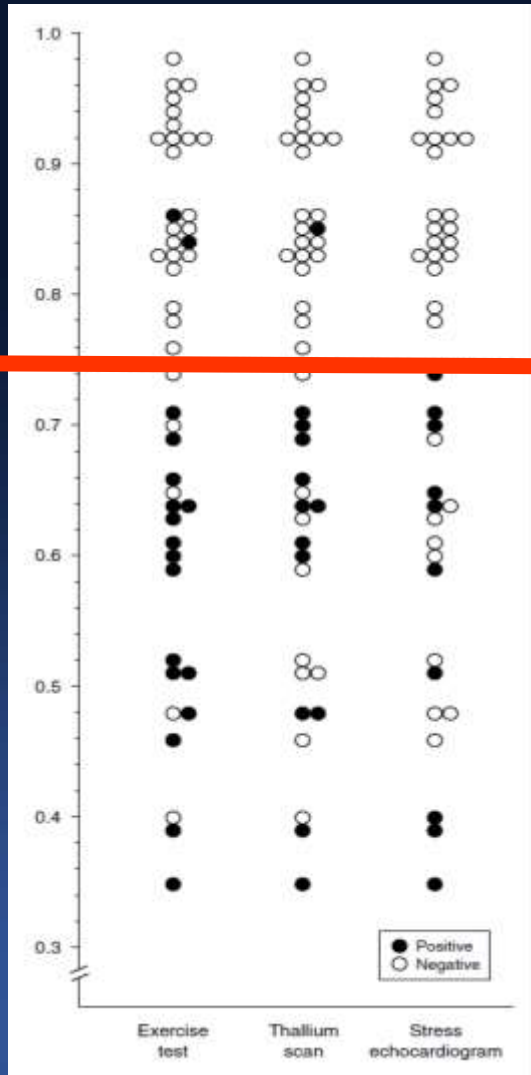


**To Treat or Not To Treat
For Gray Zone FFR (0.76~0.80)**
Data from IRIS FFR Registry

Seung-Jung Park, MD, PhD

Professor of Medicine, University of Ulsan College of Medicine,
Heart Institute, Asan Medical Center, Seoul, Korea

FFR



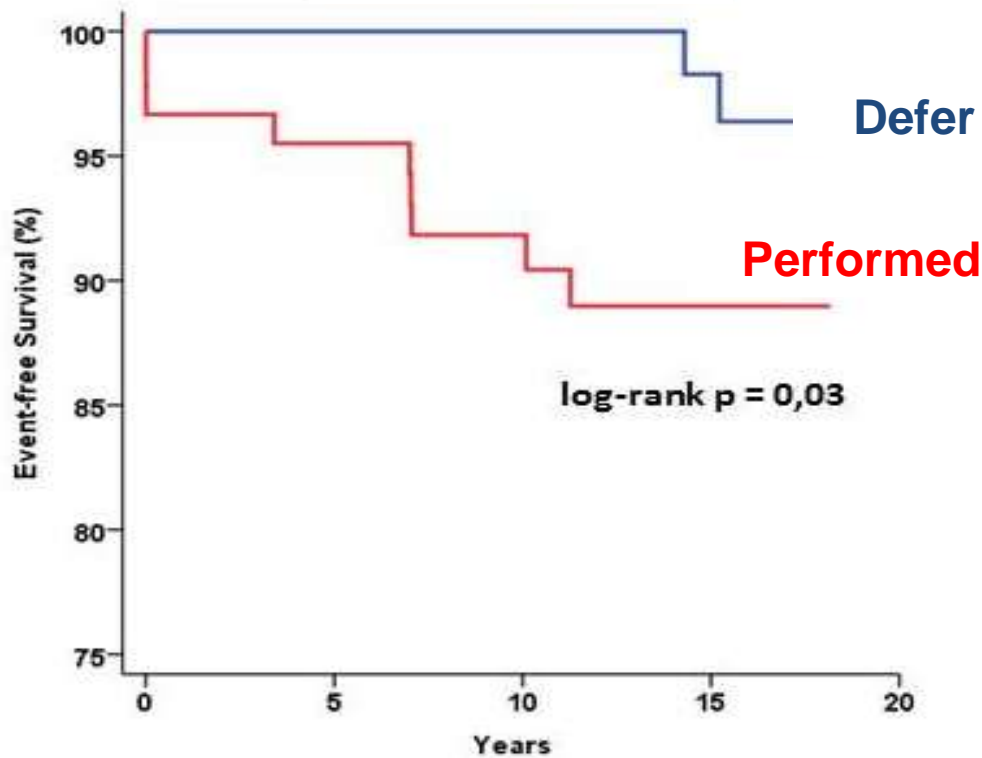
*FFR Cut-Off Value Matched
With Non-invasive Stress
Test Results (n=45)*

FFR < 0.75

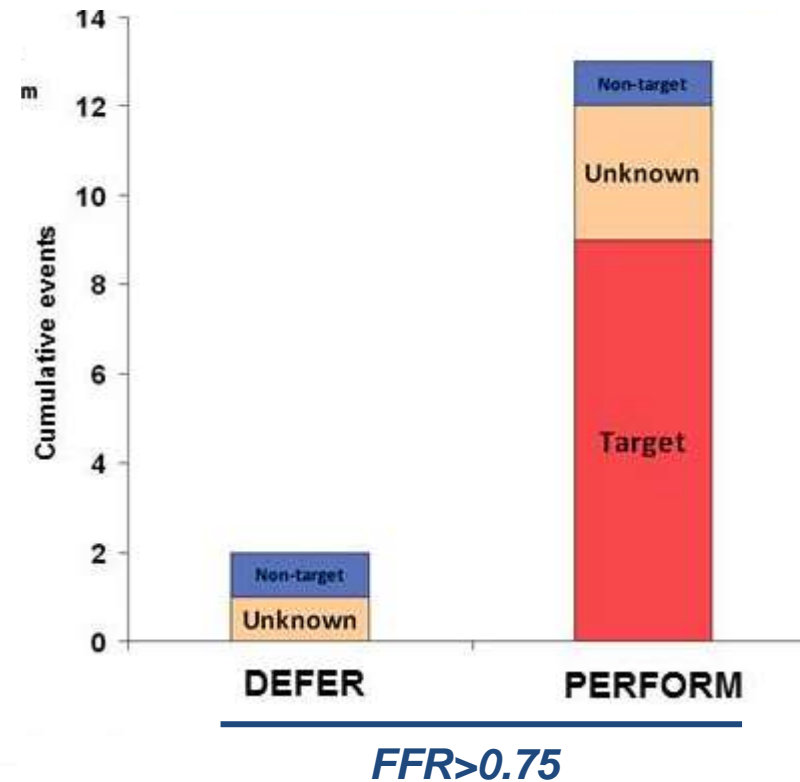
Sensitivity	88%
Specificity	100%
Positive PV	100%
Negative PV	88%
Accuracy	93%

At Beginning,

DEFER, 15 Year ($FFR_{\geq 0.75}$) Myocardial Infarction



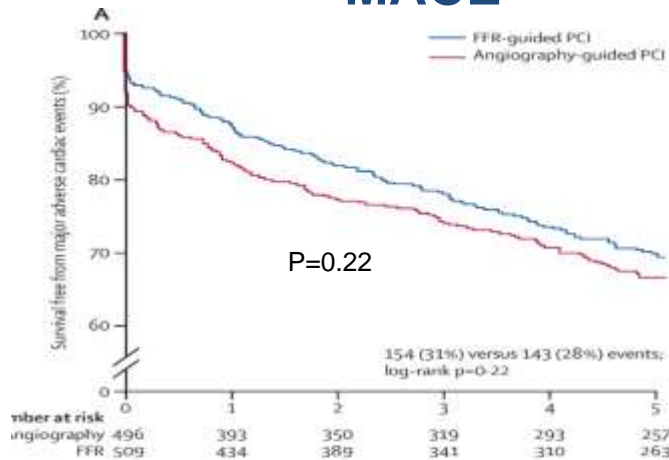
MI Territory with Target Vessel



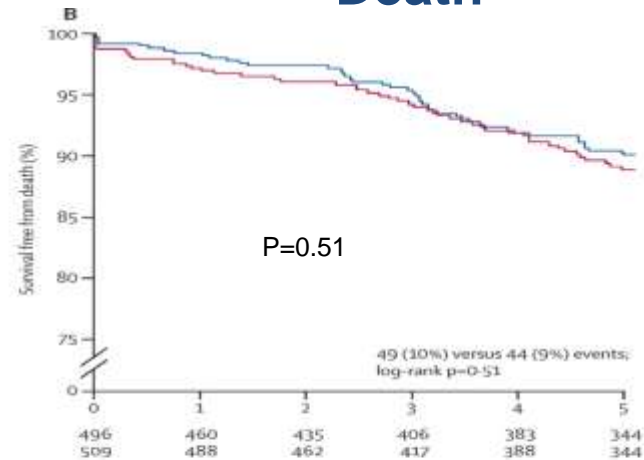
At Current Practice,

FAME 1, 5 year ($FFR_{\geq 0.80}$)

