Comparison of Sirolimus- vs. Everolimus-eluting Stents in Diabetic and Non-Diabetic Patients: Results from the IRIS-DES Registry and the ESSENCE-DIABETES trial

Diabetic Paradox: Is It Real?

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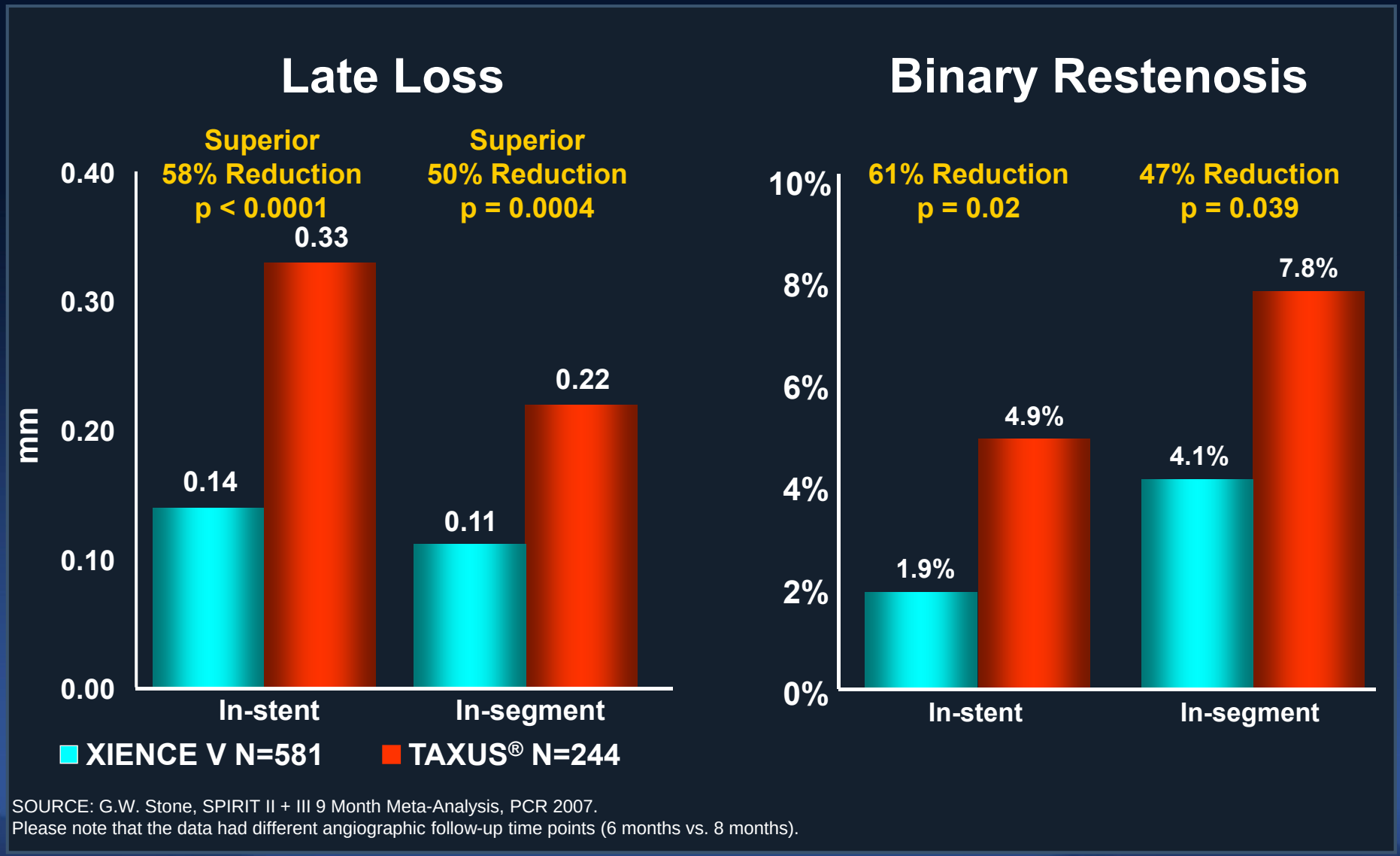
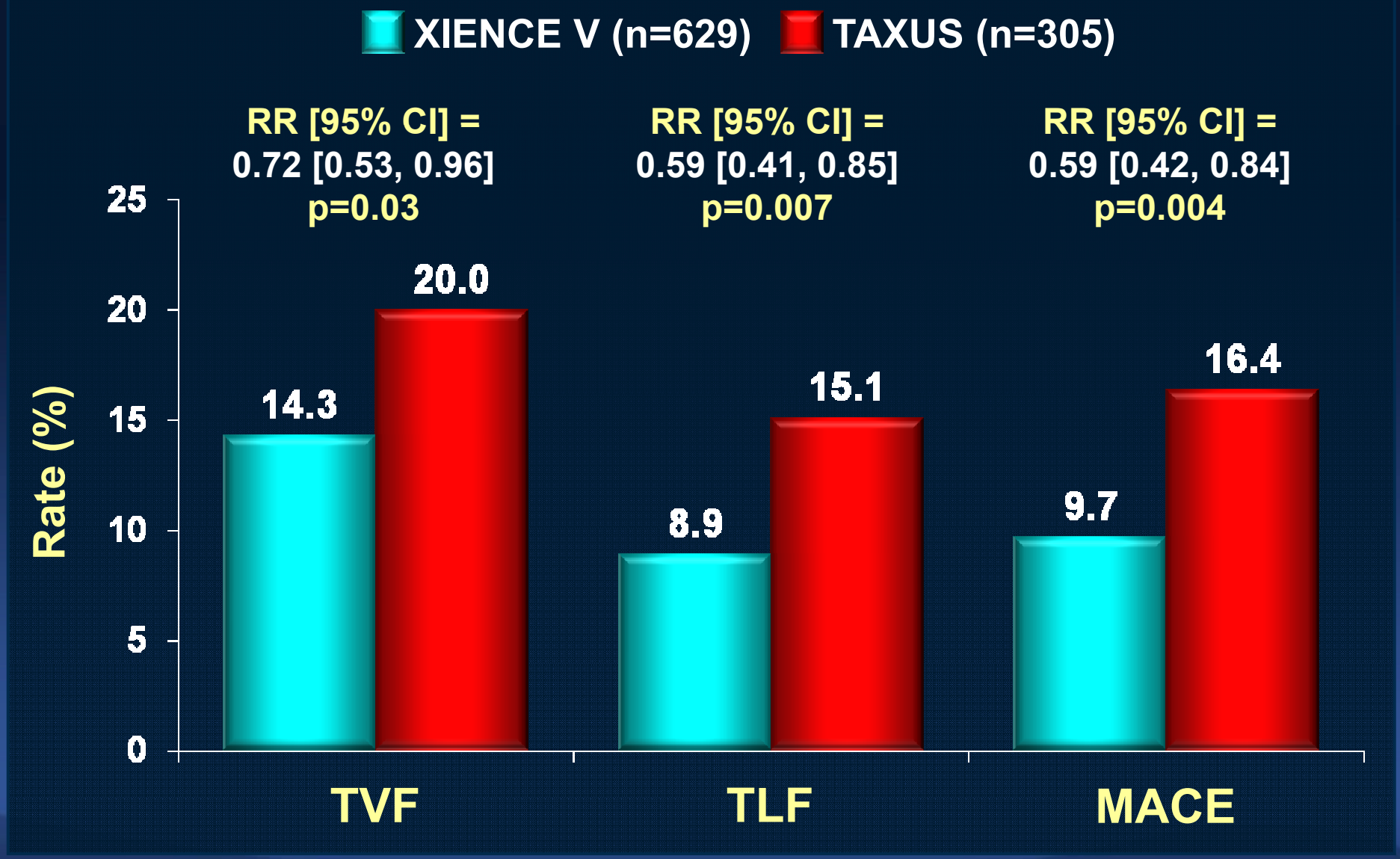
SPIRIT II + III Angiographic Results



