How To Manage Grey Zone FFR?

Data from IRIS FFR Registry

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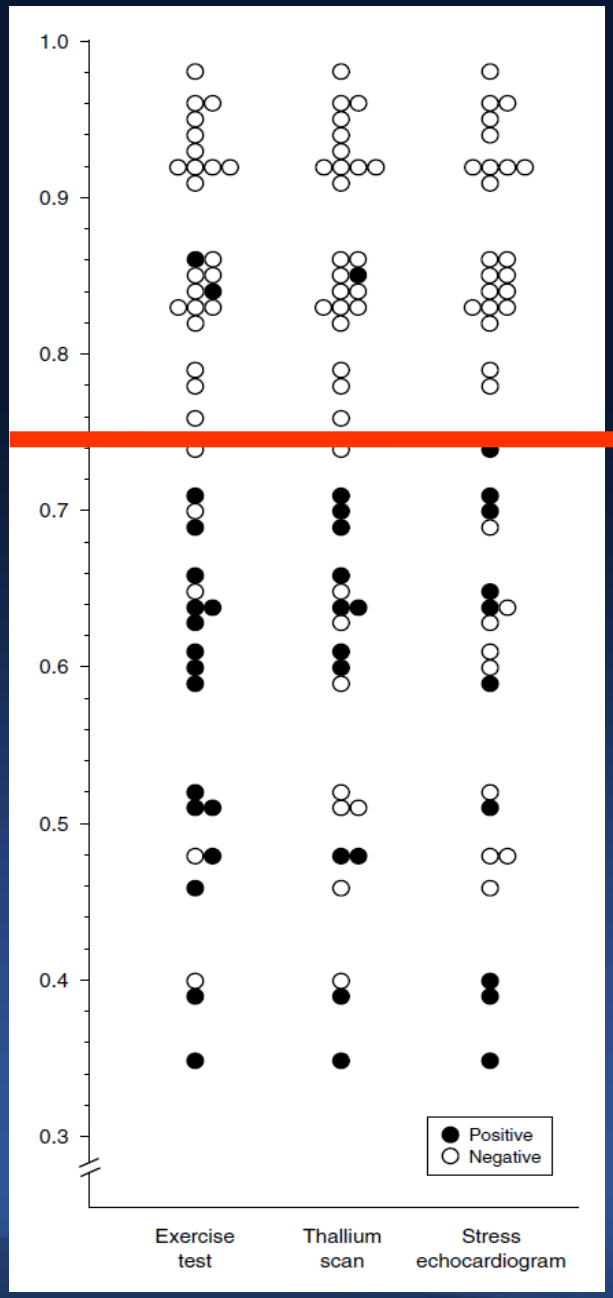
First Validation

with Non-invasive Stress Test Results

(n=45 patients, intravenous adenosine infusion)



FFR <0.75

Sensitivity 88%

Specificity 100%

Positive PV 100%

Negative PV 88%

Accuracy 93%

Pijls NHJ, NEJM 1996;334:1703-8

Cut-off Value of FFR

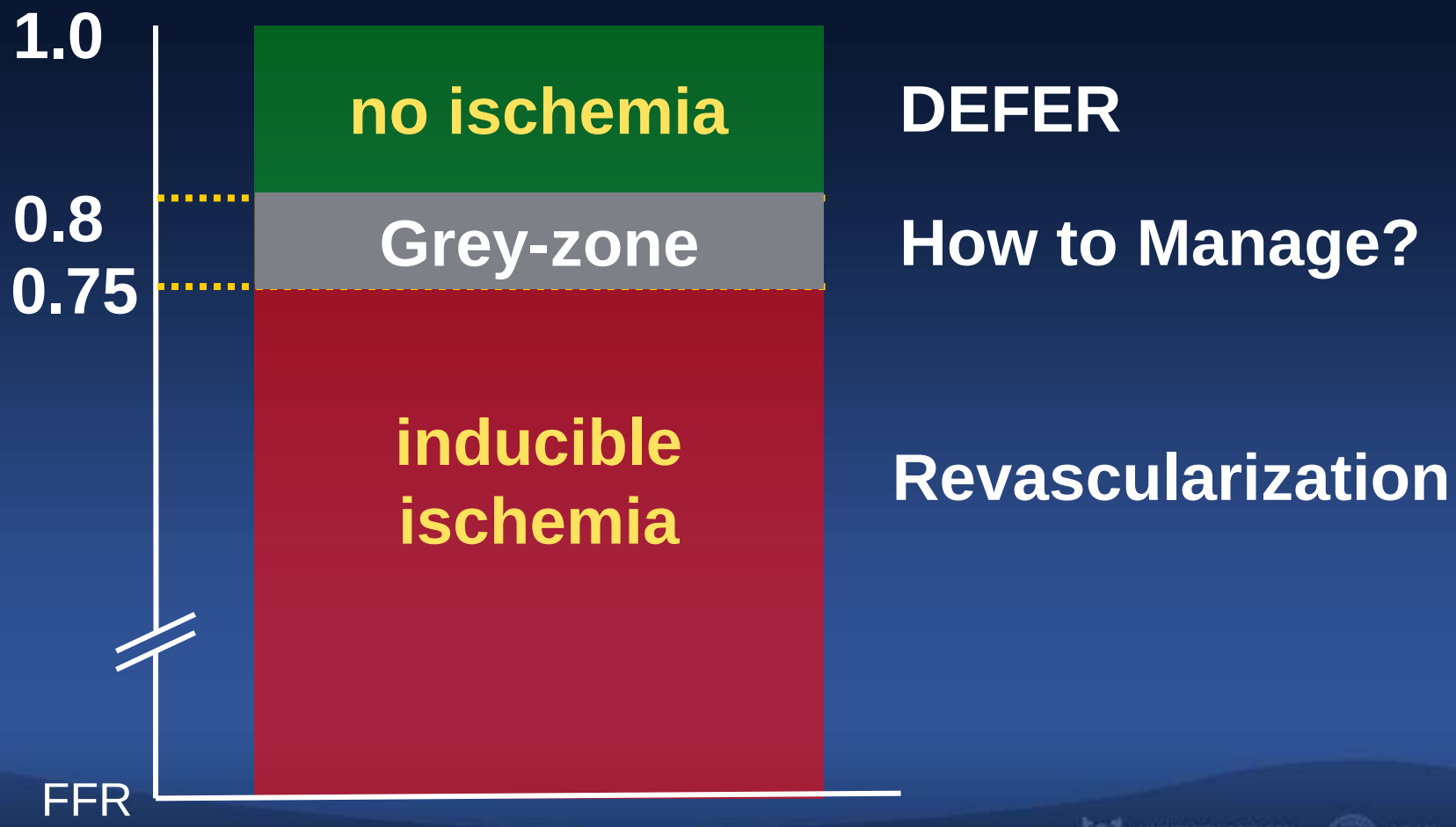
Year	Study
1996	Validation of 0.75 Cut-off by Comparing to 3 Noninvasive tests[1]
2001	DEFER study[2] FFR>0.75, Should Not be Treated
2009	FAME study[3] FFR>0.80, Defer is Safe and Good in Multi-vessel Disease
2012	FAME II study[4] FFR<0.80, Should be Treated

1. Pijls N, et al. NEJM 1996;334:26:1703-8
2. Pijls N, et al. JACC 2007;49 ;21:2105-11
3. Tonino PA, De Bruyne B, Pijls NH, et al. NEJM 2009;360(3):213-224
4. De Bruyne B, et al. NEJM 2012;367:991-1001

Which One Is Optimal Threshold ?

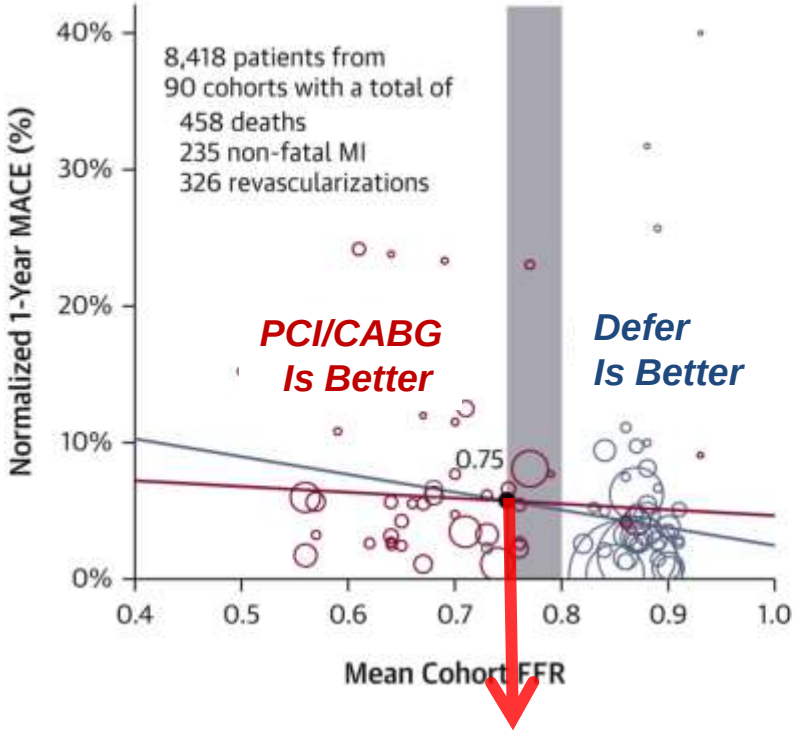
0.75 or 0.80

How to Manage Grey Zone ?
FFR (0.76~0.80)



