Update 2013: IVUS-Guided Optimization of PCI

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Cardiovascular Research Foundation

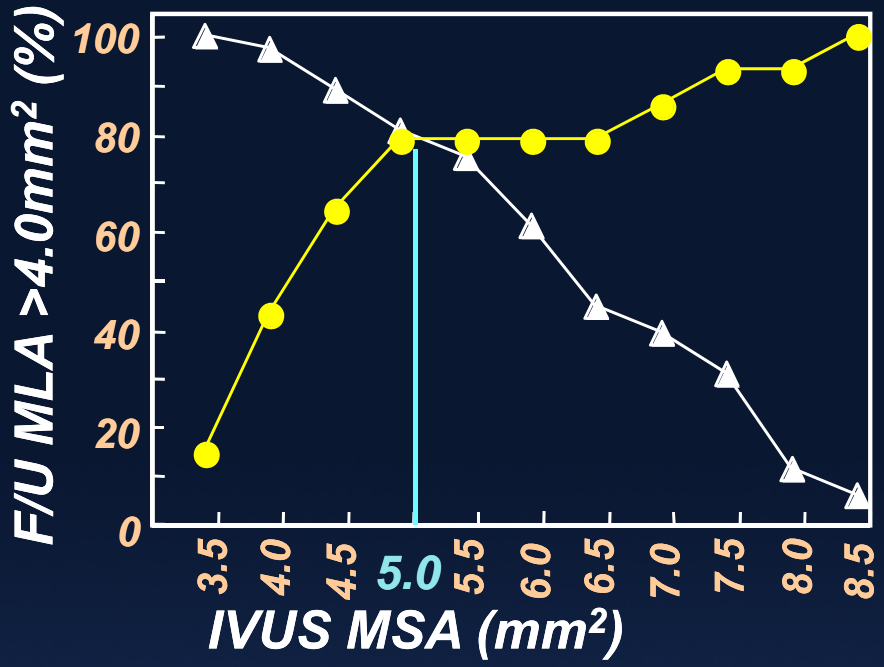
When doing PCI, there are two major questions. . .

1) **Should I do it?**
   - FFR for non-LMCA lesions
   - IVUS or FFR for LMCA lesions
2) **How should I do it?**
   - IVUS

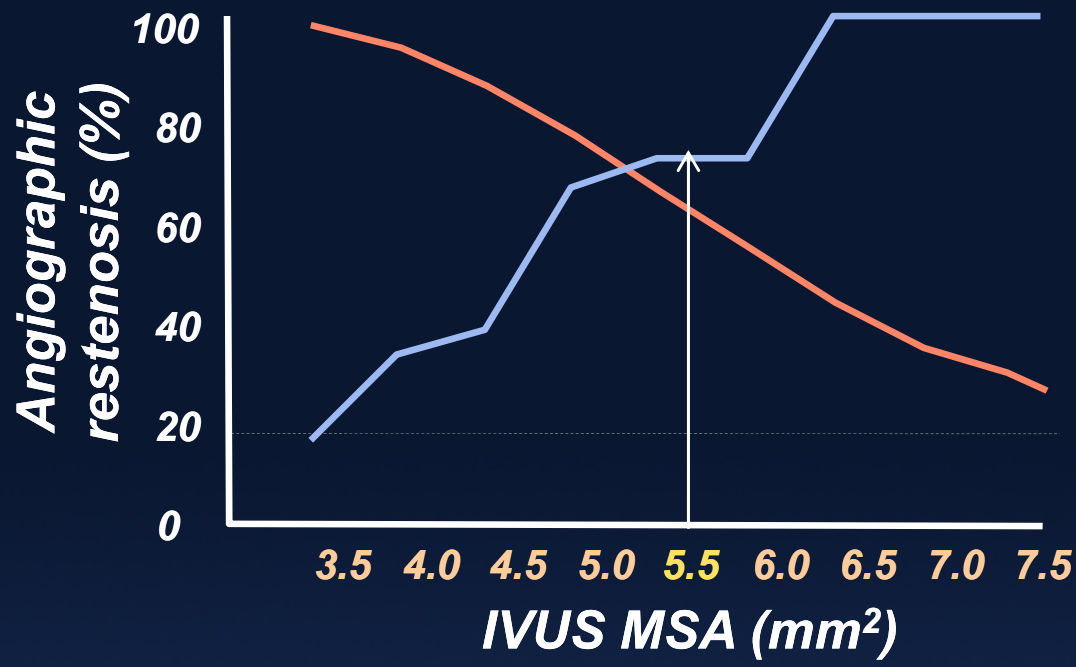
IVUS Predictors of DES Early Thrombosis & Restenosis

	Early Thrombosis	Restenosis
Small MSA or MLA or underexpansion	•*Fujii et al. J Am Coll Cardiol 2005;45:995-8)* •*Okabe et al., Am J Cardiol. 2007;100:615-20* •*Liu et al. JACC Cardiovasc Interv. 2009;2:428-34* •*Choi et al. Circ Cardiovasc Interv 2011;4:239-47*	•*Sonoda et al. J Am Coll Cardiol 2004;43:1959-63* •*Hong et al. Eur Heart J 2006;27:1305-10* •*Doi et al JACC Cardiovasc Interv. 2009;2:1269-75* •*Fujii et al. Circulation 2004;109:1085-1088* •*Kang et al. Circ Cardiovasc Interv 2011;4:9-14* •*Choi et al. Am J Cardiol 2012;109:455-60* •*Song et al. Catheter Cardiovasc Interv, in press*
Edge problems (geographic miss, secondary lesions, large plaque burden, dissections, etc)	•*Fujii et al. J Am Coll Cardiol 2005;45:995-8* •*Okabe et al., Am J Cardiol. 2007;100:615-20* •*Liu et al. JACC Cardiovasc Interv. 2009;2:428-34* •*Choi et al. Circ Cardiovasc Interv 2011;4:239-47*	•*Sakurai et al. Am J Cardiol 2005;96:1251-3* •*Liu et al.Am J Cardiol 2009;103:501-6* •*Costa et al, Am J Cardiol, 2008;101:1704-11*