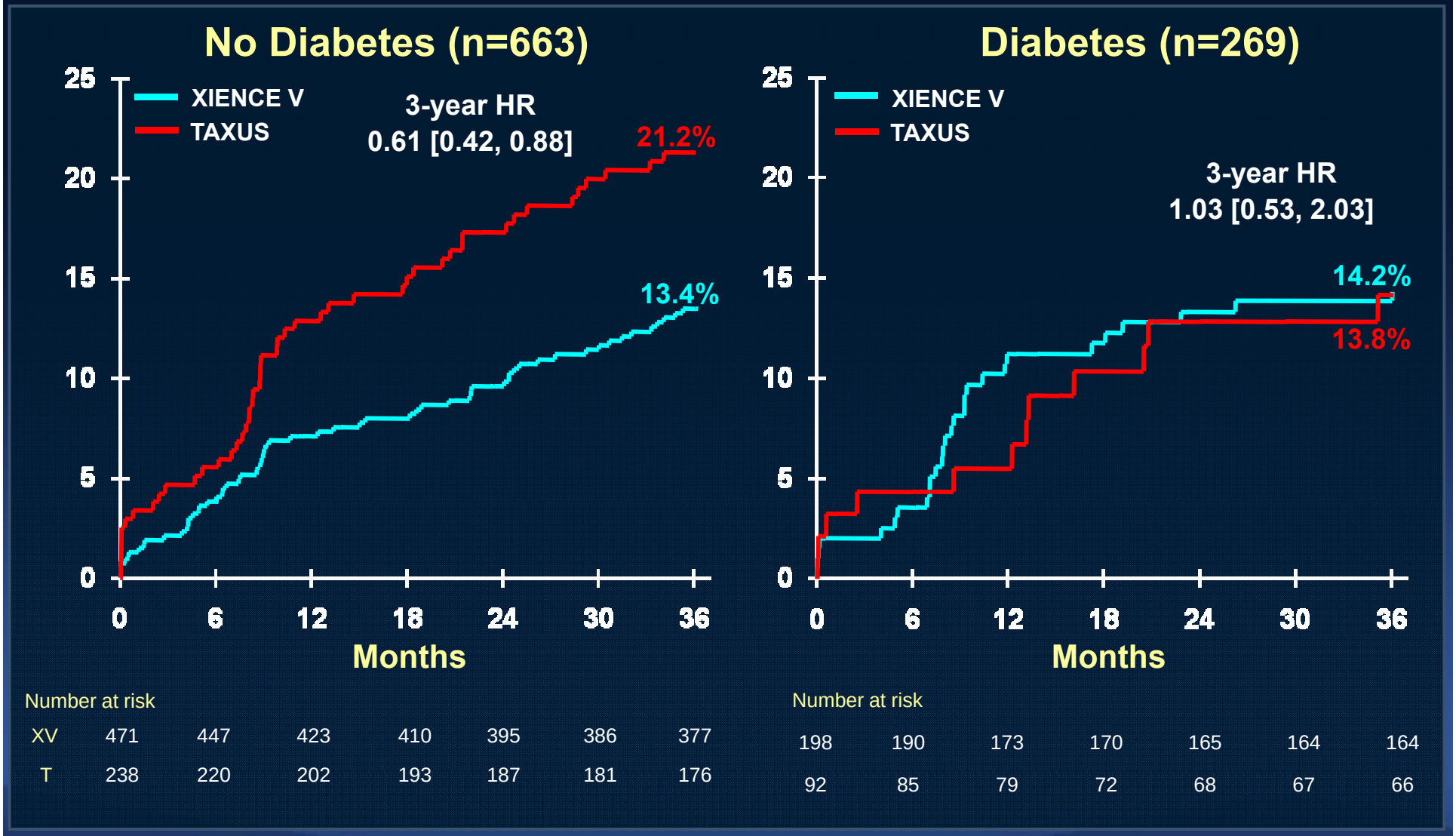
SOURCE: G.W. Stone, SPIRIT II + III 9 Month Meta-Analysis, PCR 2007.
Please note that the data had different angiographic follow-up time points (6 months vs. 8 months).

3-Year Outcomes: SPIRIT III

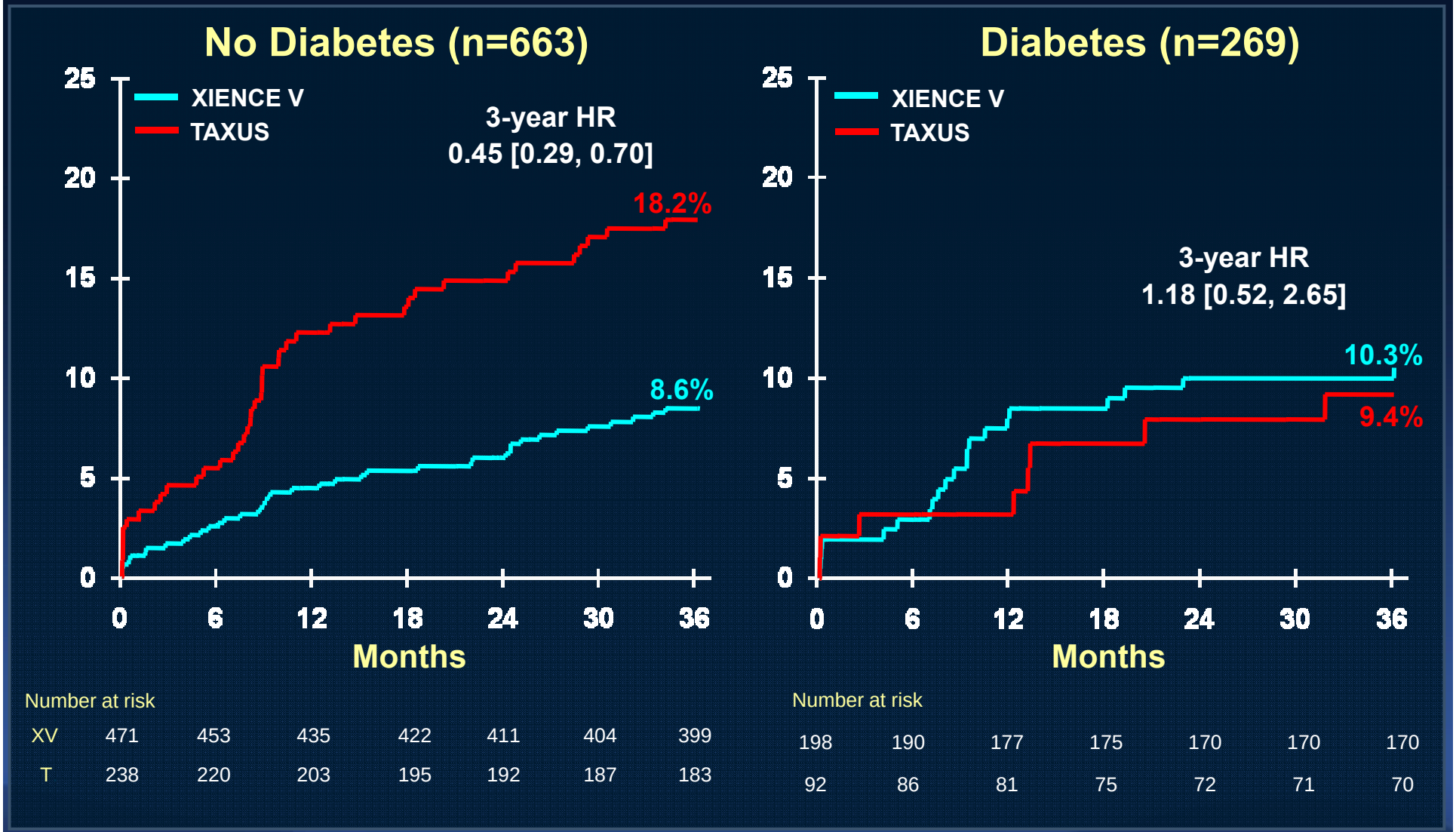


TVF = cardiac death, MI, or ID-TVR; MACE = cardiac death, MI, or ID-TLR;
TLF = cardiac death, target vessel MI, or ID-TLR

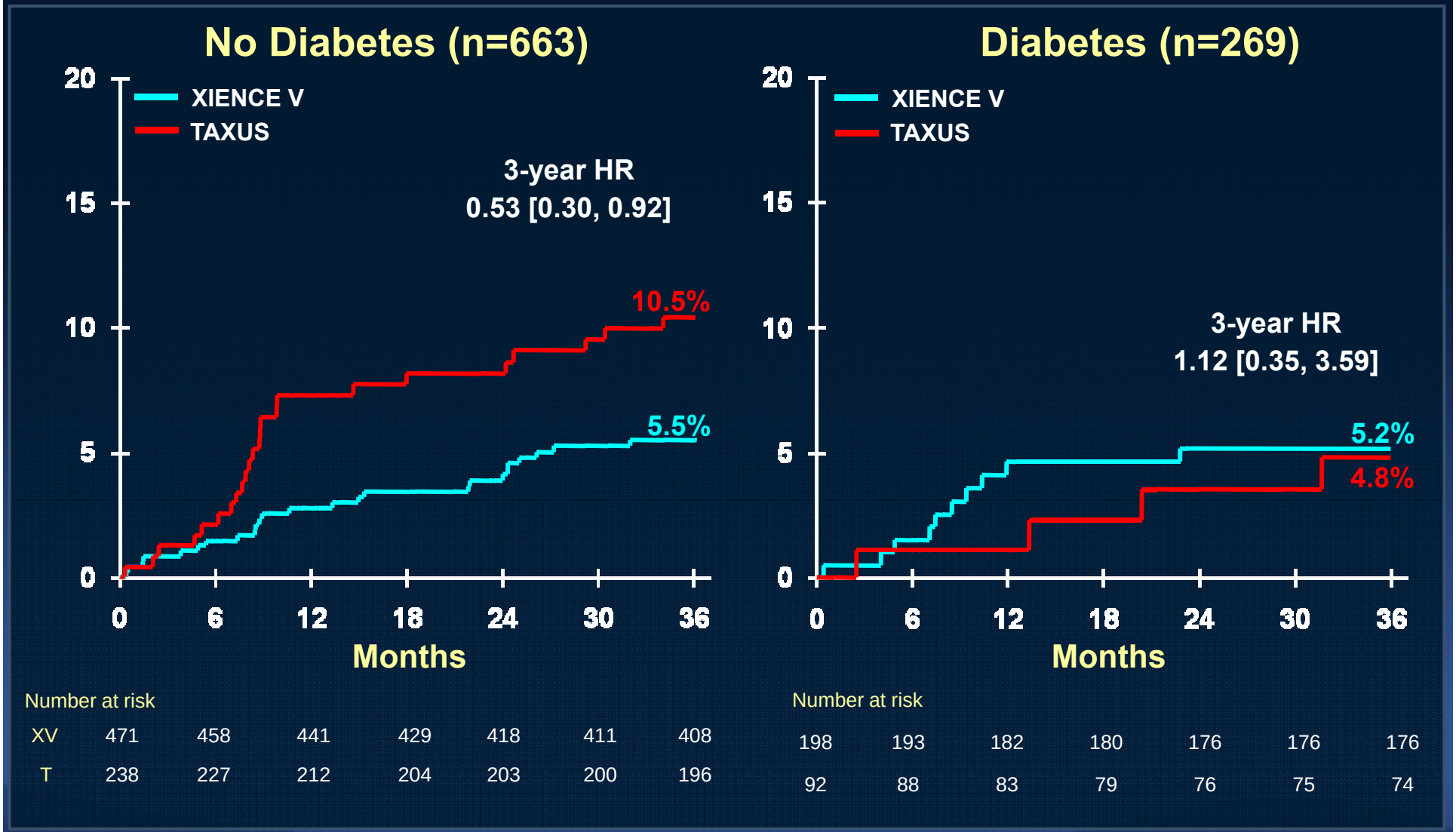
SPIRIT III Diabetes
TVF (3 years)



