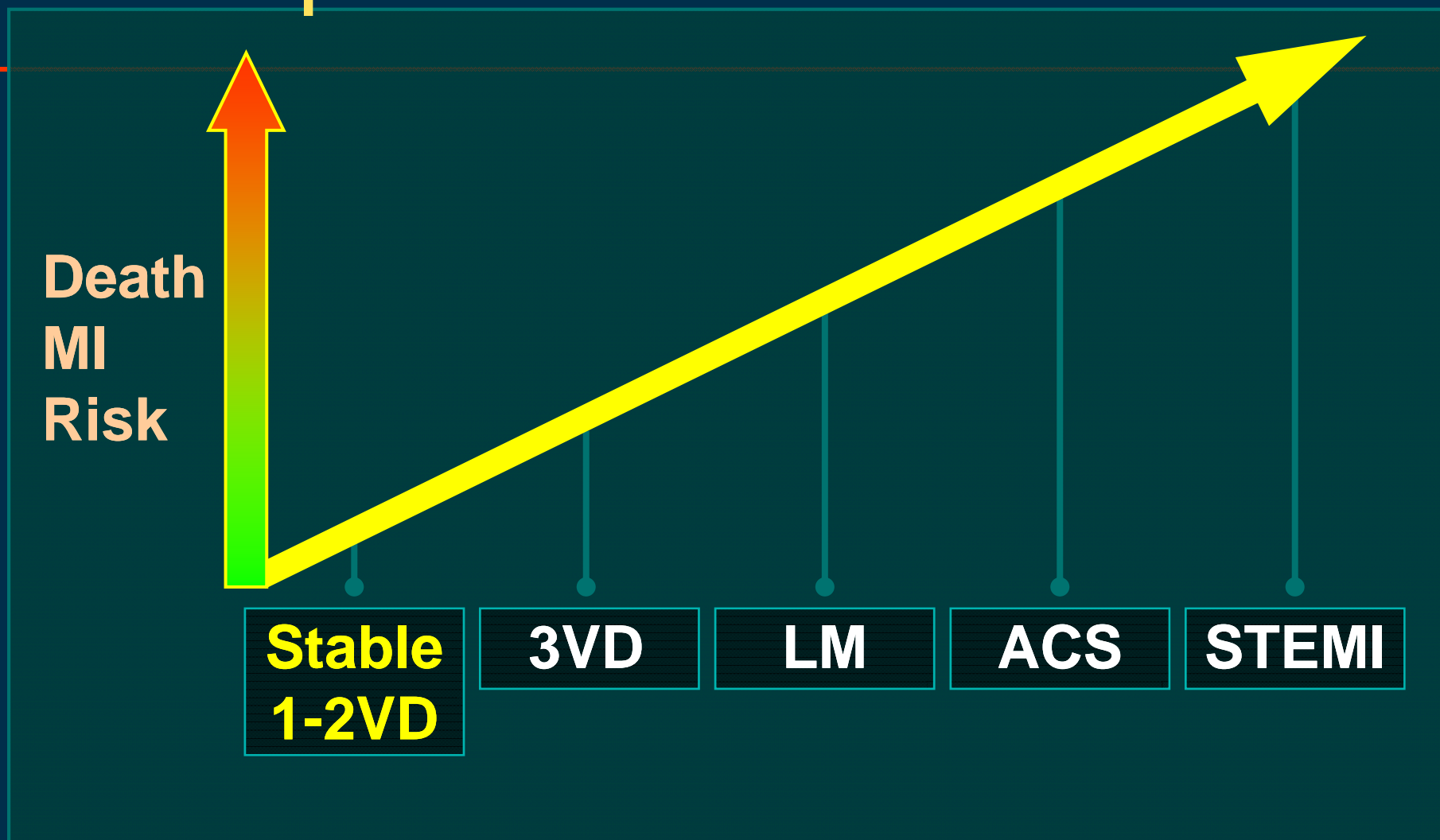


Revascularisation Challenges in Stable Angina

Niall Mulvihill, MD
Department of Cardiology,
St. James's Hospital and
Trinity College, Dublin.

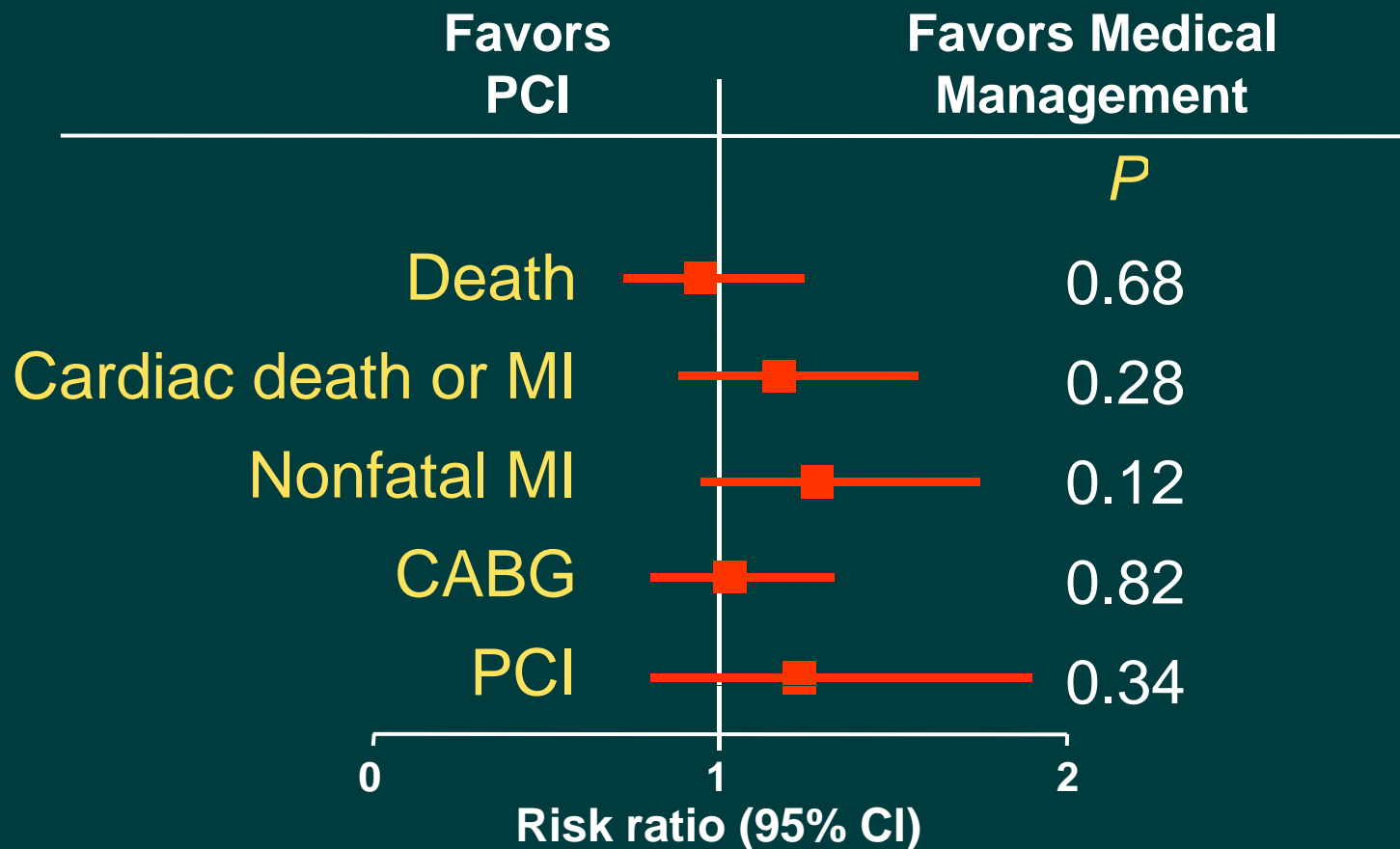


The Spectrum of CAD

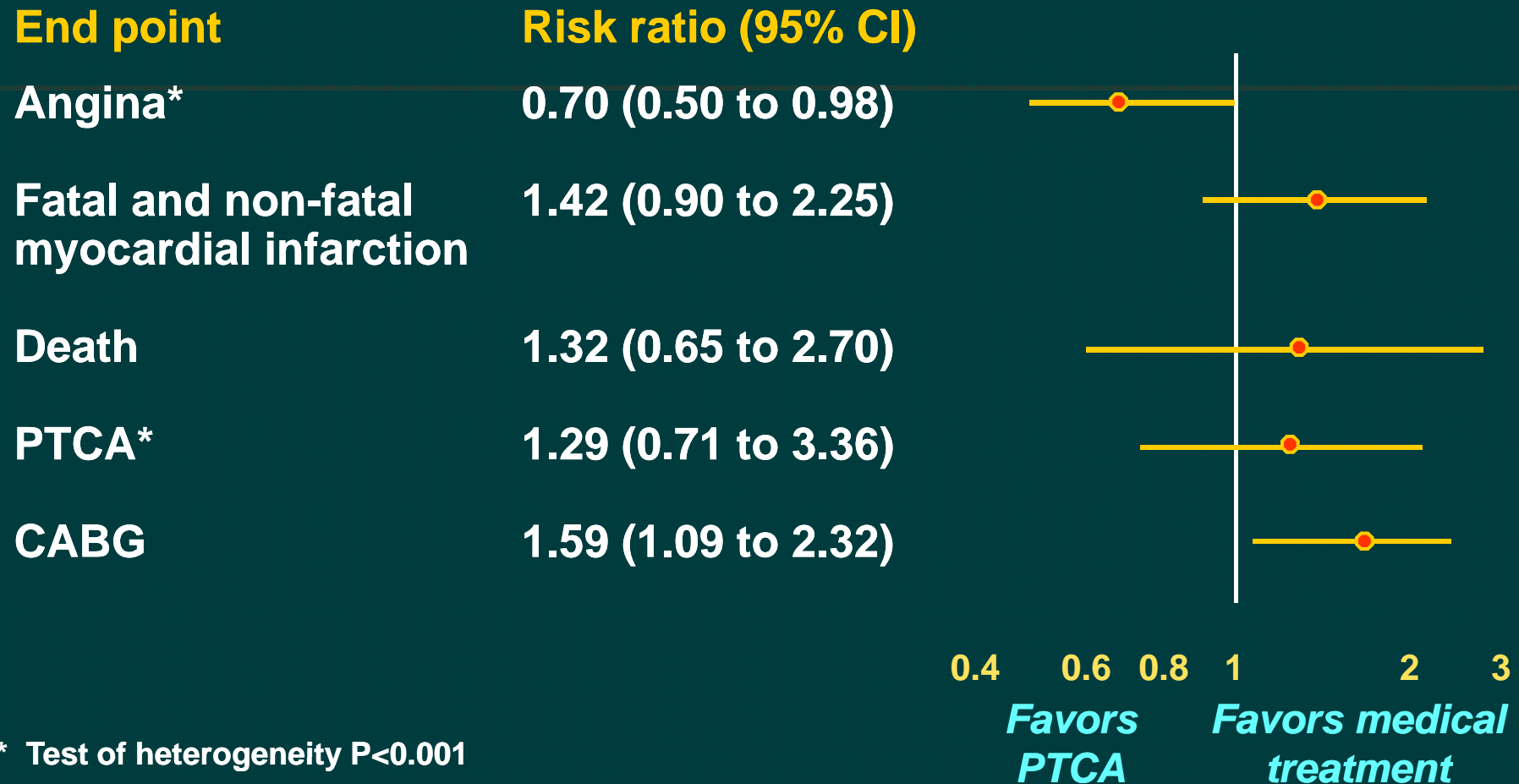


Stable CAD: PCI vs Conservative Medical Management

Meta-analysis of 11 randomized trials; N = 2,950



PCI vs Med Rx: Meta-analysis



Pooled risk ratios for various end points from six randomized controlled trials comparing percutaneous transluminal coronary angioplasty (PCTA) with medical treatment in patients with non-acute coronary heart disease; (CABG: coronary artery bypass grafting; n=953 for PTCA and 951 for medical treatment)

COURAGE: Clinical Outcomes Utilizing Revascularization and Aggressive Guideline-Driven Drug Evaluation



