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Editorial

Routine Pressure Wire Assessment at Time of Diagnostic Angiography

Is It Ready for Prime Time?

Eric Van Belle, MD, PhD; Gilles Rioufol, MD, PhD; Patrick Dupouy, MD

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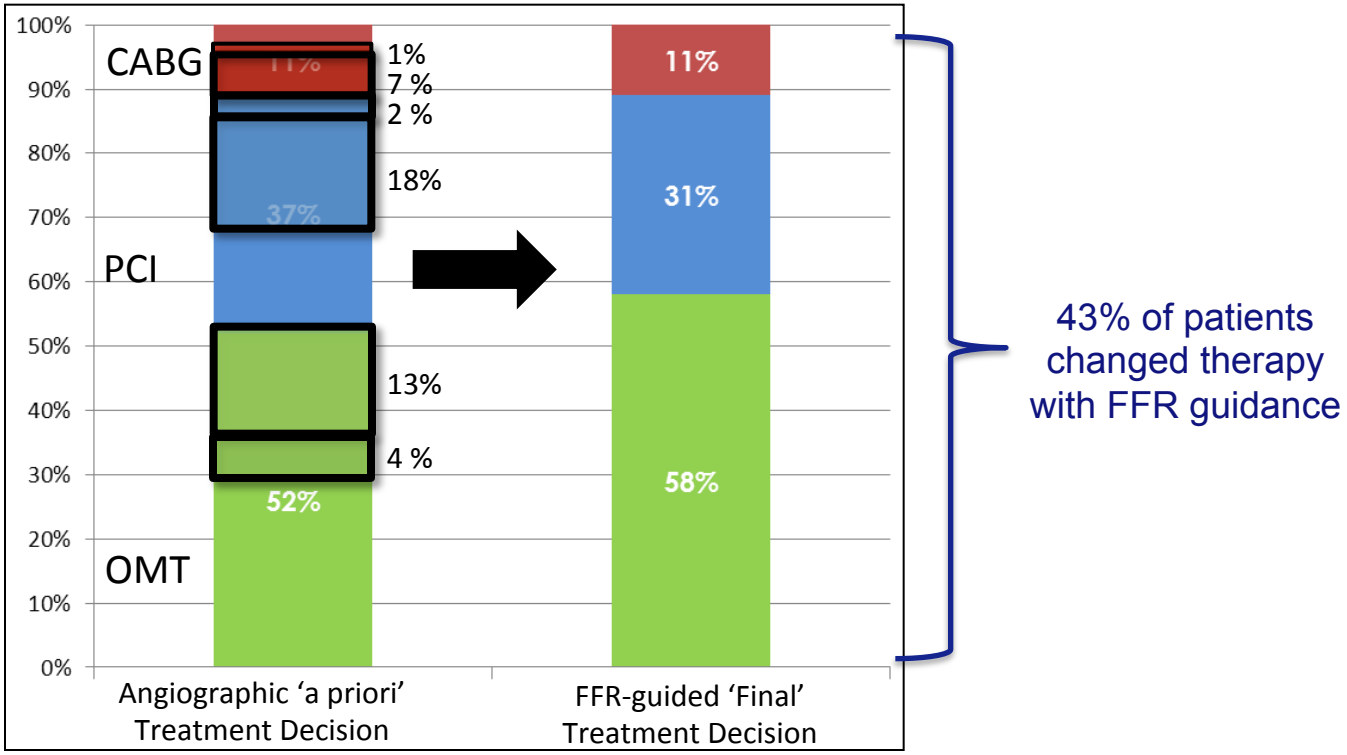
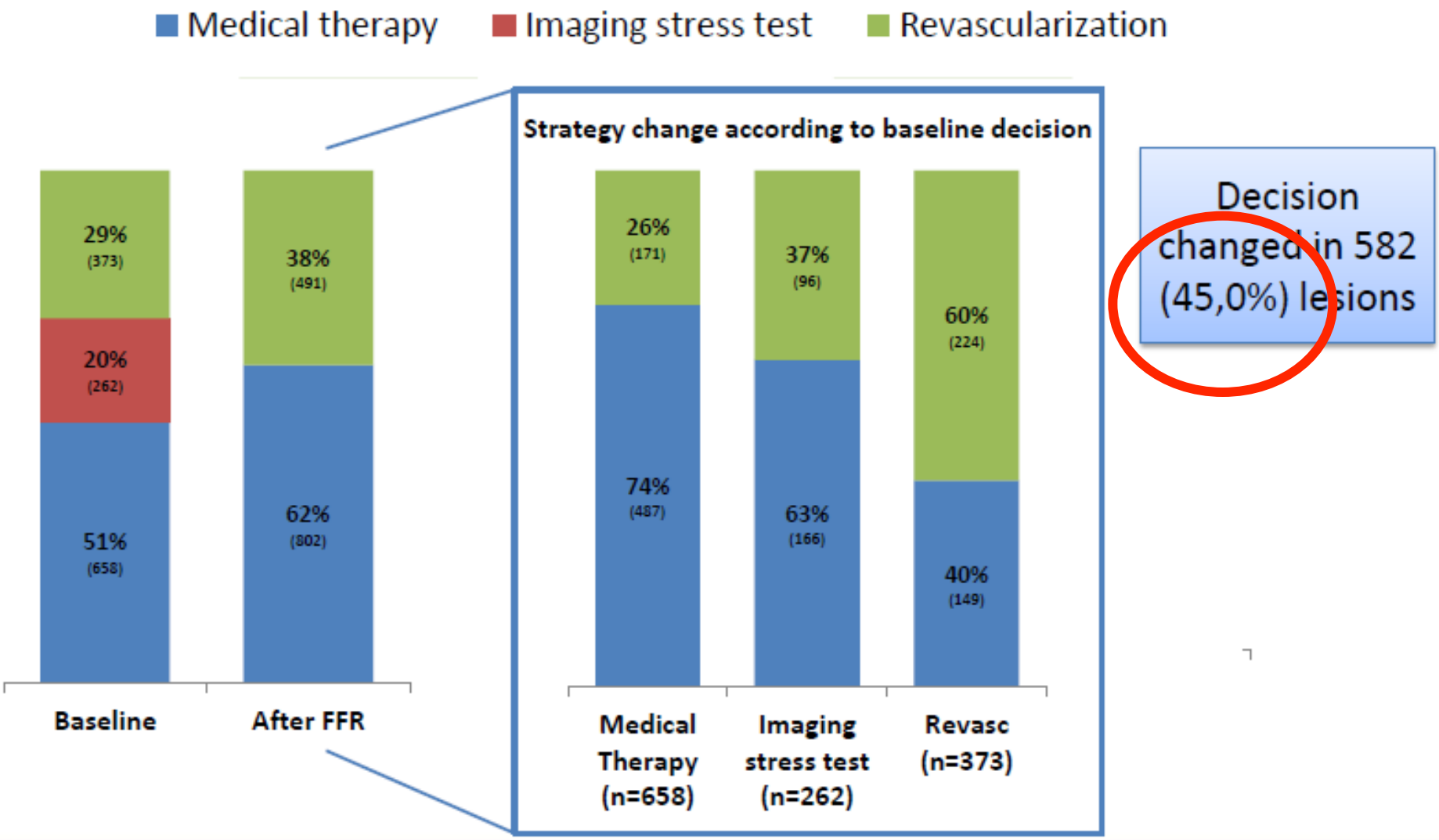
Outcome Impact of Coronary Revascularization Strategy Reclassification With Fractional Flow Reserve at Time of Diagnostic Angiography

Insights From a Large French Multicenter Fractional Flow Reserve Registry

Eric Van Belle, MD, PhD; Gilles Rioufol, MD, PhD; Christophe Pouillot, MD; Thomas Cuisset, MD, PhD; Karim Bougrini, MD; Emmanuel Teiger, MD, PhD;



Results: strategy change *per lesion*



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Post–Angiogram Decision	Post–FFR Decision: Medical	PCI	CABG	Further Info	Total
Medical	63	6	3	0	72
PCI	24	64	2	0	90
CABG	1	3	19	0	23
Further info	1	7	6	1	15
Total	89	80	30	1	200

$P<0.001$ by McNemar test. CABG indicates coronary artery bypass grafting; FFR, fractional flow reserve; and PCI, percutaneous coronary intervention.

26% of patients changed therapy with FFR guidance

Curzen et al. Circ Cardiovasc Interv 2014
Van Belle et al. Circ Cardiovasc Interv 2014

What about MVD patients?

2016 euroPCR

A prospective, observational, European, multi-center registry, collecting REAL-life information on the utilization of instantaneous wave-free ratio™ (iFR®) in the multi-vessel disease patients population

Prof. Eric Van Belle on behalf of the DEFINE REAL Investigators

DEFINE REAL

EAPCI

EUROPEAN SOCIETY OF CARDIOLOGY®

EACTS

Objectives

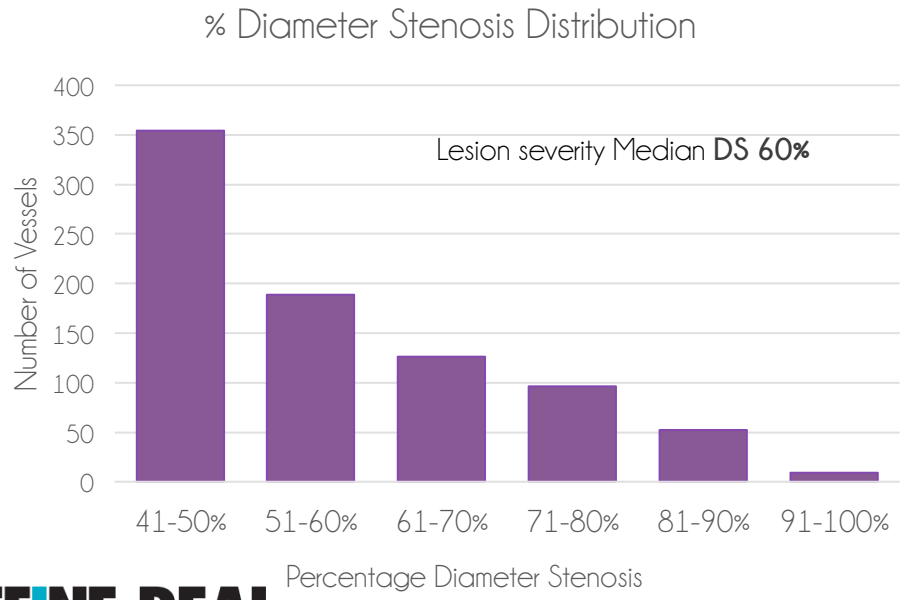
As systematic FFR multi-vessel assessment is time consuming and therefore rarely performed in routine practice, the iFR® index may help to simplify the physiology assessment of MVD patient population.

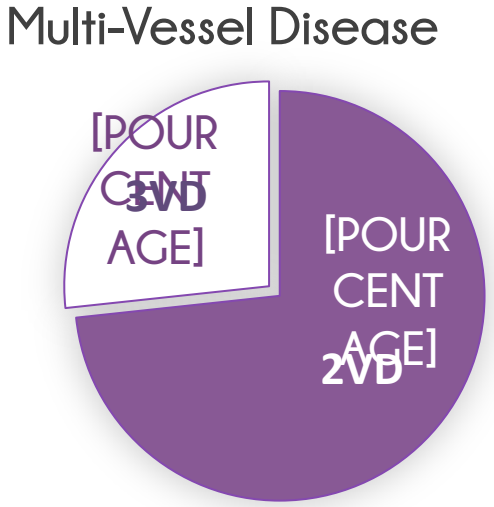
The DEFINE REAL objective is:

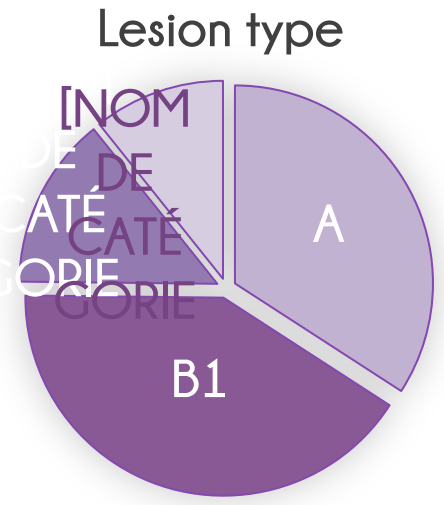
- To assess prospectively the impact of physiology on revascularization strategy of MVD patients compared to diagnostic angiogram only.

Baseline Characteristics

Patients population	**484**
• Patient with LM involved	9.1%
Vessels diseased	**1107**
• Average per patient	**2.29**
Vessels assessed by physiology	**830 (75%)**
• Average per patient	**1.71**







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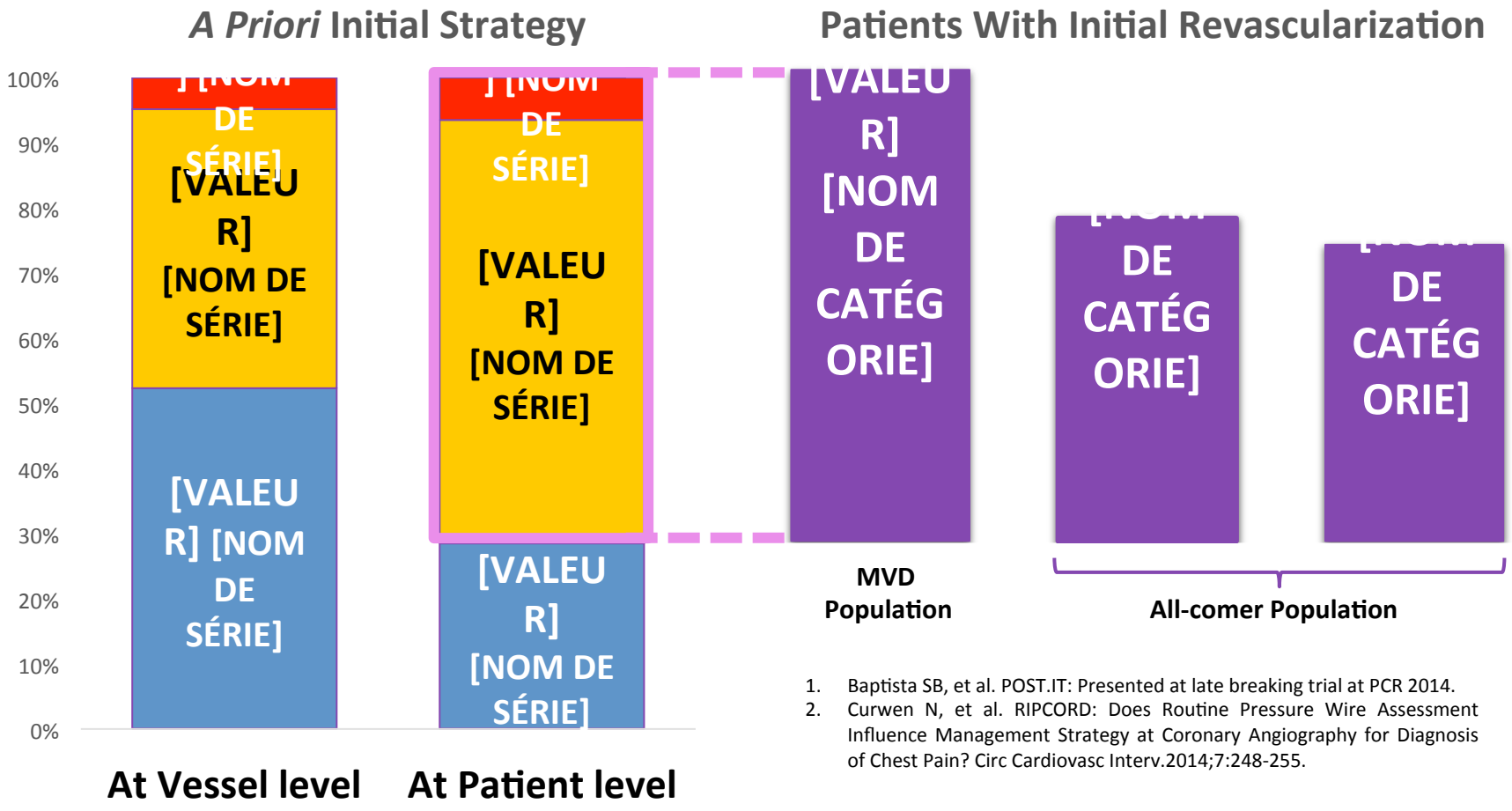
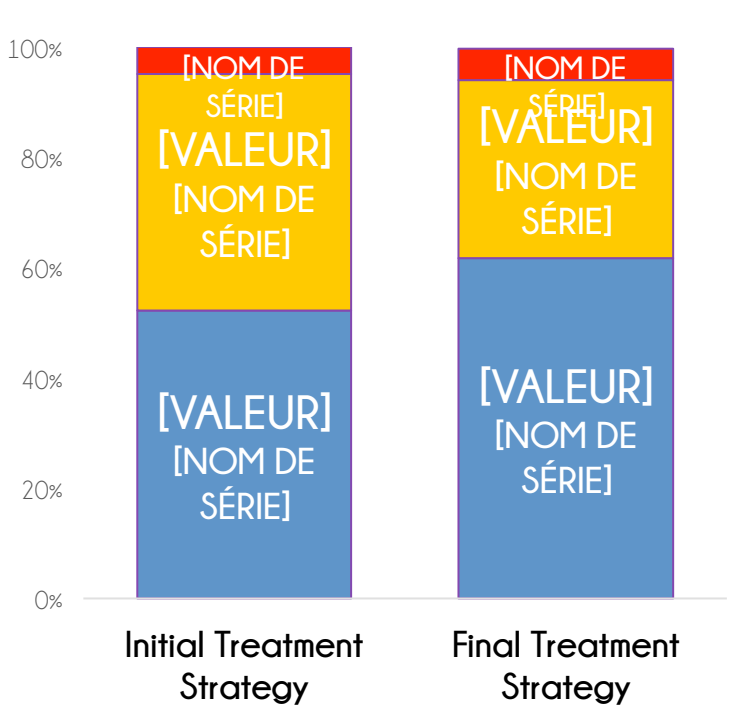
Initial Treatment Strategy By Angiography

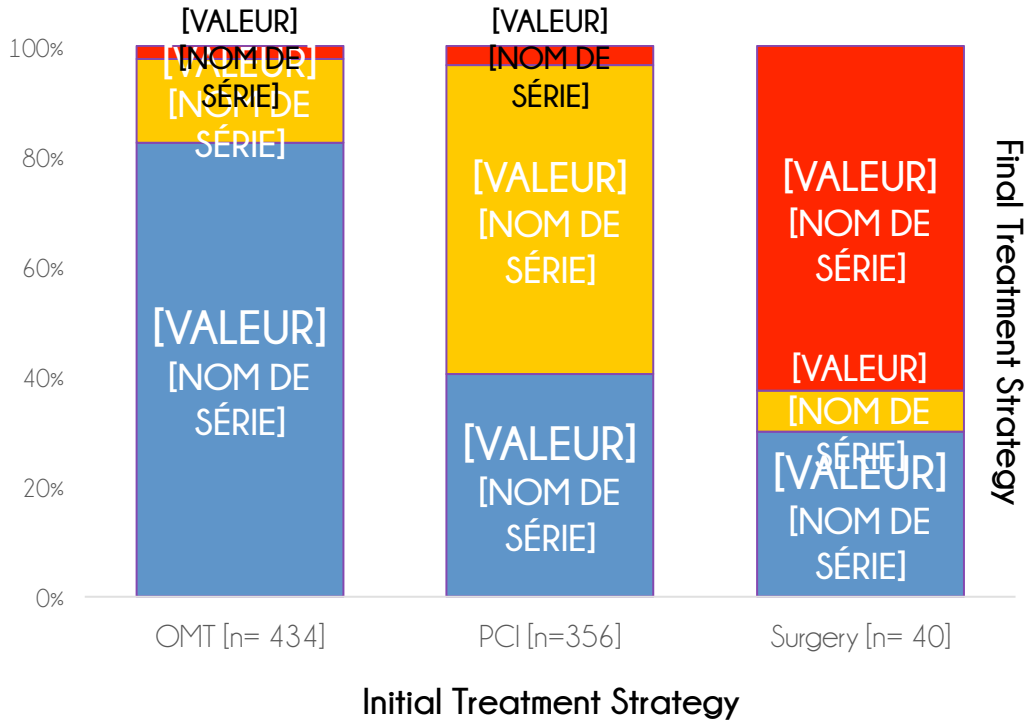


1. Baptista SB, et al. POST.IT: Presented at late breaking trial at PCR 2014.
2. Curwen N, et al. RIPCORD: Does Routine Pressure Wire Assessment Influence Management Strategy at Coronary Angiography for Diagnosis of Chest Pain? Circ Cardiovasc Interv.2014;7:248-255.

