FFR and Multivessel CAD:
Improve Patient Selection for 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	Company
Grant/ Research Support:	**Abbott, Medtronic, Acist, CathWorks, Edwards LifeSciences**
Consulting Fees/Honoraria:	**Boston Scientific**
Major Stock Shareholder/Equity Interest:	
Royalty Income:	
Ownership/Founder:	
Salary:	
Intellectual Property Rights:	
Other Financial Benefit (stock options):	**HeartFlow**

Using FFR to Decide PCI vs CABG

- Is “functionally complete” revascularization with deferral of CAD based on FFR as effective as anatomic complete revascularization?

- Does ischemia trump anatomy?

Impact of SYNTAX Score on PCI

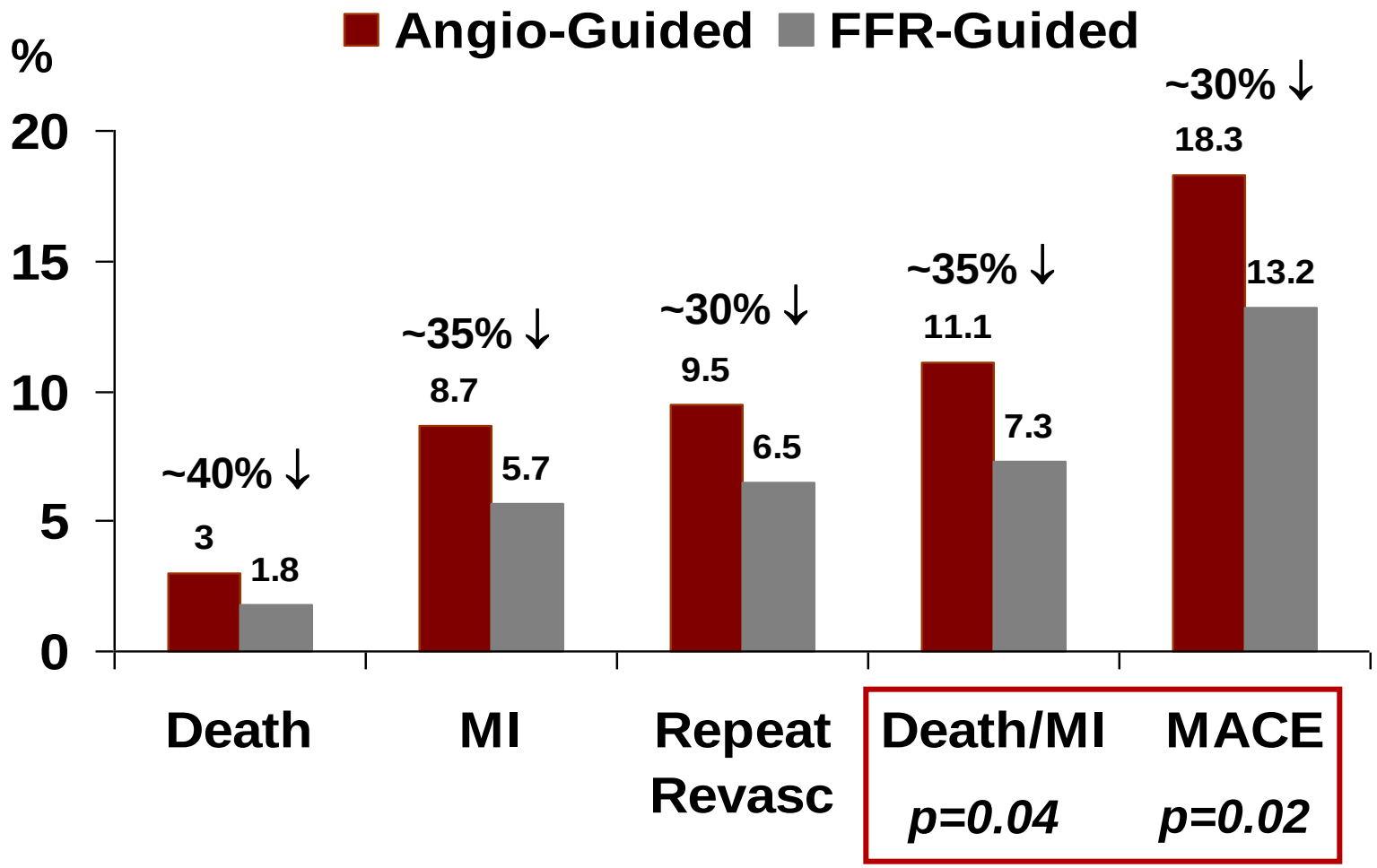
US Appropriate Use Criteria for Coronary Revascularization

