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Functional **L**esion **A**ssessment of **I**ntermediate stenosis to guide **R**evascularization

ACC.17
66th Annual Scientific Session & Expo

iFR vs FFR for guiding coronary revascularization – DEFINE-FLAIR

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WASHINGTON, DC
FRI • SAT • SUN
MARCH 17 – 19, 2017

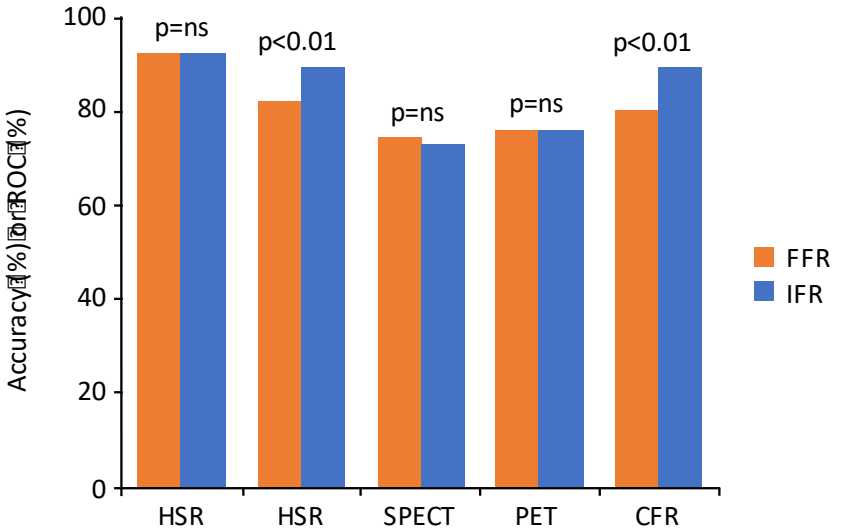
Imperial College London

Background

iFR is a pressure wire alternative to FFR

- Vasodilator-free (e.g. Adenosine, ATP)
- Similar power to detect ischemia

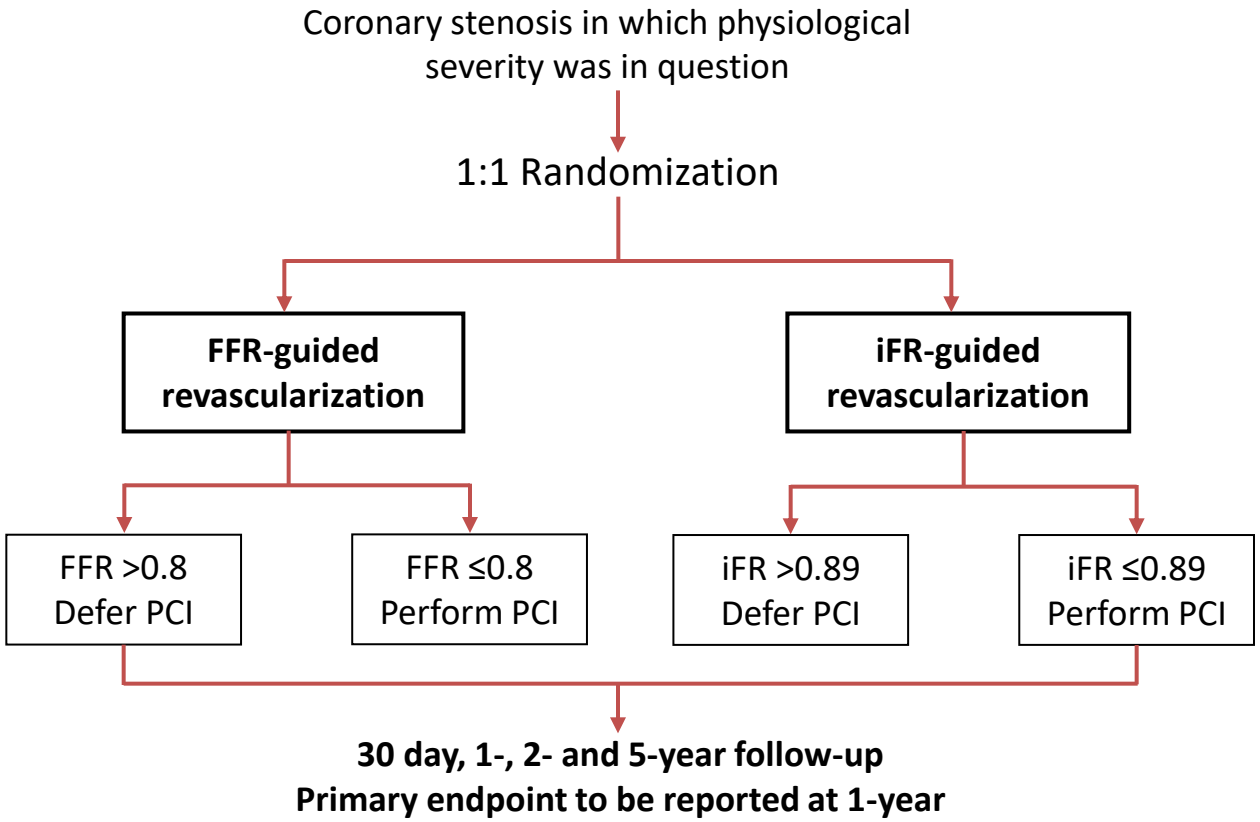
iFR and FFR have similar diagnostic power in head-to-head studies



CFR, Coronary Flow Reserve; HSR, Hyperaemic Stenosis Resistance; ROC, receiver-operating characteristic; PET, positron emission tomography; SPECT, single-photon emission computed tomography

1. Van de Hoef TP et al. Circ Cardiovasc Interv. 2012;5:508-14; 2. Sen S et al. J Am Coll Cardiol. 2013;61:1409-20; 3. Van de Hoef TP et al. EuroIntervention. 2015;11:914-25;
4. Sen S et al. J Am Coll Cardiol. 2013;62:566; 5. Petraco R et al. Circ. Int. 2014;7:492-502; 6. de Waard G et al. J Am Coll Cardiol. 2014;63:A1692.

