FAME 3 Trial:
Background, Design and Update

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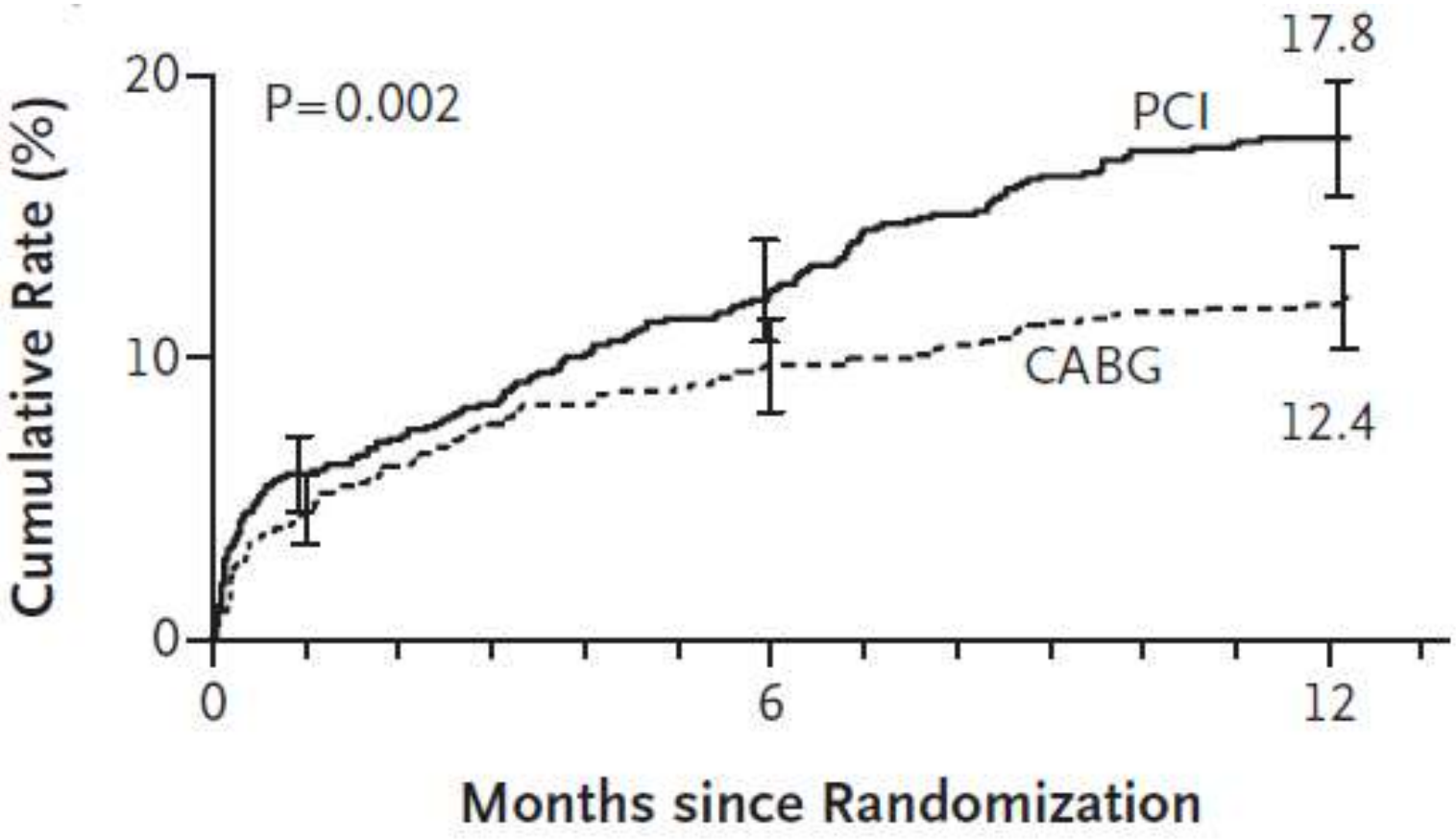
Disclosure Statement of Financial Interest

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	Company
Grant/ Research Support:	St. Jude Medical/Medtronic
Grant/ Research Support:	NIH-R01 HL093475 (PI)
Consulting Fees/Honoraria:	Medtronic
Major Stock Shareholder/Equity Interest:	
Royalty Income:	
Ownership/Founder:	
Salary:	NIH-R01 HL093475 (PI)
Intellectual Property Rights:	
Other Financial Benefit (minor stock options):	HeartFlow

