Is There a Generation Gap of DES: Results of PRECOMBAT Series

Jung-Min Ahn, MD

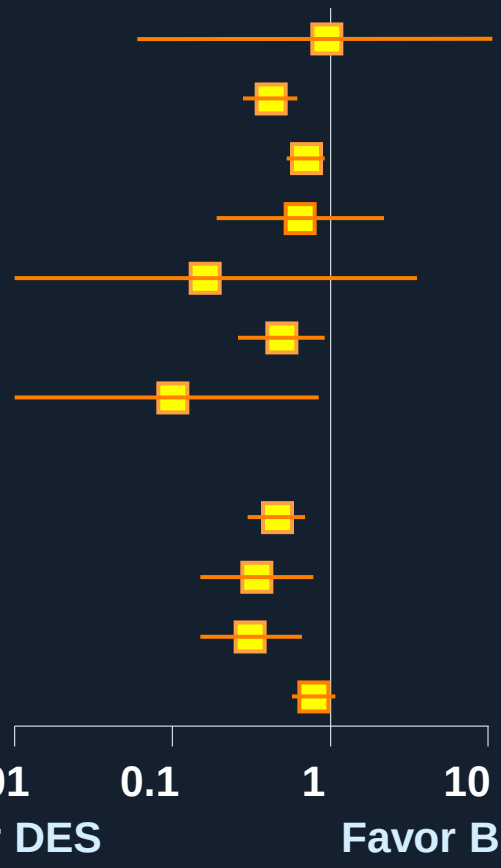
Heart Institute, Asan Medical Center

University of Ulsan, Seoul, Korea

BMS vs. 1st DES for LM

Meta-Analysis from 44 Studies and 10,342 Patients

	Time	DES (N)	BMS (N)	OR (95% CI)	P value
Death	6-12 mon	53	50	0.94(0.06-15.5)	0.97
	2 yrs	1344	496	0.42 (0.28-0.62)	<0.05
	3 yrs	1809	736	0.70 (0.53-0.92)	<0.05
MI	6-12 mon	53	50	0.64 (0.19-2.17)	0.47
	2 yrs	178	109	0.16 (0.01-3.53)	0.13
	3 yrs	611	238	0.49 (0.26-0.92)	<0.05
TVR/TLR	6-12 mon	53	50	0.10 (0.01-0.84)	<0.05
	2 yrs	-	-	-	-
	3 yrs	1809	736	0.46 (0.30-0.69)	<0.05
MACE	6-12 mon	138	114	0.34 (0.15-0.78)	<0.05
	2 yrs	398	333	0.31 (0.15-0.66)	<0.05
	3 yrs	1198	498	0.78 (0.57-1.07)	0.12

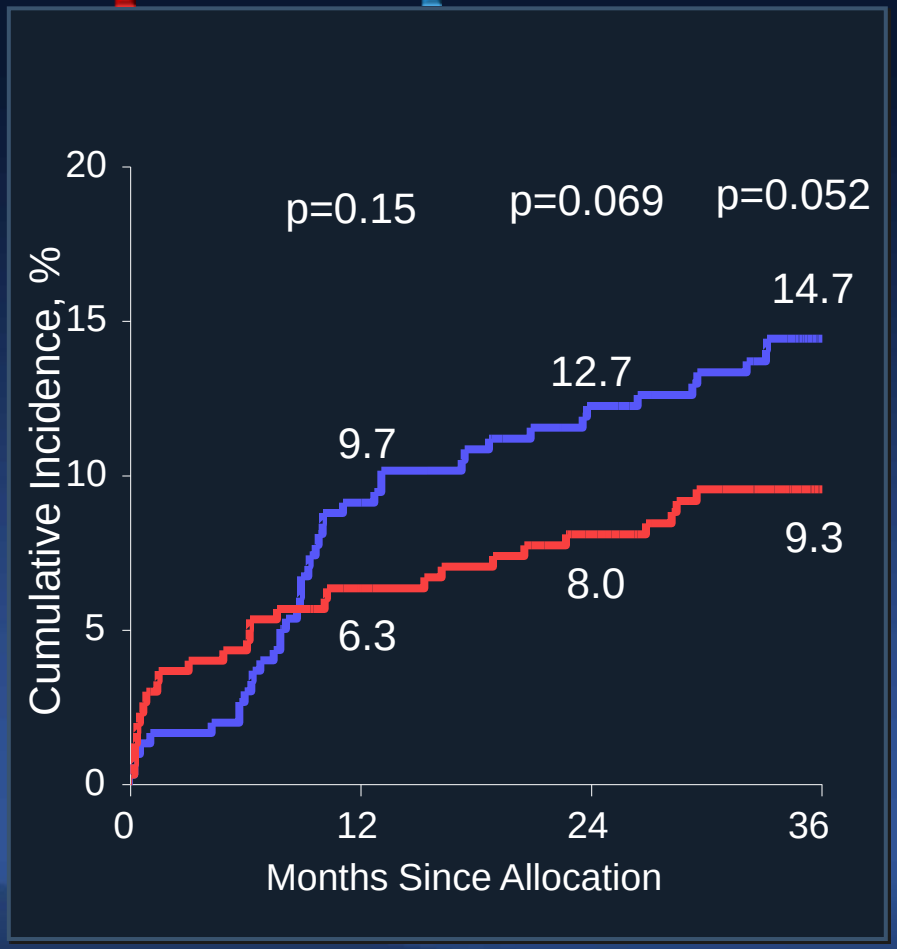


JACC Cardiovasc Interv. 2010 Jun;3(6):602-11

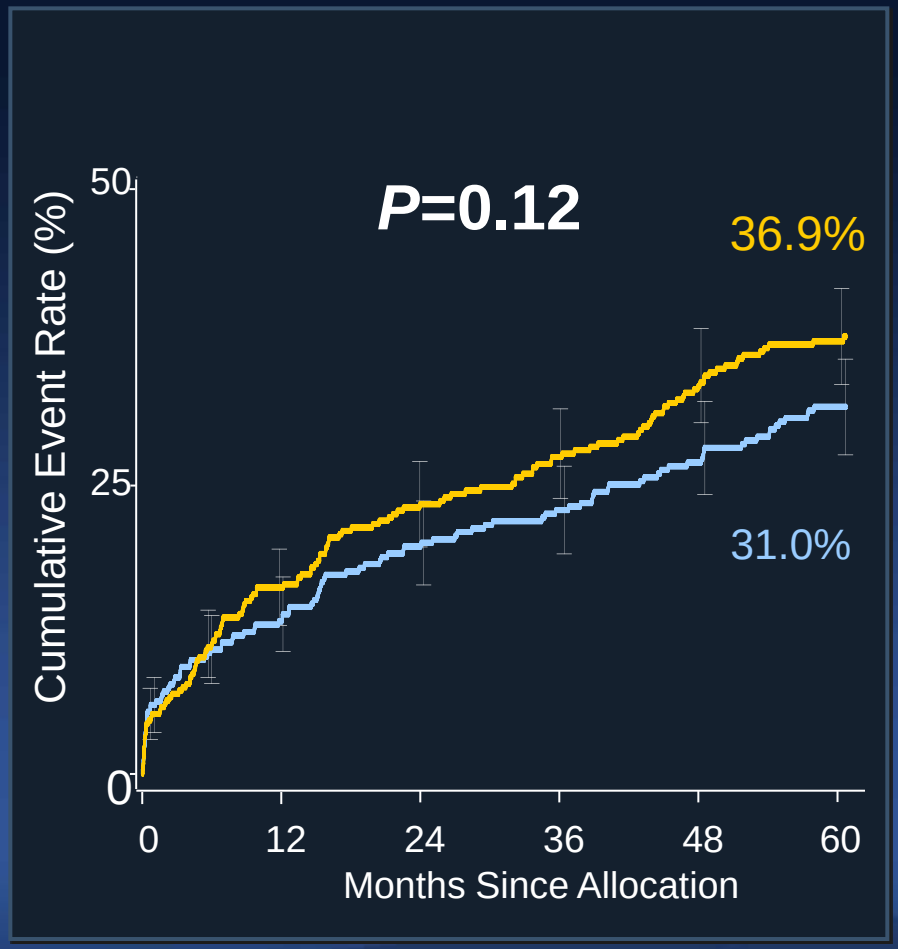
CardioVascular Research Foundation
ASAN Medical Center

LM PCI Guideline (IIa-IIb)

