Safety of coronary revascularisation deferral based on iFR and FFR measurements in stable angina and acute coronary syndromes

A pooled patient-level analysis of DEFINE FLAIR and IFR SWEDEHEART trials

Javier Escaned MD PhD FESC on behalf of the DEFINE FLAIR and IFR SWEDEHEART investigators

Potential conflicts of interest

Speaker's name: Javier Escaned

❑ **I have the following potential conflicts of interest to report:**

Speaker at educational events and consultancies: Abbott, AstraZeneca, Biosensors, Boston Scientific, Medtronic, OrbusNeich, Philips Healthcare

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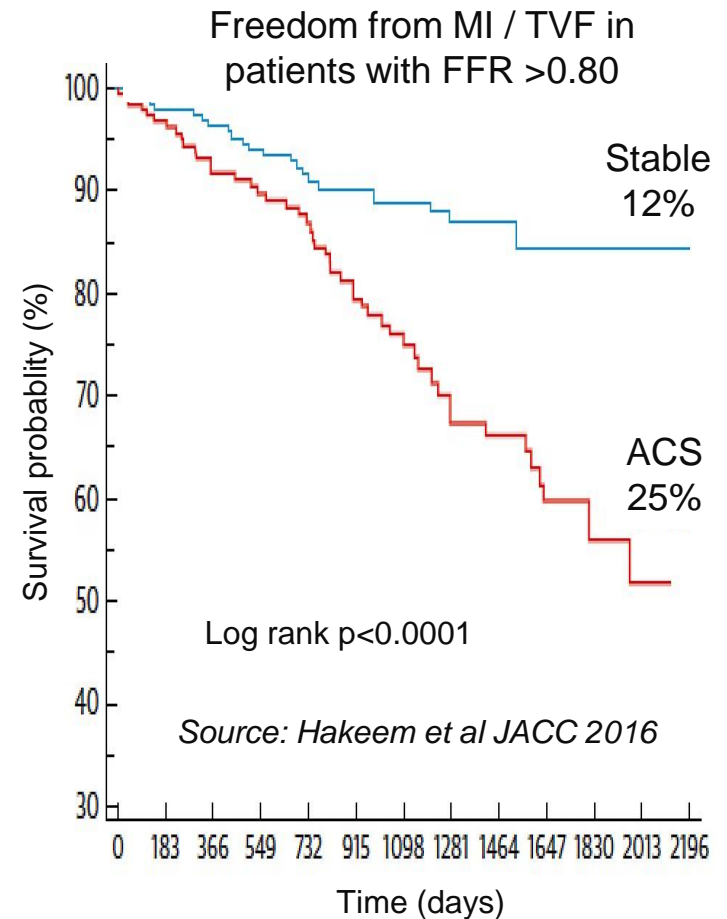
Background: Physiology-based deferral of coronary revascularisation

- Revascularisation deferral (i.e. decision to treat medically) is a key aspect of physiology-based coronary revascularisation.

- Evidence regarding the safety of revascularisation deferral in contemporary scenarios is scarce.

- Deferral was shown to be safe in the pivotal DEFER trial (1998-2001). Since then, major changes in PCI and pharmacological treatment that might affect outcomes have taken place.

Pressure sensor

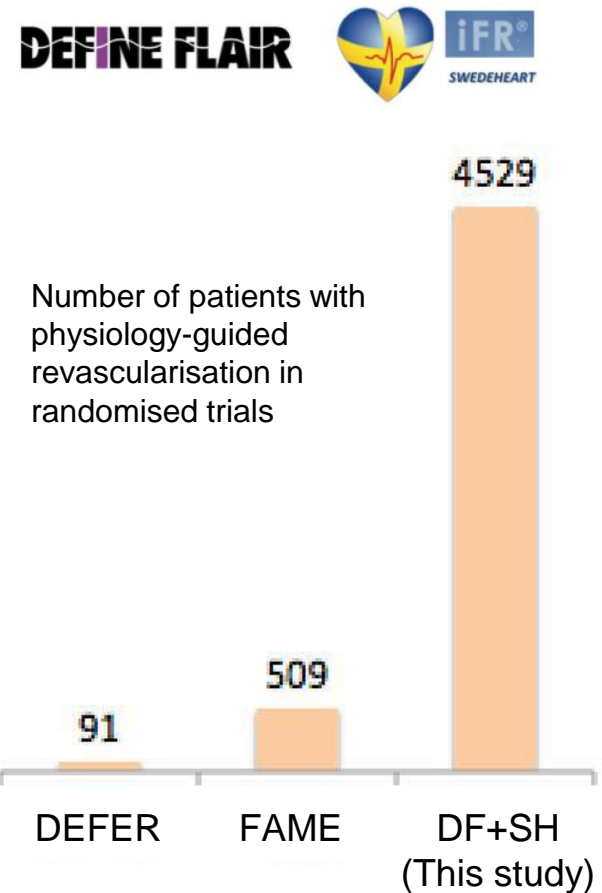Bech GJ, *al*. DEFER trial. *Circulation* 2001; **103**: 2928–34
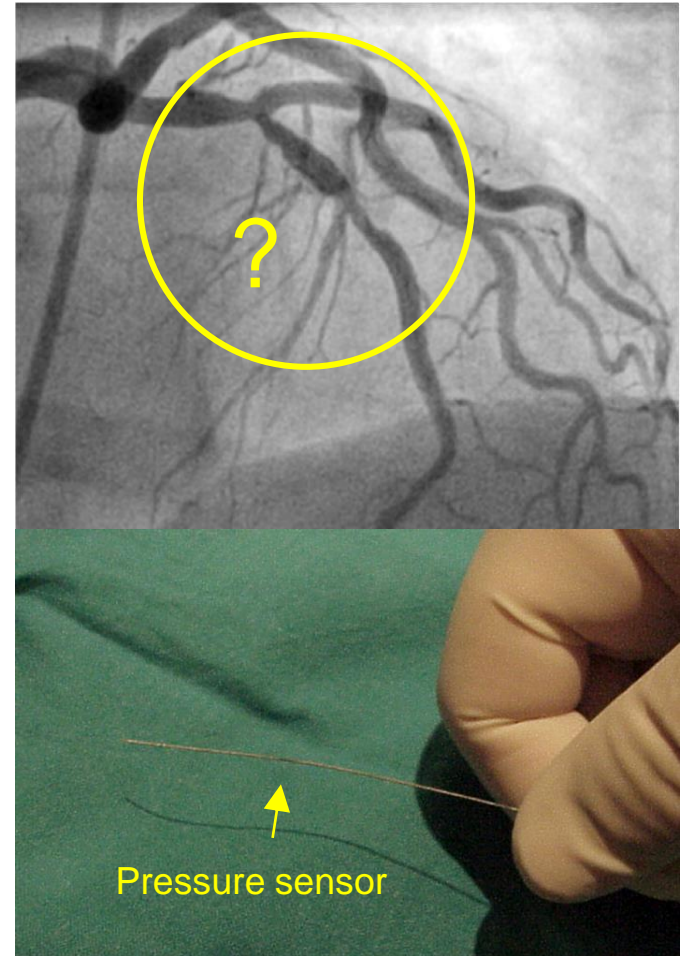
Background: Physiology-based deferral in acute coronary syndromes

- In recent years several studies have cast doubts as to the safety of deferring PCI with FFR in patients with ACS.

