

Will FFR-Directed PCI Be Better Than CABG?

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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 (minor stock options):

Company

St. Jude Medical/Medtronic

NIH-R01 HL093475 (PI)

Medtronic

NIH-R01 HL093475 (PI)

HeartFlow



Will FFR-Directed PCI be Better Than CABG?

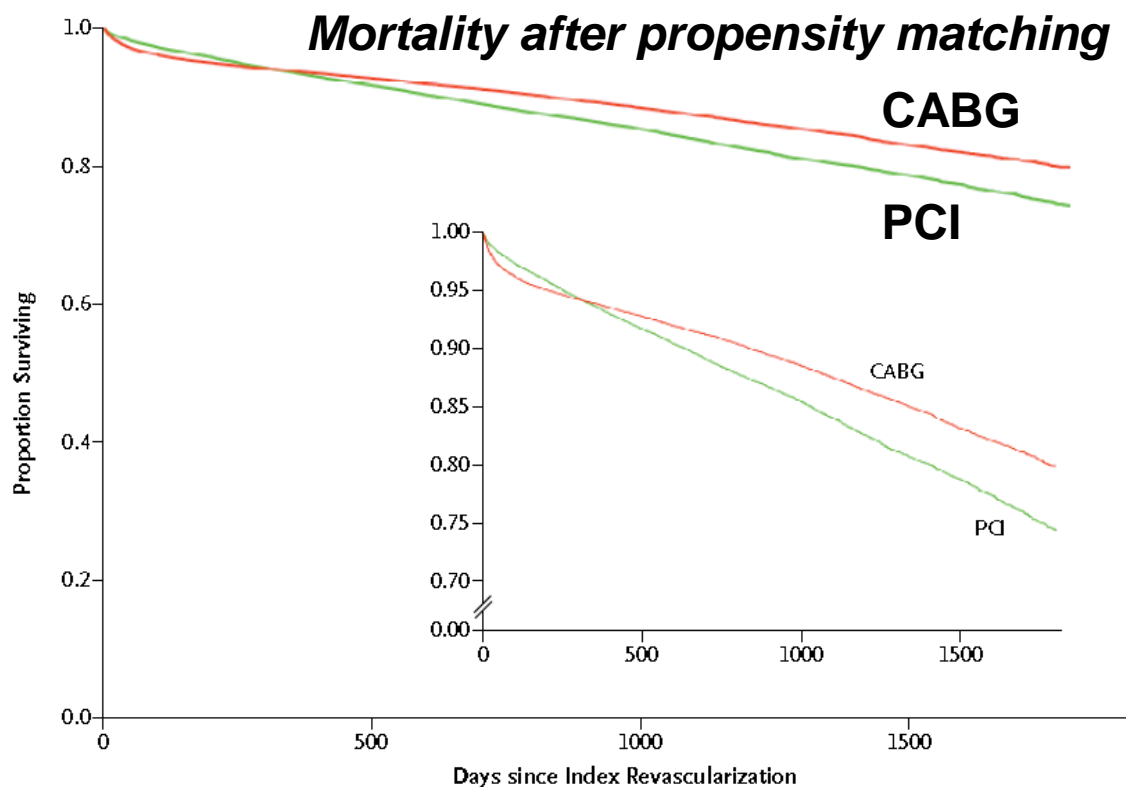
Yes!

....and No



CABG vs. PCI: ASCERT Registry

~ 189,000 stable patients ≥ 65 years old treated with either PCI or CABG



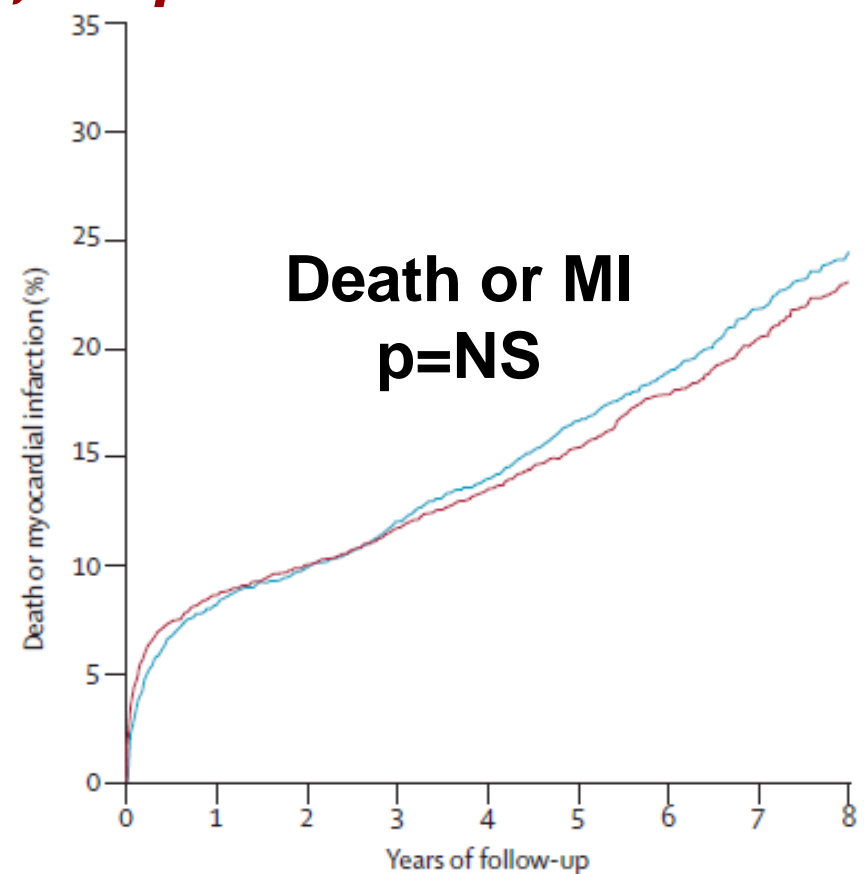
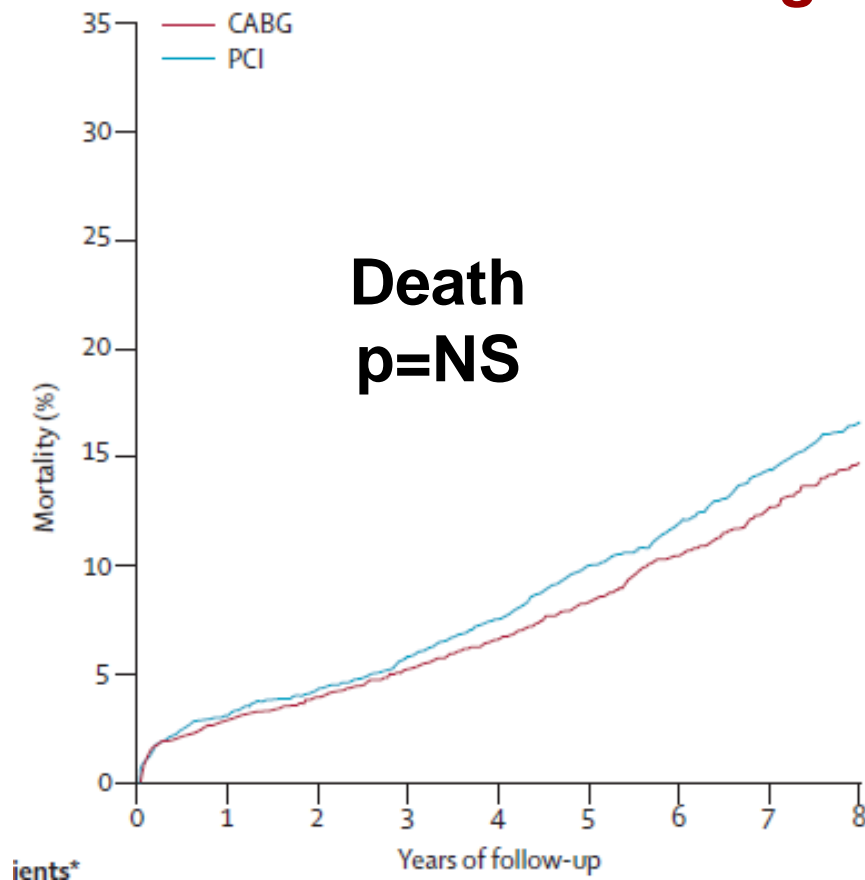
	30-Day	1-Yr	2-Yr	3-Yr	4-Yr
Mortality after CABG, % (95% CI)	2.25 (2.09–2.41)	6.24 (5.97–6.50)	8.98 (8.68–9.29)	12.4 (12.0–12.8)	16.4 (15.9–16.9)
Mortality after PCI, % (95% CI)	1.31 (1.21–1.41)	6.55 (6.35–6.76)	11.3 (11.0–11.6)	15.9 (15.6–16.3)	20.8 (20.4–21.2)
Relative risk with CABG (95% CI)	1.72 (1.52–1.89)	0.95 (0.90–1.00)	0.79 (0.76–0.83)	0.78 (0.75–0.81)	0.79 (0.76–0.82)

Weintraub, et al. New Engl J Med 2012;366:1457-76.



