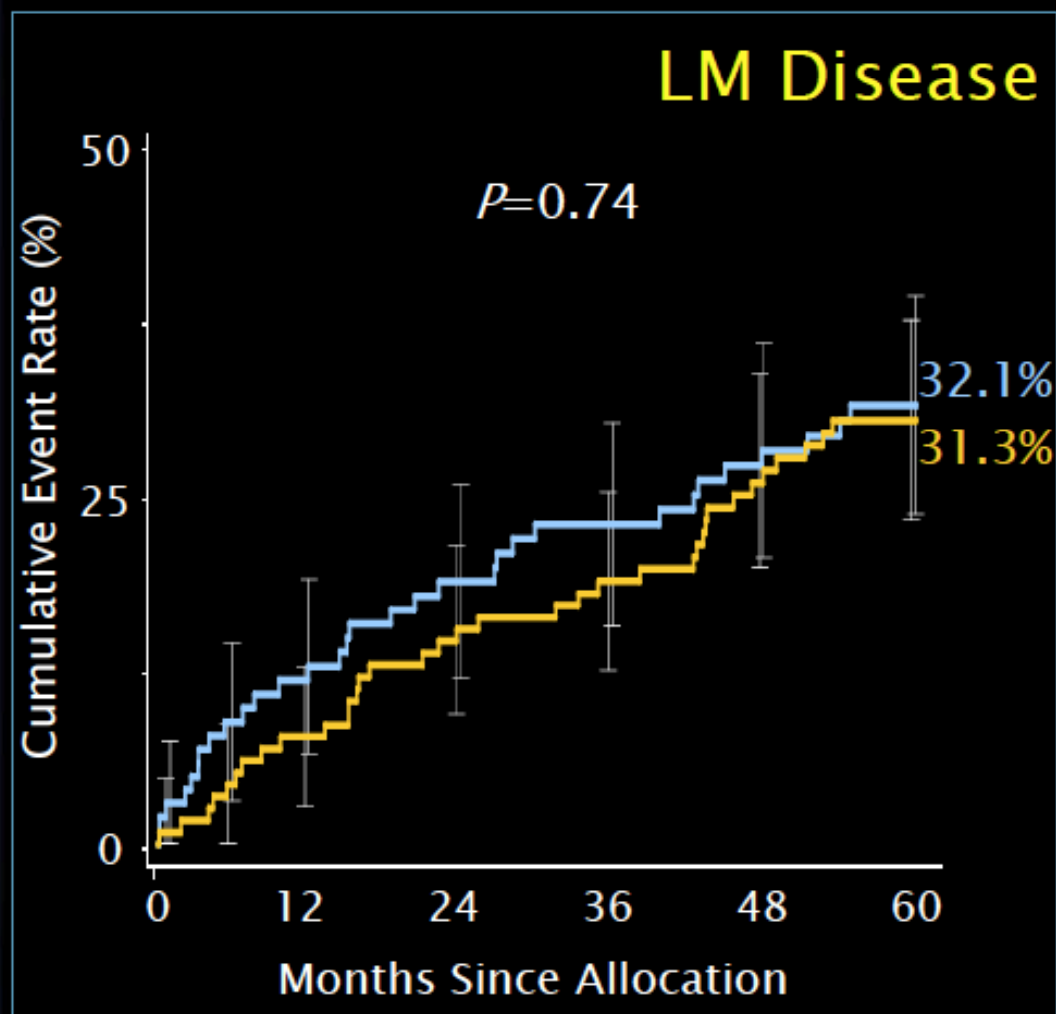
Cumulative KM Event Rate \pm 1.5 SE; log-rank P value

Site-reported Data; ITT population

MACCE to 5 Years by SYNTAX Score Tercile *Low to Intermediate Scores (0-32)*



- CABG (N=196)
- TAXUS (N=221)



	CABG	PCI	P value
Death	15.1%	7.9%	0.02
CVA	3.9%	1.4%	0.11
MI	3.8%	6.1%	0.33
Death, CVA or MI	19.8%	14.8%	0.16
Revasc.	18.6%	22.6%	0.36

