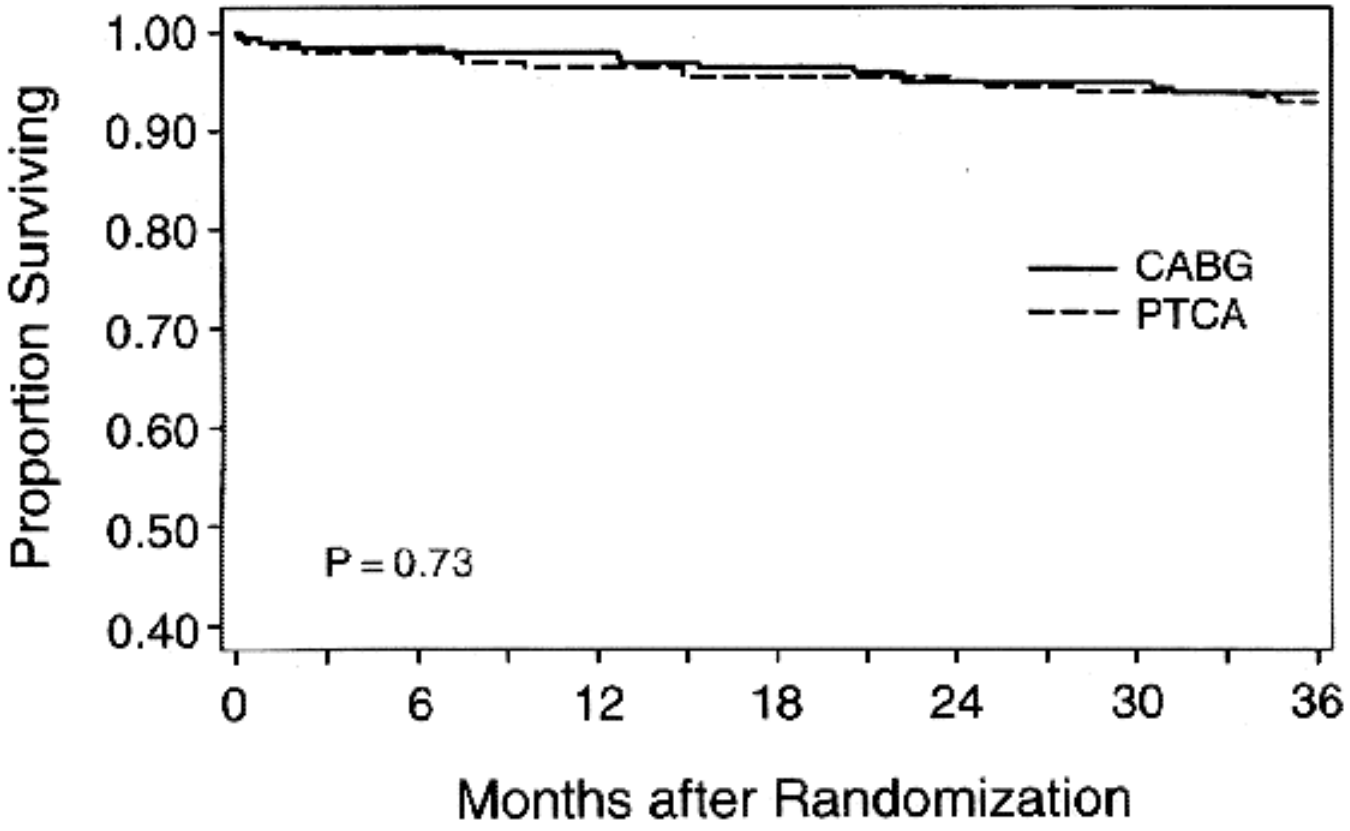
Multi-vessel PCI vs. CABG

William R. Alexis, M.D., M.P.H., F.A.C.C.

EAST

- 392 participants randomized
  - 198 PTCA
  - 194 CABG
  - Average age = 62
  - 74% men
  - 60% with two-vessel disease
  - 40% with three-vessel disease
  - Proximal LAD stenosis in 72%
  - Mean ejection fraction = 61
  - 80% with CCS class III or IV angina

EAST Survival

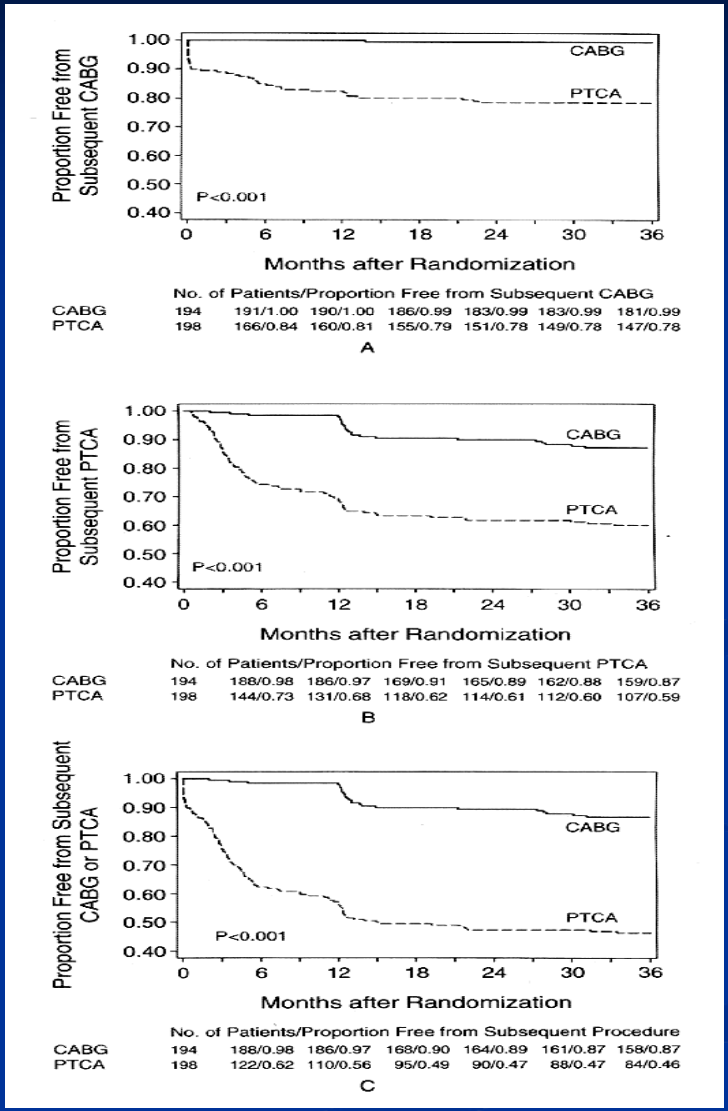


No. of Patients/Proportion Alive

CABG	194	191/0.98	190/0.97	187/0.96	184/0.94	184/0.94	182/0.94
PTCA	198	194/0.97	191/0.95	189/0.95	188/0.94	186/0.93	184/0.93

King SB, et al. NEJM 1994;331:1044-1050

EAST Revascularization



King SB, et al. NEJM 1994;331:1044-1050

EAST
Secondary End Points

- 1% of CABG patients and 22% of PTCA patients underwent additional surgery ($P<0.001$)
- PTCA or surgery required in 13% of the CABG group compared with 54% of the PTCA group ($P<0.001$)
- Most subsequent PTCAs in the PTCA group were performed during the first six months

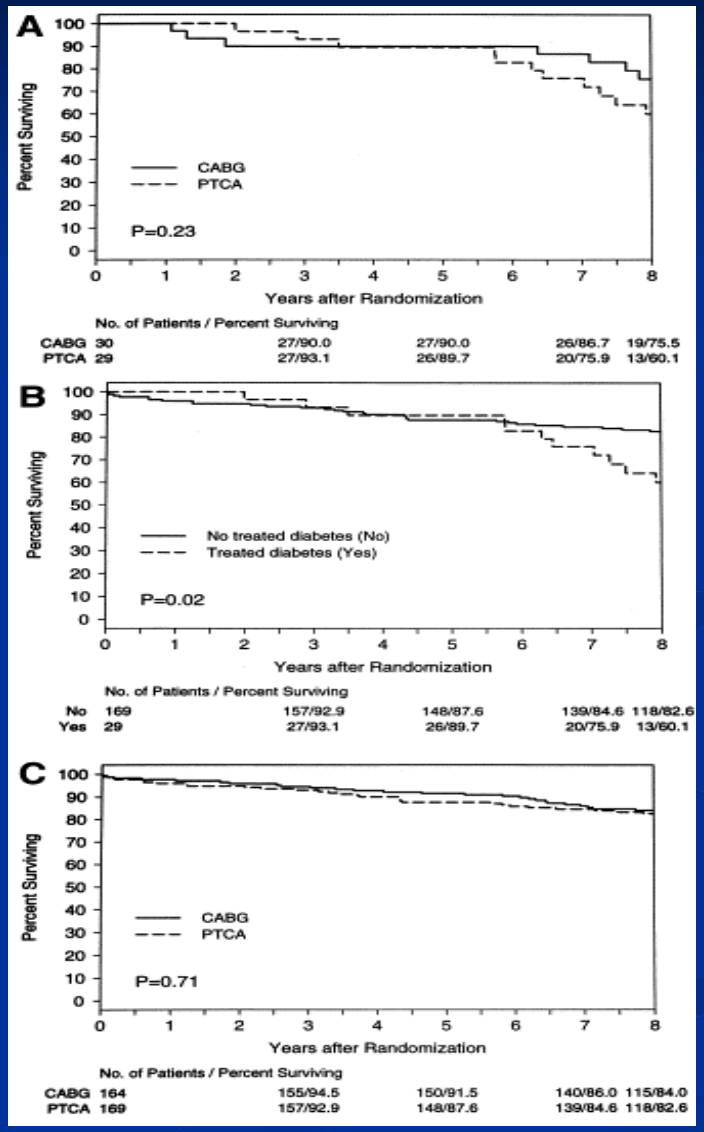
Follow-up Condition

- No difference in ejection fraction (69%)
- 20% of patients in the PTCA group had CCS Class II, III, or IV angina compared to 12% in the CABG group (P=0.039)
- No difference in terms of functional status

EAST
Conclusions

- No difference in the composite end point between the two groups at three years
- Mortality was similar in both groups although the study was insufficiently powered for this outcome
- Main difference was with need for repeat revascularization

EAST 8-Year Follow-up



EAST
8-Year Follow-up

- 100% follow-up
- CABG survival was 82.7% and PTCA survival was 79.3% (P=0.40)
- Slight, non-significant separation of survival curves in favor of surgery for 3-vessel disease
- After five years survival curves separated for diabetics (n=59) and favored surgery

Bypass Angioplasty Revascularization Investigation (BARI)

- Randomized multi center trial of CABG (N=914) vs. PTCA (N=915) in symptomatic patients with multivessel CAD
- Primary end point was mortality from all causes
- No stents used

