Clinical Outcome of DEFER

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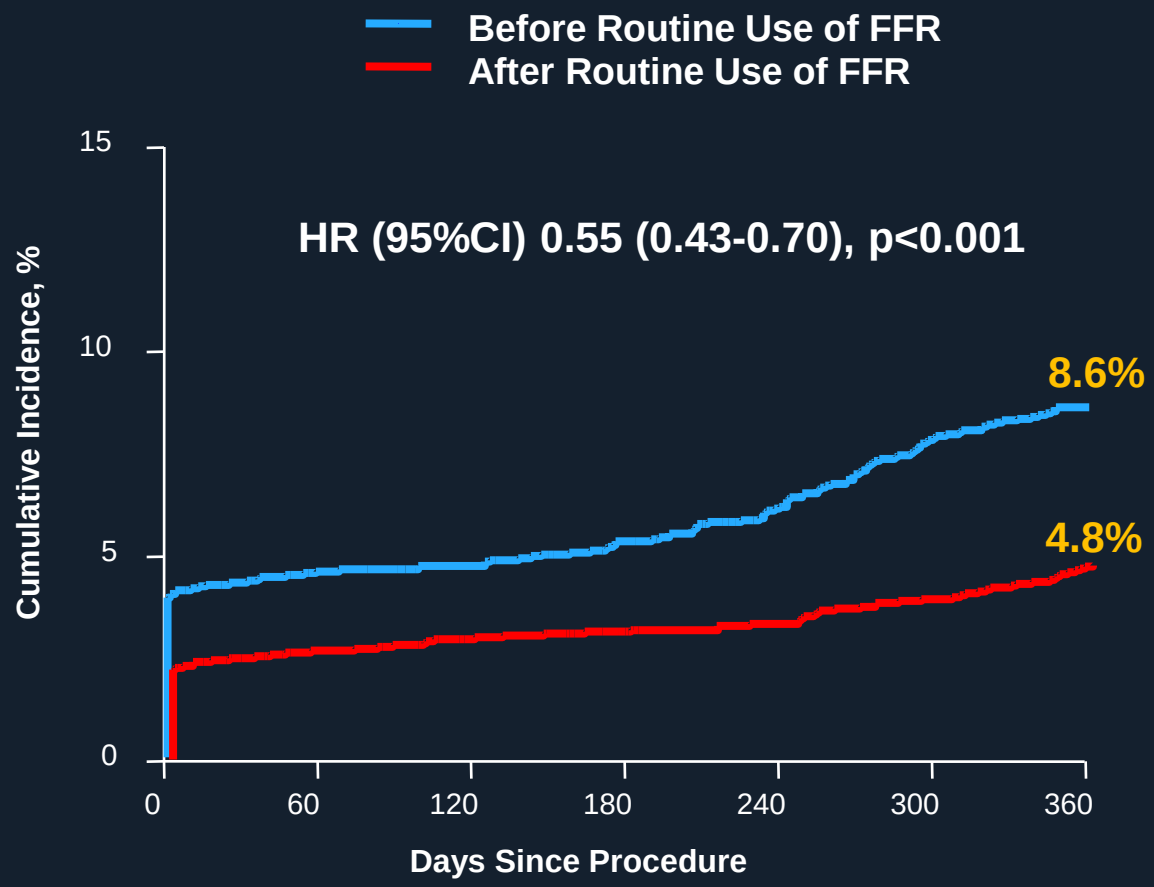
Primary End Point

(Death, MI, or Repeat Revascularization)



41%

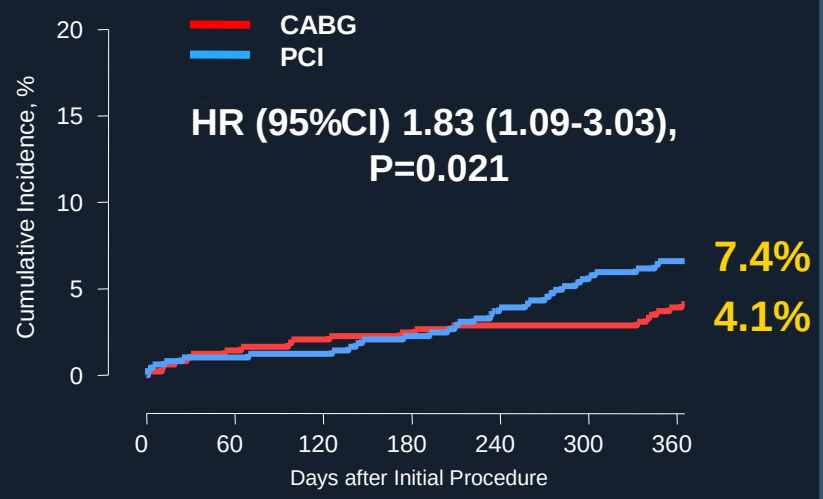
No. at Risk				
Before Routine Use	2178	2066	2011	1960
After Routine Use	2178	2092	2067	2037

Park SJ, Ahn JM et al. Eur Heart J. 2013 Nov;34(43):3353-61

Primary End Point

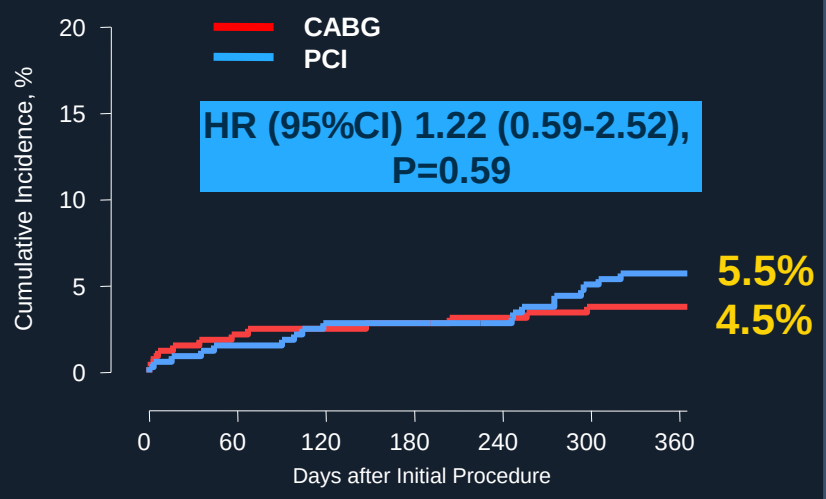
(Death, MI, Stroke or Repeat Revascularization)

Before Routine FFR (2008-2009)



CABG	488	480	472	466
PCI	488	483	465	450

After Routine FFR (2010-2011)



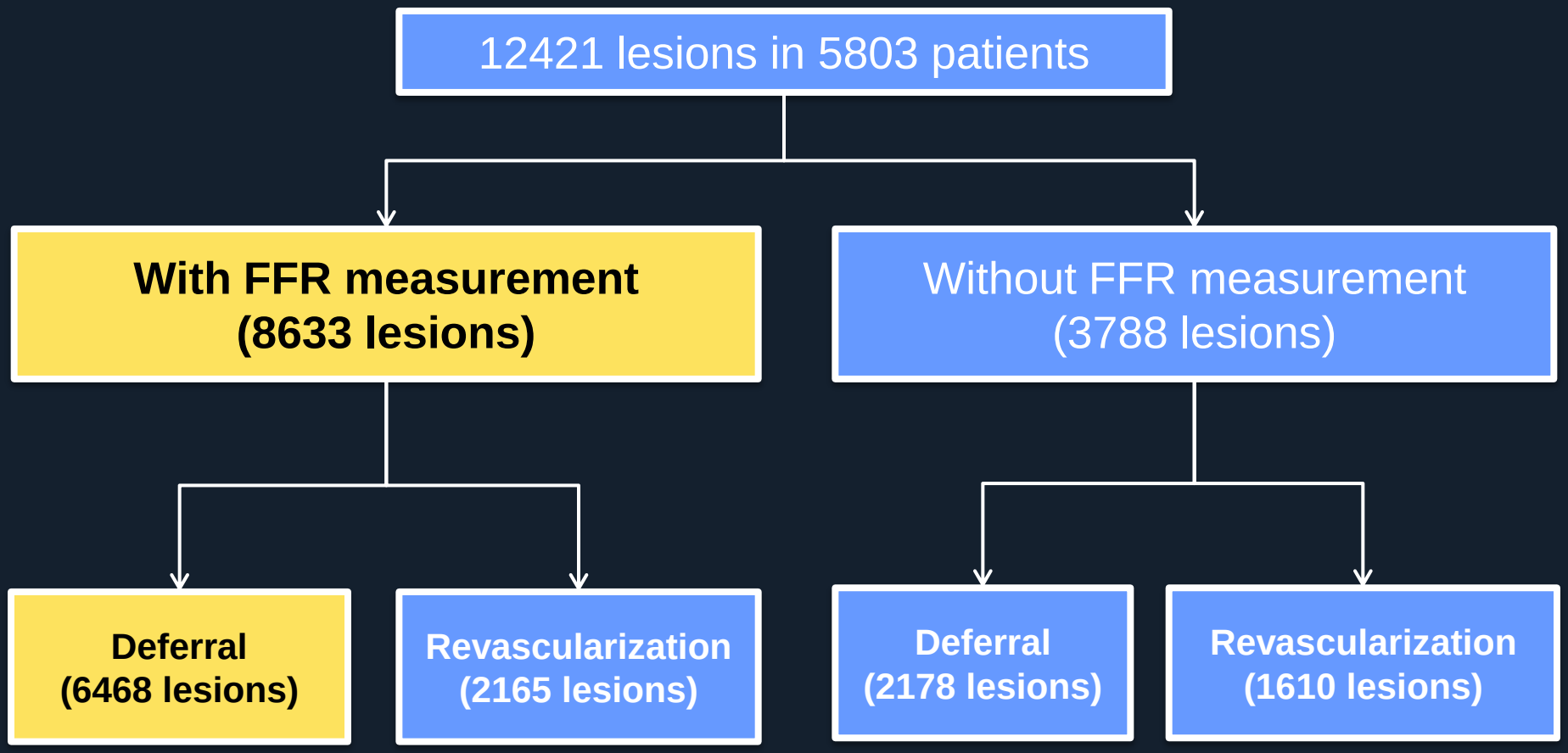
CABG	314	308	303	301
PCI	314	306	300	292

Ahn JM, Park SJ et al. Am J Cardiol 2015;116:1163-1171

Objective

- To evaluate natural prognosis of deferred or revascularized coronary stenosis after FFR measurement
- To assess the clinical outcome-derived revascularization threshold of FFR in the era of second-generation drug-eluting stent.

