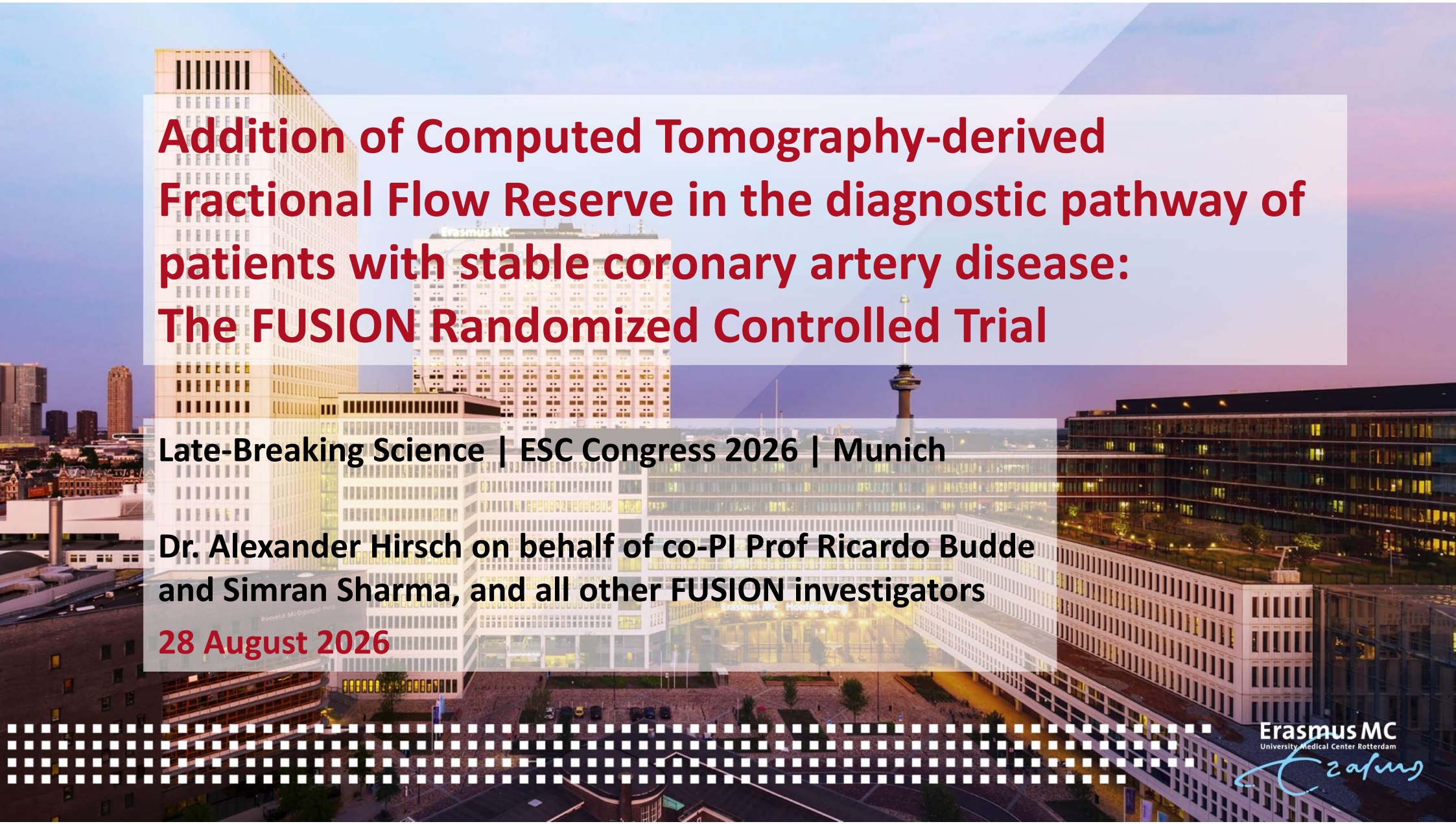


Addition of Computed Tomography-derived Fractional Flow Reserve in the diagnostic pathway of patients with stable coronary artery disease: The FUSION Randomized Controlled Trial

Late-Breaking Science | ESC Congress 2026 | Munich

Dr. Alexander Hirsch on behalf of co-PI Prof Ricardo Budde and Simran Sharma, and all other FUSION investigators

