Does Morphology Predict Future Events?

YES! Insights from PROSPECT

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CARDIOVASCULAR RESEARCH FOUNDATION
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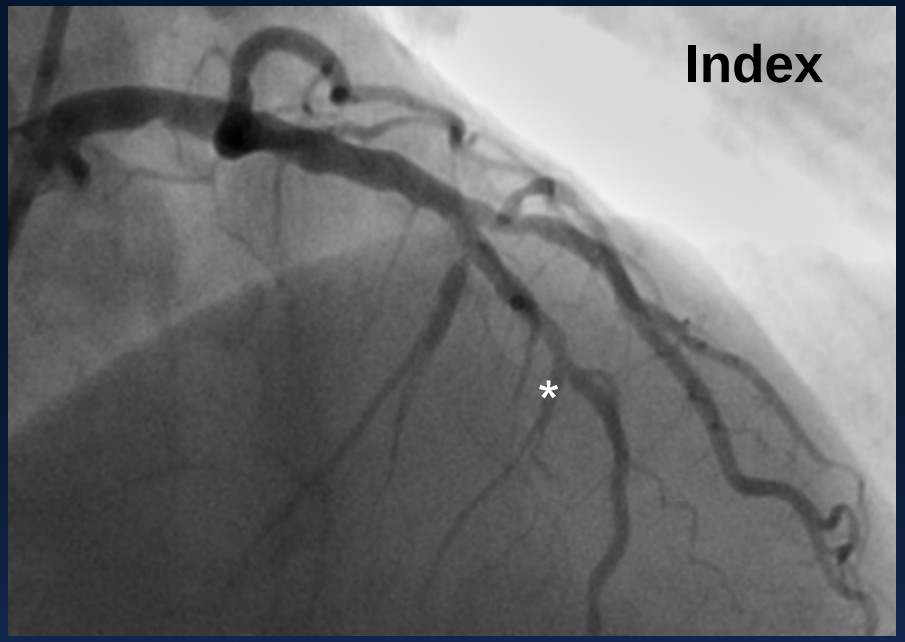
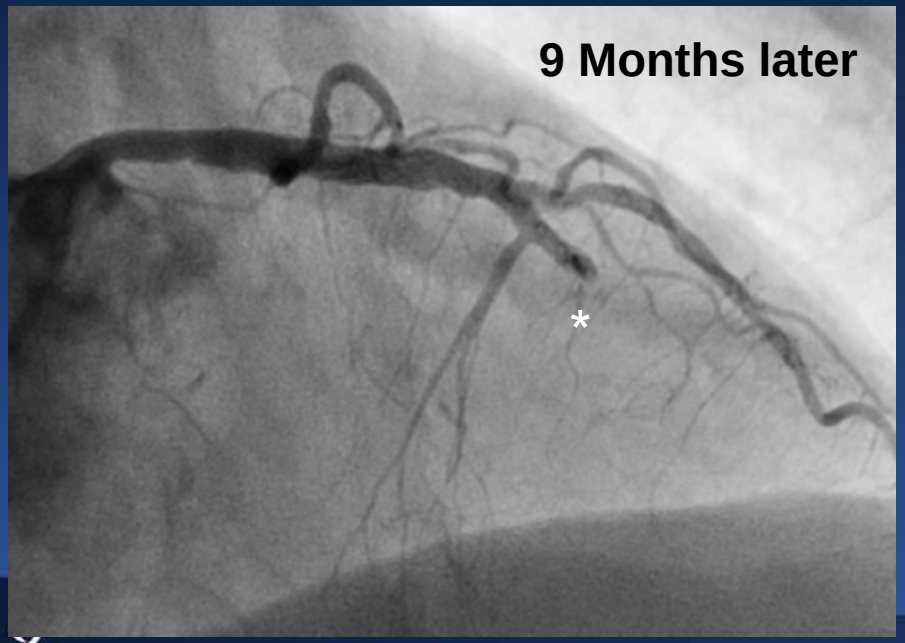
Disclosure Statement of Financial Interest

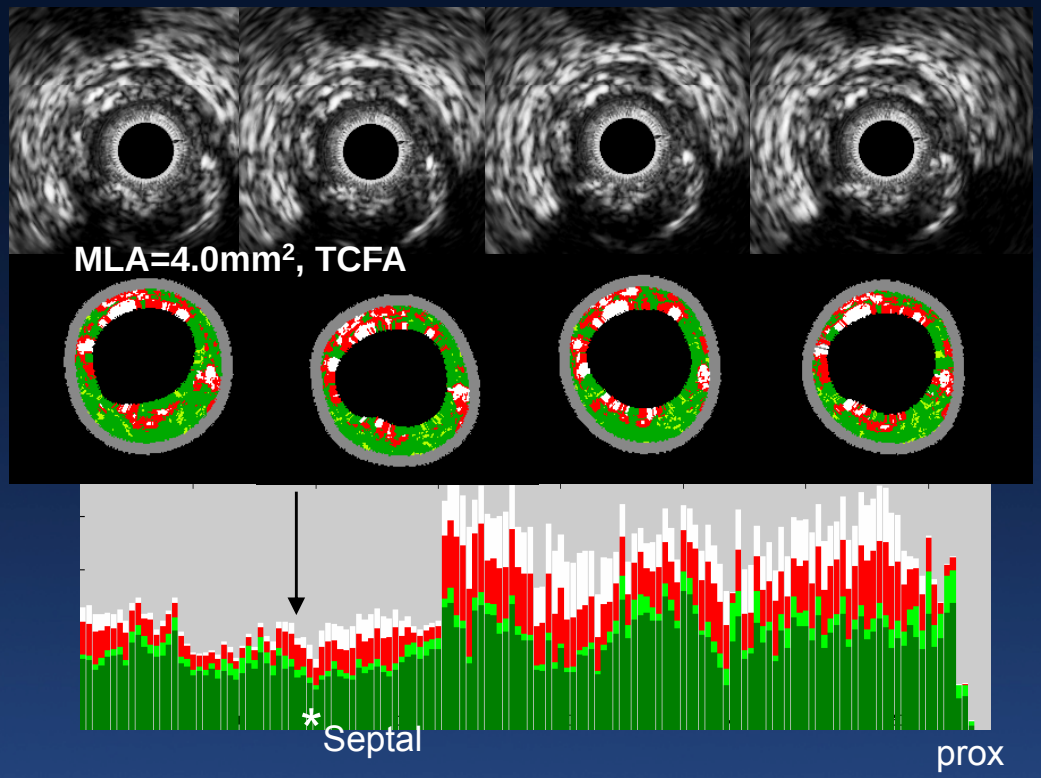
Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

Affiliation/Financial Relationship	Company
• Grant/Research Support (Institutional)	• Boston Scientific Corporation
• Consulting Fees/Honoraria	• Boston Scientific Corporation

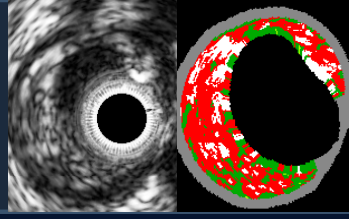
A PROSPECT Case







The PROSPECT Trial



700 pts with ACS

UA (with ECGΔ) or NSTEMI or STEMI >24º
undergoing PCI of 1 or 2 major coronary arteries
at up to 40 sites in the U.S. and Europe

Metabolic S.
- Waist circum
- Fast lipids
- Fast glu
- HgbA1C
- Fast insulin
- Creatinine

PCI of culprit lesion(s)

Successful and uncomplicated

Formally enrolled

Biomarkers
- ***Hs CRP***
- ***IL-6***
- ***sCD40L***
- ***MPO***
- ***TNFα***
- ***MMP9***
- ***Lp-PLA2***
- ***others***

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PI: Gregg W. Stone
Sponsor: Abbott Vascular; Partner: Volcano

