Long-term Clinical Outcomes After iFR vs. FFR-guided Coronary Revascularization
Insights from the SWEDEHEART National Registry

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Disclosure of Relevant Financial Relationships

Within the prior 24 months, I have had a relevant financial relationship with a company producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients:

| Nature of Financial Relationship	Ineligible Company
Consultant Fees/Honoraria	Abbott Vascular, Boston Scientific, Medtronic, Philips IGT

**All relevant financial relationships have been mitigated.**
Faculty disclosure information can be found on the app

Background

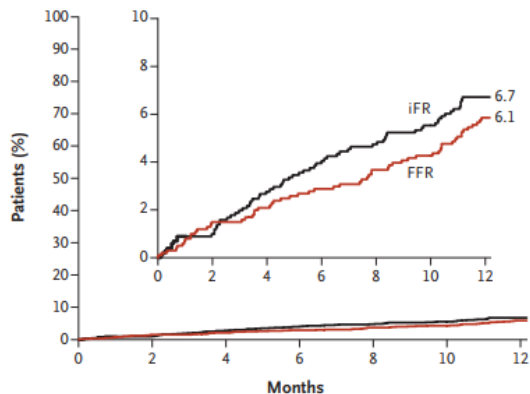**Instantaneous Wave-free ratio (iFR) is a non-hyperemic index for assessment of coronary lesion severity**
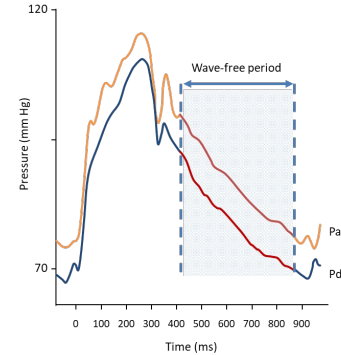
iFR-validation studies have demonstrated ≈85% agreement with Fractional Flow Reserve (FFR). iFR and FFR have similar agreement with other ischemic indices
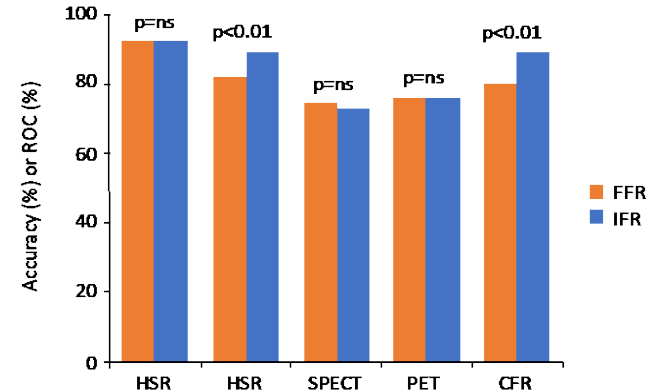
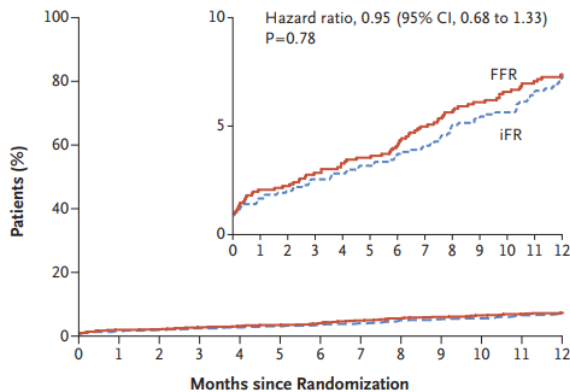# iFR vs FFR 1-year outcomes

All-cause death, MI, unplanned revascularization

iFR-SWEDEHEART

HR 1.12 (0.79-1.58)
p=0.53

DEFINE-FLAIR

HR 0.95 (0.68-1.33)
p=0.78

iFR was non-inferior to FFR at 1-year

Davies et al, N Engl J Med 2017; 376:1824-1834
Götberg et al, N Engl J Med 2017; 376:1813-1823