- Transient microcirculatory dysfunction in culprit and non-culprit vessels, blunting hyperaemic responses, has been proposed as a mechanism.

- Given the growing proportion of patients presenting with ACS, establishing whether deferral of PCI in ACS is as safe as in stable angina is an urgent matter.

Freedom from MI / TVF in patients with FFR >0.80

Stable 12%

ACS 25%

Log rank p<0.0001

Source: Hakeem et al JACC 2016

Survival probablity (%)

Time (days)

Hakeem A, *et al. J Am Coll Cardiol* 2016; **68**: 1181–91., Masrani Mehta *et al. J Am Heart Assoc* 2015; **4**: e002172.

Background: FFR- and iFR-based deferral of coronary revascularisation

- The DEFINE FLAIR (DF) and iFR SWEDEHEART (SH) trials demonstrated that iFR is as safe as FFR in guiding myocardial revascularisation.

- Yet, it is know this finding is valid for patients in whom revascularisation is deferred.

- The pooled population of both studies (4529 patients) provides a unique opportunity to investigate the discussed aspects of revascularisation deferral in contemporary clinical practice.

DEFINE FLAIR **iFR SWEDEHEART**

Number of patients with physiology-guided revascularisation in randomised trials

	DEFER	FAME	DF+SH (This study)
	91	509	4529

Davies JE *et al. N Engl J Med* 2017; Götberg M, *et al. N Engl J Med* 2017
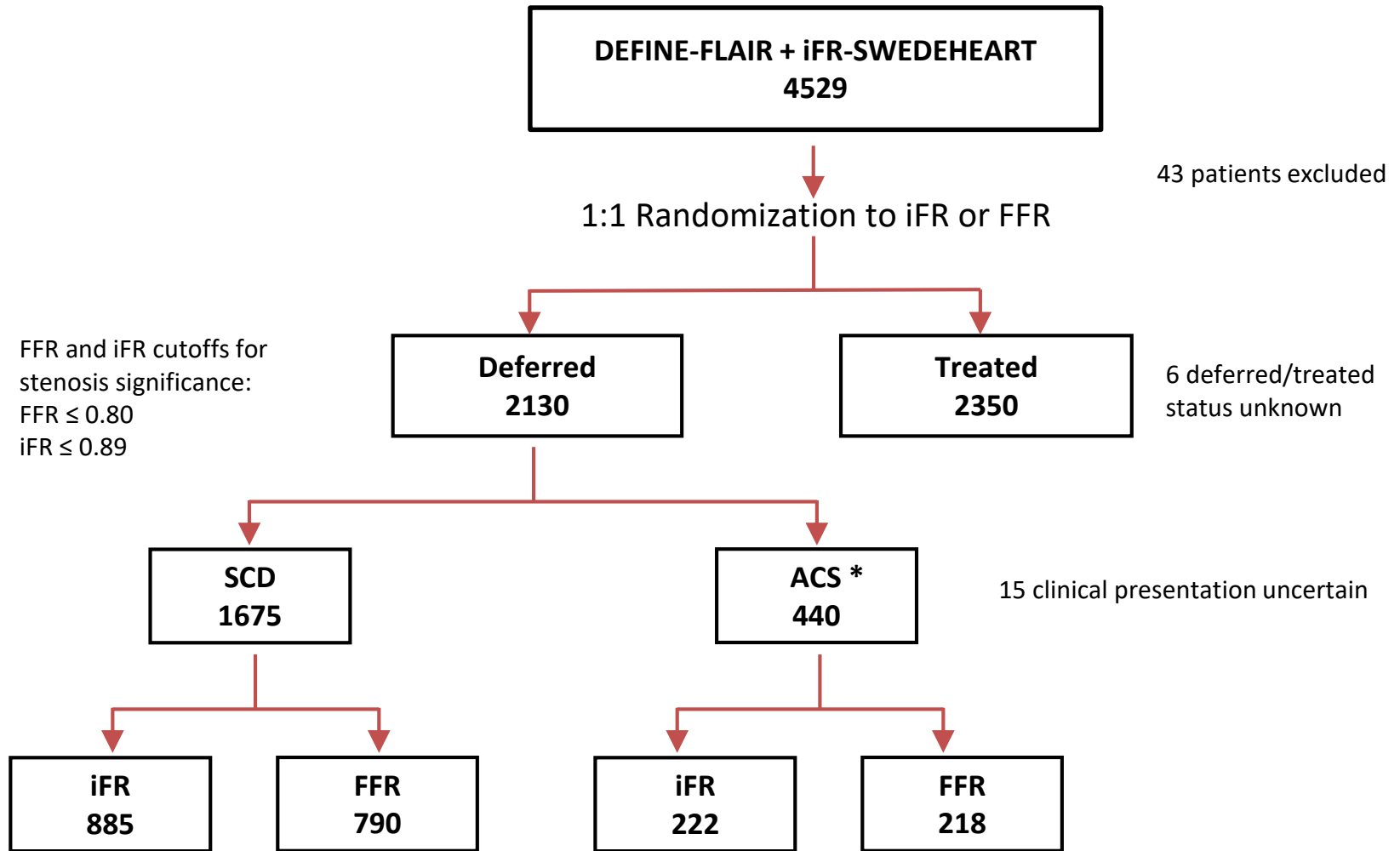
Study objectives:

To investigate if 1-year outcomes of deferred patients:

▪ Are similar when the decision is based on FFR or iFR measurements.

▪ Are influenced by clinical presentation (stable coronary disease [SCD] or acute coronary syndrome [ACS]).

Primary endpoint:

Major adverse cardiac events (MACE), defined as a composite of death, non-fatal myocardial infarction and unplanned revascularisation, at 1 year.