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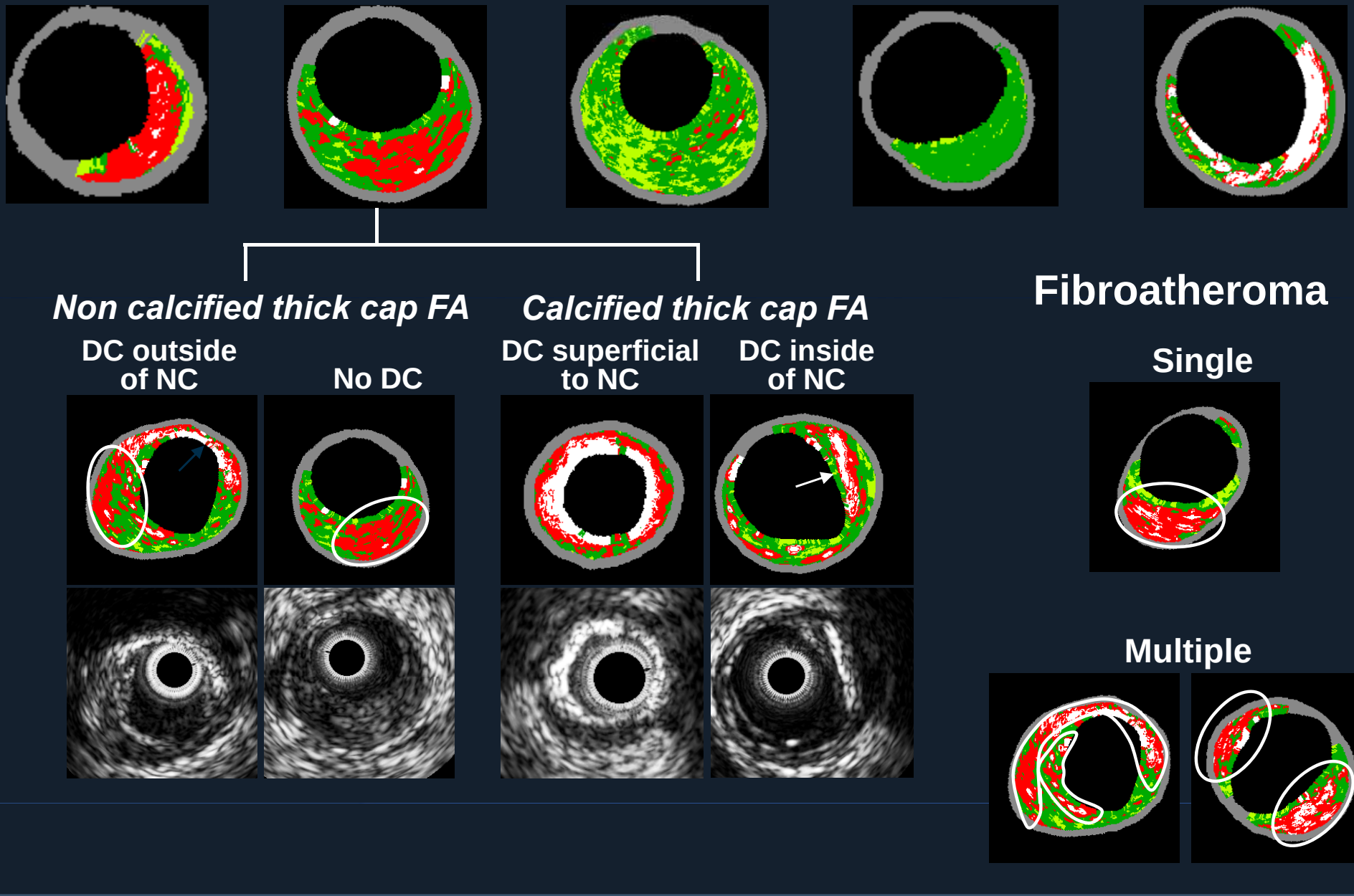
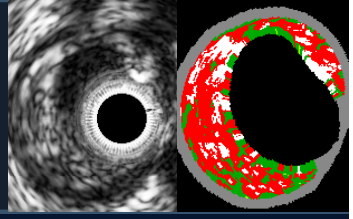
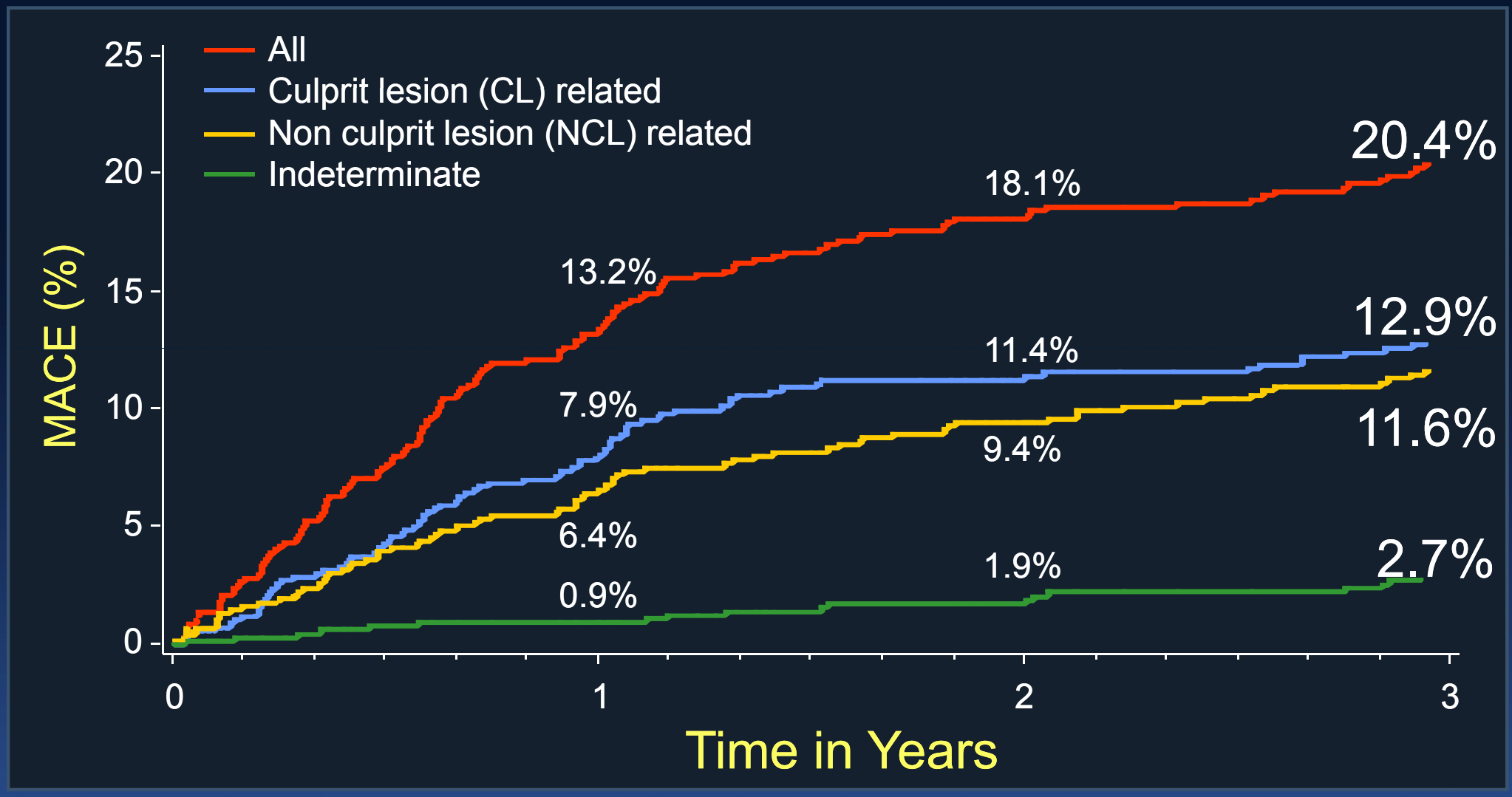
VH-IVUS Classification



PROSPECT: MACE





Number at risk

ALL	697	557	506	480
CL related	697	590	543	518
NCL related	697	595	553	521
Indeterminate	697	634	604	583

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PROSPECT: MACE

3-year follow-up, non hierarchical

	All	Culprit lesion related	Non culprit lesion related	Indeter-minate
Cardiac death	1.9% (12)	0.2% (1)	0% (0)	1.8% (11)
Cardiac arrest	0.5% (3)	0.3% (2)	0% (0)	0.2% (1)
MI (STEMI or NSTEMI)	3.3% (21)	2.0% (13)	1.0% (6)	0.3% (2)
Unstable angina	8.0% (51)	4.5% (29)	3.3% (21)	0.5% (3)
Increasing angina	14.5% (93)	9.2% (59)	8.5% (54)	0.3% (2)
Composite MACE	20.4% (132)	12.9% (83)	11.6% (74)	2.7% (17)
Cardiac death, arrest or MI	4.9% (31)	2.2% (14)	1.0% (6)	1.9% (12)

Rates are 3-yr Kaplan-Meier estimates (n of events)

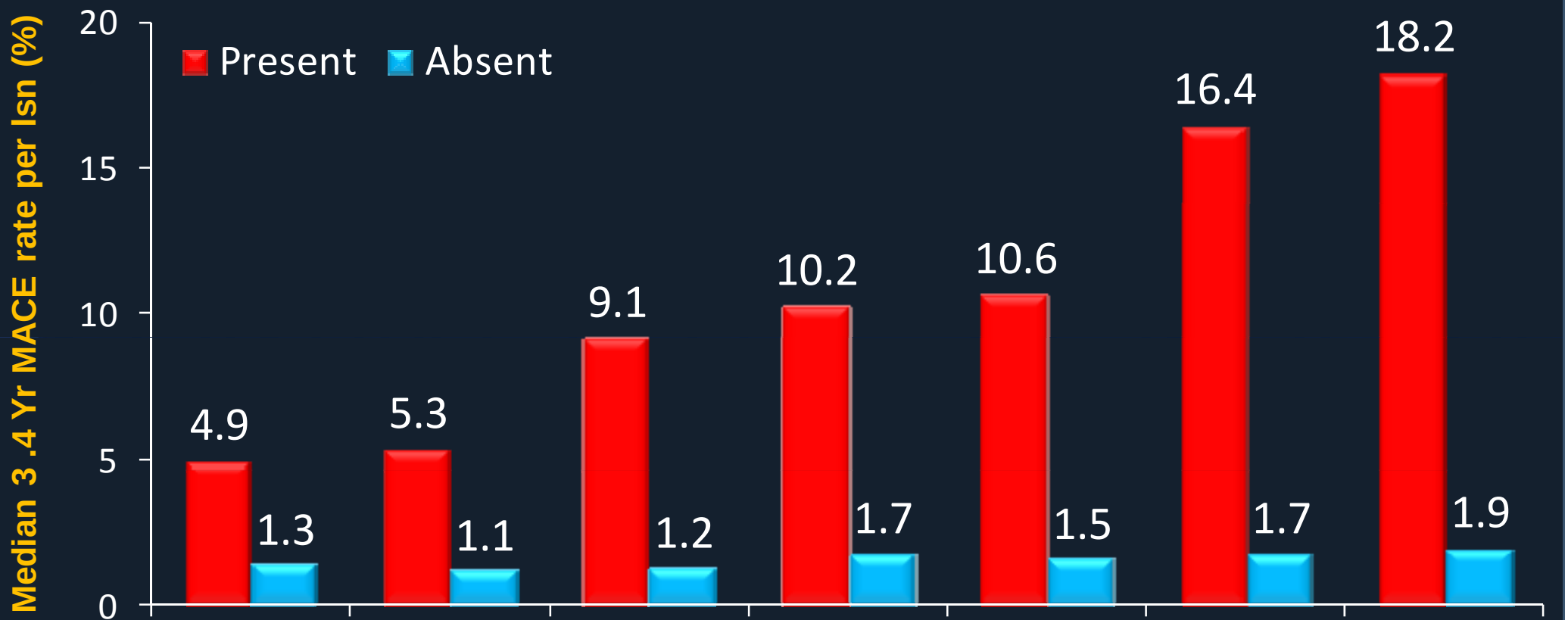
PROSPECT: Multivariable Correlates of Non Culprit Lesion Related Events

Independent predictors of lesion level events by Cox Proportional Hazards regression

Variable	HR [95% CI]	P value
PB_{MLA} ≥70%	5.03 [2.51, 10.11]	<0.0001
VH-TCFA	3.35 [1.77, 6.36]	0.0002
MLA ≤4.0 mm^2	3.21 [1.61, 6.42]	0.001

Variables entered into the model: minimal luminal area (MLA) ≤4.0 mm^2; plaque burden at the MLA (PB_{MLA}) ≥70%; external elastic membrane at the MLA (EEM_{MLA}) <median (14.1 mm^2); lesion length ≥median (11.2 mm); distance from ostium to MLA ≥median (30.4 mm); remodeling index ≥median (0.94); VH-TCFA.