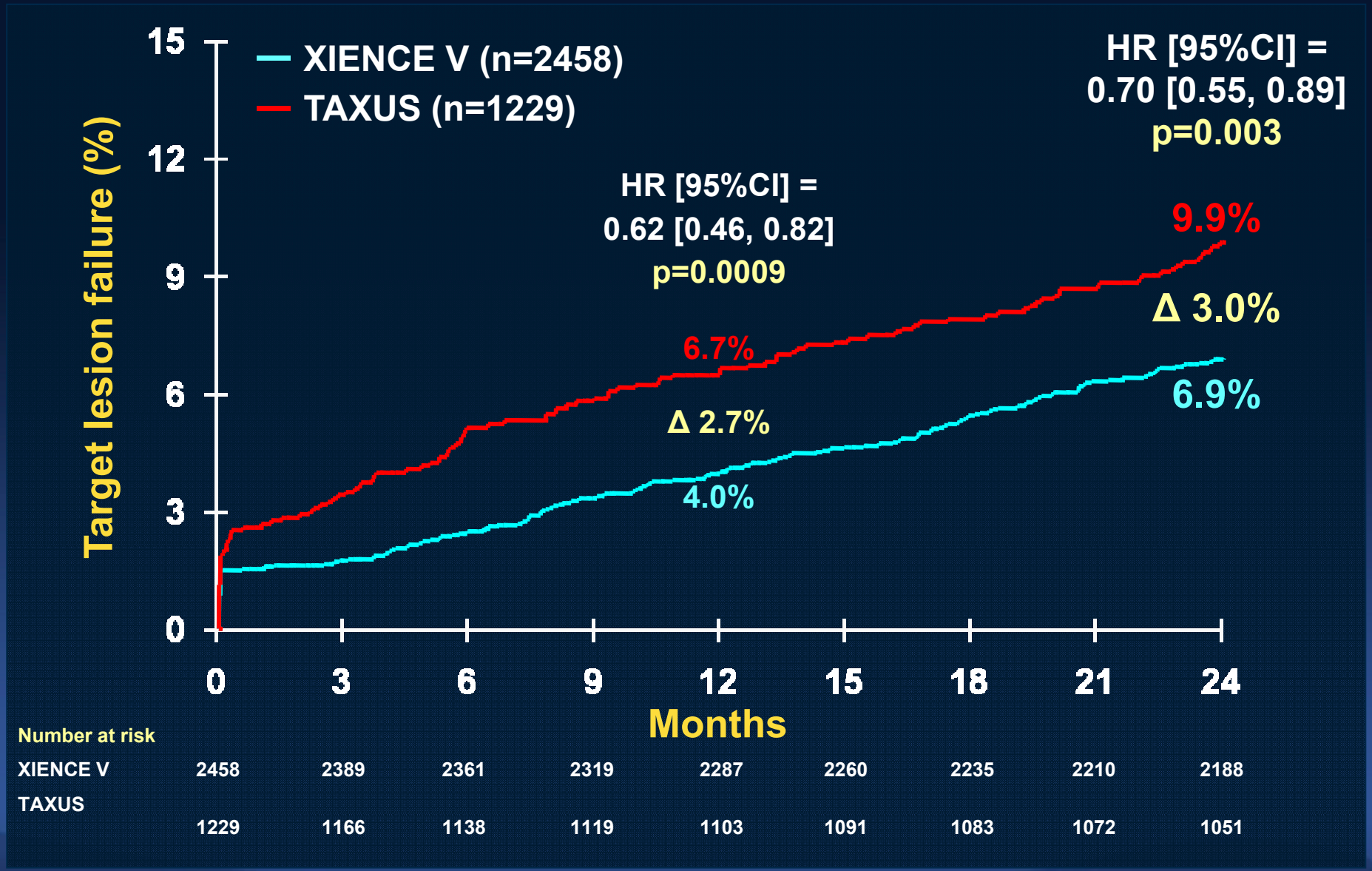
SPIRIT III Diabetes
MACE (3 years)



SPIRIT III Diabetes
TLR (3 years)