Changes of Treatment Strategy

At Vessel Level, treatment decision was changed after physiology assessment for **30.0% of Vessels**





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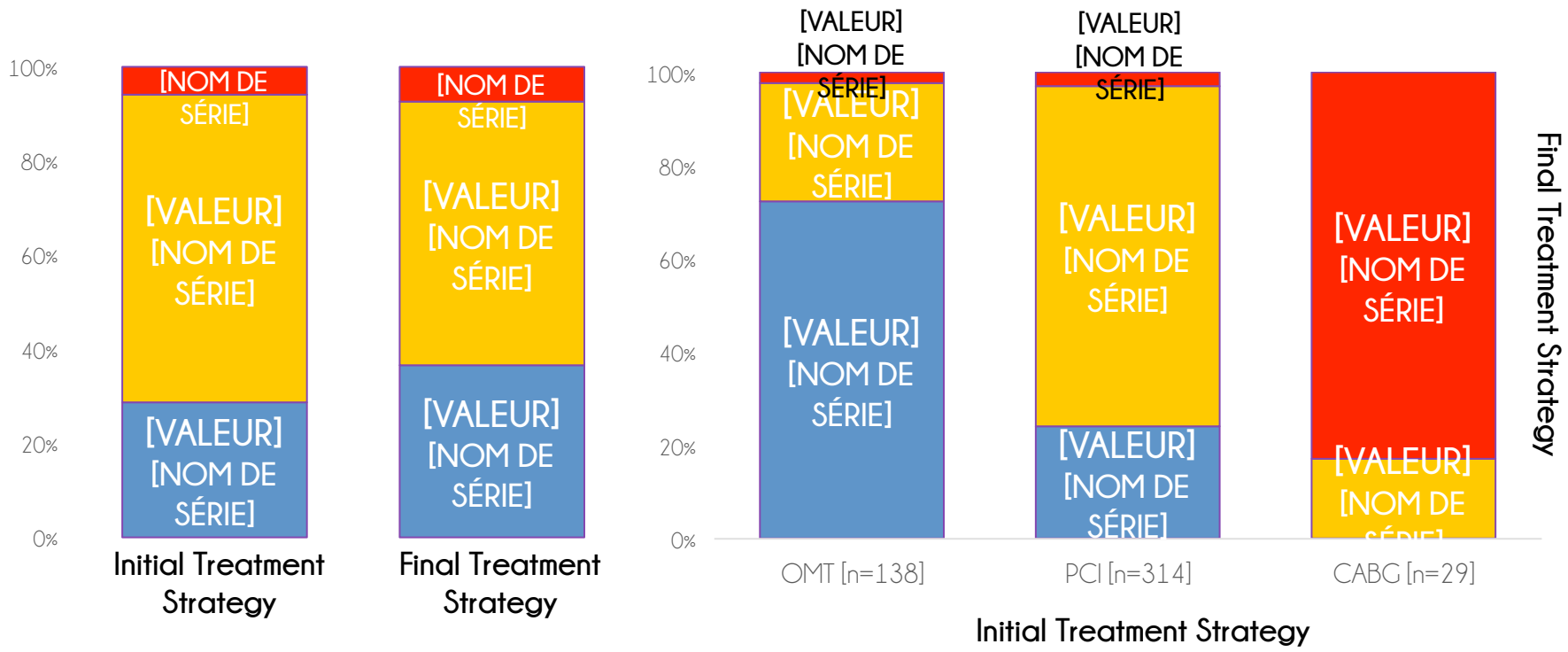
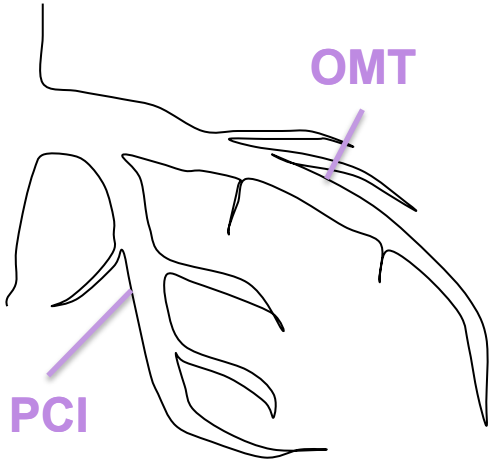
Changes of Treatment Strategy

At Patient Level (Macro Strategy), treatment decision changed after physiology assessment **for 27%** of Patients



Changes of Treatment Strategy

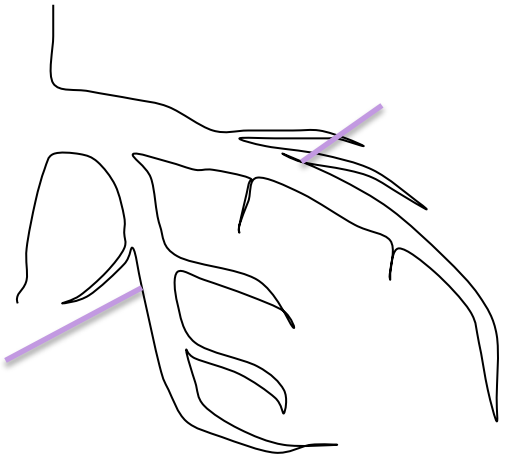
Initial Treatment by Angiography



Physiology

iFR/FFR

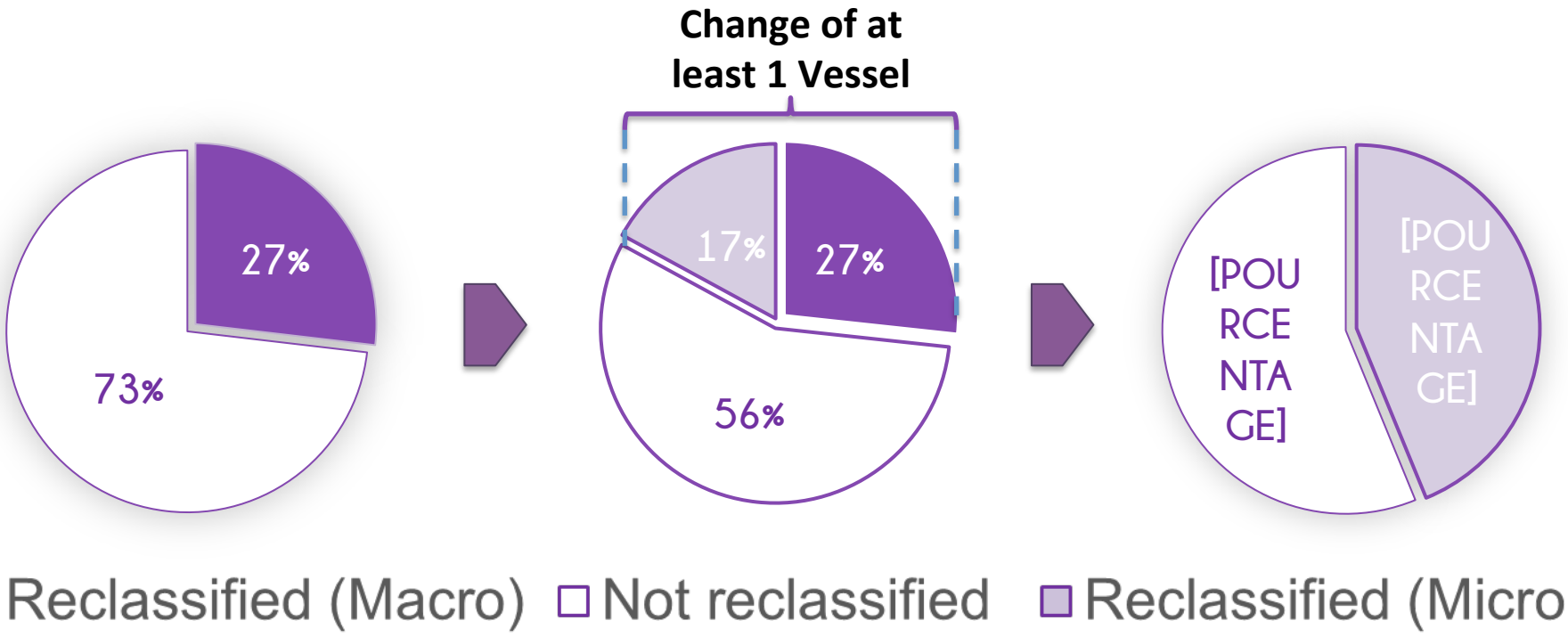
Final Treatment by Physiology



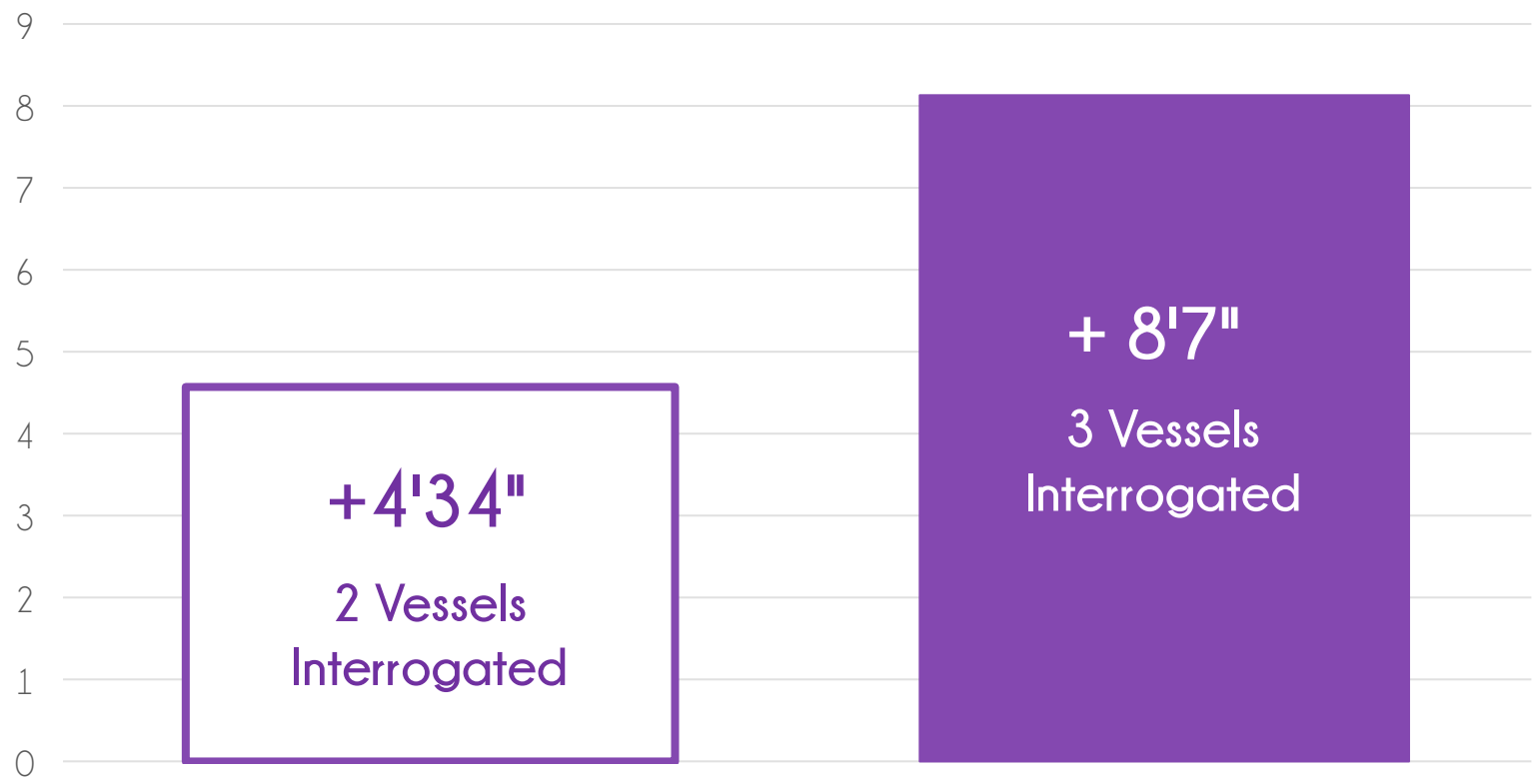
Changes of Treatment Strategy at Patient Level

Macro Strategy

Micro Strategy

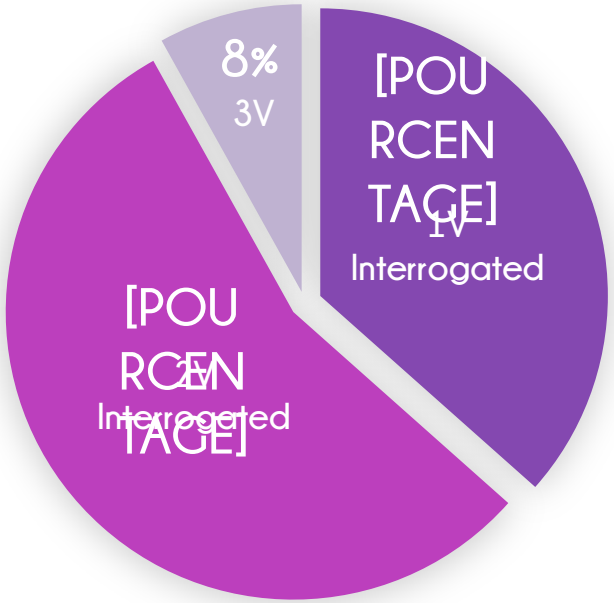


Extra time for Physiology in >1 vessel

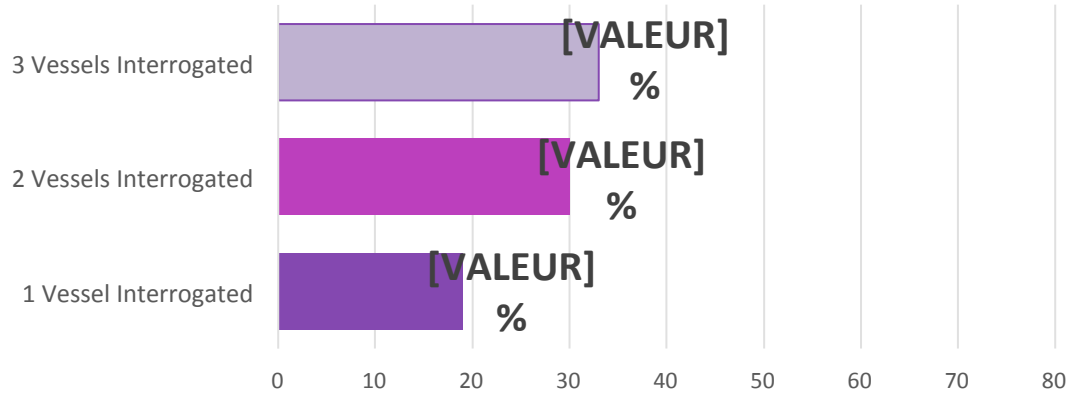


Reclassification & MVD Interrogation

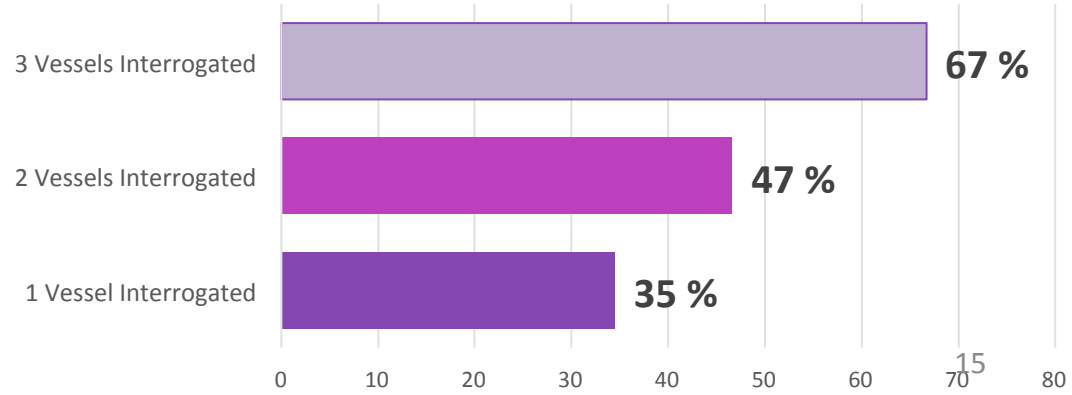
Vessels Interrogated in MVD Patients



Changed Treatment Strategy (Macro Level) / Number of Vessels Interrogated



Changed Treatment Strategy (Micro Level) / Number of Vessels Interrogated



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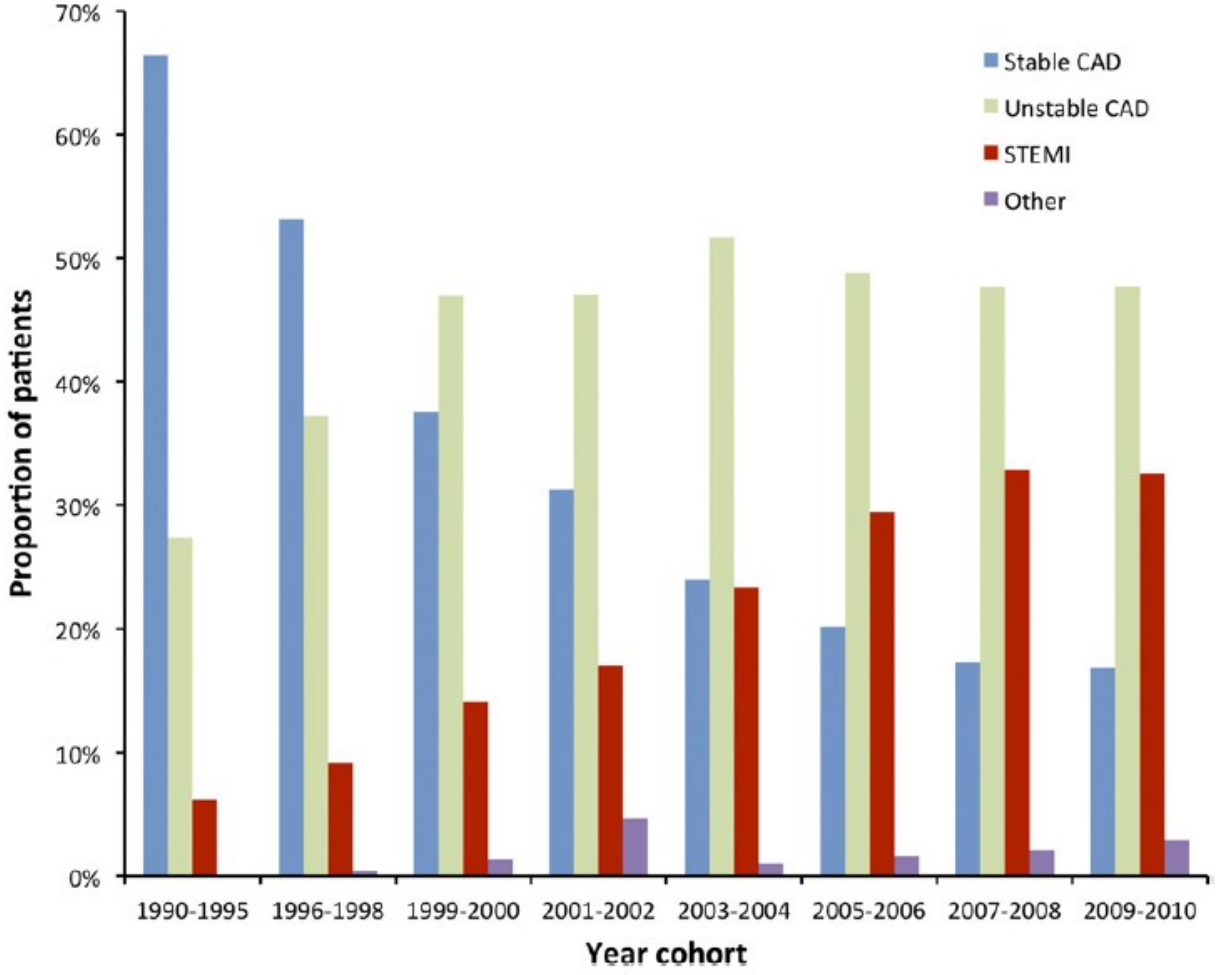
Summary

- In real life, routine physiology at time of angiography in MVD patients is feasible with 75% of vessels interrogated by physiology at a reasonable cost of extra time;
- Routine physiology in MVD patients is associated with a strategy change at patient level in 27% of MVD patients;
- Furthermore, in 44% of MVD patients, physiology assessment leads to a change of revascularization strategy in at least one vessel;
- Interrogation of more vessels leads to a higher rate of reclassification.