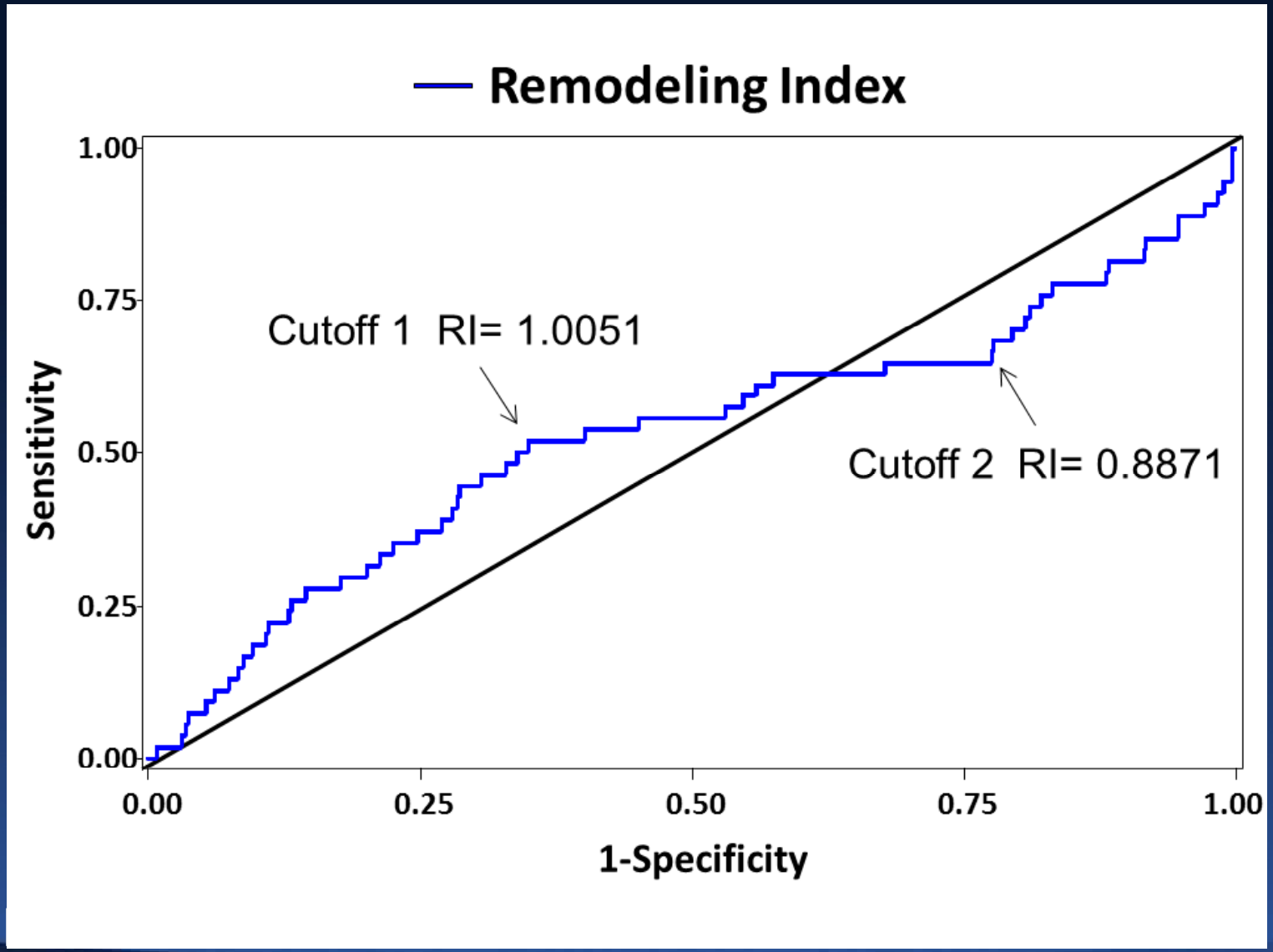
PROSPECT: Correlates of Non Culprit Lesion Related Events



	TCFA	MLA ≤4.0mm2	PB ≥70%	MLA ≤4mm2 + TCFA	PB ≥70% + MLA ≤4mm2	PB ≥70% + TCFA	PB ≥70% + MLA ≤4mm2 + TCFA
Lesion HR	3.9 (2.3, 6.8)	5.0 (2.9, 8.5)	8.7 (5.1, 14.8)	6.6 (3.4, 12.5)	7.3 (3.9, 13.6)	10.8 (5.6, 21.1)	11.1 (4.4, 27.8)
P value	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
Prevalence*	46.7%	53.3%	32.4%	15.9%	16.8%	10.1%	4.2%

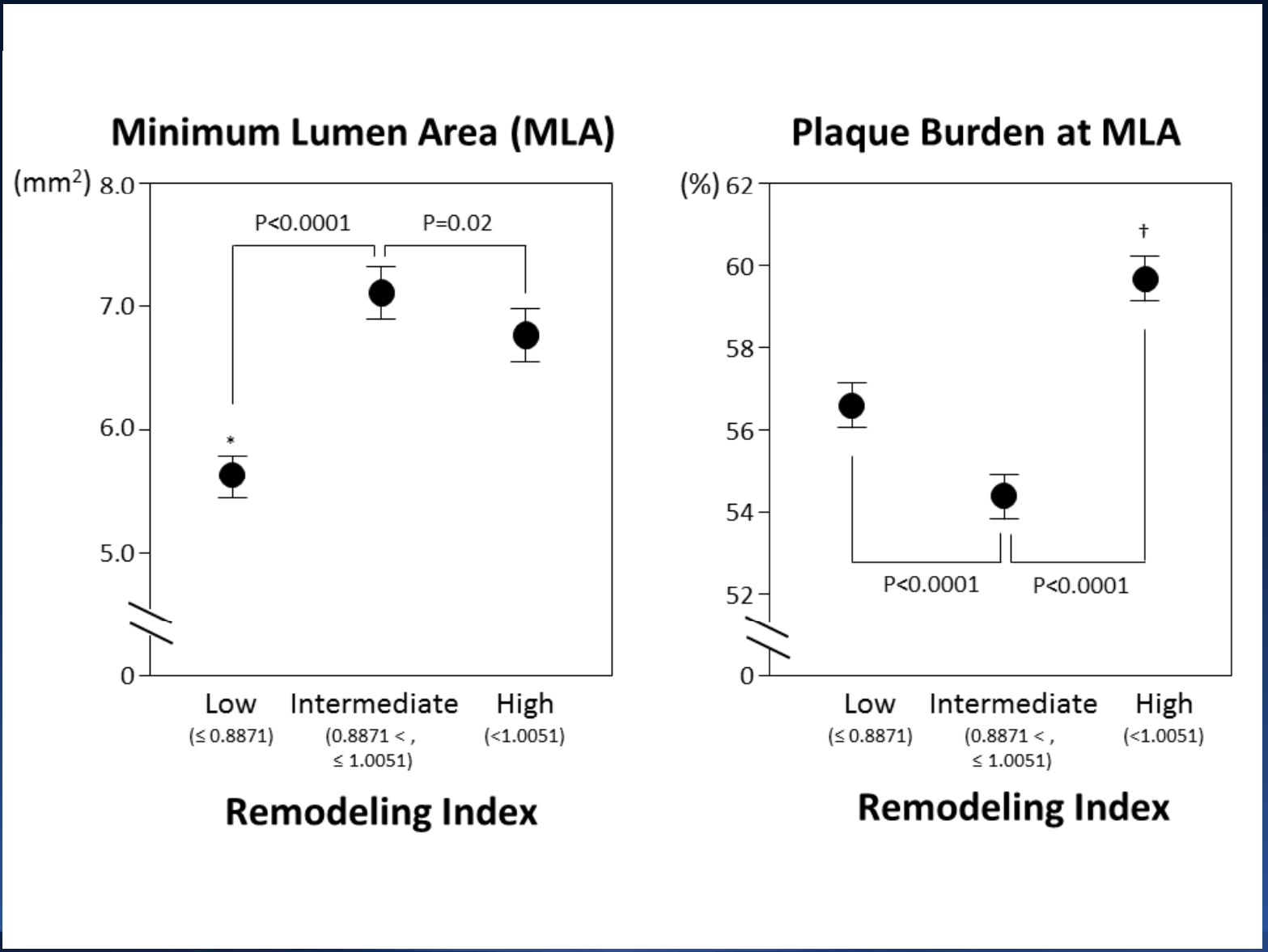
*Likelihood of one or more such lesions being present per patient. PB = plaque burden at the MLA