BARI
Mortality and MI

- 5-year cumulative survival rates were 89.3% for patients assigned to CABG and 86.3% for patients assigned to PTCA (P=0.19)
- 80.4% of CABG patients and 78% of PTCA patients were alive and free from MI at 5 years (P=0.84)

BARI
Repeated Revsacularizations

- 8% of patients CABG patients vs. 54% of PTCA patients underwent revascularization procedures in the first five years
- Most patients in the PTCA group who underwent revascularization did so in the first year of follow-up
- Thus, patients in the PTCA group required more hospitalizations during follow-up compared with the CABG group (2.5 vs. 1.9; $P<0.001$)

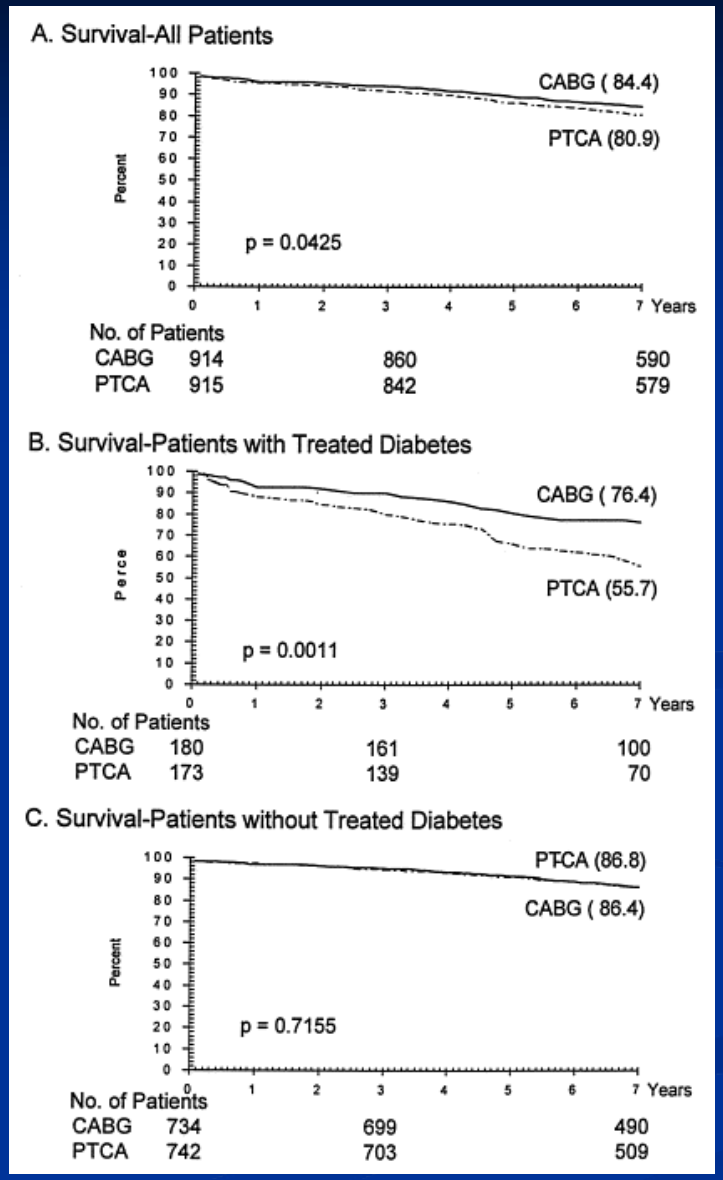
BARI
Mortality within Subgroups

- The only significant difference occurred in the subgroup with diabetes (19%)
- Five year survival was 65.5% among diabetics assigned to PTCA vs. 80.6% among diabetics assigned to CABG

BARI Conclusions

- No statistically significant difference in survival between the two treatment strategies
- Five-year survival free of MI was similar in both treatment groups
- An initial strategy of angioplasty was associated with a substantially greater need for additional revascularization procedures, especially during the first year of follow-up
- Survival was reduced in diabetic patients assigned to PTCA compared with CABG

BARI Survival



JACC 2000;35:1122-9

BARI
Seven-Year Outcome

- Seven-year survival rates for the total population were 84.4% for CABG and 80.9% for PTCA (P=0.043)
- Seven-year survival rates for diabetics (N=353) were 76.4% for CABG and 55.7% for PTCA (P=0.0011)
- Among patients without diabetes cumulative survival was similar
- The diabetic subgroup was the only one with a significant treatment difference at seven years

BARI
Seven-Year Outcome

- Diabetics who received at least one LIMA graft had better seven-year survival compared with those who received only SVGs
- Survival in the diabetic SVG group was nearly identical to that for the diabetic PTCA group
- Among non-diabetics, these three groups had nearly identical survival rates

ARTS Study

DESIGN

- **Randomized comparison of stent vs CABG in 1205 patients with multivessel CAD suitable for either technique with equivalent degree of revascularization**

CABG n = 605

STENT n = 600

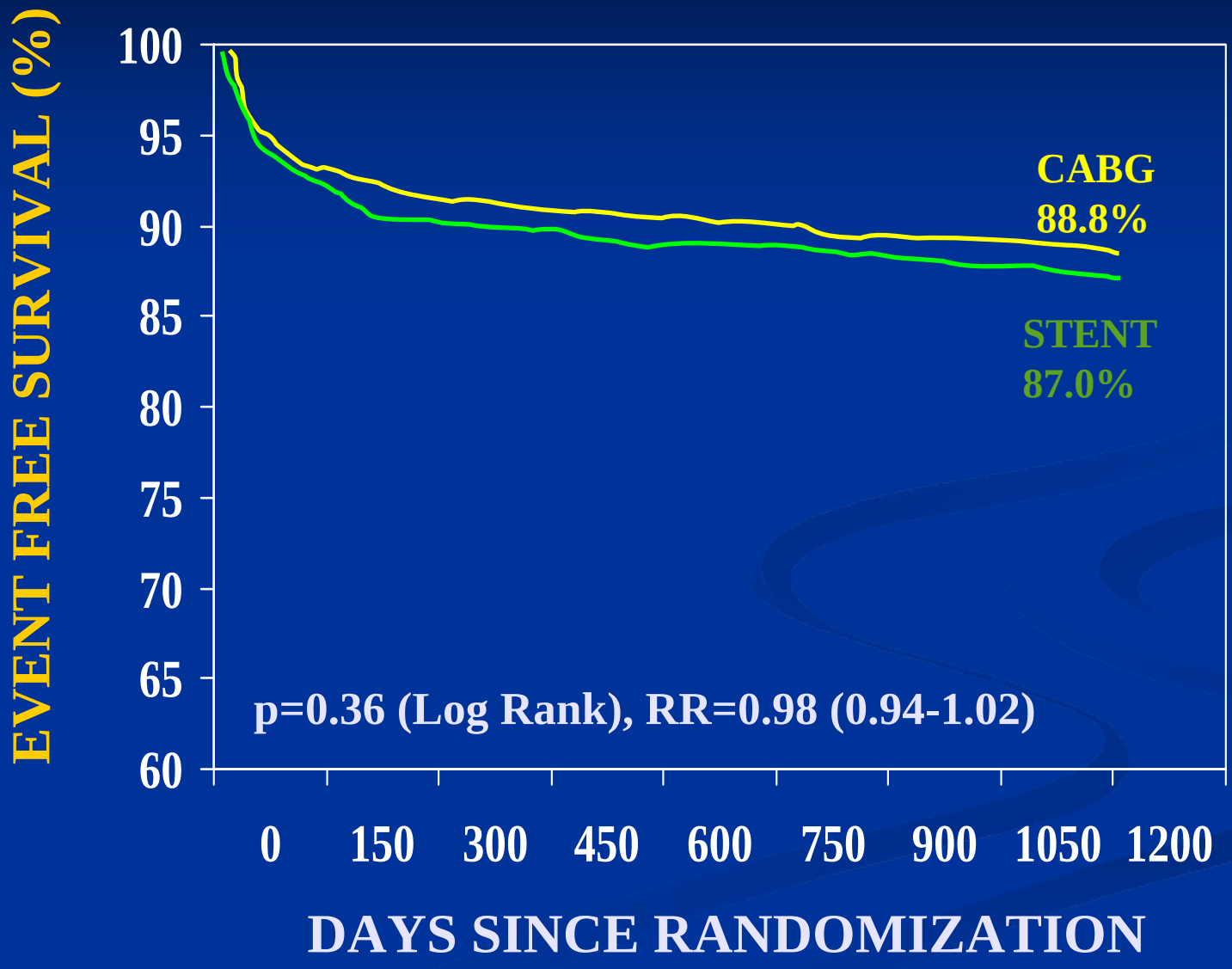
- **Excluded EF <30%, prev CVA, recent MI**
- **1^{O} endpoint =**

  freedom from MACCE (death, MI) and stroke (or TIA, RIND), or repeat revasc. at 12 mos.

