Left Main Clinical Trials

MAIN COMPARE Registry, AMC MAIN registry, SYNTAX LM, Pre-COMBAT, Pre-COMBAT-2, and IRIS-MAIN

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Professor of Medicine, University of Ulsan,
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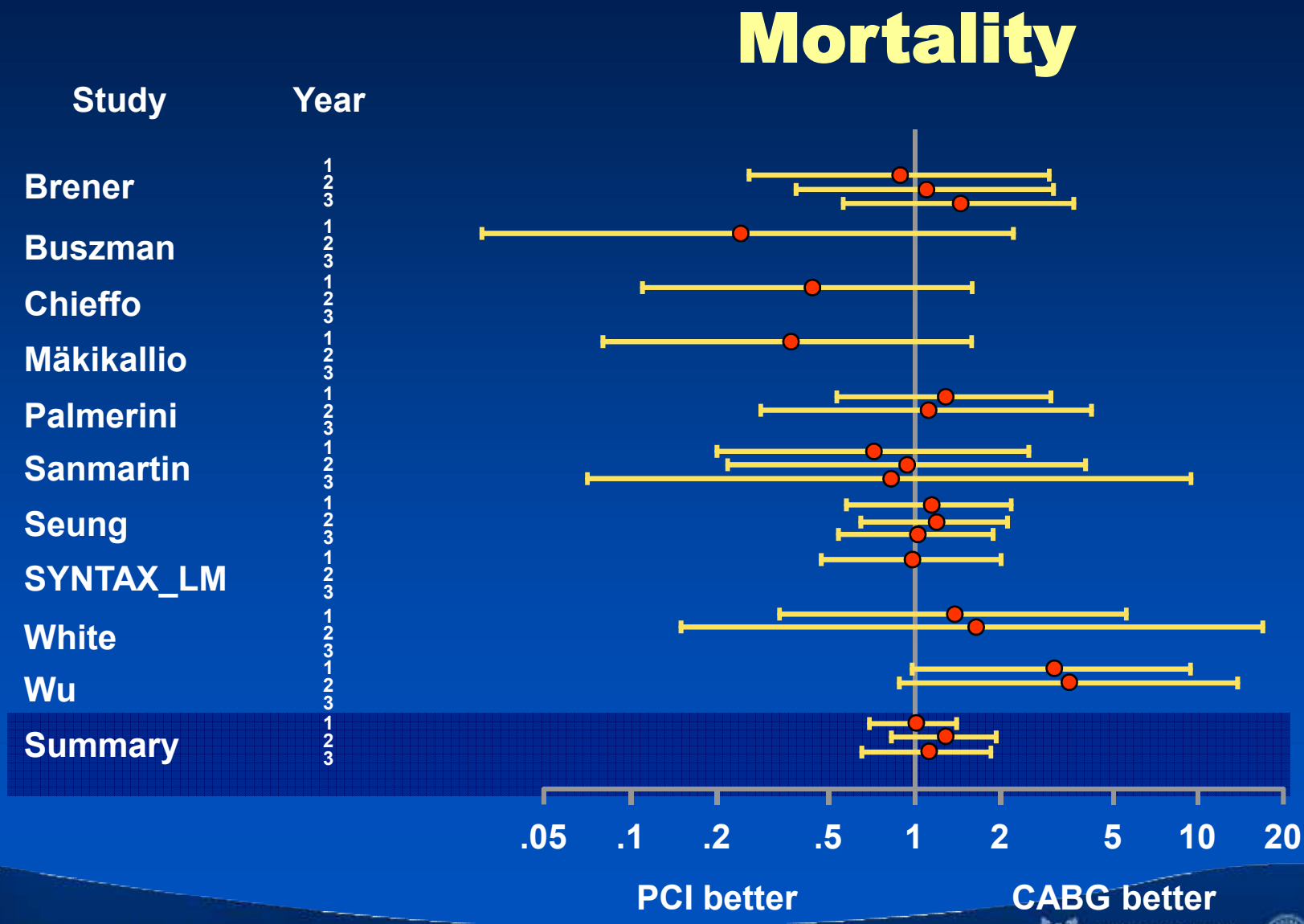
Unprotected LMCA - PCI vs CABG

Meta-analysis of 3,773 patients in 10 studies (CABG: 2,114 patients, PCI: 1,659 patients)



Naik H et al: J Am Coll Cardiol Intv 2:739-47, 2009

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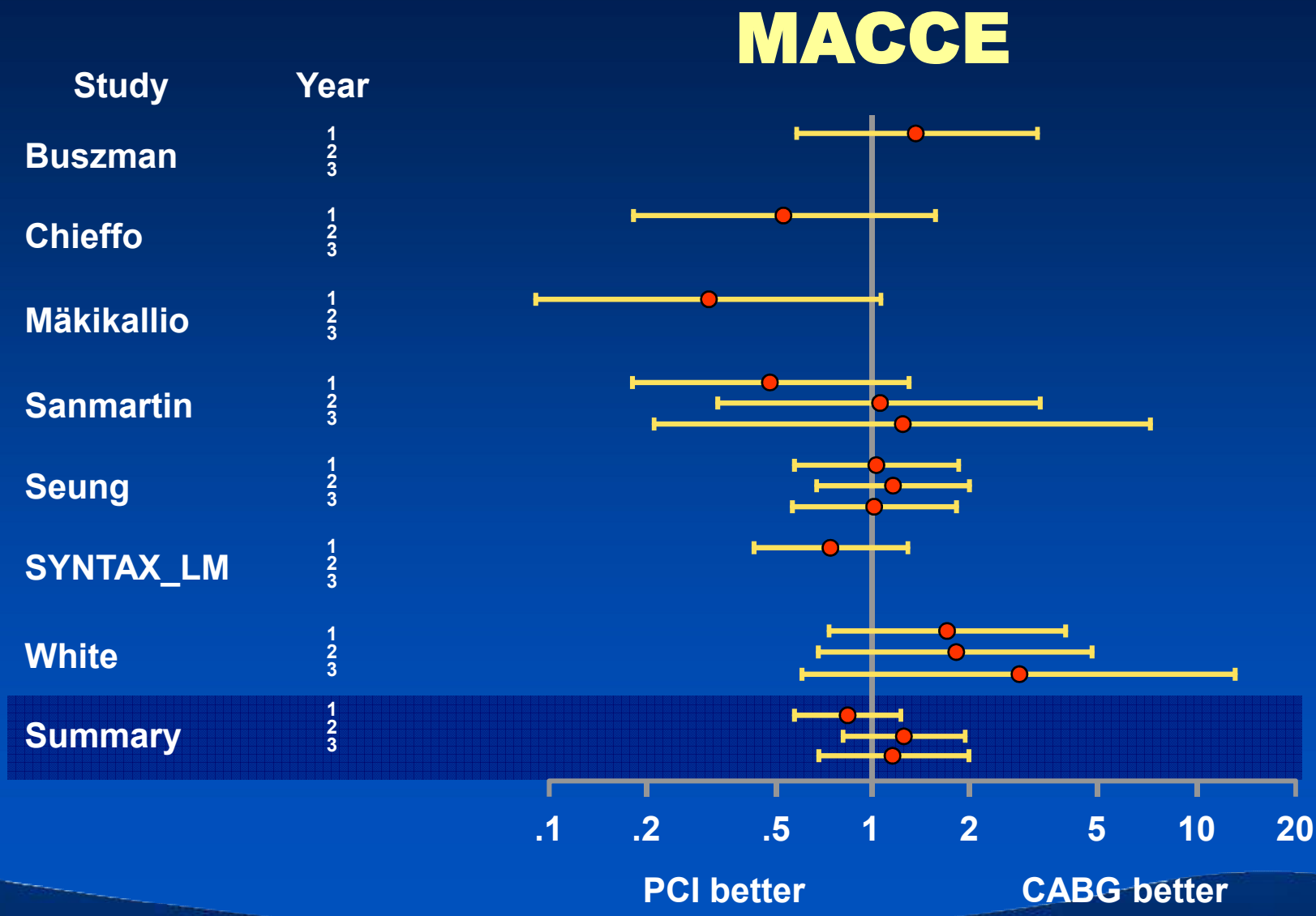

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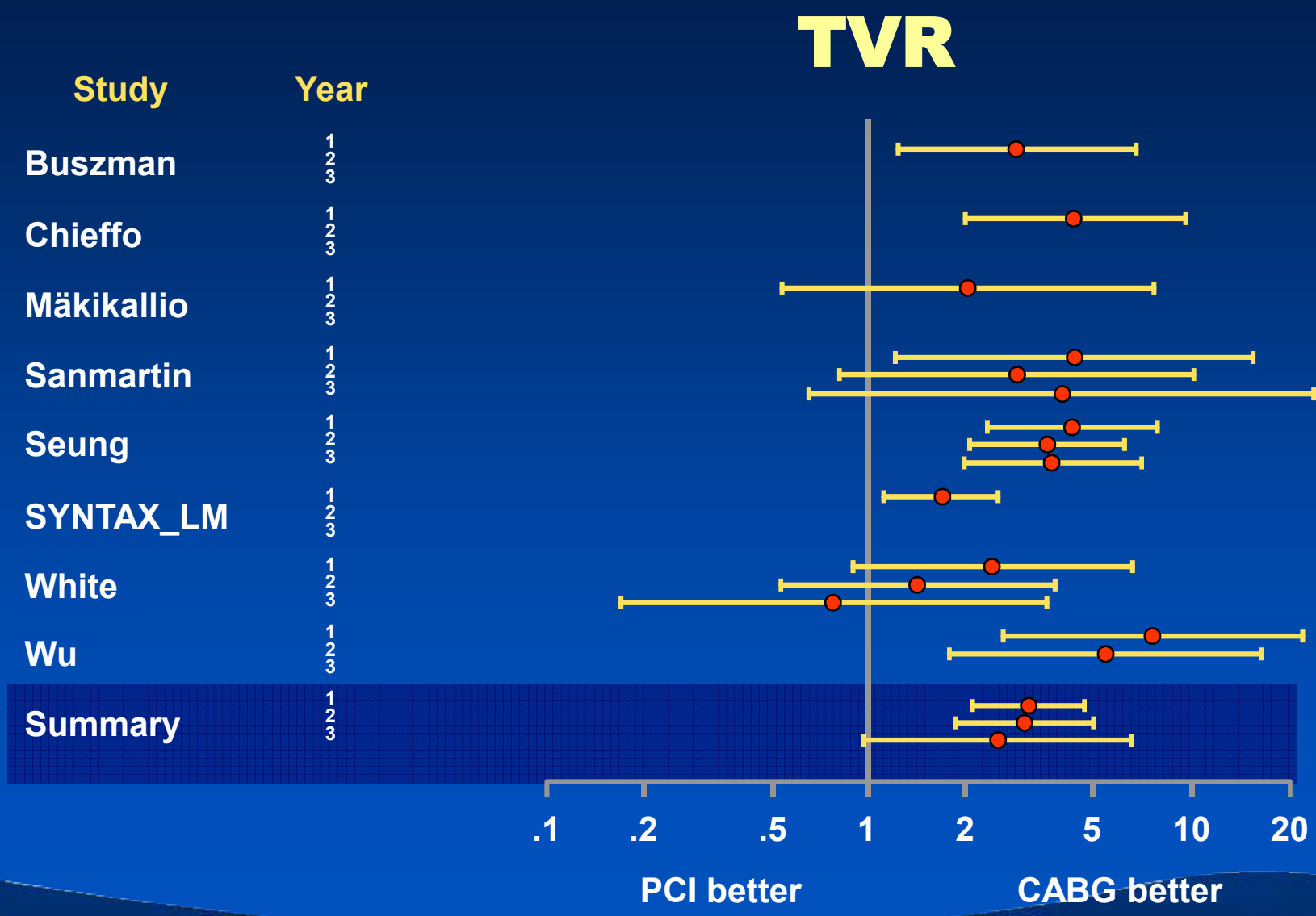


Naik H et al: J Am Coll Cardiol Intv 2:739-47, 2009

MAIN COMPARE
Registry

STENT vs **CABG** follow-up at 3 year

The MAIN-COMPARE Study
Crucial Points

- Total 2,240 patients with either PCI or CABG were included
- 97% of 1,102 patients suitable for either PCI or CABG
- DES used in 71%
- Propensity matched patients
- Central adjudication of events

Seung KB, Park DW, Park SJ, NEJM 2008;358:1781-92

MAIN COMPARE registry

Wave 1 (BMS)

LM disease treated with BMS (n=318) and CABG (n=448)

Wave 2 (DES)

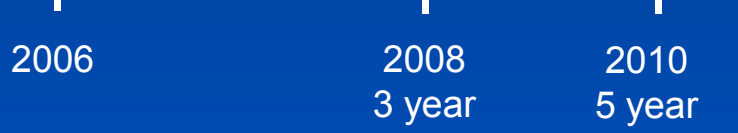
LM disease treated with DES (n=784) and CABG (n=690)

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

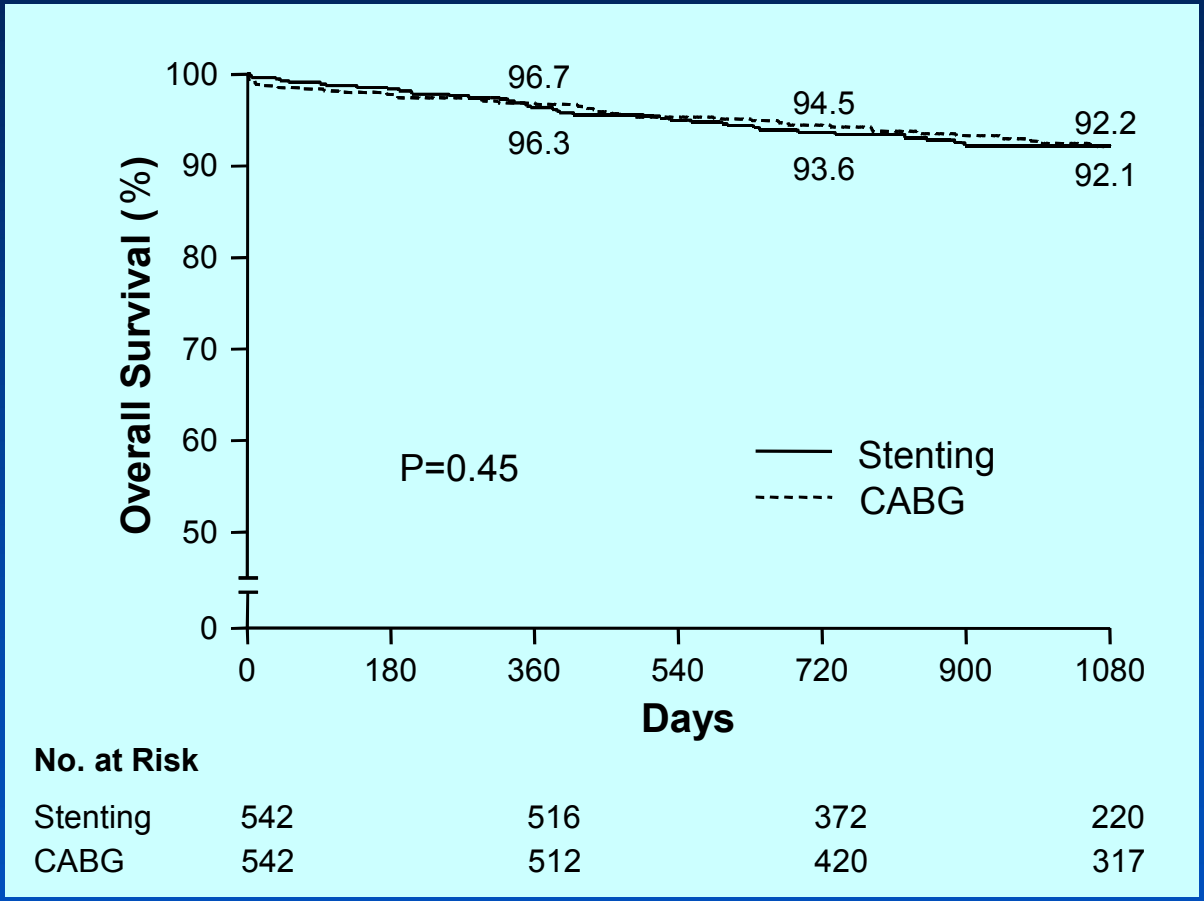
After Propensity-Matching

Overall matched cohort (n=542 pairs)

PCI vs CABG

Death

(Overall PCI and CABG matched cohort: 542 pairs)



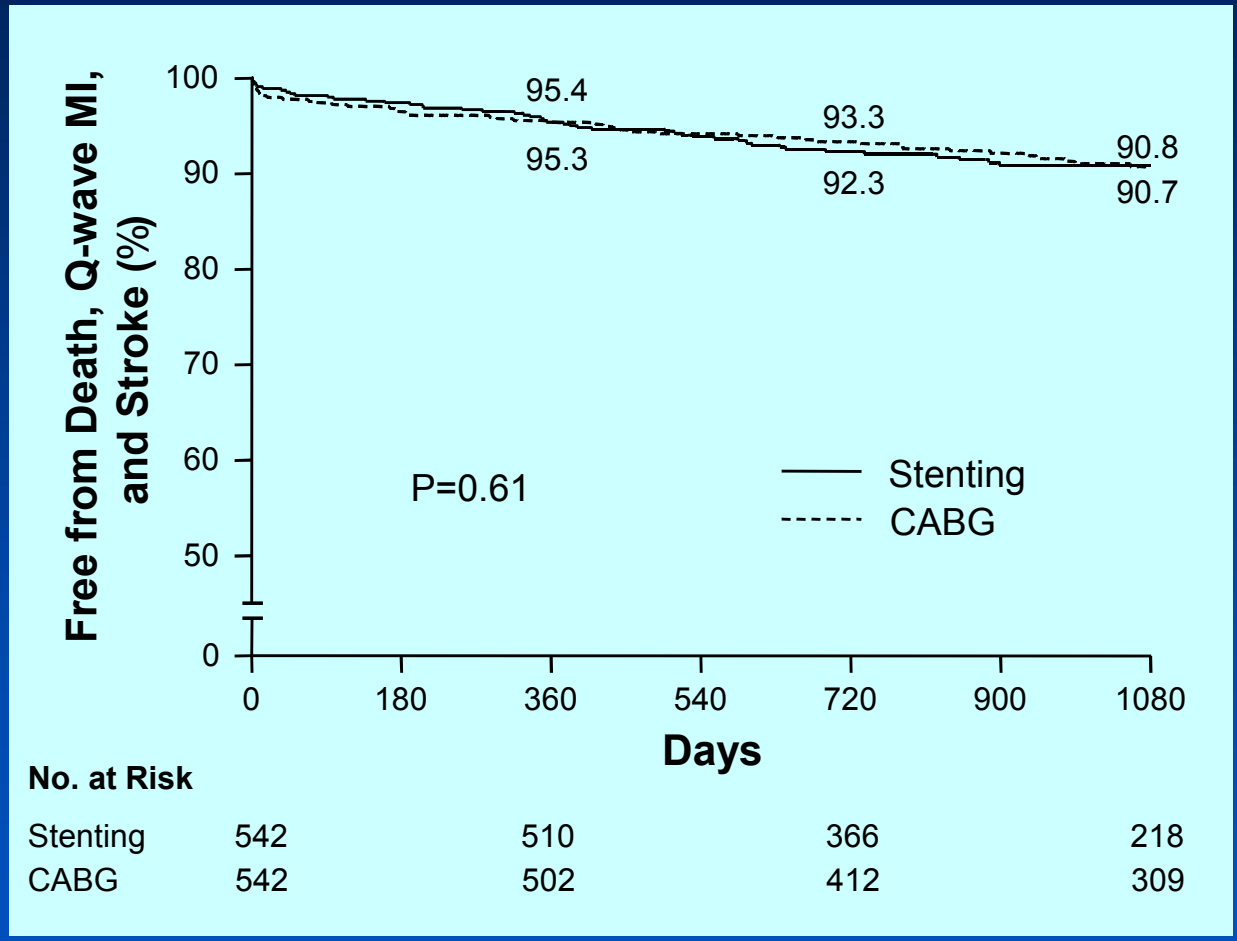
No. at Risk

Stenting	542	516	372	220
CABG	542	512	420	317

Seung KB, Park DW, Park SJ, NEJM 2008;358:1781-92

Death, Q-MI, or Stroke

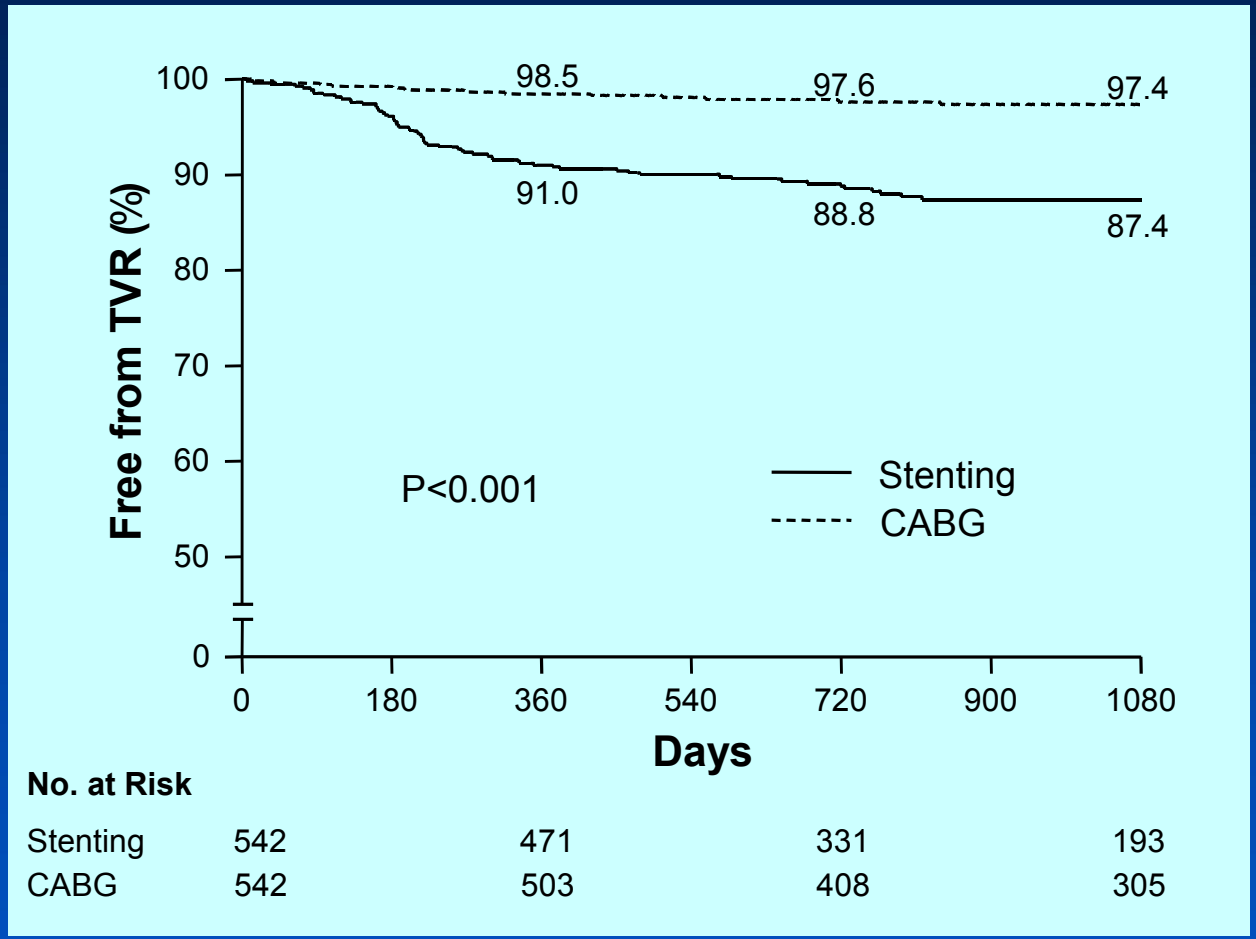
(Overall PCI and CABG matched cohort: 542 pairs)