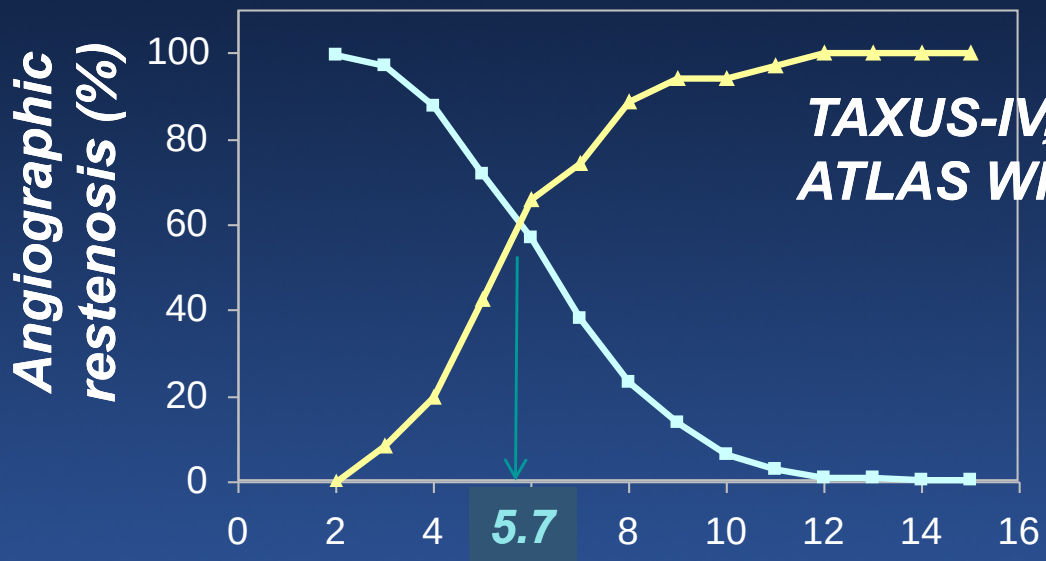
Cypher in SIRIUS*



Cypher at AMC**



TAXUS

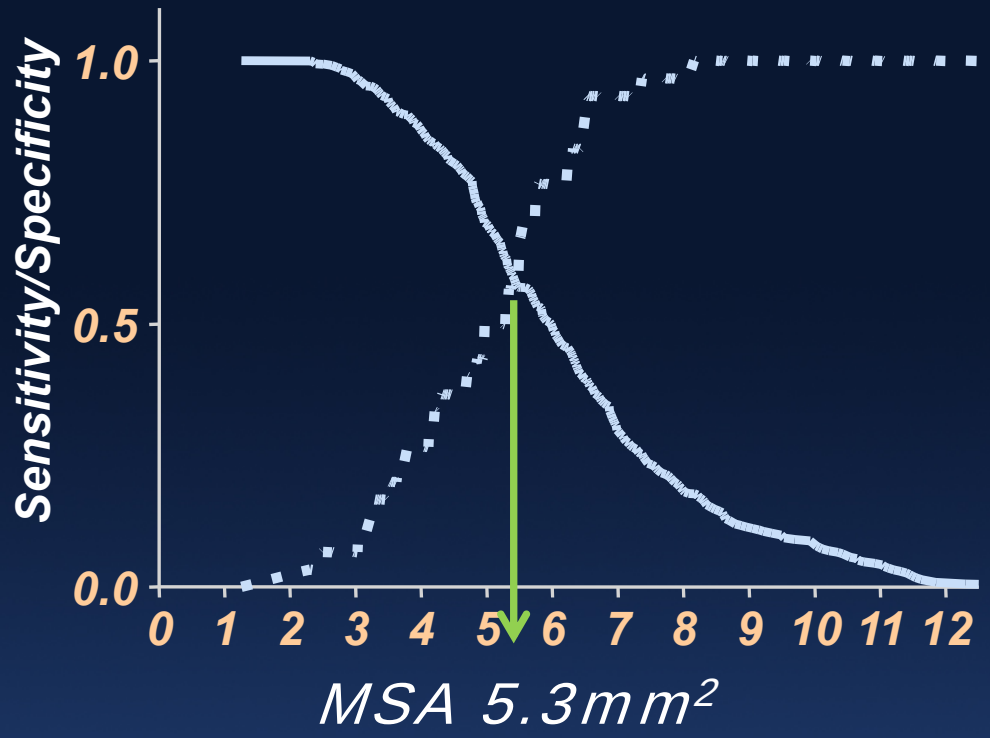


TAXUS-IV, V, VI and ATLAS WH, LL, and DS***

C-statistic for TAXUS was only 0.64

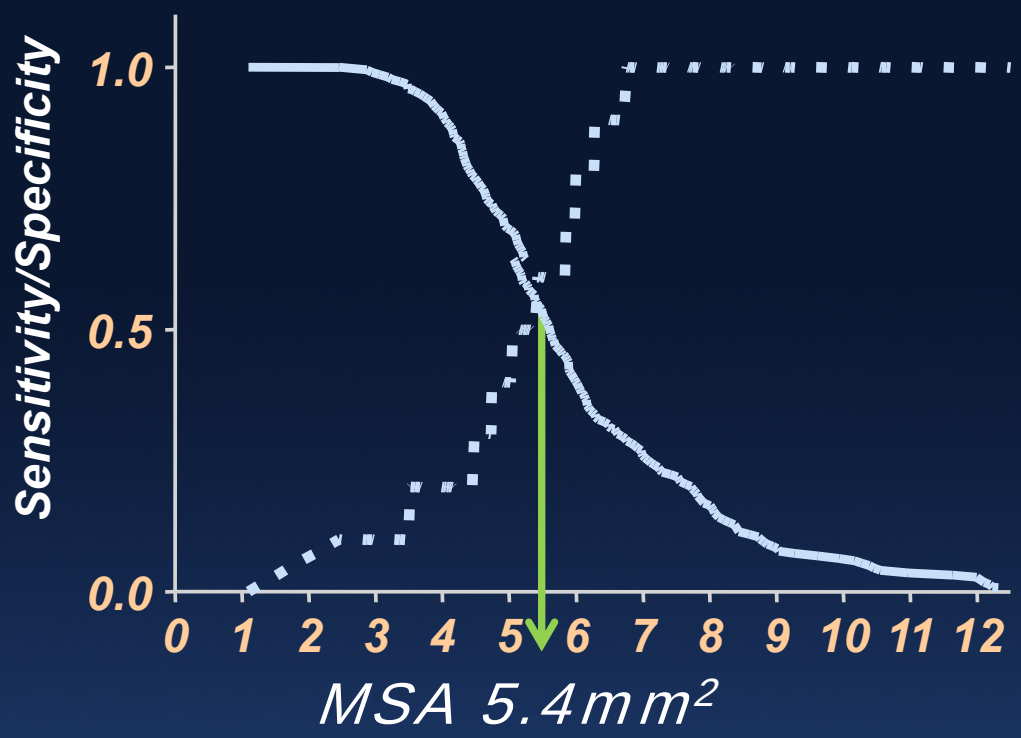
(*Sonoda et al. J Am Coll Cardiol 2004;43:1959-63)
(**Hong et al. Eur Heart J 2006;27:1305-10)
(***Doi et al. JACC Cardiovasc Interv. 2009;2:1269-75)

220 ZES



Sensitivity 56.7%
Specificity 61.8%
(AUC 0.67)

229 EES



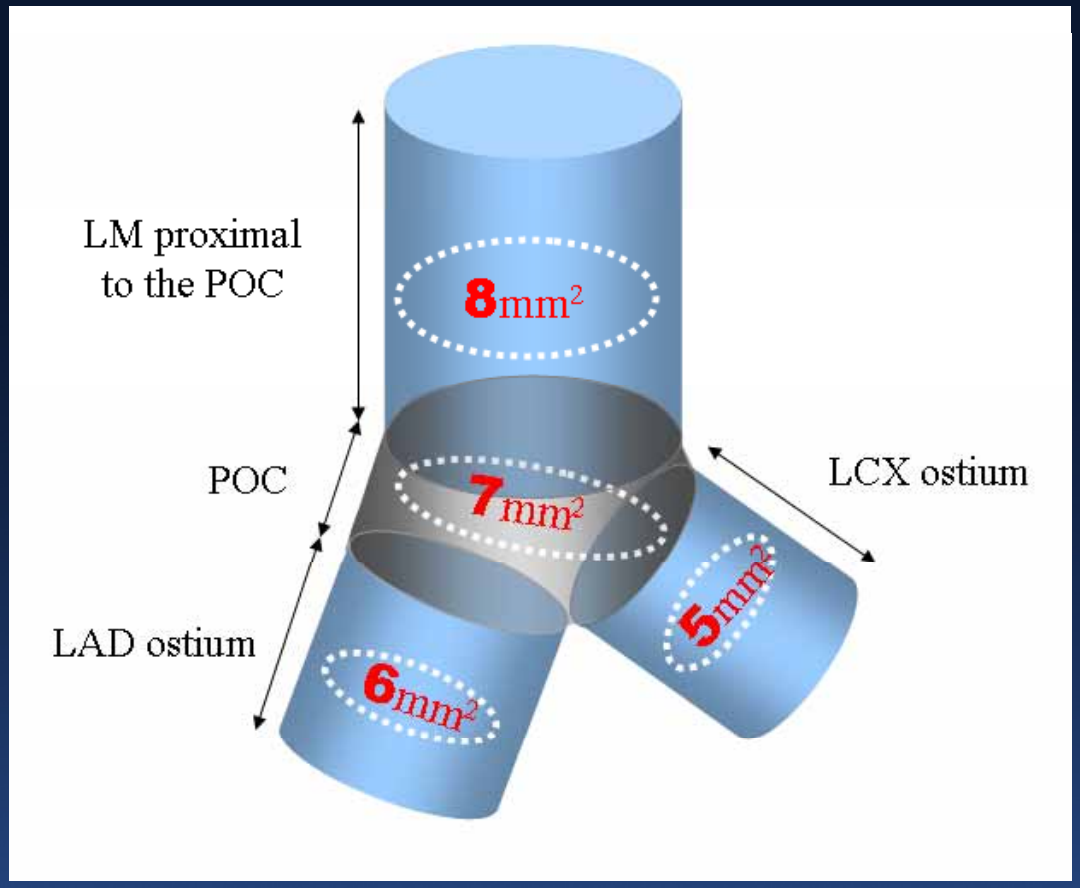
Sensitivity 60.0%
Specificity 59.9%
(AUC 0.64)

Song et al. Catheter Cardiovasc Interv 2012, in press

An ideal end point should be a clinically reasonable MSA that maximizes the probability of long-term stent patency while minimizing the risk of stent failure.

- By definition, sensitivity/specificity curve analysis “must” identify a single MSA that best separates restenosis from no restenosis. However, sensitivity and specificity are not of similar importance when predicting events.
- Is an MSA of 5.5mm^2 enough in big arteries or achievable in small arteries? Probably not.
- Furthermore, if an MSA was always sufficient, we would only need one size stent for all situations
  - 3.0mm BMS: 100% expansion=7.1mm^2
  - 2.75mm DES: 100% expansion=5.9mm^2

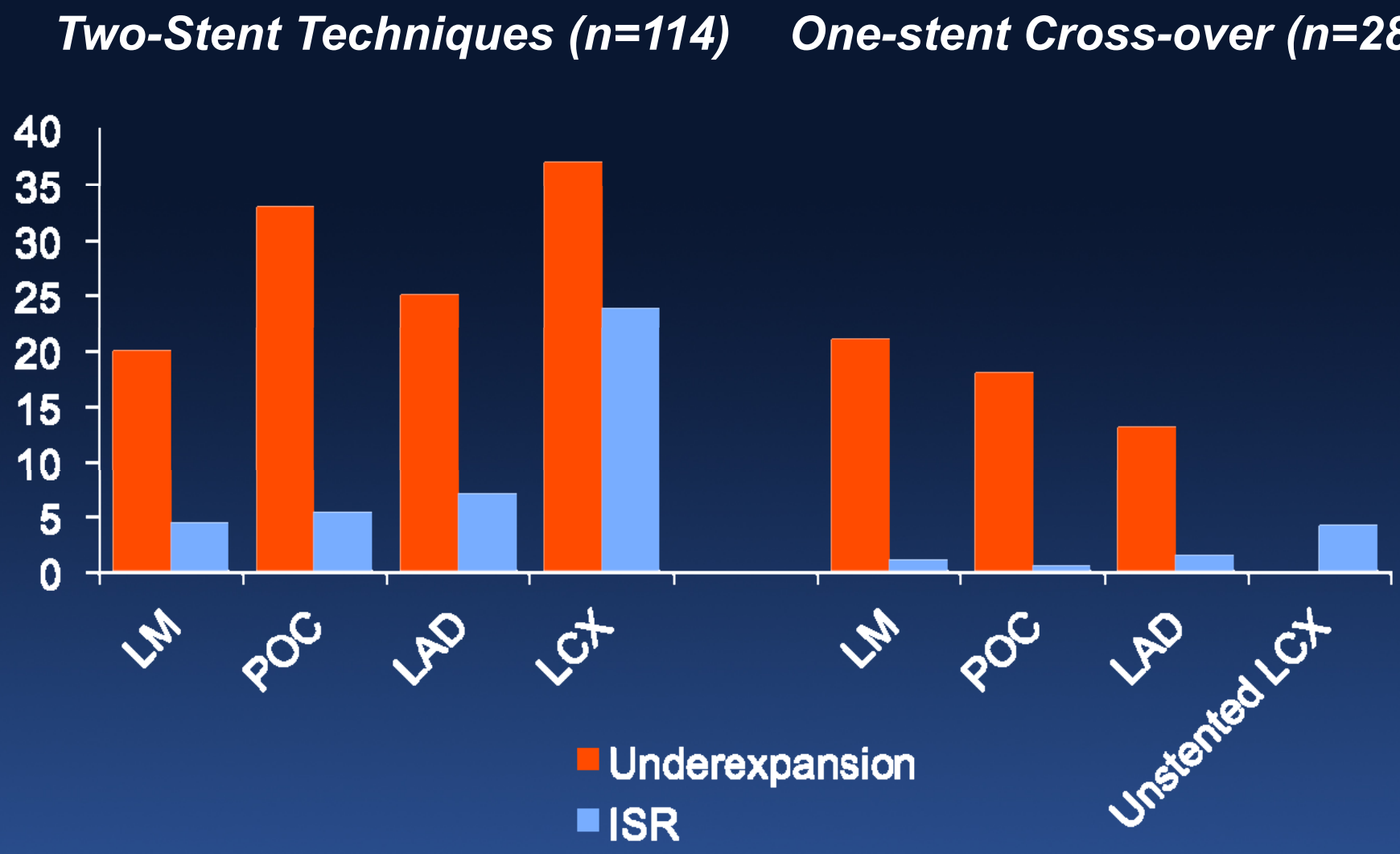
Criteria for stent underexpansion at the distal LMCA bifurcation (n=403)