Remodeling Index to predict MACE



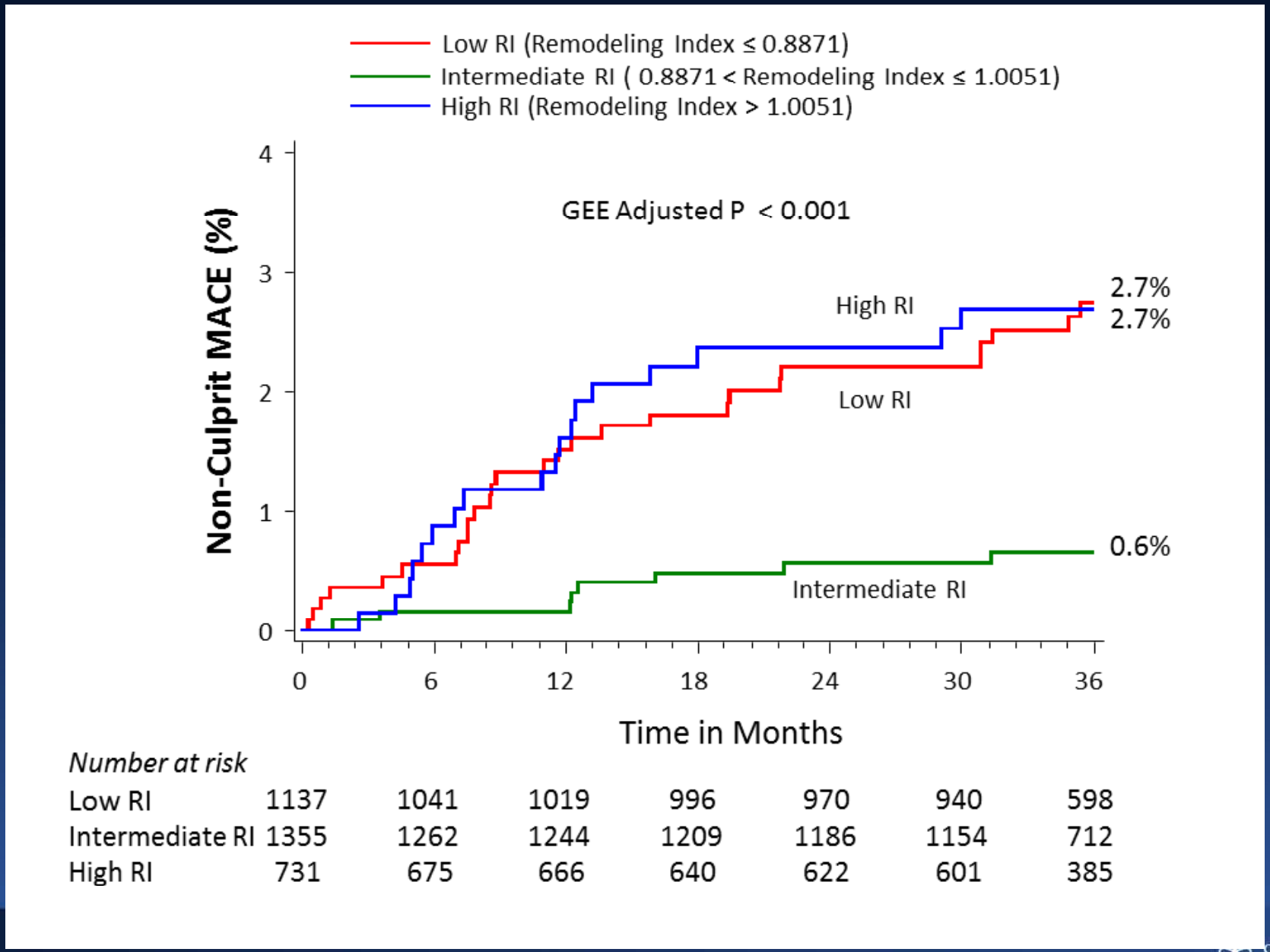
Inaba S, et al, ACC 2012

Relationship between remodeling index and MLA



Inaba S, et al, ACC 2012

Remodeling Index and MACE



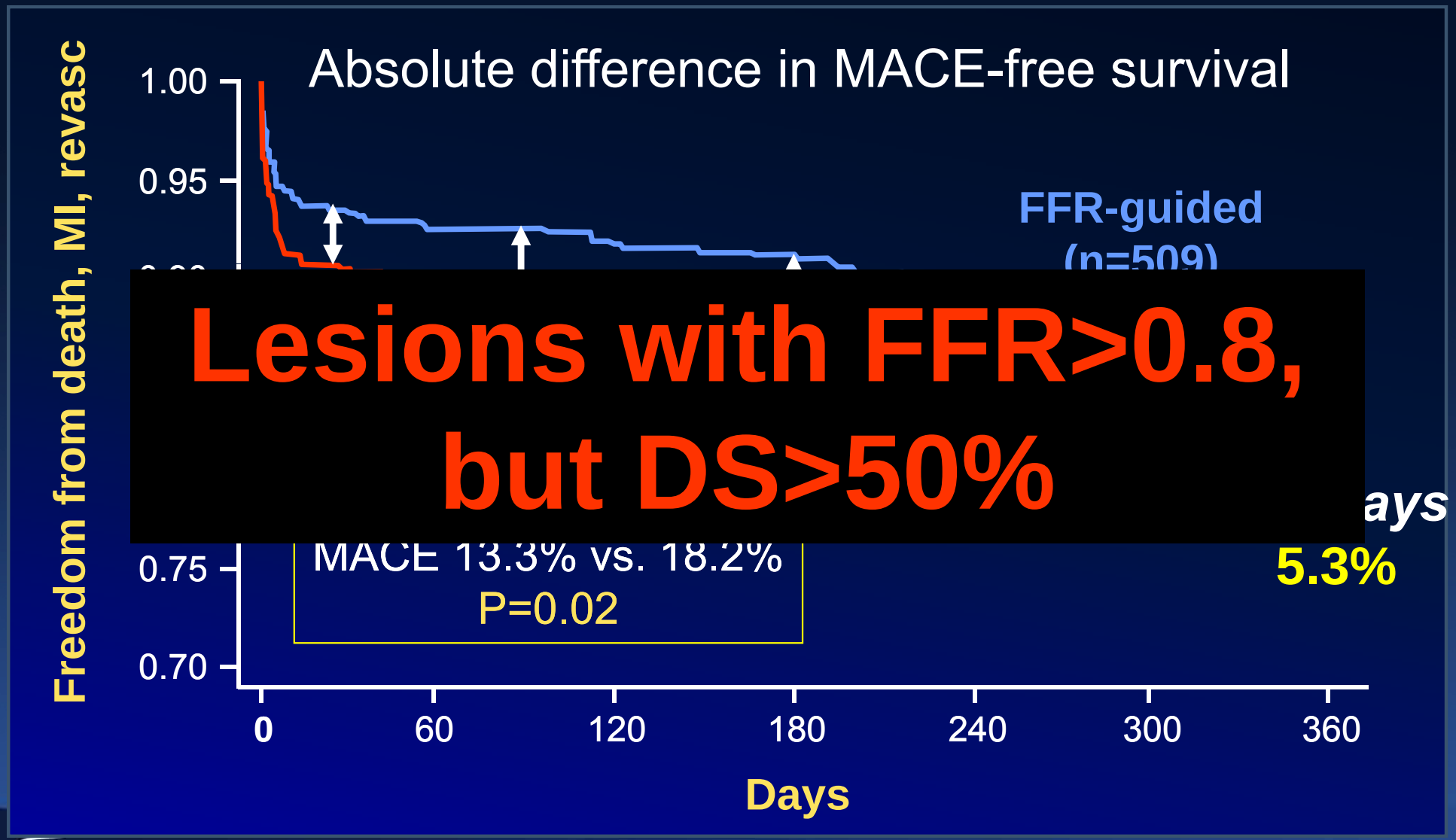
Number at risk

Low RI	1137	1041	1019	996	970	940	598
Intermediate RI	1355	1262	1244	1209	1186	1154	712
High RI	731	675	666	640	622	601	385

Inaba S, et al, ACC 2012

FAME: Primary Endpoint

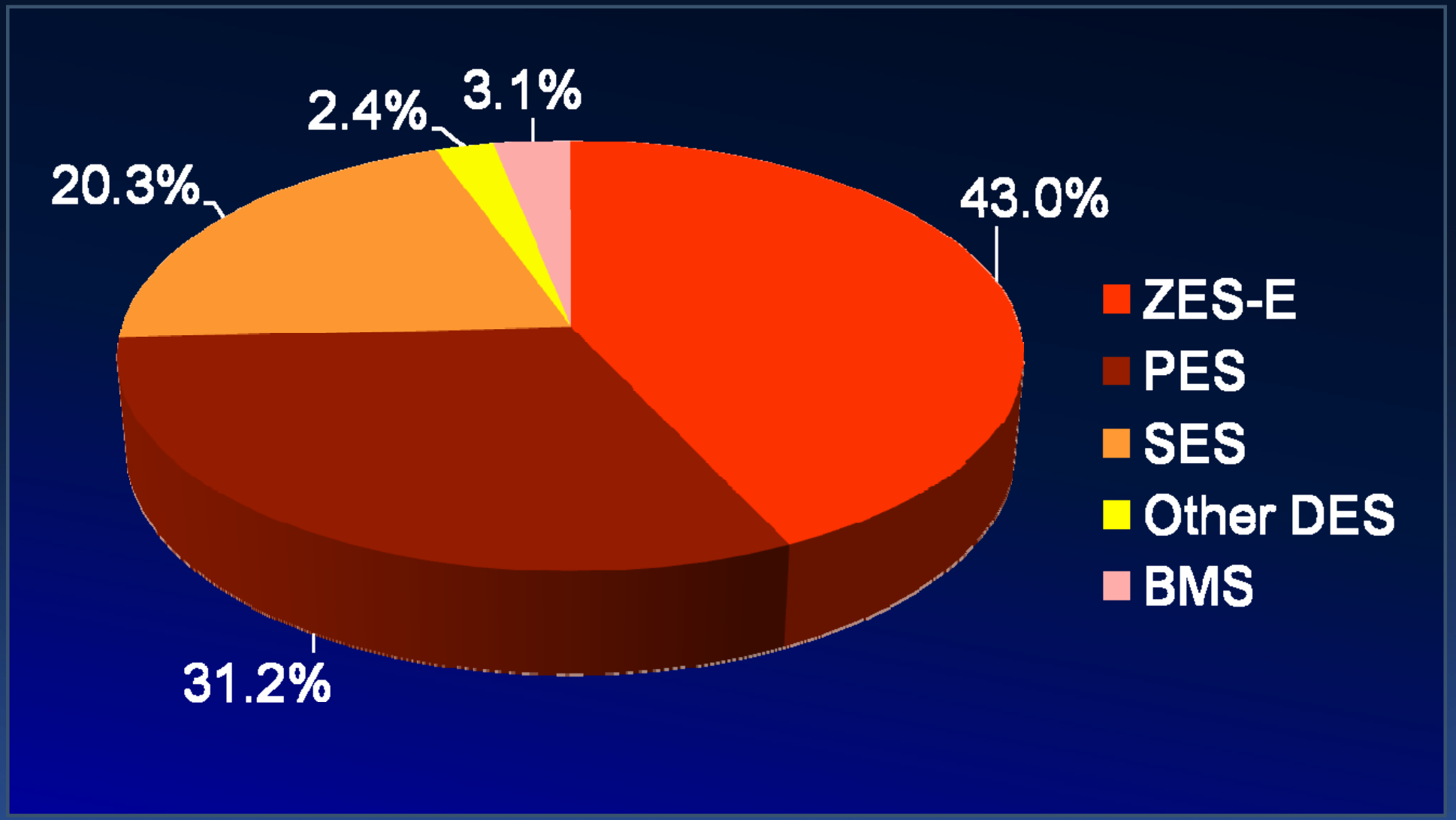
1005 pts with MVD (83% CSA) undergoing PCI with DES were randomized to FFR-guided vs. angio-guided intervention



