PROMUS PLATINUM

Four-Year Results of the PLATINUM Randomized Trial: Can Stent Metal Alloy Composition and Design Affect Late Clinical Outcomes?

Bong-Ki Lee, MD., PhD.

Kangwon National University Hospital, Chuncheon, Korea

Potential conflicts of interest

PROMUS PLATINUM

- **Speaker's name: Bong-Ki Lee**
- ☑ **I have the following potential conflicts of interest regarding the topics of this presentation:**

Speaker at educational events: Boston Scientific

The PLATINUM Study

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1530 patients with 1 or 2 *de novo* native coronary artery target lesions

RVD ≥2.5 to ≤4.25; Lesion length ≤24 mm

Peri-proc: ASA ≥300 mg, clopidogrel ≥300 mg load unless on chronic Rx

Randomized 1:1

Stratified by diabetes, intention to treat 1 vs. 2 target lesions, & study site

Cobalt chromium everolimus-eluting stent	Platinum chromium everolimus-eluting stent

ASA indefinitely, thienopyridine ≥6 mos (≥12 mos if not high risk for bleeding)

Clinical f/u only: 1, 6, 12, 18 months then yearly for 2-5 years

Everolimus-Eluting Stents

Xience V™ and PROMUS Element™

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Same Drug and Polymer

Everolimus concentration: 100 ug/cm^2

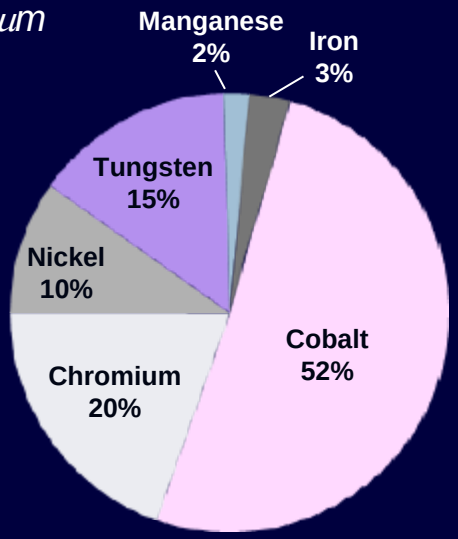
Polymer: PVDF

Polymer Thickness: 7.8μm

Xience V™ Stent (CoCr-EES)

Strut Thickness: 81 μm

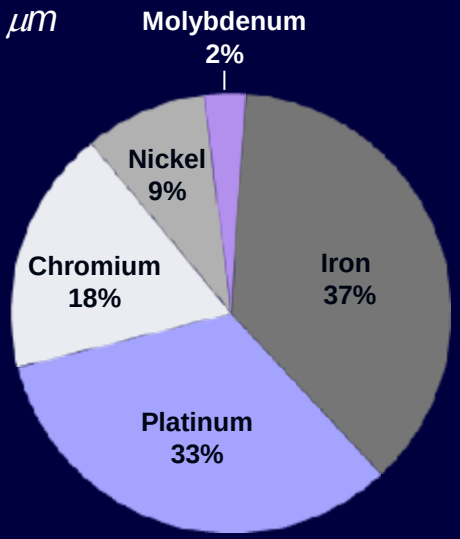
Cobalt Chromium



PROMUS Element™ Stent (PtCr-EES)

Strut Thickness: 81 μm

Platinum Chromium



Metal composition source: Menown et al, Adv Ther, 2010

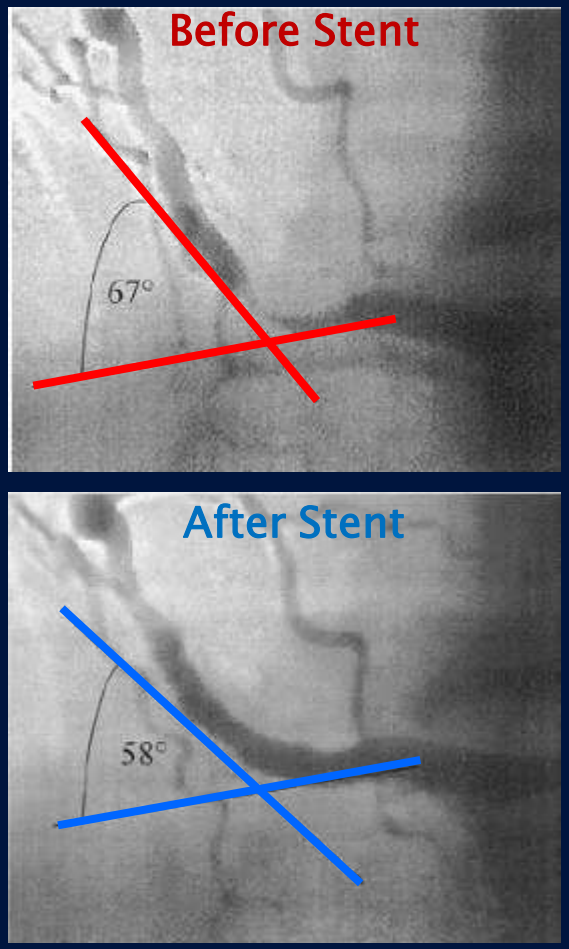
Flexibility – Conformability of DES Platform

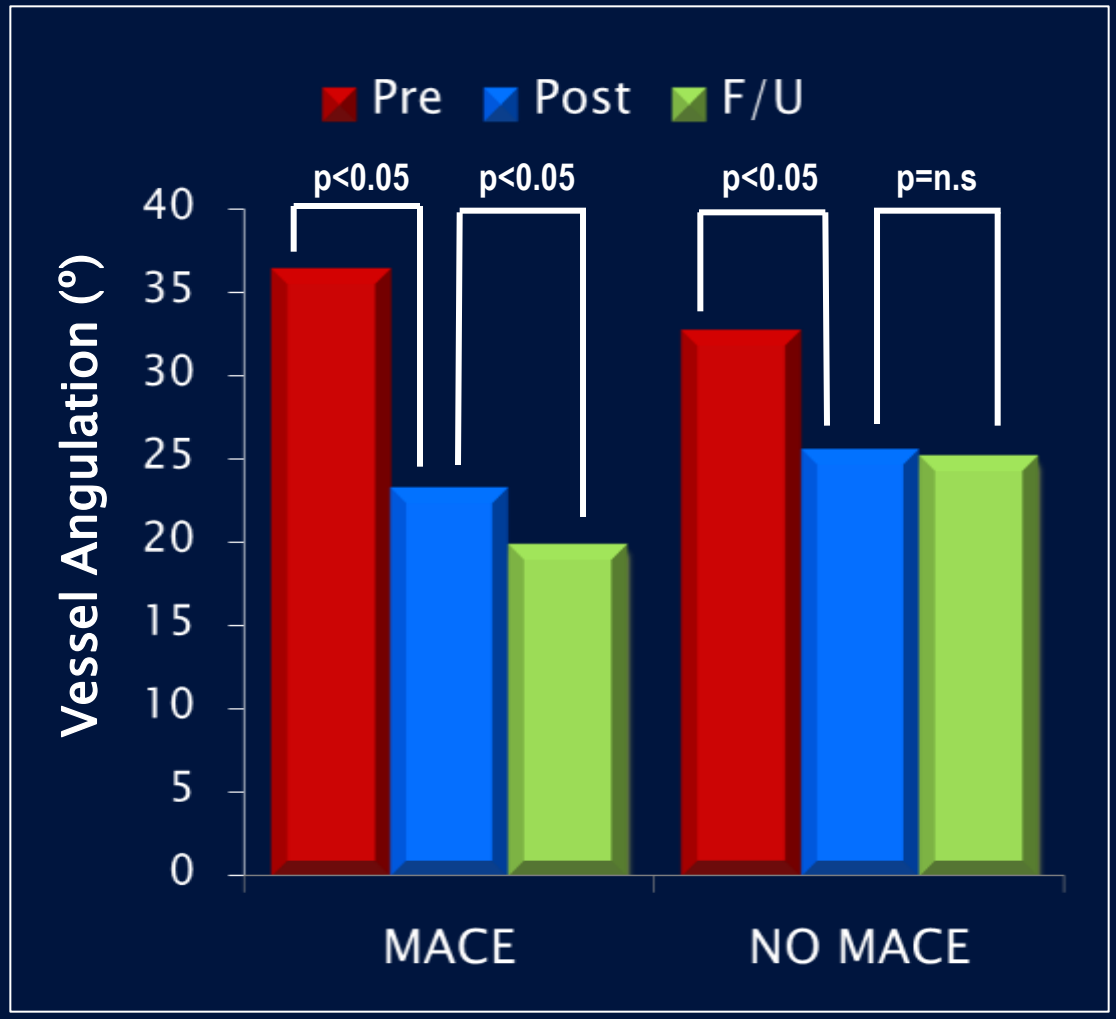
- *Coronary flow velocity*
- *Shear stress*
- *Geometric distortion*
- *Fracture resistance*

Geometric Distortion: Vessel Angulation and Straightening

Pronounced straightening of stented artery associated with MACE

Measurement Methodology





Baseline vessel angulation ≥33.5° and *change in vessel angulation post-stent ≥9.1°* found to be significant predictors of MACE

