
Will FFR-Directed PCI Be Better Than CABG?

Update on the FAME 3 Trial

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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

Grant/ Research Support:

Grant/ Research Support:

Consulting Fees/Honoraria:

Major Stock Shareholder/Equity Interest:

Royalty Income:

Ownership/Founder:

Salary:

Intellectual Property Rights:

Other Financial Benefit:

Company

St. Jude Medical

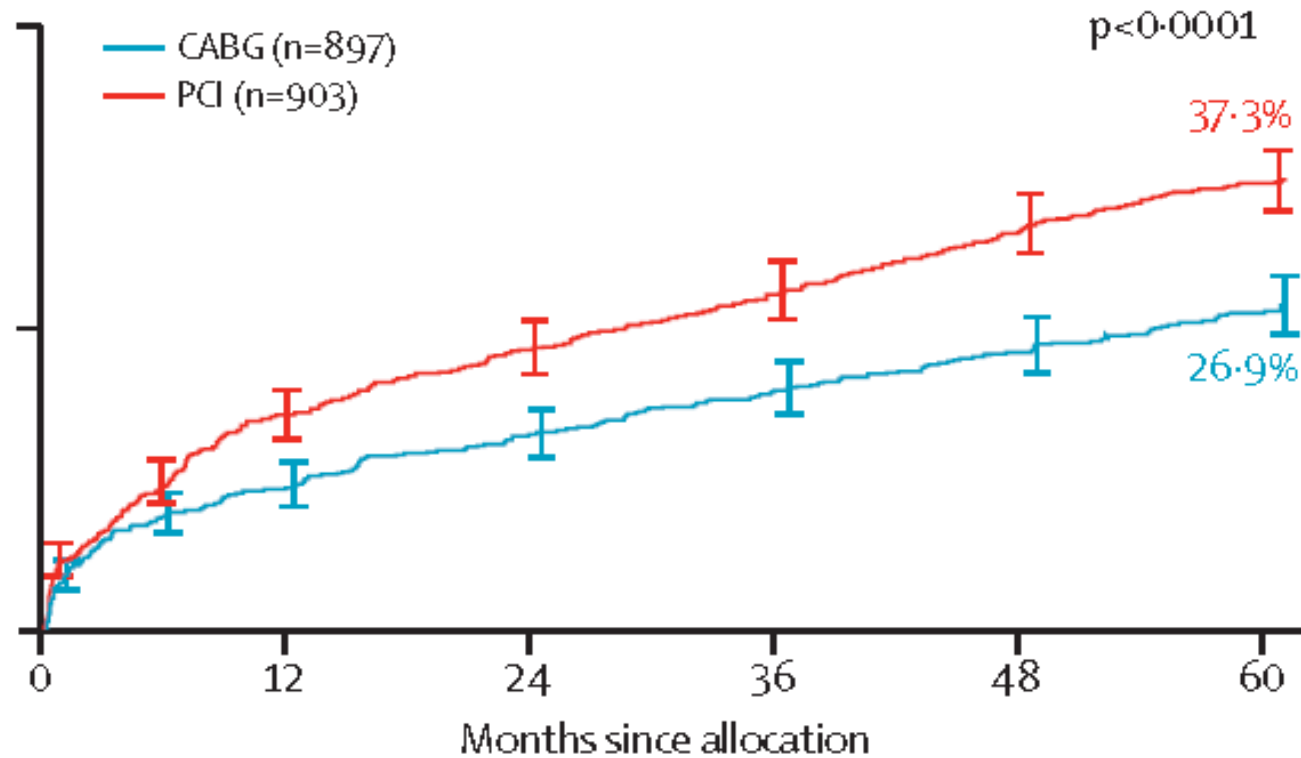
Medtronic

Medtronic, HeartFlow



SYNTAX Trial

5 Year Outcomes: MACCE

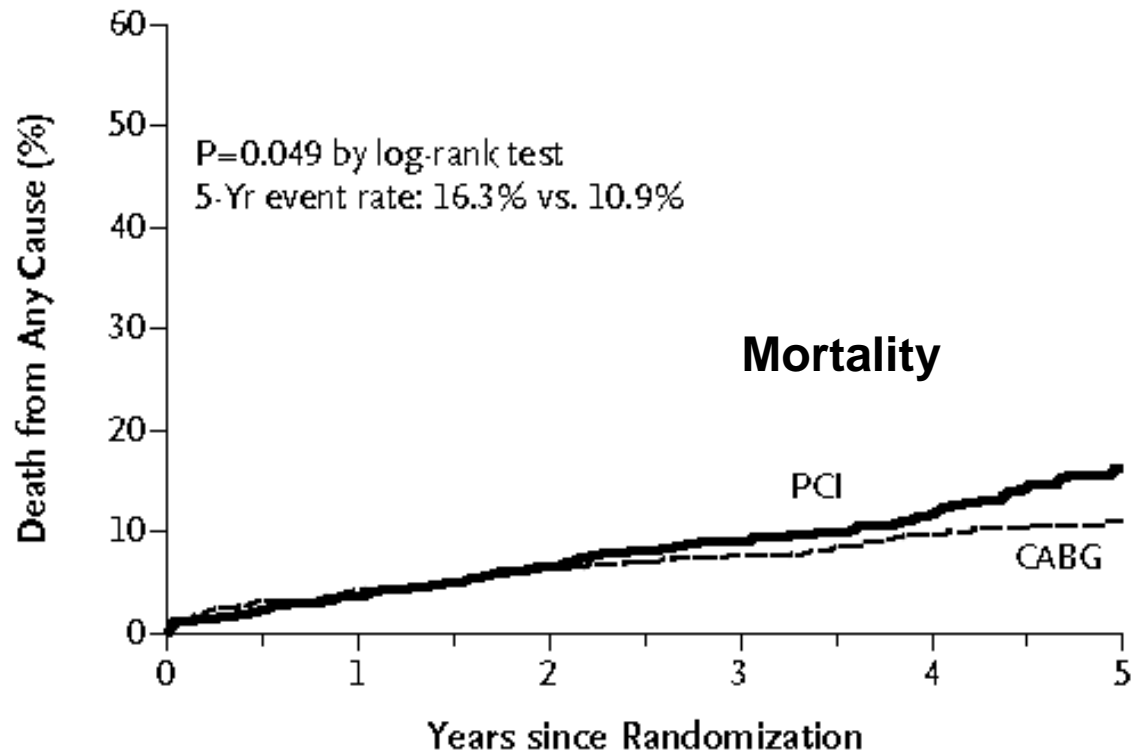


897	751	739	694	654	512
903	747	733	681	634	483



FREEDOM Trial

1900 diabetics with 3 vessel CAD randomized to PCI or CABG



No. at Risk

PCI	953	897	845	685	466	243
CABG	947	855	806	655	449	238



FAME 3 Trial:

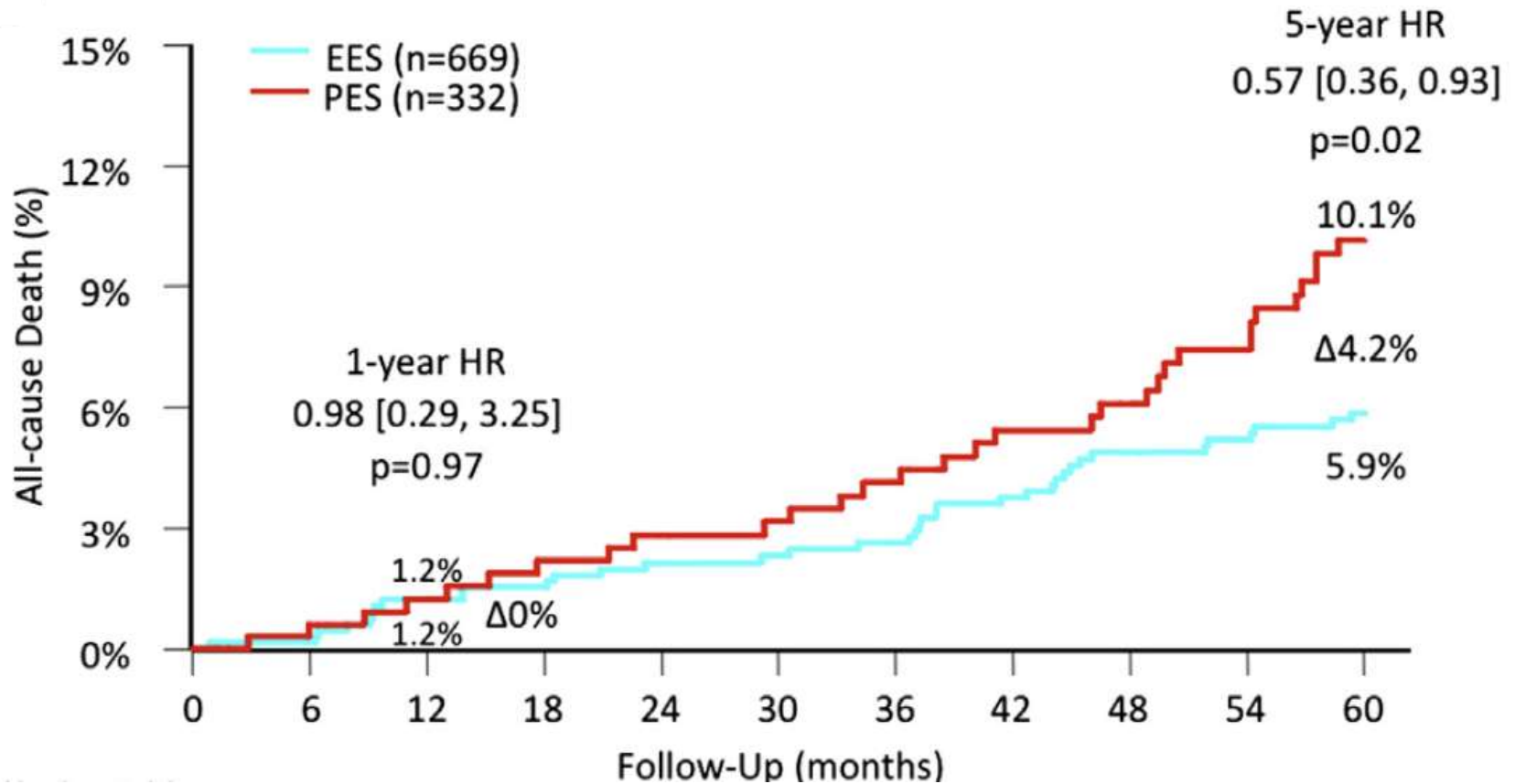
Background

- Why should we expect a different result with FAME 3?
 - 2nd Generation DES outperform 1st Generation.
 - Fractional Flow Reserve-guided PCI outperforms angiography-guided PCI.



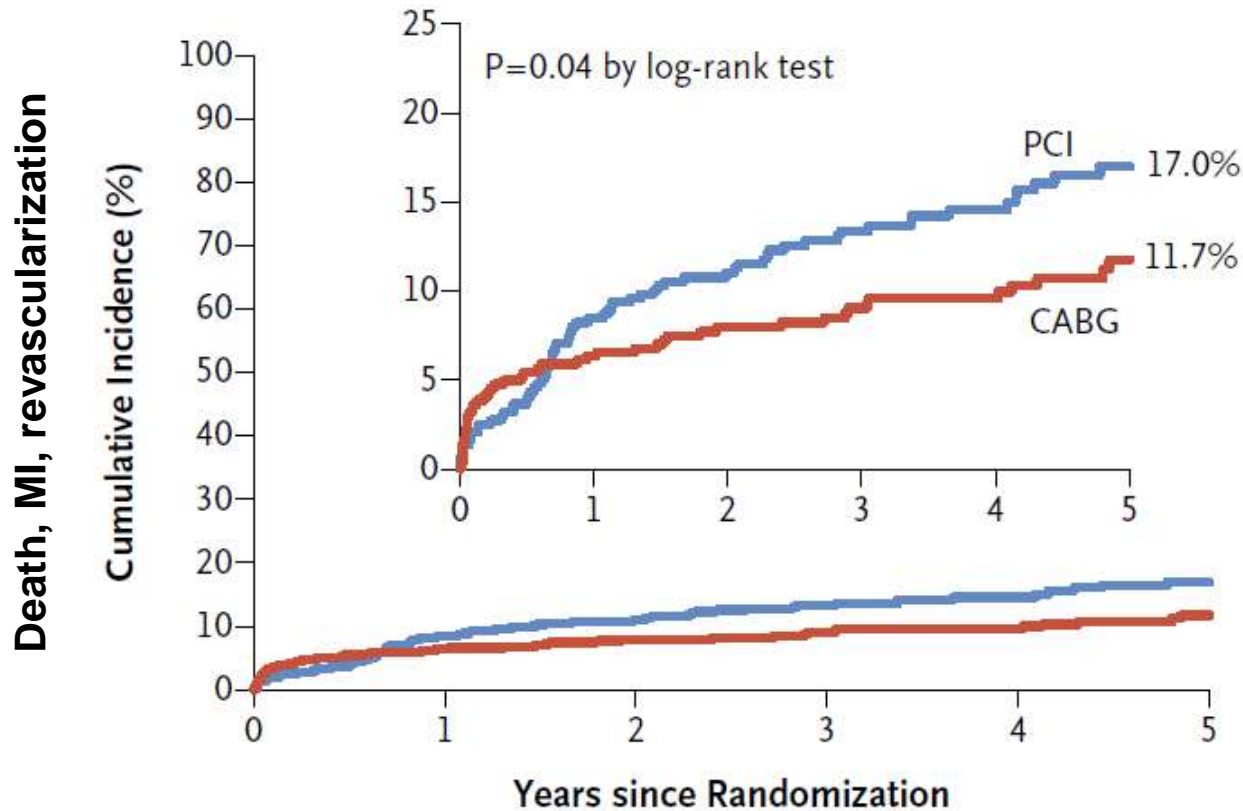
Background:

5 Year Mortality Benefit of 2nd Generation DES (SPIRIT III)



BEST Trial

880 MVD patients randomized to PCI with everolimus-eluting 2nd generation stent or to CABG

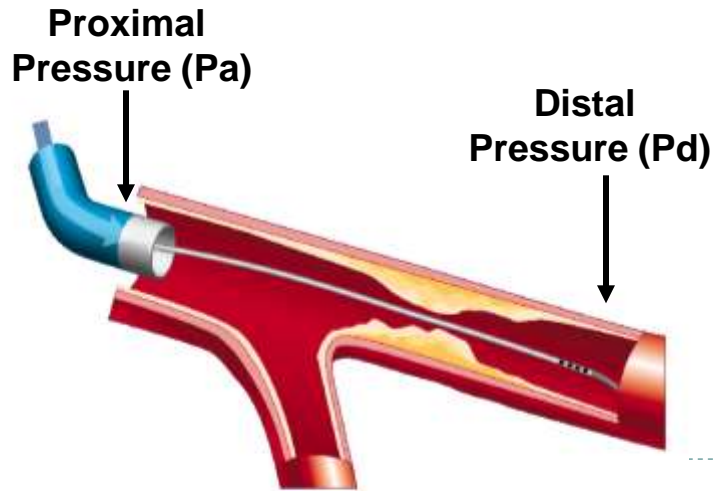


No. at Risk

PCI	438	402	362	305	242	126
CABG	442	415	377	326	262	145

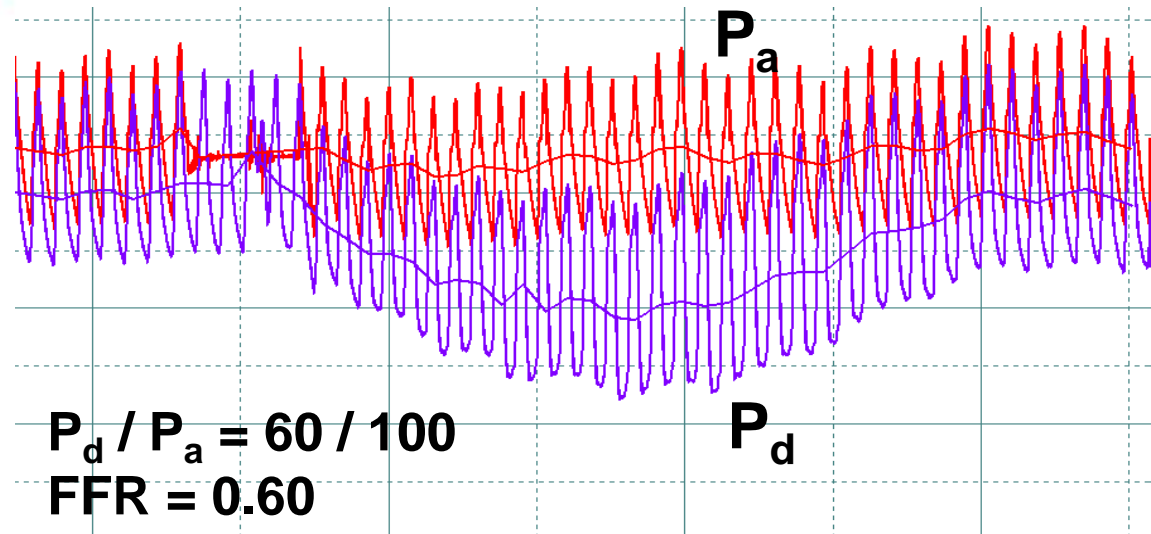


What else has changed?