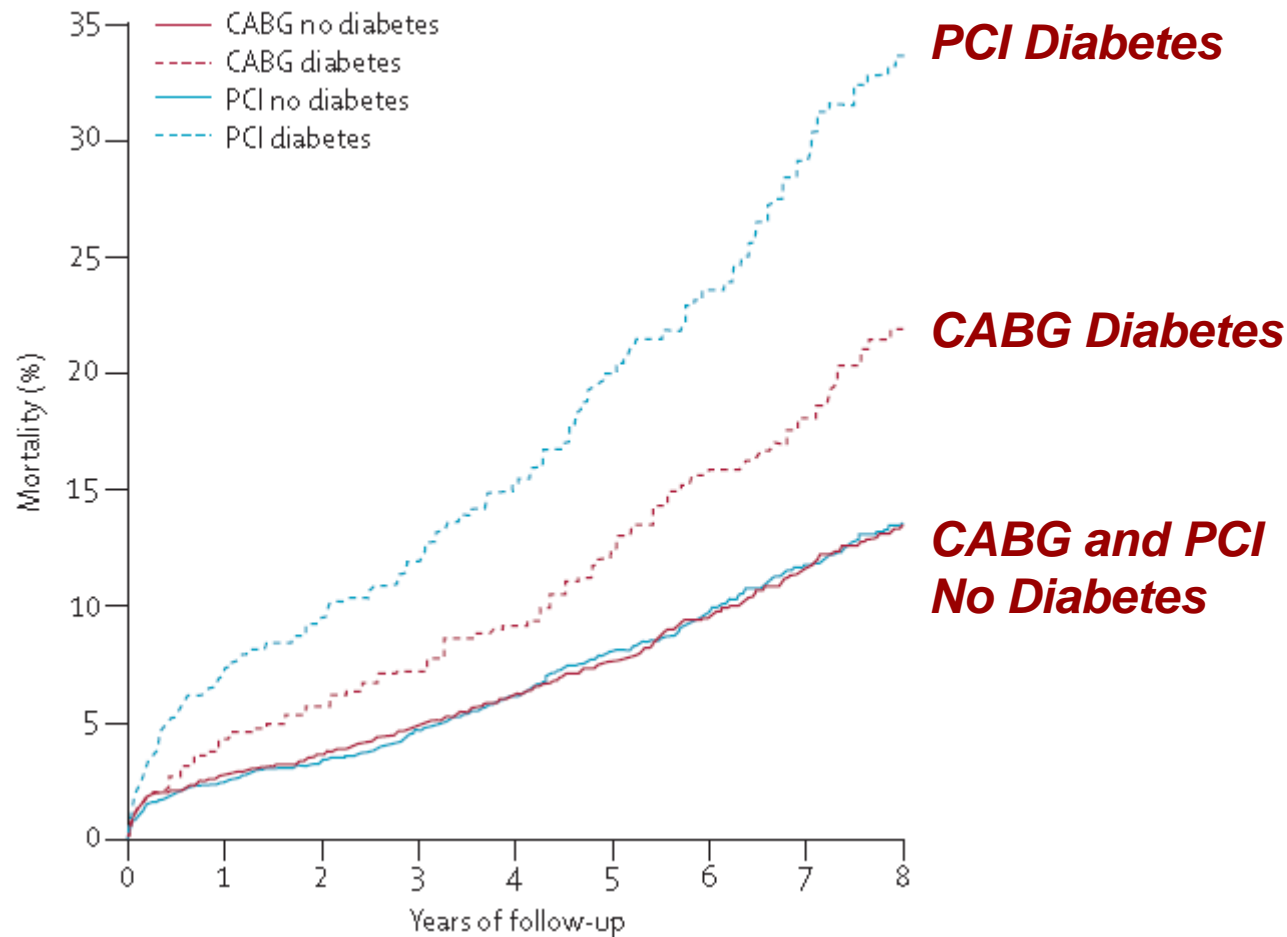
Randomized Trials

***Meta-Analysis of 10 randomized CABG vs. PCI trials
including >7,000 patients***



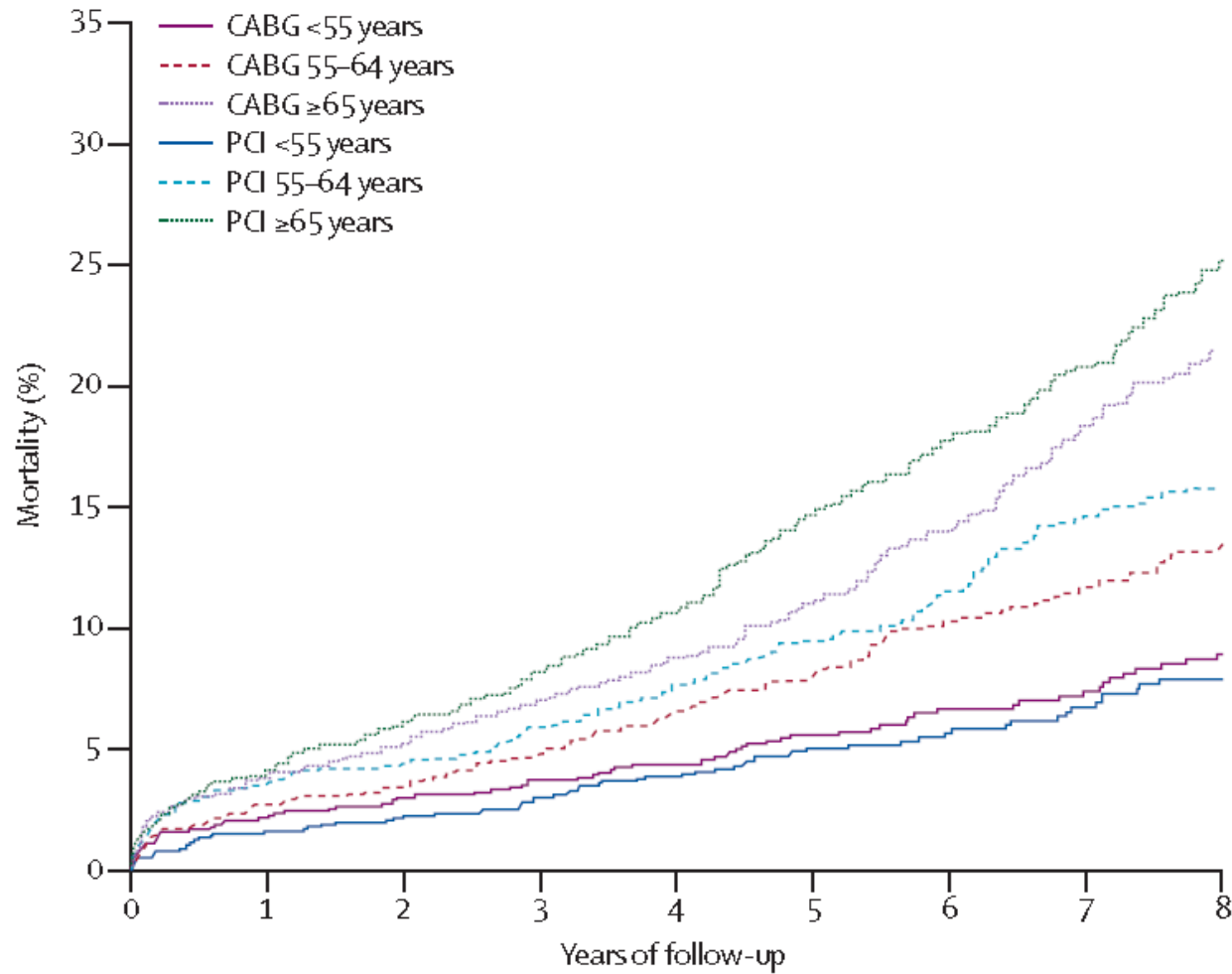
Meta-Analysis of CABG vs. PCI Trials

Impact of Diabetes



Meta-Analysis of CABG vs. PCI Trials

Impact of Age



PCI ≥65 Years

CABG ≥65 Years

PCI 55-64 Years

CABG 55-64 Years

***CABG and PCI
<55 Years***



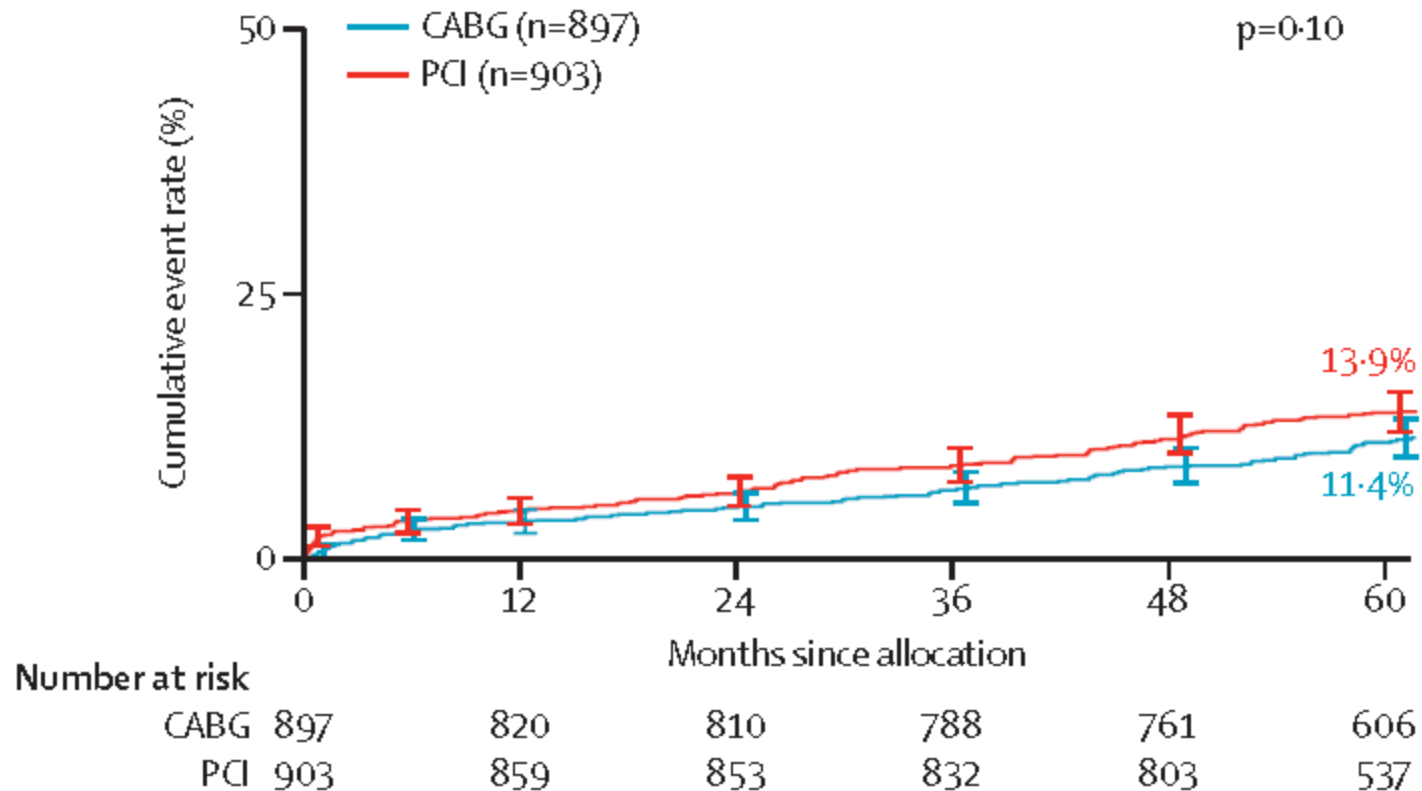
SYNTAX Trial:

- 1800 patients with 3 vessel CAD randomized to PCI with Taxus drug-eluting stents or CABG
 - ~28% diabetic
 - ~33% with LM disease
 - 4.6 stents per patient
 - Average of 86 mm of stent (1/3 with >100 mm)