Seung KB, Park DW, Park SJ, NEJM 2008;358:1781-92

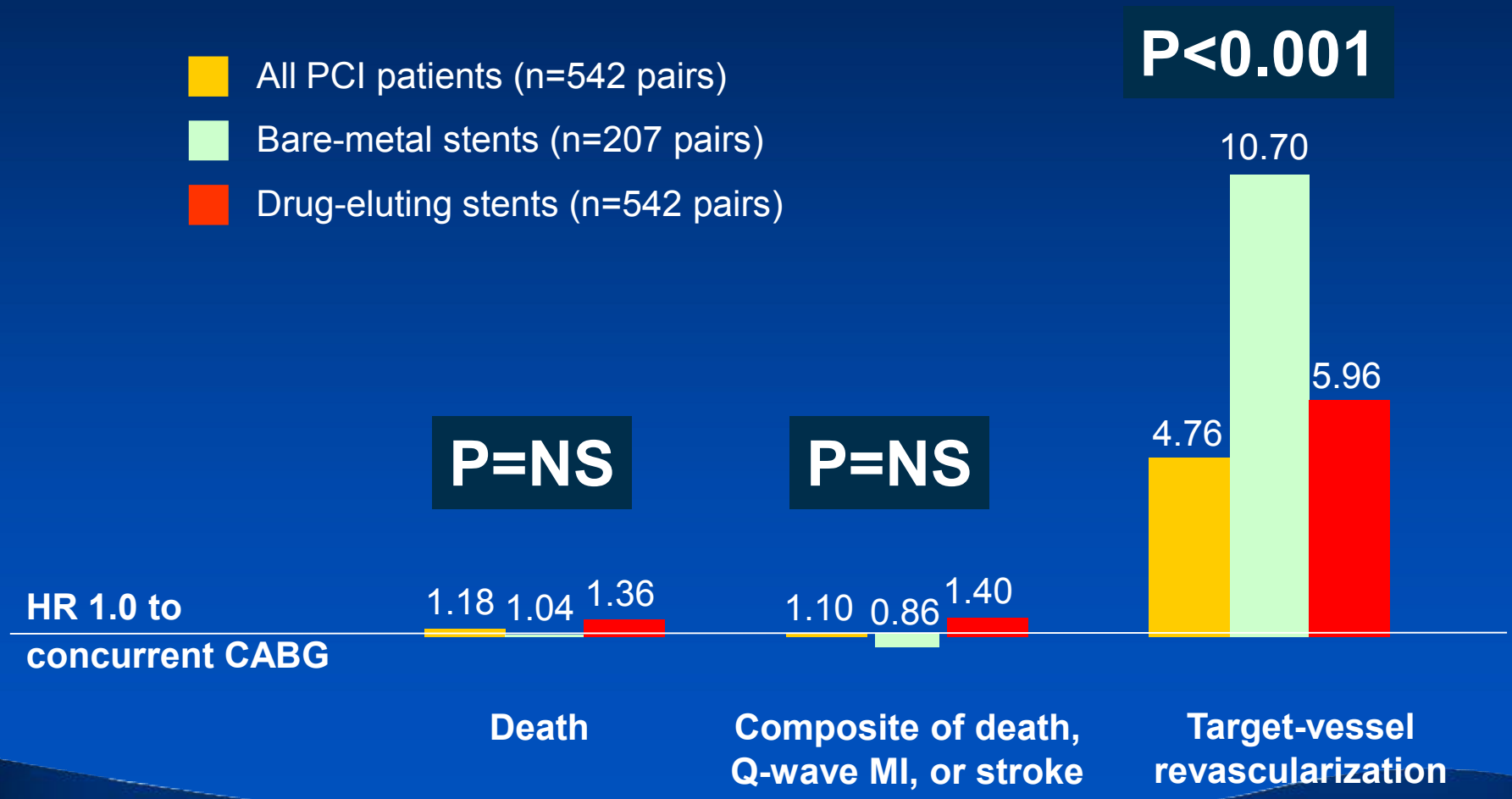
Target-vessel revascularization

(Overall PCI and CABG matched cohort: 542 pairs)



Seung KB, Park DW, Park SJ, NEJM 2008;358:1781-92

Hazard Ratios for Clinical Outcomes
: Median 3-Year Outcomes



Key Subgroup Analysis in **MAIN-COMPARE Registry**

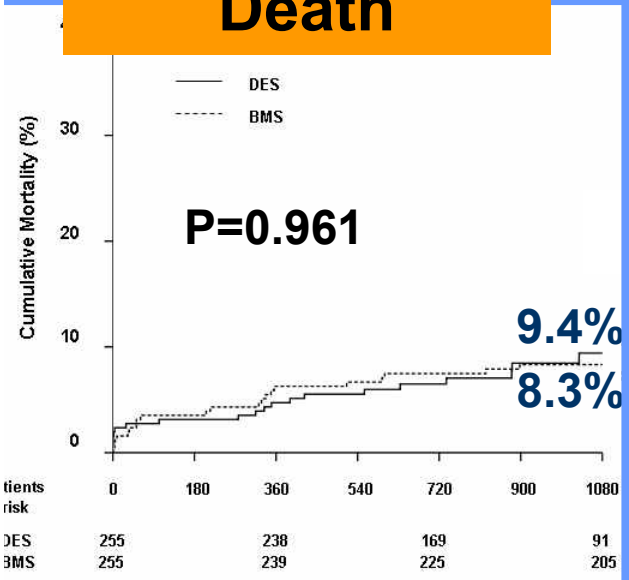
- BMS vs. DES
- IVUS guided vs. Angio-guided
- Cypher vs. TAXUS
- Non-distal vs. Distal
- 1 stent vs. 2 stents for distal LM
- Isolated LM disease
- Impact of disease extent
- Impact of DM
- Predictor analysis

BMS vs. DES

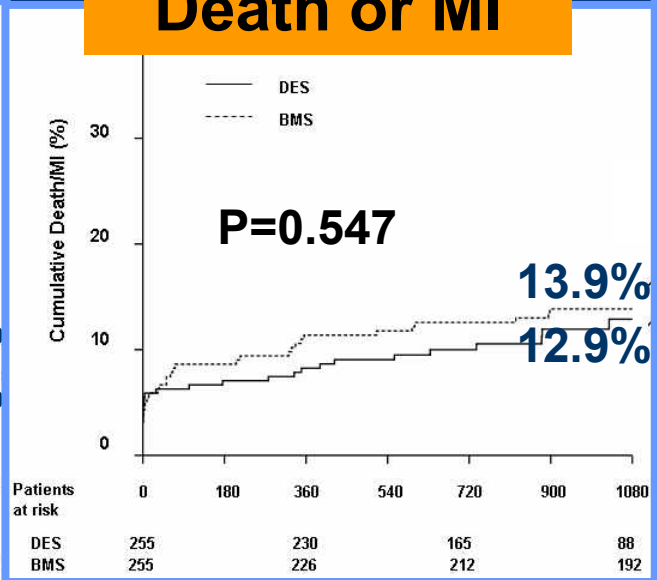
255 Propensity Matched-Pairs

Clinical Outcomes at 3 year F/U

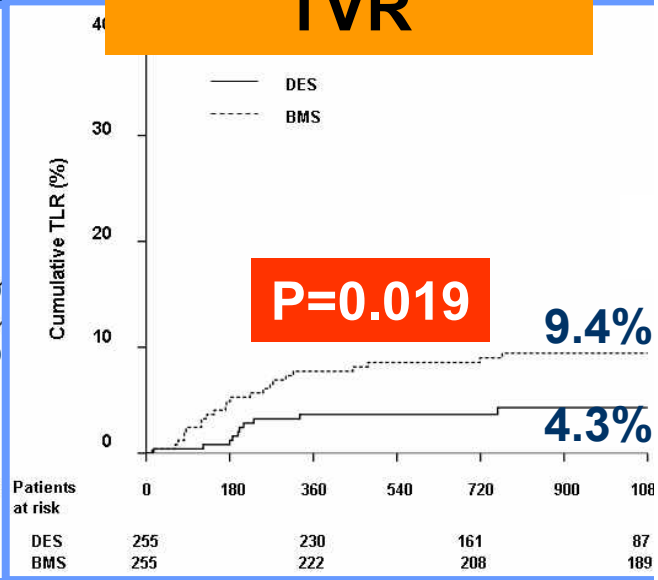
Death



Death or MI



TVR

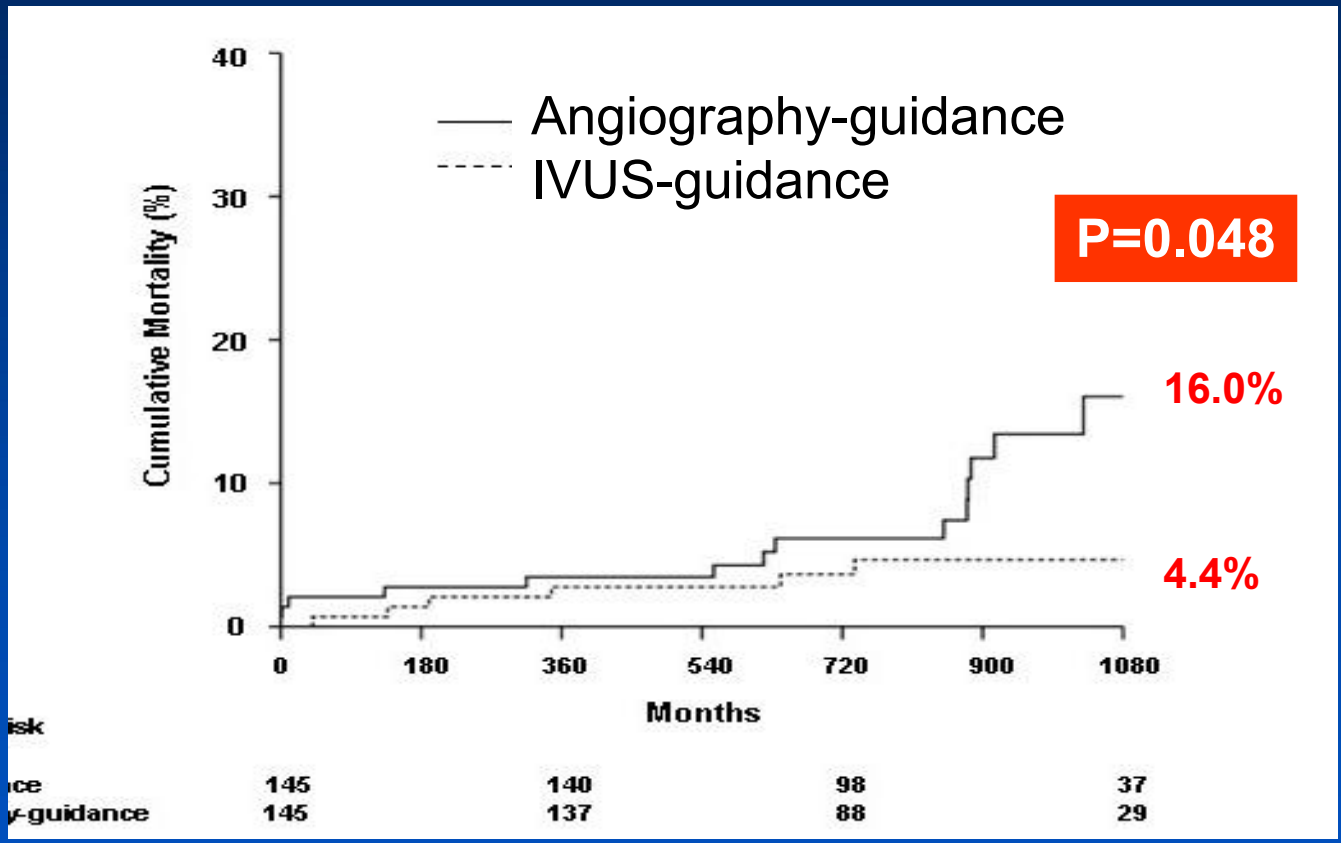


Kim YH, Park SJ, et al. Circulation 2009

IVUS guided in DES

201 Propensity Matched-Pairs

All cause Mortality at 3 year F/U



Park SJ et al, Circulation Cardiovasc Intervent 2009

Cypher vs. TAXUS

Crude and Adjusted HRs of Clinical Outcomes According to DES Type

	Crude		Multivariable adjusted†		Adjusted for propensity	
Outcome	Hazard Ratio (95% CI)	*P*	Hazard Ratio (95% CI)	*P*	Hazard Ratio (95% CI)	*P*
Death	0.88 (0.49-1.56)	0.66	0.92 (0.47-1.80)	0.82	0.93 (0.50-1.71)	0.81
MI	0.95 (0.54-1.70)	0.87	0.80 (0.43-1.48)	0.47	0.87 (0.48-1.59)	0.66
TVR	1.27 (0.64-2.51)	0.49	1.10 (0.53-2.29)	0.81	1.11 (0.55-2.26)	0.77
Death, MI, or TVR	1.02 (0.71-1.49)	0.90	0.95 (0.64-1.41)	0.79	0.99 (0.67-1.46)	0.95

*HR for cypher with reference to taxus.

Lee JY, Park SJ, et al. JACC 2009

Non-distal vs. Distal LM

Crude and Multivariable-Adjusted Cox Regression Analysis ;

Non-Distal lesions :

DES (N=363) vs. CABG (N=355)

Distal Bifurcation lesions :

DES (N=467) vs. CABG (N=566)

Hazard Ratios of Clinical outcomes
DES in Non-Distal Lesions

Outcome	Crude		Multivariable adjusted	
	Hazard Ratio (95% CI)	P	Hazard Ratio (95% CI)	P
Death	0.97 (0.59-1.59)	0.90	1.001 (0.50-1.99)	0.99
Stroke	2.0 (0.61-6.67)	0.25	1.42 (0.37-5.45)	0.61
TVR	3.83(1.43-10.25)	0.004	**7.71 (1.78-33.38)**	**0.006**
Death, Q-MI, or Stroke	0.97 (0.61-1.55)	0.90	1.06 (0.57-1.99)	0.852
Death, Q-MI, Stroke, or TVR	1.23 (0.82-1.85)	0.31	1.51 (0.91-2.49)	0.111

*HR for stents with reference to CABG.

Hazard Ratios of Clinical outcomes
DES in Distal Bifurcation Lesions

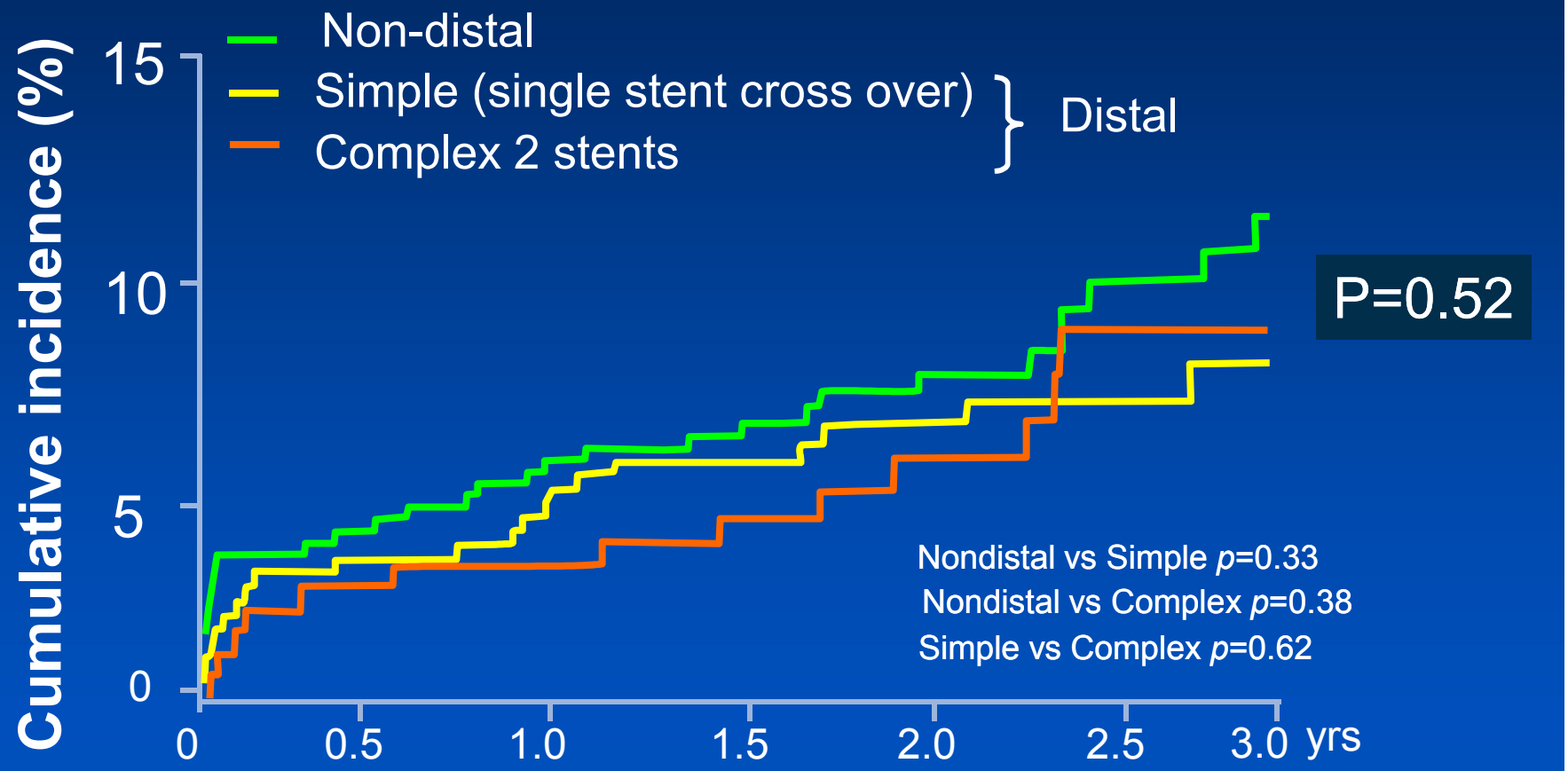
Outcome	Multivariable adjusted	
	Hazard Ratio (95% CI)	P
Death	0.66 (0.35-1.26)	0.21
Stroke	0.72 (0.23-2.23)	0.57
TVR	**6.23 (3.12-12.44)**	**<0.001**
Death, Q-MI, or Stroke	0.95 (0.56-1.82)	0.62
Death, Q-MI, Stroke, or TVR	**1.42 (1.02-1.97)**	**0.04**

*HR for stents with reference to CABG.

