FFR vs. IVUS to Guide PCI

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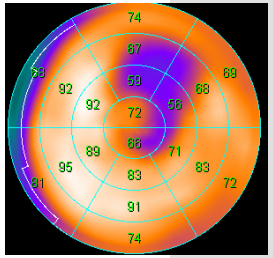
Disclosure Statement of Financial Interest

Within the past 12 months, I, [Bon-Kwon Koo] have had a financial interest/arrangement or affiliation with the organizations listed below:

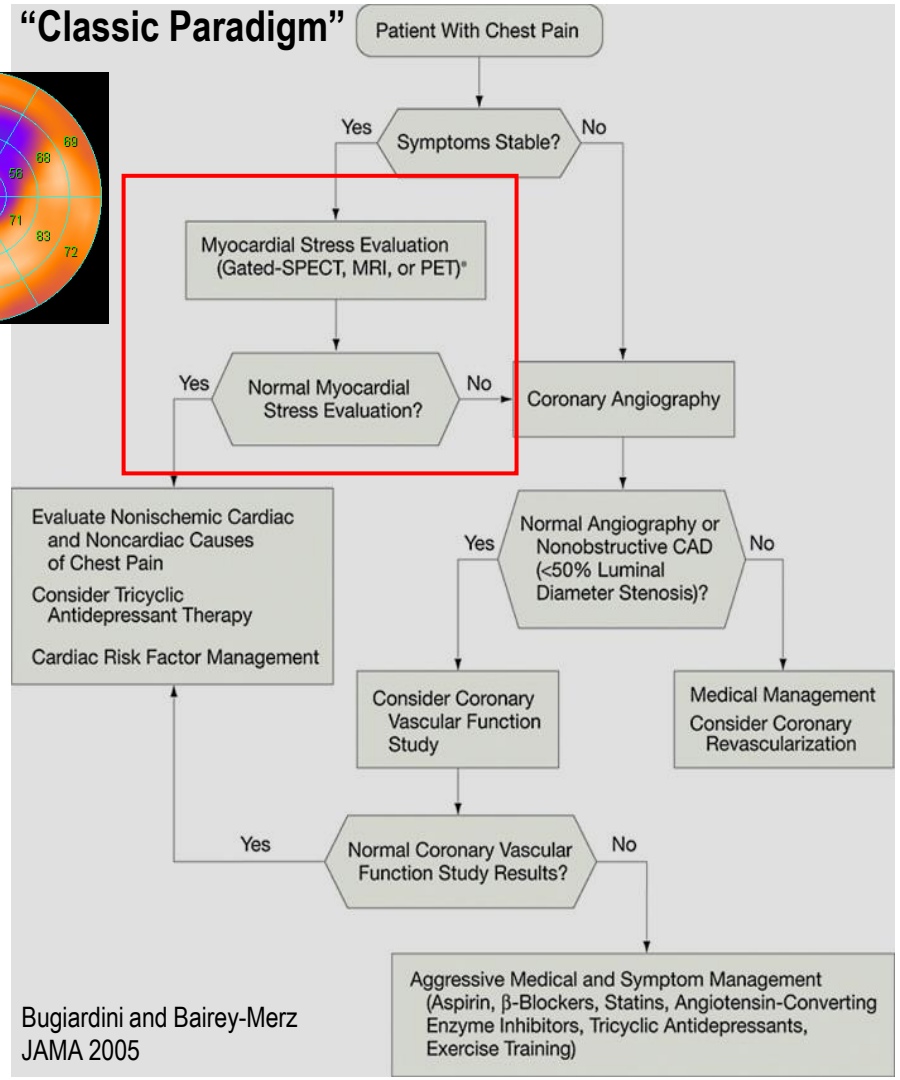
- Grant/Research Support: Institutional Research Grants from Abbott, Philips, and HeartFlow

Basics of CAD management:

Find and Fix "ISCHEMIA"



"Classic Paradigm"



Bugiardini and Bairey-Merz
JAMA 2005

2018 ESC/EACTS Guidelines on myocardial revascularization

The Task Force on myocardial revascularization of the European Society of Cardiology (ESC) and European Association for Cardio-Thoracic Surgery (EACTS)

Developed with the special contribution of the European Association for Percutaneous Cardiovascular Interventions (EAPCI

Recommendations on functional testing and intravascular imaging for lesion assessment

Recommendations	Class[a]	Level[b]
When evidence of ischaemia is not available, FFR or iwFR are recommended to assess the haemodynamic relevance of intermediate-grade stenosis.[15,17,18,39]	I	A
FFR-guided PCI should be considered in patients with multivessel disease undergoing PCI.[29,31]	IIa	B
IVUS should be considered to assess the severity of unprotected left main lesions.[35–37]	IIa	B

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CLINICAL PRACTICE GUIDELINE: FULL TEXT

2021 ACC/AHA/SCAI Guideline for Coronary Artery Revascularization

A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines

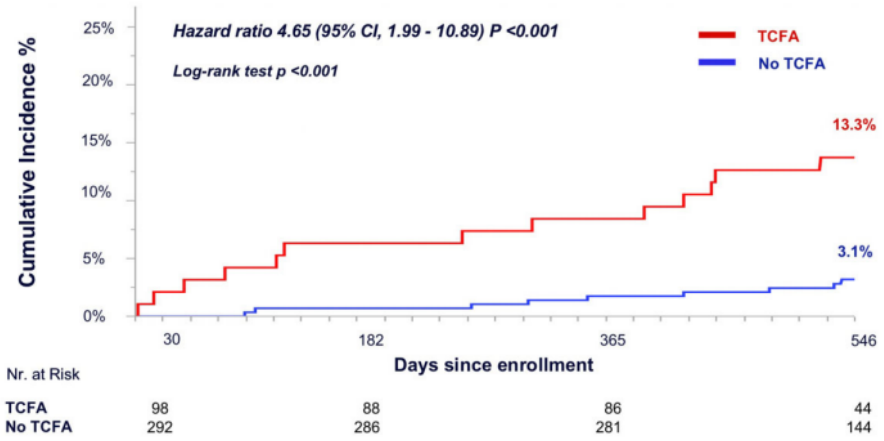
4.3. Use of Coronary Physiology to Guide Revascularization With PCI

Recommendations for the Use of Coronary Physiology to Guide Revascularization With PCI
Referenced studies that support the recommendations are summarized in Online Data Supplement 5.