Study design



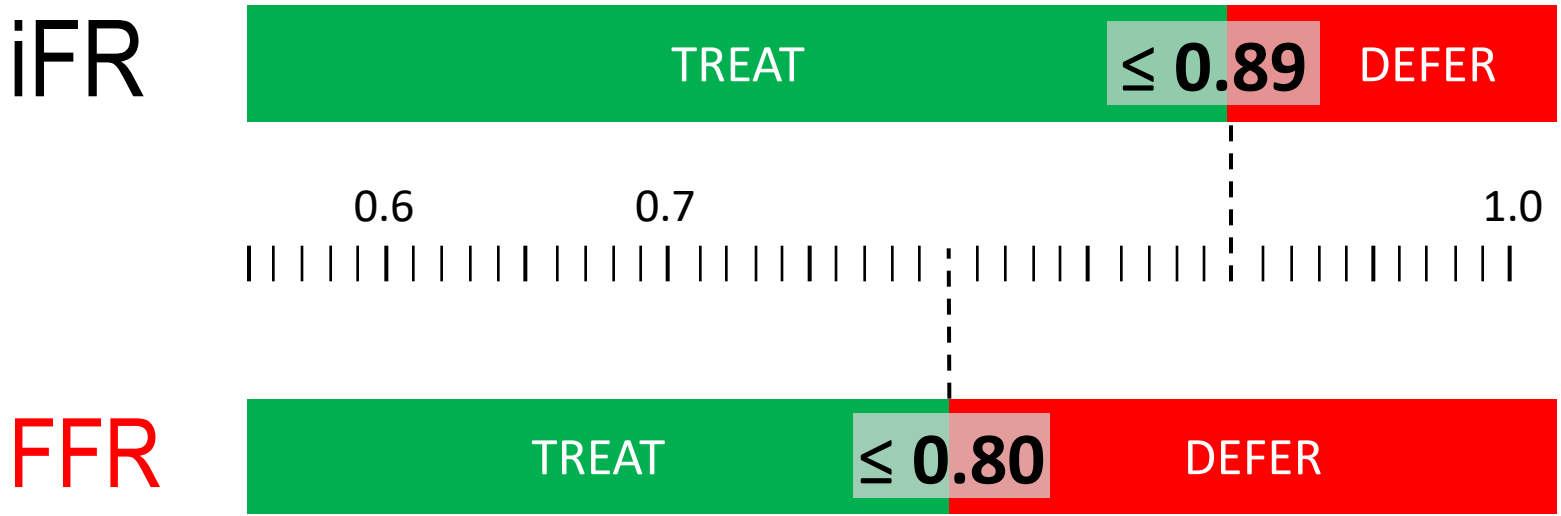
MACE composite endpoint of:

- Death
- Non-fatal myocardial infarction
- Unplanned revascularization

Non-inferiority margin for risk difference: 3.4%

DEFINE FLAIR. https://clinicaltrials.gov/ct2/show/NCT02053038.

Clinical iFR and FFR Cut-points



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ADVISE 2 Study, JACC Cardiovasc Interv 2015;8(6):824–33.
RESOLVE Study, JACC 2014 Apr 8;63(13):1253-61