- *MACE-free survival was lower in pts with underexpansion vs those without underexpansion (89.4% vs 98.1%)*
- *TLR-free survival was lower in pts with underexpansion vs no underexpansion (90.9% vs 98.5%).*
- *Although acute malapposition was observed in 28 pts, malapposition was not related to MACE at follow-up.*

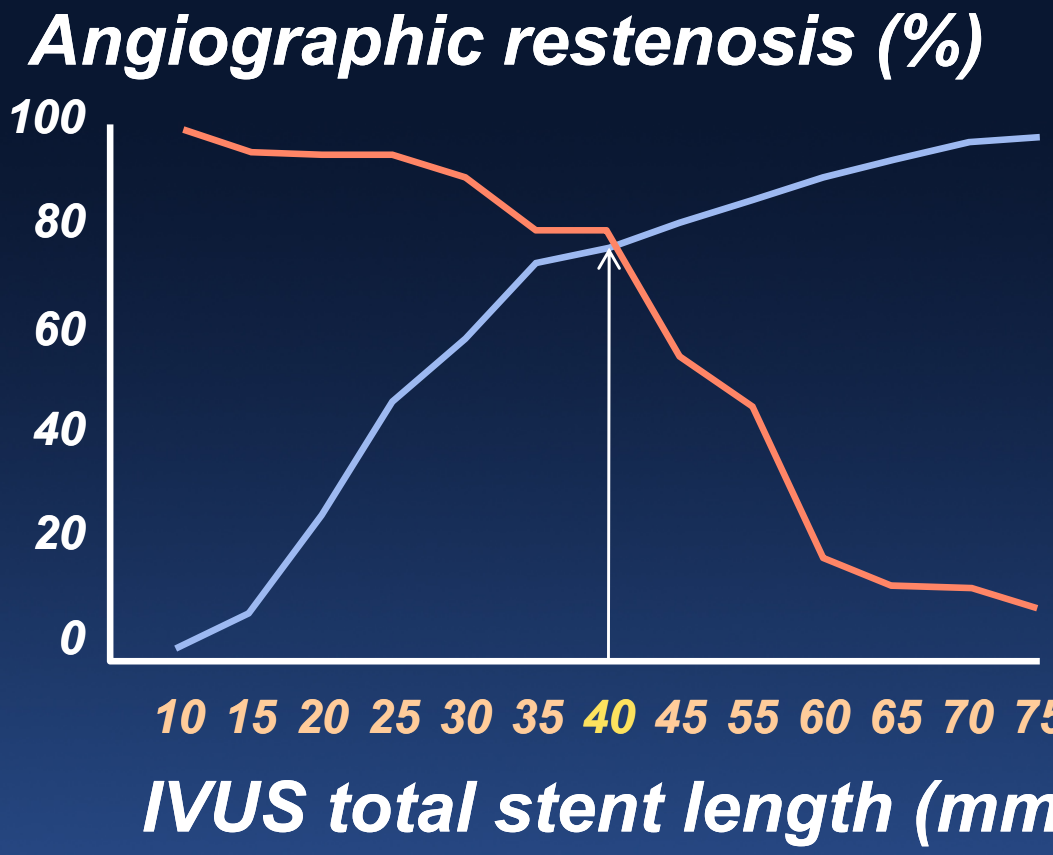
Kang et al. Circulation Cardiovasc Interv. 2011;4:562-9

Impact of underexpansion on ISR in patients treated with either two stents or a single stent cross-over



Kang et al. Circulation Cardiovasc Interv. 2011;4:562-9

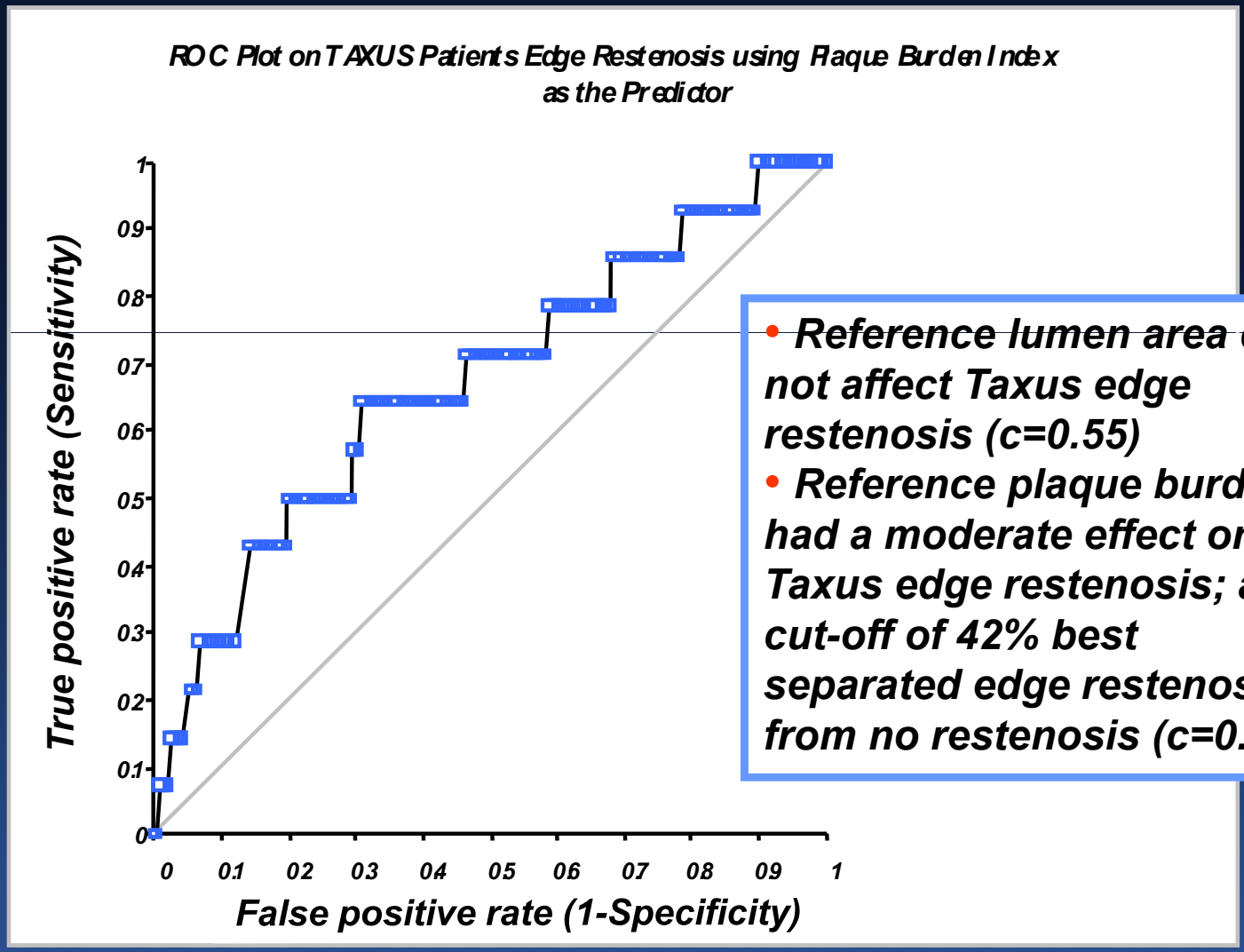
Stent length as a predictors of angiographic restenosis in 550 pts with 670 native lesions treated with Cypher stents



	MSA	
Stent length	<5.5mm^2	≥5.5mm^2
≤40mm	2.4%	0.4%
>40mm	17.7%	8.6%

Hong et al. Eur Heart J 2006;27:1305-10

Comparison of 9-month QCA edge restenosis vs reference lumen area and plaque burden in TAXUS-IV, V, and VI (n=810)