COR	LOE	RECOMMENDATIONS
1	A	1. In patients with angina or an anginal equivalent, undocumented ischemia, and angiographically intermediate stenoses, the use of fractional flow reserve (FFR) or instantaneous wave-free ratio (iFR) is recommended to guide the decision to proceed with PCI (1-6).
3: No benefit	B-R	2. In stable patients with angiographically intermediate stenoses and FFR >0.80 or iFR >0.89, PCI should not be performed (7-10).

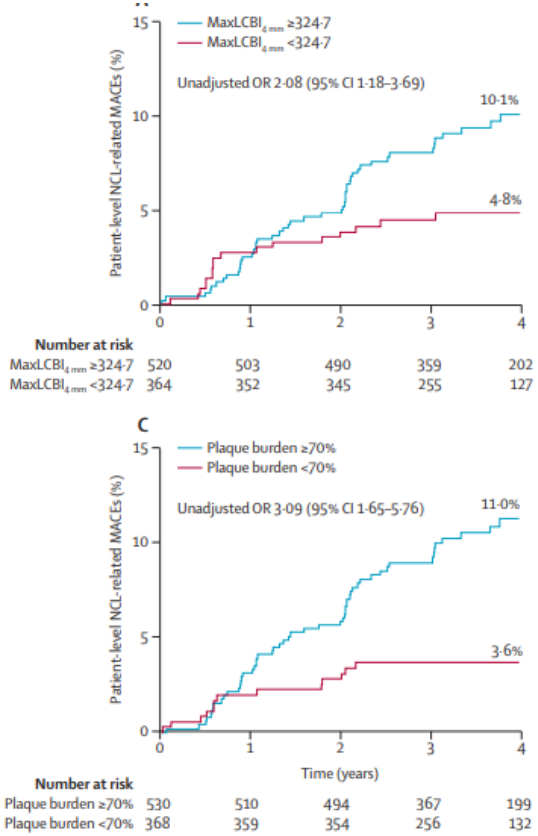
Vulnerability also matters!

COMBINE OCT-FFR



Kedhi E, et al, Eur Heart J 2021

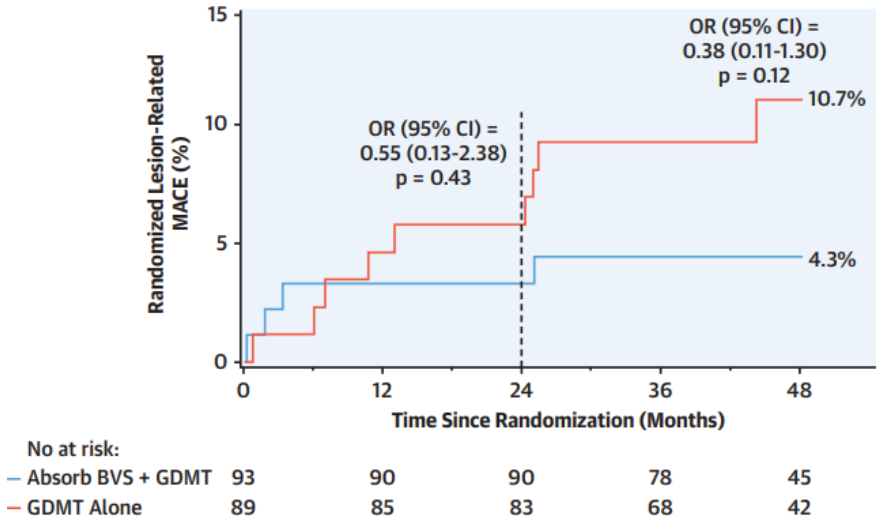
PROSPECT II



Erlinge D, et al. Lancet 2021

PROSPECT II ABSORB

(Target lesion-related MACE)



Stone GW, et al,JACC 2020

Yang SH and Koo BK. JACC Asia 2023 in press

Physiology vs. Imaging: Head to Head comparison

JACC: CARDIOVASCULAR INTERVENTIONS VOL. 13, NO. 1, 2020

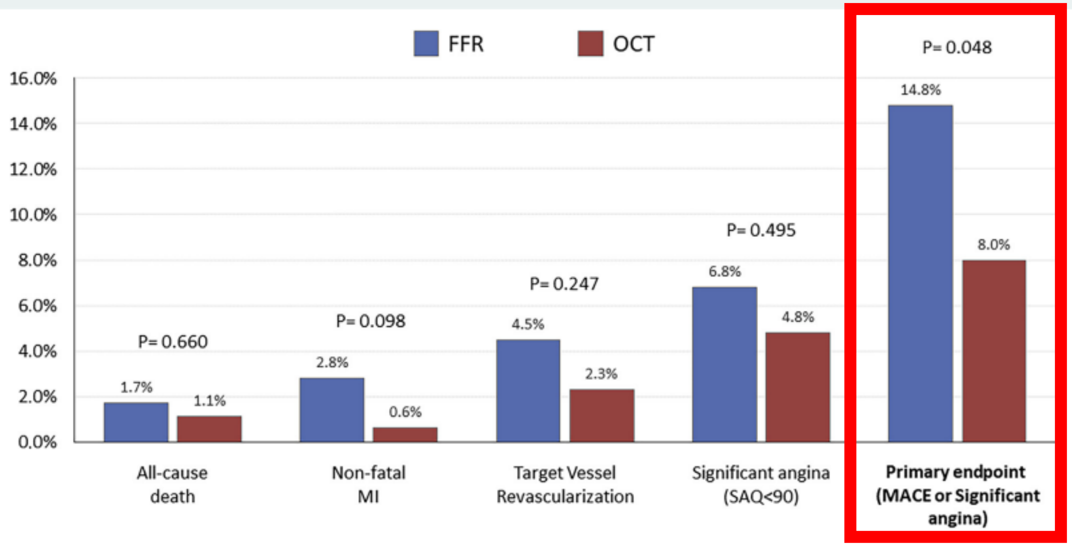
PUBLISHED BY ELSEVIER

Fractional Flow Reserve or Optical Coherence Tomography to Guide Management of Angiographically Intermediate Coronary Stenosis

A Single-Center Trial

Francesco Burzotta, MD, PhD,[a,b,*] Antonio Maria Leone, MD, PhD,[a,*] Cristina Aurigemma, MD, PhD,[a]

FIGURE 2 Primary Study Endpoint and Its Individual Components at 13-Month Follow-Up



FFR = fractional flow reserve; MACE = major adverse cardiac event(s); MI = myocardial infarction; OCT = optical coherence tomography; SAQ = Seattle Angina Questionnaire.