iFR vs FFR 5-year outcomes
All-cause death, MI, unplanned revascularization

iFR-SWEDEHEART

iFR 21.5%

FFR 19.9%

HR 1.09 (0.90-1.33)
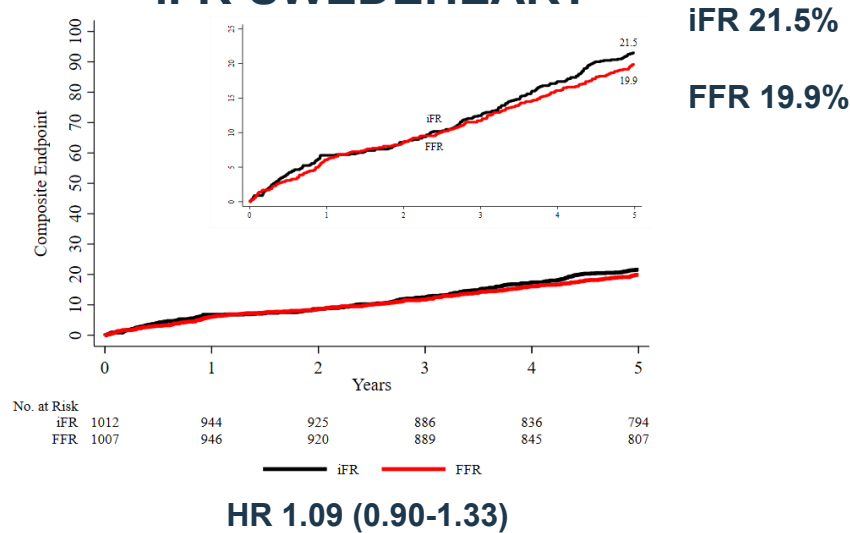
No difference in MACE, death, MI, or unplanned revasc. at 5 years

Götberg et al, J Am Coll Cardiol 2022 Mar 15:79(10):965-974

iFR vs FFR 5-year outcomes

All-cause death, MI, unplanned revascularization

DEFINE-FLAIR

iFR 21.1%

FFR 18.4%
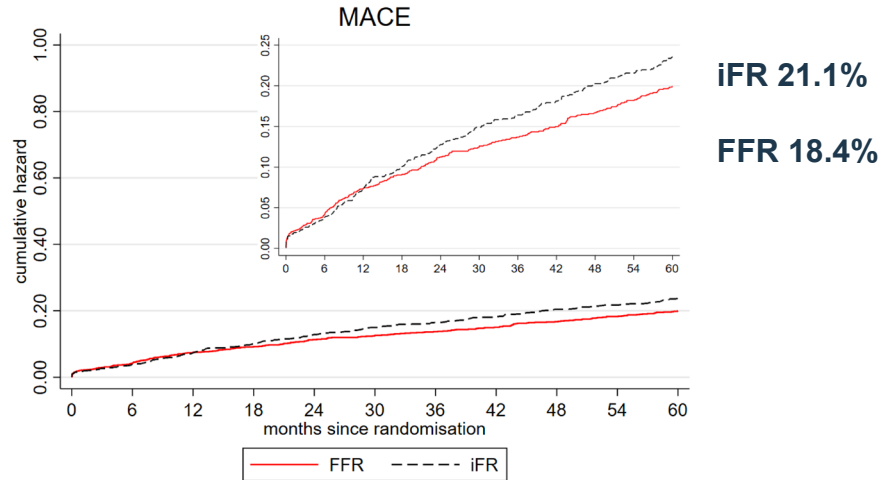
HR 1.18 (95%CI 0.99-1.42), p=0.06

No difference in MACE at 5 years

iFR vs FFR 5-year outcomes
DEFINE-FLAIR

All-cause death

MACE deferred
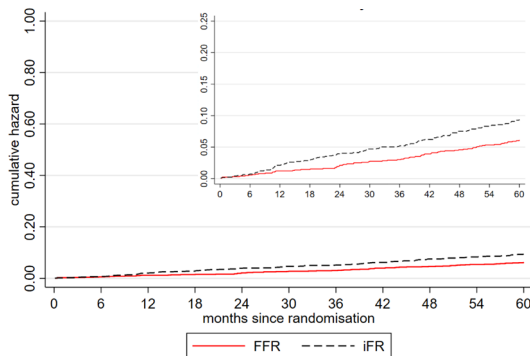
MACE treated

HR 1.56 (95% CI 1.16-2.09)
P<0.01
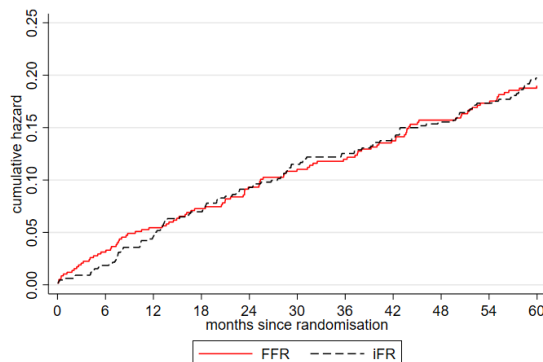
HR 1.03 (95% CI 0.79-1.35)
p=0.80
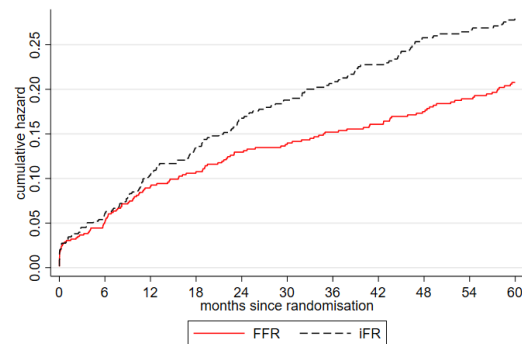
HR 1.36 (95% CI 1.07-1.72)
p=0.01