What about ACS?

Increasing Prevalence of ACS

144,039 Swedish patients (SCAAR Registry) undergoing PCI between 1990-2010



Fokkema, et al. J Am Coll Cardiol 2013;61:1222-30

Acute Microvascular Damage and FFR

STEMI

Variable Degree of Reversible Microvascular Stunning

Maximum Achievable Flow is Less

Smaller Gradient and Higher FFR across Any Given Stenosis

With time, the microvasculature may recover, maximum achievable flow may increase, and a larger gradient with a lower FFR may be measured

Overview of FFR in ACS:

- STEMI
  - Acute
  - Chronic
- Non-STEMI
  - Acute

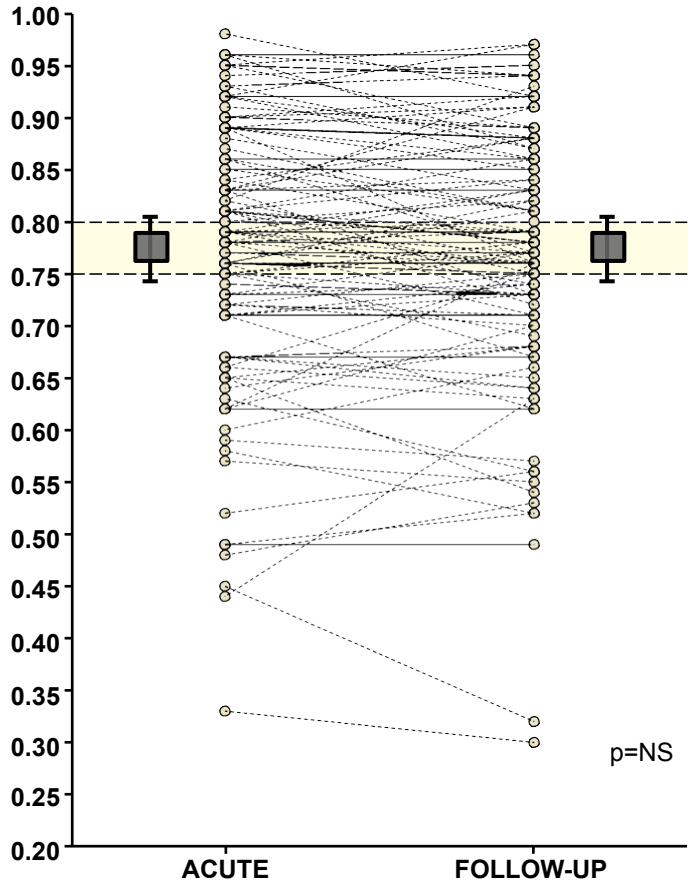
- Culprit vessel
- Non-Culprit vessel

FFR STEMI (Non-Culprit Vessels)

- During acute STEMI, is FFR measurement of non-culprit vessels reliable?

FFR STEMI (Non-Culprit Vessels)

101 patients with an acute coronary syndrome (75 STEMI, 26 NSTEMI)
112 non culprit stenoses FFR measured acutely and 35±24 days later

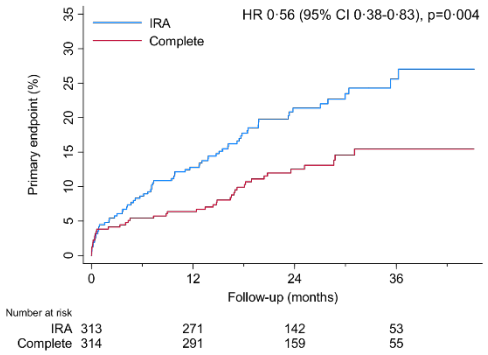


In only 2/112 stenoses was the FFR >0.80 during the ACS and <0.75 at follow-up.

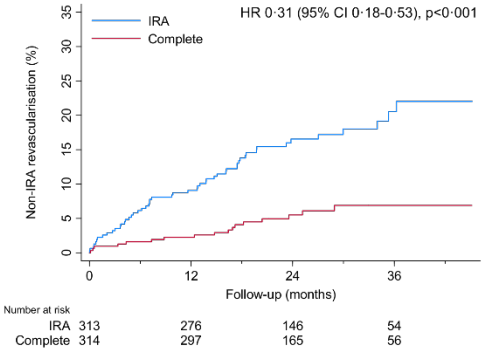
Ntalianis, et al. J Am Coll Cardiol Intv 2010;3:1274

DANAMI3-PRIMULTI

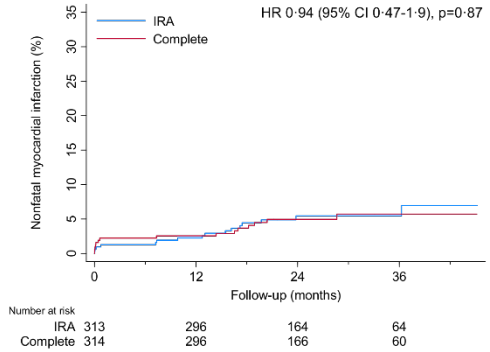
Individual components of primary endpoint



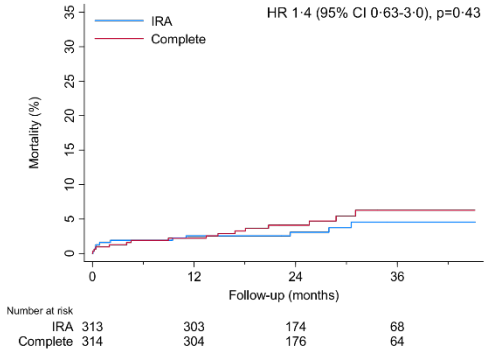
Composite



Revascularisation



Non fatal MI



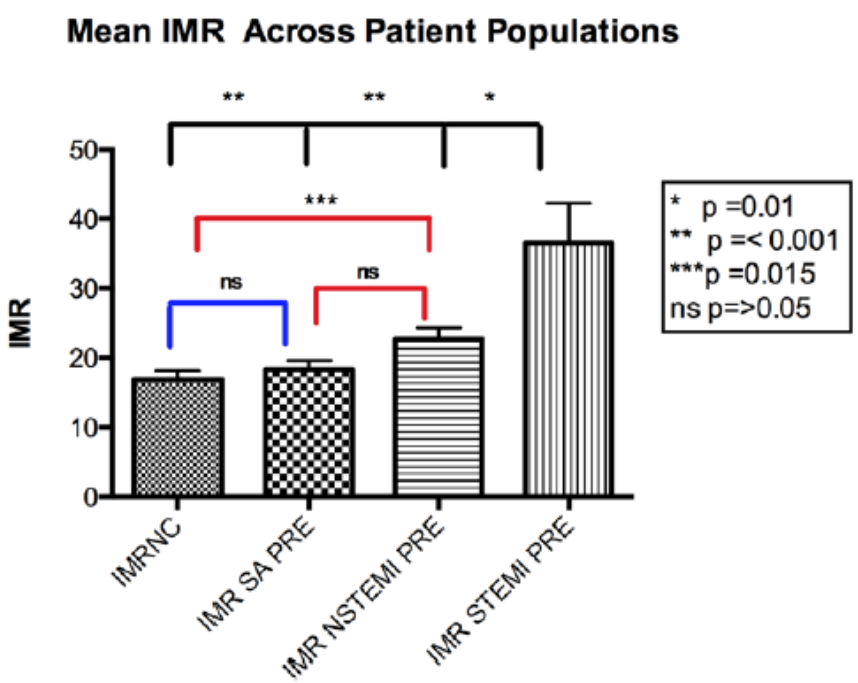
All cause death

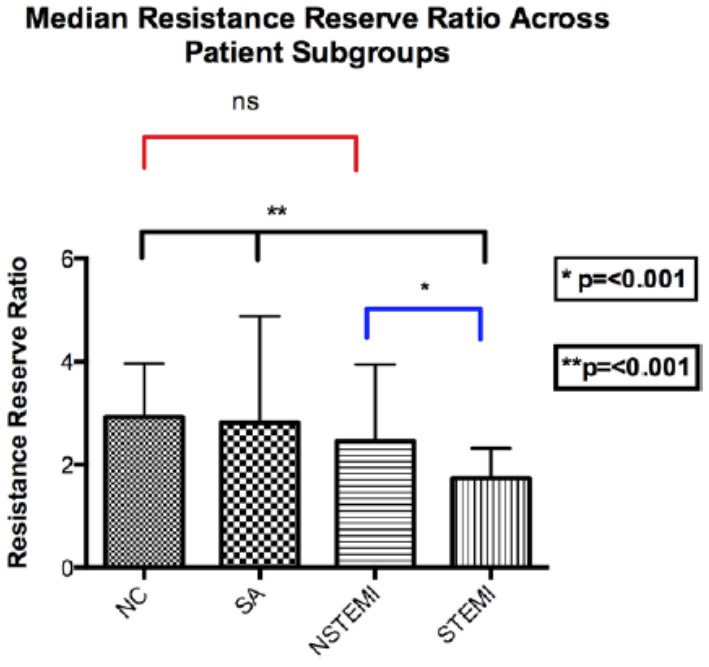
FFR during NSTEMI

- Can we measure FFR in non ST elevation acute myocardial infarction?
  - In the culprit vessel?
  - In the non-culprit vessel?
  - When we don’t know whether it the culprit or not?

Vasodilatory Capacity of the Coronary Microcirculation is Preserved in Selected Patients With Non–ST-Segment–Elevation Myocardial Infarction

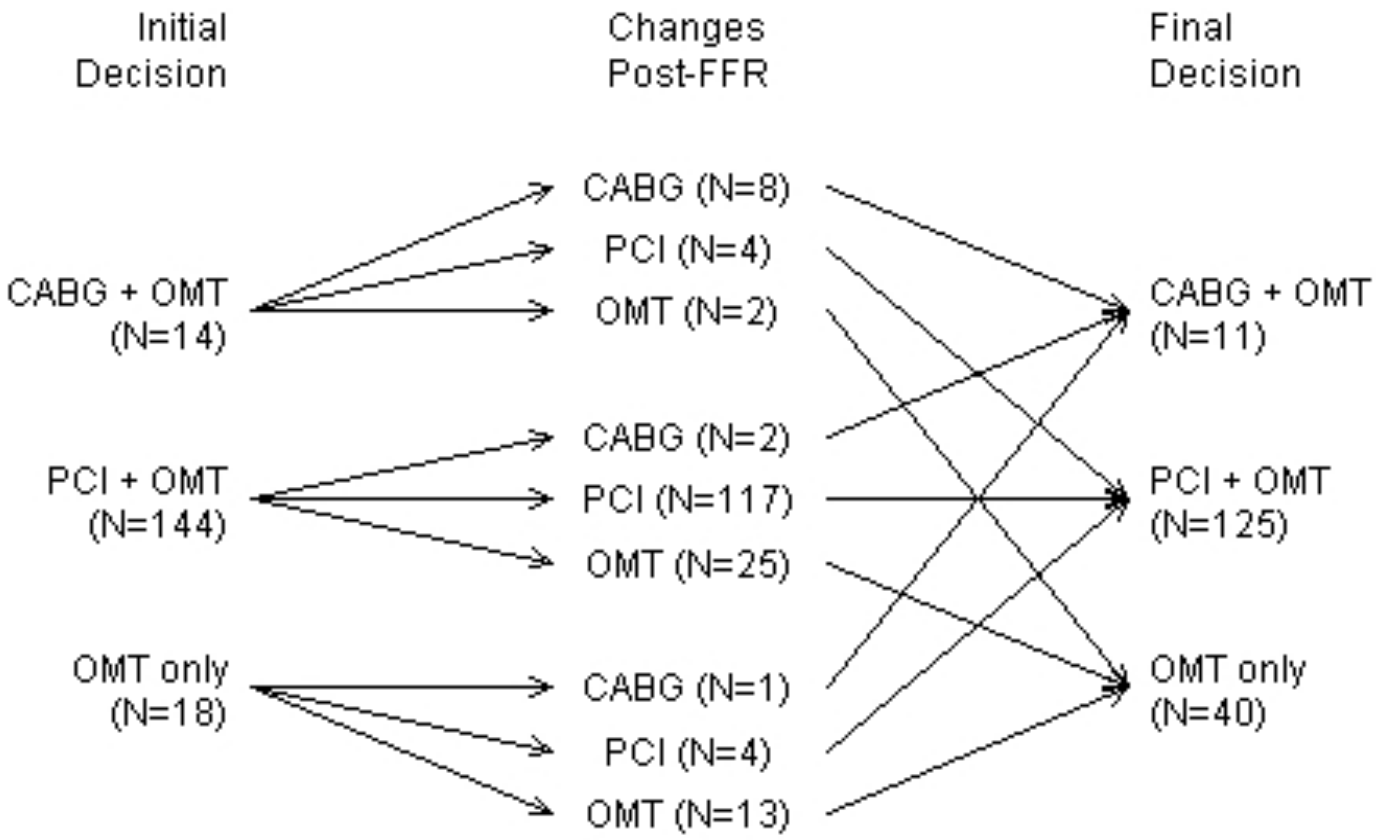
Jamie Layland, MBChB; David Carrick, MBChB; Margaret McEntegart, MBChB, PhD; Nadeem Ahmed, BSc; Alex Payne, MBChB; John McClure, PhD; Arvind Sood, MBChB, MD; Ross McGeoch, MBChB, MD; Andrew MacIsaac, MBBS, MD; Robert Whitbourn, MBBS, Bsc; Andrew Wilson, MBBS, PhD; Keith Oldroyd, MBChB, MD; Colin Berry, MBChB, PhD





Layland, et al. Circ Cardiovasc Interv 2013

FAMOUS-NSTEMI trial

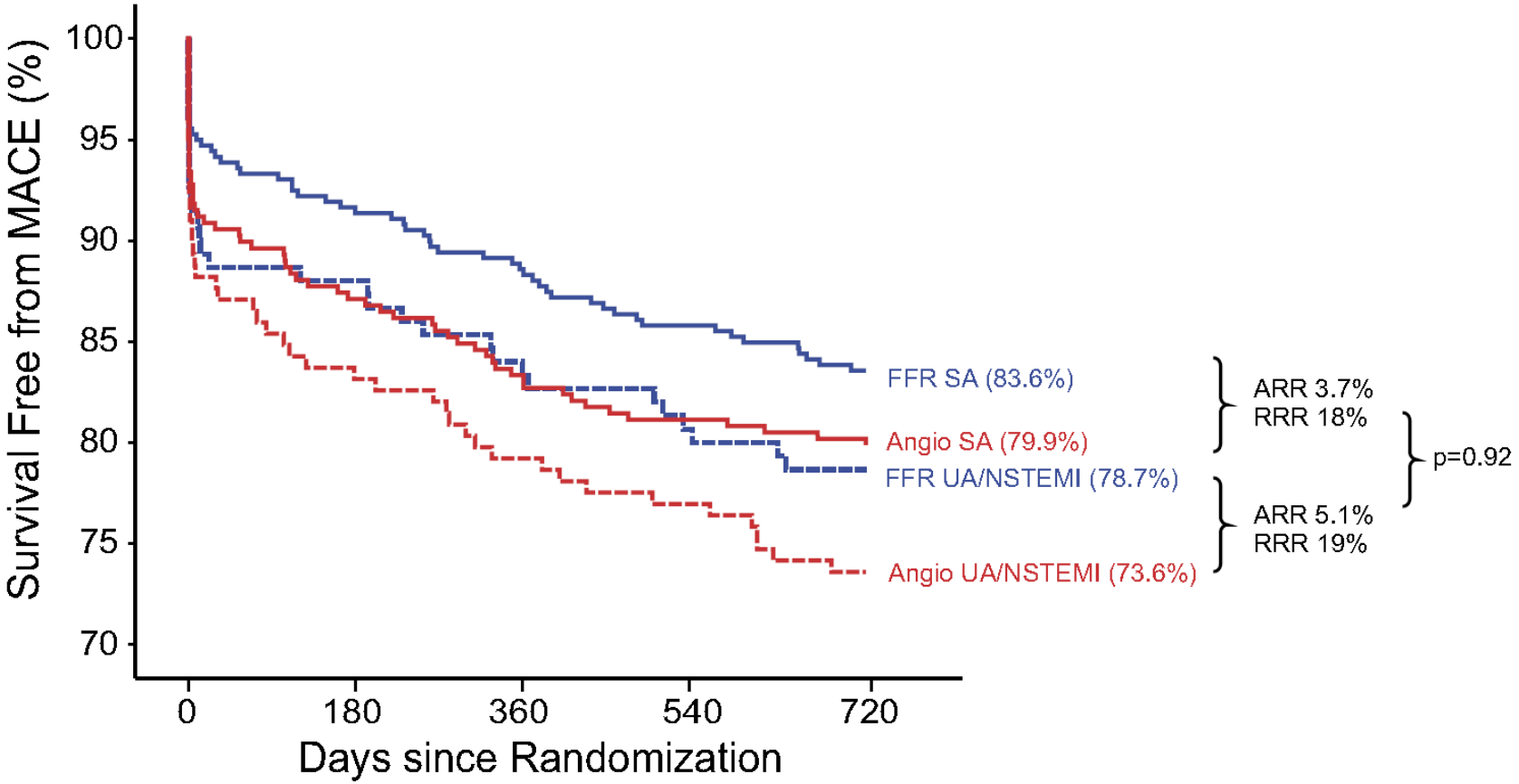


FFR treatment change ~ 22% of patients

ESC Hotline 1 Sep 2014

FFR NSTE ACS (Mixed Culprit + Non Culprit Vessel)

Benefit of FFR-guided PCI in patients with ACS (n=328) –FAME



Tonino, et al. J Am Coll Cardiol Intv 2011;4:1182-9.

Impact of routine Fractional Flow Reserve on management decision and 1-year clinical outcome of ACS patients: Insights from the POST-IT and R3F Integrated Multicenter registriEs - Implementation of FFR in Routine Practice (**PRIME-FFR**)

Eric Van Belle, Sergio-Bravo Baptista, **Luís Raposo**, John Henderson, Patrick Dupouy and others.