TABLE 1 Baseline Clinical, Angiographic, and Procedural Characteristics

	FFR (n = 176)	OCT (n = 174)	p Value
Demographics			
Age, yrs	68 ± 10	69 ± 9	0.51
Male	126 (71.6)	135 (77.6)	0.22
BMI, kg/m^2	27 ± 10	27 ± 5	0.74
Risk factors			
Diabetes	61 (34.7)	63 (36.2)	0.82
Hypertension	148 (84.1)	151 (86.8)	0.54
Dyslipidemia	120 (68.2)	130 (84.7)	0.19
Smoking	70 (39.8)	66 (37.9)	0.74
Chronic kidney disease	32 (18.2)	30 (17.2)	0.90
Cardiac history			
Previous PCI	73 (41.5)	76 (43.7)	0.74
Previous CABG	4 (2.3)	5 (2.9)	0.75
Previous MI	33 (18.8)	52 (29.9)	0.02
Clinical presentation			
Stable ischemic heart disease	139 (79.0)	143 (82.2)	0.50
Acute coronary syndrome	37 (21.0)	31 (17.8)	
LVEF, %	60 ± 8	56 ± 9	0.74
Baseline angiographic features			
Multivessel disease	92 (52.3)	83 (47.7)	0.45
Investigated lesion location			0.02
LAD	150 (66.7)	134 (60.6)	
LCx	37 (16.4)	27 (12.2)	
RCA	[illegible]	[illegible]	
Management			
Patients treated with PCI	57 (32.4)	92 (52.9)	<0.001
Number of balloons per patient	[illegible]	[illegible]	<0.001
Number of stents per patient	0.33 ± 0.57	0.64 ± 0.70	<0.001
Optimal result (according to study protocol) obtained	19 (47.5)	55 (64.7)	0.001
Discharge therapy			
Aspirin	166 (94.3)	163 (93.6)	0.83
$P2Y_{12}$ inhibitors	115 (65.3)	133 (76.4)	0.02
Beta-blockers	[illegible]	[illegible]	[illegible]
Calcium-channel blockers	56 (31.8)	55 (31.6)	0.97
Statins	152 (86.3)	161 (92.5)	0.08
Nitrates	25 (14.2)	19 (10.9)	0.42
Ranolazine	31 (17.6)	24 (13.7)	0.38

SNUH Seoul National University Hospital Cardiovascular Center

FFR vs. IVUS for intermediate lesions: FLAVOUR trial

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 SEPTEMBER 1, 2022 VOL. 387 NO. 9

Fractional Flow Reserve or Intravascular Ultrasonography to Guide PCI

B.-K. Koo, X. Hu, J. Kang, J. Zhang, J. Jiang, J.-Y. Hahn, C.-W. Nam, J.-H. Doh, B.-K. Lee, W. Kim, J. Huang, F. Jiang, H. Zhou, P. Chen, L. Tang, W. Jiang, X. Chen, W. He, S.-G. Ahn, M.-H. Yoon, U. Kim, J.-M. Lee, D. Hwang, Y.-J. Ki, E.-S. Shin, H.-S. Kim, S.-J. Tahk, and J. Wang, for the FLAVOUR Investigators*

ABSTRACT

BACKGROUND

In patients with coronary artery disease who are being evaluated for percutaneous coronary intervention (PCI), procedures can be guided by fractional flow reserve (FFR) or intravascular ultrasonography (IVUS) for decision making regarding revascularization and stent implantation. However, the differences in clinical outcomes when only one method is used for both purposes are unclear

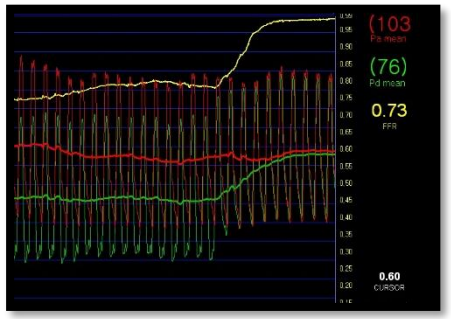
The authors' full names, academic degrees, and affiliations are listed in the Appendix. Dr. Wang can be contacted at wja@zju.edu.cn or at the Department of Cardiology, Second Affiliated Hospital, Zhejiang University School of Medicine,

- 18 sites from Korea and China
- Principal Investigators: Bon-Kwon Koo, JianAn Wang, Seung-Jea Tahk

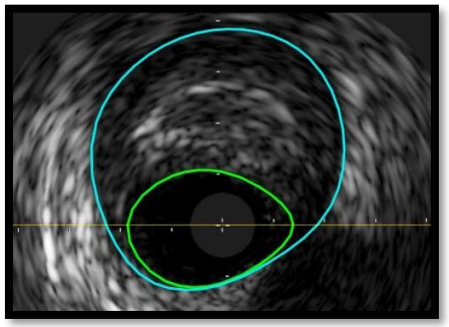
Patients with de novo intermediate stenosis (40-70% stenosis) eligible for PCI

Randomization

FFR-guided PCI



IVUS-guided PCI



Patient-oriented composite outcome* at 24 months after the index procedure

* Primary Endpoint: a composite of death from any cause, myocardial infarction, and any revascularization