Patient demographics

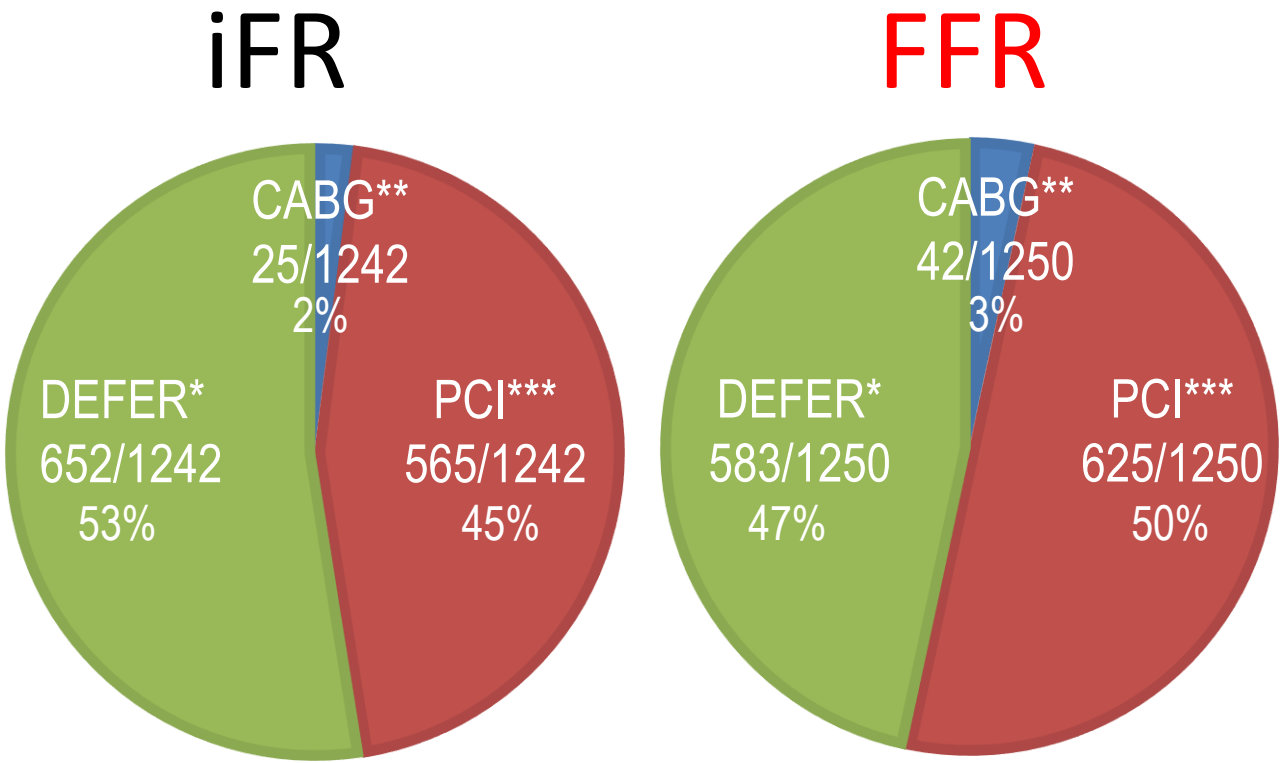
		iFR	FFR
Number of patients		1242	1250
Age, Years, mean (sd)		65.5 (10.8)	65.2 (10.6)
Gender, N (%)			
	Female	280 (22.5)	321 (25.7)
	Male	962 (77.5)	929 (74.3)
Disease type, N (%)			
	>48hr post STEMI*	49 (3.9)	42 (3.4)
	Acute coronary syndrome*	186 (15.0)	184 (14.7)
	Stable disease	986 (79.4)	1012 (81.0)

* Non-culprit lesions only

Procedural characteristics

	iFR (N=1242)	FFR (N=1250)	p-value
Radial access, N (%)	896 (72.1)	888 (71.0)	0.54
Vessels evaluated, N (%)			
All	1575	1608	0.58
LAD	844 (53.6)	845 (52.5)	0.56
LCx	323 (20.5)	333 (20.7)	0.89
RCA	374 (23.7)	393 (24.4)	0.65
Other	33 (2.1)	31 (1.9)	0.74
Unknown	1 (0.1)	6 (0.4)	0.06
Hyperemic agents, N (%)			
IC adenosine	-	455 (28.3)	
IV adenosine	-	950 (59.1)	
Other agents	-	203 (12.6)	
Multi-vessel disease, N (%)	505 (40.7)	519 (41.5)	0.66
Vessels evaluated or treated, N	1879	1940	0.42
Functionally significant lesions, N	451	557	0.004
Treated or evaluated vessels/patient; mean (sd)	1.51 (0.76)	1.55 (0.80)	0.42