The NEW ENGLAND
JOURNAL *of* MEDICINE

Optimal Medical Therapy with or without PCI
for Stable Coronary Disease

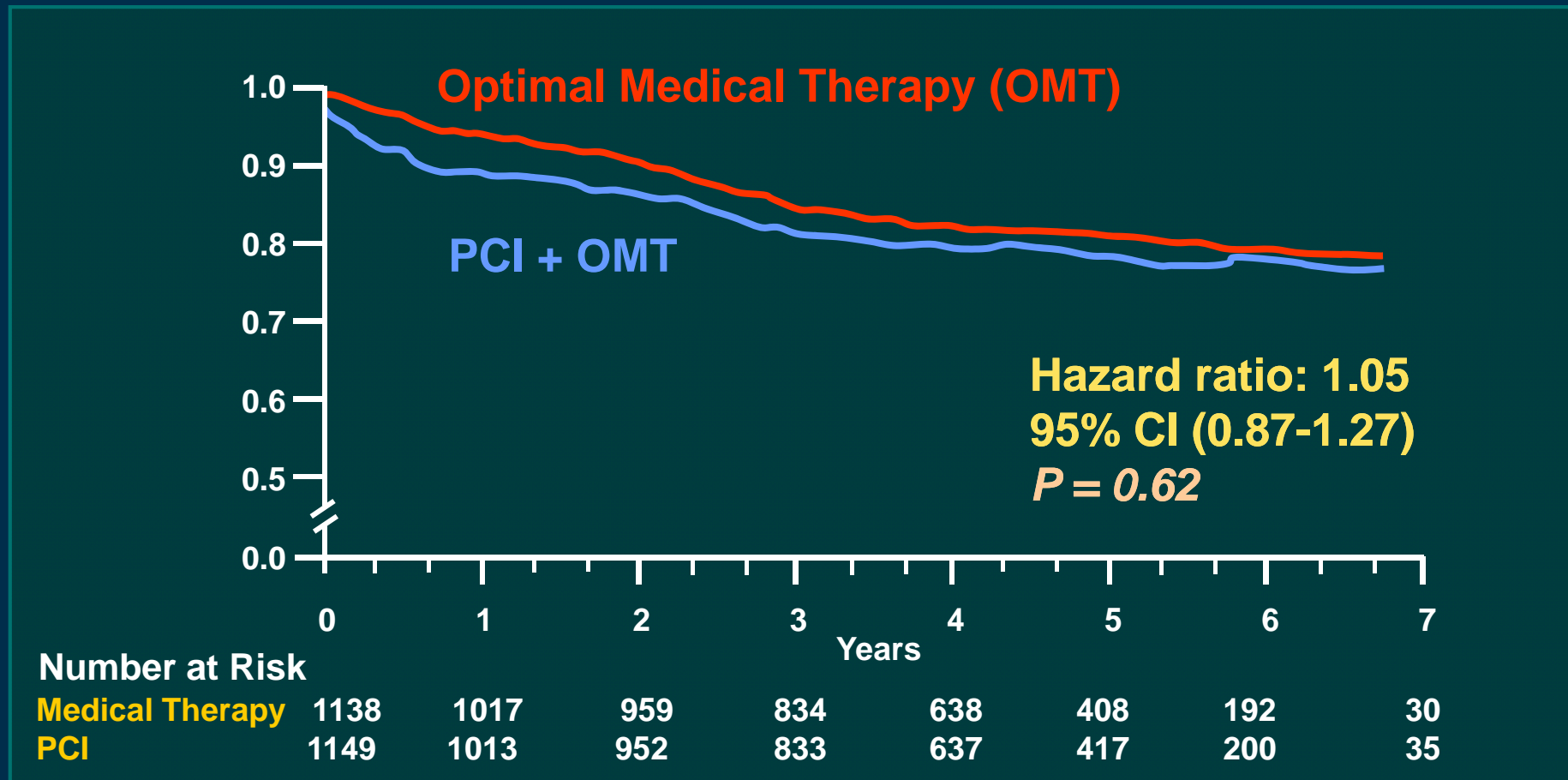
William E. Boden, M.D., Robert A. O'Rourke, M.D., Koon K. Teo, M.B., B.Ch., Ph.D., Pamela M. Hartigan, Ph.D., David J. Maron, M.D., William J. Kostuk, M.D., Merrill Knudtson, M.D., Marcin Dada, M.D., Paul Casperson, Ph.D., Crystal L. Harris, Pharm.D., Bernard R. Chaitman, M.D., Leslee Shaw, Ph.D., Gilbert Gosselin, M.D., Shah Nawaz, M.D., Lawrence M. Title, M.D., Gerald Gau, M.D., Alvin S. Blaustein, M.D., David C. Booth, M.D., Eric R. Bates, M.D., John A. Spertus, M.D., M.P.H., Daniel S. Berman, M.D., G.B. John Mancini, M.D., and William S. Weintraub, M.D., for the COURAGE Trial Research Group*

Optimal Medical Therapy with or without PCI for Stable Coronary Disease

randomized trial involving 2287 patients who had objective evidence of myocardial ischemia and significant coronary artery disease

death from any cause and nonfatal myocardial infarction during a follow-up period of 2.5 to 7.0 years (median, 4.6)

Survival Free of Death from Any Cause and Myocardial Infarction



The Message to the Public



Stent Shocker: They Don't Stop Heart Attacks



Study: Drugs trump angioplasty for chest pain



**The Courage to Let Clogged Arteries Be
Heart Stents Failed 'Courage' Test**



Angioplasty no better than drugs, study says



Study questions the widespread use of angioplasty

COURAGE

**Exclusion criteria included:
persistent CCS class IV angina,
a markedly positive stress test
refractory heart failure or cardiogenic
shock,
an ejection fraction of less than 30%,
revascularization within the previous 6
months**

COURAGE

1149 Were assigned to PCI group

46 Did not undergo PCI (and 27 were not dilatable)

107 Were lost to follow-up

So 996 patients had PCI and were followed (of which apparently 97 had POBA and only 31(3%) had DES)

COURAGE

**BUT.....Of the 1138 patients in the
medical group**

348 crossed over to revascularisation

YES THAT'S 348 (32.6%)...

**(of course you can't cross over the other
way except that they actually didn't
angioplasty 46(4%) of them...)**

COURAGE

AND

**Of 35,539 patients screened
ONLY 2287 were enrolled**

I make that 6.3%...

HPS was criticised for its screening to inclusion ratio, which was 63603 screened, 32145 run in and 20536 randomised (ie : 32% inclusion - COURAGE has 6.3% inclusion which is astonishingly low: why???)...

COURAGE

So what COURAGE has actually shown is:

(of the 6% of screened patients that physicians etc actually allowed to be randomised)

To maintain a similar outcome to PCI with bare metal stents or POBA (i.e. outdated treatment), 32.6% of patients having medical management will require revascularisation within 5 years (and even then get significantly more angina over the intervening years)

COURAGE

The only real conclusion that can honestly be taken from COURAGE is that:

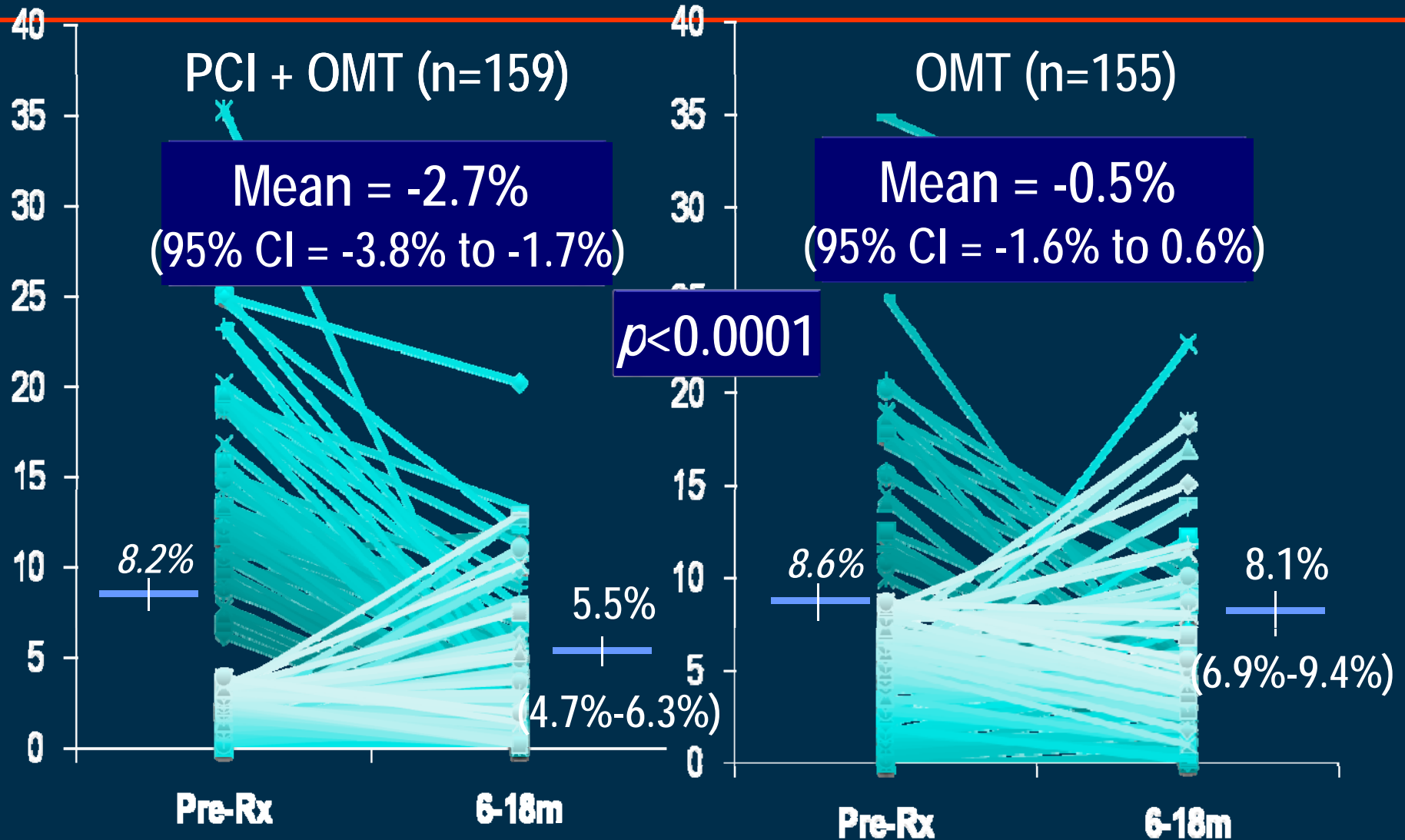
DELAYING PCI IN ASYMPTOMATIC AND MINIMALLY SYMPTOMATIC PATIENTS UNTIL INTERVENTION IS FORCED BY SYMPTOMS IS SLIGHTLY WORSE THAN IMMEDIATE PCI FOR SYMPTOM CONTROL...

