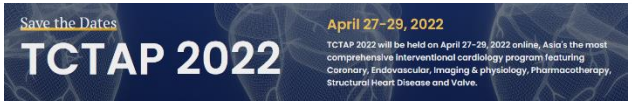


FAVOR
Series of QFR Studies

FAVOR III China

A Sham-Controlled Randomized Trial Comparing QFR-Guided and Angiography-Guided PCI

Bo Xu, Shengxian Tu, Lei Song, Zening Jin, Bo Yu, Guosheng Fu, Yujie Zhou, Jian'an Wang, Yundai Chen, Jun Pu, Lianglong Chen, Xinkai Qu, Junqing Yang, Xuebo Liu, Lijun Guo, Chengxing Shen, Yaojun Zhang, Qi Zhang, Hongwei Pan, Xiaogang Fu, Jian Liu, Yanyan Zhao, Javier Escaned, Yang Wang, William F. Fearon, Kefei Dou, Ajay J. Kirtane, Yongjian Wu, Patrick W. Serruys, Weixian Yang, William Wijns, Changdong Guan, Martin B. Leon, Shubin Qiao, Gregg W. Stone

FAVOR III China Study Group

Disclosure Statement of Financial Interest

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

Affiliation/Financial Relationship	Company
Grant/Research Support	Beijing Municipal Science and Technology Commission
Grant/Research Support	Chinese Academy of Medical Sciences
Grant/Research Support	National Clinical Research Center for Cardiovascular Diseases, Fuwai Hospital

Background

- Compared with visual angiographic assessment, pressure wire-based physiological measurement more accurately identifies flow-limiting lesions
- Nonetheless, this method is largely underused in practice due to prolonged procedural time, potential complications from pressure wire instrumentation, side effects from hyperemic agents, and costs
- Quantitative flow ratio (QFR), derived from 3D coronary artery reconstruction and fluid dynamics computations from the angiogram, enables online estimation of FFR without the use of a pressure wire or pharmacologic agents to induce hyperemia
- Prior studies have demonstrated the feasibility and accuracy of online QFR assessment compared with pressure wire-based FFR measurement
- Whether lesion selection for PCI using a QFR-guided strategy might improve outcomes compared with a standard angiography-guided strategy is unknown

Toth G, et al. *Eur Heart J* 2014; van Nunen LX, et al. *Lancet* 2015; Parikh RV, et al. *J Am Coll Cardiol* 2020; Kogame N, et al. *JACC Cardiovasc Interv* 2020; Piccolo R, et al. *Lancet* 2015.

Quantitative Flow Ratio (QFR)

FAVOR
Series of QFR Studies

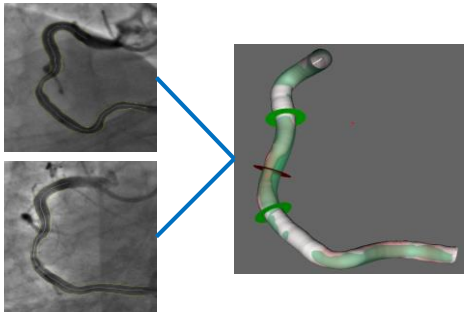
Standard Angiogram

Data Transmission System

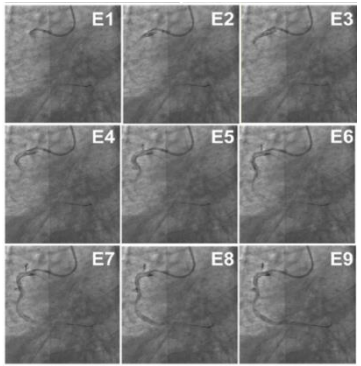
Two image runs with angle difference ≥25°

AngioPlus System

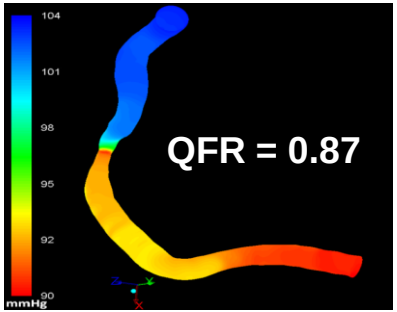
3D Reconstruction



Modified Frame Count



QFR



Without Inducing Hyperemia

Tu S, et al. *JACC Cardiovasc Interv* 2016; Xu B, et al. *J Am Coll Cardiol* 2017.