IRIS FFR Registry (2009.8-2015.8)



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Patient Characteristics

Variables	N=5846
Age	63.6±9.8
Sex (men)	4187 (71.6%)
Diabetes	1807 (30.9%)
Hypertension	3687 (63.1%)
Current smoker	1402 (24.0%)
Hyperlipidemia	3507 (60.0%)
Previous myocardial infarction	378 (6.5%)
Previous PCI	1138 (19.5%)
Previous stroke	345 (5.9%)
Chronic renal failure	119 (2.0%)
Chronic lung disease	125 (2.1%)
Peripheral artery disease	139 (2.4%)
Family history	600 (10.3%)

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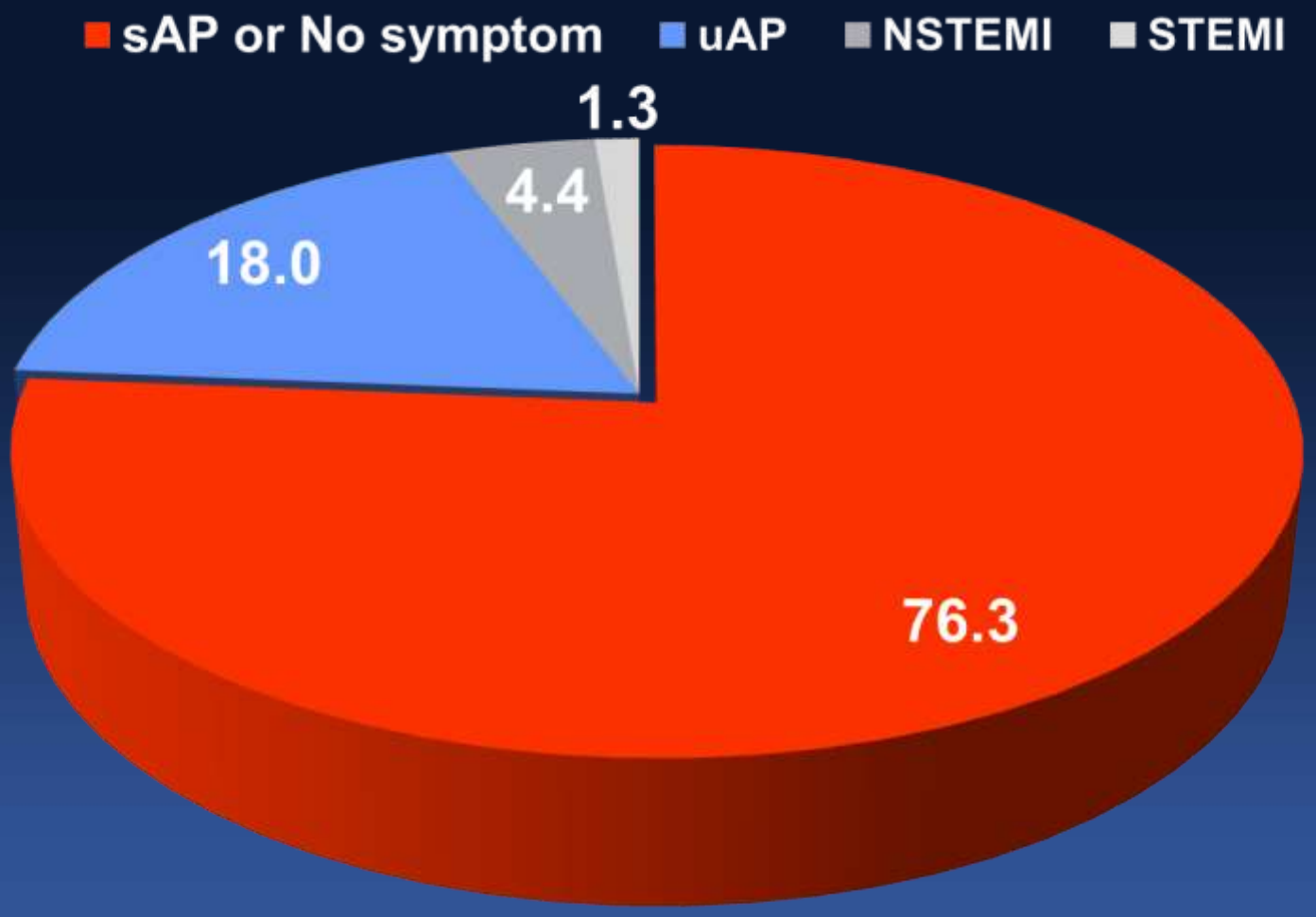
Clinical Presentation



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Lesion Characteristics

Variables	N=8633
Lesion territory	
Left main	345 (4.1%)
Left anterior descending artery	4372 (50.6%)
Left circumflex artery	2070 (24.0%)
Right coronary artery	1407 (16.3%)
ACC/AHA B2C lesion	4819 (55.8%)
Long lesion (>20mm)	3680 (42.6%)
Moderate to severe calcification	269 (3.1%)
Thrombus containing lesion	63 (0.7%)
Angiographic ulcerated lesion	55 (0.6%)
Diameter stenosis	
30-50%	2659 (30.7%)
50-70%	4057 (47.0%)
70-99%	1927 (22.3%)

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FFR

Variables	8633 lesions
Fractional flow reserve	
Mean	0.83±0.11
Median	0.85 (0.77, 0.91)
<0.75	1903 (22.1%)
0.75-0.80	1001 (11.6%)
>0.80	5729 (66.3%)
Route of adenosine	
Intravenous	7881 (91.3%)
Intracoronary	752 (8.7%)
Hyperemic Agent	
Adenonsine	8393 (97.2%)
Others	240 (2.8%)

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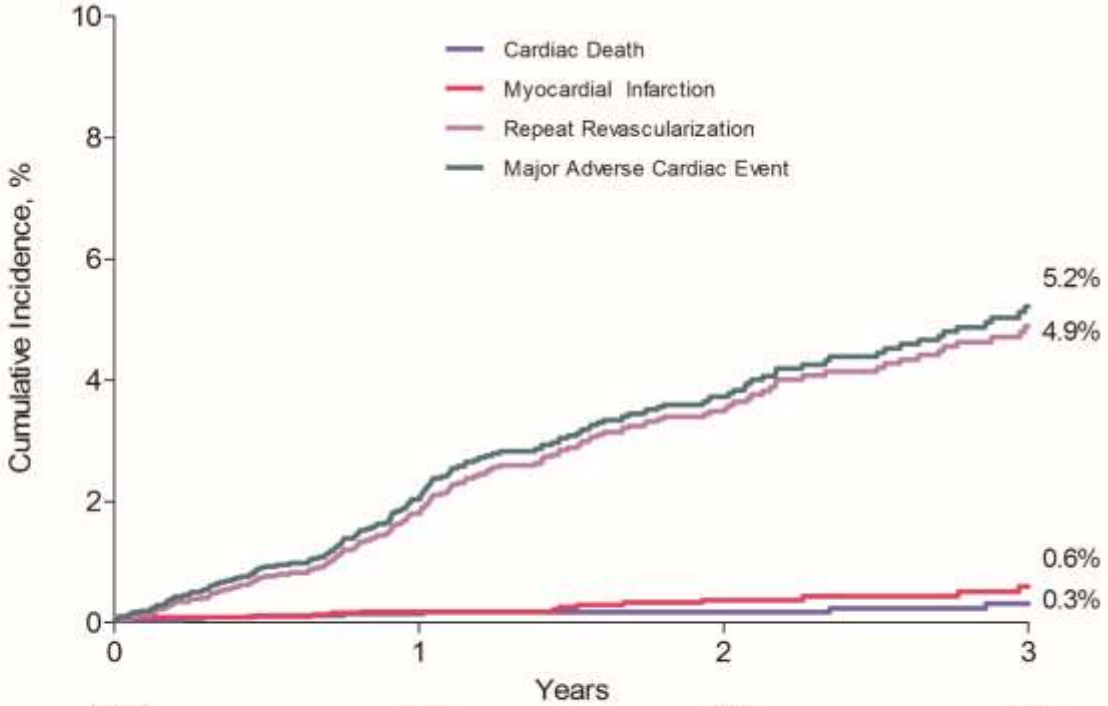
Deferred Lesion Outcome (1)



Cardiac Death	4608	3393	2069	1036
Myocardial Infarction	4608	3445	2107	1059
Repeat Revascularization	4608	3337	1998	987
Major Adverse Cardiac Event	4608	3333	1996	987

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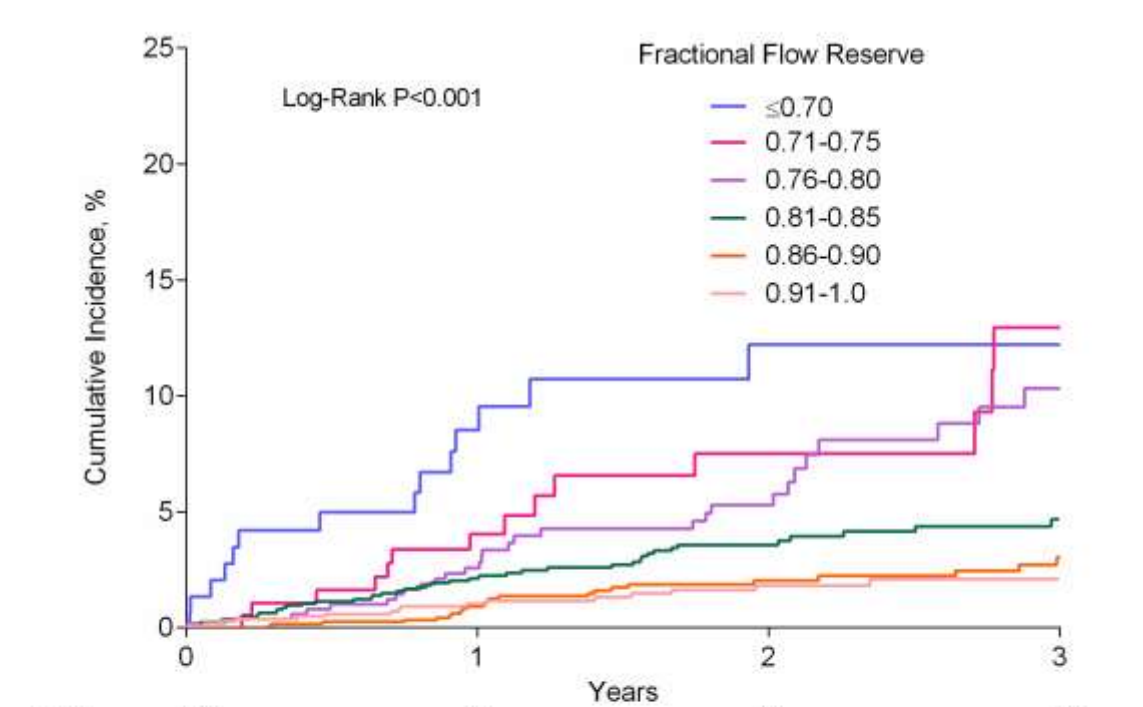
Deferred Lesion Outcome (2)



≤0.70	148	93	52	27
0.71-0.75	195	140	89	40
0.76-0.80	540	379	216	97
0.81-0.85	1320	953	601	309
0.86-0.90	1329	961	583	292
0.91-1.0	1076	784	482	222

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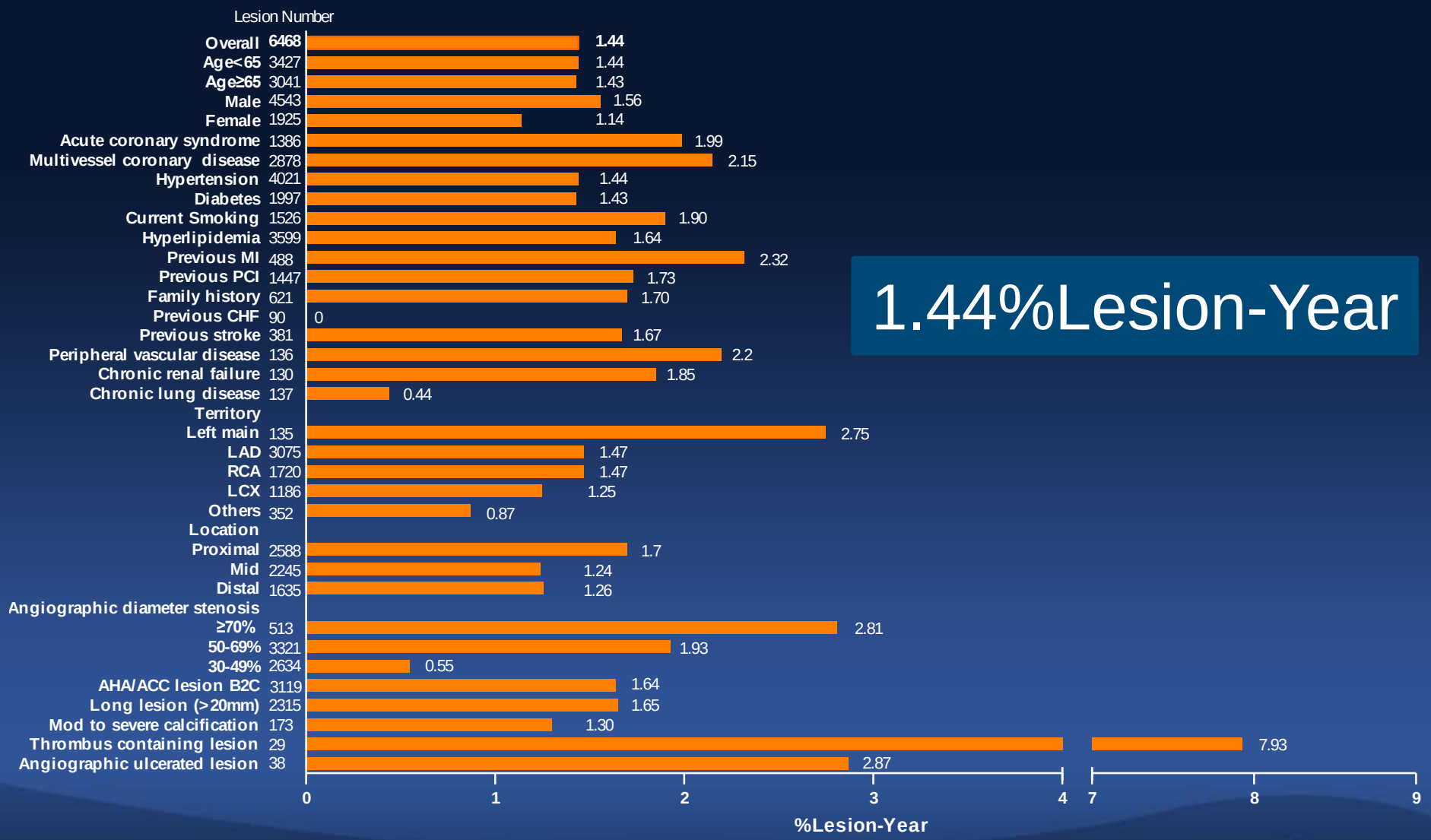
Incidence Rate of Deferred Lesion Failure