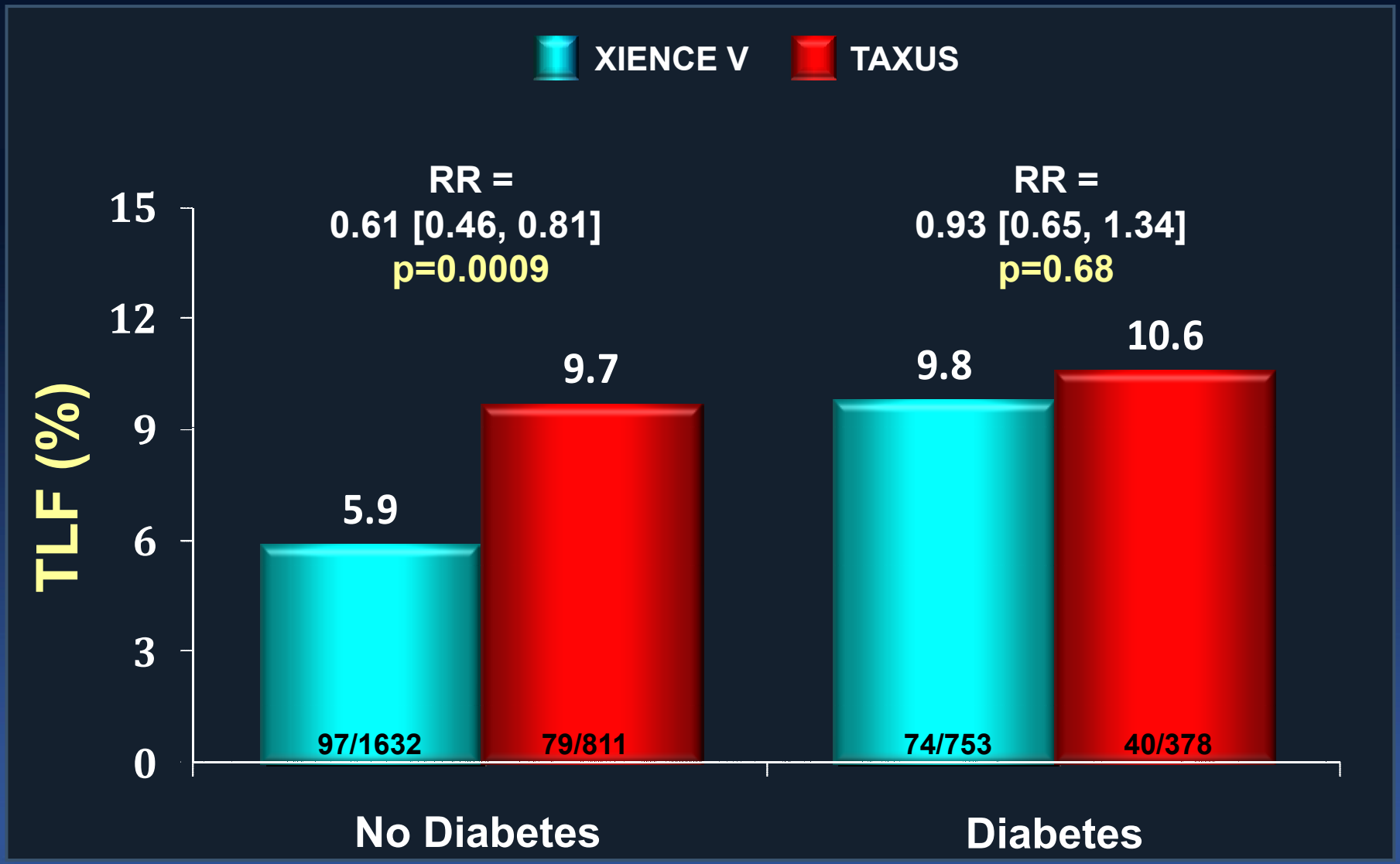


2 Yrs TLF : SPIRIT IV



Stone GW et al., NEJM 2010;362:1663-74

Impact of Diabetes on TLF at 2 years



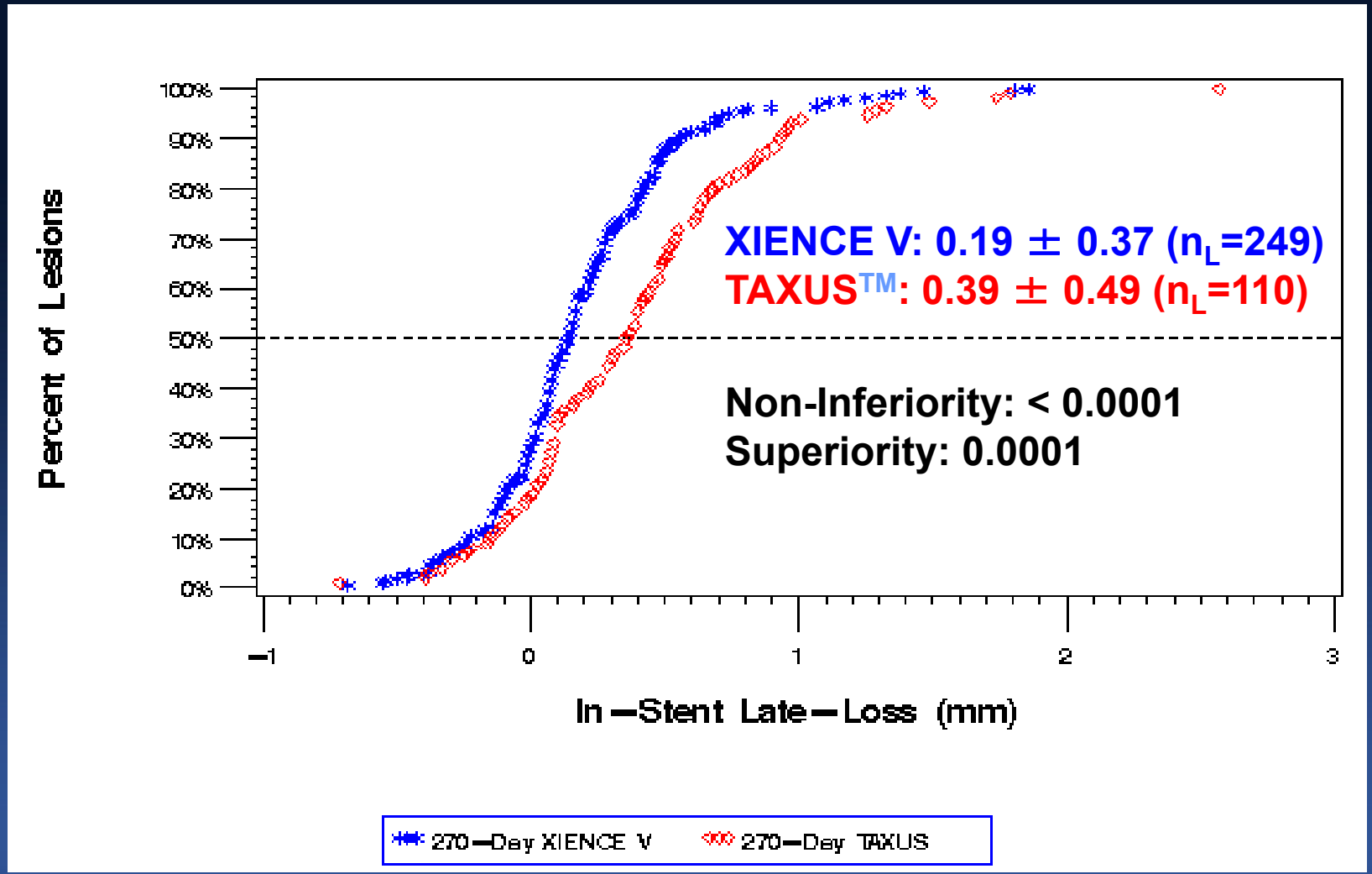
TLF = cardiac death, target-vessel MI, or ischemia-driven TLR
Categorical (binary) event rates

Stone GW et al., NEJM 2010;362:1663-74

Conclusion from SPIRIT II, III, IV

- The safety and efficacy of EES over PES have been demonstrated in these RCTs
- However, explanation for the different results from diabetic subgroup remains uncertain

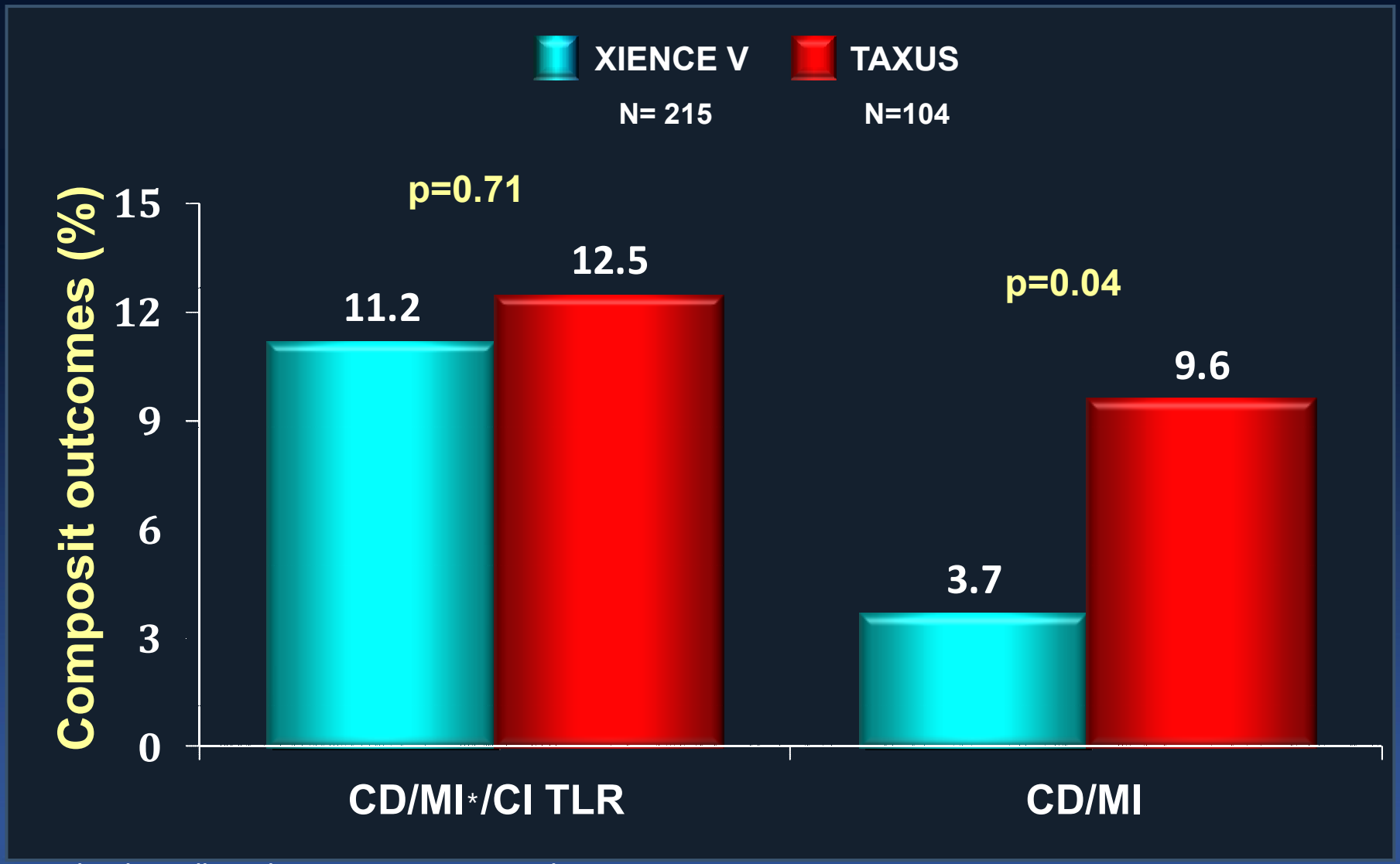
SPIRIT V Diabetic RCT: Primary Endpoint: 9 Mo LL



Angiographic follow-up at 270-days: XIENCE V: 88% TAXUS: 86%

Grube, EuroPCR 2010

SPIRIT V Diabetic RCT: 1-Year Outcomes



*Not clearly attributed to a non target vessel

p-values are not from formal hypothesis testing and are displayed for descriptive purposes only

Grube, EuroPCR 2010

SPIRIT V Diabetic RCT: Conclusion

- XIENCE V is superior to TAXUS Liberte in the primary endpoint of in-stent late loss, 0.19 vs. 0.39, p=0.0001