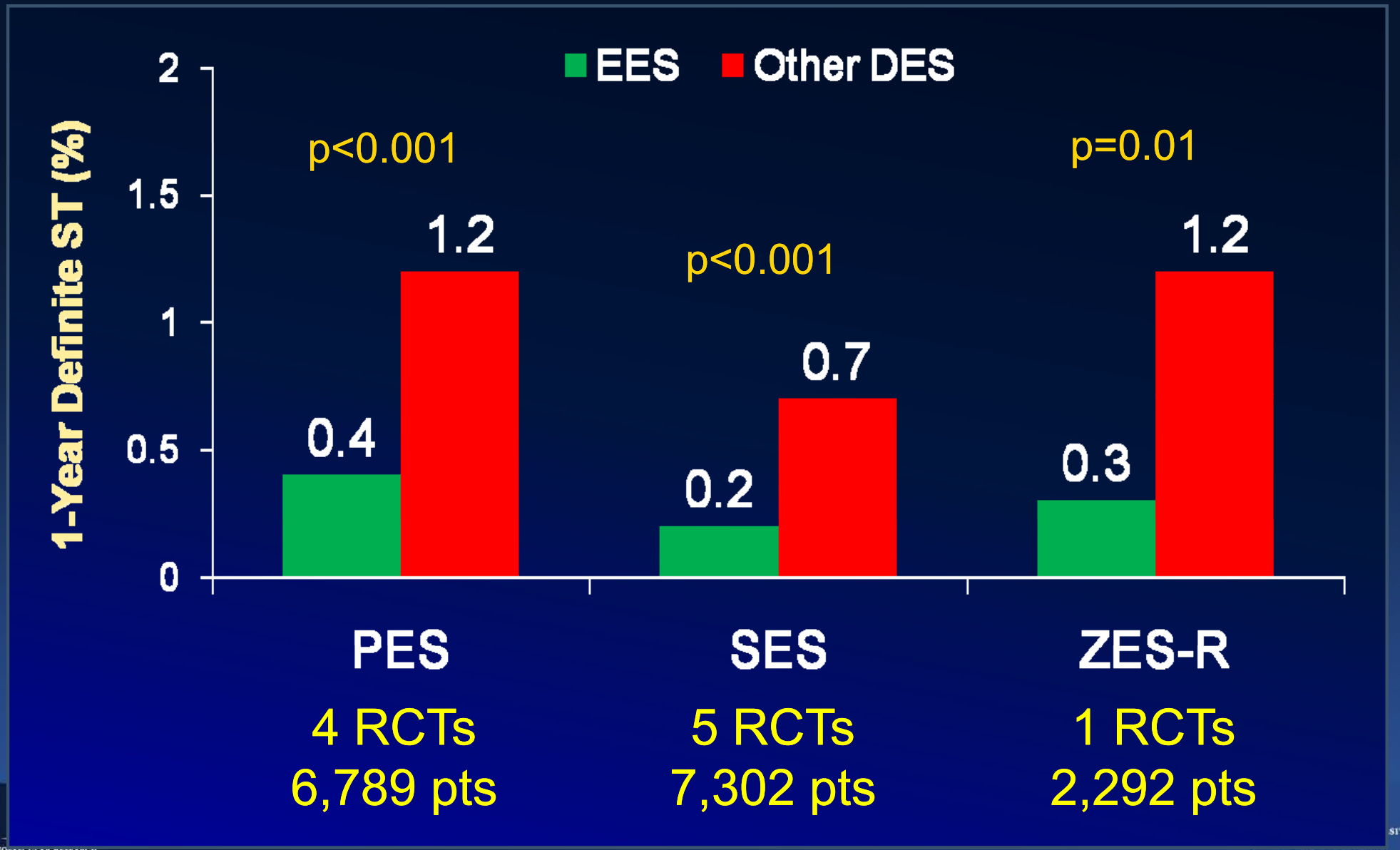
Lesions with FFR>0.8, but DS>50%

Tonino PAL et al. NEJM 2009;360:213–24

FAME Trial: Stent Use



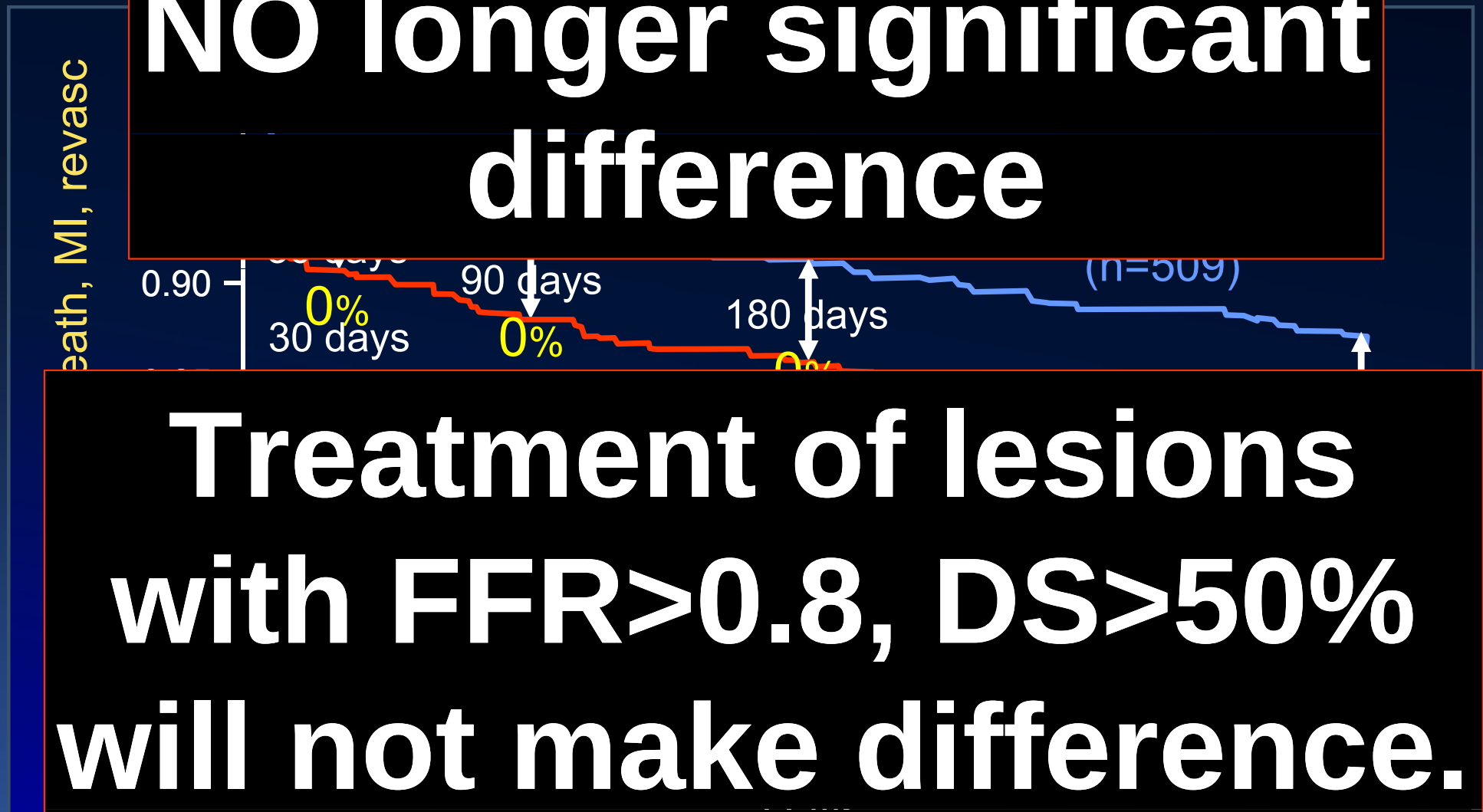
RCTs of EES vs. Other DES (n-16,383): 1-year definite stent thrombosis



FAME: With better stents????

1005 pts with MVD (83% CSA) undergoing PCI with DES were randomized to FFR guided vs angio guided intervention

NO longer significant difference



Treatment of lesions with FFR>0.8, DS>50% will not make difference.

