



Fractional Flow Reserve-Guided PCI Compared with Coronary Bypass Surgery:

The True Message of the FAME 3 Trial

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Disclosures

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

Grant/Research Support

Consulting Fees/Stock Options

Major Stock Shareholder/Equity

Royalty Income

Ownership/Founder

Intellectual Property Rights

Other Financial Benefit

Company

Abbott, Boston Scientific, Medtronic
NIH R61 HL139929-01A1 (PI)

CathWorks, Siemens, HeartFlow



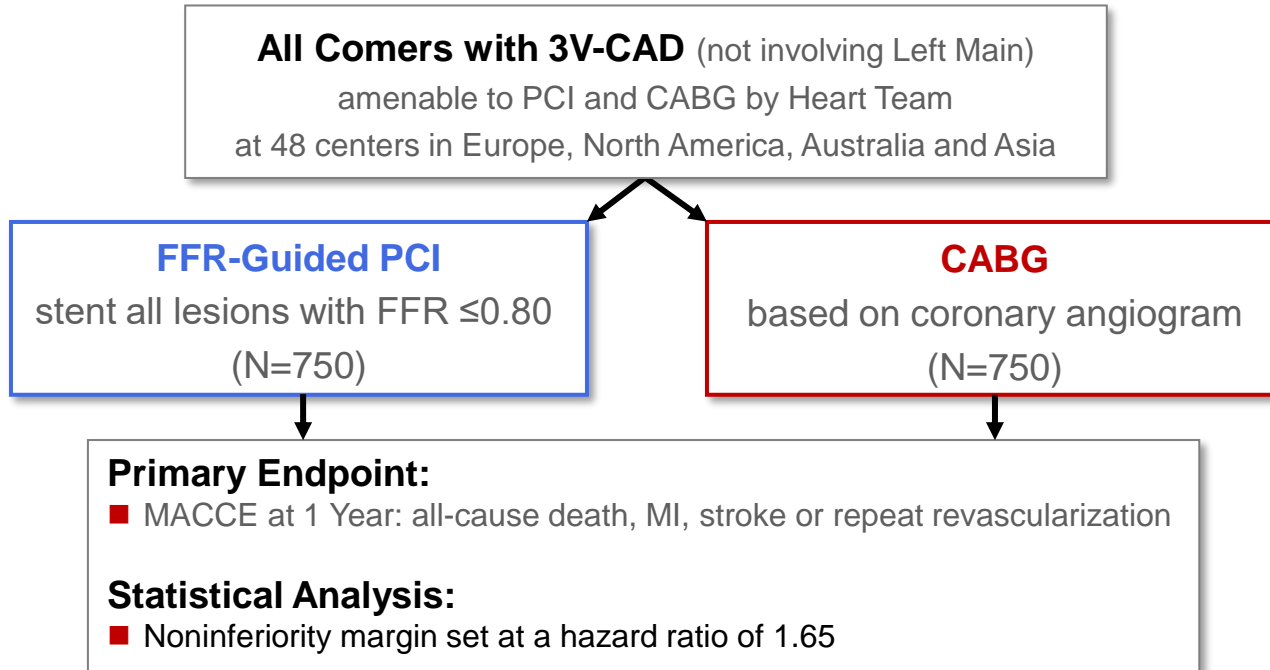
Outline

- Review the main results of the FAME 3 Trial
- Message 1: Improved outcomes
- Message 2: FFR and disease complexity
- Message 3: Endpoint definitions
- Message 4: Quality of life



FAME 3: *Study Design*

Investigator-initiated, multicenter, randomized, controlled study



Baseline Characteristics

| Variable | PCI (n=757) | CABG (n=743) |
|---------------------|----------------|-----------------|
| Age | 65 ± 8 years | 65 ± 8 years |
| Male | 81% | 83% |
| Caucasian | 94% | 92% |
| HTN | 71% | 75% |
| Dyslipidemia | 69% | 72% |
| Current Tobacco Use | 19% | 18% |
| Diabetes | 28% | 29% |
| Insulin dependent | 7% | 8% |
| ACS presentation | 40% | 39% |
| EF≤50% | 18% | 18% |
| Prior PCI | 13% | 14% |