MACE includes death,nonfatal MI, and revascularization

Gyongyosi et al, JACC 2000;35:1580-9

Stent Design Influences Geometric Distortion Post PCI: QCA Analysis* Of PLATINUM

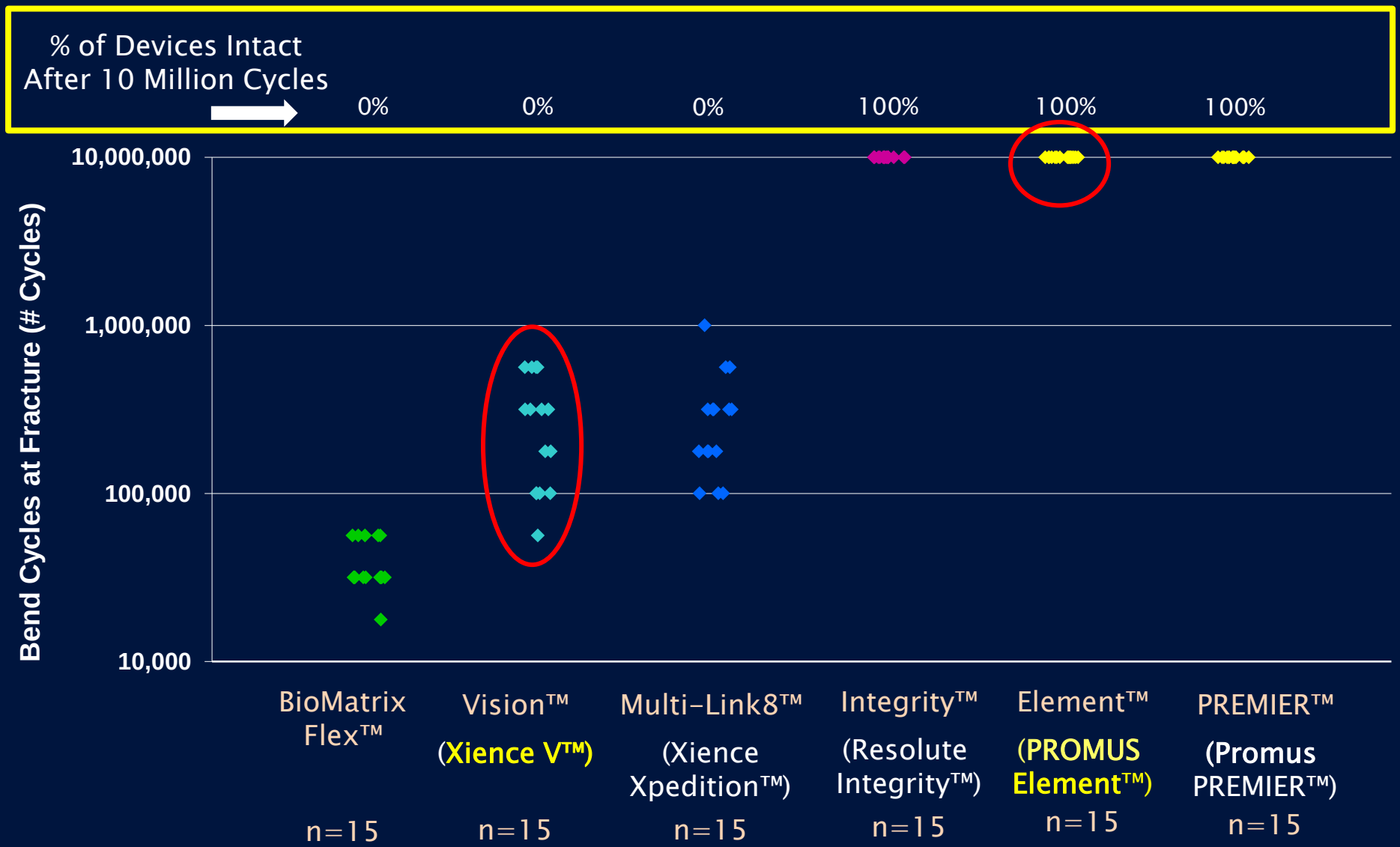
Factor	XIENCE V (n=50 lesions)	PROMUS Element (n=50 lesions)	P Value
Lesion length, mm	12.4 ± 5.7	15.2 ± 6.2	0.020
Stent length, mm	19.4 ± 10.4	22.0 ± 7.5	0.159
Baseline bend, degrees (at min MLD)	79.1 ± 13.5	79.0 ± 11.7	0.969
Pre-procedure angulation, degrees			
Minimum	80.5 ± 22.9	76.0 ± 24.0	0.335
Maximum	97.0 ± 24.8	91.2 ± 25.9	0.255
Post-procedure angulation, degrees			
Minimum	55.4 ± 27.1	60.5 ± 28.1	0.356
Maximum	65.1 ± 30.4	71.5 ± 29.5	0.284
Change in angulation, degrees			
Minimum	25.2 ± 18.8	15.5 ± 19.2	0.013
Maximum	31.9 ± 26.4	19.7 ± 21.3	0.012

**Post-hoc analysis of 100 most severely angled stenoses*

Popma et al. JACC 2013;61:A410 (abstract 2101-229)

Stent Platform Flexibility Correlates with Fracture Resistance

Bend Fatigue Bench Test (12 degree flexion arc)



Ormiston et al. Circ Cardiovasc Interv 2014;7:Dec 24 13 [E-pub]

BSC Fracture Resistance Test Method Focal Bend

Sequence from high speed video of Fracture Resistance Focal Bend test

Benchtest results may not necessarily be indicative of clinical performance. Data on file at BSC

Late Revascularizations in PLATINUM

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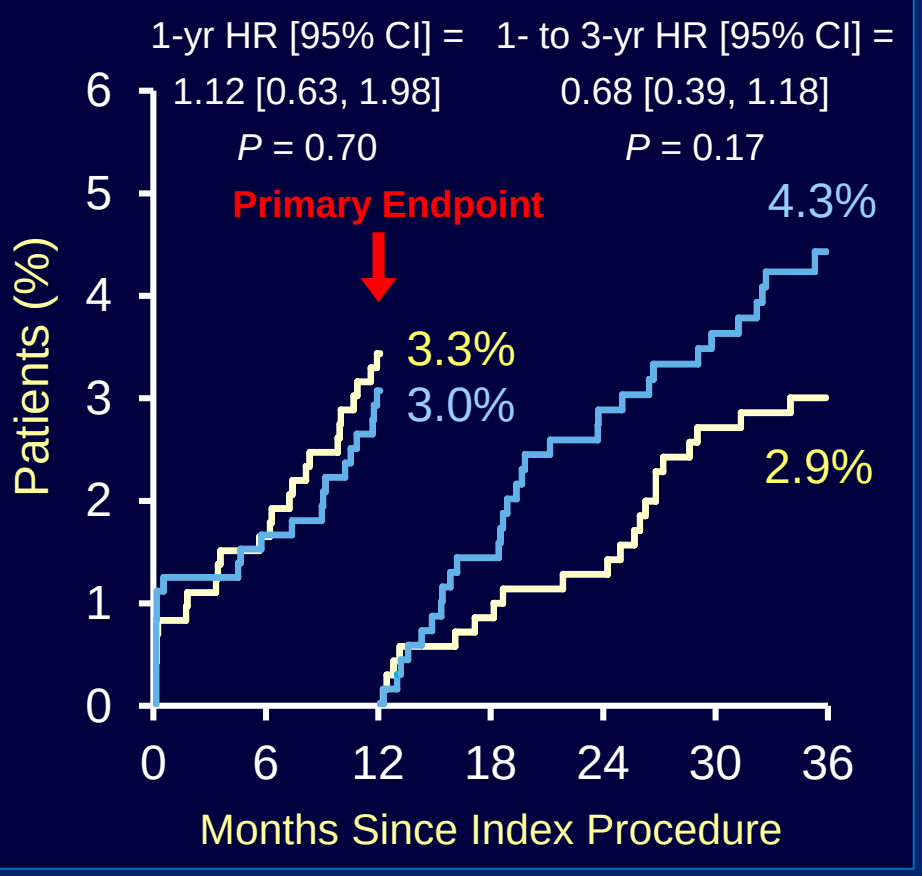
3-Year Landmark Analysis