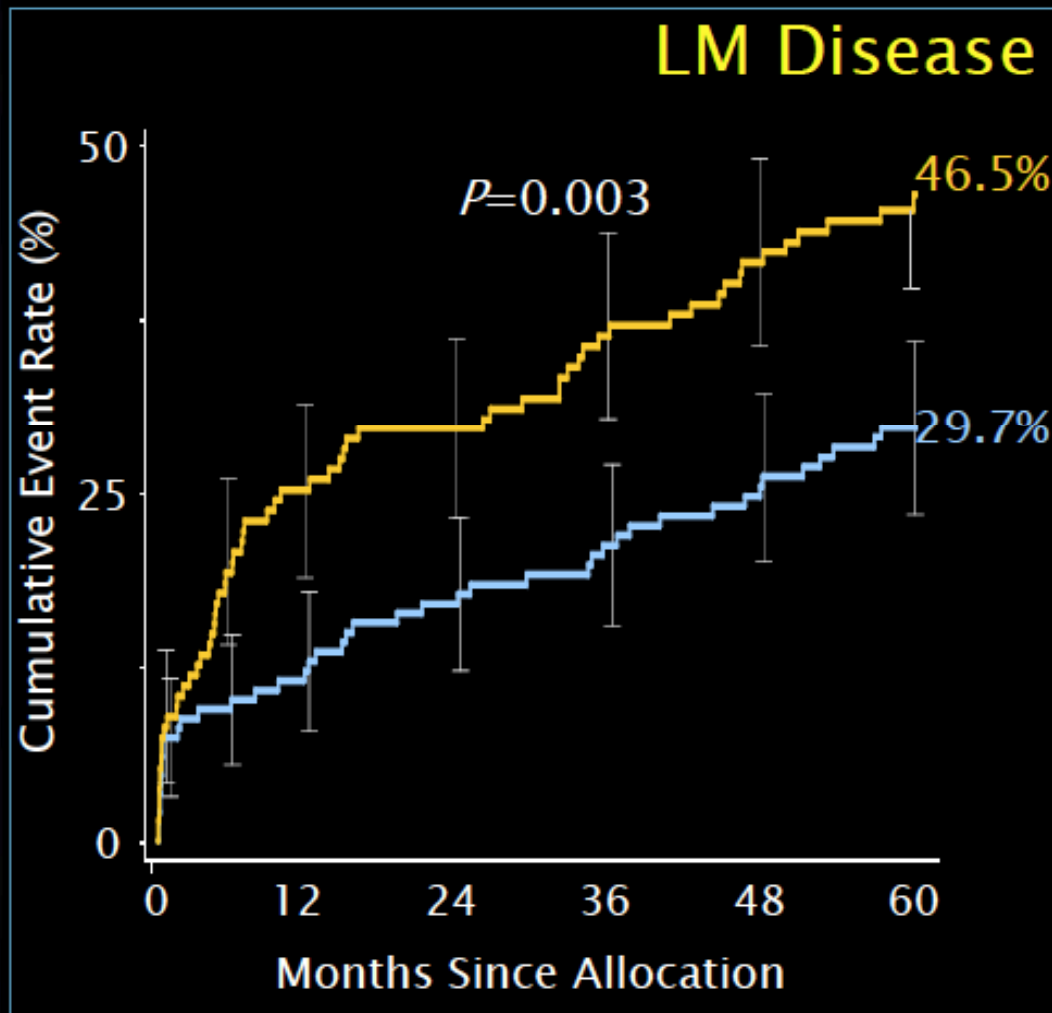
Serruys PW et al. Lancet 2013;381:629-38

MACCE to 5 Years by SYNTAX Score Tercile

LM Subset *High Scores* ≥ 33



■ CABG (N=149)
 ■ TAXUS (N=135)



	CABG	PCI	P value
Death	14.1%	20.9%	0.11
CVA	4.9%	1.6%	0.13
MI	6.1%	11.7%	0.13
Death, CVA or MI	22.1%	26.1%	0.40
Revasc.	11.6%	34.1%	<0.001