1 stent *vs* 2 stents

For Distal LM disease

Death
at 3 year F/U



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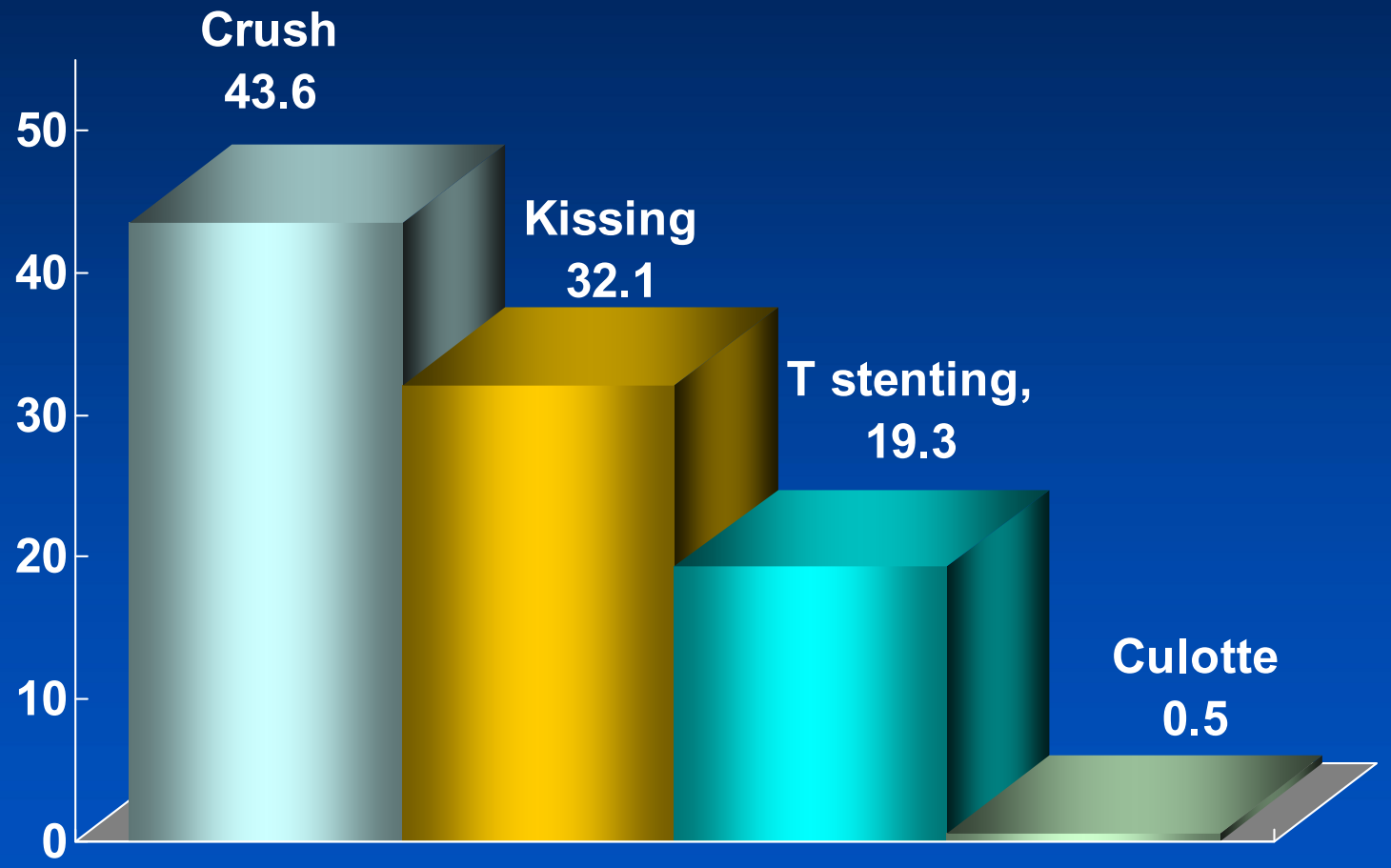
Data from MAIN COMPARE Registry 2009

2 Stenting Techniques

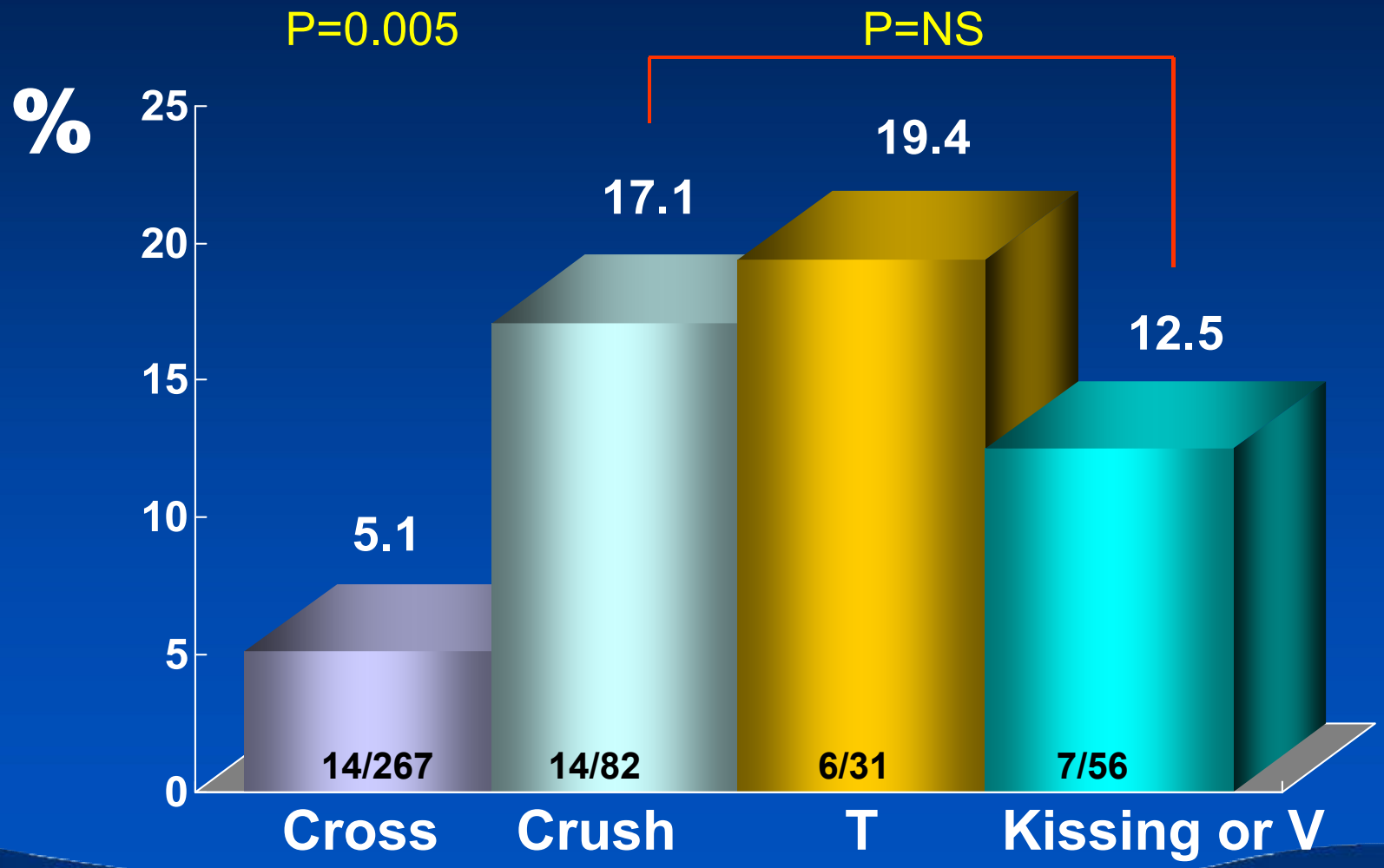
for LM bifurcation (DES, N=503 patients)



Data from MAIN COMPARE Registry

TLR at 4 year

According to LM Bifurcation Stenting Technique



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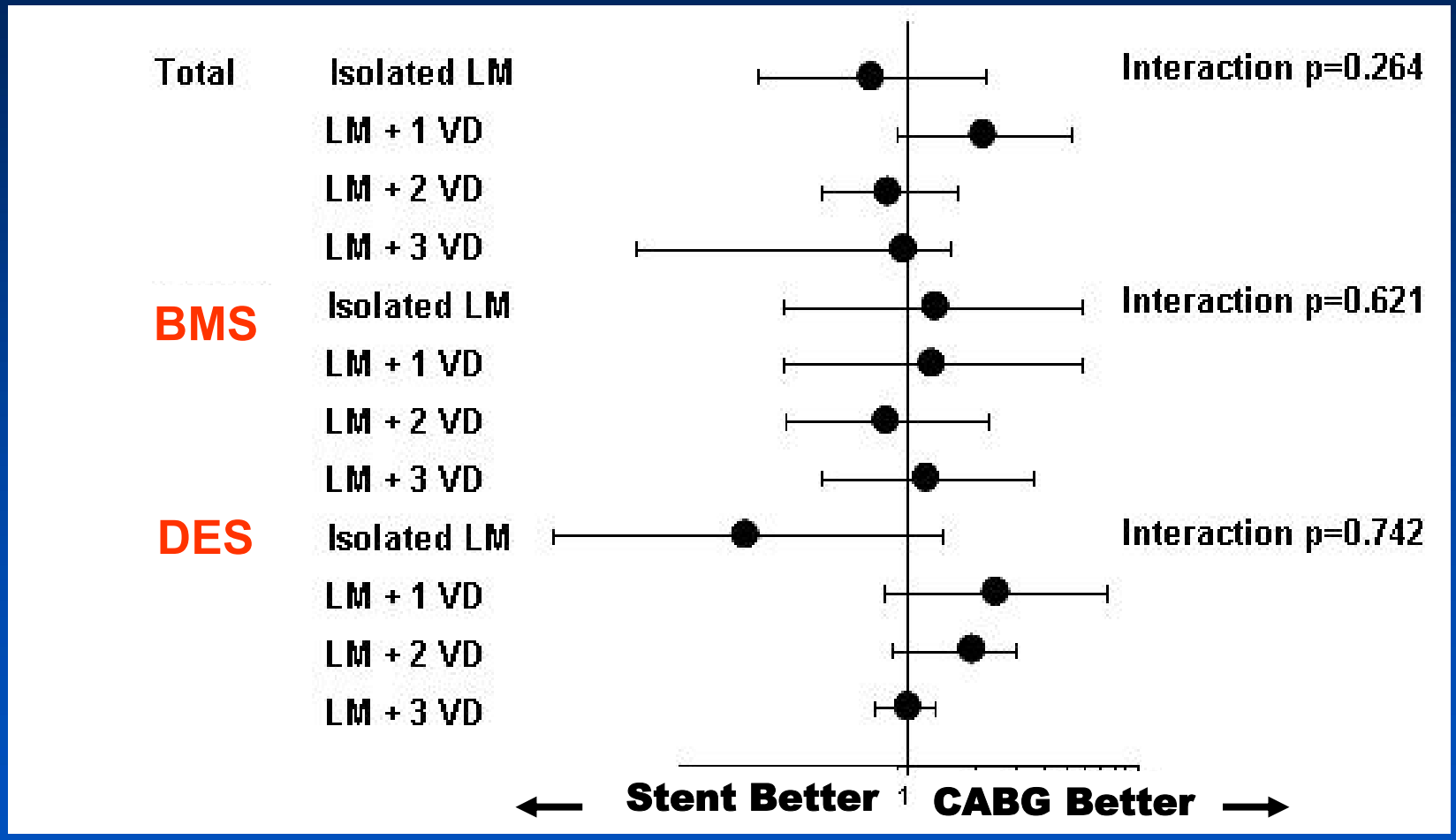
Data from MAIN COMPARE Registry