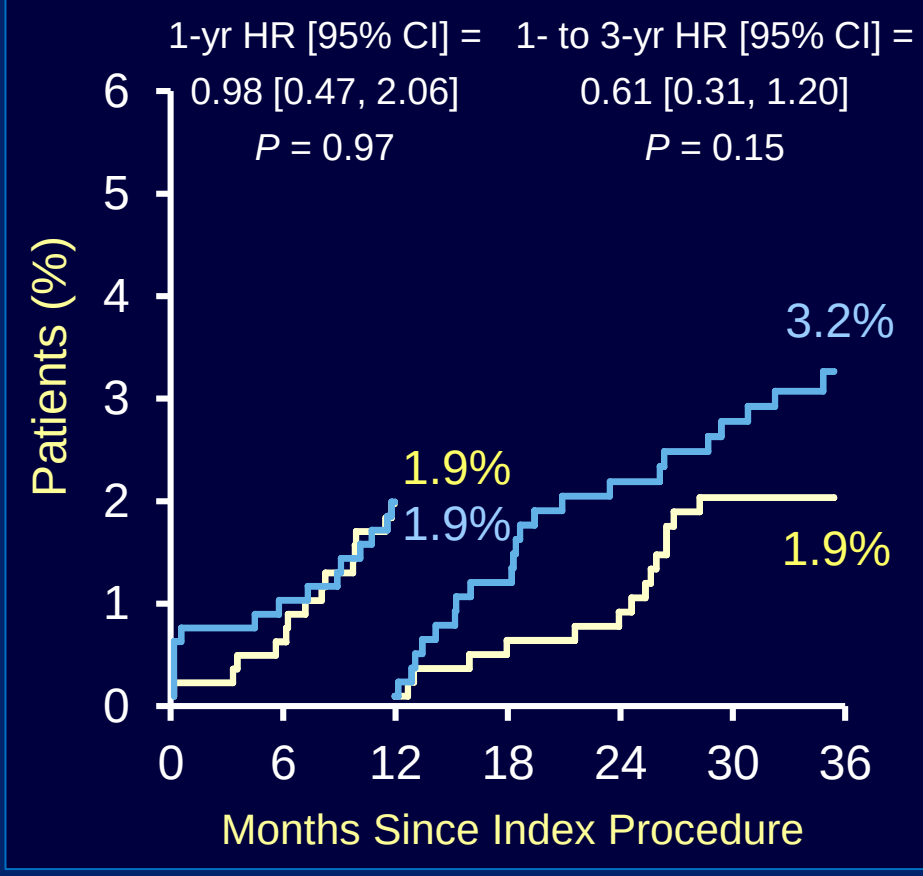
CoCr-EES (N=749 at time 0, n=722 at 1 year)

PtCr-EES (N=758 at time 0, n=736 at 1 year)

Target Lesion Failure



Target Lesion Revascularization



TLF = cardiac death or MI related to the target vessel or ischemia-driven TLR; Patients with Study Stents.

Objective

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- To determine the cumulative effect of different metal alloy composition and stent design on late clinical events with the PtCr-EES and CoCr-EES through 4 years in the Platinum Workhorse trial

PLATINUM 4-Year Analysis

1530 patients randomized at 132 clinical sites in Asia/Pacific (N=56), European Union (N=562), Japan (N=124), & United States (N=788)

CoCr-EES (N=762)	PtCr-EES (N=768)
No 4-yr f/u (N=45) Withdrew consent: 14 Missed 3-yr visit: 20 Lost to follow-up: 11	No 4-yr f/u (N=40) Withdrew consent: 8 Missed 3-yr visit: 22 Lost to follow-up: 8 Other: 2
No Study Stent Implanted* (N=13)	No Study Stent Implanted* (N=10)
4-Year Follow-up 94.0% (704/749)	4-Year Follow-up 94.7% (718/758)

* Patients who did not receive a study stent were only followed through 1 year

Baseline Demographics

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	CoCr-EES (N=762)	PtCr-EES (N=768)	*P* value
Age, years	63.1 ± 10.3	64.0 ± 10.3	0.09
Male	71.1%	71.6%	0.83
Hypertension	73.2%	70.9%	0.32
Hyperlipidemia	76.2%	78.2%	0.36
Diabetes	25.1%	22.0%	0.16
- Insulin treated	6.3%	7.7%	0.29
Current smoker	17.7%	21.0%	0.10
Prior MI	21.1%	21.0%	0.99
Unstable angina	24.7%	24.1%	0.80

Baseline Lesion Characteristics (QCA)

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	CoCr-EES (N=762 Patients) (N=841 Lesions)	PtCr-EES (N=768 Patients) (N=853 Lesions)	*P* value
Target lesions	1.10 ± 0.31	1.11 ± 0.31	0.66
- 2 lesions treated	10.1%	11.1%	0.54
RVD, mm	2.63 ± 0.49	2.67 ± 0.49	0.09
MLD, mm	0.74 ± 0.34	0.75 ± 0.35	0.40
DS, %	71.9 ± 11.5	71.8 ± 11.5	0.87
Type B2 or C	63.5%	65.4%	0.42
Ostial location	3.6%	3.9%	0.74
Bend ≥45 degrees	7.4%	8.5%	0.41
Calcification (mod/severe)	28.1%	27.9%	0.95
Lesion length, mm	12.5 ± 5.5	13.0 ± 5.7	0.10

Procedural Characteristics

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	CoCr-EES (N=762 Patients) (N=841 Lesions)	PtCr-EES (N=768 Patients) (N=853 Lesions)	*P* value
Stents per patient	1.20 ± 0.48	1.16 ± 0.44	0.16
Stents per target lesion	1.08 ± 0.35	1.05 ± 0.26	0.01
Max stent diam. per lesion (mm)	3.05 ± 0.44	3.09 ± 0.45	0.07
Stent length per lesion (mm)	19.7 ± 8.9	20.5 ± 7.0	0.06
Post-dilatation	49.3%	49.8%	0.84
Max pressure overall (atm)	15.9 ± 3.2	16.3 ± 3.1	0.002

Antiplatelet Therapy at 4 Years

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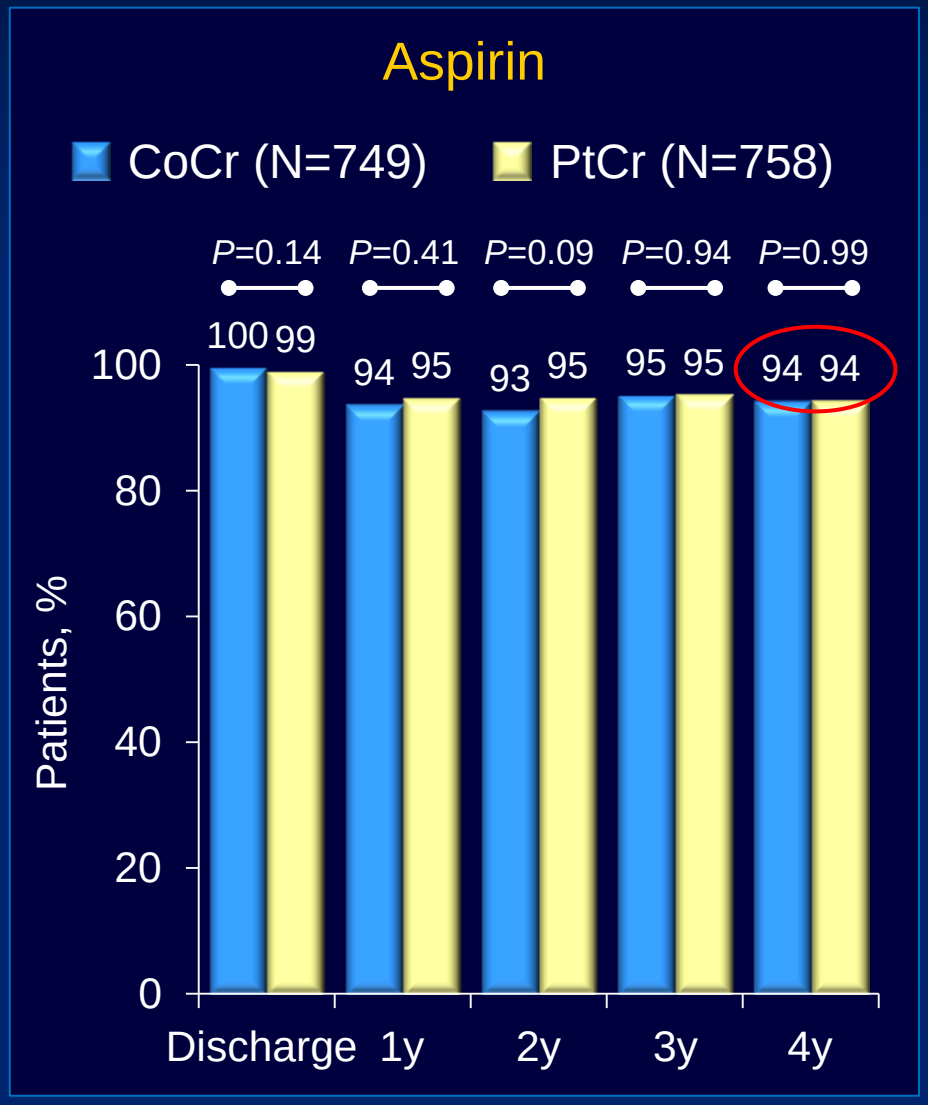