DEFINE-FLAIR:Significant increase in mortality with iFR

Signal restricted to treated patients driving MACE

No difference in MI or unplanned revascularization

Escaned et al EUROPCR 2023

Swedeheart National Registry Analysis
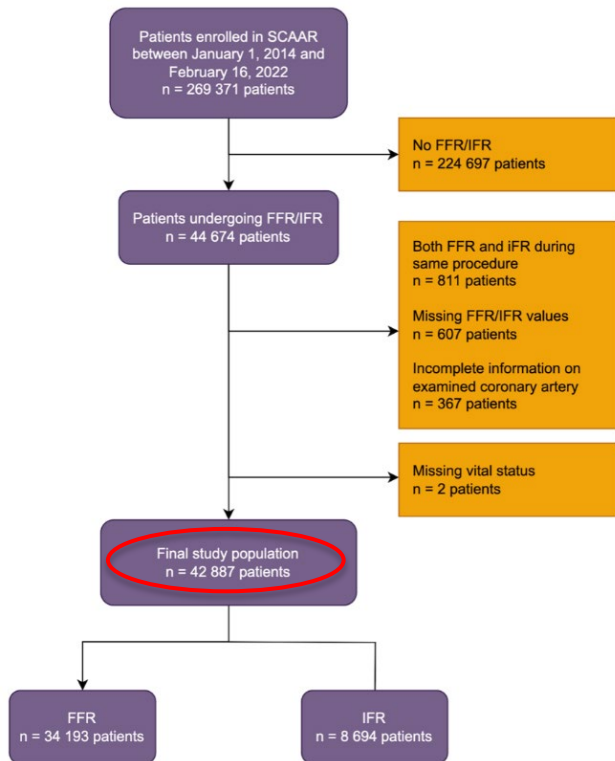
42887 patients included in the analysis

Follow-up up to 5 years:

National Population Registry (mortality)

SWEDEHEART (revasc with PCI)

National Patient Registry (MI, revasc with CABG)

100% tracking of all patients

Patients enrolled in SCAAR between January 1, 2014 and February 16, 2022
n = 269 371 patients

No FFR/IFR
n = 224 697 patients

Patients undergoing FFR/IFR
n = 44 674 patients

Both FFR and iFR during same procedure
n = 811 patients

Missing FFR/IFR values
n = 607 patients

Incomplete information on examined coronary artery
n = 367 patients

Missing vital status
n = 2 patients

Final study population
n = 42 887 patients

FFR
n = 34 193 patients

IFR
n = 8 694 patients

Baseline characteristics

	Total	FFR	IFR	P–value
	42887 (100.0%)	34193 (79.7%)	8694 (20.3%)	
Age (years) – median (IQR)	69.0 (61.0–75.0)	69.0 (61.0–75.0)	69.0 (61.0–75.0)	0.08
Men	31797 (74.1%)	25509 (74.6%)	6288 (72.3%)	<0.001
Diabetes	10312 (24.0%)	8129 (23.8%)	2183 (25.1%)	0.01
Hypertension	31725 (74.0%)	25246 (73.8%)	6479 (74.5%)	0.19
Previous myocardial infarction	12897 (30.1%)	10138 (29.6%)	2759 (31.7%)	<0.001
Previous PCI	15863 (37.0%)	12640 (37.0%)	3223 (37.1%)	0.87
Stroke	2598 (6.1%)	2026 (5.9%)	572 (6.6%)	0.02
Chronic heart failure	4410 (10.3%)	3510 (10.3%)	900 (10.4%)	0.81
Peripheral artery disease	1947 (4.5%)	1549 (4.5%)	398 (4.6%)	0.85
Chronic obstructive pulmonary disease	2771 (6.5%)	2139 (6.3%)	632 (7.3%)	0.001
Renal failure	1637 (3.8%)	1283 (3.8%)	354 (4.1%)	0.17
Cancer	1547 (3.6%)	1203 (3.5%)	344 (4.0%)	0.05