Study Design

Investigator-Initiated, Multicenter, Sham-Controlled Blinded Randomized Trial

FAVOR Series of QFR Studies

Patients with coronary artery disease scheduled for coronary angiography

Meet all general inclusion and not meet any exclusion criteria

Inclusions: age ≥ 18 years; stable, unstable angina, or post-AMI (≥72 hours). Exclusions: moderate or severe chronic kidney disease (defined as creatinine >150 μmol/L or estimated glomerular filtration rate (GFR) <45 ml/kg/1.73 m^2).

Informed consent

Coronary angiography

Meet all angiographic inclusion and not meet any exclusion criteria

Inclusions: patients must have at least one lesion with a percent diameter stenosis between **50% and 90%** in a coronary artery with a **≥2.5 mm** reference vessel diameter by visual assessment. Exclusions: patients had only one lesion with DS%>90% and TIMI flow <3; interrogated lesions are related with AMI.

Identify target vessels intended to be treated with standard angiography guidance

N=3830 (1:1 randomization)

Randomization Stratifications
- Diabetes Mellitus
- Multivessel Disease
- Presence of any vessel with DS% >90% and TIMI flow <3
- Center

Independent Organizations
- Core Lab
- CEC
- DSMB
- Data Management
- Statistical Analysis

QFR-guided strategy N=1915	Angiography-guided strategy N=1915
QFR was measured in all coronary arteries containing any lesion with visually-assessed DS% ≥50% and ≤90% and RVD ≥2.5 mm • QFR ≤0.80: PCI • QFR >0.80: deferral • All measured vessel QFR >0.80: OMT alone	PCI was performed based on visual angiographic assessment per local standard of practice

Imaging core lab analysis; clinical follow-up at 1 month, 6 months,1, 2, 3, 4, and 5 years; EQ-5D questionnaires collected at 1, 6, and 12 months

ClinicalTrial.gov Identifier: NCT03656848

Song L, et al. *Am Heart J* 2020.

Endpoints

Primary Endpoint:

1-year rate of major adverse cardiac events (MACE), defined as the composite of death from any cause, MI, or ischemia-driven revascularization