28 August 2026

Erasmus MC
University Medical Center Rotterdam

Disclosures

Alexander Hirsch

- **Research grant and consultancy fees:** GE Healthcare
- **Speaker fees:** GE Healthcare, Bristol Myers Squibb, Bayer, Siemens Healthineers, Heartflow
- **Medical advisory board:** Medis Medical Imaging Systems

Trial funding

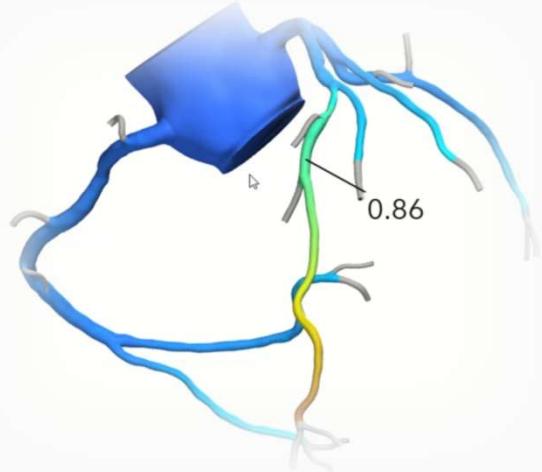
- Dutch Ministry of Health and the Dutch National Health Care Institute (Zorginstituut Nederland, project 80-86200-98-19012)
- Additional financial support from Heartflow Inc., which had no role in study design, conduct, data collection, analysis or reporting

Ethics and registration

Approved by the Medical Ethics Committee of Erasmus MC (MEC-2021-0189)
Registered on clinicaltrials.gov NCT05174247
All patients provided written informed consent

CT-derived Fractional Flow Reserve

- CCTA provides high-resolution anatomical information; however, no functional information about coronary stenoses
- CCTA tends to overestimate severity, and patients referred for ICA frequently have no hemodynamically significant stenosis
- FFRct provides non-invasive, lesion-specific, functional information and has the potential to reduce ICAs without obstructive CAD
- Previous trials evaluated FFRct:
  - As part of broader diagnostic strategies, randomizing patients before CCTA (FORECAST/PRECISE)
  - In a low-risk population (China CT-FFR Study 3)
  - Compared to a control group including standard functional testing, predominantly X-ECG (TARGET)



Trial aim

The FUSION trial investigates the impact of adding FFRct to the diagnostic pathway of patients with a 50-90% stenosis on CCTA on the rate of ICAs without obstructive CAD

FUSION trial

- Investigator-initiated, multicenter, randomized controlled trial
- 12 hospitals in the Netherlands (academic and non-academic)
- Stable CAD patients with a **50–90% stenosis** in ≥1 coronary artery of ≥2 mm on CCTA
- **528** patients randomized in a 1:1 ratio, stratified by center, to
  - **FFRct-guided care (n=263)**
    - CCTA sent off-site to Heartflow; deferral from ICA recommended when FFRct was negative
  - **Usual care (n=265)**
    - Management at the discretion of the treating physician

Study endpoints

- **Primary endpoint: <u>ICA without obstructive CAD at 90 days</u>**

  Definition: ICA without a significant stenosis based on:

  - Invasive FFR/iFR (no FFR ≤0.80 or iFR ≤0.89)
  - QCA (no diameter stenosis ≥50%)
  - Visual assessment (no diameter stenosis LM ≥50% & ≥70% all other segments)