Tonino PAL et al. NEJM 2009;360:213–24

FFR ≥0.8
Don't touch now

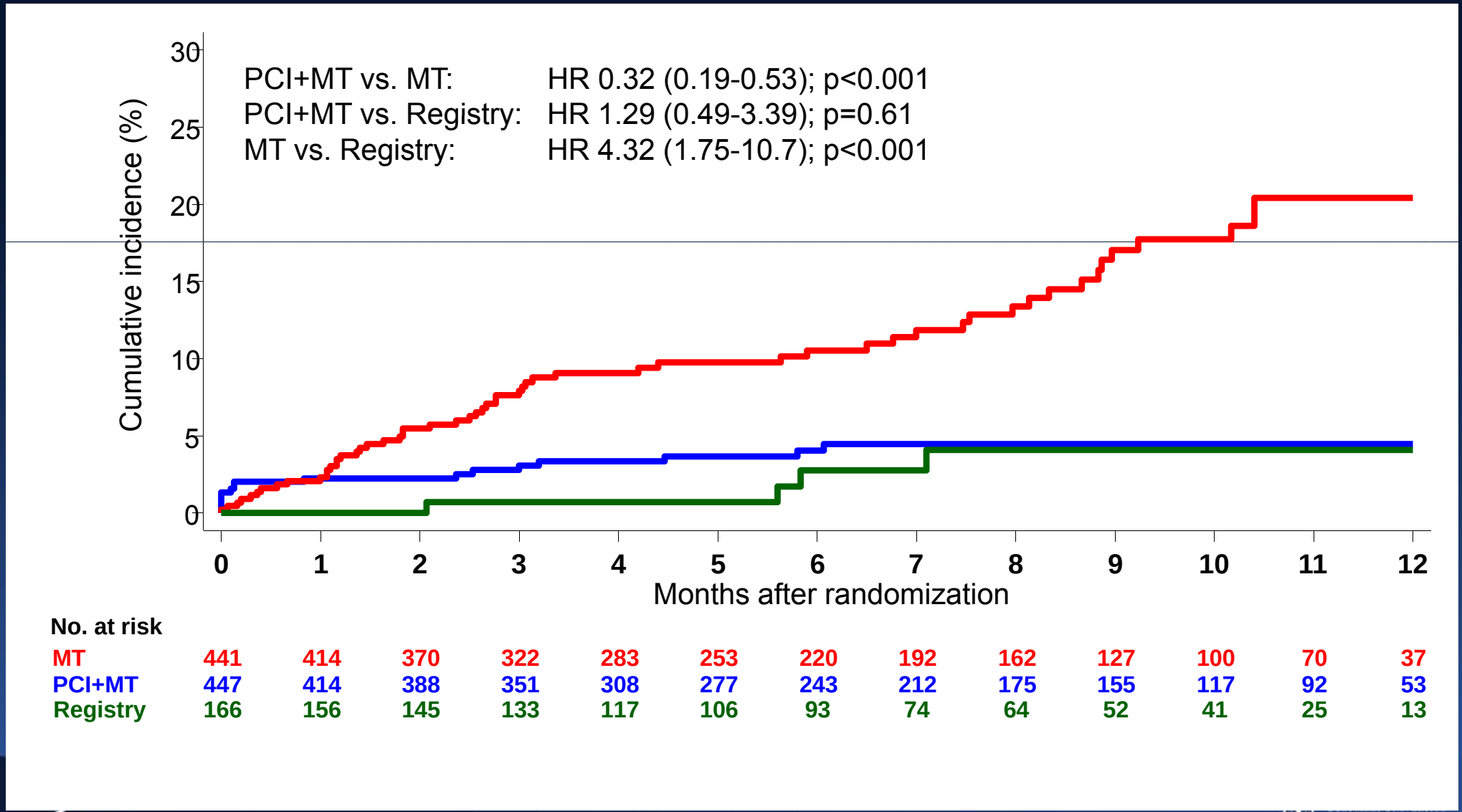
FFR<0.8

Treat

?

MLA<4mm^2,
PB>70%

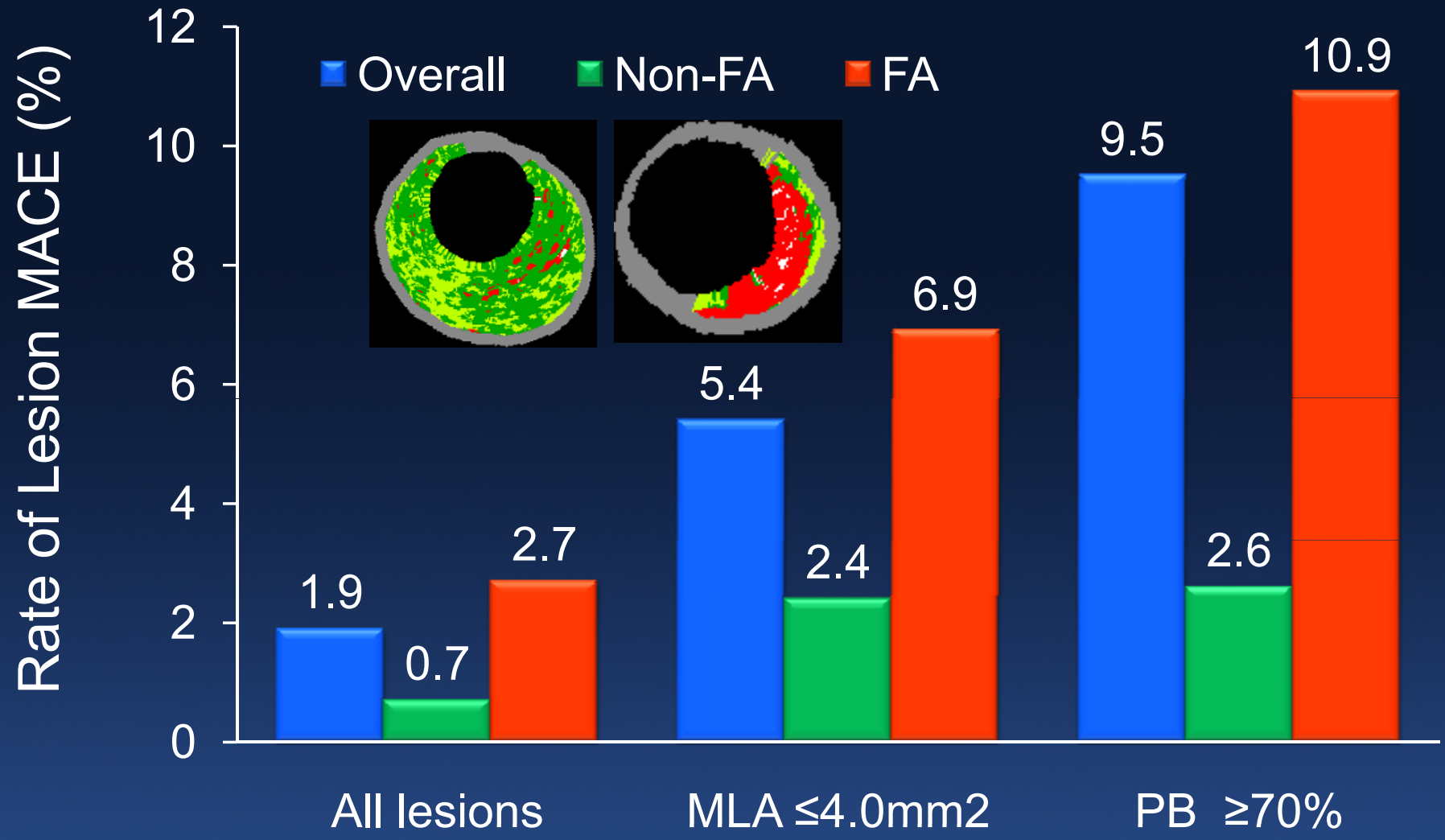
FAME 2: Primary Outcomes
Death, MI, Urgent Revascularization



No. at risk												
MT	441	414	370	322	283	253	220	192	162	127	100	70	37
PCI+MT	447	414	388	351	308	277	243	212	175	155	117	92	53
Registry	166	156	145	133	117	106	93	74	64	52	41	25	13

De Bruyne, et al. New Engl J Med 2012;367:991-1001.

PROSPECT: Non-FA Lesions



	All lesions	MLA ≤4.0mm2	PB ≥70%
Lesion numbers (Non-FA/FA)	1147/1733	172/368	43/210

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Dohi et al, ***JACC Img In press***