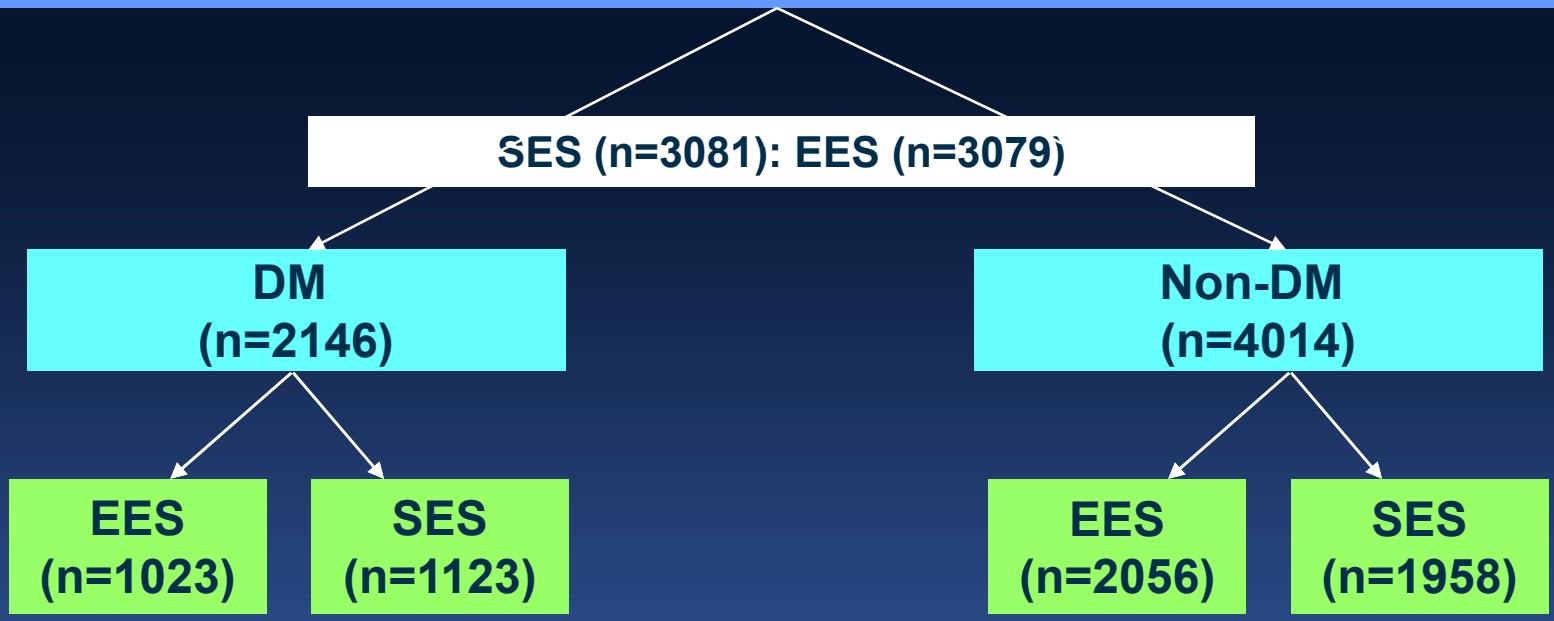
- XIENCE V is safe when compared to TAXUS Liberte in diabetic patients at 1 year:

  - composite endpoint of cardiac death & MI of 3.7% vs. 9.6%, p=0.04

  - No incidence of stent thrombosis for XIENCE V through 1 year

IRIS-DES Registry: 55 Centers

Overall 6160 patients from April 2008 to June 2010



Primary end-point: MACE (death, non-fatal MI, TVR) at 1year
Secondary end-point: Death, MI, Death or MI, TLR, TVR, ST, Procedural Success

Baseline Clinical Characteristics

No. of Patients	DM (n=2146)		Non-DM (n=4014)	
	CYPHER (n=1123)	XIENCE (n=1023)	CYPHER (n=1958)	XIENCE (n=2056)
Age, yrs	64.5±10.0	64.6±9.6	62.9±11.2	63.3±11.3
Male gender	701 (62)	564 (62)	1350 (69)	1444 (70)
BMI, kg/m^2	24.8±3.1	25.0±3.2	24.6±3.0	24.5±3.2
Hypertension	802 (71)	746 (73)	1108 (57)	1175 (57)
Current smoking	290 (26)	275 (27)	54 (28)	610 (30)
Hyperlipidemia	468 (42)	421 (41)	769 (39)	734 (36)
Clinical diagnosis				
Silent ischemia	39 (4)	31 (3)	66 (3)	46 (2)
Stable angina	350 (31)	324 (32)	655 (34)	598 (29)
Unstable angina	509 (45)	456 (45)	785 (40)	883 (43)
NSTEMI	133 (12)	100 (10)	226 (12)	236 (12)
STEMI	92 (8)	112 (11)	226 (12)	293 (14)

Baseline Clinical Characteristics

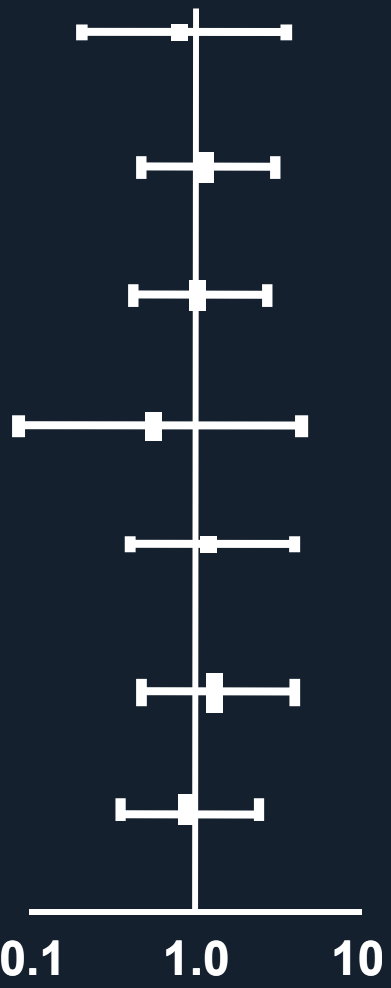
No. of Patients	DM (n=2146)		Non-DM (n=4014)	
	CYPHER (n=1123)	XIENCE (n=1023)	CYPHER (n=1958)	XIENCE (n=2056)
ECG findings				
Sinus rhythm	1081 (96)	987 (97)	1901 (97.1)	1995 (97)
Atrial fib.	40 (4)	35 (3)	54 (3)	57 (3)
Others	2 (0.2)	1 (0.1)	3 (0.2)	4 (0.2)
LVEF (%)	58.7±10.5	58.9±10.7	59.3±9.6	59.7±9.8
Previous CABG	40 (4)	27 (3)	43 (2)	34 (2)
Previous PCI	236 (21)	186 (18)	341 (17)	266 (13)
Previous MI	93 (8)	60 (6)	133 (7)	97 (5)
Family Hx. of CAD	51 (5)	35 (3)	107 (6)	77 (4)
Previous CHF	41 (4)	27 (3)	36 (2)	38 (2)
Previous stroke	99 (9)	96 (9)	118 (6)	152 (7)
Renal failure	84 (8)	63 (6)	35 (2)	40 (2)

Procedural Characteristics

No. of Patients	DM (n=2146)		Non-DM (n=4014)	
	CYPHER (n=1123)	XIENCE (n=1023)	CYPHER (n=1958)	XIENCE (n=2056)
Disease extent				
1VD	464 (41)	439 (43)	1000 (51)	1010 (49)
2VD	400 (36)	349 (34)	619 (32)	676 (33)
3VD	259 (23)	235 (23)	339 (17)	370 (18)
Left main disease	82 (7.3)	108 (10.6)	100 (5)	203 (10)
LAD disease	866 (77.1)	791 (77.3)	1515 (77)	1545 (75)
PCI Indications				
Elective	844 (75)	824 (81)	1460 (75)	1606 (78)
Urgent	109 (10)	89 (9)	236 (12)	246 (12)
Emergent	170 (15)	110 (11)	262 (13)	204 (10)
Complete revascularization	908 (91)	881 (86)	1638 (84)	1813 (88)
Total No. of stents	1.9±1.0	1.9±1.2	1.7±0.9	1.8±1.1

Diabetic Patient

Outcomes	HR (95% CI)	P
Death	0.82 (0.41-1.66)	0.58
MI	1.09 (0.81-1.47)	0.58
Death or MI	1.03 (0.78-1.36)	0.83
Stent thrombosis	0.52 (0.13-2..07)	0.35
TLR	1.11 (0.63-1.97)	0.72
TVR	1.22 (0.72-2.06)	0.46
MACE	0.95 (0.58-1.57)	0.85