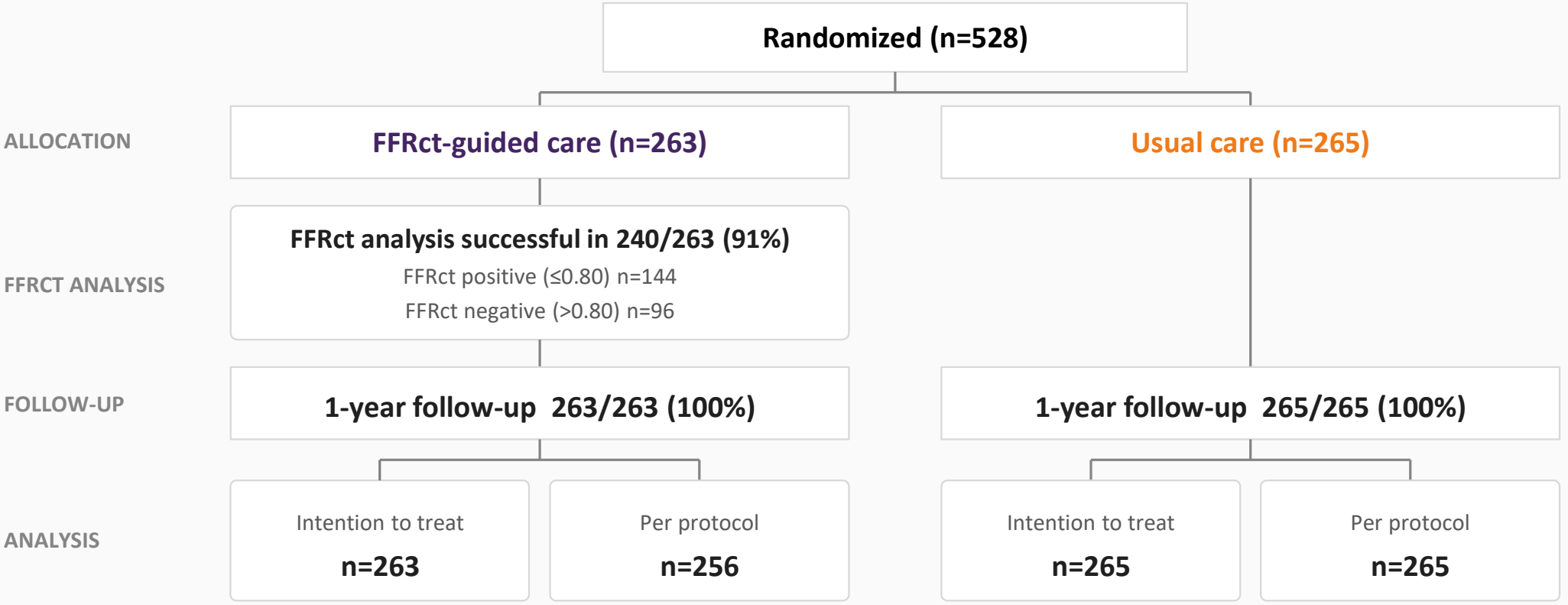
- **Secondary endpoints**

  ICA without obstructive CAD at 1 year; any ICA; revascularization; ICA complications; additional non-invasive testing; MACE; quality of life and angina status; CAD-related healthcare costs

- **Adjudication**

  A blinded clinical event committee reviewed and adjudicated all ICAs and clinical events

Study flow chart



7 patients (3%) were excluded from the per-protocol analysis because an available FFRct result was not incorporated into clinical decision-making.

Baseline characteristics

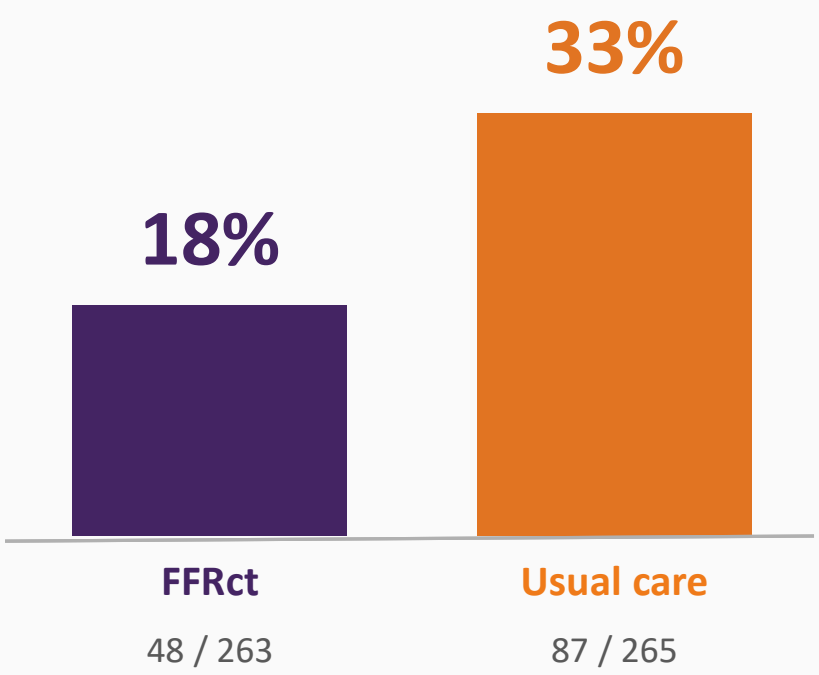
Characteristic	FFRct (n=263)	Usual care (n=265)
Age, years	63 [57–70]	63 [58–68]
Male sex	160 (61%)	152 (57%)
Body mass index, kg/m²	27 [24–29]	26 [24–29]
Diabetes mellitus	40 (15%)	39 (15%)
Hypertension	129 (49%)	132 (50%)
Hypercholesterolemia	125 (48%)	144 (54%)
Family history of CAD	100 (38%)	104 (39%)
Current smoker	38 (14%)	41 (16%)
Typical or atypical chest pain	170 (65%)	159 (60%)
Coronary artery calcium score	229 [103–521]	227 [60–464]
One-vessel disease ≥50%	178 (68%)	185 (70%)
Two-vessel disease	59 (22%)	51 (19%)
Three-vessel and/or left main	26 (10%)	29 (11%)
Left main and/or proximal LAD involved	114 (43%)	122 (46%)
Hemodynamically significant focal lesion on FFRct (≤0.80)	144 (60%)	NA