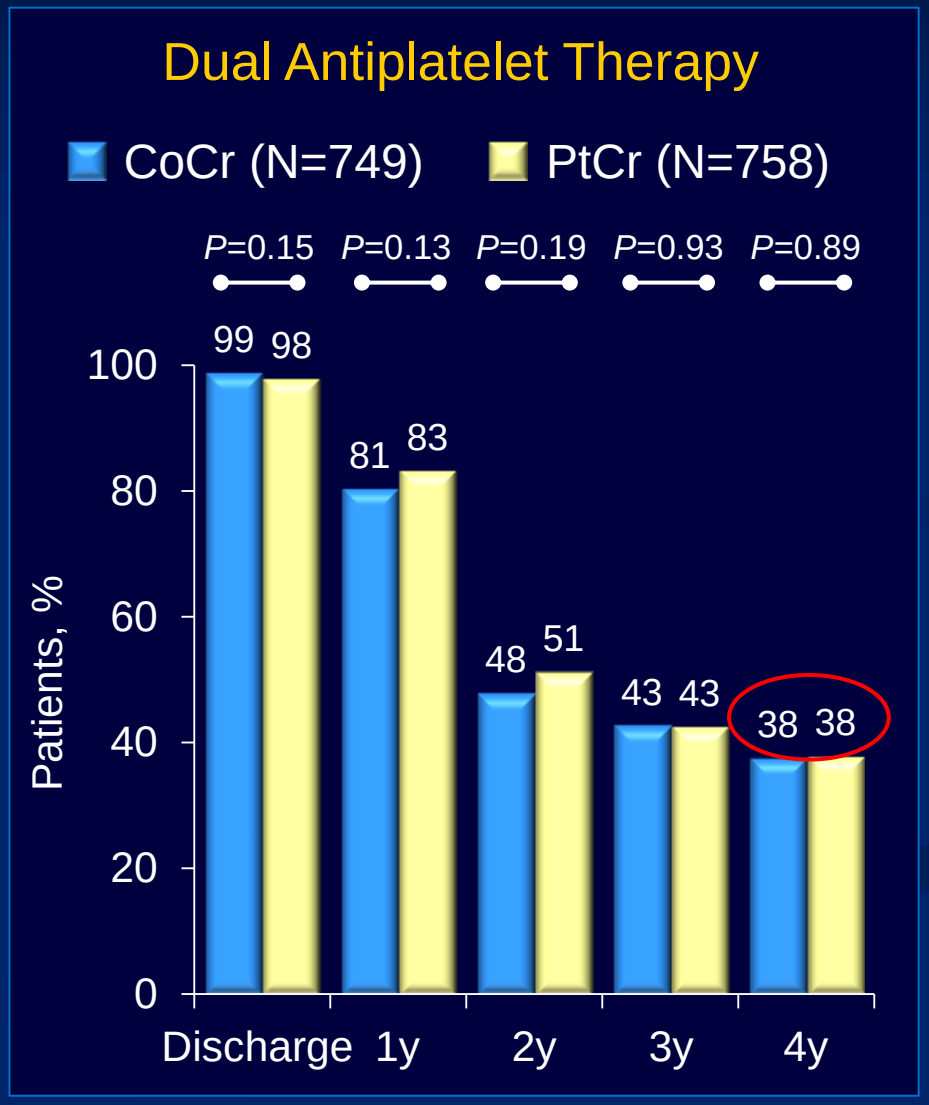

Target Lesion Failure

4-Year Follow-up (Primary Endpoint at 1 Year)

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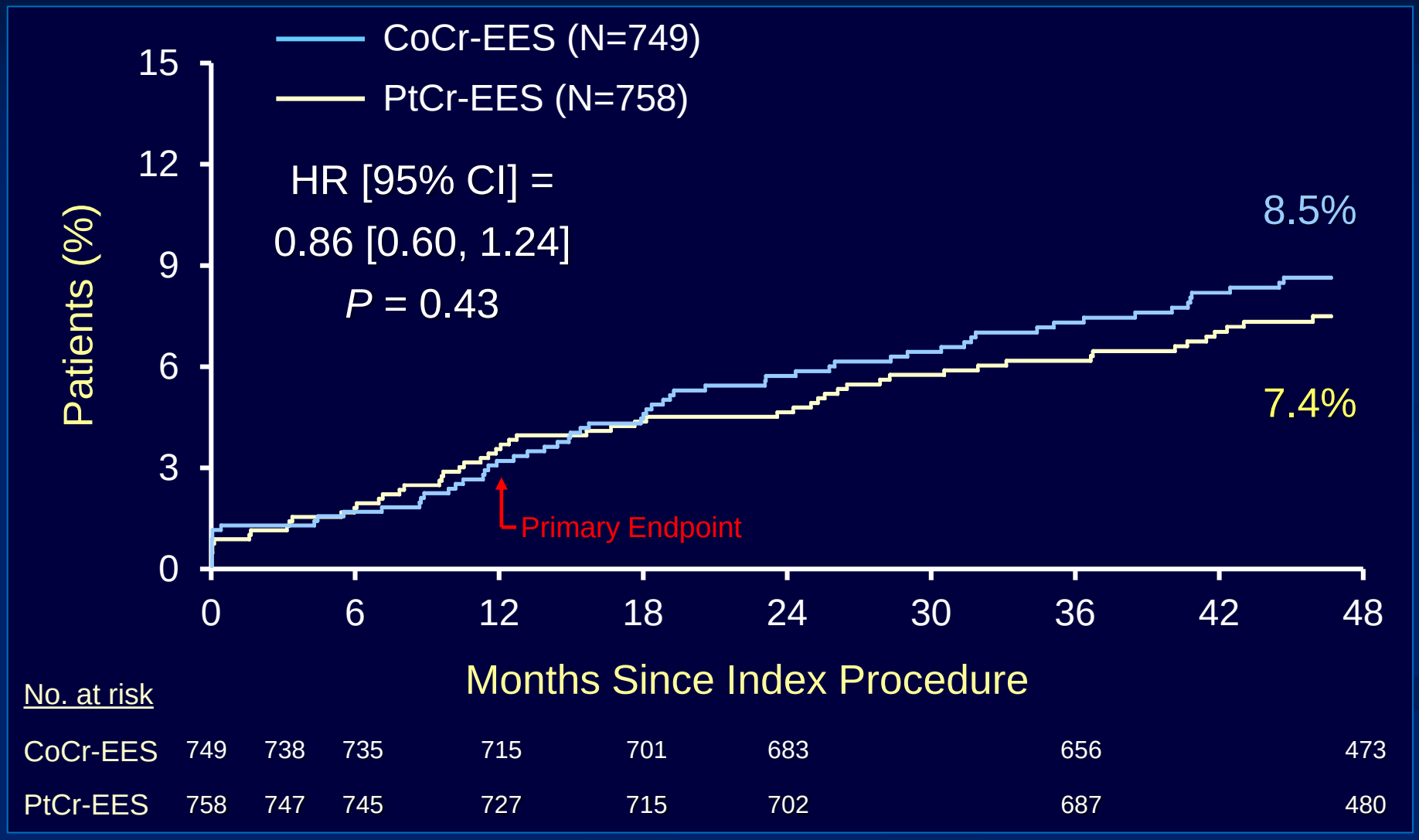

Target Lesion Failure = cardiac death or MI related to the target vessel or ischemia-driven target lesion revascularization

Target Lesion Failure

4-Year Landmark Analysis

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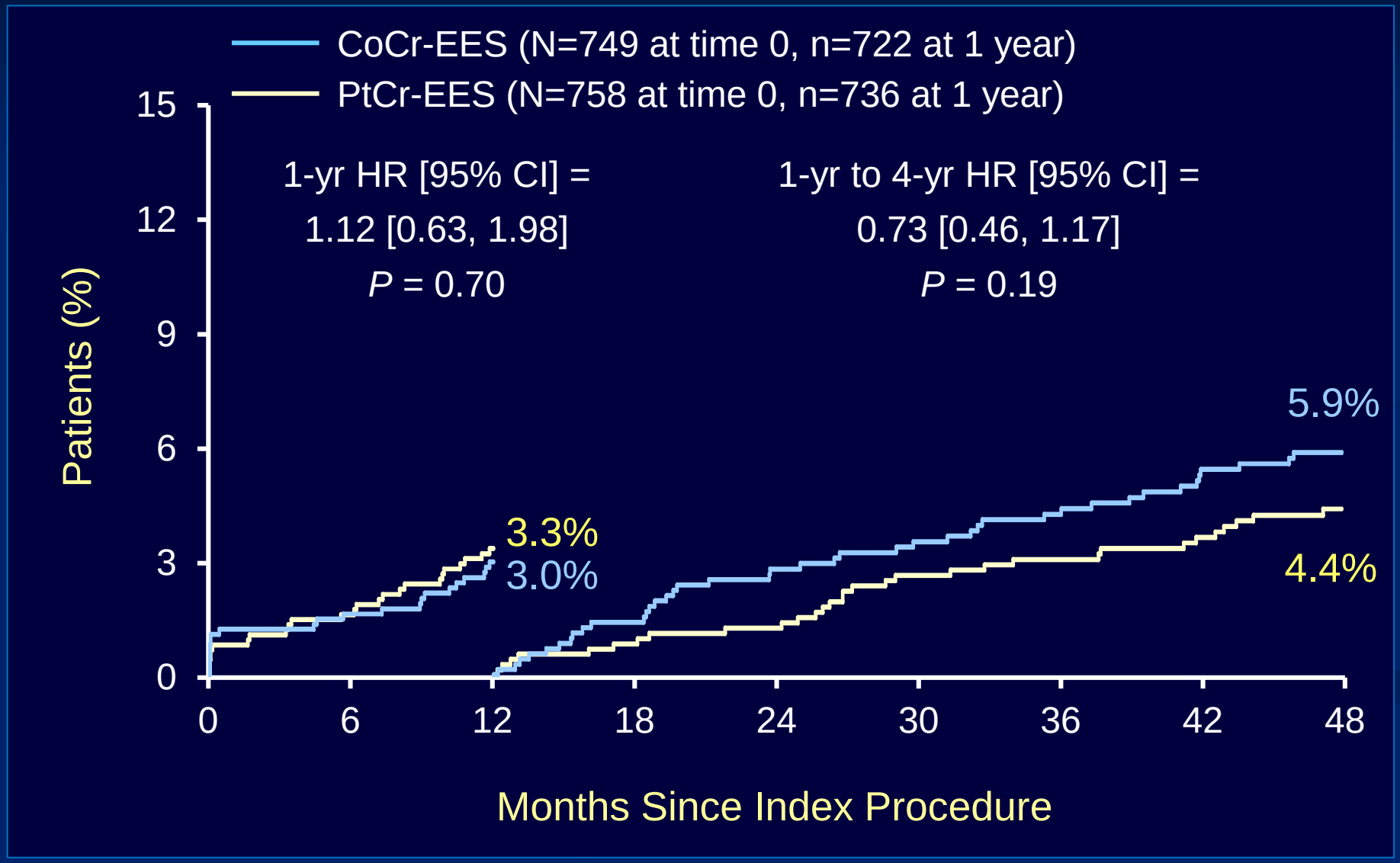