COURAGE

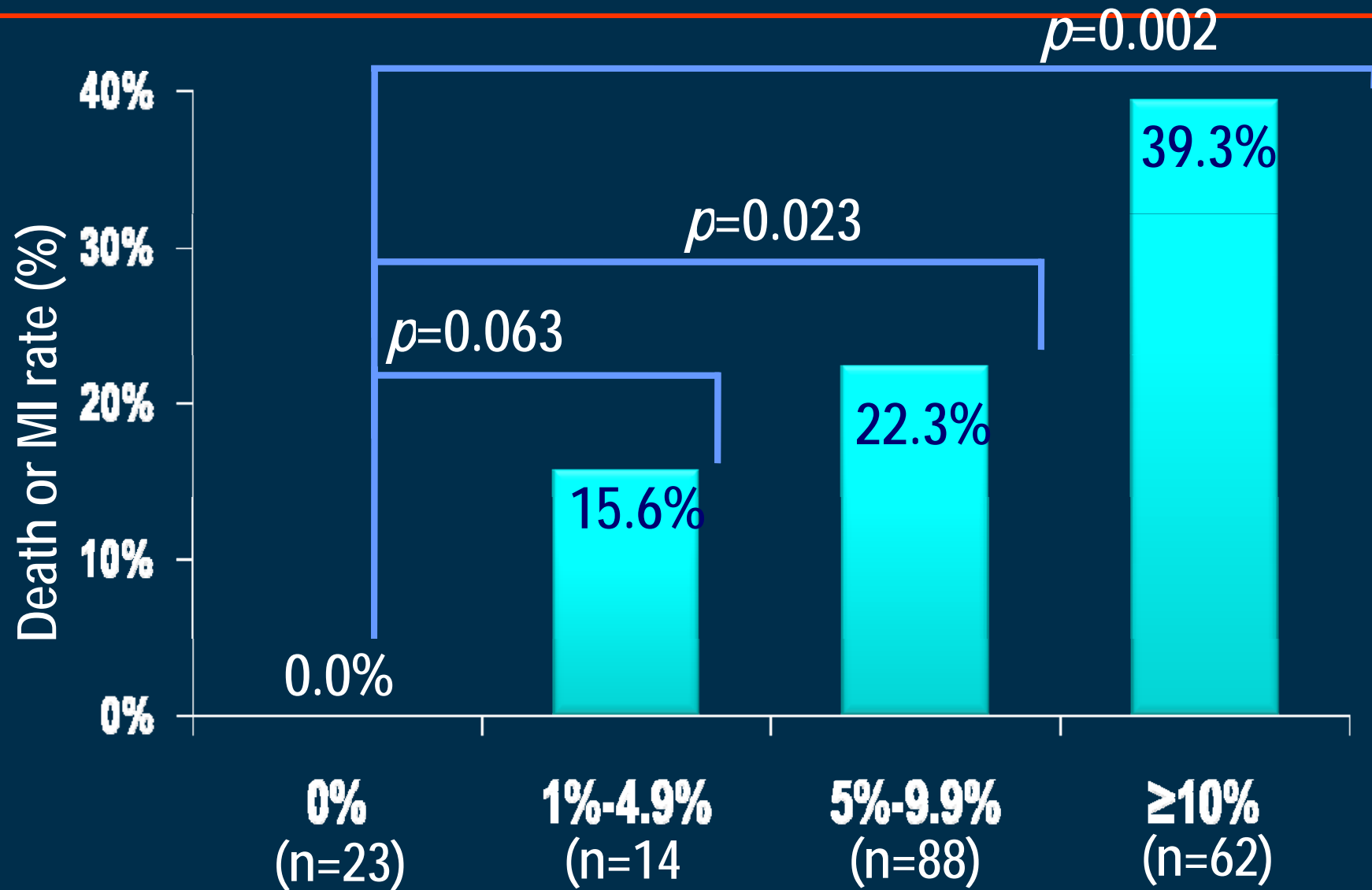
BUT.....Silent Ischaemia

**Myocardial perfusion scan
substudy (313 patients up to 18 months
post randomization)**

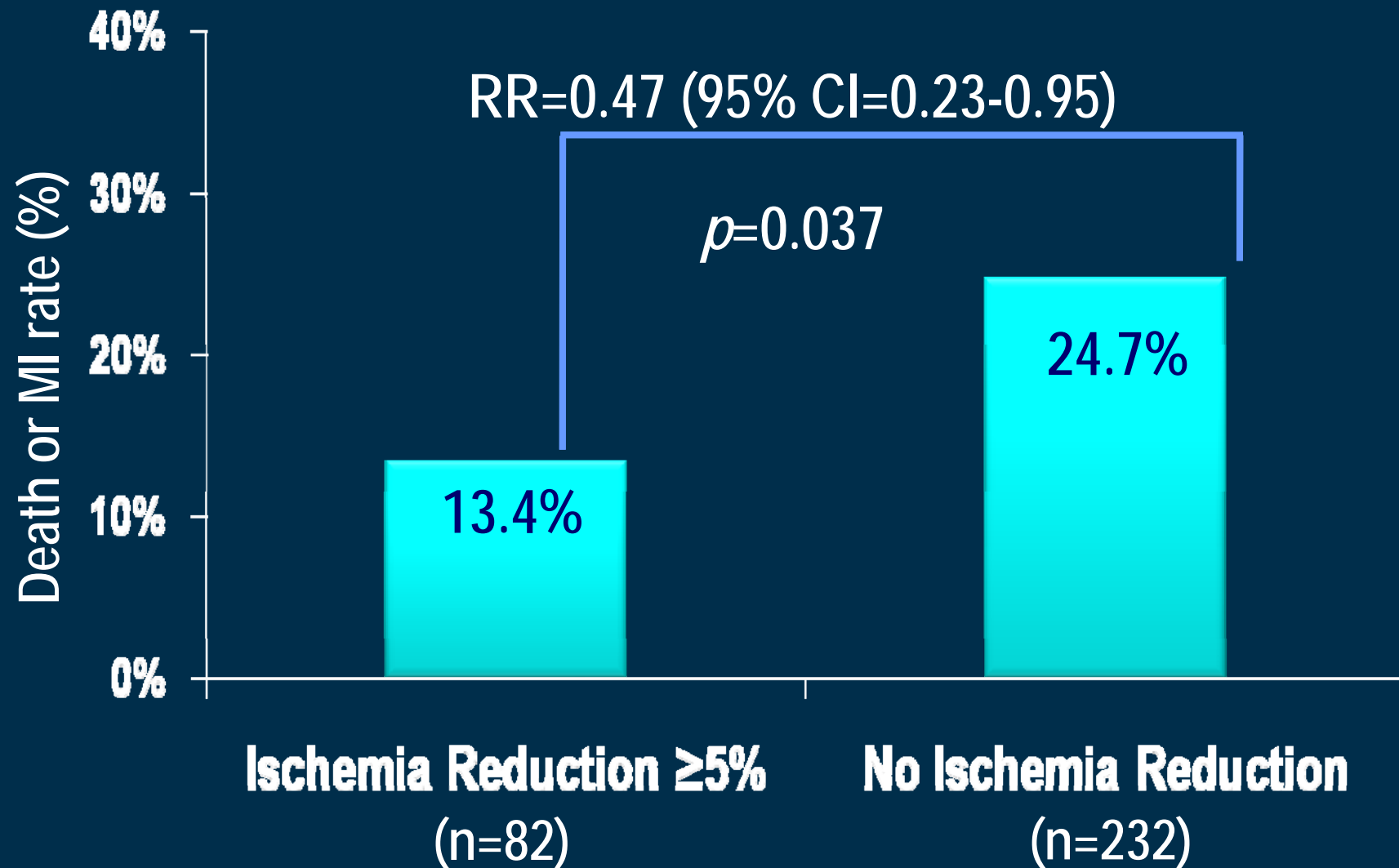
MPS % ischemic myocardium (95% CI) pre-Rx & 6-18m



Rates of death or MI by residual ischemia on 6-18m MPS



Rates of death or MI by ischemia reduction

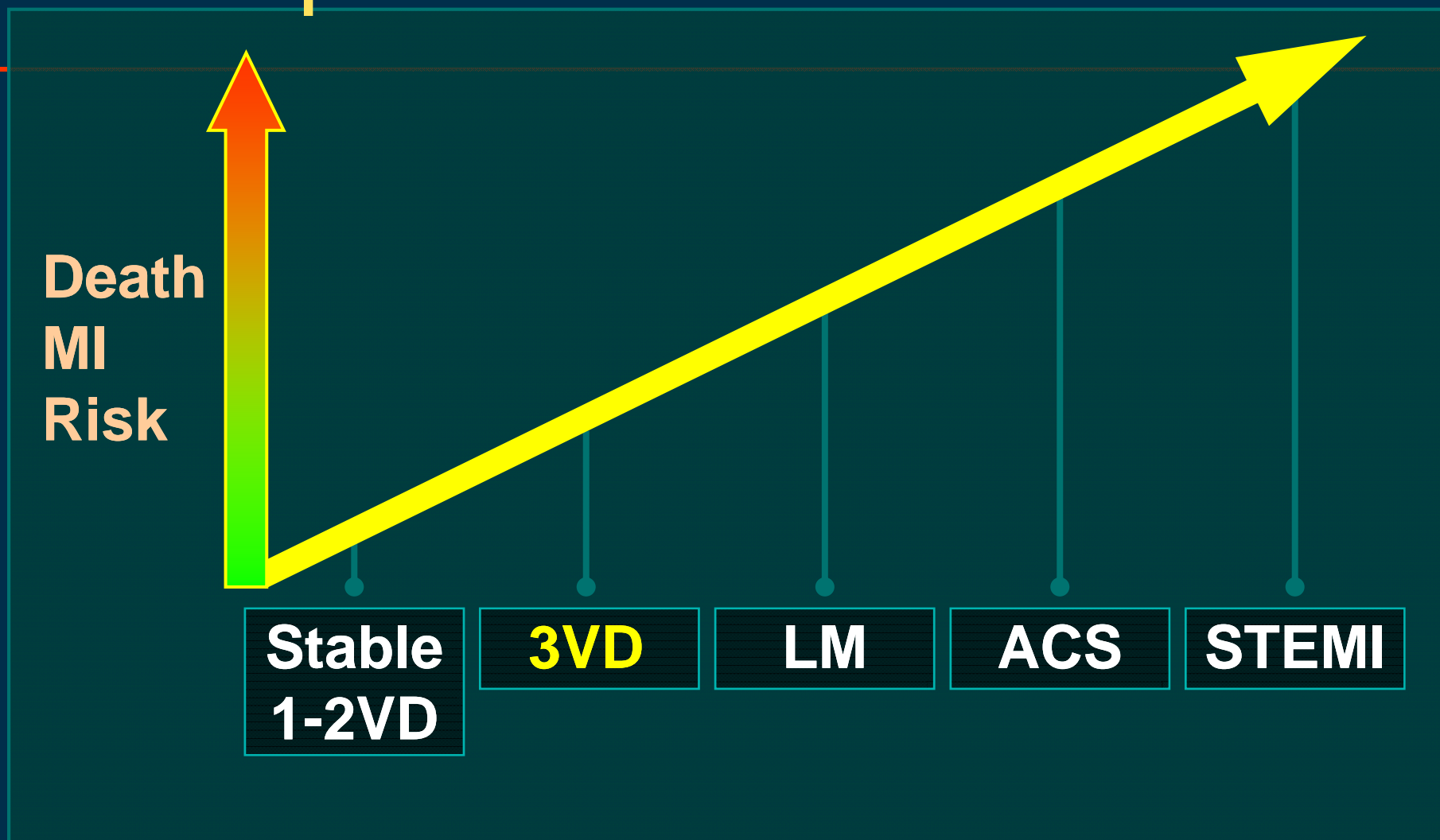


COURAGE

So actually the COURAGE results *now* suggest that:

Whilst a policy of delaying PCI in patients with minimal symptoms is only slightly worse than immediate PCI for symptom control, it may lead to increased residual ischaemia and increased mortality ...

The Spectrum of CAD



CABG vs. PCI

Most Recent Meta-Analysis (of Randomized Trials)

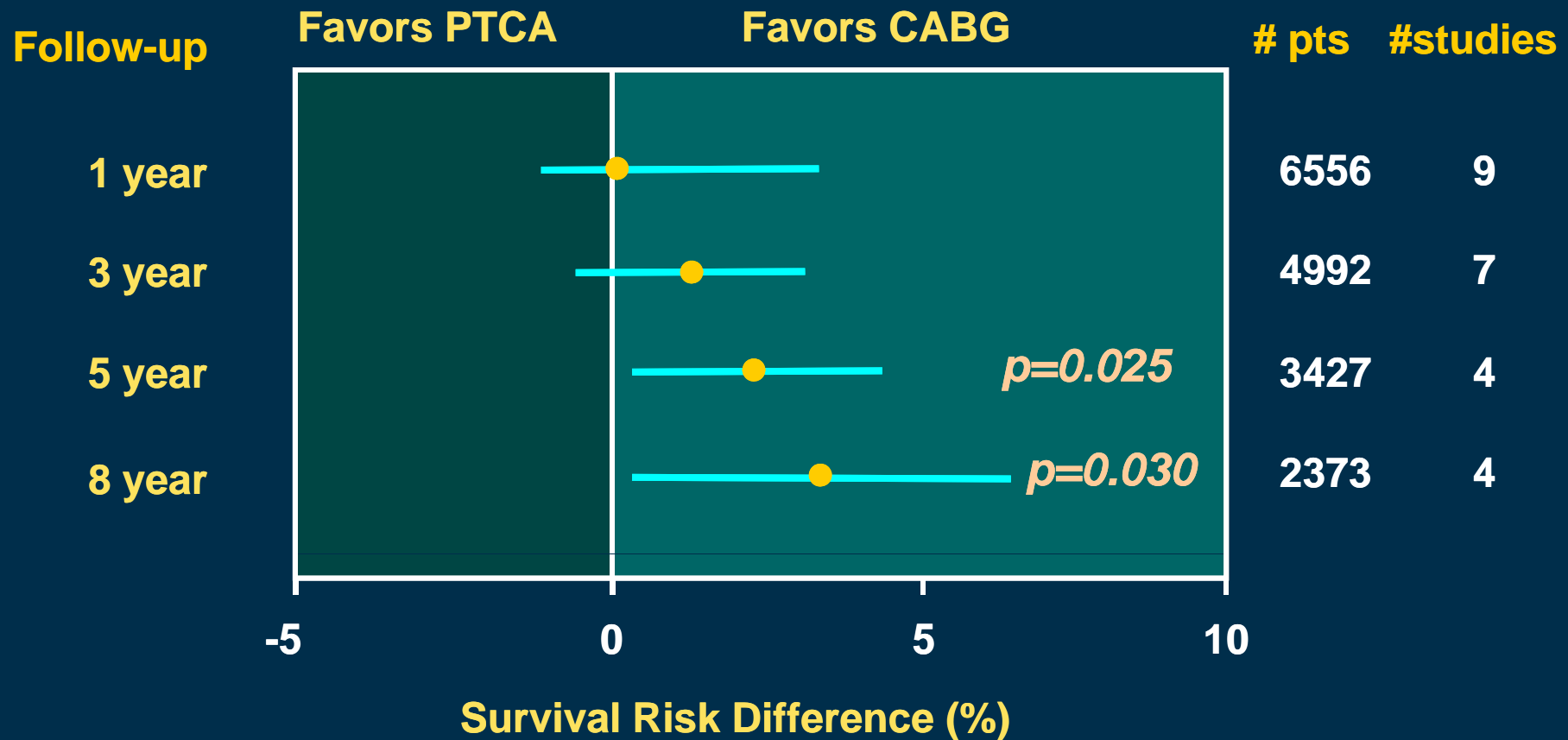
RITA	(n = 1011)	BARI	(n = 1829)
ERACI	(n = 127)	Toulouse	(n = 152)
Lousanne	(n = 134)	SIMA	(n = 121)
GABI	(n = 359)	ERACI II	(n = 450)
EAST	(n = 392)	ARTS	(n = 1205)
CABRI	(n = 1054)	SoS	(n = 988)
MASS	(n = 142)		