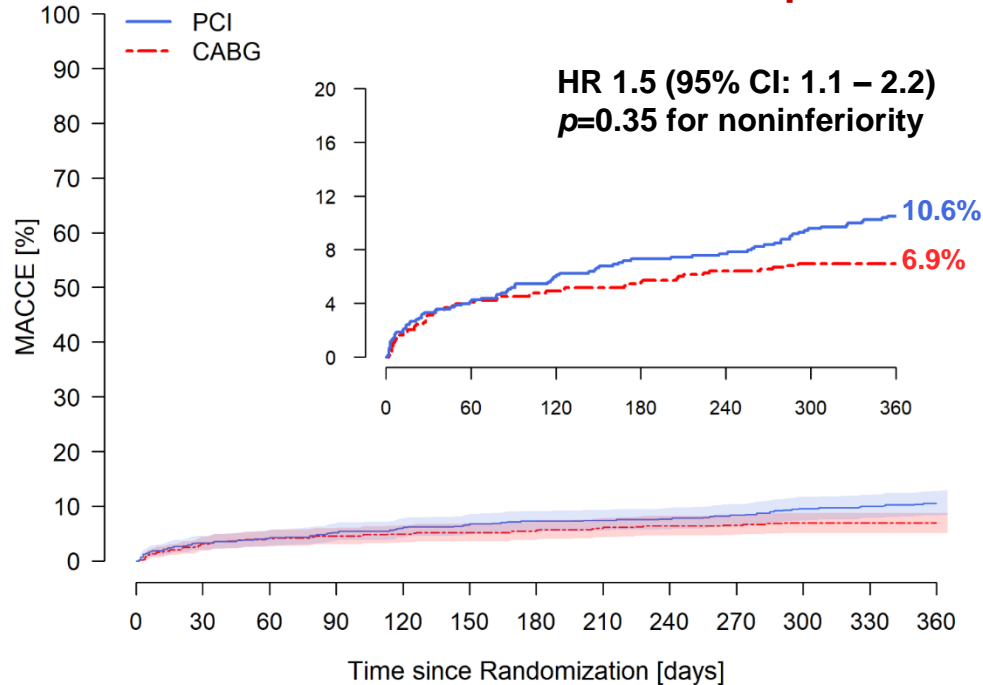


Procedural Characteristics

| Variable | PCI (n=757) | CABG (n=743) |
|-------------------------|----------------|-----------------|
| Time to procedure | 4 days | 13 days |
| Procedure duration | 87 min | 197 min |
| Length of hospital stay | 3 days | 11 days |
| Number of lesions | 4.3 | 4.2 |
| ≥1 Chronic occlusion | 21% | 23% |
| ≥1 Bifurcation lesion | 69% | 66% |
| SYNTAX Score | 26 | 26 |
| Low (0-22) | 32% | 35% |
| Intermediate (23-32) | 50% | 48% |
| High (>33) | 18% | 17% |

Primary Endpoint

MACCE (Death, MI, stroke or repeat revascularization) at 1 Year



| | No. at Risk | | | | | | | | | | | | |
|------|-------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| PCI | 757 | 728 | 721 | 713 | 707 | 702 | 697 | 696 | 693 | 687 | 678 | 674 | 670 |
| CABG | 743 | 709 | 701 | 698 | 695 | 693 | 691 | 686 | 683 | 682 | 679 | 679 | 679 |



Message #1

- Compared with historical data, outcomes with both FFR-guided PCI with current generation DES and CABG have improved significantly.