Study population

DEFINE-FLAIR + iFR-SWEDEHEART
4529

43 patients excluded

1:1 Randomization to iFR or FFR

FFR and iFR cutoffs for
stenosis significance:
FFR ≤ 0.80
iFR ≤ 0.89

Deferred
2130

Treated
2350

6 deferred/treated
status unknown

SCD
1675

ACS *
440

15 clinical presentation uncertain
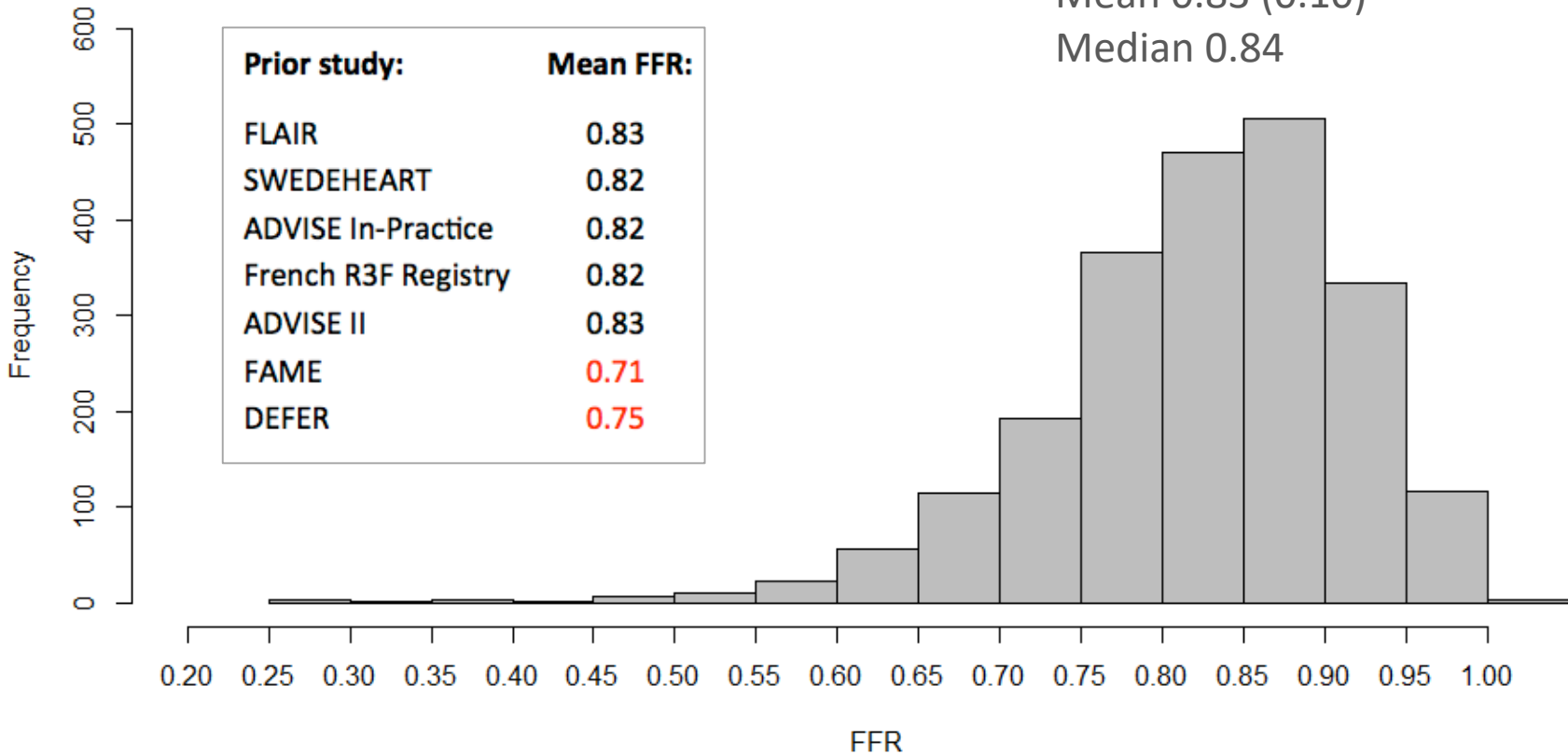
iFR
885

FFR
790

iFR
222

FFR
218

* In ACS, only non-culprit vessels were evaluated with pressure guidewires

FFR values reflect interrogation of predominantly intermediate stenoses

DEFINE FLAIR   iFR® SWEDEHEART

Patients in FFR arm = 2246
Mean 0.83 (0.10)
Median 0.84

Prior study:	Mean FFR:
FLAIR	0.83
SWEDEHEART	0.82
ADVISE In-Practice	0.82
French R3F Registry	0.82
ADVISE II	0.83
FAME	0.71
DEFER	0.75

Patient characteristics in the deferred and treated groups

	Deferred	Treated	P value
Number of patients	2130	2350	
Age (yr), mean (sd)	66.3 (10.3)	66.3 (10.1)	0.72
Male, N (%)	1493 (70.1)	1887 (80.3)	<0.01
Diabetes mellitus, N (%)	494 (23.2)	696 (29.6)	<0.01
Previous myocardial infarction, N (%)	644 (30.2)	746 (31.7)	0.51
Previous PCI, N (%)	1207 (56.7)	1411 (60.0)	0.03

Deferred patients had a lower cardiovascular risk profile than treated patients

Clinical presentation

	Treated *	Deferred *	P value	iFR	FFR	P value
Number of patients	2350	2130		2240	2246	
Clinical presentation			<0.01			NS
Post-STEMI**, N (%)	48 (2.0)	41 (1.9)		48 (2.0)	41 (1.9)	
Non ST ACS**, N (%)	727 (30.9)	399 (18.7)		571 (25.5)	559 (24.9)	
SCD**, N (%)	1562 (66.5)	1675 (78.6)		1604 (71.6)	1635 (72.8)	

* 6 patients with revascularization status unknown
** 28 patients with clinical presentation uncertain

ACS = Post-STEMI + Non ST ACS

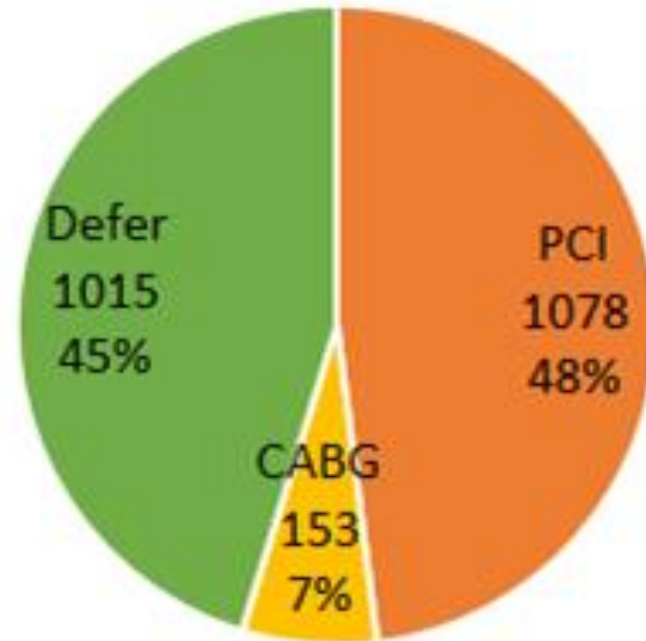Clinical presentation was balanced between iFR and FFR