SYNTAX

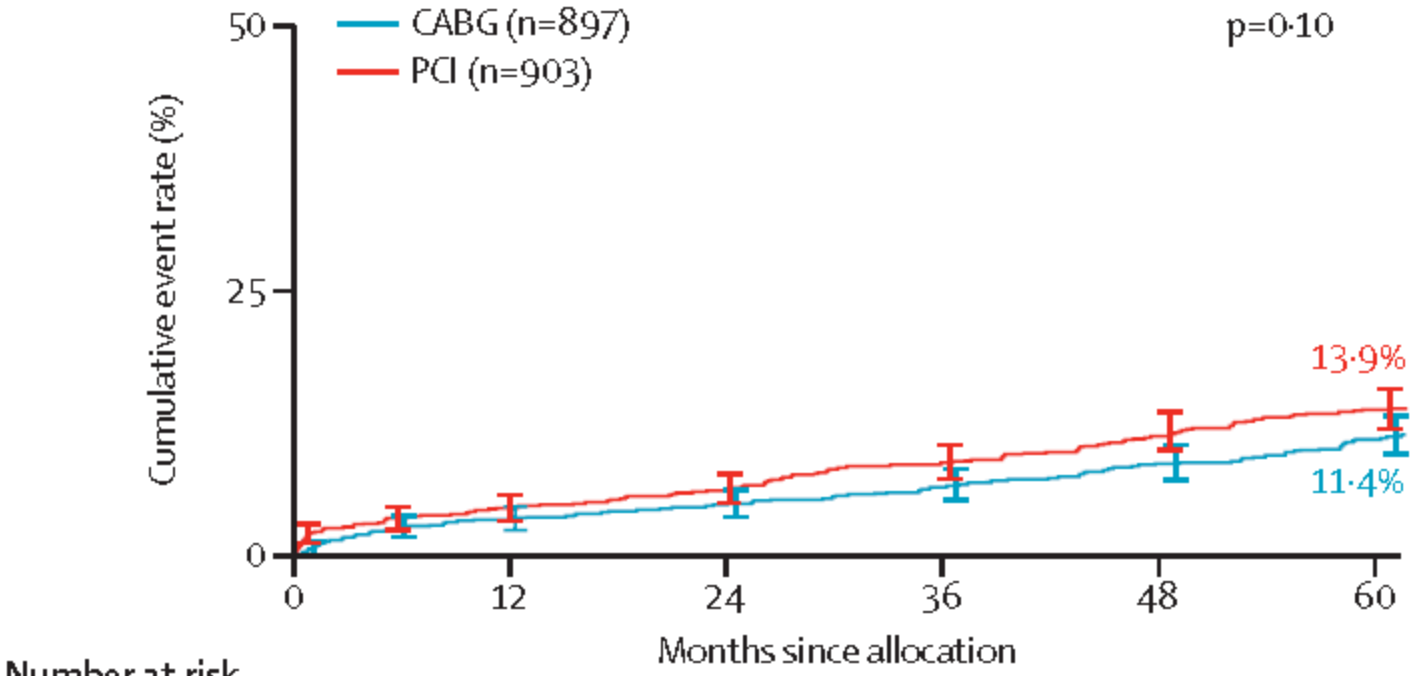
MACCE at 12 months



Serruys, et al. N Engl J Med 2009;360:961-72

SYNTAX

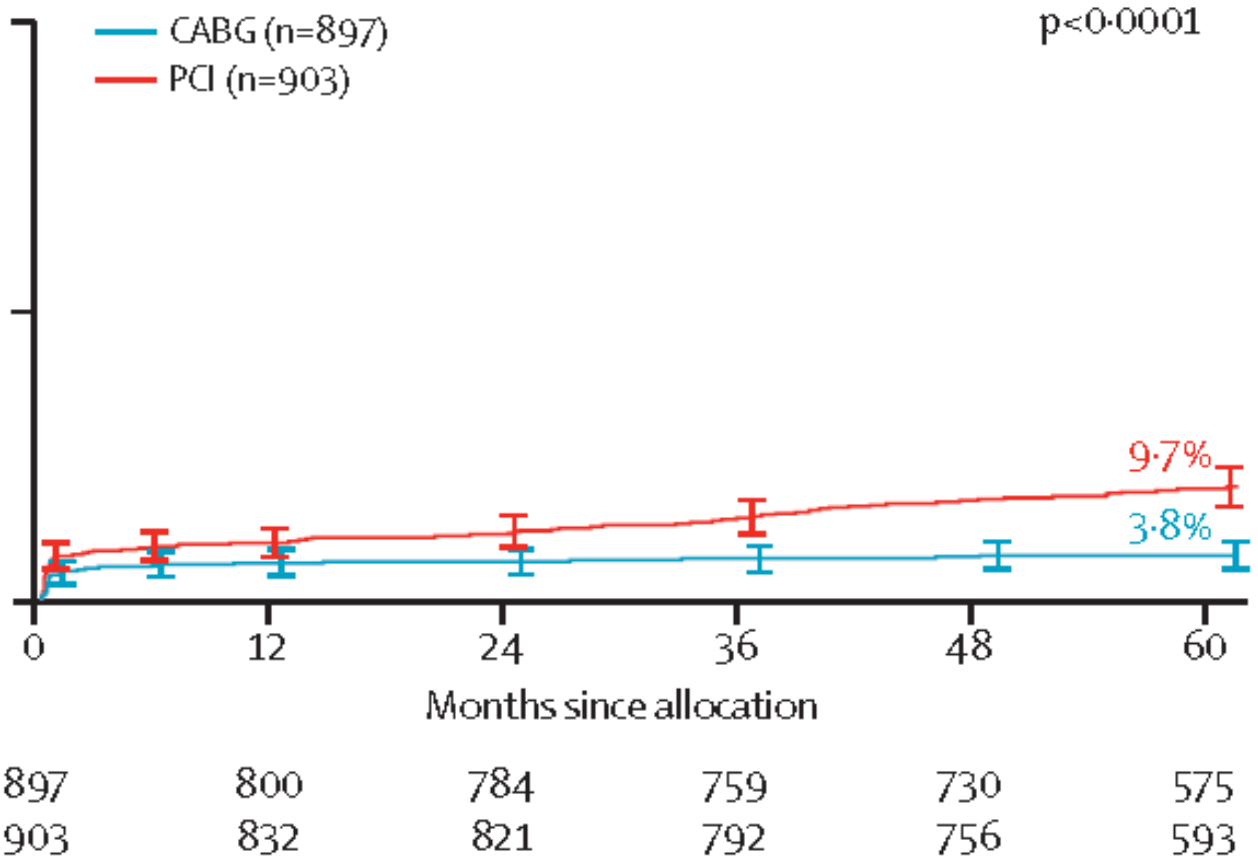
5 Year Outcomes: All Cause Mortality



Mohr, et al. Lancet 2013;381:629-38

SYNTAX

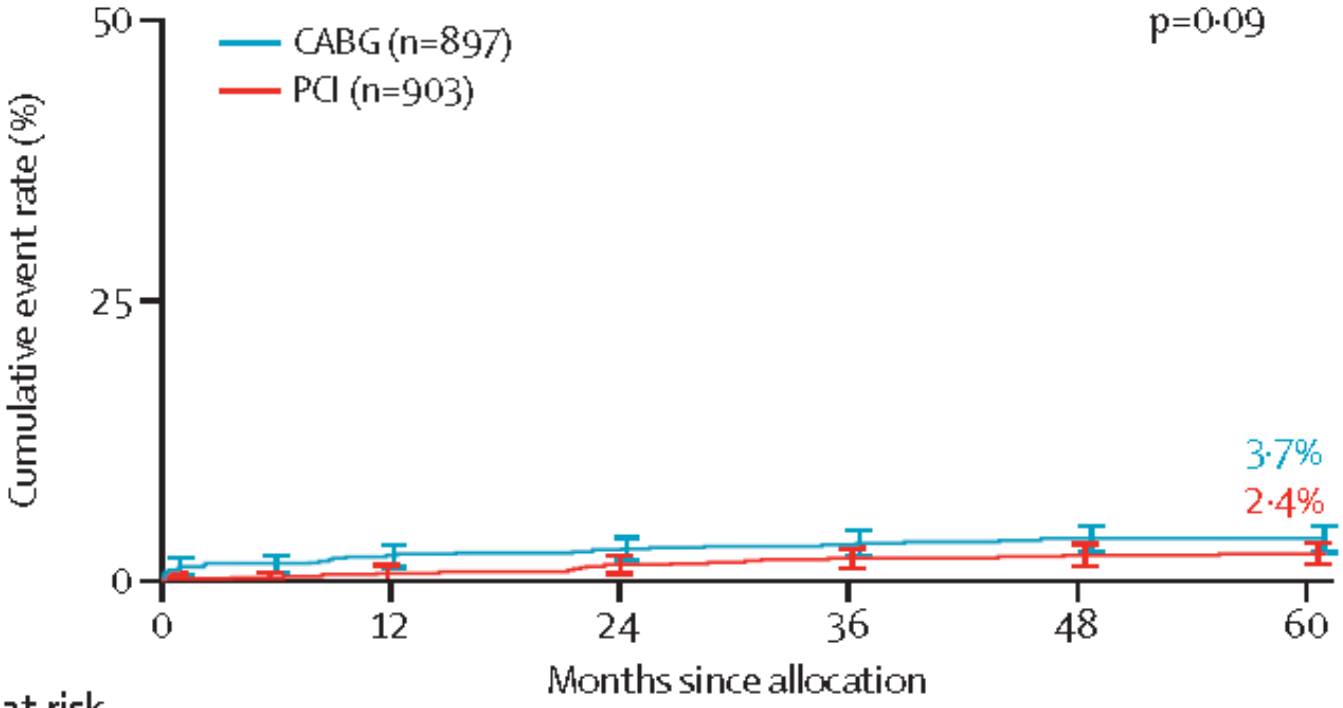
5 Year Outcomes: Myocardial Infarction



Mohr, et al. Lancet 2013;381:629-38

SYNTAX

5 Year Outcomes: Stroke



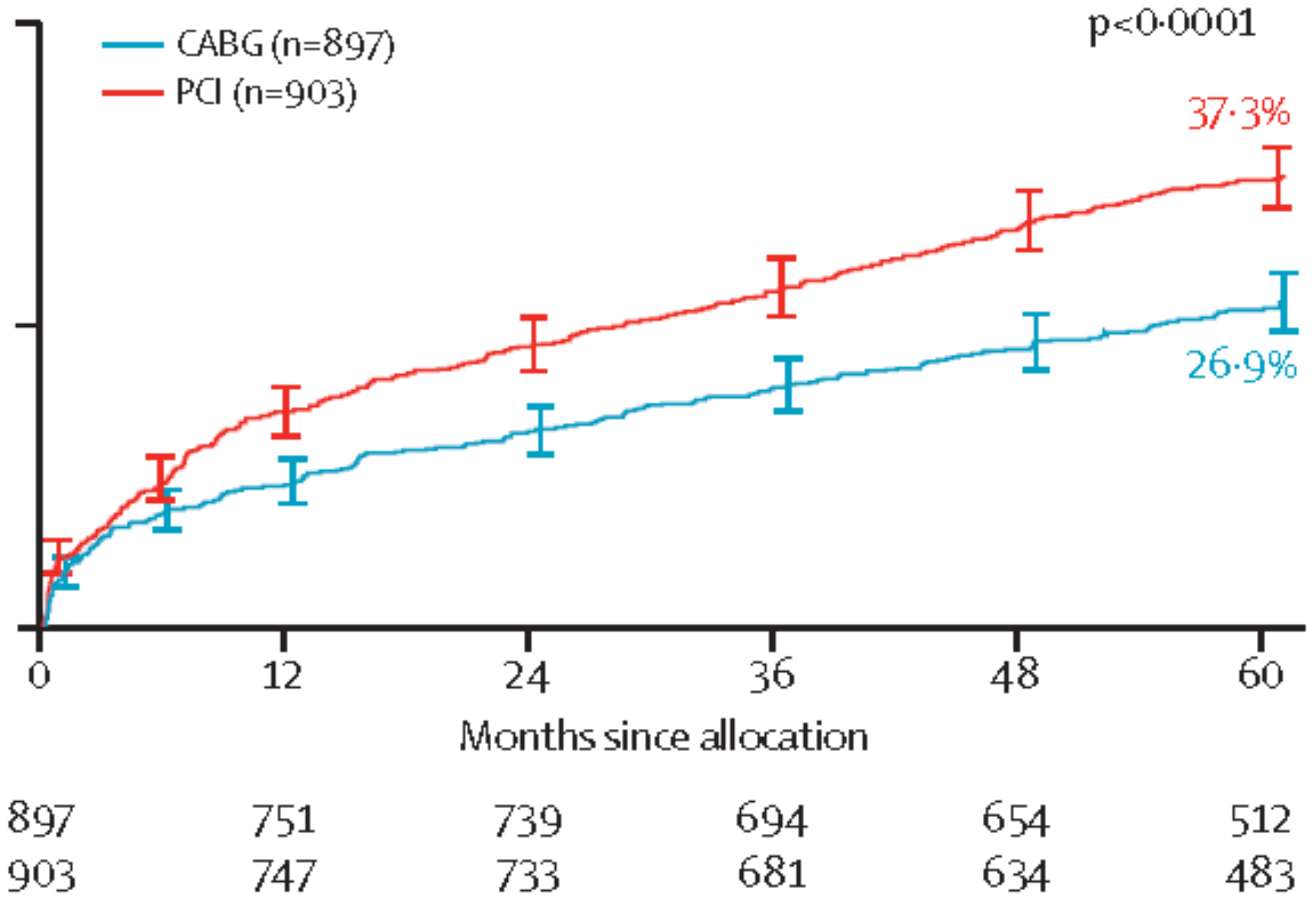
Number at risk

CABG	897	806	790	763	732	579
PCI	903	854	842	815	782	622

Mohr, et al. Lancet 2013;381:629-38