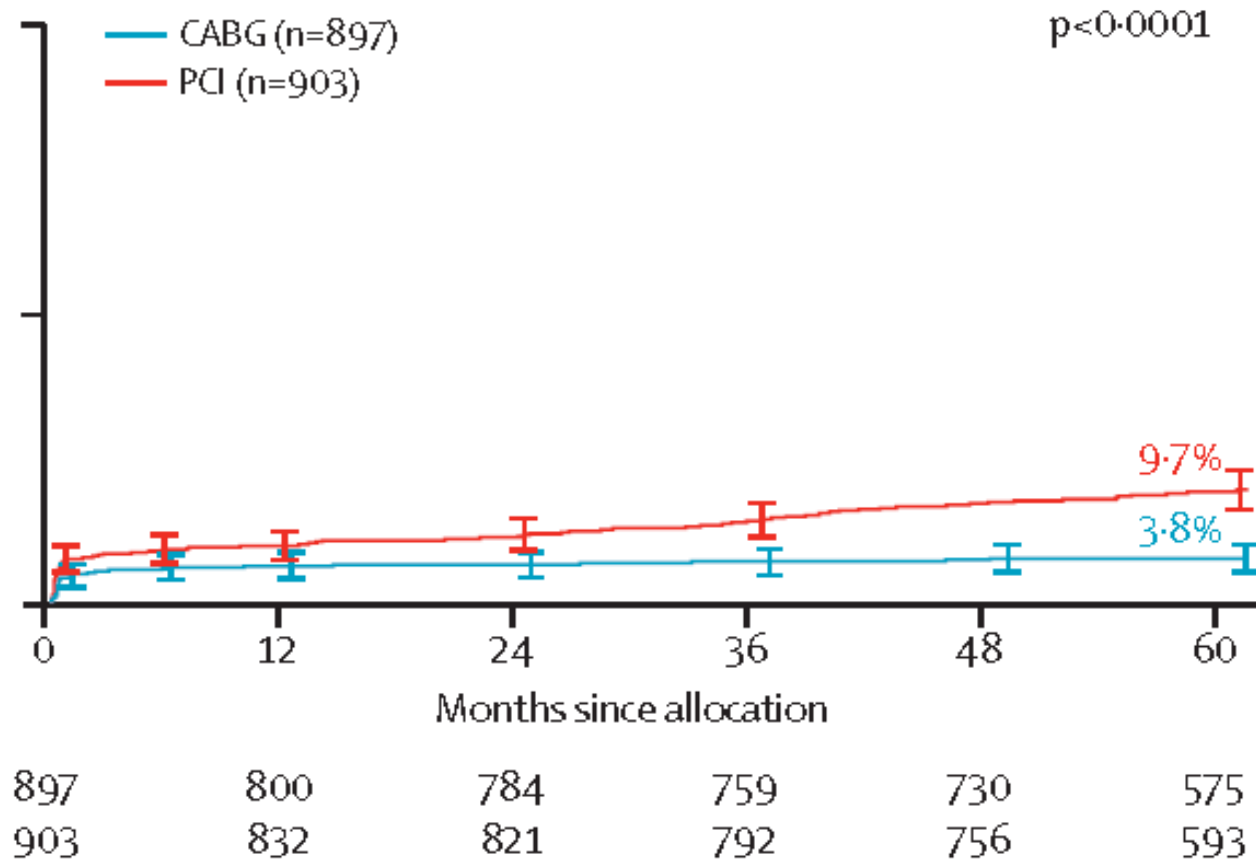
SYNTAX

5 Year Outcomes: All Cause Mortality



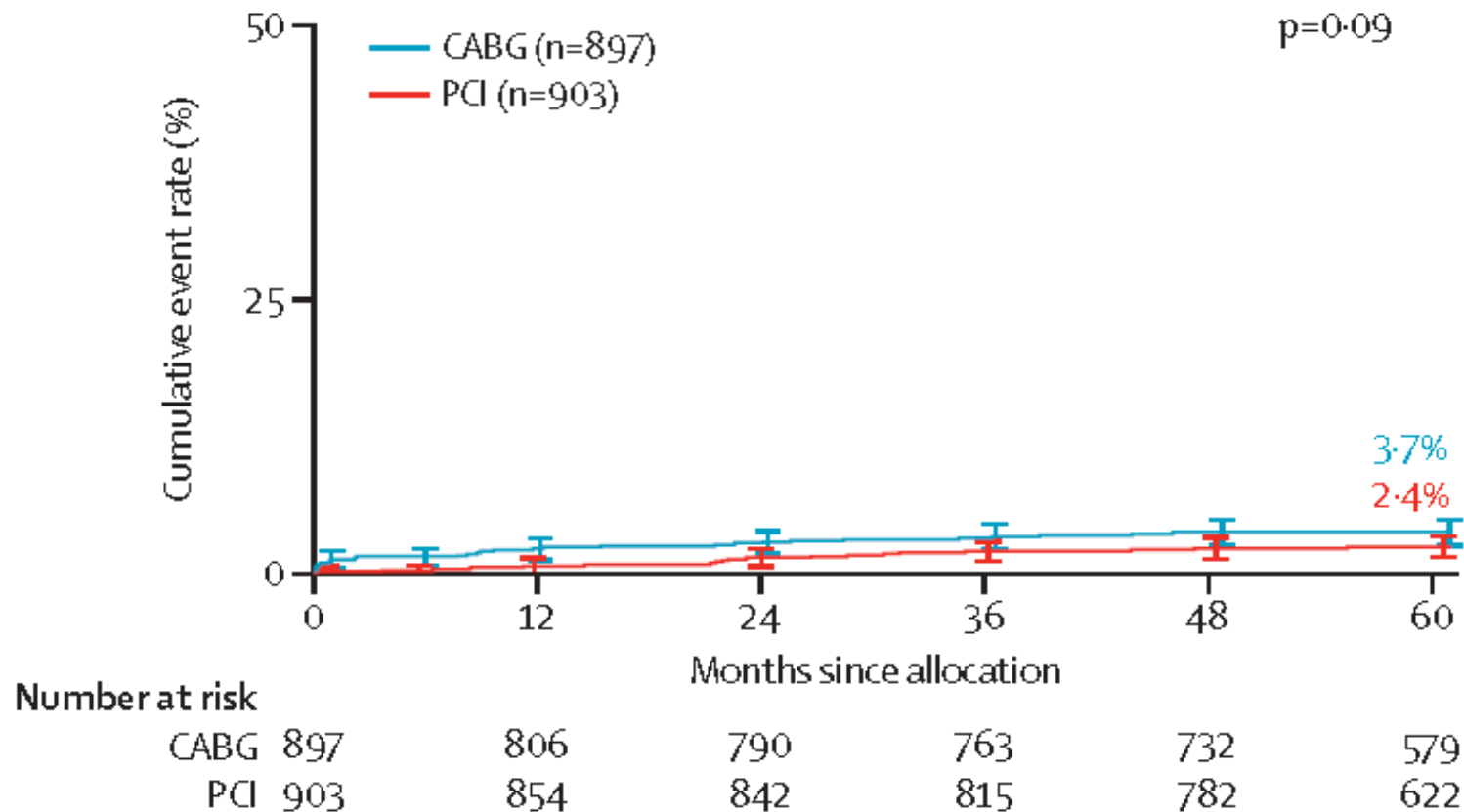
SYNTAX

5 Year Outcomes: Myocardial Infarction



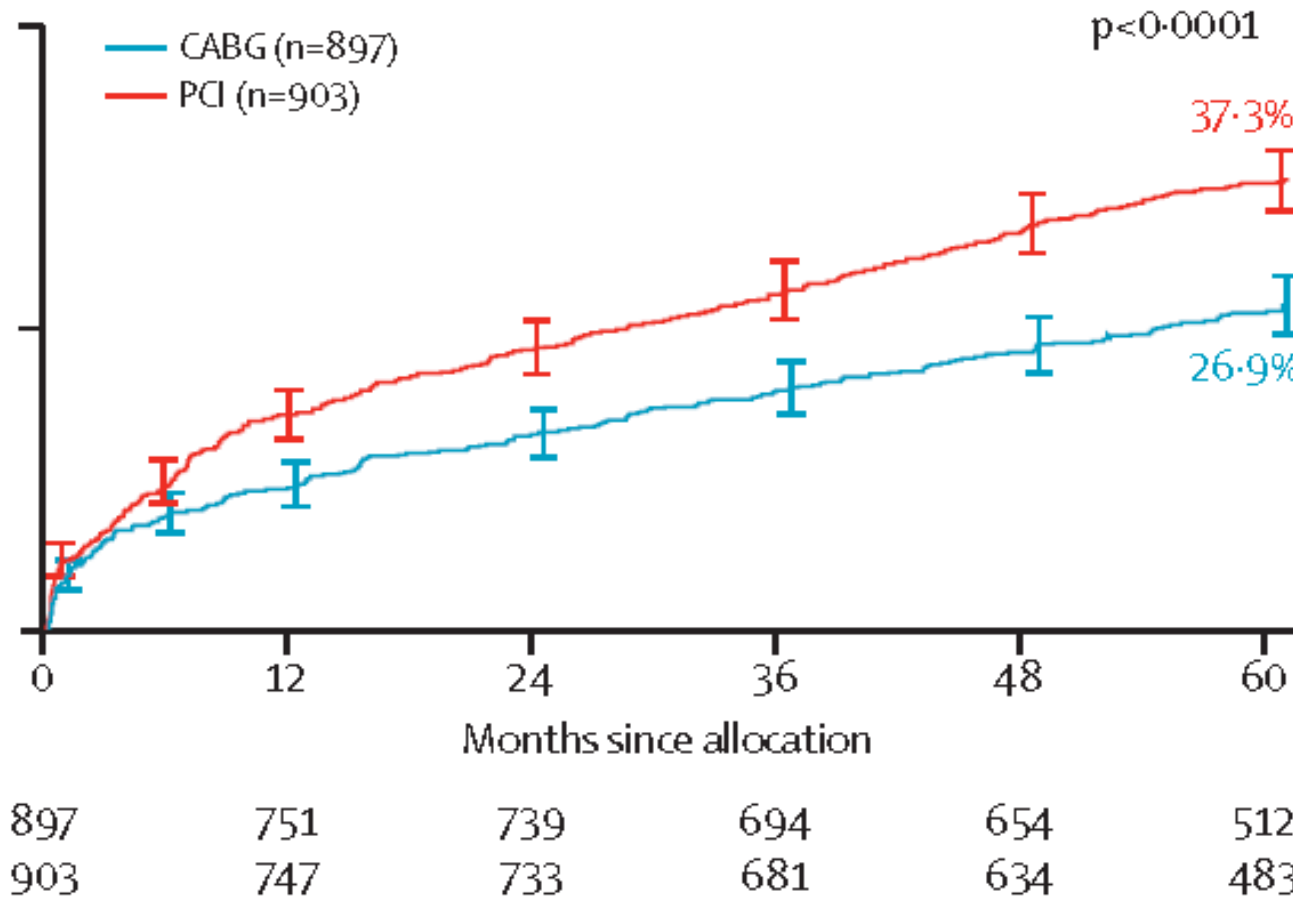
SYNTAX

5 Year Outcomes: Stroke

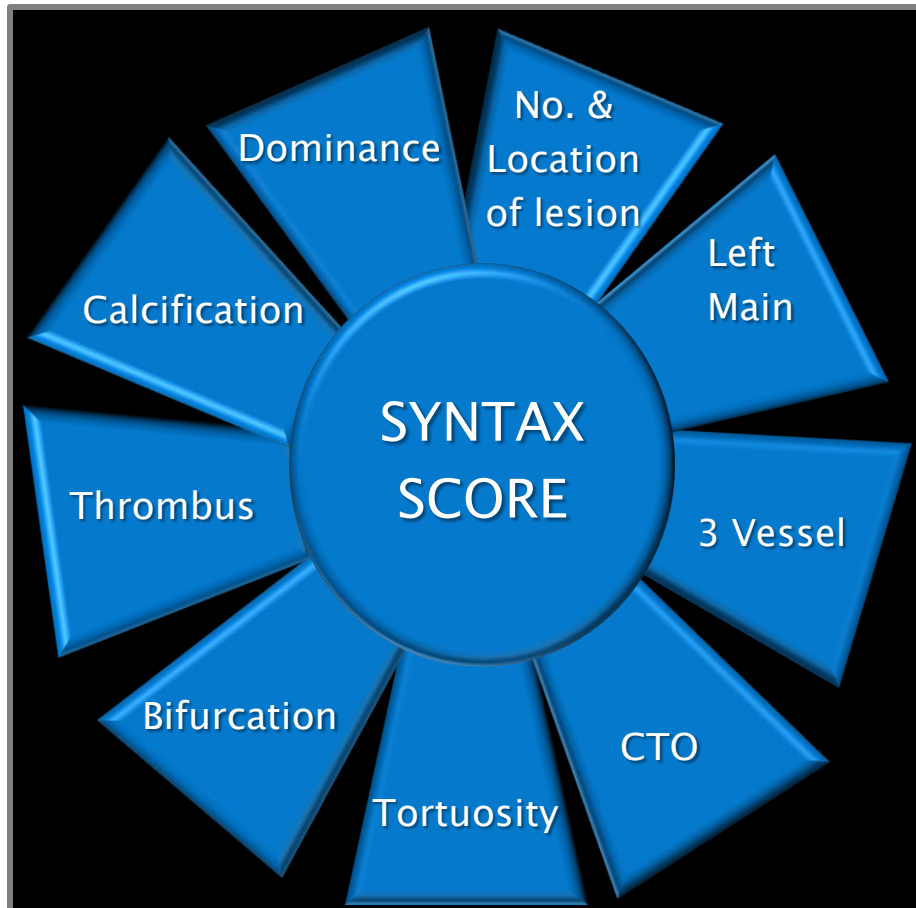


SYNTAX

5 Year Outcomes: MACCE



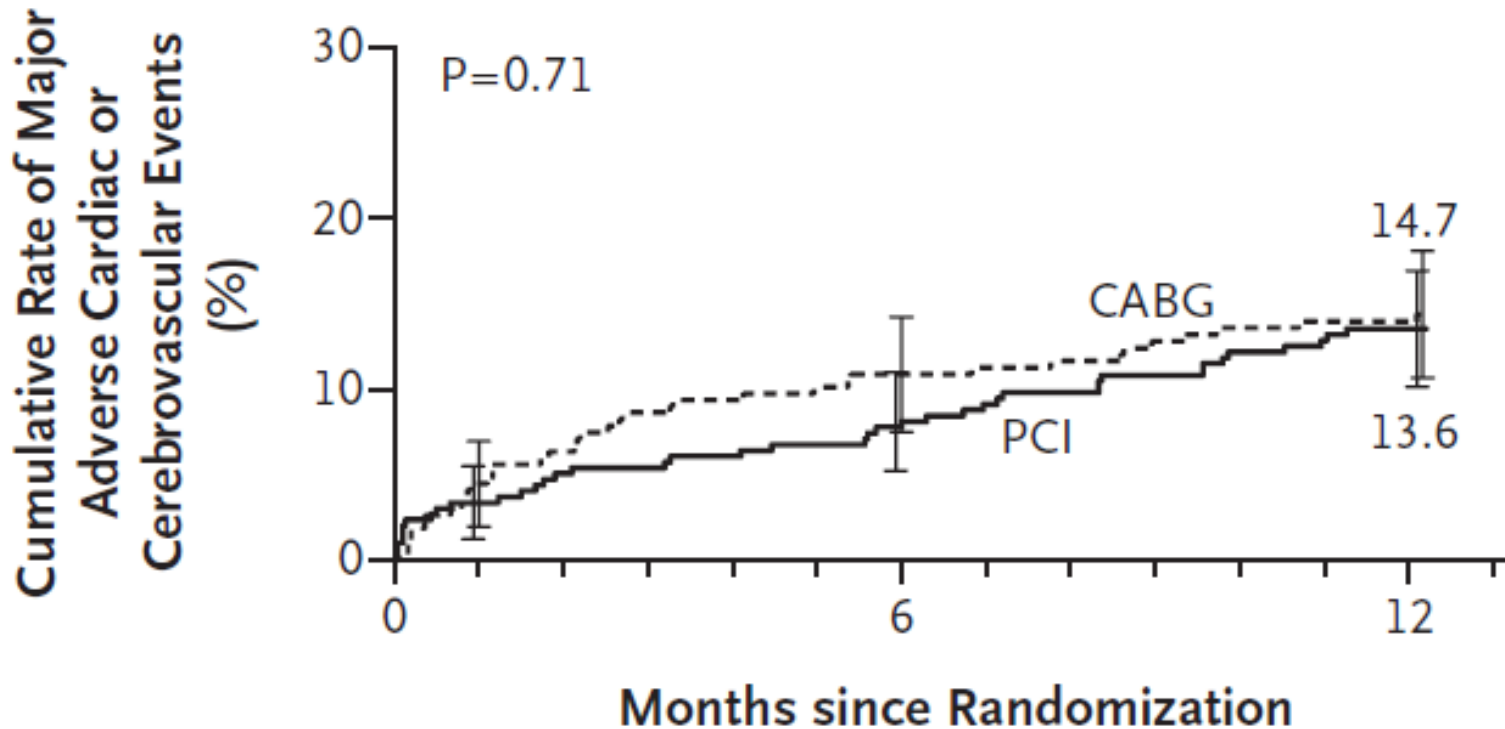
SYNTAX Score



SYNTAX

Similar outcomes with PCI vs CABG with lower SYNTAX score

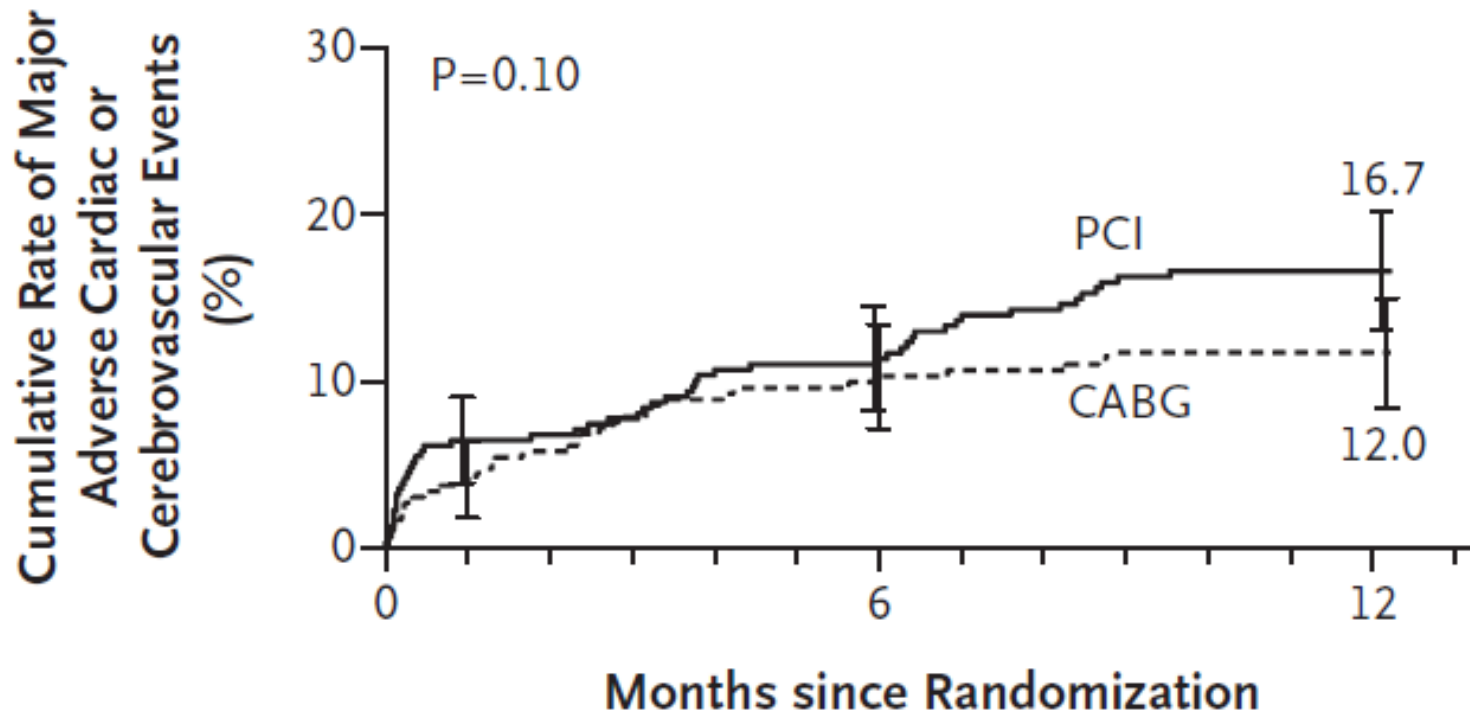
Lowest Tertile (SYNTAX score ≤ 22)