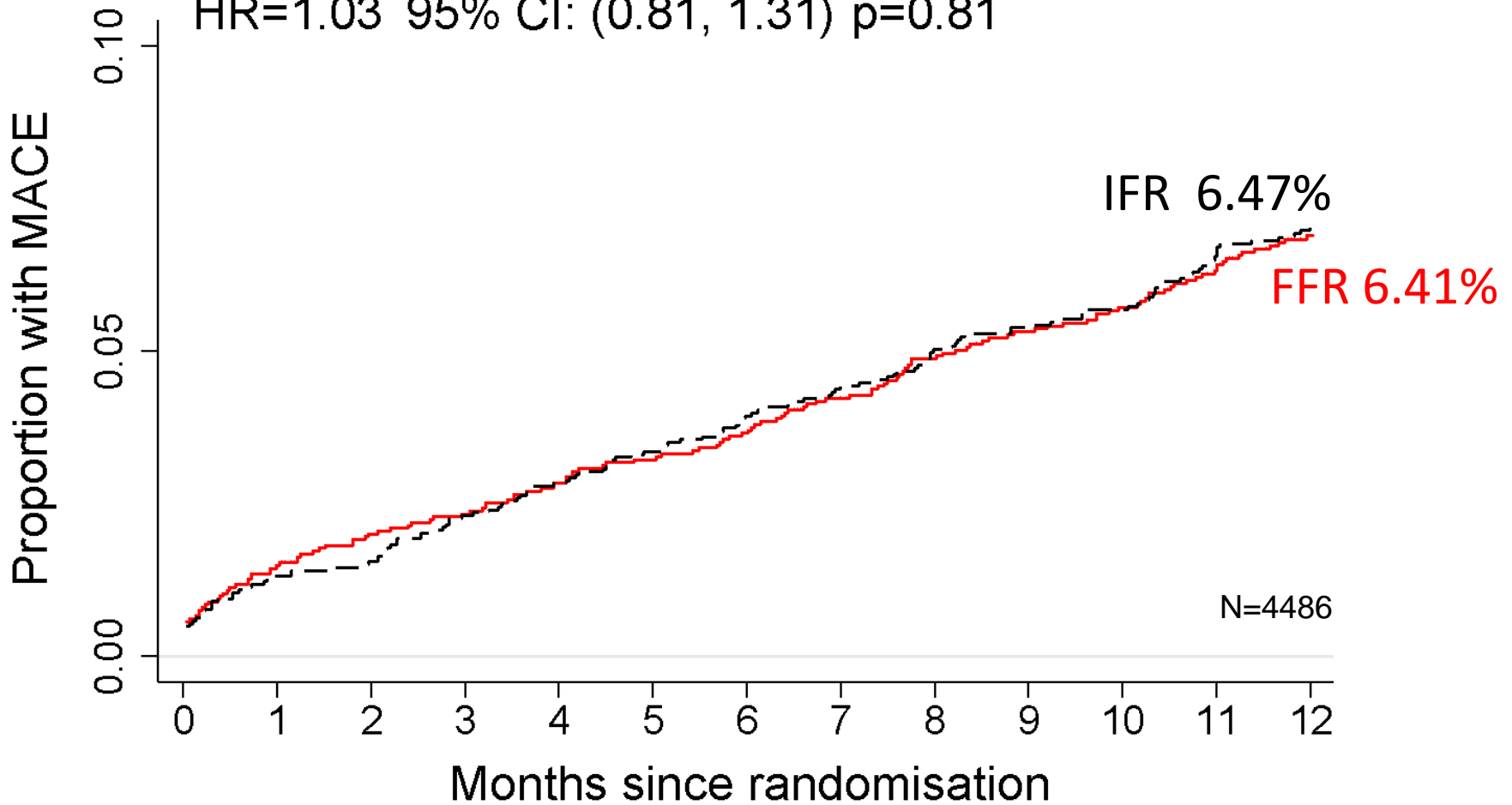# Treatment allocations with iFR and FFR

iFR (n=2240)
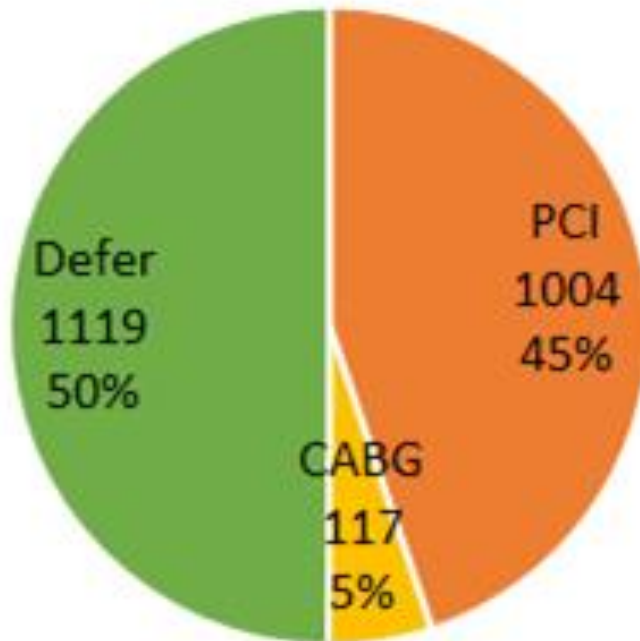
FFR (n=2246)

Significantly less revascularisation based on iFR interrogation (P < 0.01)