PRECOMBAT



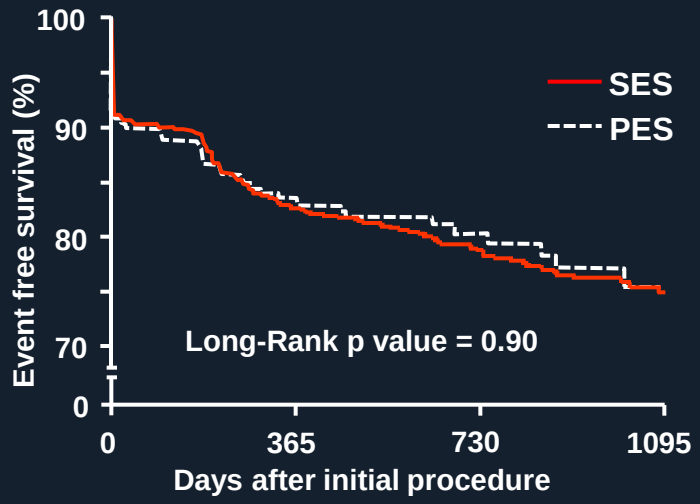
SYNTAX-LM



SES vs. PES for LM

MAINCOMPARE

Death, MI, or TVR



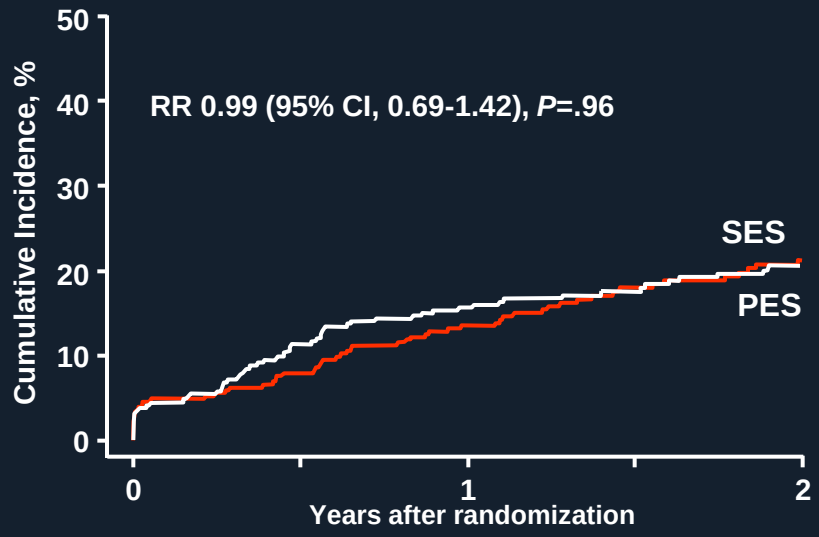
Number at risk

PES	189	153	94	31
SES	669	551	367	169

Lee et al. J Am Coll Cardiol 2009;54:853-9

ISAR LM-1

Death, MI or TVR



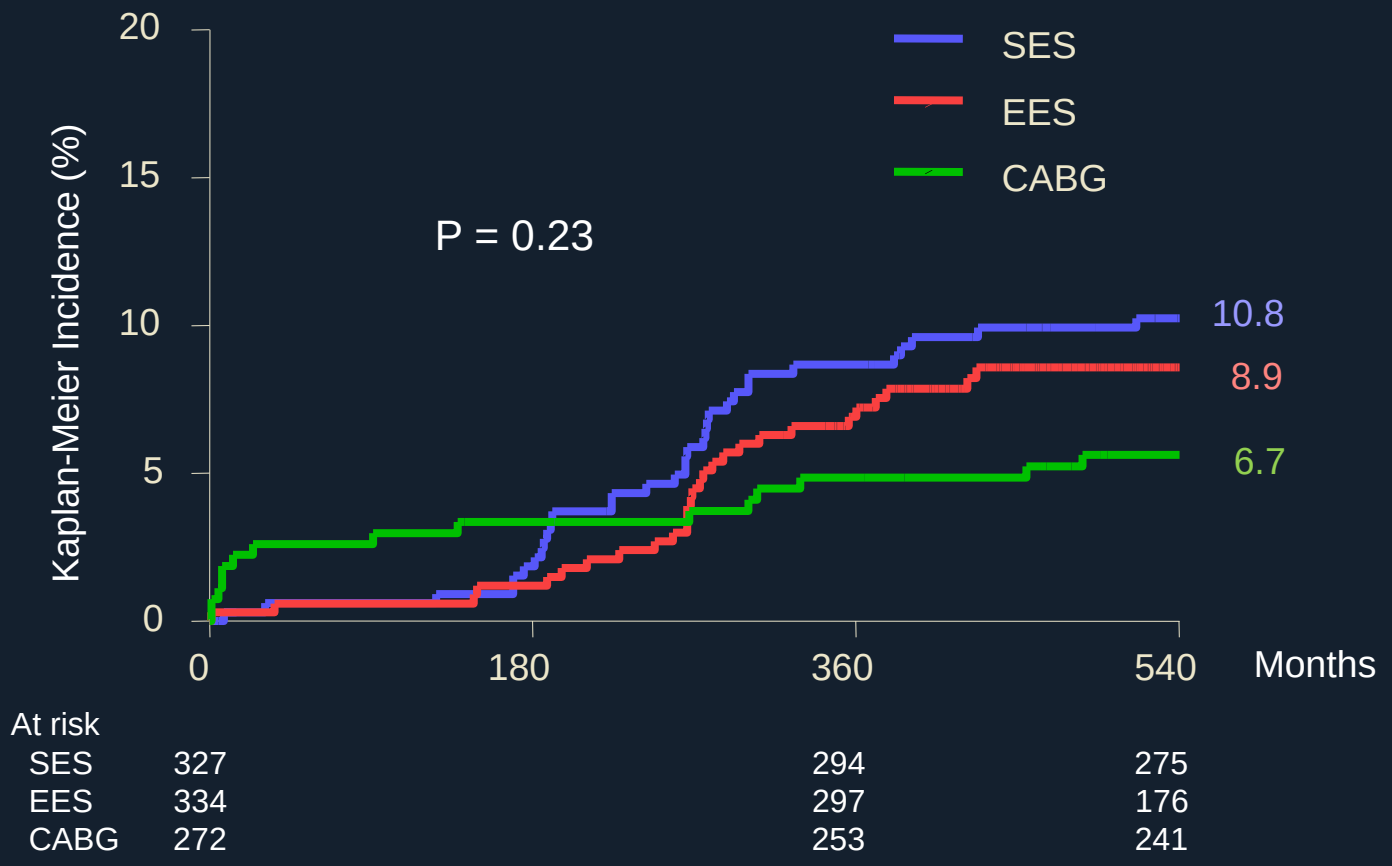
Patients at Risk

PES	302	278	250	189	160
SES	305	271	252	198	176

Mehilli et al. J Am Coll Cardiol 2009; 53:1760-3

1st vs. 2nd DES for LM
PRECOMBAT-2 Study

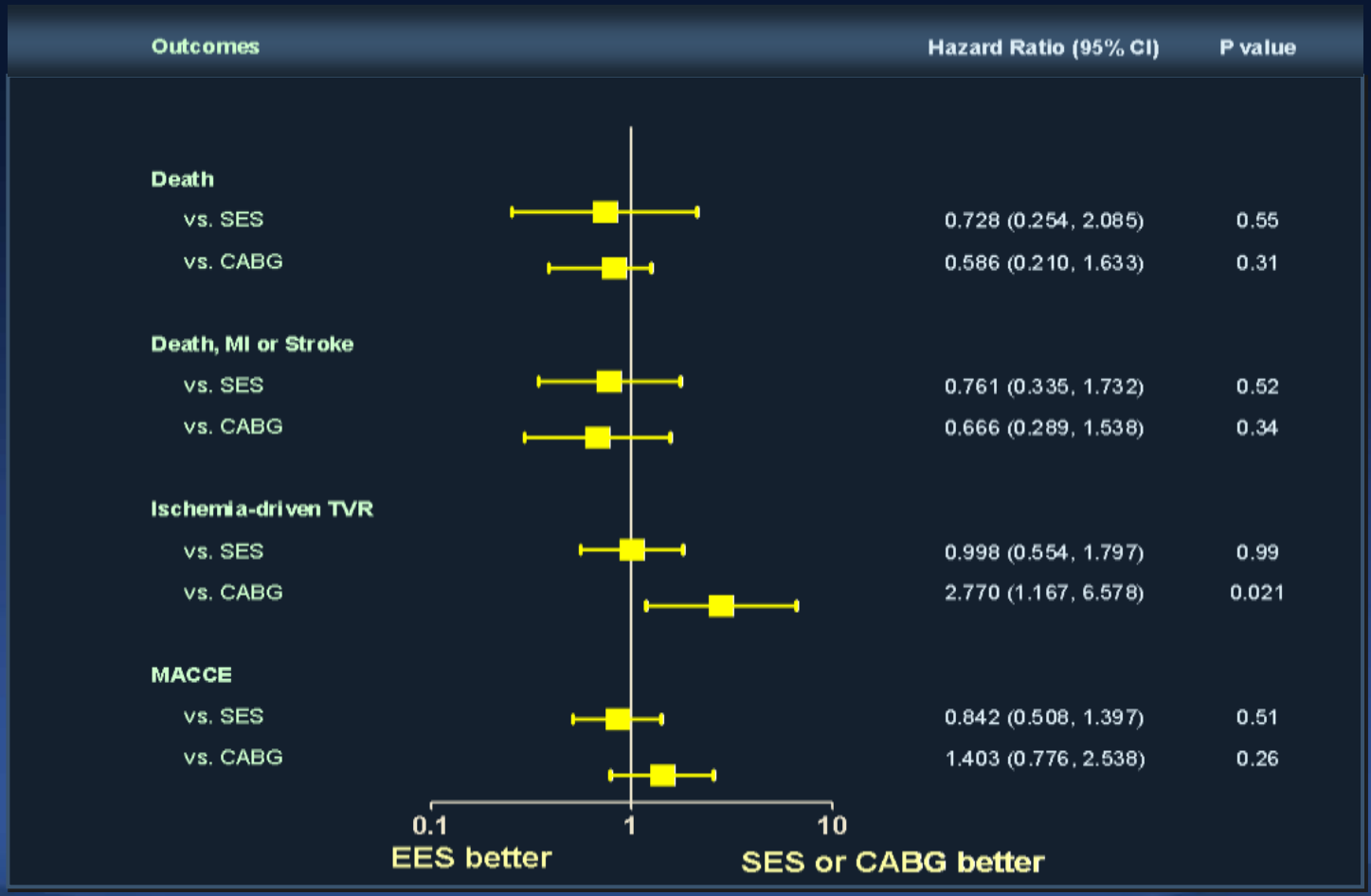
MACCE



Kim YH et al. J Am Coll Cardiol Intv 2012;5:708

1st vs. 2nd DES for LM
PRECOMBAT-2 Study

Hazard Ratios of EES after Adjustment



Kim YH et al. J Am Coll Cardiol Intv 2012;5:708

1st vs. 2nd DES for LM
EXCELLENT registry

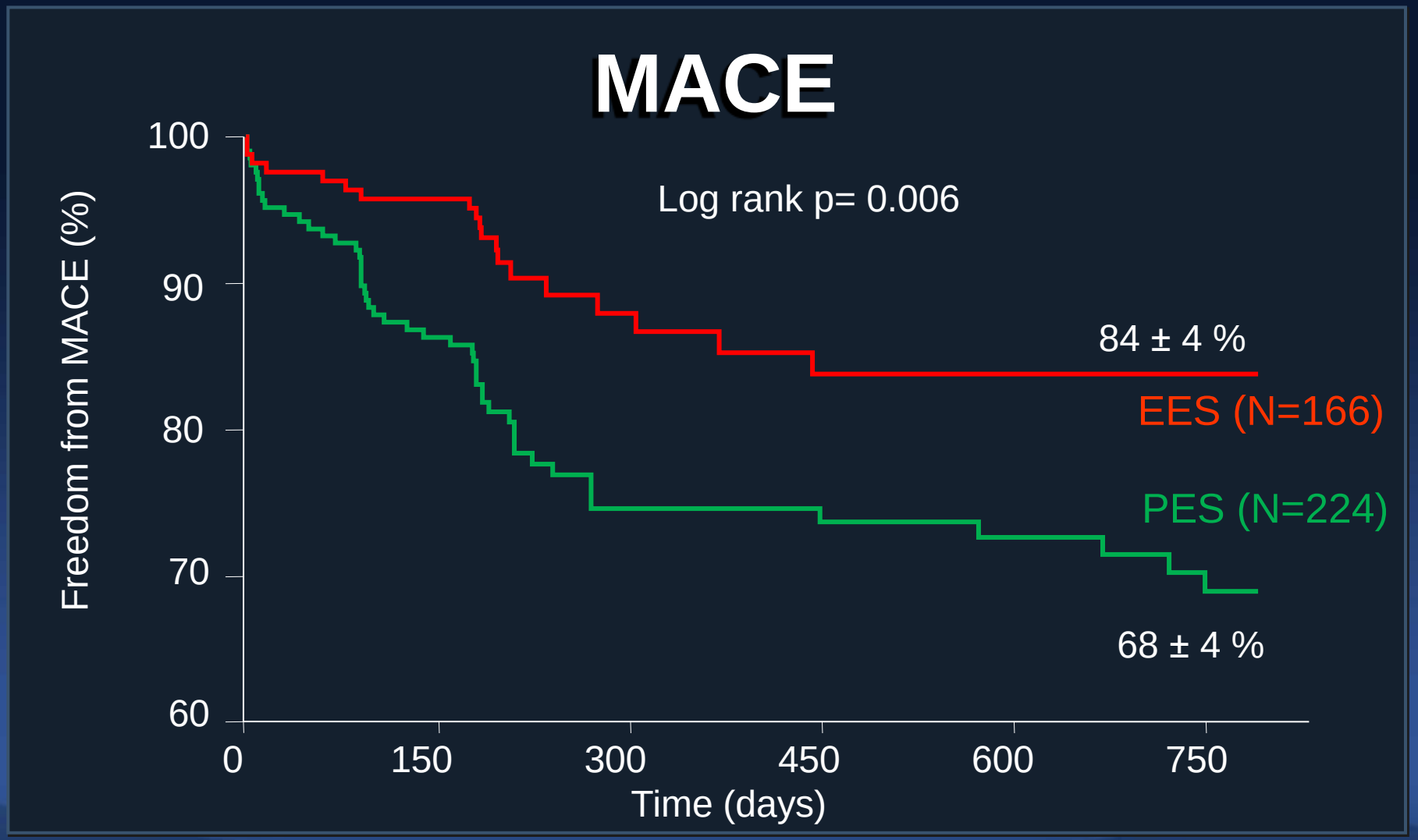
1 Year Outcome

	Events			Propensity Score Adjustment	
	EES (N=160)	SES (N=115)	P value	HR (95% CI)	P value
Death/MI/TVR	12 (7.5%)	16 (13.9%)	0.117	0.43 (0.20-0.95)	**0.037**
Death	7 (4.4%)	8 (7.0%)	0.383	0.52 (0.18-0.51)	0.23
Death/MI	8 (5.0%)	8 (7.0%)	0.529	0.60 (0.21-0.67)	0.323
TVR	4 (2.5%)	8 (7.0%)	0.096	0.28 (0.08-0.98)	0.046