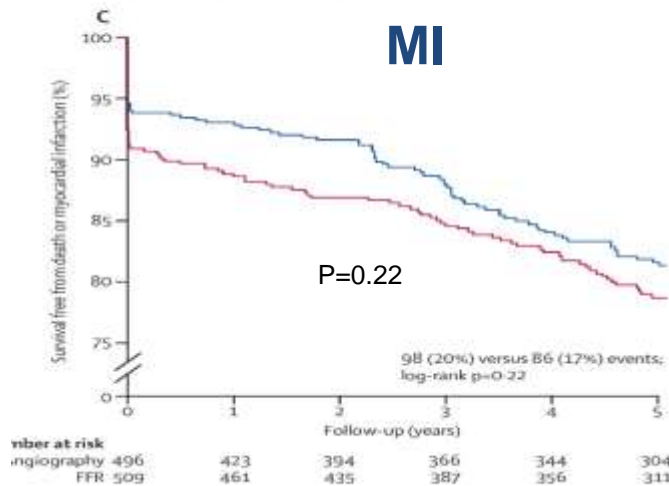
MACE



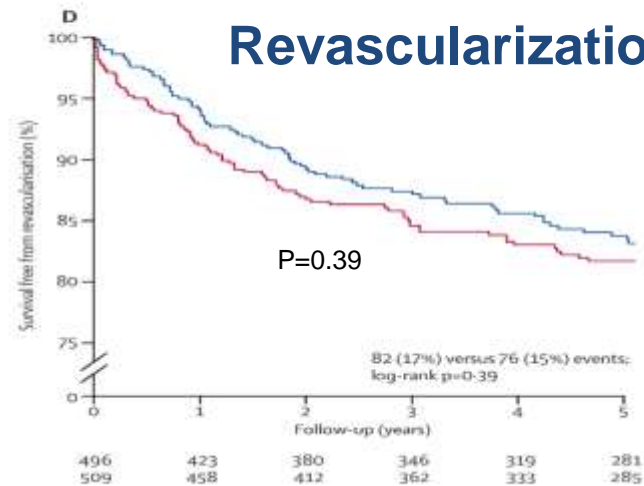
Death



MI

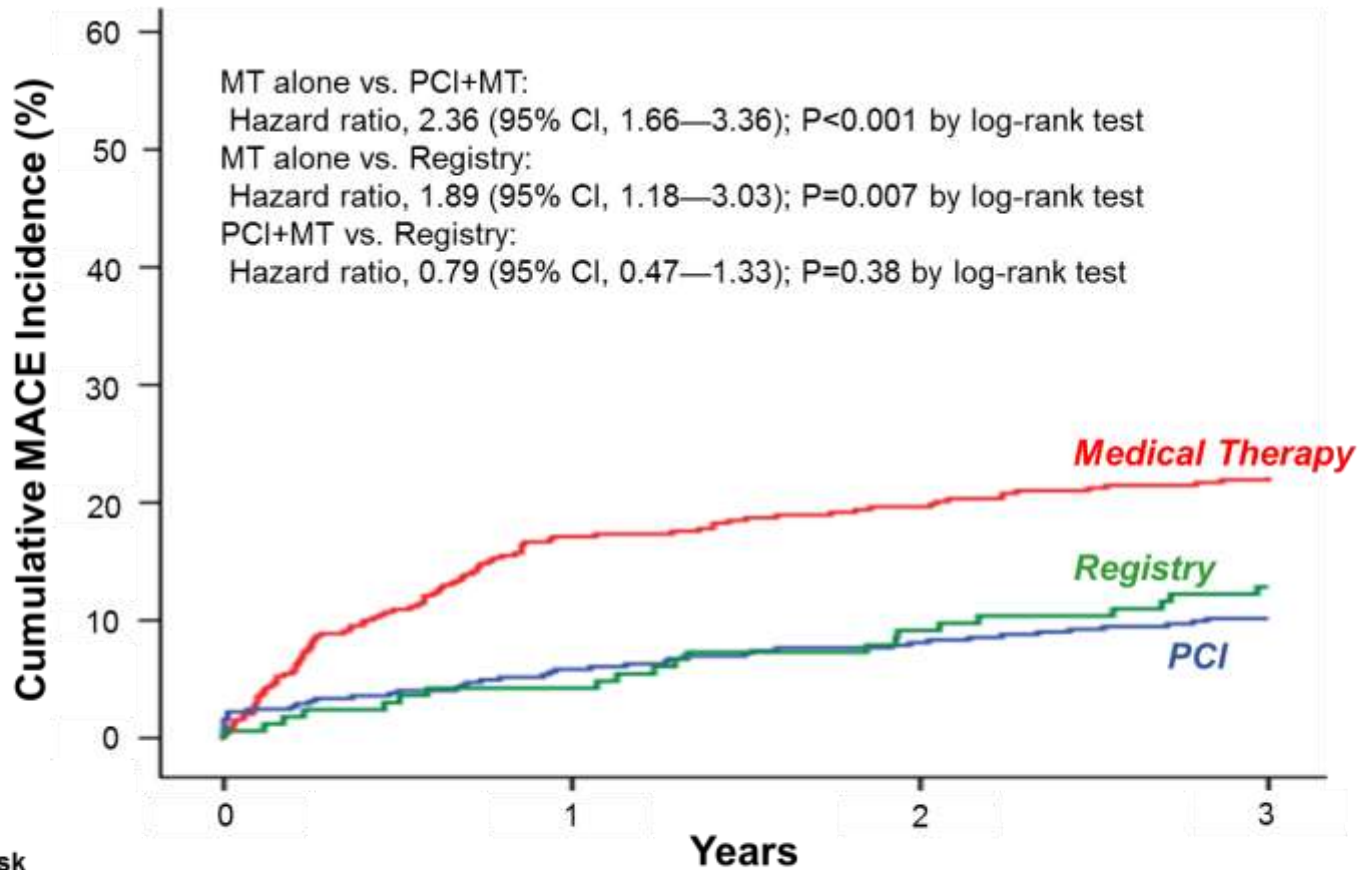


Revascularization



FAME II, 3 Year ($FFR < 0.80$)

Death, MI, or Urgent Revascularization



No. at Risk

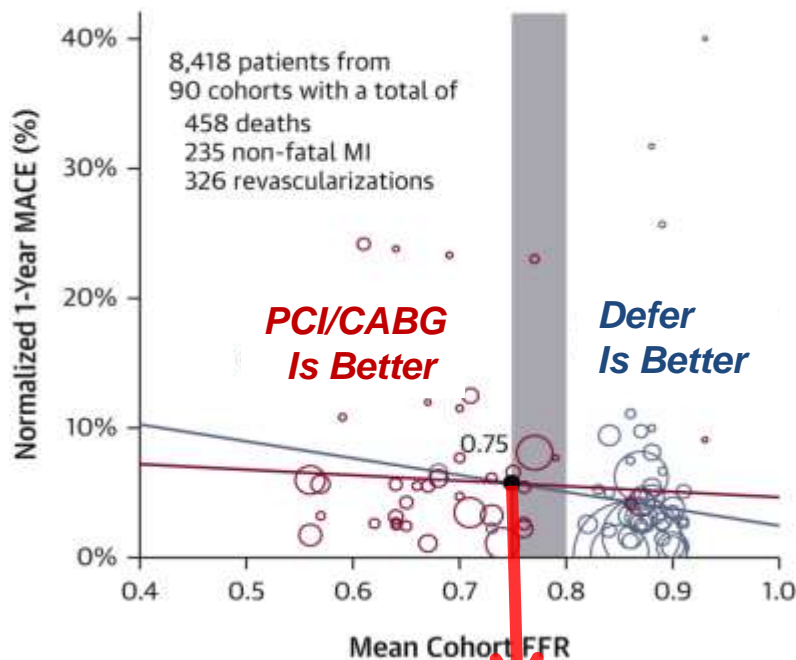
MT alone	441	362	350	339
PCI+MT	447	417	405	392
Registry	166	156	148	141

***Outcome Derived
Optimal Threshold of FFR***

Meta-Analysis for Optimal Threshold Based on the Outcomes (n=9,173)

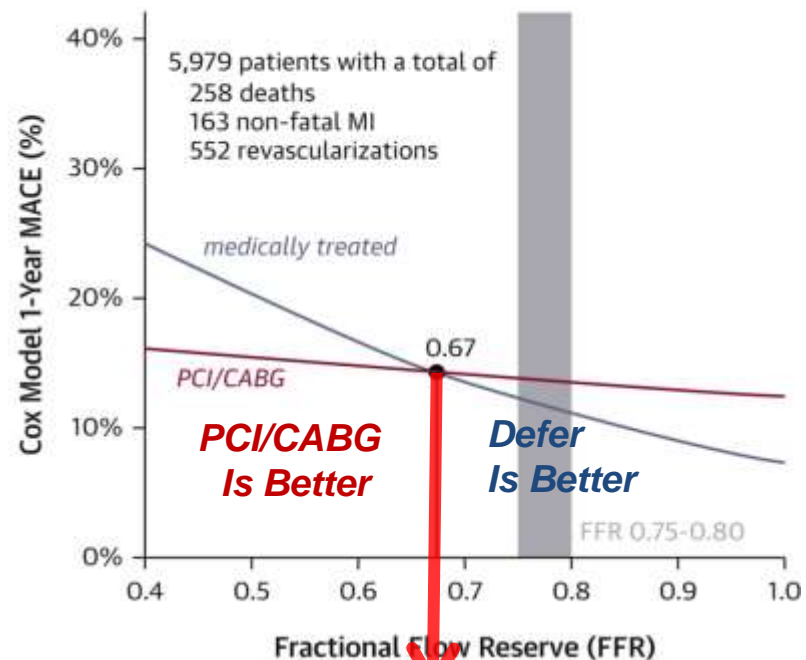
MACE at 1 Year

Study-level analysis



0.75

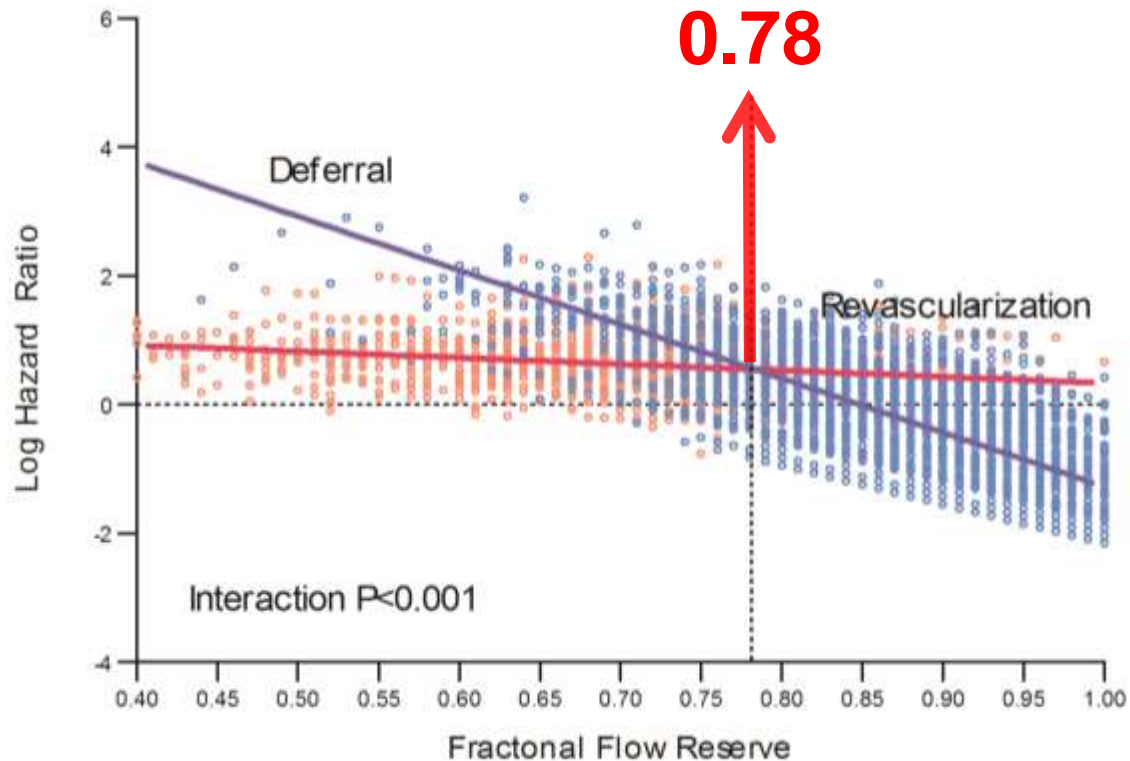
Patient-level analysis.



0.67

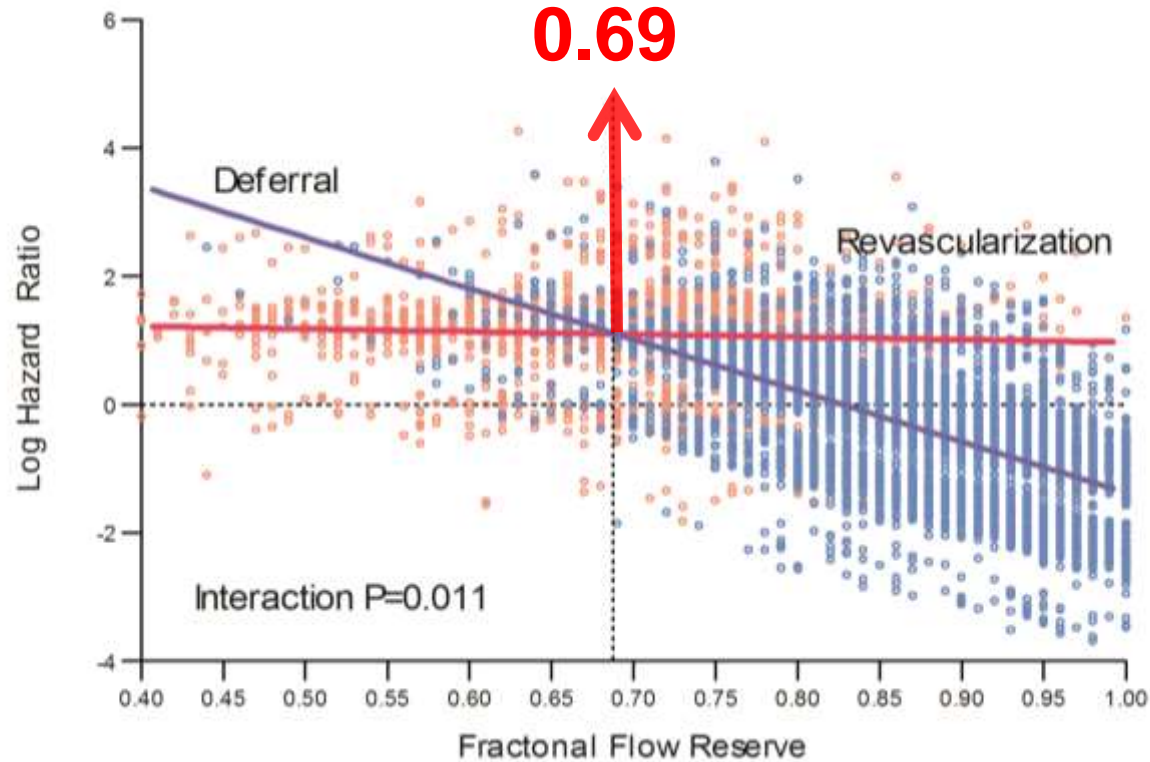
Outcome Derived Optimal Threshold of FFR (IRIS-FFR Registry, n=8,632)