MACE in iFR and FFR guided revascularisation (all patients)
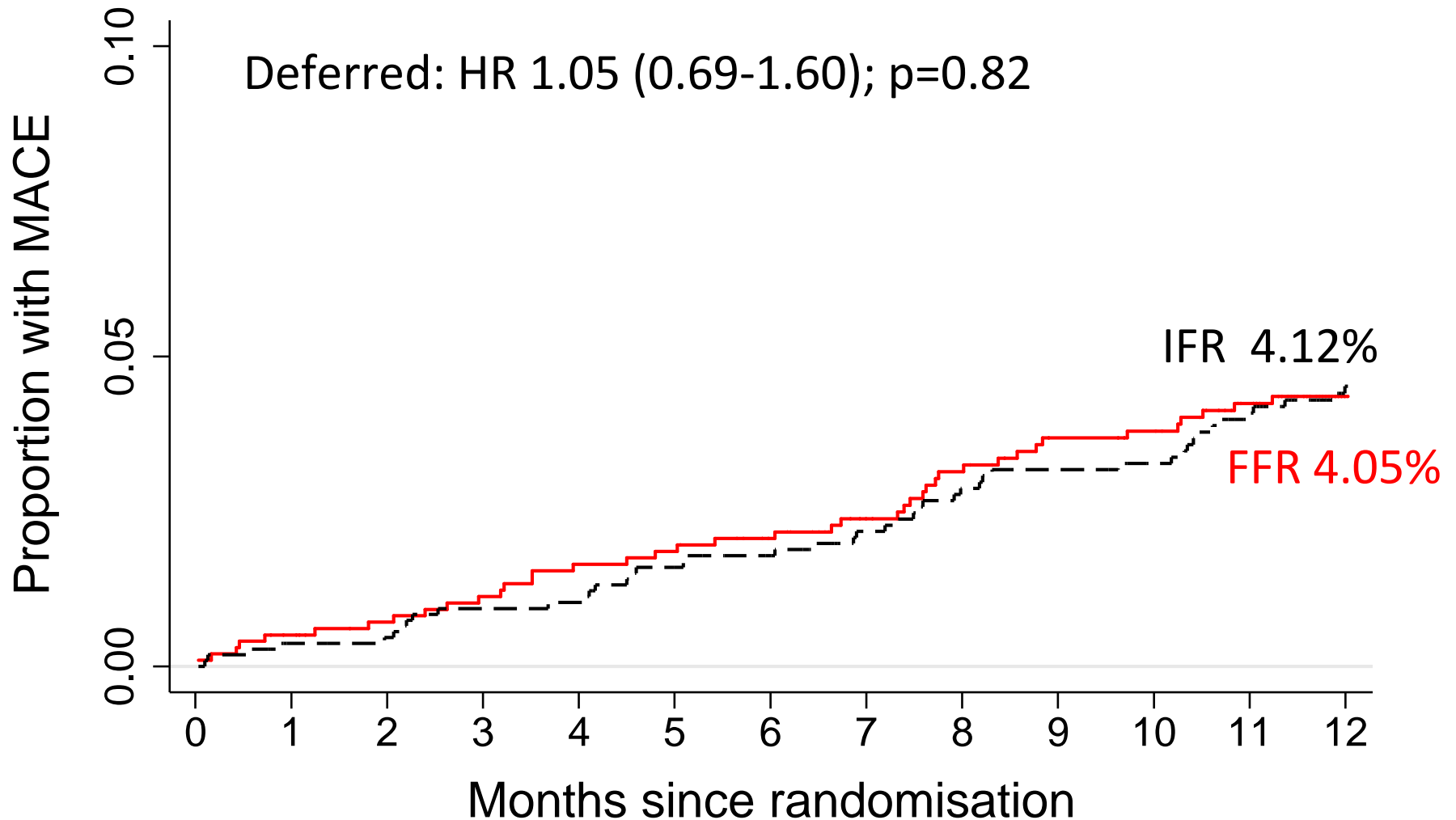
HR=1.03 95% CI: (0.81, 1.31) p=0.81

IFR 6.47%

FFR 6.41%

N=4486

Proportion with MACE

Months since randomisation

MACE similar and low at 1 year after iFR- and FFR-based revascularisation decision-making

MACE components in iFR and FFR guided revascularisation (all patients)

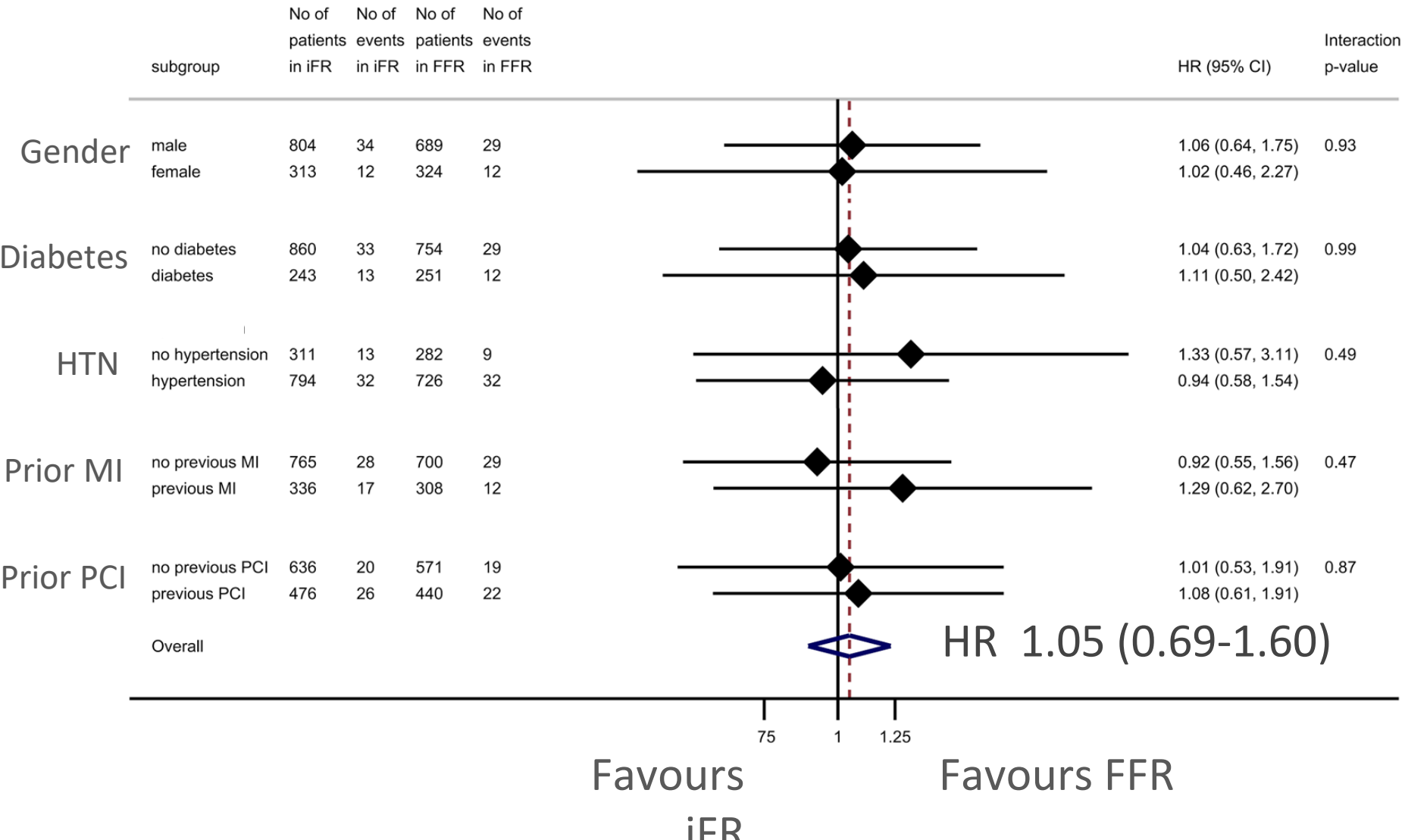| Outcome	iFR Group N=2240 no.(%)	FFR Group N=2246 no. (%)	Hazard Ratio (95% CI)	P value
Primary outcome: death from any cause, nonfatal myocardial infarction, or unplanned revascularisation	145 (6.47)	144 (6.41)	1.03 (0.81-1.31)	0.81
Death from cardiovascular causes	15 (0.67)	10 (0.45)	1.52 (0.68-3.39)	0.3
Death from noncardiovascular causes	21 (0.94)	15 (0.67)	1.42 (0.73-2.76)	0.3
Nonfatal myocardial infarction	53 (2.37)	45 (2.00)	1.19 (0.76-1.85)	0.45
Unplanned revascularisation	93 (4.15)	109 (4.85)	0.91 (0.69-1.21)	0.53