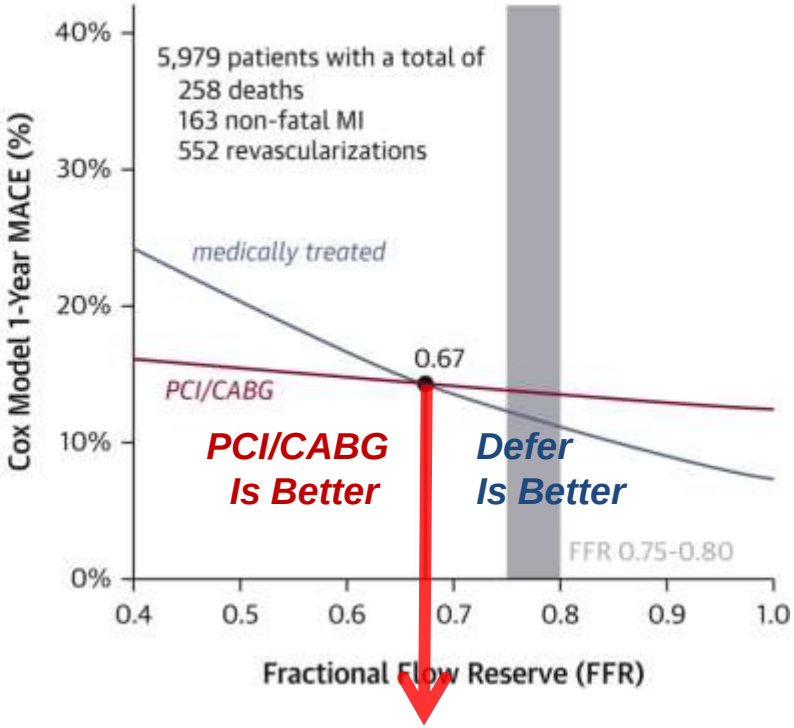
MACE at 1 Year (Meta-Analysis, 9,173 lesions)

Study-level analysis



0.75

Patient-level analysis.

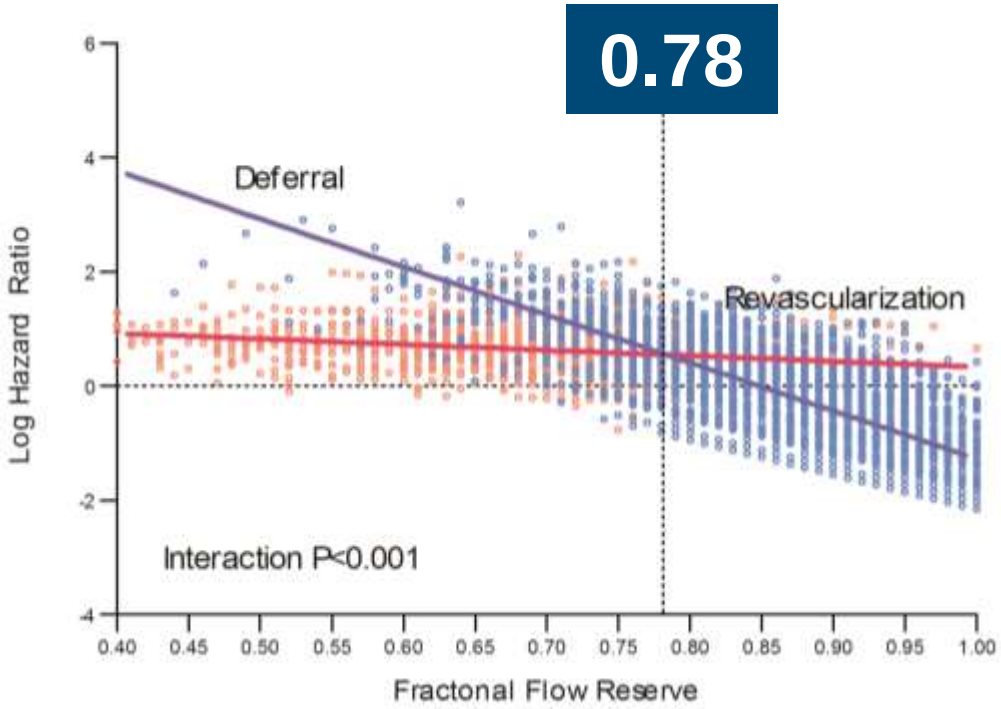


0.67

Johnson NP et al, J Am Coll Cardiol. 2014;64(16):1641-1654.

Outcome Derived Revascularization Threshold of FFR (The IRIS-FFR registry N=5846 patients)

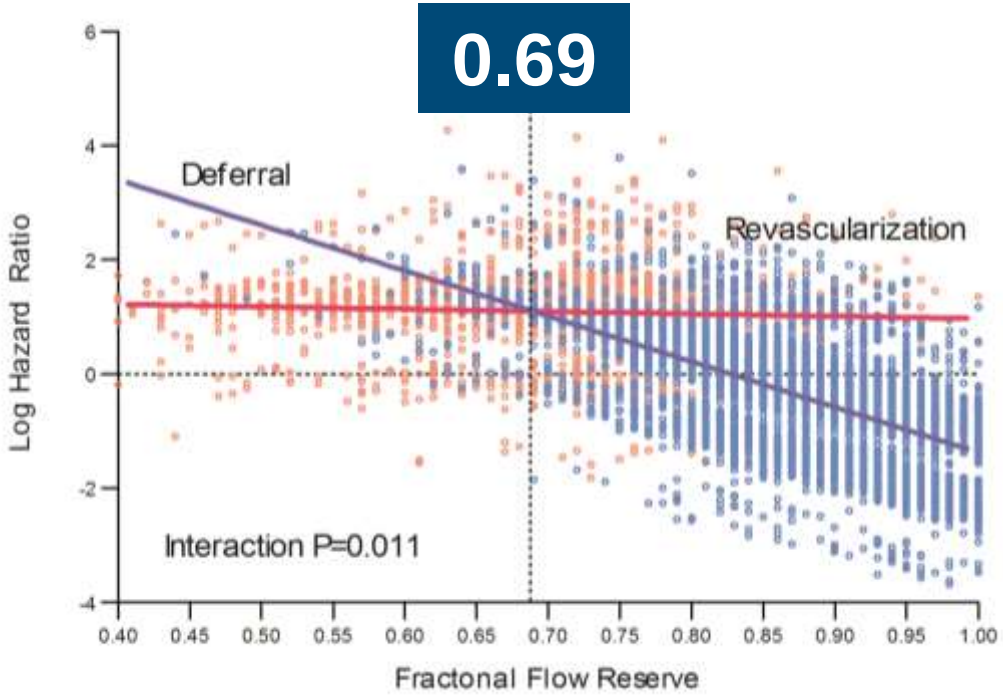
MACE



Ahn JM, Park SJ et al, Circulation. 2017 Mar 29.

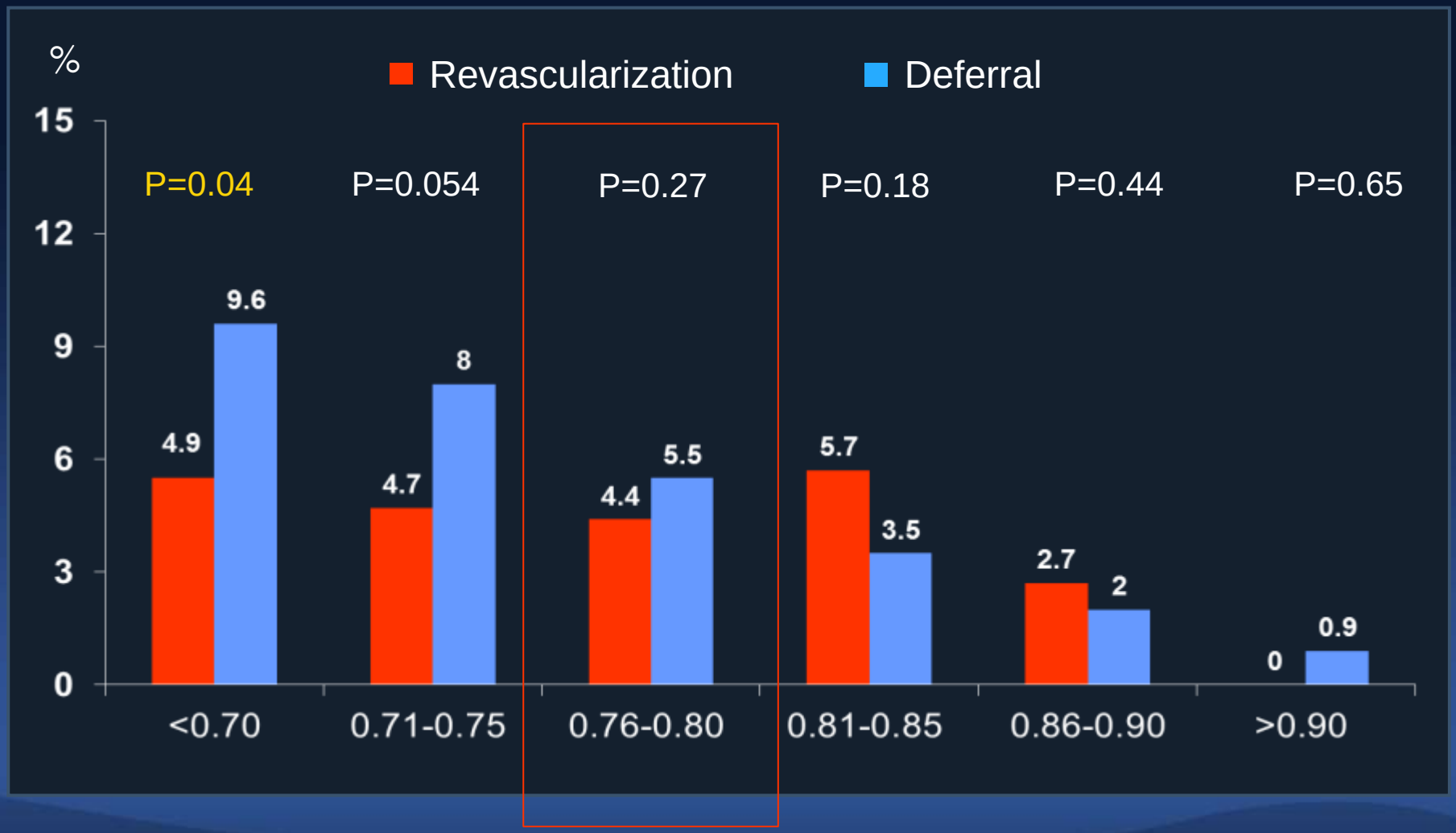
Outcome Derived Revascularization Threshold of FFR (The IRIS-FFR registry N=5846 patients)