Baseline differences between iFR vs. FFR

iFR more often utilized in women, DM, MI, stroke, COPD

Deferred vs. treated

	Deferred				Treated			
	Total	FFR	iFR	P-value	Total	FFR	iFR	P-value
Age (years) – median (IQR)	69.0 (62.0-75.0)	69.0 (62.0-75.0)	69.0 (61.0-75.0)	0.053	68.0 (61.0-74.0)	68.0 (61.0-74.0)	70.0 (61.0-75.0)	<0.001
Men	19983 (71.3%)	15609 (71.3%)	4374 (71.1%)	0.772	11814 (79.6%)	9900 (80.5%)	1914 (75.3%)	<0.001
Diabetes	6464 (23.1%)	5039 (23.0%)	1425 (23.2%)	0.808	3848 (25.9%)	3090 (25.1%)	758 (29.8%)	<0.001
Hypertension	20837 (74.3%)	16283 (74.4%)	4554 (74.0%)	0.588	10888 (73.3%)	8963 (72.9%)	1925 (75.7%)	0.003
Previous myocardial infarction	8282 (29.5%)	6371 (29.1%)	1911 (31.1%)	0.003	4615 (31.1%)	3767 (30.6%)	848 (33.3%)	0.007
Previous PCI	10252 (36.6%)	7998 (36.5%)	2254 (36.6%)	0.881	5611 (37.8%)	4642 (37.7%)	969 (38.1%)	0.732
Stroke	1753 (6.3%)	1366 (6.2%)	387 (6.3%)	0.882	845 (5.7%)	660 (5.4%)	185 (7.3%)	<0.001
Chronic heart failure	3026 (10.8%)	2381 (10.9%)	645 (10.5%)	0.384	1384 (9.3%)	1129 (9.2%)	255 (10.0%)	0.180
Peripheral artery disease	1289 (4.6%)	1012 (4.6%)	277 (4.5%)	0.693	658 (4.4%)	537 (4.4%)	121 (4.8%)	0.381
Chronic obstructive pulmonary disease	1961 (7.0%)	1479 (6.8%)	482 (7.8%)	0.003	810 (5.5%)	660 (5.4%)	150 (5.9%)	0.281
Renal failure	1098 (3.9%)	853 (3.9%)	245 (4.0%)	0.757	539 (3.6%)	430 (3.5%)	109 (4.3%)	0.052
Cancer	1063 (3.8%)	814 (3.7%)	249 (4.0%)	0.231	484 (3.3%)	389 (3.2%)	95 (3.7%)	0.138

Treated iFR-group: older, more often women, DM, HT, MI, stroke

Baseline characteristics influence revascularization decision differently in iFR- vs FFR-group
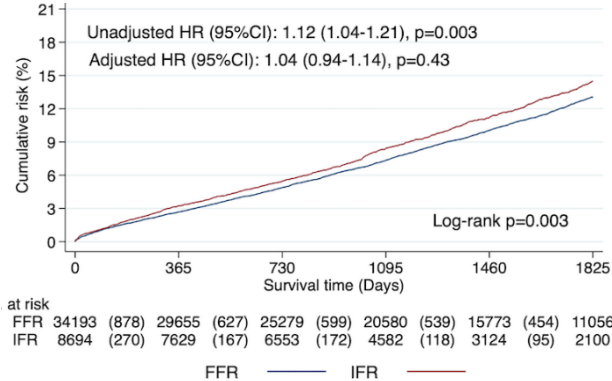
iFR vs FFR 5-year MACE

All-cause death, MI, unplanned revascularization

*Adjusted HR 0.99 (0.93-1.05)
p=0.72
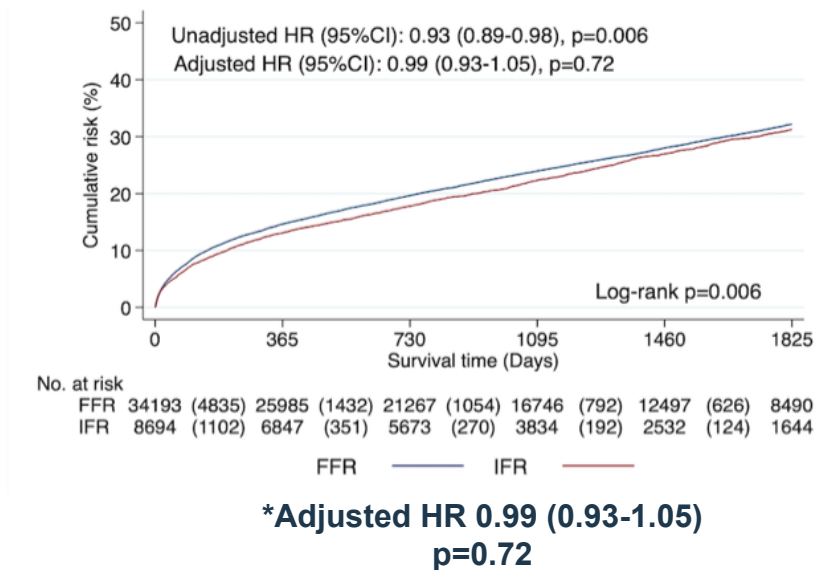
No difference in MACE between iFR and FFR