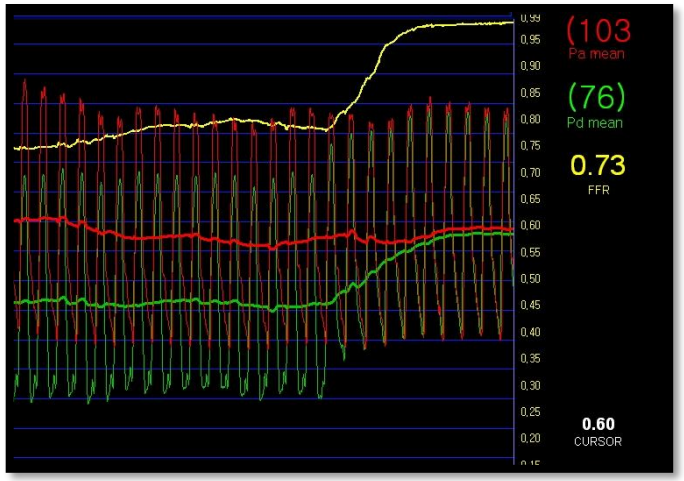
Objective

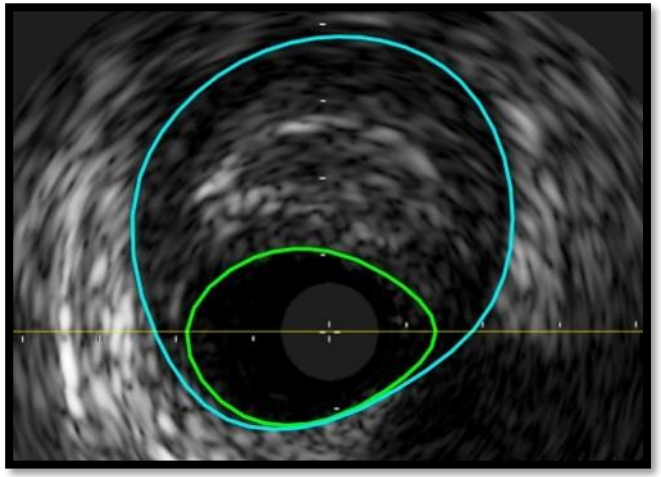
- To compare the efficacy of FFR-guided PCI strategy with IVUS-guided PCI strategy in patients with intermediate coronary stenosis.

Working Hypothesis

*The FFR-guided PCI strategy will be **non-inferior** to the IVUS-guided PCI strategy*

in regard to clinical outcomes at 2 years after the index procedure.





Indications for PCI & PCI Optimization

FFR-guided PCI	IVUS-guided PCI
Indications for PCI	
FFR ≤ 0.80	Minimum lumen area (MLA) ≤ 3mm^2 or 3 < MLA ≤ 4mm^2 & Plaque burden > 70%
Criteria for optimal PCI	
Post-PCI FFR ≥ 0.88 or Post-PCI ΔFFR (FFR across the stent) < 0.05	Plaque burden at stent edge ≤ 55% Minimal stent area ≥ 5.5mm^2 or Minimal stent area ≥ distal reference lumen area