Park KW et al. Int J Cardiol 2013;168:2738-44

1st vs. 2nd DES for LM

PCI Florence Registry

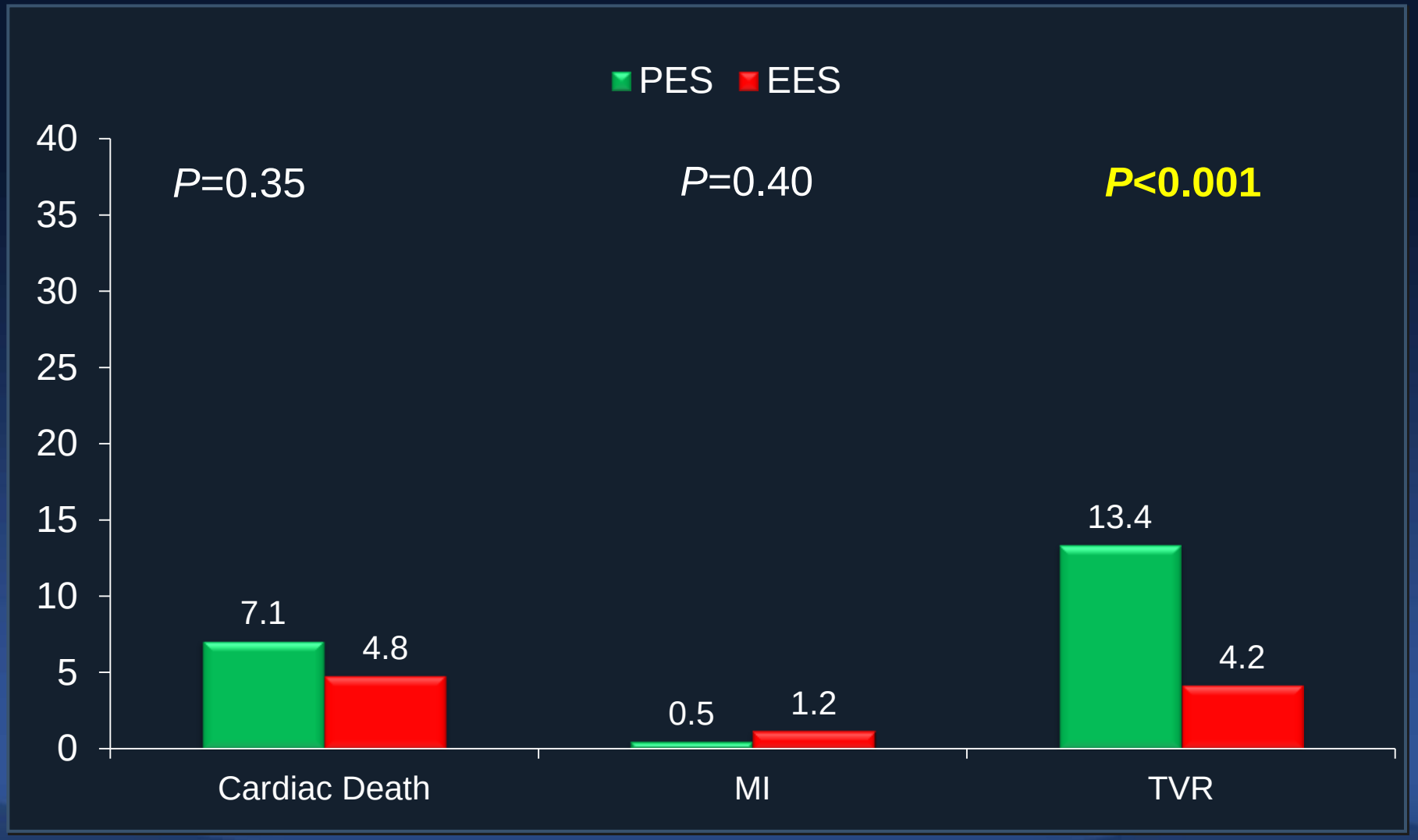


Valenti et al. JACC 2012;60(14):1217-1222

CardioVascular Research Foundation
UNIVERSITY OF ULSAN COLLEGE MEDICINE
ASAN Medical Center

1st vs. 2nd DES for LM

PCI Florence Registry



Valenti et al. JACC 2012;60(14):1217-1222

CardioVascular Research Foundation
UNIVERSITY OF ULSAN COLLEGE MEDICINE
ASAN Medical Center

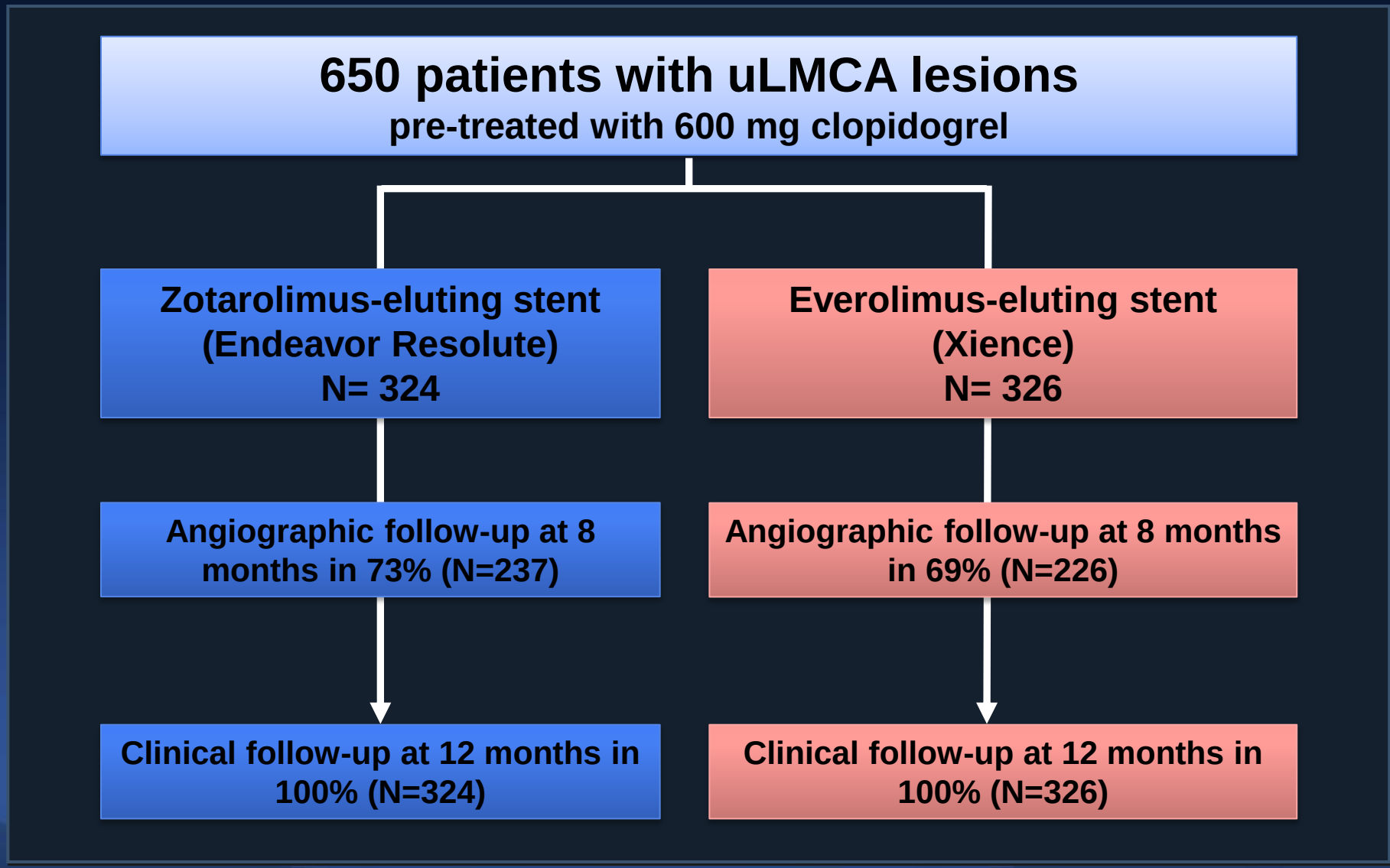
1st vs. 2nd DES for LM
ESTROFA-LM registry