MACE components similar and low at 1 year after iFR- and FFR-guided revascularisation decision-making
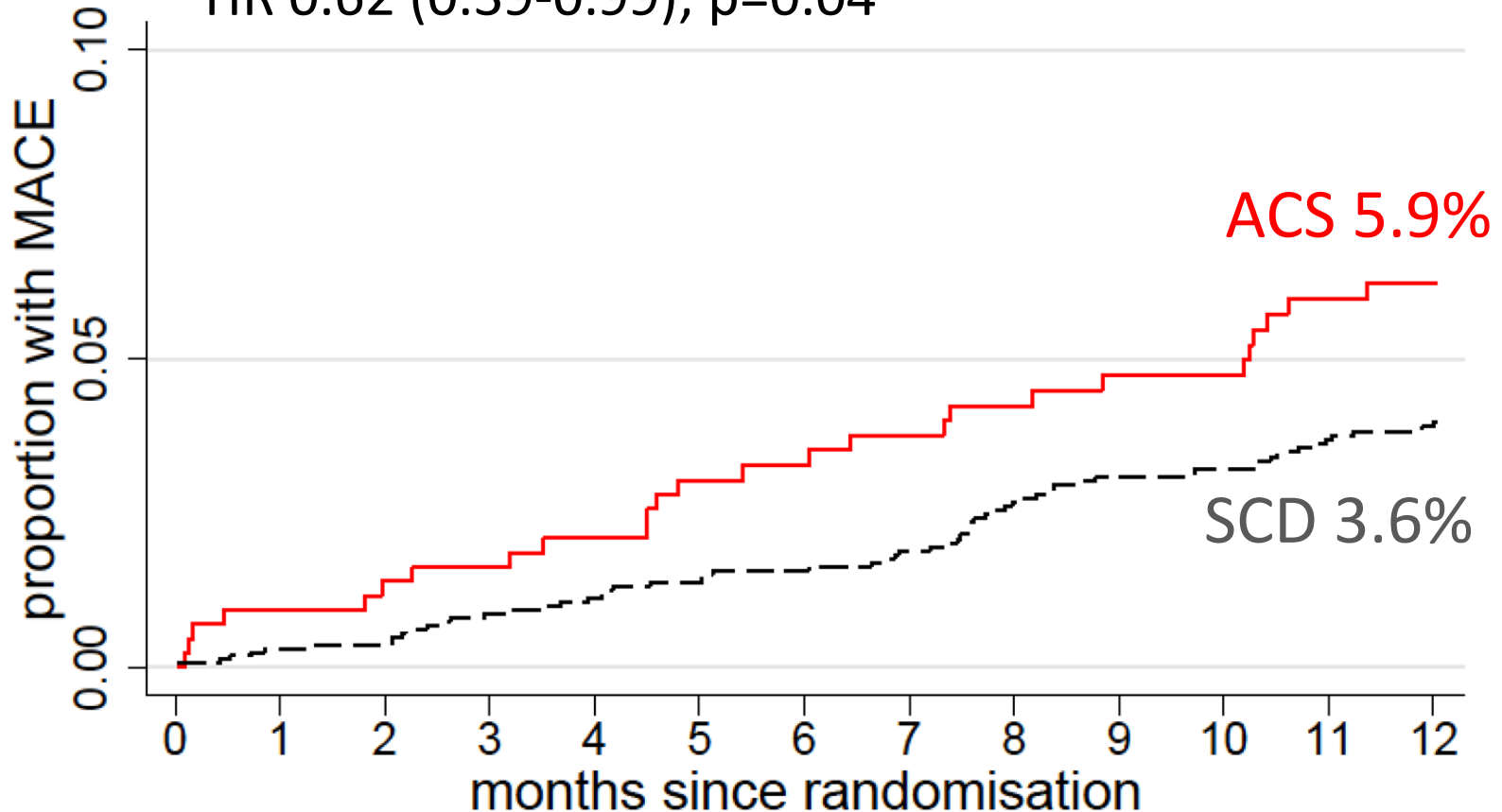
Outcomes in deferred patients

Deferred: HR 1.05 (0.69-1.60); p=0.82

IFR 4.12%

FFR 4.05%

Proportion with MACE

Months since randomisation

Similar and low MACE rates at 1 year after iFR- and FFR- based deferral

MACE in deferred patients - subgroup analyses

subgroup		No of patients in iFR	No of events in iFR	No of patients in FFR	No of events in FFR	HR (95% CI)	Interaction p-value
Gender	male	804	34	689	29	1.06 (0.64, 1.75)	0.93
	female	313	12	324	12	1.02 (0.46, 2.27)	
Diabetes	no diabetes	860	33	754	29	1.04 (0.63, 1.72)	0.99
	diabetes	243	13	251	12	1.11 (0.50, 2.42)	
HTN	no hypertension	311	13	282	9	1.33 (0.57, 3.11)	0.49
	hypertension	794	32	726	32	0.94 (0.58, 1.54)	
Prior MI	no previous MI	765	28	700	29	0.92 (0.55, 1.56)	0.47
	previous MI	336	17	308	12	1.29 (0.62, 2.70)	
Prior PCI	no previous PCI	636	20	571	19	1.01 (0.53, 1.91)	0.87
	previous PCI	476	26	440	22	1.08 (0.61, 1.91)	
	Overall						

HR 1.05 (0.69-1.60)