Impact of Disease Extents

Kim YH, Park SJ, et al. JACC 2009

Adjusted HR:
Treatment effect of Stents to CABG

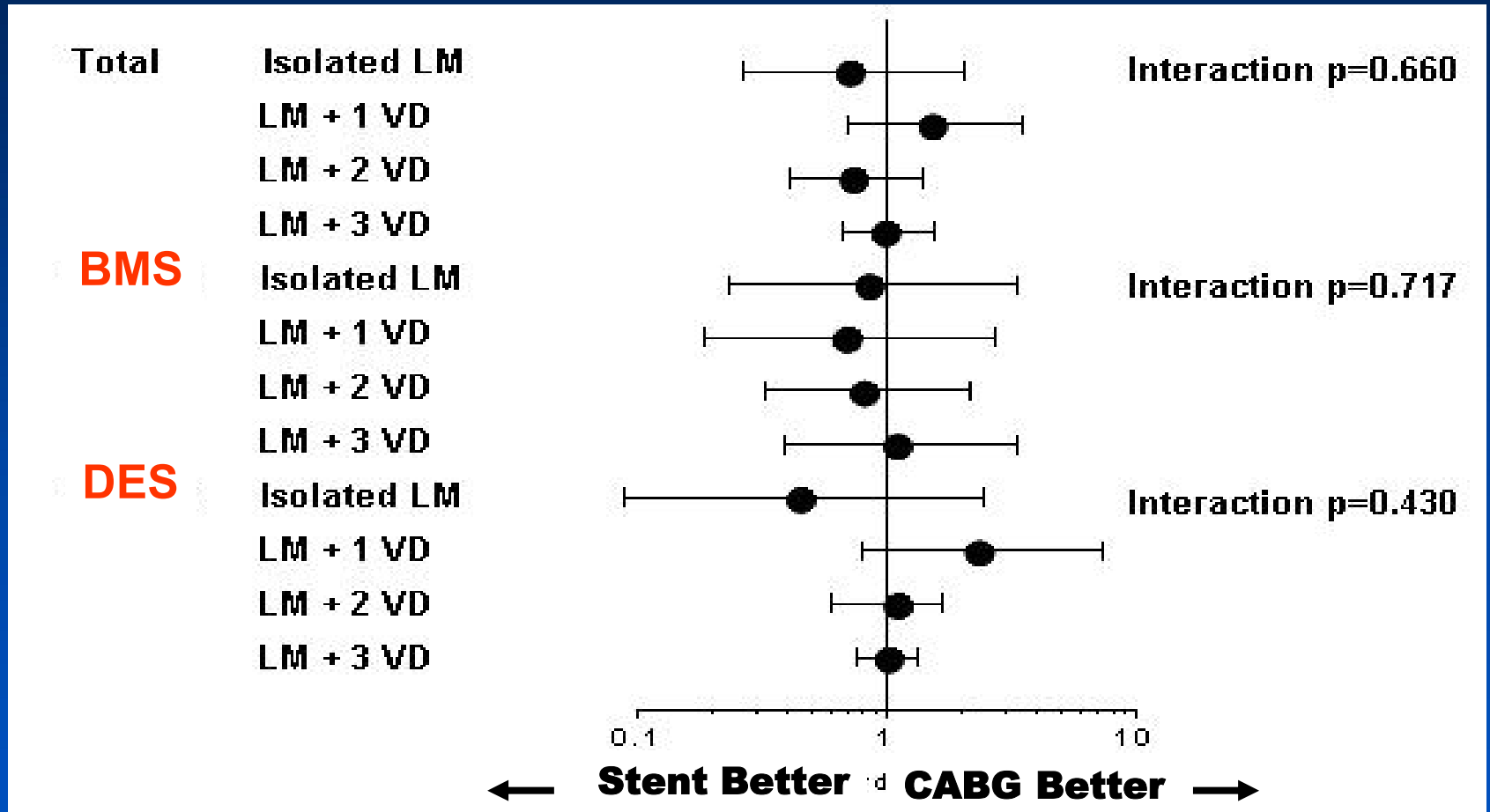
Death



Kim YH, Park SJ, et al. JACC 2009

Adjusted HR:
Treatment effect of Stents to CABG

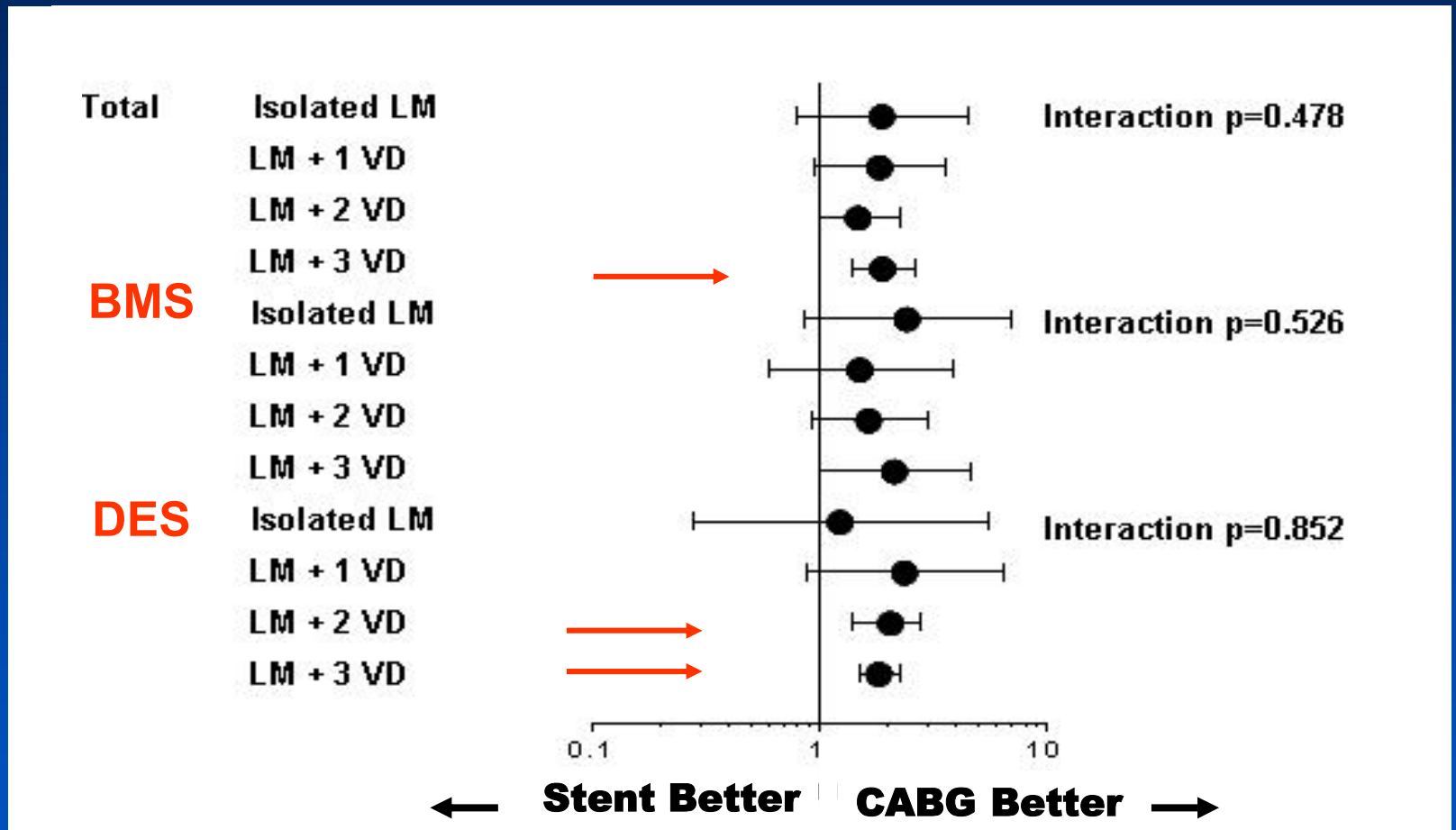
Death, Q-MI, or Stroke



Kim YH, Park SJ, et al. JACC 2009

Adjusted HR:
Treatment effect of Stents to CABG

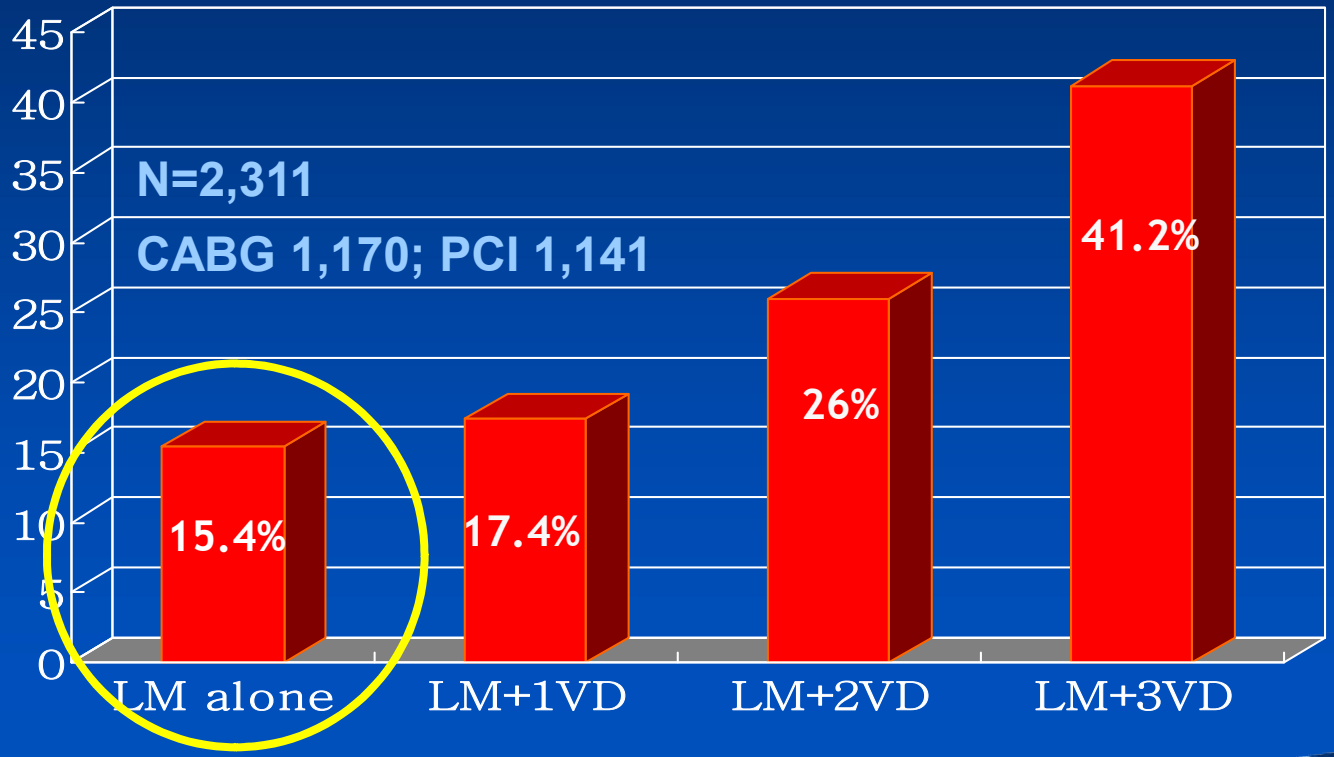
Death, QMI, Stroke, or TVR



Kim YH, Park SJ, et al. JACC 2009

Isolated
Left Main Stenosis

Supportive data from MAIN COMPARE registry about **Isolated LM disease**

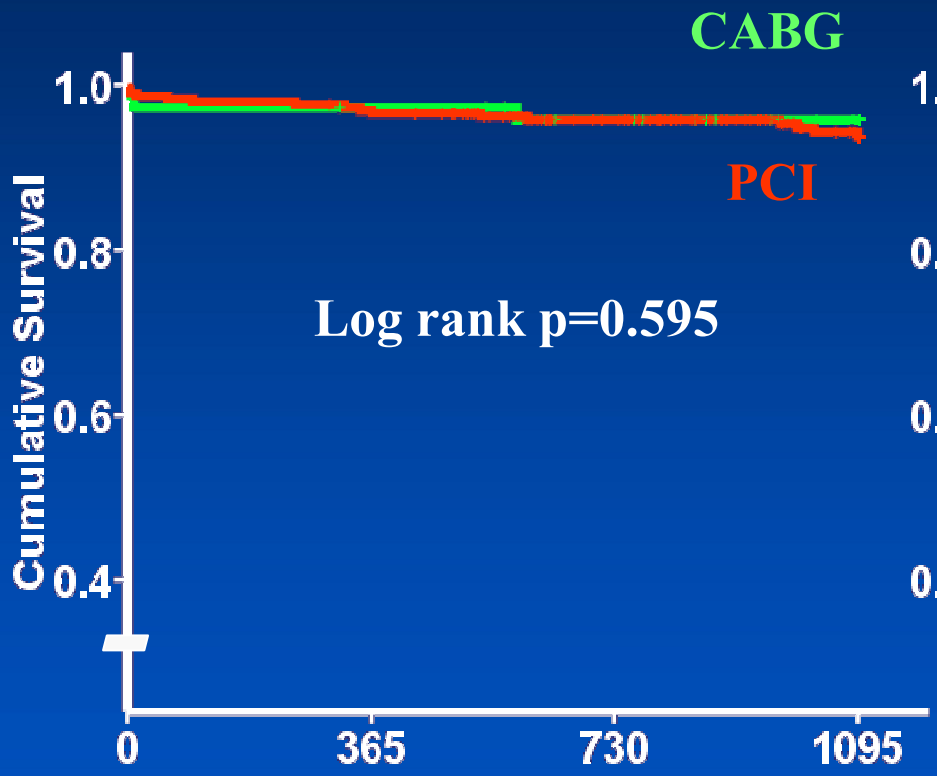


LM Involved Site

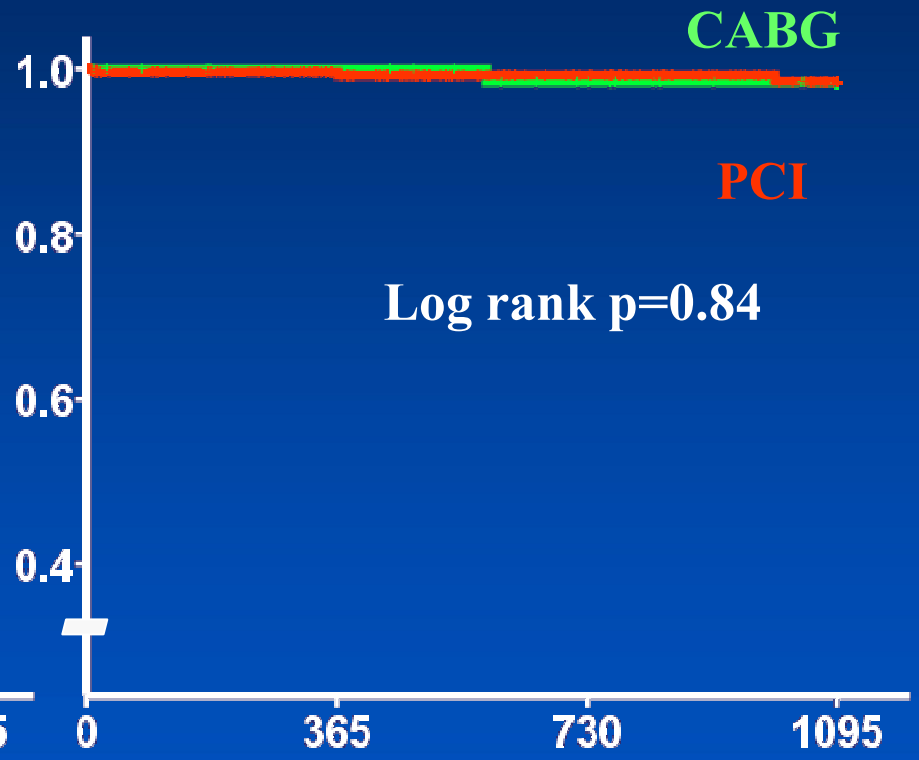
	CABG (n=73)	PCI (n=291)
Ostium	18 (25.7%)	122 (41.9%)
Shaft	27 (38.6%)	103 (35.4%)
Bifurcation	25 (35.7%)	63 (21.6%)

Clinical Outcomes in Isolated LM disease at 3 years

Death

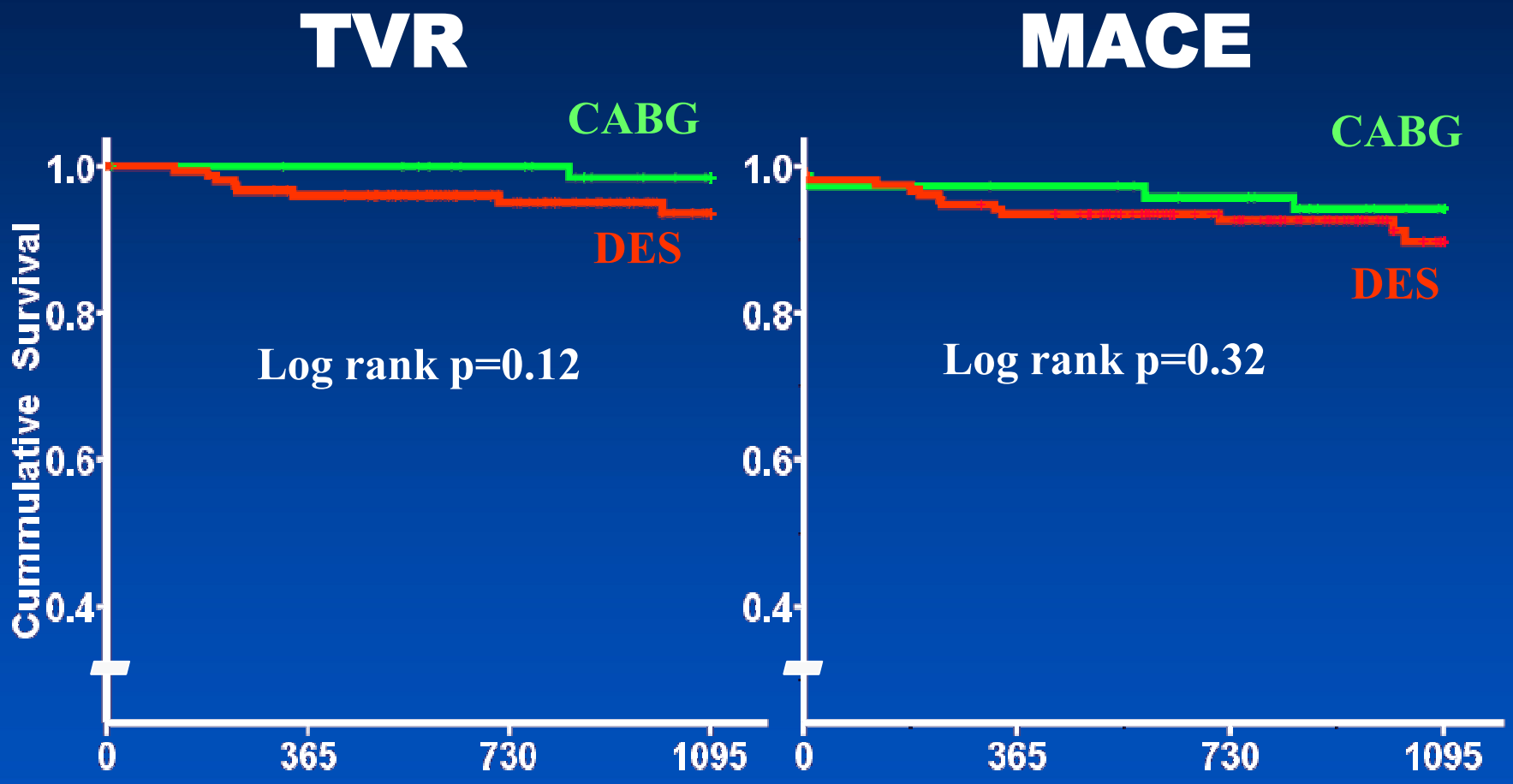


Q- MI



CABG	73	70	65	55	73	67	59	49
PCI	291	281	236	179	291	231	172	116

Clinical Outcomes in Isolated LM disease at 3 years



CABG	73	70	65	54	73	70	65	54
PCI	155	144	105	54	155	144	105	54

Isolated LM disease may be unique disease entity and has comparable clinical outcomes (all-cause mortality, Q-MI, TVR and composite MACE) with surgery.

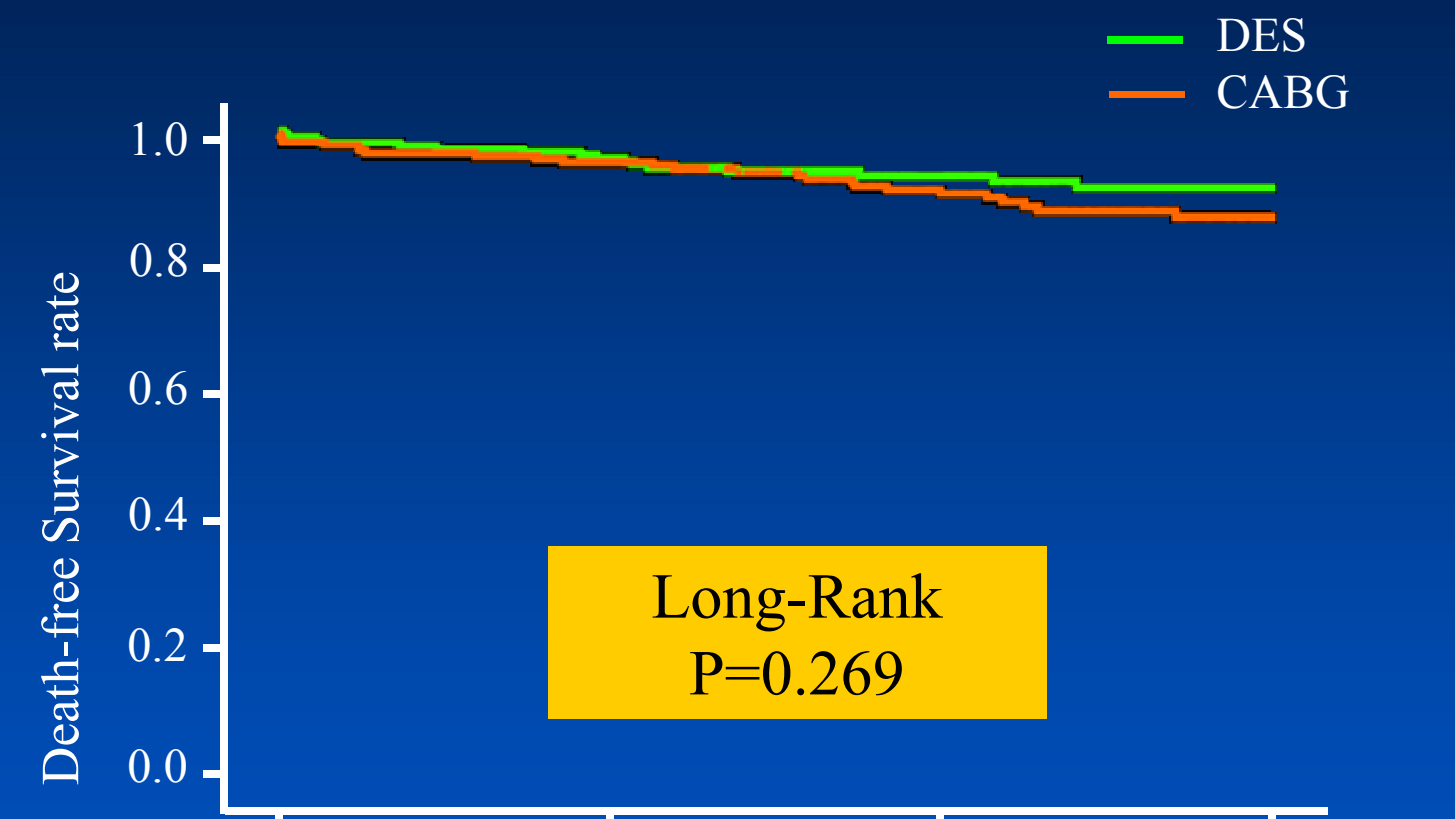
Based on the data from MAIN COMPARE Registry and Syntax trial

Impact of DM

Kim WJ et al, JACC Intv, 2009; 2: 956 – 963

Unadjusted Kaplan-Meier Curves

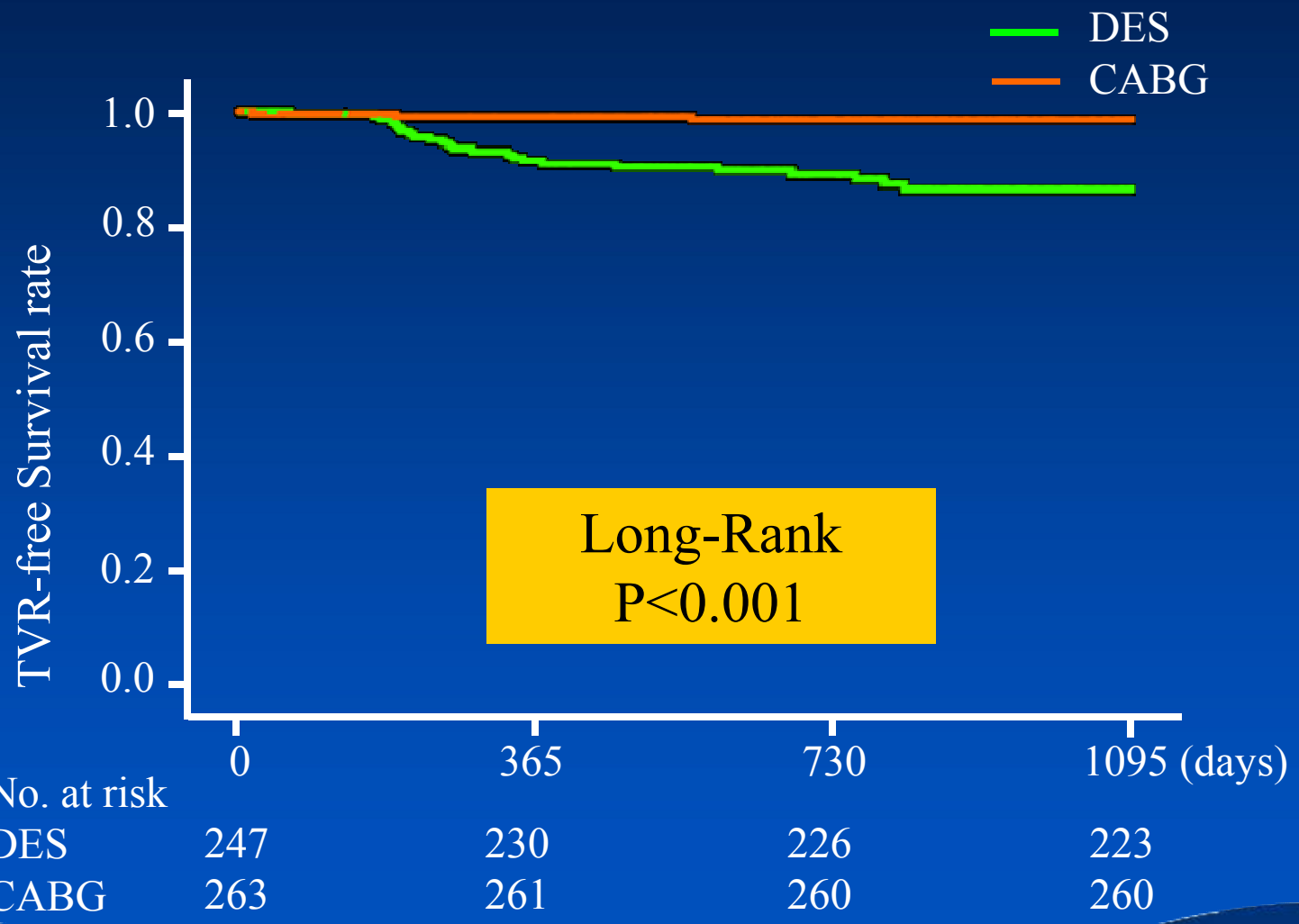
Death in Diabetics



No. at risk				
DES	247	238	233	231
CABG	263	252	243	238

Unadjusted Kaplan-Meier Curves

TVR in Diabetics



Hazard Ratios of Clinical outcomes
: DES vs. CABG for Diabetic Patients

	Crude		Multivariable adjusted*	
	Adjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value
Death	0.70 (0.38-1.32)	0.27	0.78 (0.38-1.60)	0.50
Q–MI	0.38 (0.04-3.67)	0.39	0.30 (0.02-4.81)	0.39
TVR	9.00 (2.71-29.90)	<0.001	13.14 (3.09-55.92)	<0.001
Stroke	1.29 (0.39-4.22)	0.68	1.72 (0.49-6.02)	0.39
Death/Q-MI/TVR	1.53 (0.95-2.48)	0.08	1.64 (0.96-2.82)	0.07
Death/Q-MI/TVR/CVA	1.41 (0.91-2.20)	0.12	1.95 (1.19-3.22)	0.01

*HR for stents with reference to CABG.

Kim WJ et al, JACC Intv, 2009; 2: 956 – 963

Predictors

MACE : Death /MI /Stroke

MACCE : Death /MI /Stoke and *TVR*

Subgroup Analysis in
MAIN-COMPARE Study

Multivariate Predictors by Cox Model
For MACE (Death/ MI/ Stroke)

Outcomes	Hazard Ratio	95% CI	P value
Overall patients			
EuroSCORE	1.25	1.16, 1.34	<0.001
Chronic lung disease	2.14	1.07, 4.29	0.032
Chronic renal failure	2.67	1.54, 4.63	<0.001
Atrial fibrillation	2.21	1.11, 4.42	0.024
PCI patients			
EuroSCORE	1.17	1.05, 1.31	0.004
Prior congestive heart failure	3.86	1.58, 9.44	0.003
Chronic renal failure	6.15	2.90, 13.01	<0.001
CABG patients			
EuroSCORE	1.27	1.16, 1.39	<0.001
Diabetes mellitus	1.76	1.13, 2.75	0.013
Chronic lung disease	4.03	1.79, 9.05	<0.001
Prior cerebrovascular disease	2.36	1.29, 4.31	0.005
Hyperlipidemia	0.60	0.36, 0.99	0.043

Multivariate Predictors by Cox Model
For MACCE (Death/ MI/ Stroke and TVR)

Outcomes	Hazard Ratio	95% CI	P value
Overall patients			
EuroSCORE	1.10	1.04, 1.16	<0.001
CABG	0.71	0.54, 0.92	0.010
Chronic renal failure	2.32	1.40, 3.85	0.001
Prior cerebrovascular disease	1.58	1.08, 2.33	0.020
Use of intra-aortic balloon pump	2.00	1.09, 3.64	0.024
PCI patients			
Prior congestive heart failure	2.98	1.44, 6.16	0.003
Use of intra-aortic balloon pump	2.25	1.23, 4.10	0.008
Chronic renal failure	4.17	2.27, 7.64	<0.001
CABG patients			
EuroSCORE	1.22	1.12, 1.33	<0.001
Chronic lung disease	2.52	1.15, 5.49	0.021
Prior MI	1.76	1.06, 2.94	0.030
Prior cerebrovascular disease	2.32	1.36, 3.99	0.002

MAIN COMPARE Registry
5 year Follow-Up

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5 Year
Long-term Outcomes

Complete follow-up for major clinical events was obtained in 97.9% of the overall cohort (98.1% for the PCI group and 97.6% for the CABG group; P=0.45).