3 Year Event Free Survival

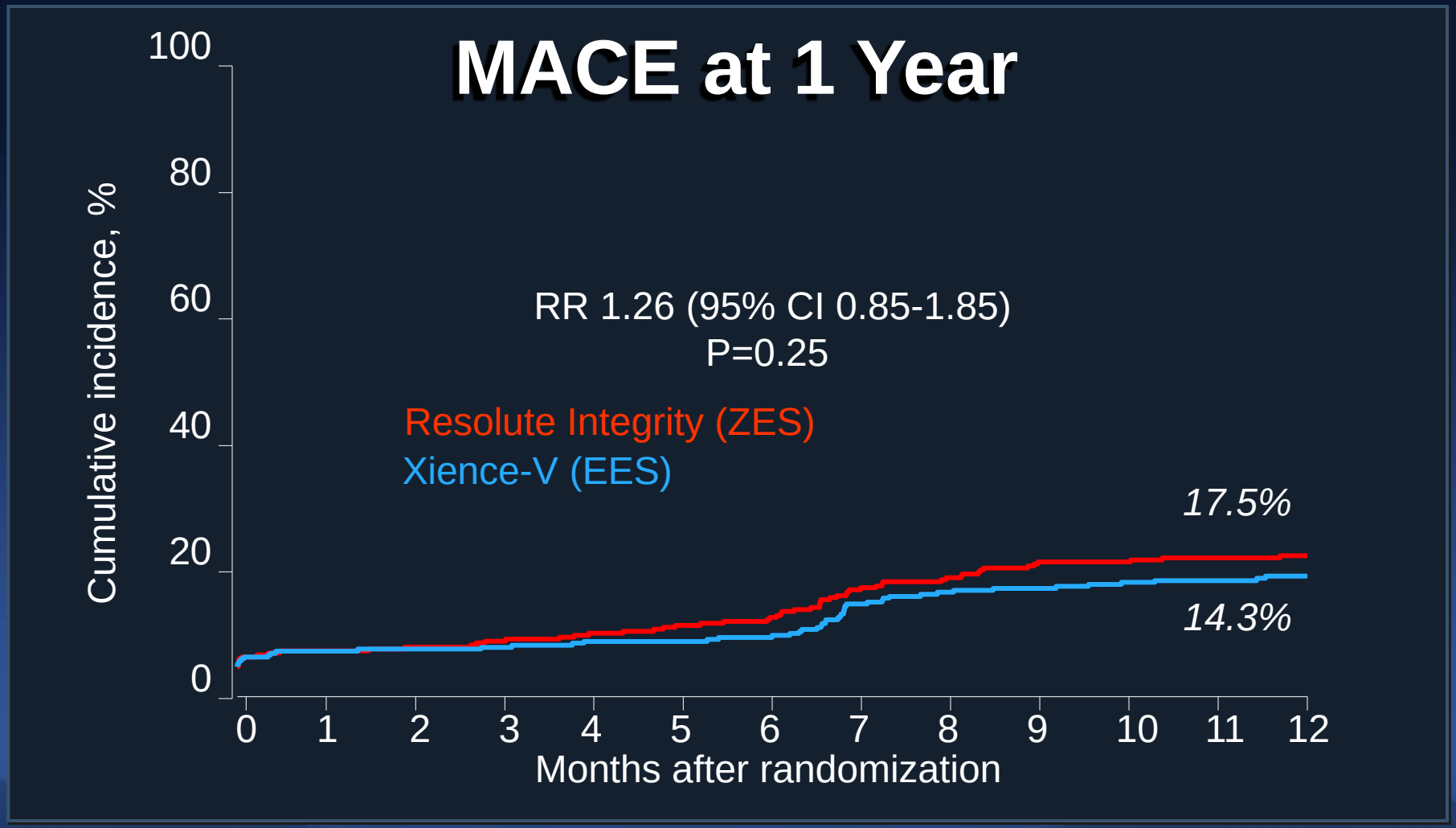
	Events		P value
	PES (N=415)	EES (N=355)	
Death and MI	86%	87%	0.50
Cardiac Death and MI	92%	91%	0.90
TLR	96%	94%	0.10
All revascularization	84%	86%	0.10
Death, MI, and TLR	84%	82%	0.60

De la Hernandez JM et al. Am J Cardiol 2013;111:676-83

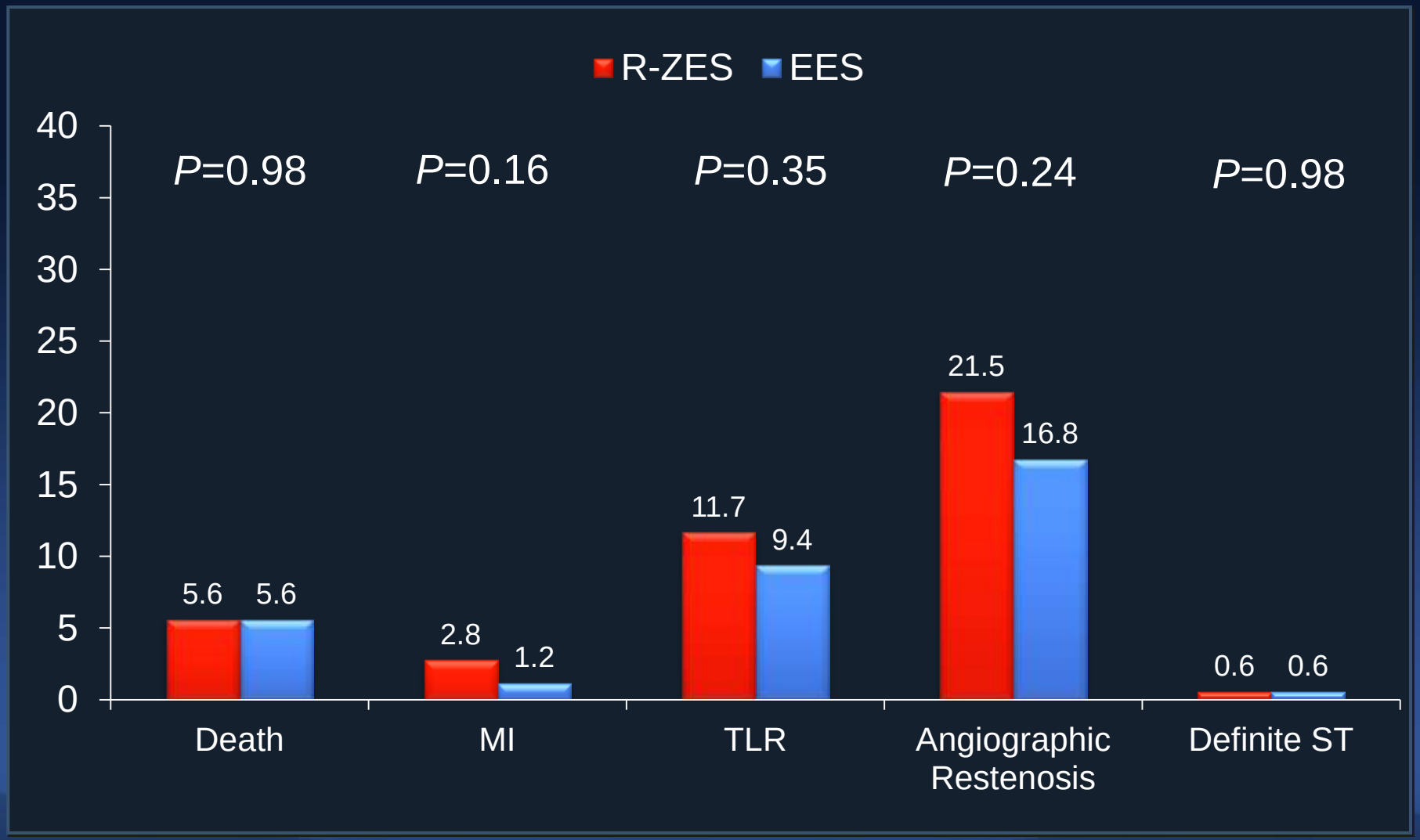
ISAR-LEFT MAIN 2 Trial



2nd DES for LM
ISAR Left Main 2 (n=650)



ISAR Left Main 2 (n=650)
Outcomes at 1 Year



PRECOMBAT Series
New DES Evaluation !

PRE-COMBAT
for unprotected left main disease
Multi-centers in Korea

Randomization

- **PCI with Cypher N=300**
- **CABG N=300**

PRE-COMBAT-2
for unprotected left main disease

Treated with Xience V Stent

Pts randomizable in the PRECOMBAT N=300

PRE-COMBAT-3
for unprotected left main disease

Treated with Promus Element stent

Pts randomizable in the PRECOMBAT N=300

PRE-COMBAT-4
for unprotected left main disease

Treated with Resolute Integrity

Pts randomizable in the PRECOMBAT N=300

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

PRECOMBAT-3 Trial

Design

- DESIGN: a prospective, single arm, registry

- OBJECTIVE: To evaluate the outcomes of PCI with everolimus-eluting **PROMUS ELEMNT (PtCr-EES)** stents for patients with ULMCA stenosis, the results were compared with those of patients receiving SES, CoCr-EES and CABG in the PRECOMBAT trial

- PRINCIPAL INVESTIGATOR

  Seung-Jung Park, MD, PhD, Asan Medical Center, Seoul, Korea

Purpose of PRECOMBAT-3

- To evaluate the safety and efficacy of PCI using platinum chromium everolimus-eluting Promus Element stent (Boston Scientific) for patients with ULMCA stenosis.

- The results were compared with those of historical controls of patients receiving PCI with Cypher, Xience V or CABG in the PRECOMBAT-1 and 2 study

Subjects

- Between August 2010 and July 2013, 300 patients who met the inclusion and exclusion criteria of PRECOMBAT randomized study were entered from 330 patients undergoing ULMCA stenting with PtCr-EES in 23 Korean cardiac centers.

Inclusion and Exclusion

- Identical to the PRECOMBAT randomized study

- In brief, patients with angiographic ULMCA stenosis (> 50% stenosis), who did not have ST-segment elevation MI, cardiogenic shock, other serious comorbidity or contraindication of DES, were included.

Procedures and Follow-up

- PtCr-EES (Promus Element) was the default stent for all lesions with LMCA in the study period
- IVUS and other devices were used at the operator's discretion.
- Annually clinical follow-up to 5 years

End Points

Identical to those used in the PRECOMBAT.

- MACCE : Primary end point, a composite of death, MI, stroke and ischemia-driven TVR.
- Death : cardiac and non-cardiac deaths.
- MI : Q-MI within 48 hours after procedure and spontaneous MI thereafter.
- TVR : ischemia-driven revascularization.

Statistics

- Analysis among as-treated groups
- ANOVA and t-test for continuous variables
- Chi-square and Fisher-exact for categorical variables
- Censoring at 2 years (720 days) or events
- Log-rank for survival analysis
- Multivariate Cox analysis to adjust different baseline characteristics

Baseline Characteristics

	SES (N=327)	CoCr-EES (N=334)	PtCr-EES (N=300)	CABG (N=272)	P value
Age, years	62.0±10.0	62.9±10.4	64.3±10.3	62.5±9.4	0.026
Male sex	249 (76.1)	236 (70.7)	231 (77.0)	209 (76.8)	0.19
Diabetes mellitus	109 (33.3)	116 (34.7)	94 (31.3)	82 (30.1)	0.63
Hypertension	176 (53.8)	189 (56.6)	191(63.7)	140 (51.5)	0.018
Hyperlipidemia	139 (42.5)	149 (44.6)	155 (51.7)	107 (39.3)	0.021
Current smoker	97 (29.7)	75 (22.5)	70 (23.3)	74 (27.2)	0.13
Previous PCI	42 (12.8)	27 (8.1)	51 (17.0)	34 (12.5)	0.009
Previous MI	16 (4.9)	13 (3.9)	15 (5.0)	17 (6.3)	0.62
Previous heart failure	0	4 (1.2)	11 (3.7)	2 (0.7)	0.001