Serruys et al, NEJM 2001;344:1117

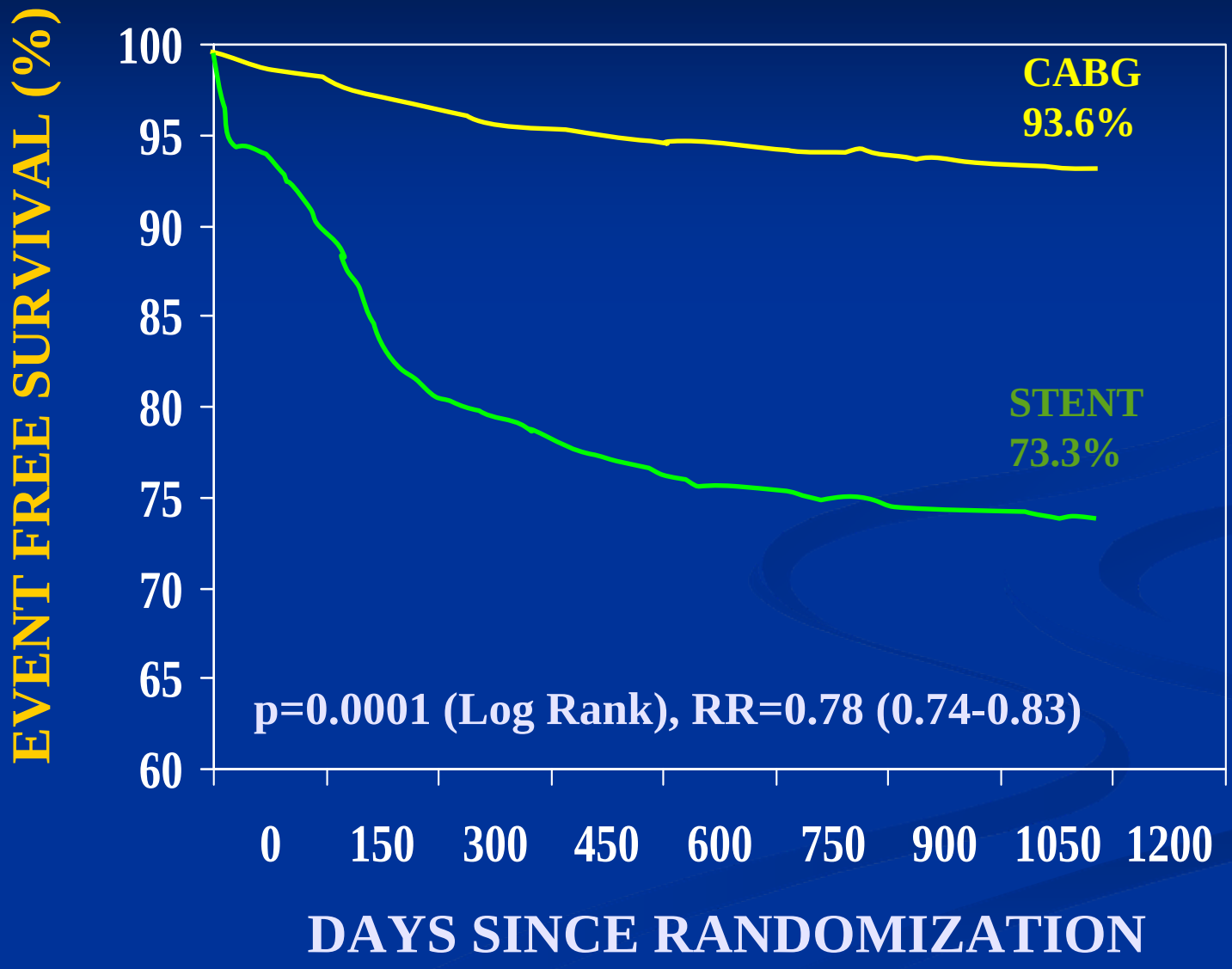
ARTS Study

Death / CVA / MI



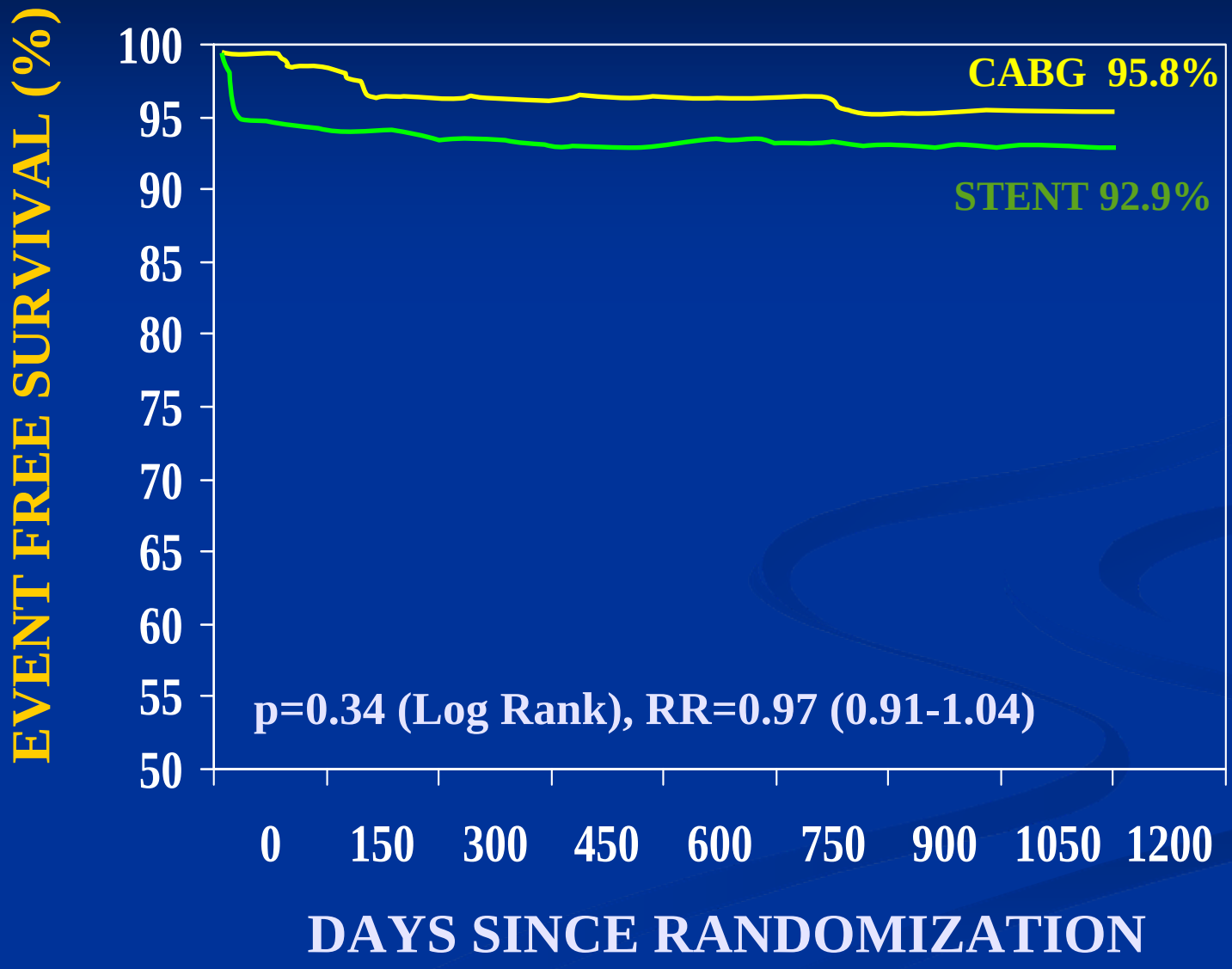
ARTS Study

CABG and Re-PTCA

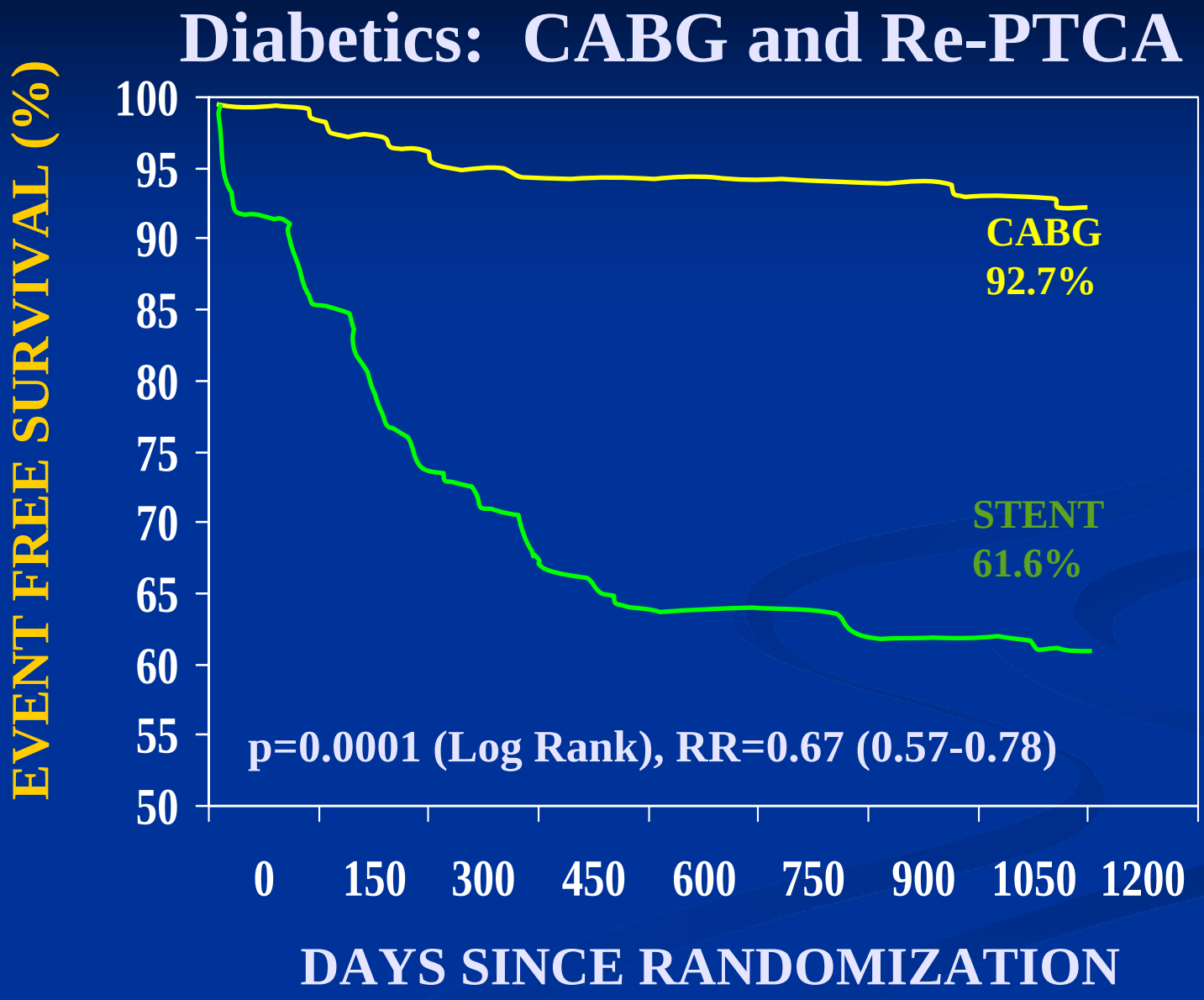


ARTS Study

Diabetics: Death



ARTS Study


Diabetics: CABG and Re-PTCA
EVENT FREE SURVIVAL (%)
100
95
90
85
80
75
70
65
60
55
50
CABG
92.7%
STENT
61.6%
p=0.0001 (Log Rank), RR=0.67 (0.57-0.78)
0
150
300
450
600
750
900
1050
1200
DAYS SINCE RANDOMIZATION

ANGINA at 2 and 3 Year F/U

	Stent		CABG	
	2 years	*3 years*	*2 years*	*3 years*
None	79.6%	81.6%	87.3%	87.0%
Unstable	0.4%	1.2%	0.2%	0.4%
Stable	19.0%	16.5%	12.1%	11.7%
Silent	1.1%	0.7%	0.4%	0.9%
All	N = 553	N=569	N=529	N=554

Conclusion

- Diabetic patients show poor clinical outcome in the stent group when compared to the CABG group.