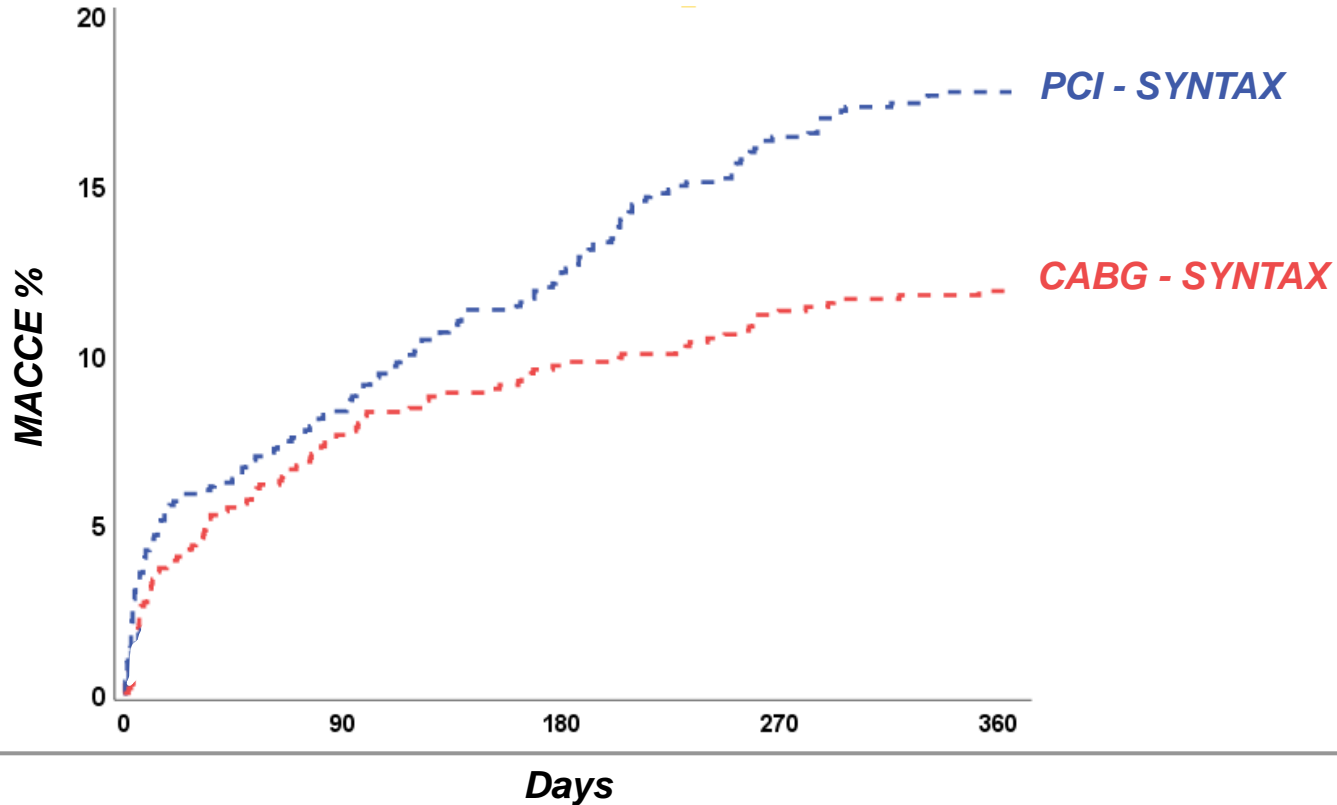
FAME 3 and SYNTAX Trials

| Variable | FAME 3 | SYNTAX |
|---------------------|----------|----------|
| Age | 65 years | 65 years |
| Male | 82% | 78% |
| Diabetes | 29% | 25% |
| Insulin Dependent | 8% | 10% |
| Hypertension | 73% | 67% |
| Dyslipidemia | 70% | 78% |
| Current Tobacco Use | 19% | 20% |
| ACS presentation | 39% | 29% |
| EF≤50% | 18% | 20% |
| Prior PCI | 14% | 0% |
| Number of Lesions | 4.3 | 4.4 |
| SYNTAX Score | 26 | 29 |



FAME 3 and SYNTAX Trials

MACCE (Death, MI, Stroke, or Repeat Revascularization) at 1 Year



Message #2

- For any test (e.g., FFR) to have a positive impact on outcomes, it needs to be used in a population and/or in a manner where it will impact decision-making.



FAME 3 and FFR

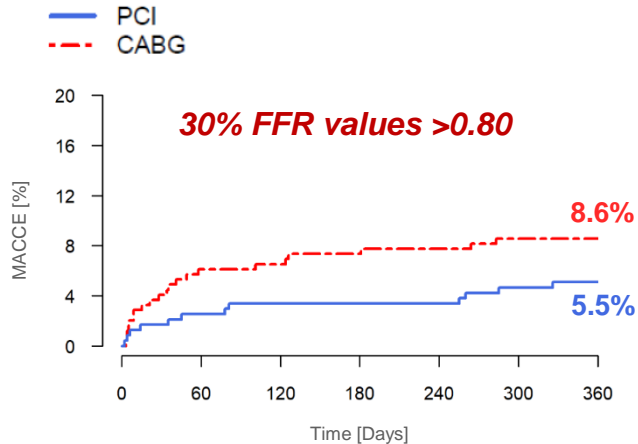
- FFR could only be measured in 82% of lesions, meaning in about 20% of lesions FFR played no role in decision-making.
- In those lesions where FFR was measured, FFR was negative in only 24%.
- For reference, in studies of intermediate lesions, FFR is typically negative in 60-70% of lesions.
- A main benefit of FFR is deferring unnecessary PCI when FFR is negative.