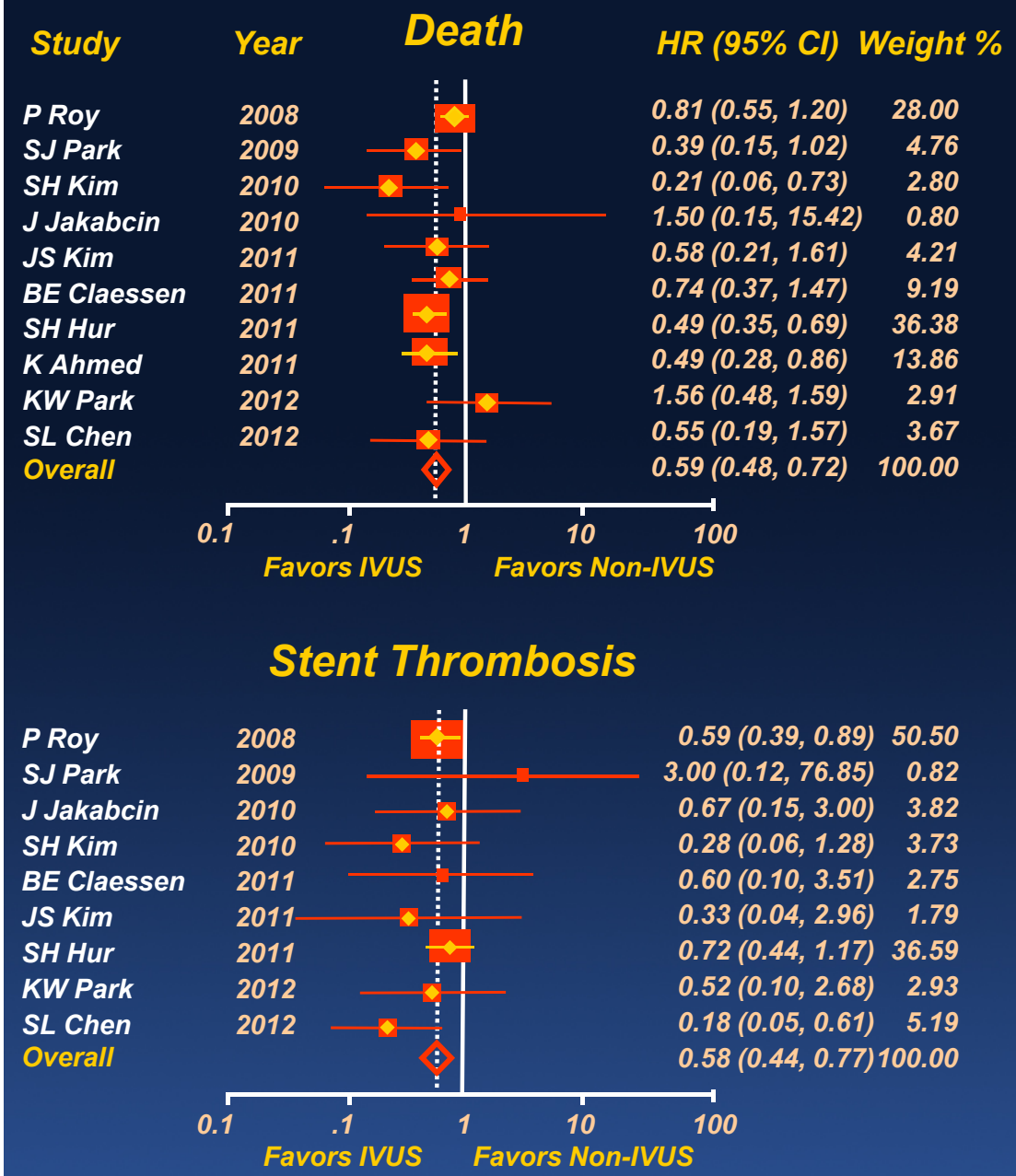
- *Reference lumen area did not affect Taxus edge restenosis (c=0.55)*
- *Reference plaque burden had a moderate effect on Taxus edge restenosis; a cut-off of 42% best separated edge restenosis from no restenosis (c=0.67)*

Liu et al. Am J Cardiol. 2009;103:501-6

Although it was one of the original Colombo criteria, there is little or no data linking *isolated* acute stent malapposition to adverse clinical events including ST and restenosis.

- **Stent malapposition is associated with *less* intimal hyperplasia – the drug can cross small stent vessel-wall gaps**
  - *Hong et al, Circulation. 2006;113:414-9*
  - *Kimura et al, Am J Cardiol . 2006;98:436-42*
  - *Steinberg et al, JACC Cardiovasc Intervent 2010;3:486-94*
  - *Balakrishnan et al., Circulation 2005;111:2958-65*
- **In the integrated analysis of slow release formulation PES in TAXUS IV, V, and VI and TAXUS ATLAS Workhorse, Long Lesion, and Direct Stent Trial, there was no effect of acute stent malapposition on MACE or ST within the first 9 months – whether BMS or DES**
  - *Steinberg et al, JACC Cardiovasc Intervent 2010;3:486-94*
- **In HORIZONS-AMI, acute stent malapposition was detected in 33.8% of 68 lesions treated with PES and 38.7% of 24 lesions treated with BMS (p=0.7). There was no difference in MACE between pts with versus without acute stent malapposition in either BMS or PES cohorts; and acute malapposition was not a predictor of early ST**
  - *Guo et al. Circulation 2010;122:1077-84*
  - *Choi et al. Circ Cardiovasc Interv 2011;4:239-47*
- **Although acute malapposition was observed in 28/403 pts with LMCA lesions treated with DES implantation, malapposition was not related to MACE at follow-up.**
  - *Kang et al. Circ Cardiovasc Interv 2011;4:562-9*

Meta-Analysis of 11 Studies (n=19,619 patients)



Compared with angiography-guidance, IVUS-guided DES implantation was associated with a reduced incidence of

- *Death (HR: 0.59, 95% CI: 0.48-0.73, p<0.001)*
- *Stent thrombosis (HR: 0.58, 95% CI: 0.44-0.77, p<0.0001)*
- *Major adverse cardiac events (HR: 0.87, 95% CI: 0.78-0.96, p=0.008)*

TCT2012

Zhang et al. Eurointervention 2012;8:855-65

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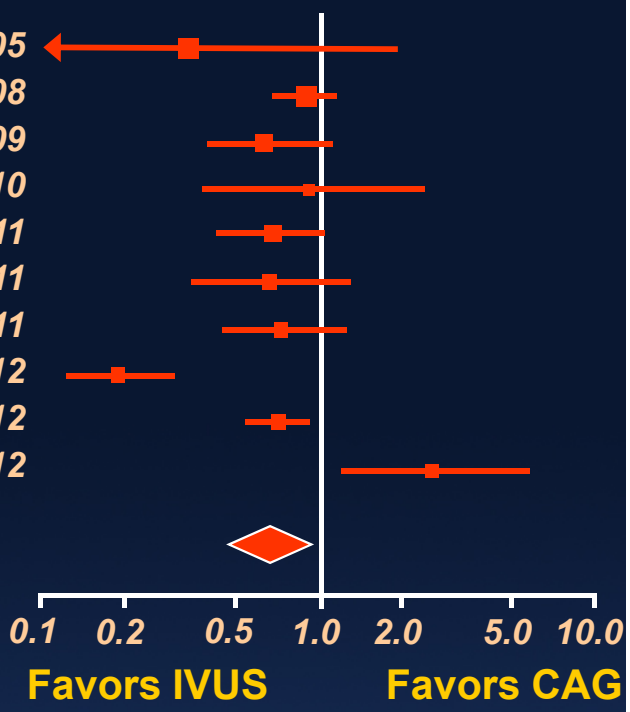
MACE

Study or Subgroup	Log [Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Yr
Agostoni	-1.048	0.8517	3.1%	0.35 [0.07, 1.86]	2005
Roy	-0.1309	0.1322	13.2%	0.88 [0.68, 1.14]	2008
MAIN-COMPARE	-0.4512	0.2502	10.9%	0.64 [0.39, 1.04]	2009
HOME DES IVUS	-0.0977	0.4423	7.2%	0.91 [0.38, 2.16]	2010
MATRIX	-0.3883	0.1981	12.0%	0.58 [0.45, 1.00]	2011
Youn	-0.4062	0.3209	9.4%	0.67 [0.36, 1.25]	2011
COB18	-0.3235	0.2538	10.8%	0.72 [0.44, 1.19]	2011
Patel	-1.624	0.2228	11.5%	0.20 [0.13, 0.31]	2012
Hur	-0.3853	0.1094	13.5%	0.69 [0.56, 0.96]	2012
EXCELLENT	0.8765	0.3759	8.4%	2.40 [1.15, 5.02]	2012
Total (95% CI)			100.0%	0.68 [0.49-0.94]	

Heterogeneity: $Tau^2=0.20$; $Chi^2=47.08$; df=9 (P<.0.00001); $x^2=81\%$

Test for overall effect: Z=2.30; (P=0.02)



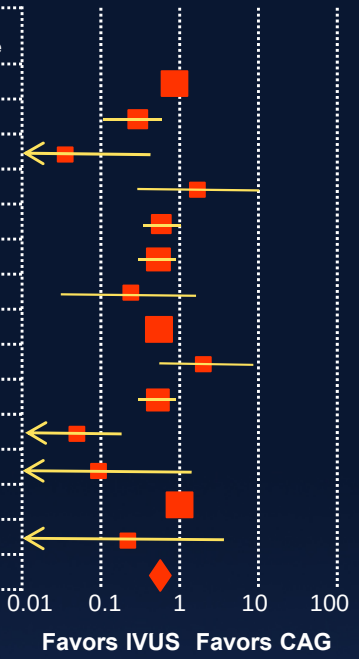
Ten observational and one randomized study (10,916 pts) were included: 5980 IVUS-guided and 4936 angio-guided. Compared with angiography-guidance, IVUS-guided DES implantation was associated with a reduced incidence of

- *MACE: OR=0.68 (95% CI 0.49 to 0.94), p=0.02*
- *Mortality: OR=0.64 (95% CI 0.49 to 0.83), p=0.001)*
- *Myocardial Infarction: OR=0.55 (95% CI 0.35 to 0.88), p=0.01*