Target Lesion Failure = cardiac death or MI related to the target vessel or ischemia-driven target lesion revascularization

Ischemia-Driven TLR

4-Year Follow-up

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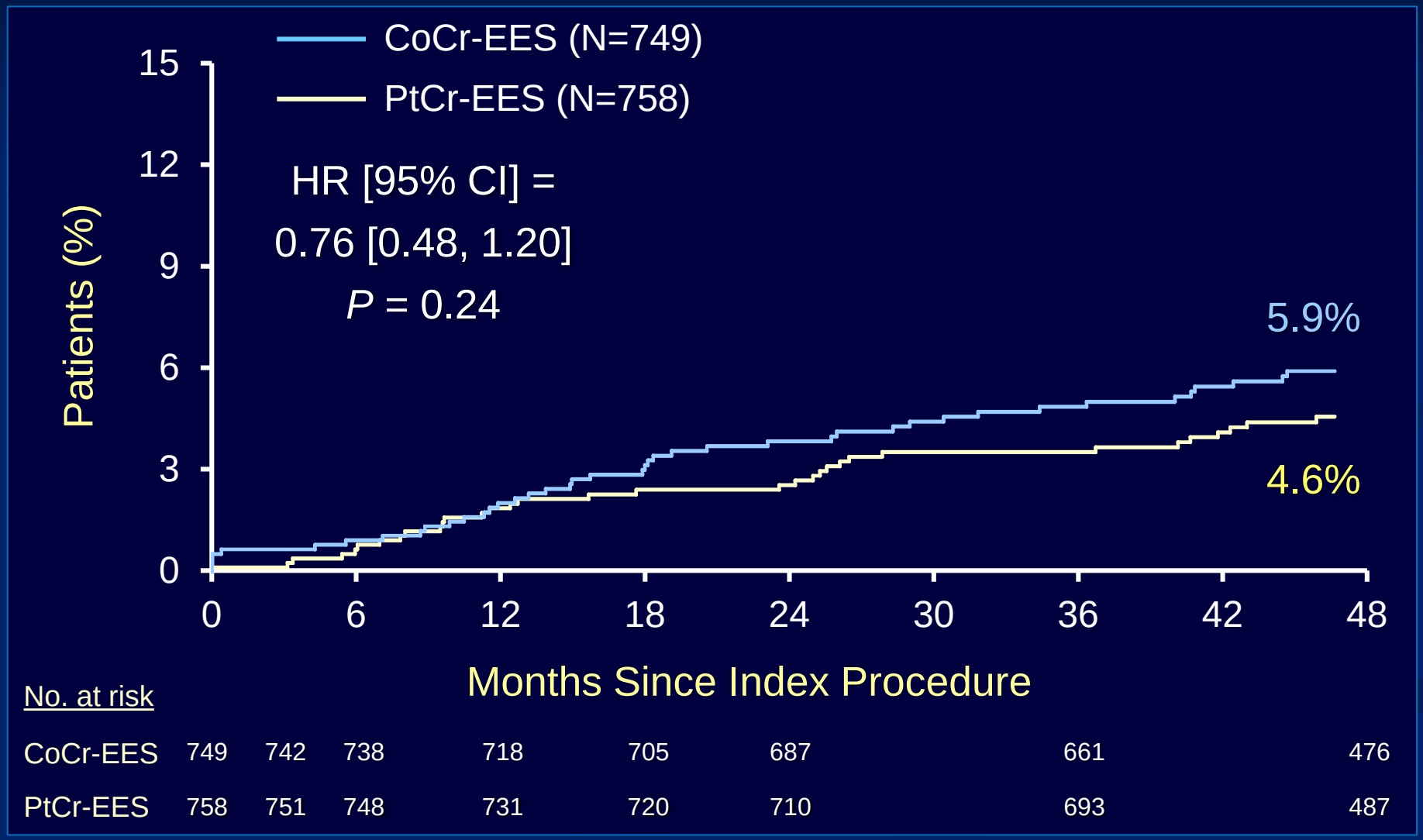
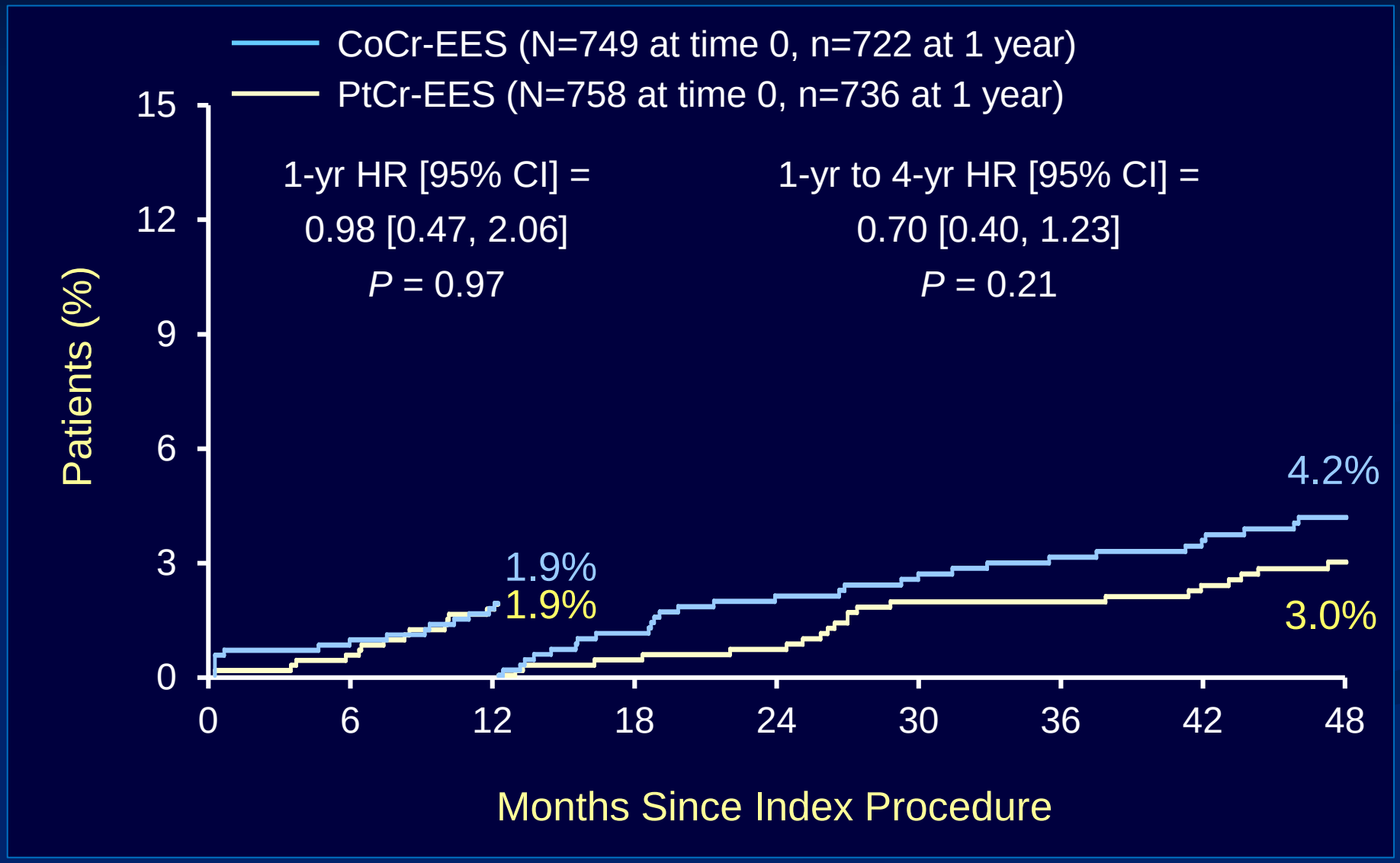