- Consequently surgery may be preferable to stenting in diabetic patients with multivessel coronary disease, although surgery carries a significant risk of cerebrovascular accident

Baseline and Procedural Characteristics: ARTS II vs ARTS I Patients

Baseline Characteristics	ARTS II (n=607)	ARTS I	
		CABG (n=605)	PCI (n=600)
Age (years)	62	61	61
Female (%)	77	76	77
Triple-vessel disease (%)	54	33	30
Diabetes (%)	26	16	19
Insulin dependant (%)	4.6	2.6	3.8
Hypertension (%)	67	45	45
Hyperlipidemia (%)	74	58	58
Current smoker (%)	19	26	28
Procedural Characteristics			
GP IIb/IIIa inhibitors (%)	33	0	0
Stent per patient ratio	3.7±1.5	NA	2.8±1.3
CK-MB >5 UNL (%) periprocedural release	1.5	12.7	6.2

CABG=coronary artery bypass graft; PCI=percutaneous coronary intervention; NA=not applicable

One-year event-free survival outcomes in the ARTS trials

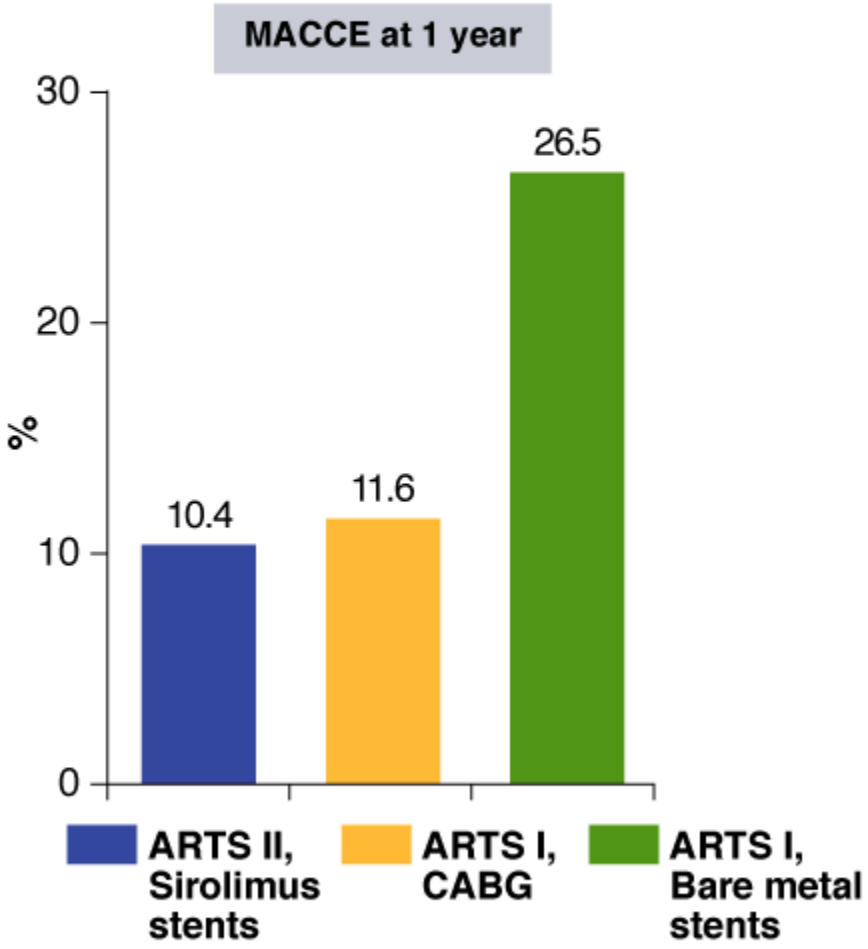
End point	ARTS II, n=607 (%)	p, ARTS II vs ARTS I CABG	ARTS I CABG, n=602 (%)	ARTS I PCI, n=600 (%)
Survival free from death/CVE/MI	96.9	<0.001	92.0	90.7
Survival free from reintervention	91.5	0.003	95.9	78.1
Survival free from MACCE*	89.5	0.46	88.5	73.7

*Primary end point. CVE=cerebrovascular event. MACCE=major adverse cardiac and cerebrovascular events

Serruys P. American College of Cardiology 2005 Scientific Sessions; March 6-9, 2005; Orlando, FL.

ARTS-II

Trial Design: ARTS-II was a non-randomized, open-label study of treatment with sirolimus-eluting stents (SES) compared with historical controls in the ARTS 1 trial of patients undergoing revascularization with CABG or bare metal stents (BMS) in patients with multivessel disease.



Results

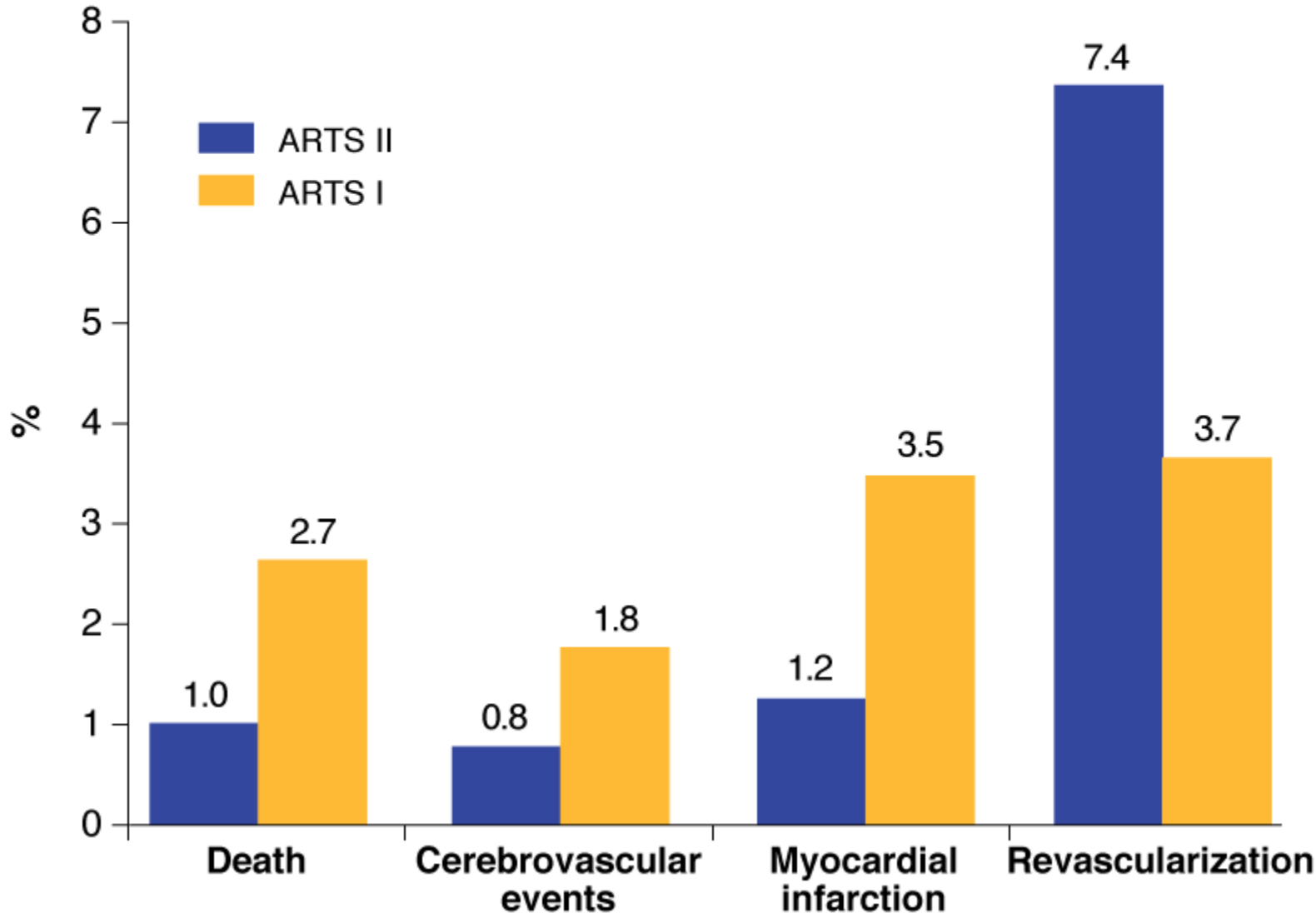
- Baseline differences found when comparing ARTS 2 to ARTS 1
- At 1 year, no difference in major adverse cardiac and cerebrovascular events (MACCE) comparing ARTS 2 SES registry patients with CABG randomized patients in ARTS 1 trial but MACCE ↓ in ARTS 2 SES vs BMS patients in ARTS 1 (Figure)
- Also no difference in 1 year death (1.0% for ARTS 2 registry SES patients vs 2.7% for ARTS 1 CABG patients), cerebrovascular events (0.8% vs 1.8%), MI (1.2% vs 3.5%), or revascularization with CABG (2.0% vs 0.7%) or PCI (5.4% vs 3.0%)

Conclusions

- Among patients suitable for either CABG or PCI, this registry experience demonstrates that sirolimus-eluting stent placement was associated with a low need for repeat revascularization
- However, given the registry, non-randomized nature of study and comparison to historical controls, conclusions cannot be made about the superiority of one approach over another

Presented at ACC 2005

Differences in 1-Year Event Rates for ARTS II Sirolimus-Eluting Stent Patients vs. CABG Arm of ARTS I



ARTS Diabetic Subgroup: 12-Month Data

	ARTS II CYPHER® Stent	ARTS I Surgical
Death	2.5%	3.1%
CVA	0.0	5.2%
Myocardial infarction	0.6%	2.1%
MACCE*	15.7%	14.6%

*Primary endpoint

CVA=cerebrovascular accident; MACCE=major adverse cardiac and cerebrovascular events

Observational Studies

- The NYS Database suggested superior outcomes for CABG when compared to PCI with DES
  - Controversial given non-randomized study design susceptible to bias
  - Safety issues driven by "Stent thrombosis"
  - Possibly a true reflection of "The real world" experience of cardiovascular physicians

Optimal revascularization strategy in patients with three-vessel disease and/or left main disease

The 2-year Outcomes of the SYNTAX Trial

A. Pieter Kappetein, MD PhD
Erasmus MC, Rotterdam, NL
On behalf of the SYNTAX investigators

Clinical Trial Update III
2 September 2009, Room Barcelona Zone 2
9:24 AM to 9:37 AM

Conflicts of Interest: None

SYNTAX Study Objectives

- With technological advances and changes in clinical practice, the respective values of coronary artery bypass surgery and percutaneous coronary intervention needed to be reassessed

- The SYNTAX randomized trial is an attempt to provide an evidence base to determine the best treatment option for patients in a real-world population seen by the surgeon and the interventional cardiologist in their daily practice

SYNTAX Trial Design

62 EU Sites +  23 US Sites

De novo 3VD and/or LM (isolated, +1,2,3 VD)

Limited Exclusion Criteria

Previous interventions , Acute MI with CPK>2x, Concomitant cardiac surgery

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

Patient Profiling

Local Heart team (surgeon & interventional cardiologist) assessed each patient with regards to:

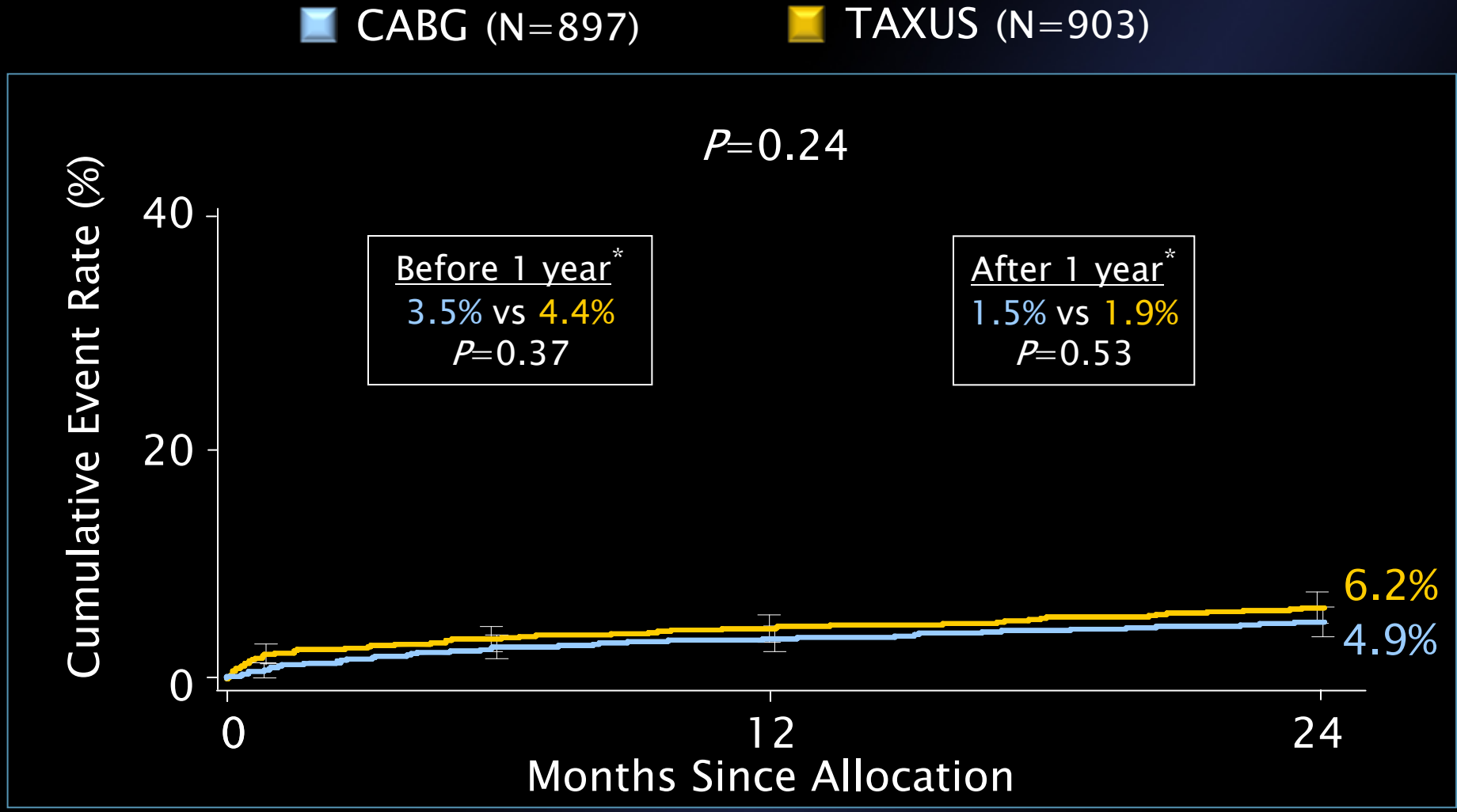
- Patient's operative risk (euroSCO
- Coronary (Newly d Score)
- Goal: SYNTAX score to provide guidance on optimal revascularization strategies for patients with high risk lesions

www.syntaxscore.com
available now

Sianos et al, EuroIntervention 2005;1:219-27
Valgimigli et al, Am J Cardiol 2007;99:1072-81
Serruys et al, EuroIntervention 2007;3:450-9

Coronary tree segments AHA classification and modified for the ARTS study, Circulation 1975; 51:5-40 & Semin Interv Cardiol 1999; 4:209-19
Modified Leaman score, Circ 1981;63:285-92
Lesions classification ACC/AHA , Circ 2001;103:3019-41
Bifurcation classification, CCI 2000;49:274-83
CTO classification, J Am Coll Cardiol 1997;30:649-56