1.44%Lesion-Year

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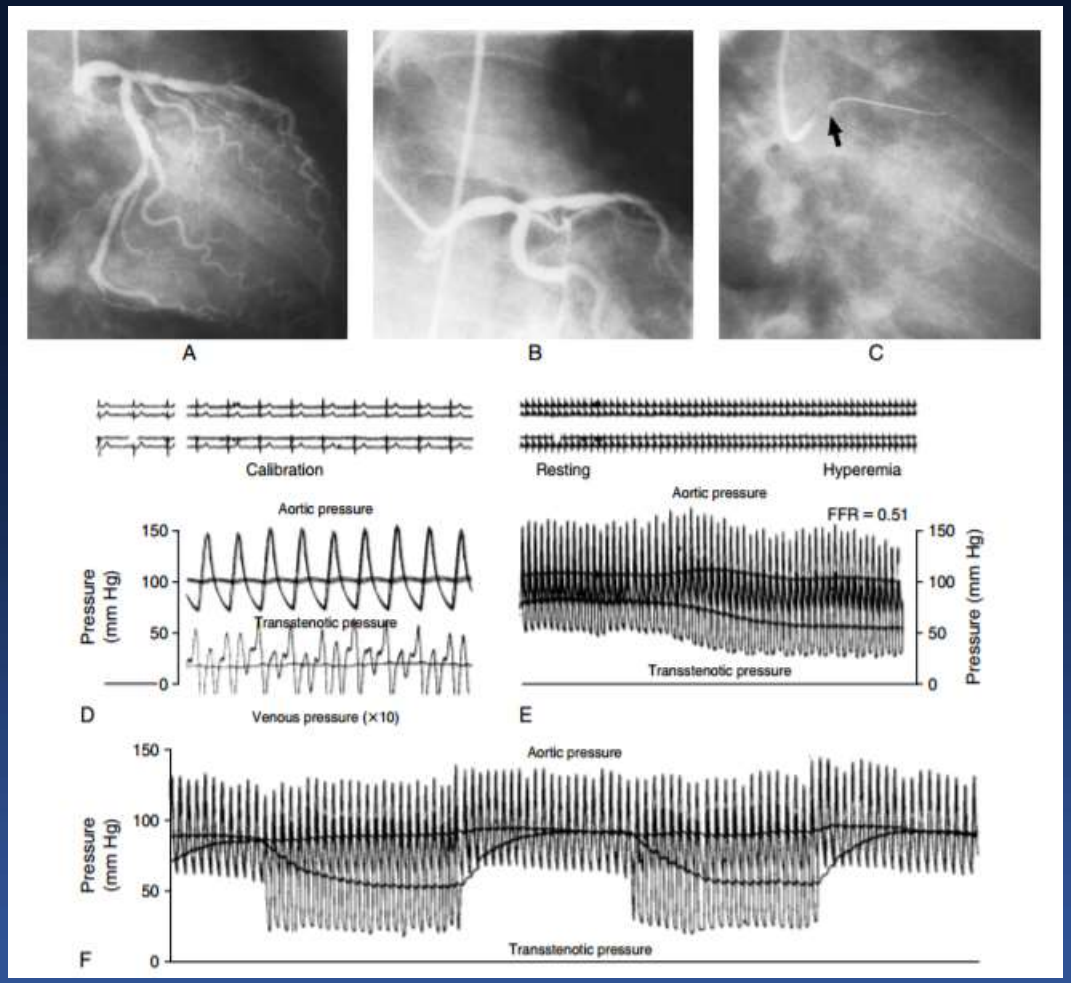
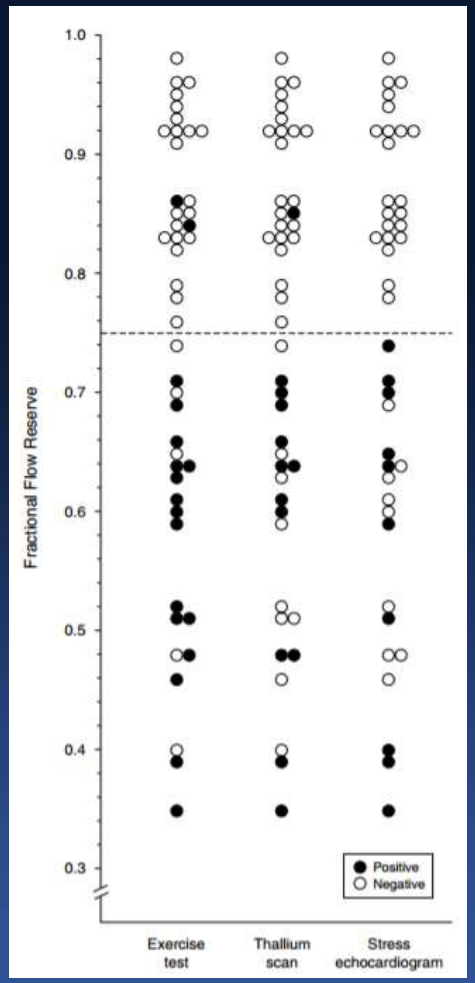
Predictors of Deferred Lesion Failure

	HR (95% CI)	P value
FFR (by increase of 0.01)	0.94 (0.93-0.96)	<0.001
Multivessel CAD	1.66 (1.19-2.33)	0.003
Thrombus containing lesion	5.46 (1.98-15.0)	0.001
Diameter stenosis		<0.001
30-50%	1 (reference)	
50-70%	2.20 (1.41-3.44)	<0.001
>70%	2.50 (1.41-4.44)	0.002

FFR Cut-Off From Noninvasive Functional Study



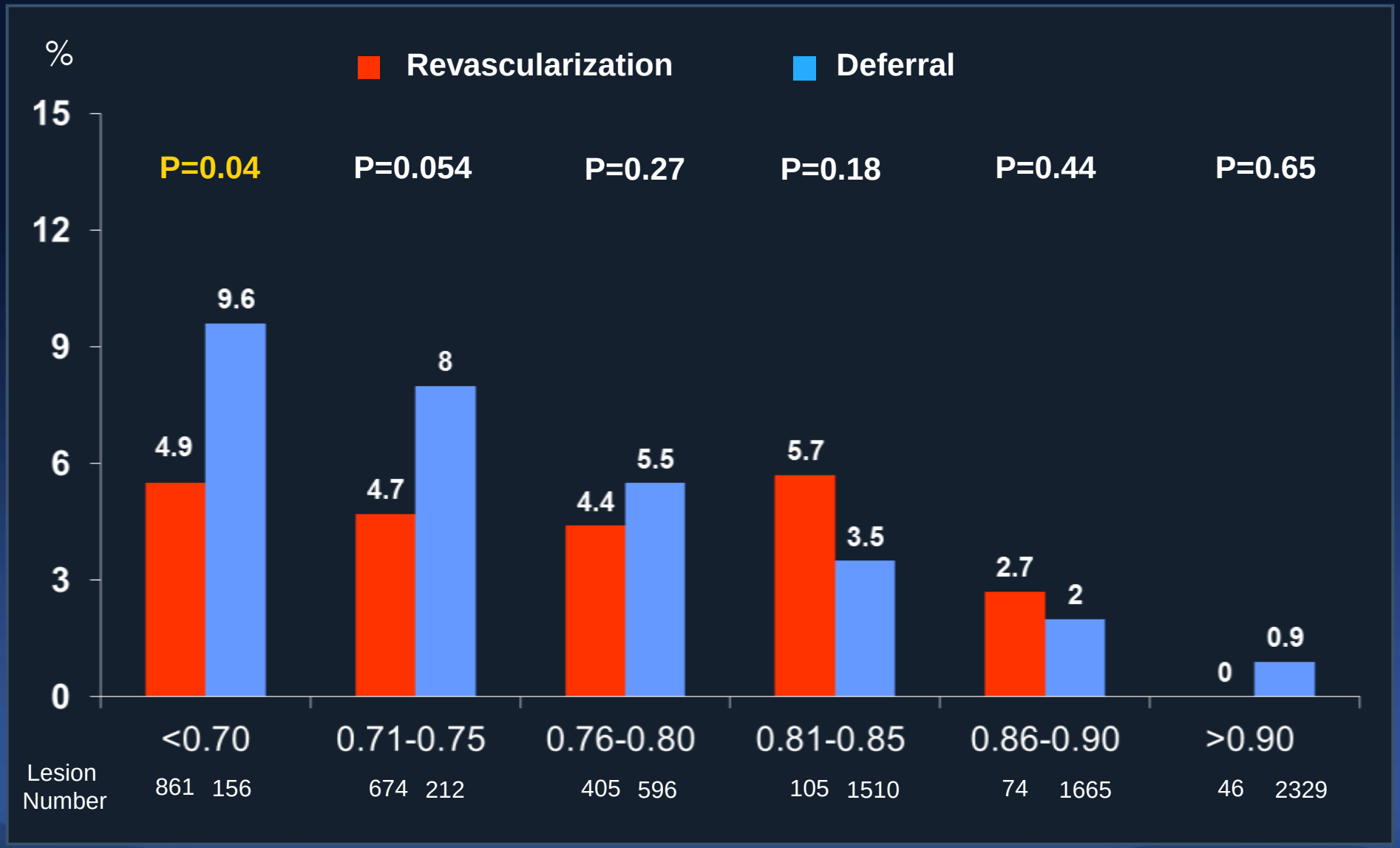


0.75

FFR cut-off value was compared with noninvasive functional study: ***Exercise test, Thallium scan, Stress Echo***

Pijls NH et al. N Engl J Med. 1996 Jun 27;334(26):1703-8.