Cardiac Death or MI



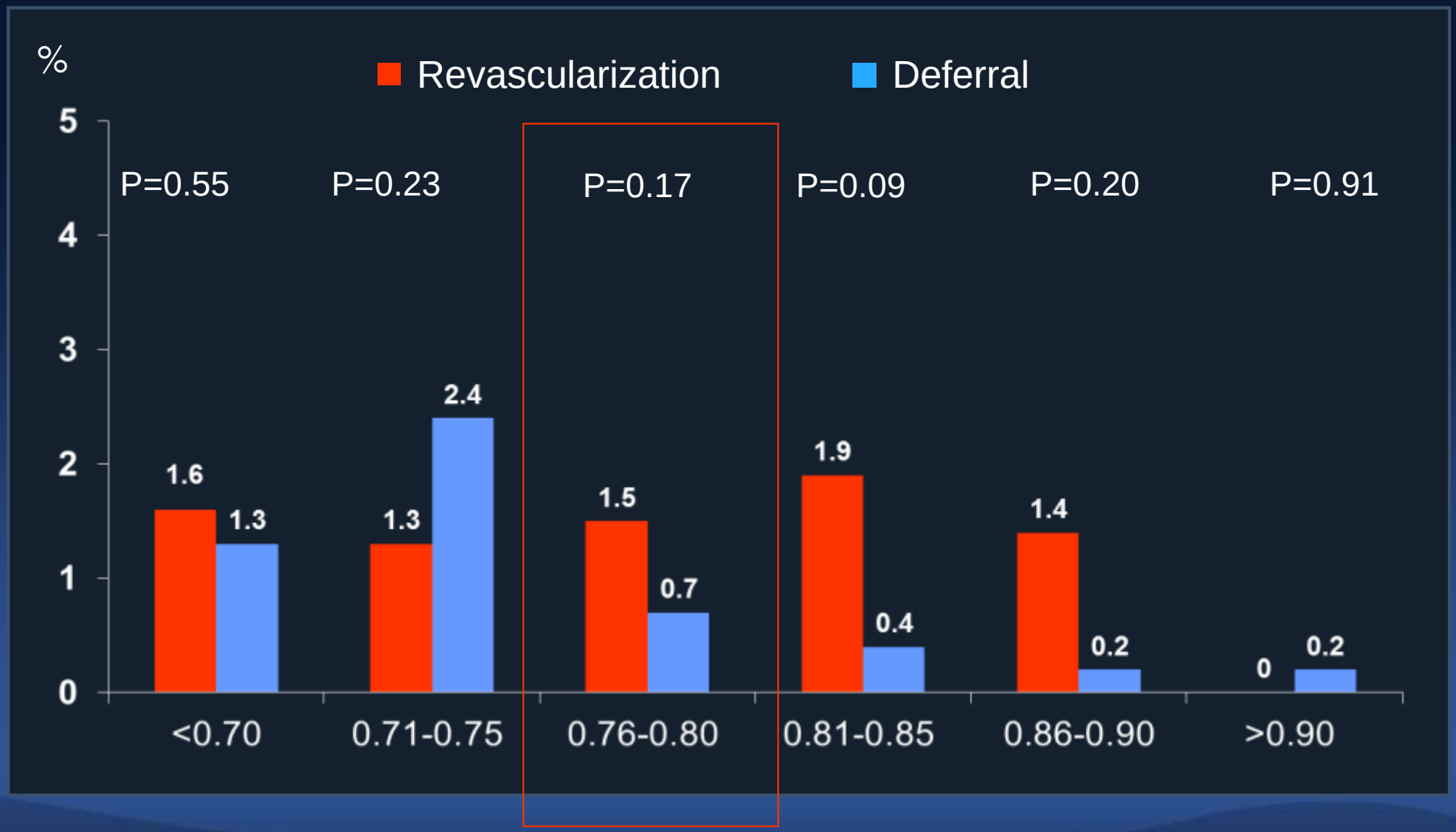
Ahn JM, Park SJ et al, Circulation. 2017 Mar 29.

Major Adverse Cardiac Events



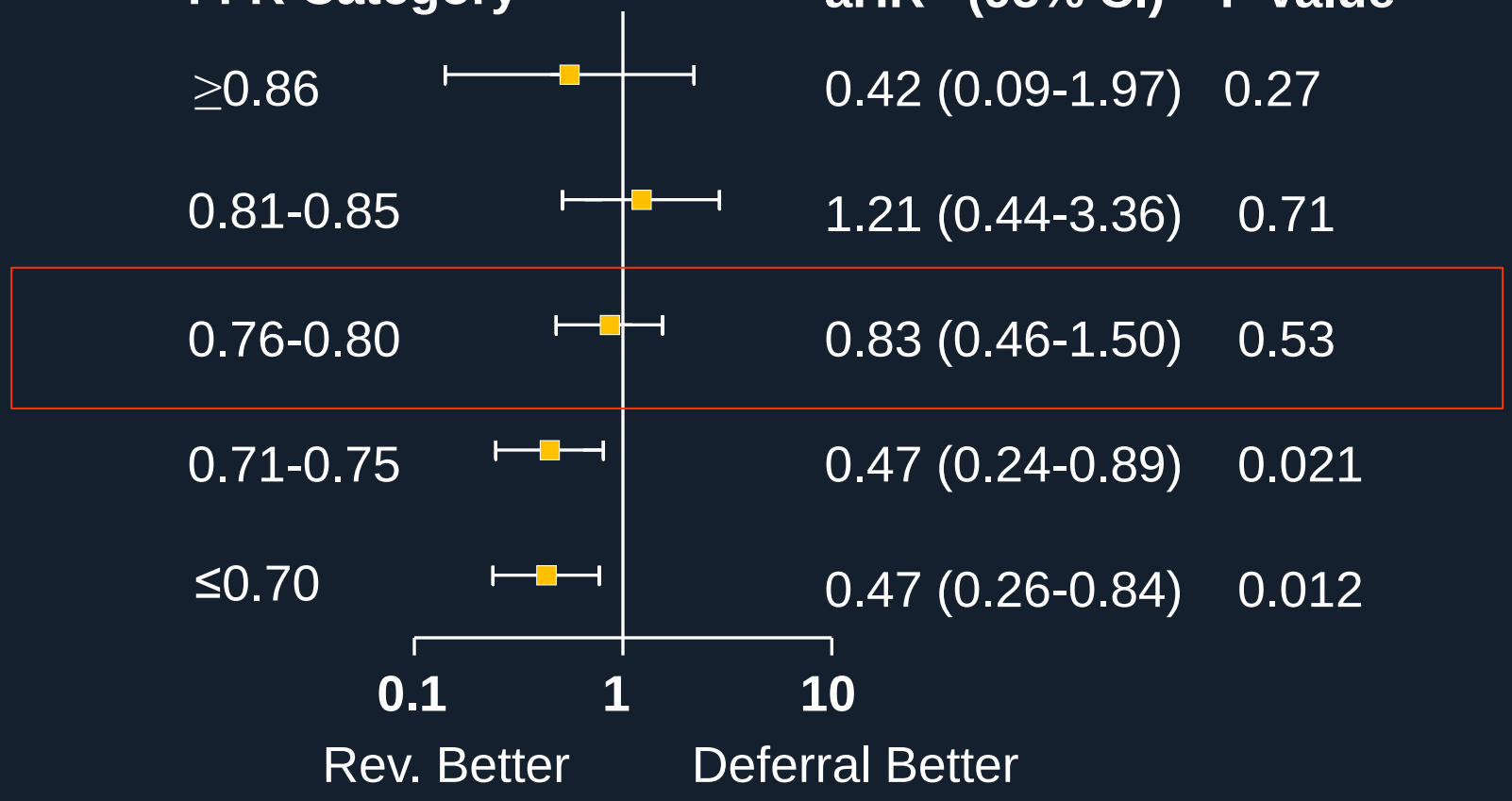
Ahn JM, Park SJ et al, Circulation. 2017 Mar 29.