Baseline Characteristics

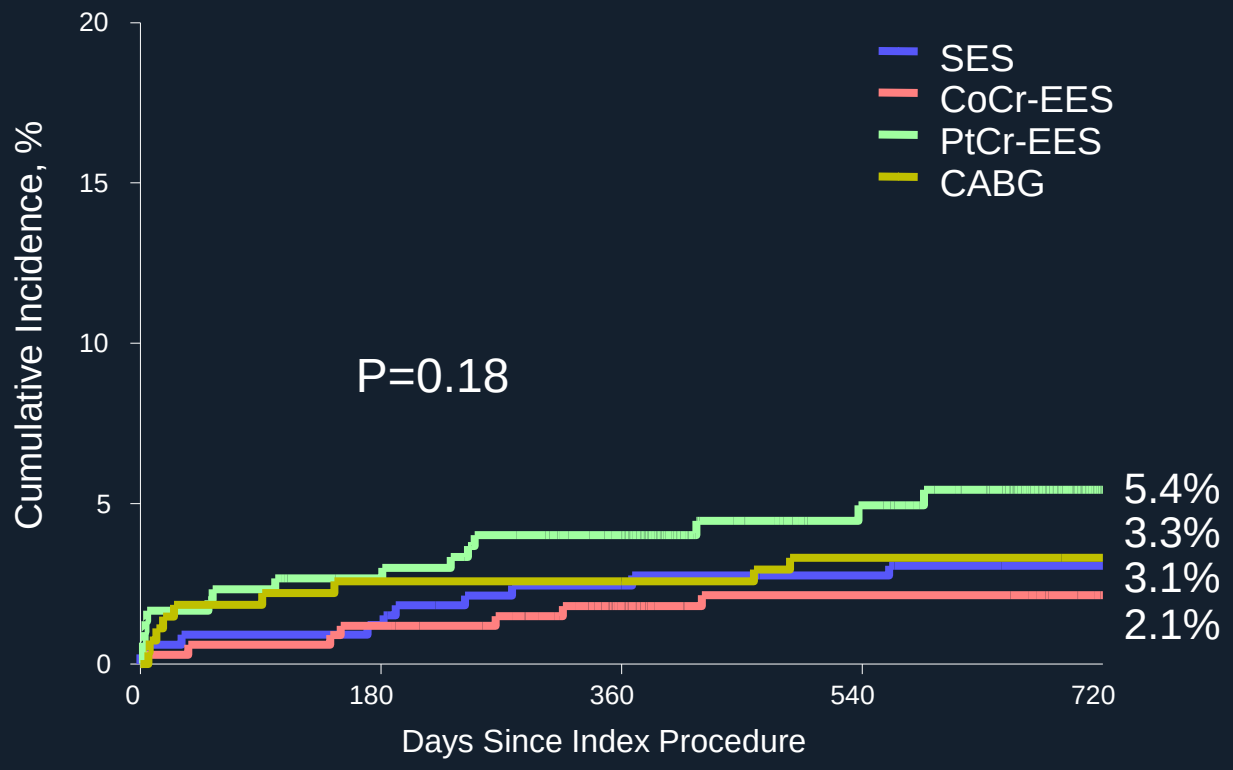
	SES (N=327)	CoCr-EES (N=334)	PtCr-EES (N=300)	CABG (N=272)	P value
Chronic renal failure	3 (0.9)	4 (1.2)	15 (5.0)	2 (0.7)	< 0.05
Peri. vascular disease	15 (4.6)	6 (1.8)	18 (6.0)	7 (2.6)	0.02
Chronic lung disease	8 (2.4)	4 (1.2)	9 (3.0)	7 (2.6)	0.46
ACS	155 (47.4)	151 (45.2)	151 (50.3)	147 (54.0)	0.16
Ejection fraction, %	61.5±8.4	61.1±8.2	59.0±9.9	60.8±8.4	<0.05
EuroSCORE	2.8±1.9	2.9±2.0	3.4±2.4	2.9±2.0	<0.05
Multivessel disease	231 (70.6)	191 (57.2)	198 (66.0)	205 (75.4)	< 0.05
LM bifurcation	219 (67.0)	240 (71.9)	207 (69.0)	163 (59.9)	< 0.05
SYNTAX Score	23.8±9.5	21.1±8.8	21.0±9.6	26.8±10.4	<0.05

Procedures

	SES (N=327)	CoCr-EES (N=334)	PtCr-EES (N=300)	CABG (N=272)	P value
Total stent N. in left main	1.6±0.8	1.8±0.9	1.7±0.8	–	<0.05
Total stent N. per patient	2.6±1.4	2.3±1.3	2.3±1.2	–	<0.05
IVUS	294 (89.9)	302 (90.4)	270 (90.0)	–	0.83
Two-stent technique	112 (34.3)	88 (26.3)	81 (27.0)	–	0.049
Angiographic follow-up	249 (76.1)	203 (60.8)	121 (40.3)	–	< 0.05
N. of conduits	–	–	–	2.7±0.9	
N. of arterial conduits	–	–	–	2.1±0.9	
Off-pump surgery	–	–	–	166 (61.0)	
Use of LIMA	–	–	–	254 (93.4)	

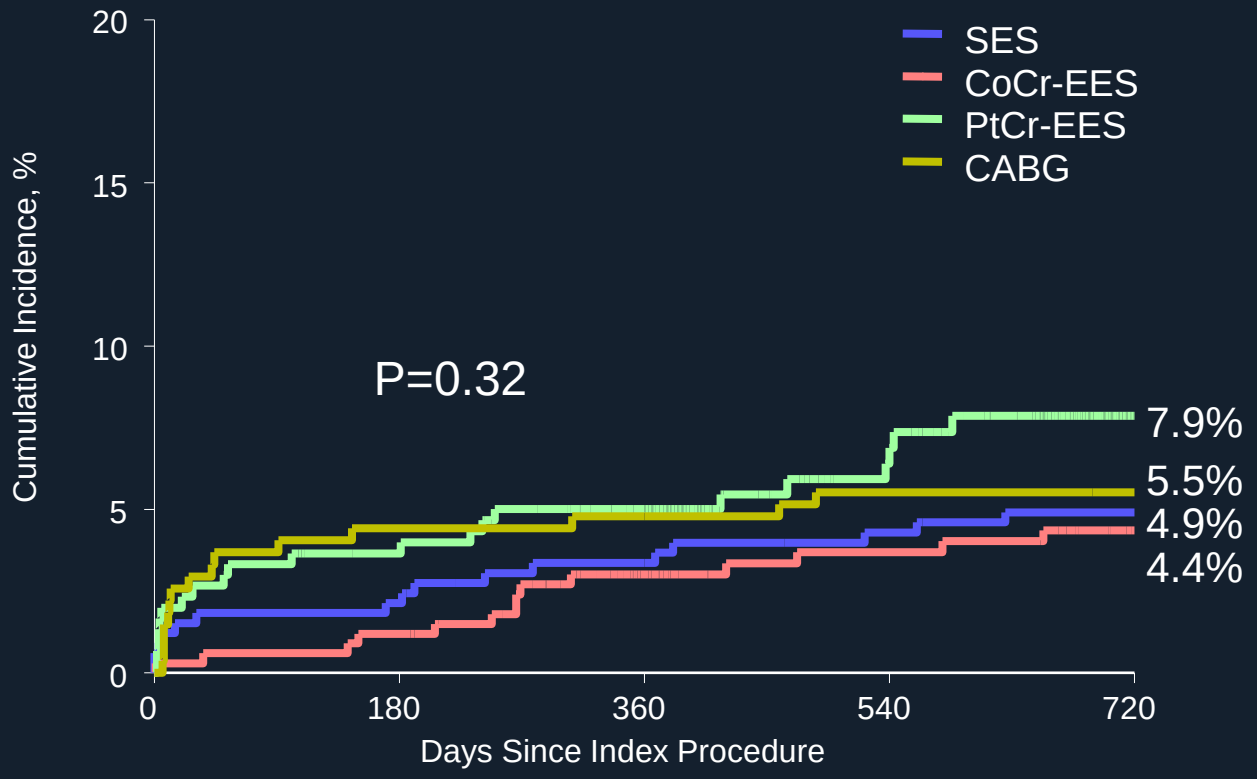
Clinical Outcomes

Death



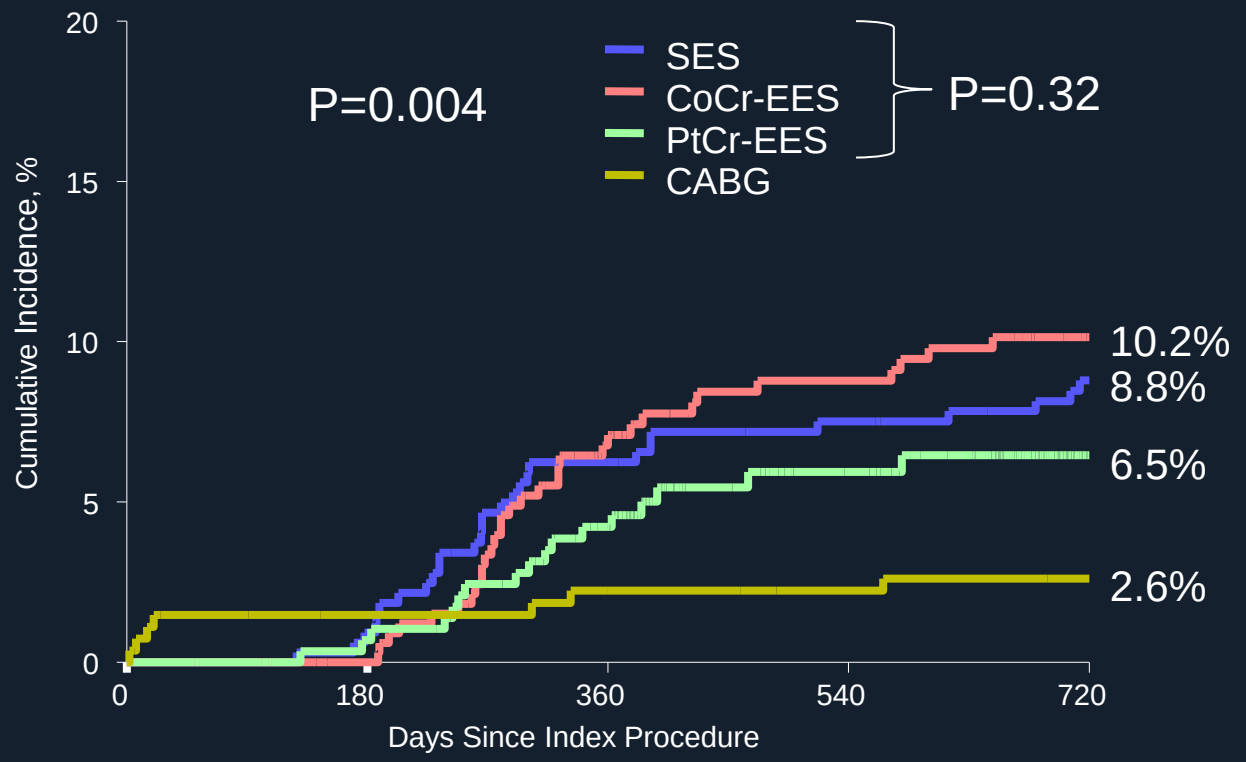
N. at risk					
SES	327	324	317	315	311
CoCrEES	334	331	308	292	282
PtCrEES	300	289	273	200	119
CABG	272	265	264	262	260