Major Adverse Cardiac Events



% from crude proportion

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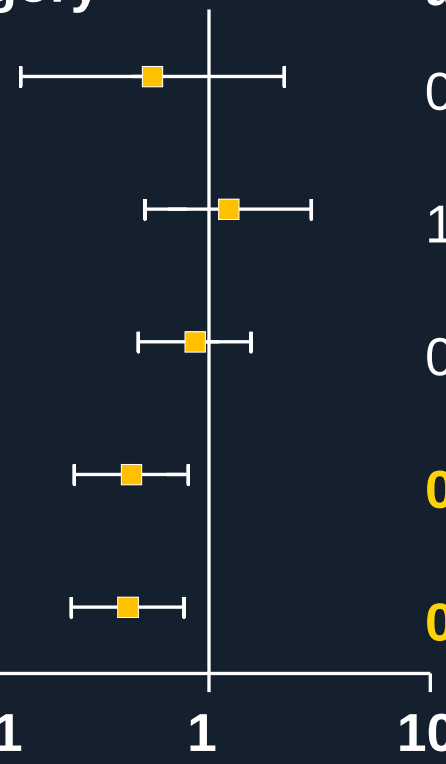
Adjust Hazard Ratio: MACE



FFR Category	aHR (95% CI)	P value
≥0.86	0.42 (0.09-1.97)	0.27
0.81-0.85	1.21 (0.44-3.36)	0.71
0.76-0.80	0.83 (0.46-1.50)	0.53
0.71-0.75	**0.47 (0.24-0.89)**	**0.021**
≤0.70	**0.47 (0.26-0.84)**	**0.012**

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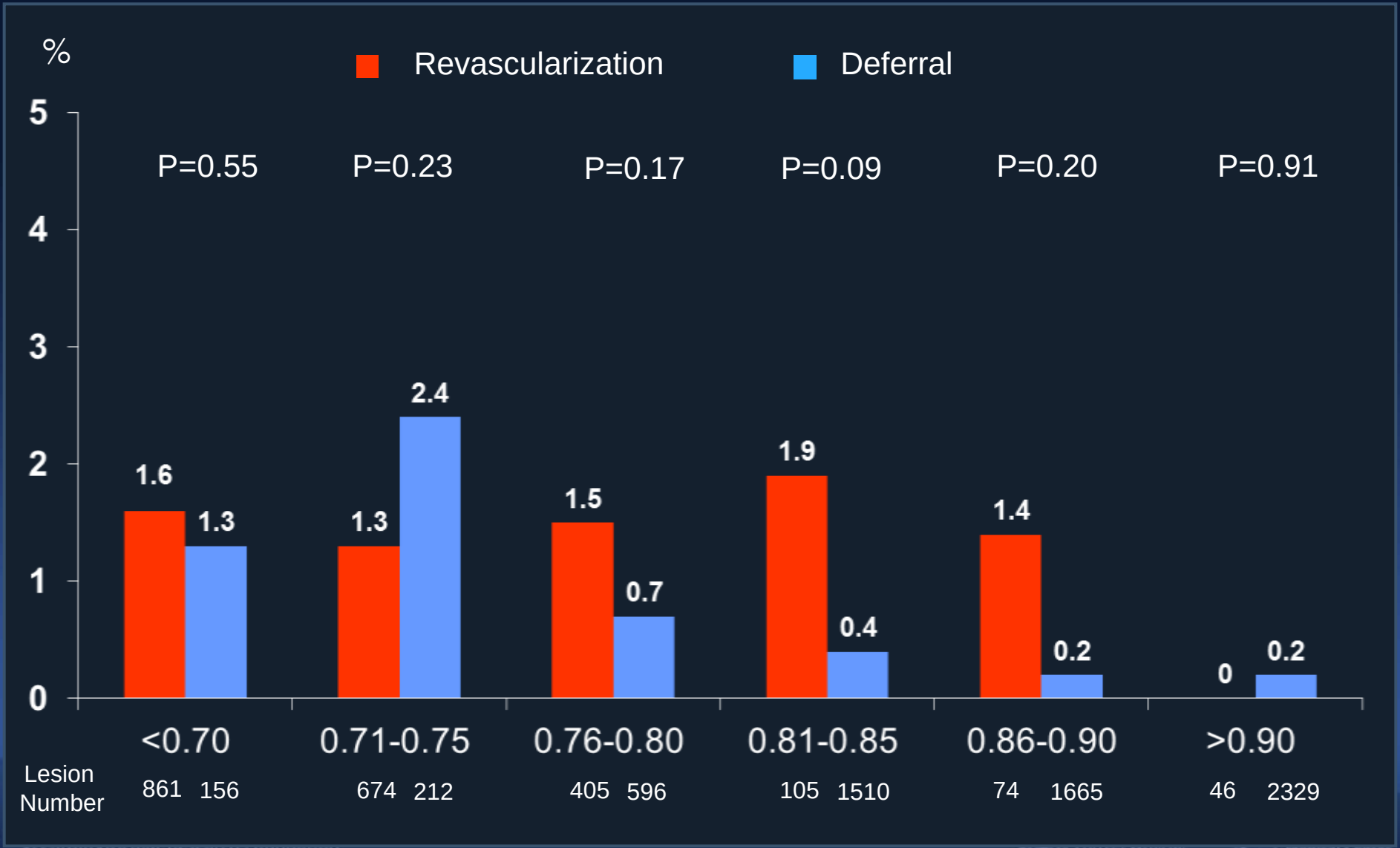
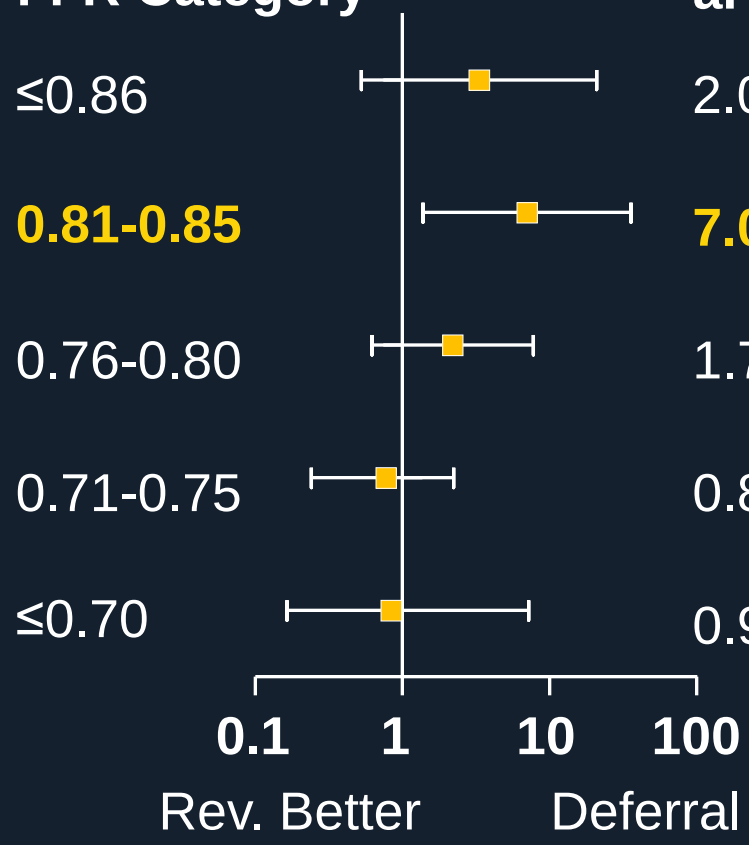
Cardiac Death or MI



% from crude proportion

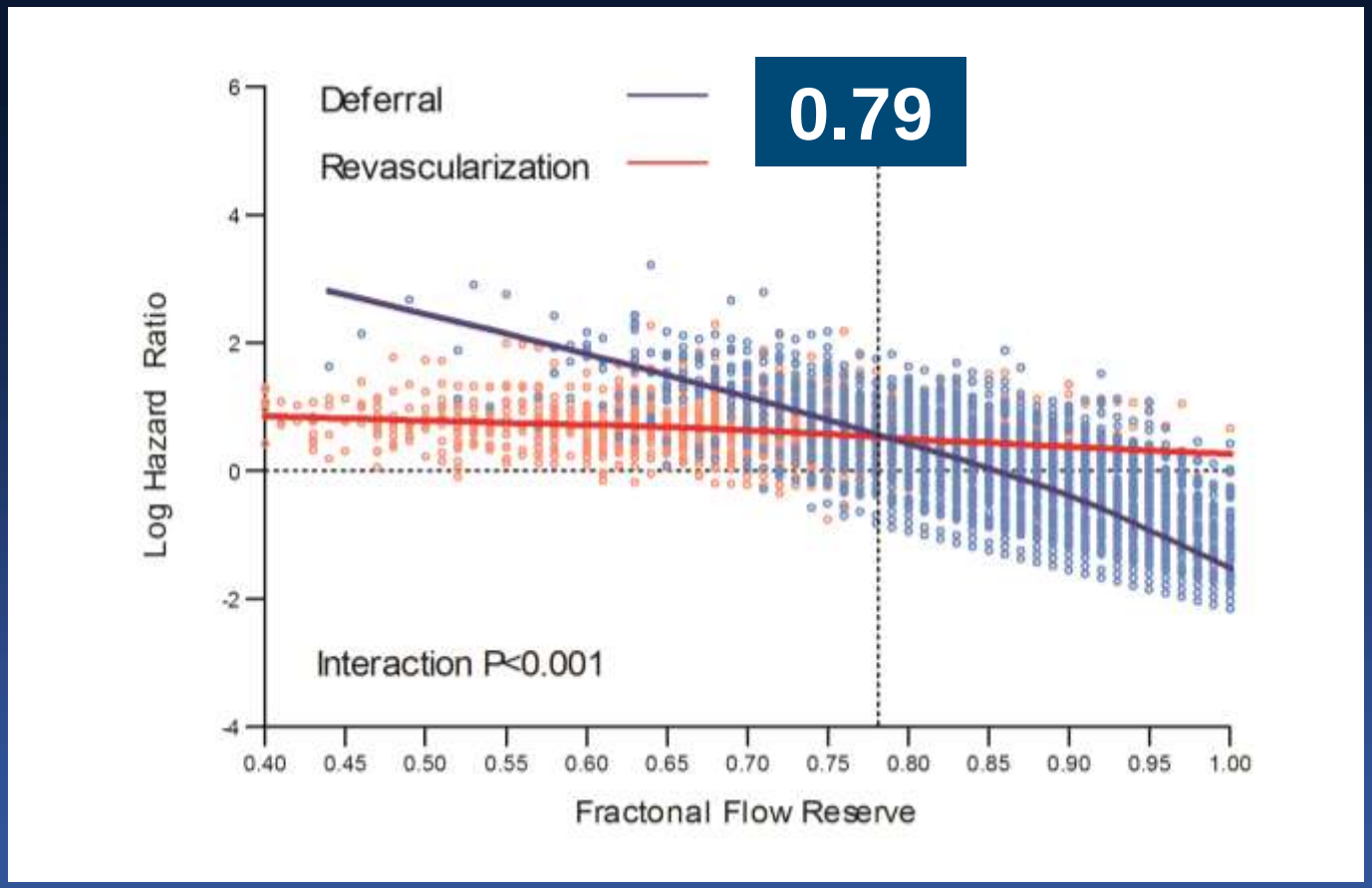
Adjust HR: Cardiac Death and MI



FFR Category	aHR (95% CI)	P value
≤0.86	2.03 (0.52-7.84)	0.31
0.81-0.85	**7.04 (1.60-30.9)**	**0.01**
0.76-0.80	1.72 (0.42-7.06)	0.45
0.71-0.75	0.87 (0.29-2.58)	0.80
≤0.70	0.92 (0.20-4.21)	0.92