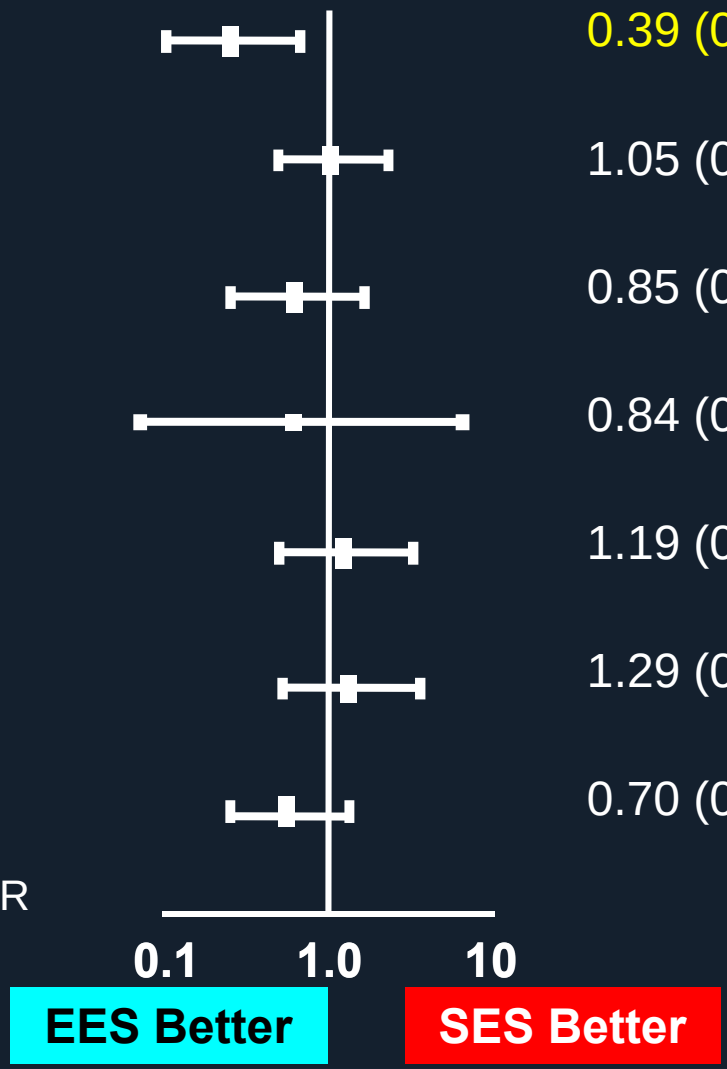
*MACE = death, MI, TVR

EES Better **SES Better**

Non-Diabetic Patient

Outcomes	HR (95% CI)	P
Death	0.39 (0.19-0.81)	0.01
MI	1.05 (0.75-1.46)	0.78
Death or MI	0.85 (0.69-1.05)	0.13
Stent thrombosis	0.84 (0.24-2.92)	0.79
TLR	1.19 (0.65-2.16)	0.57
TVR	1.29 (0.77-2.14)	0.33
MACE	0.70 (0.45-1.07)	0.10

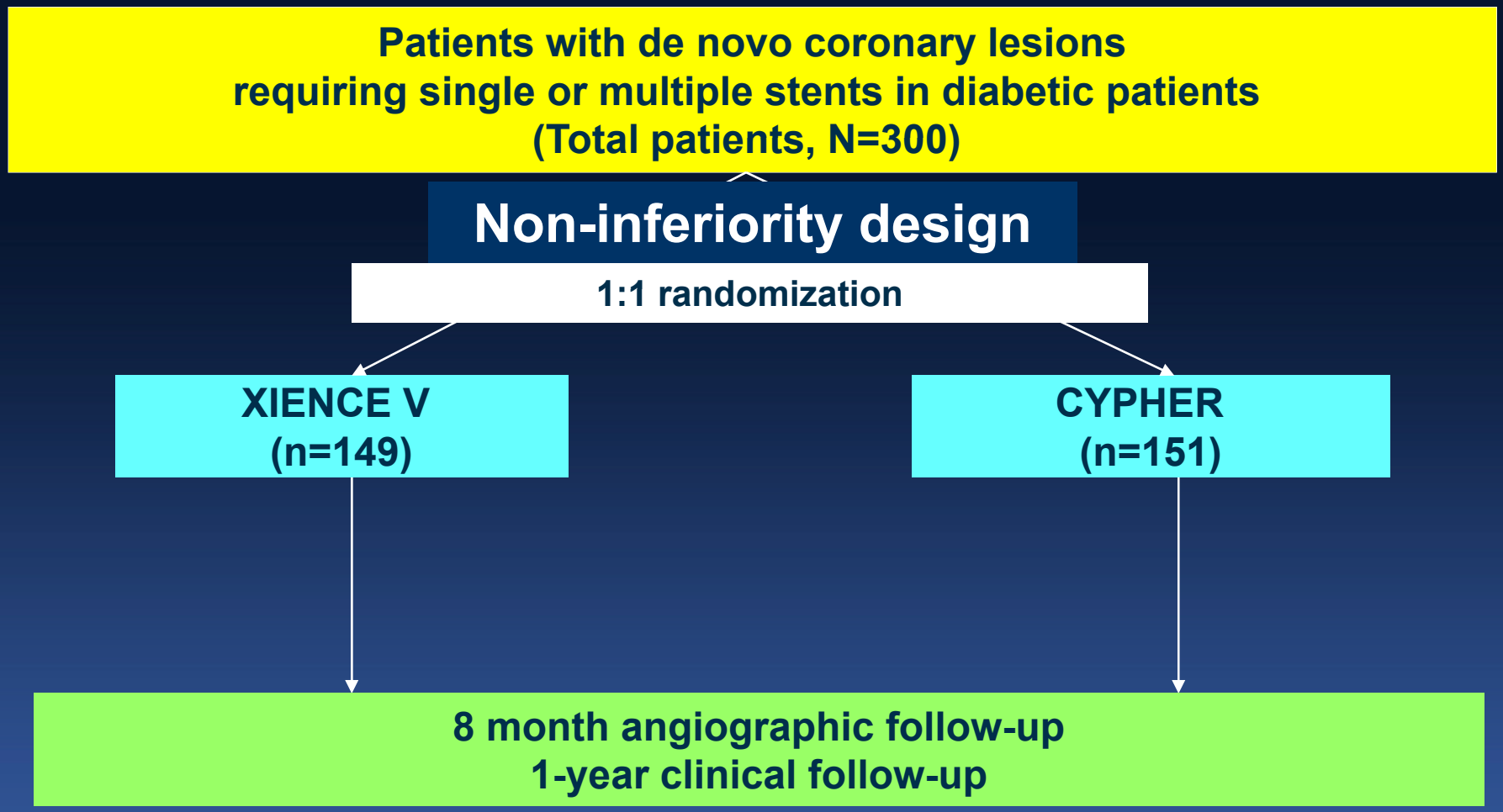
*MACE = death, MI, TVR



Conclusions: IRIS-DES registry

- In this large, multi-center observational PCI cohort in “real-world” during 1 year,
  - Diabetics : MACE was similar in EES vs. SES
  - Non-diabetics : MACE was lower trend in EES
  - **Death : EES was significantly lower than SES)**
  - Stent thrombosis, TLR, and TVR were similar between the two groups

ESSENCE-DIABETES



Primary end-point: Angiographic in-segment late loss at 8-month angiography
Secondary end-point: Clinical outcomes at 12 month follow-up
IVUS results at 8 month angiographic follow-up (selected center)

Patient Demographics

	EES (n=149)	SES (n=151)	*p*
Age (yrs)	63.2±8.3	63.5±8.1	0.831
Men	78 (52.3%)	99 (65.6%)	0.020
Treatment of DM			0.400
OHA	105 (70.5%)	115 (76.2%)	
Insulin	24 (18.1%)	19 (12.6%)	
Dietary alone	17 (11.4%)	17 (11.3%)	
Glycosylated Hb	7.9±1.6%	7.7±1.4%	0.274
Hypertension	102 (68.5%)	110 (72.8%)	0.404
Smoking	31 (20.8%)	41 (27.2%)	0.199
Hypercholesterolemia	62 (41.6%)	53 (35.1%)	0.246
LVEF (%)	59.9±7.6	61.4±5.9	0.084

Target lesion and Clinical Presentation

	EES (n=149)	SES (n=151)	*p*
Stented site			0.837
LAD	91 (61.1%)	89 (58.9%)	
LCX	21 (14.1%)	25 (16.6%)	
RCA	37 (24.8%)	37 (24.5%)	
Multi-vessel disease	84 (56.4%)	81 (53.6%)	0.634
Diagnosis			0.073
Stable angina	85 (57.0%)	90 (59.6%)	
Unstable angina	60 (40.3%)	49 (32.5%)	
Myocardial infarction	4 (2.7%)	12 (7.9%)	