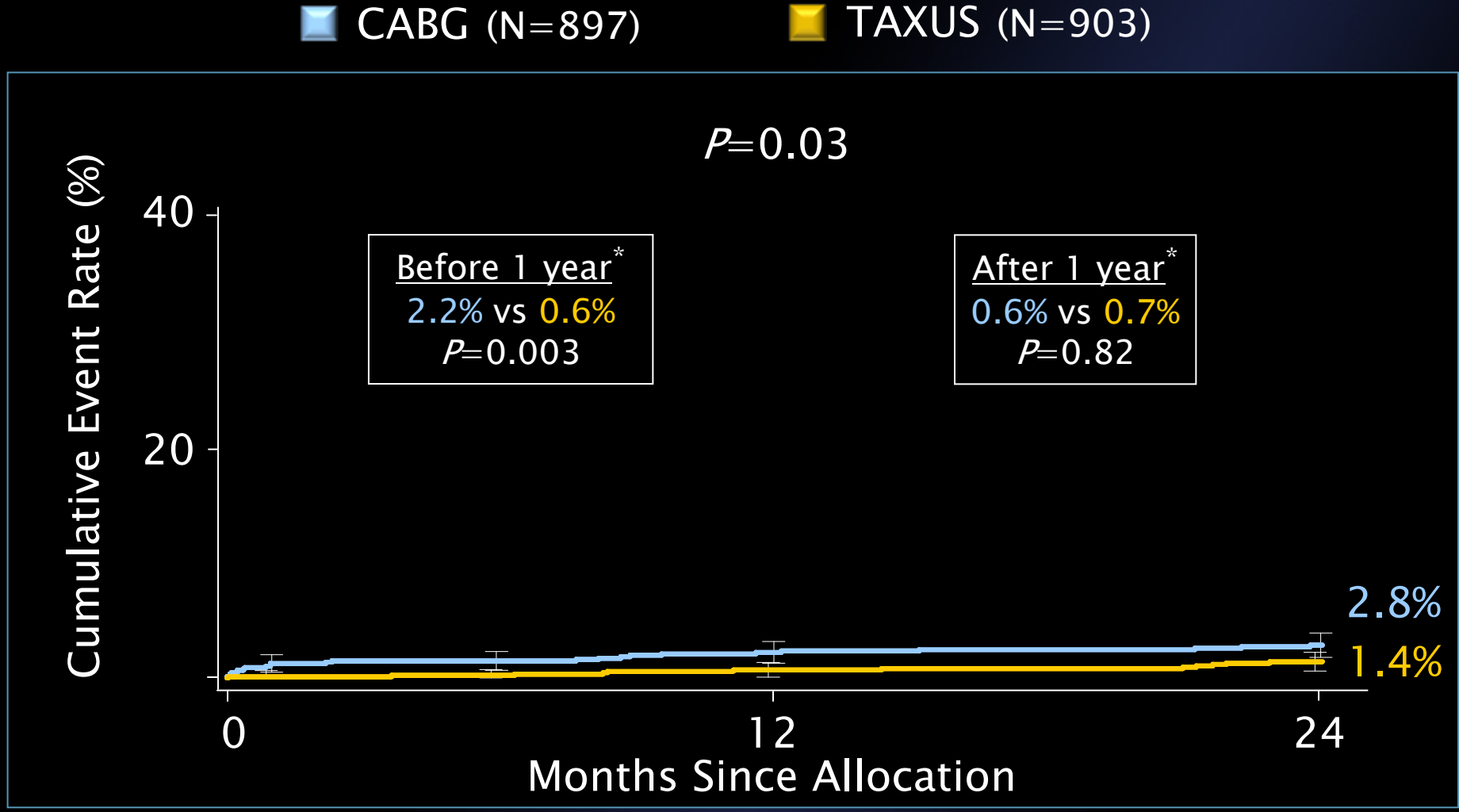
All-Cause Death to 2 Years



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

ITT population

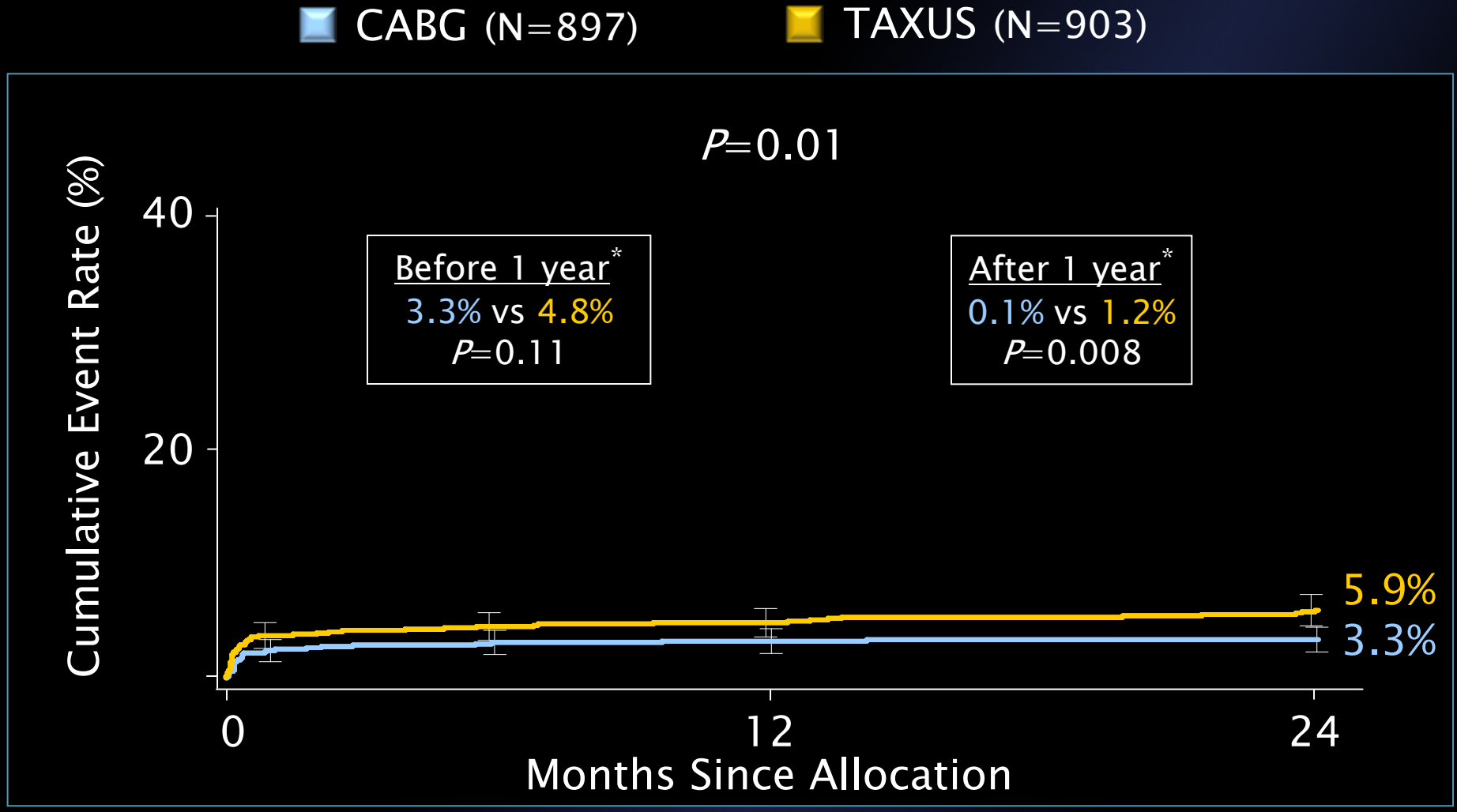
CVA to 2 Years



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

ITT population

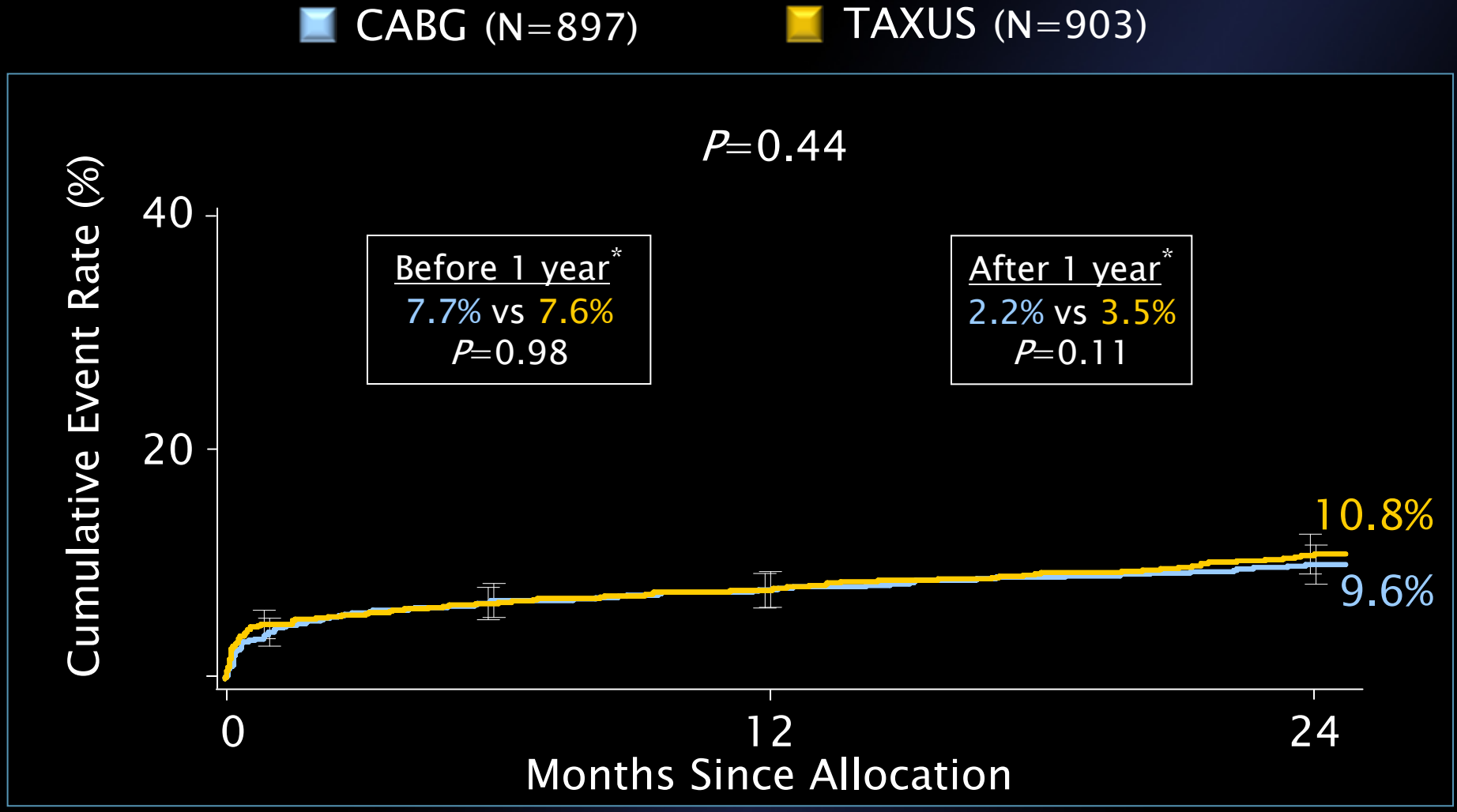
Myocardial Infarction to 2 Years



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

ITT population

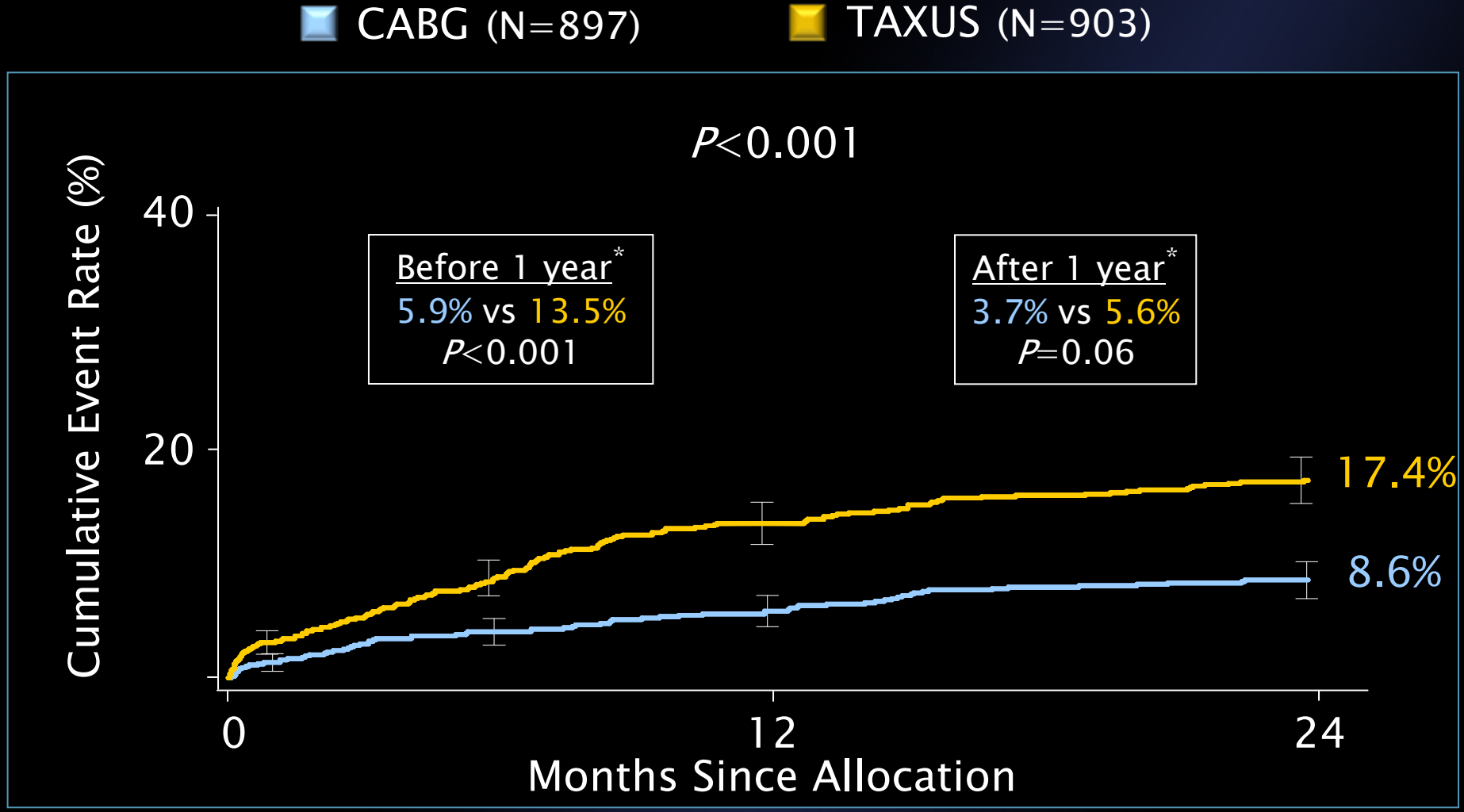
All-Cause Death/CVA/MI to 2 Years



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

ITT population