Cumulative KM Event Rate \pm 1.5 SE; log-rank P value

Site-reported Data; ITT population

Summary

Left Main Subset

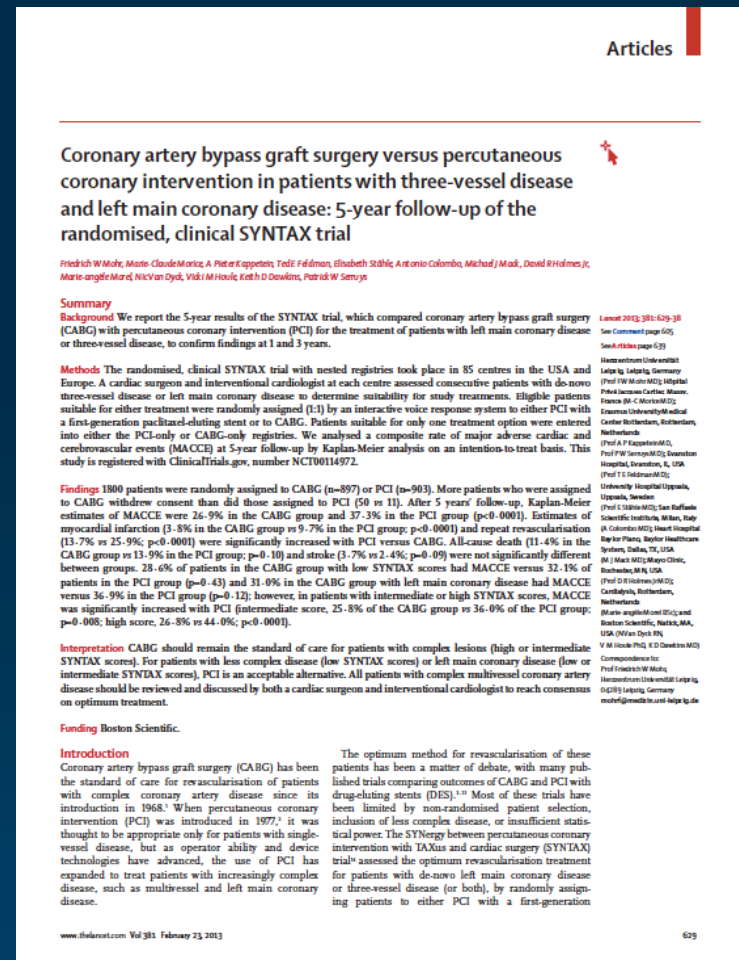


- At 5 years, overall MACCE in the PCI group was comparable with CABG (31.0% CABG vs 36.9% PCI)
- Similar overall safety outcomes (Death/CVA/MI) between CABG and PCI at 5 years (20.8% CABG vs 19.0% PCI)
- There was a higher rate of revascularization in the PCI group (15.5% CABG vs 26.7% PCI), driven primarily by patients with high baseline SYNTAX scores
- A higher rate of CVA in the CABG group (4.3% CABG vs 1.5% PCI) was driven mostly by periprocedural events, with no difference between groups after 1 year
- PCI outcomes are excellent relative to CABG in LM isolated and LM+1VD

SYNTAX (2009-2013): Which Legacy?