MACE

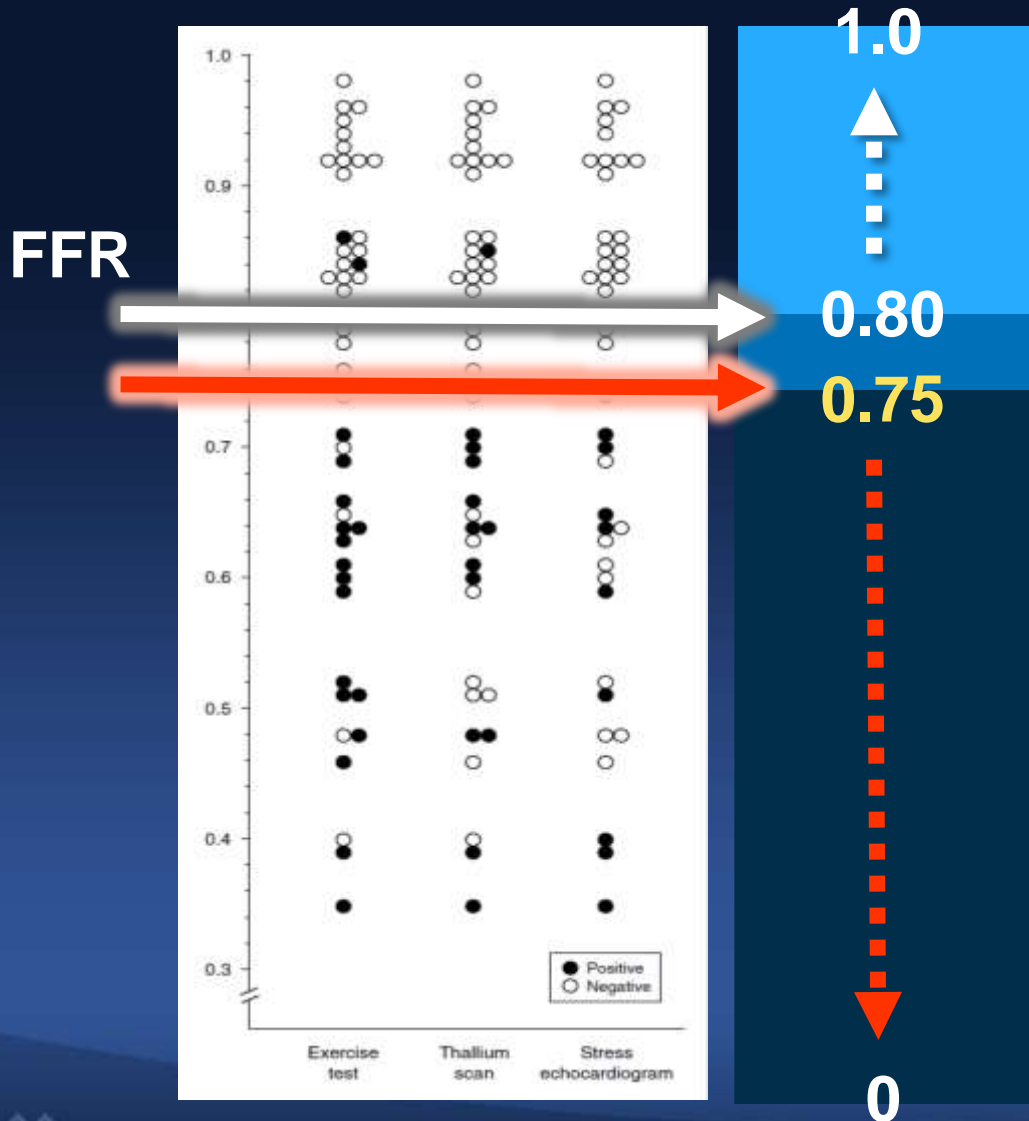


Outcome Derived Optimal Threshold of FFR (IRIS-FFR Registry, n=8,632)

Cardiac Death and MI



Current Practice



Defer

To Treat or Not ?

To Treat

Study Objective

To Compare the Prognosis of *Deferred and Performed Revascularization* in Coronary Stenoses with Grey-Zone FFR (0.75-0.80) in the Prospective IRIS-FFR Registry

Study Flow

10,881 lesions in 7735 patients
With FFR measurement
(Aug 2009 to Oct 2016)

1334 lesions in 1334 patients
with Grey-Zone FFR (0.75-0.80)
(Median 3 years follow-up)

Deferred group
(683 patients)

Performed group
(651 patients)

1:1 Propensity score matching

Deferred group
(368 patients)

Performed group
(368 patients)

Primary End Point

Major Adverse Cardiac Events (MACE),

A Composite Clinical Outcomes of

- Death of all-cause
- Target Vessel Myocardial Infarction
 - Periprocedural MI: CK-MB $>$ 5 times UNL with Sx
 - Spontaneous MI: any cardiac enzyme elevation
- Target Vessel Revascularization

Baseline Characteristics of Overall Population

	Deferred (N=683)	Performed (N=651)	P value
Age (years)	64.2±9.8	63.8±9.9	0.52
Male sex	535 (78.3%)	478 (73.4%)	0.042
Body mass index (kg/m ²)	24.9±3.1	25.1±3.0	0.18
Acute coronary syndrome	125 (18.3%)	163 (25.0%)	0.003
Hypertension	441 (64.6%)	418 (64.2%)	0.94
Diabetes	220 (32.2%)	203 (31.2%)	0.73
Current smoking	164 (24.0%)	130 (20.0%)	0.09
Hyperlipidemia	388 (56.8%)	363 (55.8%)	0.74
Previous MI	47 (6.9%)	38 (5.8%)	0.50
Previous PCI	153 (22.4%)	102 (15.7%)	0.002
Peripheral vascular disease	18 (2.6%)	21 (3.2%)	0.63
Chronic renal failure	19 (2.8%)	15 (2.3%)	0.70
Multi-vessel disease	375 (54.9%)	413 (63.4%)	0.002
LVEF, %	60.5±11.4	60.8±11.0	0.67

Lesion Characteristics of Overall Population

	Deferred (N=683)	Performed (N=651)	P value
FFR	0.78±0.02	0.77±0.02	<0.001
Diseased vessel			0.001
Left main	20 (2.9%)	48 (7.4%)	
LAD	513 (75.1%)	448 (68.8%)	
RCA	72 (10.5%)	86 (13.2%)	
LCX	54 (7.9%)	56 (8.6%)	
Lesion location			0.002
Proximal	315 (46.1%)	362 (55.6%)	
Mid	264 (38.7%)	215 (33.0%)	
Distal	81 (11.9%)	65 (10.0%)	
Diameter stenosis			<0.001
≥ 70%	88 (12.9%)	349 (53.6%)	
50-69%	446 (65.3%)	295 (45.3%)	
30-49%	149 (21.8%)	7 (1.1%)	
AHA/ACC B2C lesion	444 (65.0%)	484 (74.3%)	<0.001
Long lesion (>20mm)	320 (46.9%)	384 (59.0%)	<0.001

Baseline Characteristics of Propensity score-Matched Population

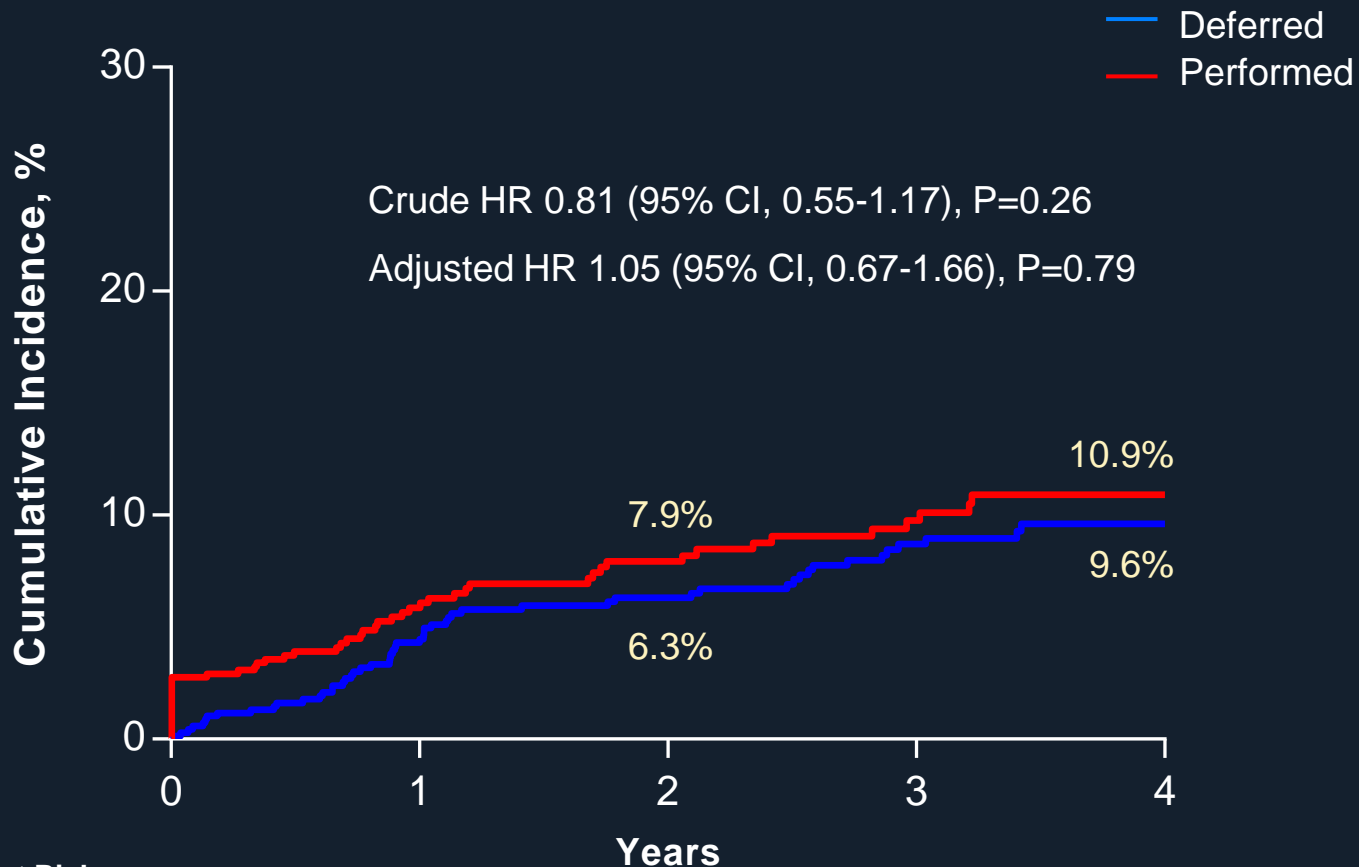
	Deferred (N=368)	Performed (N=368)	P value
Age (years)	64.5±9.9	64.2±9.9	0.73
Male sex	285 (77.4%)	275 (74.7%)	0.44
Body mass index (kg/m ²)	24.9±3.2	24.9±2.8	0.95
Acute coronary syndrome	71 (19.3%)	73 (19.8%)	0.85
Hypertension	232 (63.0%)	234 (63.6%)	0.94
Diabetes	112 (30.4%)	119 (32.3%)	0.63
Current smoking	97 (26.4%)	81 (22.0%)	0.20
Hyperlipidemia	205 (55.7%)	207 (56.2%)	0.94
Previous MI	26 (7.1%)	22 (6.0%)	0.65
Previous PCI	80 (21.7%)	68 (18.5%)	0.31
Peripheral vascular disease	8 (2.2%)	14 (3.8%)	0.28
Chronic renal failure	13 (3.5%)	8 (2.2%)	0.38
Multi-vessel disease	223 (60.6%)	228 (62.0%)	0.76
LVEF, %	61.7±6.9	61.5±7.8	0.82

Lesion Characteristics of Propensity score-Matched Population

	Deferred (N=368)	Performed (N=368)	P value
FFR	0.78±0.02	0.78±0.02	0.14
Diseased vessel			0.98
Left main	15 (4.1%)	17 (4.6%)	
LAD	258 (70.1%)	262 (71.2%)	
RCA	49 (13.3%)	47 (12.8%)	
LCX	34 (9.2%)	32 (8.7%)	
Lesion location			0.80
Proximal	193 (52.4%)	191 (51.9%)	
Mid	125 (34.0%)	132 (35.9%)	
Distal	38 (10.3%)	37 (10.1%)	
Diameter stenosis			0.20
≥ 70%	83 (22.6%)	90 (24.5%)	
50-69%	270 (73.4%)	271 (73.6%)	
30-49%	15 (4.1%)	7 (1.9%)	
AHA/ACC B2C lesion	249 (67.7%)	262 (71.2%)	0.34
Long lesion (>20mm)	180 (48.9%)	199 (54.1%)	0.18

Primary End Point

(Death, TV-MI, Target Vessel Revascularization)