SYNTAX

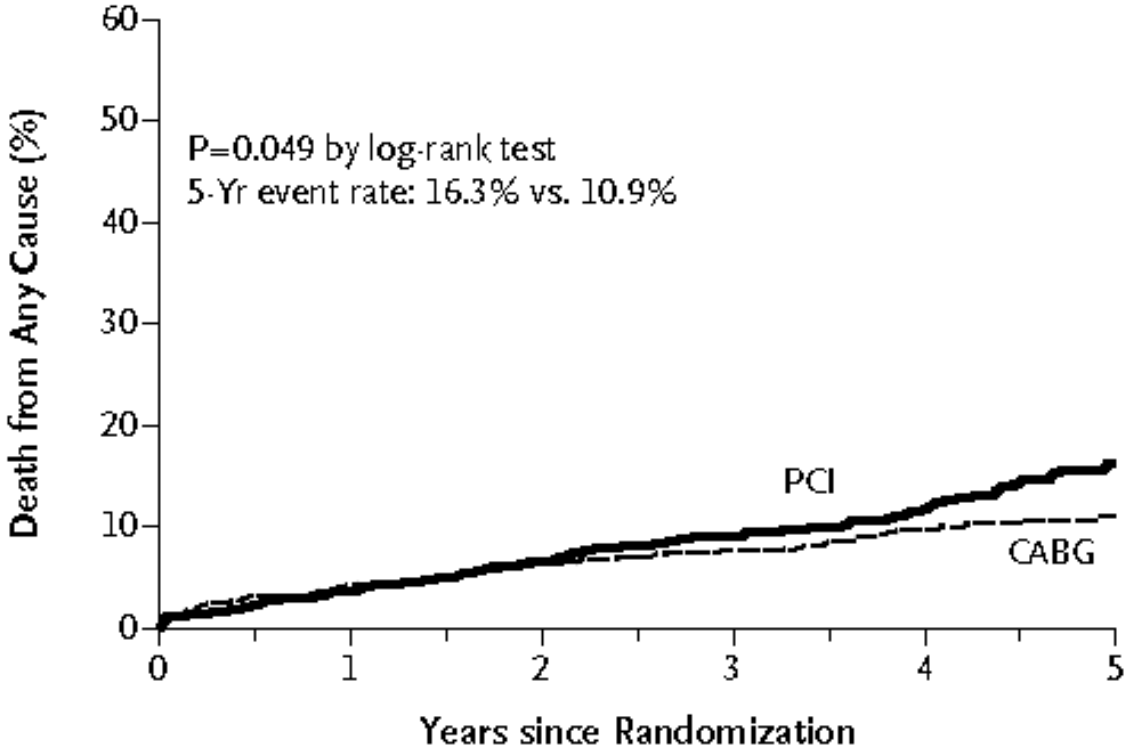
5 Year Outcomes: MACCE



Mohr, et al. Lancet 2013;381:629-38

FREEDOM Trial

Mortality



No. at Risk						
PCI	953	897	845	685	466	243
CABG	947	855	806	655	449	238

Farkouh, et al. N Engl J Med 2012;367:2375-84

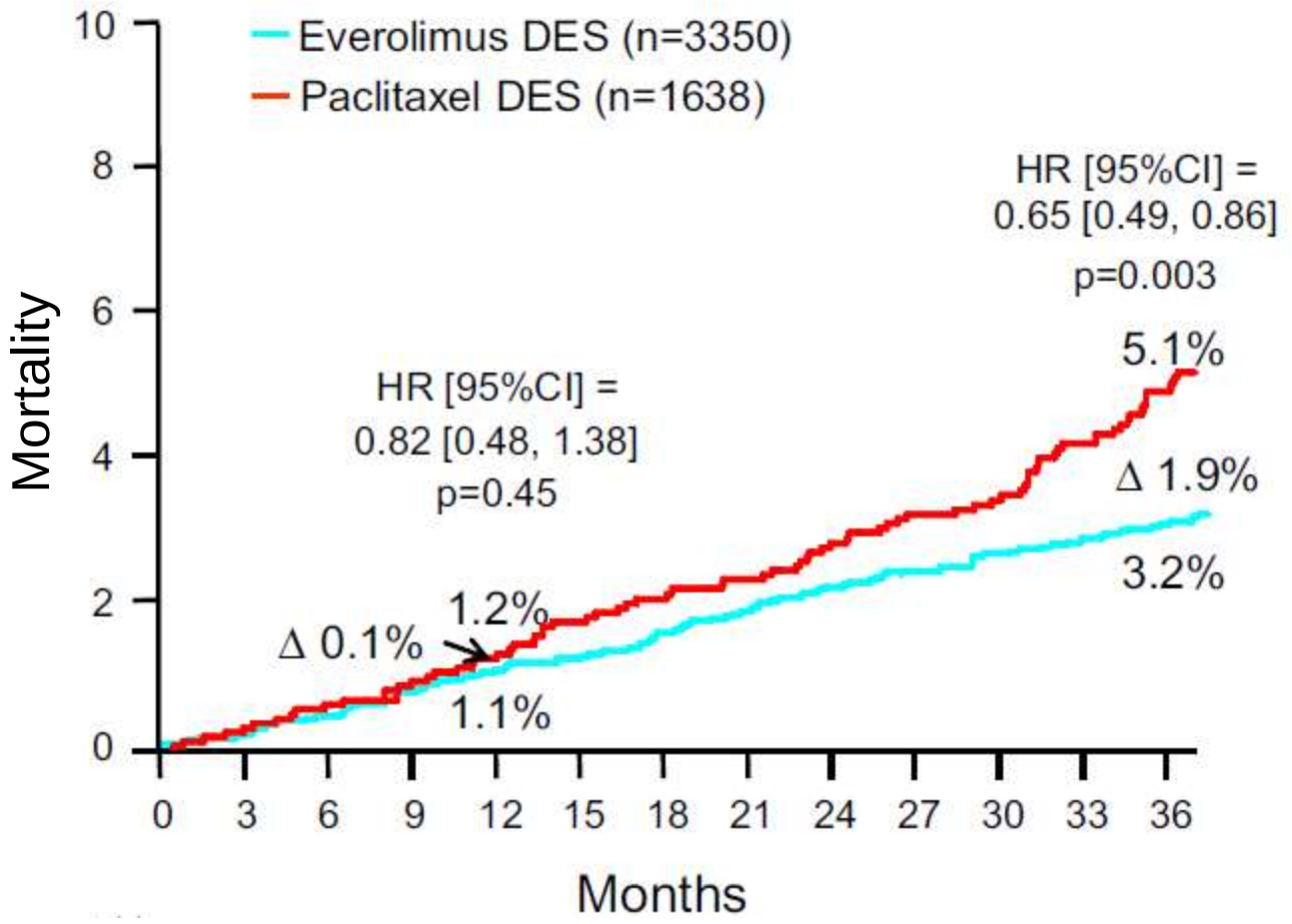
FAME 3:

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:

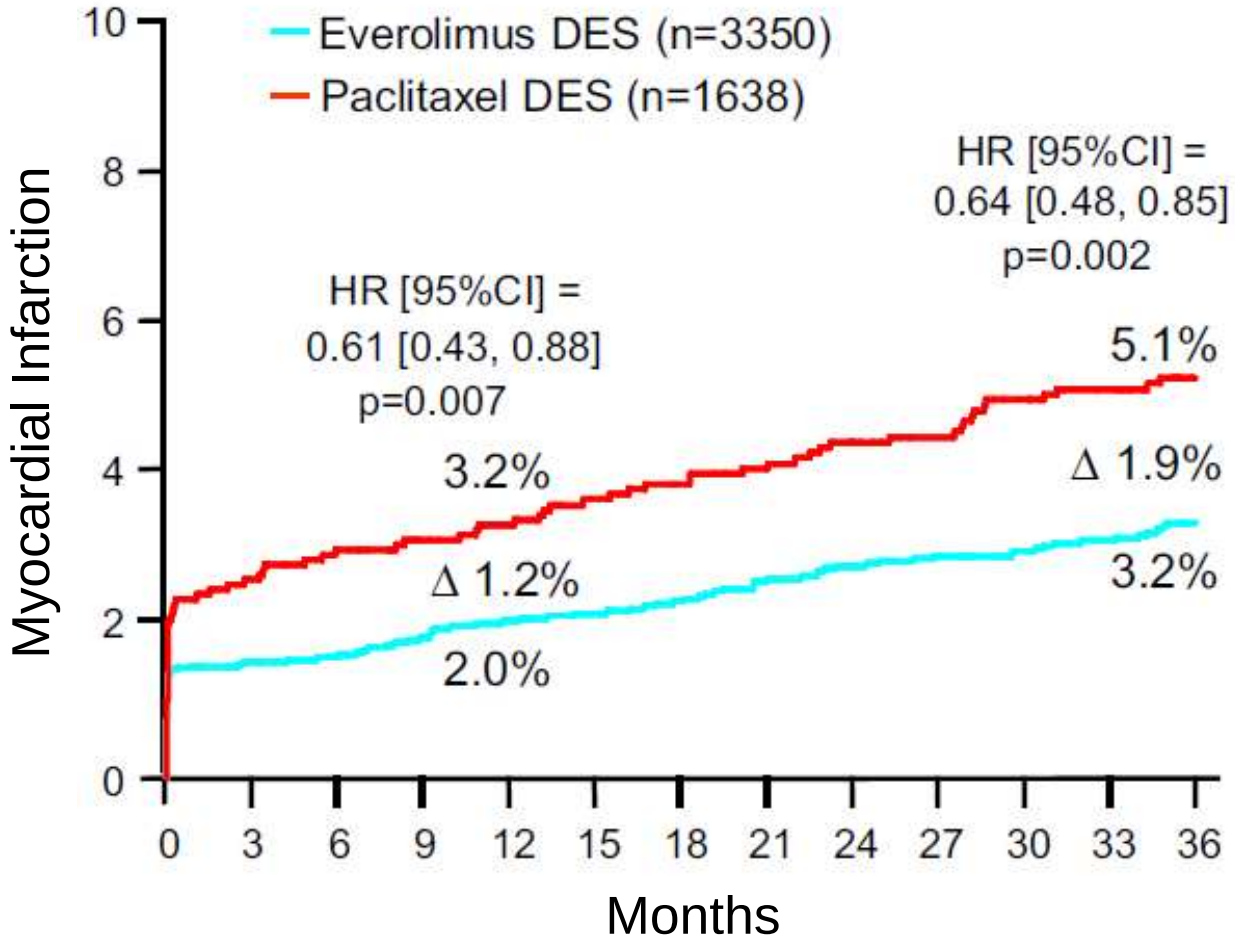
3 Year Mortality Benefit of 2nd Generation DES (SPIRIT II,III,IV)



Dangas, et al. J Am Coll Cardiol Intv 2013;6:914-22.