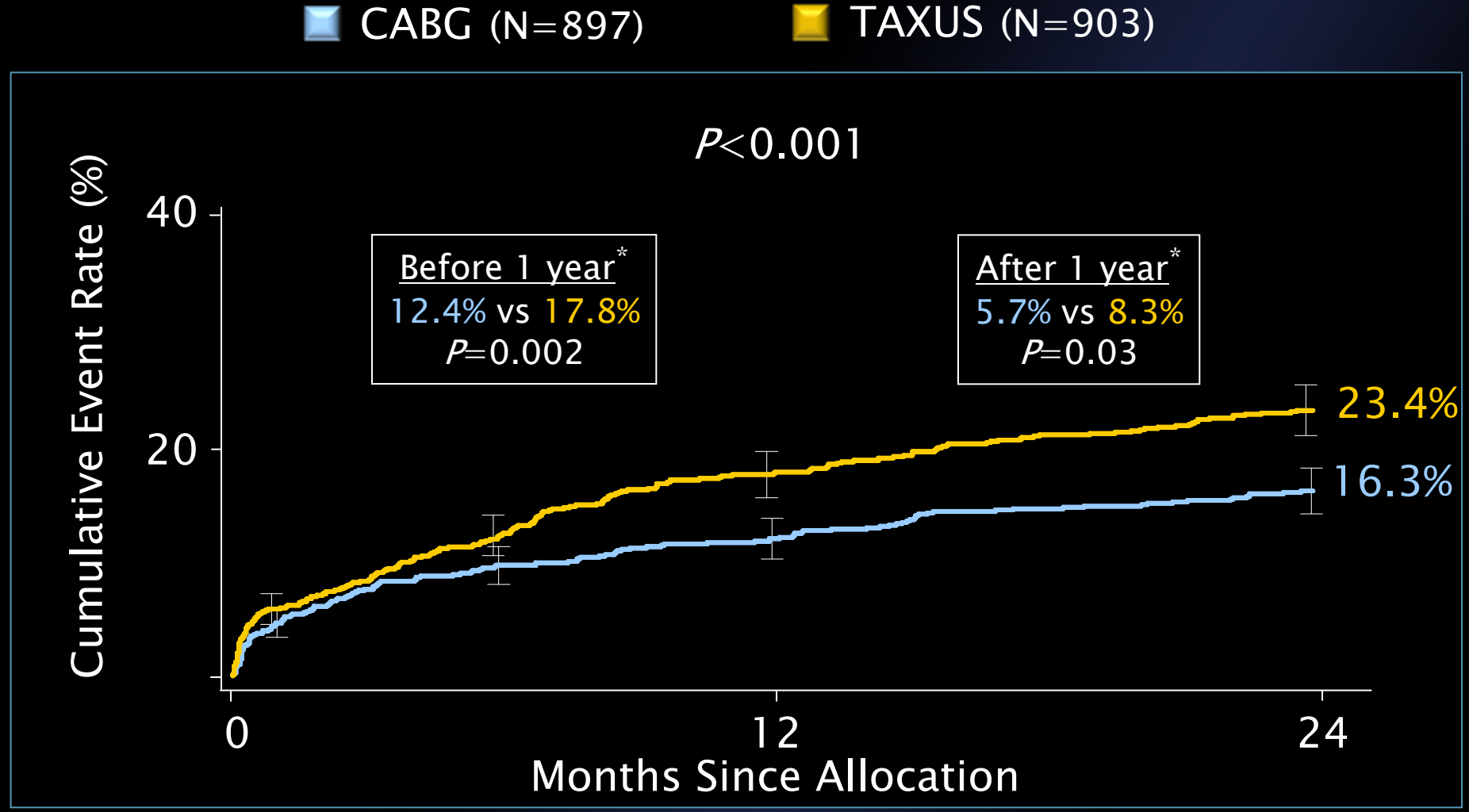
Repeat Revascularization to 2 Years



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

ITT population

MACCE to 2 Years

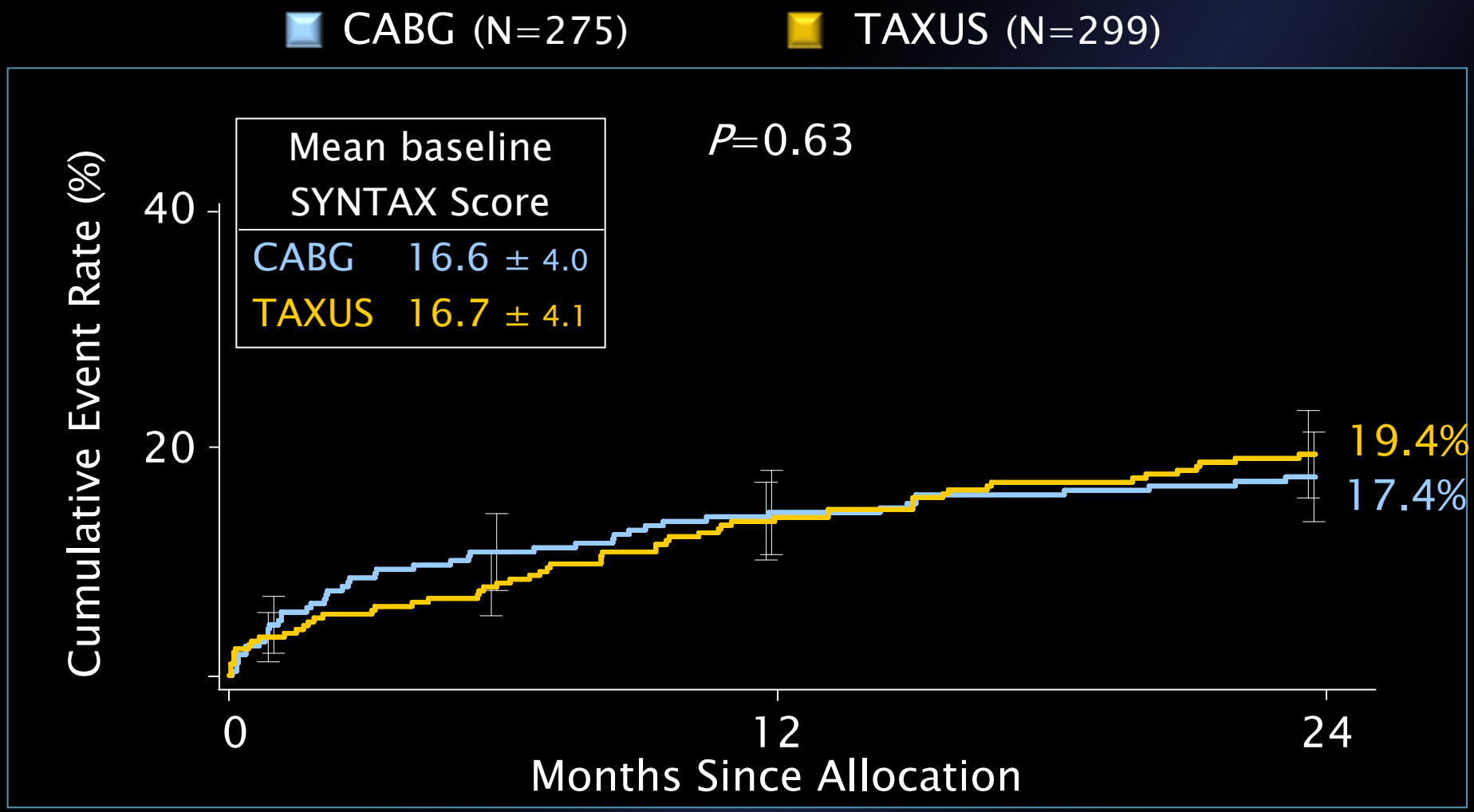


Cumulative KM Event Rate ± 1.5 SE; log-rank *P* value;*Binary rates

ITT population

MACCE to 2 Years by SYNTAX Score Tercile

Low Scores (0–22)

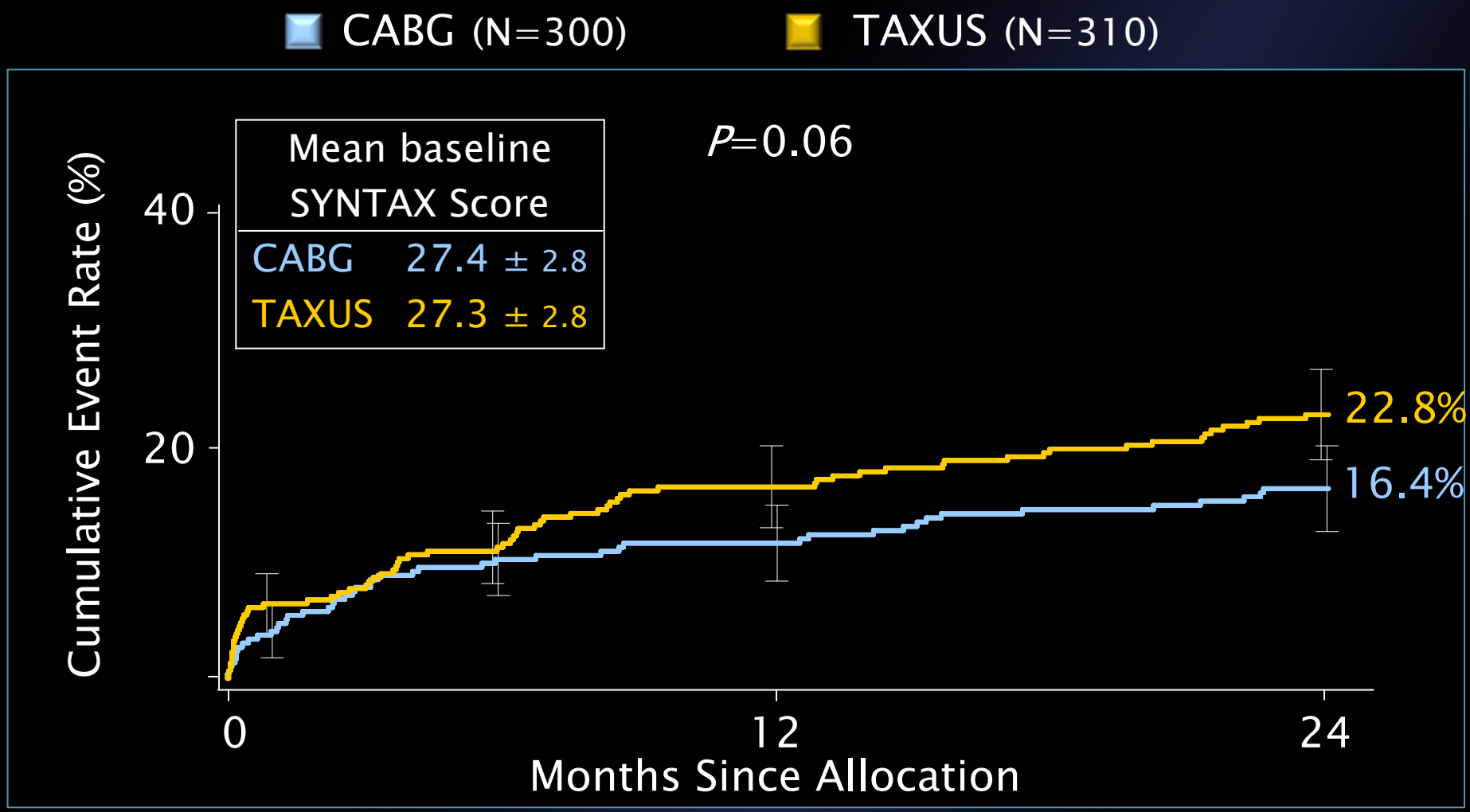


Cumulative KM Event Rate ± 1.5 SE; log-rank *P* value

Calculated by core laboratory; ITT population

MACCE to 2 Years by SYNTAX Score Tercile

Intermediate Scores (23–32)