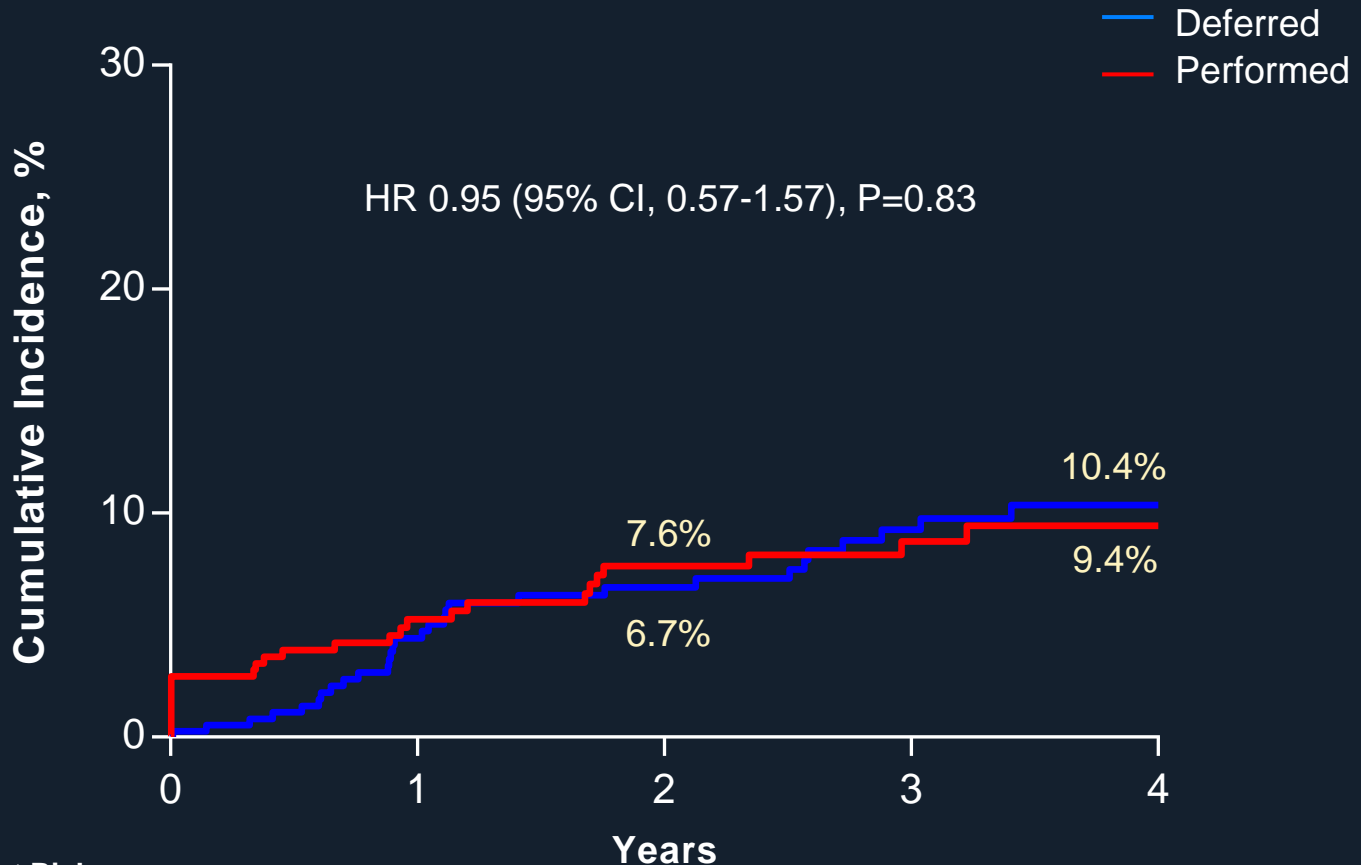


No. at Risk

Deferred	683	591	493	361	171
Performed	651	449	343	247	144

Primary End Point

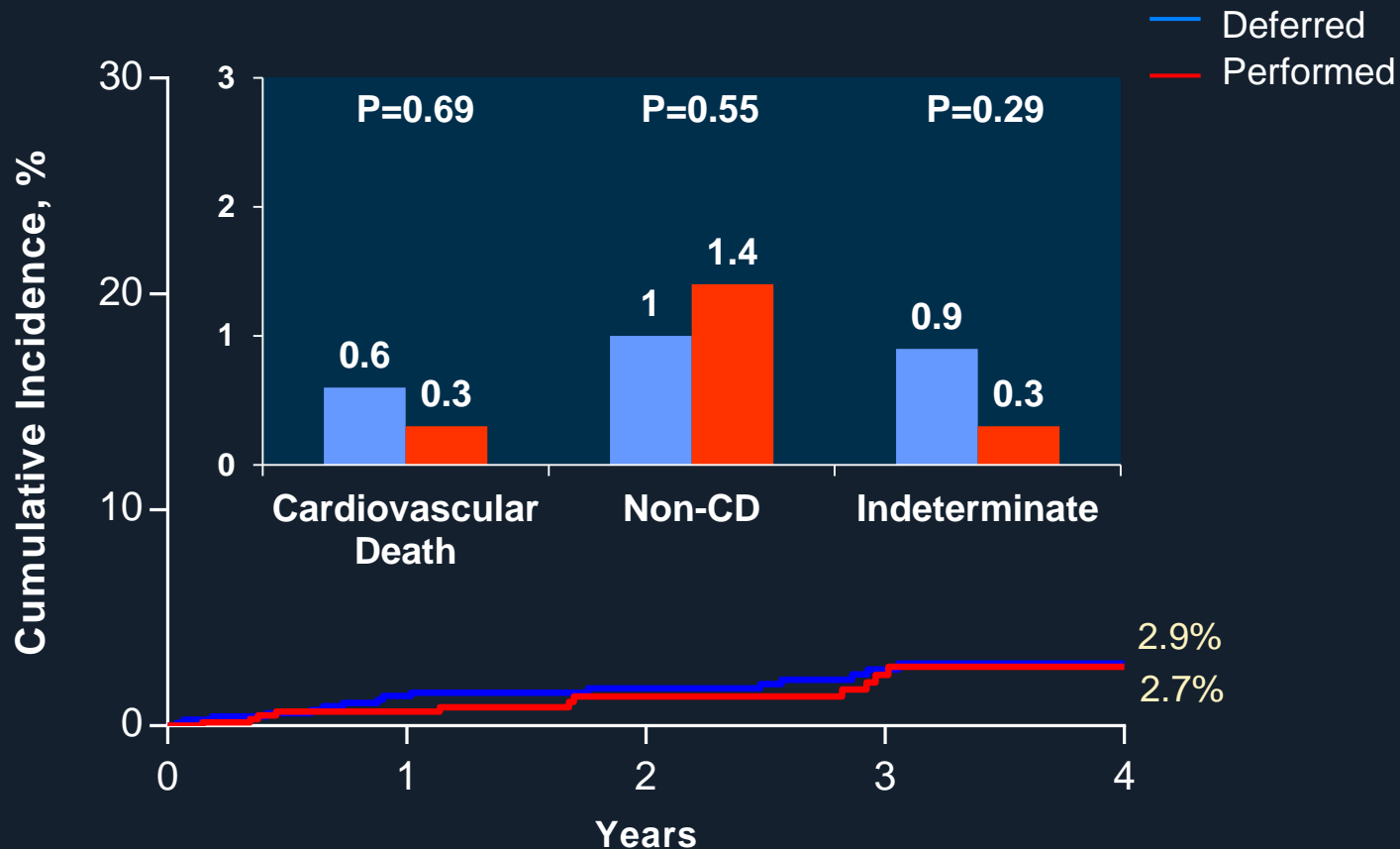
(Death, TV-MI, Target Vessel Revascularization)



No. at Risk

Deferred	368	308	249	186	99
Performed	368	263	204	144	84

Death from any cause



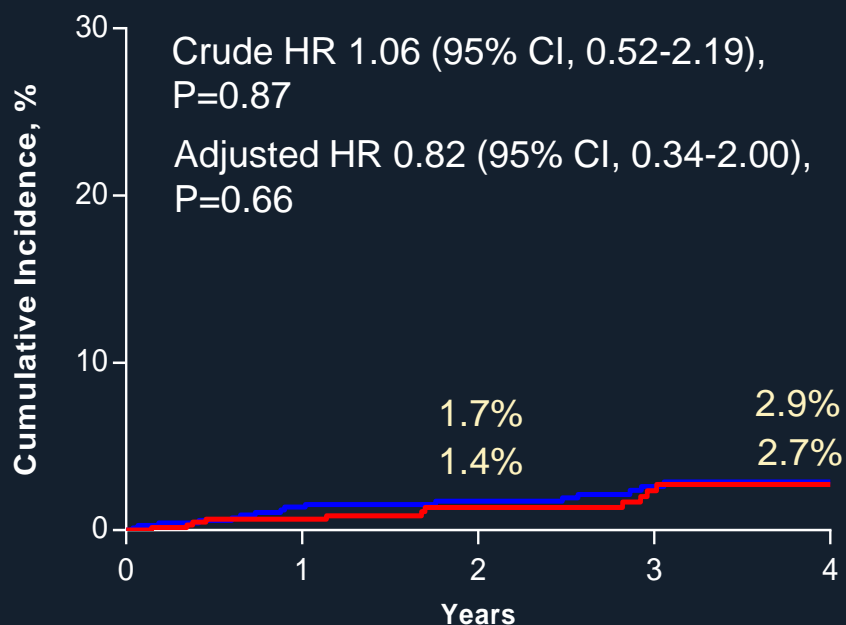
No. at Risk

Deferred	683	609	517	387	189
Performed	651	476	373	271	162

Death from any cause

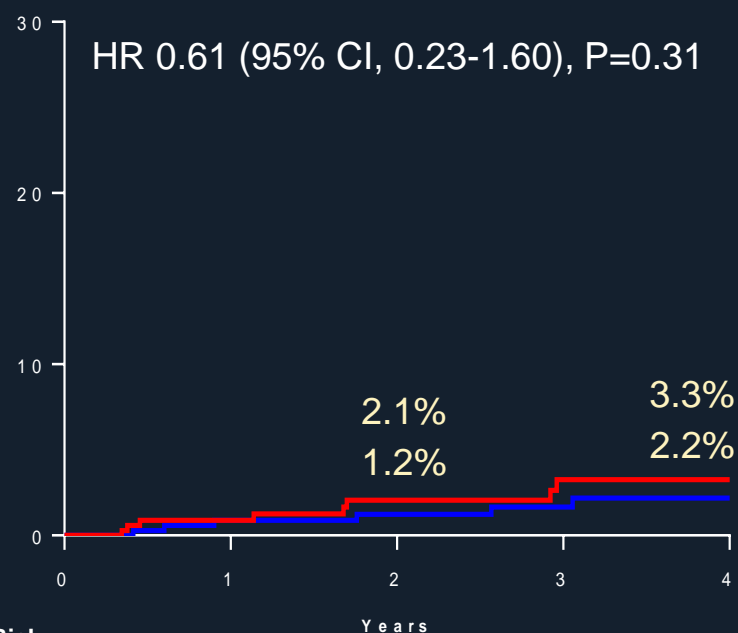
— Deferred
— Performed

Overall Population



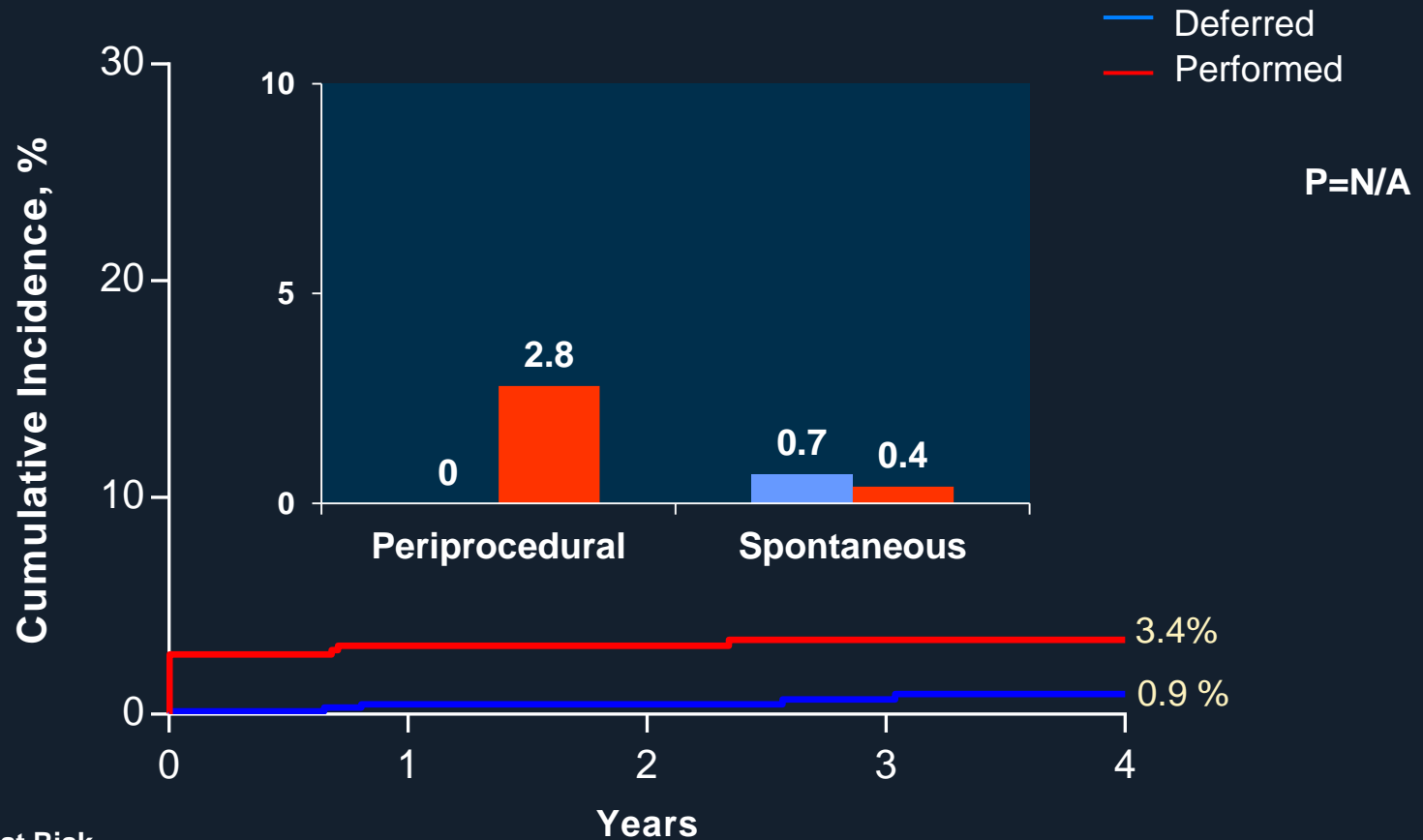
No. at Risk	Years				
	0	1	2	3	4
Deferred	683	609	517	387	189
Performed	651	476	373	271	162