UPLM or complex CAD		
CABG and PCI	I—Heart Team approach recommended	C
CABG and PCI	IIa—Calculation of STS and SYNTAX scores	B
UPLM*		
CABG	I	B
PCI	IIa—For SIHD when *both* of the following are present: ■ Anatomic conditions associated with a low risk of PCI procedural complications and a high likelihood of good long-term outcome (e.g., a low SYNTAX score of ≤22, [illegible]k left main CAD) ■ Clinical characteristics that predict a significantly increased risk of adverse surgical outcomes (e.g., STS-predicted risk of operative mortality ≥5%)	B
	IIa—For UA/NSTEMI if not a CABG candidate	B
	IIa—For STEMI when distal coronary flow is TIMI flow grade <3 and PCI can be performed more rapidly and safely than CABG	C
	IIb—For SIHD when *both* of the following are present: ■ Anatomic conditions associated with a low to intermediate risk of PCI procedural complications and an intermediate to high likelihood of good long-term outcome (e.g., low-intermediate SYNTAX score of <33, b[illegible]eft main CAD) ■ Clinical characteristics that predict an increased risk of adverse surgical outcomes (e.g., moderate—severe COPD, disability from prior stroke, or prior cardiac surgery; STS-predicted operative mortality >2%)	B
	III: Harm—For SIHD in patients (versus performing CABG) with unfavorable anatomy for PCI and who are good candidates for CABG	B

Patel, et al. J Am Coll Cardiol 2017;69:2212-41

FAME 1: One Year Outcomes

1,005 patients with multivessel CAD randomized to FFR-guided vs angiography-guided PCI



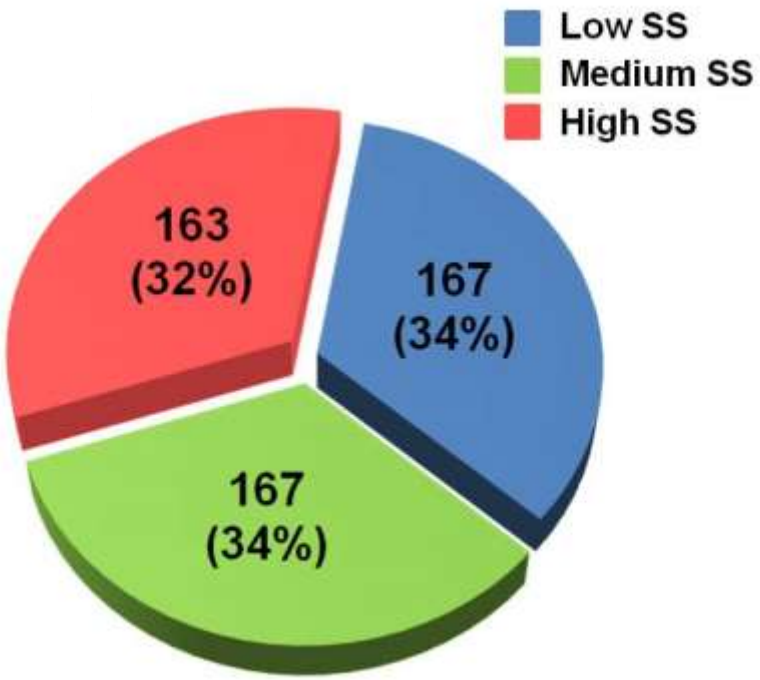
Tonino, et al. New Engl J Med 2009;360:213-24.