iFR vs FFR 5-year outcomes

All-cause death

Unadjusted HR (95%CI): 1.12 (1.04-1.21), p=0.003
Adjusted HR (95%CI): 1.04 (0.94-1.14), p=0.43

Log-rank p=0.003

at risk
FFR 34193 (878) 29655 (627) 25279 (599) 20580 (539) 15773 (454) 11056
IFR 8694 (270) 7629 (167) 6553 (172) 4582 (118) 3124 (95) 2100

FFR ——— IFR ———

**Adjusted HR 1.04 (0.94-1.14)
p=0.43**

Myocardial infarction

Unadjusted HR (95%CI): 0.88 (0.83-0.94), p≤0.001
Adjusted HR (95%CI): 1.00 (0.92-1.08), p=0.98

Log-rank p≤0.001

. at risk
FFR 34193 (3297) 27398 (829) 23062 (524) 18723 (353) 14410 (264) 10162
IFR 8694 (713) 7198 (190) 6145 (128) 4294 (90) 2945 (50) 1992

FFR ——— IFR ———
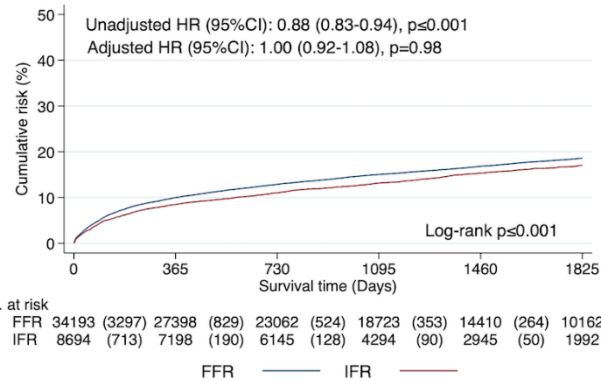
**Adjusted HR 0.94 (0.85-1.05)
p=0.30**

Unplanned revascularization

Unadjusted HR (95%CI): 0.93 (0.85-1.01), p=0.09
Adjusted HR (95%CI): 0.94 (0.85-1.05), p=0.30

Log-rank p=0.09

at risk
FFR 34193 (1508) 29048 (513) 24821 (340) 20380 (232) 15811 (189) 11266
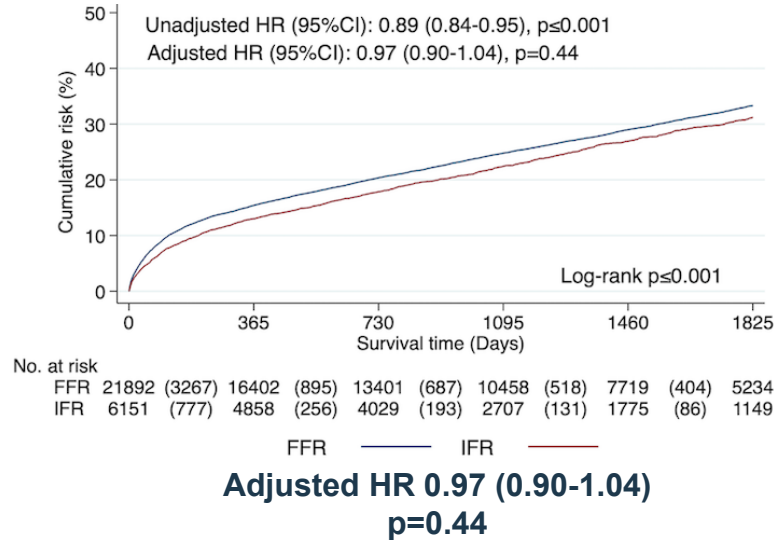IFR 8694 (313) 7588 (132) 6552 (94) 4626 (68) 3177 (34) 2166