Cardiac Death or MI

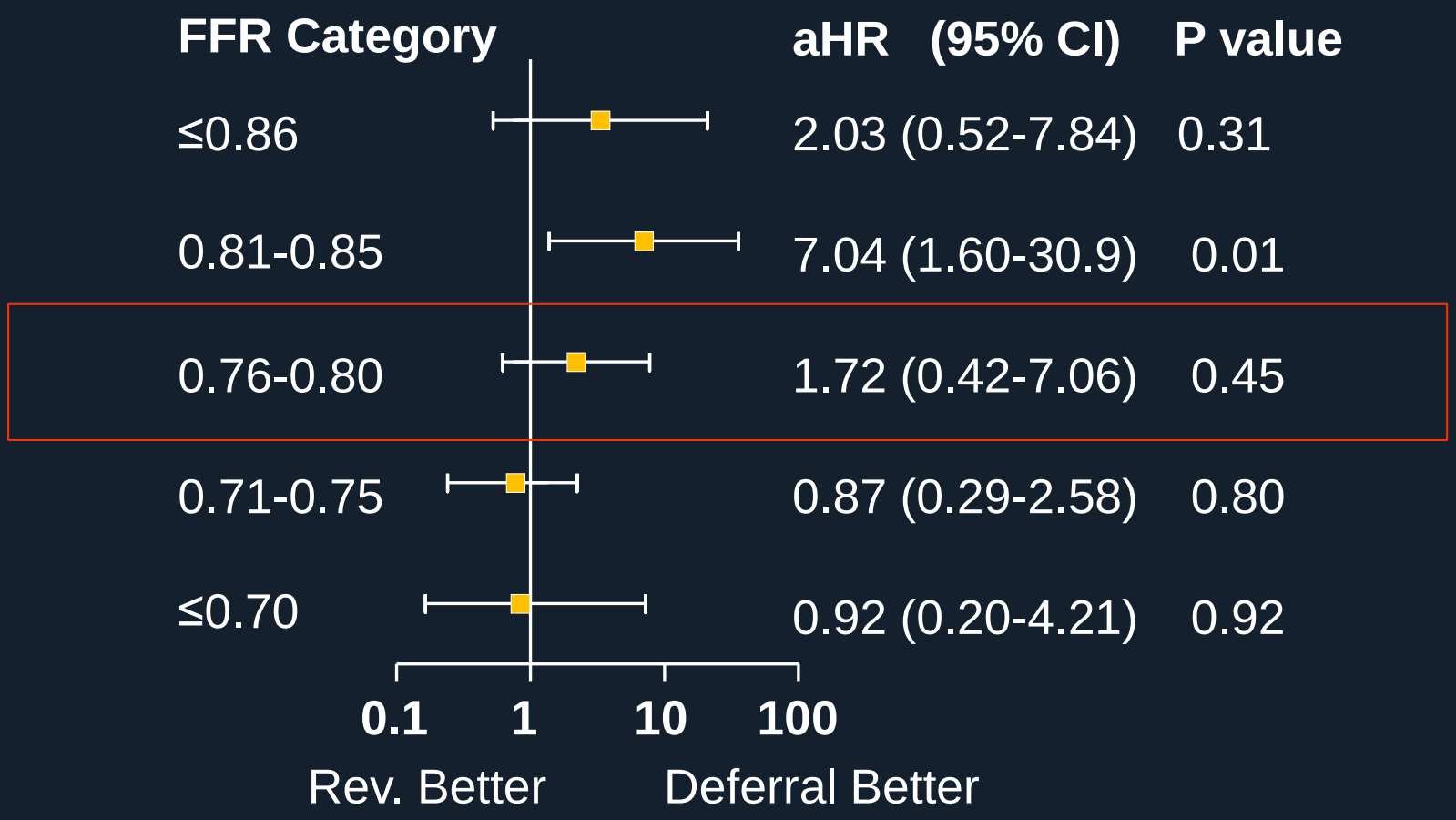


Ahn JM, Park SJ et al, Circulation. 2017 Mar 29.

Adjust Hazard Ratio: MACE



Adjust HR: Cardiac Death and MI



Study Objective

To Compare the Prognosis of Deferred and Revascularized stenoses with Grey-zone FFR (0.76-0.80) in the Prospective IRIS-FFR Registry

IRIS-FFR Registry

Design

- DESIGN: a multicenter, prospective registry
- OBJECTIVE: To evaluate the natural history of coronary stenosis assessed by FFR
- PRINCIPAL INVESTIGATOR
  Seung-Jung Park, MD, PhD,
  Asan Medical Center, Seoul, Korea
- PARTICIPATING CENTERS: 30 Centers in Korea

Major Inclusion Criteria

- Patients with ≥1 FFR evaluated Lesions
- De novo coronary stenosis with FFR of 0.76-0.80

Major Exclusion Criteria

- TIMI flow grade < 3
- Bypass graft
- Overt heart failure
- Technical unsuitability for FFR evaluation
- Patients with life expectancy < 2 years

Primary End Point

Major Adverse Cardiac Events (MACE),

a composite clinical outcomes of

- Death of all-cause
- Myocardial Infarction

  Periprocedural MI: CK-MB > 5 times UNL with Sx

  Spontaneous MI: any cardiac enzyme elevation
- Target Vessel Revascularization

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)

Baseline Characteristics of Overall Population

	Deferral (N=623)	Revascularization (N=503)	P value
Age (years)	64.3±9.8	64.7±9.7	0.50
Male sex	488 (78.3%)	365 (72.6%)	0.025
Body mass index (kg/m^2)	24.9±3.1	24.9±2.9	0.87
Acute coronary syndrome	168 (27.0%)	153 (30.4%)	0.13
Hypertension	408 (65.5%)	320 (63.6%)	0.51
Diabetes	203 (32.6%)	157 (31.2%)	0.62
Current smoking	148 (23.8%)	98 (19.5%)	0.09
Hyperlipidemia	361 (57.9%)	296 (58.8%)	0.76
Previous MI	43 (6.9%)	29 (5.8%)	0.44
Previous PCI	139 (22.3%)	84 (16.7%)	0.019
Peripheral vascular disease	18 (2.9%)	18 (3.6%)	0.51
Chronic renal failure	17 (2.7%)	8 (1.6%)	0.20
Multi-vessel disease	279 (44.8%)	189 (37.6%)	0.015
LVEF, %	61.8±7.3	62.0±7.6	0.70

Lesion Characteristics of Overall Population

	Deferral (N=623)	Revascularization (N=503)	P value
FFR	0.785±0.014	0.778±0.013	<0.001
Diseased vessel			0.004
Left main	18 (2.9%)	34 (6.8%)	
LAD	465 (74.6%)	347 (69.0%)	
RCA	68 (10.9%)	64 (12.7%)	
LCX	48 (7.7%)	48 (9.5%)	
Lesion location			0.02
Proximal	283 (45.4%)	271 (53.9%)	
Mid	240 (38.5%)	170 (33.8%)	
Distal	76 (12.2%)	52 (10.3%)	
Diameter stenosis			<0.001
≥ 70%	78 (12.5%)	267 (53.1%)	
50-69%	410 (65.8%)	230 (45.7%)	
30-49%	107 (17.2%)	4 (0.8%)	
AHA/ACC B2C lesion	406 (65.2%)	369 (73.4%)	0.003
Long lesion (>20mm)	288 (46.2%)	291 (57.9%)	<0.001