Ischemia-Driven TLR

4-Year Landmark Analysis



PLATINUM Subgroup Analyses

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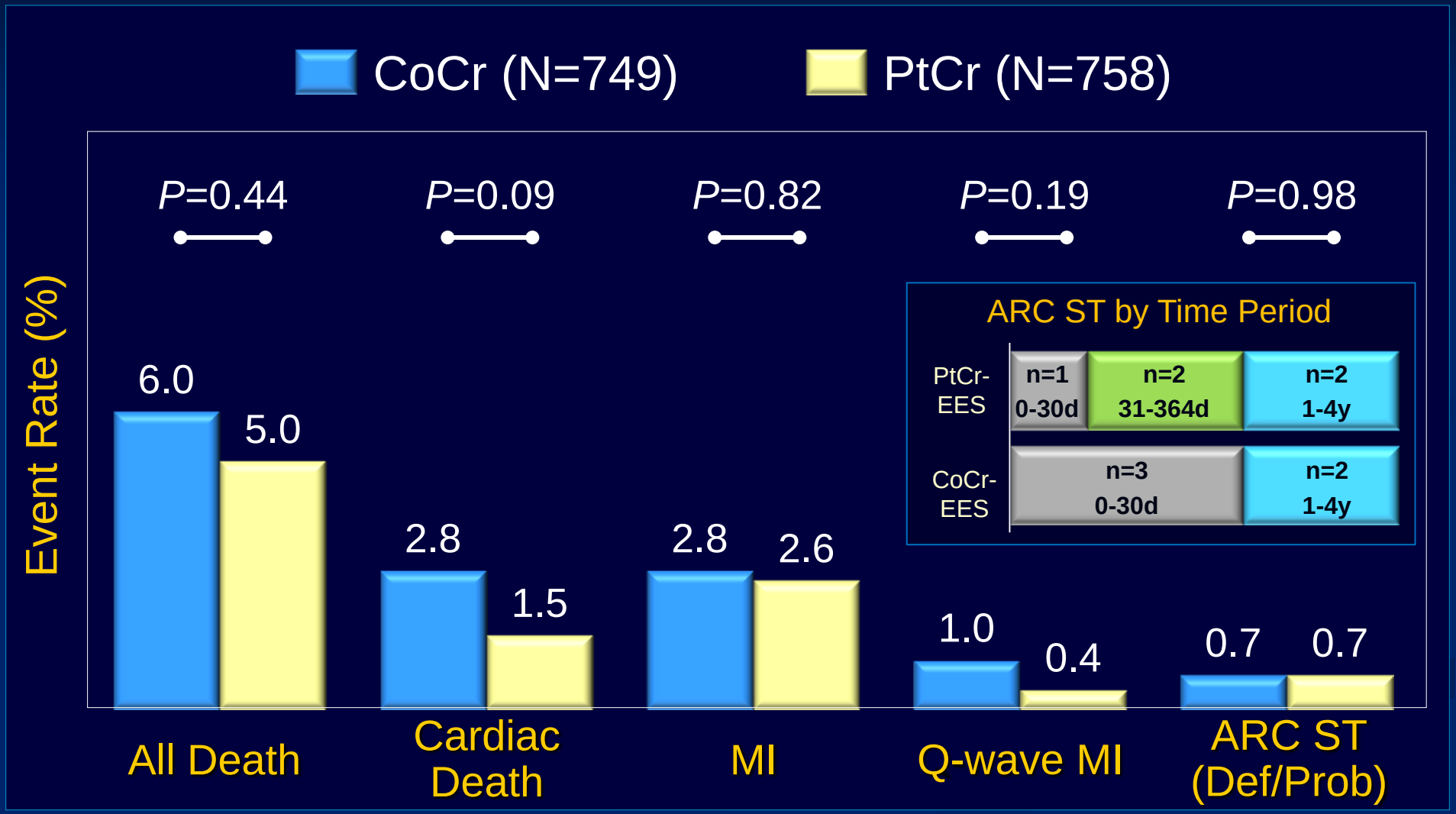
TLF at 4 Years

	CoCr (%)	PtCr (%)	Relative Risk (95% CI)	Relative Risk (95% CI)	*P* Interaction
All randomized (n=1507)	9.1%	7.8%		0.86 [0.61, 1.22]	
Age < 65 yrs (n=779)	9.1%	7.2%		0.79 [0.48, 1.30]	0.65
Age ≥ 65 yrs (n=728)	8.9%	8.4%		0.93 [0.57, 1.54]	
Male (n=1074)	7.9%	8.5%		1.08 [0.71, 1.65]	0.05
Female (n=433)	12.1%	6.1%		0.50 [0.26, 0.98]	
Diabetic (n=351)	13.6%	12.5%		0.92 [0.51, 1.65]	0.88
Nondiabetic (n=1156)	7.6%	6.6%		0.86 [0.56, 1.33]	
Single vessel Tx (n=1399)	9.4%	7.7%		0.82 [0.57, 1.17]	0.25
Dual vessel Tx (n=108)	4.3%	9.3%		2.13 [0.43, 10.5]	
BMI < 29 kg/m^2 (n=842)	8.5%	5.7%		0.68 [0.40, 1.14]	0.18
BMI ≥ 29 kg/m^2 (n=663)	9.7%	10.7%		1.10 [0.68, 1.77]	
RVD ≤ 2.62 mm (n=778)	10.2%	9.5%		0.93 [0.59, 1.45]	0.73
RVD > 2.62 mm (n=728)	7.6%	6.2%		0.82 [0.46, 1.43]	
Lesion ≤ 13.0 mm (n=870)	9.1%	7.6%		0.84 [0.53, 1.33]	0.85
Lesion > 13.0 mm (n=636)	9.0%	8.1%		0.90 [0.52, 1.53]	

Binary Rates

Safety Measures at 4 Years



Time to event rates

Conclusions

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- Event rates are very low through 4 years follow-up for both the PtCr-EES and the CoCr-EES arms in this non-complex anatomic cohort. *
  - Non-signficant differences were observed between groups in the rates of death, cardiac death, QMI,TLF or ischemia-driven TLR (favoring PtCr-EES).
- Limitations
  - Study not powered for individual endpoints or event rates >1 year
  - No systematic angio/IVUS follow-up for mechanistic insights (FRX)
  - Limited lesion complexity in study population diminishes ability to differentiate between these 2 stent platforms over time.
    - Differences in stent platform flexibility/conformability would likely have greater impact on clinical events in a more complex cohort. Late adverse outcomes following CoCr-EES are ~ proportional to complexity of CAD in prior studies.
- Trend towards reduced late ID-TLR with PtCr-EES (vs.CoCr-EES) is hypothesis-generating and should be further investigated