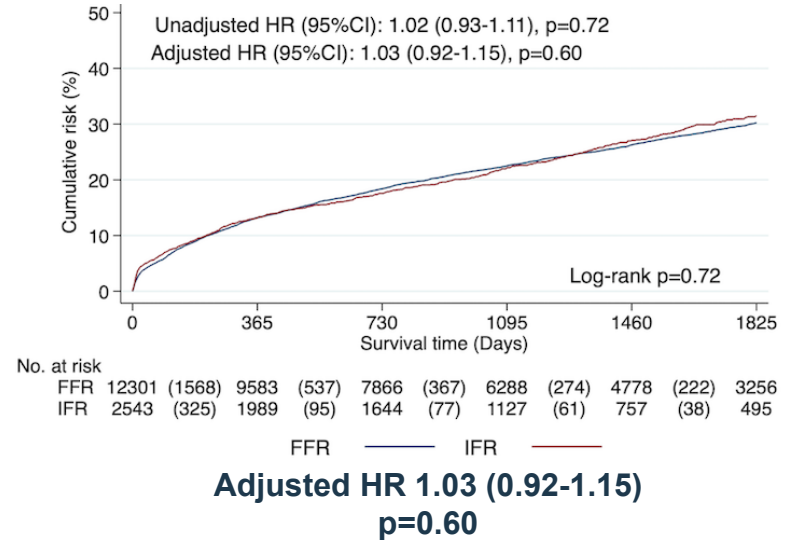FFR ——— IFR ———
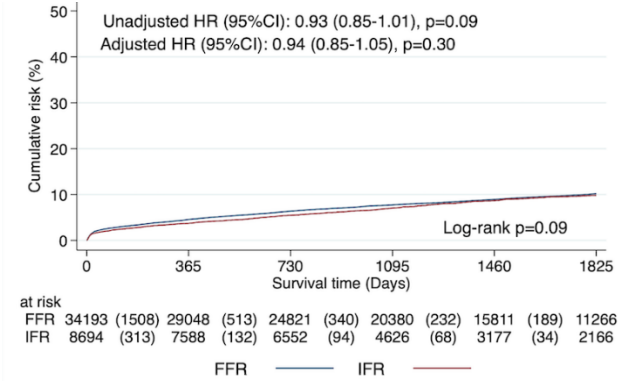
**Adjusted HR 1.00 (0.92-1.08)
p=0.98**

Similar outcome in all components of MACE
(all-cause death, MI, or unplanned revascularization)

CRF
TCT

Deferred vs. treated patients

MACE (Deferred)

Adjusted HR 0.97 (0.90-1.04)
p=0.44

MACE (Treated)

Adjusted HR 1.03 (0.92-1.15)
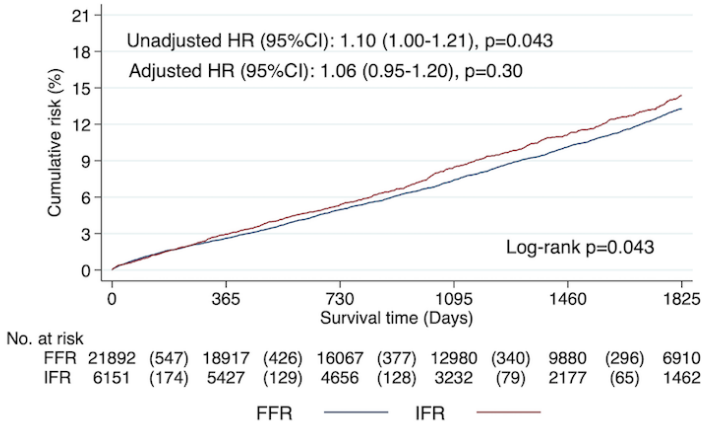**p=0.60**

No difference in MACE between iFR and FFR

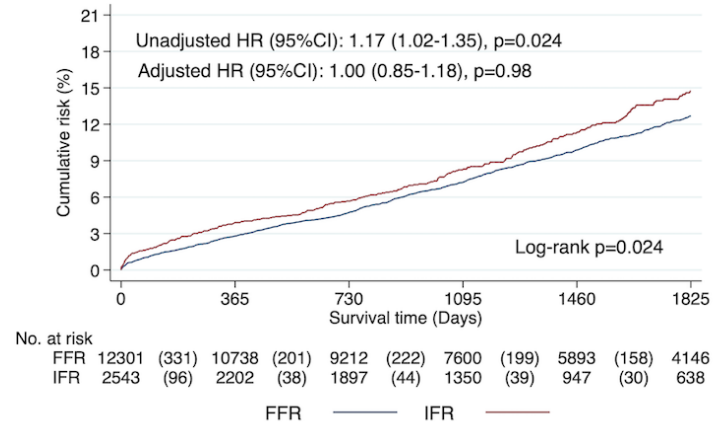## No interaction between treatment decision and outcome