Outcome Derived Revascularization Threshold of FFR

Major Adverse Cardiac Events



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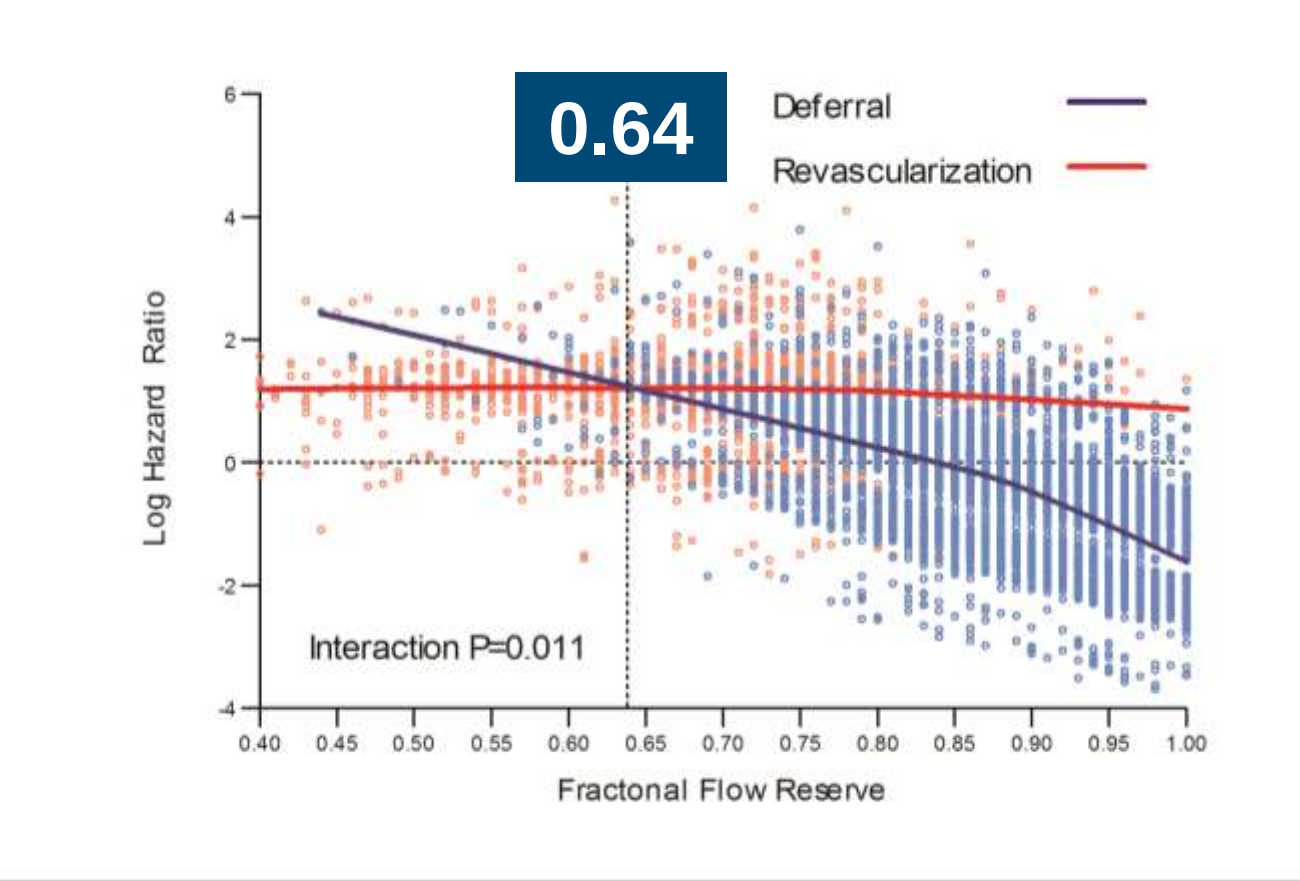
Outcome Derived Revascularization Threshold of FFR

Cardiac Death or Myocardial Infarction



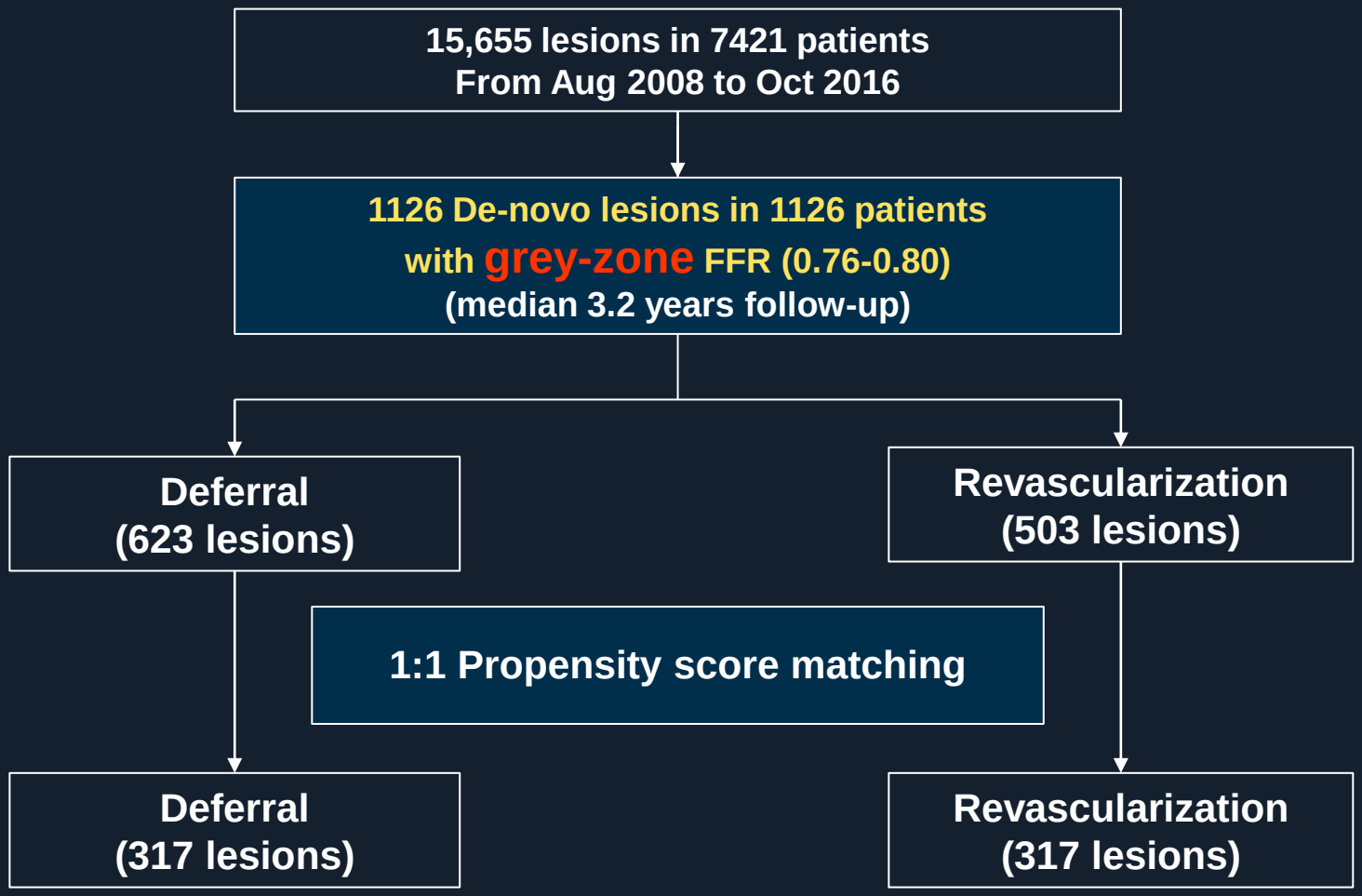
Best Cut-off Value of FFR

0 ⟷ 0.75 ⟷ 0.80 ⟷ 1.0

Significant	grey zone	Non-significant

Author	Number	Stress Test	BCV	Accuracy
Pijls et al.	60	X-ECG	0.74	97
DeBruyne et al.	60	X-ECG/SPECT	0.72	85
Pijls et al.	45	X-ECG/SPECT/pacing/DSE	0.75	93
Bartunek et al.	37	DSE	0.68	90
Abe et al.	46	SPECT	0.75	91
Chamuleau et al.	127	SPECT	0.74	77
Caymaz et al.	40	SPECT	0.76	95
Jimenez-Navarro et al.	21	DSE	0.75	90
Usui et al.	167	SPECT	0.75	79
Yanagisawa et al.	167	SPECT	0.75	76
Meuwissen et al.	151	SPECT	0.74	85
DeBruyne et al.	57	MIBI-SPECT post-MI	0.78	85
Samady et al.	48	MIBI-SPECT post-MI	0.78	85
Ahn JM et al.(2011)	151	SPECT	0.77	89

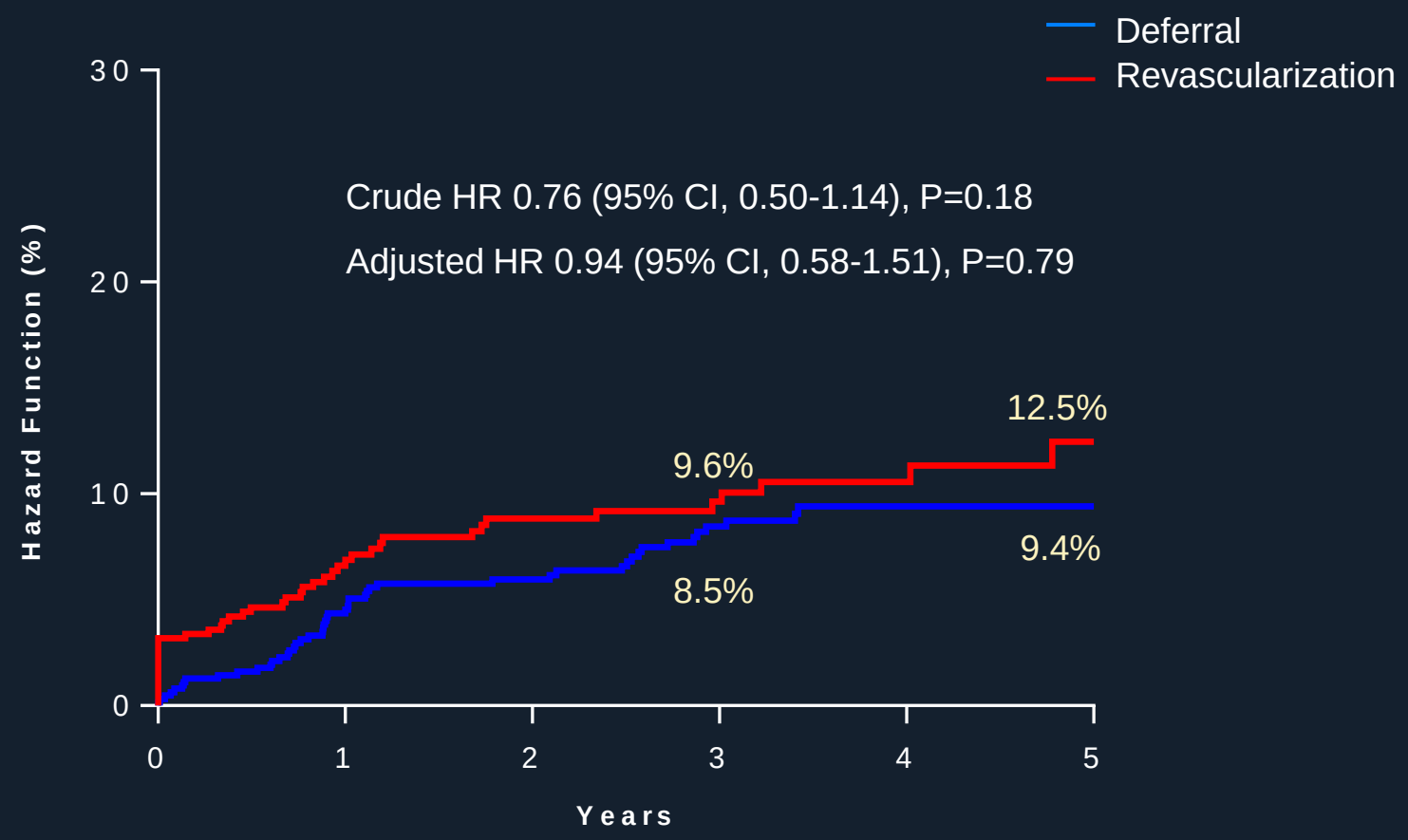
Study Flow


15,655 lesions in 7421 patients
From Aug 2008 to Oct 2016
1126 De-novo lesions in 1126 patients
with grey-zone FFR (0.76-0.80)
(median 3.2 years follow-up)
Deferral
(623 lesions)
Revascularization
(503 lesions)
1:1 Propensity score matching
Deferral
(317 lesions)
Revascularization
(317 lesions)

Overall Population

Primary End Point

(Death, MI, Target Vessel Revascularization)