**13 randomized trials
7,946 patients**

CABG vs. PCI

Most Recent Meta-Analysis

Survival – MVD Trials

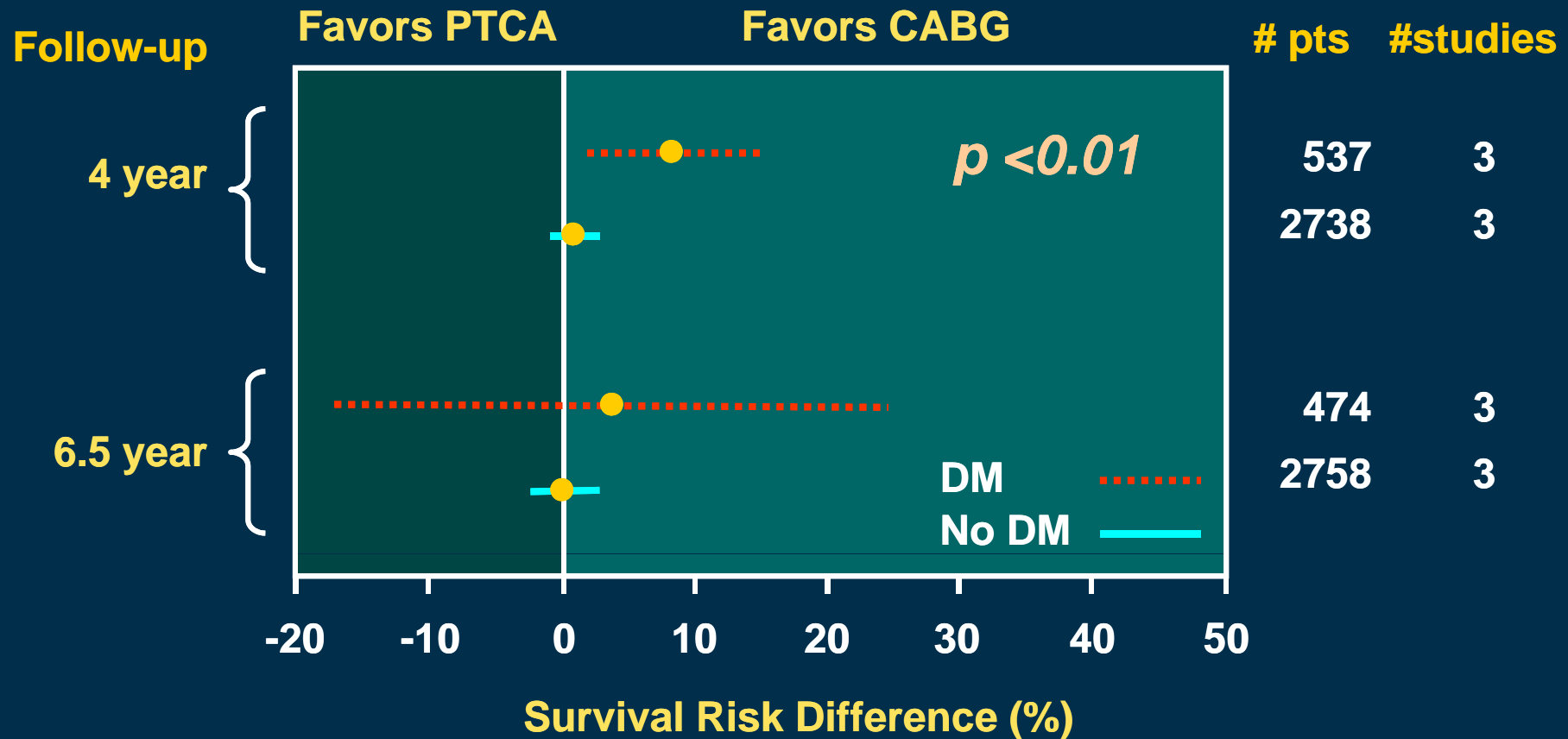


Hoffman et al. JACC. 2003;41:1293-1304.

CABG vs. PCI

Most Recent Meta-Analysis

Survival – Diabetics



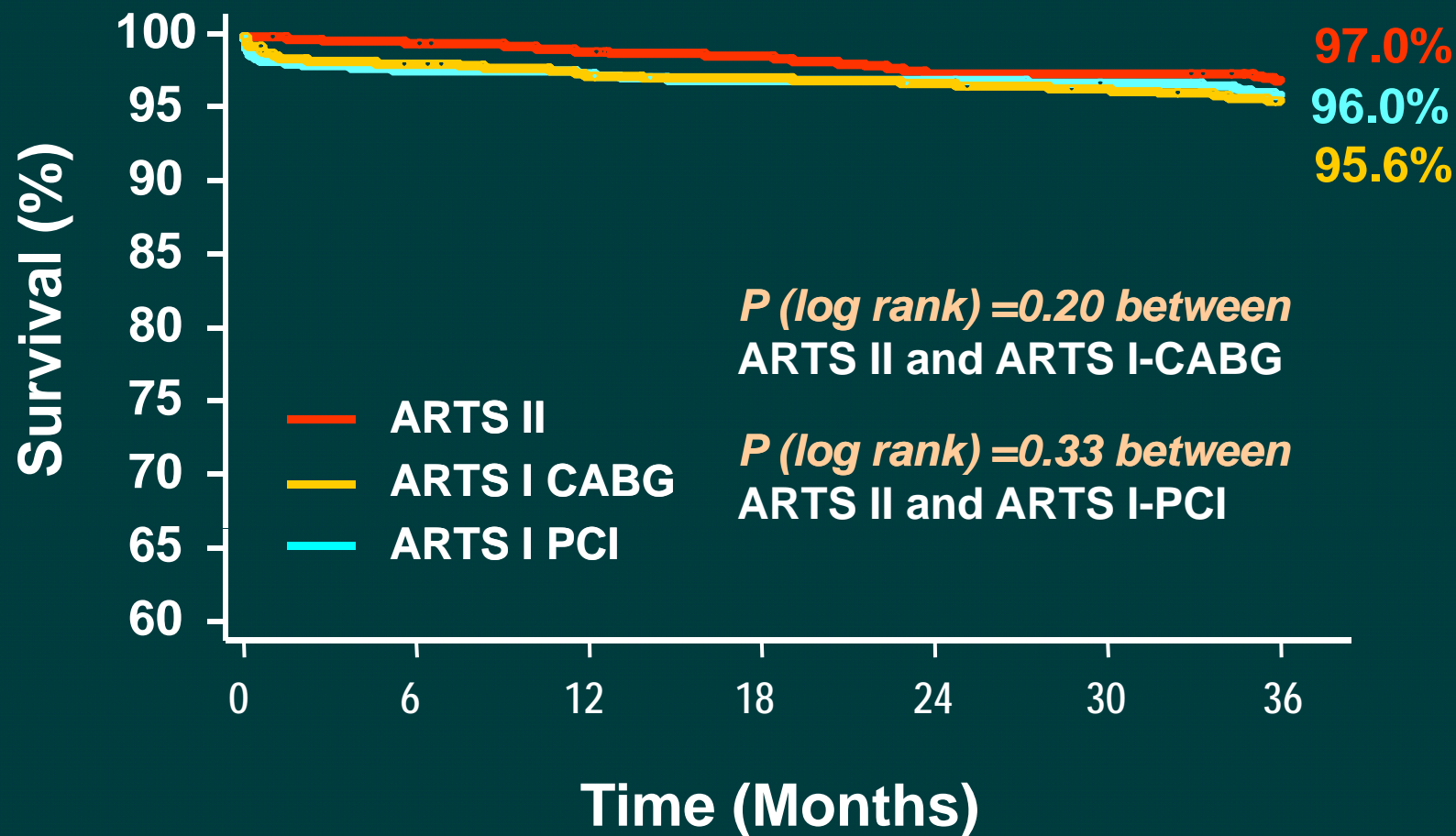
Hoffman et al. JACC. 2003;41:1293-1304.

ARTS II – Procedural Characteristics

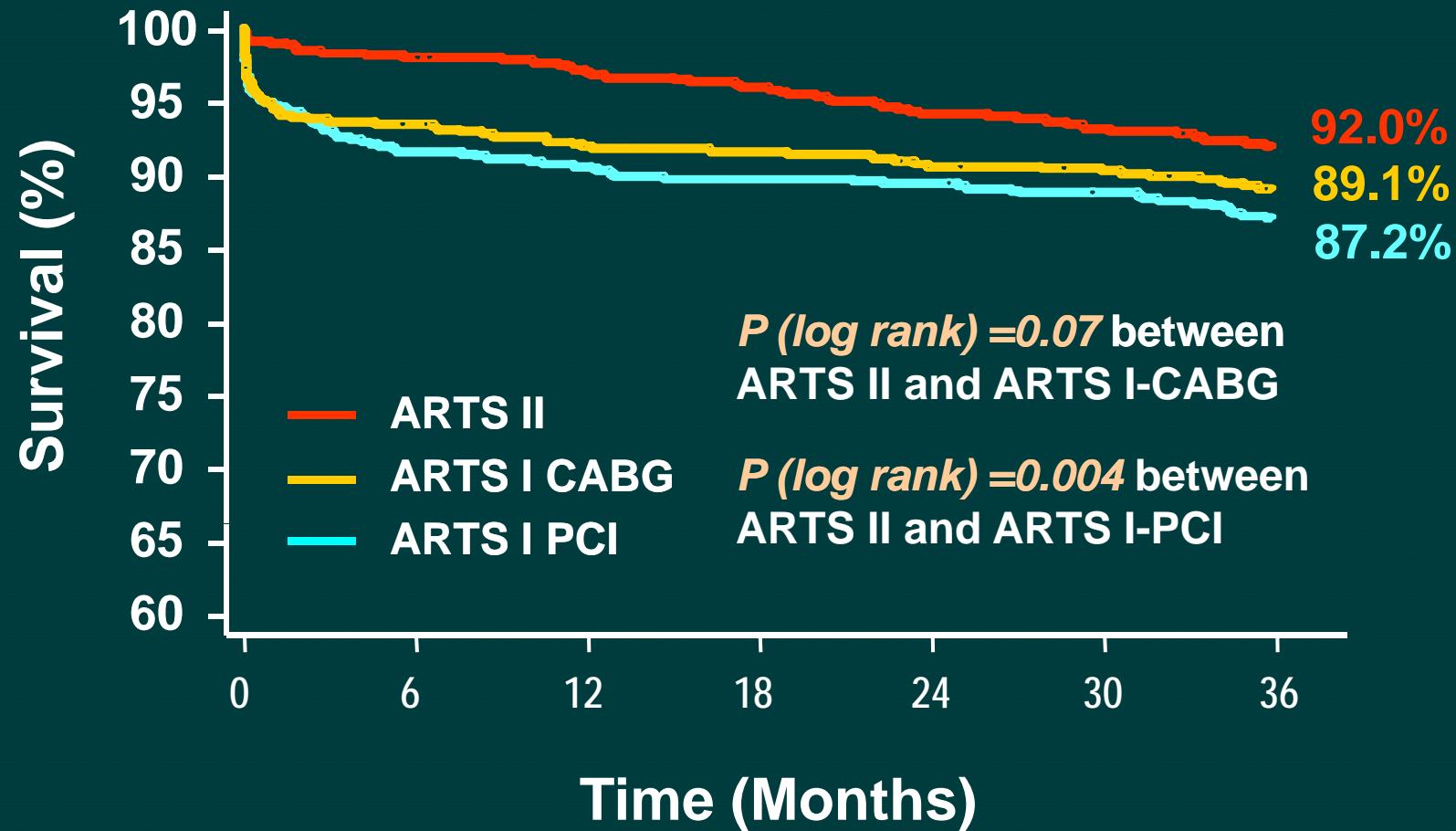
	ARTS II N=607 pts N=2160 les.	ARTS I (CABG) N=605 pts N=1638 les.	ARTS I (PCI) N=600 pts N=1606 les.
Lesions, #	3.6 ↗	2.8	2.8
Stented les. / anast. seg., #	3.2 ↗	2.8	2.5
Stents, #	3.7 ↗	-	2.8
Max. inflation pressure, atm	16.4 ↗	-	14.6
Total stent length, mm	72 ↗	-	48
(range)	12-253	-	8-165
GP IIb/IIIa inhibitor use, %	32	-	-
Use of arterial conduit, %	-	93	-
Duration of procedure, mins	85 ↘	193	99
Hospital stay, days since procedure	3.4	9.6	3.9

Figures in *Italics* indicate statistical difference (95% CI) between ARTS II and ARTS I groups.