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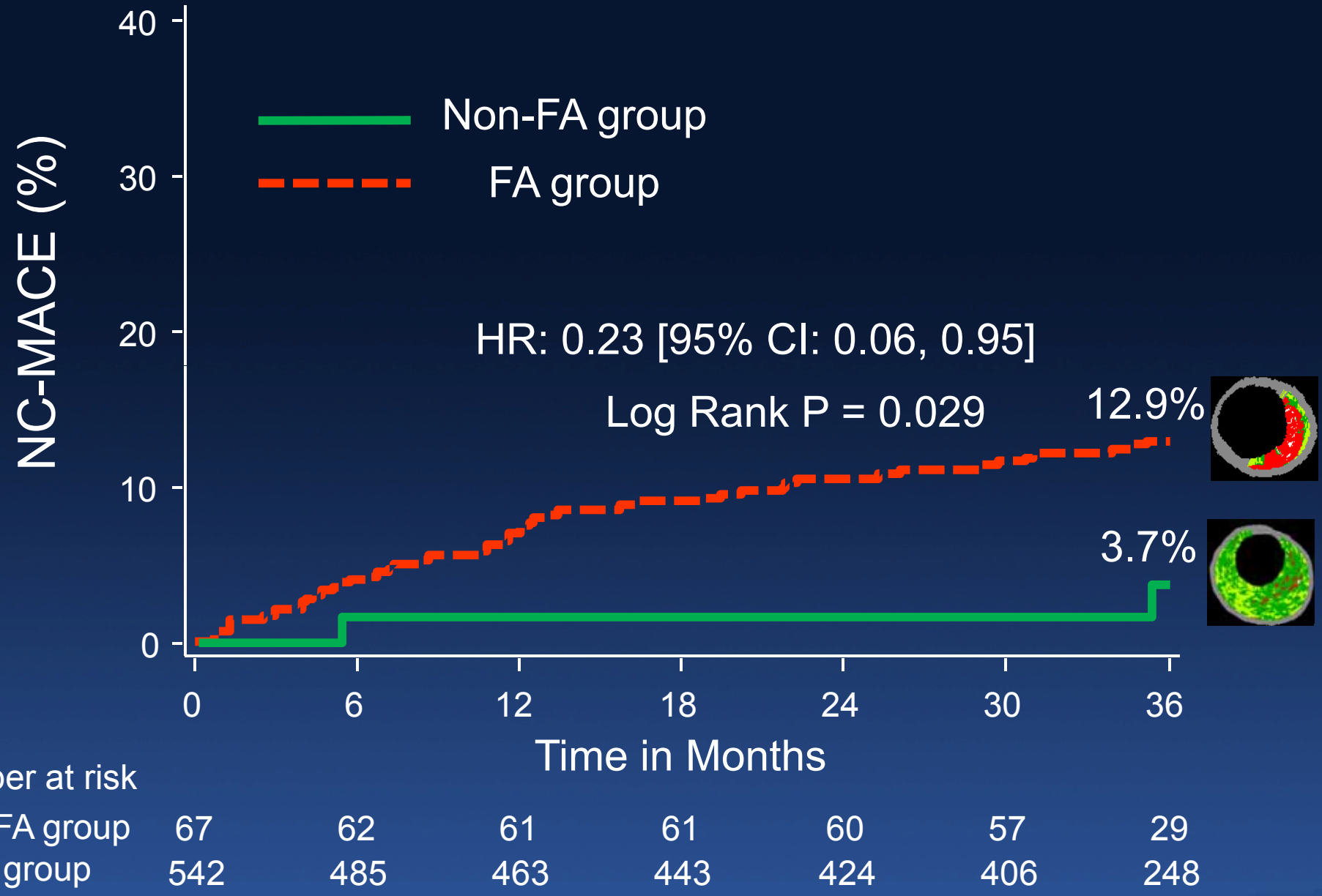
PROSPECT: Non-FA Lesions



Number at risk

Non-FA group	67	62	61	61	60	57	29
FA group	542	485	463	443	424	406	248

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Dohi et al, ***JACC Img In press***

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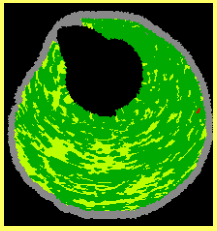
FFR ≥0.8
Don’t touch now

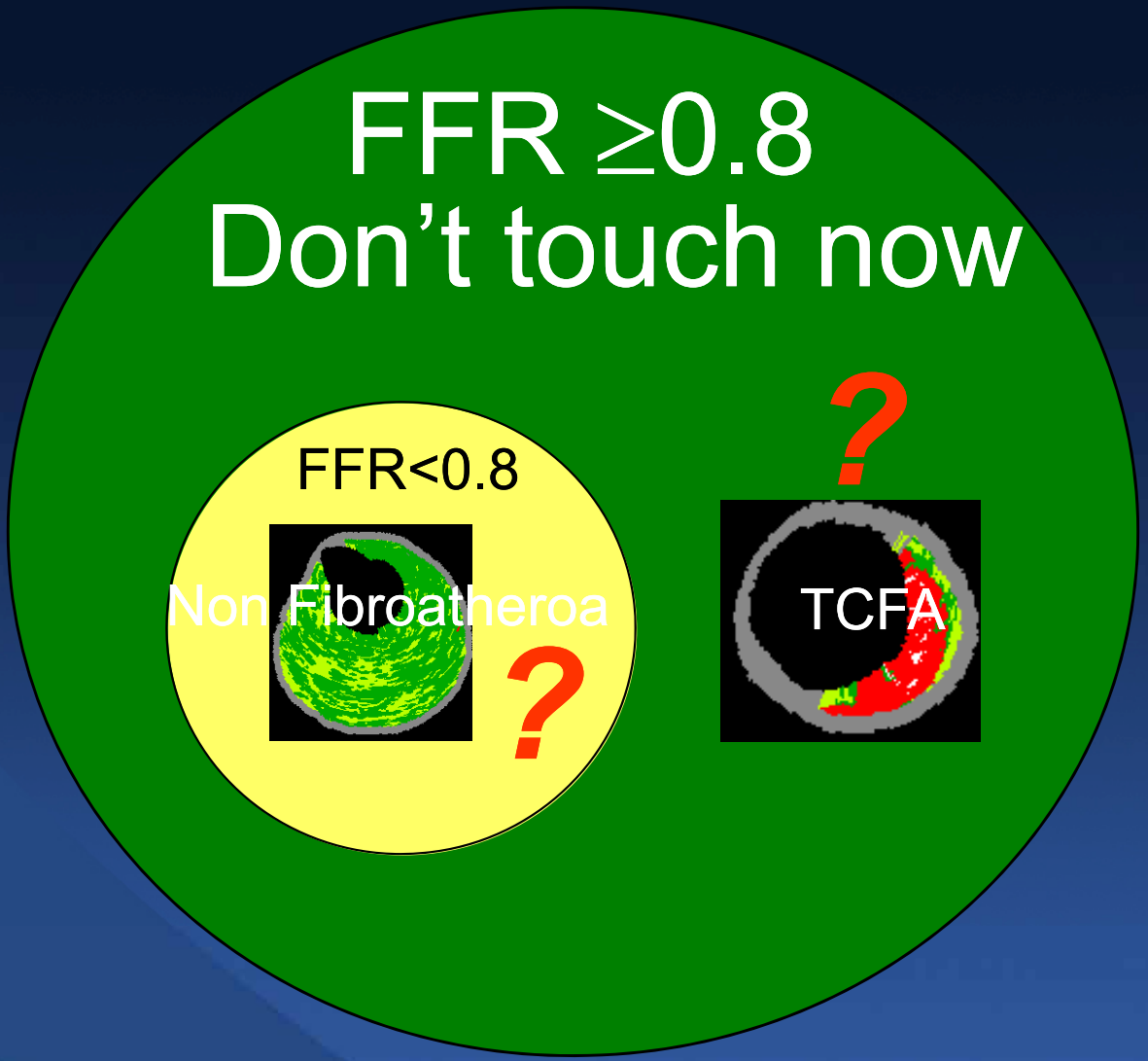
FFR<0.8

Non Fibroatheroa



?

1. FFR<0.8 should be treated - FAME2
2. FFR≥0.8, but vulnerable plaque using the best stent (2nd generation, bioabsorbable stent).