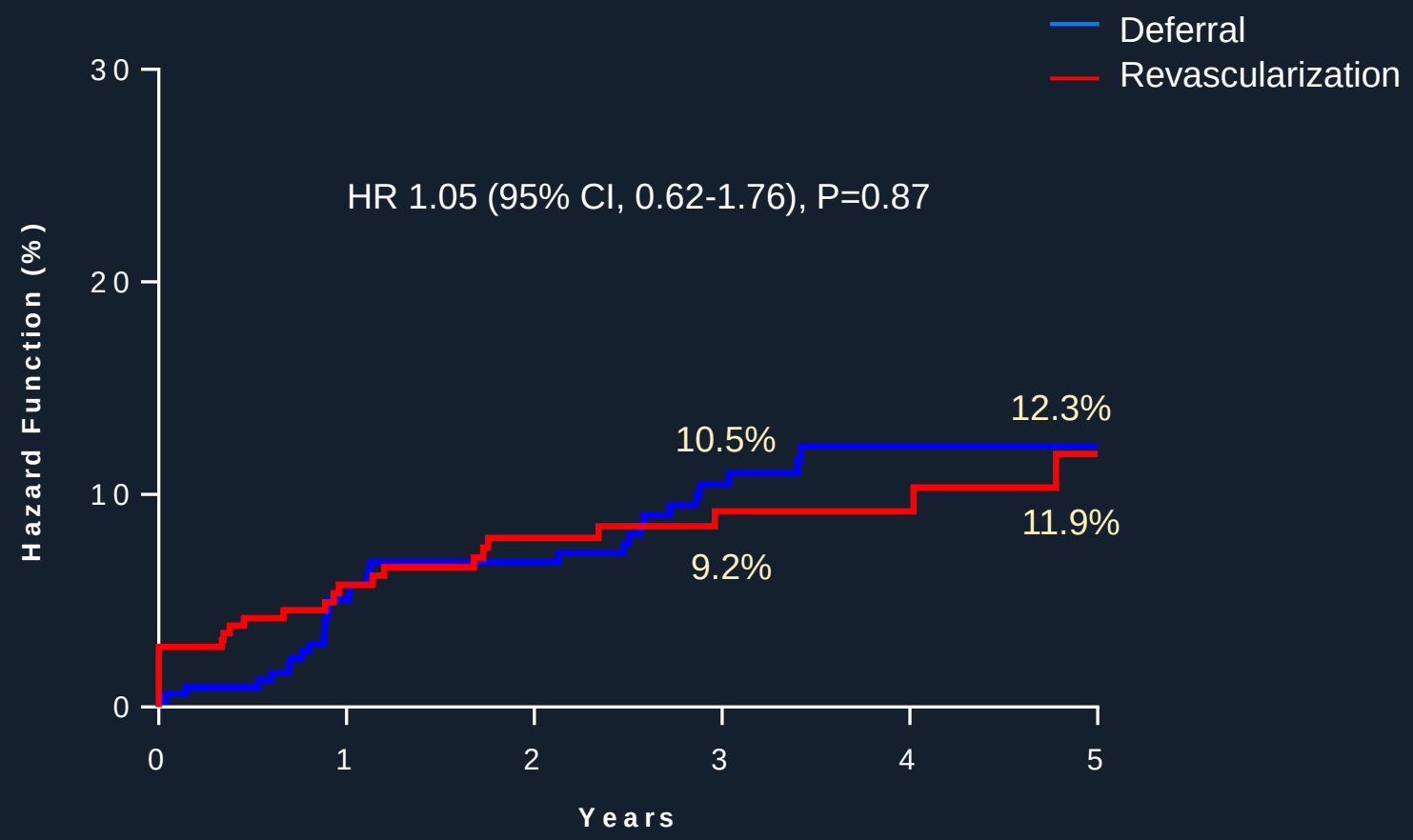


No. at Risk						
Deferral	623	544	468	346	158	75
Revasc	503	357	280	205	116	75

Matched Population

Primary End Point

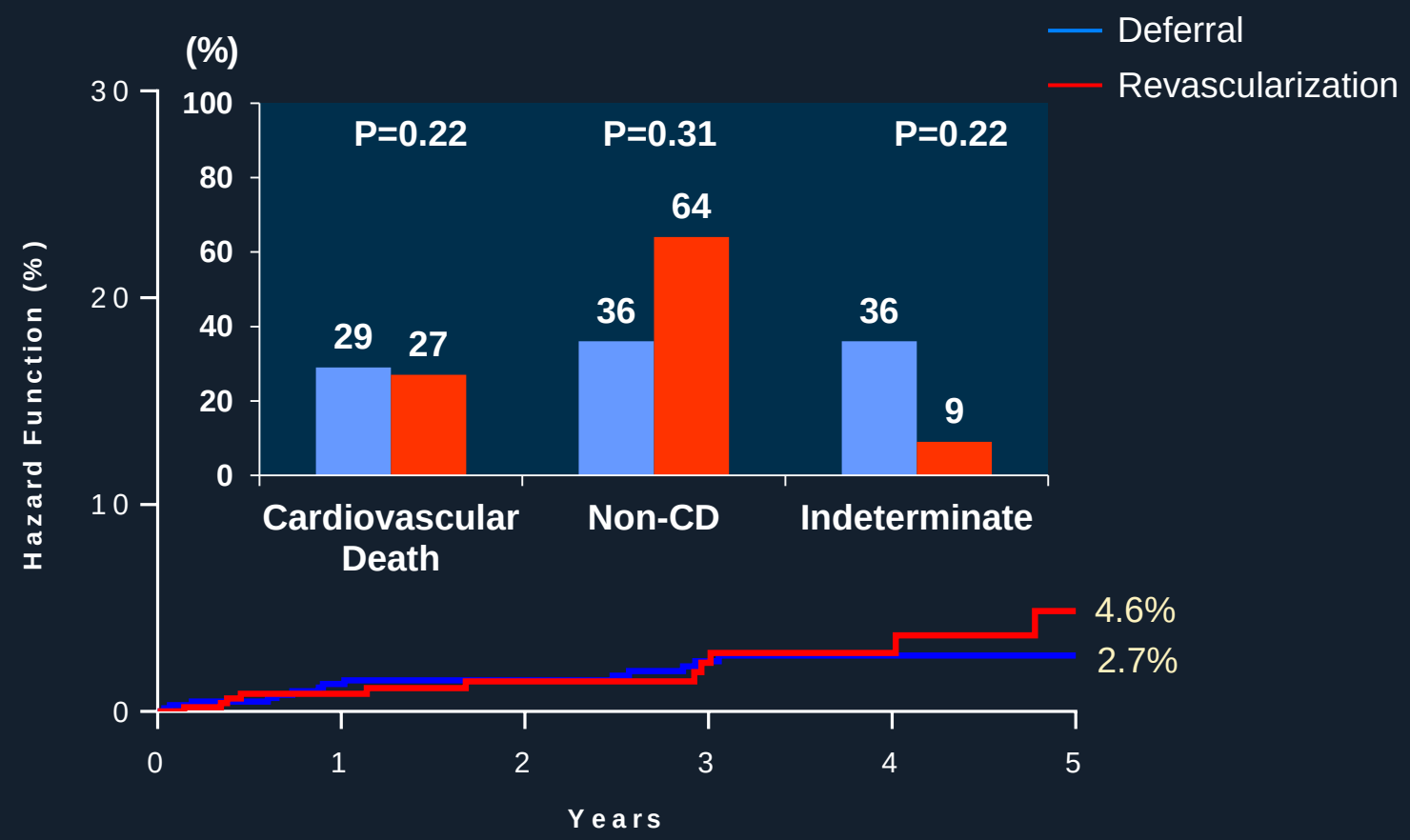
(Death, MI, Target Vessel Revascularization)