Koo BK, Hu X, Kang JH, et al. N Engl J Med 2022

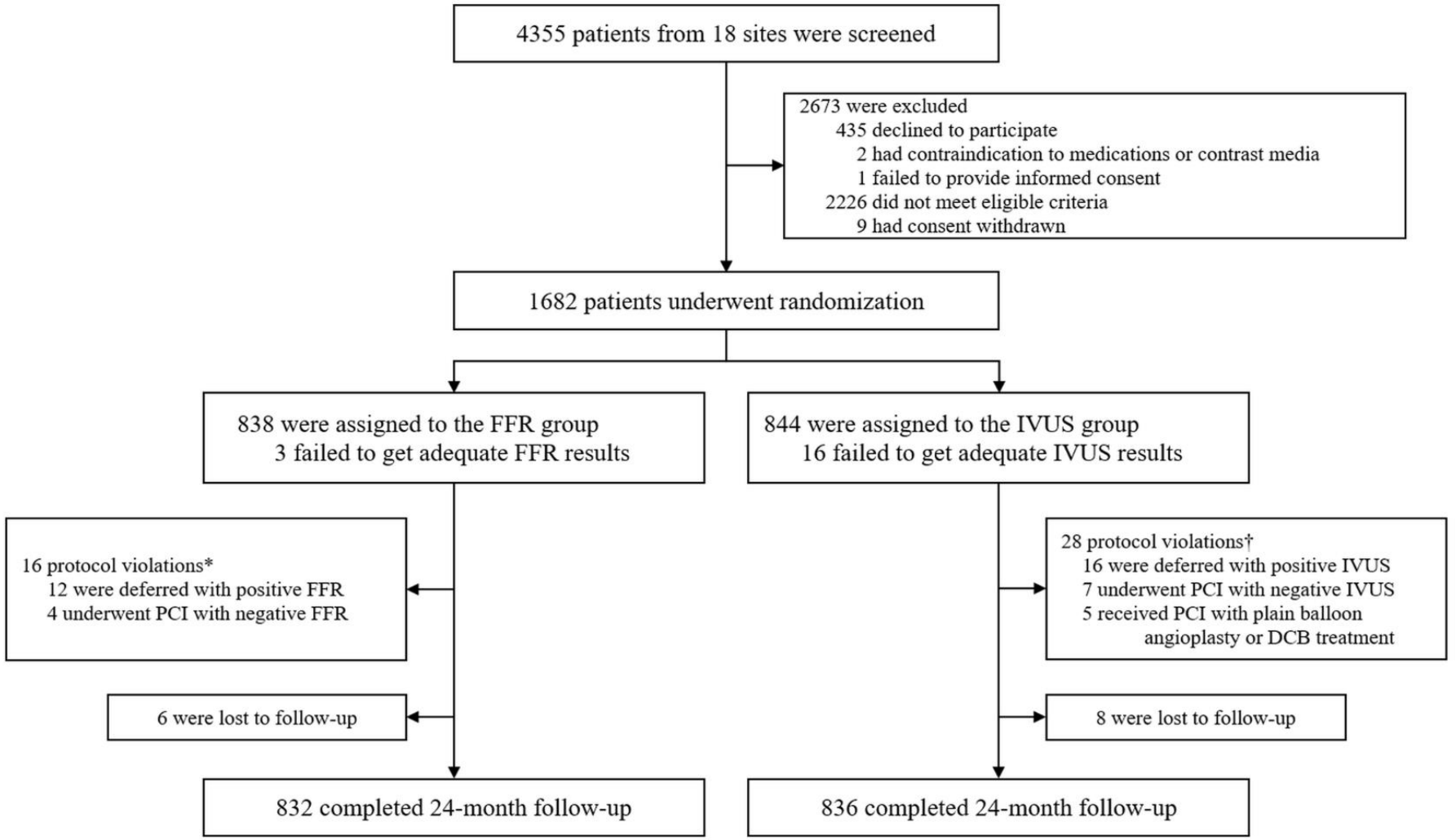
Endpoints and Sample Size Calculation

- **Endpoints**
  - **Primary Endpoint:** Patient-oriented composite outcome (POCO) at 24 months
    - A composite of death from any cause, myocardial infarction (MI), and any revascularization at 24 months
  - **Secondary Endpoints**
    - Individual components of the primary end point, number of stents used, stroke, and patient-reported outcomes measured with Seattle Angina Questionnaire (SAQ)

- **Sample size calculation**
  - Assumed 24-month POCO in the FFR-guided PCI group: 10.0%
  - Assumed 24-month POCO in the IVUS-guided PCI group: 12.0%
  - Type I error: 0.05, Power: 90%
  - Non-inferiority margin: 2.5%

A total of 1,700 patients was needed.

Study Flow

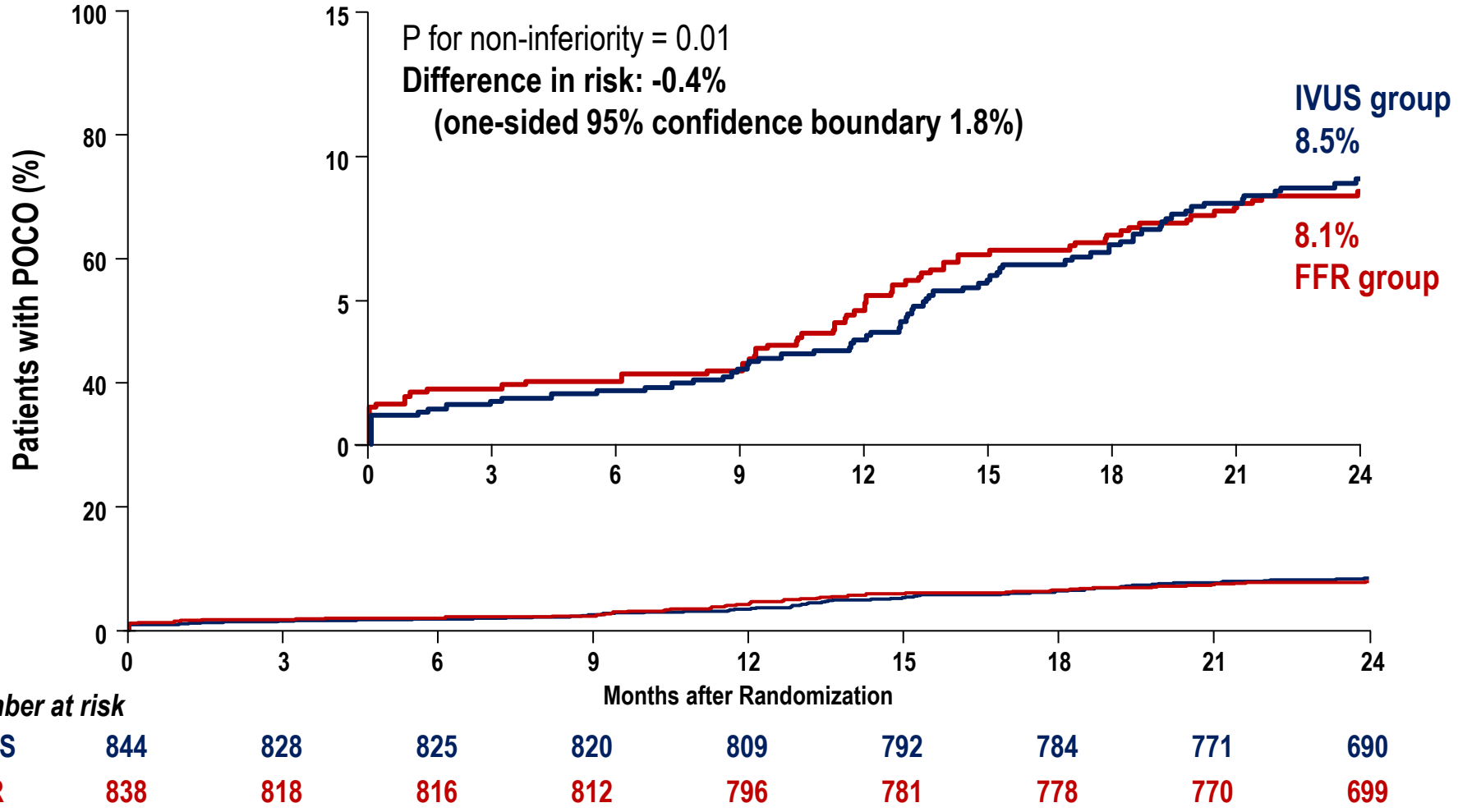


Koo BK, Hu X, Kang JH, et al. N Engl J Med 2022

Baseline Characteristics

	Total (N=1682)	FFR Group (N=838)	IVUS Group (N=844)	*P value*
Age, years	65.1±9.6	65.4±9.4	64.8±9.9	0.143
Male	1187 (70.6%)	584 (69.7%)	603 (71.4%)	0.461
Stable angina	1063 (63.2%)	519 (61.9%)	544 (64.5%)	0.432
Diabetes mellitus	554 (32.9%)	272 (32.5%)	282 (33.4%)	0.716
Target vessel QCA				
Reference vessel diameter, mm	3.0±0.5	3.0±0.5	3.0±0.5	0.784
Diameter stenosis, %	**56.8±10.1**	56.7±10.1	56.9±10.1	0.633
IVUS findings				
Minimal luminal area, mm^2			**3.4±1.3**	
Plaque burden, %			**70.1±10.2**	
FFR findings				
FFR		**0.83±0.09**		
PCI and Medications				
Target vessel PCI	831 (45.7%)	**305 (33.2%)**	**526 (58.4%)**	**<0.001**