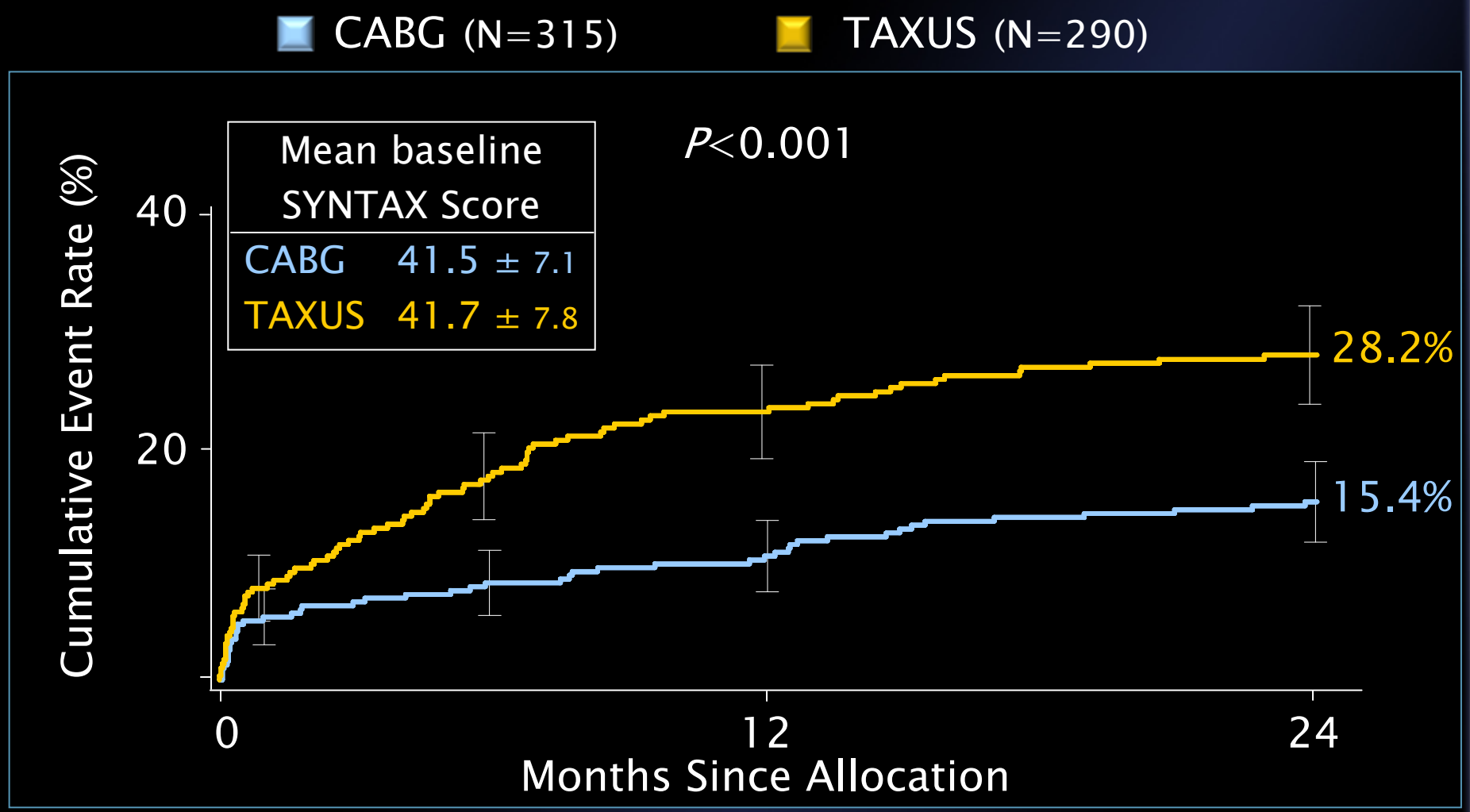


Cumulative KM Event Rate ± 1.5 SE; log-rank *P* value

Calculated by core laboratory; ITT population

MACCE to 2 Years by SYNTAX Score Tercile

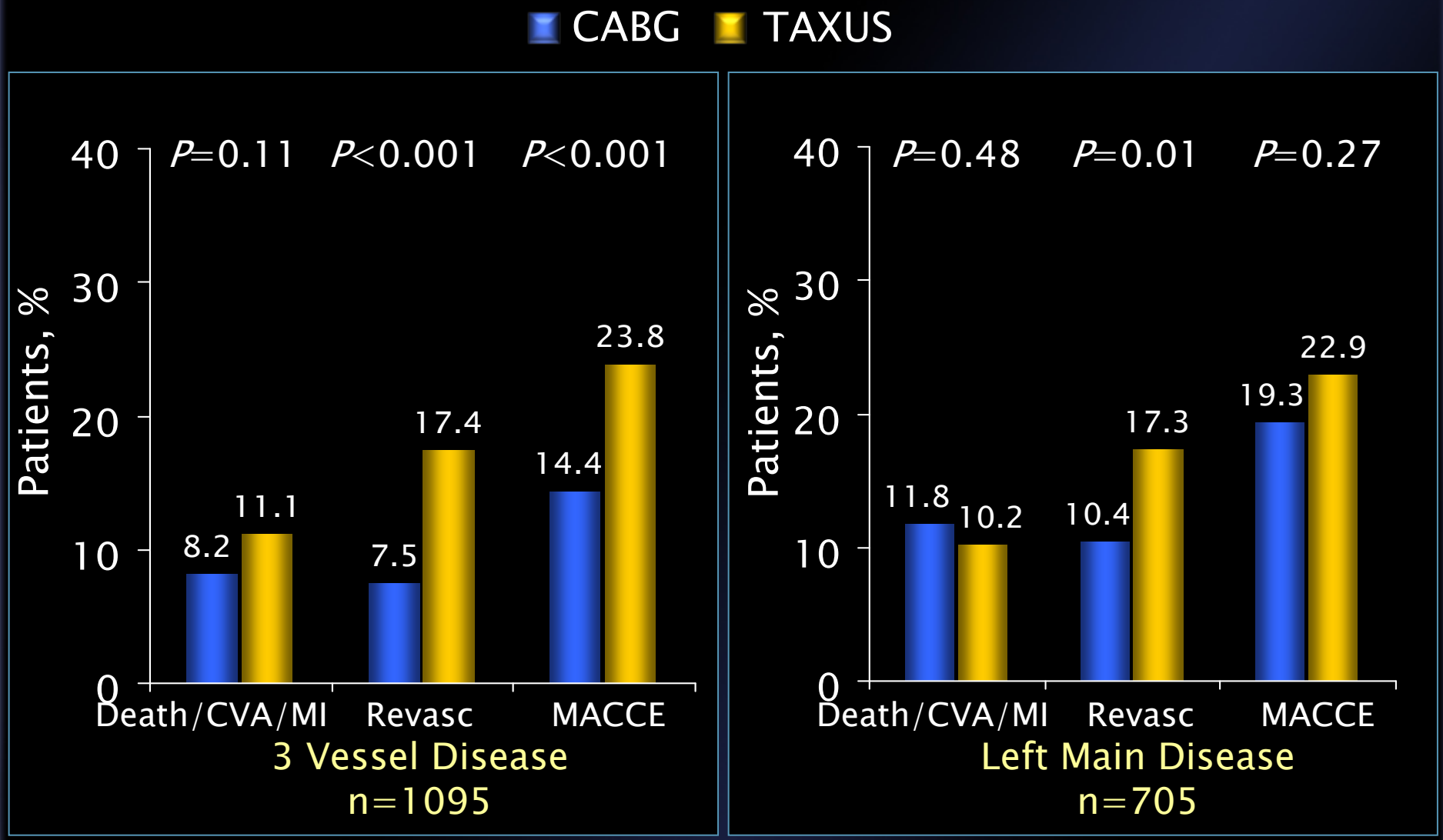
High Scores (≥33)



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

Calculated by core laboratory; ITT population

2 Year Outcomes in 3VD and LM Subgroups

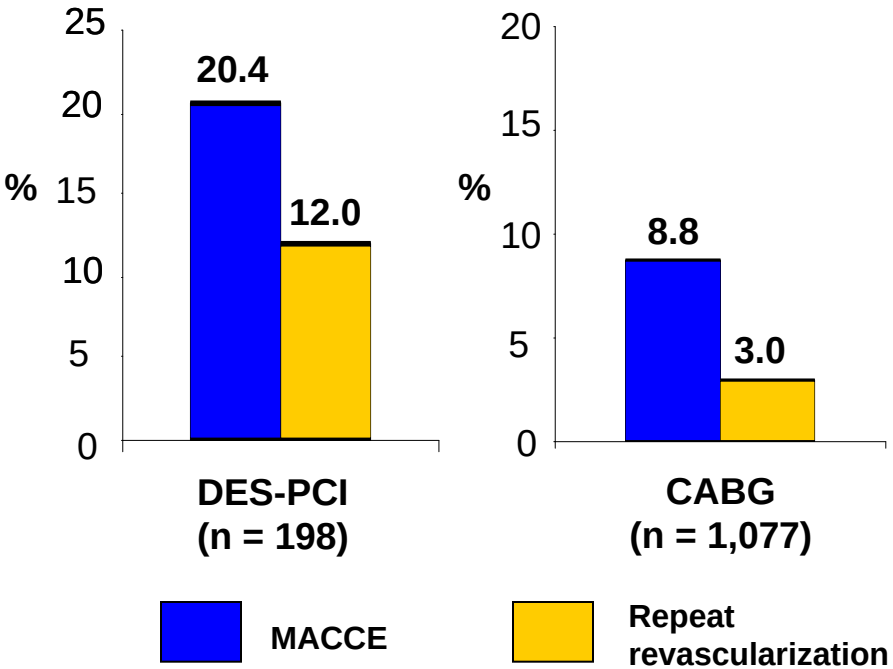


Time-to Event; Log-rank *P* value

ITT population

SYNTAX Registry

Trial design: Patients with severe three-vessel or left main (LM) disease who did not meet criteria for entry into the SYNTAX trial were followed for 12 months in the SYNTAX CABG and PCI registry.



Results

- Main reason for PCI only: inoperable (comorbidities); main reason for CABG only: complex anatomy
- PCI outcomes: MACCE (20.4%), mortality (7.3%), MI (4.2%), repeat revascularization (12%), CVA (0)
- CABG outcomes: MACCE (8.8%), mortality (2.5%), MI (2.5%), repeat revascularization (3%), CVA (2.2%)

Conclusions

- The SYNTAX registry describes outcomes in PCI and CABG in patients not eligible for the SYNTAX trial
- Of all-comers with three-vessel and/or LM disease, 6.4% were considered inoperable; 35% not feasible for PCI

Presented by Dr. Friedrich Mohr at ESC 2008

Summary: I

- In the SYNTAX randomized patients, 2-year MACCE rates were significantly higher for PCI than CABG, mainly driven by higher repeat revascularization in the PCI arm.
  - Significant increase of MI compared to CABG at 2 years driven by higher PCI MI rate between years 1and 2
  - Significantly higher CVA rate in CABG compared to PCI with the majority of CVAs occurring in the first year
  - Composite safety (death/CVA/MI) remains similar between arms at 2 years
- MACCE rates at 2 years not significantly different for patients with a low (0-22) or intermediate (23-32) baseline SYNTAX Score; for patients with high SYNTAX Scores (≥33), MACCE continued to be increased at 2 years in patients treated with PCI

Summary: II

- In the predefined subgroups of patients with either 3VD or LM disease:
  - Safety outcomes (death/CVA/MI) in the 3VD group were similar for PCI and CABG, but the 2-year revascularization and MACCE rates favored CABG.
  - In the LM group, safety outcomes and MACCE rates were similar for PCI and CABG, but the 2-year revascularization rate was lower in the CABG group.
- The 2-year SYNTAX results suggest that CABG remains the standard of care for patients with complex disease (high SYNTAX Scores); however, PCI may be an acceptable alternative revascularization method to CABG when treating patients with less complex (low or intermediate SYNTAX Score) disease.
- SYNTAX patients will continue to be followed for 5 years.

Future Directions

- Hybrid Procedures
  - Combines the best aspects of surgical and percutaneous treatments
    - Minimally invasive LIMA graft with DES to non-LAD lesions
    - Percutaneous intervention to MI culprit lesion followed by CABG
- In contemporary practice, surgeons are becoming more like interventionalists and interventionalists more like surgeons