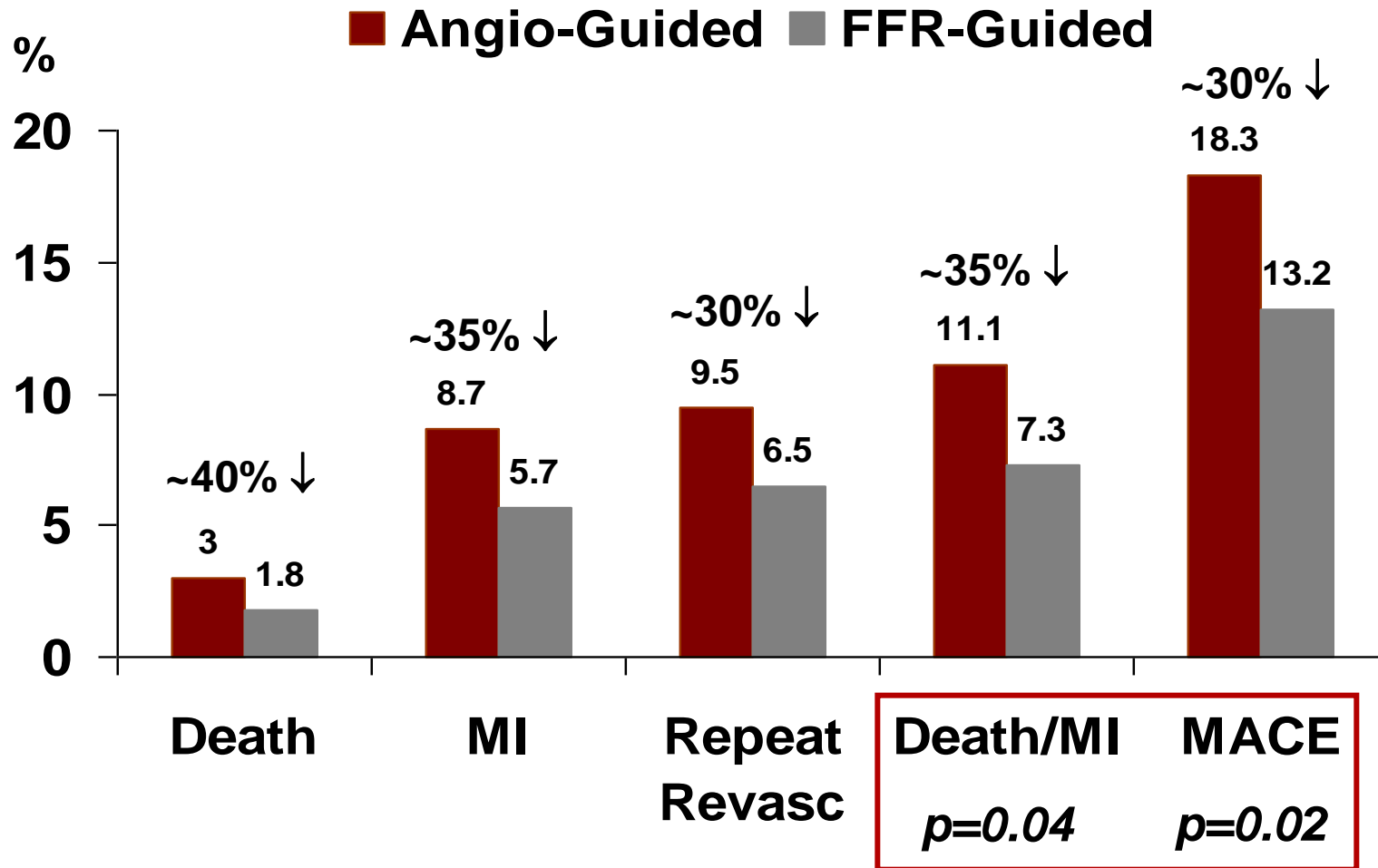
$$FFR = P_d / P_a$$

during maximal flow



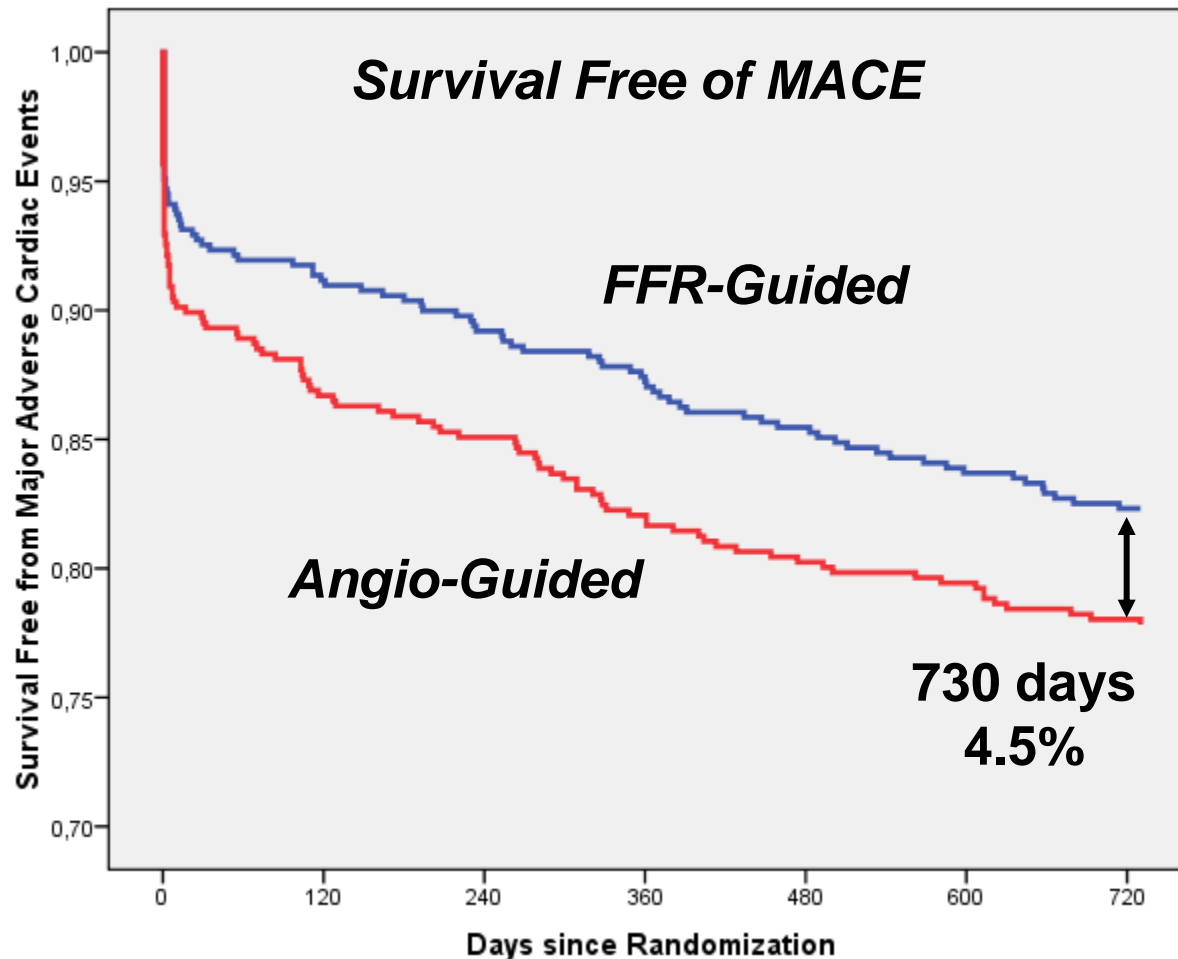
FAME Study: One Year Outcomes

1005 patients with 2-3 vessel CAD randomized to angio or FFR-guided PCI



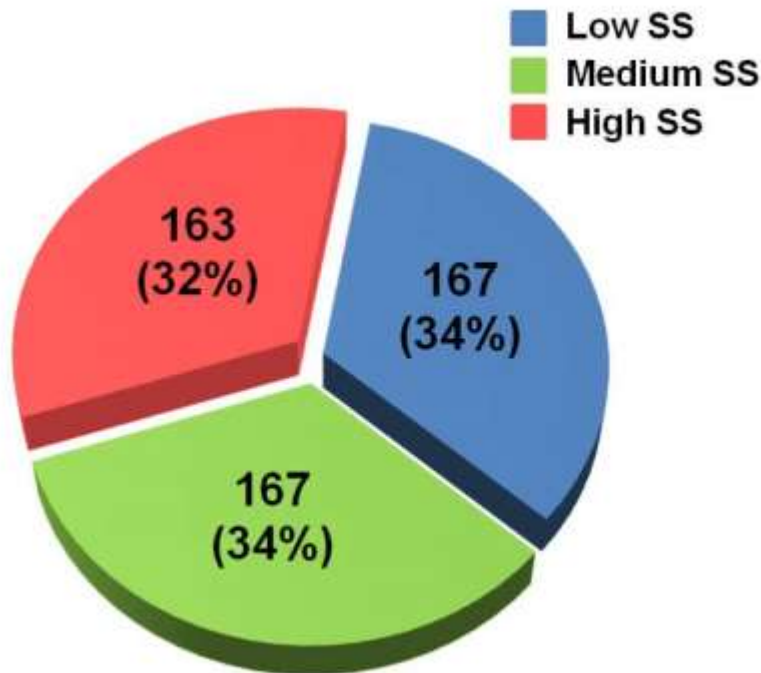
FAME Study: Two Year Outcomes

Death/MI was significantly reduced from 12.9% to 8.4% (p=0.02)