Deferred vs. treated patients

All-cause death (Deferred)

Adjusted HR 1.06 (0.95-1.20)
p=0.30
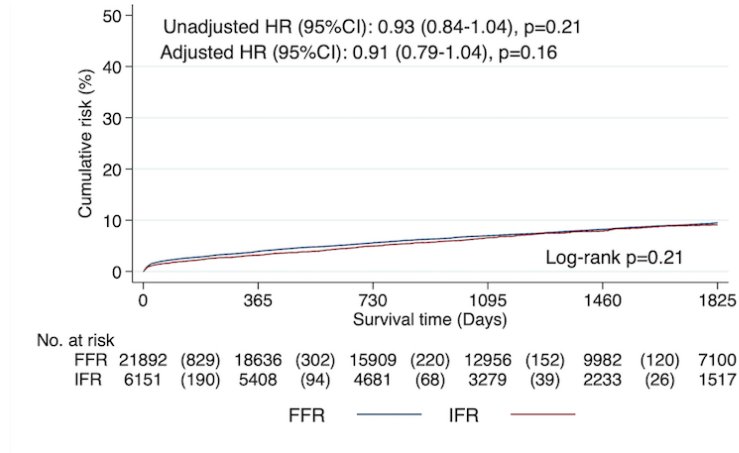
All-cause death (Treated)

Adjusted HR 1.00 (0.85-1.18)
p=0.98

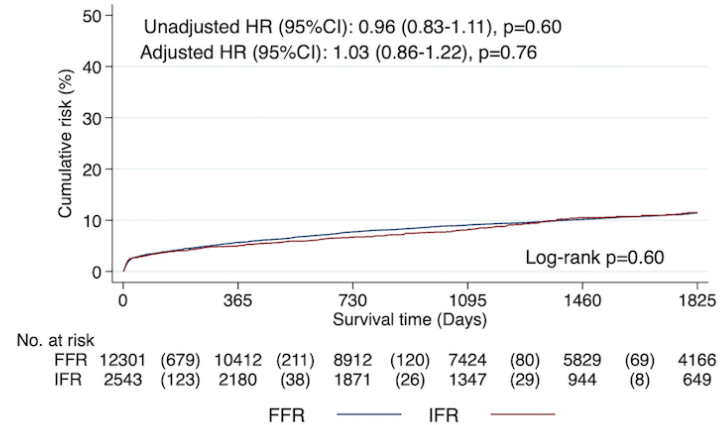## No difference in All-cause death between iFR and FFR

Deferred vs. treated patients

Myocardial infarction (Deferred)

Myocardial infarction (Treated)

Unadjusted HR (95%CI): 0.93 (0.84-1.04), p=0.21
Adjusted HR (95%CI): 0.91 (0.79-1.04), p=0.16

Log-rank p=0.21

No. at risk
FFR 21892 (829) 18636 (302) 15909 (220) 12956 (152) 9982 (120) 7100
IFR   6151 (190)   5408   (94)   4681   (68)   3279   (39) 2233   (26) 1517

Adjusted HR 0.91 (0.79-1.04)
p=0.16

Unadjusted HR (95%CI): 0.96 (0.83-1.11), p=0.60
Adjusted HR (95%CI): 1.03 (0.86-1.22), p=0.76

Log-rank p=0.60

No. at risk
FFR 12301 (679) 10412 (211)   8912 (120)   7424   (80) 5829   (69) 4166
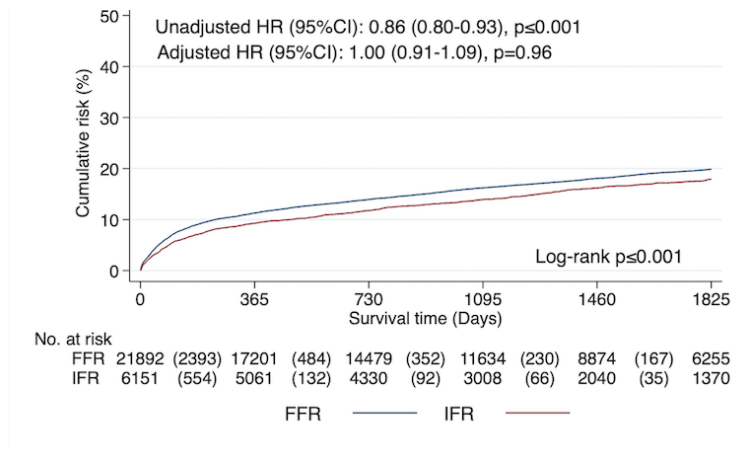IFR   2543 (123)   2180   (38)   1871   (26)   1347   (29)   944   (8)   649