Primary Outcome



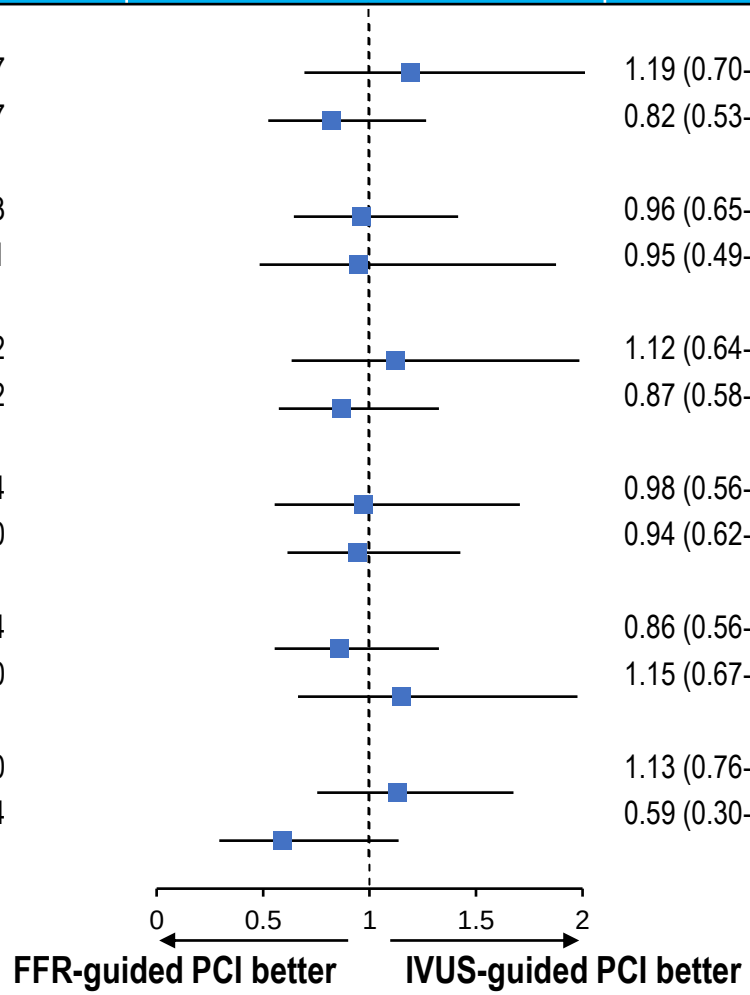
Number at risk

IVUS	844	828	825	820	809	792	784	771	690
FFR	838	818	816	812	796	781	778	770	699

* Primary Endpoint: death from any cause, myocardial infarction, and any revascularization

Subgroup Analysis

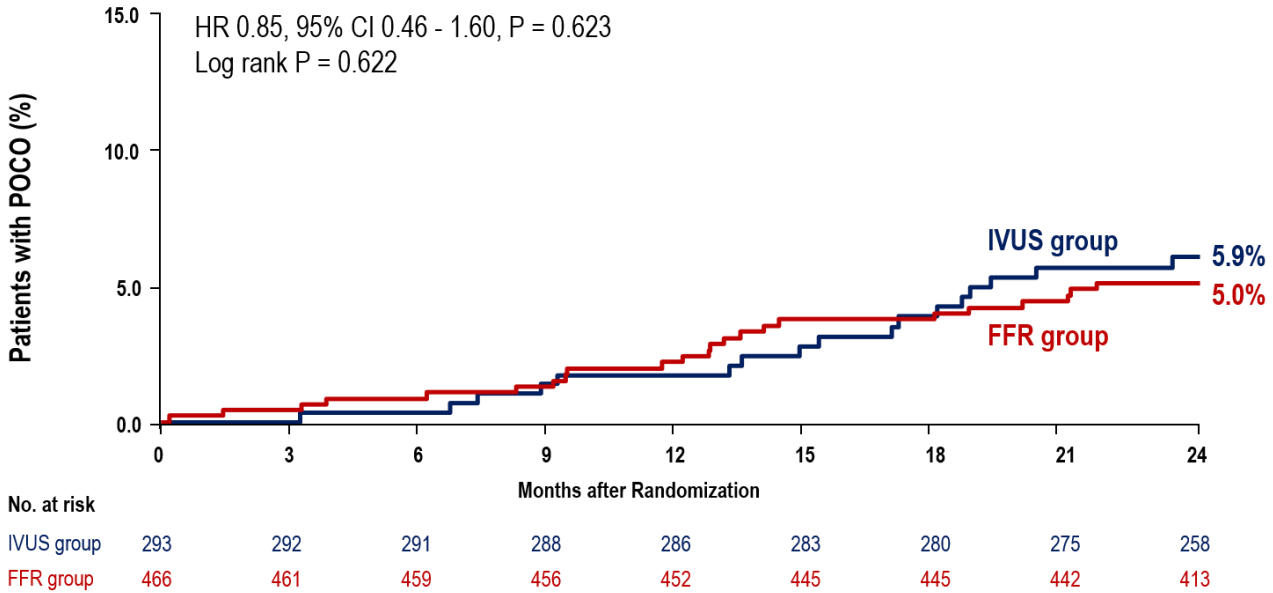
Subgroup	FFR group (events/patients)	IVUS group (events/patients)	Hazard Ratio (95% CI)
Age			
< 65 years	29/376	26/397	1.19 (0.70-2.02)
≥ 65 years	38/462	45/447	0.82 (0.53-1.26)
Sex			
Male	50/584	54/603	0.96 (0.65-1.41)
Female	17/254	17/241	0.95 (0.49-1.87)
Diabetes mellitus			
Yes	25/272	23/282	1.12 (0.64-1.98)
No	42/566	48/562	0.87 (0.58-1.32)
Clinical presentation as ACS			
Yes	25/252	25/244	0.98 (0.56-1.70)
No	42/586	46/600	0.94 (0.62-1.42)
LAD as the target vessel			
Yes	40/573	45/554	0.86 (0.56-1.32)
No	27/265	26/290	1.15 (0.67-1.97)
Multivessel coronary artery disease			
Yes	53/445	46/430	1.13 (0.76-1.67)
No	14/393	25/414	0.59 (0.30-1.13)