Matched Population



No. at Risk	Years				
	0	1	2	3	4
Deferred	368	319	262	201	109
Performed	368	276	222	154	89

Myocardial Infarction



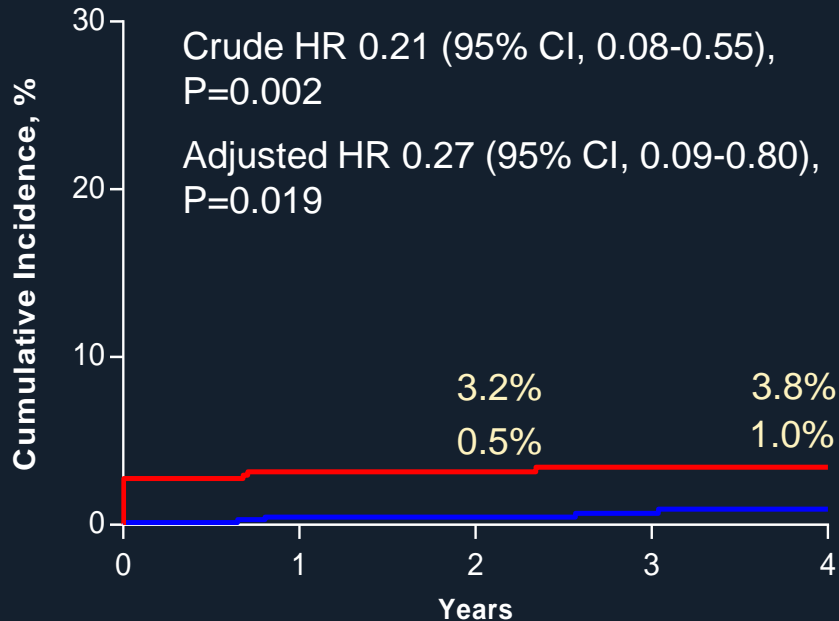
No. at Risk

Deferred	683	606	514	387	188
Performed	651	452	353	261	156

Myocardial Infarction

— Deferred
— Performed

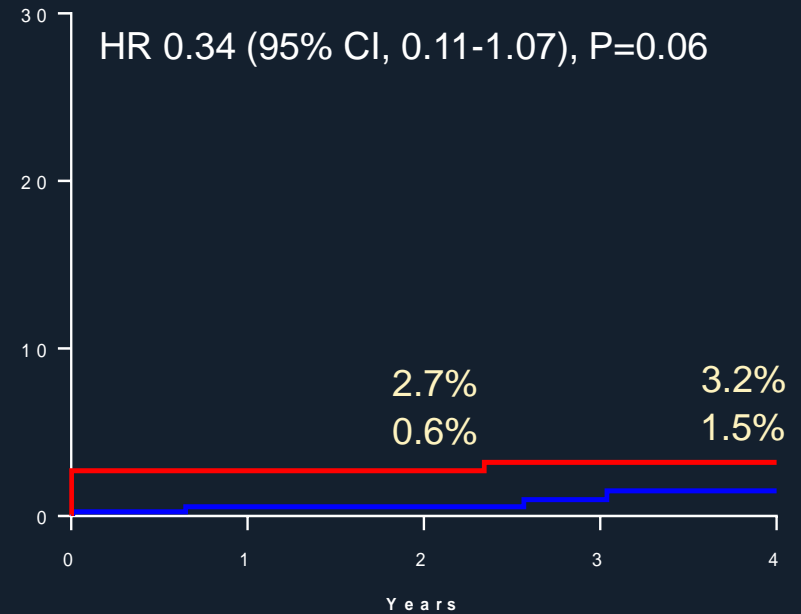
Overall Population



No. at Risk

	0	1	2	3	4
Deferred	683	606	514	387	188
Performed	651	452	353	261	156

Matched Population



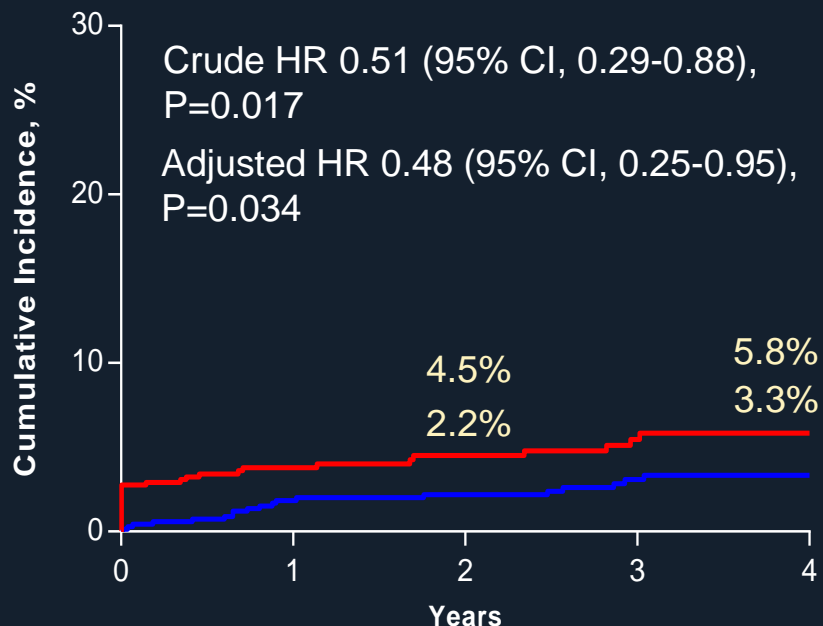
No. at Risk

	0	1	2	3	4
Deferred	368	318	260	200	109
Performed	368	264	210	151	89

Death and Myocardial Infarction

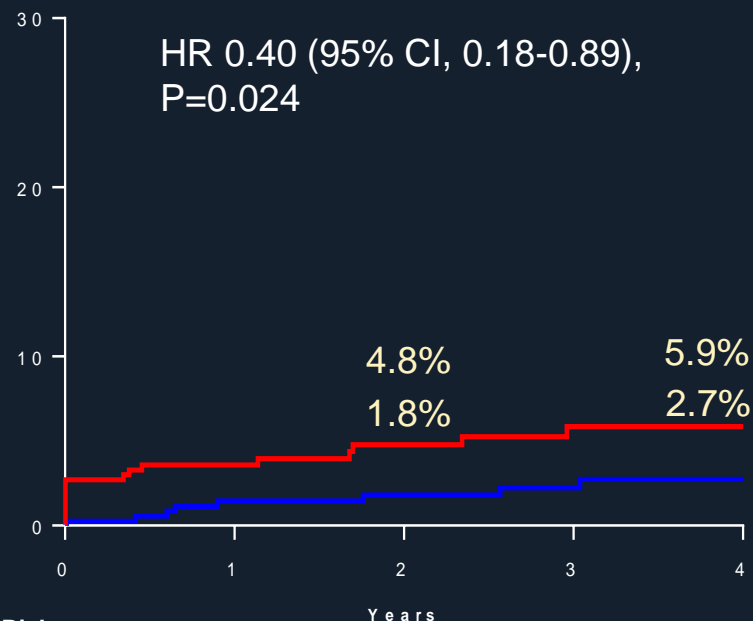
— Deferred
— Performed

Overall Population



No. at Risk	Years				
	0	1	2	3	4
Deferred	683	606	514	388	189
Performed	651	460	358	260	154

Matched Population

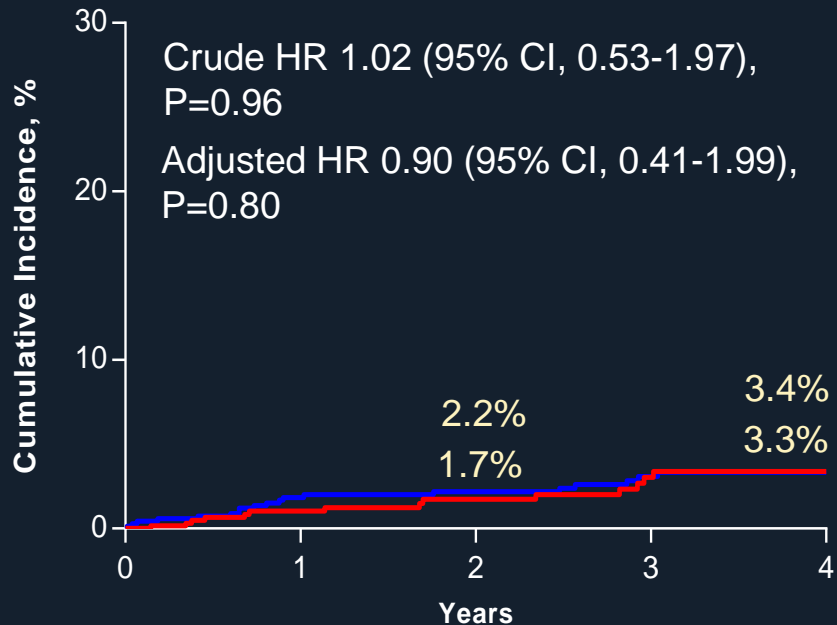


No. at Risk	Years				
	0	1	2	3	4
Deferred	368	317	260	200	109
Performed	368	268	212	150	87