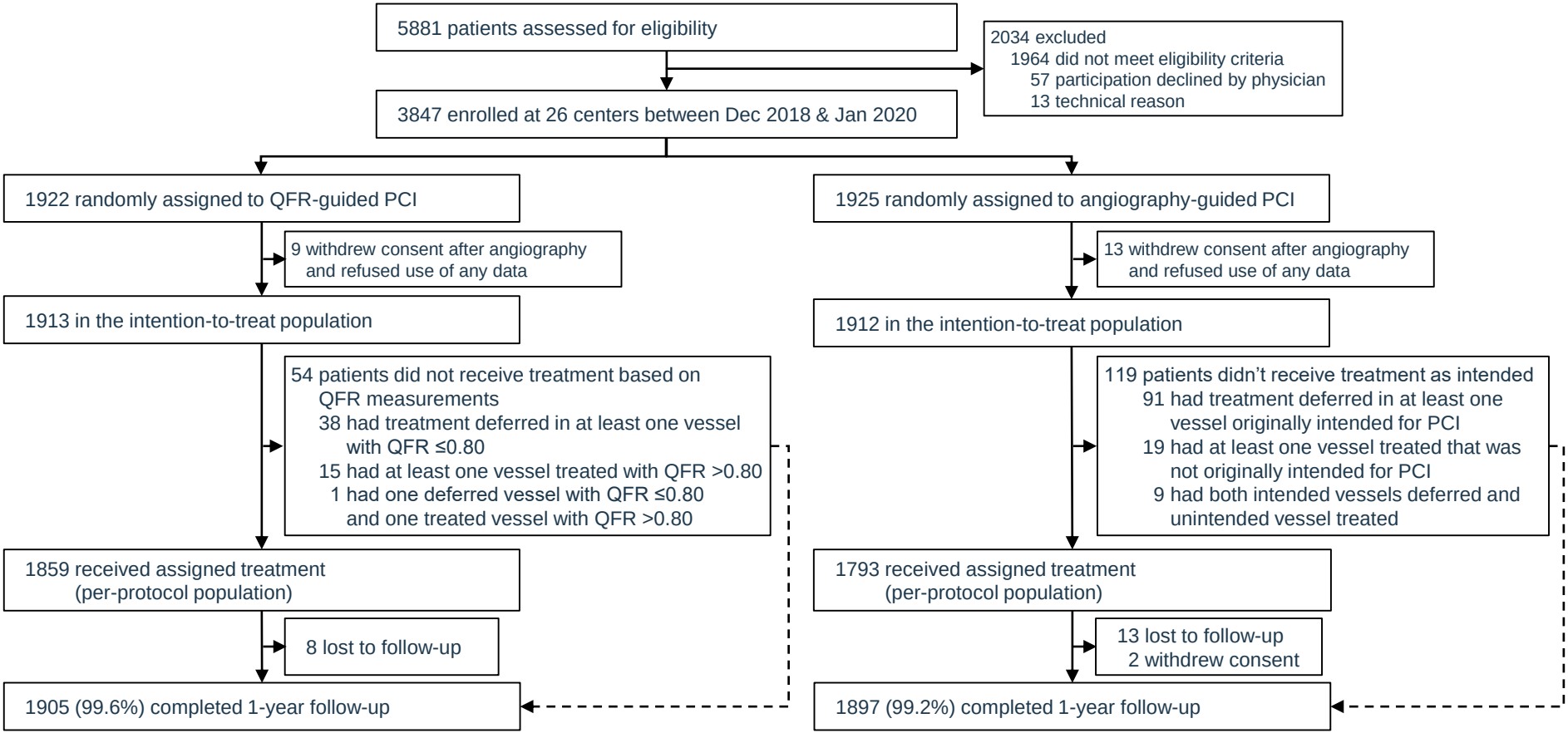
Major Secondary Endpoint:

1-year rate of MACE excluding peri-procedural MI arising from the index or planned staged procedures

Other Secondary Endpoints:

- MACE at 1 month, 6 months, 2 years, and 3 years
- Death (cardiovascular, non-cardiovascular, and undetermined) at 1 month, 6 months, 1 year, 2 years, and 3 years
- MI (peri-procedural and non-procedural) at 1 month, 6 months, 1 year, 2 years, and 3 years
- Repeat revascularization (ischemia driven and non-ischemia driven) at 1 month, 6 months,1 year, 2 years, and 3 years
- Target vessel revascularization (ischemia driven and non-ischemia driven) at 1 month, 6 months,1 year, 2 years, and 3 years
- Definite/probable stent thrombosis (acute, subacute, late, and very late according to ARC-2 definition)
- PCI strategy changes following QFR and 3D-QCA
- Cost-effectiveness and quality-of-life outcomes at 1 month, 6 months, and 1 year

Patient Flow



Xu B, et al. *Lancet* 2021.