Death, MI, or Stroke



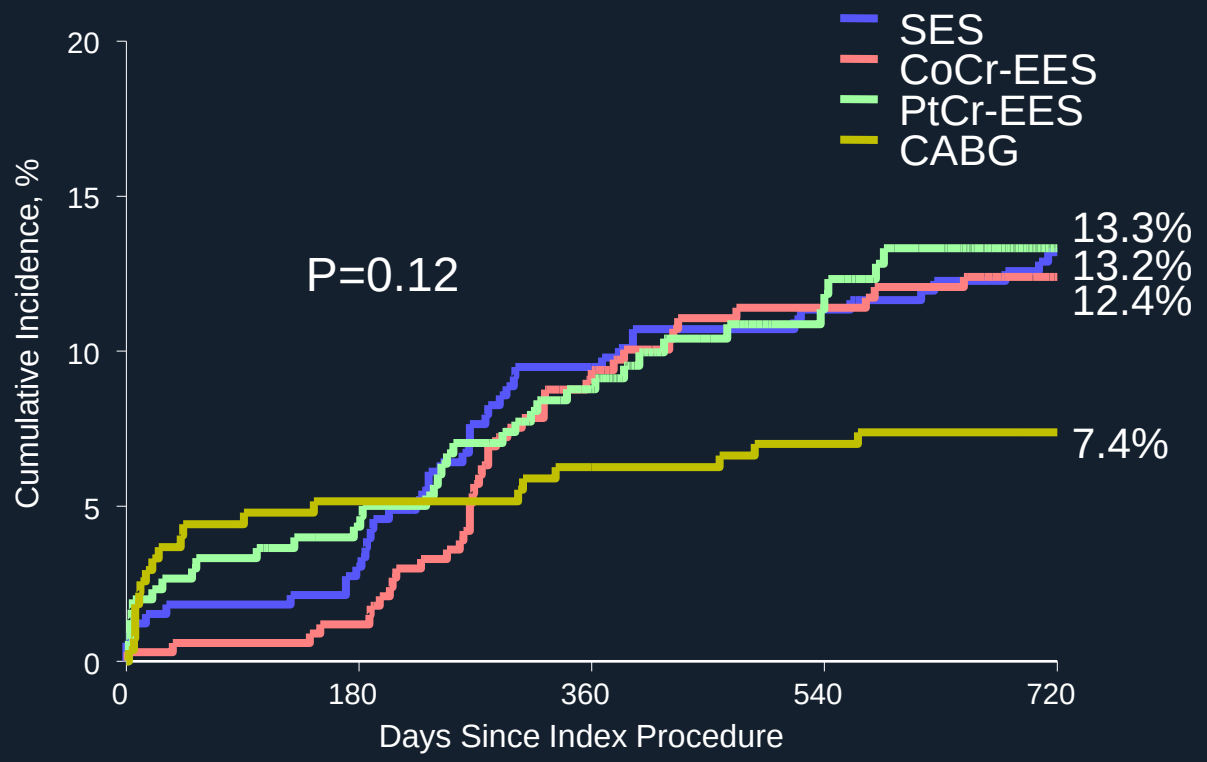
N. at risk					
SES	327	321	314	310	306
CoCrEES	334	331	304	287	275
PtCrEES	300	286	270	194	116
CABG	272	260	258	256	254

TVR



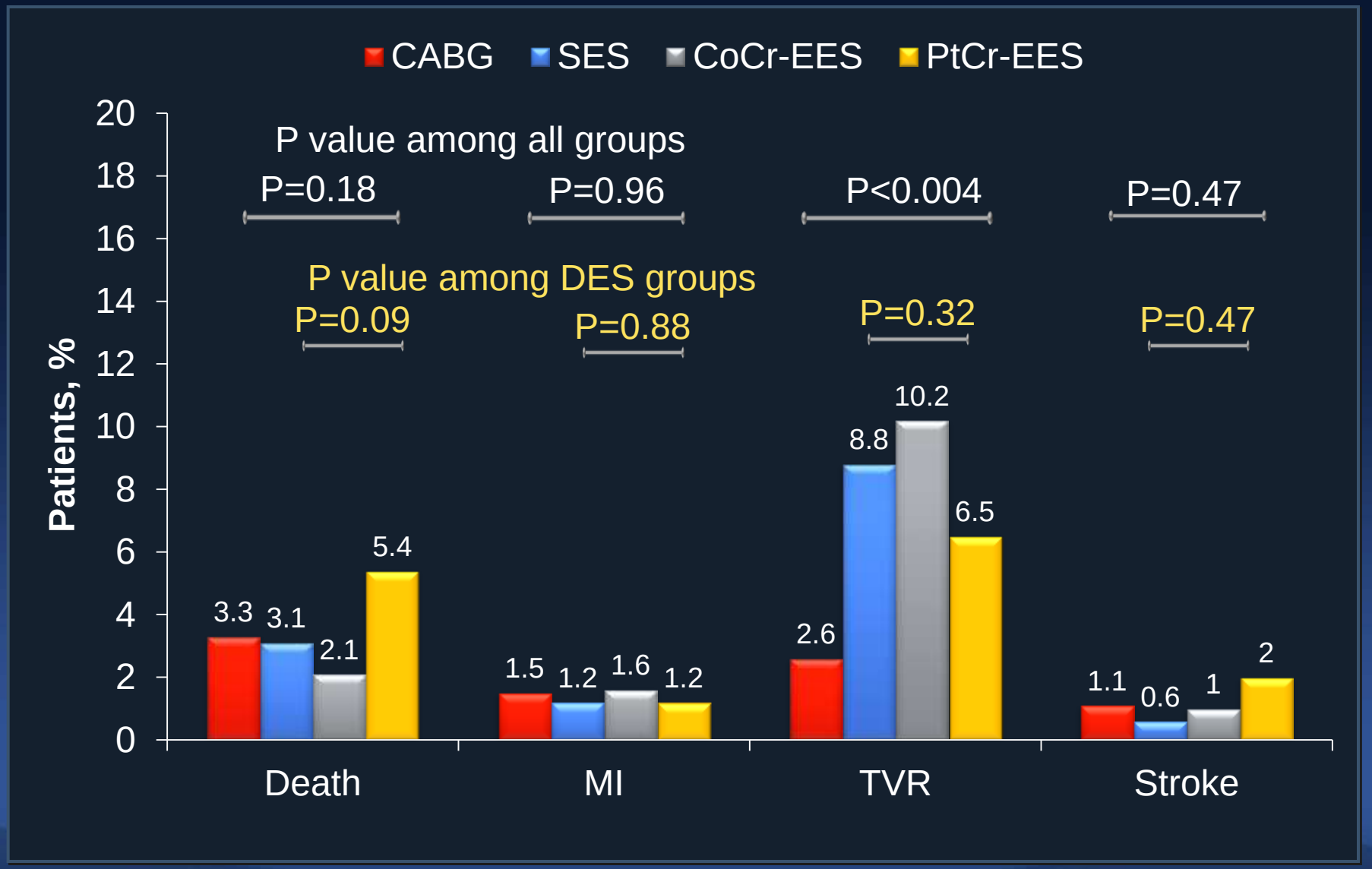
N. at risk					
SES	327	321	298	292	284
CoCrEES	334	331	289	269	255
PtCrEES	300	287	263	188	114
CABG	272	263	260	258	255

MACCE: Death, MI, Stroke, or TVR



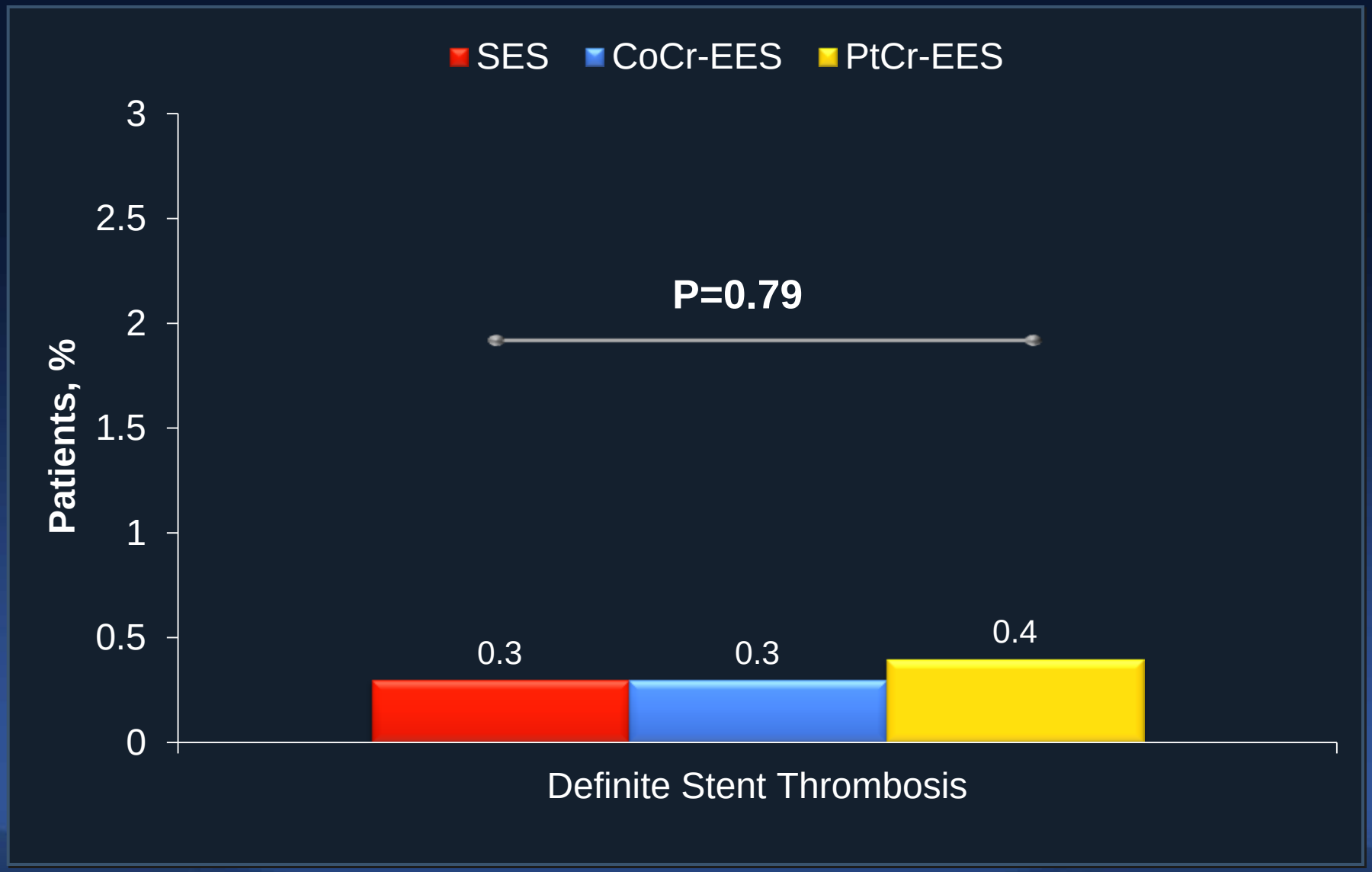
N. at risk					
SES	327	318	295	288	280
CoCrEES	334	331	286	266	253
PtCrEES	300	284	259	183	112
CABG	272	258	254	252	249