** SPIRIT III-like (max 2 target lesions / max 2 vessels)*

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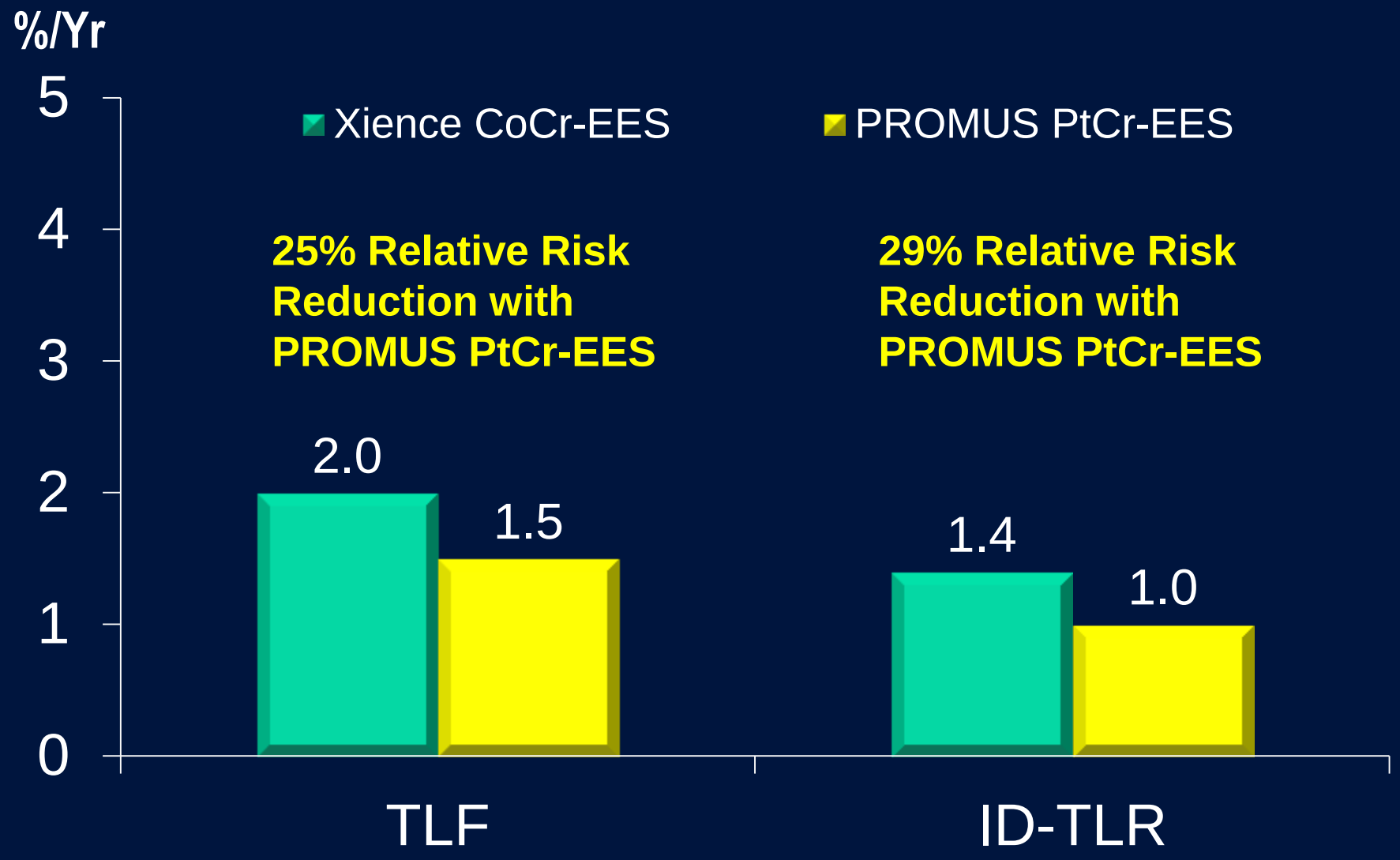
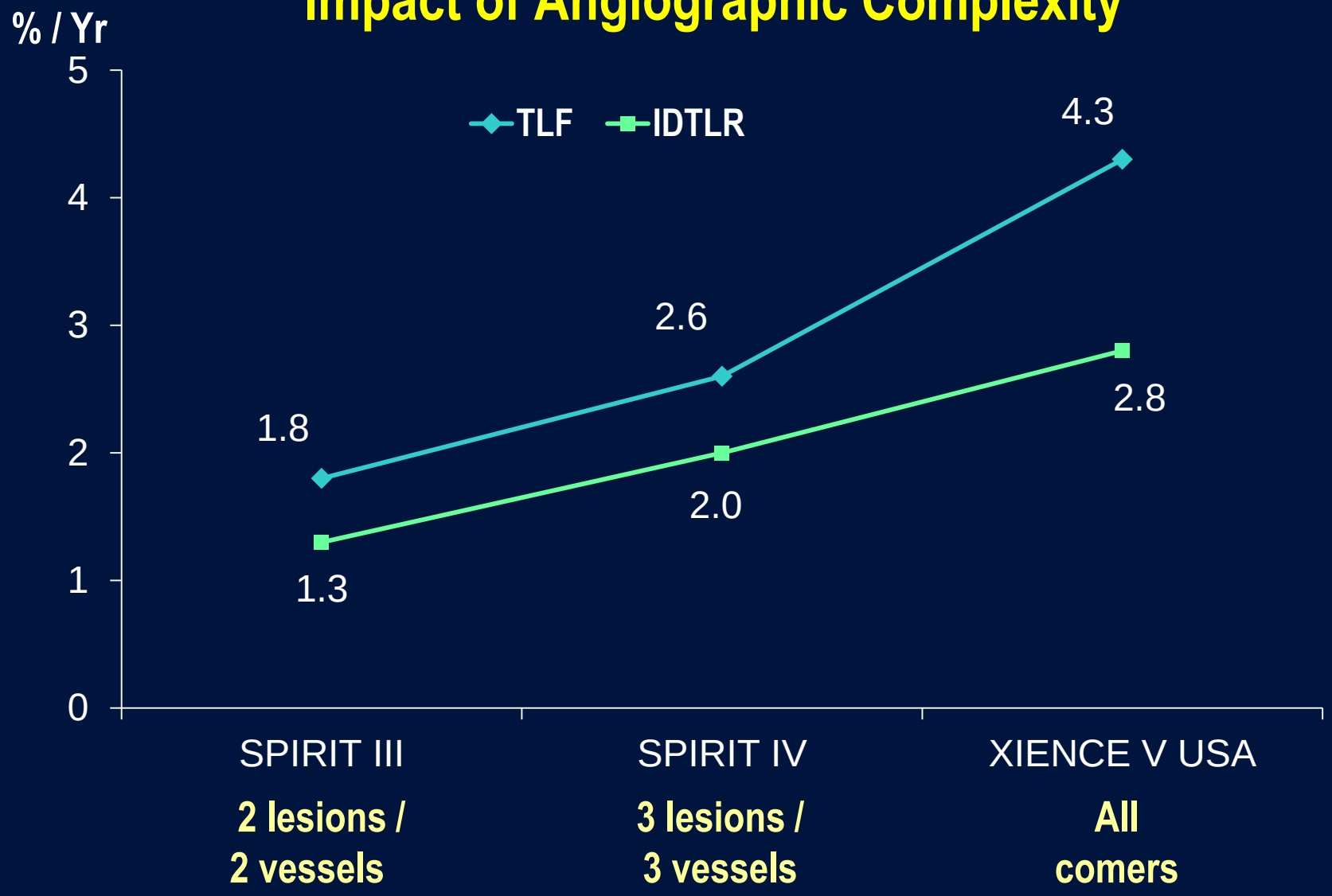
NOT USED/BACKUP

% / Year Clinical Events Beyond 1 Year: PLATINUM*



- *SPIRIT III-like (max 2 target lesions / max 2 vessels)*
- *1 stent fracture observed (Xience) with limited (non-protocol driven) angio follow-up*

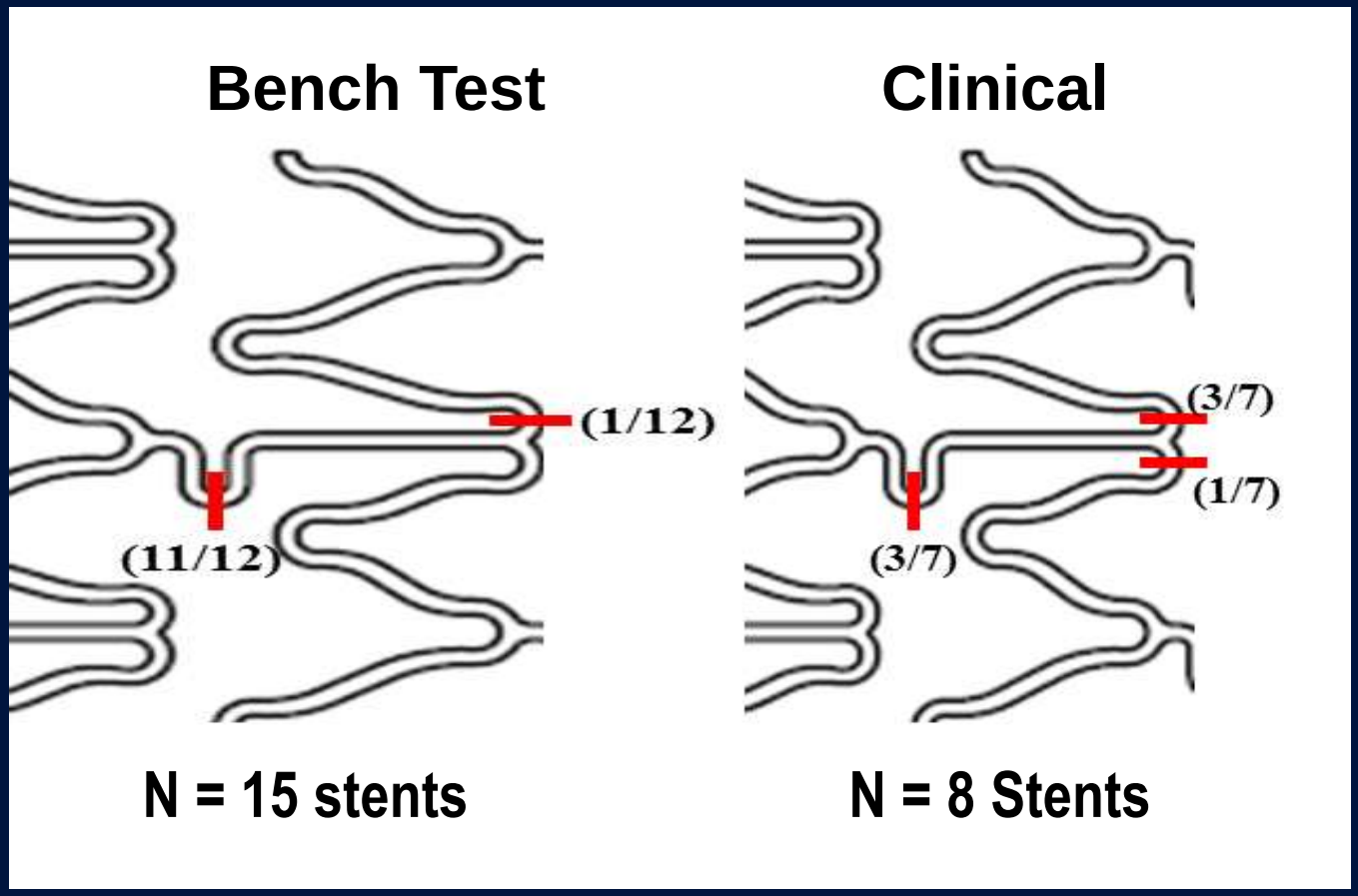
Clinical Events Beyond 1 Year *: Impact of Angiographic Complexity