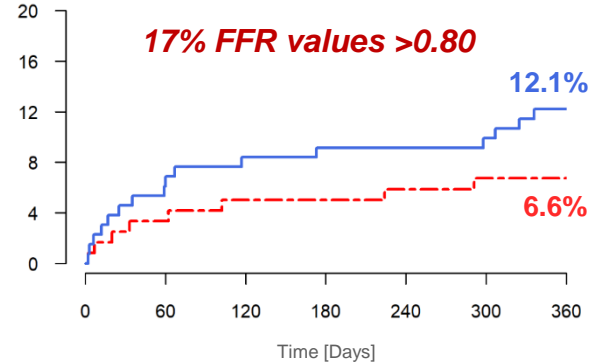
MACCE According to SYNTAX Score...

...and according to percentage of lesions with FFR values >0.80

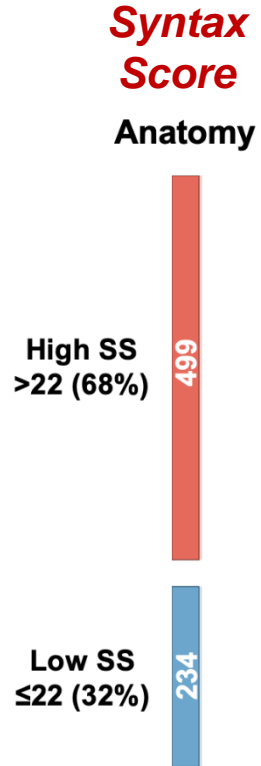
LOW (<23) SYNTAX SCORE



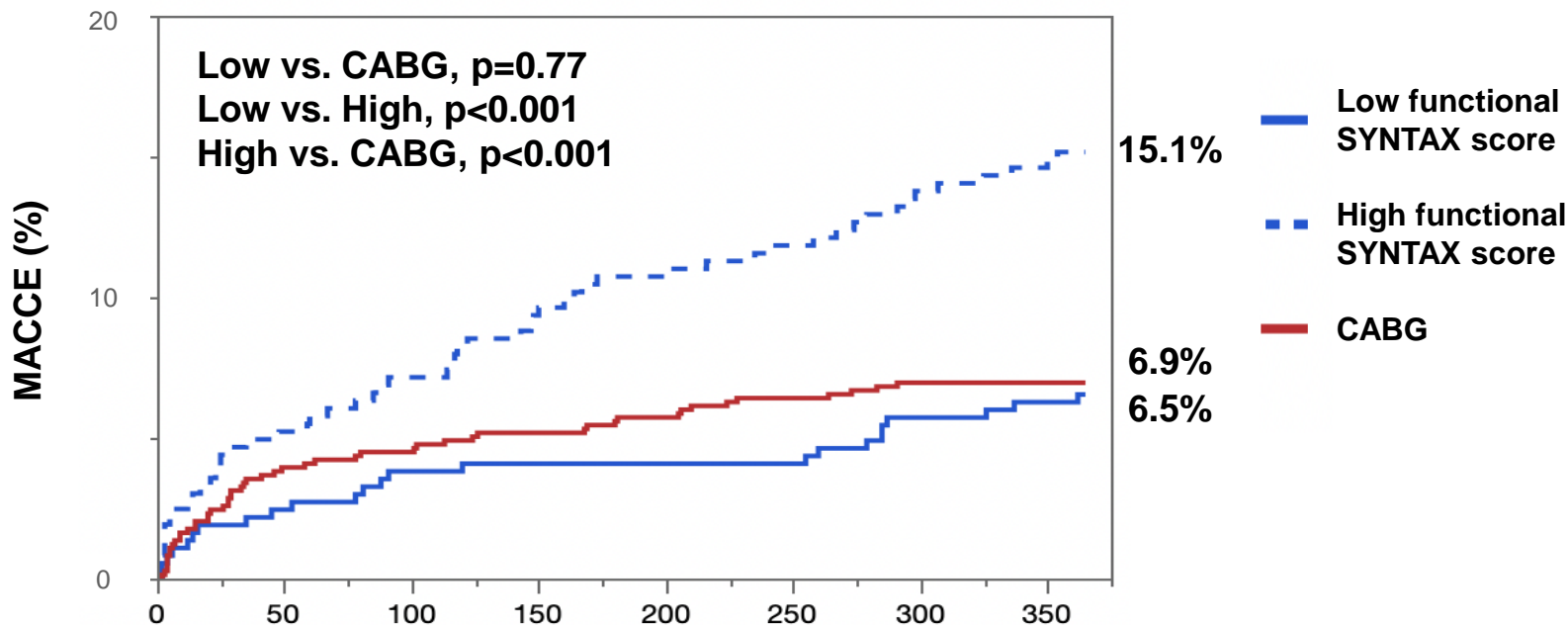
HIGH (>32) SYNTAX SCORE



Reclassification with FFR Information



MACCE According to Functional SYNTAX Score



| | | | | | |
|------|-----|-----|-----|-----|-----|
| Low | 368 | 354 | 353 | 346 | 342 |
| High | 365 | 338 | 325 | 313 | 306 |
| CABG | 743 | 699 | 689 | 680 | 678 |