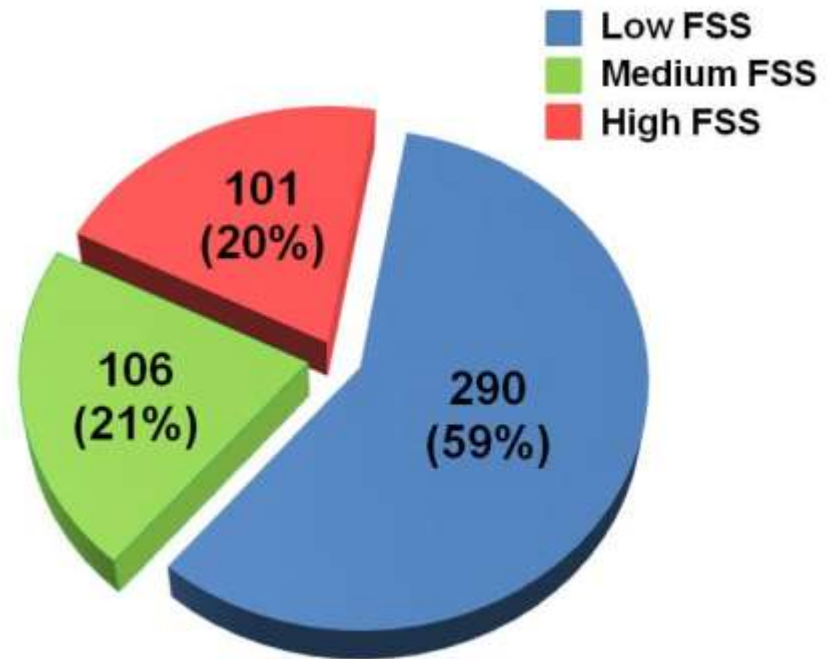


Functional SYNTAX Score

Reclassifies > 30% of cases



Without FFR

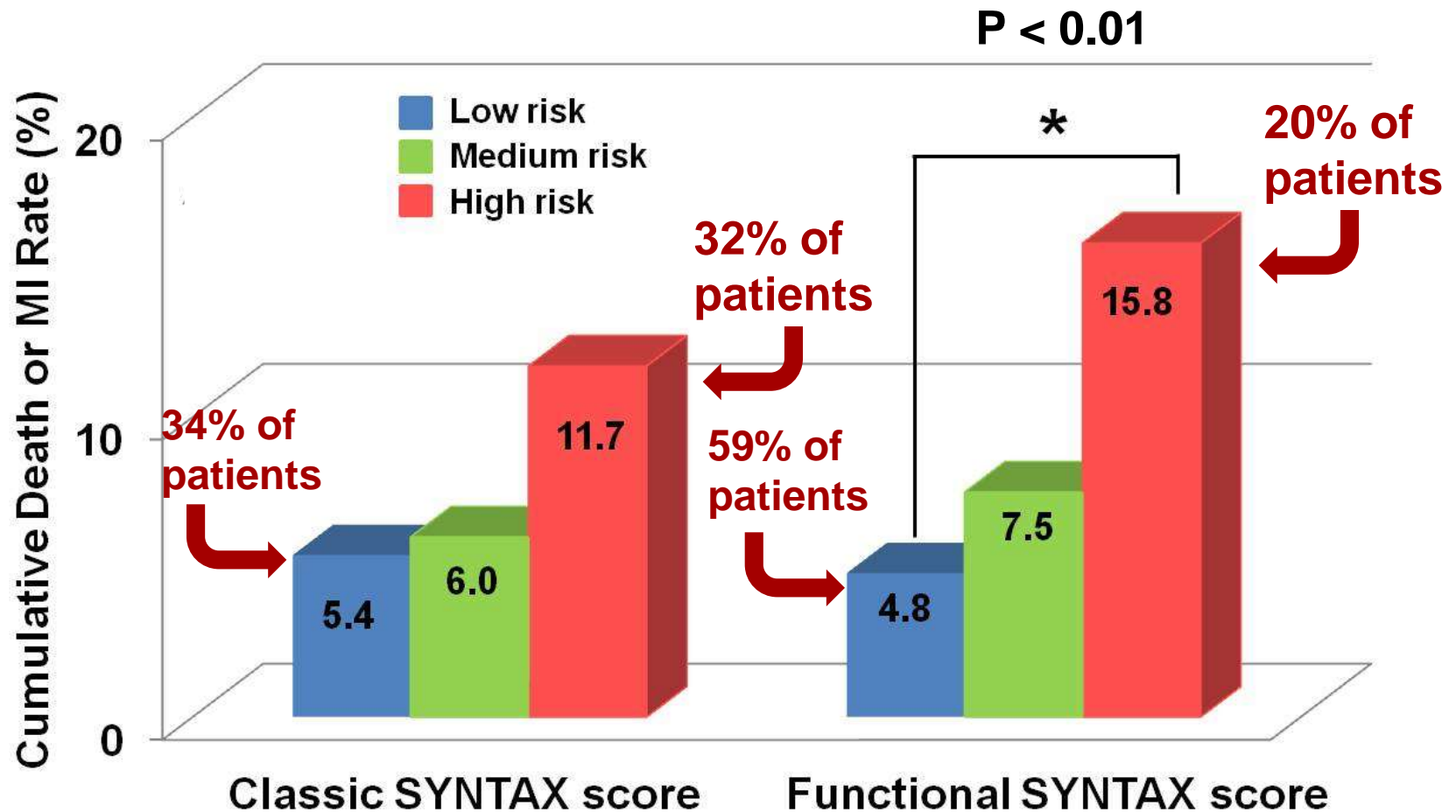


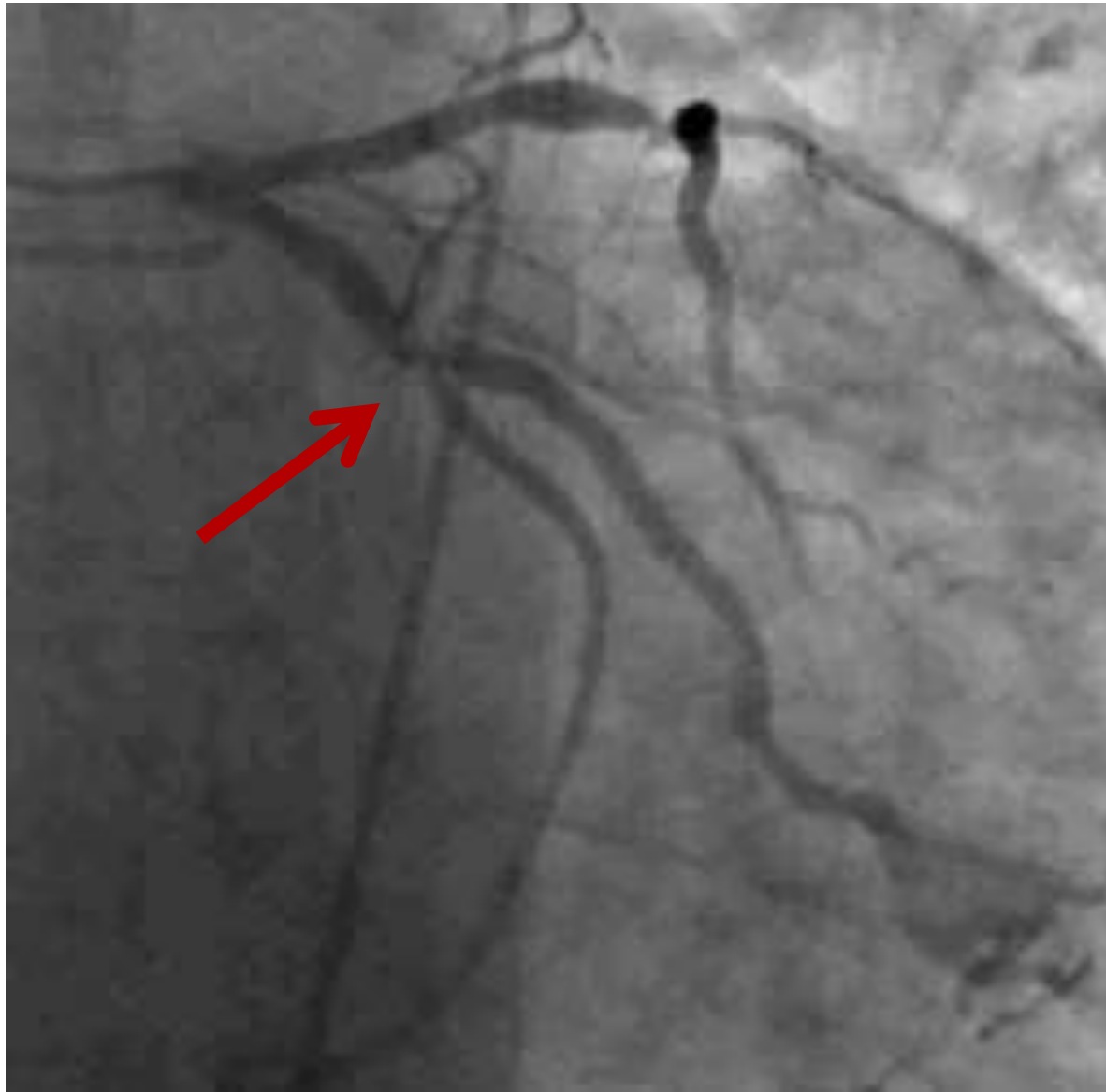
With FFR