Baseline Characteristics (i)

	QFR-guided group (N=1913)	Angiography-guided group (N=1912)
Age, years	62.7 ± 10.1	62.7 ± 10.2
Male sex	70.5%	70.6%
Body mass index, kg/m^2	25.1 (22.9, 27.0)	24.7 (22.7, 27.0)
Diabetes mellitus	33.9%	33.8%
Hypertension	66.4%	65.5%
Hypercholesterolemia	38.1%	38.1%
Current smoker	30.0%	29.7%
Family history of coronary artery disease	7.7%	7.8%
Previous myocardial infarction	9.4%	9.4%
Previous percutaneous coronary intervention	25.4%	24.4%
Previous stroke	9.6%	9.2%
Peripheral artery disease	2.9%	3.7%

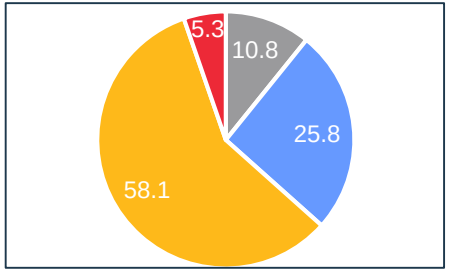
Baseline Characteristics (ii)

FAVOR Series of QFR Studies

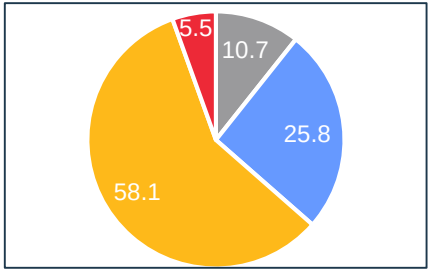
Clinical presentation

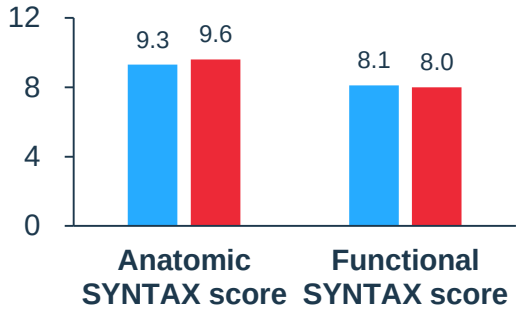
- Asymptomatic ischemia
- Stable angina
- Unstable angina
- Post myocardial infarction (within 30 days)

QFR-guided group



Angiography-guided group

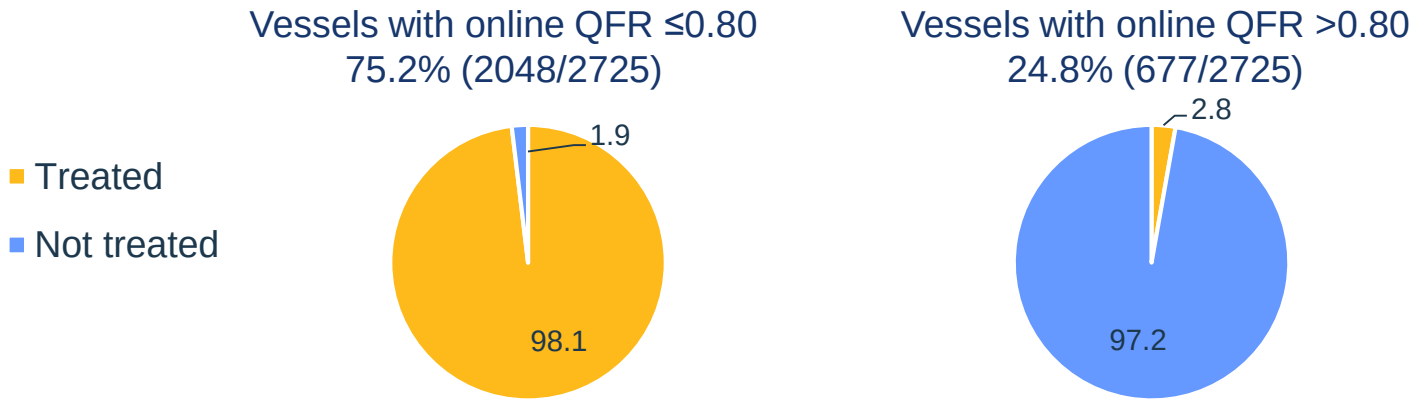




	QFR-guided group (N=1913)	Angiography-guided group (N=1912)
Estimated glomerular filtration rate, ml/min/1.73m^2	70.3 (58.4, 83.4)	70.0 (58.0, 83.9)
Left ventricular ejection fraction, %	63.0 (61.0, 66.0)	63.0 (60.0, 66.0)
Multivessel disease	53.5%	54.6%
Any vessel with one or more lesions with diameter stenosis >90% and TIMI flow <3	8.9%	9.5%