Jang et al. Circulation 2012;126:A14107

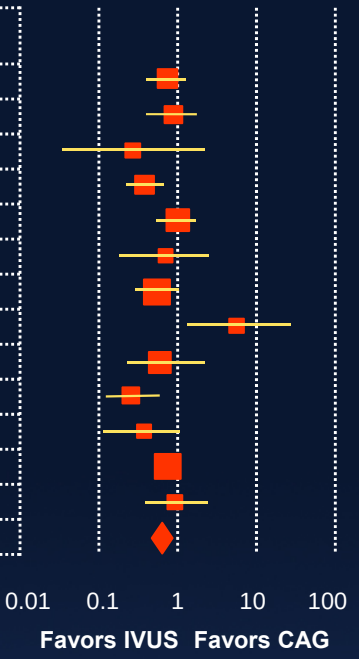
Death from any cause

		OR	Lower	Upper	Z-value	P-value
Roy	2008	0.79	0.54	1.16	-1.20	0.23
MAIN-COMPARE	2009	0.26	0.11	0.63	-2.96	0.00
Kim	2010	0.03	0.00	0.44	-2.57	001
HOME DES IVUS	2010	1.52	0.26	8.87	0.46	0.64
MATRIX	2011	0.53	0.29	0.97	-2.07	0.04
COBIS	2011	0.47	0.26	0.83	-2.62	0.01
Youn	2011	0.21	0.03	1.70	-1.46	0.14
Hur	2012	0.49	0.36	0.66	-4.60	0.00
EXCELLENT	2012	1.84	0.42	7.99	0.82	0.41
Ahn	2012	0.48	0.29	0.79	-2.88	0.00
Patel	2012	0.04	0.01	0.24	-3.66	0.00
Chen	2012	0.09	0.00	1.58	-1.65	0.10
ADAPT-DES	2012	0.88	0.64	1.20	-0.82	0.41
AVIO	2013	0.20	0.01	4.17	-1.04	0.30
Random pooled esttimate		0.50	0.36	0.69	-4.10	0.00



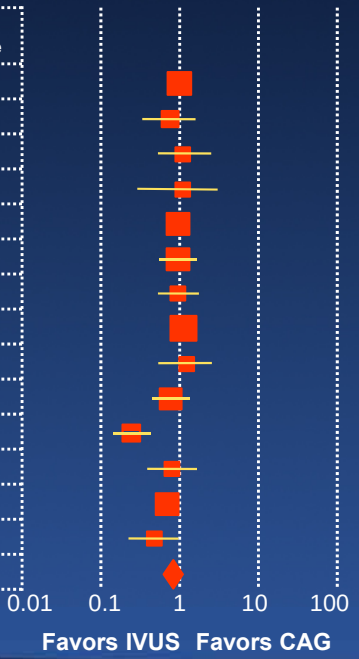
Myocardial Infarction

		OR	Lower	Upper	Z-value	P-value
Roy	2008	0.67	0.37	1.22	-1.31	0.19
MAIN-COMPARE	2009	0.81	0.37	1.75	-0.54	0.59
HOME DES IVUS	2010	0.24	0.03	2.09	-1.29	0.20
MATRIX	2011	0.35	0.18	0.71	-2.96	0.00
COBIS	2011	0.86	0.43	1.72	-0.43	0.66
Youn	2011	0.64	0.17	2.46	-0.65	0.52
Hur	2012	0.50	0.25	1.01	-1.95	0.05
EXCELLENT	2012	5.60	1.16	26.95	2.15	0.03
Ahn	2012	0.60	0.19	1.85	-0.89	0.37
Patel	2012	0.23	0.10	0.53	-3.44	0.00
Chen	2012	0.31	0.10	1.00	-1.97	0.05
ADAPT-DES	2012	0.66	0.51	0.86	-3.11	0.00
AVIO	2013	0.81	0.34	1.94	-0.47	0.64
Random pooled esttimate		0.59	0.45	0.79	-3.63	0.00



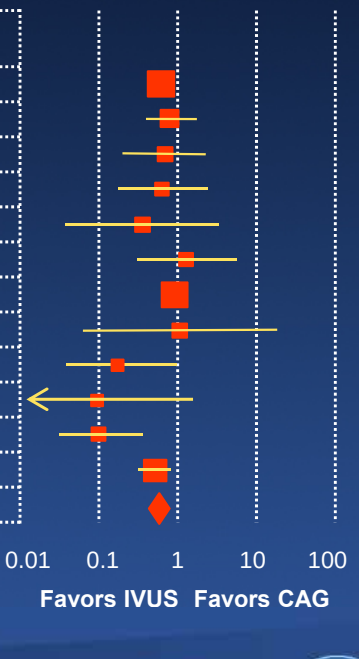
Target vessel revascularization

		OR	Lower	Upper	Z-value	P-value
Roy	2008	0.94	0.68	1.31	-0.37	0.71
MAIN-COMPARE	2009	0.72	0.31	1.67	-0.77	0.44
Kim	2010	1.08	0.45	2.60	0.18	086
HOME DES IVUS	2010	1.00	0.32	3.12	0.00	1.00
MATRIX	2011	0.90	0.62	1.30	-0.57	0.57
COBIS	2011	0.90	0.55	1.47	-0.43	0.67
Youn	2011	0.90	0.46	1.75	-0.32	0.75
Hur	2012	1.09	0.89	1.44	1.04	0.30
EXCELLENT	2012	1.09	0.46	2.58	0.20	0.84
Ahn	2012	0.74	0.46	1.16	-1.31	0.19
Patel	2012	0.24	0.13	0.43	-4.80	0.00
Chen	2012	0.80	0.38	1.71	-0.57	0.57
ADAPT-DES	2012	0.64	0.46	0.88	-2.70	0.01
AVIO	2013	0.46	0.21	0.99	-1.99	0.05
Random pooled esttimate		0.78	0.63	0.96	-2.30	0.02



Stent Thrombosis

		OR	Lower	Upper	Z-value	P-value
Roy	2008	0.58	0.39	0.87	-2.67	0.01
Kim	2010	0.76	0.35	1.67	-0.68	0.50
HOME DES IVUS	2010	0.65	0.18	2.31	-0.66	0.51
MATRIX	2011	0.60	0.15	2.36	-0.74	0.46
COBIS	2011	0.33	0.03	3.30	-0.94	0.35
Youn	2011	1.27	0.28	5.72	-0.31	0.76
Hur	2012	0.85	0.56	1.32	-0.72	0.47
EXCELLENT	2012	1.00	0.06	17.87	0.00	1.00
Ahn	2012	0.17	0.03	0.88	-2.11	0.03
Patel	2012	0.09	0.00	1.65	-1.63	0.10
Chen	2012	0.09	0.03	0.33	-3.63	0.00
ADAPT-DES	2012	0.50	0.29	0.85	-2.53	0.01
Random pooled esttimate		0.55	0.39	0.77	-3.43	0.00



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Park et al, unpublished

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RESET is a prospective, randomized, open label, multi-center trial to demonstrate non-inferiority of ZES plus 3-mo DAPT vs any other DES plus vs 12-month DAPT. In the pre-specified long lesion subset (lesions requiring a ≥28mm long stent in a vessel with a distal reference diameter ≥2.5mm), pts were randomized to ZES vs EES and then to IVUS-vs angiography-guidance.

	IVUS-guidance	Angiography-guidance	RR	p
N	269	274		
MACE (cardiac death, MI, ST, TVR)	4.5%	7.3%	0.59 (0.28-1.24)	0.16

n=41 cross-over n=13

	IVUS-guidance	Angiography-guidance	RR	p
N	297	246		
MACE (cardiac death, MI, ST, TVR)	4.0%	8.1%	0.48 (0.23-0.99)	0.048

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Kim et al., JACC Cardiovasc Interv, in press

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ADAPT-DES – IVUS vs No-IVUS Cohort -

Assessment of **D**ual **A**nti**P**latelet **T**herapy with **D**rug-**E**luting **S**tents

8,575 pts prospectively enrolled
No clinical or anatomic exclusion criteria
11 sites in US and Germany

↓

PCI with ≥1 non-investigational DES
Successful and uncomplicated

↙ ↘

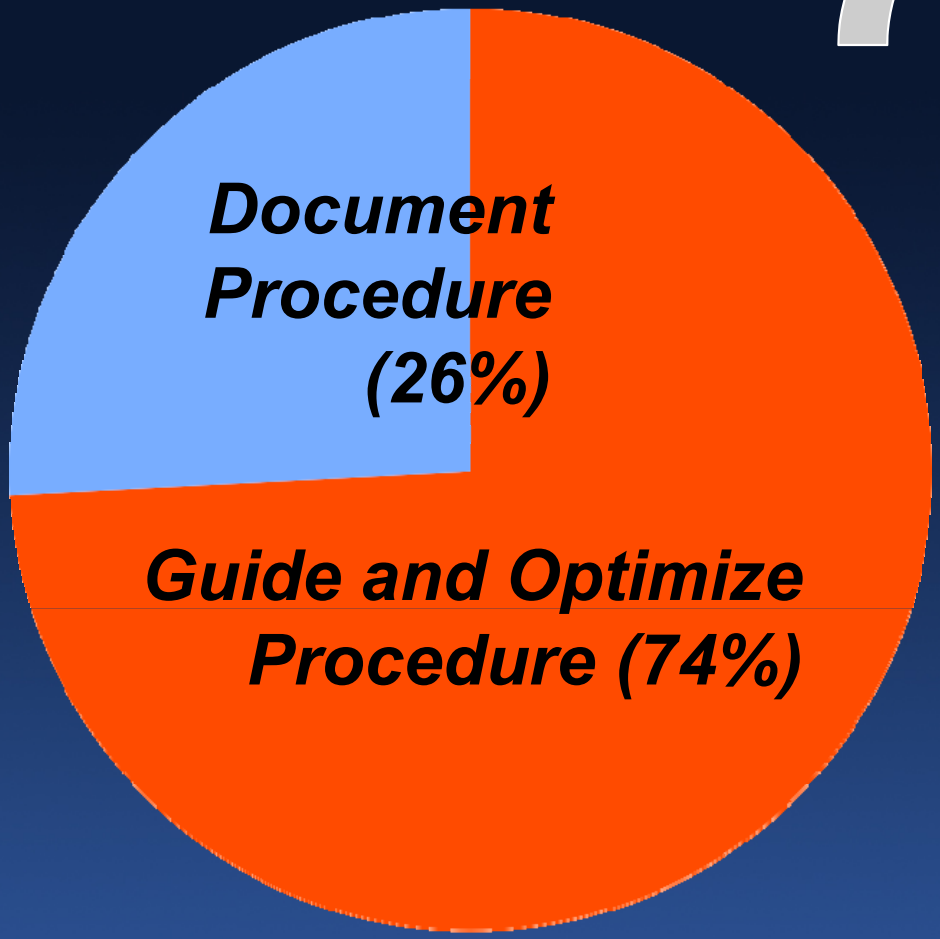
IVUS Use: 3349 pts | **No IVUS: 5234 pts**