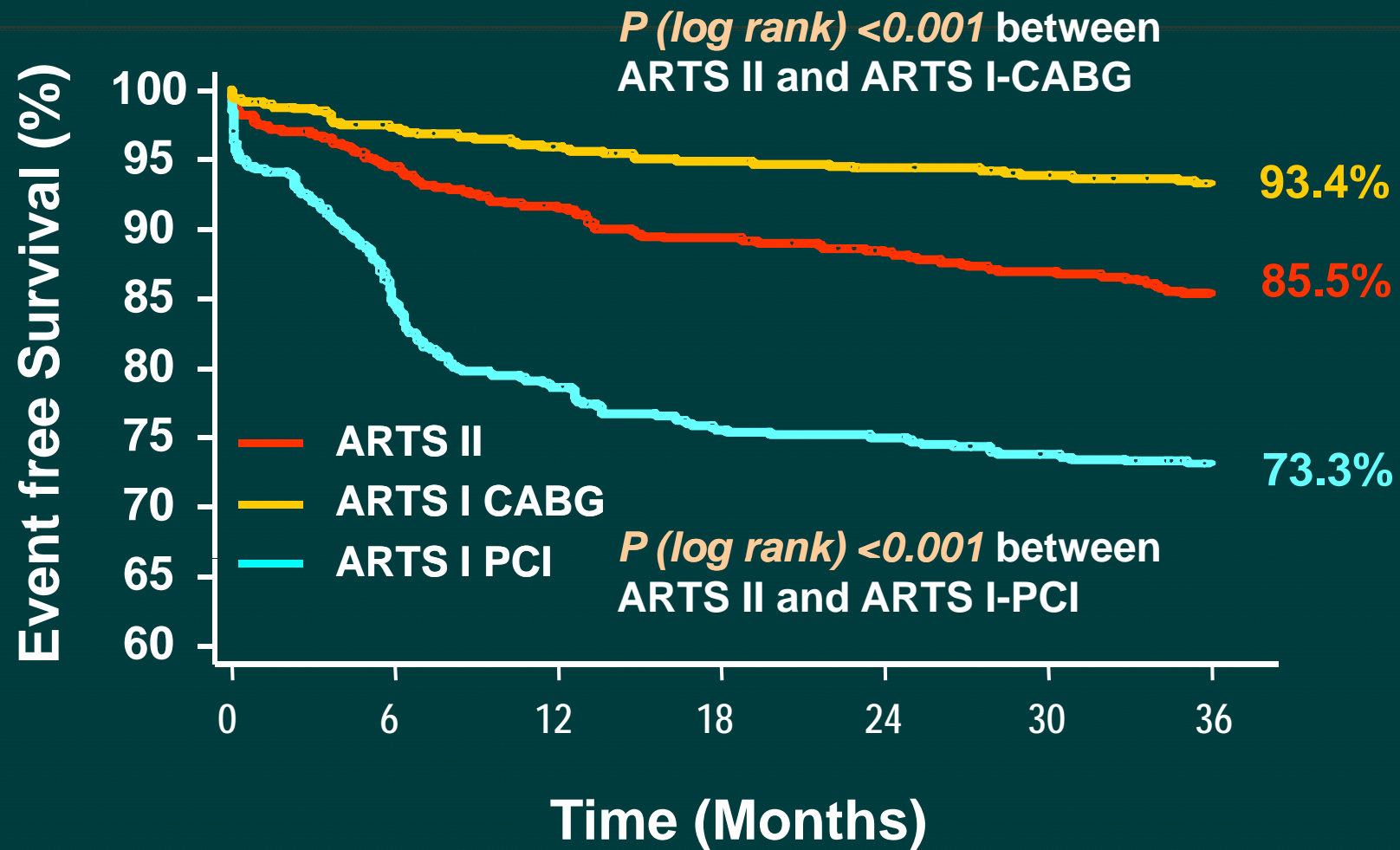
ARTS II – Deaths up to 3 Years



ARTS II – Death/CVA/MIs up to 3 Years



ARTS II - Re-Intervention up to 3 Years



ARTS II: Summary

Despite the higher risk profile, the overall MACCE rates at 30 days, 6 and 12 months are consistently lower in ARTS II than in both the ARTS I-PCI and ARTS I-CABG arms.

In addition, the composite endpoint of Death / CVA / MI is lower for ARTS II as compared to ARTS I-CABG ($p < 0.07$).

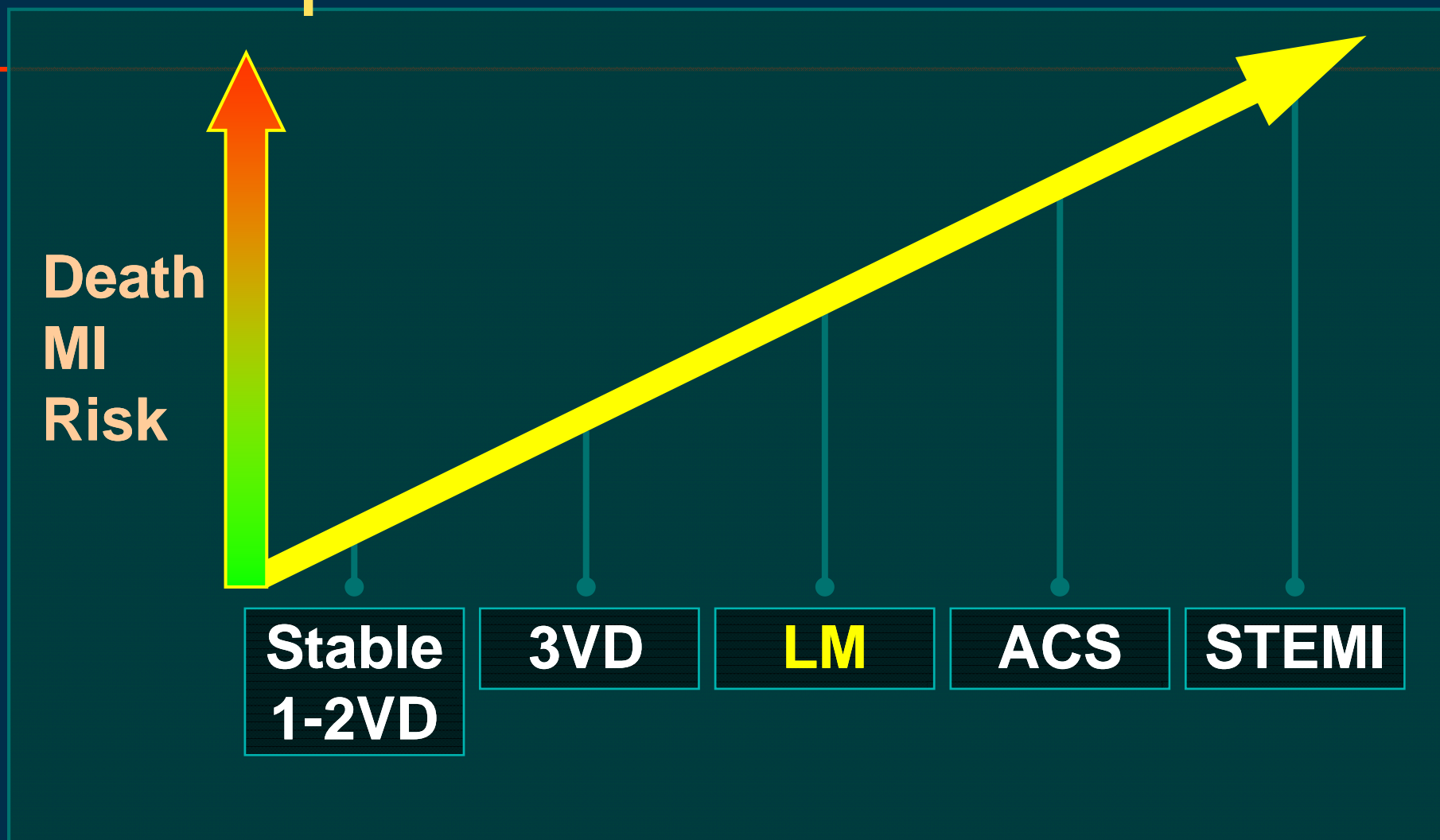
However, the reintervention rate of the ARTS I-CABG is still significantly lower than in ARTS II ($p = 0.003$).

ARTS II

Selected lower risk cohort of patients without significant LV impairment

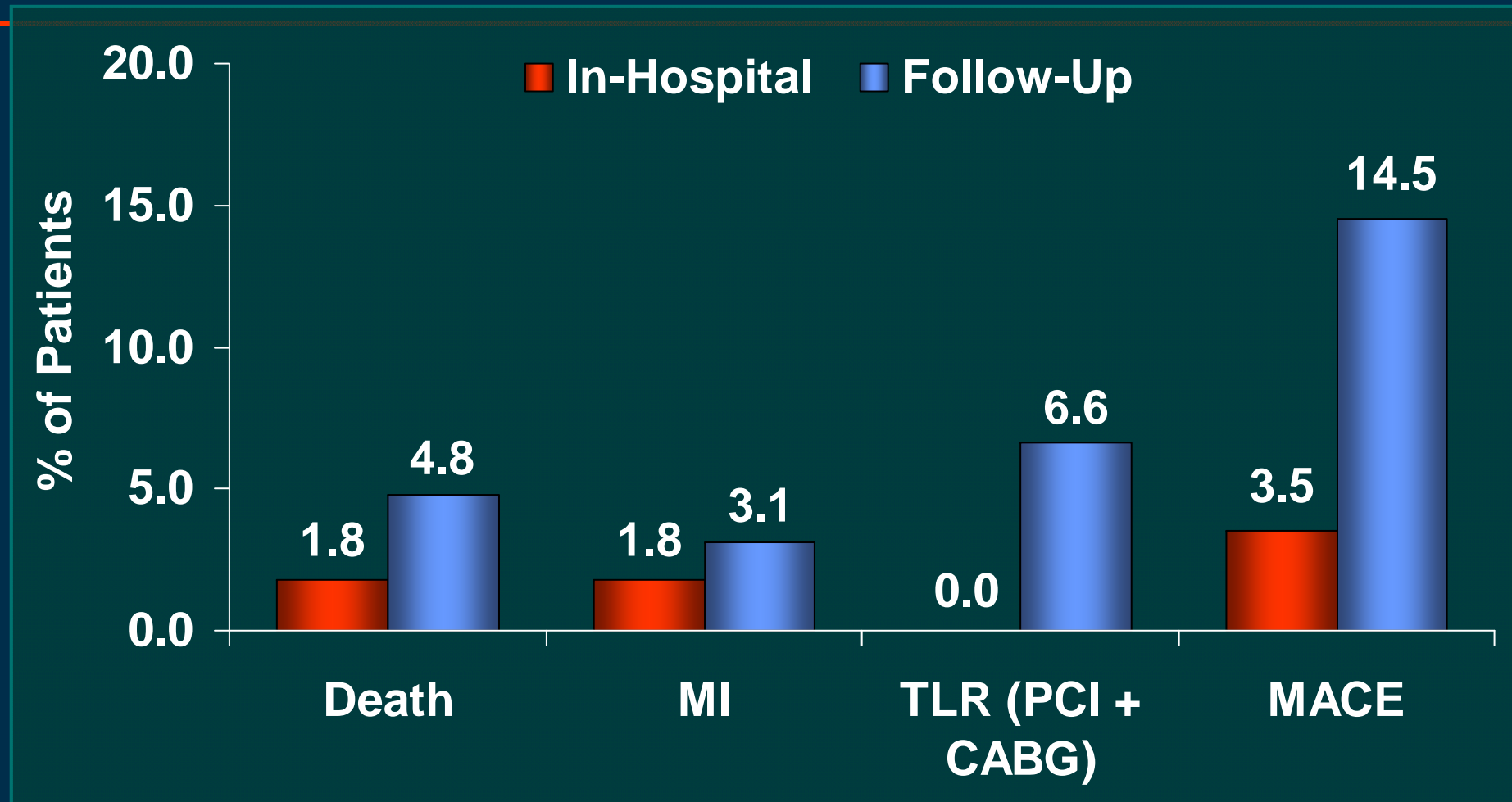
PCI with DES is a good option with increased risk of repeat revascularisation

The Spectrum of CAD



SES Left Main Registry

N=294

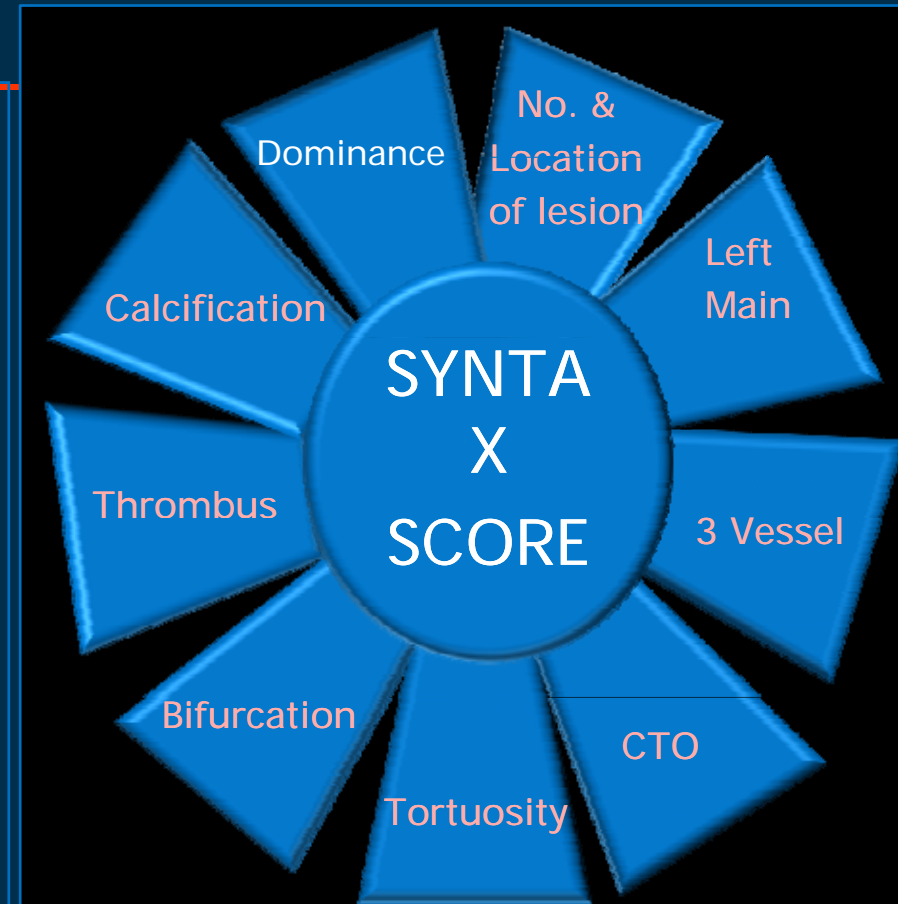


SYNTAX

Heart team meeting
- surgeon(s) and
interventional
cardiologist(s) assess
each patient