No. at Risk						
Deferral	317	269	230	173	79	45
Revasc	317	231	182	129	82	52

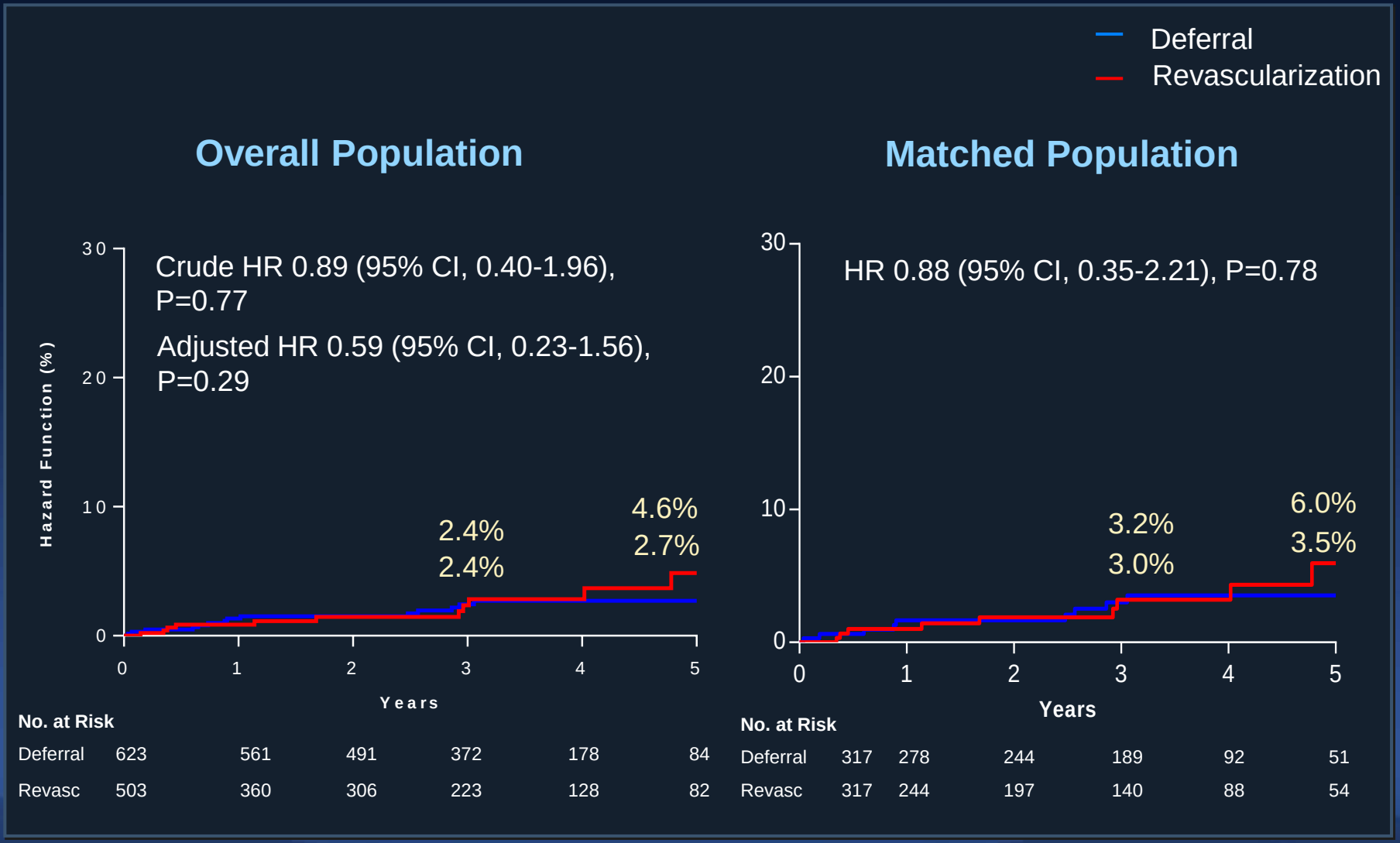
Unpublished Data From IRIS-FFR Registry

Death from any cause



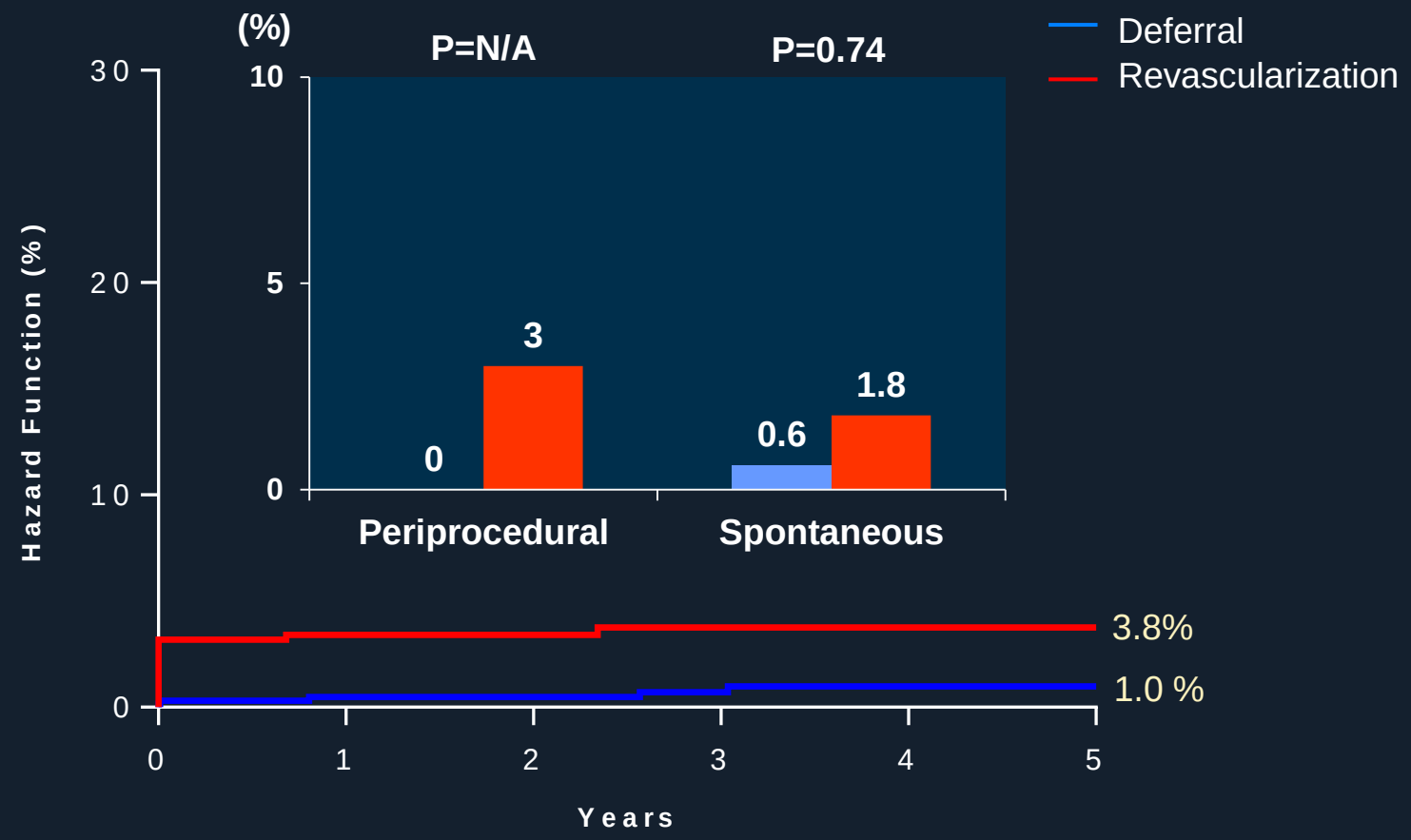
No. at Risk						
Deferral	623	561	491	372	178	84
Revasc	503	360	306	223	128	82