Background:

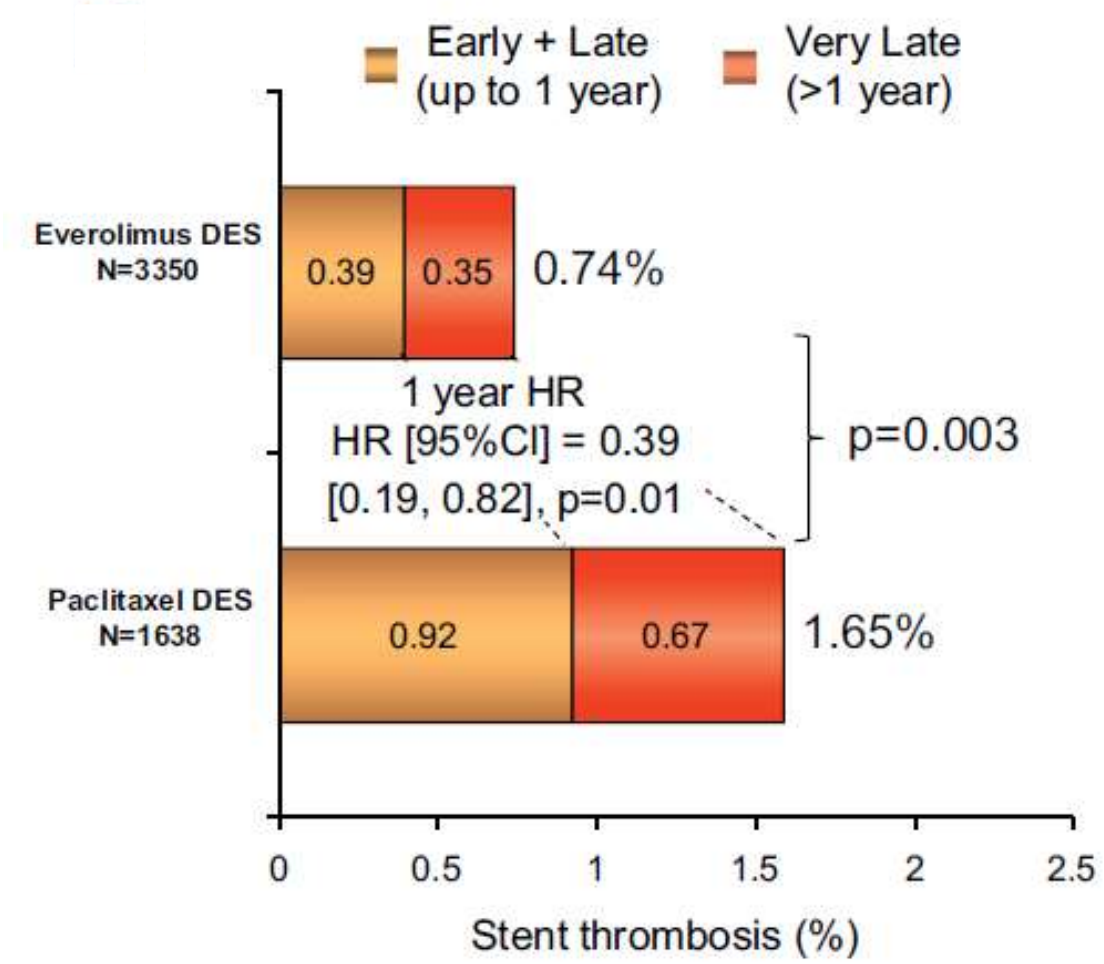
3 Year MI Benefit of 2nd Generation DES



Dangas, et al. J Am Coll Cardiol Intv 2013;6:914-22.

Background:

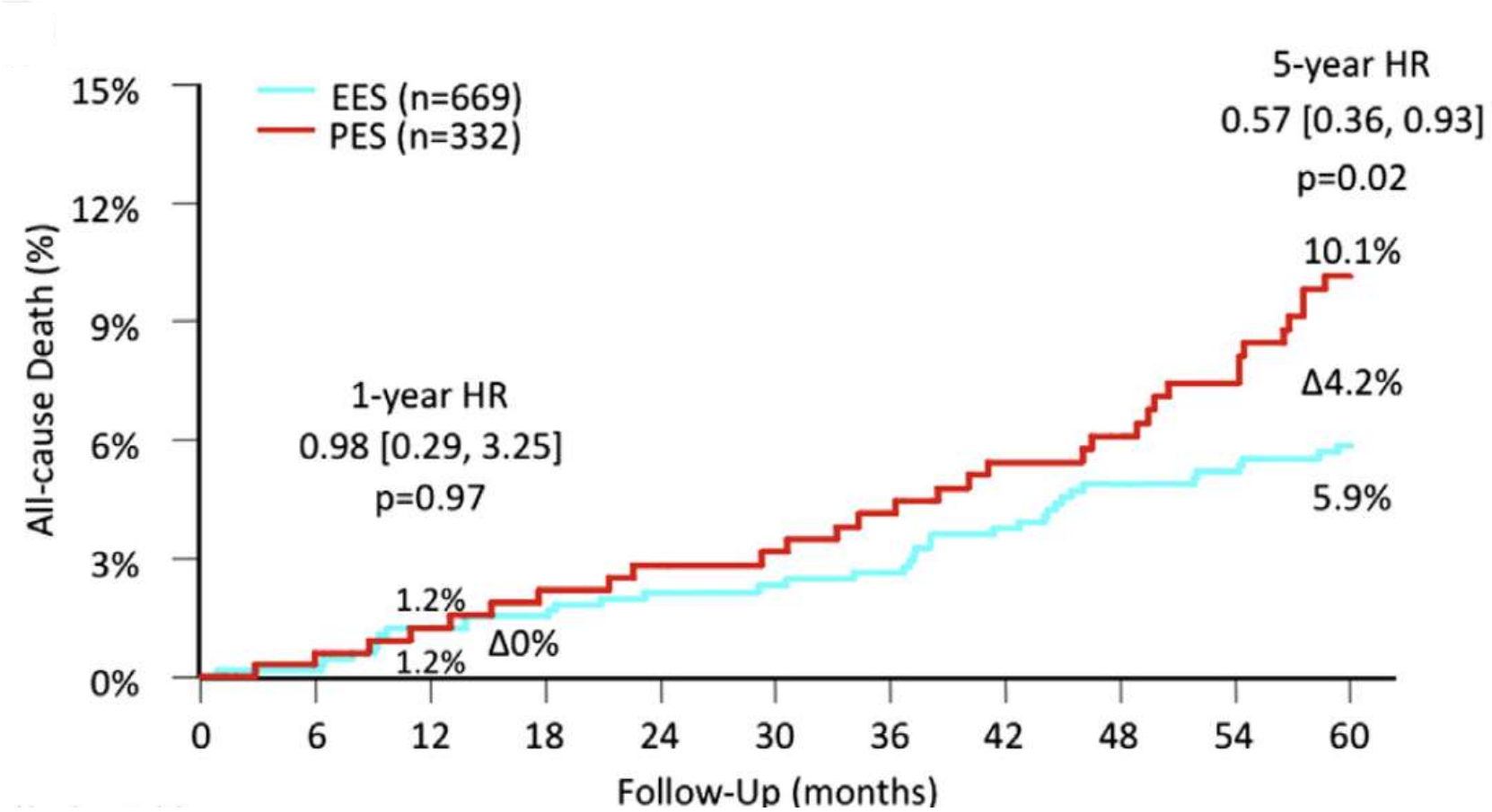
3 Year Stent Thrombosis Benefit of 2nd Generation DES



Dangas, et al. J Am Coll Cardiol Intv 2013;6:914-22.

Background:

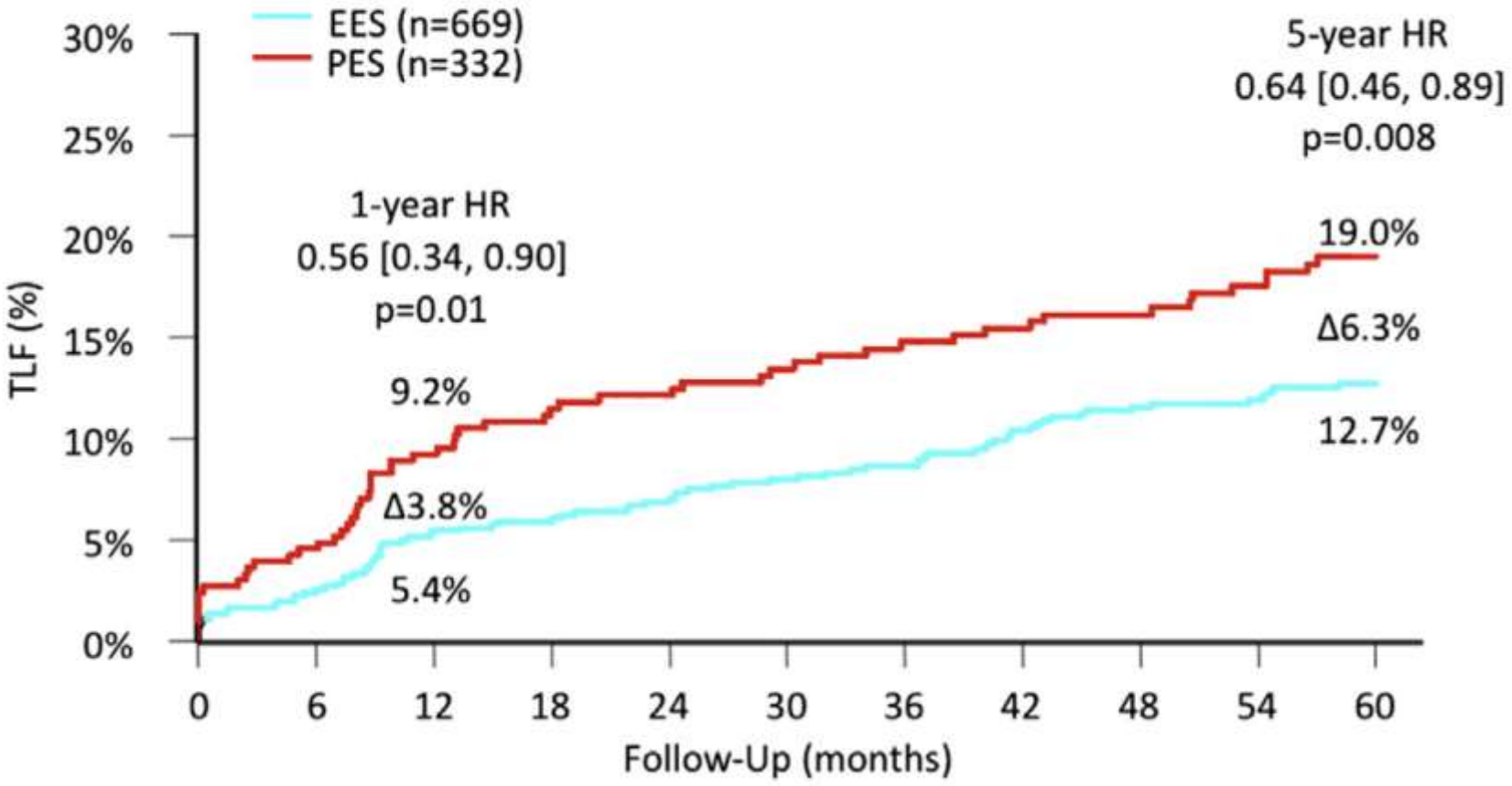
5 Year Mortality Benefit of 2nd Generation DES (SPIRIT III)



Gada, et al. J Am Coll Cardiol Intv 2013;6:1263-6.