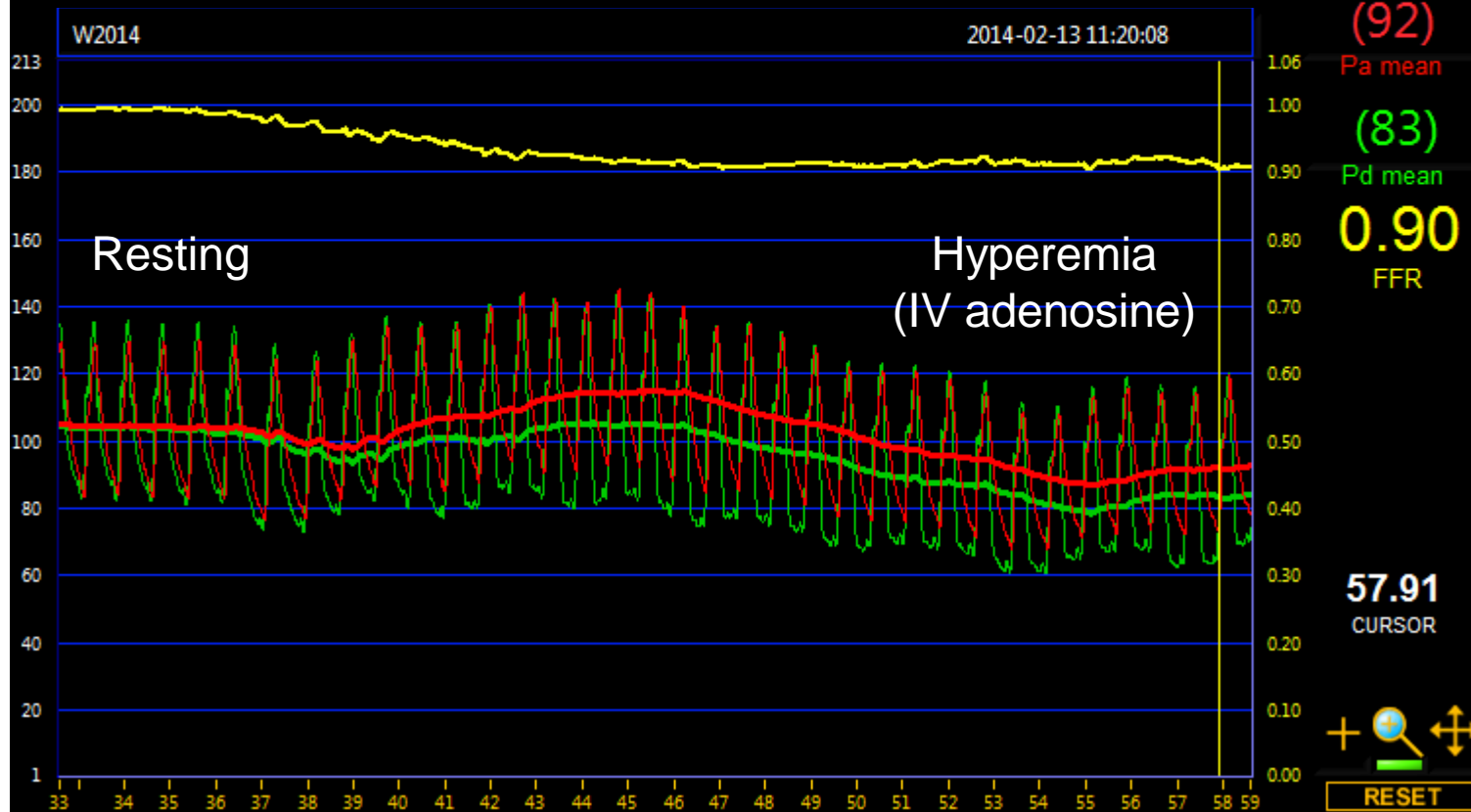
Functional SYNTAX Score

Discriminates Risk for Death/MI





FFR L Cx/OM = 0.90



Angiographic vs. Functional Complete Revascularization

Residual SYNTAX Score (RSS):