Death and Spontaneous MI

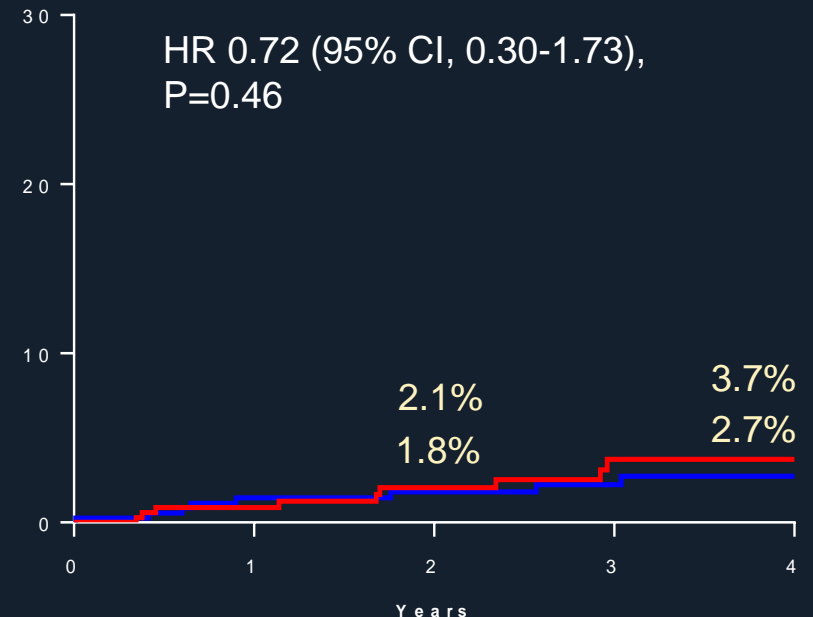
— Deferred
— Performed

Overall Population



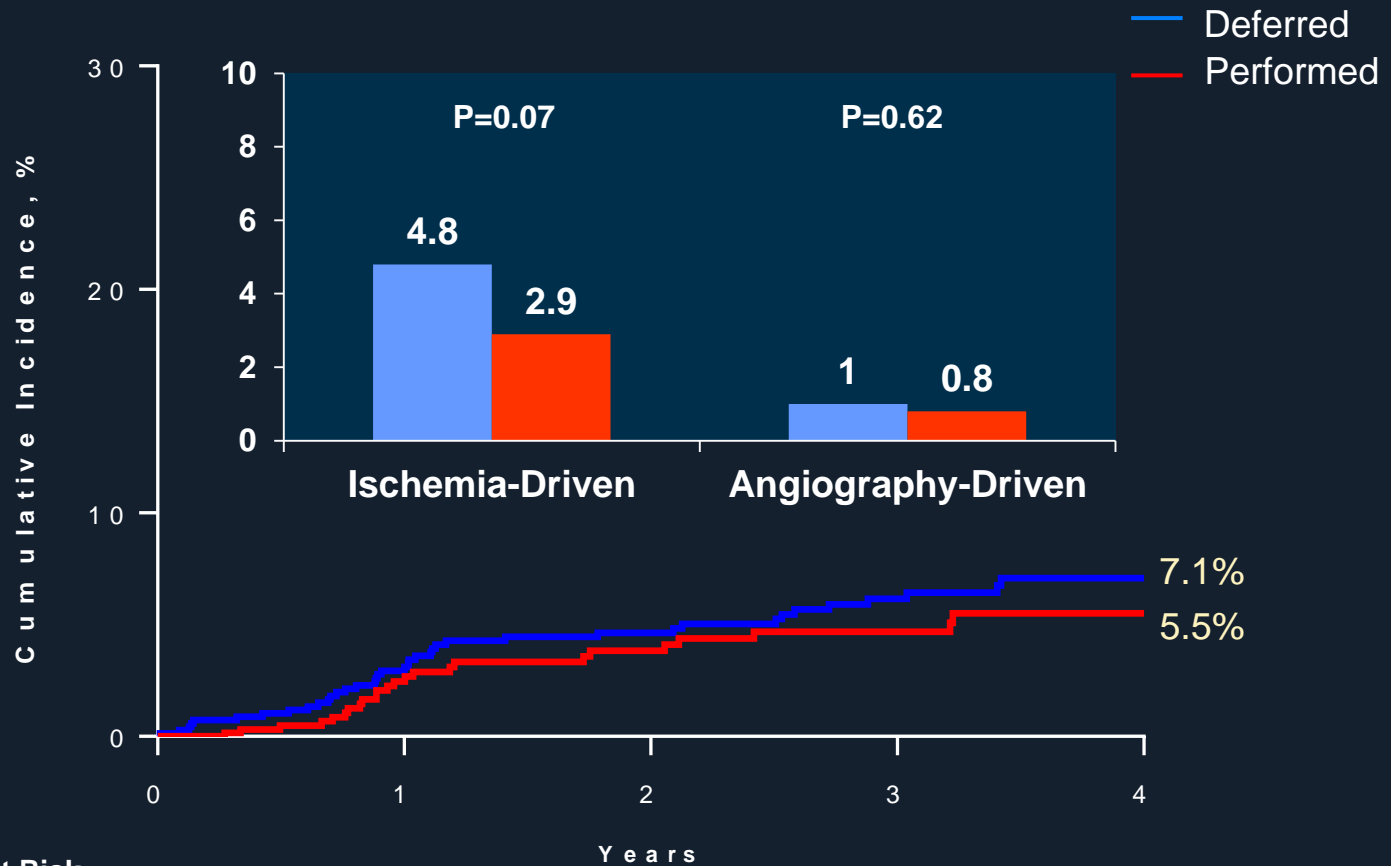
No. at Risk	Years				
	0	1	2	3	4
Deferred	683	607	515	387	189
Performed	651	475	372	272	162

Matched Population



No. at Risk	Years				
	0	1	2	3	4
Deferred	368	318	260	200	109
Performed	368	276	219	154	90

Target Vessel Revascularization



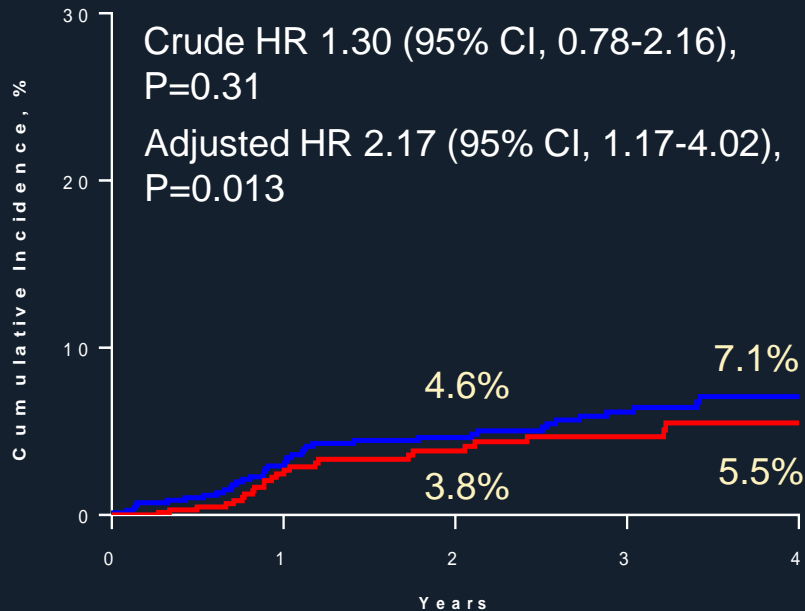
No. at Risk

	0	1	2	3	4
Deferred	683	598	500	371	176
Performed	683	467	361	261	154

Target Vessel Revascularization

— Deferred
— Performed

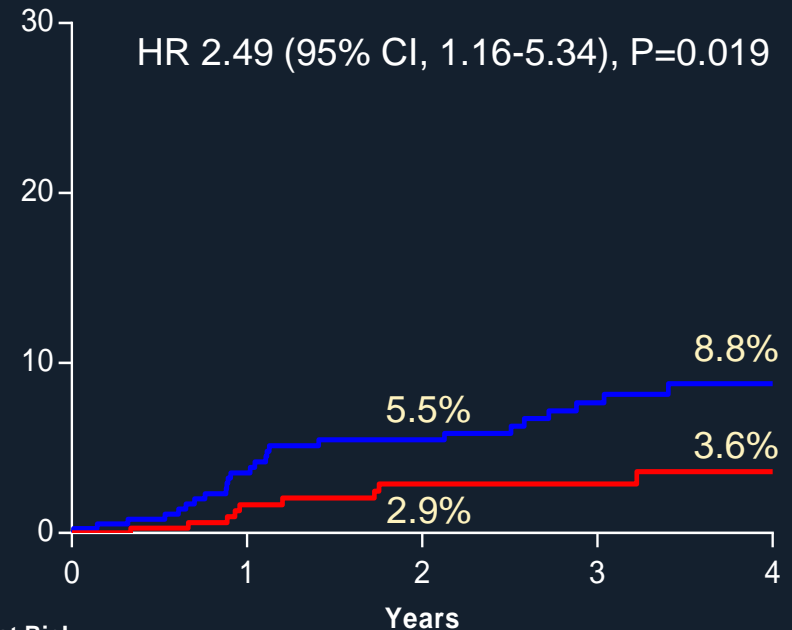
Overall Population



No. at Risk

	0	1	2	3	4
Deferred	683	592	494	362	171
Performed	651	463	356	259	151

Matched Population



No. at Risk

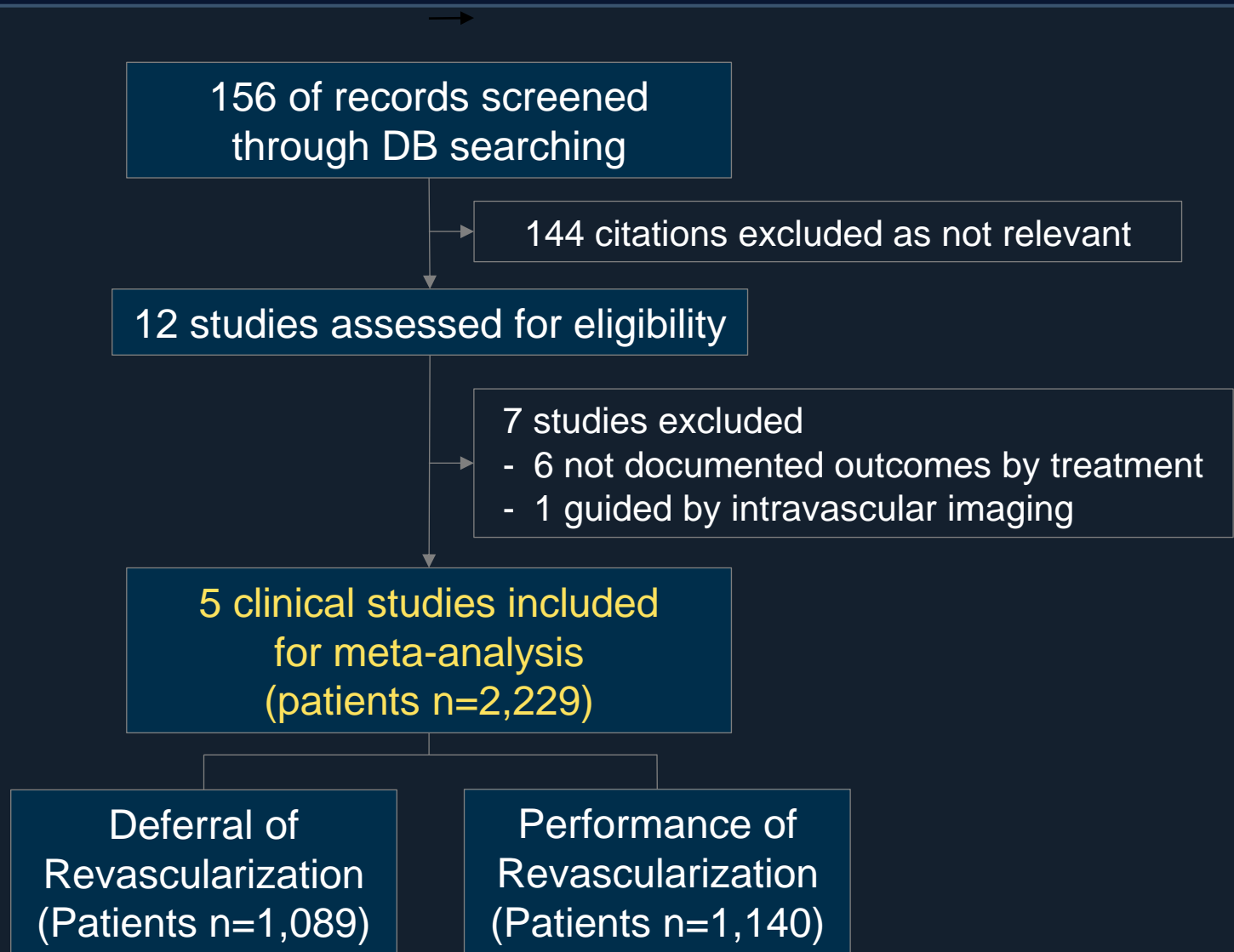
	0	1	2	3	4
Deferred	368	309	249	186	99
Performed	368	271	211	148	87

Results

- The risk of a composite of death, MI, and TVR was **not significantly different** between deferred and performed groups with the grey zone FFR.
- Death, spontaneous MI did not differ btw groups.
- Higher risk of periprocedural MI in performed group was offset by higher risk of TVR in deferred group.
- The trend was consistent after adjustment by propensity-score matching and IPTW.

Meta-Analysis
**To Treat or Not To Treat
For Gray Zone FFR (0.76~0.80)**

Study Flow Diagram



5 Studies Analyzed

	Design	Number (MT / PCI)	F/U (mo)	Cardiac death	MI	TVR	MACE
Courtis et al. (2008)	Retrospective, single-center	107 (44 / 61)	13	0 / 0	0 / 2	23 / 5	CD+TV-MI+TLR 23 / 5
Lindstaedt et al. (2010)	Retrospective, single-center	97 (48 / 49)	24	0 / 6.1	0 / 12.2	10.4/24.5	CD+TVMI+TVR 12.5 / 28.6
Adjedj et al. (2016)	Retrospective, single-center	453 (266 / 187)	26	2.3 / 0.5	2.3 / 1.6	8.6 / 7.5	Death+MI+TVR 13.9 / 11.2
Agarwal et al. (2017)	Retrospective, single-center	238 (48 / 190)	30	18 / 8	8.3 / 1.0	19 / 8	Death+Spont MI+TVR 40 / 16
Kang et al. In review.	Prospective, Multi-center	1334 (683 / 651)	34	1.3 / 0.6	0.7 / 3.2	5.7 / 3.7	Death+TV- MI+TVR 8.1 / 8.4

Courtis J, et al. Catheter Cardiovasc Interv 2008;71(4):541-8,

Lindstaedt M et al. Clin Cardiol 2010;33(2):77-83

Adjedj J et al. Circulation 2016;133(5):502-8

Agarwal SK et al. J Invasive Cardiol. 2017;29(11)371-6.