Data are median [25th–75th percentile] or n (%)

Primary endpoint

ICA without obstructive CAD at 90 days (%)

OR 0.46 (0.31-0.69), p<0.001



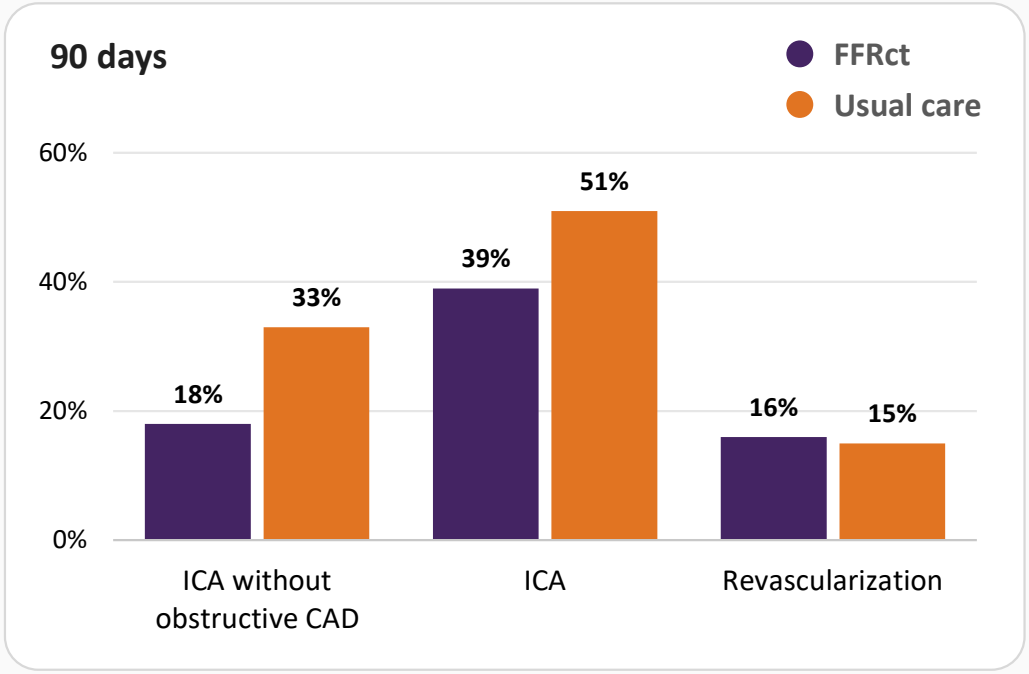
CONSISTENT ACROSS SENSITIVITY ANALYSES

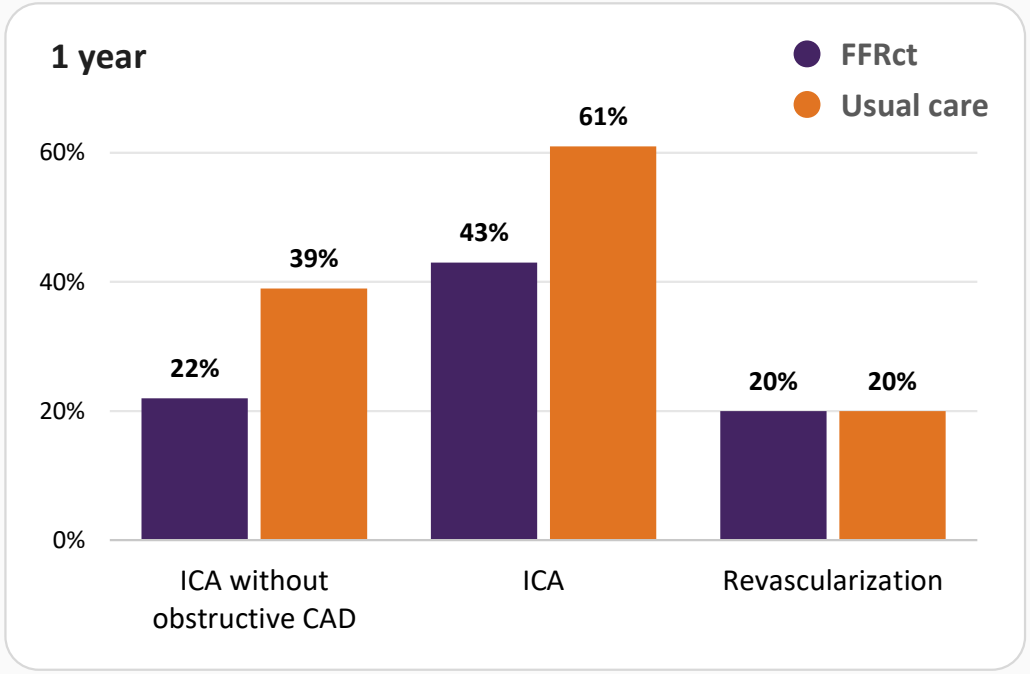
Analysis	OR (95% CI)	P-value
Intention to treat, unadjusted	**0.46 (0.31–0.69)**	<0.001
Intention to treat, adjusted*	**0.47 (0.31–0.71)**	<0.001
Intention to treat, adjusted#	**0.44 (0.29–0.67)**	<0.001
Per protocol, unadjusted	**0.39 (0.26–0.59)**	<0.001
Per protocol, adjusted*	**0.40 (0.26–0.61)**	<0.001
Per protocol, adjusted#	**0.38 (0.24–0.58)**	<0.001