Treatment allocation with iFR and FFR

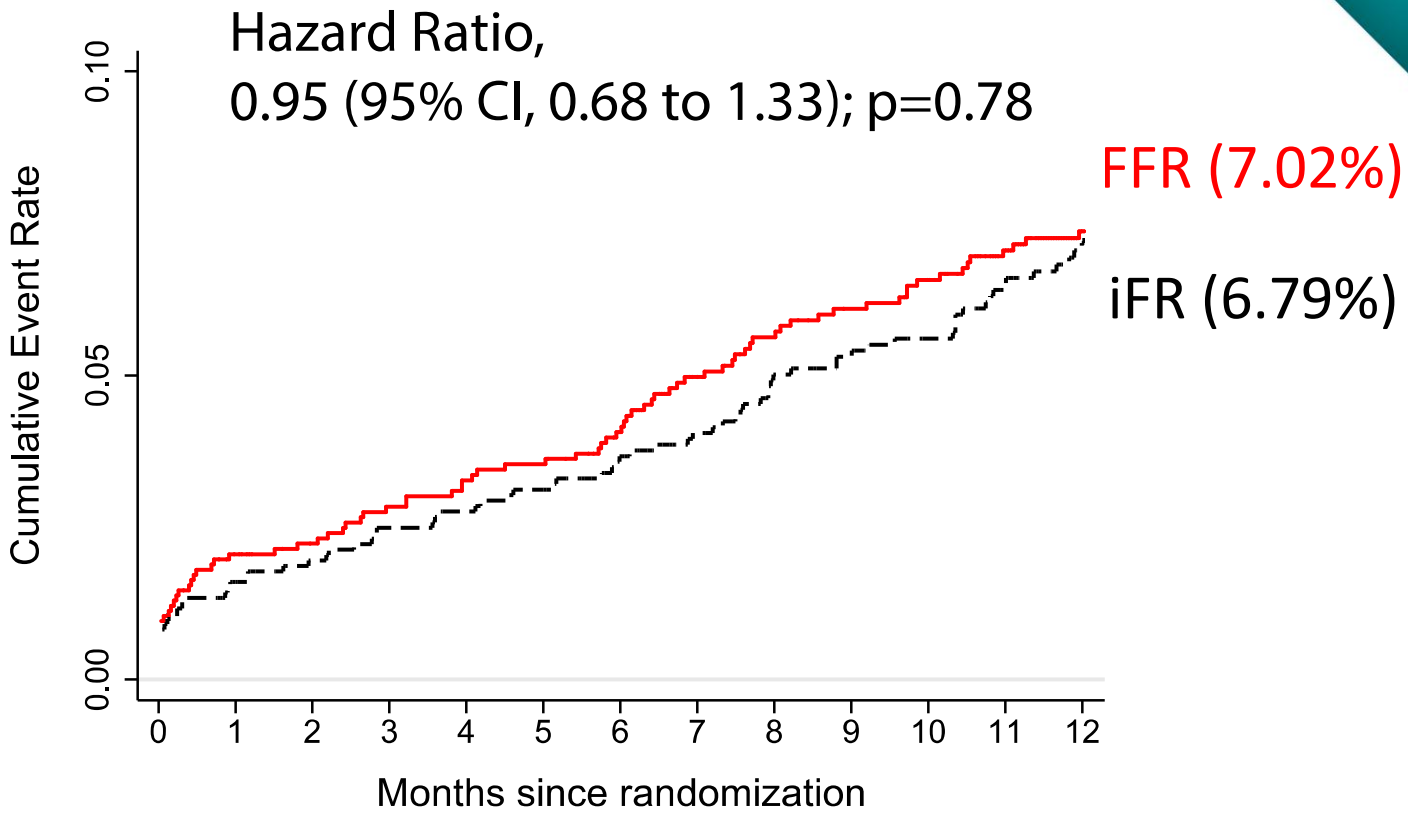


p for comparison between patients randomized to iFR and FFR

DEFER* p=0.003
CABG** p=0.04
PCI*** p=0.02

Significantly less revascularization based on iFR interrogation

Primary endpoint (MACE)
iFR equivalent to FFR (non-inferiority)



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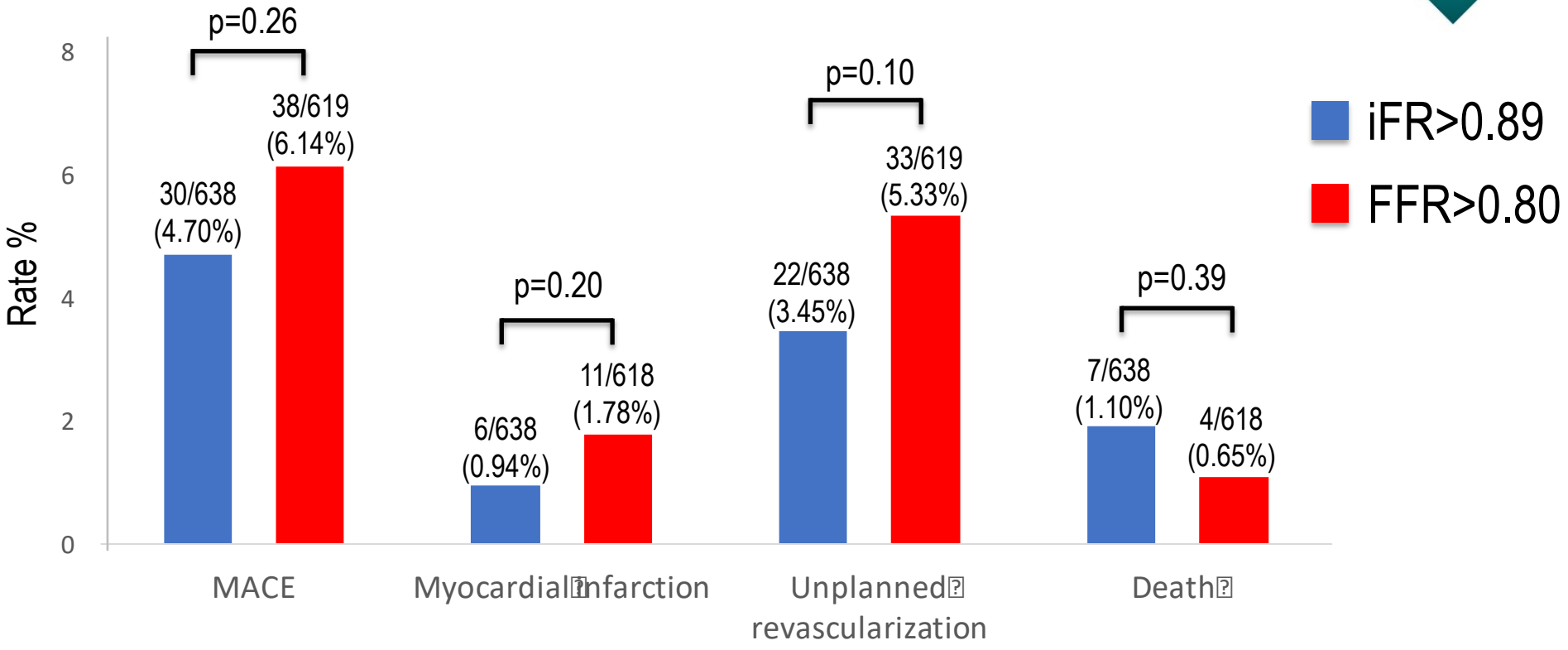
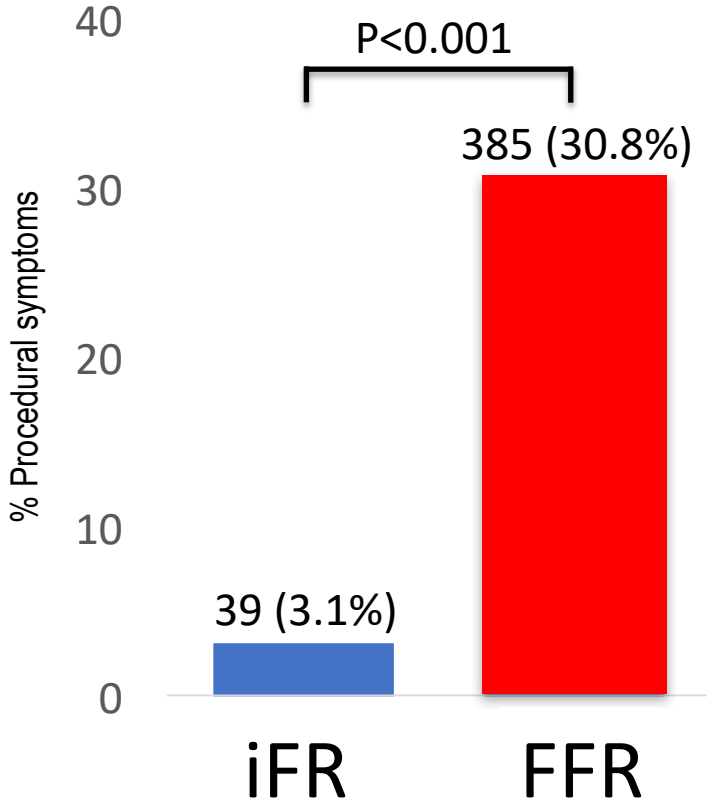
Event rates in deferred patients