MACE (Death, MI, and TVR)

Study **Odds ratio (95% CI)**

Courtis et al. 2008 5.88 (1.51-22.85)

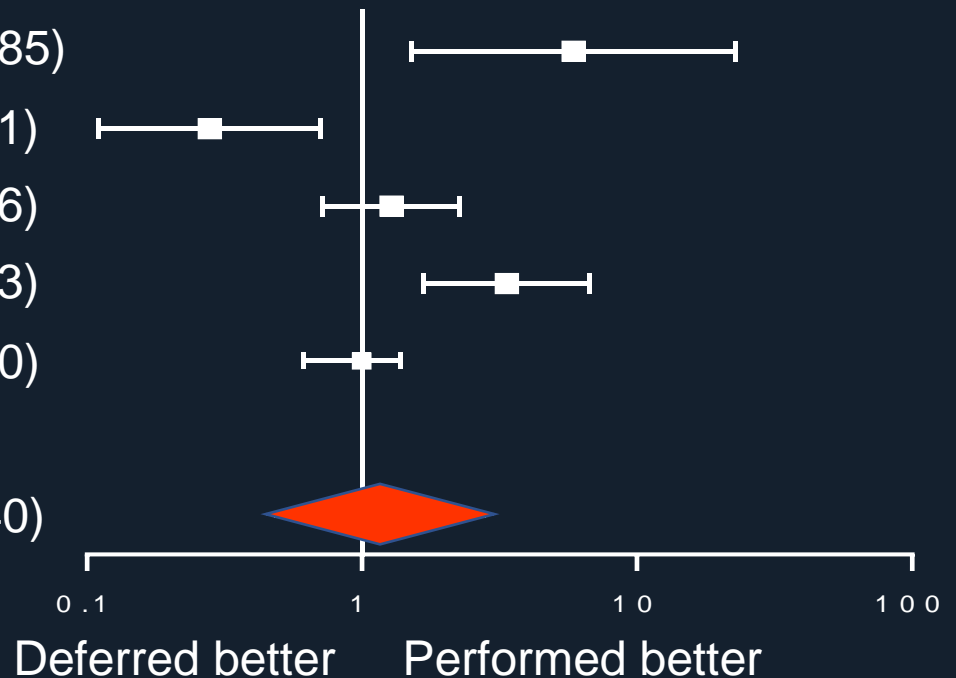
Lindstaedt et al. 2010 0.28 (0.11-0.71)

Adjedj et al. 2016 1.28 (0.72-2.26)

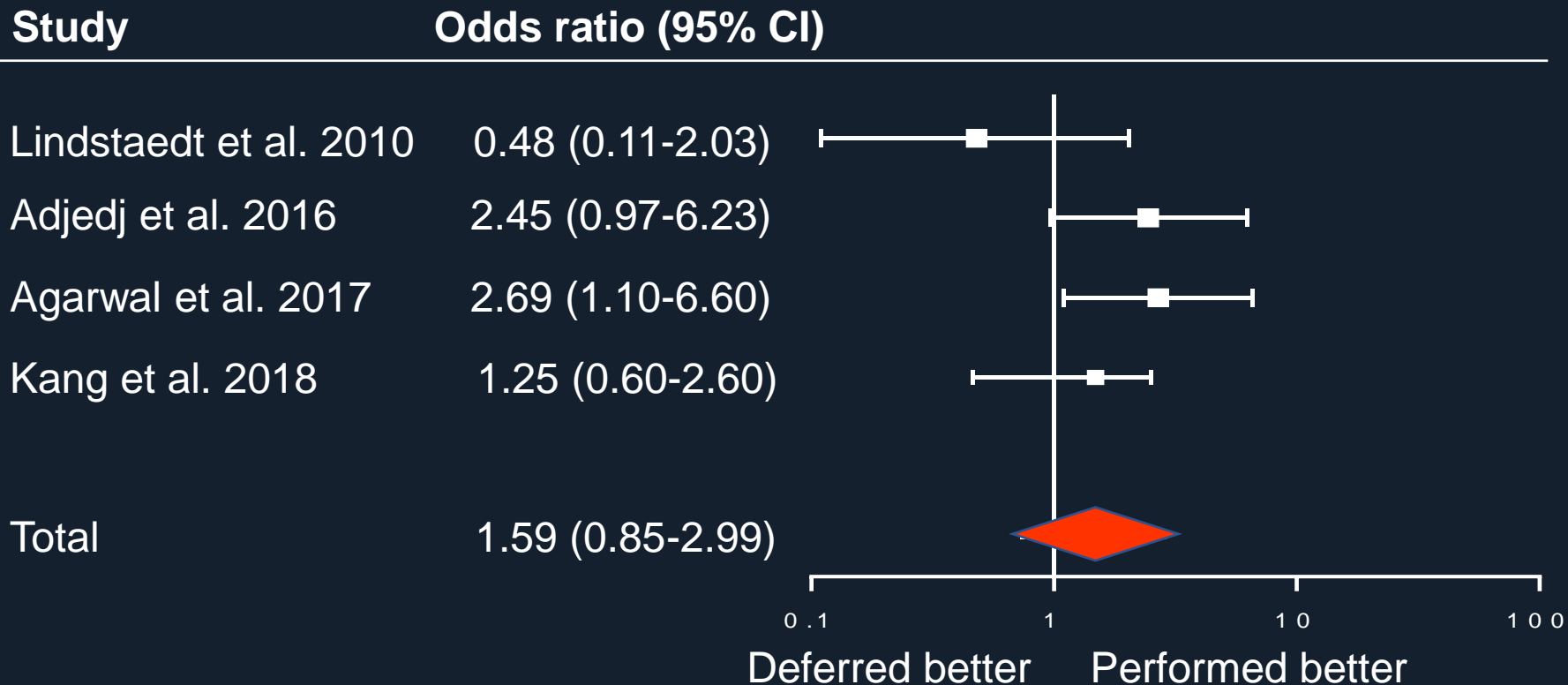
Agarwal et al. 2017 3.36 (1.68-6.73)

Kang et al. 2018 0.95 (0.64-1.40)

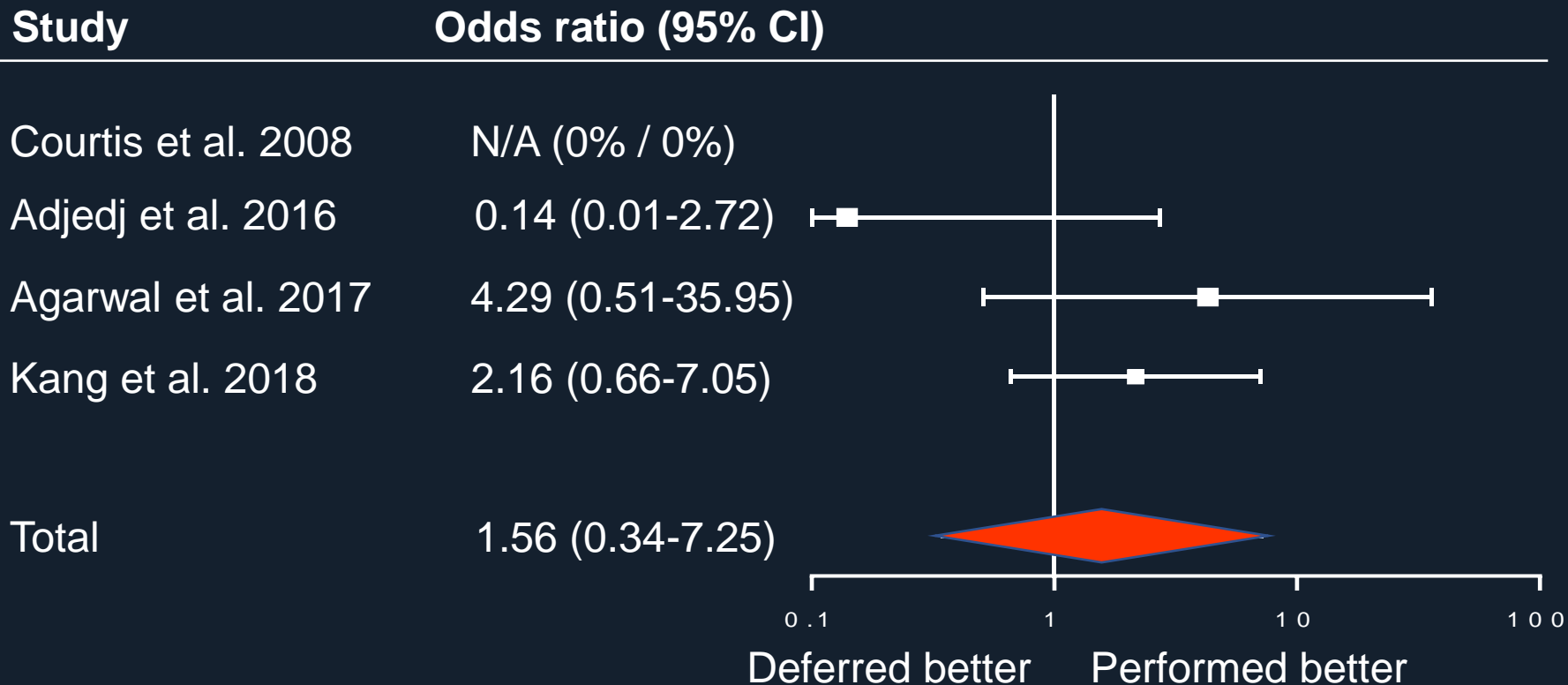
Total 1.37 (0.64-1.40)