Background:

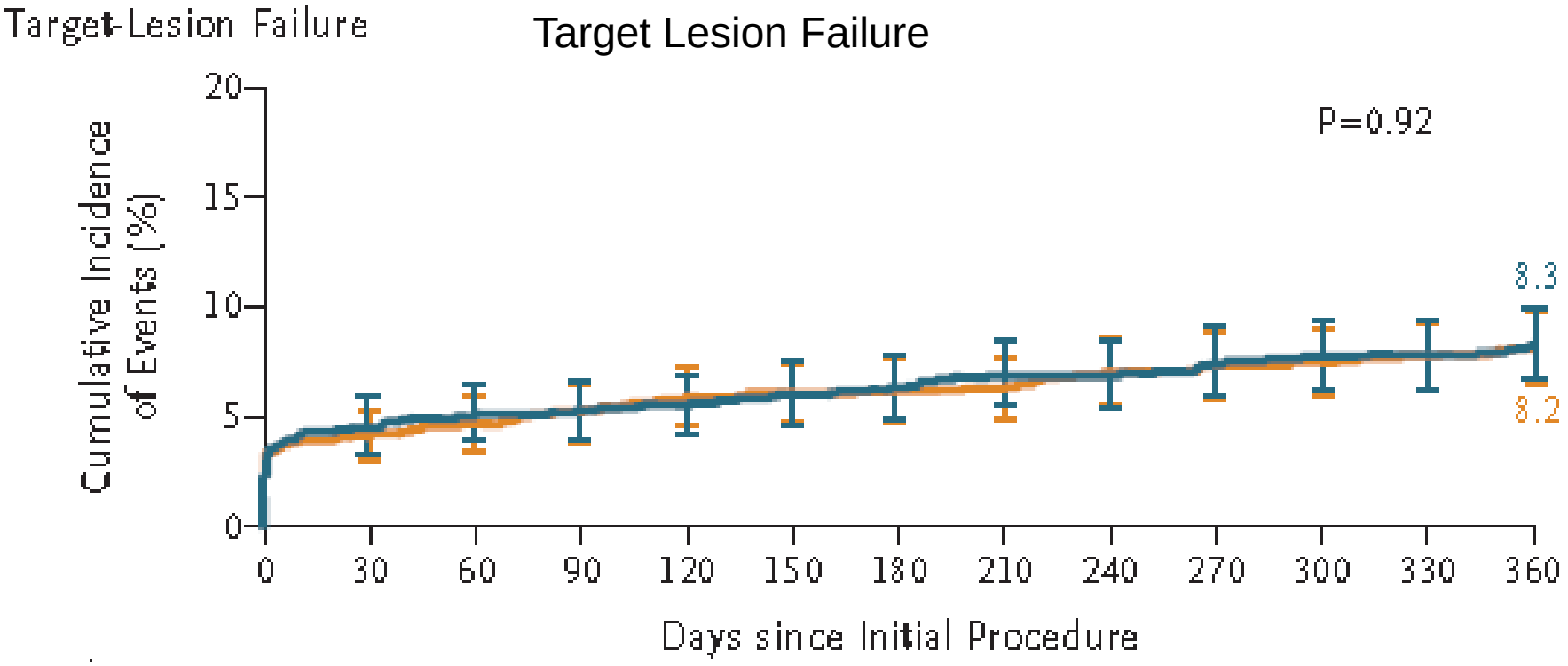
5 Year TLF Benefit of 2nd Generation DES (SPIRIT III)



Gada, et al. J Am Coll Cardiol Intv 2013;6:1263-6.

Background:

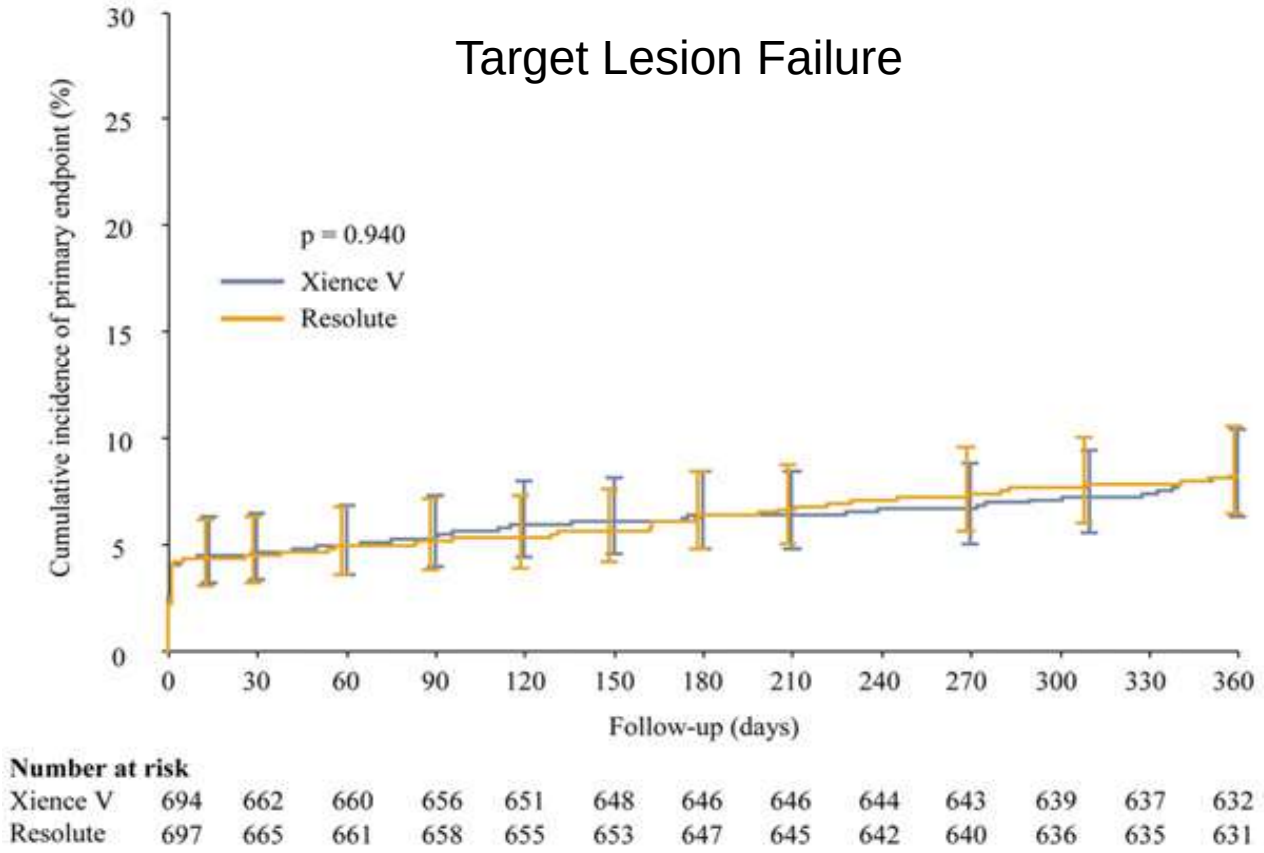
Randomized comparison of two 2nd generation DES (Resolute and Xience stents)



Serruys, et al. NEJM 2010;363:136-46.

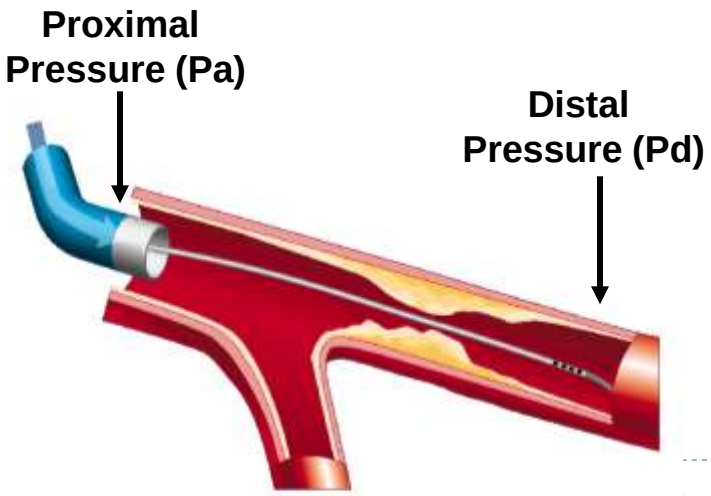
Background:

Randomized comparison of 2nd generation Resolute and Xience stents in the TWENTE trial