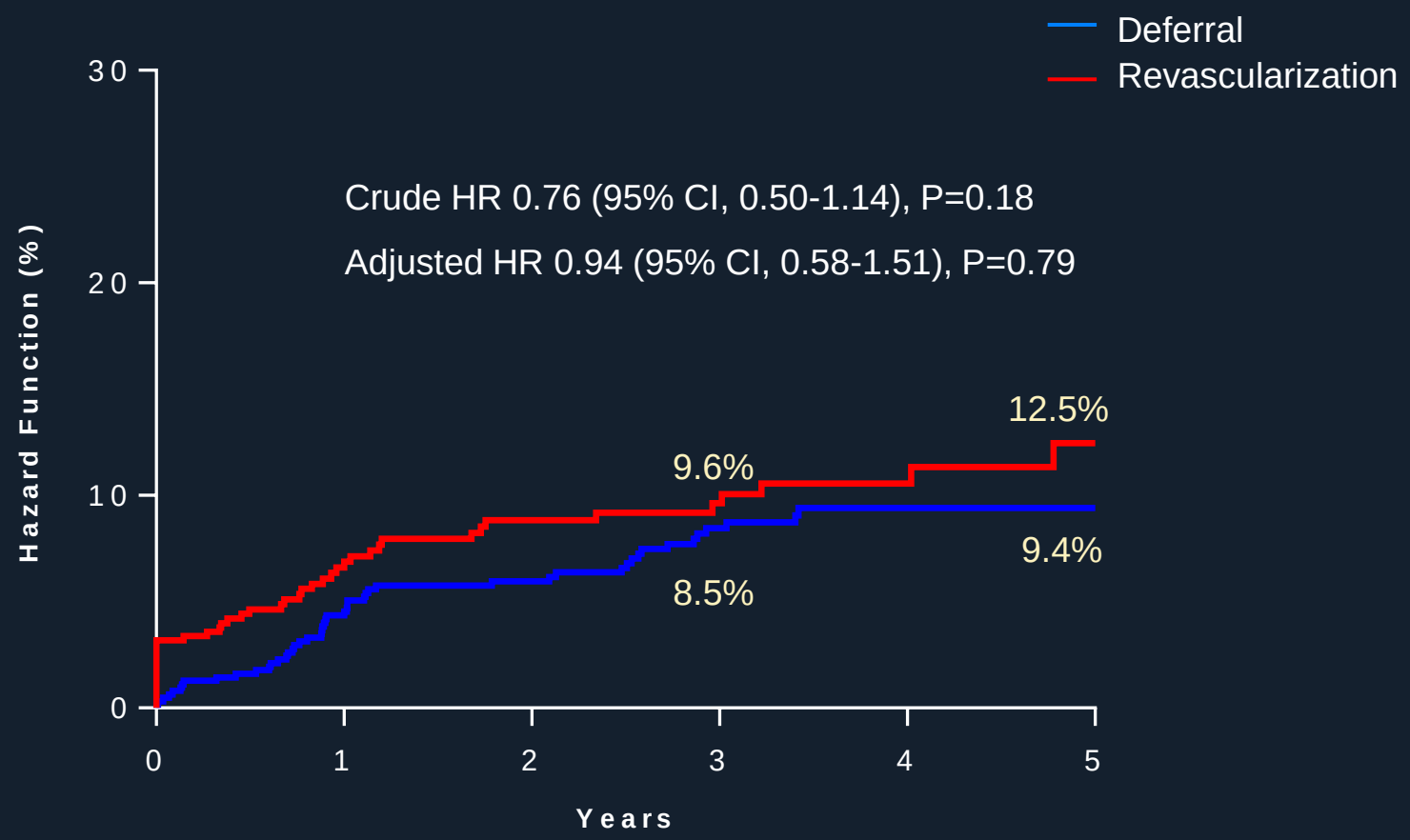
Baseline Characteristics of Propensity score-Matched Population

	Deferral (N=317)	Revascularization (N=317)	P value
Age (years)	65.2±10.2	64.7±10.0	0.56
Male sex	236 (74.4%)	238 (75.1%)	0.93
Body mass index (kg/m^2)	24.9±3.2	24.7±2.9	0.43
Acute coronary syndrome	61 (19.2%)	73 (23.0%)	0.13
Hypertension	206 (65.0%)	203 (64.0%)	0.87
Diabetes	108 (34.1%)	101 (31.9%)	0.61
Current smoking	72 (22.7%)	65 (20.5%)	0.56
Hyperlipidemia	178 (56.2%)	183 (57.7%)	0.75
Previous MI	22 (6.9%)	19 (6.0%)	0.75
Previous PCI	65 (20.5%)	60 (18.9%)	0.69
Peripheral vascular disease	12 (3.8%)	16 (5.0%)	0.56
Chronic renal failure	8 (2.5%)	7 (2.2%)	1.00
Multi-vessel disease	194 (61.2%)	192 (60.6%)	0.87
LVEF, %	62.3±6.1	61.6±7.7	0.23

Lesion Characteristics of Propensity score-Matched Population

	Deferral (N=317)	Revascularization (N=317)	P value
FFR	0.779±0.014	0.780±0.014	0.57
Diseased vessel			0.68
Left main	13 (4.1%)	21 (6.6%)	
LAD	229 (72.2%)	221 (69.7%)	
RCA	41 (12.9%)	39 (12.3%)	
LCX	26 (8.2%)	26 (8.2%)	
Lesion location			0.89
Proximal	166 (52.4%)	172 (54.3%)	
Mid	111 (35.0%)	103 (32.5%)	
Distal	32 (10.1%)	32 (10.1%)	
Diameter stenosis			0.56
≥ 70%	74 (23.3%)	84 (26.5%)	
50-69%	233 (73.5%)	227 (71.6%)	
30-49%	8 (2.5%)	4 (1.3%)	
AHA/ACC B2C lesion	228 (71.9%)	224 (70.7%)	0.79
Long lesion (>20mm)	165 (52.1%)	170 (53.6%)	0.75

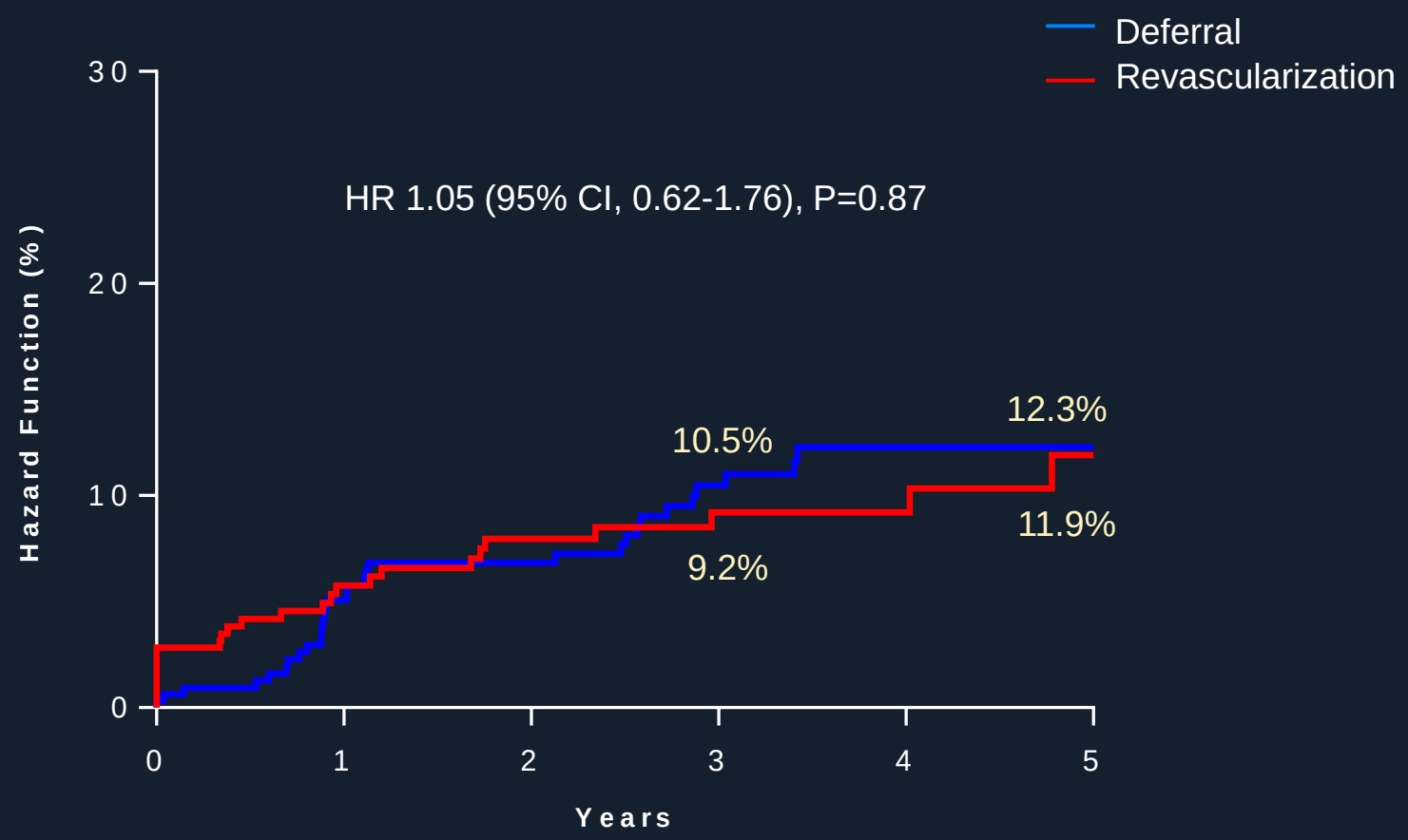
Primary End Point
(Death, MI, Target Vessel Revascularization)