Operative risk
(EuroSCORE & Parsonnet score)

Coronary lesion complexity
(SYNTAX score)



BARI classification of coronary segments

Leaman score, *Circ* 1981;63:285-299

Lesions classification ACC/AHA, *Circ* 2001;103:3019-3041

Bifurcation classification, *CCI* 2000;49:274-283

CTO classification, *J Am Coll Cardiol* 1997;30:649-656

Sianos et al, *EuroIntervention* 2005;1:219-227
Valgimigli et al, *Am J Cardiol* 2007;99:1072-1081
Serruys et al, *EuroIntervention* 2007;3:450-459

SYNTAX Trial- Eligible Patients

De novo disease

Isolated left main

left main +
1-vessel disease

left main +
2-vessel disease

left main +
3-vessel disease

3-vessel disease

Revascularisation in
all 3 vascular territories

Limited Exclusion Criteria

- Previous interventions (PCI or CABG)
- Acute MI with CPK > 2x
- Concomitant cardiac surgery

SYNTAX Trial Design

 62 EU Sites +  23 US Sites

All Pts with de novo 3VD
and/or LM disease (N=4,337)

- Treatment preference (9.4%)
- Referring doctor or patient refused informed consent (7.0%)
- Inclusion/exclusion (4.7%)
- Withdrew before consent (4.3%)
- Other (1.8%)
- Medical treatment (1.2%)

71% enrolled (N=3,075)

SYNTAX Trial Design

 62 EU Sites +  23 US Sites

Heart Team (surgeon & interventionalist)

Amenable for both
treatment options

Amenable for only
one treatment
approach

Stratification:
LM and Diabetes

Randomised Arms
n=1800

Two Registry Arms

CABG
N=897

vs

TAXUS*
N=903

CABG
N=1077

PCI
N=198

3VD 66.3%
LM 33.7%

3VD 65.4%
LM 34.6%

Procedural Characteristics

PCI Randomised Cohort

Patient-based

TAXUS*
N=903

Staged Procedure, %

14.1

Vessels treated, %

LAD

36.3

Circumflex

32.5

RCA

29.2

LM

11.2

Bi/trifurcation, %

64.4

Lesions treated/pt, mean \pm SD

3.6 \pm 1.6

No. stents implanted, mean \pm SD

4.6 \pm 2.3

Total length implanted, mm \pm SD

86.1 \pm 47.9

Range, mm

8 – 324

Long stenting (>100 mm), %

33.2

Procedural Characteristics

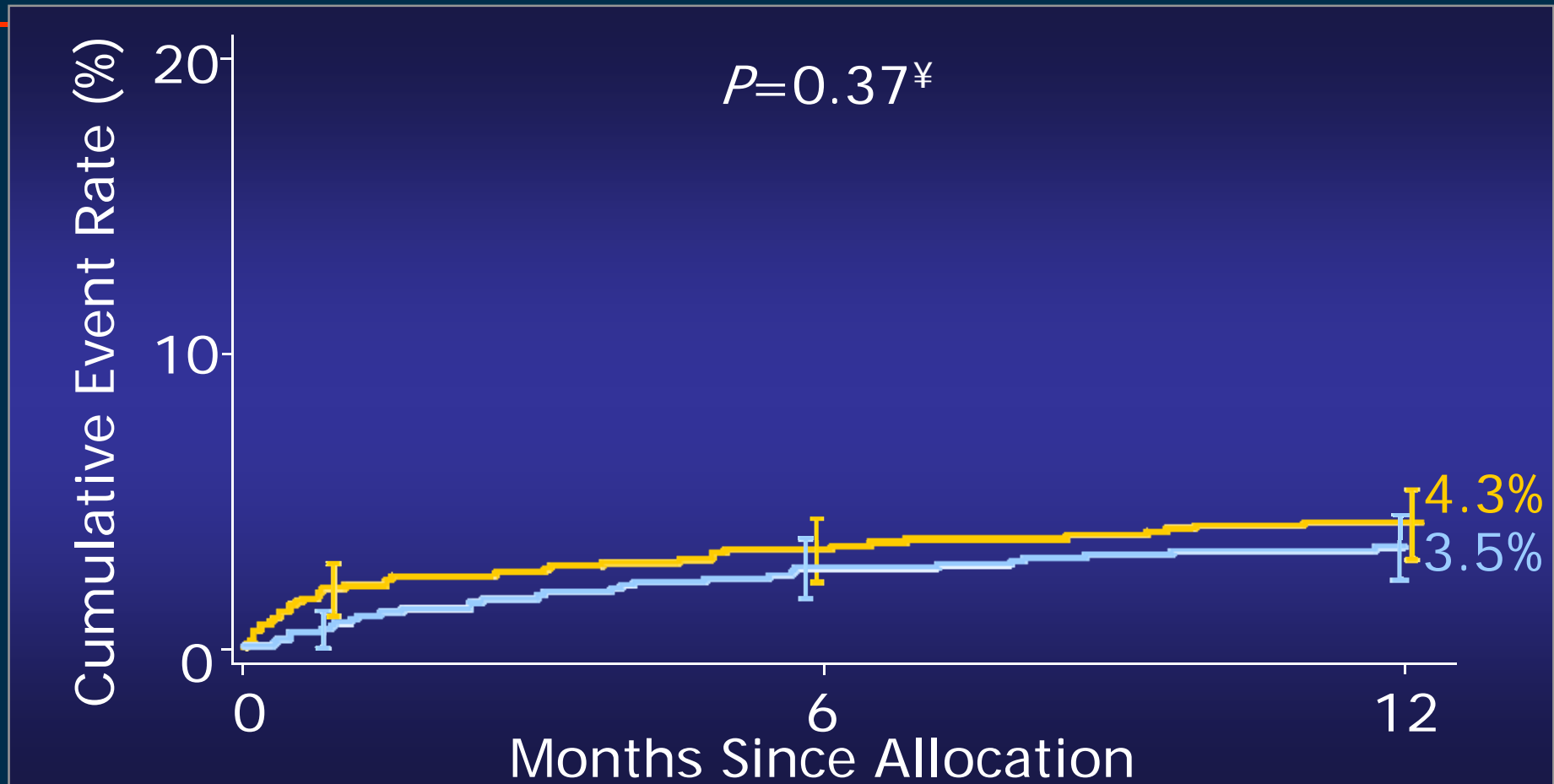
CABG Randomised Cohort

<i>Procedure-related</i>	CABG N=897
Off-pump surgery, %	15.0
Graft revascularization, %	
Complete arterial revascularisation	18.9
At least one arterial graft	97.3
Double LIMA/RIMA	27.6
LIMA+venous	78.1
Arterial graft to LAD	95.6
Radial Artery	14.1
Venous graft only	2.6
Grafts per patient, mean \pm SD	2.8 \pm 0.7
Distal anastomosis/pt, mean \pm SD	3.2 \pm 0.9

SYNTAX - All-cause mortality to 12 Months

■ CABG (N=897)

■ TAXUS* (N=903)

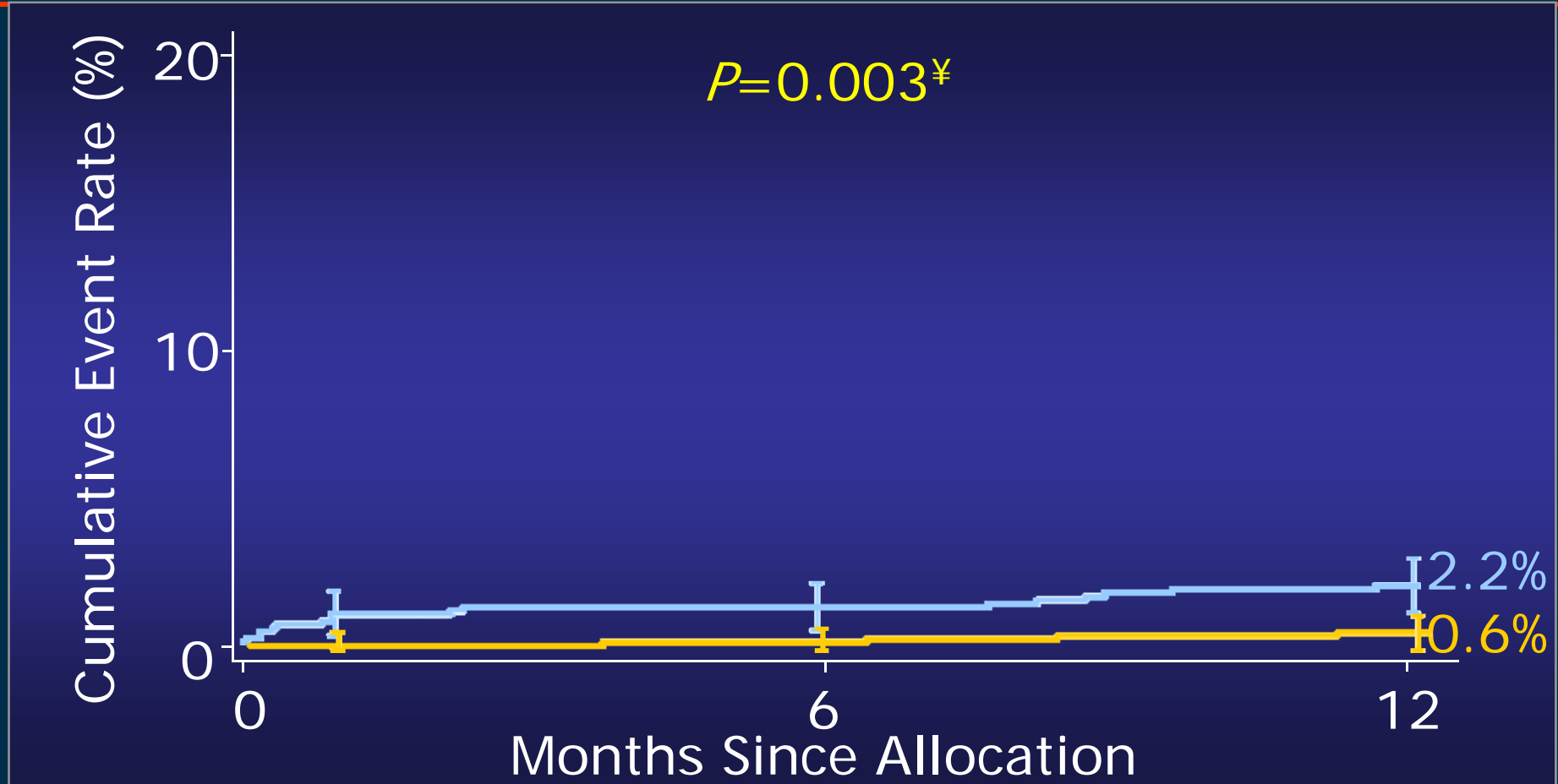


ITT; [‡]Fisher Exact Test

SYNTAX - Cerebrovascular Events to 12 Months

■ CABG (N=897)

■ TAXUS* (N=903)