The median follow-up was 62.0 months (IQR range, 48.0 to 78.3 months) in the overall patients.

After Propensity-Matching

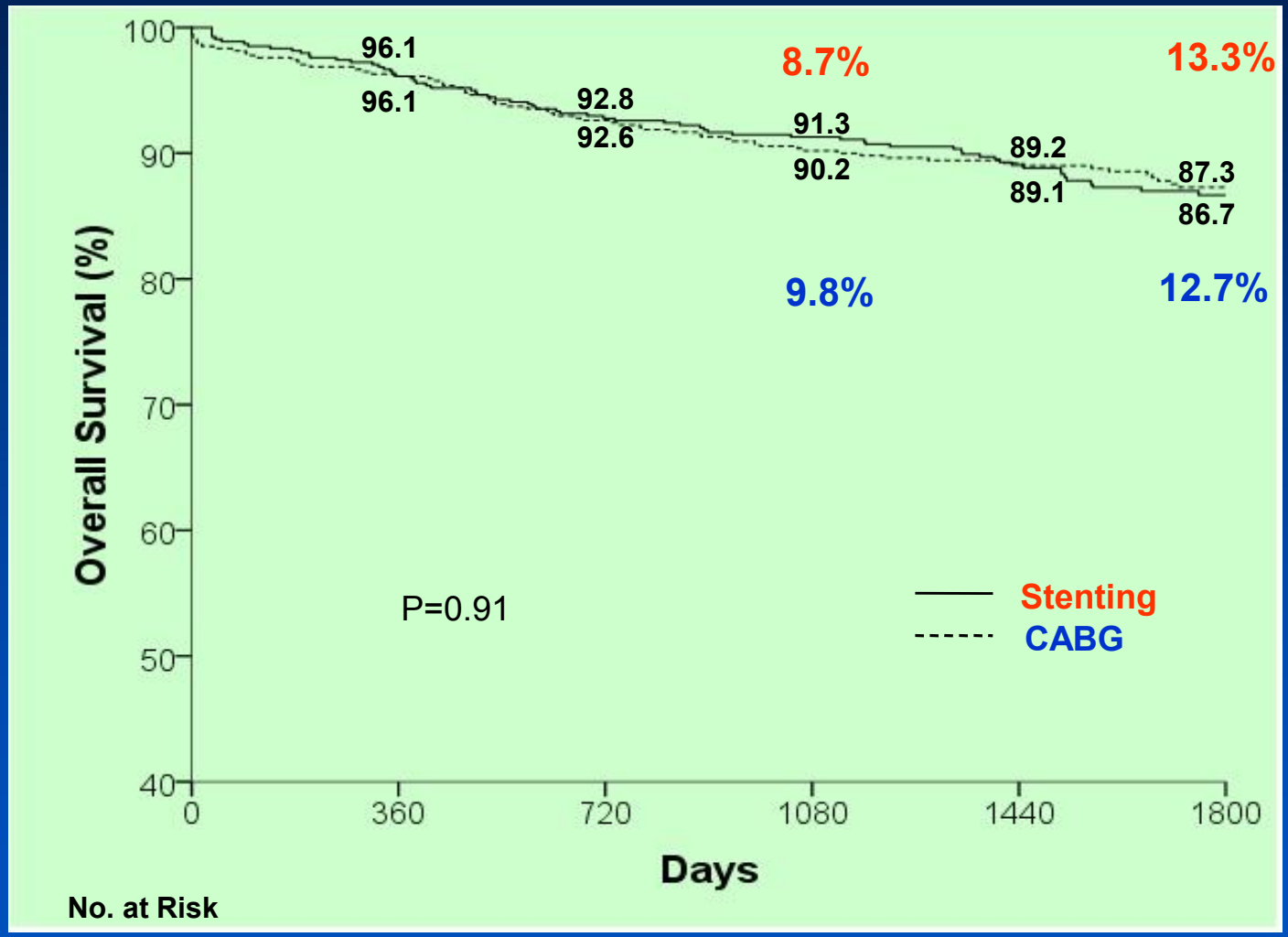
Overall matched cohort (n=542 pairs)

Wave 1; BMS vs. contemporary CABG (n=207 pairs)

Wave 2; DES vs. contemporary CABG (n=396 pairs)

5-Year: Death

(Overall : 542 pairs)



4.6% ↑

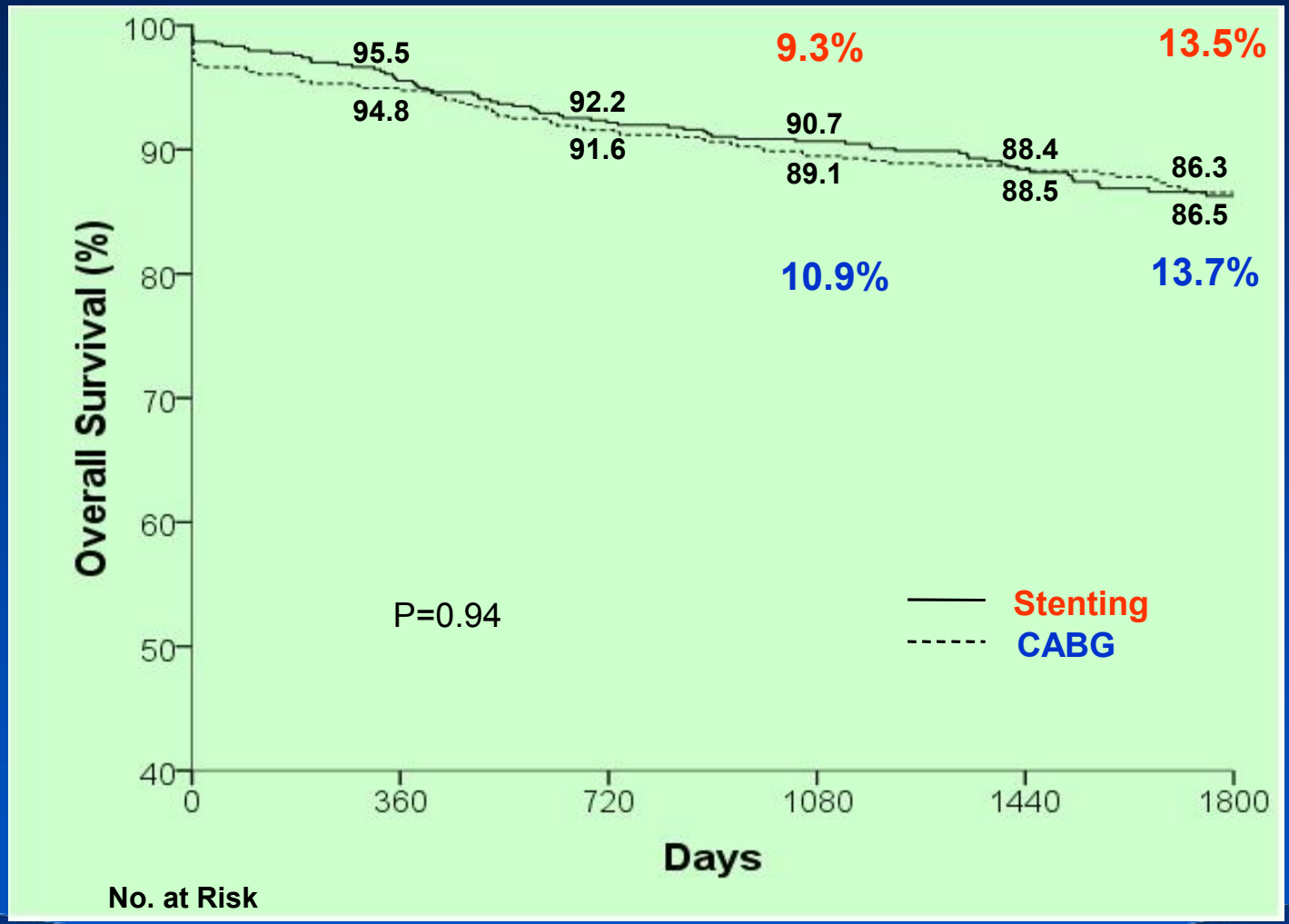
2.9% ↑

No. at Risk

Stenting	542	519	499	486	388	241
CABG	542	521	499	478	421	320

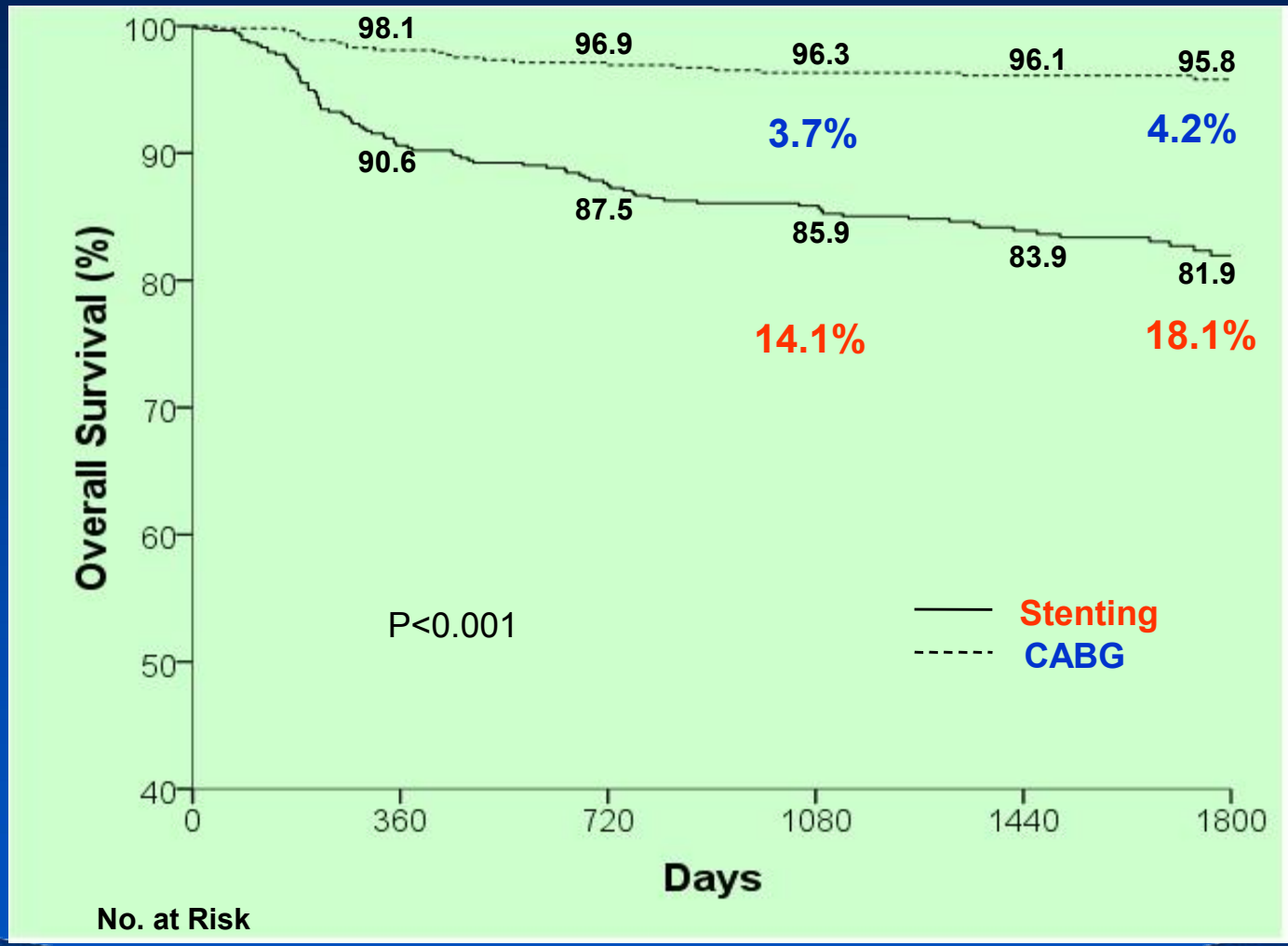
5-Year: Death, Q-MI, or Stroke

(Overall 542 pairs)



5-Year: TVR

(Overall : 542 pairs)



No. at Risk

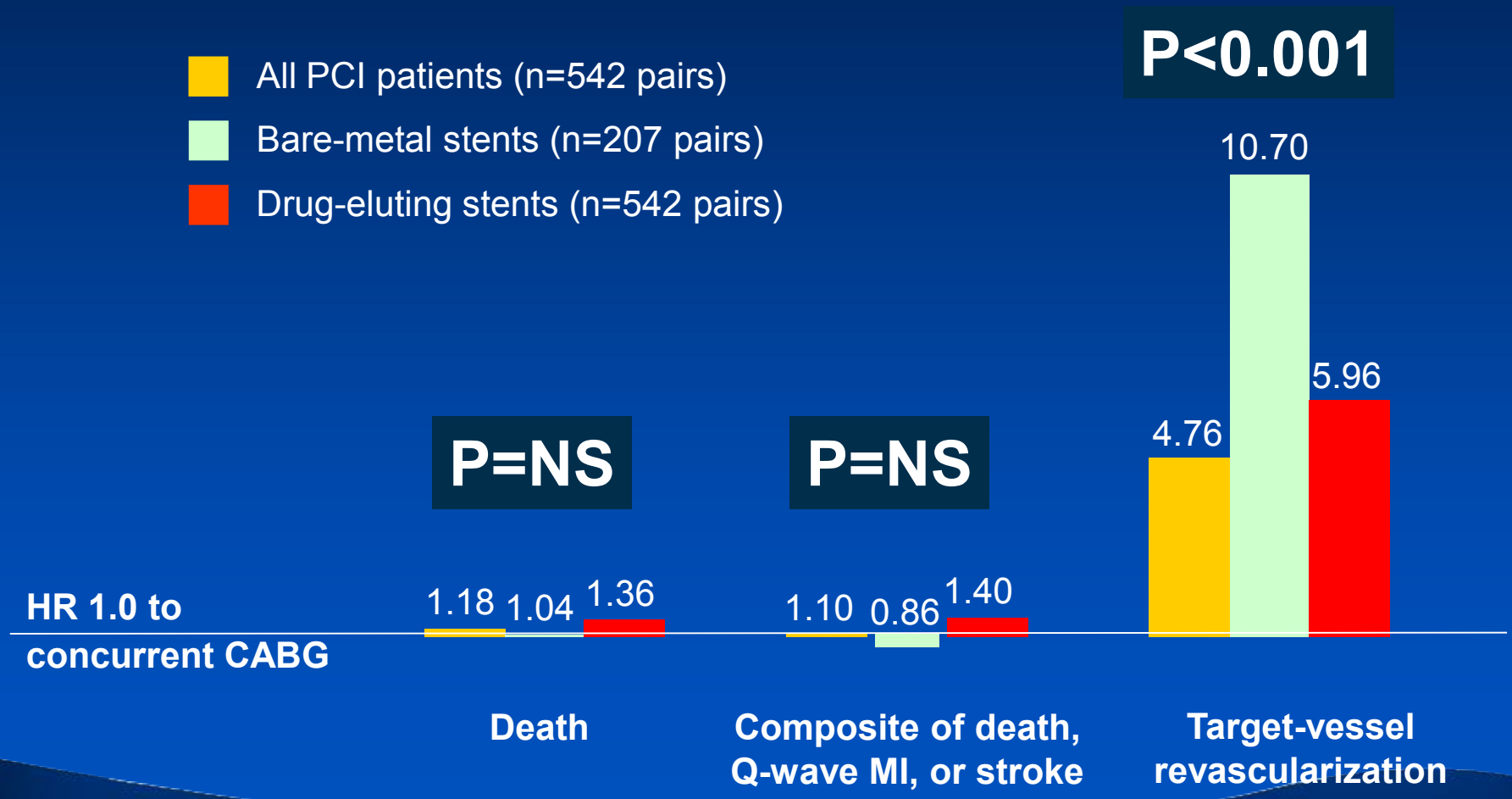
Stenting	542	472	438	421	328	198
CABG	542	511	484	460	403	305

HR for Clinical Outcomes after Stenting as Compared with after CABG among **Propensity**

	Overall Patients (N=542 pairs)		Wave 1* (N=207 pairs)		Wave 2* (N=396 pairs)	
Outcome	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P
Death	1.02 (0.74-1.39)	0.91	1.04 (0.66-1.64)	0.86	1.26 (0.85-1.87)	0.24
Composite outcome	1.10 (0.74-1.38)	0.94	0.94 (0.60-1.47)	0.79	1.27 (0.86-1.87)	0.24
TVR	4.55 (2.88-7.20)	<0.001	7.97 (3.34-19.00)	<0.001	6.69 (3.44-13.03)	<0.001