On behalf of the PRIME-FFR study group

Hotline EuroPCR 2016

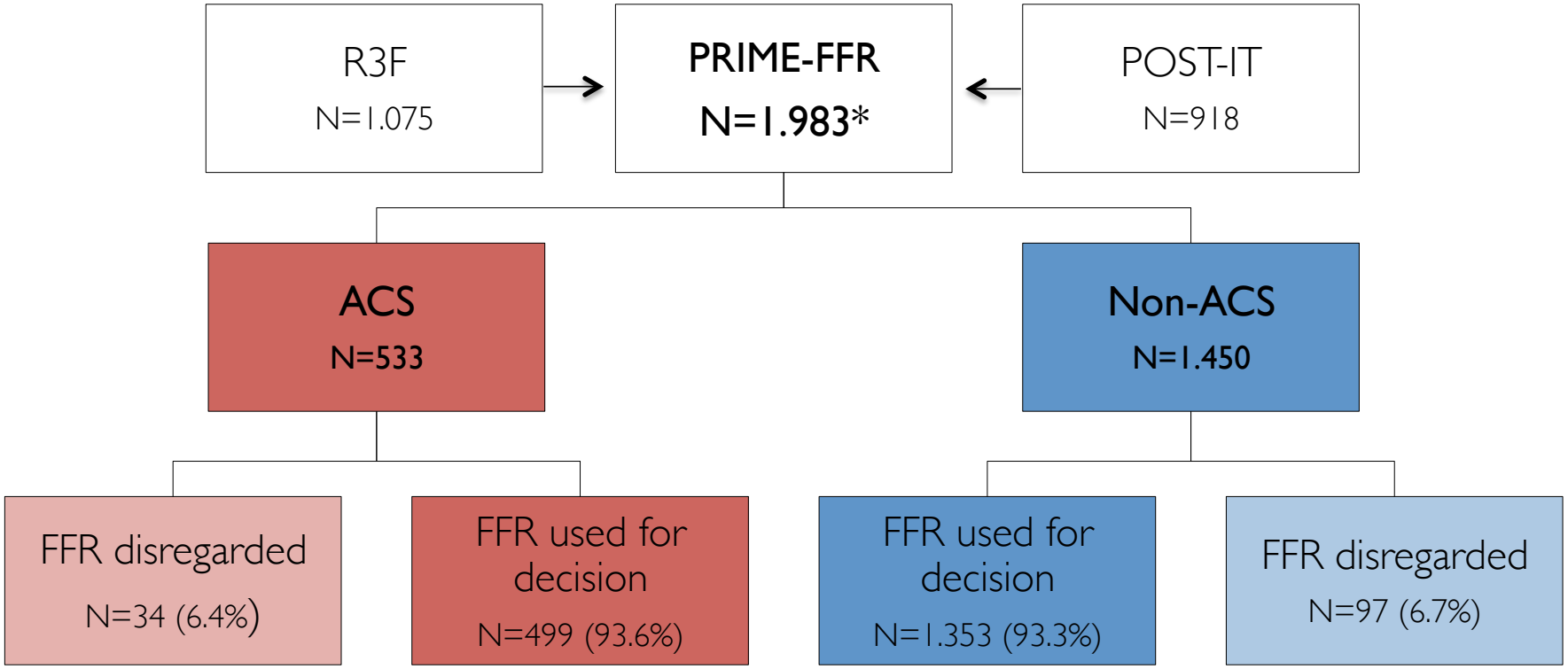
PRIME-FFR

POST-IT and R3F Integrated Multicenter registriEs - Implementation of FFR in Routine Practice

Why it will be important ?

- In ACS, what is rate of reclassification of the management strategy (medical, PCI, CABG) with routine FFR usage?
- How does the rate of reclassification compare with non-ACS patients?
- Is FFR–based reclassification of the management strategy; i.e. against strategy suggested by angiography; safe in ACS patients?
- Is FFR-based deferral to medical treatment able to identify a population at low risk?

Study Design & Endpoints



Impact of FFR on management strategy

Safety of changing treatment strategy

1-year MACE (Total Death/MI/unplanned revascularization)

*FFR result unavailable in 10 patients

Baseline Characteristics

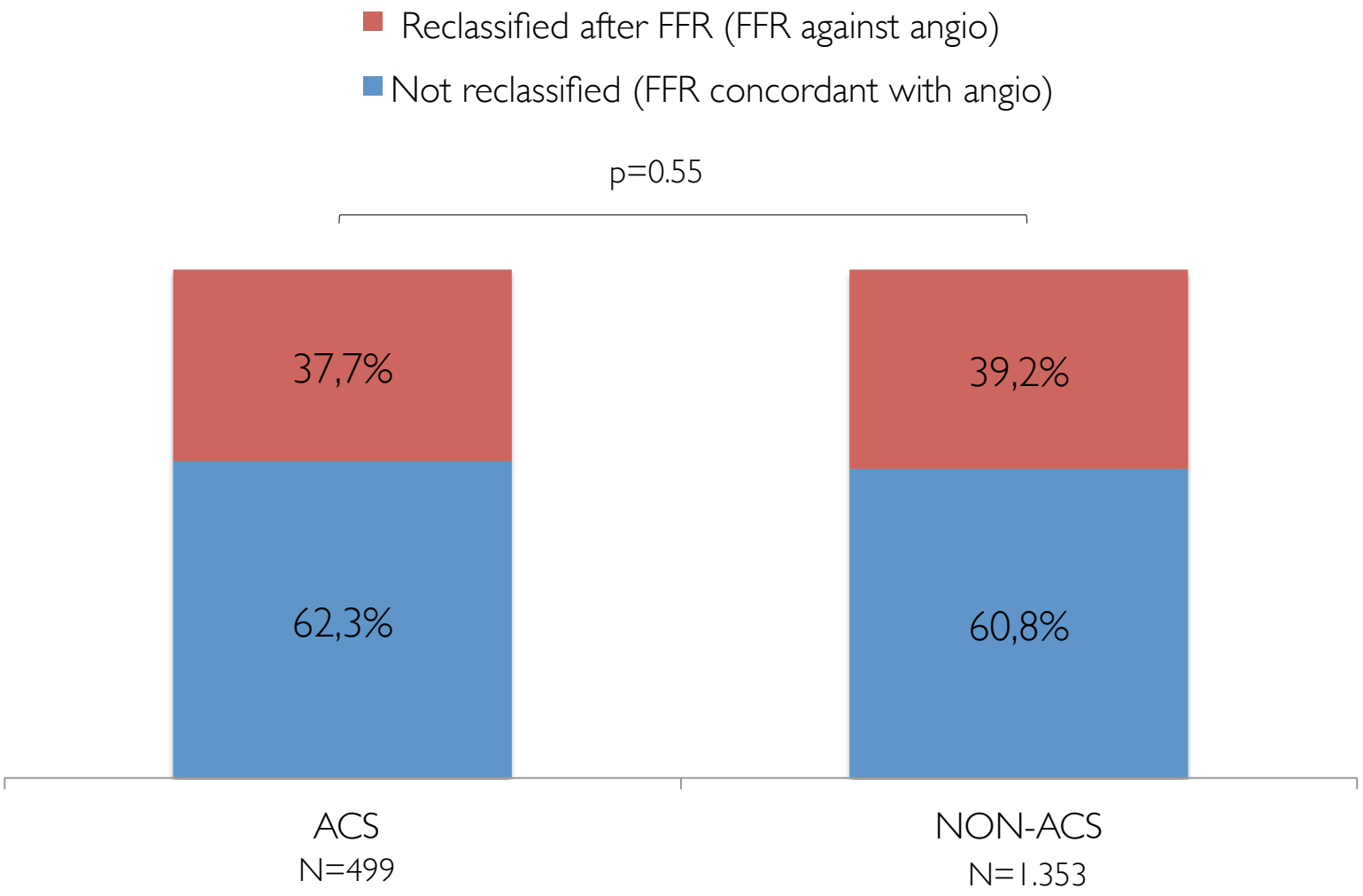
Variable (n;%)	ACS Population	Non-ACS population	*p* value
Age (years) [mean±SD]	64.0±11.5	65.3±10.1	0.019
Male Gender	401 (75.2%)	1102 (76.0%)	0.724
Diabetes mellitus	160 (30.8%)	541 (38.2%)	0.003
Hypertension	365 (70.3%)	1073 (75.7%)	0.016
Smoking (current/former<1year)	234 (43.9%)	558 (38.5%)	0.091
High Cholesterol	335 (64.9%)	1044 (73.8%)	<0.001
Myocardial infarction	187 (44.3%)	360 (31.0%)	<0.001
PCI	199 (47.2%)	538 (46.1%)	0.720
CABG	11 (2.6%)	56 (4.8%)	0.054
Left Ventricular EF ≤50%	84 (15.8%)	249 (17.2%)	0.757
Dual Antiplatelet therapy	314 (60.2%)	742 (51.6%)	<0.001
Statin	398 (76.2%)	1119 (78.0%)	0.402
ACEI/ARB	319 (62.3%)	839 (58.9%)	0.175
Beta-Blockers	318 (61.6%)	880 (61.6%)	0.999
Typical Angina Syndrome	-	562 (38.8%)	<0.001
On-going ACS	229 (43.0%)	-	
Recent ACS STEMI	91 (17.1%)	-	
Recent ACS NSTEMI/UA	213 (40.0%)	-	

Baseline Characteristics

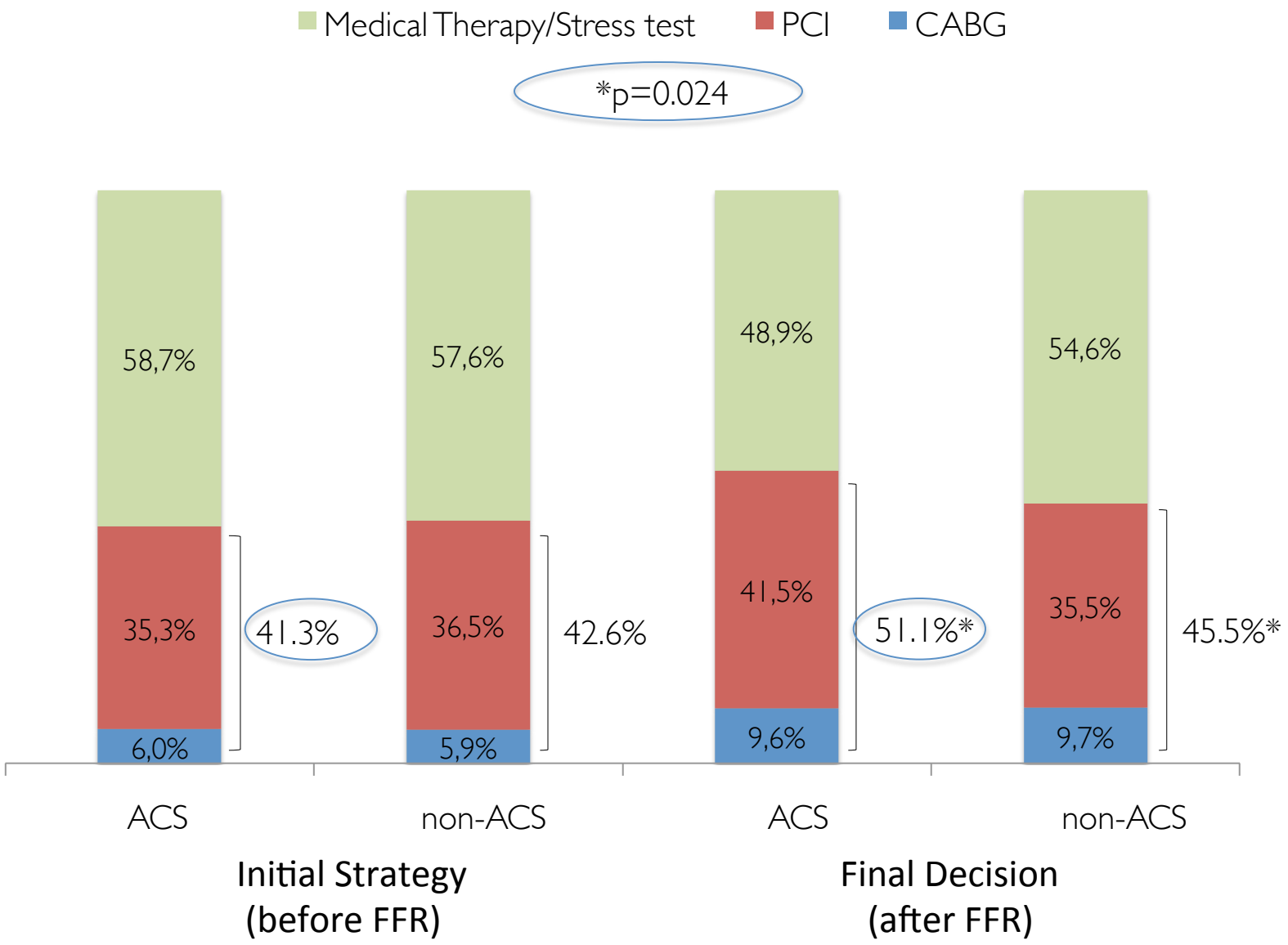
Variable (n;%)	ACS Population	Non-ACS population	*p* value
Number of diseased vessels (>50%)			
0-1	284 (53.3%)	846 (58.4%)	0.055
2	156 (29.3%)	384 (26.5%)	
3	93 (17.4%)	220 (15.2%)	
Number of lesions evaluated			
1	391 (73.4%)	1049 (72.3%)	0.921
2	103 (19.3%)	300 (20.7%)	
3	31 (5.8%)	81 (5.6%)	
>3	8 (1.5%)	20 (1.4%)	
Lesion Characteristics			
Left Anterior Descending	414 (57.7%)	1146 (57.9%)	0.511
Left Main	32 (4.5%)	117 (5.9%)	0.121
Proximal LAD	125 (17.4%)	389 (19.7%)	0.187
Any proximal lesion	239 (33.3%)	687 (34.7%)	0.485
Lesion - % stenosis [mean±SD]	57.6±12.4	55.4±13.9	<0.001
ACC/AHA Classification B2/C	310 (43.2%)	757 (38.3%)	0.020
Lesions with FFR $\leq$0.80	288 (40.0%)	786 (39.7%)	0.902

FFR & Treatment strategy change

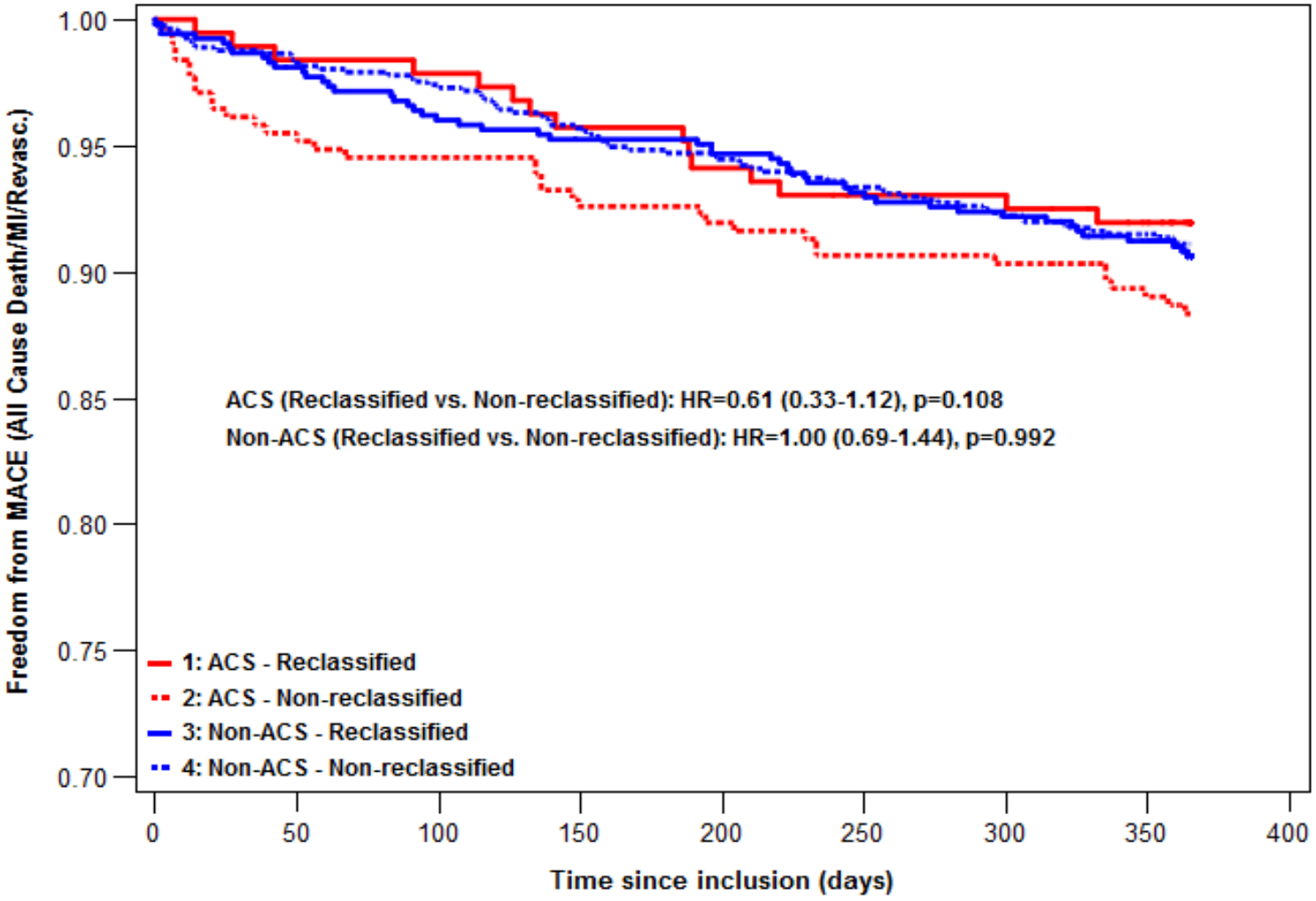
Overall management change in patients in whom FFR was used for decision



FFR & Treatment strategy change

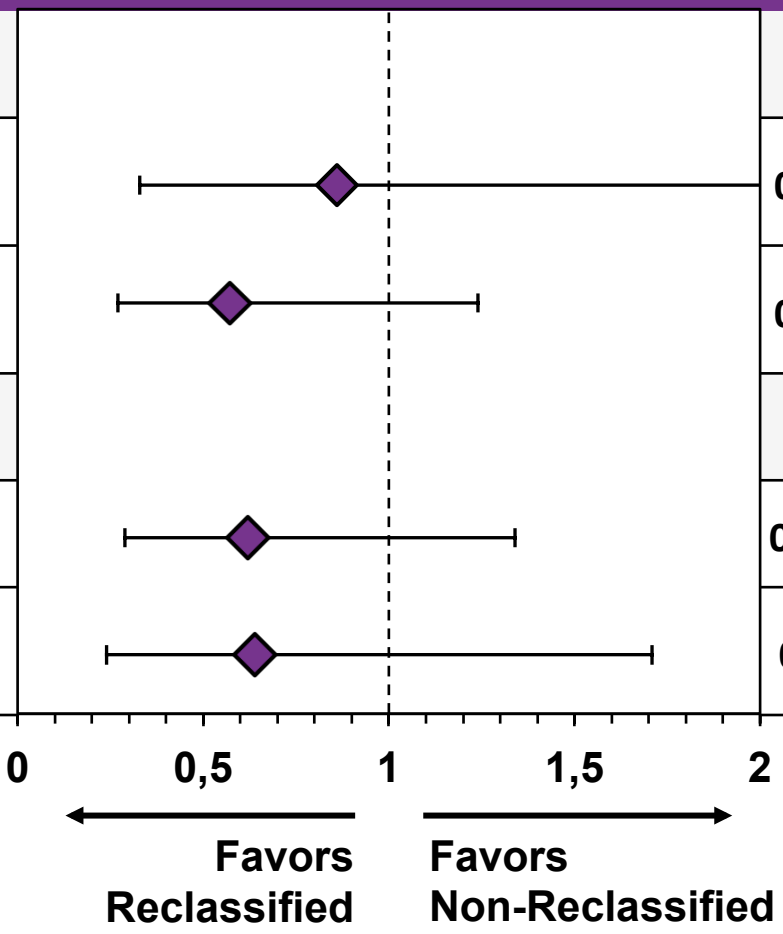


Safety of FFR-based reclassification in ACS

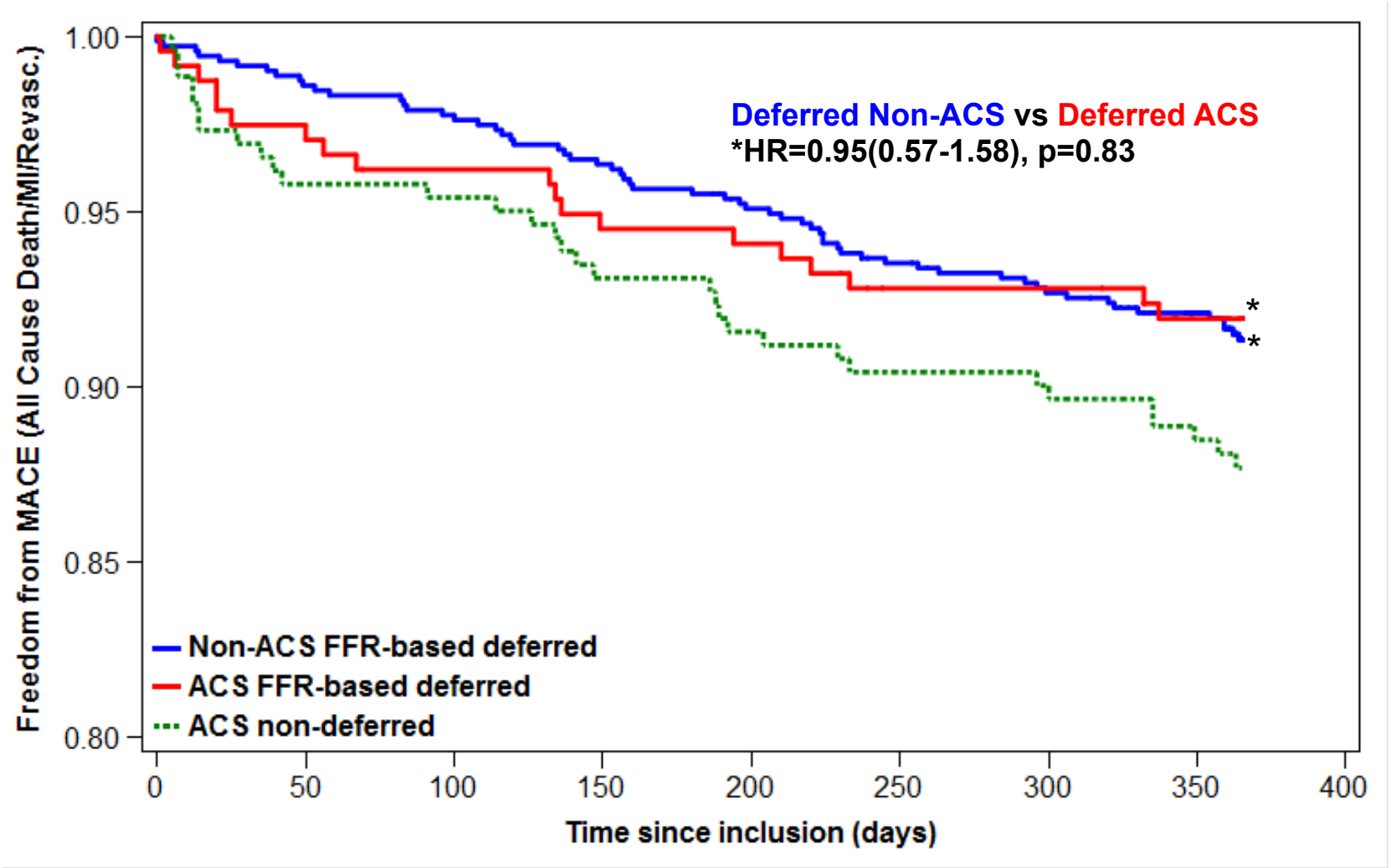


Is it safe to Reclassify in the culprit vessel ?