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

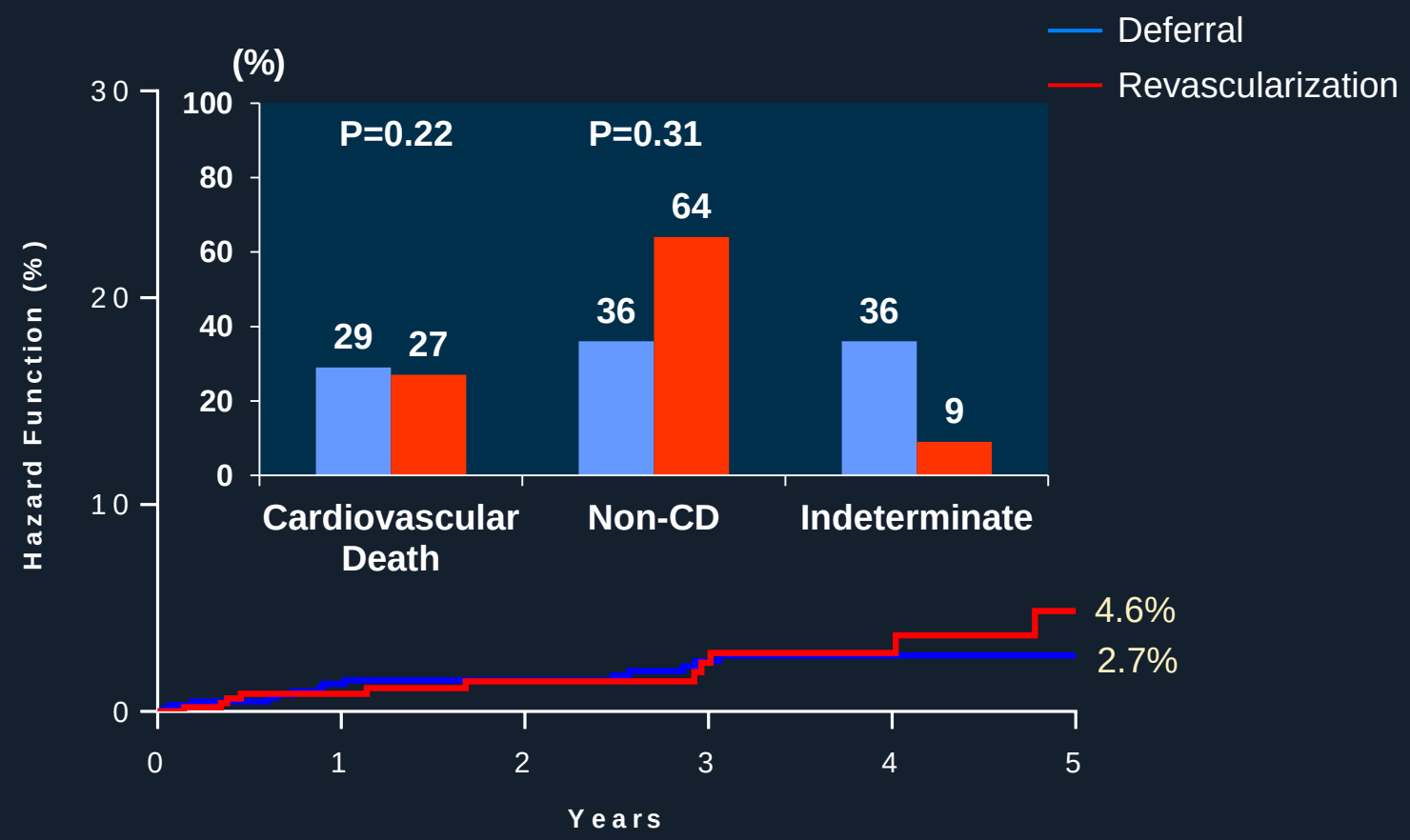
Matched Population

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

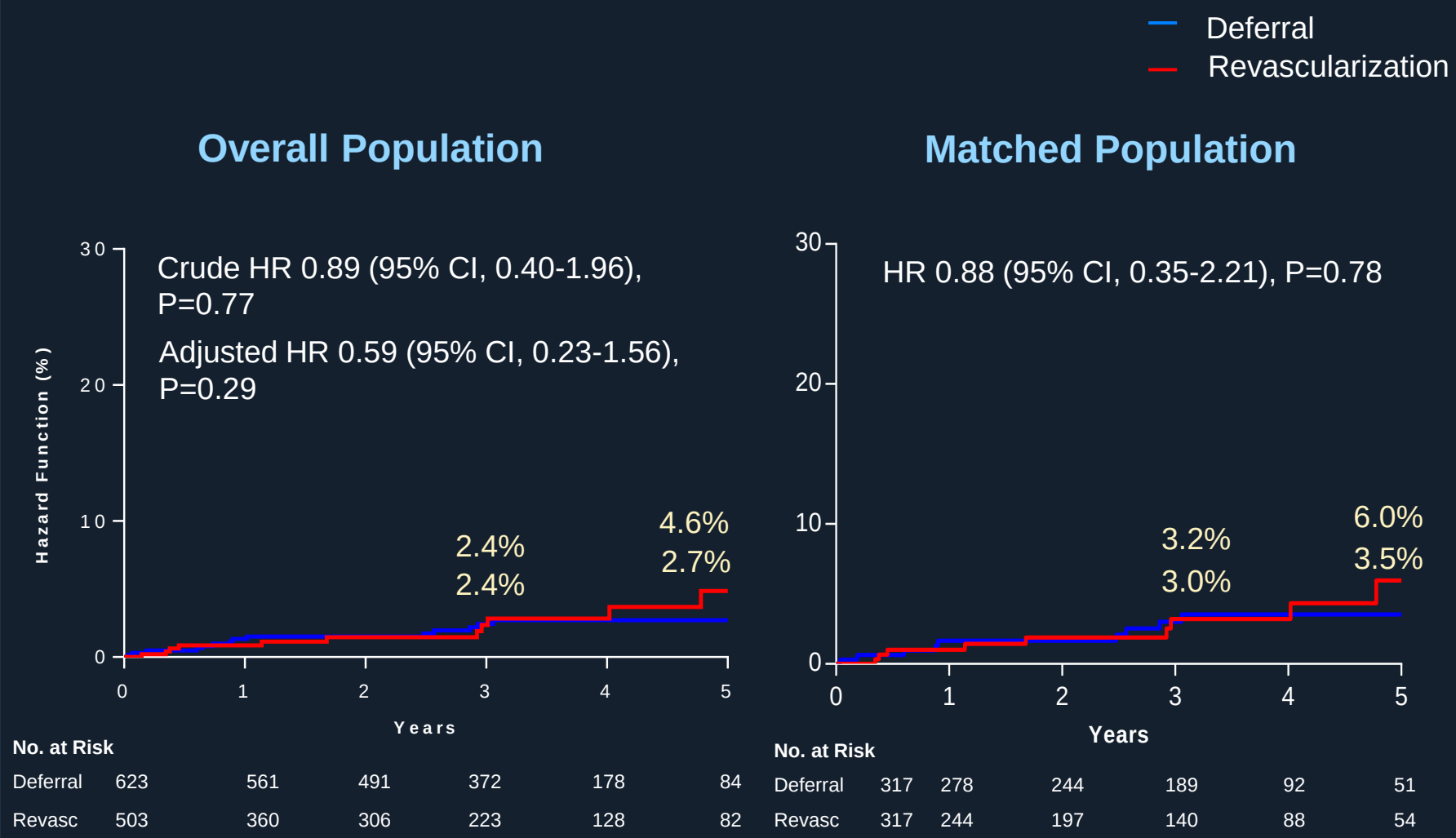
Death from any cause



No. at Risk

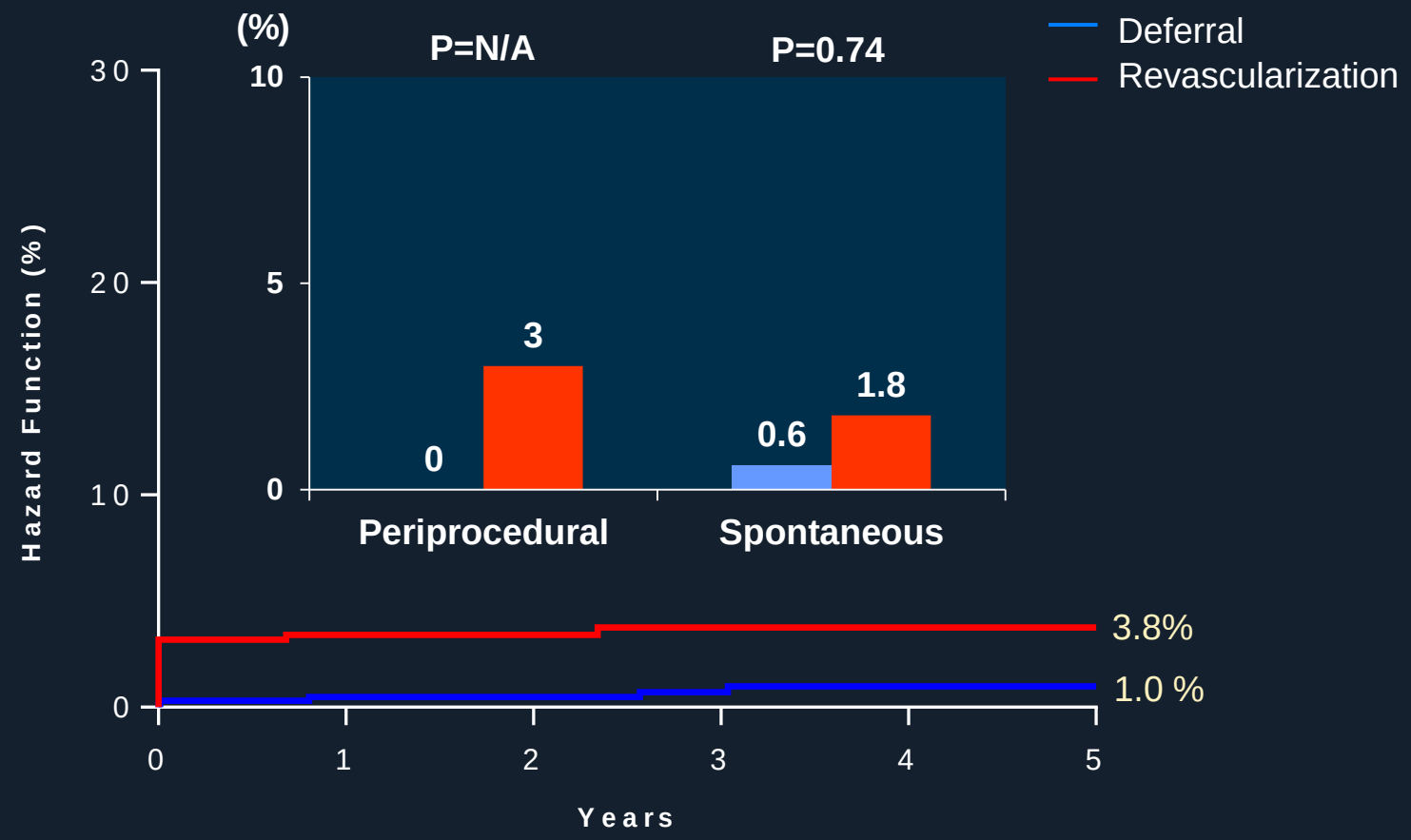
Deferral	623	561	491	372	178	84
Revasc	503	360	306	223	128	82