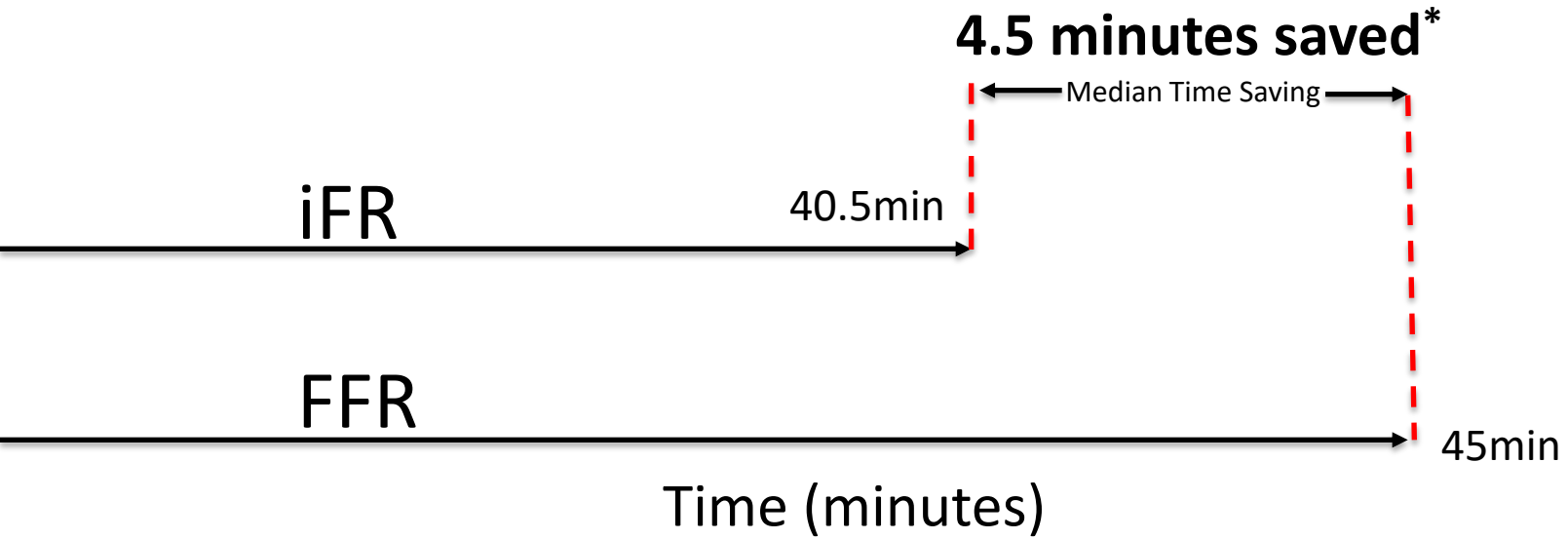


10-fold fewer procedural symptoms and signs



	iFR	FFR
Dyspnea	13 (1.0%)	250 (20.0%)
Chest pain	19 (1.5%)	90 (7.2%)
Rhythm disturbance	2 (0.2%)	60 (4.8%)
Hypotension	4 (0.3%)	13 (1.0%)
Vomiting / Nausea	1 (0.1%)	11 (0.9%)
Bronchospasm/VT	1 (0.1%)	8 (0.6%)
Other	4 (0.3%)	38 (3.0%)

iFR guided revascularization reduces procedure time



* Threshold for reduction in median time (p=0.001)