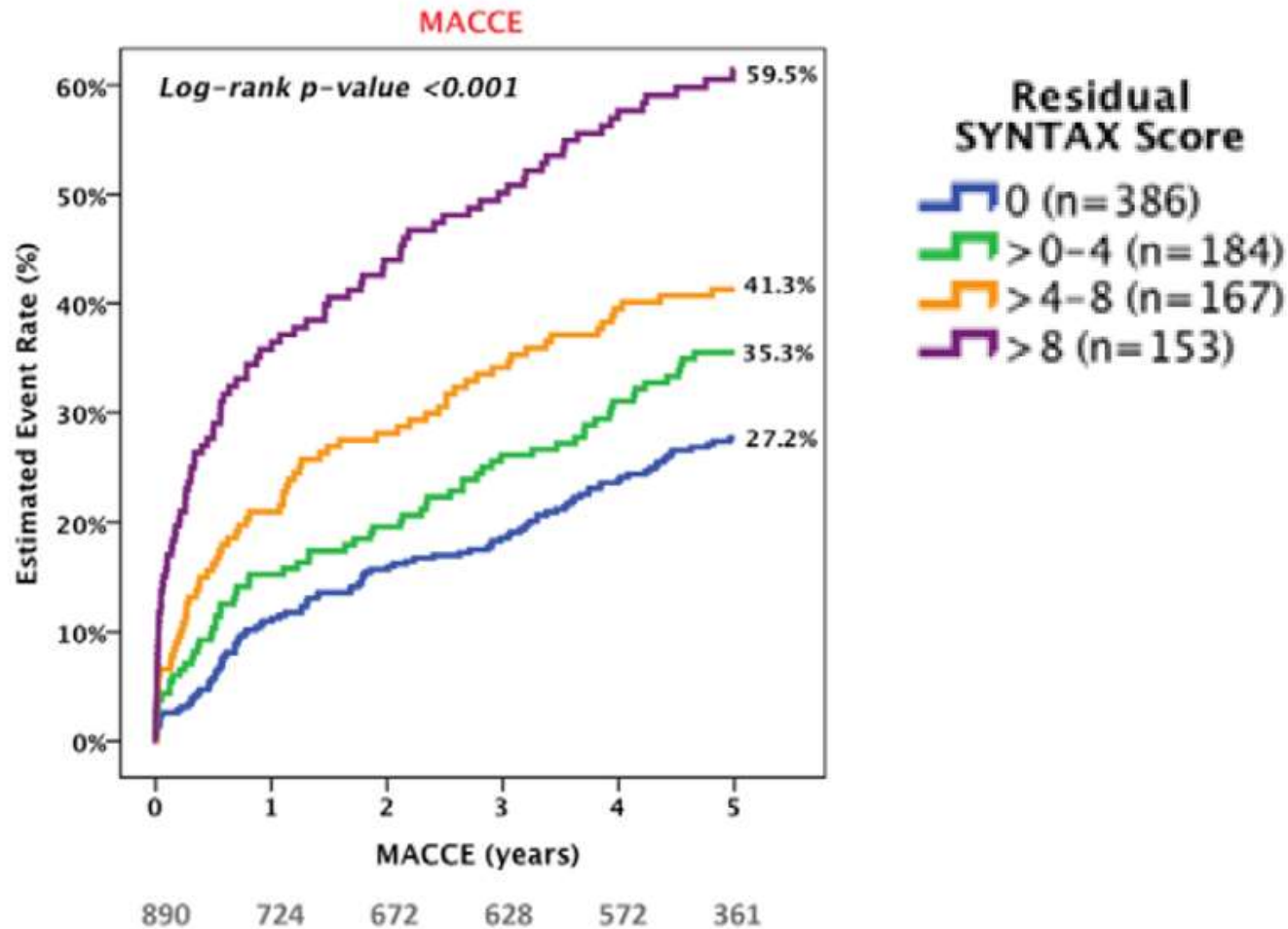
SYNTAX Score after PCI

SYNTAX Revascularization Index (SRI):

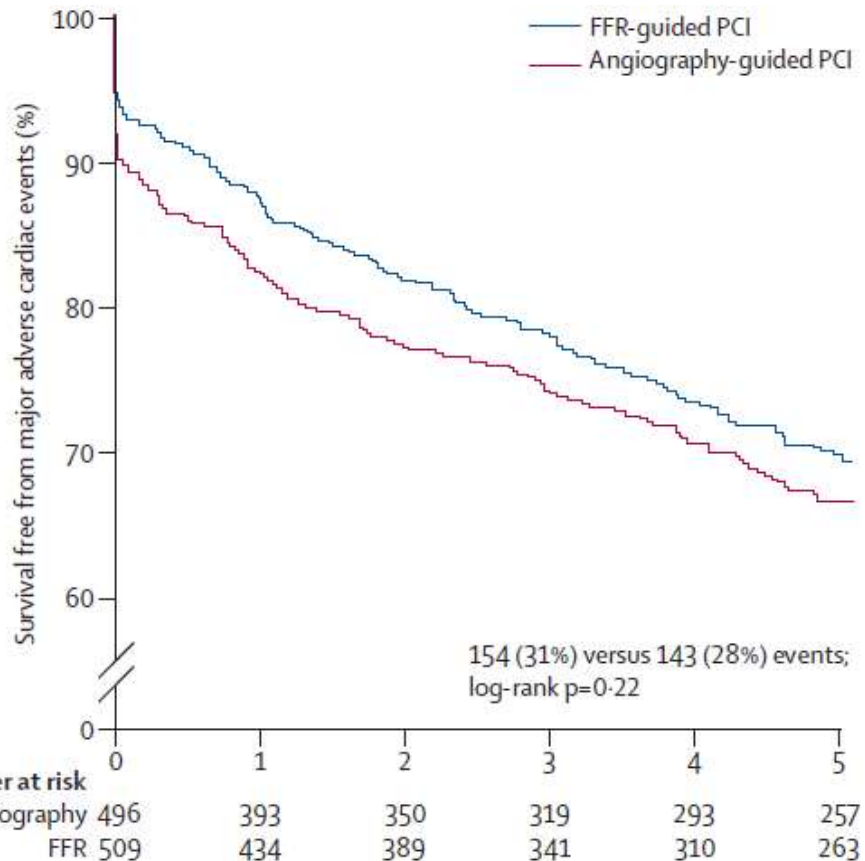
$$100\% * (1 - RSS/SS)$$



Importance of Angiographic Complete Revascularization?



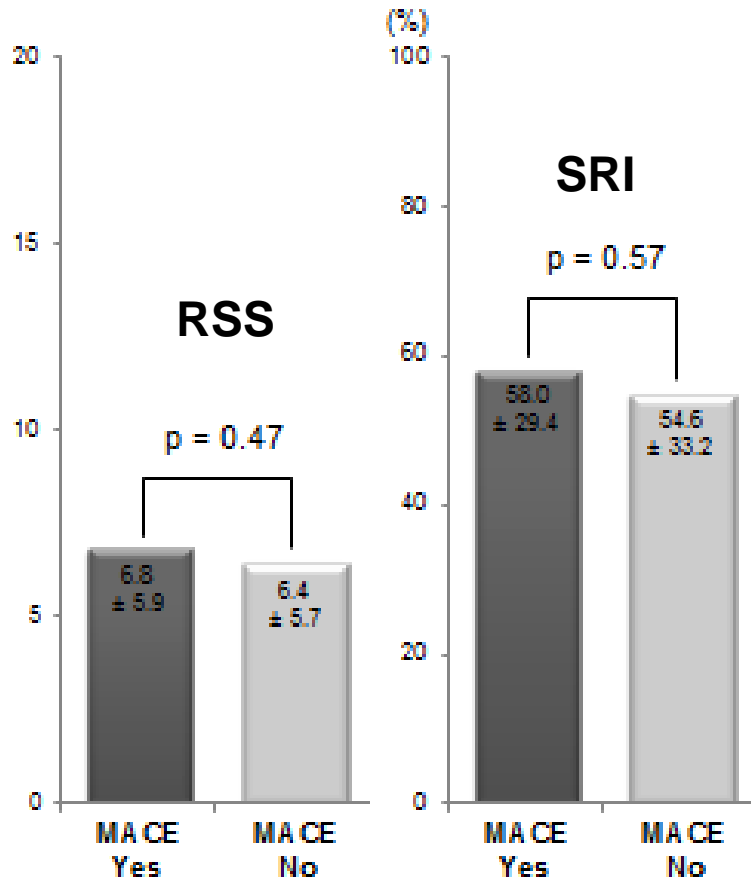
FAME Study: Five Year Outcomes



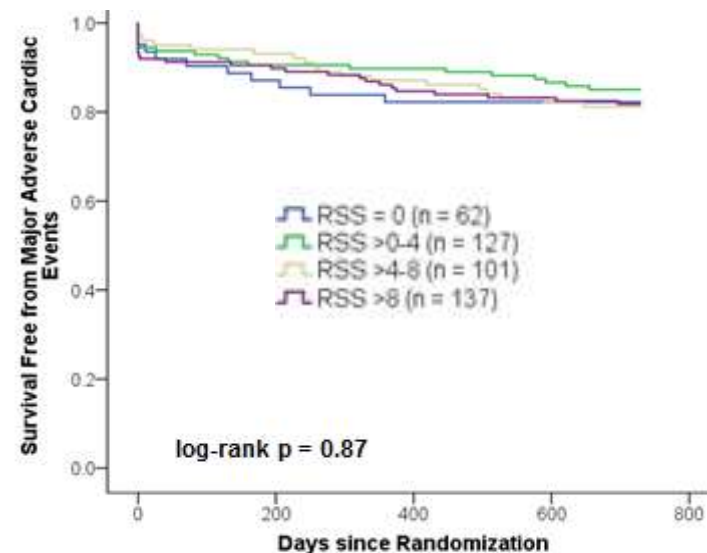
	Angiography-guided PCI (n=496)	Fractional flow reserve-guided PCI (n=509)	Absolute difference*
All-cause mortality			
1-year follow-up	3.0%	1.8%	1.2%
2-year follow-up	3.8%	2.6%	1.2%
5-year follow-up	9.9%	8.6%	1.3%
Cardiac mortality			
1-year follow-up	2.0%	1.4%	0.6%
2-year follow-up	2.4%	1.8%	0.6%
5-year follow-up	5.6%	4.1%	1.5%
Number of events per patient			
1-year follow-up	0.23 (0.53)	0.15 (0.41)	0.08
2-year follow-up	0.29 (0.60)	0.21 (0.48)	0.08
5-year follow-up	0.41 (0.76)	0.35 (0.67)	0.06