Outcome of Deferred Lesions at 1 Year

- Among all deferred lesions (n=597):
 - MI rate = 0.5% (n=3)
 - Revascularization rate = 3.2% (n=19)

Message #3

- Not all “hard” endpoints are really that hard!



Definition of Myocardial Infarction

Procedural (FAME 3)

- Defined in the same way for CABG and PCI
- Troponin > 10x URL (or an increase of > 20%, if the baseline values are elevated) AND at least one of the following:
 - *New pathologic Q waves or new LBBB*
 - *Angiographic documented new graft or new major native coronary occlusion*
 - *Imaging demonstration of new loss of viable myocardium or new regional wall motion abnormality*



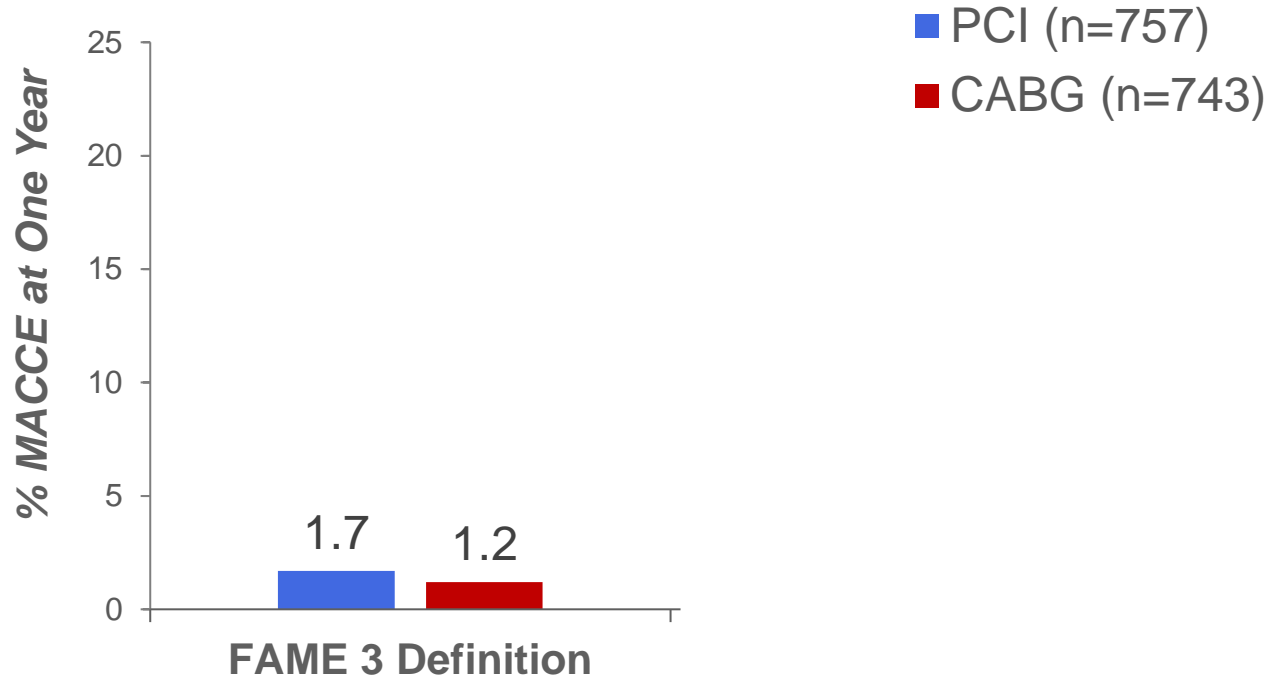
Definition of Myocardial Infarction

Procedural (SCAI)

- CK-MB 10x URL (or 70x troponin) OR
- CK-MB >5x URL (35x troponin ULN) PLUS
 - *New pathologic Q-waves in 2 contiguous leads or new persistent LBBB*



Procedural MI Definitions



¹ Moussa ID, et al. *J Am Coll Cardiol* 2013;62:1563-70.