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SWEDE HEART

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iFR vs FFR-guided Coronary Intervention – iFR-SWEDEHEART

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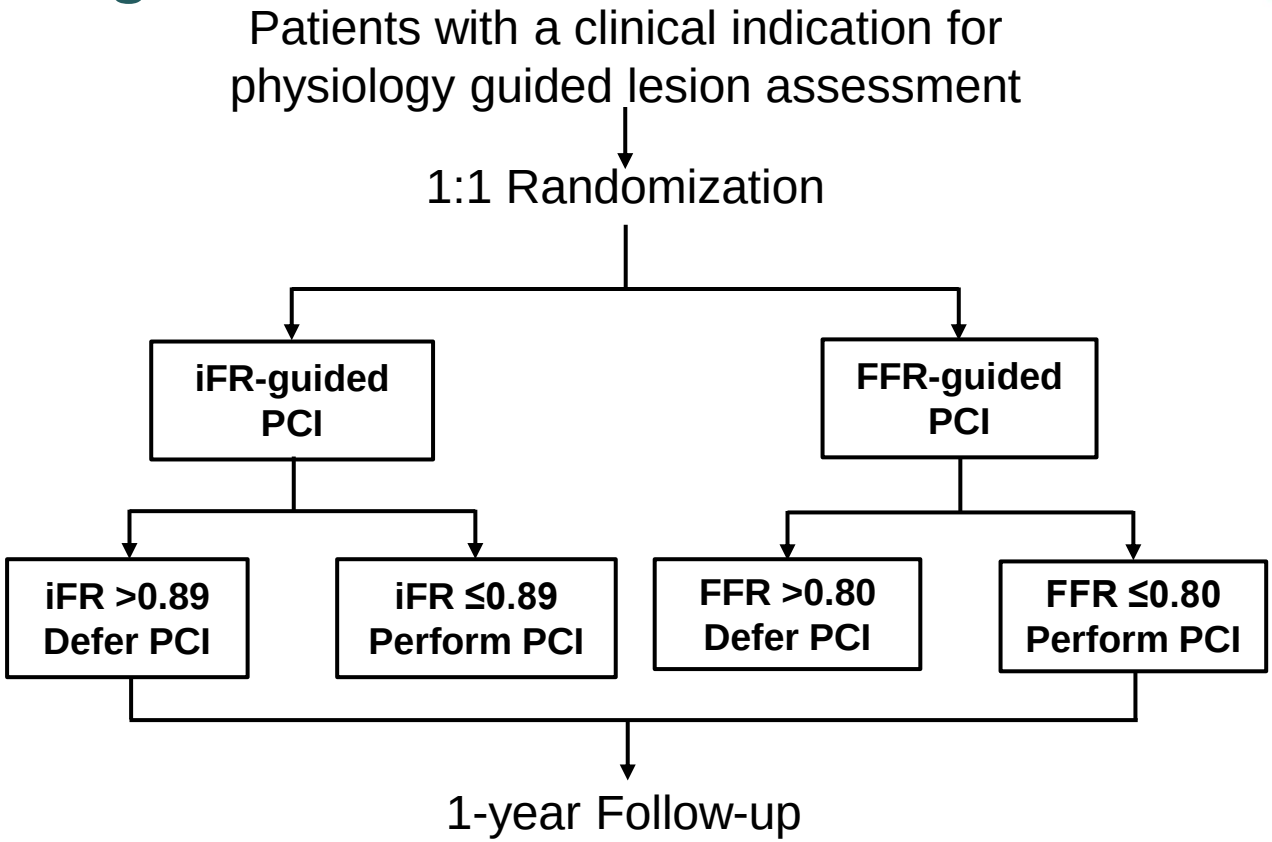
Study Design