Death from any cause



Unpublished Data From IRIS-FFR Registry

Myocardial Infarction

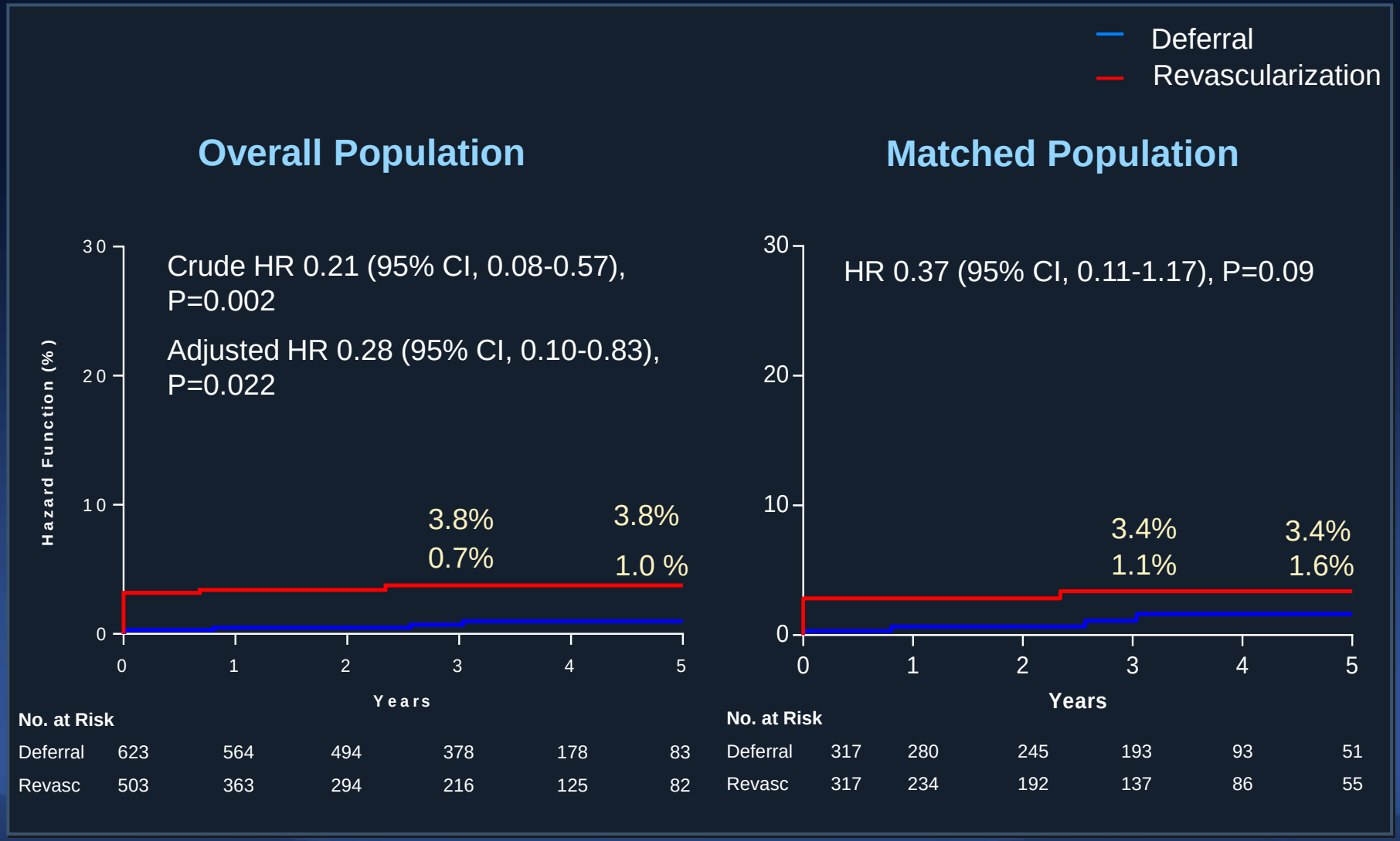


No. at Risk

Deferral	623	564	494	378	178	83
Revasc	503	363	294	216	125	82

Unpublished Data From IRIS-FFR Registry

Myocardial Infarction

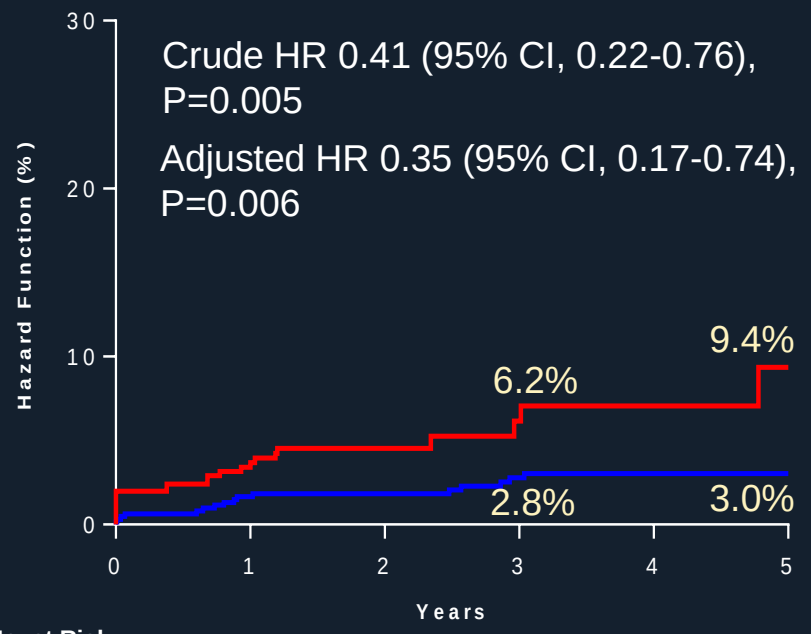


Unpublished Data From IRIS-FFR Registry

Death and Myocardial Infarction

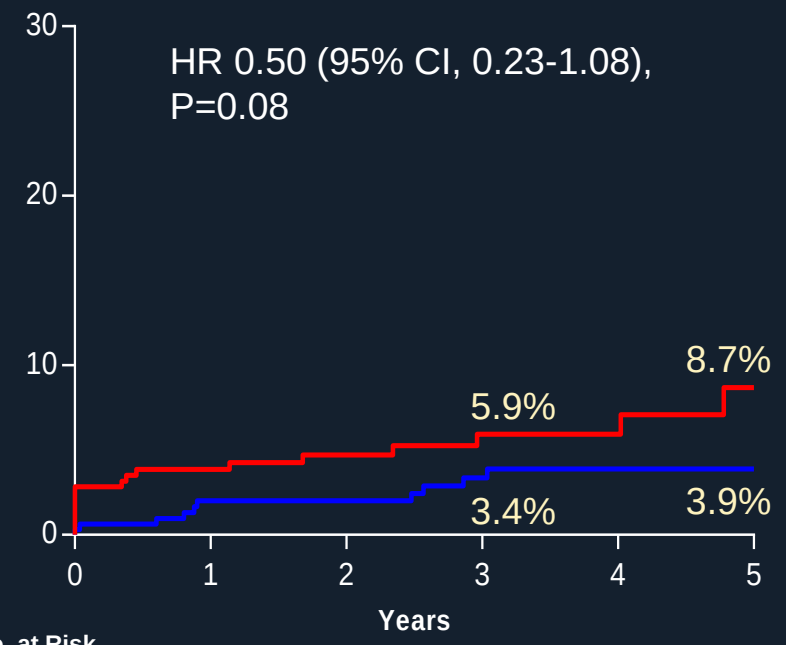
Deferral
Revascularization

Overall Population



No. at Risk						
Deferral	623	559	489	371	176	84
Revasc	503	367	294	215	123	79

Matched Population

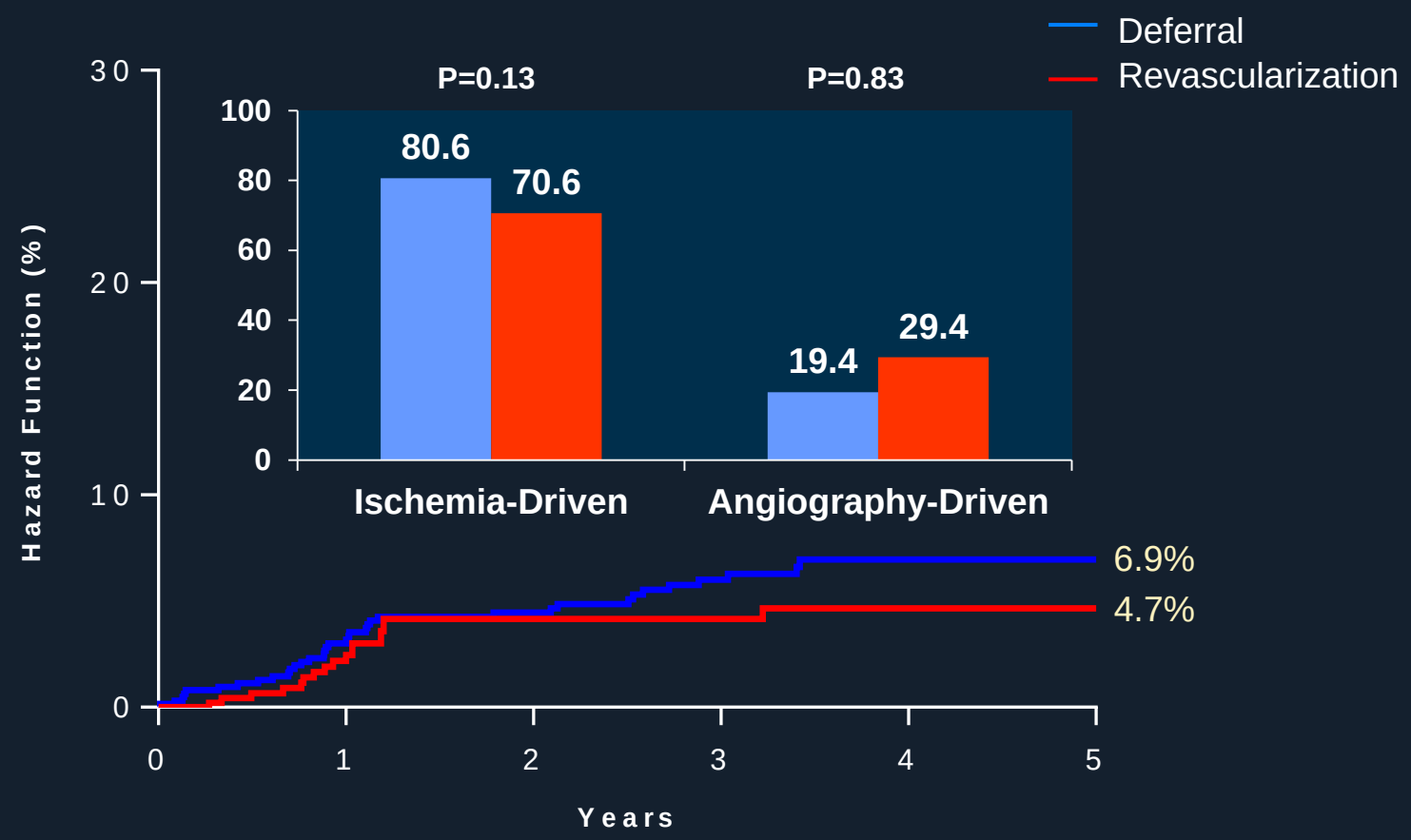


No. at Risk						
Deferral	317	277	243	189	92	51
Revasc	317	236	190	135	85	53

Unpublished Data From IRIS-FFR Registry

Overall Population

Target Vessel Revascularization



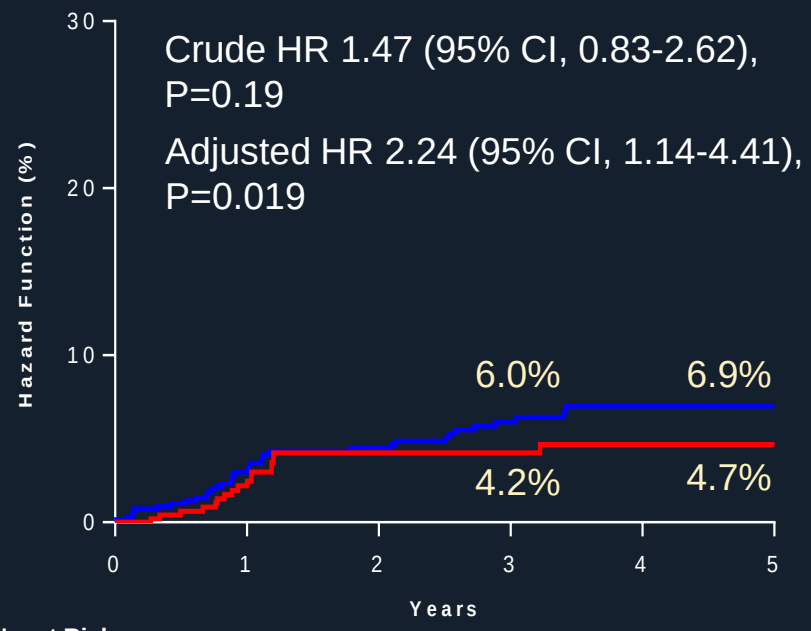
No. at Risk						
Deferral	623	551	475	356	163	76
Revasc	503	374	297	218	125	81

Unpublished Data From IRIS-FFR Registry

Target Vessel Revascularization

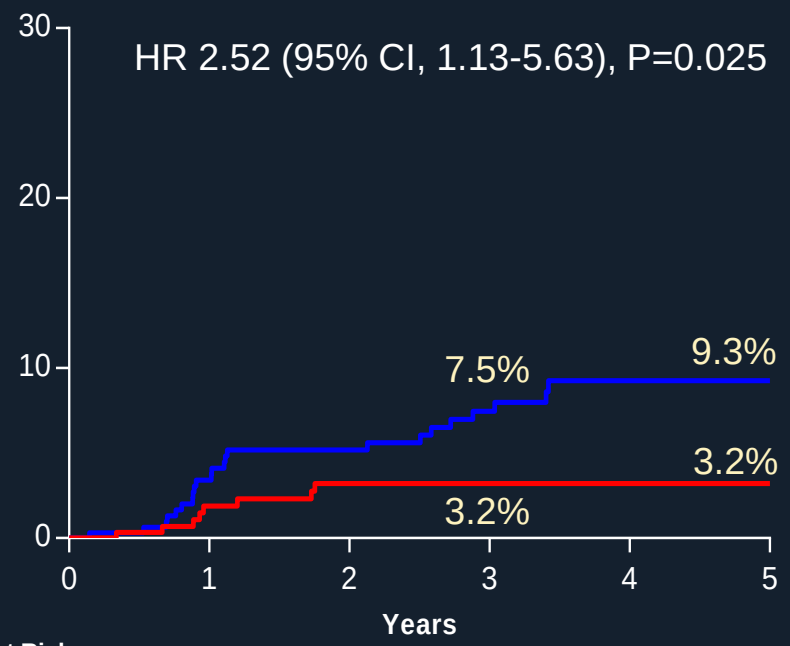
Deferral
Revascularization

Overall Population



No. at Risk						
Deferral	623	551	475	356	163	76
Revasc	503	374	297	218	125	81

Matched Population

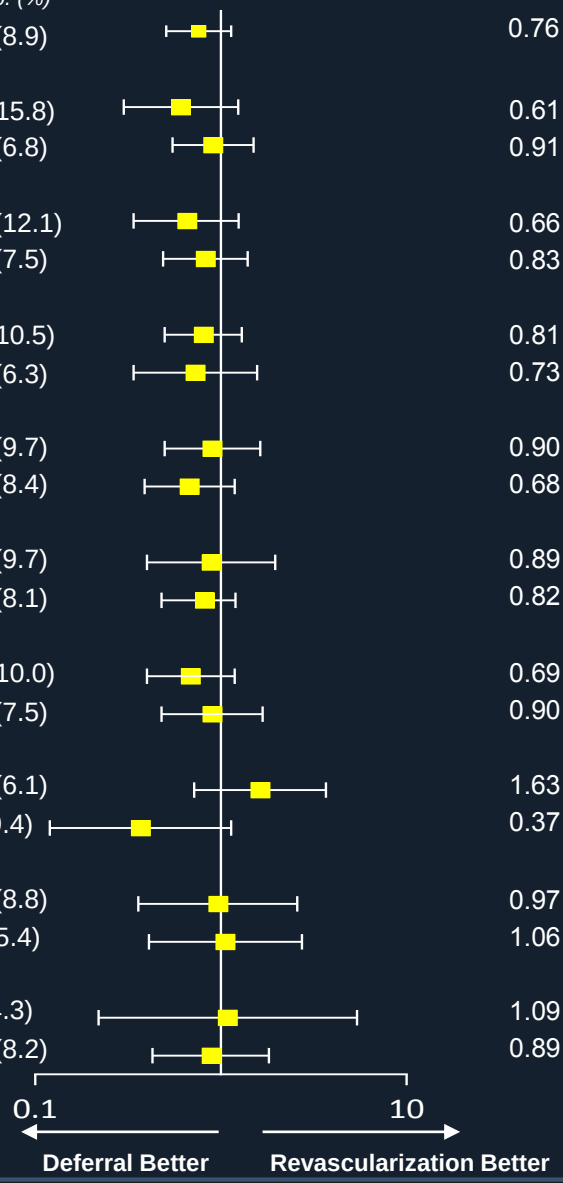


No. at Risk						
Deferral	317	273	233	179	82	45
Revasc	317	242	194	139	88	55

Unpublished Data From IRIS-FFR Registry

Subgroup Analysis

Subgroup	Deferral	Revascularization	Hazard ratio (95% CI)	p value for interaction
	no. of patients with event/total no. (%)			
Overall	49/623 (7.9)	45/503 (8.9)	0.76 (0.51−1.14)	
Acute coronary syndrome				0.67
Yes	13/115 (11.3)	19/120 (15.8)	0.61 (0.30−1.24)	
No	36/508 (7.1)	26/383 (6.8)	0.91 (0.55−1.50)	
Diabetes				0.56
Yes	18/203 (8.9)	191/157 (12.1)	0.66 (0.34−1.25)	
No	31/420 (7.4)	26/346 (7.5)	0.83 (0.49−1.40)	
Multivessel coronary artery disease				0.90
Yes	34/344 (9.9)	33/314 (10.5)	0.81 (0.50−1.30)	
No	15/279 (5.4)	12/189 (6.3)	0.73 (0.34−1.57)	
Left main or proximal LAD disease				0.47
Yes	23/224 (10.3)	21/216 (9.7)	0.90 (0.50−1.63)	
No	26/399 (6.5)	24/287 (8.4)	0.68 (0.39−1.19)	
Diameter stenosis				0.89
≥ 70%	8/78 (10.3)	26/267 (9.7)	0.89 (0.40−1.97)	
< 70%	41/545 (7.5)	19/236 (8.1)	0.82 (0.48−1.42)	
Lesion length				0.47
≥ 20mm	23/288 (8.0)	29/291 (10.0)	0.69 (0.40−1.19)	
< 20mm	26/335 (7.8)	16/212 (7.5)	0.90 (0.48−1.68)	
Minimal lumen area on IVUS				**0.036**
≤ 2.5 mm^2	12/107 (11.2)	11/180 (6.1)	1.63 (0.72−3.69)	
> 2.5 mm^2	5/115 (4.3)	8/85 (9.4)	0.37 (0.12−1.14)	
Plaque burden on IVUS				0.95
≥ 80%	6/63 (9.5)	12/136 (8.8)	0.97 (0.36−2.58)	
< 80%	11/159 (6.9)	7/129 (5.4)	1.06 (0.41−2.74)	
Rupture or thrombus on IVUS				0.79
Yes	3/57 (5.3)	3/69 (4.3)	1.09 (0.22−5.41)	
No	14/165 (8.5)	16/196 (8.2)	0.89 (0.43−1.82)	



Conclusion

- Although the risk of MACE in the deferred lesion increased significantly while FFR decreased, the risk of MACE was not significantly different in the range of FFR ≥0.76 (including “grey zone”) between deferred and revascularized lesions

- Only in the lesions with FFR of ≤0.75, the significant benefit of revascularization over deferral was observed in terms of the risk of MACE. Subsequently, the outcome-derived revascularization threshold of FFR was located at the FFR of 0.79.

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Thank You !!

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