SYNTAX

Worse outcomes with PCI vs CABG with higher SYNTAX score

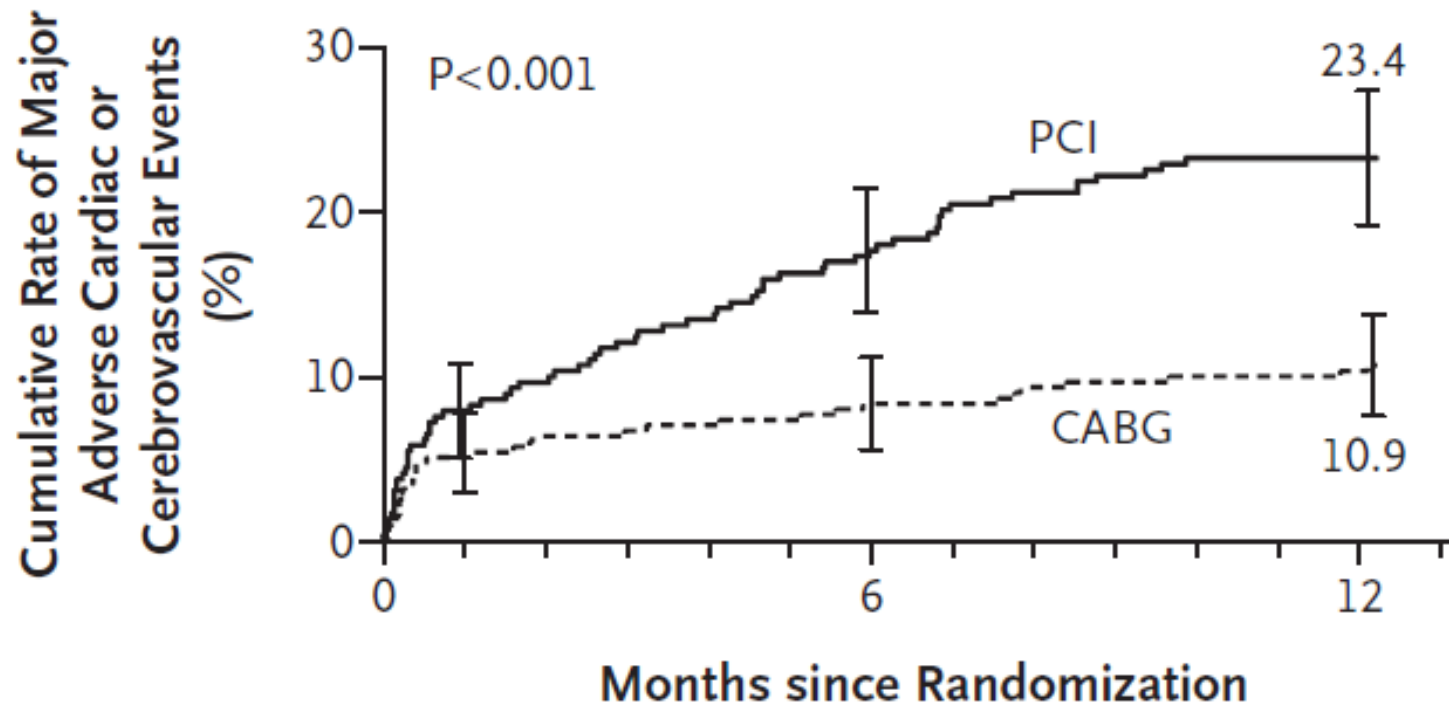
Intermediate Tertile (SYNTAX score 23-32)



SYNTAX

Worse outcomes with PCI vs CABG with higher SYNTAX score

High Tertile (SYNTAX score ≥ 33)



FREEDOM Trial

- 2005-2010: 1900 diabetics enrolled from 140 international centers
- Mostly first generation drug-eluting stents
- Mean SYNTAX score = 26
- 3.5 lesions stented/patient



FREEDOM Trial

Early Outcomes

Event	30 Days after Procedure			12 Months after Procedure		
	PCI	CABG	P Value	PCI	CABG	P Value
	number (percent)			number (percent)		
Major adverse cardiovascular and cerebrovascular events	45 (4.8)	47 (5.2)	0.68	157 (16.8)	106 (11.8)	0.004
Death	8 (0.8)	15 (1.7)	0.12	32 (3.4)	38 (4.2)	0.35
Myocardial infarction	17 (1.8)	15 (1.7)	0.82	54 (5.8)	30 (3.4)	0.02
Stroke	3 (0.3)	16 (1.8)	0.002	8 (0.9)	17 (1.9)	0.06
Repeat revascularization	31 (3.3)	10 (1.1)	0.002	117 (12.6)	42 (4.8)	<0.001



FREEDOM Trial

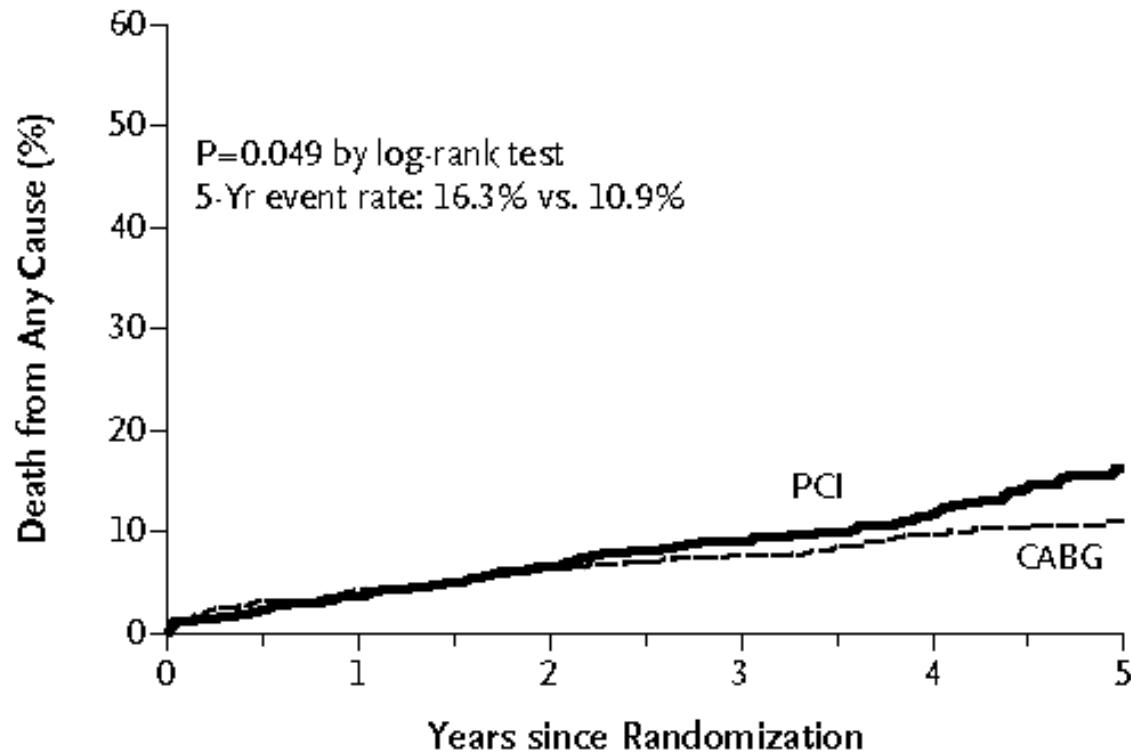
Late Outcomes

Outcome	2 Years after Randomization		5 Years after <u>Randomization</u>		Patients with Event		P Value*
	PCI	CABG	PCI	CABG	PCI	CABG	
	number (percent)				number		
Primary composite†	121 (13.0)	108 (11.9)	200 (26.6)	146 (18.7)	205	147	0.005‡
Death from any cause	62 (6.7)	57 (6.3)	<u>114 (16.3)</u>	<u>83 (10.9)</u>	118	86	0.049
Myocardial infarction	62 (6.7)	42 (4.7)	<u>98 (13.9)</u>	<u>48 (6.0)</u>	99	48	<0.001
Stroke	14 (1.5)	24 (2.7)	20 (2.4)	37 (5.2)	22	37	0.03§
Cardiovascular death	9 (0.9)	12 (1.3)	73 (10.9)	52 (6.8)	75	55	0.12



FREEDOM Trial

Mortality



No. at Risk

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

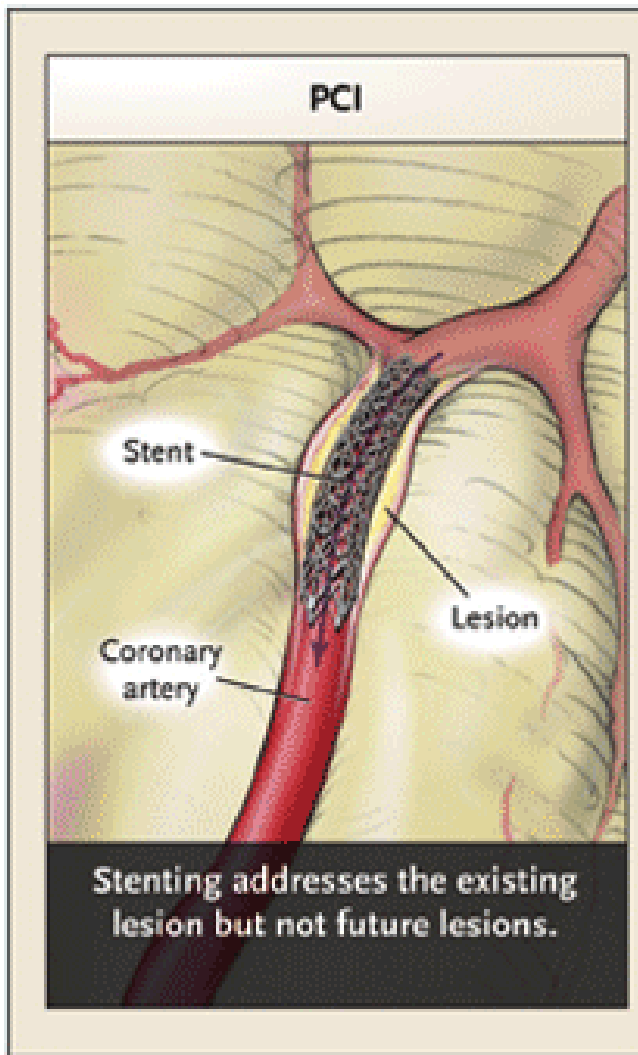


What have we learned?

- Older patients, patients with more severe CAD, and diabetics fare better with CABG when compared to *angiography*-guided PCI with *first* generation drug-eluting stents.



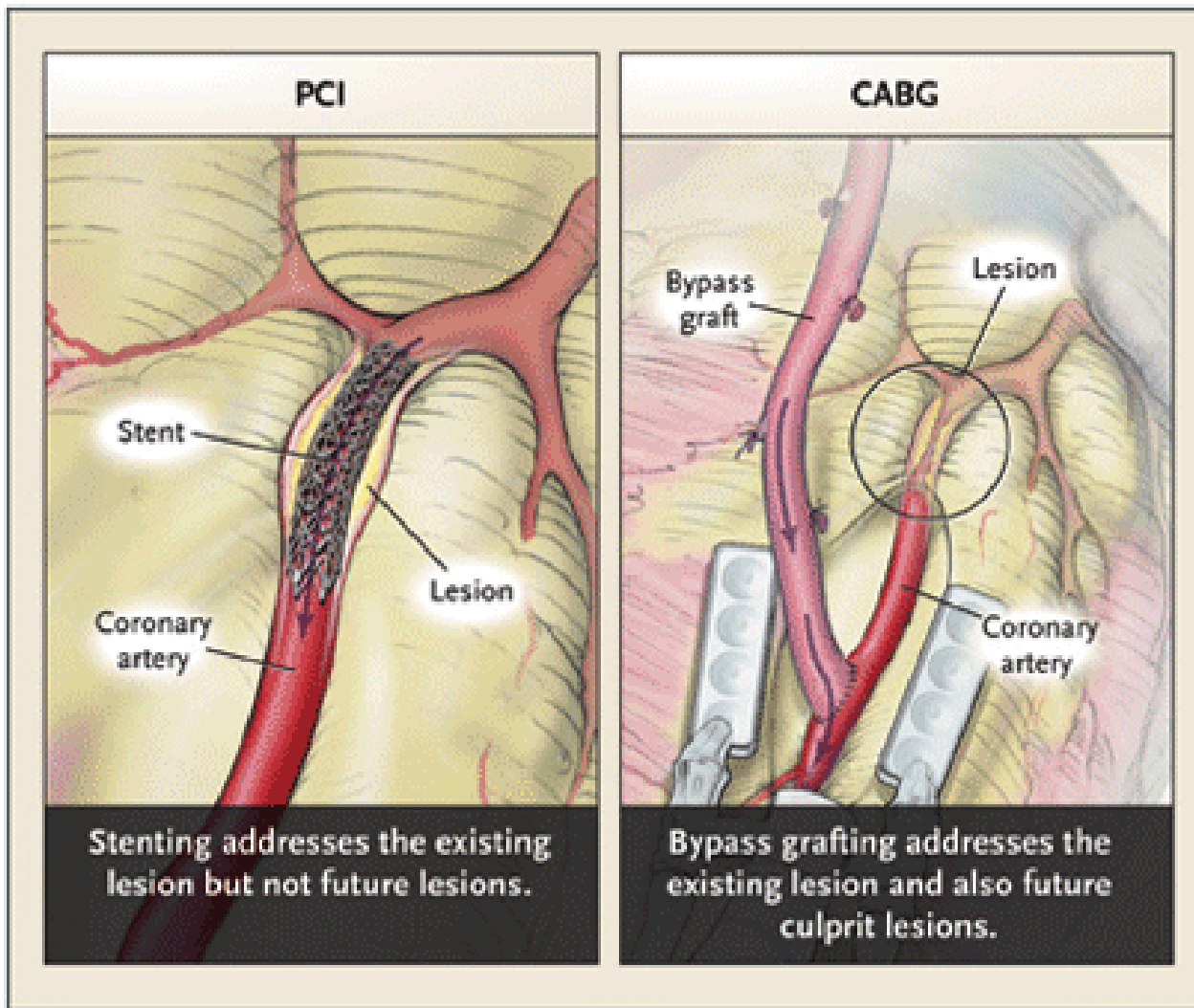
How do we explain this?



Gersh and Frye. New Engl J Med 2005;352:2235.



How do we explain this?