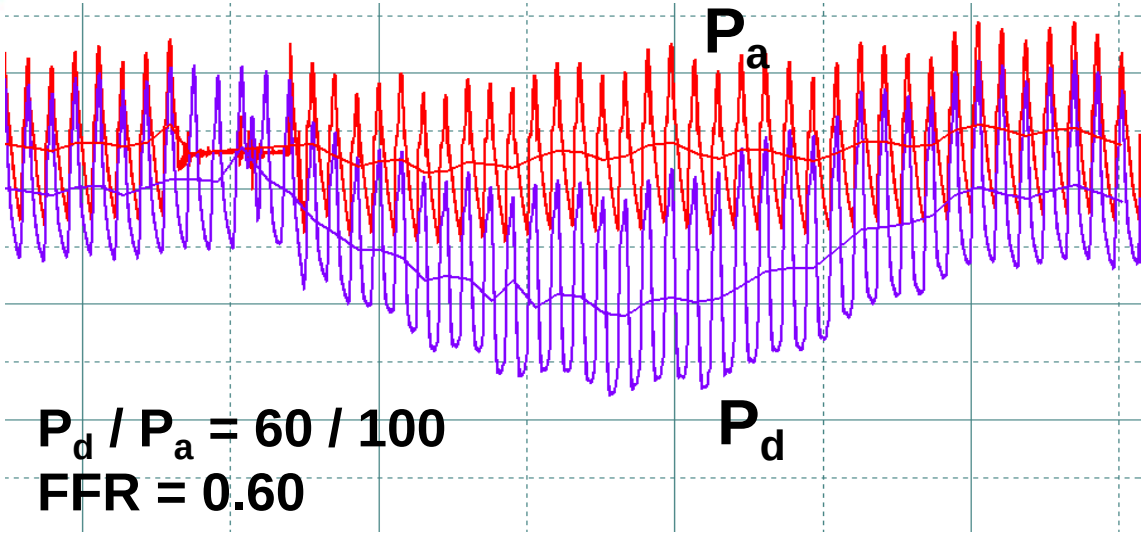
Von Birgelen, et al. JACC 2012;59:1350-61.

What else has changed?



FFR = P_d / P_a

during maximal flow

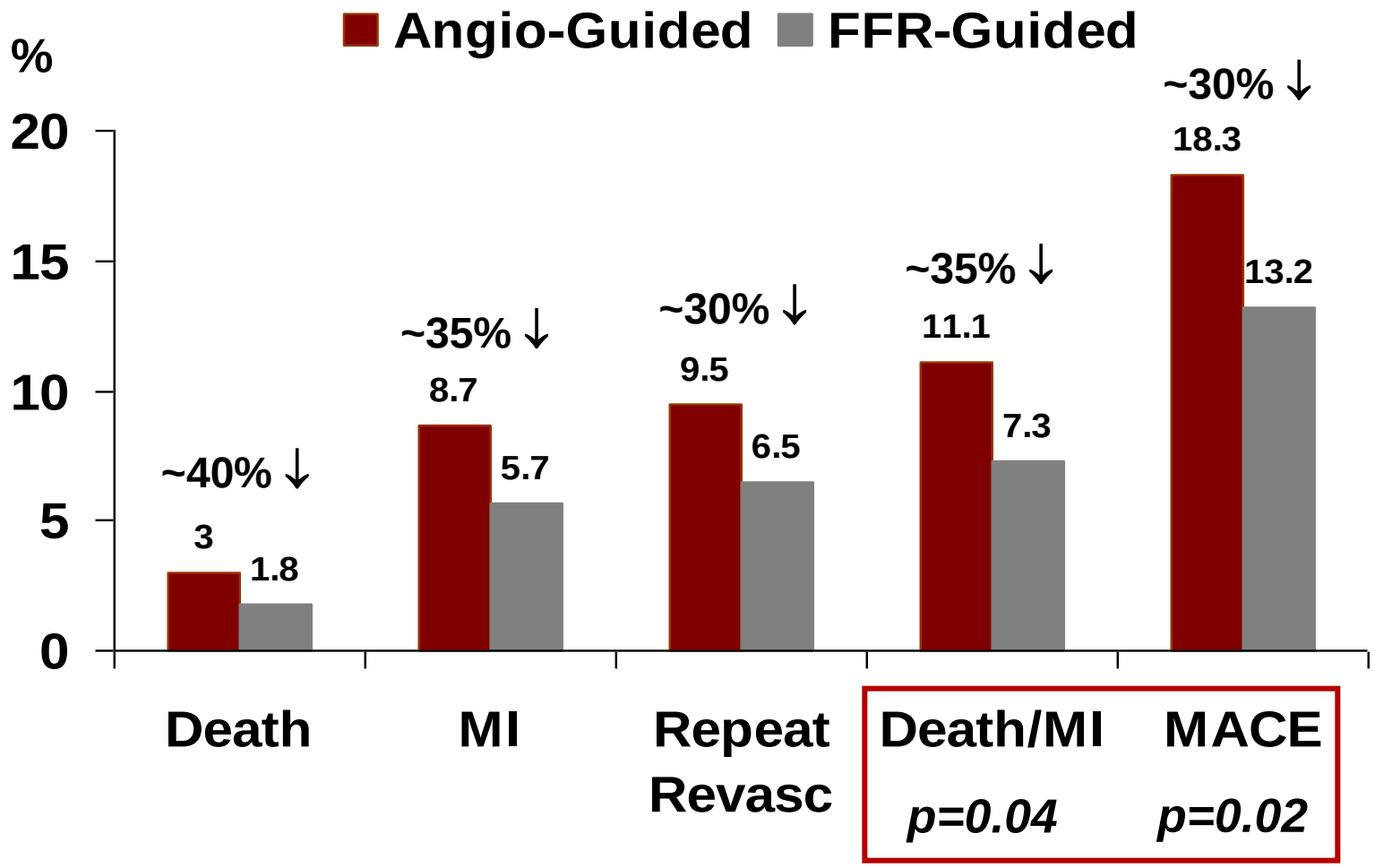


P_d / P_a = 60 / 100

FFR = 0.60

FAME Study: One Year Outcomes

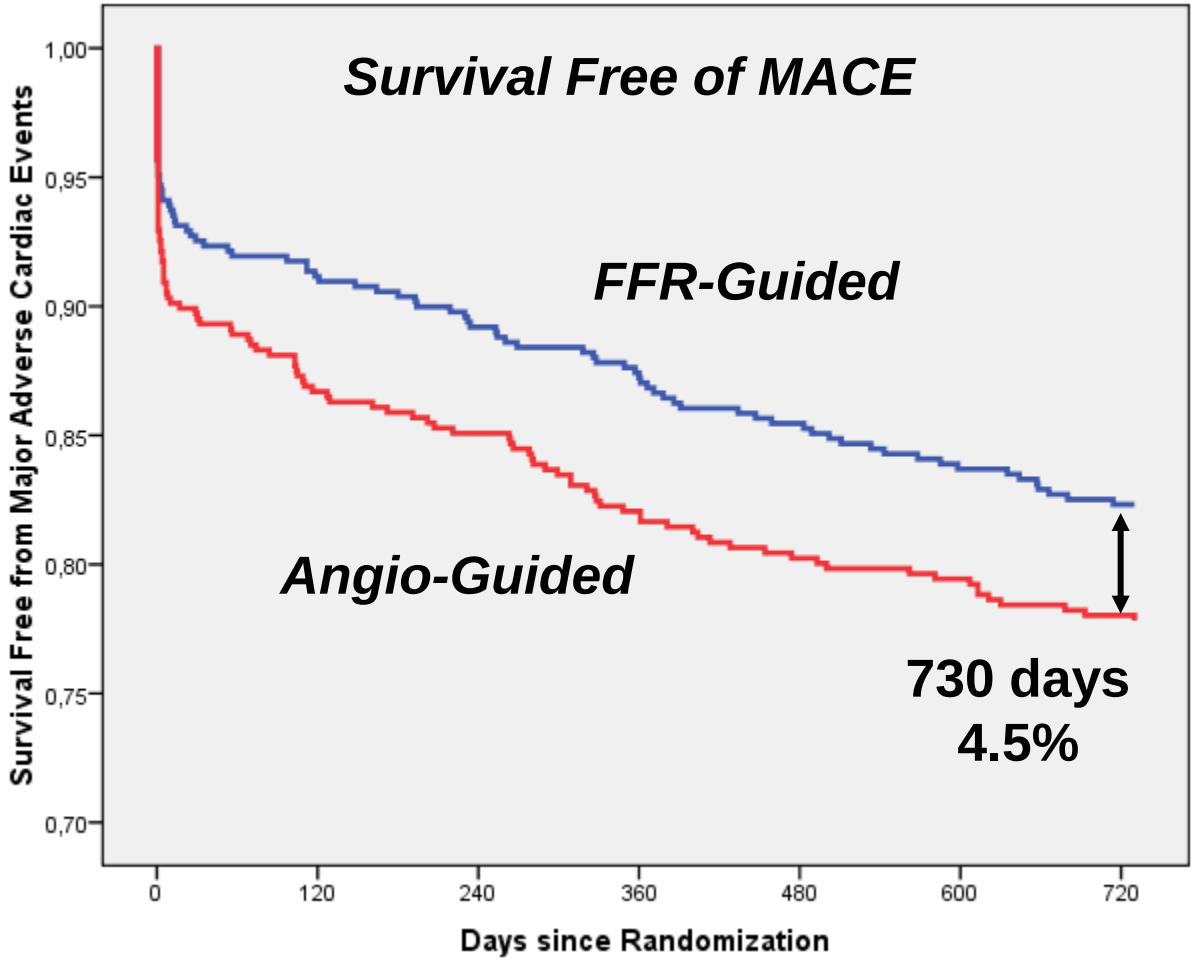
1005 patients with 2-3 vessel CAD randomized to angio or FFR-guided PCI



New Engl J Med 2009;360:213-24.