	Hazard Ratio (95% CI)	p-value	Interaction p-value
ACS Type			**0.52**
Ongoing ACS	**0.86** (0.33 - 2.26)	**0.76**	
Other ACS	**0.57** (0.27 - 1.24)	**0.16**	
No. of Diseased Vessels			**0.97**
>1 Diseased Vessels	**0.62** (0.29 - 1.34)	**0.22**	
≤1 Diseased Vessel	**0.64** (0.24 -1.71)	**0.37**	

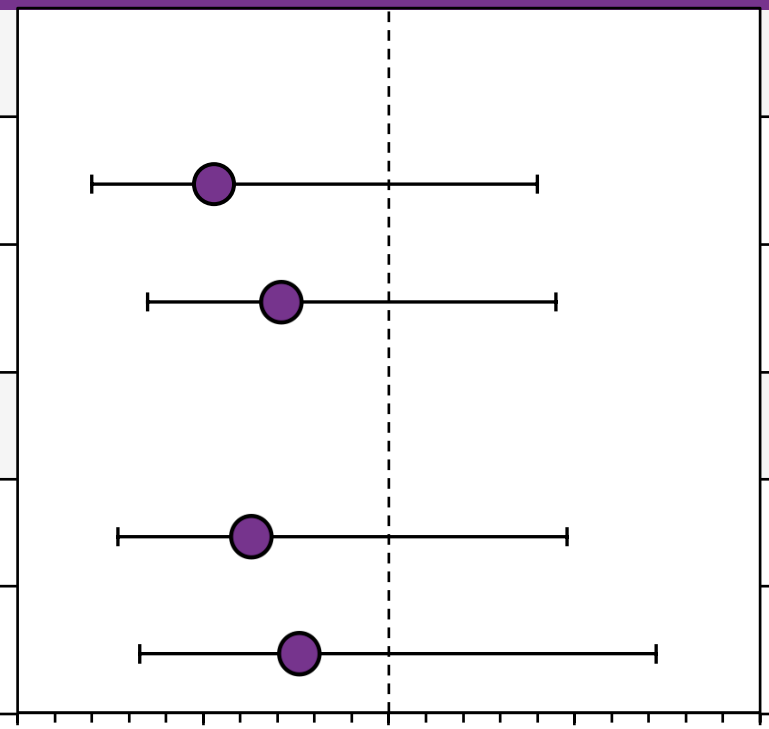


Safety of FFR-based deferral in ACS

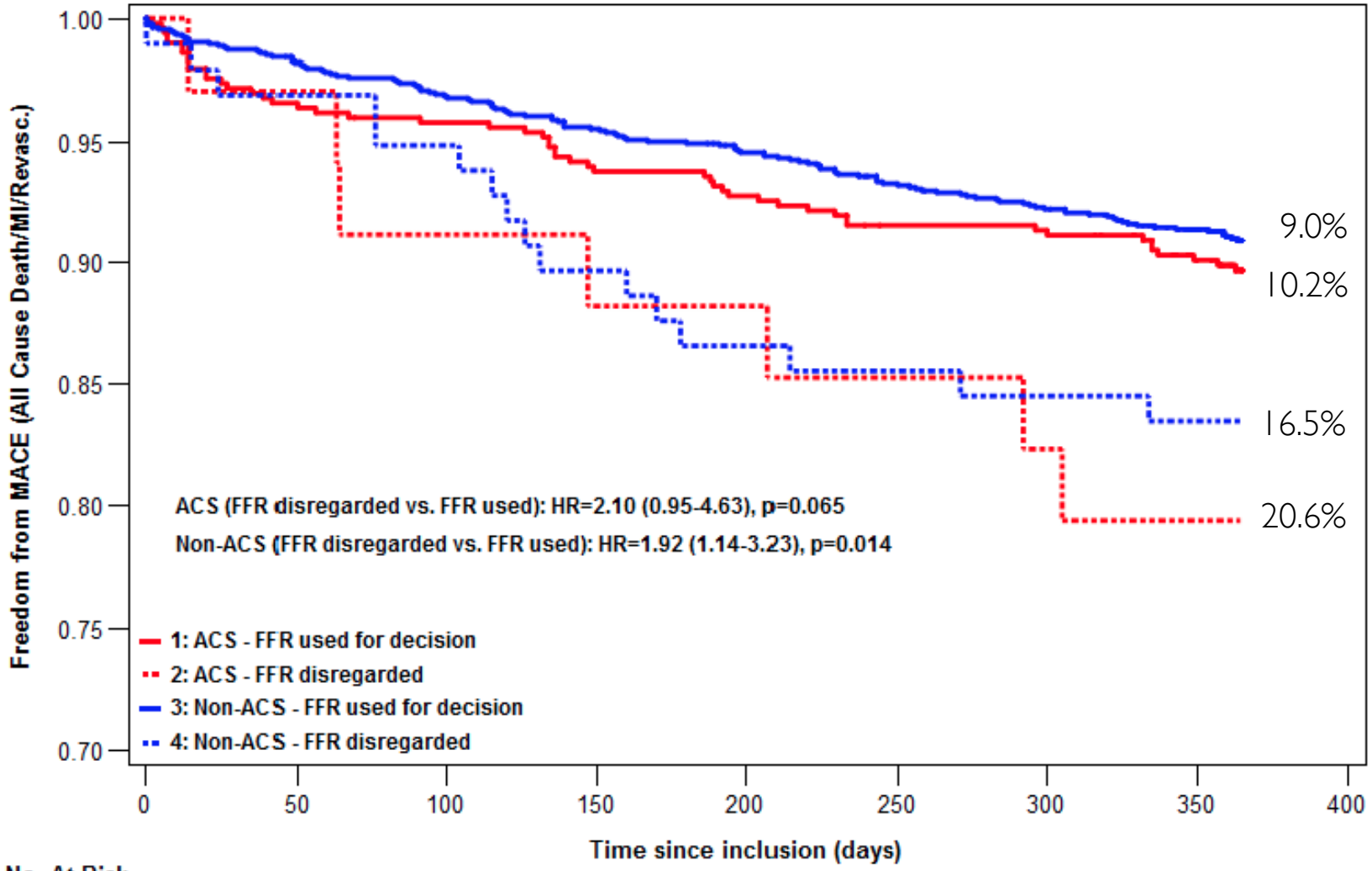


Is it safe to Defer the culprit vessel ?

	Hazard Ratio (95% CI)	p-value	Interaction p-value
ACS Type			**0.62**
Ongoing ACS	**0.53** (0.20 - 1.40)	**0.20**	
Other ACS	**0.71** (0.35 - 1.45)	**0.35**	
No. of Diseased Vessels			**0.76**
>1 Diseased Vessels	**0.63** (0.27 - 1.48)	**0.29**	
≤1 Diseased Vessel	**0.76** (0.33 - 1.72)	**0.51**	



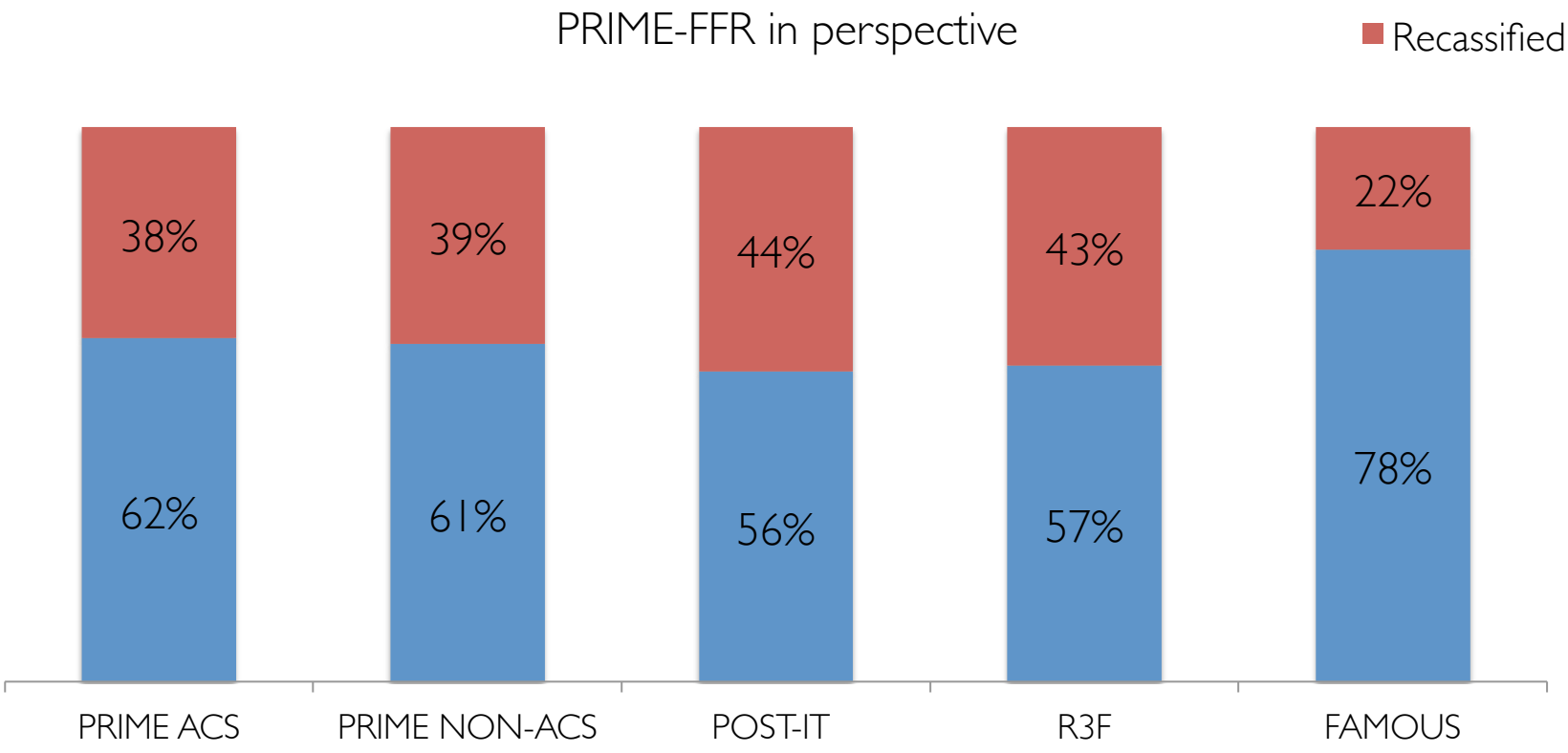
Safety of integrating FFR on management



No. At Risk

1:	498	480	476	466	461	452	450	435	0
2:	34	33	31	30	30	29	28	27	0
3:	1345	1315	1296	1278	1262	1241	1226	1192	0
4:	96	94	92	87	84	83	82	81	0

Conclusions



Conclusions

- ✓ Routine use of FFR in patients with on-going UA/NSTEMI or recent ACS is associated with a high rate of reclassification of management strategy (>35%).

- ✓ Integrating FFR on clinical decision making and pursuing a treatment strategy divergent from angiography (including revascularization deferral) was as safe in ACS as in stable CAD patients.

The POST-IT & R3F Investigators

POST-IT (Portugal)

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Ruben Ramos, MD (Lisbon)
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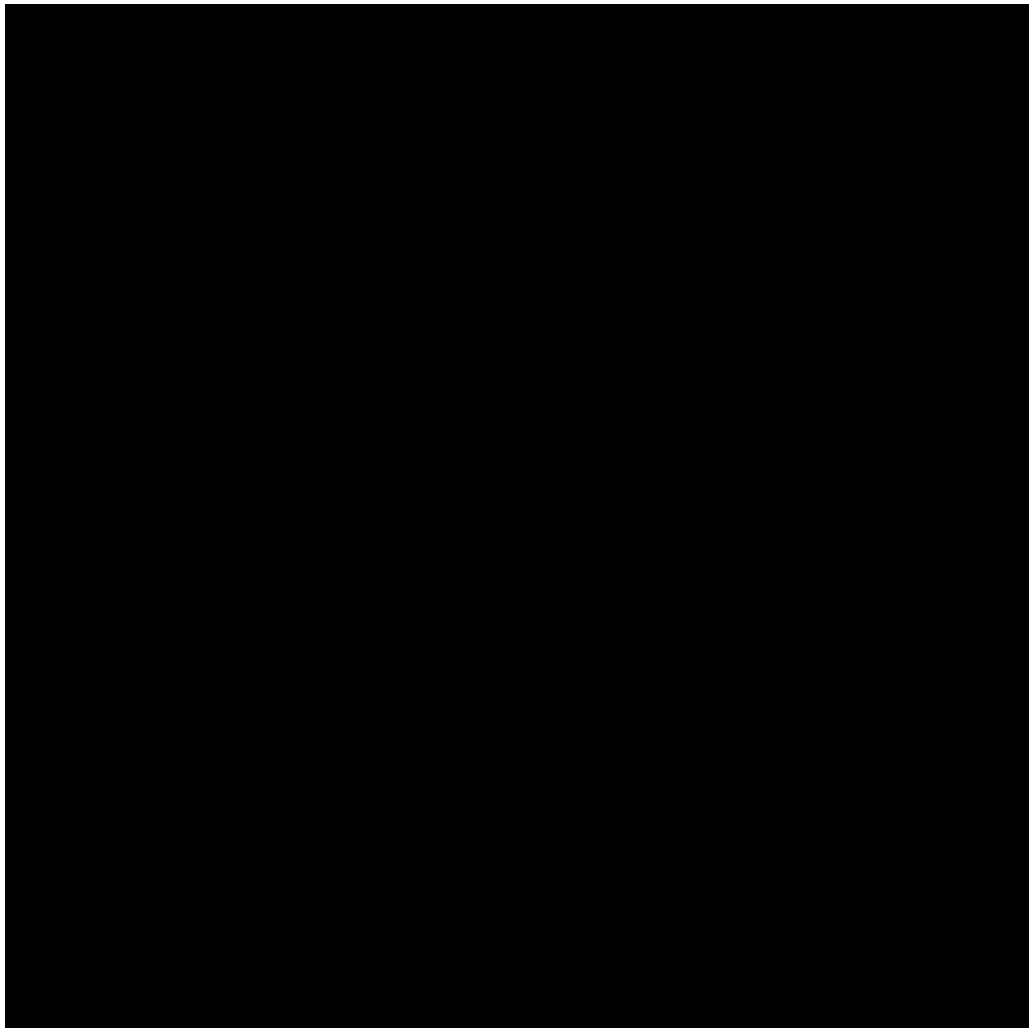
Elisabete Jorge, MD (Coimbra)
Carina Machado, MD (Ponta Delgada)
Marco Costa, MD (Coimbra)
Eduardo Oliveira, MD (Lisbon)
João Costa, MD (Braga)
João Pipa, MD (Viseu)
Nuno Fonseca, MD (Setúbal)
Jorge Guardado, MD (Leiria)
Bruno Silva, MD (Funchal)
Maria João Sousa, MD (Porto)
João Carlos Silva, MD (Porto)
Alberto Rodrigues, MD (Penafiel)
Luís Seca, MD (Vila Real)
Renato Fernandes, MD (Évora)

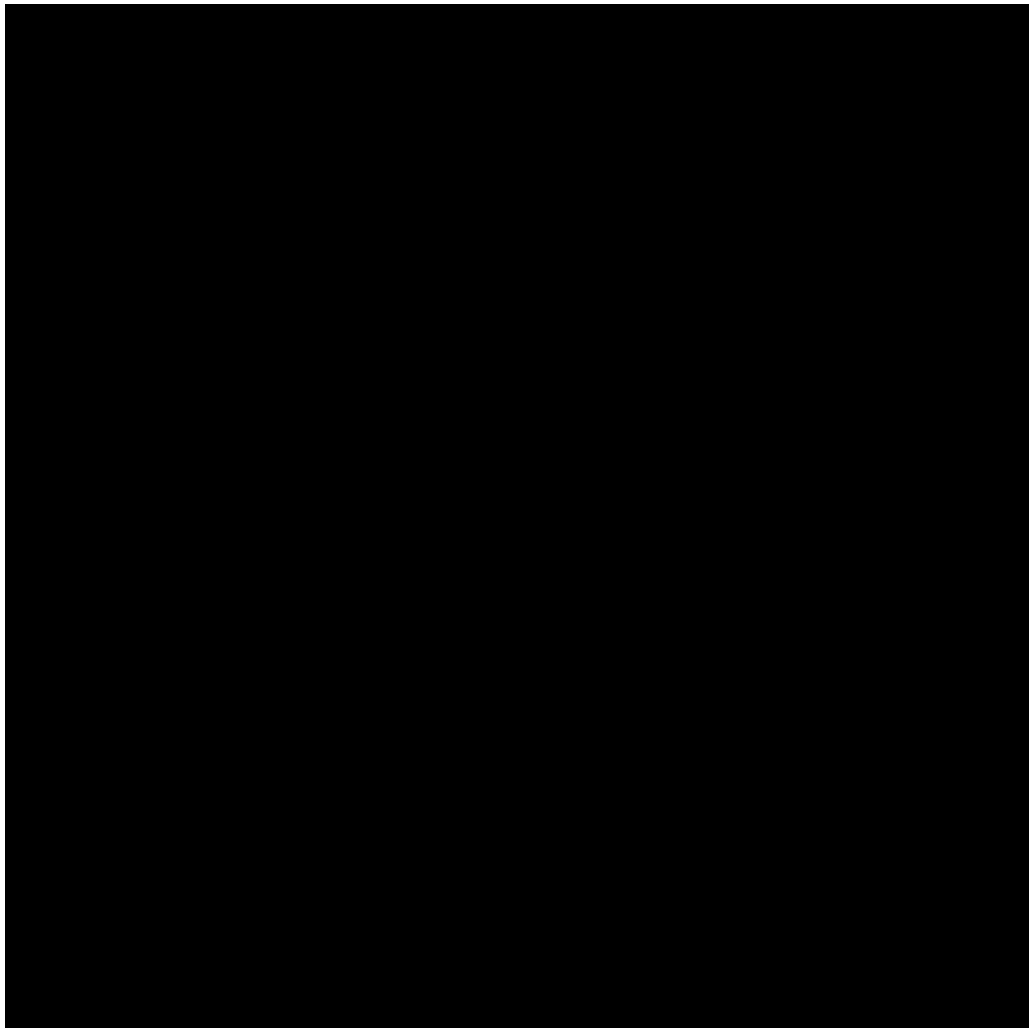
R3F (France)