** Adjusted for age, sex, type of chest pain, and CAC score.*

 # Adjusted for age, sex, type of chest pain, CAC score, and center.

Downstream clinical management





ICA without obstructive CAD

90 d **OR 0.46 (0.31–0.69)** P<0.001
1 y **OR 0.44 (0.30–0.64)** P<0.001

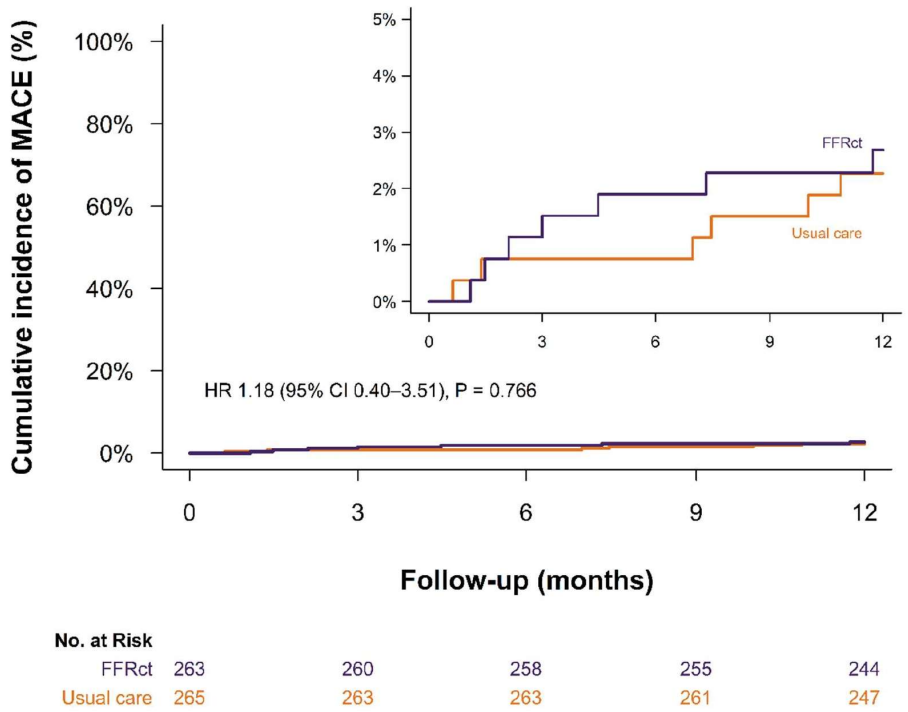
ICA

90 d **OR 0.60 (0.43–0.85)** P=0.004
1 y **OR 0.49 (0.35–0.70)** P<0.001

Revascularization

90 d **OR 1.04 (0.65–1.66)** P=0.875
1 y **OR 0.99 (0.64–1.51)** P=0.948

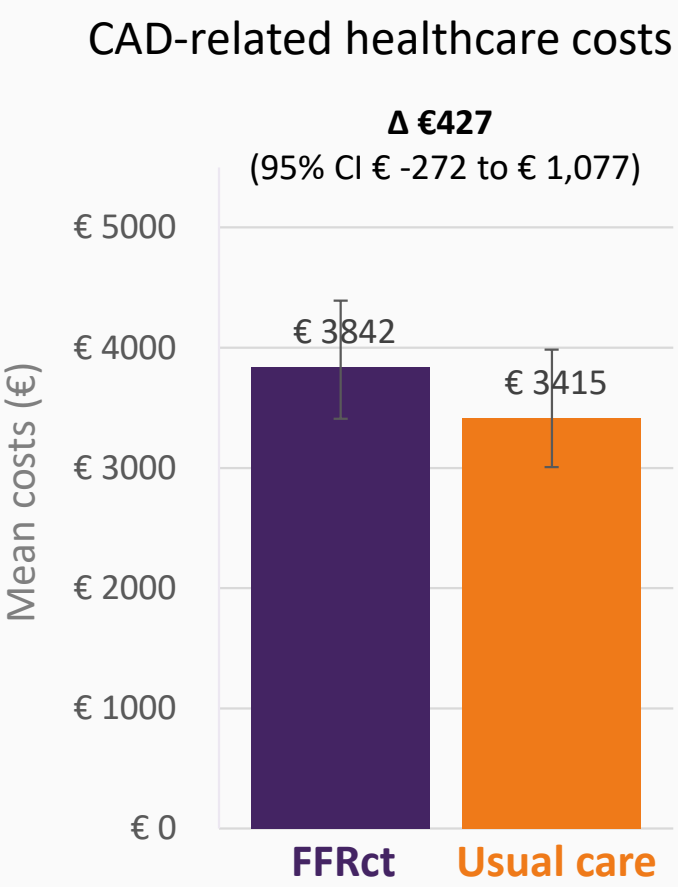
Clinical outcomes at 1 year



Clinical event rates were similar, although low

EVENTS AT 1 YEAR	FFRct	Usual care
At least one MACE	7 (3%)	6 (2%)
All-cause mortality	4 (2%)	1 (0.4%)
Non-fatal myocardial infarction	3 (1%)	5 (2%)
Unplanned hospitalization leading to urgent revascularization	2 (1%)	4 (2%)
Cardiovascular mortality	1 (0.4%)	0
Non-fatal stroke	2 (1%)	0
ICA complications	3 (1%)	3 (1%)

Other secondary outcomes at 1 year



- No difference in CAD-related healthcare costs
- No difference in additional non-invasive testing
  - 28/263 (11%) vs 37/265 (14%), p=0.25
- No difference in quality of life or angina

Conclusions

Adding FFRct to the diagnostic pathway of patients with 50-90% stenosis on CCTA reduced the rate of ICA without obstructive CAD and overall ICA use at 90 days and 1 year, with no differences in revascularizations, quality of life, or costs compared to usual care. Clinical event rates were similar, although low.

Principal investigators: Prof R.P.J. Budde & Dr. A. Hirsch
Coordinator investigator: Drs. S. Sharma

Simultaneously published in JACC