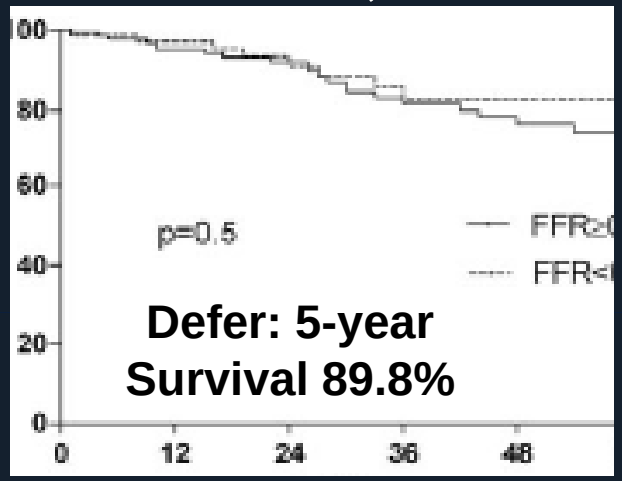


LMCA Defer by FFR

Any Death
LMCA revasc
Other revasc

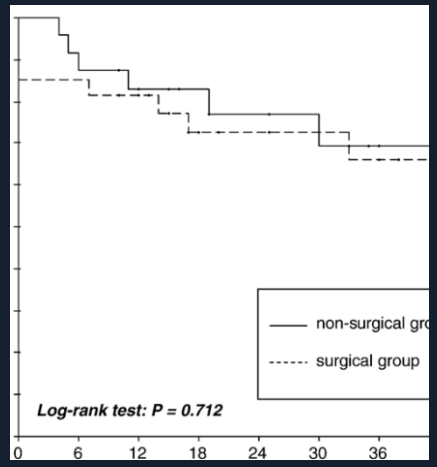
FFR=0.8

Hamilos, 2009

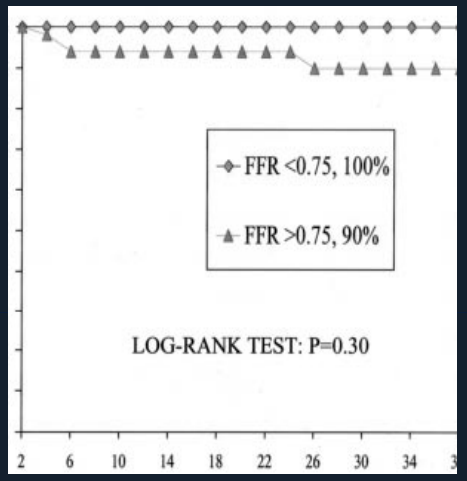


FFR=0.75

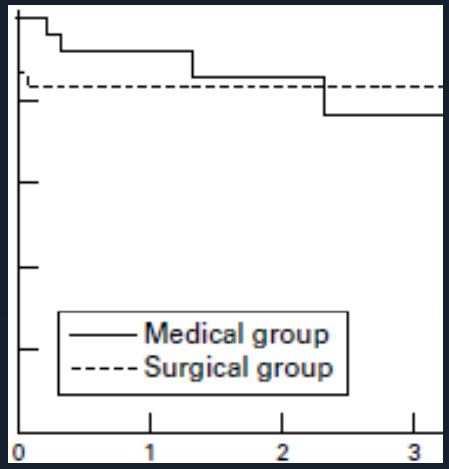
Lindstaedt, 2006

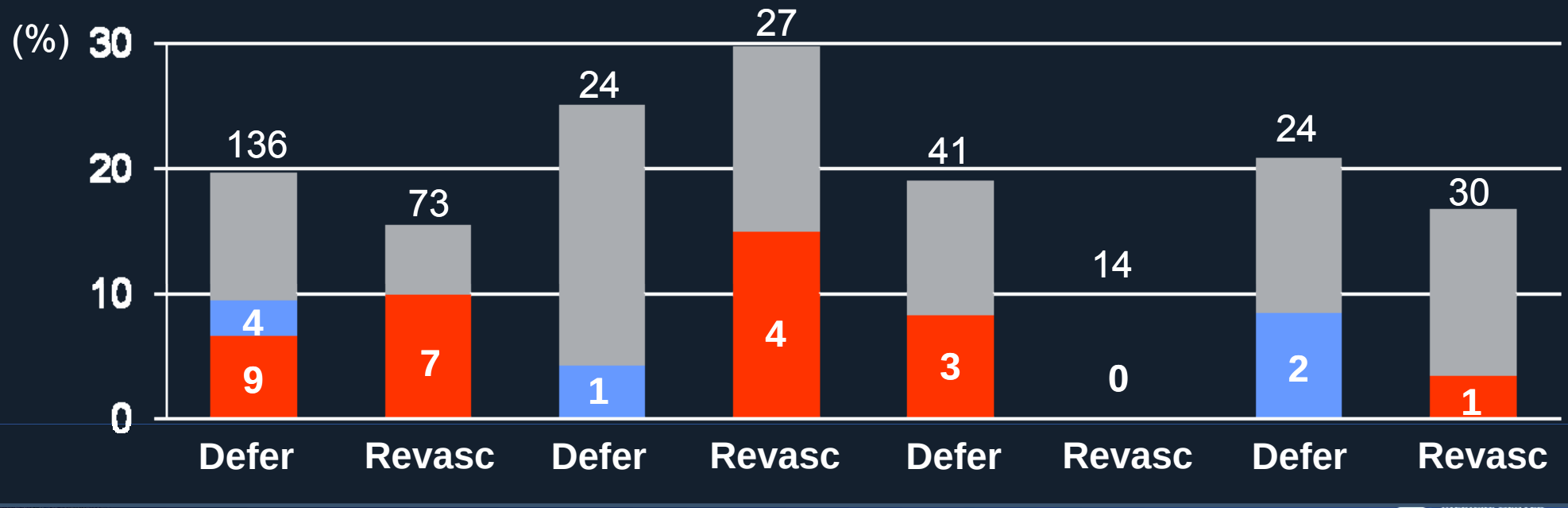


Jasti, 2004



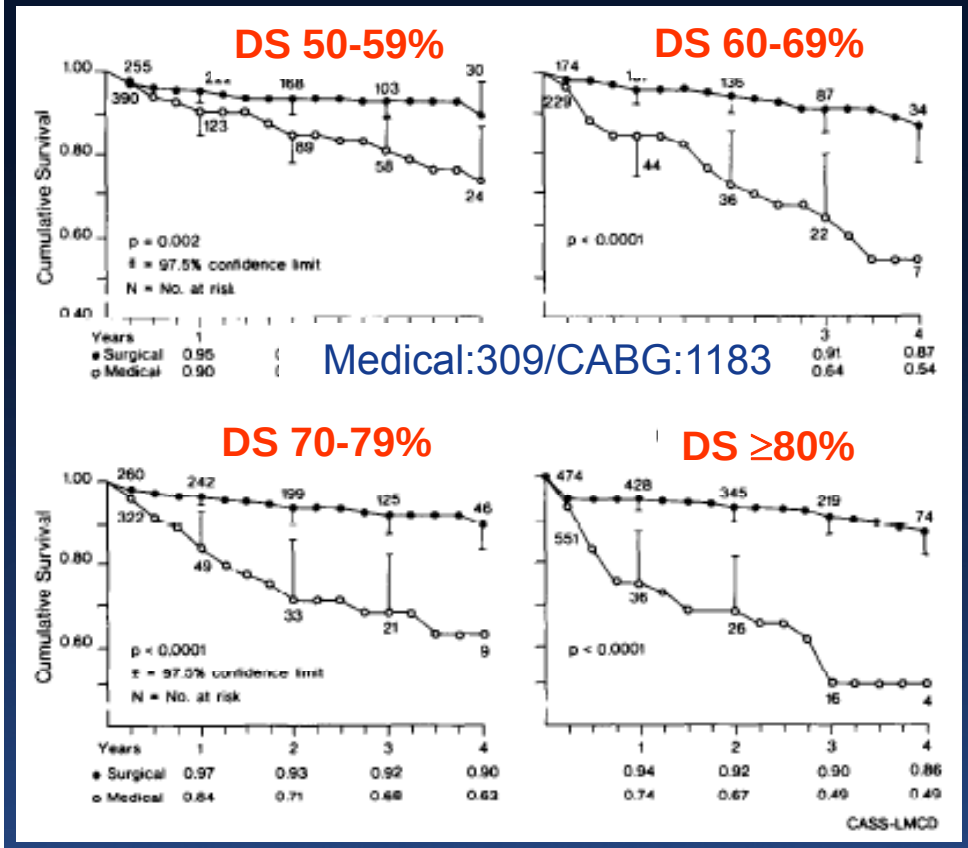
Bech, 2001





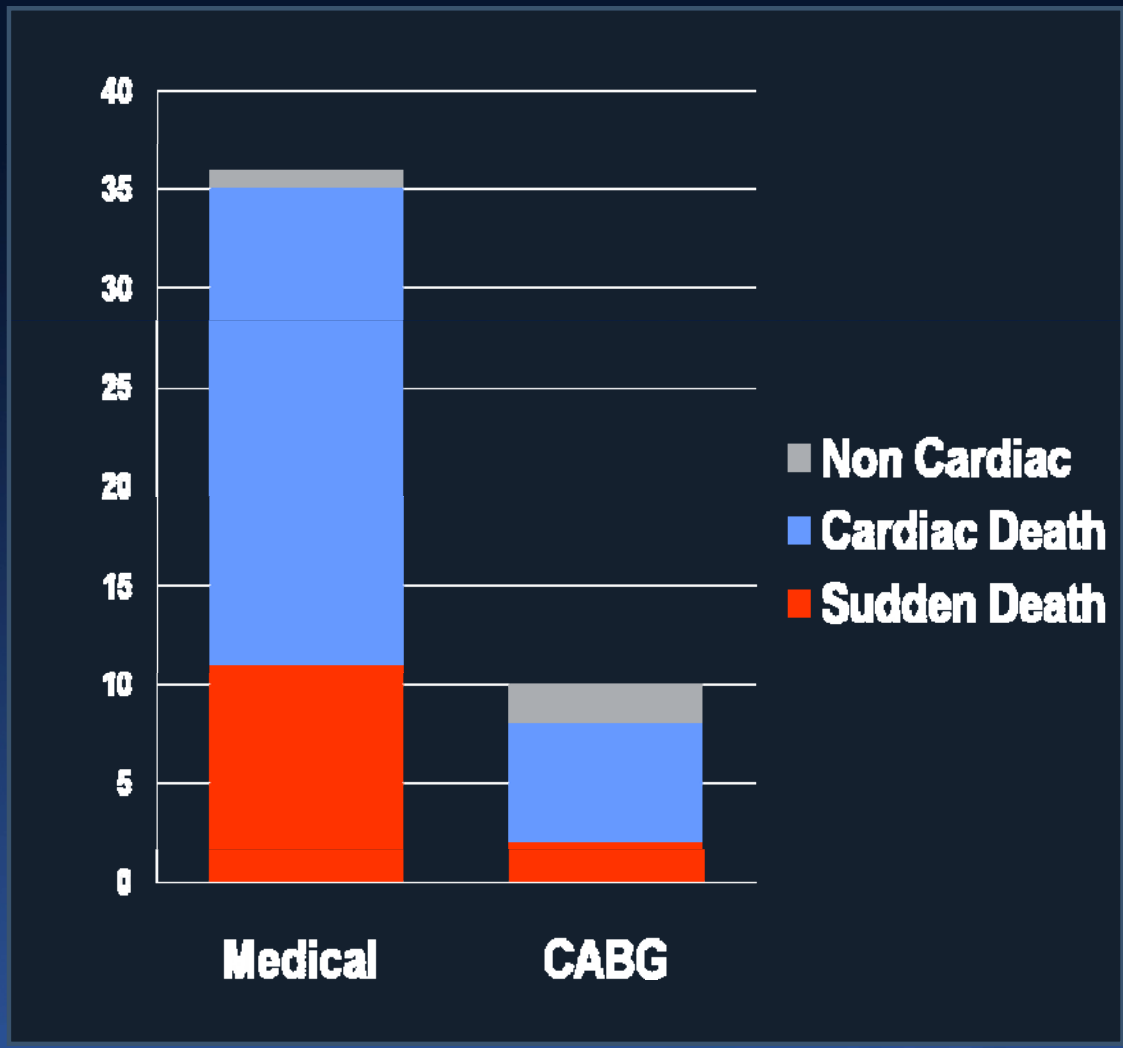
Hamilos, *Circ,* 120:1505, Lindstaedt, Am H J, 2006;152;156, Jasti ,Circ, 2004;110:2831, Bech, Heart, 2001;86:547

Natural History of Left Main Disease



Medical:309/CABG:1183

Chaitman et al, *AJC* 1981;48: 765-777



Summary

- Does morphology predict future event?

YES!

- Does physiology predict future event?

YES!

- Is only morphology enough?

NO…

- Is only physiology enough?

I believe NO…