Adjusted HR 1.03 (0.86-1.22)
p=0.76

No difference in Myocardial infarction between iFR and FFR

Deferred vs. treated patients

**Unplanned revasc. (Deferred)**

Unadjusted HR (95%CI): 0.86 (0.80-0.93), p≤0.001
Adjusted HR (95%CI): 1.00 (0.91-1.09), p=0.96

Log-rank p≤0.001

**Adjusted HR 1.00 (0.91-1.09)
p=0.96**

Unplanned revasc. (Treated)

Unadjusted HR (95%CI): 0.88 (0.78-1.00), p=0.048
Adjusted HR (95%CI): 0.99 (0.85-1.15), p=0.85

Log-rank p=0.048
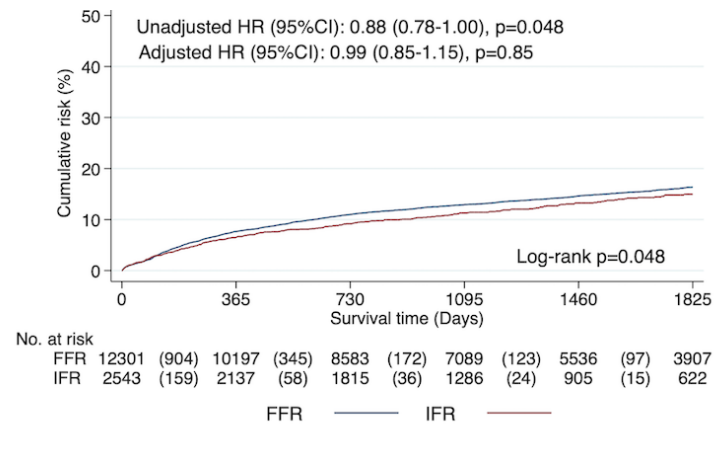
**Adjusted HR 0.99 (0.85-1.15)
p=0.85**

No difference in Unplanned revascularization between iFR and FFR

Subgroup analyses 5-year MACE
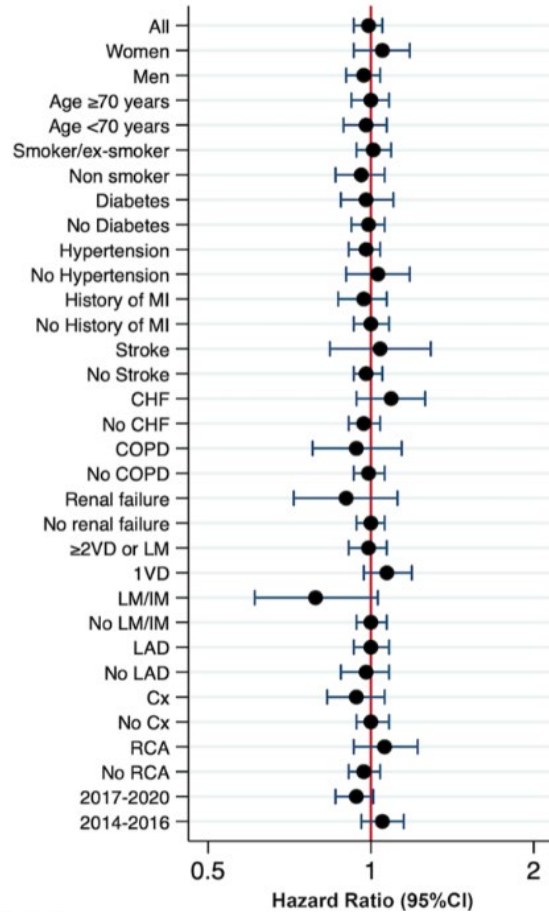
No difference in MACE between iFR and FFR in any of the subgroups

Summary I

In a national registry analysis of 42 887 patients investigated with iFR or FFR with a follow-up up to 5-years:

Similar outcome between iFR and FFR

- MACE (all-cause death, MI, unplanned revasc)
- All-cause death
- Myocardial infarction
- Unplanned revascularization
- Deferred and treated populations

Summary II

The observed difference in mortality between iFR and FFR among treated patients in DEFINE-FLAIR could not be verified in this large nation-wide real-world all-comers registry analysis