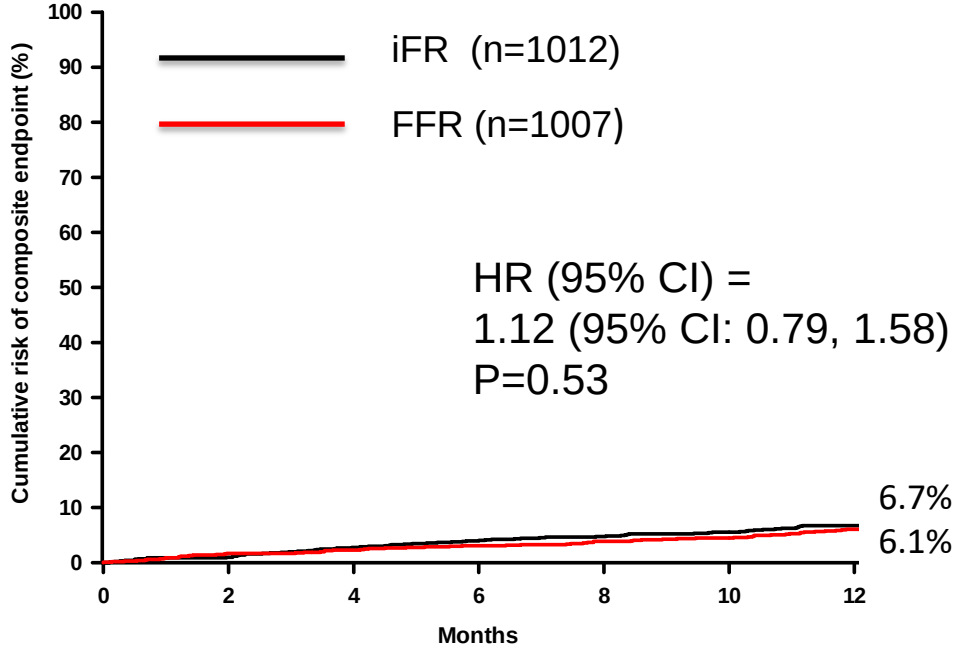


Baseline clinical characteristics

	iFR (N=1019)	FFR (N = 1018)
Age - yr. (mean (± SD))	67.6 (9.6)	67.4 (9.2)
Male sex - no. (%)	756 (74.2)	766 (75.3)
Indication for angiography - no. (%)		
Stable angina	632 (62.0)	632 (62.0)
Unstable angina	211 (20.7)	208 (20.4)
NSTEMI	176 (17.3)	178 (17.5)
Diabetes mellitus - no. (%)	232 (22.8)	213 (20.9)
Hypertension - no. (%)	730 (71.6)	710 (69.7)
Hyperlipidemia - no. (%)	733 (71.9)	704 (69.1)
Current smoker	159 (15.6)	167 16.3)
Previous myocardial infarction - no. (%)	337 (33.1)	335 (32.9)
Previous PCI - no. (%)	429 (42.1)	425 (41.7)
Previous coronary artery by-pass grafting - no. (%)	49 (4.8)	43 (4.2)

Primary Endpoint at 1 year

Death, MI, Unplanned revascularization (non-inferiority)



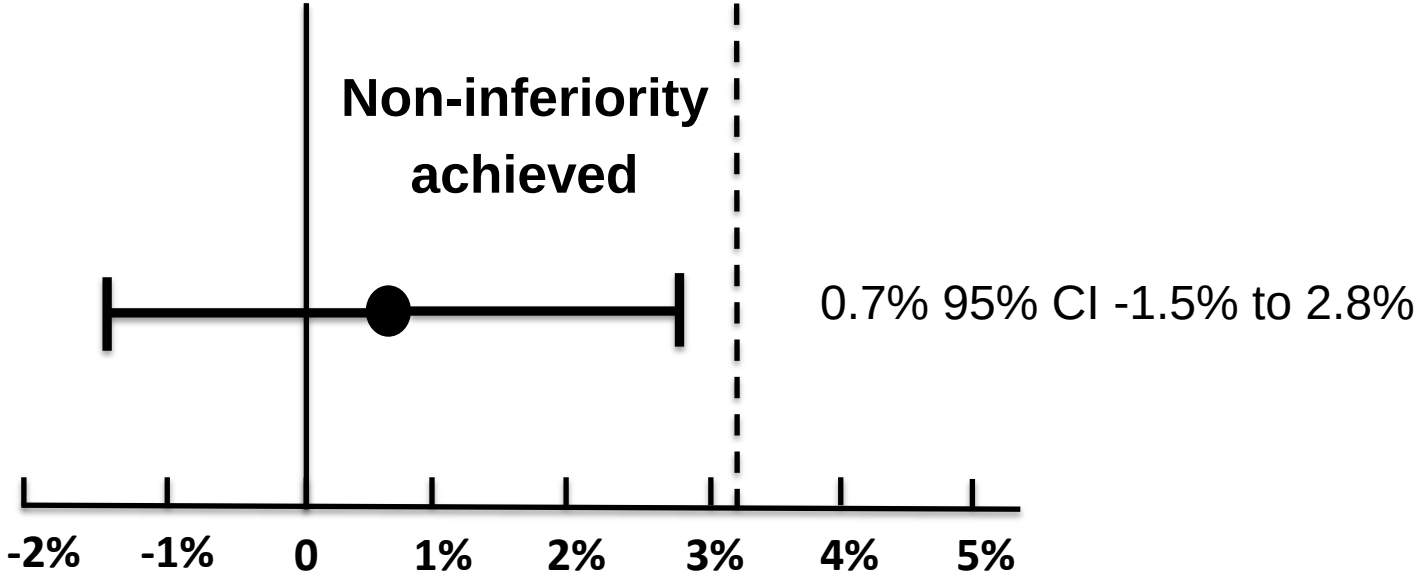
No. at Risk

iFR	1012	1002	984	971	963	956	944
FFR	1007	990	984	976	968	961	946

Primary Endpoint at 1 year

Non-inferiority Analysis

Pre-specified non-inferiority margin
= 3.2% for the upper 2-sided 95% confidence interval

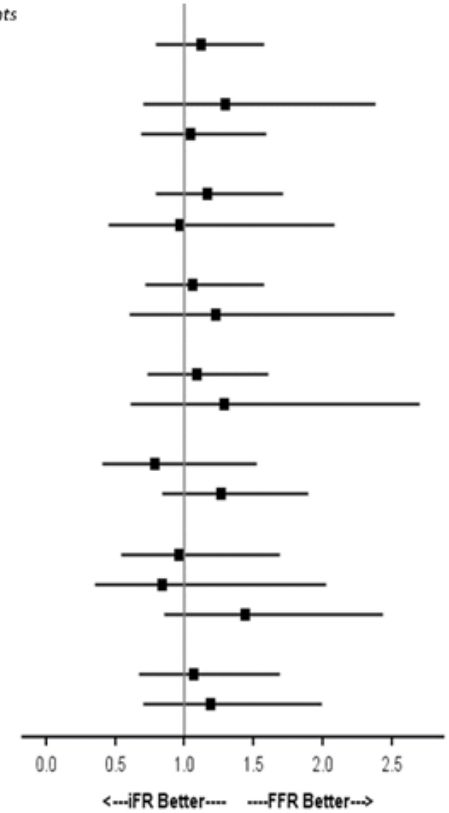


Risk Difference in All-cause Death, MI and Unplanned Revascularization (%)