Online QFR Assessment

	QFR-guided group (N=1913)
Vessels eligible for online QFR assessment	2727
Vessels with online QFR calculated	99.9%
Mean online QFR calculation time per patient, min	3.9 ± 1.4
Online QFR value	0.70 ± 0.16



How QFR Guidance Changed the Strategy

FAVOR Series of QFR Studies

Vessels intended to be treated pre randomization	QFR-guided group N=2503	Angiography-guided group N=2559
LM, p=0.46	1.3%	1.6%
LAD, p=0.069	52.6%	50.1%
LCX, p=0.084	20.9%	22.9%
RCA, p=0.80	25.2%	25.5%

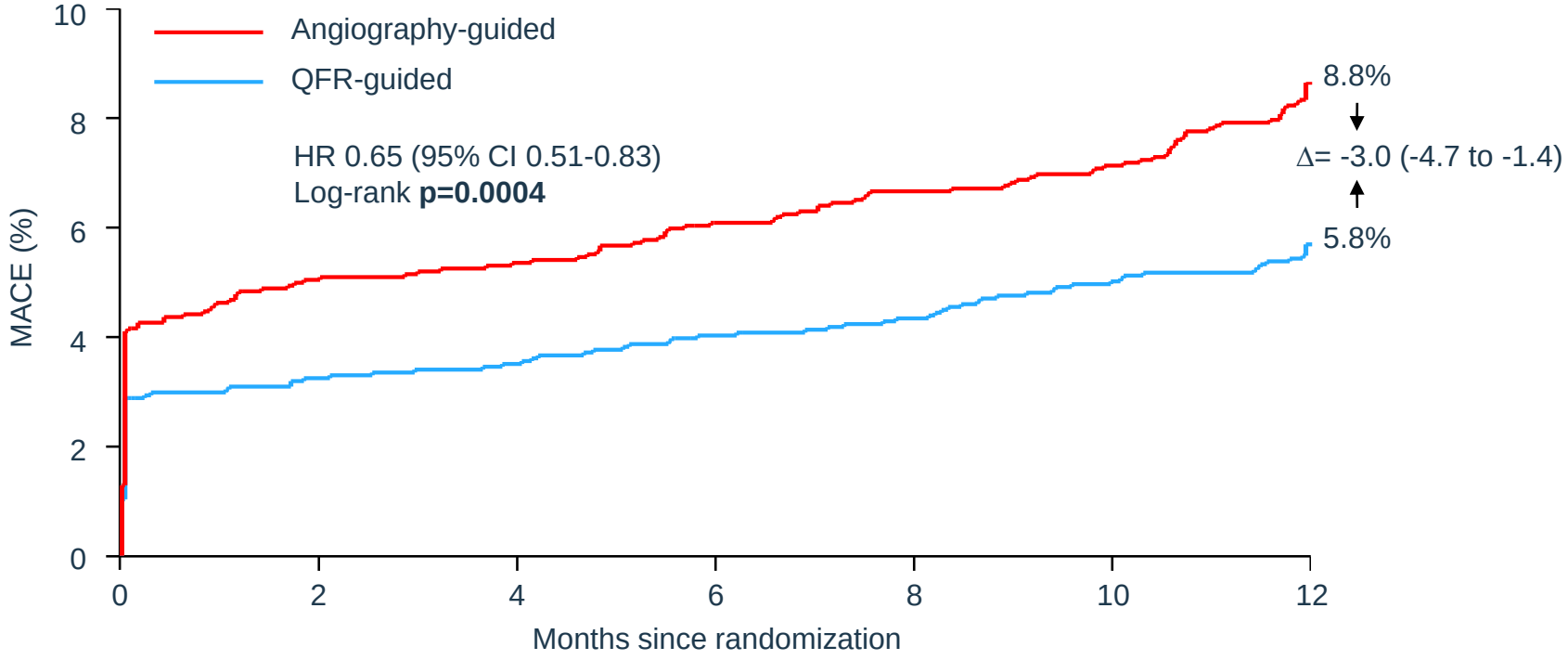
Vessels actually treated of those originally intended	QFR-guided group N=2112	Angiography-guided group N=2449
LM, p=0.62	1.4%	1.6%
LAD, **p=0.0007**	55.6%	50.6%
LCX, **p=0.015**	19.8%	22.7%
RCA, p=0.14	23.2%	25.1%