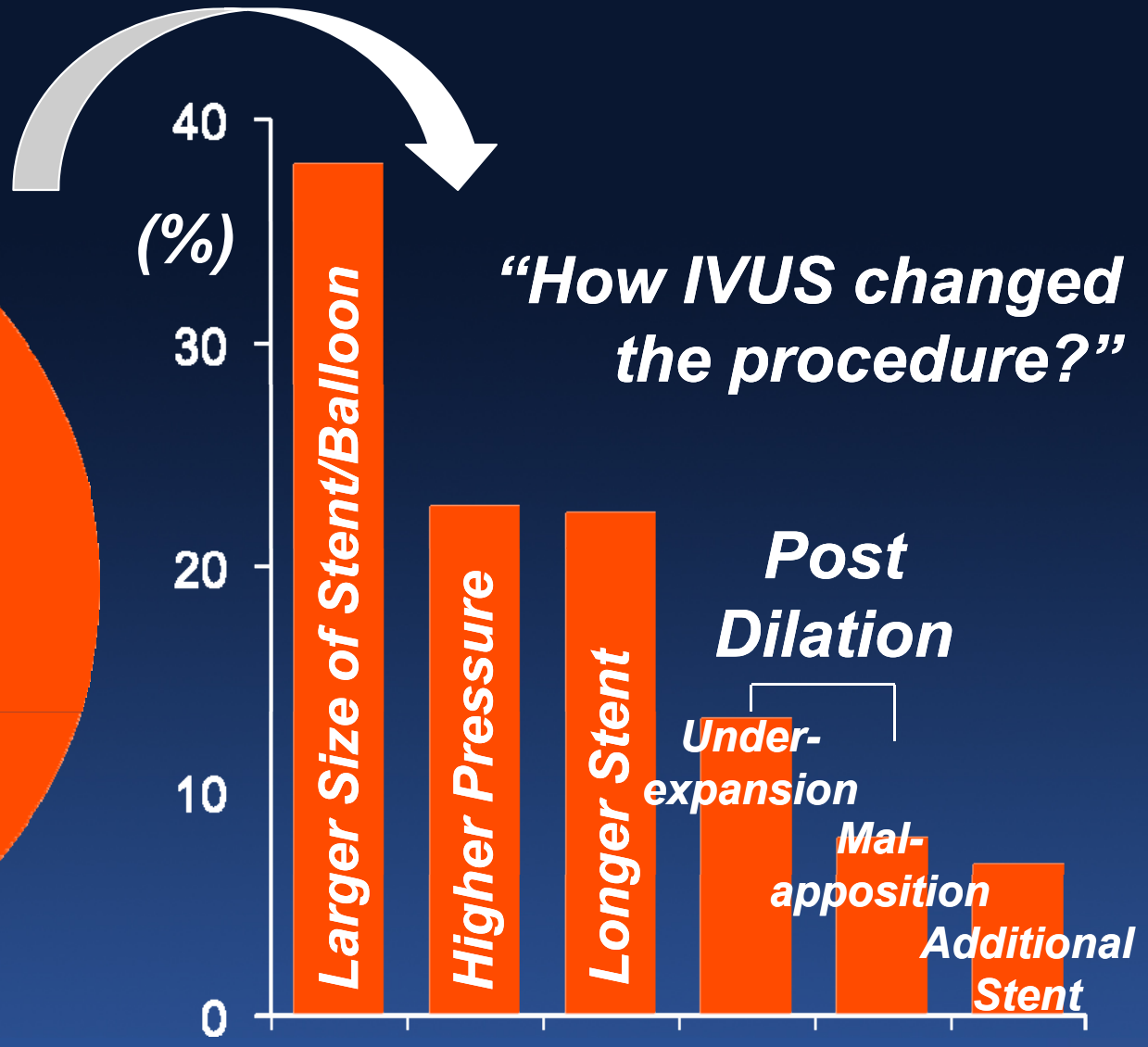
↓ ↓

Clinical FU at 30 days, 1 year

Witzenbichler, et al. TCT2012

Reason for IVUS Use



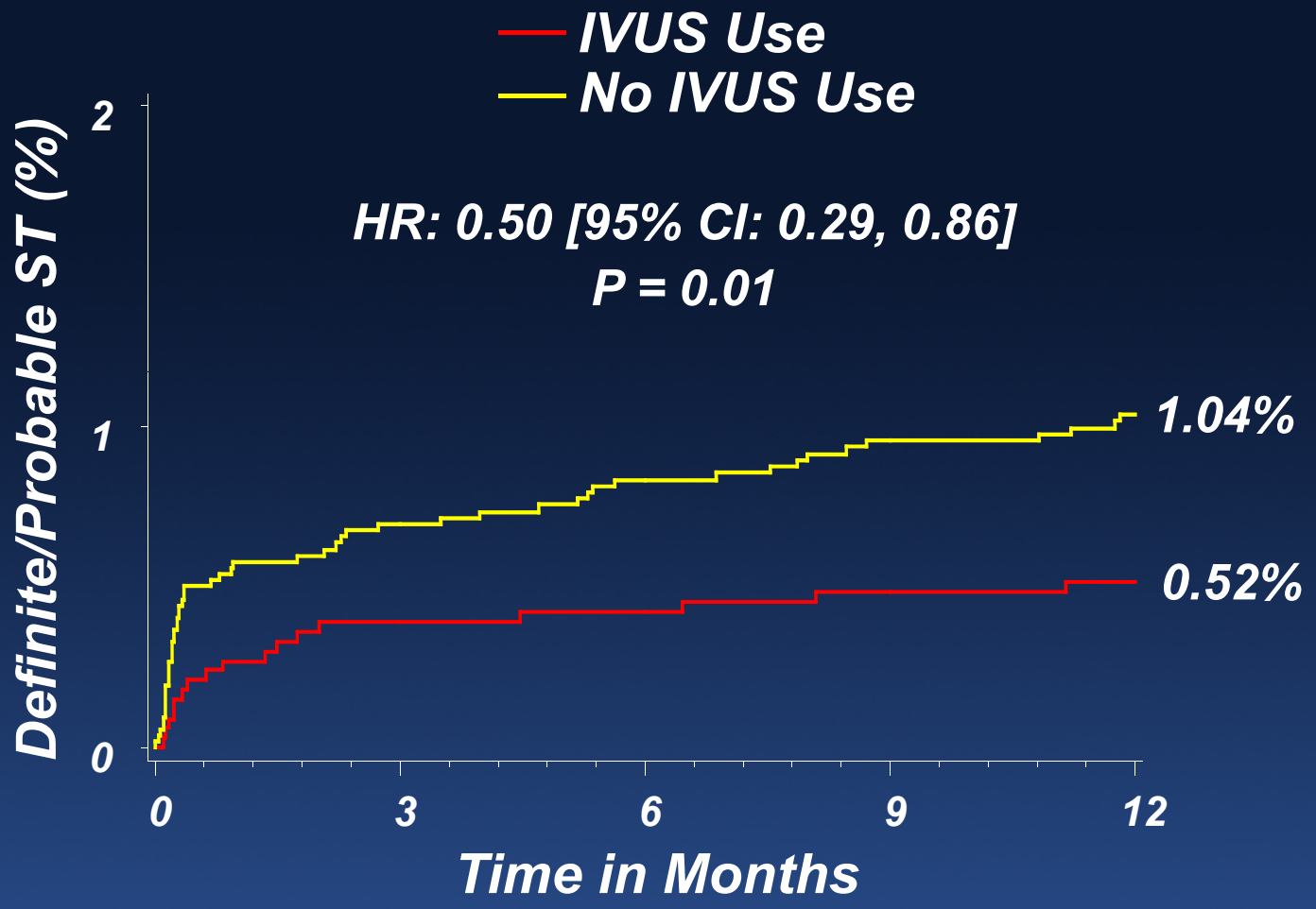


"How IVUS changed the procedure?"