No significant interaction between the treatment effect and key subgroups

Primary Outcome According to Treatment

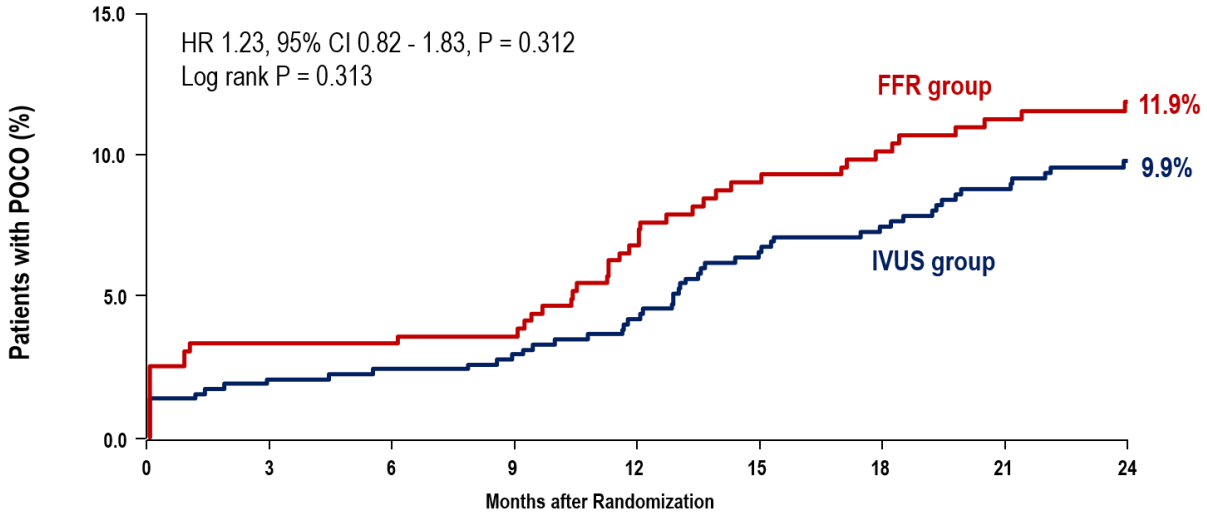
Medical treatment



No. at risk

IVUS group	293	292	291	288	286	283	280	275	258
FFR group	466	461	459	456	452	445	445	442	413

PCI



No. at risk

IVUS group	551	536	534	532	523	509	504	496	432
FFR group	372	357	357	356	344	336	333	328	286

Indications for PCI & PCI Optimization

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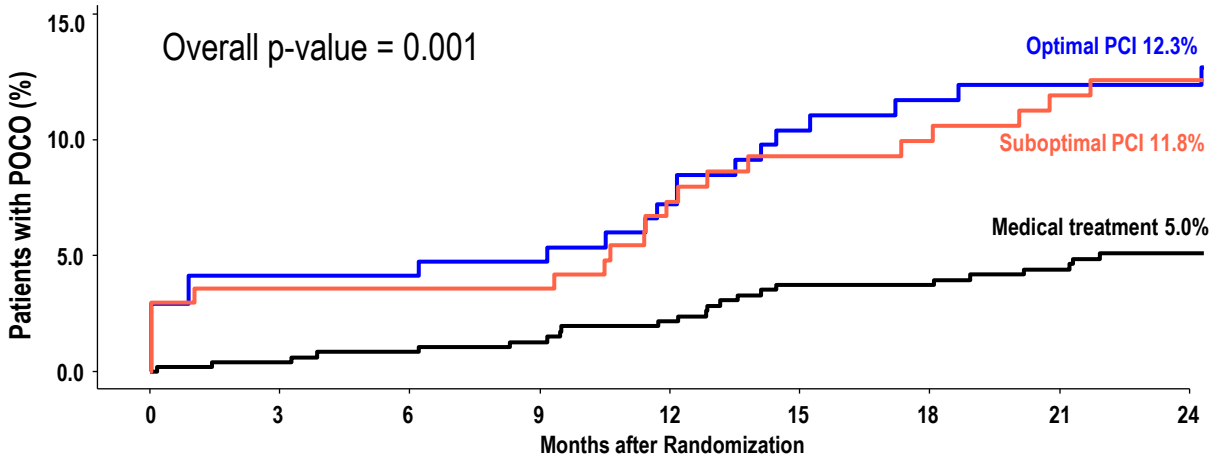
Post-PCI FFR ≥ 0.88 or Post-PCI ΔFFR (FFR across the stent) < 0.05	Plaque burden at stent edge ≤ 55% Minimal stent area ≥ $5.5mm^2$ or Minimal stent area ≥ distal reference lumen area