Primary Endpoint at 12 months

All-cause Death, MI, Unplanned Revascularization

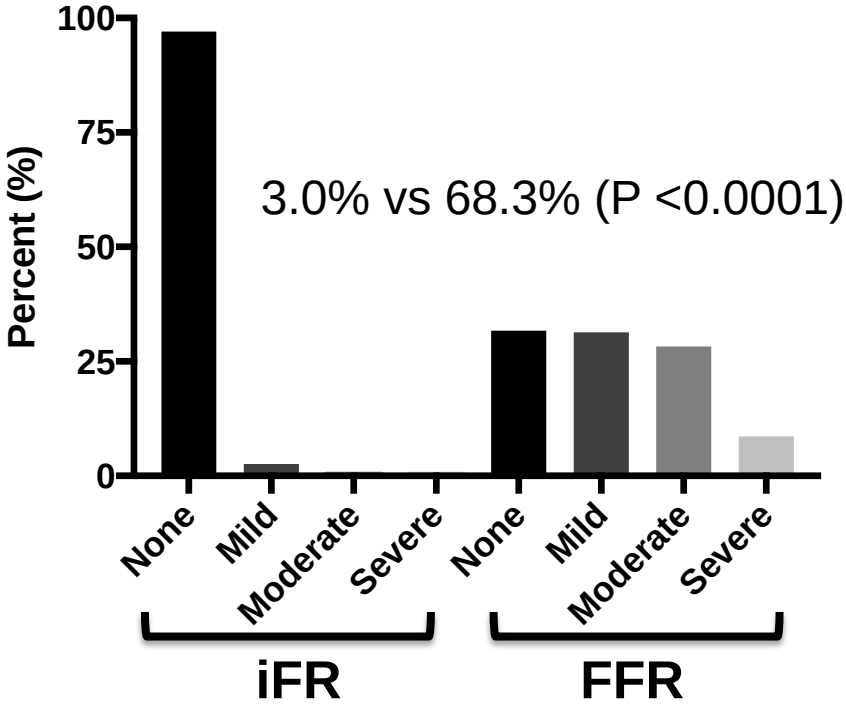
Subgroup	iFR	FFR	Hazard Ratio (95% CI)	P Value
	no of events/total no of patients			
All patients	68/1012	61/1007	1.12 (0.79-1.58)	
Age				0.57
≤65 yr	24/377	18/363	1.29 (0.70-2.4)	
>65 yr	44/635	43/644	1.04 (0.69-1.59)	
Gender				0.68
Female	13/258	13/248	0.97 (0.45-2.09)	
Male	55/753	48/759	1.16 (0.79-1.71)	
Hypertension				0.72
Yes	51/724	47/703	1.06 (0.71-1.58)	
No	16/281	14/301	1.23 (0.60-2.52)	
Hyperlipidemia				0.69
Yes	53/727	47/696	1.09 (0.73-1.61)	
No	15/279	13/308	1.29 (0.61-2.70)	
Diabetes				0.23
Yes	16/227	19/212	1.26 (0.84-1.89)	
No	52/782	42/789	0.78 (0.40-1.52)	
Smoking status				0.30
Never	23/349	25/363	0.96 (0.54-1.69)	
Former smoker	35/496	23/464	1.44 (0.85-2.44)	
Smoker	9/159	11/163	0.84 (0.35-2.03)	
Angina status				0.76
Stable Angina	37/627	35/630	1.06 (0.67-1.69)	
Unstable or NSTEMI	31/385	26/377	1.19 (0.70-2.00)	



Secondary Endpoints

	iFR (N=1012)	FFR (N=1007)	Hazard Ratio (95% CI)	P Value
All cause death - no. (%)	15 (1.5)	12 (1.2)	1.25 (0.58-2.66)	0.57
Myocardial infarction - no. (%)	22 (2.2)	17 (1.7)	1.29 (0.68-2.44)	0.42
Unplanned revascularization - no. (%)	47 (4.6)	46 (4.6)	1.04 (0.69-1.57)	0.84
Target lesion revascularization (TLR) - no. (%)	29 (2.9)	27 (2.7)	1.21 (0.70-2.07)	0.49
Restenosis - no. (%)	19 (1.9)	18 (1.8)	1.05 (0.55-2.01)	0.87
Stent thrombosis - no. (%)	1 (0.1)	2 (0.2)		

Chest Discomfort from the procedure



I.v. adenosine 69%

I.c. adenosine 31%

Conclusions

DEFINE-FLAIR and iFR-SWEDEHEART confirm that in stable and ACS patients with coronary stenoses:

- iFR is ***non-inferior*** to FFR for major adverse cardiac events (MACE) at 1 year in patients undergoing physiological-guided revascularization.