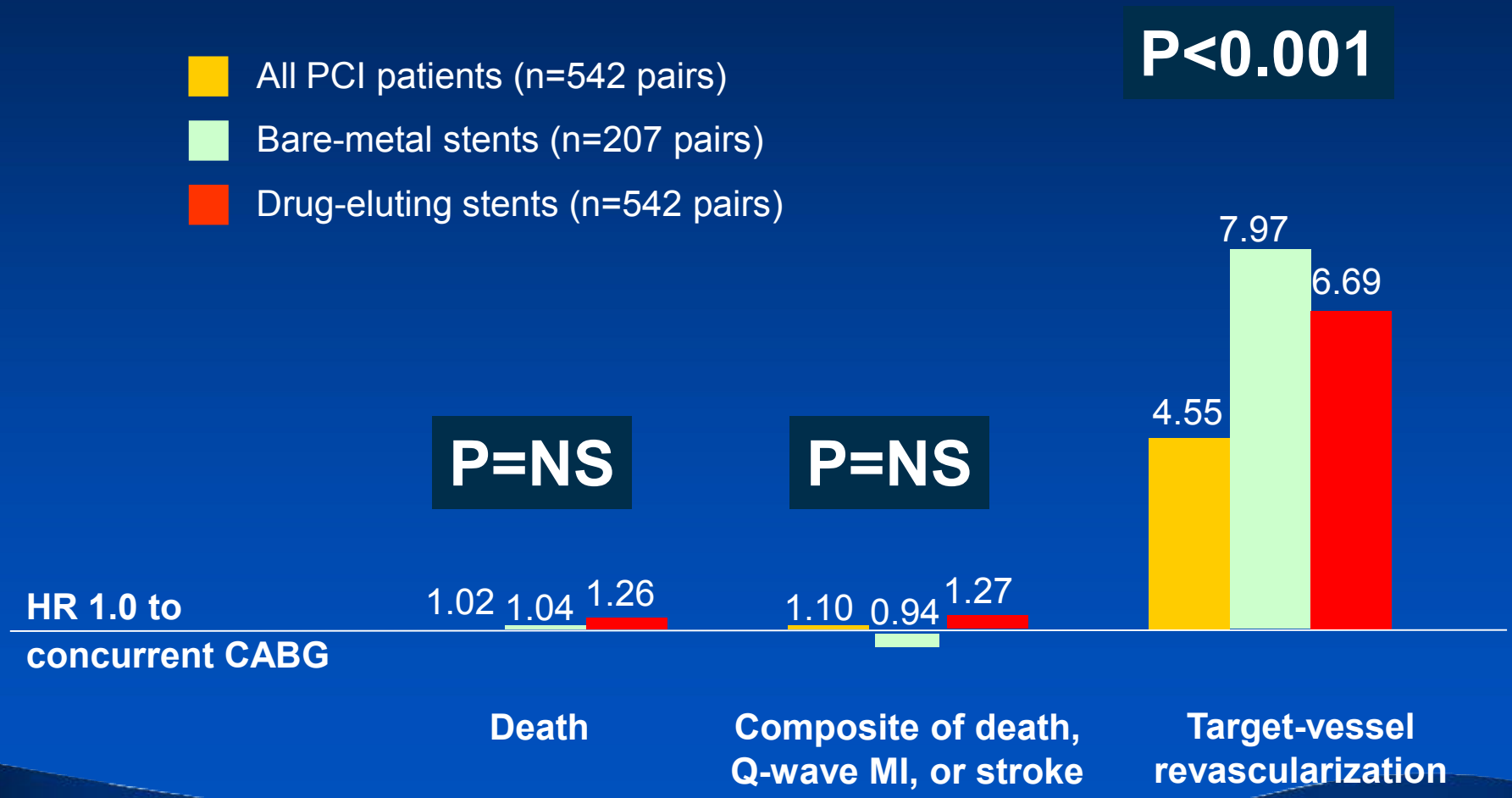
Hazard Ratios for Clinical Outcomes

: Median 3-Year Outcomes



Hazard Ratios for Clinical Outcomes

: Median 5-Year Outcomes



ASAN MAIN Registry
5 – 10 year Follow-Up

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AMC Works since 1998

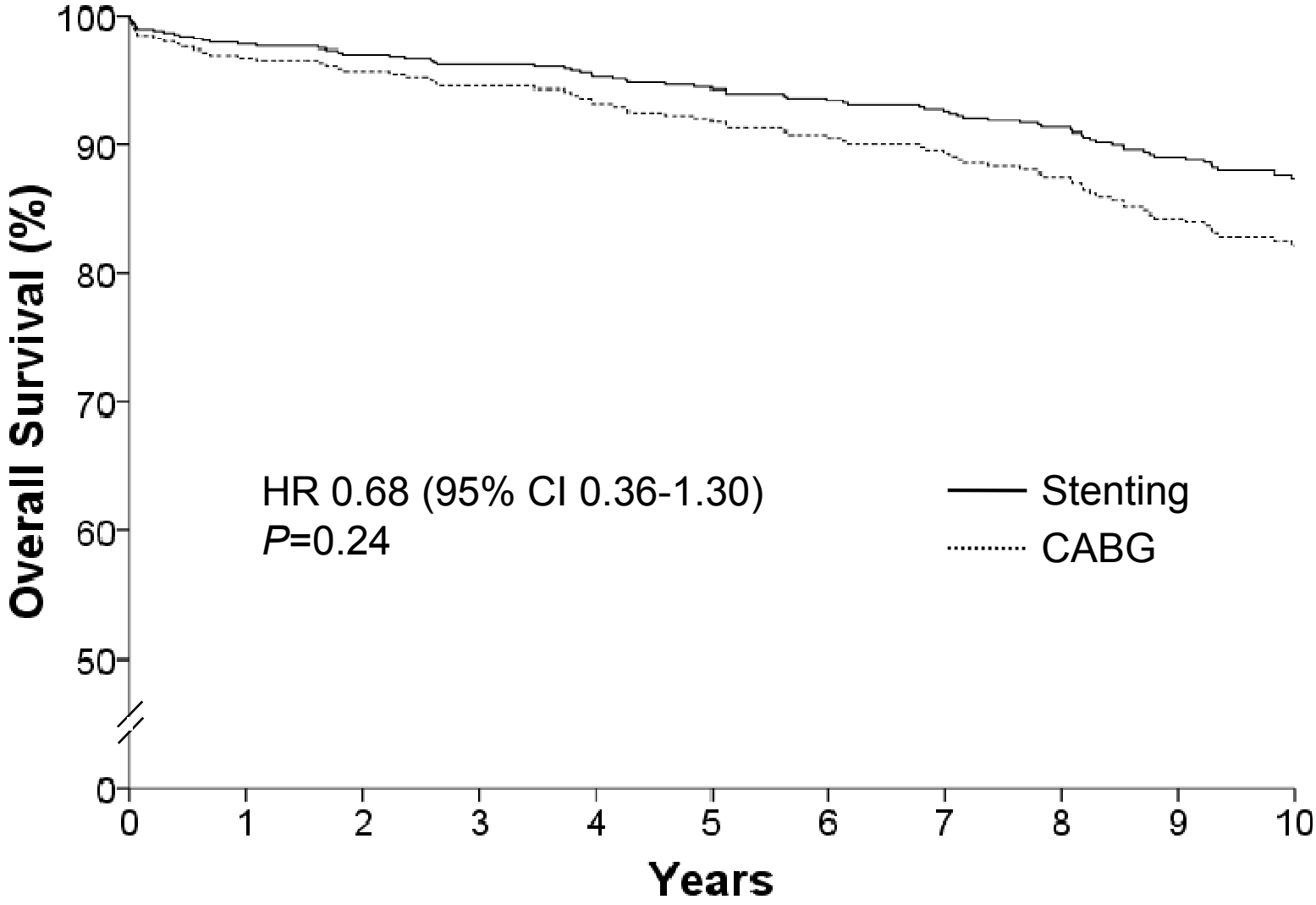
1997	J Am Coll Cardiol 1998;31:37-42 : Early experience
1998	Am J Cardiol 1998;82:670-3 : IVUS analysis
1999	J Am Coll Cardiol 2001;38:1054-60 : Role of debulking
2000	Circulation 2001;104:1609-1614 : ULTIMA registry
2003	JACC 2005;45:351-6 : SES stenting.
2004	Am J Cardiol 2006;98:1567-1570 : EuroSore evaluation
2005	Int Jour of Cardiology 2007. 208-213 : 5 year F/U data
2007	Cathter Cardio Interv 70:840-846, 2007: Kissing stent technique longterm
2008	NEJM. 2008 Apr 24;358(17):1781-92. MAIN COMPARE registry

More than 1,200 patients have been preformed unprotected left main stenting in AMC