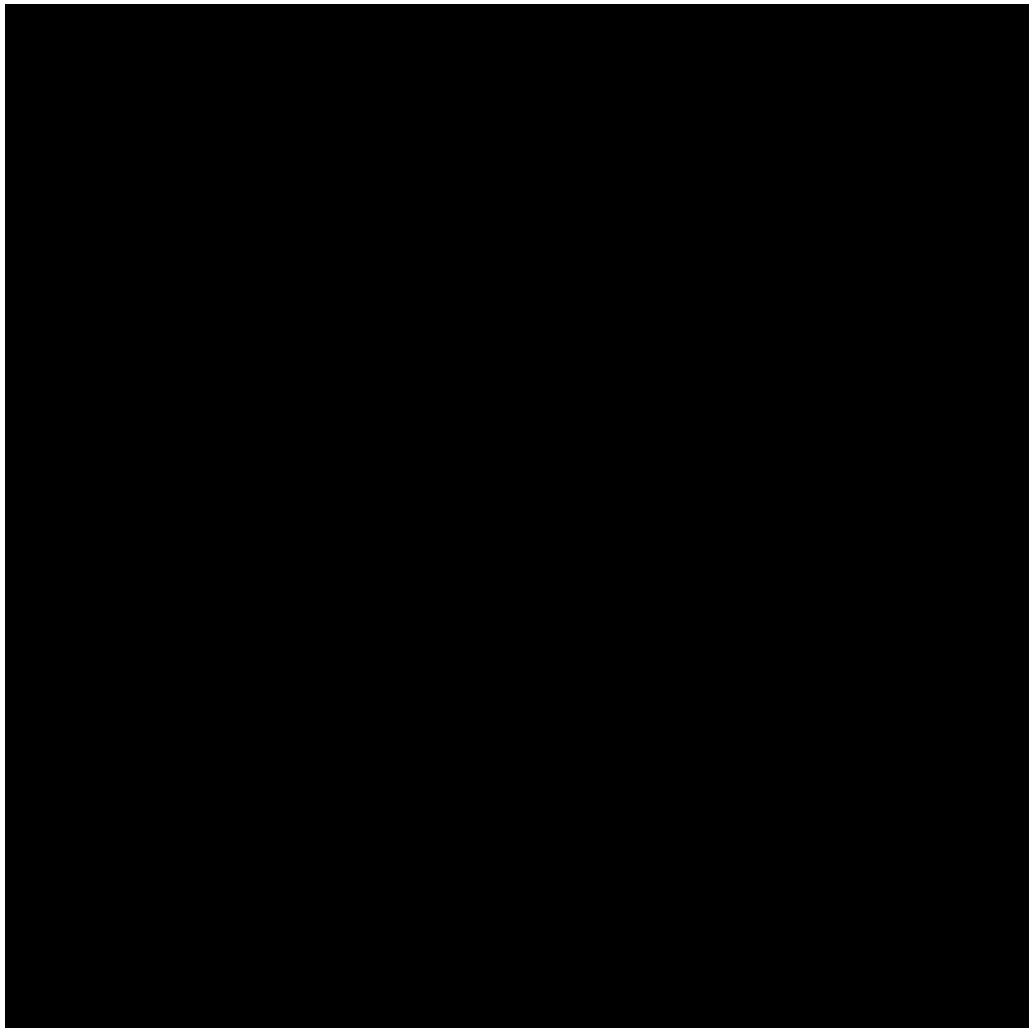
Eric Van Belle, MD, PhD (Lille)
Patrick Dupouy, MD (Antony)
Gilles Rioufol, MD, PhD (Lyon)
Christophe Pouillot, MD (St Denis, La Réunion)
Thomas Cuisset, MD, PhD (Marseille)
Karim Bougrini, MD (St Denis, La Réunion)
Emmanuel Teiger, MD, PhD (Créteil)
Stéphane Champagne, MD (Créteil)
Loic Belle, MD (Annecy)
Didier Barreau, MD (Toulon)
Michel Hanssen, MD (Haguenau)
Cyril Besnard, MD (Lyon)
Jean Dallongeville, MD, PhD (Lille)
Georgios Sideris, MD (Paris)
Christophe Bretelle, MD (Valence)
Nicolas Lhoest, MD (Colmar)
Pierre Barnay, MD (Avignon)
Raphael Dauphin (Lyon)
Laurent Leborgne, MD, PhD (Amiens)
Flavien Vincent (Lille)

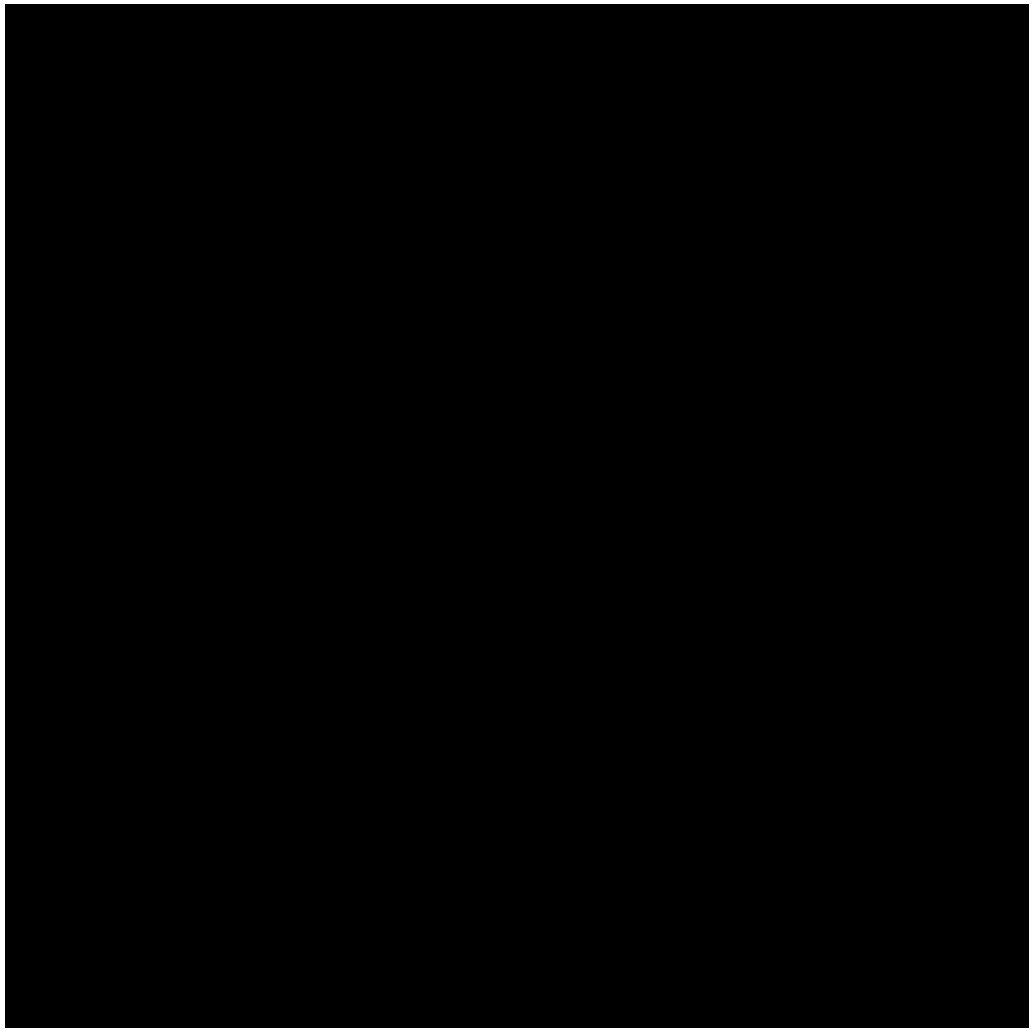
Patient with non-STEMI-ACS

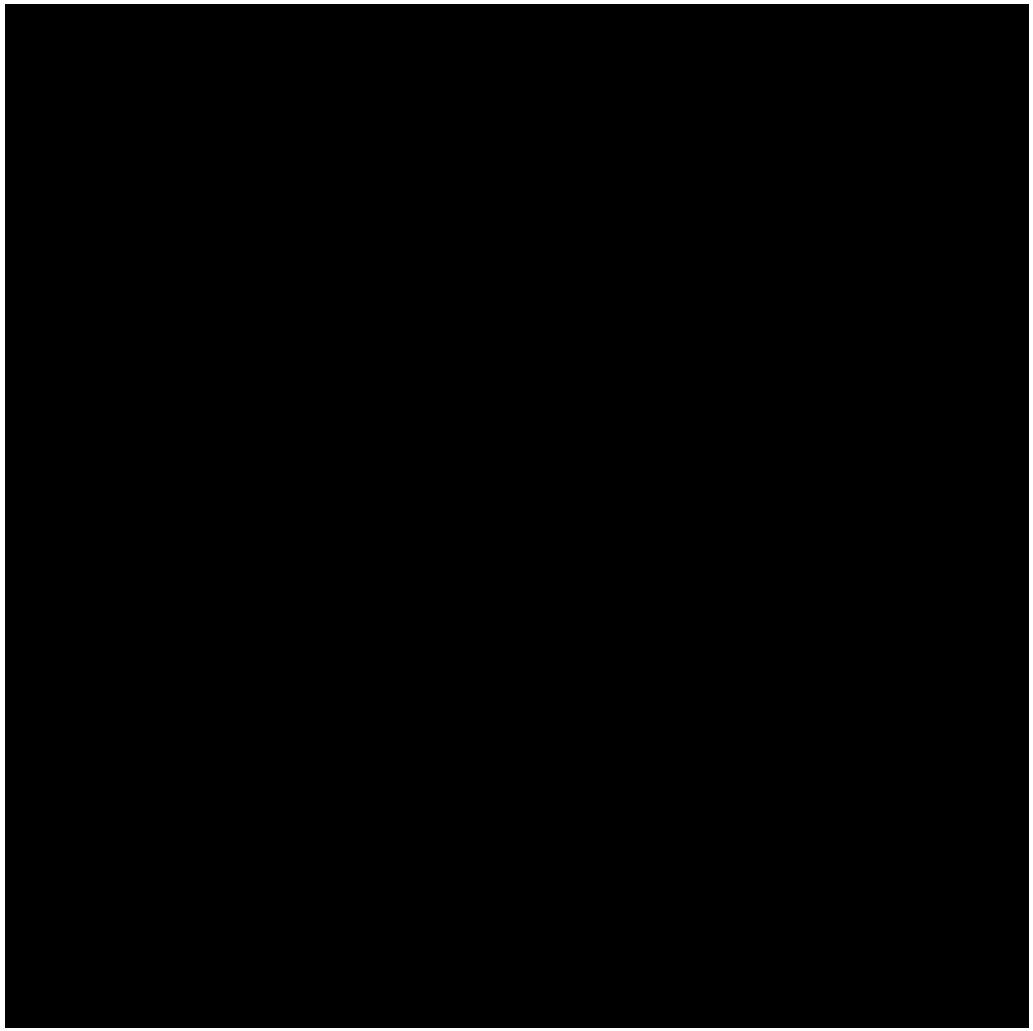
- Male
- 65 years old
- Previous smokers
- Chest pain for 6 hours
- Admitted in acute care
- ECG: ambiguous changes in inferior leads
- Troponine rise











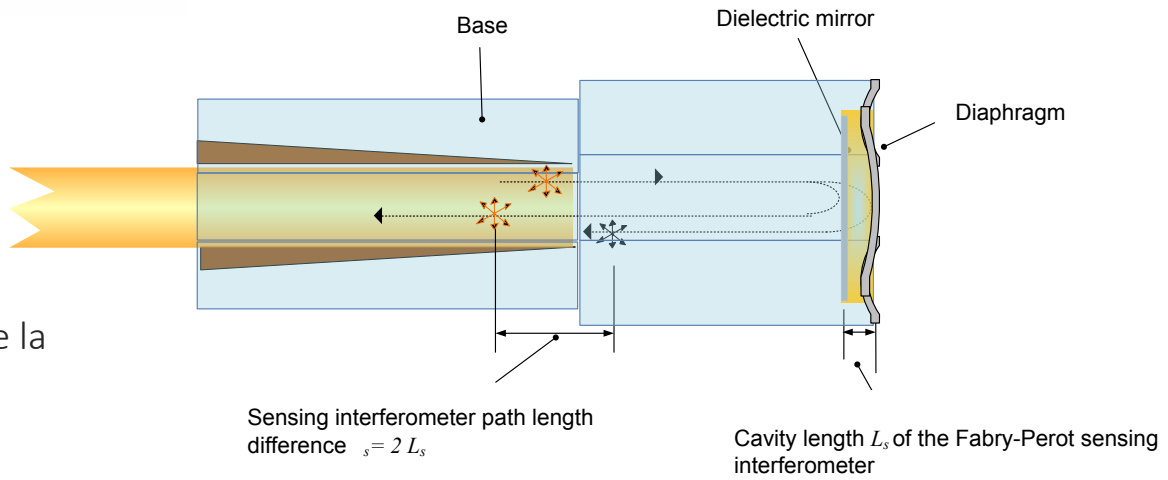
Opsens – La technologie derrière le succès

Caractéristique Unique - *White-light interferometry – Optical Coherence method*

(US patent 7.259.862)

- Mesure absolu de la différence de la distance entre les deux faisceaux.
- La mesure est insensible à

- l'intensité lumineuse et
- aux variations d'intensité (courbure de la fibre, connexion, vieillissement et lampes).

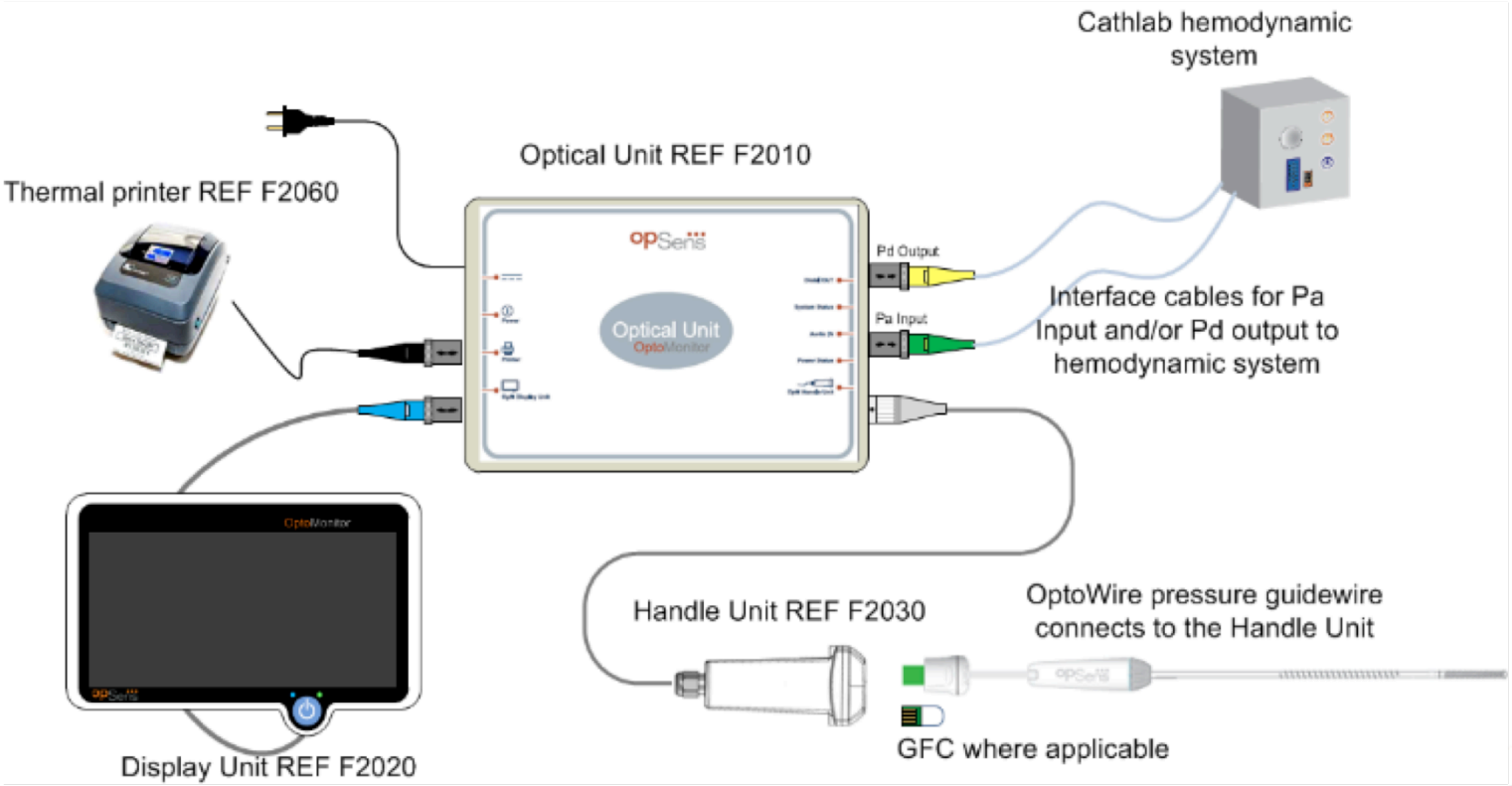


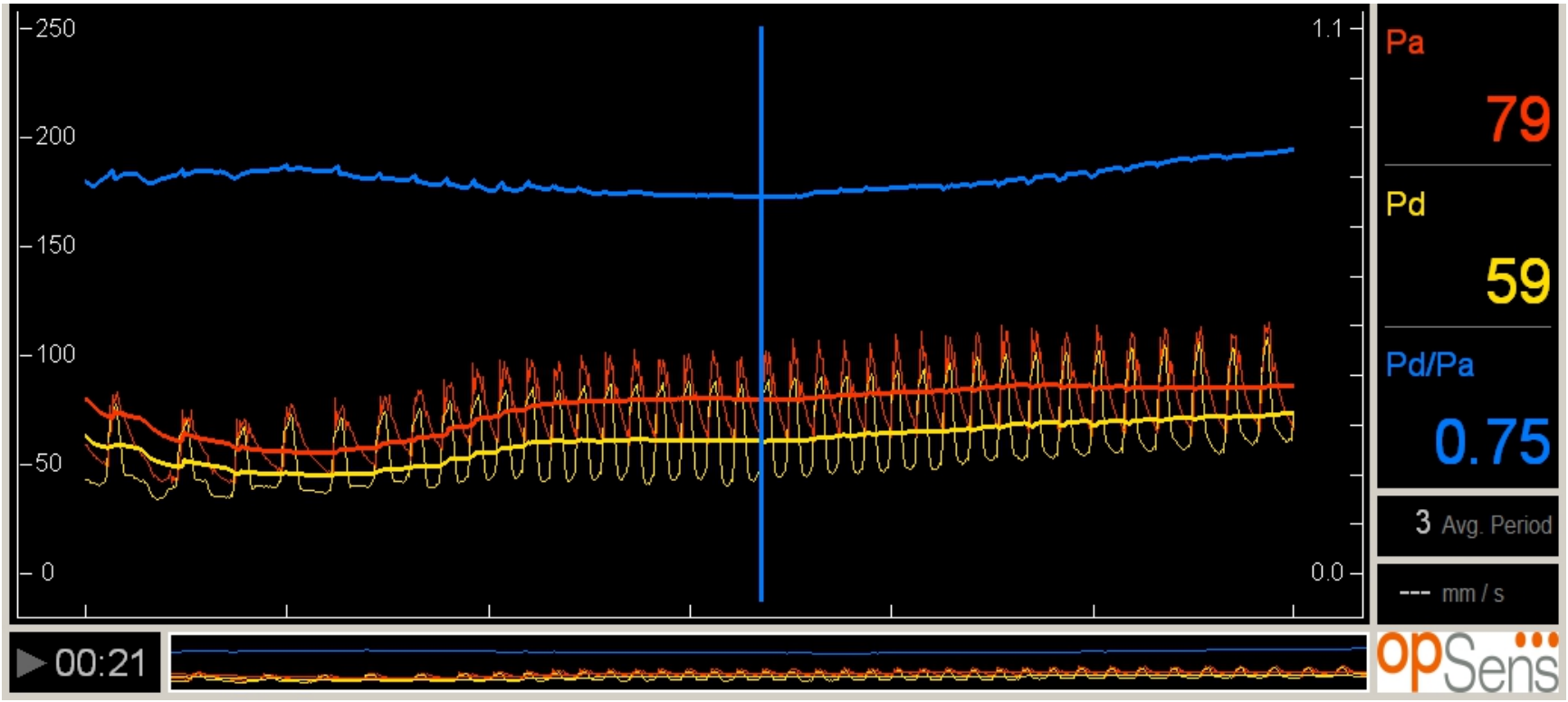
Caractéristique unique – *Optical MEMS based pressure sensor*

(Brevet US 7.689.071 et 8.752.435)

- Construction unique du diaphragme du capteur pour une sensibilité de pression optimale.
- Assemblage robuste du capteur permettant une force tensile un *pull* supérieur.