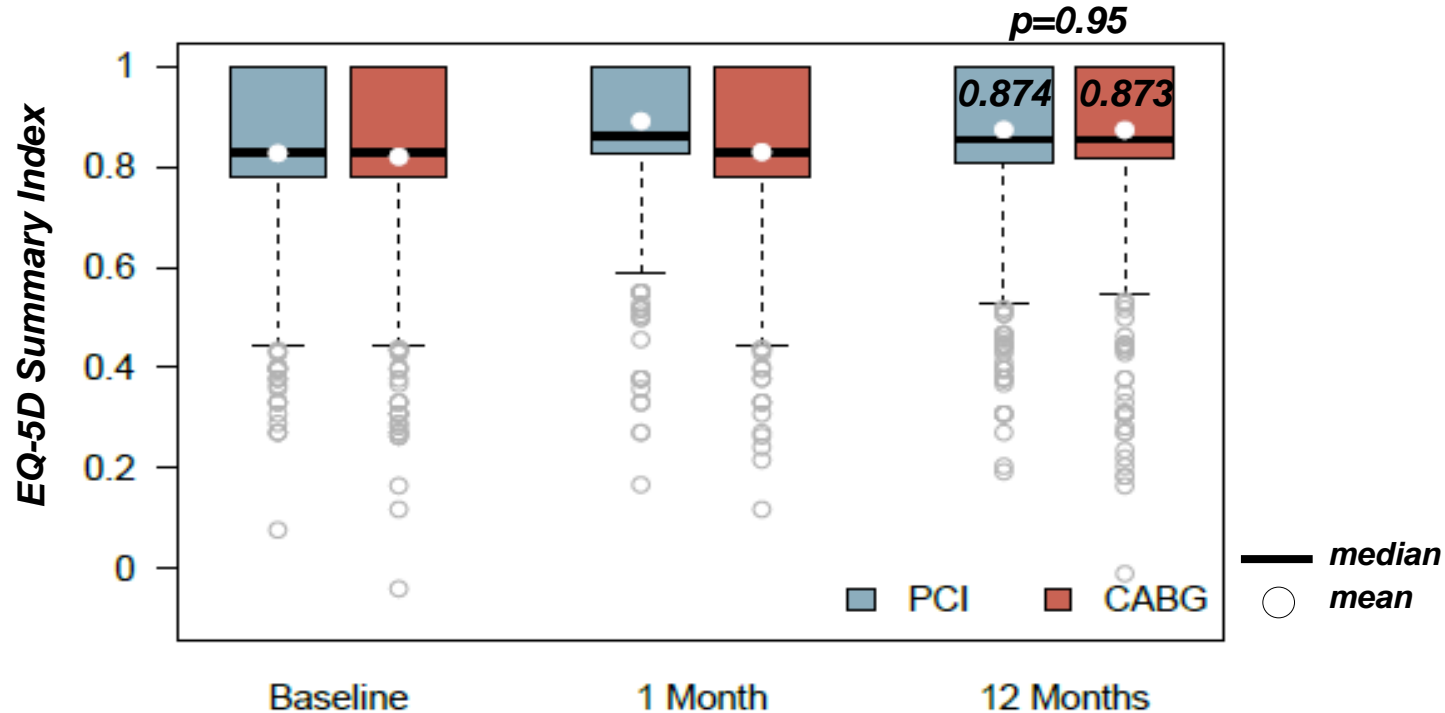
Message #4

- Because the clinical event rate is similar between FFR-guided PCI and CABG (only 3.7% absolute difference in MACCE and no difference in death and stroke) other endpoints, like quality of life and angina relief become even more important to both the patient and the physician.