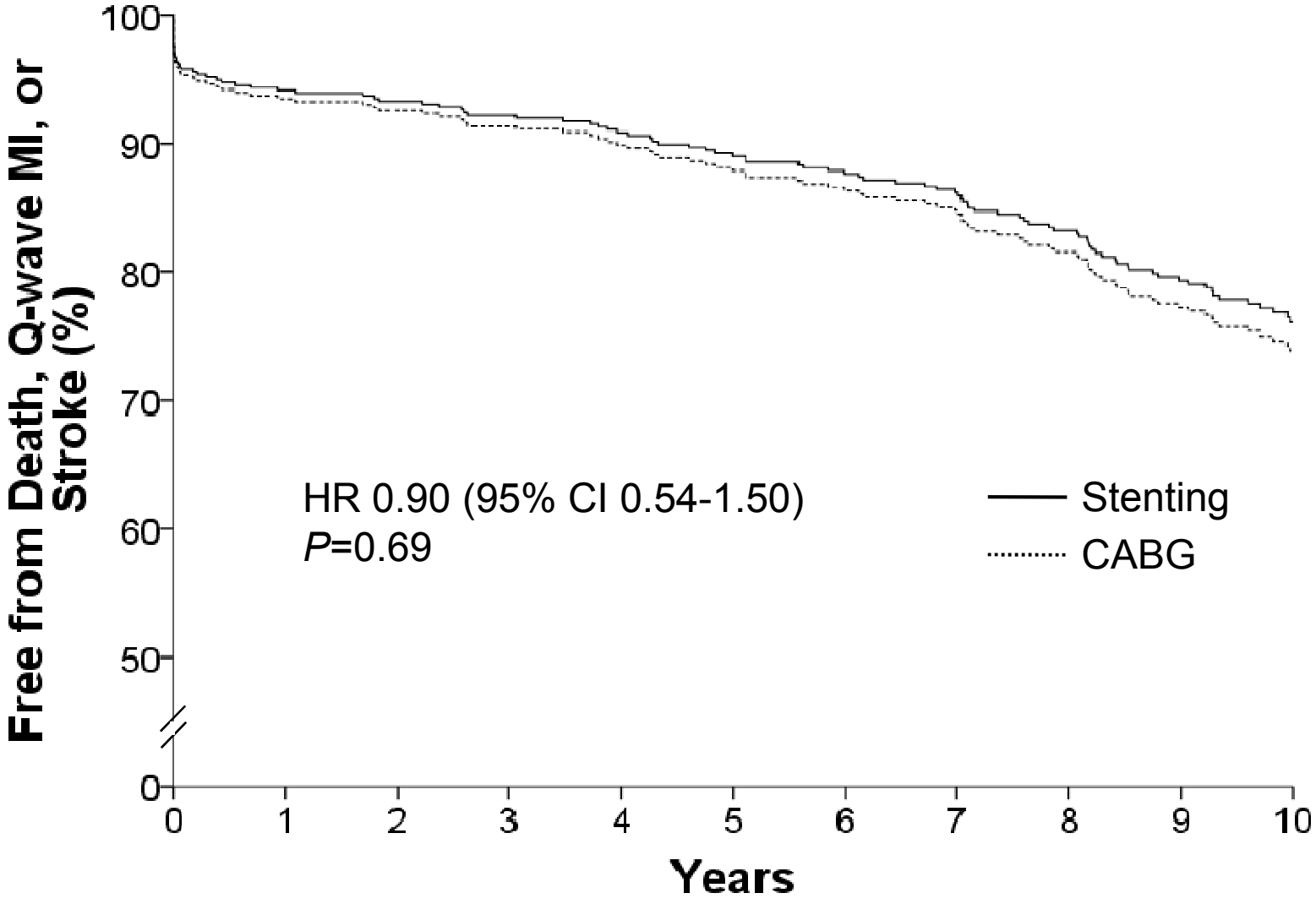
10 Year Clinical Outcomes

BMS vs. CABG
(100 : 250 pts)
for Unprotected LMCA Disease

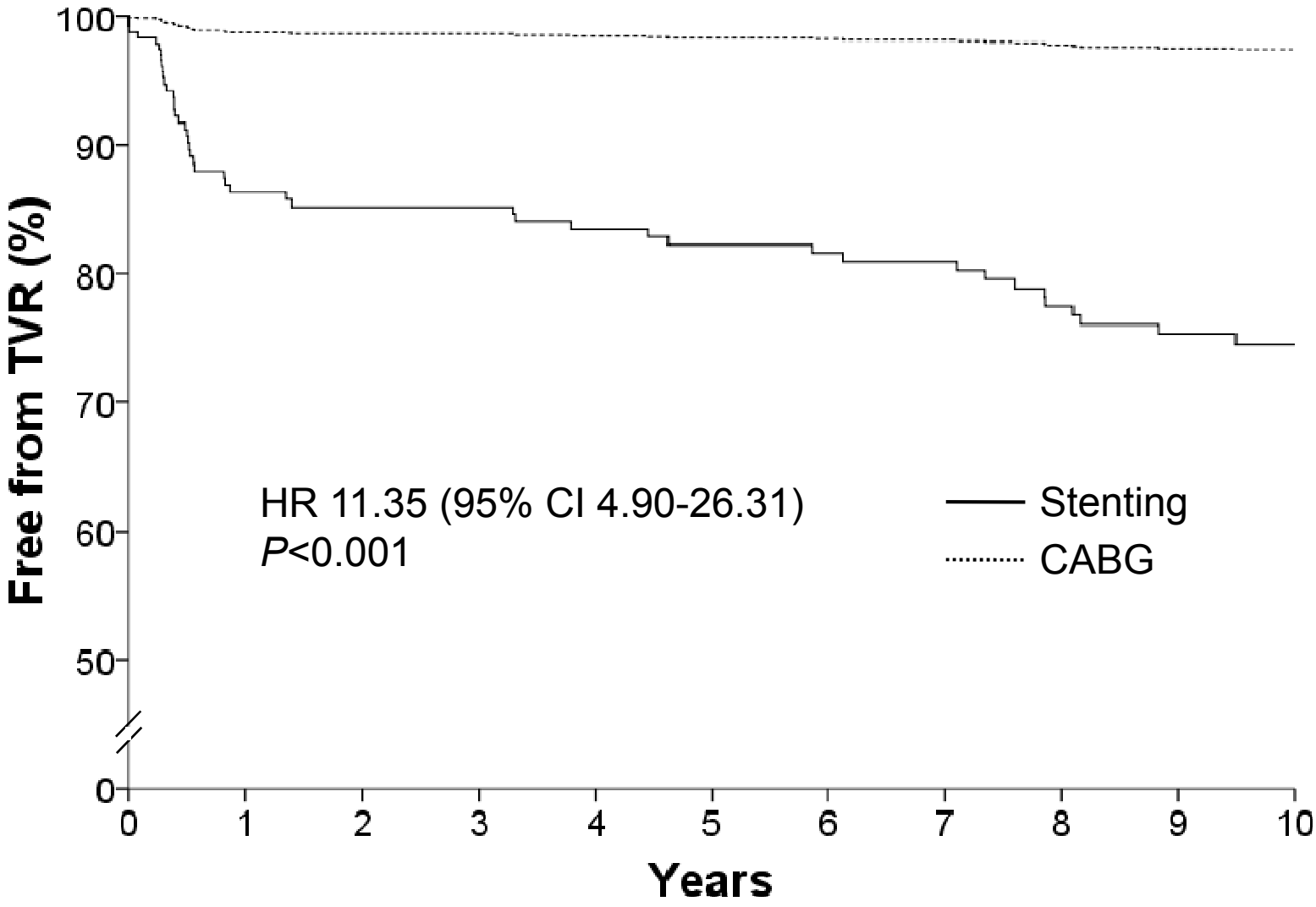
Adjusted Outcomes: Death



Adjusted Outcomes: Death, Q-MI, Stroke



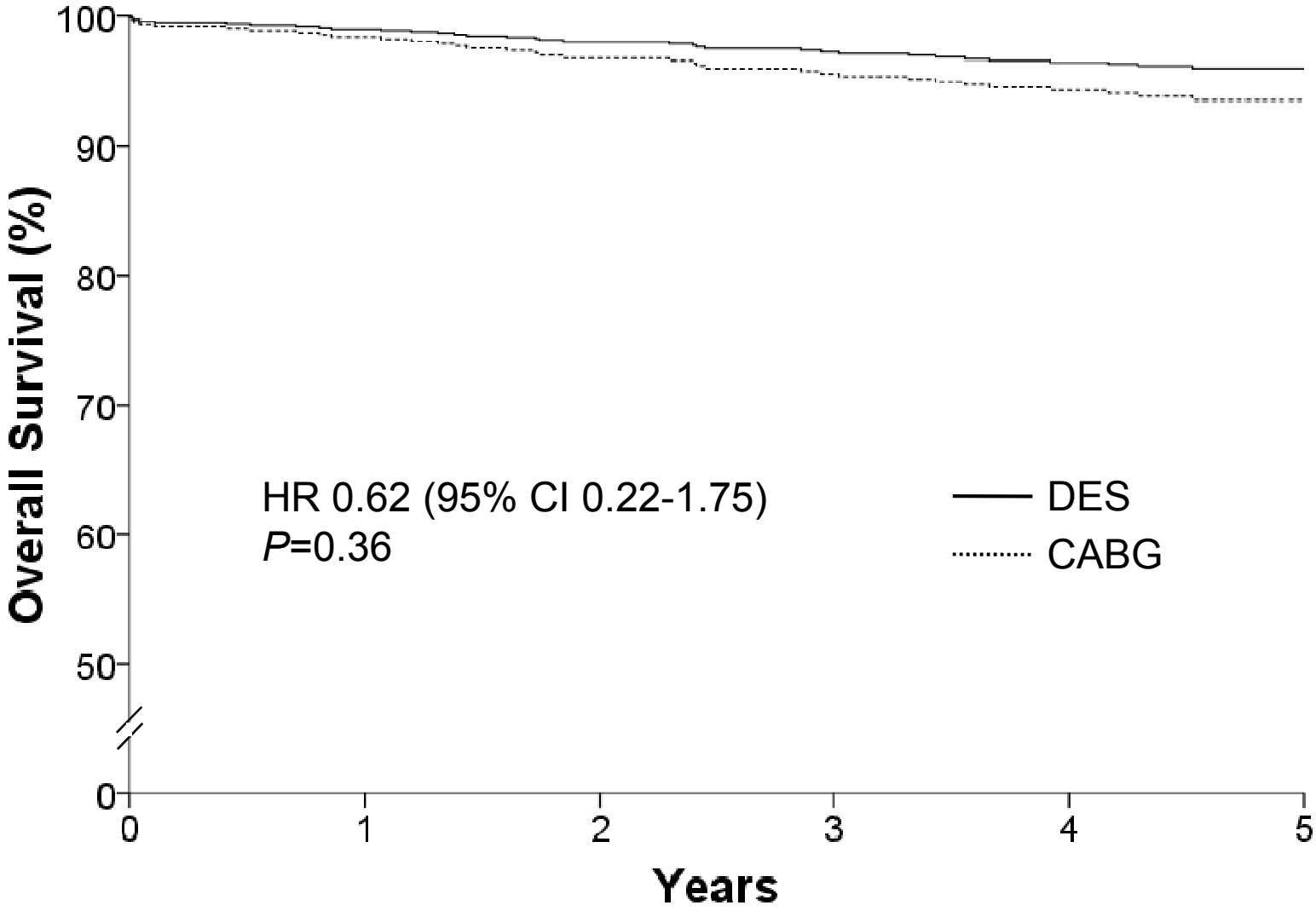
Adjusted Outcomes: TVR



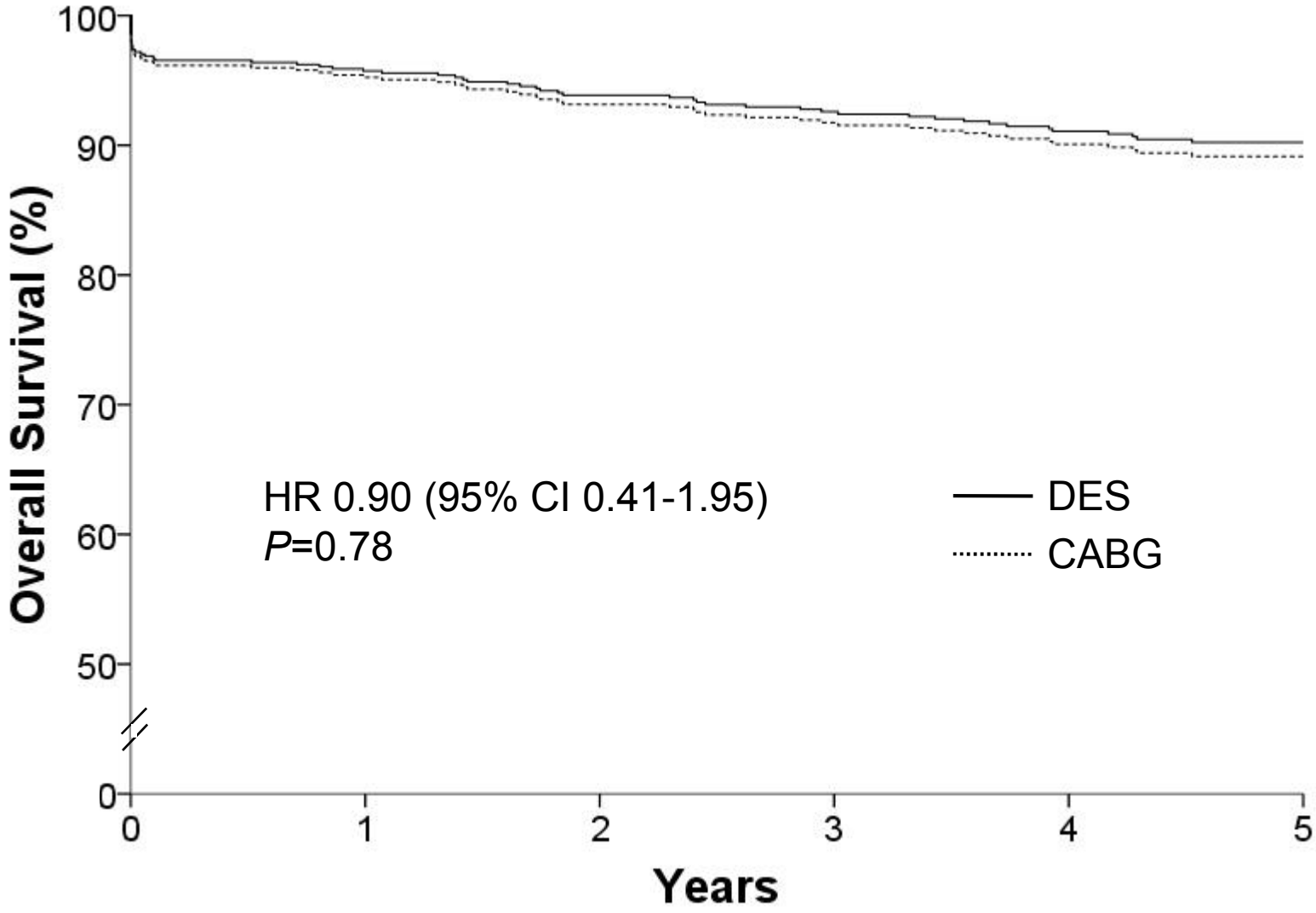
5 Year Clinical Outcomes

DES vs. CABG
(176 : 219 pts)
for Unprotected LMCA Disease

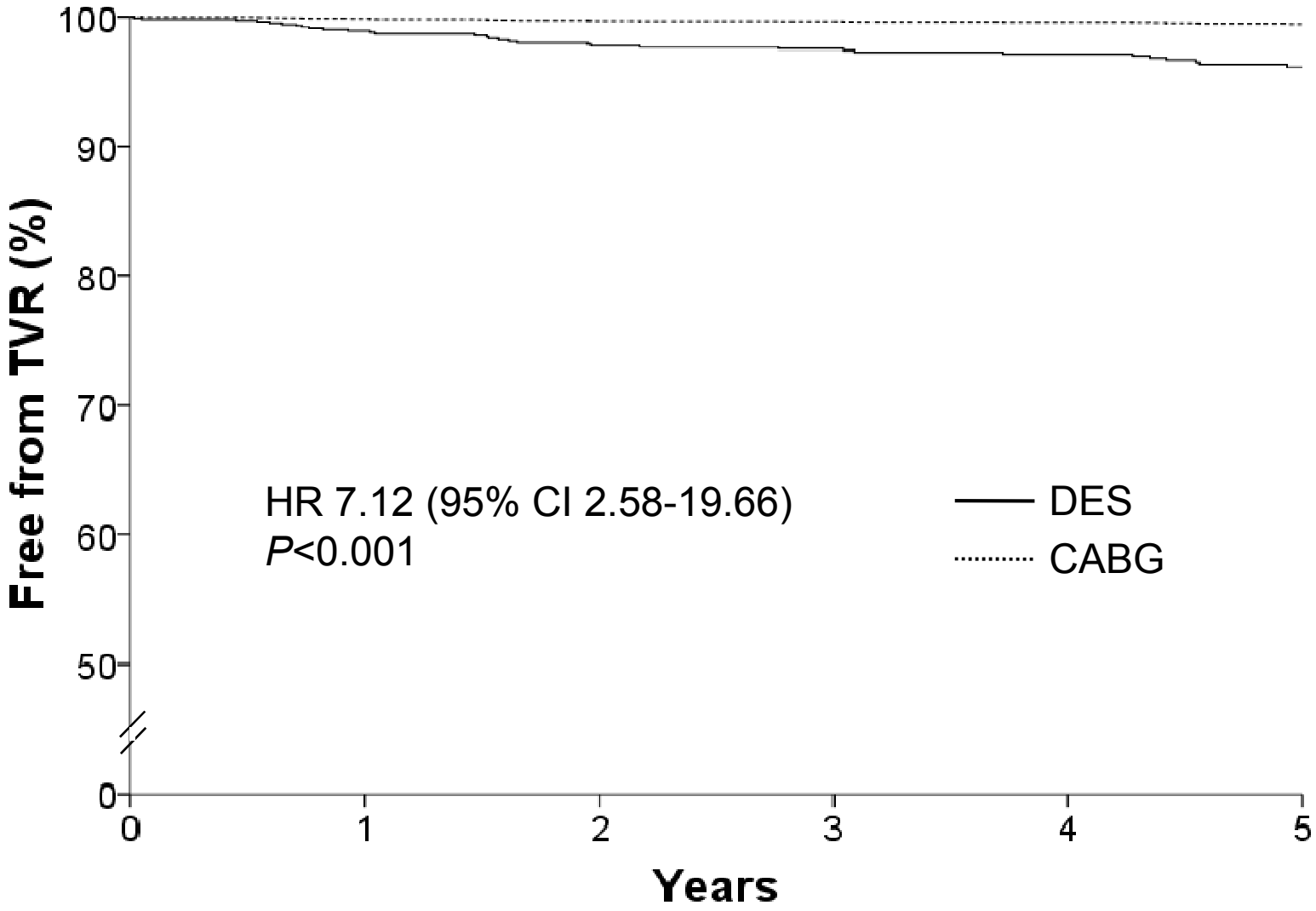
Adjusted Outcomes: Death



Adjusted Outcomes: Death, Q-MI, Stroke



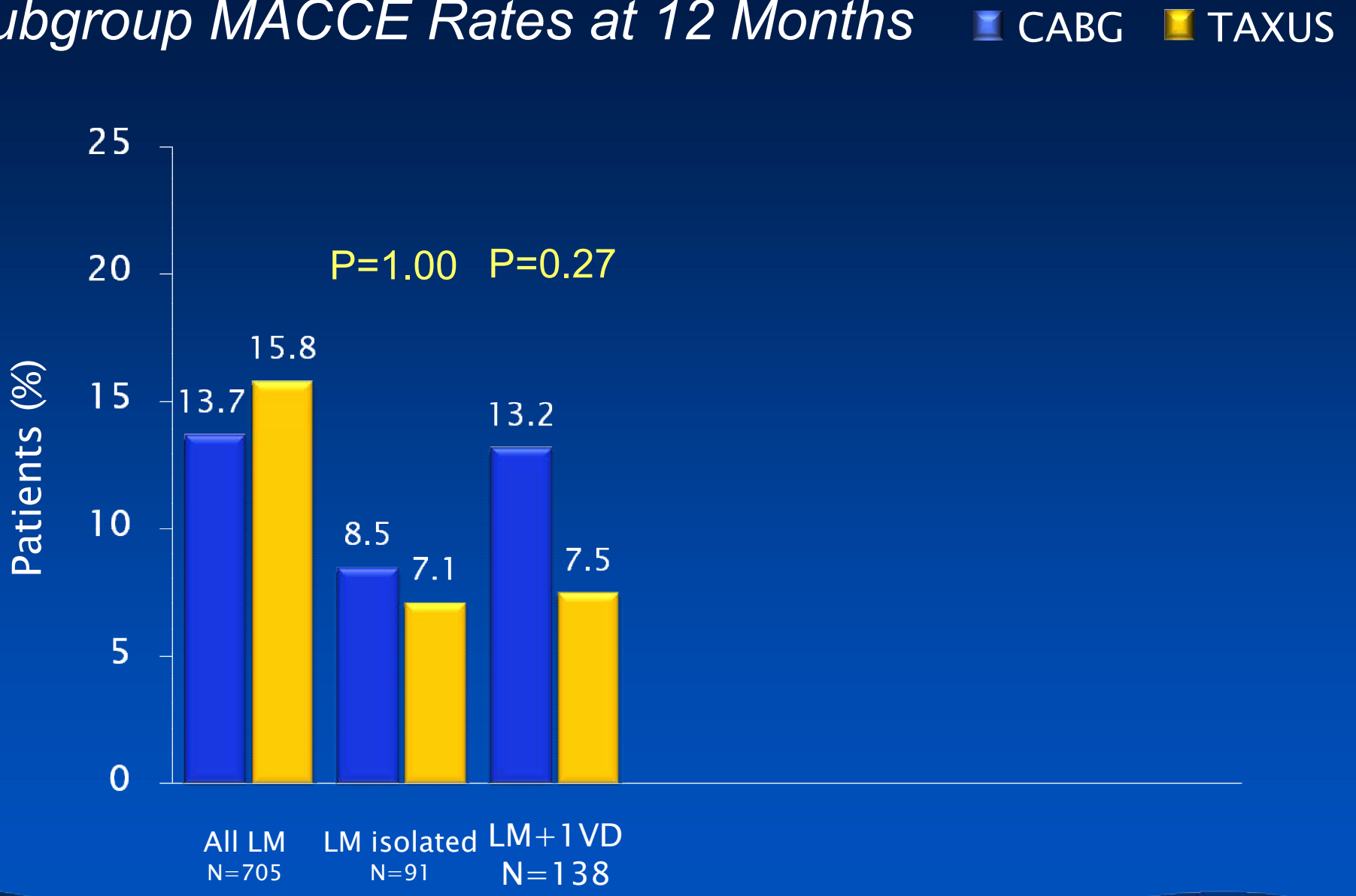
Adjusted Outcomes: TVR



SYNTAX
LM subgroup

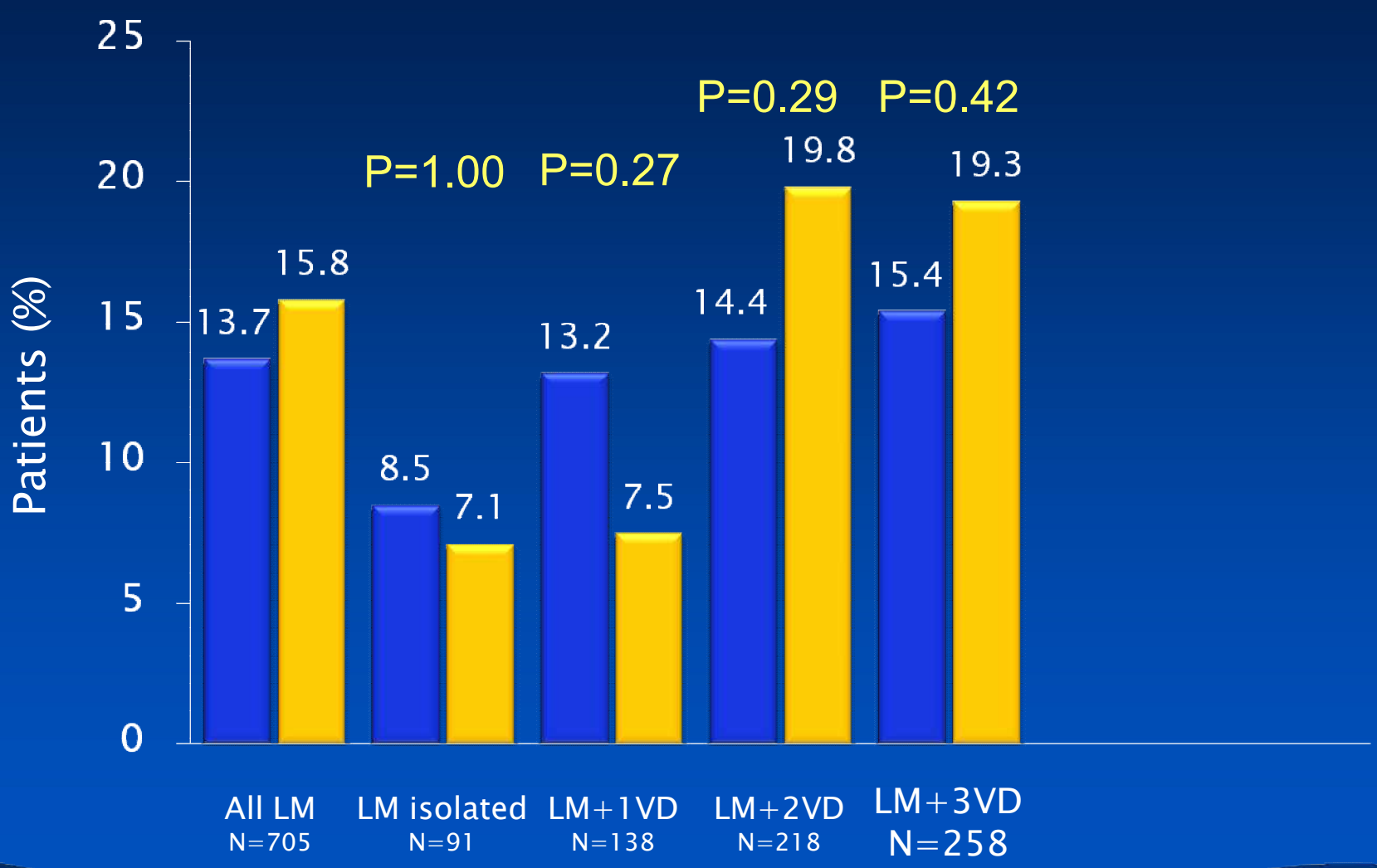
Left Main and Three Vessel Disease

Subgroup MACCE Rates at 12 Months



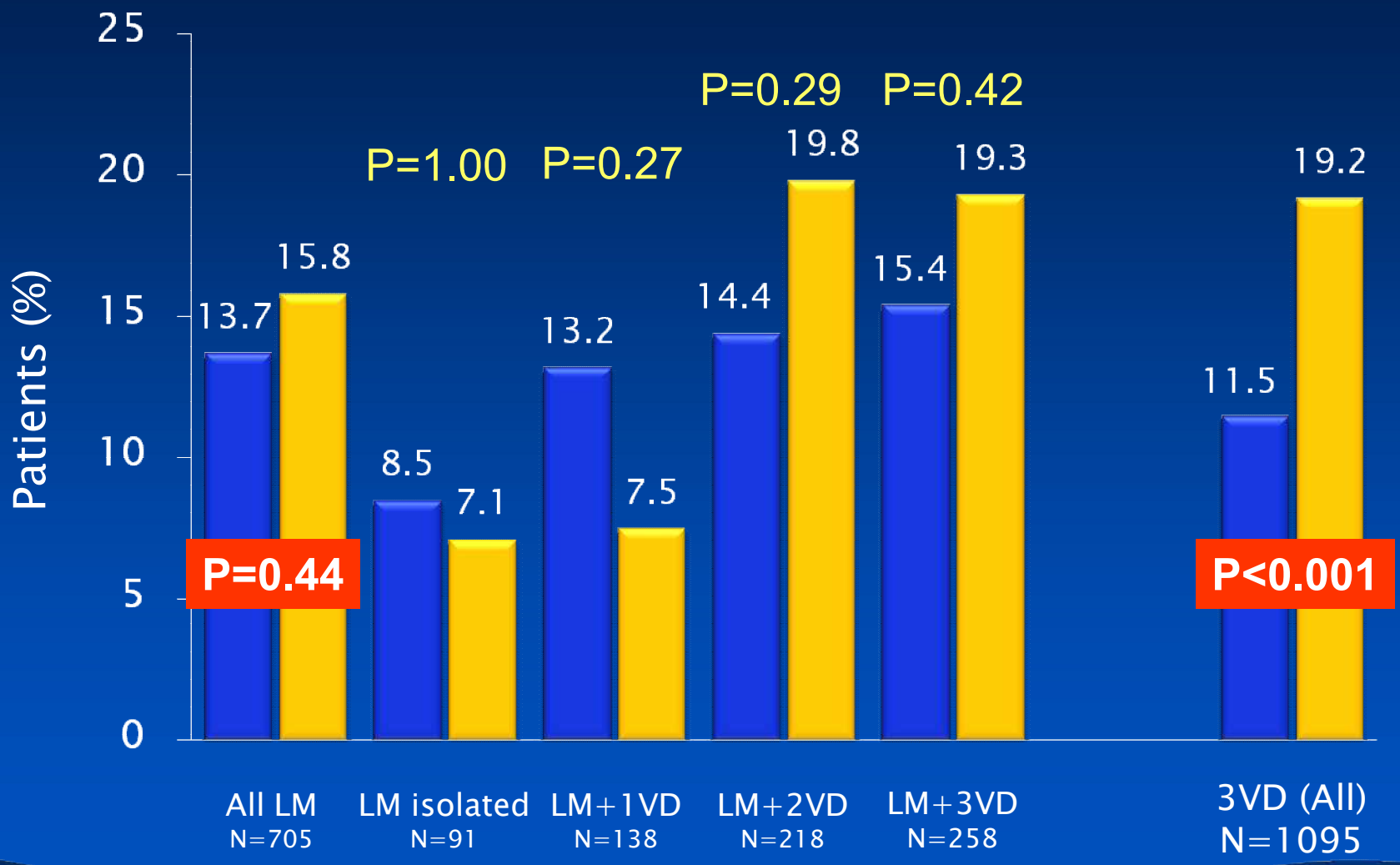
Left Main and Three Vessel Disease

Subgroup MACCE Rates at 12 Months



Left Main and Three Vessel Disease

Subgroup MACCE Rates at 12 Months



SYNTAX trial end points in 3VD subset

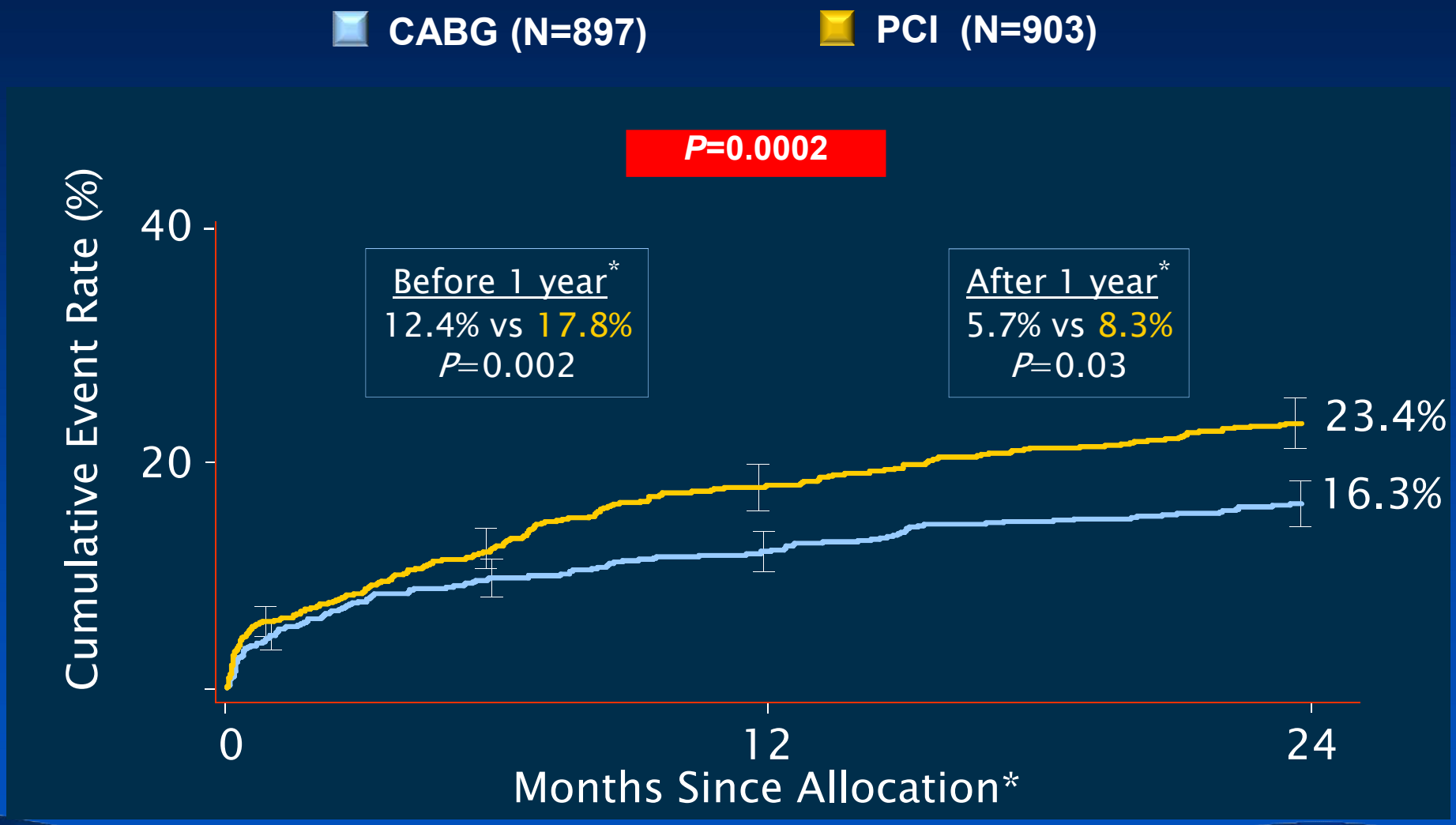
End point	CABG (%)	Taxus (%)	p
Death	2.9	4.4	0.18
Stroke	1.9	0.8	0.09
MI	2.6	5.2	0.04
Revascularization	5.4	14.7	<0.001
Death/stroke/MI	6.4	7.9	0.39
MACCE	11.2	19.1	<0.001

SYNTAX trial end points in left main subset

End point	CABG (%)	Taxus (%)	p
Death	4.4	4.2	0.88
Stroke	2.7	0.3	0.009
MI	4.1	4.3	0.97
Revascularization	6.7	12.0	0.02
Death/stroke/MI	9.1	7.0	0.29
MACCE	13.6	15.8	0.44

SYNTAX LM
2-Year Outcomes

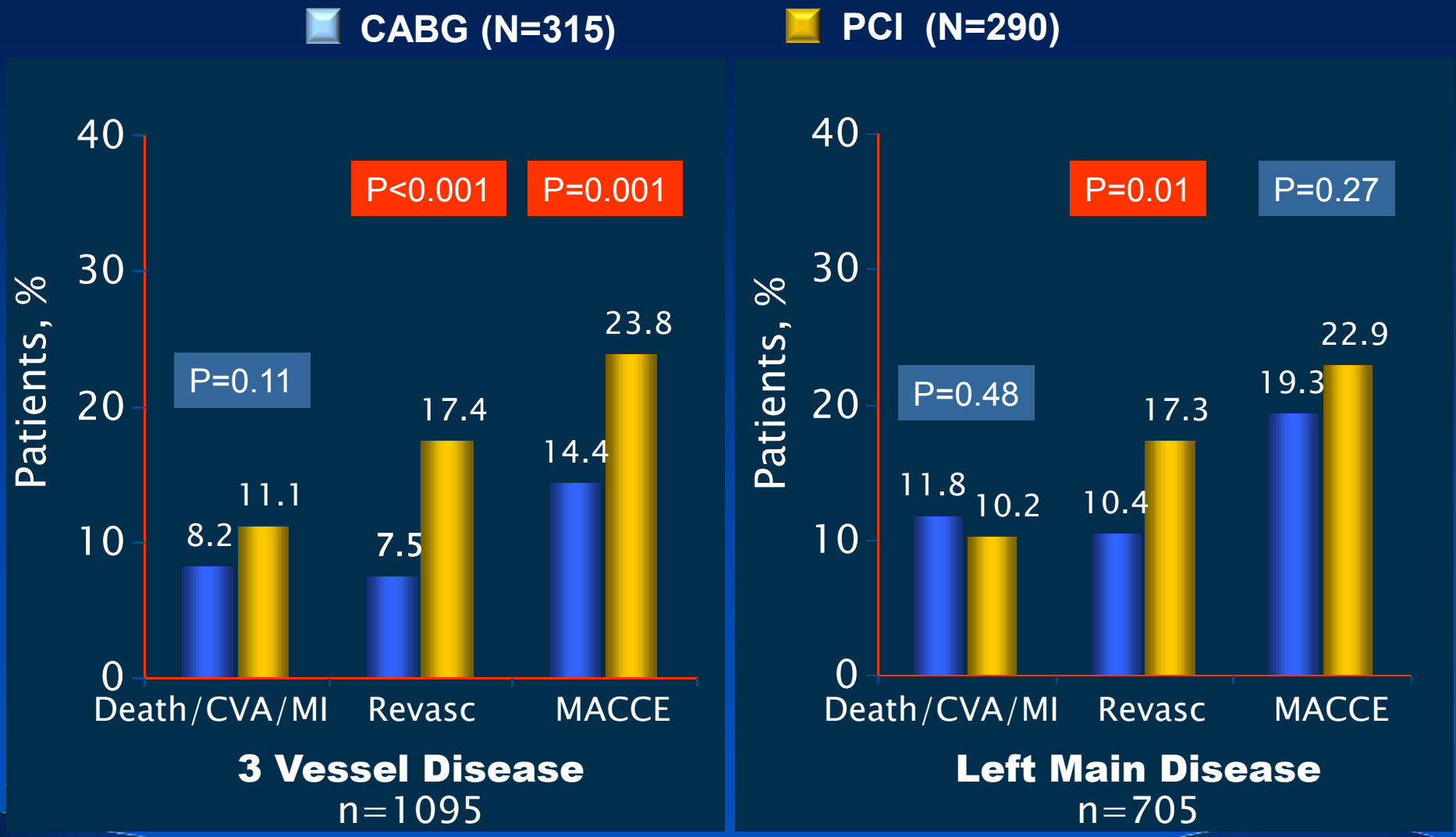
MACCE to 2 Years



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

ITT population

SYNTAX Trial 2 Year Outcomes
in 3VD and LM Subgroups



Presented at ESC September 2009 by A. Pieter Kappetein MD PhD. The SYNTAX Score™ is made possible by support from Boston Scientific Corporation and Cardialysis BV.