** through 3 years*

SPIRIT III: Gregg Stone, MD TCT 2011; SPIRIT IV: Gregg Stone, MD TCT 2011;
XIENCE V USA: James Hermillller Jr, MD, TCT 2012; PLATINUM: Ian Meredith AM, MBBS, PhD, ACC 2013

Xience V™ Fracture Maps



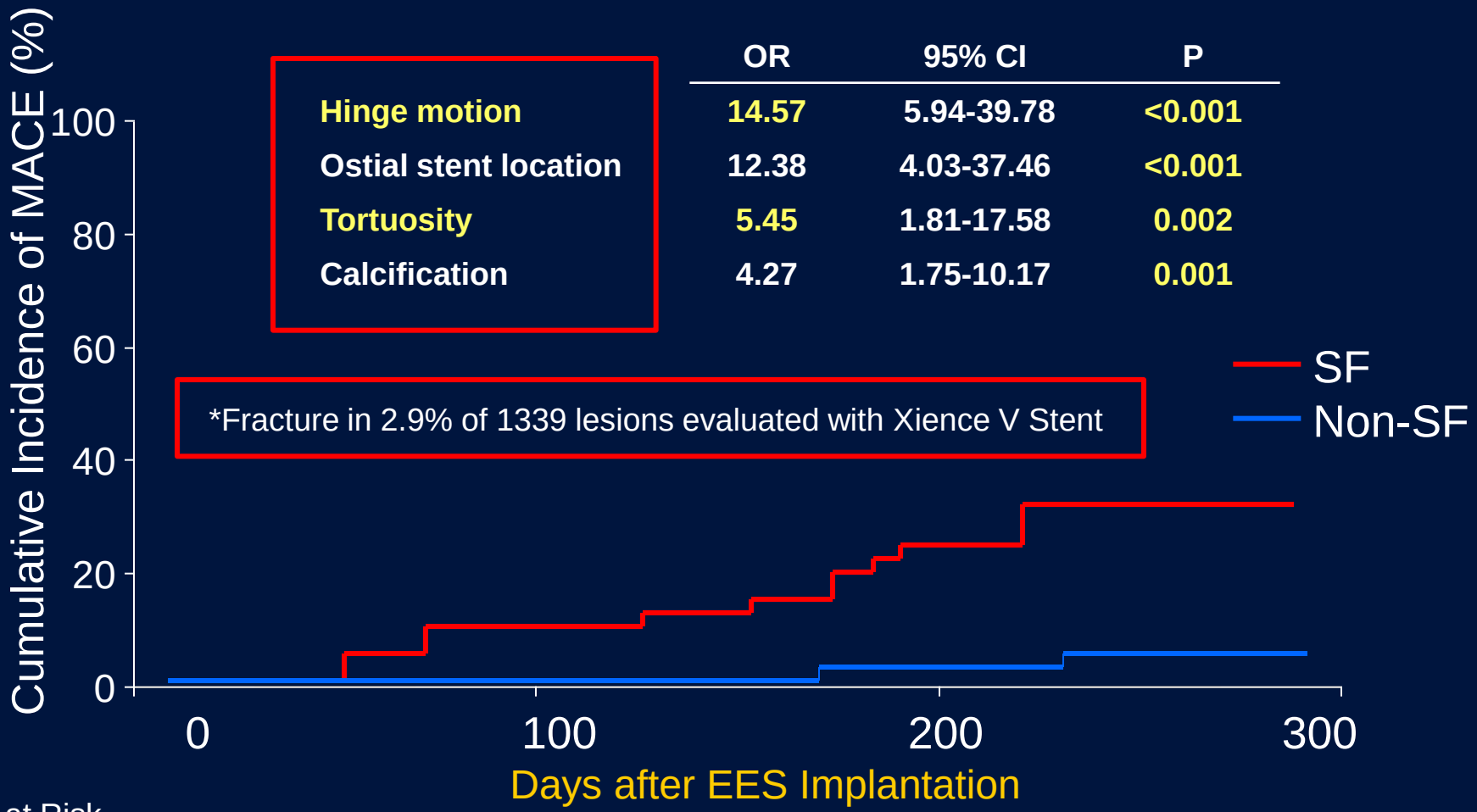
Reported Fracture Locations match bench testing results

(Foerst, J.R. et al. JACC Card Intv 2012;5:239-242
Otsuka et.al. Circulation 2014,129:211-223)

Multivariate Predictors of Stent Fracture* at 6-9 Months and MACE Following Xience V™ Deployment

	OR	95% CI	P
Hinge motion	14.57	5.94-39.78	<0.001
Ostial stent location	12.38	4.03-37.46	<0.001
Tortuosity	5.45	1.81-17.58	0.002
Calcification	4.27	1.75-10.17	0.001

*Fracture in 2.9% of 1339 lesions evaluated with Xience V Stent

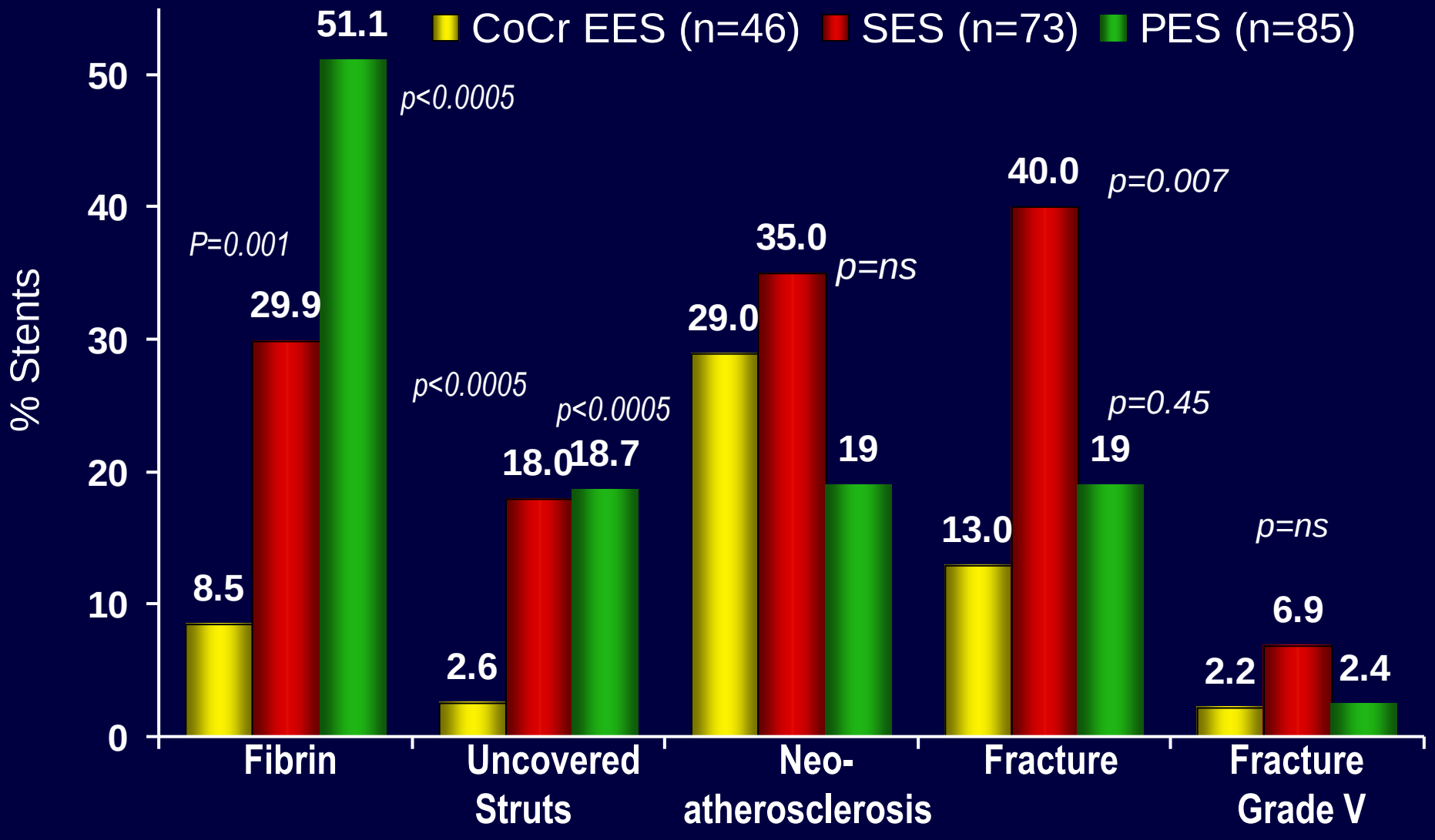


# at Risk				
SF	39	36	32	29
Non-SF	998	990	981	911

MACE defined as CD/ MI/ CI-TLR/ ST

Kuramitsu et al. Circ Cardiovasc Int 2012 (epub)

Pathology of DES in Humans



Adapted from Otsuka, Virmani et al Circ 2014 (epub)