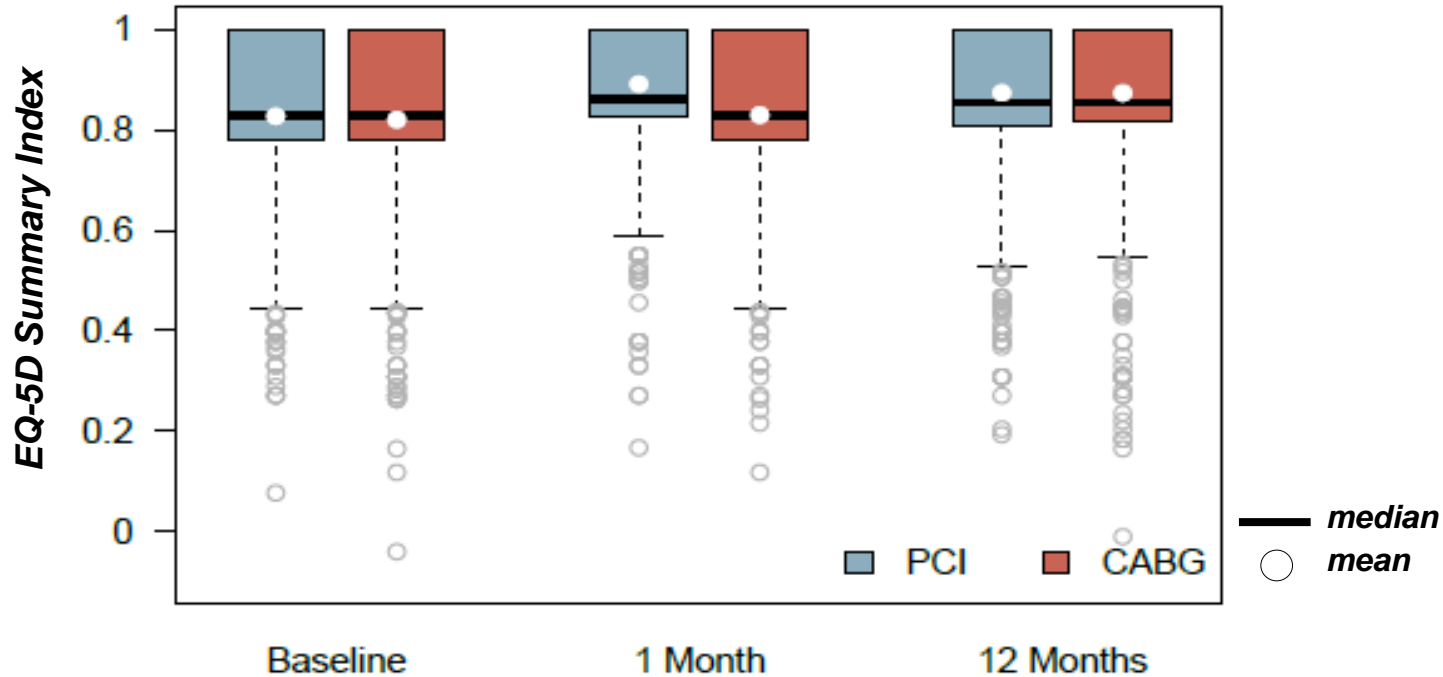
FAME 3 Quality of Life

Primary Endpoint: EQ-5D Summary Score at 1 year



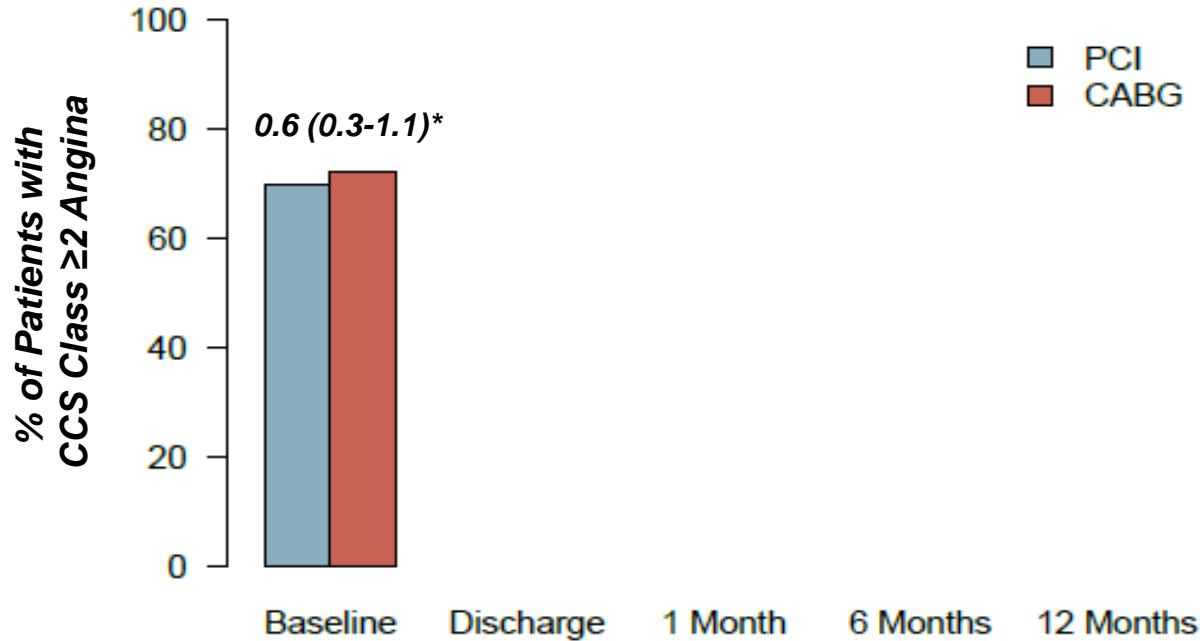
FAME 3 Quality of Life

P<0.001 for the trajectory of improvement in EQ-5D Summary Index favoring FFR-Guided PCI