Clinical Outcomes at 2 Years

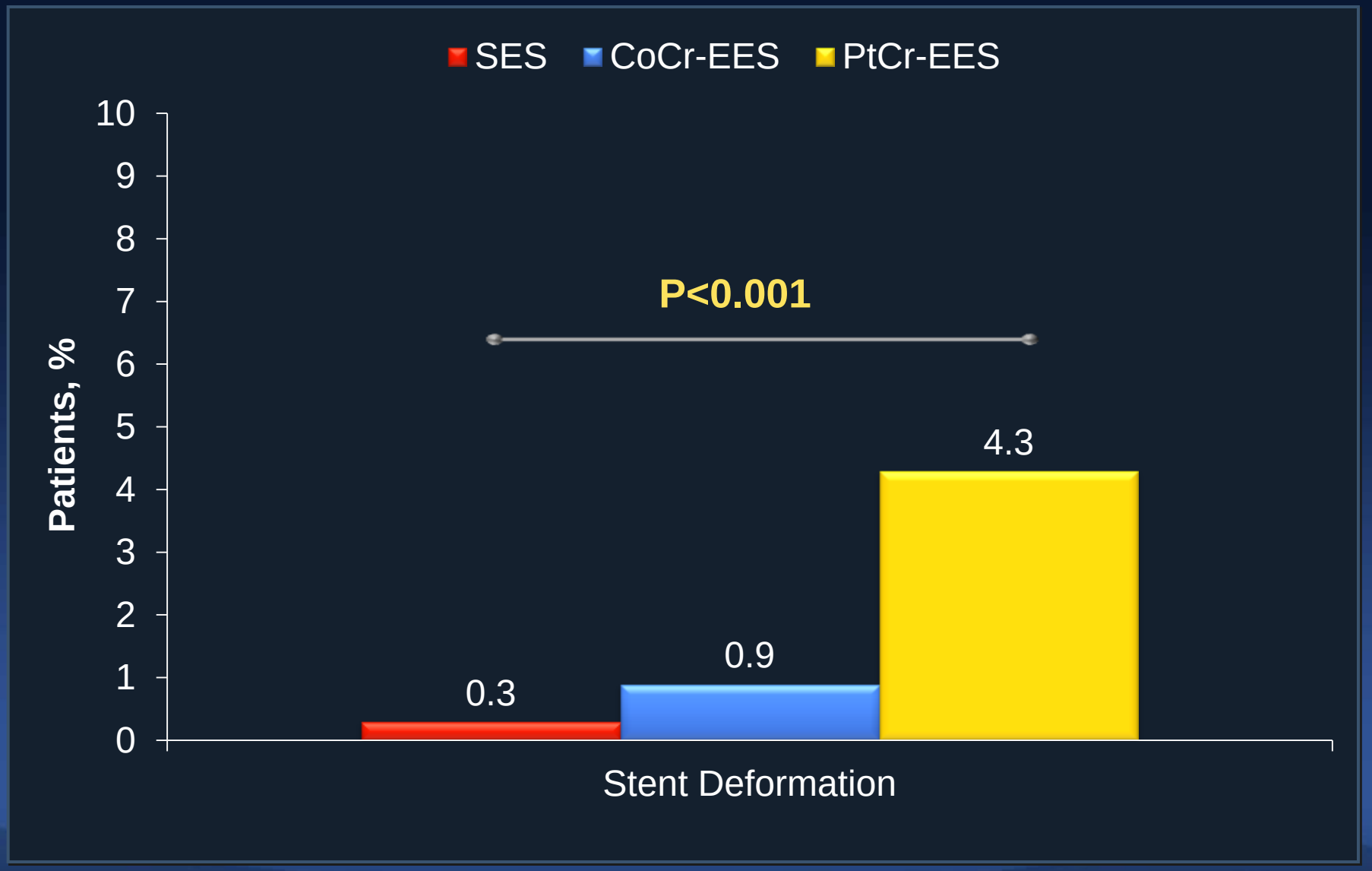


Cumulative KM Event Rate; log-rank P value; *Binary rates

Definite Stent Thrombosis at 2 Years

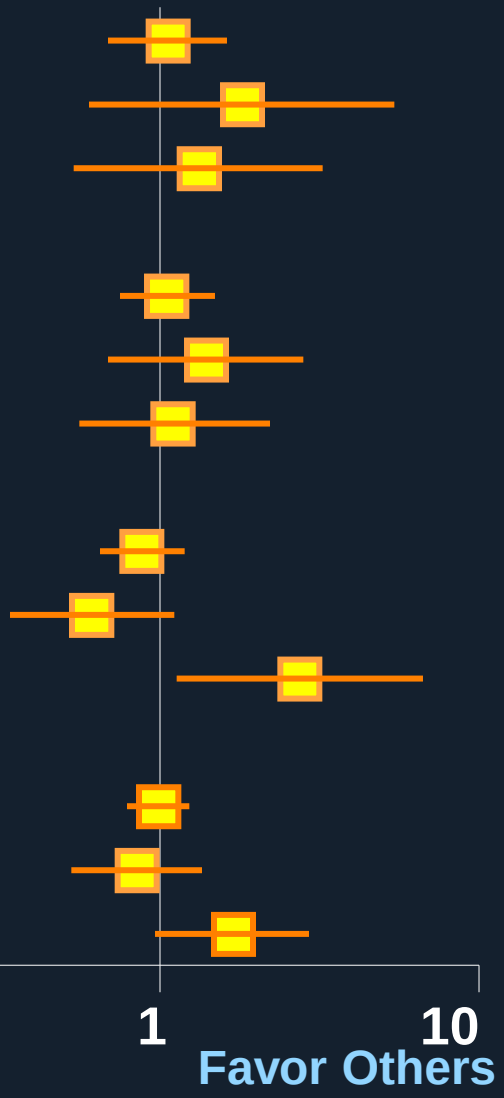


Stent Deformation

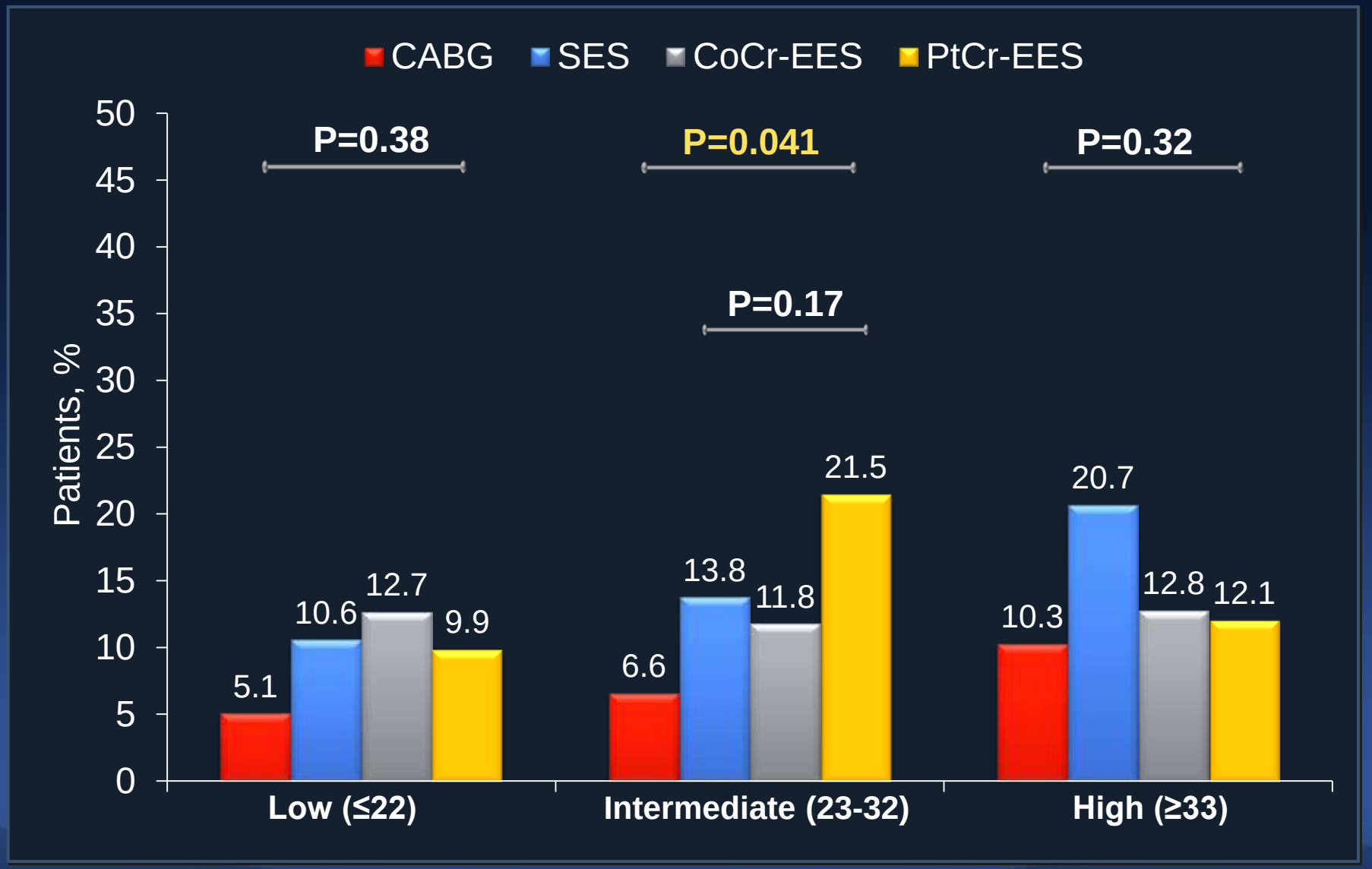


Adjusted HR for PtCr-EES

	Adjusted Hazard ratio	95% CI	P value
Death			
vs SES	1.06	0.69 - 1.63	0.78
vs. CoCr-EES	1.81	0.60 – 5.44	0.29
vs. CABG	1.33	0.54 – 3.25	0.53
Death, MI, or stroke			
vs. SES	1.05	0.75 – 1.49	0.77
vs. CoCr-EES	1.40	0.69 – 2.83	0.35
vs. CABG	1.10	0.56 – 2.22	0.79
TVR			
vs. SES	0.88	0.65 – 1.20	0.42
vs. CoCr-EES	0.61	0.34 – 1.11	0.10
vs. CABG	2.75	1.13 – 6.69	0.026
MACCE			
vs. SES	0.99	0.79 – 1.24	0.95
vs. CoCr-EES	0.85	0.53 – 1.36	0.50
vs. CABG	1.70	0.97 – 2.95	0.062