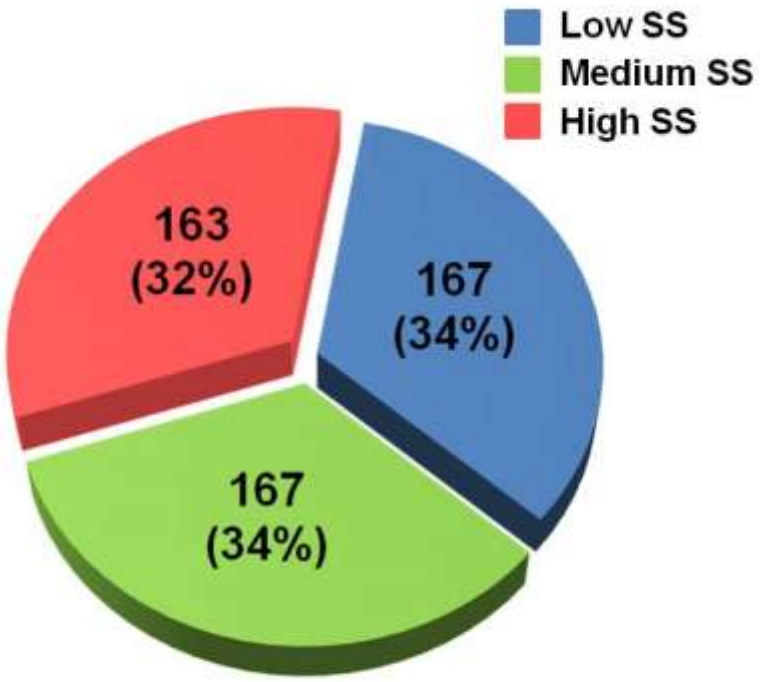
FAME Study: Two Year Outcomes

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



Pijls, et al. J Am Coll Cardiol 2010;56:177-184

Functional SYNTAX Score

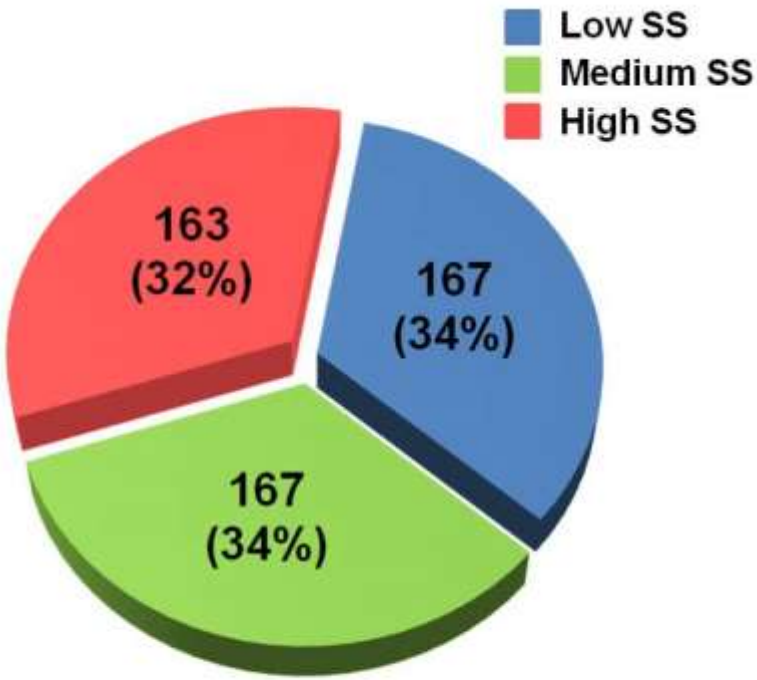


Without FFR

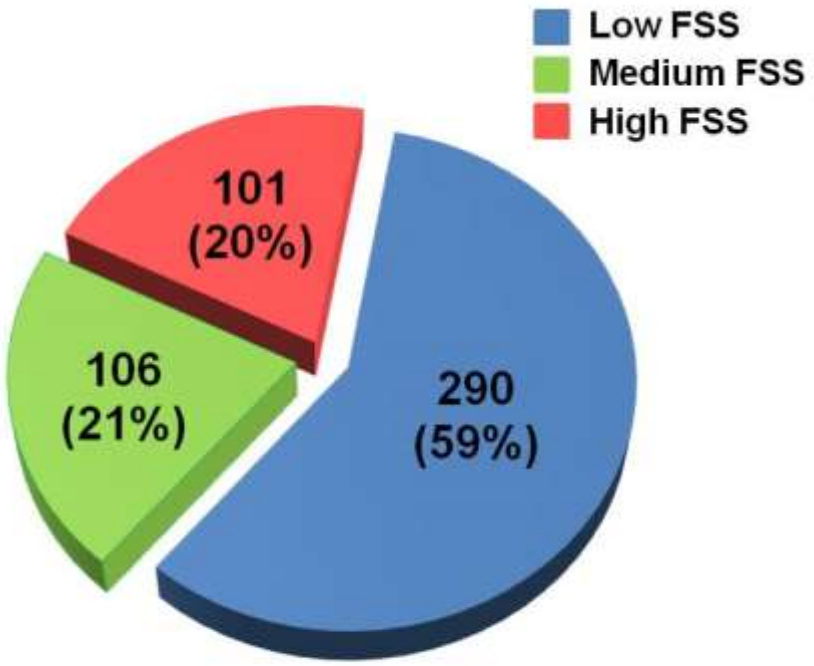
Nam CW, et al. J Am Coll Cardiol 2011;58:1211-8