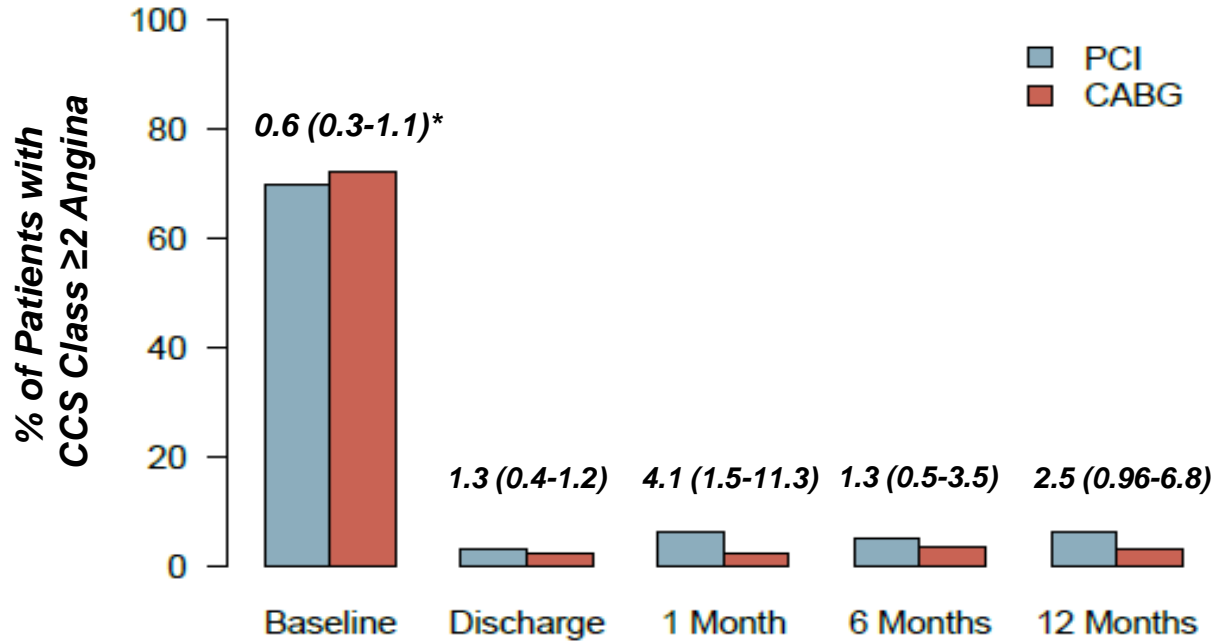
FAME 3 Quality of Life

% of Patients with CCS Class \geq 2 Angina at Each Time Point



FAME 3 Quality of Life

% of Patients with CCS Class \geq 2 Angina at Each Time Point



Conclusion

- FAME 3 has a number of true messages:
 - FFR-guided PCI did not meet the criterion for noninferiority to CABG
 - Outcomes with both FFR-guided PCI and CABG are significantly improved when compared with historical data.
 - In less complex disease, where measuring FFR can actually have an impact, FFR-guided PCI performed very favorably in comparison with CABG. The Functional SYNTAX score identifies patients who benefit most from PCI.
 - Endpoint definition (particularly procedural MI) clearly affects one's interpretation of FAME 3.
 - Quality of life at one year is similar after FFR-guided PCI compared with CABG; overall quality of life during the first year is better after PCI; and significant angina is infrequent and similar in both arms at one year.



What is next for FAME 3?

FAME 3: Three Year Follow-up

Frederik Zimmermann, MD, PhD



The image shows a purple poster for the EuroPCR Late Breaking Trial. At the top right is a small calendar icon. The text on the poster includes the EuroPCR logo, the title 'Late Breaking Trial', the course name 'EuroPCR', a description 'The World-Leading Course in interventional cardiovascular medicine #EuroPCR', the dates '16-19 MAY 2023', the location 'France Palais des congrès, Paris', and logos for PCR and EAPCI (European Society of Cardiology).

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PCR *Late Breaking Trial*

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