75   1   1.25

Favours iFR   Favours FFR

Outcomes in <u>deferred</u> patients according to clinical presentation

HR 0.62 (0.39-0.99); p=0.04

ACS 5.9%

SCD 3.6%

proportion with MACE

months since randomisation

In deferred patients, clinical presentation did influence MACE rate

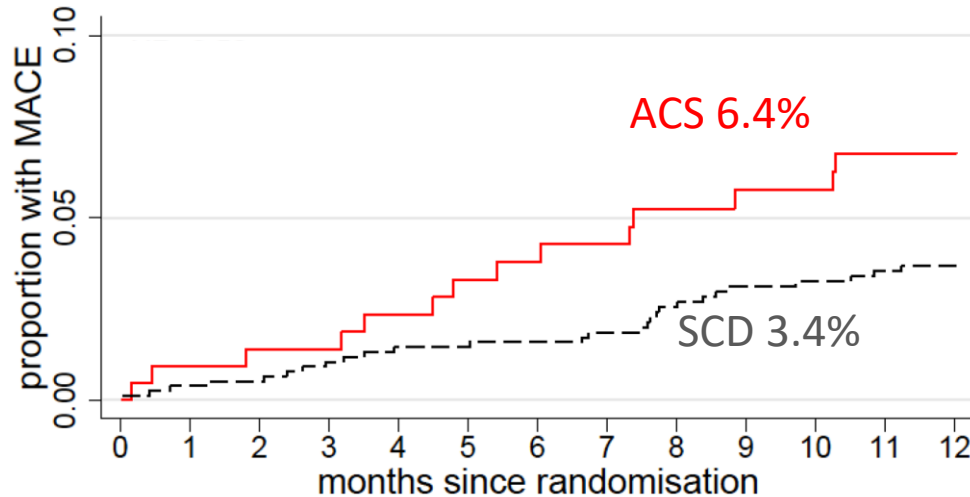# Outcomes in <u>treated</u> patients according to clinical presentation
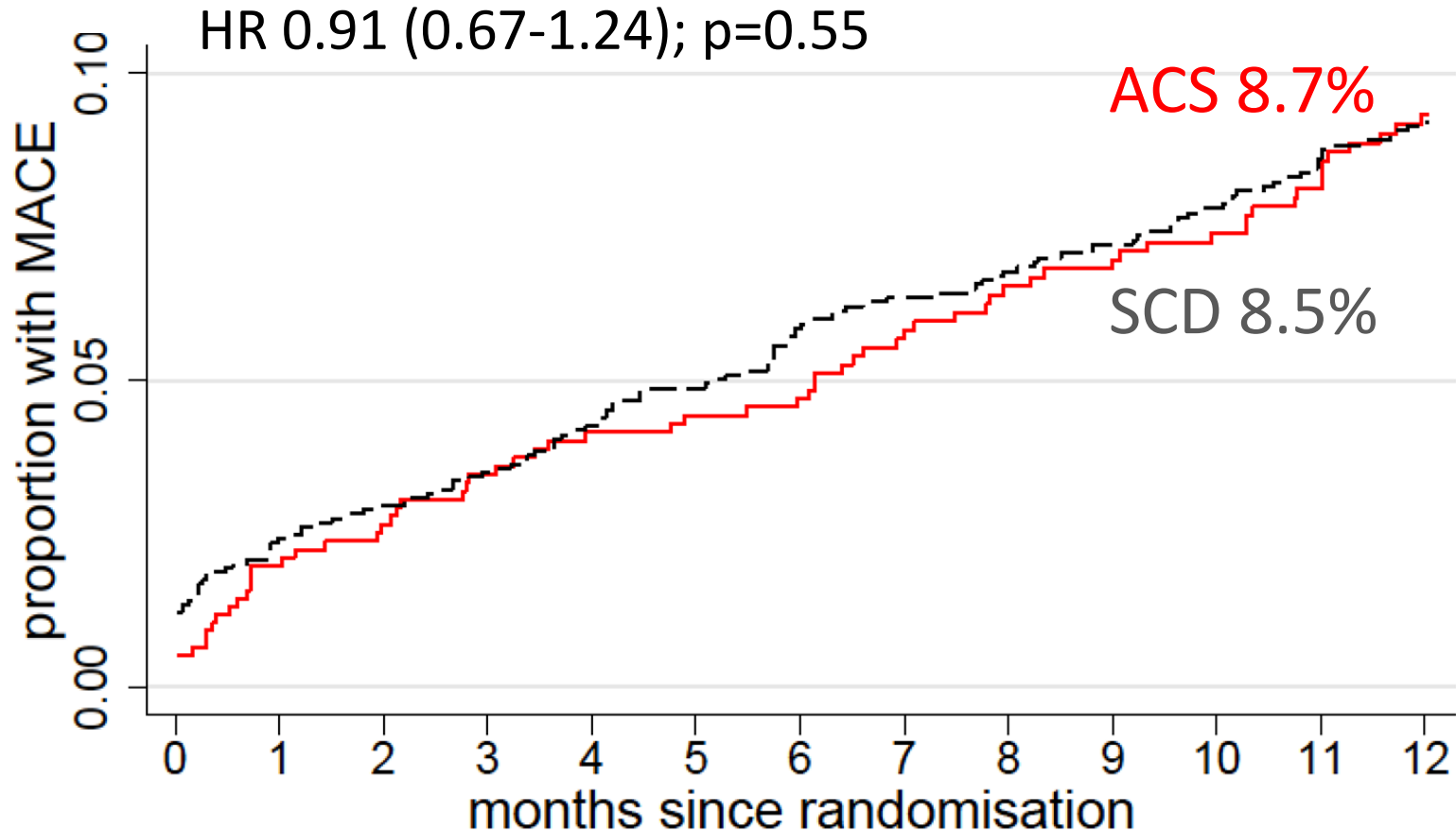
In treated patients, clinical presentation did not influence MACE rate

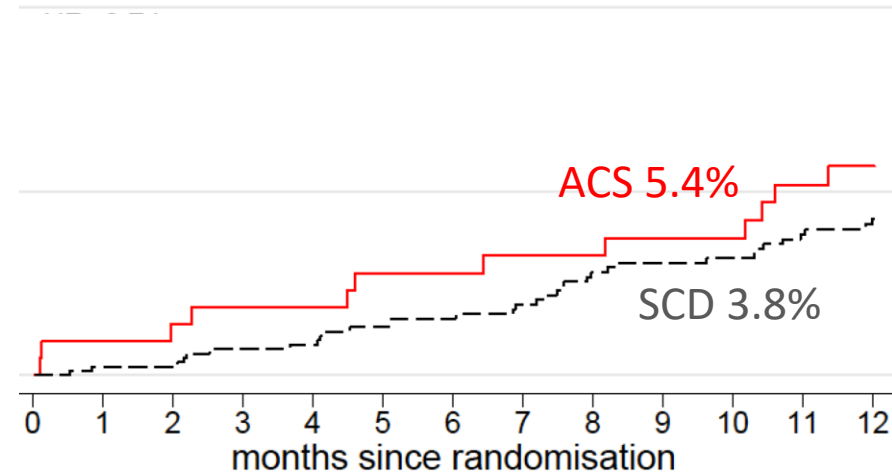# Unadjusted outcomes after deferral by clinical presentation and iFR or FFR