1-Year Outcomes



5-Year Outcomes

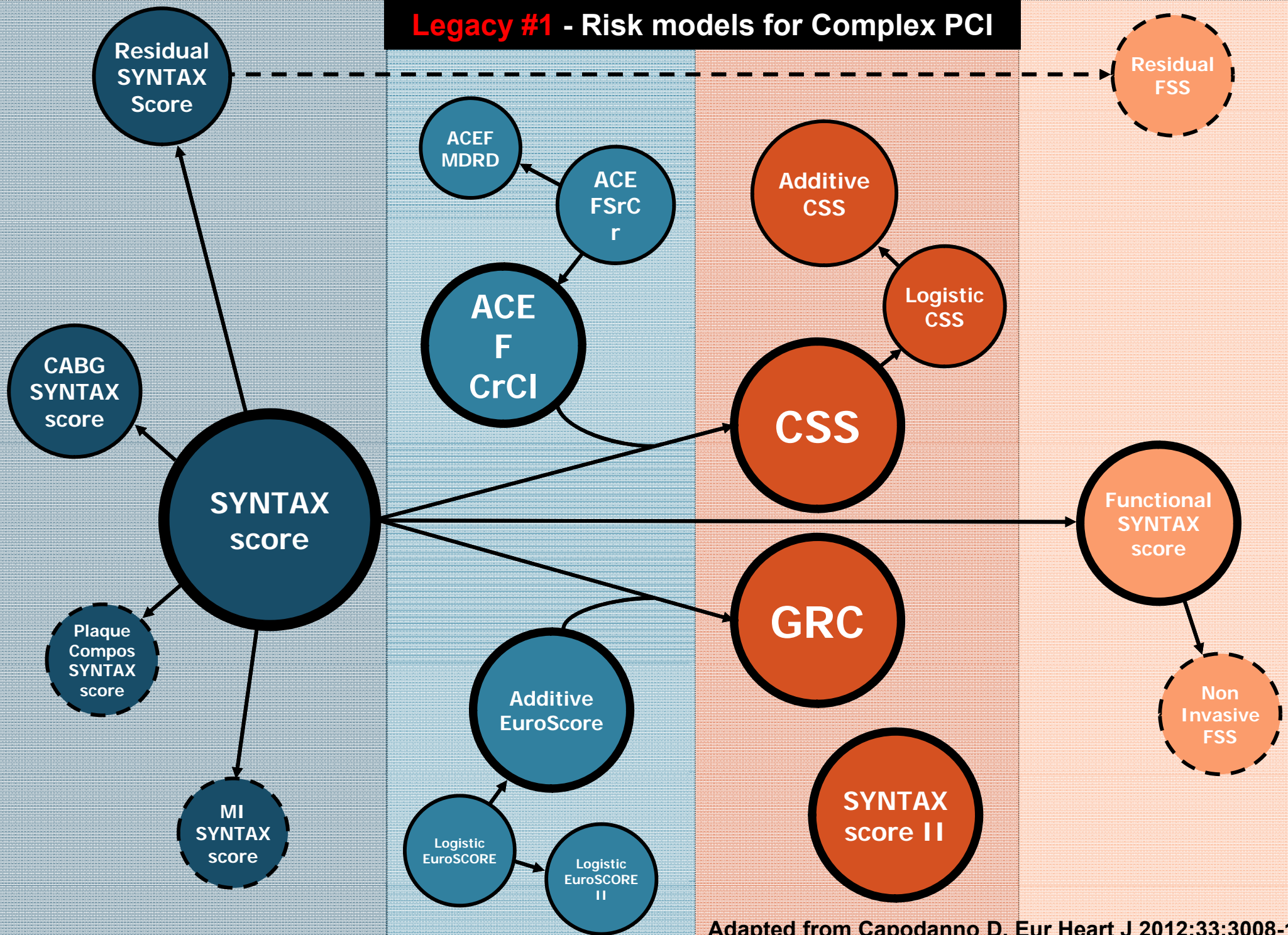


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Serruys PW, et al. *N Engl J Med* 2009;360:961-72
Mohr FW, et al. *Lancet* 2013; 381: 629-38