Clinical Outcomes at 1 year

	IVUS n = 3349	No IVUS n = 5234	P Value
Definite/probable ST	0.52% (17)	1.04% (53)	0.011
- Acute<1day	0.06% (2)	0.04% (2)	0.66
- Subacute (1-30day)	0.27% (9)	0.56% (29)	0.051
- Late (>30day to 1yr)	0.25% (8)	0.46% (23)	0.12
All death	1.79% (58)	2.04% (103)	0.40
Cardiovascular death	0.99% (32)	1.35% (68)	0.14
All MI	2.46% (81)	3.68% (188)	0.0022
- Peri-procedural MI	1.26% (42)	1.53% (80)	0.29
- ST-related MI	0.37% (12)	0.59% (30)	0.16
- MI non-ST-related	0.87% (28)	1.58% (79)	0.0054

Relationship between IVUS Use and Definite or Probable ST within 1 year



Number at risk:					
IVUS Use	3349	3251	3221	3197	3023
No IVUS Use	5234	5015	4978	4938	4585

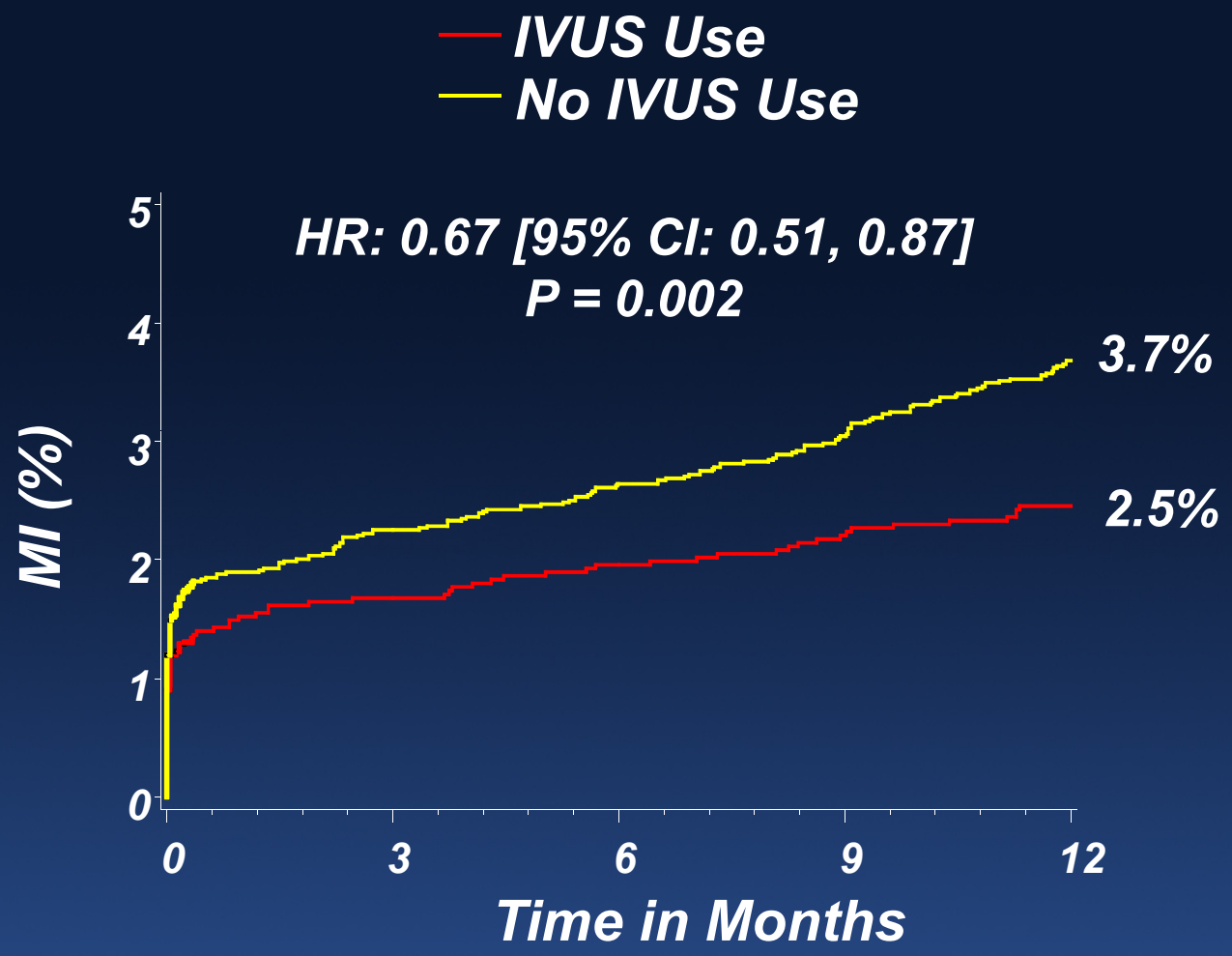
Mutivariable Cox PHR Models of 1-year Stent Thrombosis

Number events=68, Total at risk=8401

	HR [95%CI]	P value
IVUS use	0.37 [0.20, 0.69]	0.0019
PRU>208	2.37 [1.42, 3.96]	0.0009
Diabetes	1.65 [1.00, 2.70]	0.048
STEMI presentation	2.76 [1.51, 5.05]	0.0010
EES use	0.49 [0.30, 0.82]	0.0065
Total stent length (mm)	1.01 [1.00, 1.02]	0.019
Max stent diameter (mm)	0.60 [0.35, 1.02]	0.058
On DAPT at MACE	1.80 [0.92, 3.55]	0.087

Other non significant covariates entered to the model: ARU≥550
Model c-statistics=0.483

Relationship between IVUS Use and MI within 1 year



Number at risk:					
IVUS Use	3349	3209	3171	3141	2969
No IVUS Use	5234	4932	4882	4830	4460

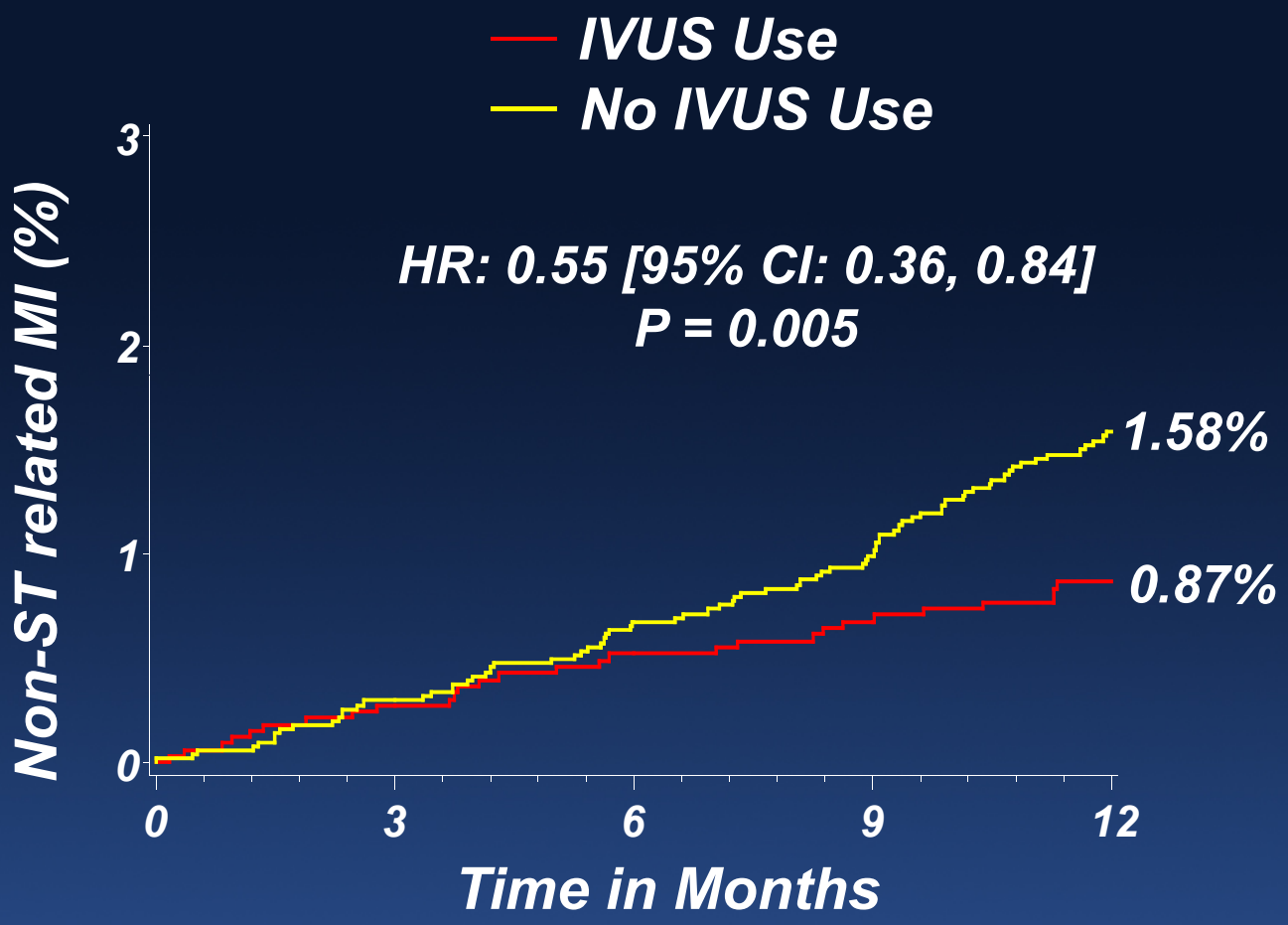
Mutivariable Cox PHR Models of 1-year MI

Number events=269, Total at risk=8547

	HR [95%CI]	P value
IVUS use	0.65 [0.49, 0.87]	0.0034
Cr Clearance <60 ml/min	1.64 [1.19, 2.27]	0.0025
Three vessel CAD	1.57 [1.22, 2.02]	0.0005
Diabetes	1.48 [1.15, 1.89]	0.0021
Acute coronary syndrome	1.41 [1.10, 1.80]	0.0064
Prior MI	1.35 [1.04, 1.75]	0.023