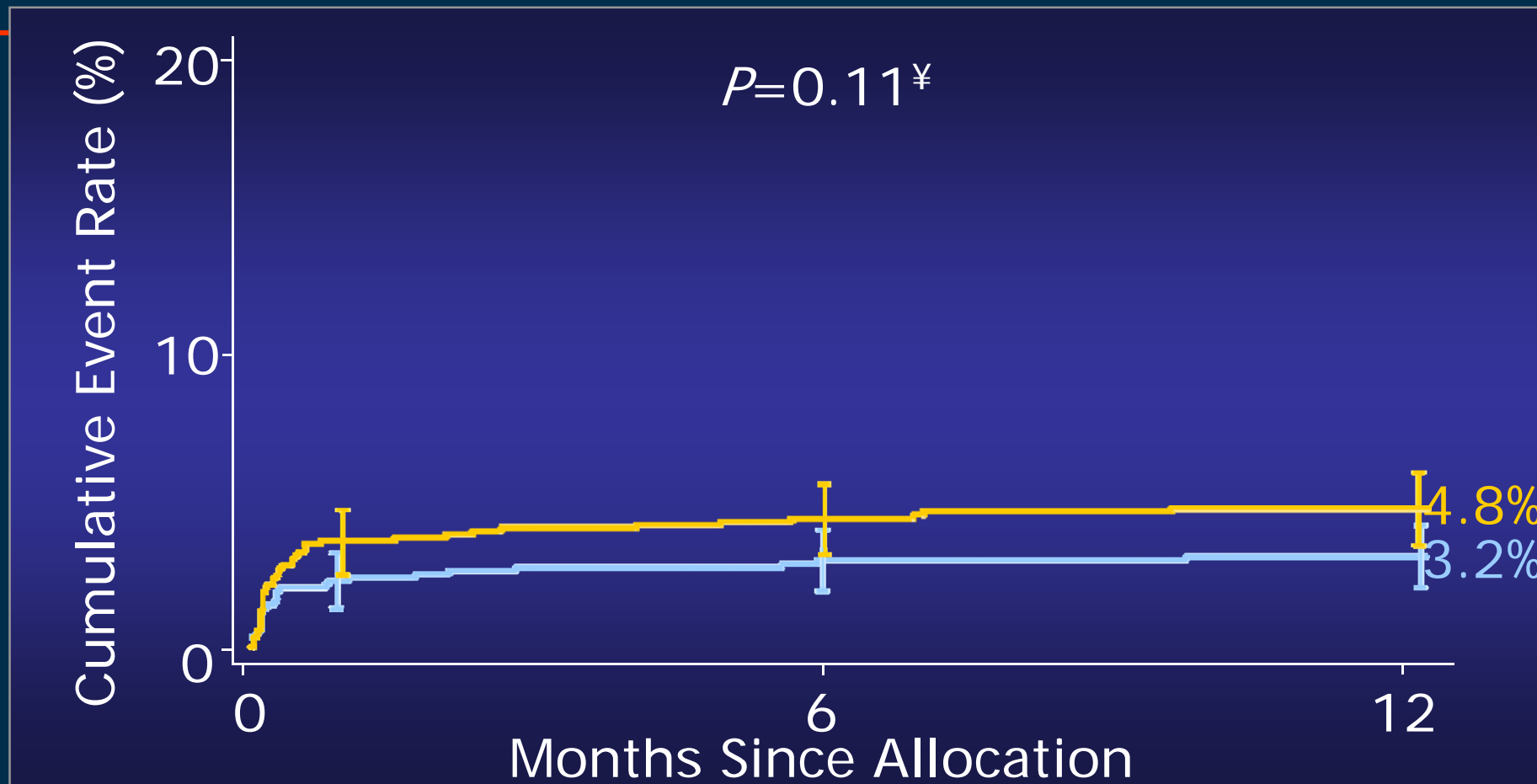


ITT; *Fisher Exact Test

SYNTAX - Myocardial Infarction to 12 Months

■ CABG (N=897)

■ TAXUS* (N=903)

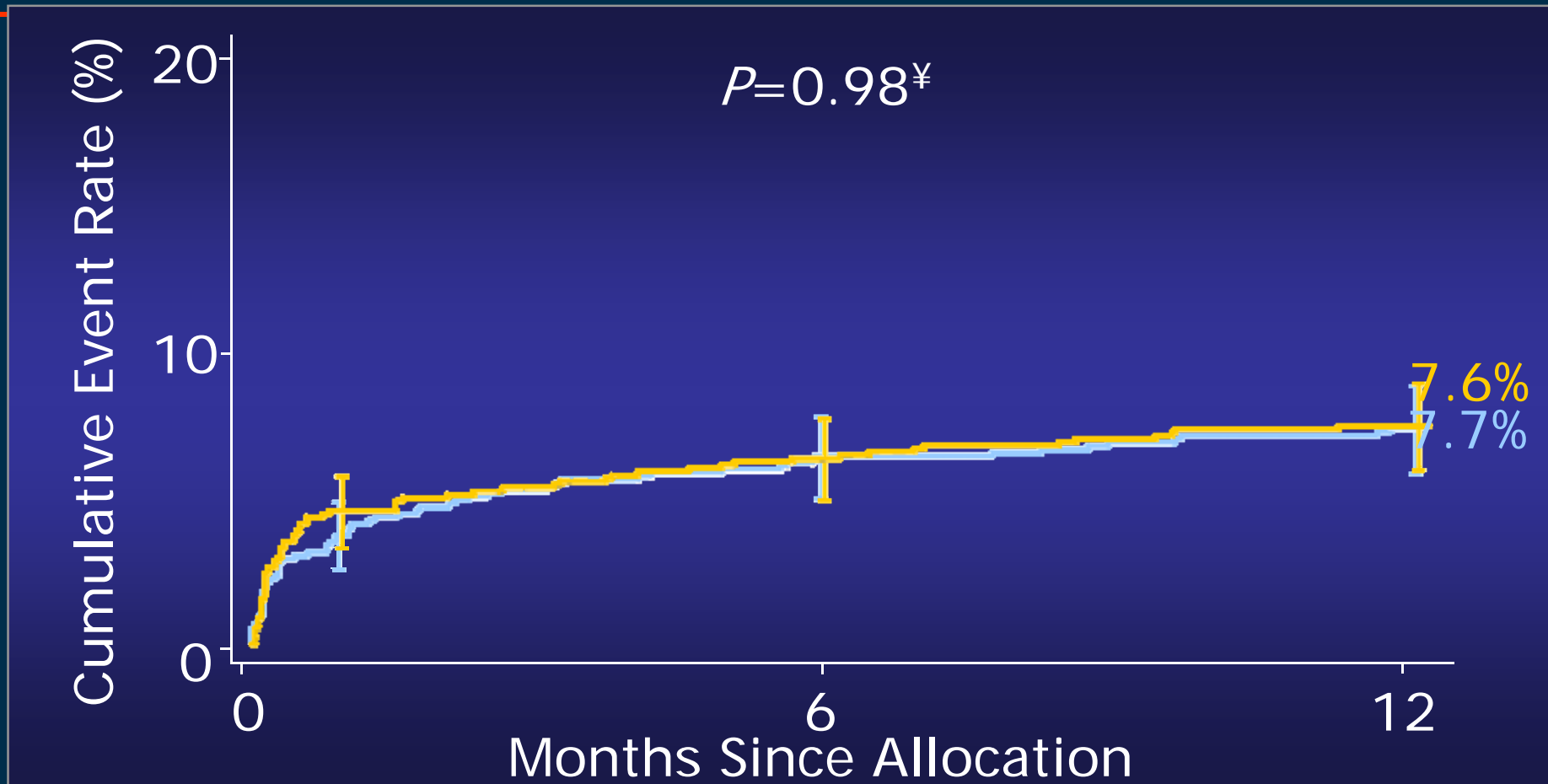


ITT; ¥Fisher Exact Test

SYNTAX - Death/CVA/MI to 12 Months

■ CABG (N=897)

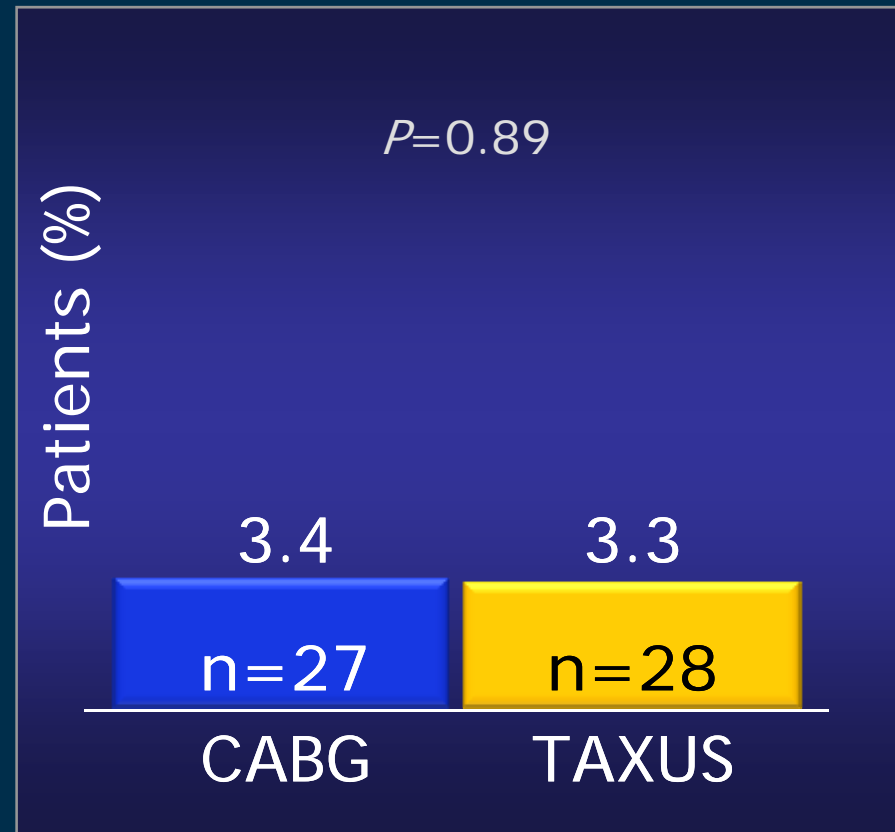
■ TAXUS* (N=903)



ITT; ¥Fisher Exact Test

SYNTAX - Symptomatic Graft Occlusion & Stent Thrombosis

■ CABG (N=897) ■ TAXUS* (N=903)

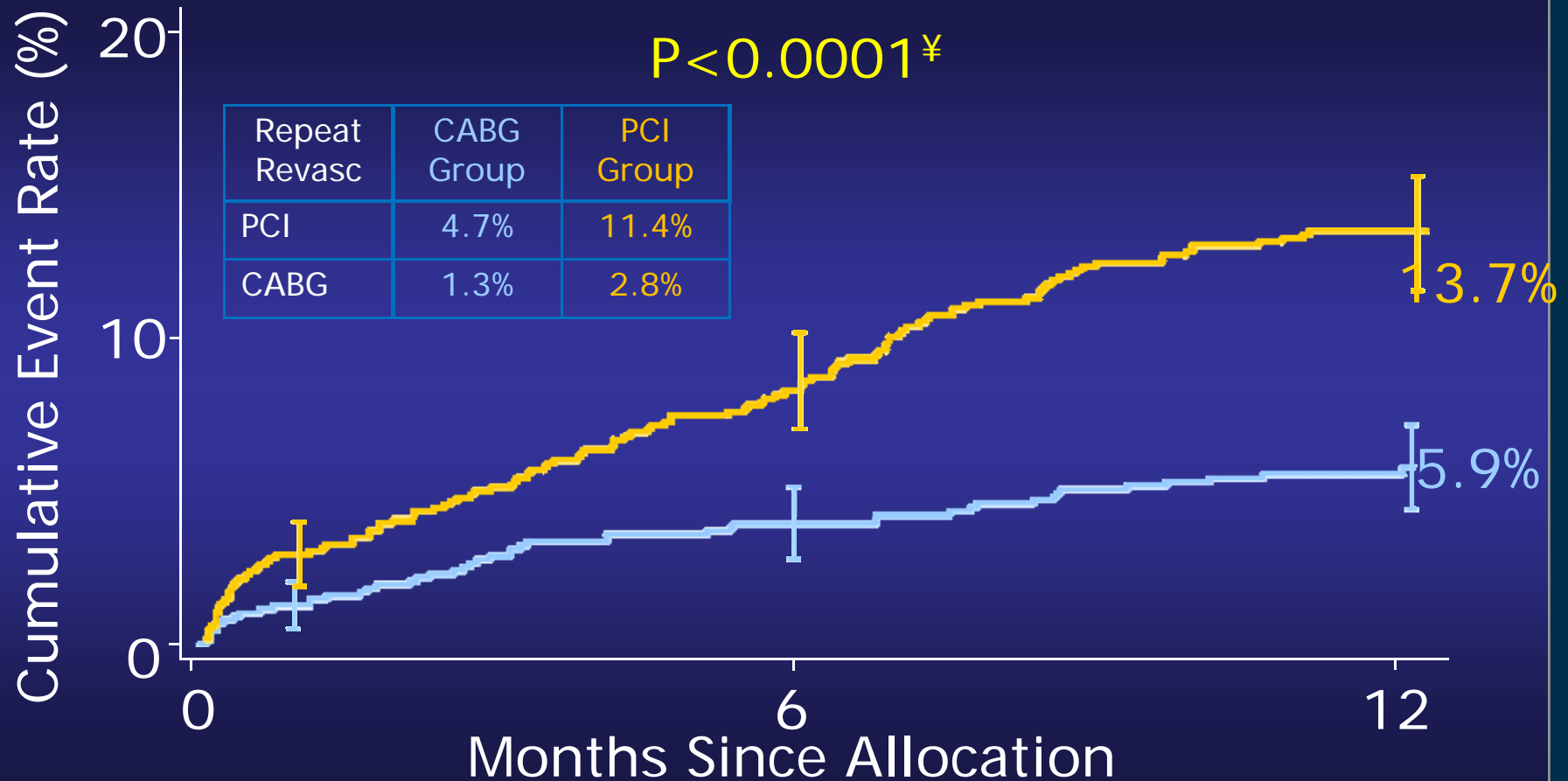


ITT population

SYNTAX - Repeat Revascularisation to 12 Months

■ CABG (N=897)

■ TAXUS* (N=903)