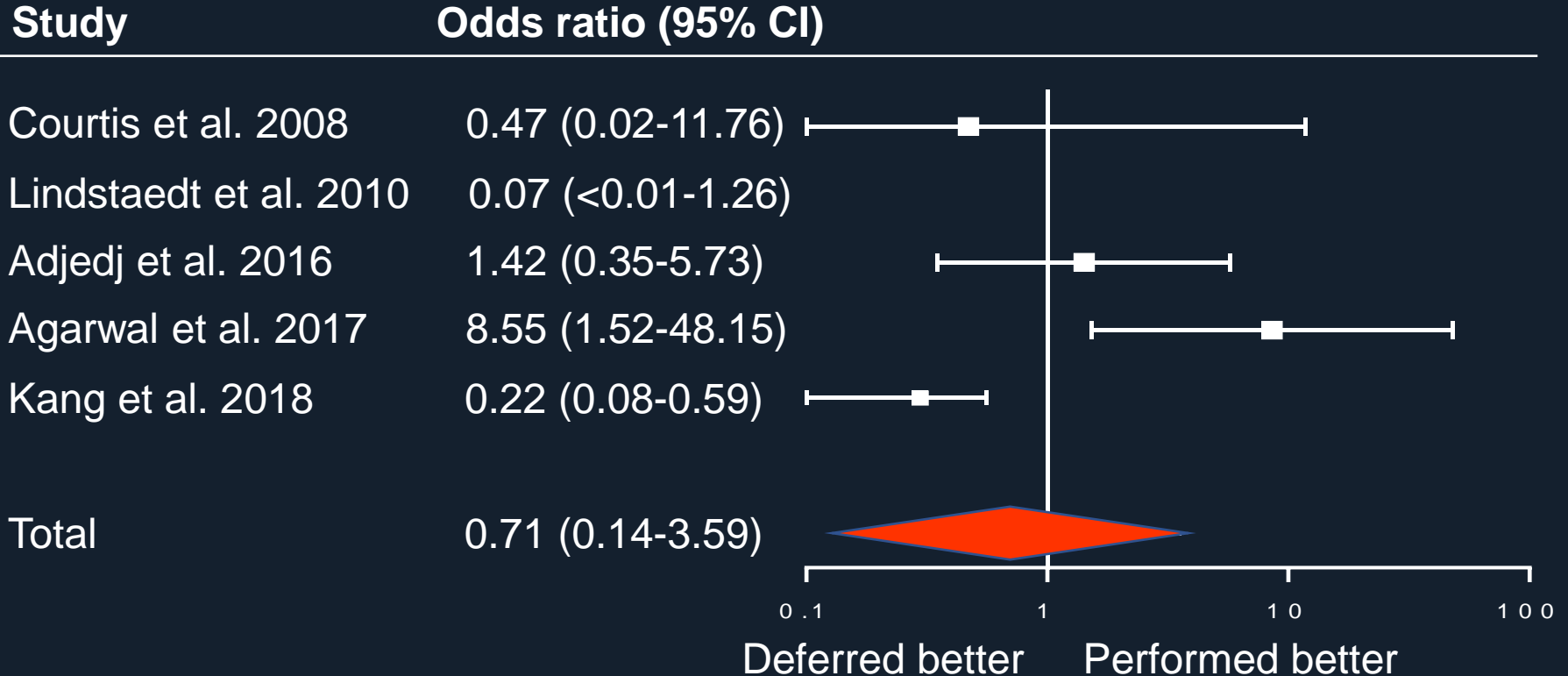
Death



Cardiac Death



Myocardial infarction



Death or MI

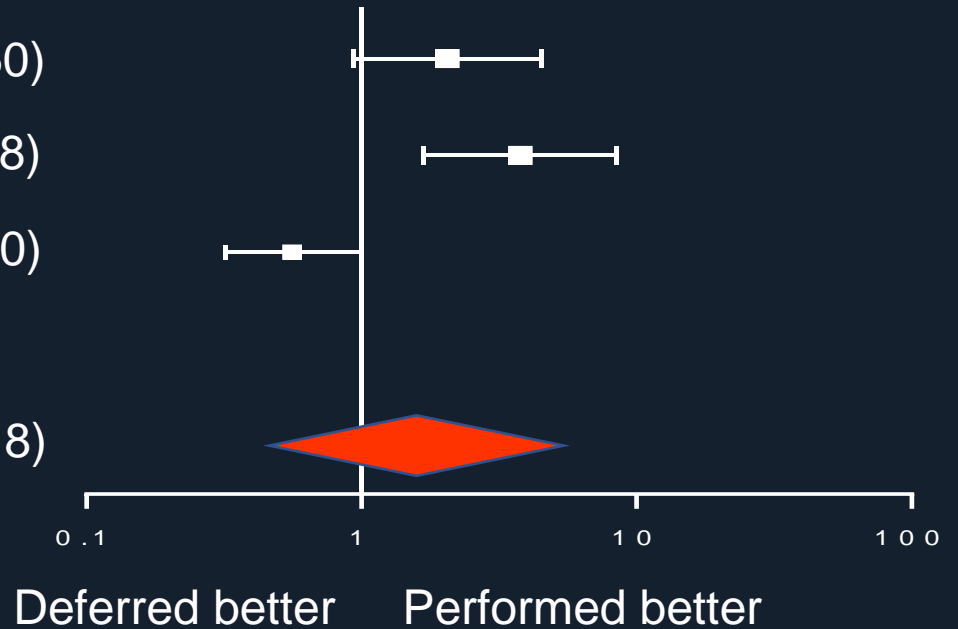
Study **Odds ratio (95% CI)**

Adjedj et al. 2016 2.05 (0.93-4.50)

Agarwal et al. 2017 3.78 (1.68-8.48)

Kang et al. 2018 0.56 (0.32-1.00)

Total 1.59 (0.49-5.18)



TVR

Study **Odds ratio (95% CI)**

Courtis et al. 2008 5.88 (01.51-22.85)

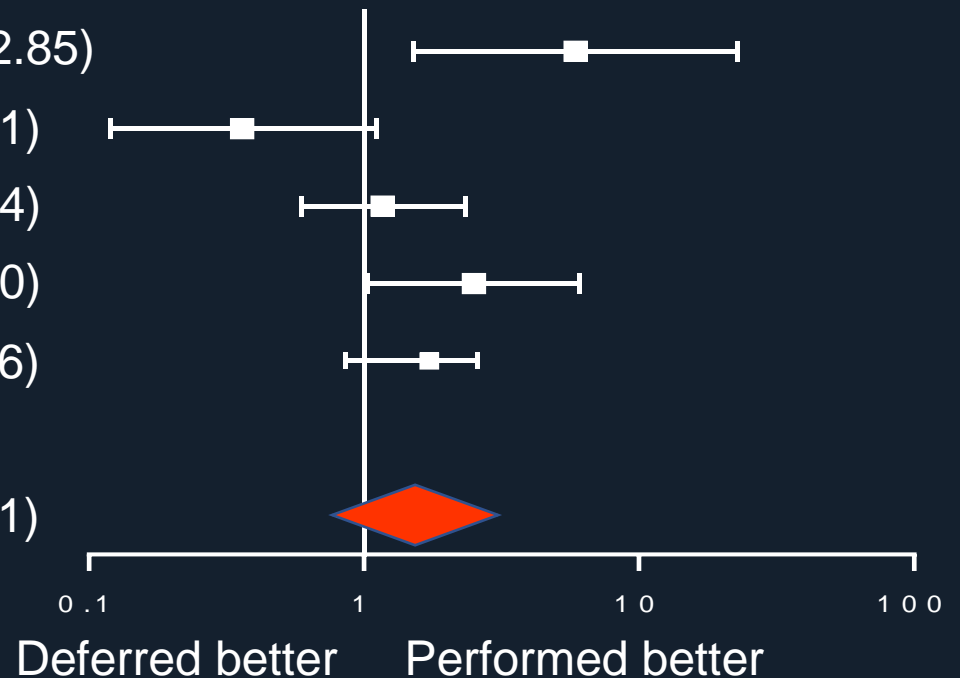
Lindstaedt et al. 2010 0.36 (0.12-1.11)

Adjedj et al. 2016 1.17 (0.59-2.34)

Agarwal et al. 2017 2.51 (1.03-6.10)

Kang et al. 2018 1.58 (0.94-2.66)

Total 1.51 (0.79-2.91)

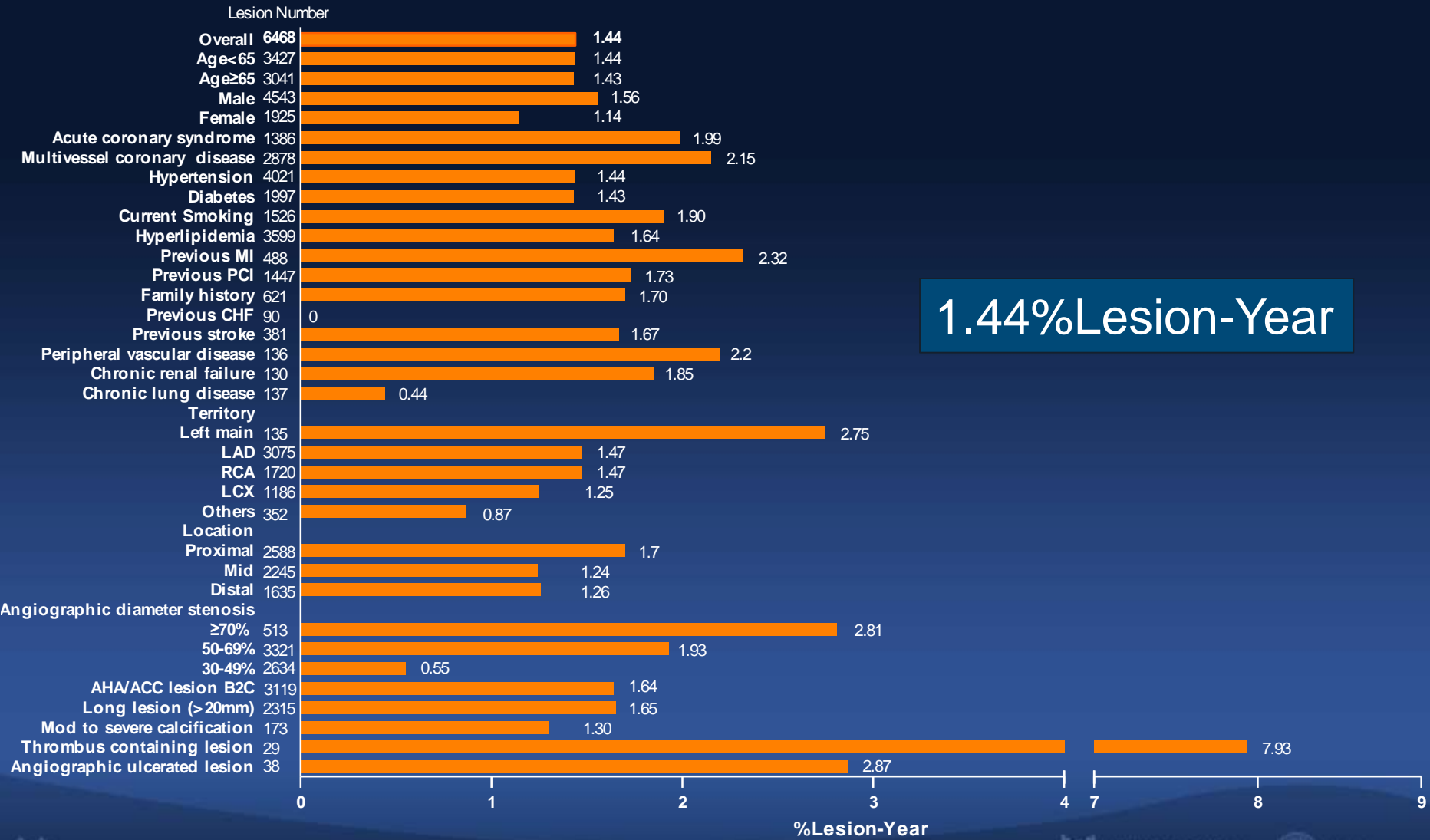


Conclusion

- Large prospective multicenter registry (IRIS-FFR) and Meta-analysis demonstrated that the revascularization was not associated with better clinical outcomes for the coronary stenoses with grey zone FFR (0.76~0.80).
- Medical treatment of lesions with grey zone FFR would be a reasonable and safe strategy.

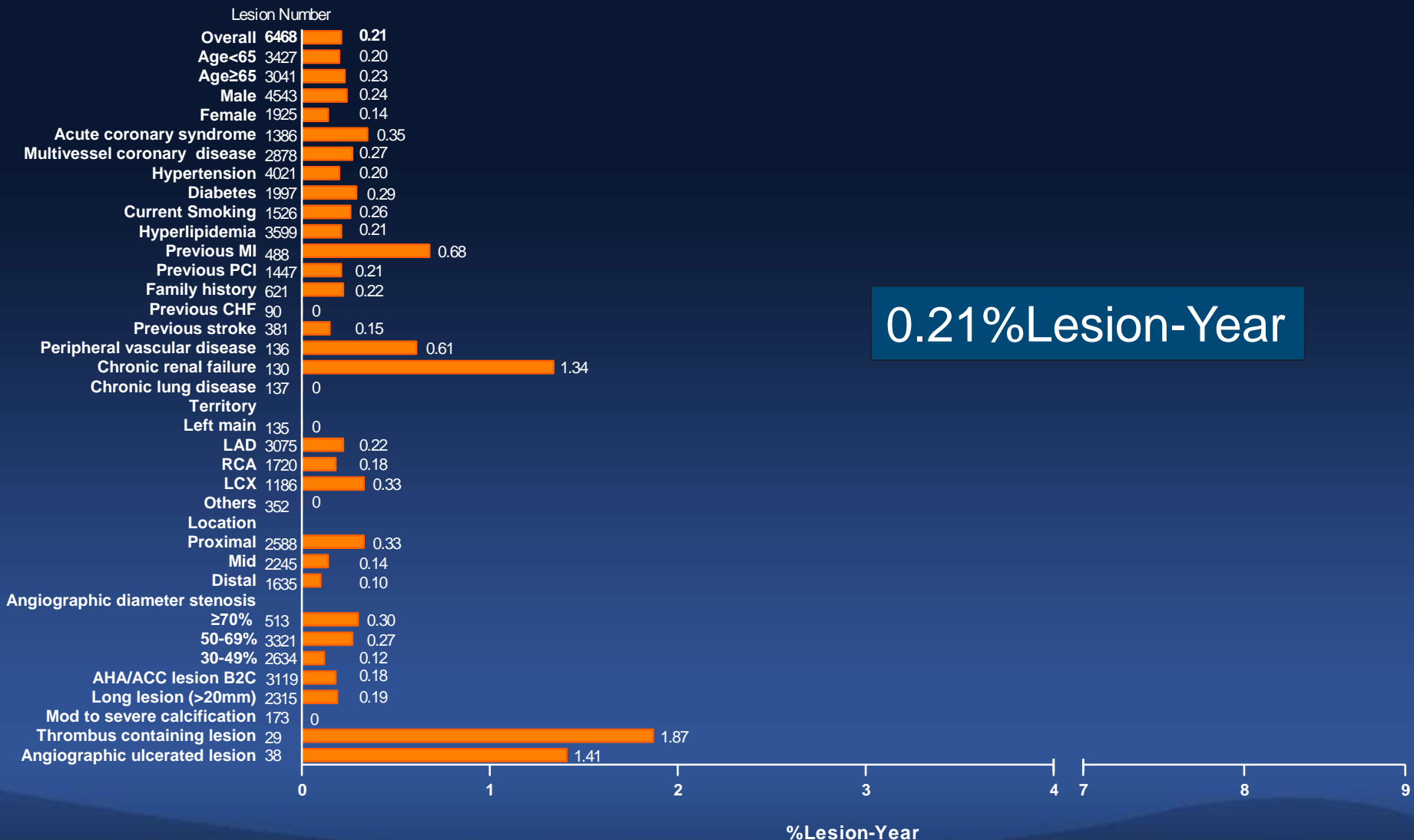
However,

Incidence Rate of Deferred Lesion Failure



1.44% Lesion-Year

Incidence Rate of Cardiac Death/MI





Thank You !!

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