OptoMonitor – Vue d'ensemble




250
200
150
100
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1.1
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Pd
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Pd/Pa
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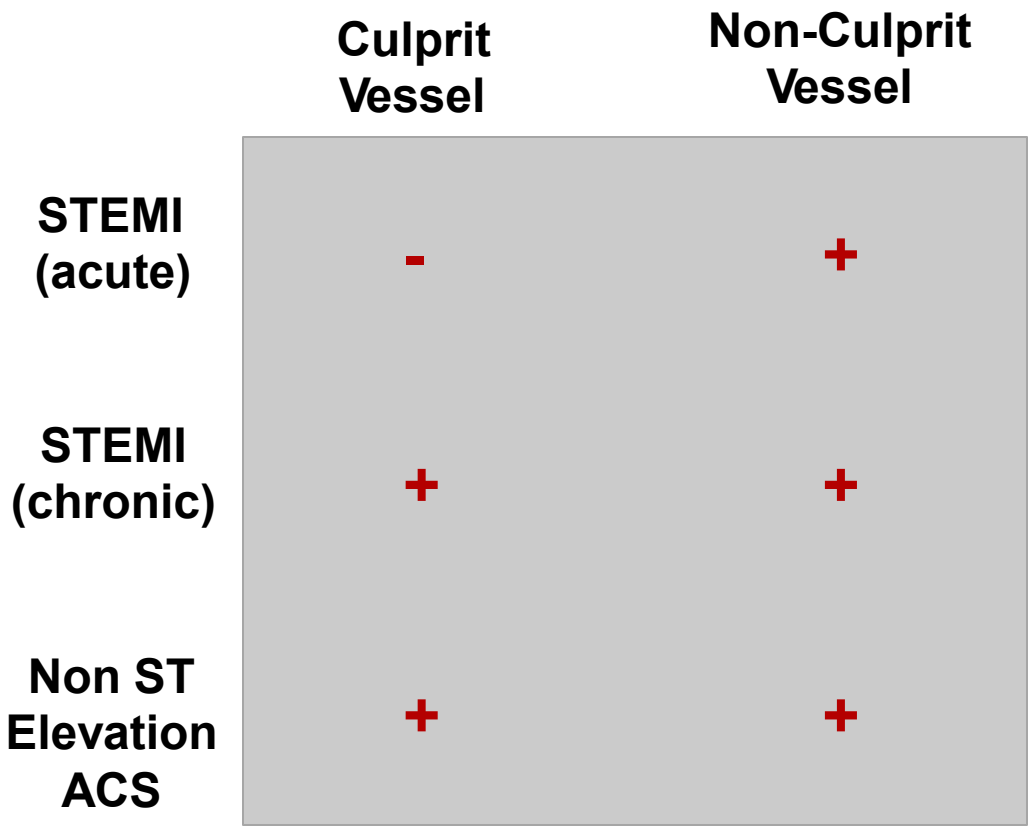
Summary

Indications for FFR in Acute Coronary Syndromes

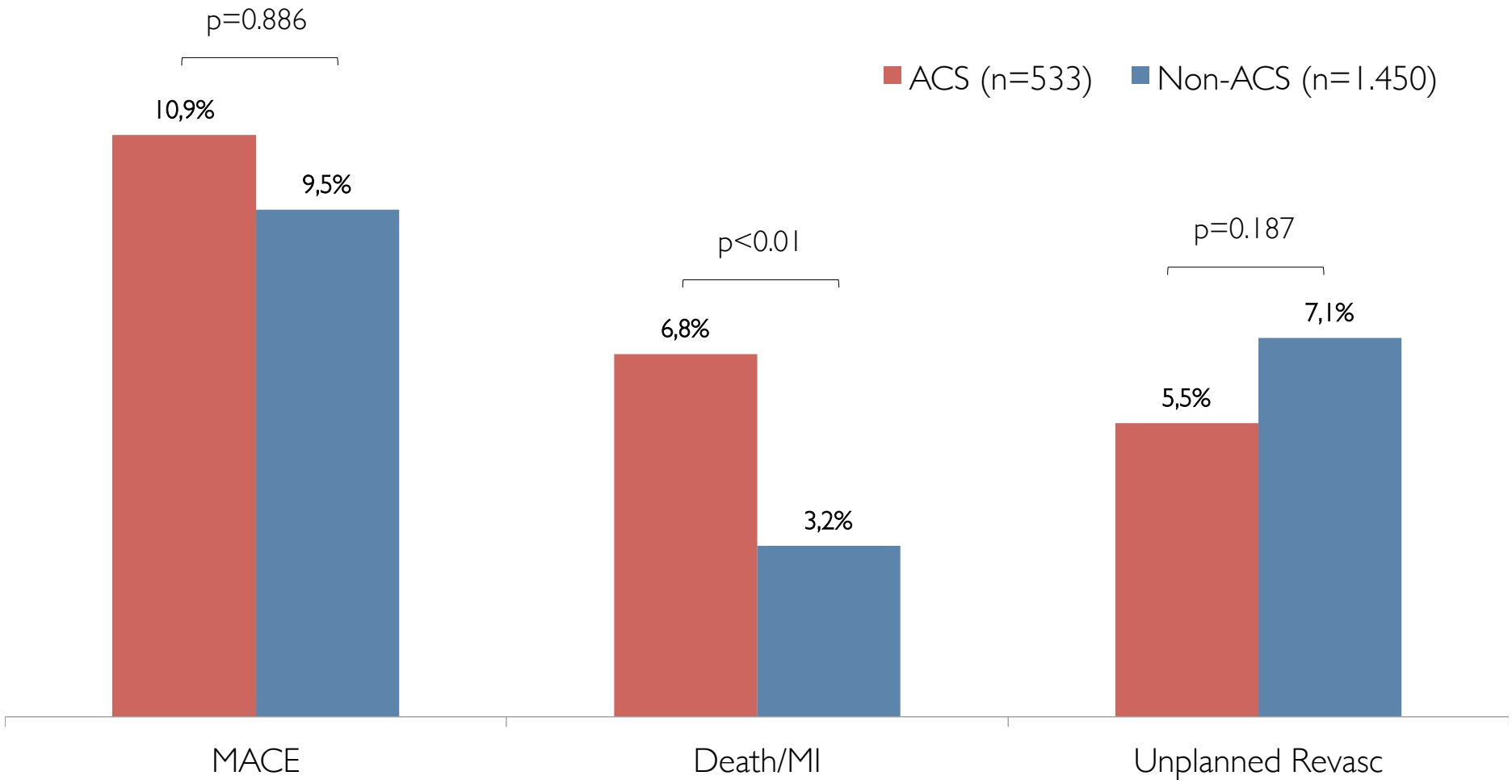


Invasive physiology as the « All-in-one-device» for management of CAD patients?

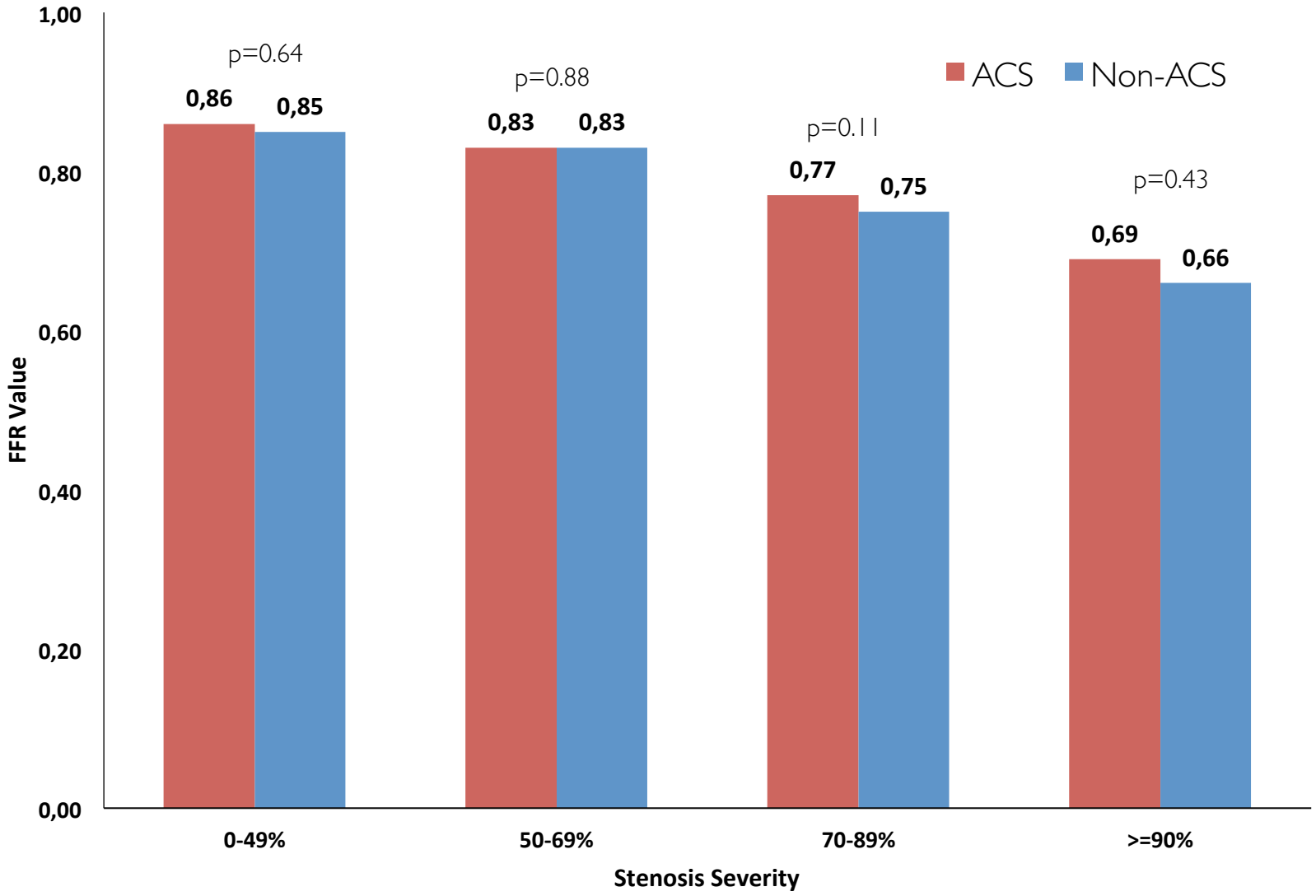
- **Macromanagement of CAD (patient level):**
  - **Diagnostic tool:**
    - **Classify patient risk (Defer)**
    - **Reclassify treatment approach (R3F, Post-it, RipCord)**
  - **Identify patients who benefit from coronary revascularization (Fame, Fame 2)**

- **Micromanagement of CAD (Vessel/lesion level)**
  - **Vessel: Which vessel to treat (Fame, R3F)**
  - **Lesion: Which lesion to treat in the vessel ? How to treat this lesion ?**