Angiographic vs. Functional Complete Revascularization



Comparison of RSS and SRI values in patients with and without MACE at 2 years after FFR-guided PCI in FAME



FAME 3:

Objective

- The primary objective of the FAME 3 Trial is to demonstrate that FFR-guided PCI with the 2nd generation Resolute DES is non-inferior to CABG in patients with multivessel CAD.



FAME 3:

Design

- Multicenter, worldwide, prospective, randomized trial
- Non-inferiority design
- 1500 patients from 50 sites
- Plan for up to 5 year follow-up



Study Flow:

**All Comers with 3 V CAD
(not involving LM)**



**Heart team identifies lesions for PCI/CABG
and then patient is randomized**

**FFR-Guided PCI with Resolute DES
Stent all lesions with $FFR \leq 0.80$
(n=750)**

**Perform CABG based on
coronary angiogram
(n=750)**

**Primary: One Year follow-up for Death, MI, CVA, Revascularization
Key Secondary: Three Year follow-up for Death/MI/CVA**

Non-inferior Design



FAME 3:

Inclusion Criteria

- Age \geq 21 years
- Three vessel CAD, defined as \geq 50% diameter stenosis by visual estimation in each of the three major epicardial vessels, but not involving left main coronary artery, and amenable to revascularization by both PCI and CABG as determined by the Heart Team
- Willing and able to provide informed, written consent



FAME 3:

Key Exclusion Criteria

- Requirement for other cardiac or non-cardiac surgical procedure (e.g., valve replacement)
- Previous CABG
- Left main disease requiring revascularization
- Cardiogenic shock and/or need for mechanical/pharmacologic hemodynamic support
- Recent STEMI (<5 days)
- Ongoing Non STEMI with biomarkers (e.g., cardiac troponin) still rising
- Known left ventricular ejection fraction <30%



FAME 3:

Major Endpoints

- Primary Endpoint:
 - One year rate of Death, MI, Stroke and Revascularization
- Key Secondary Endpoint:
 - Three year rate of Death, MI and Stroke



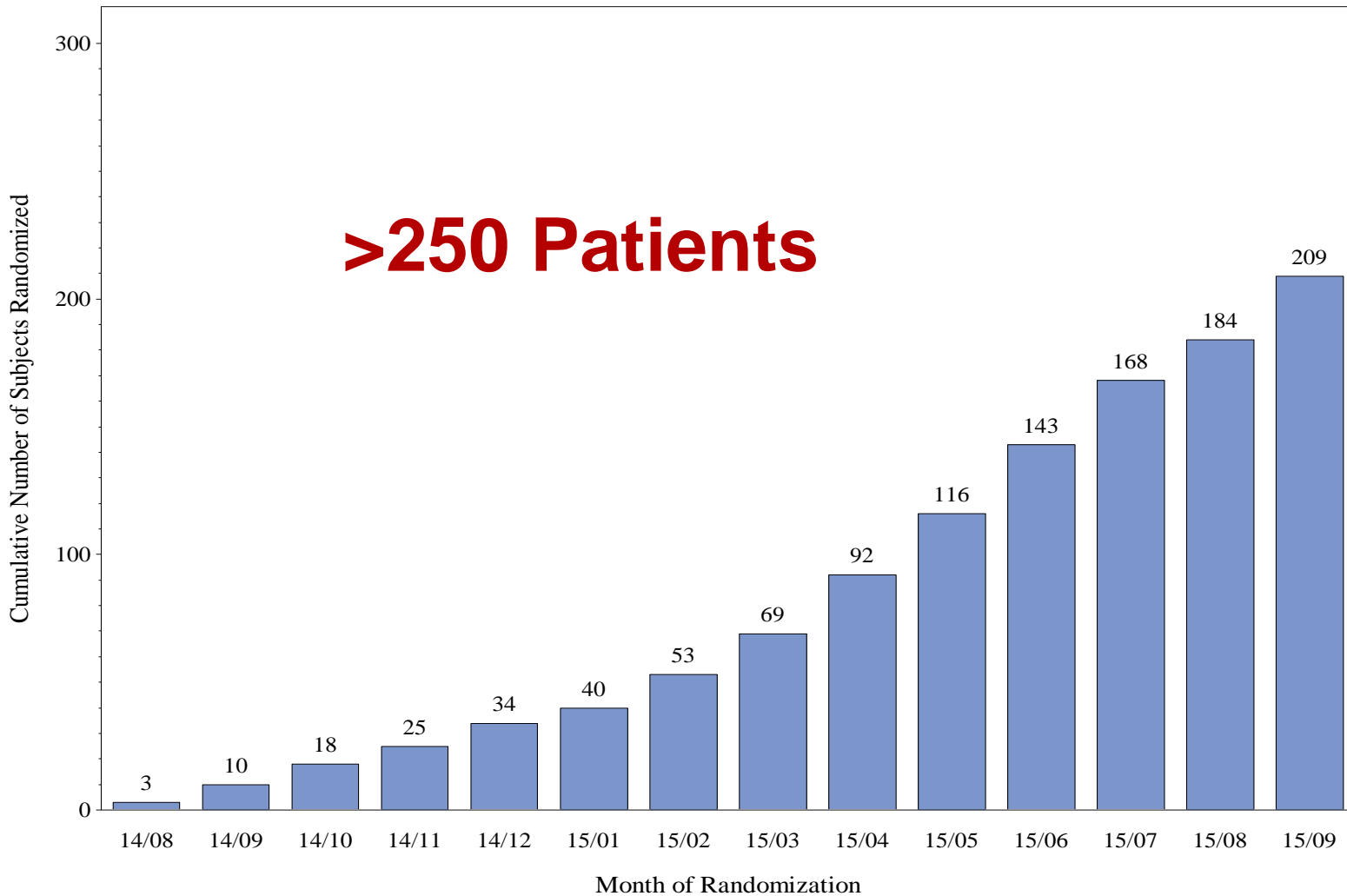
FAME 3

Study Organization

- Investigator-initiated trial
- Coordinated by Stanford with support of a CRO
- Funded by research grants from Medtronic and St. Jude Medical
- Independent DSMB and CEC



FAME 3 Enrollment Update:



Conclusion:

- By incorporating FFR-guided PCI and utilizing the 2nd generation Resolute Integrity stent, FAME 3 aims to demonstrate that FFR-guided PCI is non-inferior to CABG in patients with 3-vessel coronary disease not involving the left main coronary artery.