Procedural Characteristics

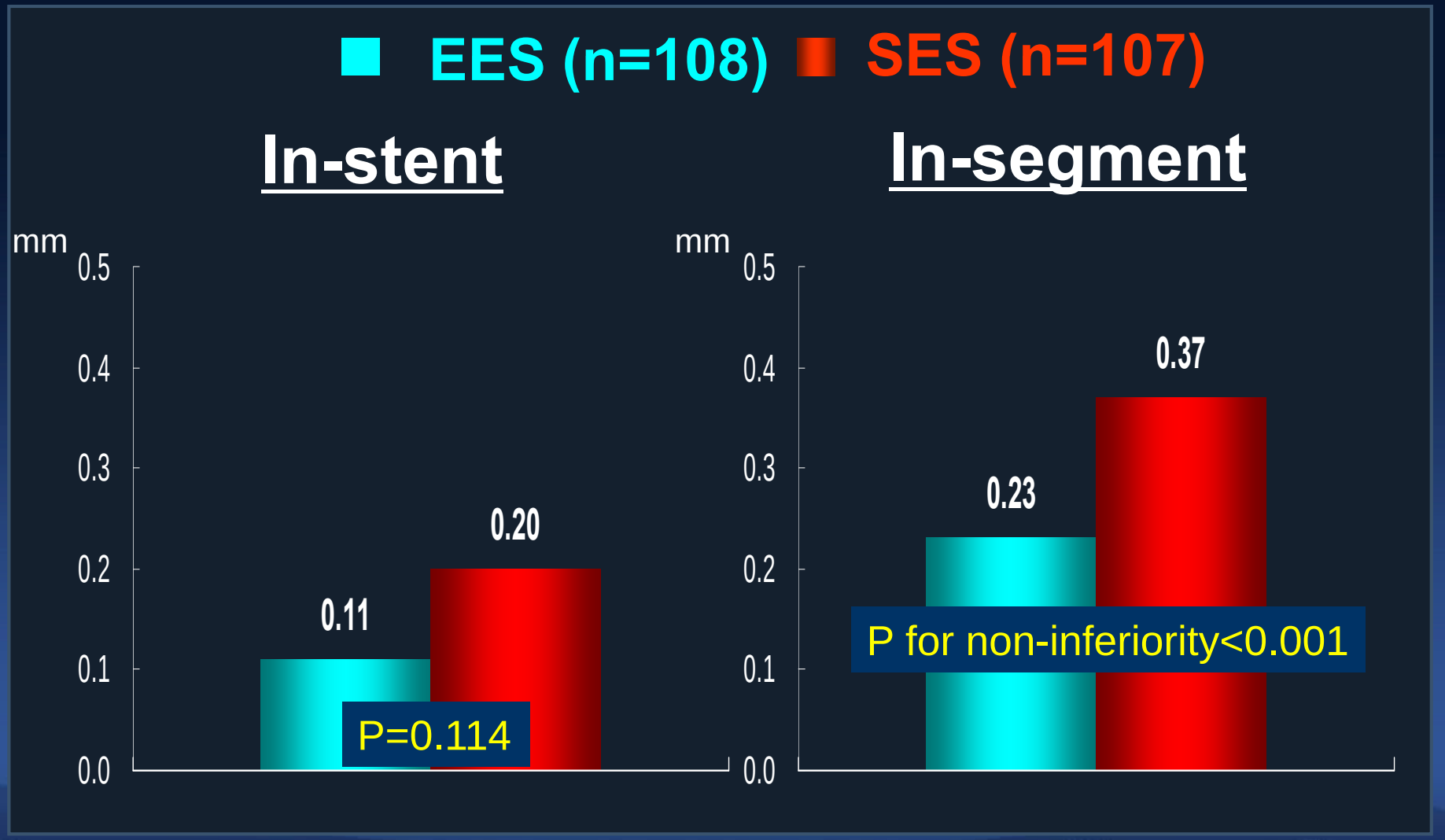
	EES (n=149)	SES (n=151)	*p*
Maximal pressure (atm)	12.9±3.8	13.6±3.8	0.077
Use of IVUS	117 (78.5%)	119 (78.8%)	0.952
Use of GP IIb/IIIa inhibitor	2 (1.3%)	7 (4.6%)	0.173
Number of stents per lesion	1.3±0.6	1.3±0.5	0.865
Multi-vessel stenting	41 (27.5%)	46 (30.5%)	0.574
Total stent length	27.7±12.7	29.7±14.8	0.217

Baseline Angiographic Characteristics

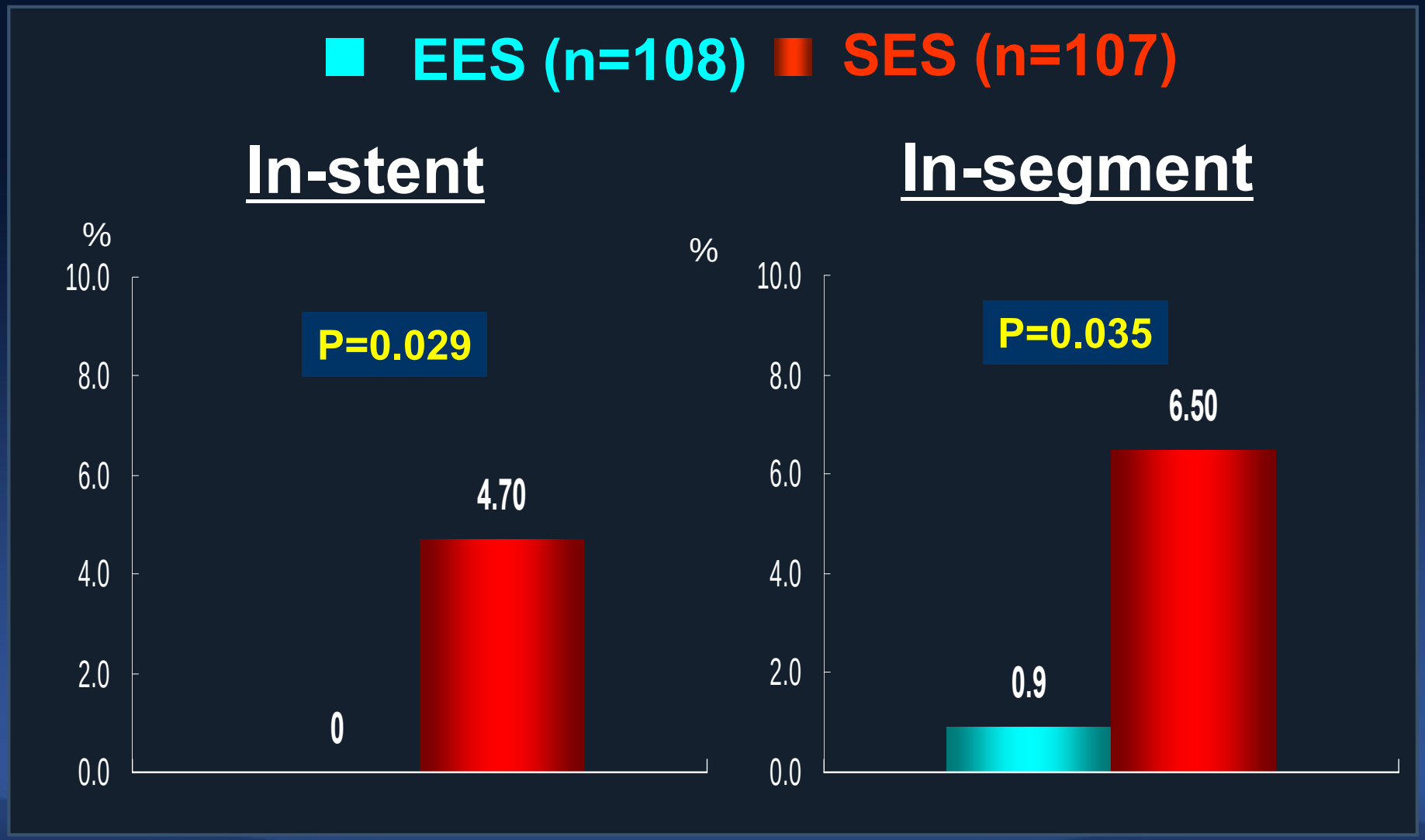
	EES (n=149)	SES (n=151)	*p*
Reference vessel (mm)	2.77±0.53	2.77±0.45	0.965
Lesion length (mm)	22.4 ±12.9	23.9 ±14.0	0.337
MLD (mm)	0.90±0.41	0.87±0.46	0.497
Diameter stenosis (%)	69.1±13.6	70.7±14.4	0.423

8 Mo Late loss: Primary End point

Late loss was calculated using maximal regional late loss



Restenosis rate



MACE at 12-Month

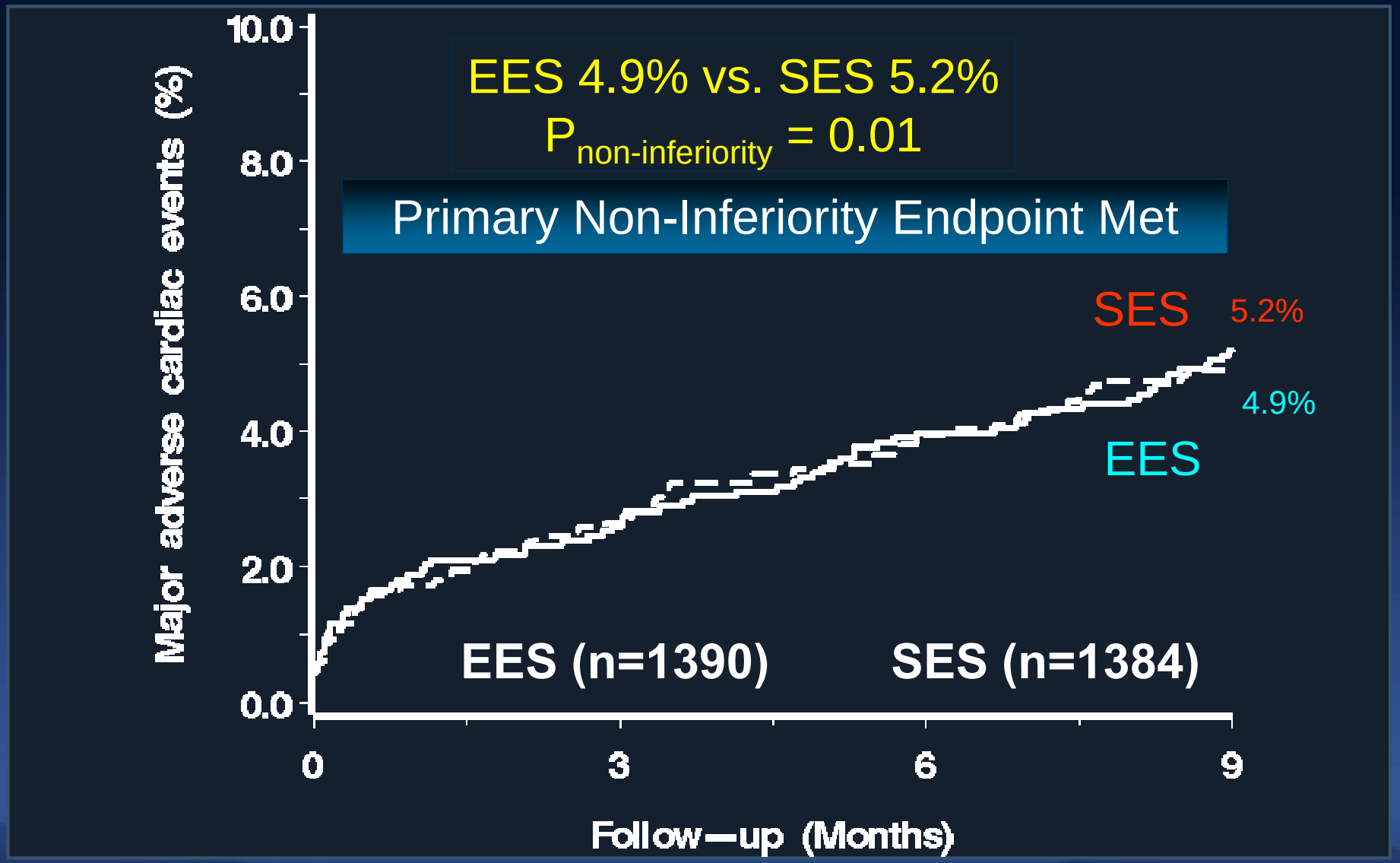
	EES	SES	P
Patients	149	151	
Death	2 (1.3%)	5 (3.3%)	
Cardiac	1 (0.7%)	2 (1.3%)	0.448
Non-cardiac	1 (0.7%)	3 (2.0%)	
MI	0	2 (1.3%)	0.498
Stent thrombosis	1	1	
Acute	0	0	
Subacute	1 (0.7%)	1 (0.7%)	0.999
Late	0	0	
Ischemic driven TVR	1 (0.7%)	6 (4.0%)	0.121
Ischemic driven TLR	1 (0.7%)	4 (2.6%)	0.371
Death/MI/ischemic driven TVR	3 (2.0%)	10 (6.6%)	0.085
Death/MI/ischemic driven TLR	3 (2.0%)	8 (5.3%)	0.218