FAME 3:

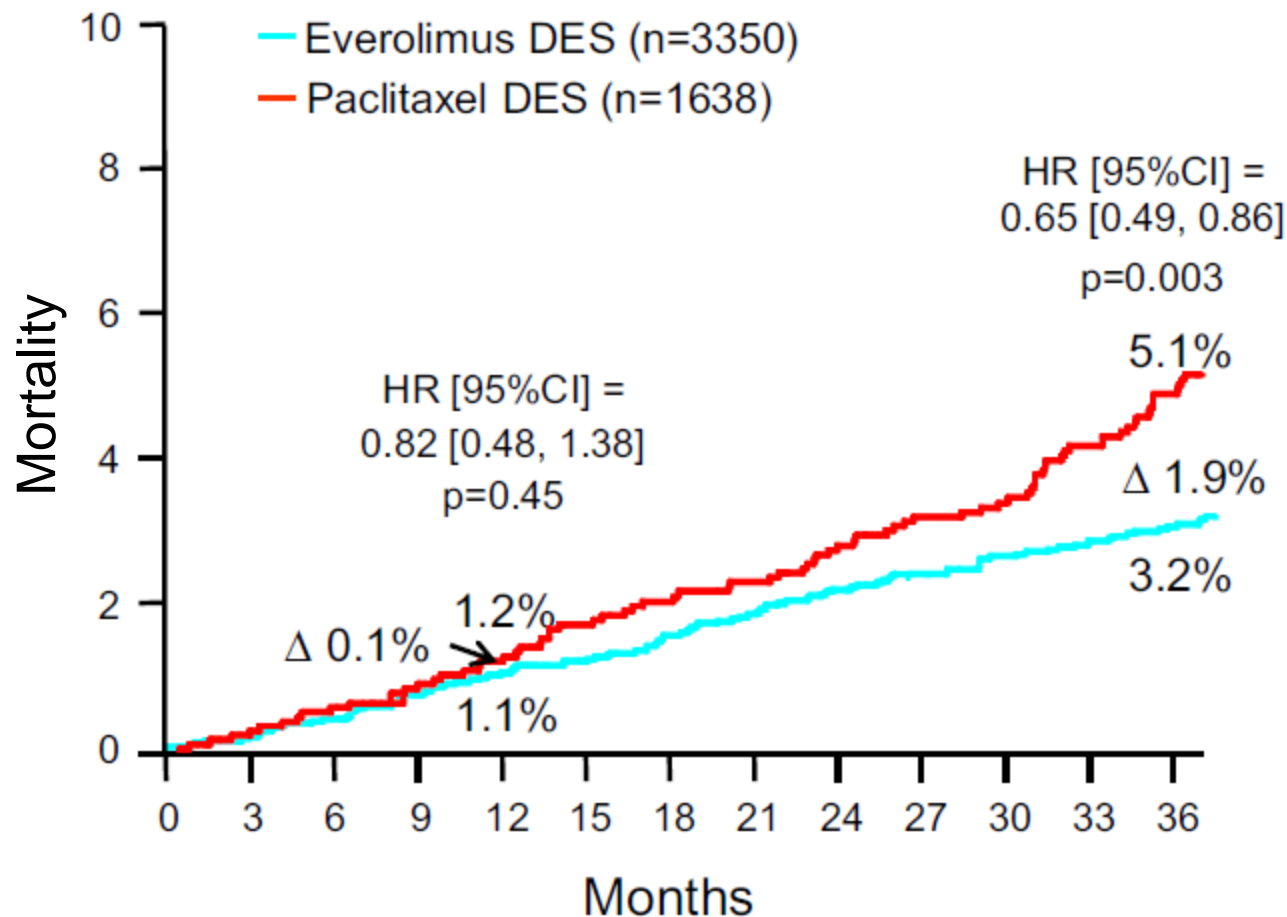
Background

- 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.



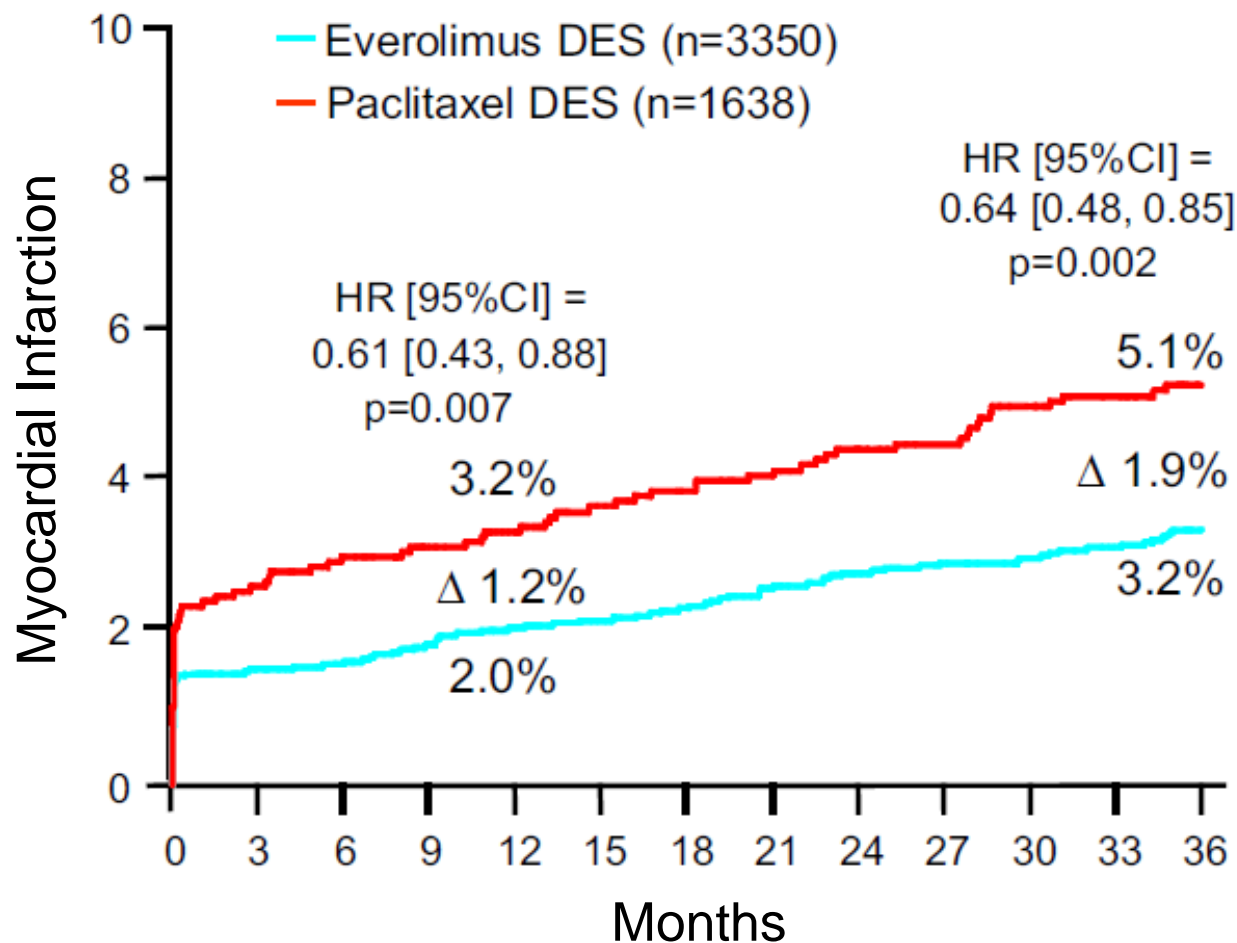
Background:

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



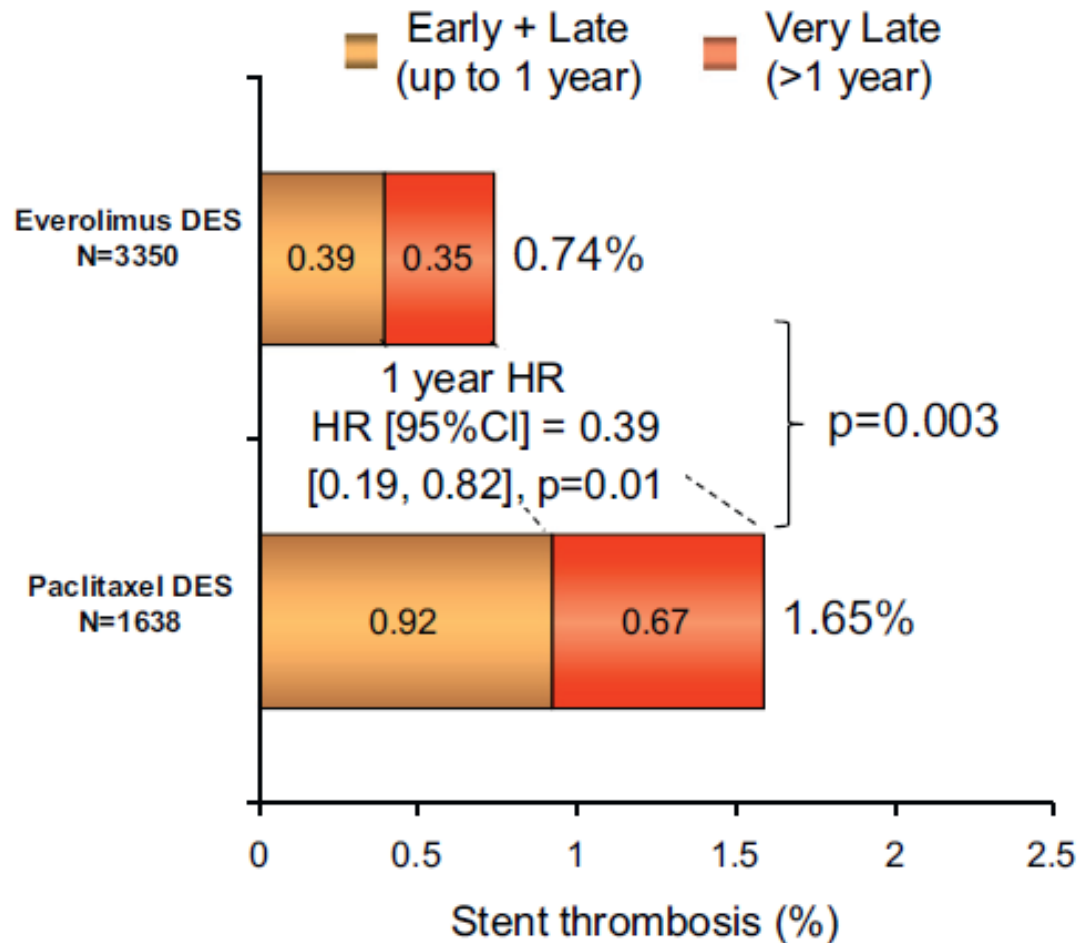
Background:

3 Year MI Benefit of 2nd Generation DES



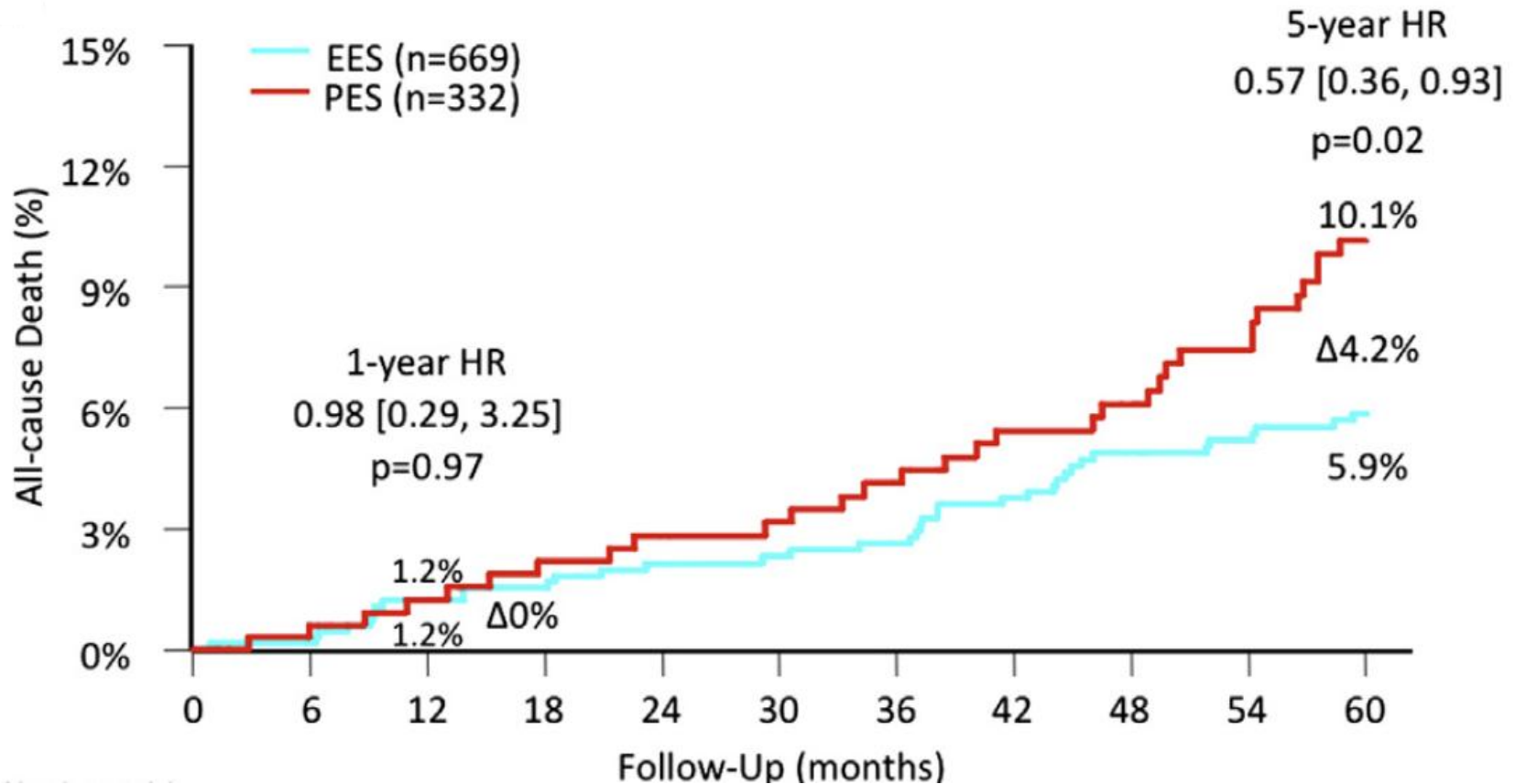
Background:

3 Year Stent Thrombosis Benefit of 2nd Generation DES



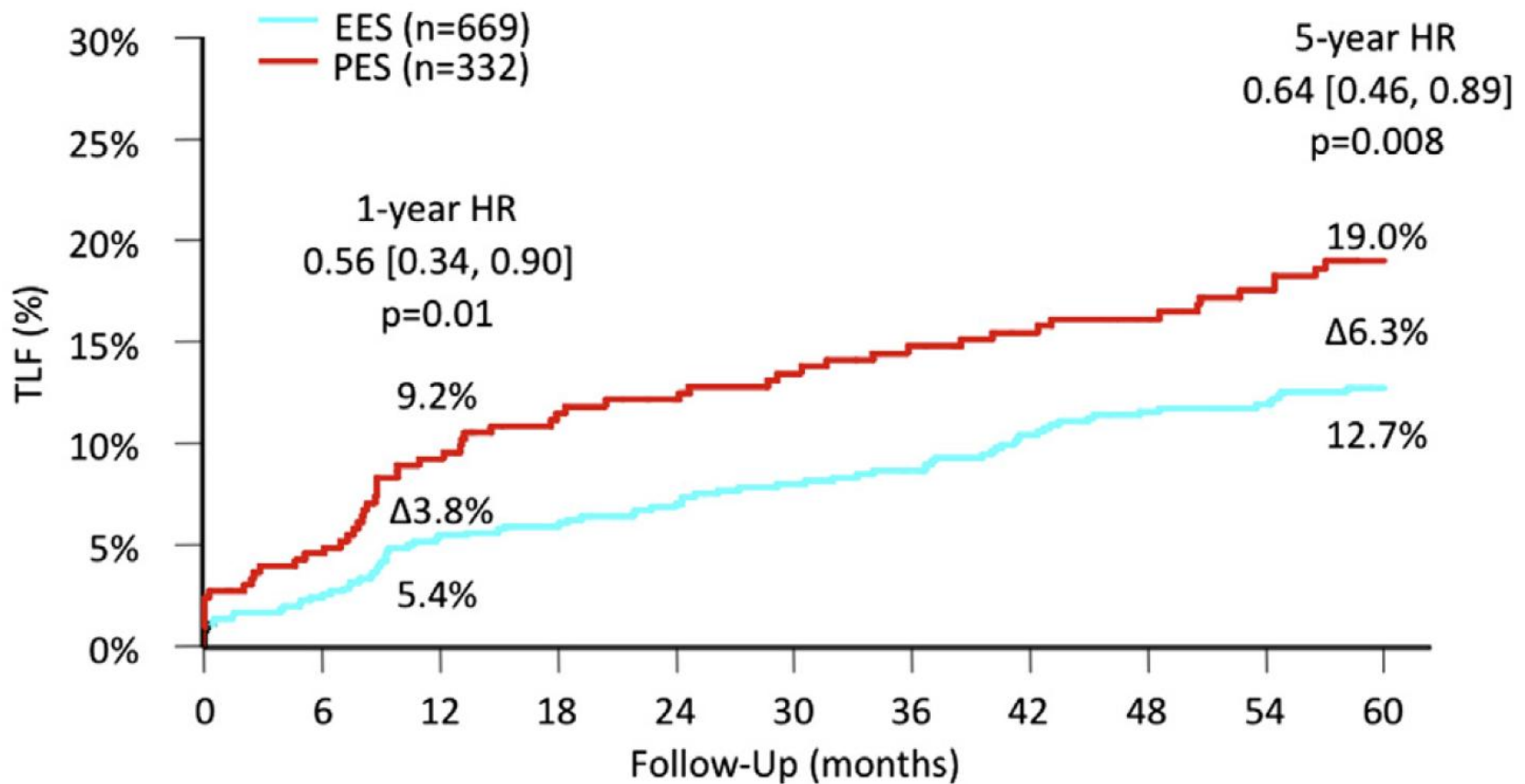
Background:

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



Background:

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

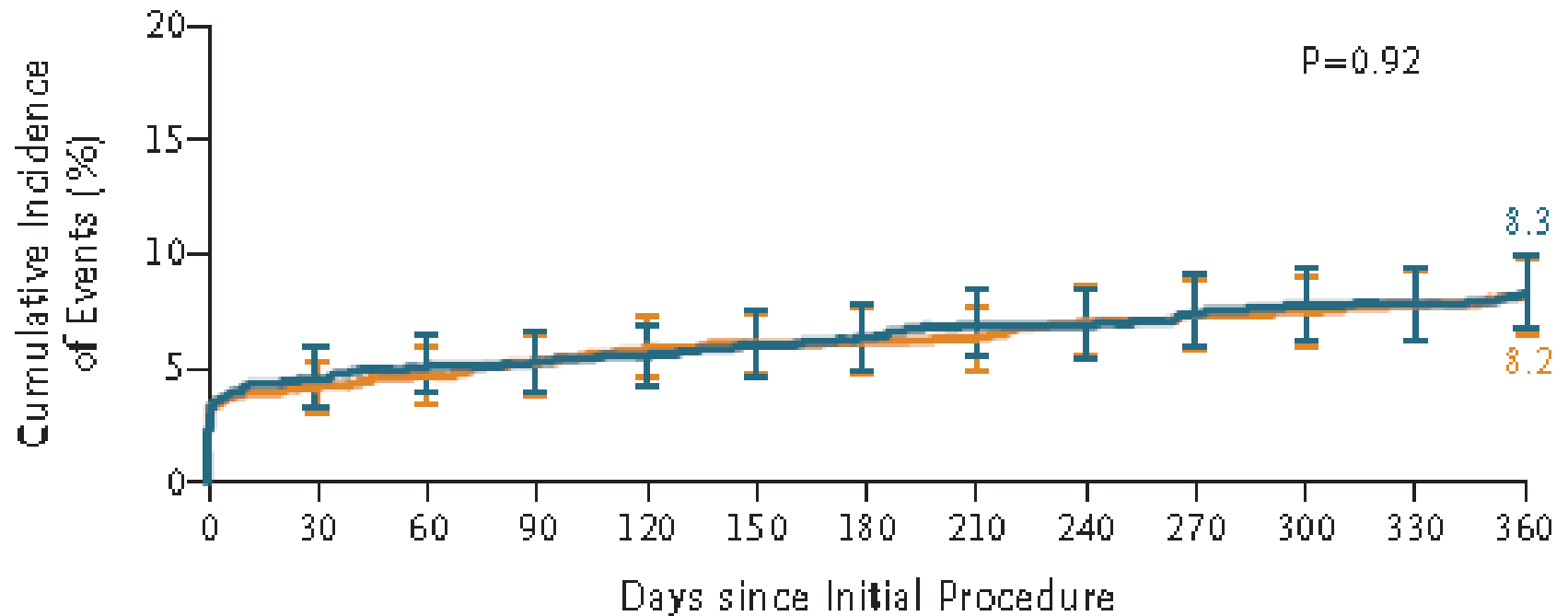


Background:

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

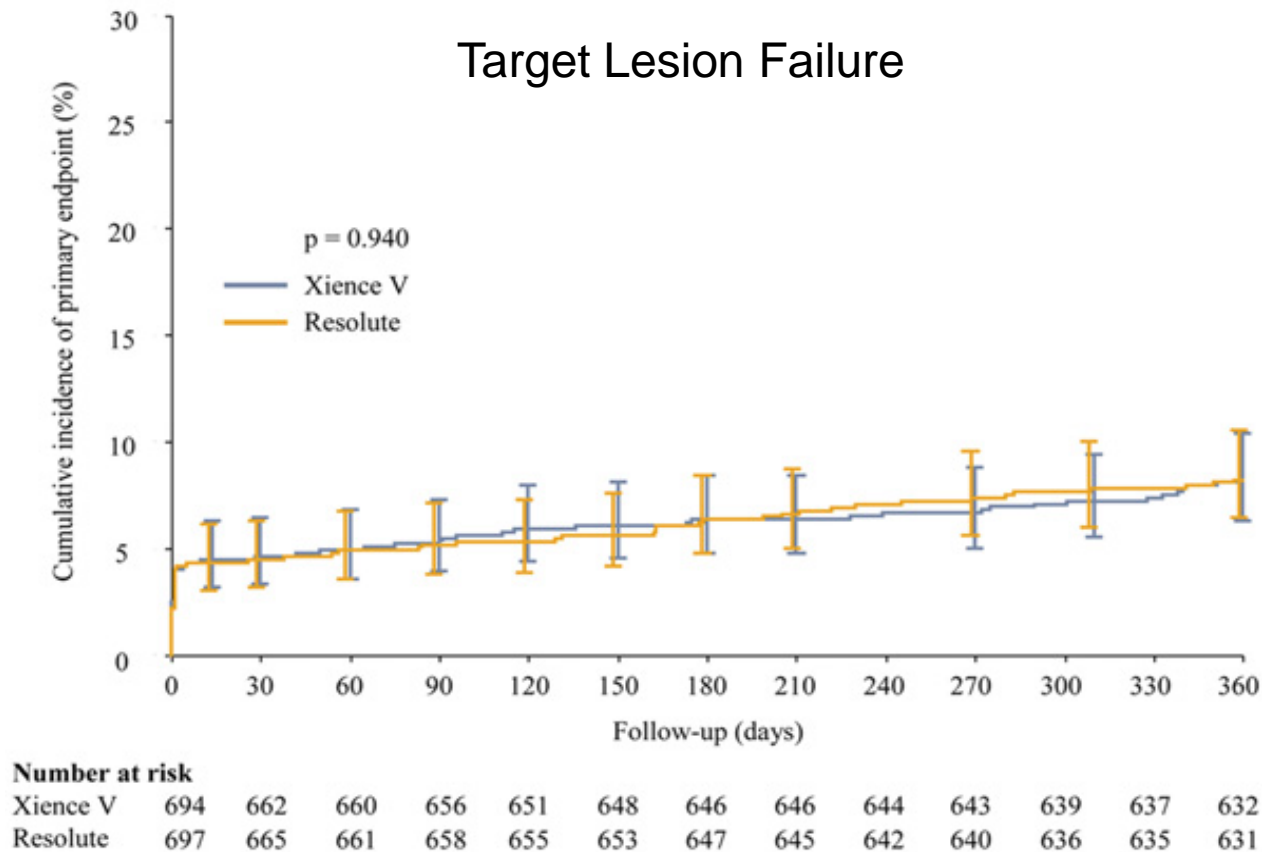
Target-Lesion Failure

Target Lesion Failure



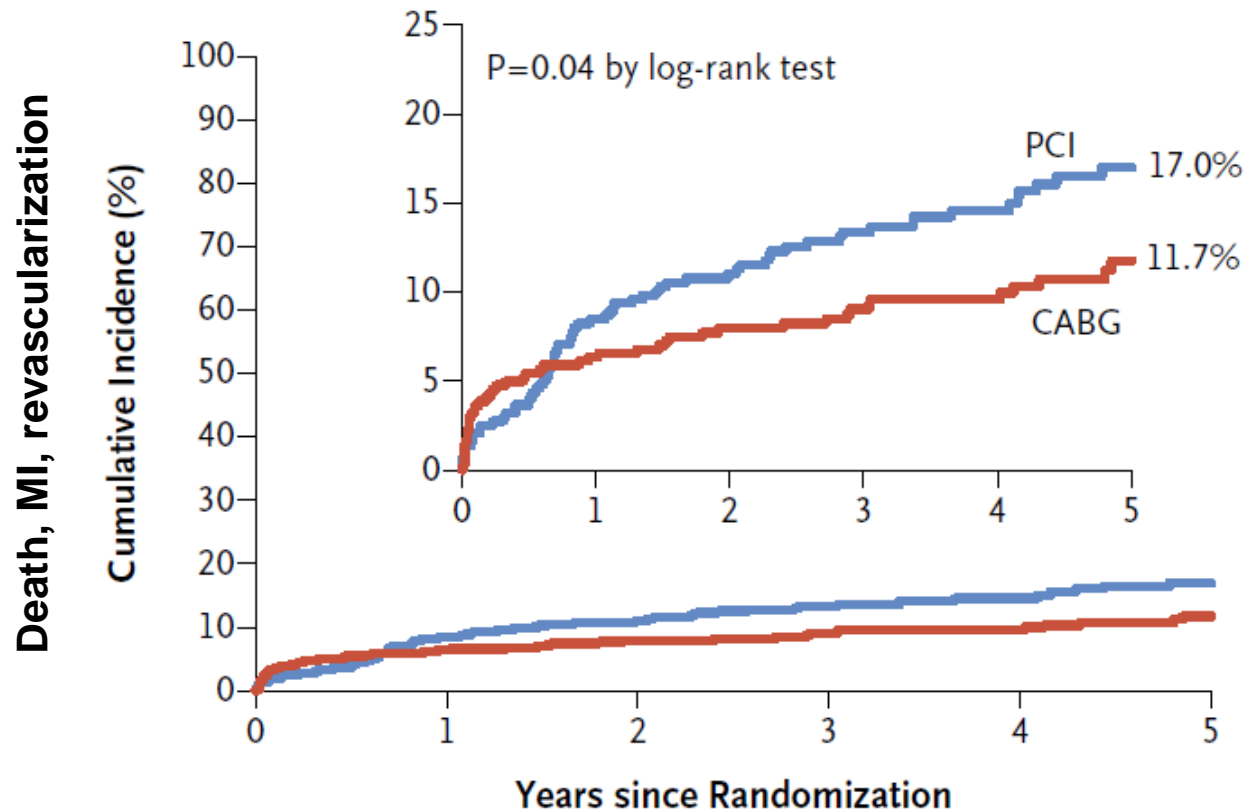
Background:

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



BEST Trial

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



No. at Risk

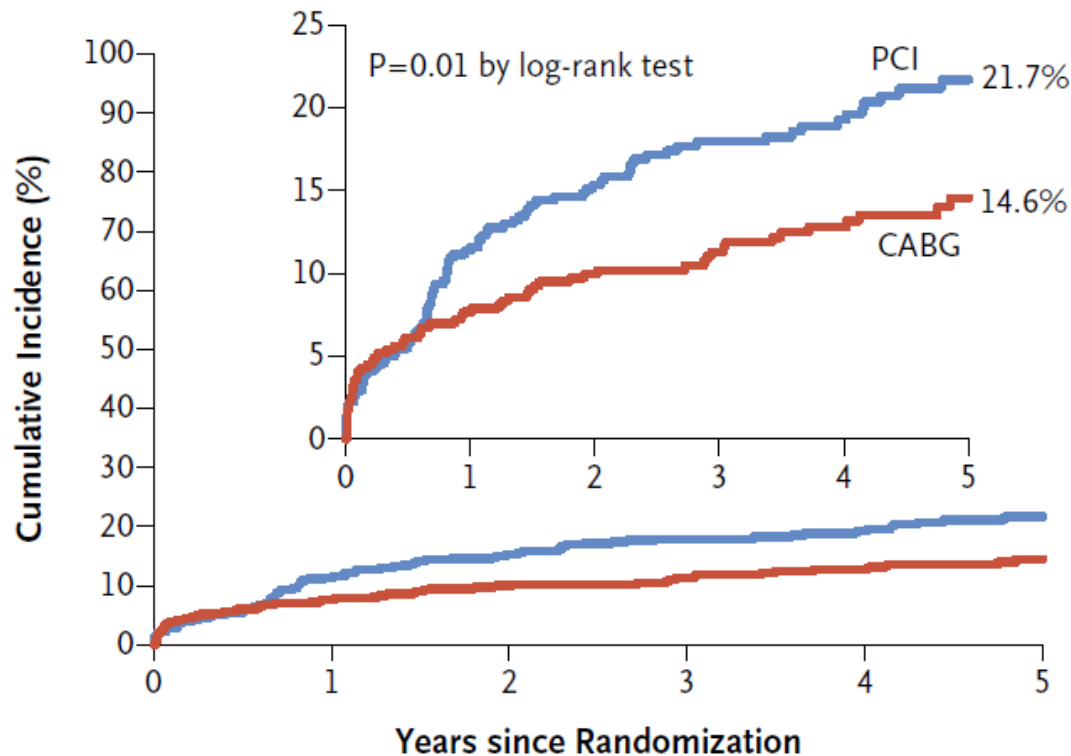
PCI	438	402	362	305	242	126
CABG	442	415	377	326	262	145