Legacy #1 - Risk models for Complex PCI



Adapted from Capodanno D, Eur Heart J 2012;33:3008-10

Angiographic

Clinical

Combined

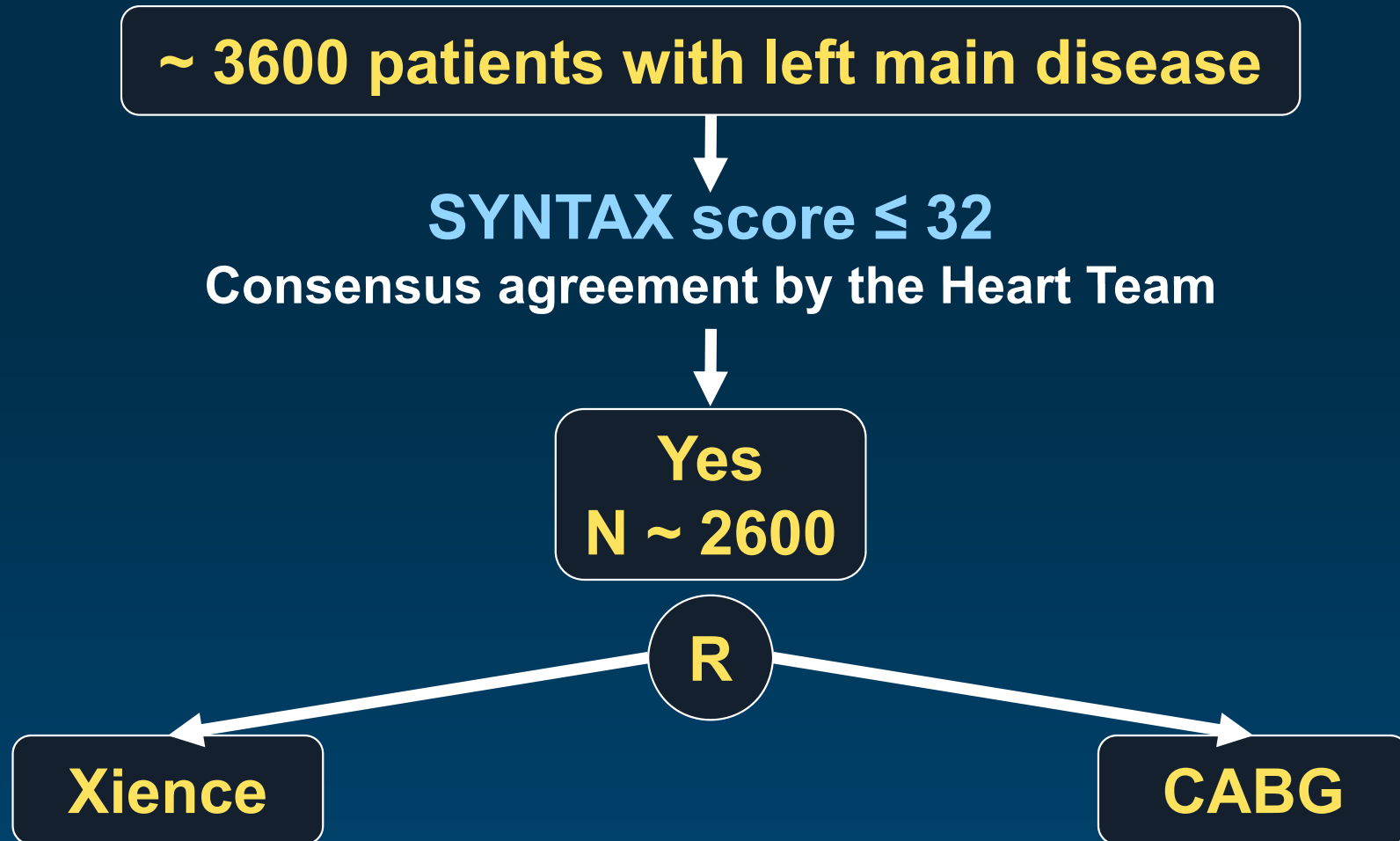
Functional

Legacy #2 – SYNTAX Advanced Our understanding On How to Improve The Outcomes of LM PCI

- Use best in class DES
 - Thienopyridine pre-loading
- Optimal pharmacotherapy
 - Statin pre-loading
 - Bivalirudin anticoagulation
- IVUS/FFR to assess the intermediate LM Isn
- FFR to avoid unnecessary stenting, but also to ensure complete ischemic revascularization
- IVUS guided LM stenting
 - 1- vs 2-stent techniques
 - Debulking
- Optimal LM stent technique
 - Hemodynamic support
 - Staging
 - Routine angiographic FU



Legacy #3 – From the Ashes of the SYNTAX, a New Trial: The EXCEL



Legacy #4 - The Heart Team Approach

The rationale for Heart Team decision-making for patients with stable complex coronary artery disease

Stuart J. Head¹, Sanjay Kaul², Michael J. Mack³, Patrick W. Serruys¹,
David P. Taggart⁴, David R. Holmes Jr⁵, Martin B. Leon^{6,7}, Jean Marco⁸,
Ad J.J.C. Bogers¹, and A. Pieter Kappetein^{1*}

The Heart Team of Cardiovascular Care

David R. Holmes, JR, MD,* Jeffrey B. Rich, MD,† William A. Zoghbi, MD,‡ Michael J. Mack, MD,§

- Initially introduced in revascularization trials to select patients for randomization. The Coronary Heart Team consists of a clinical/non-invasive cardiologist, an interventional cardiologist, and a cardiac surgeon. Other physicians with specific expertise can be added if necessary.
- The Heart Team has recently become a class 1C recommendation in European and American guidelines on myocardial revascularization



5-Year from SYNTAX... key messages

For patients with left main disease

- **Revascularization with PCI has comparable safety and efficacy outcomes to CABG**
- **Although formally unproved at this stage, PCI seems a reasonable treatment alternative in this patient population, in particular, when the SYNTAX Score is low (≤ 22) or intermediate (23-32)**

Legacies from SYNTAX include evolving concepts in trial design and decision making for LM PCI