Death from any cause



Overall Population

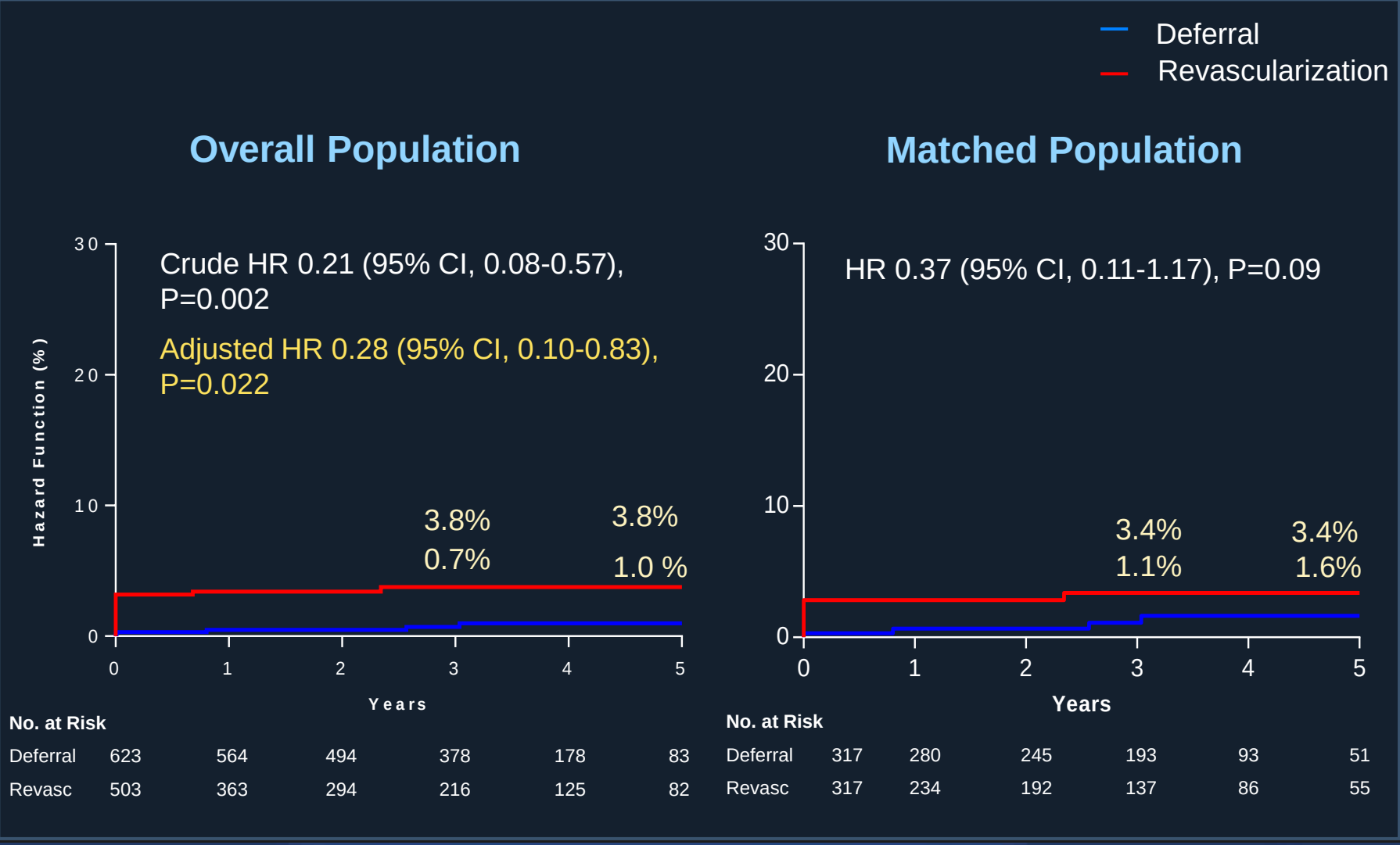
Myocardial Infarction



No. at Risk

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

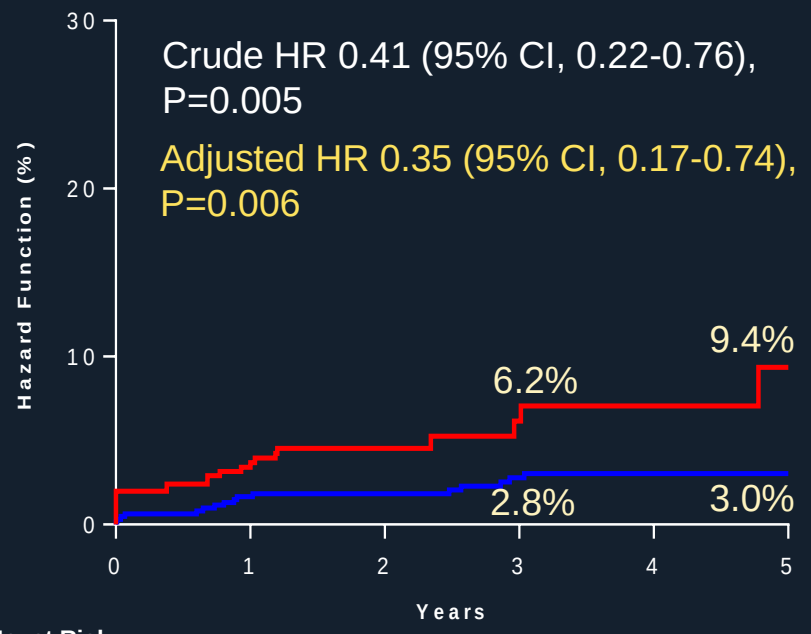
Myocardial Infarction



Death and Myocardial Infarction

Deferral
Revascularization

Overall Population



No. at Risk						
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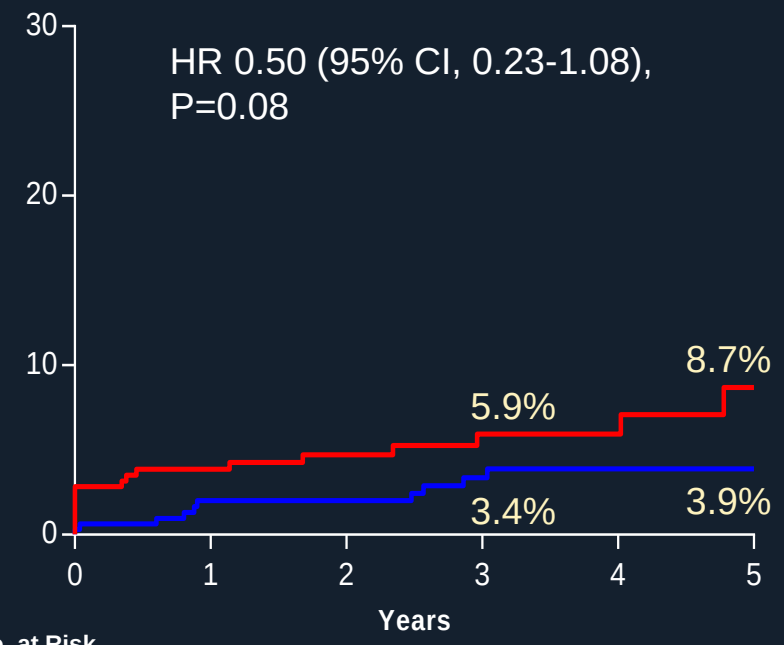
Revasc	503	367	294	215	123	79