BEST Trial

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

Death, Myocardial Infarction, Stroke, or Repeat Revascularization

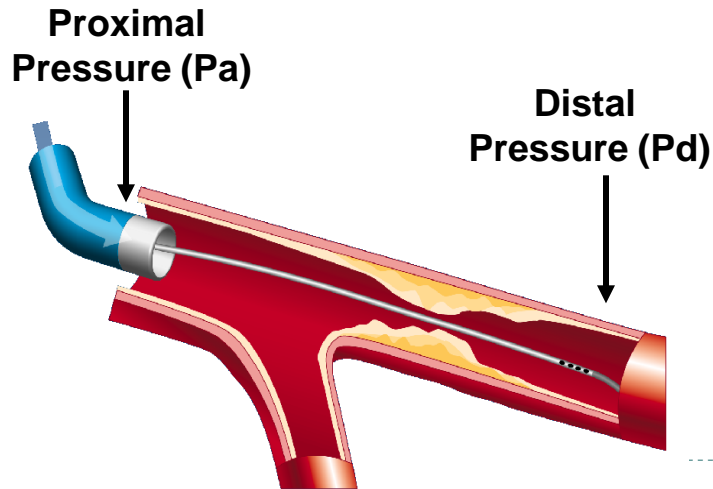


No. at Risk

PCI	438	389	341	288	229	117
CABG	442	409	368	317	250	137

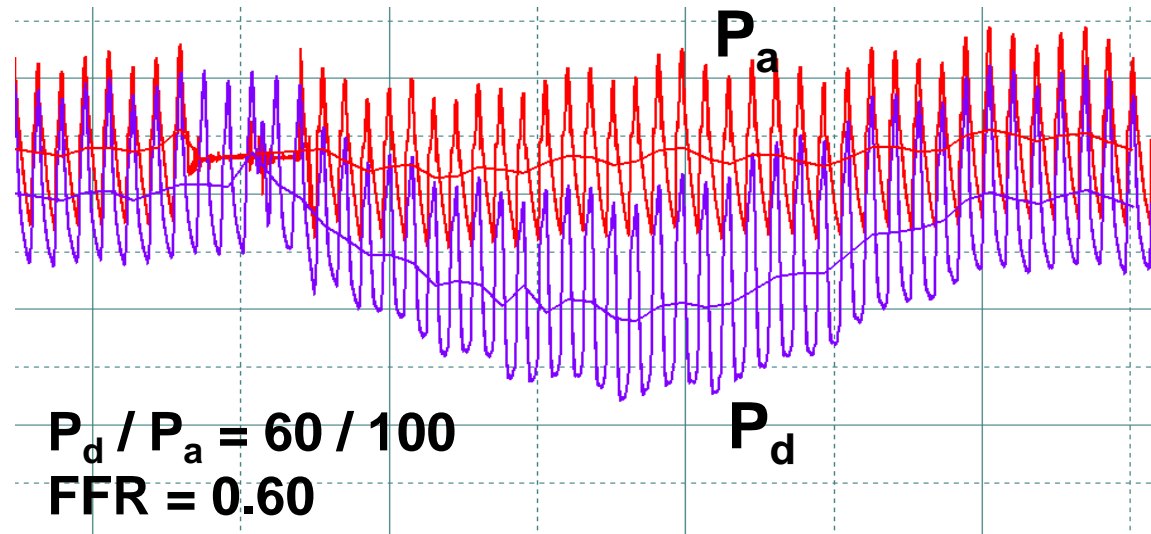


What else has changed?