	QFR-guided group	Angiography-guided group	p value
Vessels actually treated of those originally intended	84.4% (2112/2503)	95.7% (2449/2559)	**<0.0001**
Patients with intended vessel deferral or unintended vessel treatment	23.3% (445/1913)	6.2% (119/1912)	**<0.0001**
Deferral (non-treatment) of at least one vessel originally intended for PCI	19.6% (375/1913)	5.2% (100/1912)	**<0.0001**
Treatment of at least one vessel not originally intended for PCI	4.4% (85/1913)	1.5% (28/1912)	**<0.0001**

Key Procedural Results

	QFR-guided group (N=1913)	Angiography-guided group (N=1912)	p value
PCI performed	90.5%	99.1%	**<0.0001**
Number of stents placed per patient	1.45 ± 1.02	1.58 ± 0.97	**<0.0001**
Use of intravascular imaging	6.2%	6.3%	0.89
Contrast medium used per patient, ml	163.0 ± 75.6	169.7 ± 74.2	**0.0060**
Fluoroscopy time, min	14.1 ± 8.0	14.9 ± 7.4	**0.0013**
Procedure time, min	53.7 ± 30.4	59.4 ± 30.4	**<0.0001**
Adjusted procedure time, min	44.6 ± 28.8	49.5 ± 30.2	**<0.0001**
PCI lesion success	99.0%	99.3%	0.38
Residual anatomic SYNTAX score	2.4 ± 3.6	2.4 ± 4.0	0.49
Residual functional SYNTAX score	0.7 ± 2.3	1.0 ± 2.8	**<0.0001**
Residual functional SYNTAX score=0	88.1%	82.2%	**<0.0001**