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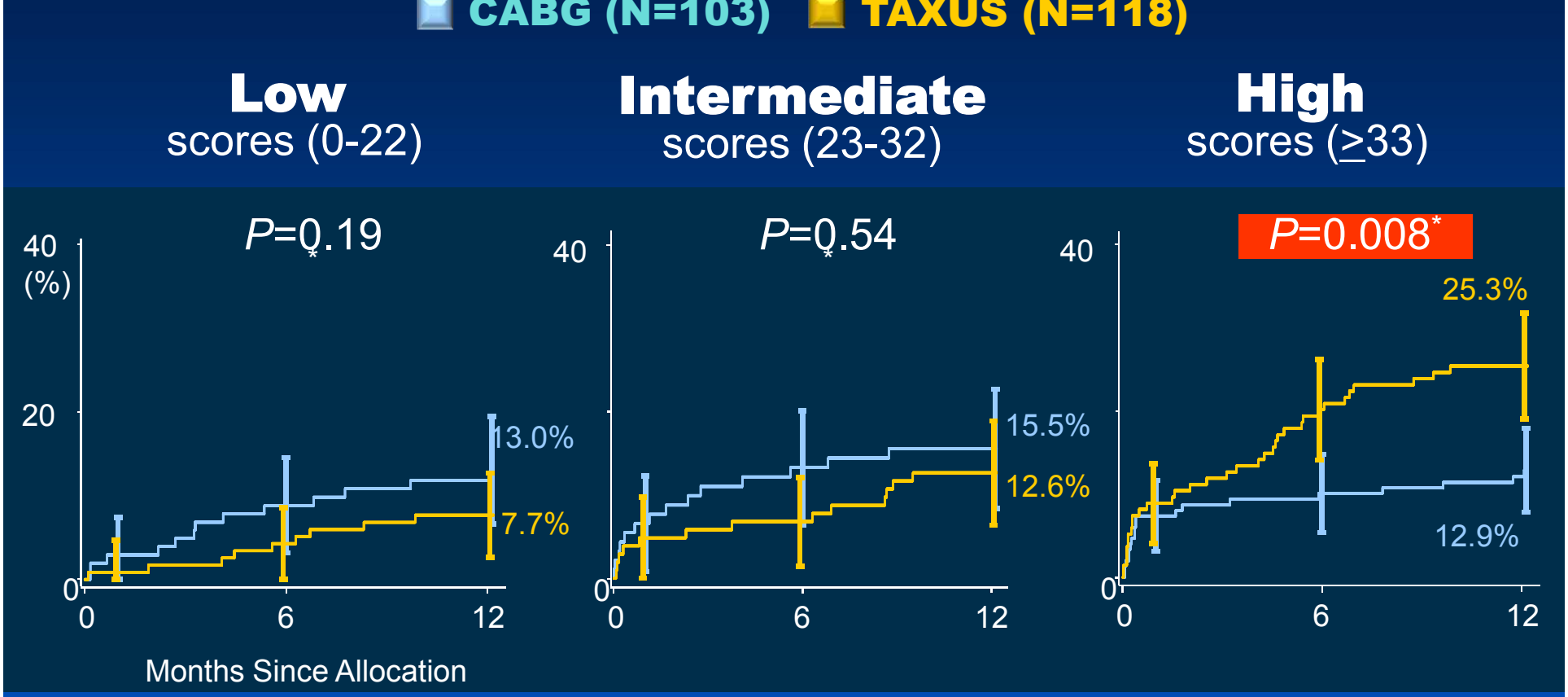
ASAN Medical Center

MACCE to 12 Months
by SYNTAX Score Tercile

LM Subset

CABG (N=103) **TAXUS (N=118)**



CABG better

CardioVascular Research Foundation

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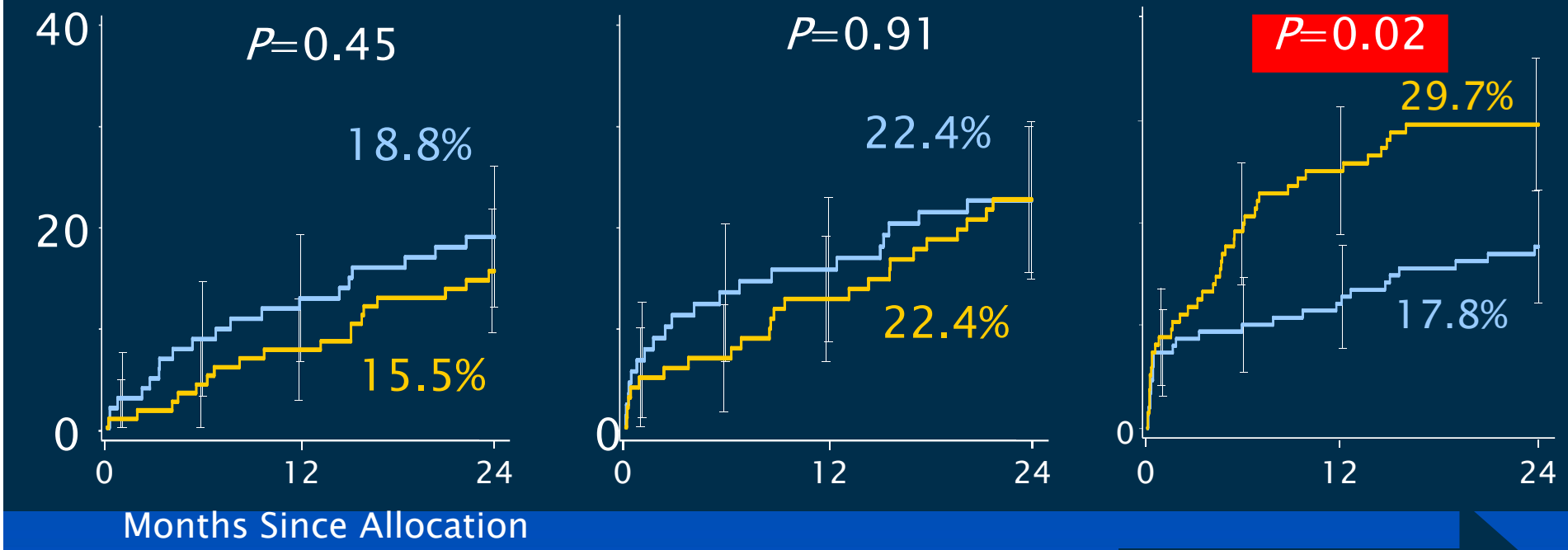
ASAN Medical Center

MACCE to 2 Years
by SYNTAX Score™ Tercile

LM subset

CABG (N=103) **TAXUS (N=118)**



CABG better

Syntax LM subgroup analysis showed,

PCI has comparable clinical outcomes with surgery (no difference in death or MI).
There is higher rate of stoke in surgery and higher rate of TVR in PCI
2-year results confirm the one-year one's.

Message

From MAIN COMPARE registry,
ASAN MAIN registry, SYNTAX LM

STENT vs CABG
for Left Main Disease Treatment

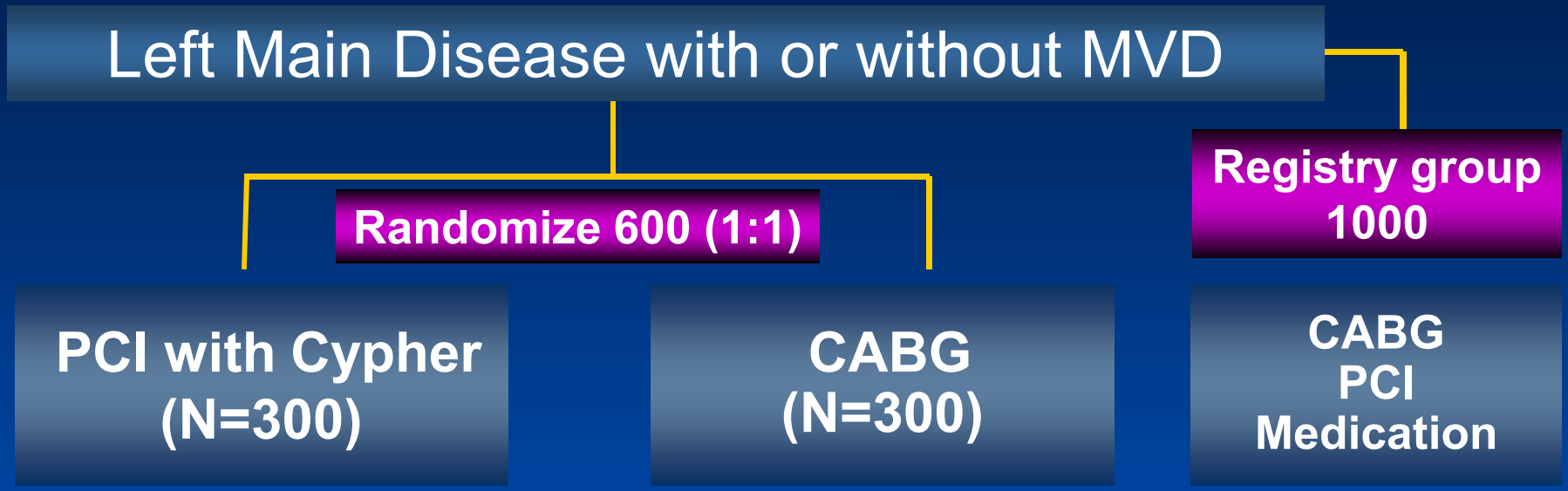
In selected group of LM disease;

- Ostial and shaft LM disease
- Isolated LM disease
- LM with 1 vessel disease
- Syntax Score <33

STENT group may have even better clinical outcomes…

What is NEXT !

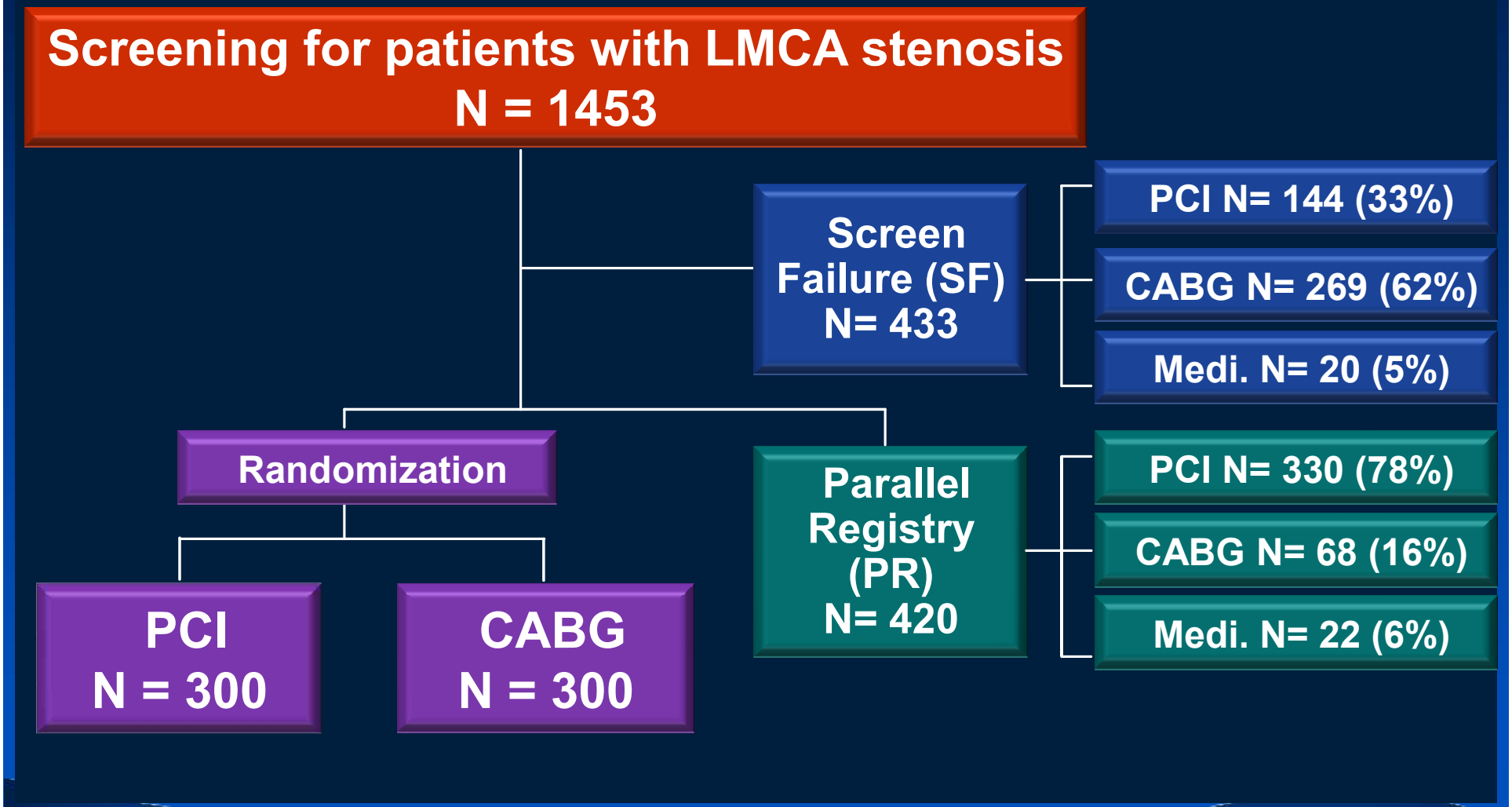
PRECOMBAT Study Design



PRIMARY Endpoint: 2-year MACCE (Death/MI/Stroke/TVR)
SECONDARY Endpoints: clinical and angiographic outcomes

PI: Seung-Jung Park
13 centers from Korea

Enrollment (Finished)



Comparison with SYNTAX Patients

	PRECOMBAT (N = 600)	SYNTAX (N = 705)
Age, year	62.1 ± 9.8	65.5 ± 9.9
Male sex, %	73.8	73.8
Diabetes mellitus, %	32.1	22.1
Hypertension , %	53.4	73.5
Hyperlipidemia , %	41.7	75.2
History of smoking, %	46.3	20.9
Total lesion numbers	2.9 ± 1.5	3.2 ± 1.8
Left main + 2 vessel, %	30.0	30.9
Left main + 3 vessel, %	42.0	36.6

PRECOMBAT

- The PRECOMBAT trial is the FIRST randomized clinical trial aimed to compare the safety and effectiveness of DES and CABG for the treatment unprotected LMCA disease with its primary end point of MACCE.

- The final outcome will be available on ACC 2011.

PRECOMBAT-2

***PRE*mier *COM*parison of *B*ypass surgery and *A*ngioplas*T*y-2 Using Everolimus Electing Stent in Patients with Left Main Coronary Disease**

Current Trial

PRE-COMBAT
for unprotected left main disease
Up to 13 cardiac centers in Korea

Randomization of 600 (1:1)

PCI with Cypher N=300

CABG N=300

PRE-COMBAT-2
for unprotected left main disease
Up to 13 cardiac centers in Korea

All patients receiving Xience V For 1 year upto 500

PRECOMBAT-Eligible Cohort

: Pts Meeting Randomization Criteria of 'PRECOMBAT' N = 300

PRECOMBAT-Not Eligible Cohort

N = 200

Primary Endpoint (MACCE): 2-year death, MI, Stroke, and ischemic driven TVR

IRIS - MAIN

(Left ***MAIN*** Disease – ***I***nterventional Cardiology ***R***esearch ***I***ncorporation ***S***ociety)

A Global, Multicenter, and Prospective,
Real World Observational Study

All Patients with Left Main Disease (3,000 pts)

PCI with Any stents (Approximately 1,500 pts)	**CABG** (Approximately 1,500 pts)	**Medical Treatment**

Primary Endpoint: 2-year composite of Death, MI, Stroke, and TVR and annually follow up to 10 years

PI: Seung-Jung Park,MD

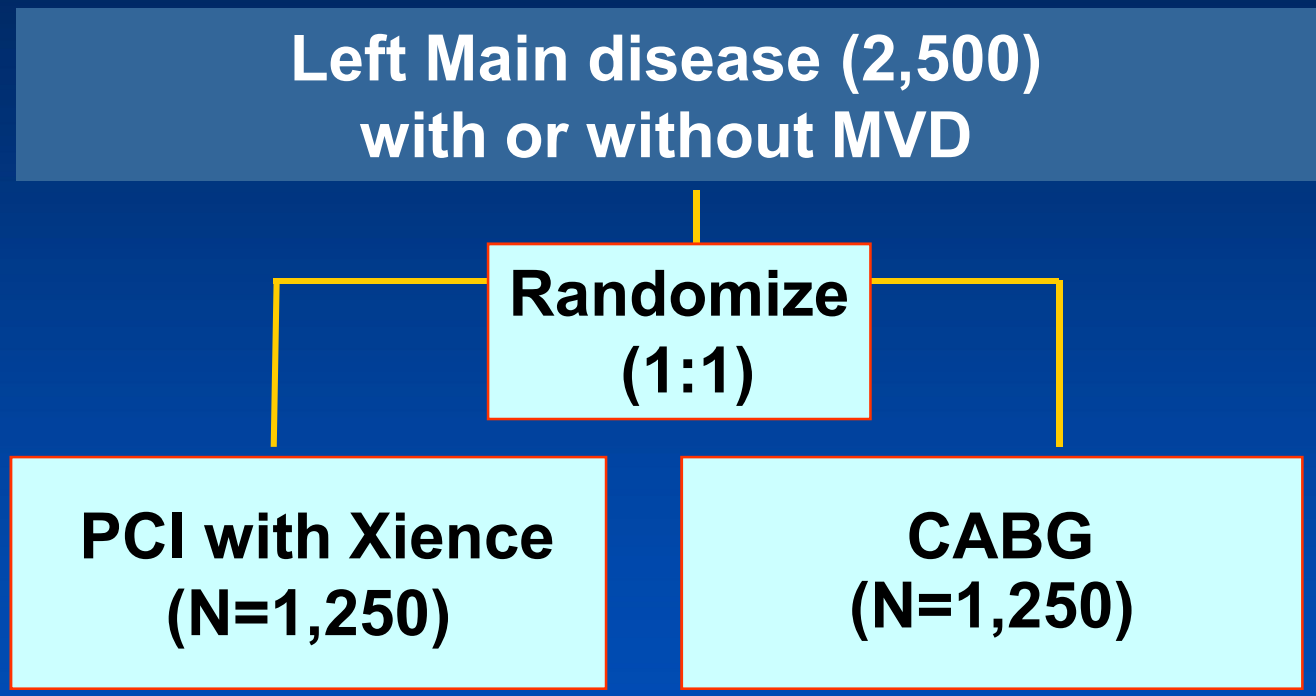
CardioVascular Research Foundation

UNIVERSITY OF ULSAN COLLEGE MEDICINE

ASAN Medical Center

EXCEL Trial

(*E*valuation of *X*ience prime versus *C*oronary artery bypass surgery for *E*ffectiveness of *L*eft main revascularization)



Primary Endpoint: 2-year composite of death, MI, or stroke

PI: Gregg Stone, Patrick Serruys