Optimal PCI vs. Suboptimal PCI

Optimal PCI: FFR-guided PCI 50.1%, IVUS-guided PCI 54.8%

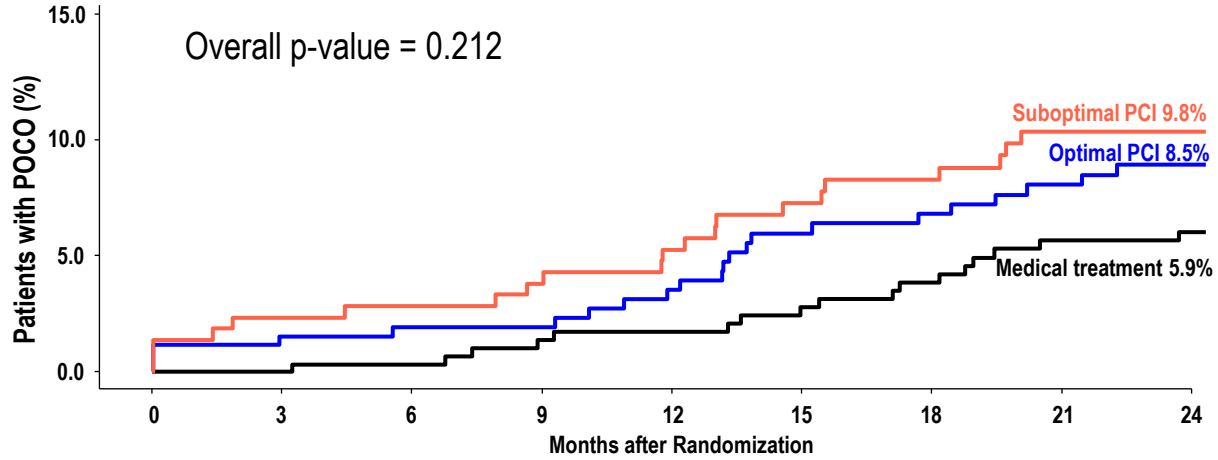
FFR-guided PCI



No. at risk

MT	466	461	459	456	452	445	445	442	413
Optimal	172	165	165	164	160	155	153	152	135
Suboptimal	171	163	163	163	157	154	153	150	129

IVUS-guided PCI

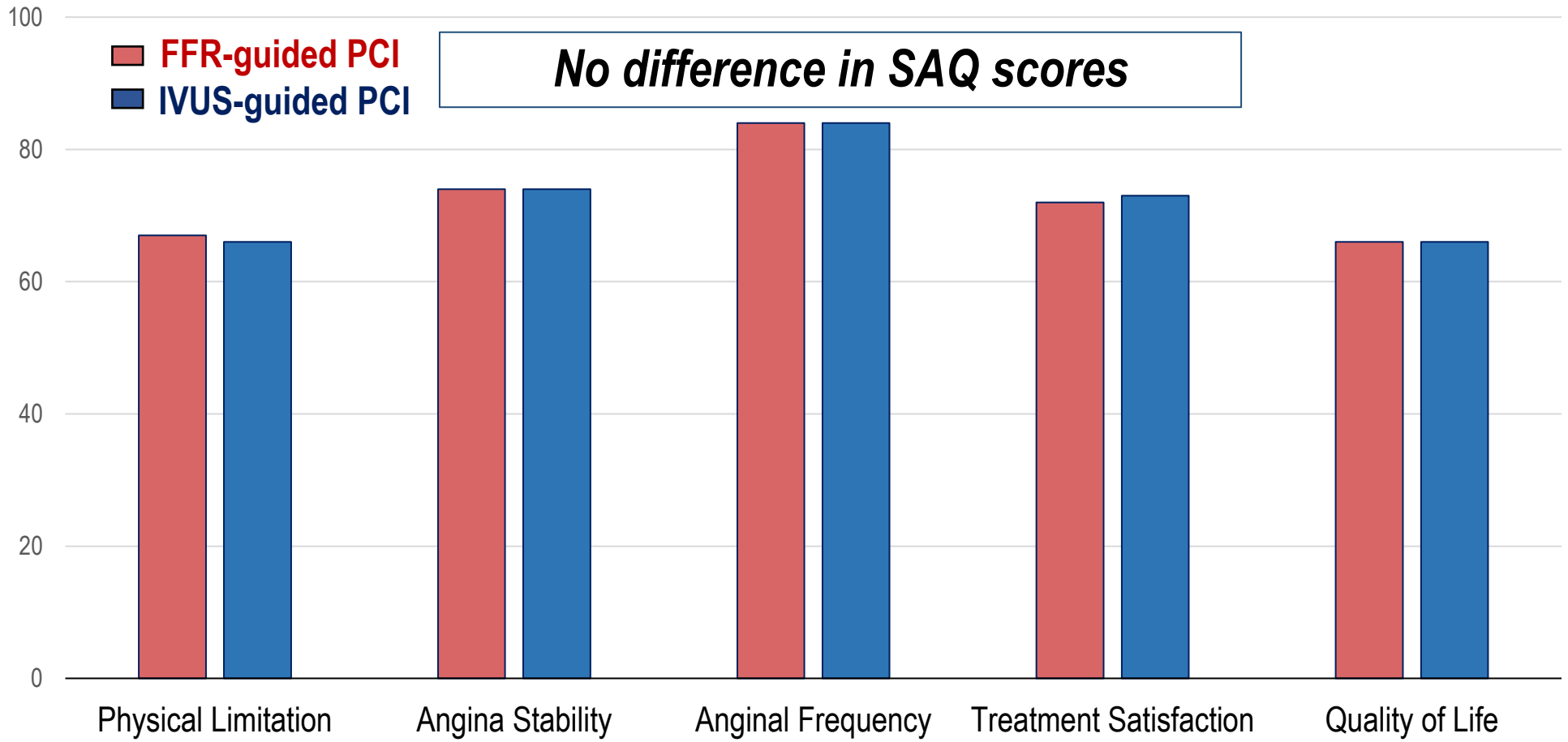


No. at risk

MT	293	292	291	288	286	283	280	275	258
Optimal	261	255	254	254	249	242	240	237	211
Suboptimal	215	209	208	206	203	198	196	192	162

Patient-Reported Outcomes

Seattle Angina Questionnaire (SAQ) scores at follow-up



FLAVOUR trial Summary

In patients with intermediate lesions, FFR in comparison with IVUS

- PCI: 43.2% less in target vessels and 32% less in patient-level
- DAPT: 19.8% less of dual antiplatelet therapy use
- No difference (non-inferior) in clinical outcomes
- No difference in patient-reported quality of life

Limitations

- **Intermediate coronary stenosis**: The impact of FFR and IVUS guidance can be different in patients with more severe stenosis.
- **FFR and IVUS**: The role of non-hyperemic pressure ratios, image-derived FFR, OCT or NIRS-IVUS needs further investigation.
- **Criteria for PCI**: Local hemodynamic significance and features of plaque vulnerability were not used.

Take Home Messages

In patients with *intermediate coronary stenosis*,

- FFR-guided PCI was noninferior to IVUS-guided PCI with respect to a composite of death from any cause, MI, and any revascularization at 24 months after the index procedure.
- FFR-guided PCI was associated with a lower rate of stent implantation.
- No difference was observed in patient-reported outcomes between the two strategies.