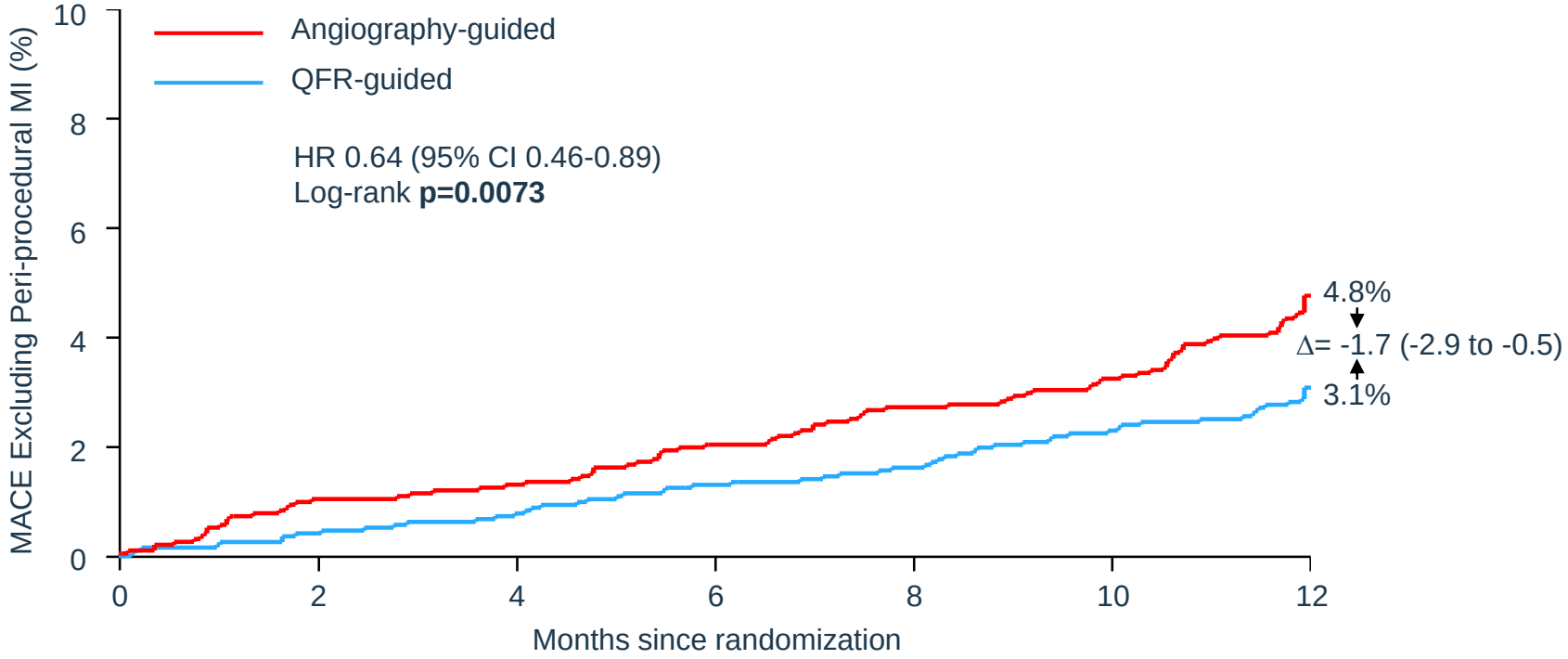
Primary Endpoint (ITT)



No. at risk

QFR-guided	1913	1845	1840	1828	1821	1809	1795
Angiography-guided	1912	1804	1798	1783	1770	1762	1732

Major Secondary Endpoint (ITT)



No. at risk

QFR-guided	1913	1900	1894	1881	1874	1862	1846
Angiography-guided	1912	1883	1877	1862	1847	1839	1808

One-Year Clinical Outcomes

FAVOR Series of QFR Studies

	QFR-guided group (N=1913)	Angiography-guided group (N=1912)	Hazard ratio (95% CI)	p value
Primary endpoint	5.8%	8.8%	**0.65 (0.51-0.83)**	**0.0004**
Death from any cause	0.7%	0.5%	1.44 (0.62-3.37)	0.40
Myocardial infarction	3.4%	5.7%	**0.59 (0.44-0.81)**	**0.0008**
Ischemia-driven revascularization	2.0%	3.1%	**0.64 (0.43-0.96)**	**0.031**
Major secondary endpoint	3.1%	4.8%	**0.64 (0.46-0.89)**	**0.0078**
Other secondary endpoints				
Cardiovascular death	0.5%	0.4%	1.28 (0.48-3.44)	0.62
Peri-procedural myocardial infarction	2.9%	4.2%	**0.69 (0.49-0.97)**	**0.033**
Non-procedural myocardial infarction	0.5%	1.6%	**0.33 (0.16-0.68)**	**0.0025**
Any revascularization	2.6%	3.5%	0.73 (0.50-1.05)	0.089
Target vessel revascularization	1.2%	1.3%	0.88 (0.50-1.56)	0.66
Stent thrombosis, definite or probable	0.2%	0.3%	0.50 (0.12-1.99)	0.33

Conclusions and Clinical Implications

- In the present multicenter, randomized, sham-controlled trial, a QFR-guided vessel and lesion selection strategy improved 1-year clinical outcomes compared with standard angiography guidance in patients undergoing PCI
  - ✓ The benefits were due both to fewer procedural complications and superior long-term results compared with standard angiography guidance, with less MIs and repeat revascularization procedures
- The simplicity and safety of QFR compared with wire-based physiological measurements should facilitate the adoption of physiologic lesion assessment into routine clinical practice