Conclusions: ESSENCE-DIABETES

- EES implantation resulted in non-inferior to SES in reducing in-segment late loss and reduced 8-month angiographic restenosis.

- Owing to the improved angiographic outcome, EES showed lower tendency of 12-month ischemic driven TVR-MACE without significant difference of MI, death or stent thrombosis.

SORT OUT IV: MACE

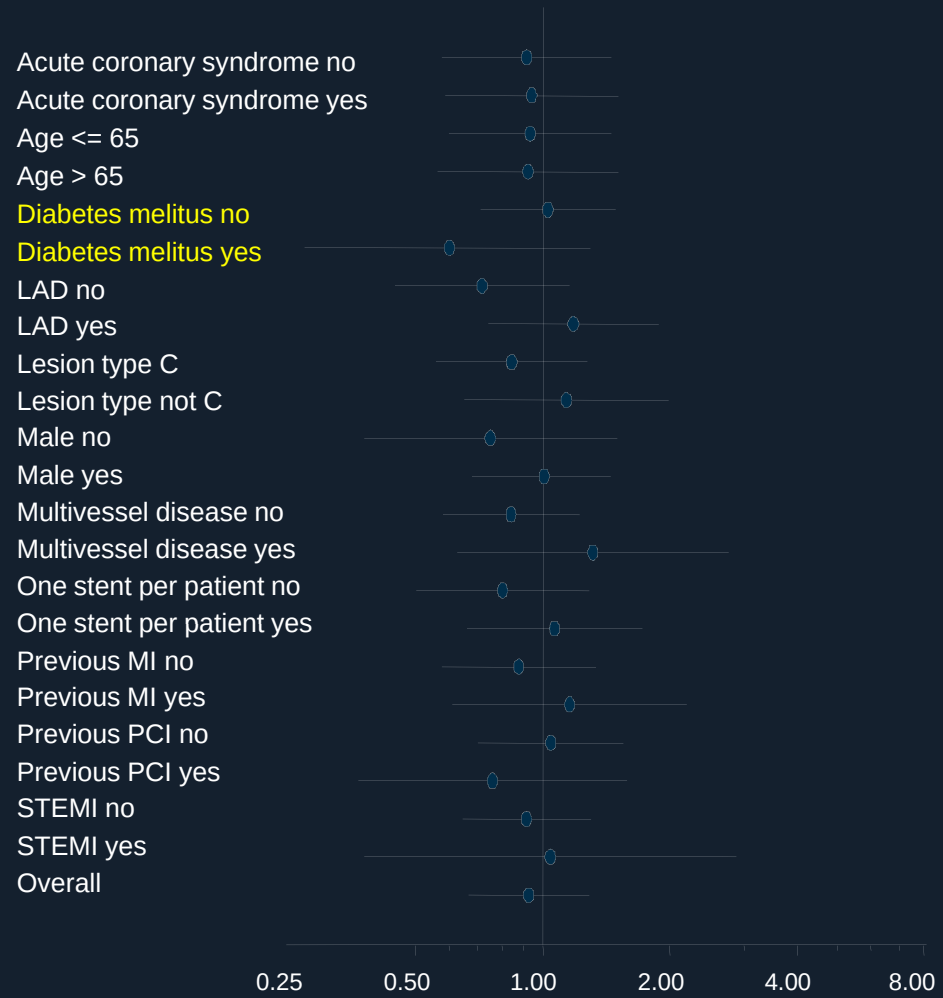


MACE: CD, MI, definite ST, TVR

Jensen LO, TCT 2010

Major Adverse Cardiac Event

PRE-SPECIFIED SUBGROUPS



	Events (%)		Hazard Ratio (95% CI)		P Value for Interaction
	Everolimus-eluting stent	Sirolimus-eluting stent			
Acute coronary syndrome no	35/773 (4.5)	36/1188 (4.9)	0.94	(0.59 - 1.50)	1.00
Acute coronary syndrome yes	33/617 (5.3)	36/630 (5.7)	0.94	(0.59 - 1.51)	-
Age <= 65	37/719 (5.1)	41/746 (5.5)	0.93	(0.60 - 1.46)	0.95
Age > 65	31/671 (4.6)	31/638 (5.0)	0.95	(0.58 - 1.57)	-
Diabetes melitus no	58/1196 (4.8)	56/1188 (4.7)	1.03	(0.71 - 1.49)	0.26
Diabetes melitus yes	10/194 (5.2)	16/196 (8.7)	0.63	(0.28 - 1.38)	-
LAD no	30/705 (4.3)	38/665 (5.9)	0.74	(0.46 - 1.19)	0.16
LAD yes	38/685 (5.5)	34/719 (4.7)	1.18	(0.74 - 1.88)	-
Lesion type C	41/580 (7.1)	49/602 (8.3)	0.86	(0.57 - 1.31)	0.43
Lesion type not C	27/810 (3.3)	23/782 (2.9)	1.14	(0.65 - 1.99)	-
Male no	14/335 (4.2)	19/343 (5.5)	0.75	(0.38 - 1.50)	0.47
Male yes	54/1055 (5.1)	53/1041 (5.2)	1.01	(0.69 - 1.47)	-
Multivessel disease no	51/1166 (4.4)	60/1182 (5.2)	0.86	(0.59 - 1.24)	0.30
Multivessel disease yes	17/224 (7.6)	12/202 (5.9)	1.32	(0.63 - 2.75)	-
One stent per patient no	32/550 (5.8)	36/511 (7.2)	0.83	(0.51 - 1.33)	0.46
One stent per patient yes	34/833 (4.1)	33/864 (3.8)	1.07	(0.66 - 1.72)	-
Previous MI no	41/947 (4.3)	46/955 (4.9)	0.90	(0.59 - 1.37)	0.51
Previous MI yes	21/276 (7.6)	17/259 (6.6)	1.16	(0.61 - 2.20)	-
Previous PCI no	50/963 (5.2)	47/964 (5.0)	1.07	(0.72 - 1.59)	0.42
Previous PCI yes	13/264 (4.9)	16/250 (6.4)	0.76	(0.37 - 1.58)	-
STEMI no	61/1268 (4.8)	64/1239 (5.2)	0.93	(0.66 - 1.32)	0.84
STEMI yes	7/122 (5.7)	8/145 (5.5)	1.04	(0.38 - 2.88)	-
Overall	68/1390 (4.9)	72/1384 (5.2)	0.94	(0.67 - 1.31)	-

Jensen LO, TCT 2010

Conclusion : SORT OUT IV

- Both the EES and the SES were associated with low major adverse cardiac events
- EES was found to be non-inferior to the SES for patients treated with percutaneous coronary intervention including diabetes.

Jensen LO, TCT 2010

Conclusion

- Efficacy of Xience stent is similar or more effective, compared with that of Taxus stent in diabetic and non-diabetic population.
- Xience stent is safe compared with Taxus stent in diabetic and non-diabetic population.

Conclusion

- Xience stent is non-inferior to Cypher stent in angiographic outcomes and showed comparable and excellent clinical outcomes in diabetic and non-diabetic population.
- So, Xience stent may be good clinical option in diabetic and non-diabetic population in the real practice.