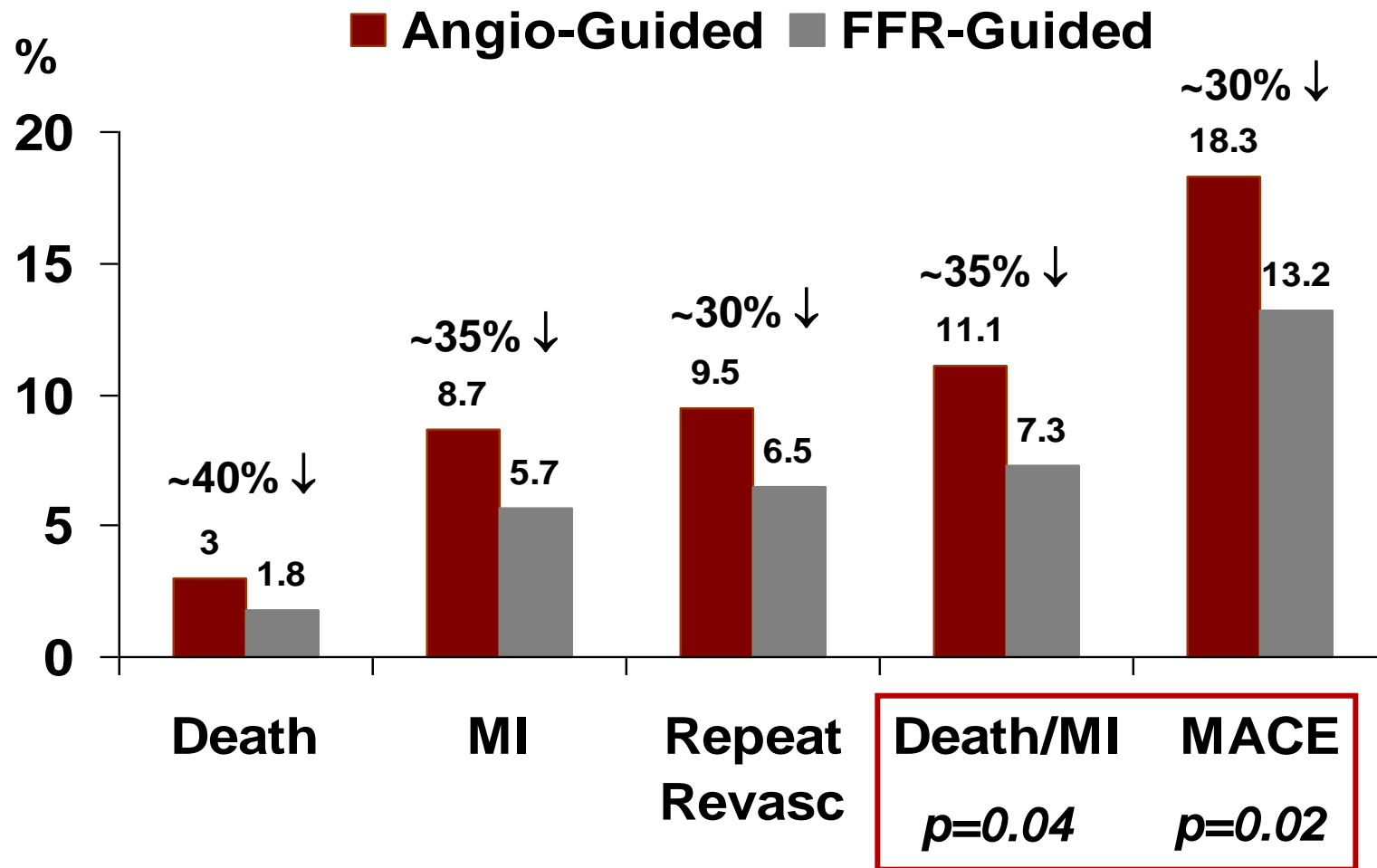
$$\text{FFR} = P_d / P_a$$

during maximal flow



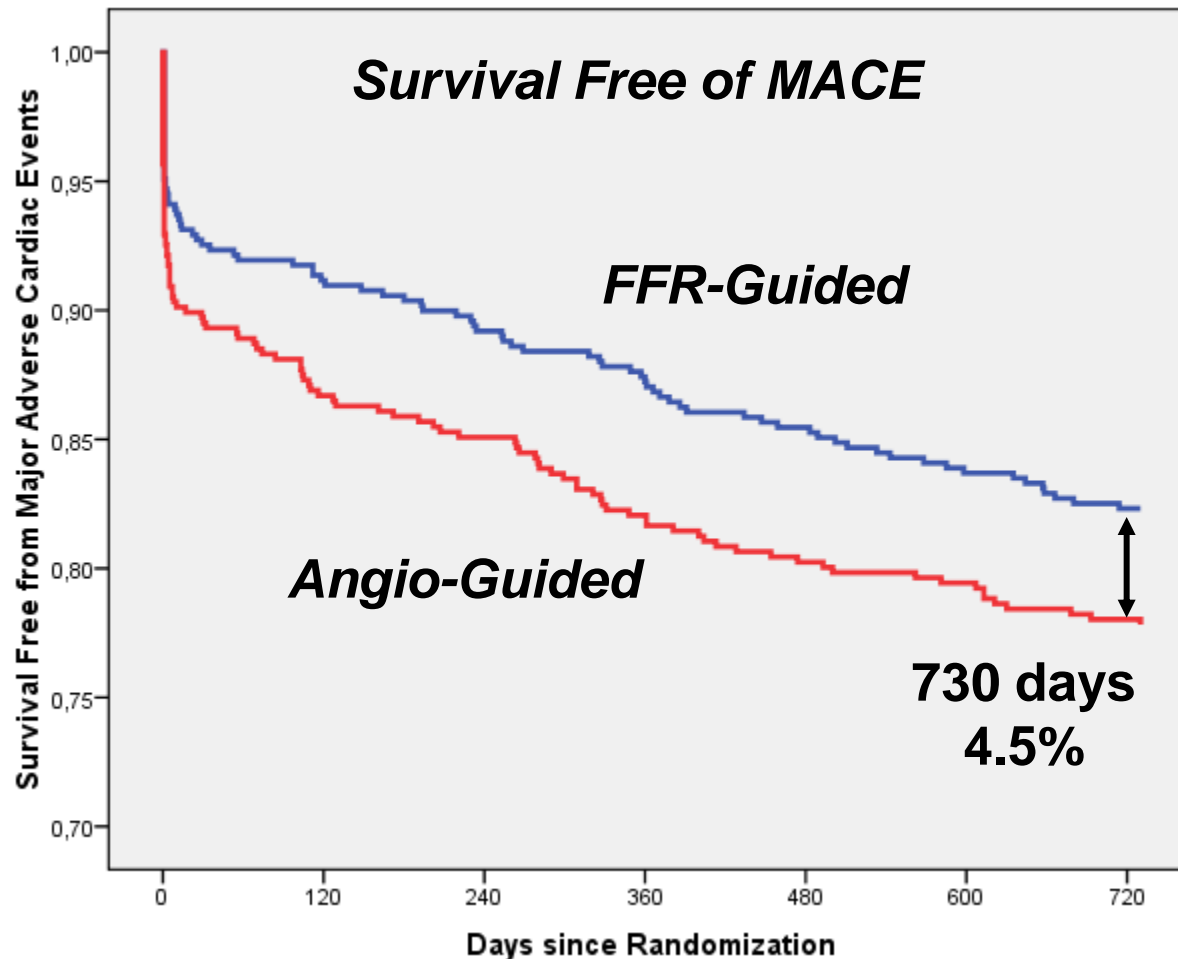
FAME Study: One Year Outcomes

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

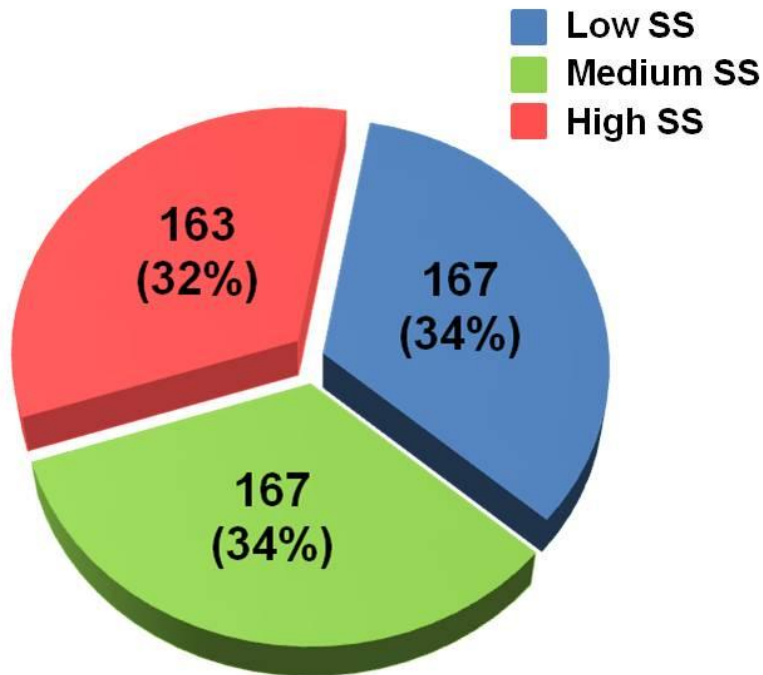


FAME Study: Two Year Outcomes

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



Functional SYNTAX Score

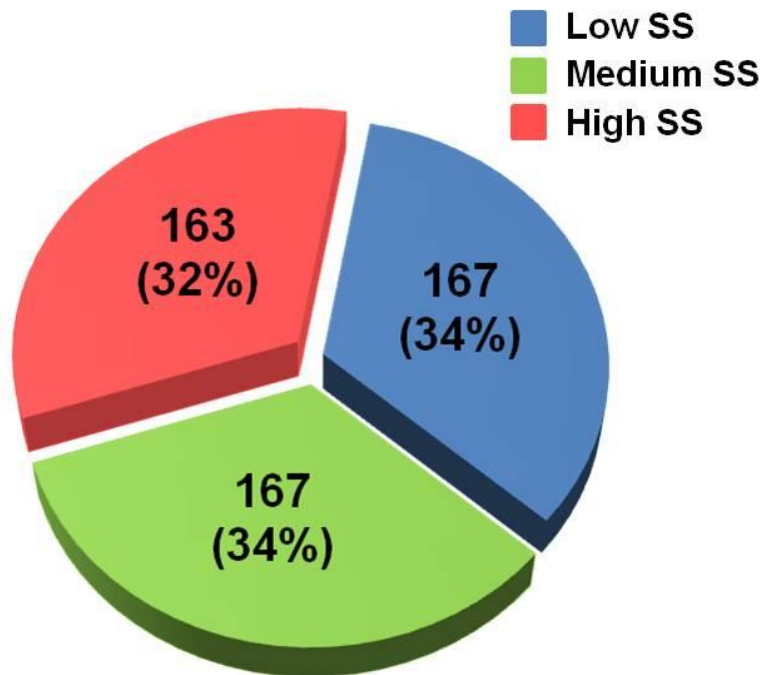


Without FFR

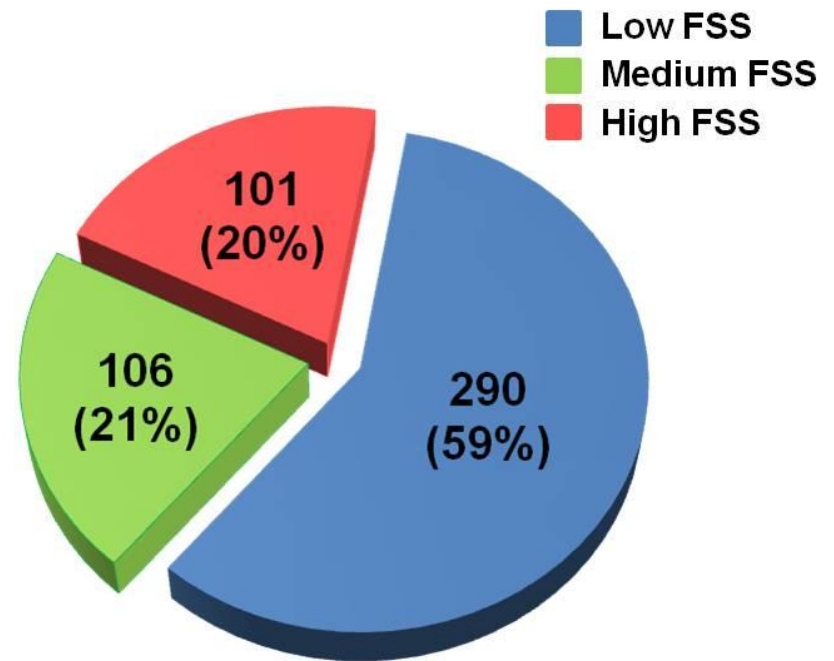


Functional SYNTAX Score

Reclassifies > 30% of cases



Without FFR

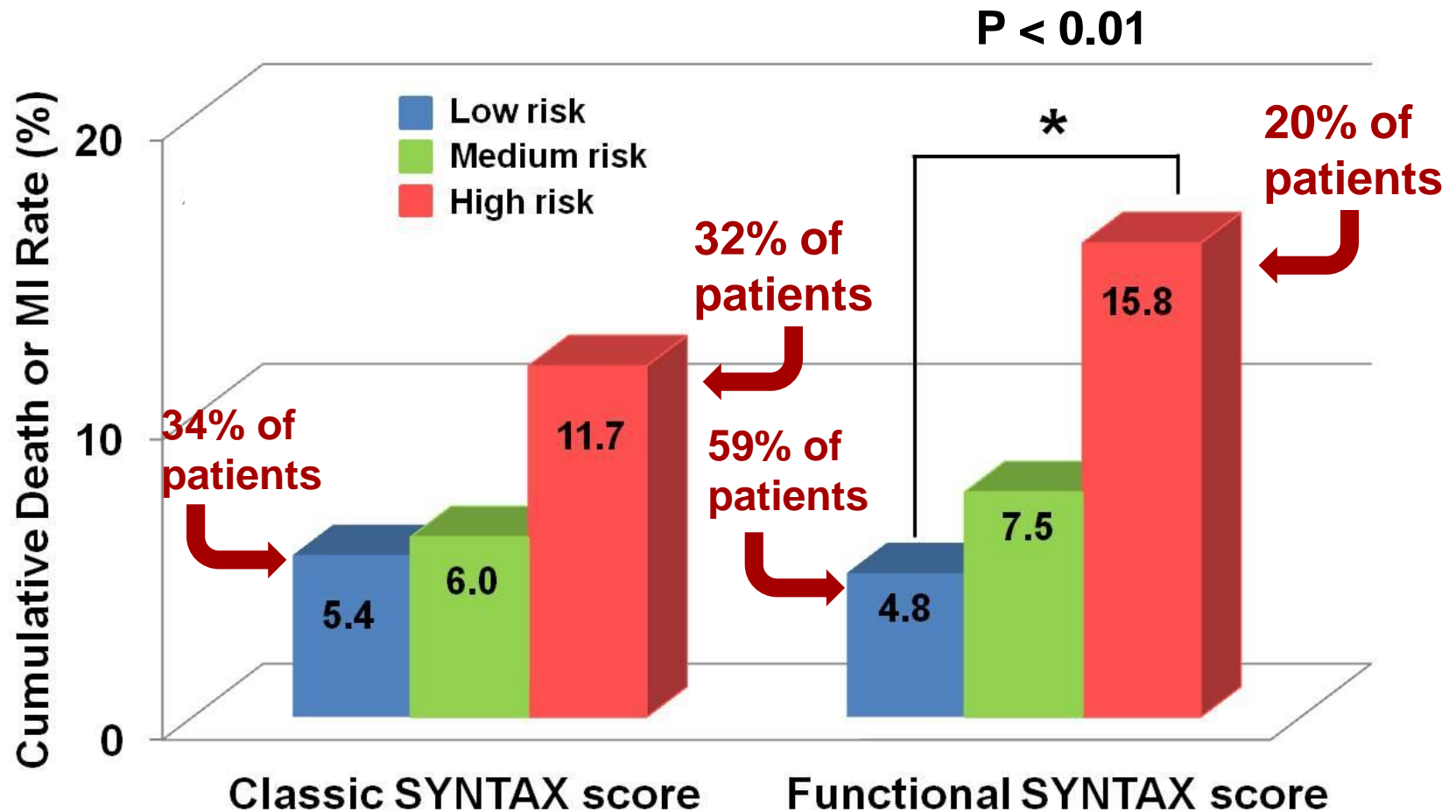


With FFR

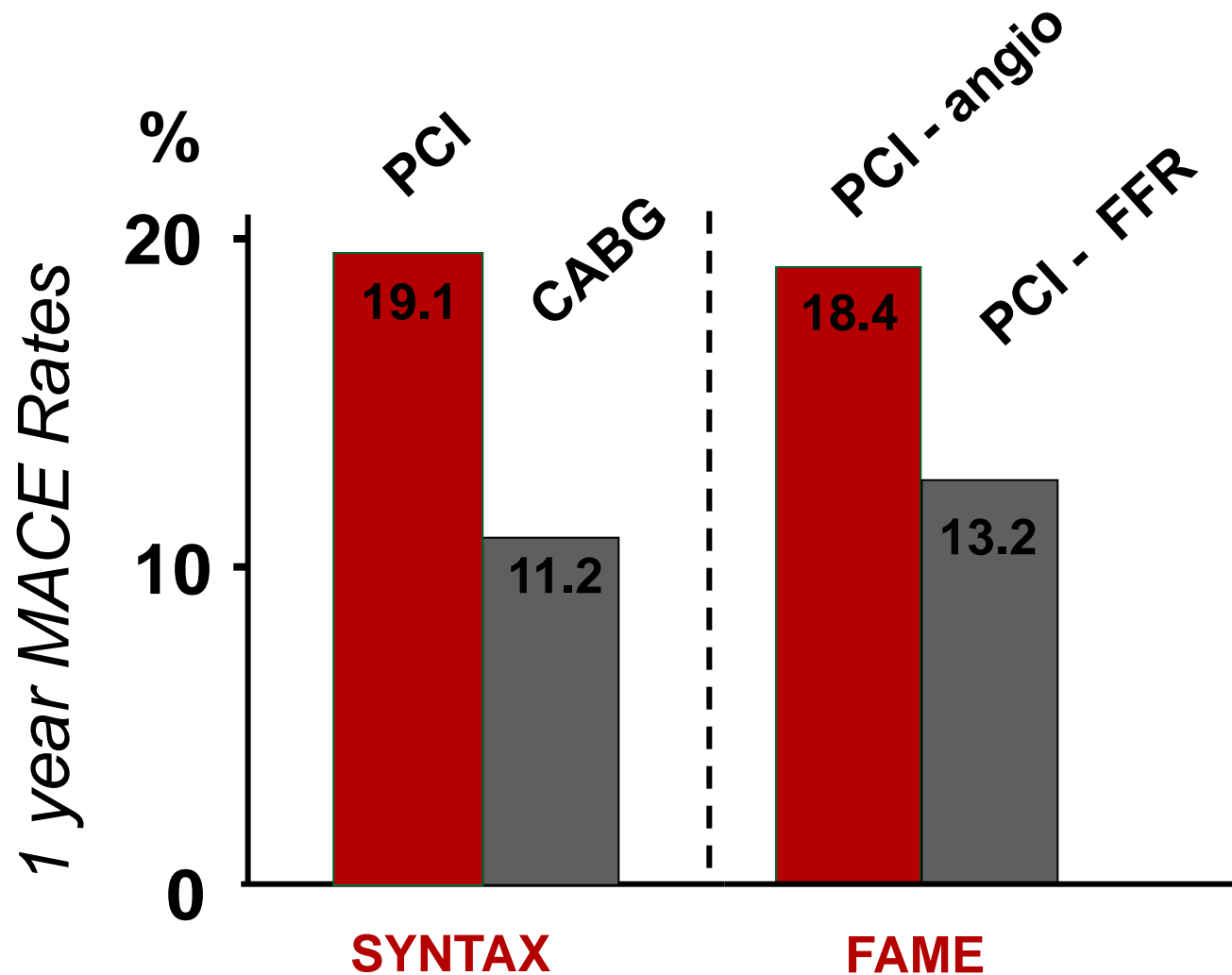


Functional SYNTAX Score

Discriminates Risk for Death/MI



Why FAME 3?



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:

**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 $\text{FFR} \leq 0.80$
(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



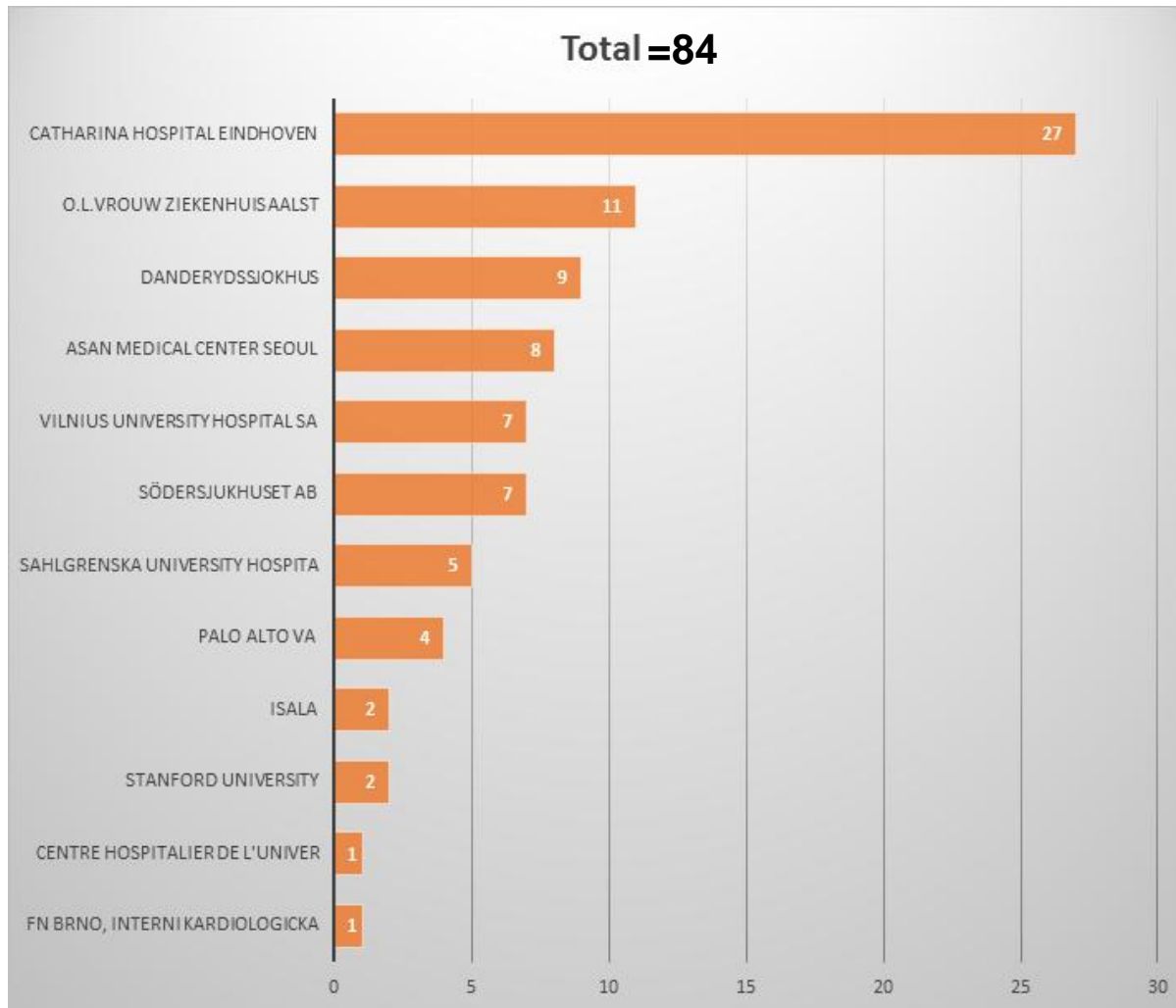
FAME 3

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.



Will FFR-Directed PCI be Better Than CABG?

Yes!

- With current generation DES
- Applying FFR guidance to optimize ischemia reduction and minimize stent complications
- Optimizing medical therapy to reduce plaque progression

....and No

- Complex disease will remain a limitation
- Long-term outcomes in diabetics will be a challenge
- Revascularization will remain higher



Thank You!