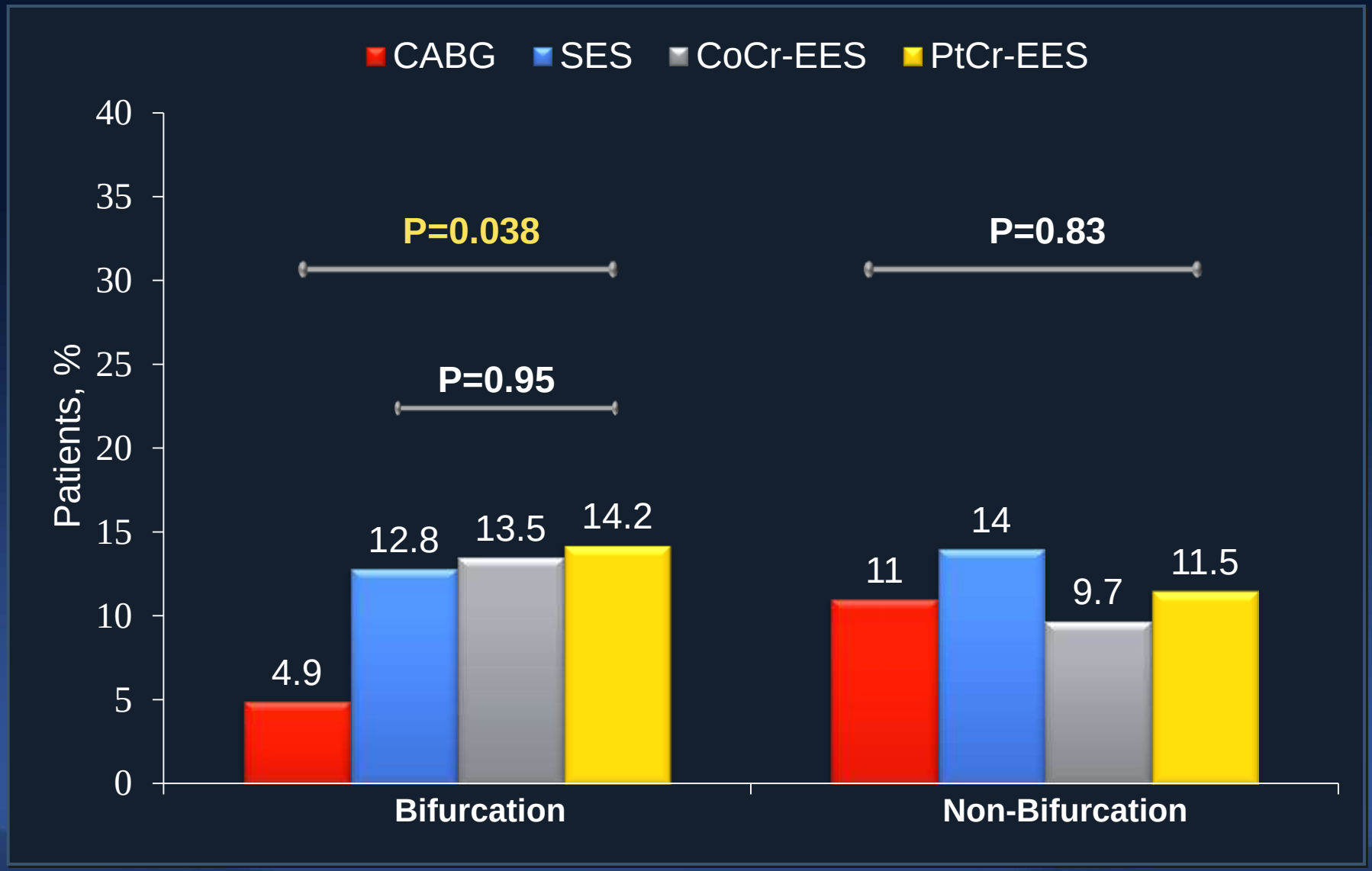


2-Y MACCE in SYNTAX Subgroup



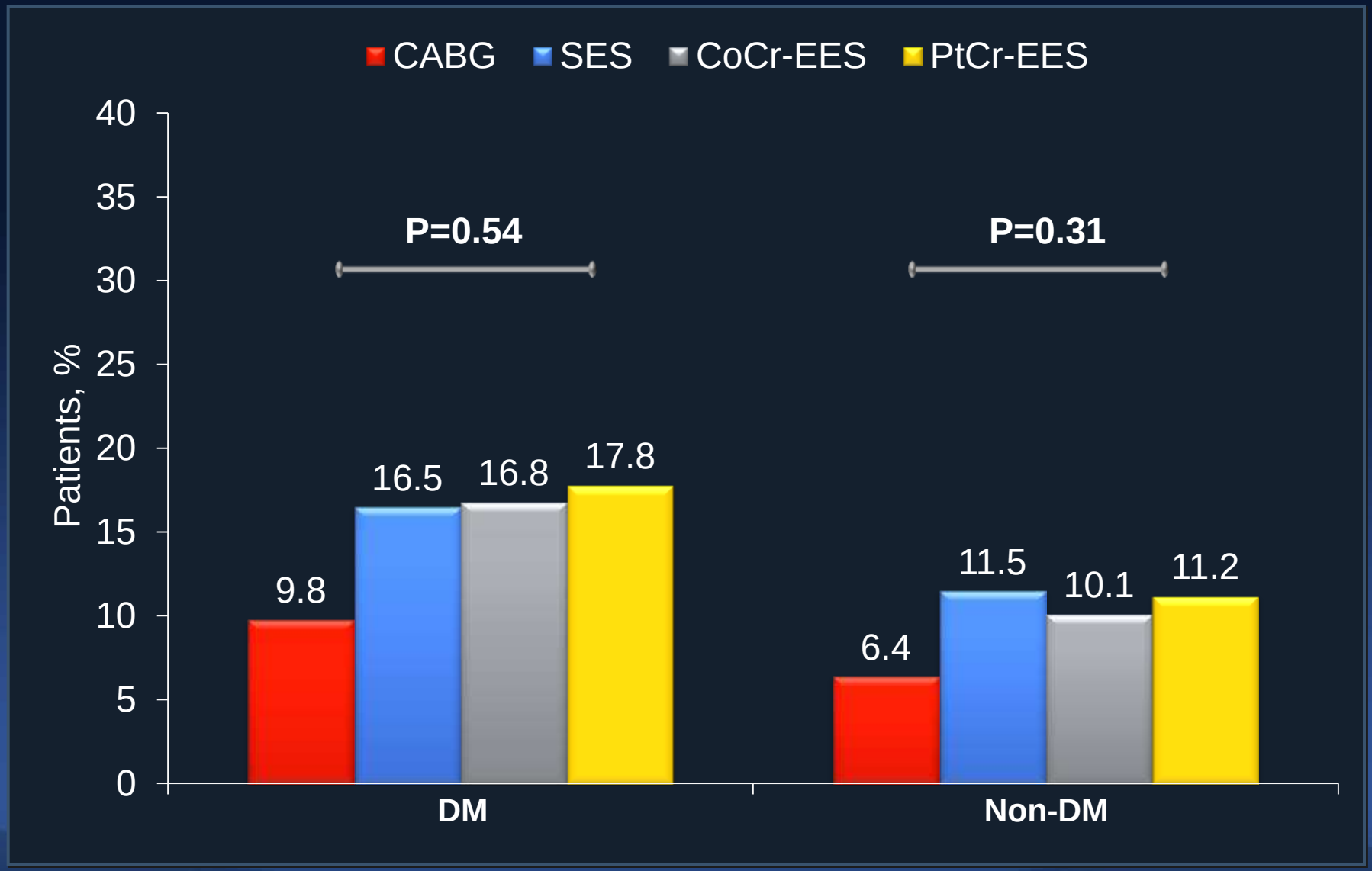
Cumulative KM Event Rate; log-rank P value; *Binary rates

2-Y MACCE in Bifurcation



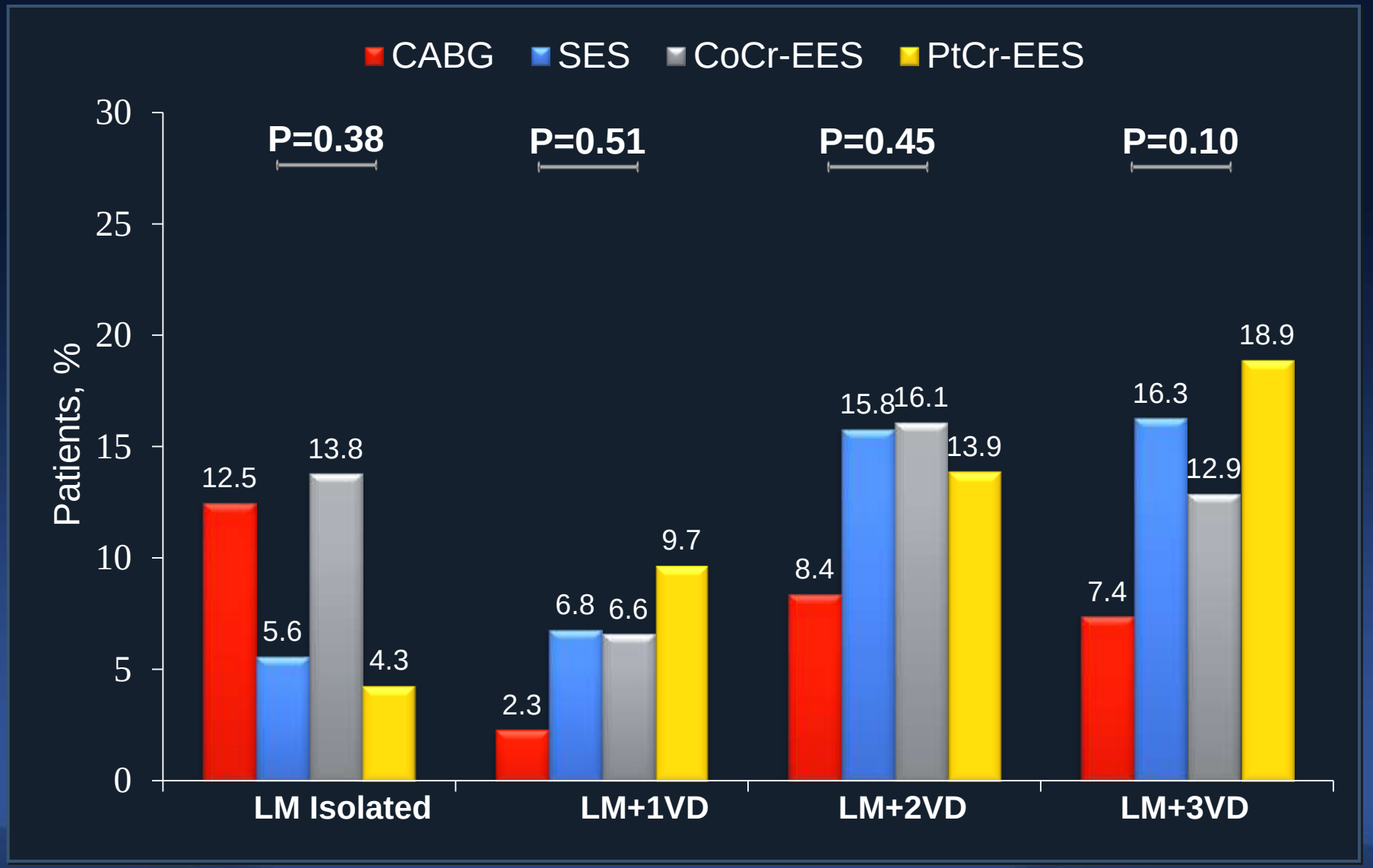
Cumulative KM Event Rate; log-rank P value; *Binary rates

2-Y MACCE in DM



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

2-Y MACCE in LM Subgroups



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

UNIVERSITY OF ULSAN COLLEGE MEDICINE
ASAN Medical Center

Conclusions

- The PRECOMBAT-3 trial demonstrated PCI for ULMCA stenosis using PtCr-EES is safe and effective compared with previous version of DES including SES and CoCr-EES.
- However, the adoption of more flexible stent design was associated with the higher rate of stent deformation.
- In addition, compared with the historical control of CABG group in PRECOMBAT-1 trial, PtCr-EES stenting was associated with the similar rate of the death, MI, or stroke but the higher rate of the repeated revascularization at 2 year follow-up.

Conclusions

- Based on the current available data, the generation gap of DES appears to be very minimal regarding the clinical endpoint.

- Therefore, physicians pay more attention to “how to stent” rather than “what kind of stent”.