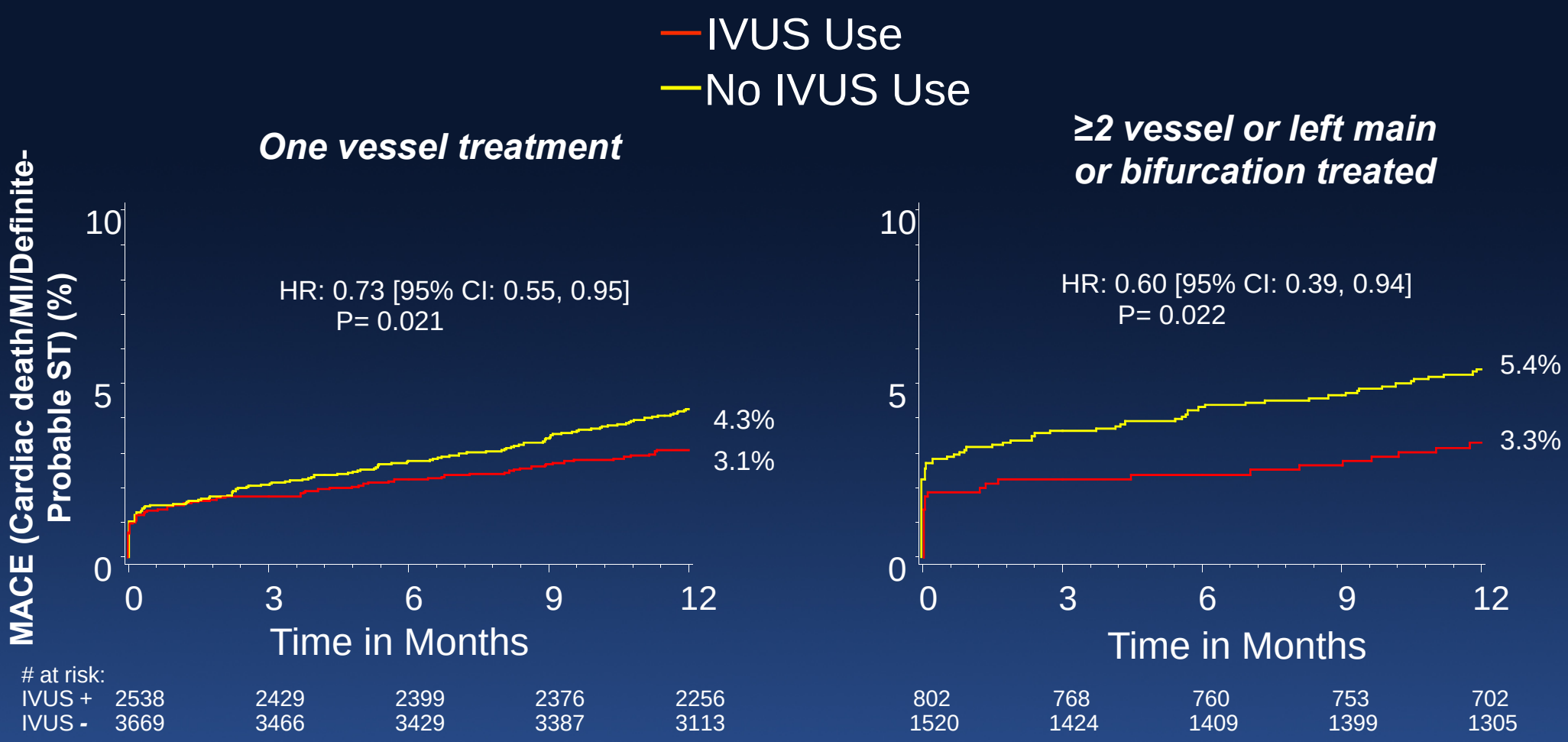
Other non significant covariates entered to the model: Male, Hemoglobin (g/dL)

Relationship between IVUS Use and MI not related to ST within 1 year

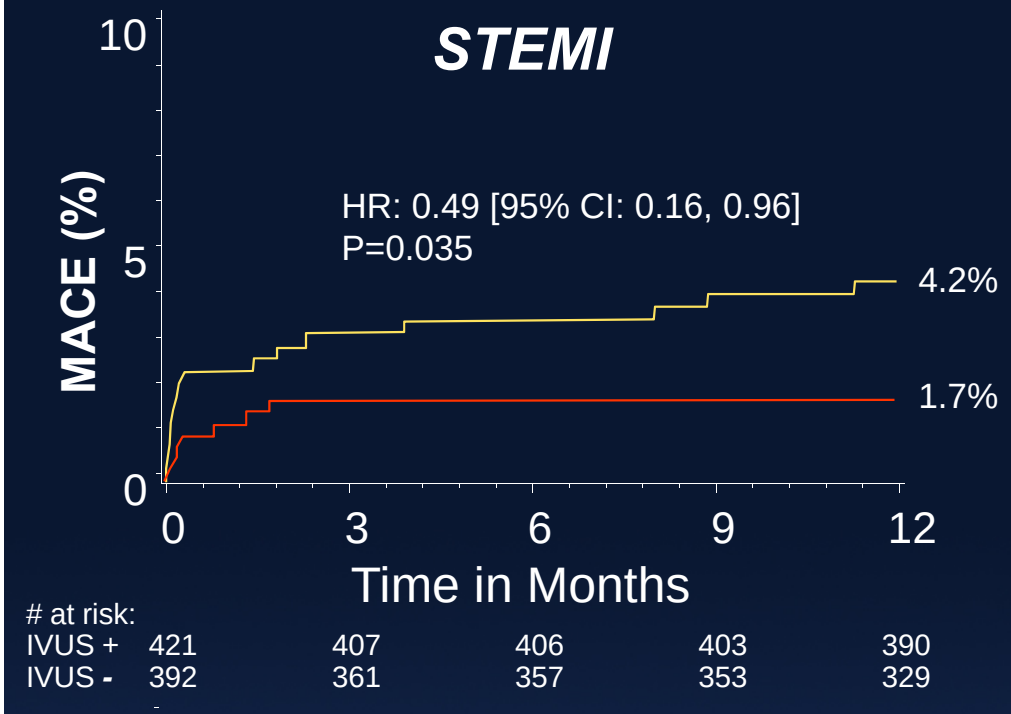


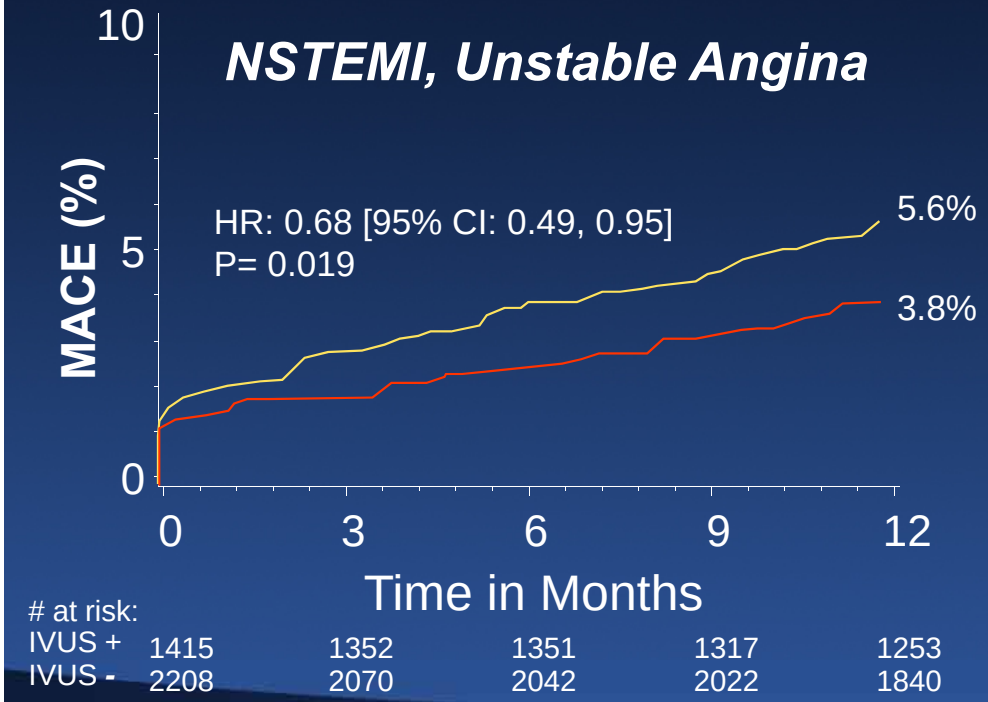
Number at risk:					
IVUS Use	3349	3253	3216	3188	3015
No IVUS Use	5234	5024	4974	4925	4555

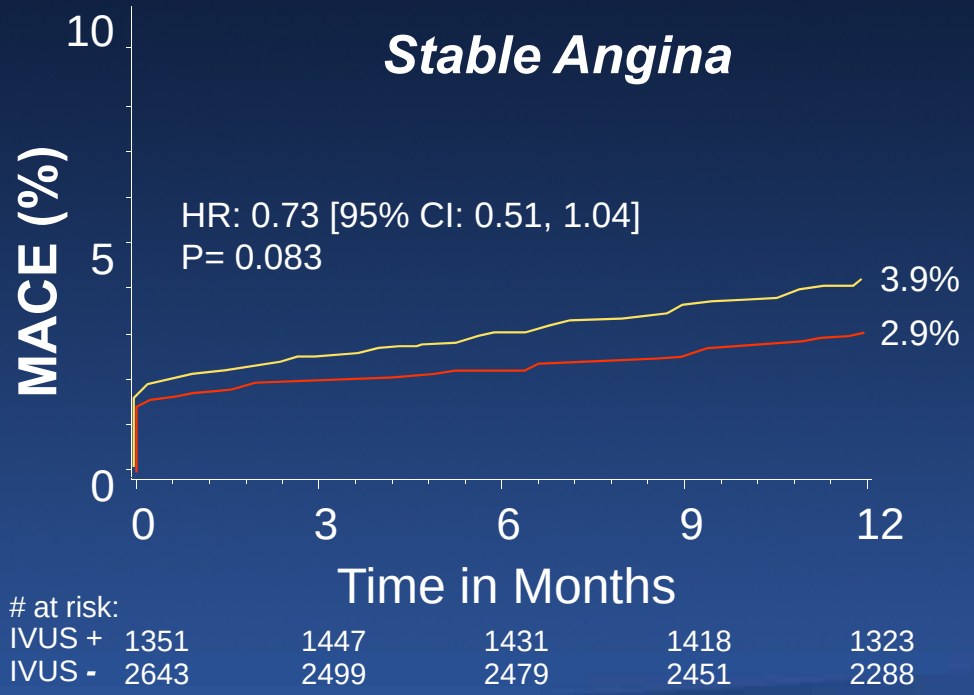
Impact of Complexity of Procedure on MACE



Impact of Patient Presentation on MACE







IVUS Use
No IVUS Use

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a passion for innovation

Stent expansion

Geographical miss

Findings not seen on IVUS

Malapposition

Tissue protrusion

Edge dissections