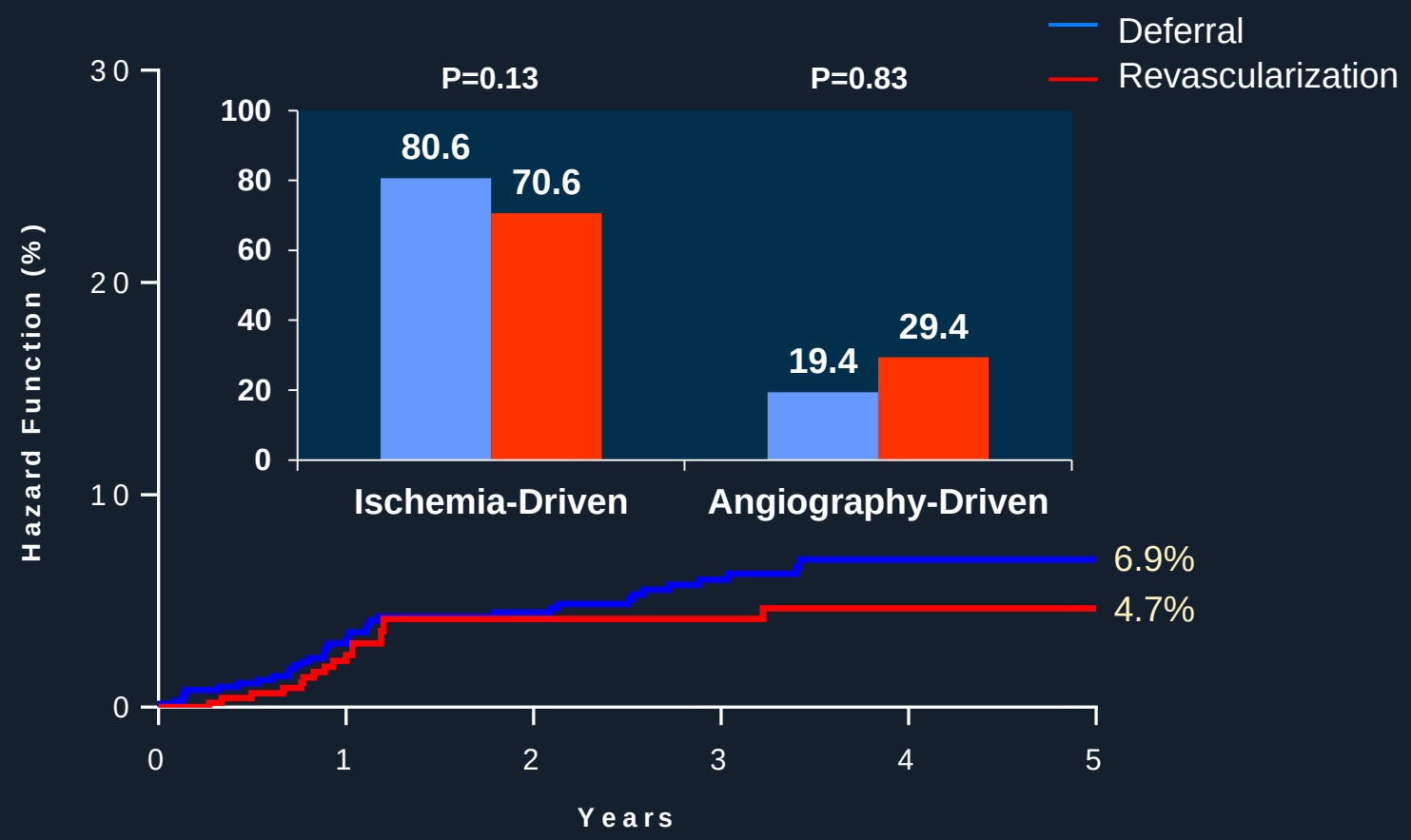
Matched Population



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

Overall Population

Target Vessel Revascularization

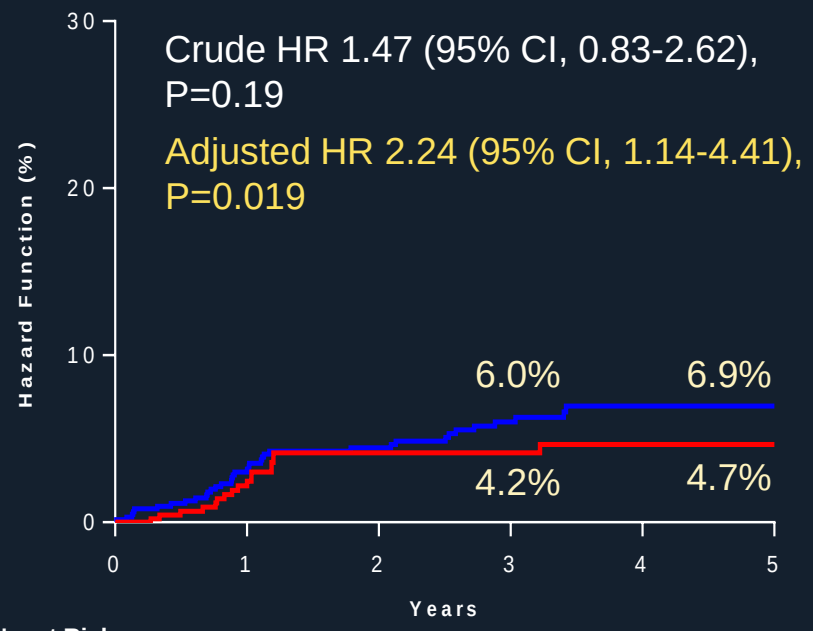


No. at Risk						
Deferral	623	551	475	356	163	76
Revasc	503	374	297	218	125	81

Target Vessel Revascularization

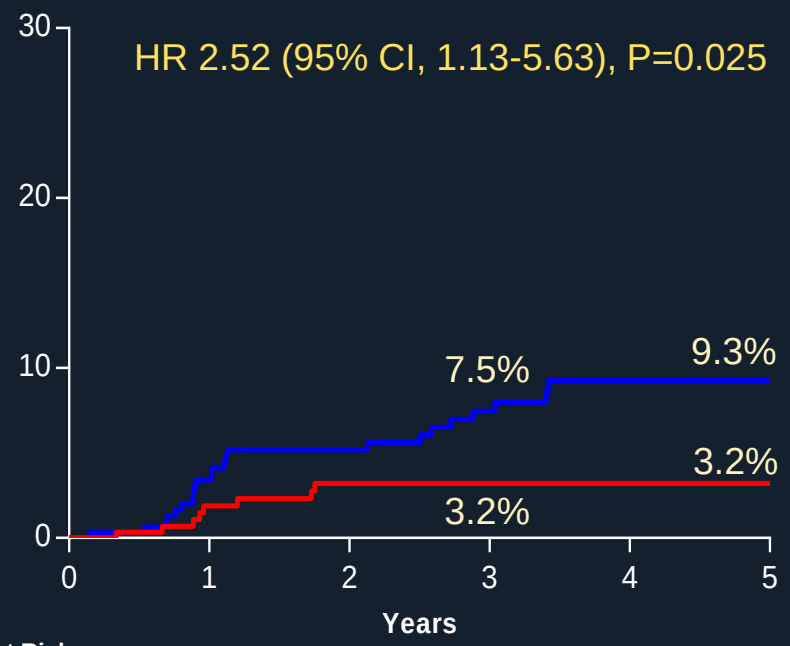
Deferral
Revascularization

Overall Population



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

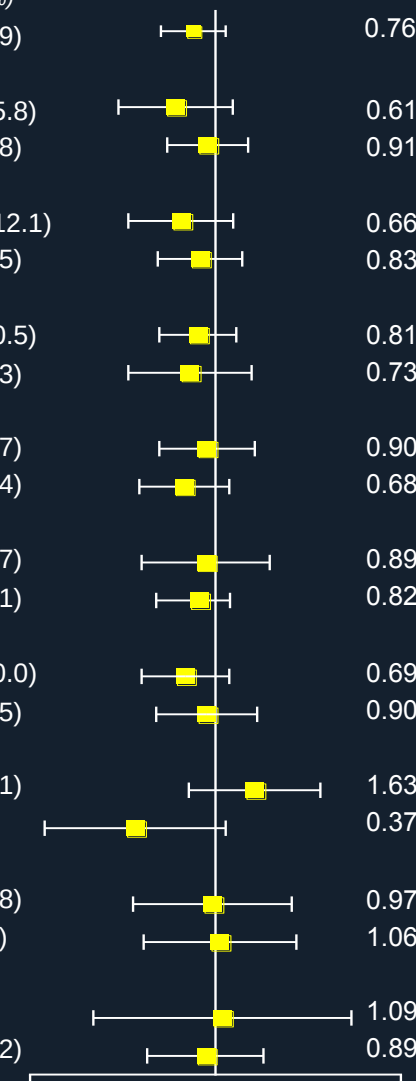
Matched Population



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

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

- Revascularization was associated with higher rate of MI, and death and MI, medical treatment (defer) was associated higher rate of TVR for the coronary stenoses with grey zone FFR.

- ***And so, medical treatment would be a reasonable strategy for lesions of grey zone (0.76~0.80)***