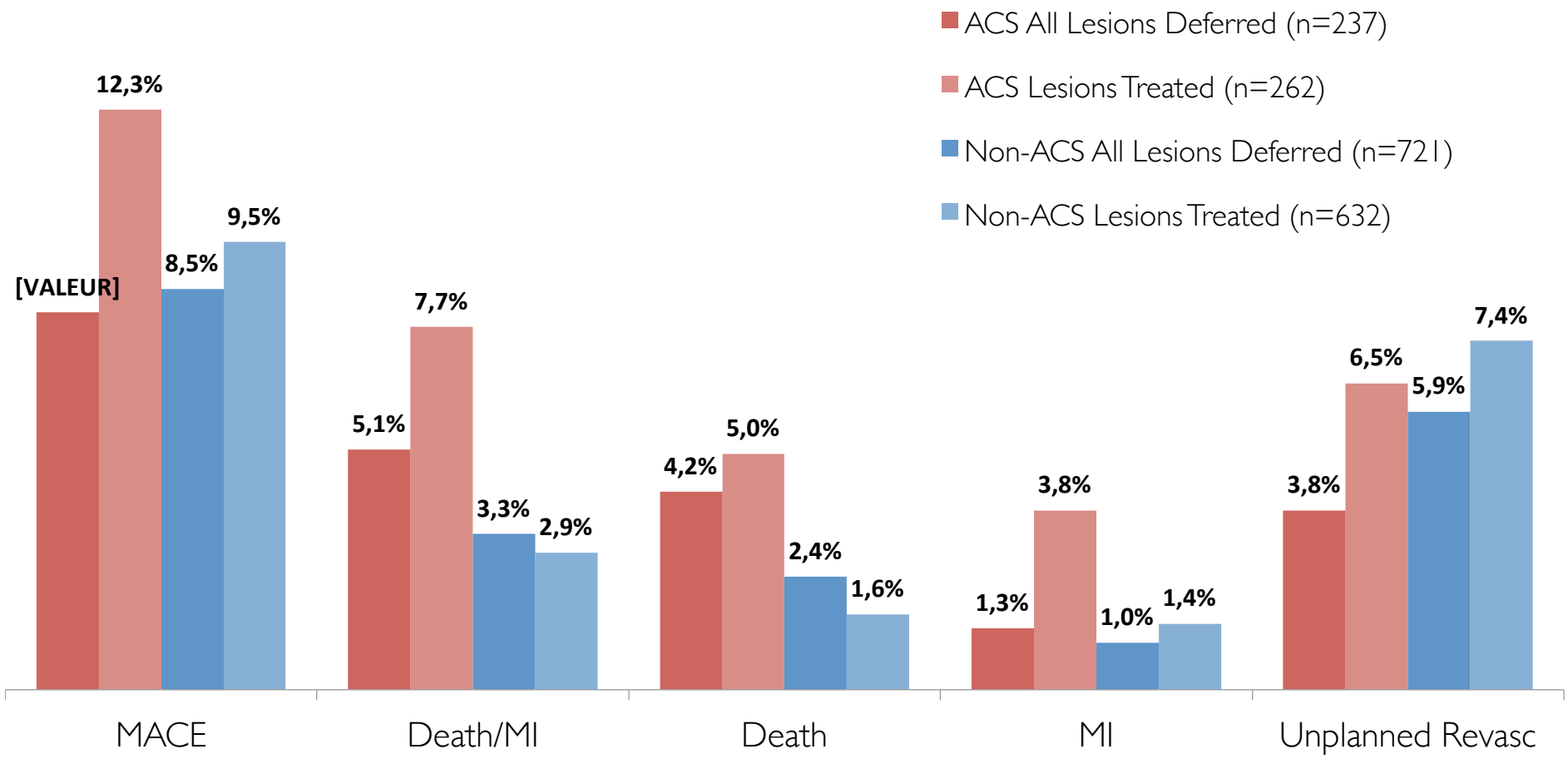
Overall 1-year Clinical Outcome



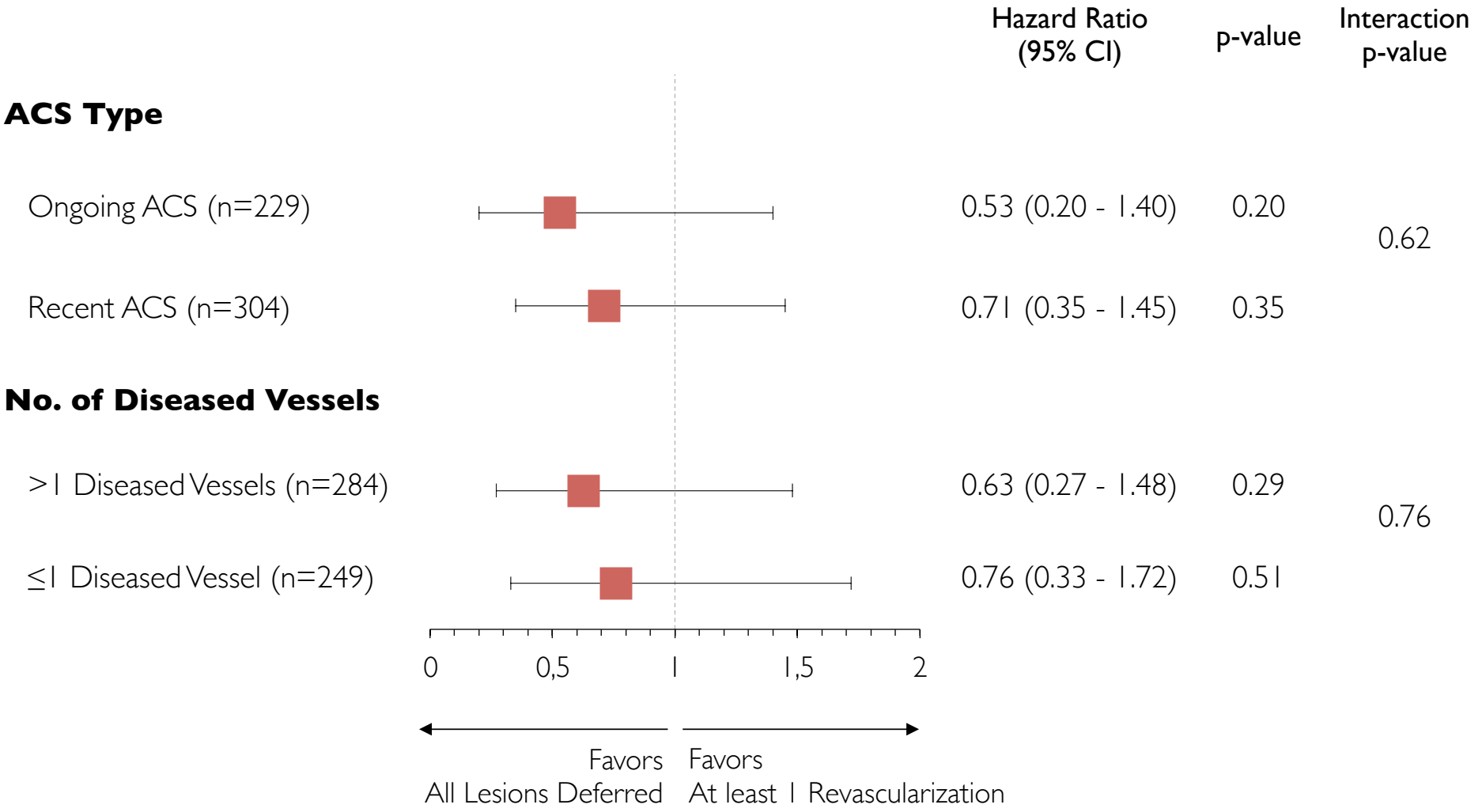
Impact of ACS status on FFR values



Safety of revascularization deferral



Management Strategy in ACS Subgroups

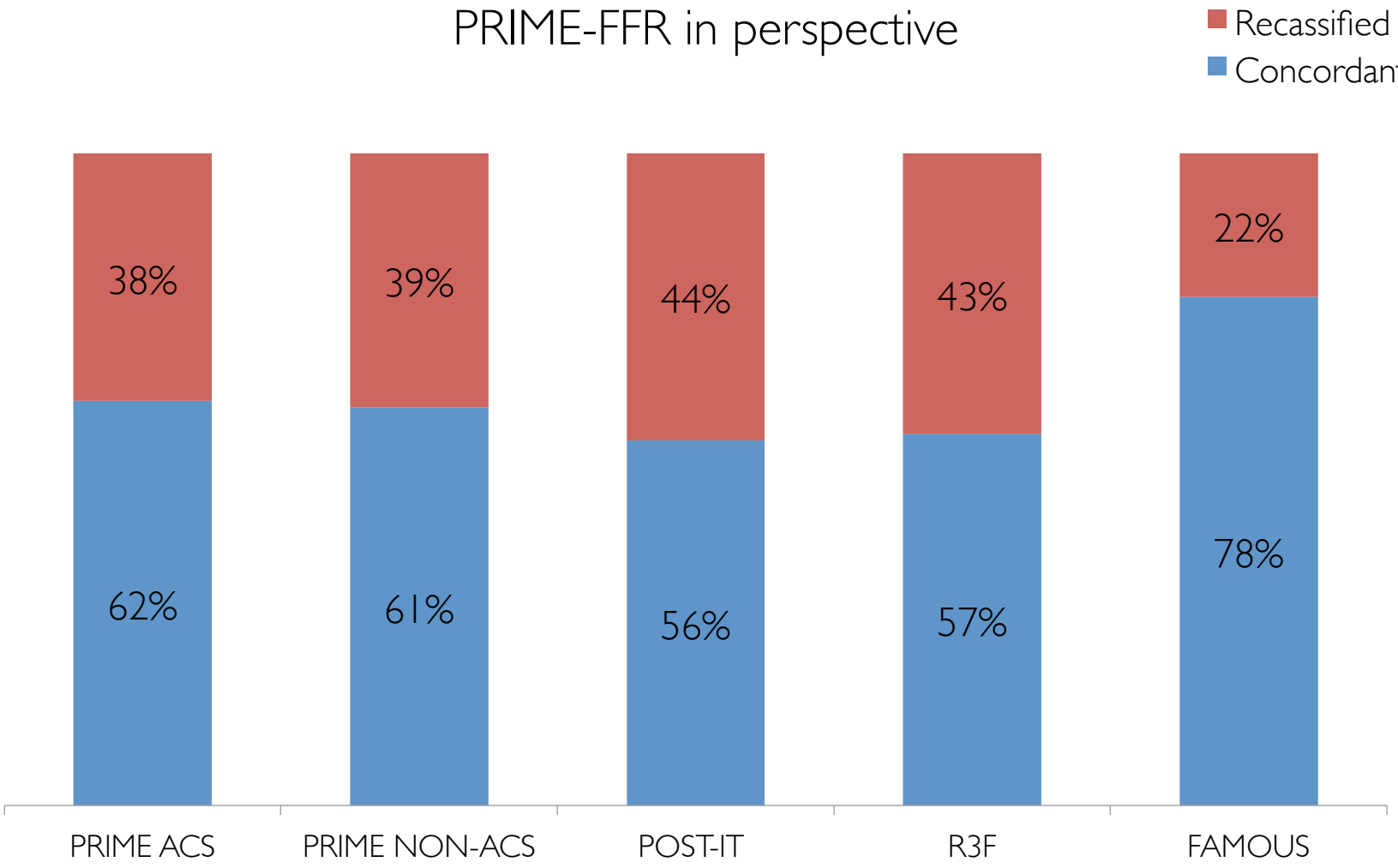


Conclusions

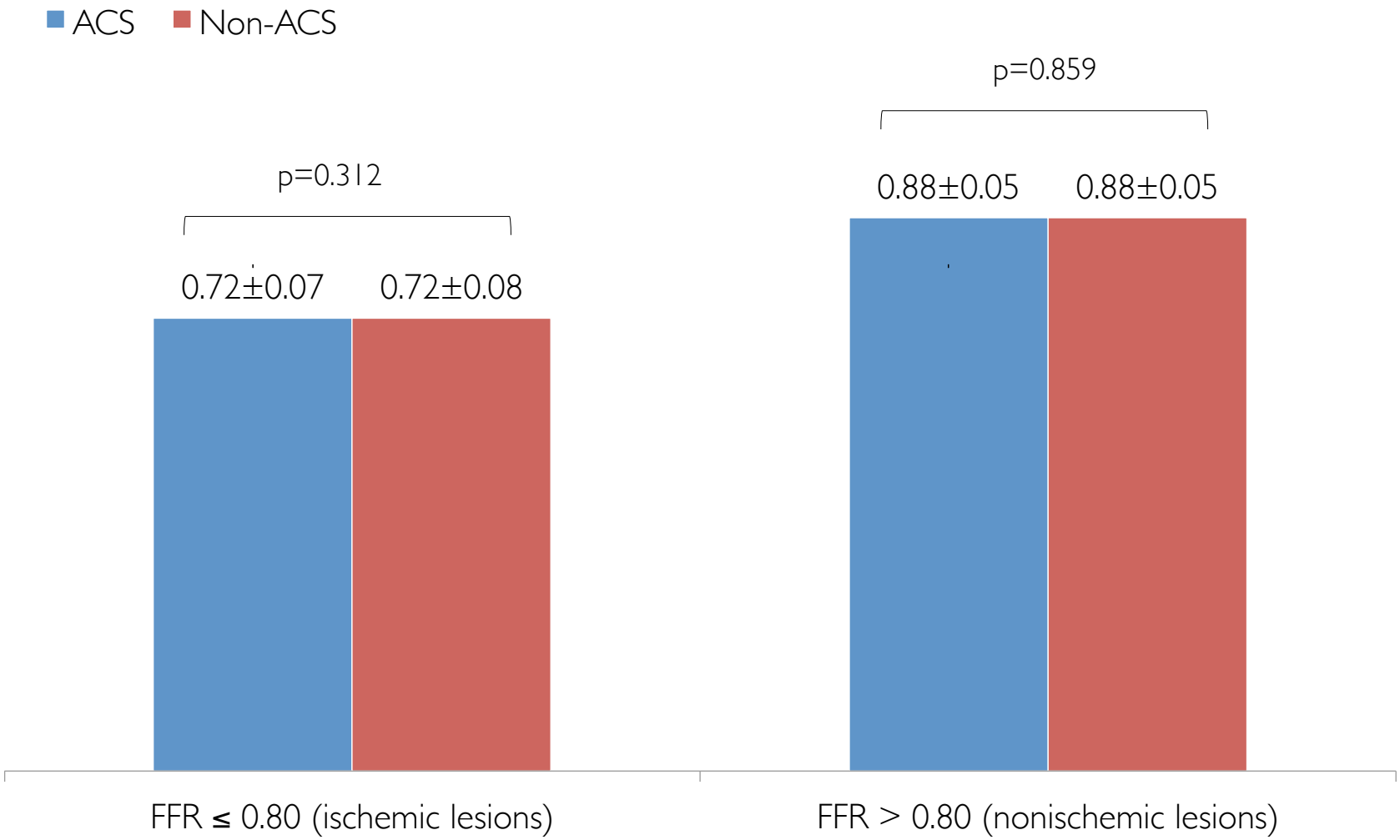
- ✓ Integrating FFR on clinical decision making and pursuing a treatment strategy divergent from angiography (including revascularization deferral) was as safe in ACS as in stable CAD patients.

- ✓ Large randomized trials powered for clinical outcomes are needed to further clarify the role of FFR in the setting of the heterogeneous clinical scenario of ACS patients.

Impact of FFR on Treatment Strategy

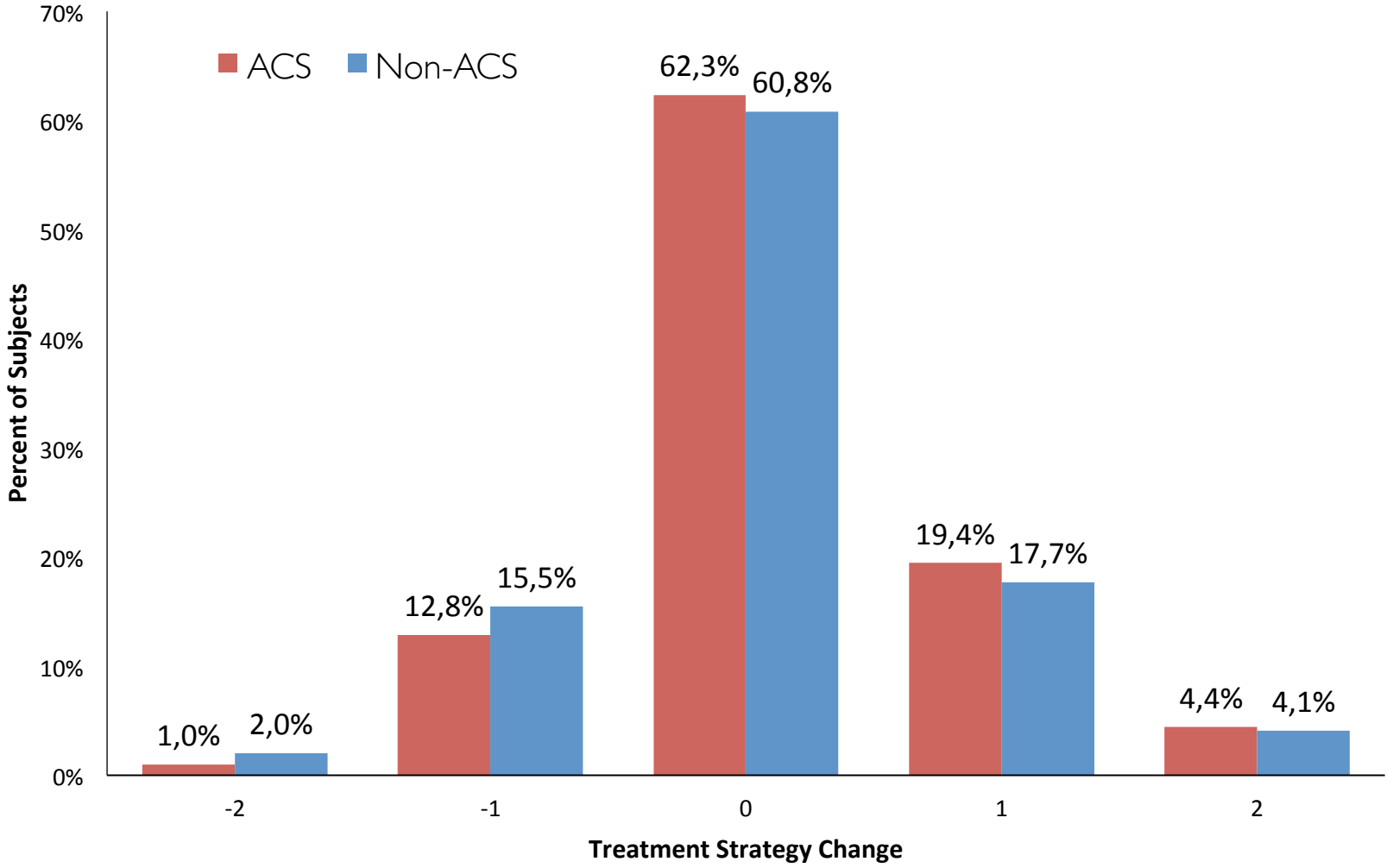


Impact of ACS status on FFR values



FFR & Treatment strategy change

"Magnitude" of strategy change according to ACS status



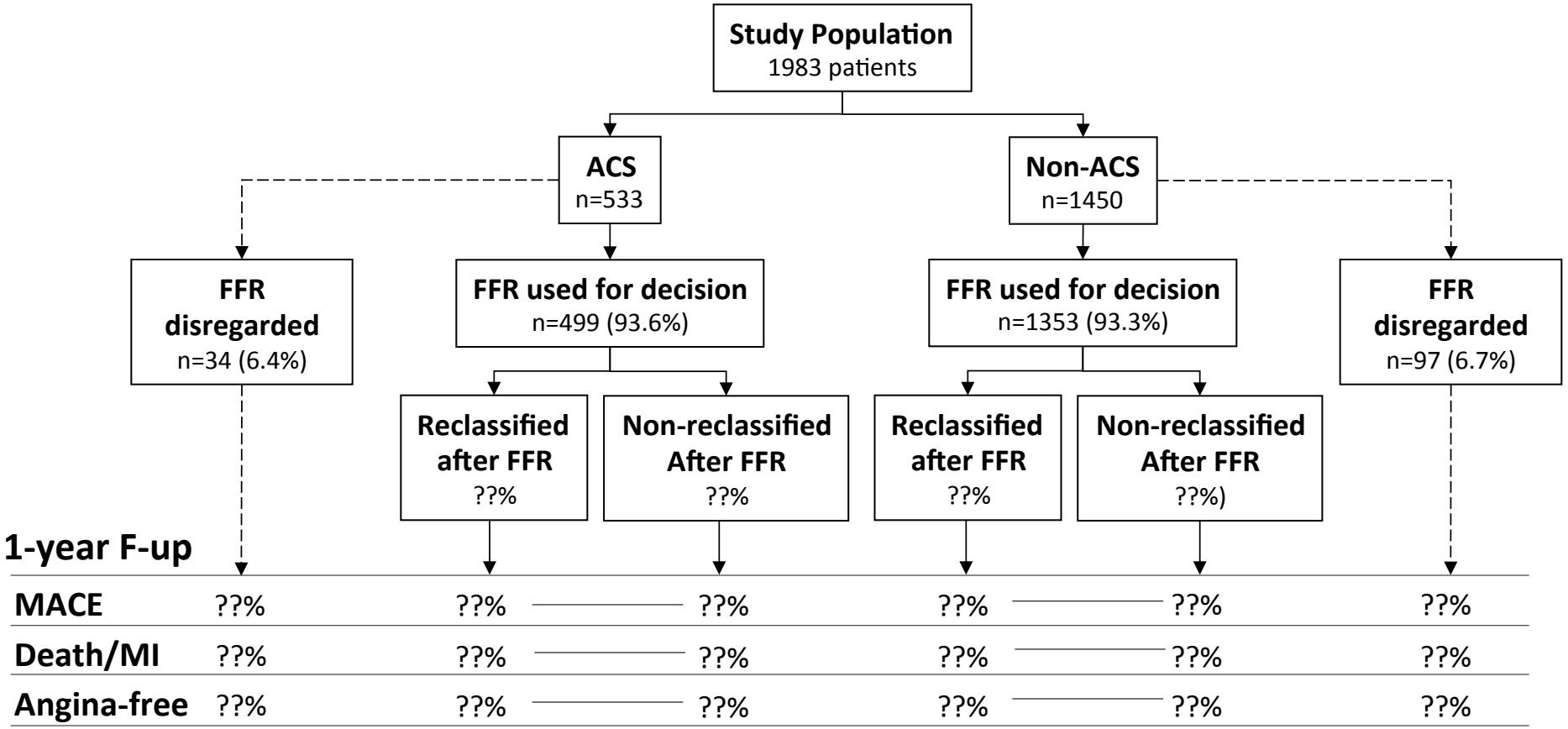
Baseline Characteristics

Variable (n;%)	ACS Population	Non-ACS population	p value
Number of diseased vessels (>50%)			
0-1	284 (53.3%)	846 (58.4%)	0.055
2	156 (29.3%)	384 (26.5%)	
3	93 (17.4%)	220 (15.2%)	
Number of lesions evaluated			
1	391 (73.4%)	1049 (72.3%)	0.921
2	103 (19.3%)	300 (20.7%)	
3	31 (5.8%)	81 (5.6%)	
>3	8 (1.5%)	20 (1.4%)	
Lesion Characteristics			
Left Anterior Descending	414 (57.7%)	1146 (57.9%)	0.511
Left Main	32 (4.5%)	117 (5.9%)	0.121
Proximal LAD	125 (17.4%)	389 (19.7%)	0.187
Any proximal lesion	239 (33.3%)	687 (34.7%)	0.485
Lesion - % stenosis [mean±SD]	57.6±12.4	55.4±13.9	<.001
ACC/AHA Classification B2/C	310 (43.2%)	757 (38.3%)	0.020
FFR results [mean±SD]			
FFR ≤ 0.80 (ischemic lesions)	0.72±0.07	0.72±0.08	0.312
FFR > 0.80 (nonischemic lesions)	0.88±0.05	0.88±0.05	0.859
Lesions with FFR ≤ 0.80 (n;%)	288 (40.0%)	786 (39.7%)	0.902

PRIME-FFR

POST-IT and R3F Integrated Multicenter registriEs - Implementation of FFR in Routine Practice

Joint French/Portuguese Prospective Study



Hotline EuroPCR Thursday Morning

PRIME-FFR

POST-IT and R3F Integrated Multicenter registriEs - Implementation of FFR in Routine Practice

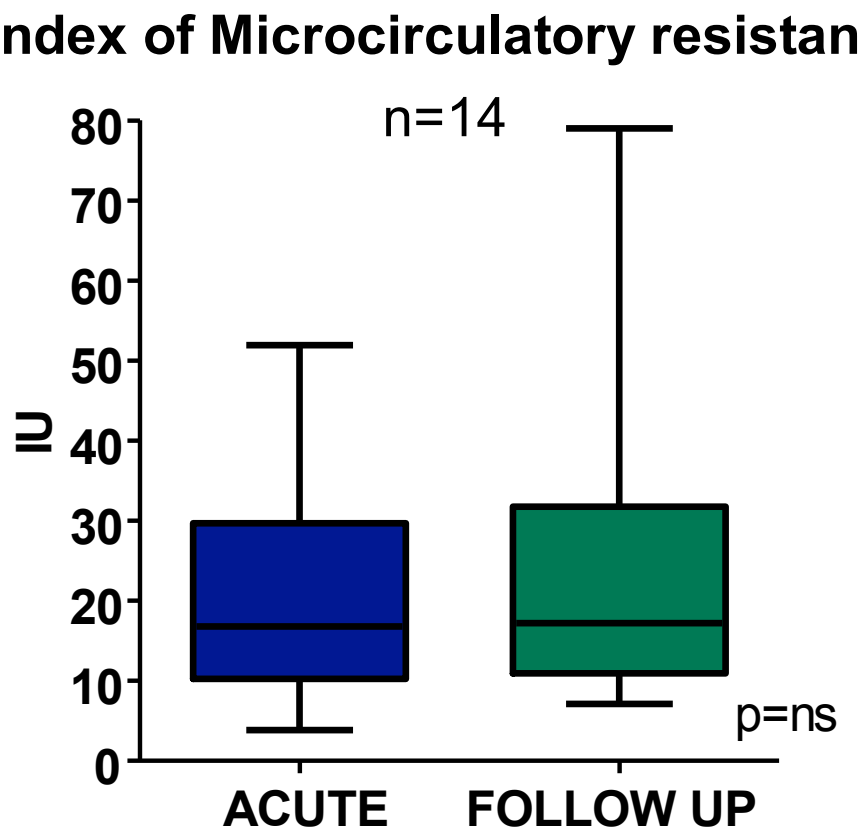
Why it will be important ?

- In ACS, what is rate of reclassification of the management strategy (medical, PCI, CABG) with routine FFR usage?
- How does the rate of reclassification compare with non-ACS patients?
- Is FFR–based reclassification of the management strategy; i.e. against stategy suggested by angiography; safe in ACS patients?
- Is FFR-based deferral to medical treatment able to identify a population at low risk?

Hotline EuroPCR

FFR STEMI (Non-Culprit Vessels)

Microvascular resistance did not change from baseline to follow-up



Ntalianis, et al. J Am Coll Cardiol Intv 2010;3:1274