Functional SYNTAX Score

Reclassifies > 30% of cases



Without FFR

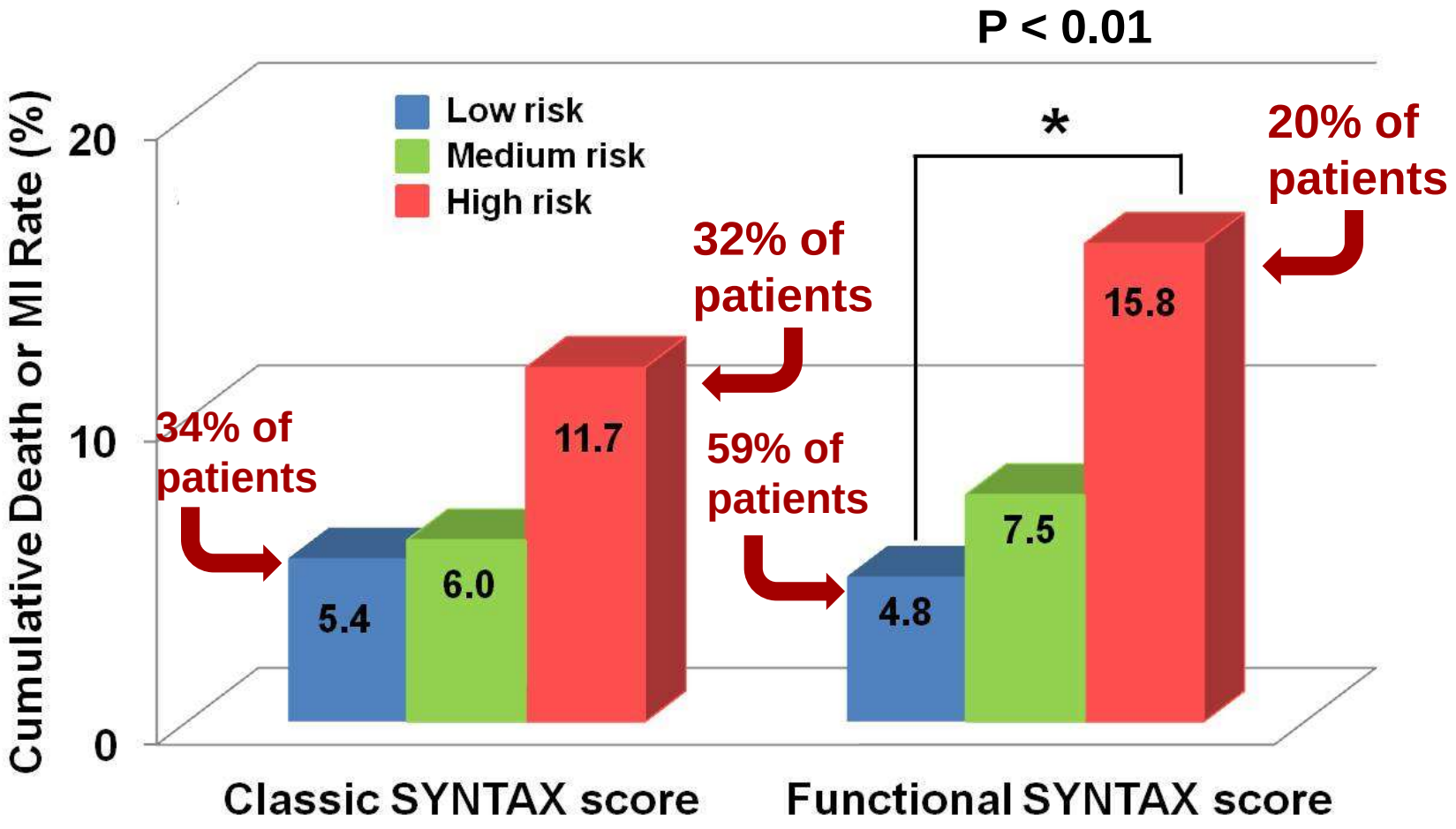


With FFR

Nam CW, et al. J Am Coll Cardiol 2011;58:1211-8

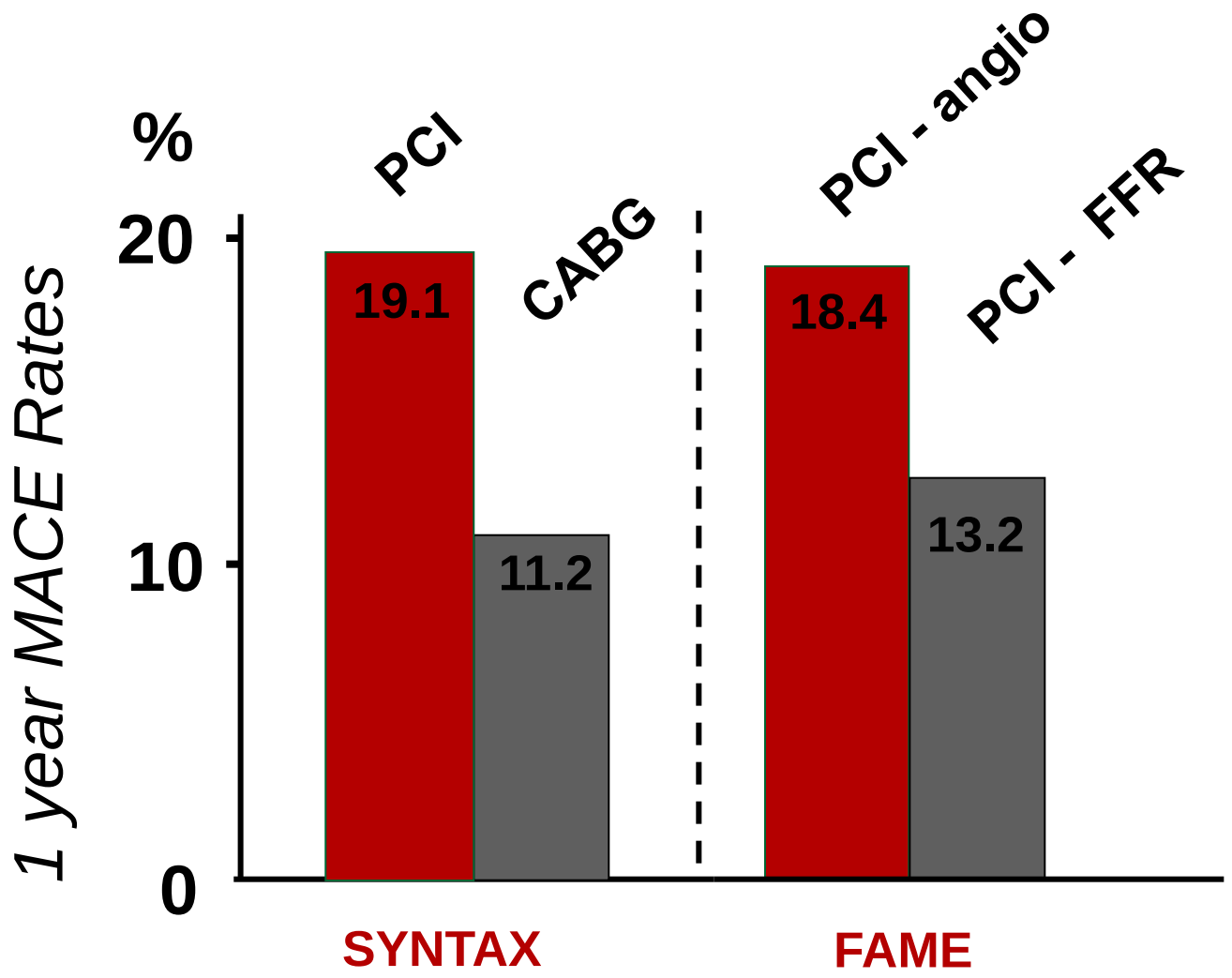
Functional SYNTAX Score

Discriminates Risk for Death/MI



Nam CW, et al. J Am Coll Cardiol 2011;58:1211-8

Where do we go from here?



FAME 3:

Objective

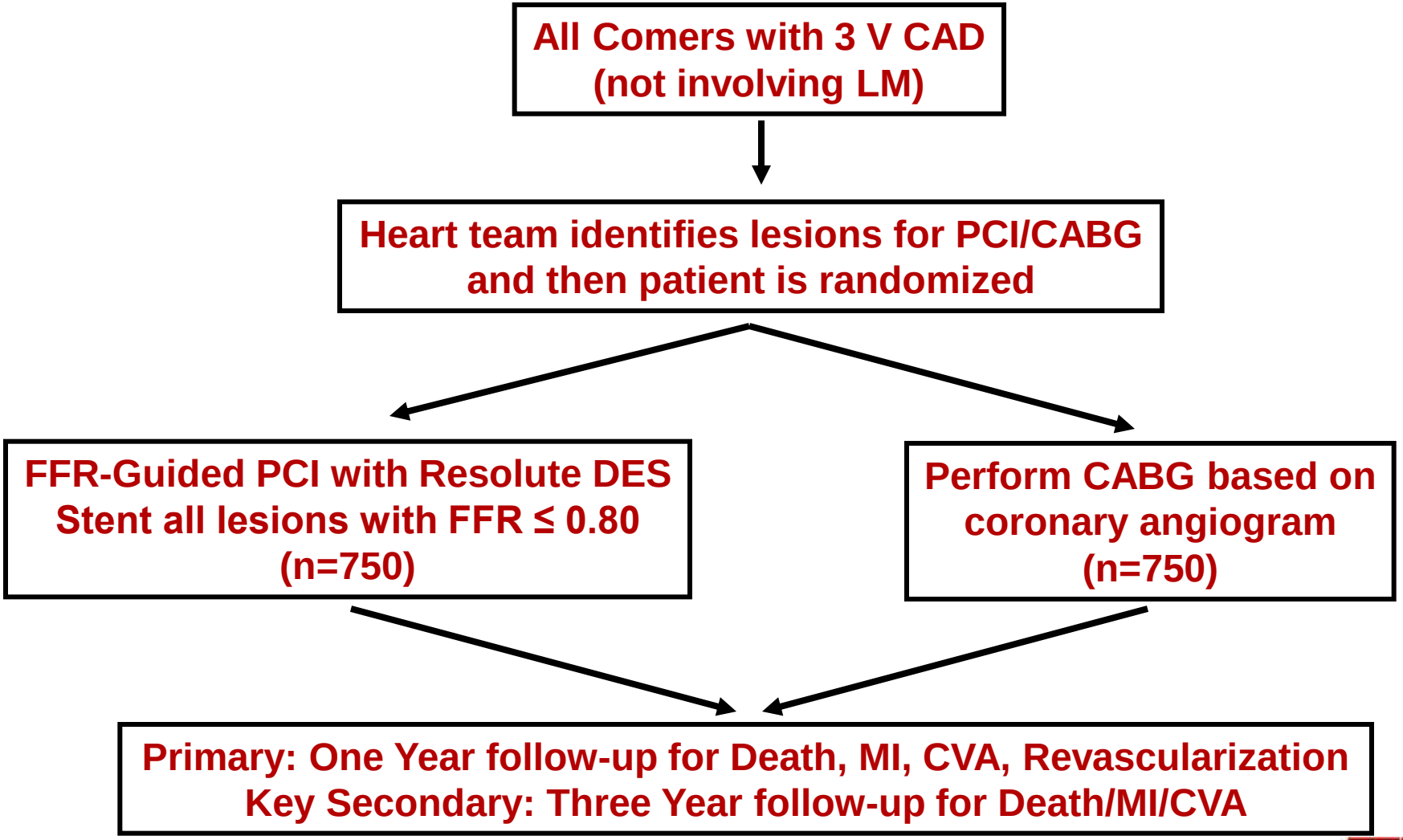
- The primary objective of the FAME 3 Trial is to demonstrate that FFR-guided PCI with the 2nd generation Resolute DES is non-inferior to CABG in patients with multivessel CAD.

FAME 3:

Design

- Multicenter, worldwide, prospective, randomized trial
- Non-inferiority design
- 1500 patients from 50 sites
- Plan for 2 years enrolment and up to 5 year follow-up

Study Flow:



Non-inferior Design

NCT02100722

FAME 3:

Inclusion Criteria

- Age ≥ 21 years
- Three vessel CAD, defined as ≥ 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

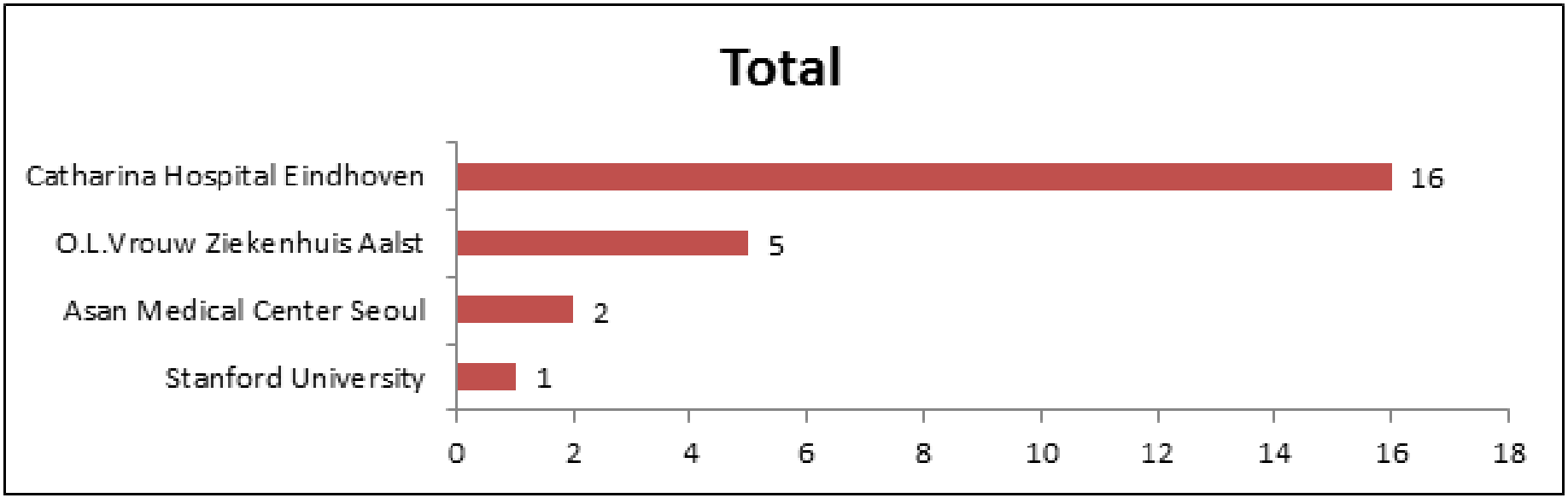
- Primary Endpoint:
  - One year rate of Death, MI, Stroke and Revascularization
- Key Secondary Endpoint:
  - Three year rate of Death, MI and Stroke

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:



Site Status Update:

- Total Participating Sites: 41
- Total Sites with EC/IRB Approval: 22
- Total Activated Sites: 7

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.