FFR

HR 0.52 (0.27-1.00); p<0.05

ACS 6.4%

SCD 3.4%

proportion with MACE

months since randomisation

In FFR-deferred patients, MACE is significantly higher in ACS than SCD

iFR

HR 0.74 (0.38-1.43); p=0.37

ACS 5.4%

SCD 3.8%

months since randomisation

In iFR-deferred patients, MACE is similar in ACS and SCD

Contemporary outcomes in treated and deferred stable patients: a comparison with the historical DEFER trial (1998-2000)
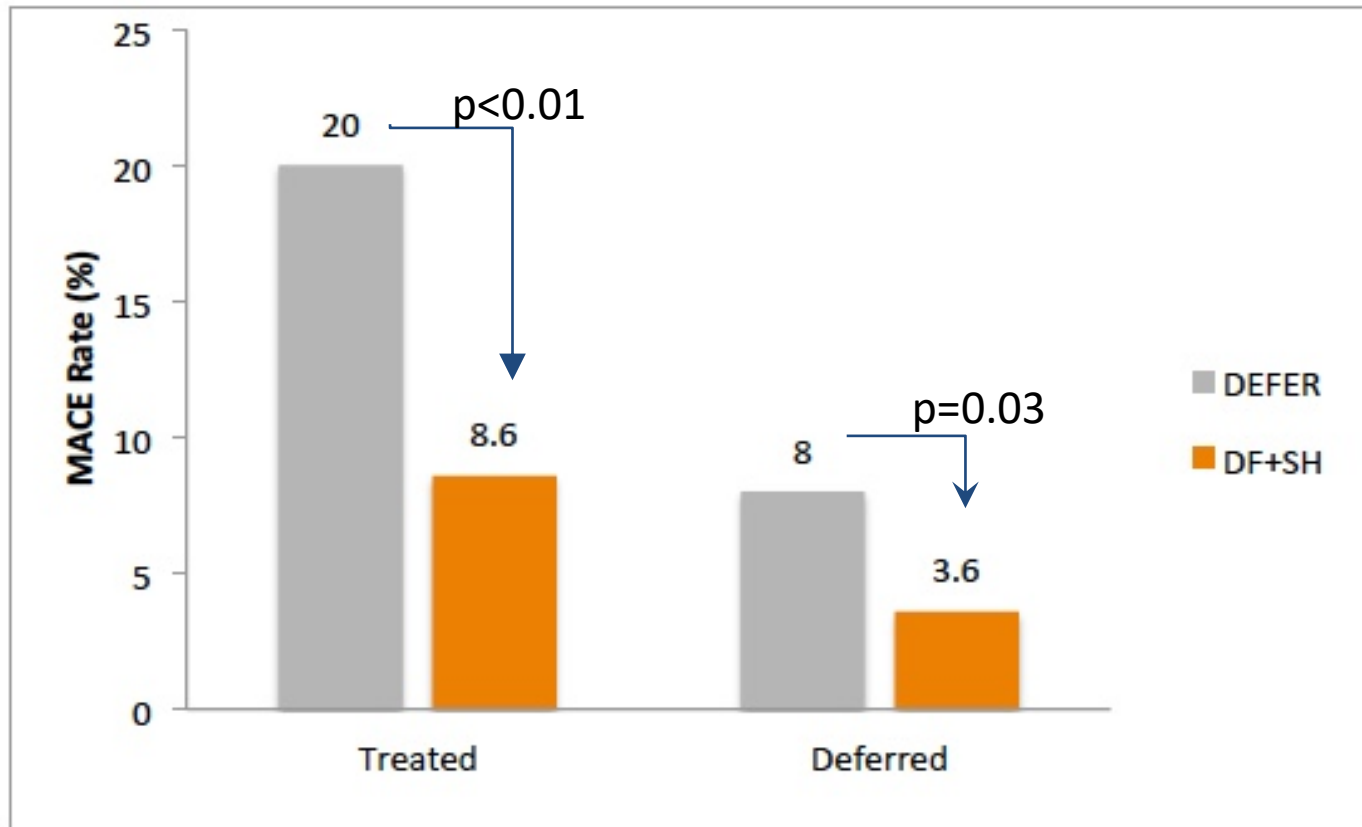
Dramatic reduction in MACE at 1 year follow up in both treated and deferred revascularisation groups compared with DEFER trial

Bech GJ et al. *Circulation* 2001; **103**: 2928–34,

Conclusions

Deferral of myocardial revascularisation based on pressure guidewire interrogation:

- Was more frequently performed when iFR was used, compared to FFR.

- Was associated with low and similar 1-year outcomes in the FFR and iFR guided arms.

- Was associated with higher MACE rate in patients presenting with ACS than with SCD.

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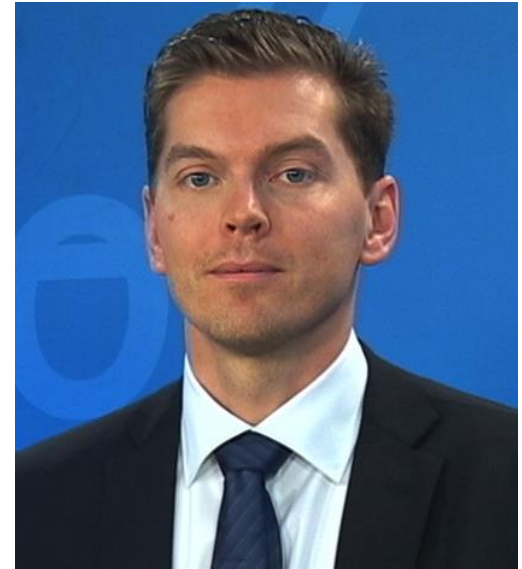
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22 countries, 63 centers, 4,529 patients

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Backup slides

Additional relevant information for this study can be found in the original publications of the DEFINE FLAIR and iFR SWEDEHEART trials.

http://www.nejm.org/doi/full/10.1056/NEJMoa1700445

http://www.nejm.org/doi/full/10.1056/NEJMoa1616540

Procedural details iFR vs FFR

	iFR	FFR	P value
Number of patients	2240	2246	
radial-artery approach - no. patients (%)	1728 (77.1)	1693 (75.4)	0.16
mean iFR/FFR - mean (sd)	0.91 (0.09)	0.83 (0.10)	
mean iFR/FFR in treated - mean (sd)	0.87 (0.11)	0.78 (0.10)	
mean iFR/FFR in deferred - mean (sd)	0.95 (0.03)	0.89 (0.05)	
PCI - no. patients (%)	1004 (44.8)	1078 (48.0)	0.03
CABG - no. patients (%)	117 (5.2)	153 (6.8)	0.02

Conclusions

Deferral of myocardial revascularisation based on pressure guidewire interrogation:

- Was more frequently performed when iFR was used, compared to FFR.

- Was associated with low and similar 1-year outcomes in the FFR and iFR guided arms.

- Was associated with higher MACE rate in patients presenting with ACS than with SCD.