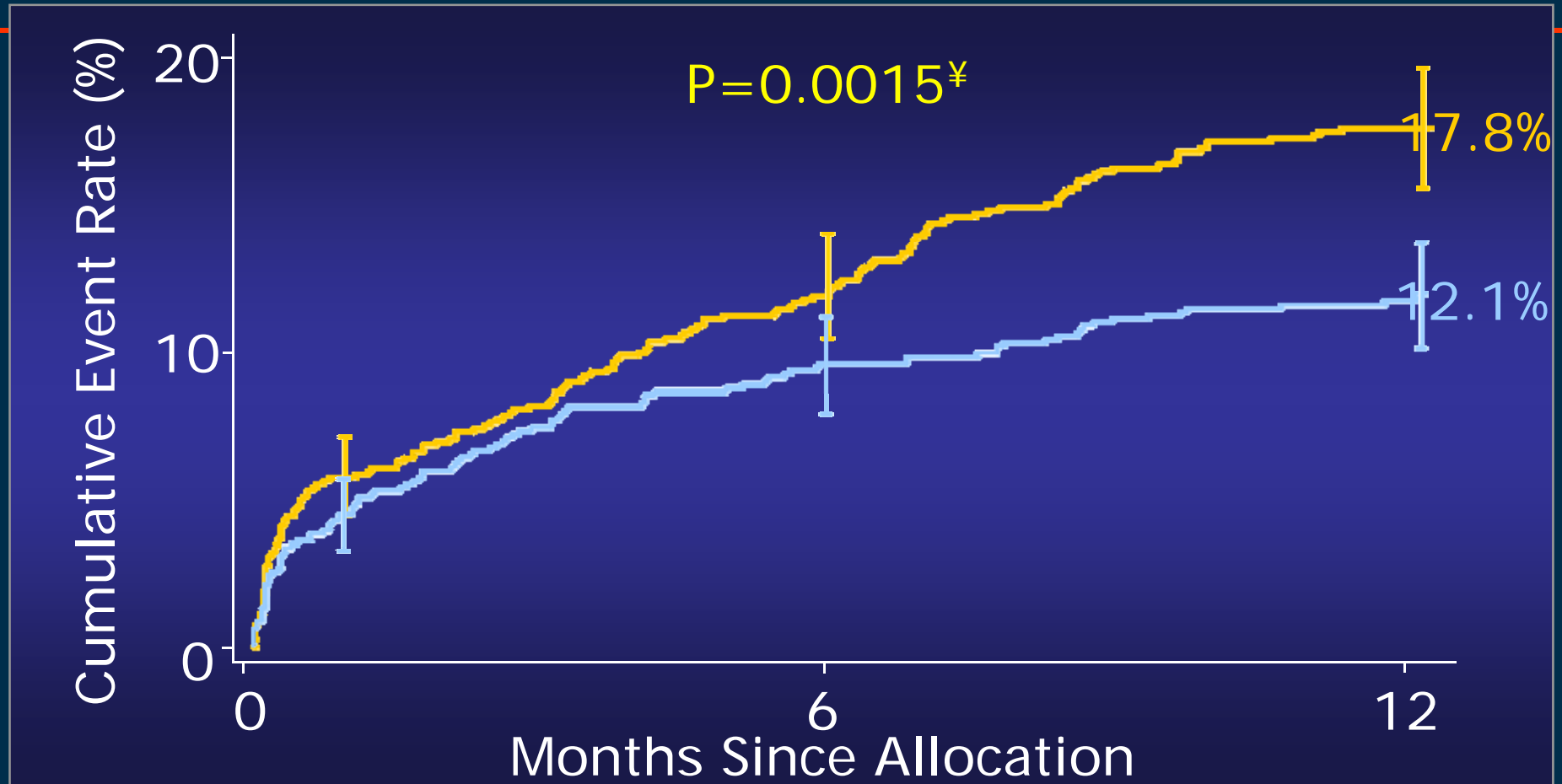


ITT; \ddagger Fisher Exact Test

SYNTAX - MACCE to 12 Months

■ CABG (N=897)

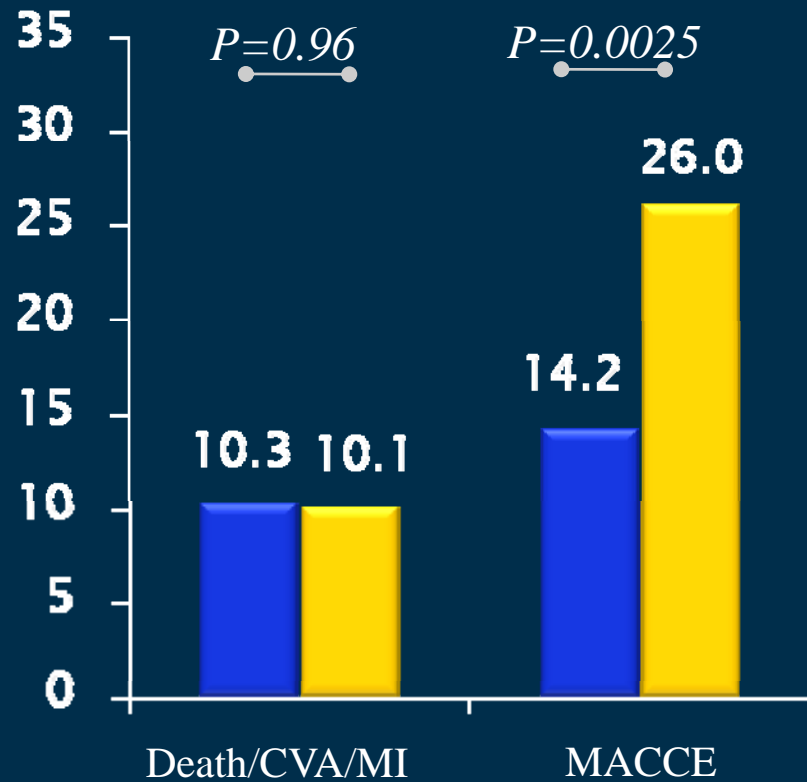
■ TAXUS* (N=903)



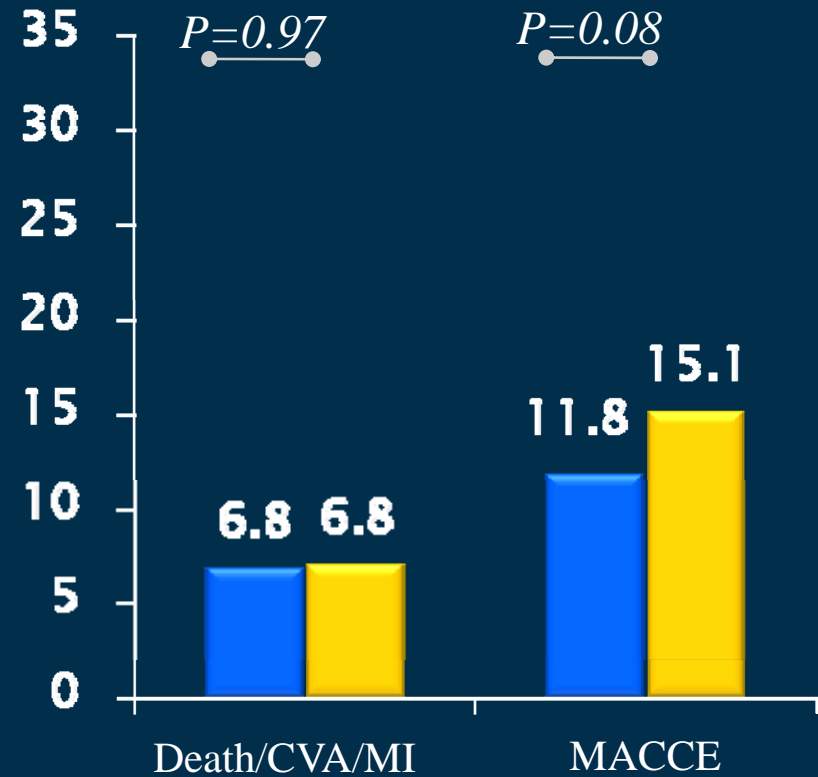
ITT; ¥Fisher Exact Test

SYNTAX - Outcome according to Diabetic Status

CABG TAXUS



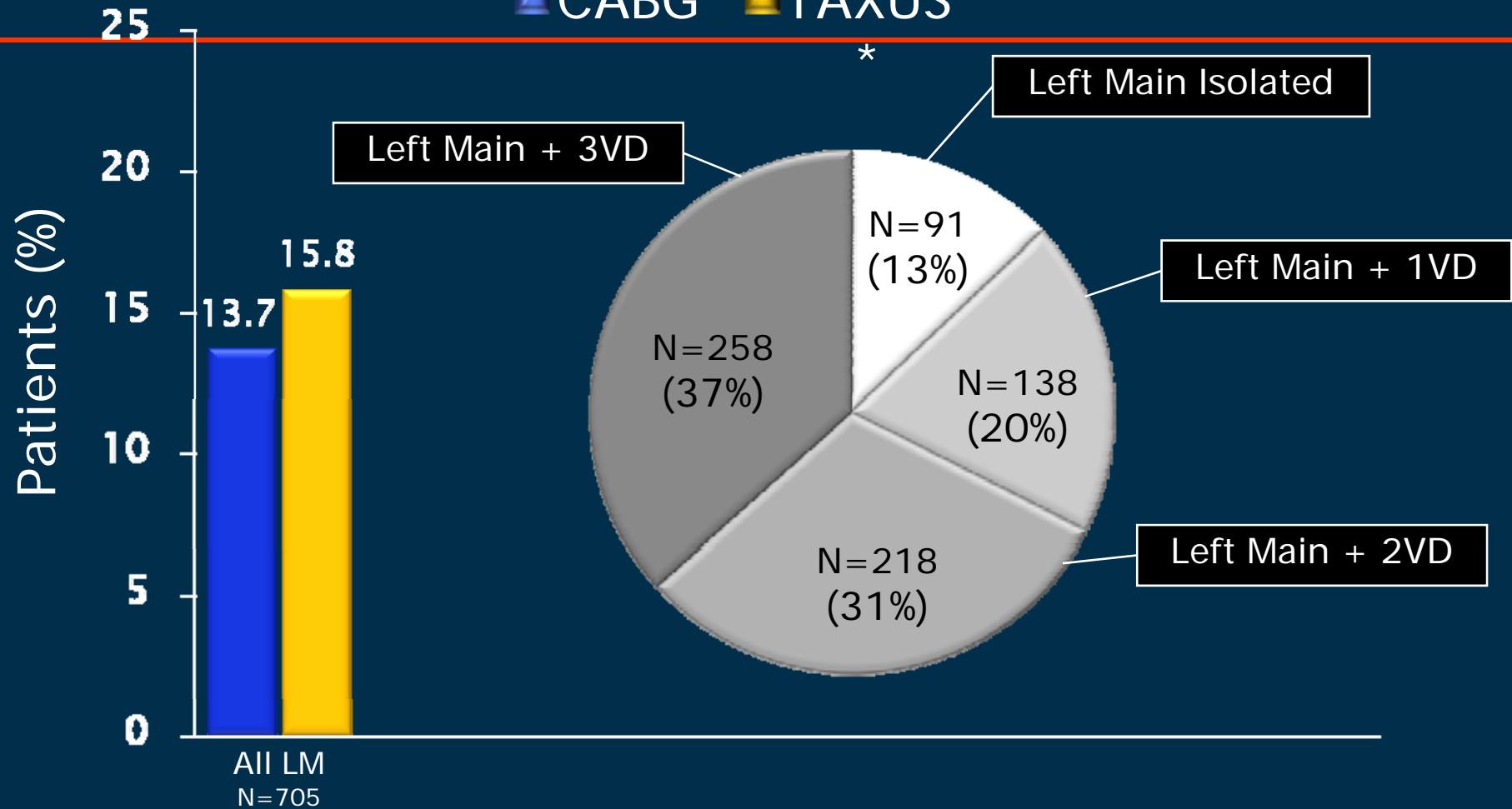
Diabetes (Medical Treatment)
N=452



Non-Diabetic
N=1348

SYNTAX - Left Main Subgroup MACCE Rates at 12 Months

CABG TAXUS



SYNTAX: Conclusions

Comparable safety outcomes for PCI and CABG

Stent thrombosis and graft occlusion rates similar

Higher rate of repeat revascularisation in the PCI group

Higher rate of CVA in the CABG group

SYNTAX: Translating results to clinical practice - Informed Consent

Doctor: This looks serious

Patient: What can we do about it ?

Doctor: First choice CABG

Patient: What is second choice ?

Doctor: Stenting: Less CVA, shorter stay but you are more likely to see me again

Patient: Lets go with stents then !!!

Revascularization Challenges in Stable Angina

Assess and investigate patients appropriately so that you can offer them the best evidenced based treatment for their coronary artery disease

When is Medical Therapy BEST ?

- *Chronic stable coronary syndromes*
 - ✓ *angina well controlled*
 - ✓ *without “critical” lesions*
 - ✓ *without markedly + stress tests*

When is Surgery BEST?

- *Acute and chronic stable coronary syndromes*
 - ✓ *high risk or overly complex lesions not well suited for PCI*
 - ✓ *recurrent PCI failures*

When is PCI BEST ?

- *Acute coronary syndromes*
 - ✓ *most patients unless anatomy unsuitable*
- *Chronic stable coronary syndromes*
 - ✓ *poorly controlled angina*
 - ✓ *“critical” lesions*
 - ✓ *markedly + stress tests*