Anatomic vs. Functional CAD

Patients with angiographically 3VD (N=115), proportions per number of diseased vessels after assessment by FFR

Tonino, et al. J Am Coll Cardiol 2010;55:2816-21.

Functional SYNTAX Score (FSS)

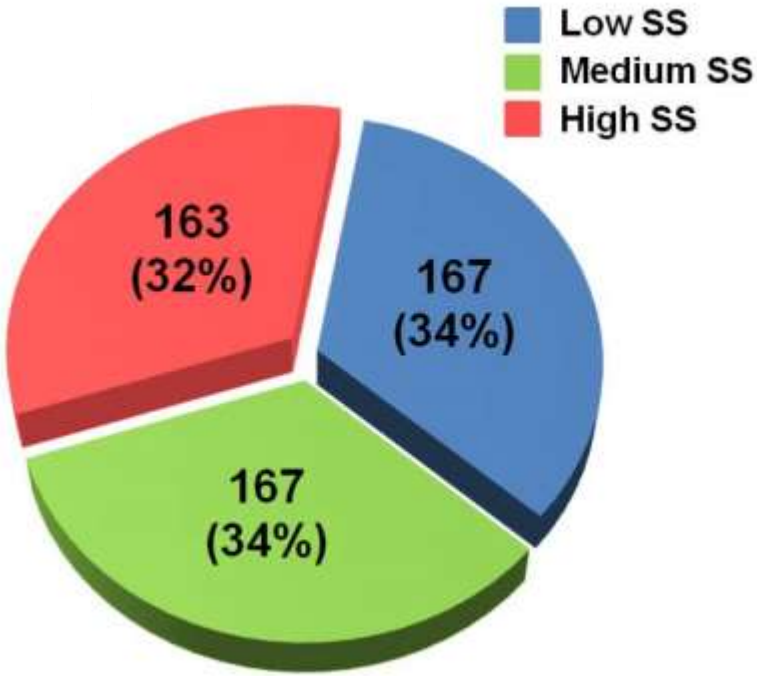


Without FFR

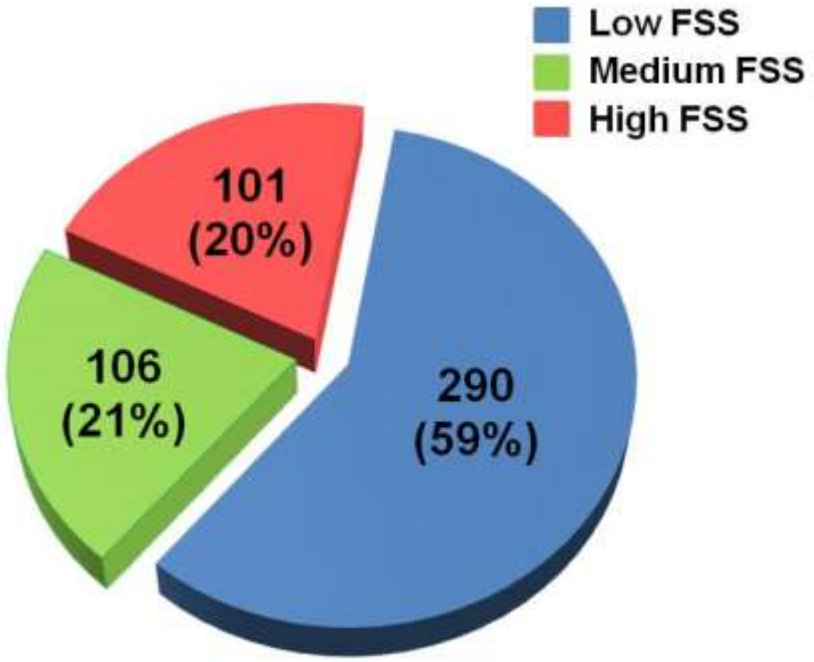
Nam CW, et al. J Am Coll Cardiol 2011;58:1211-8

Functional SYNTAX Score (FSS)

Reclassifies > 30% of Cases



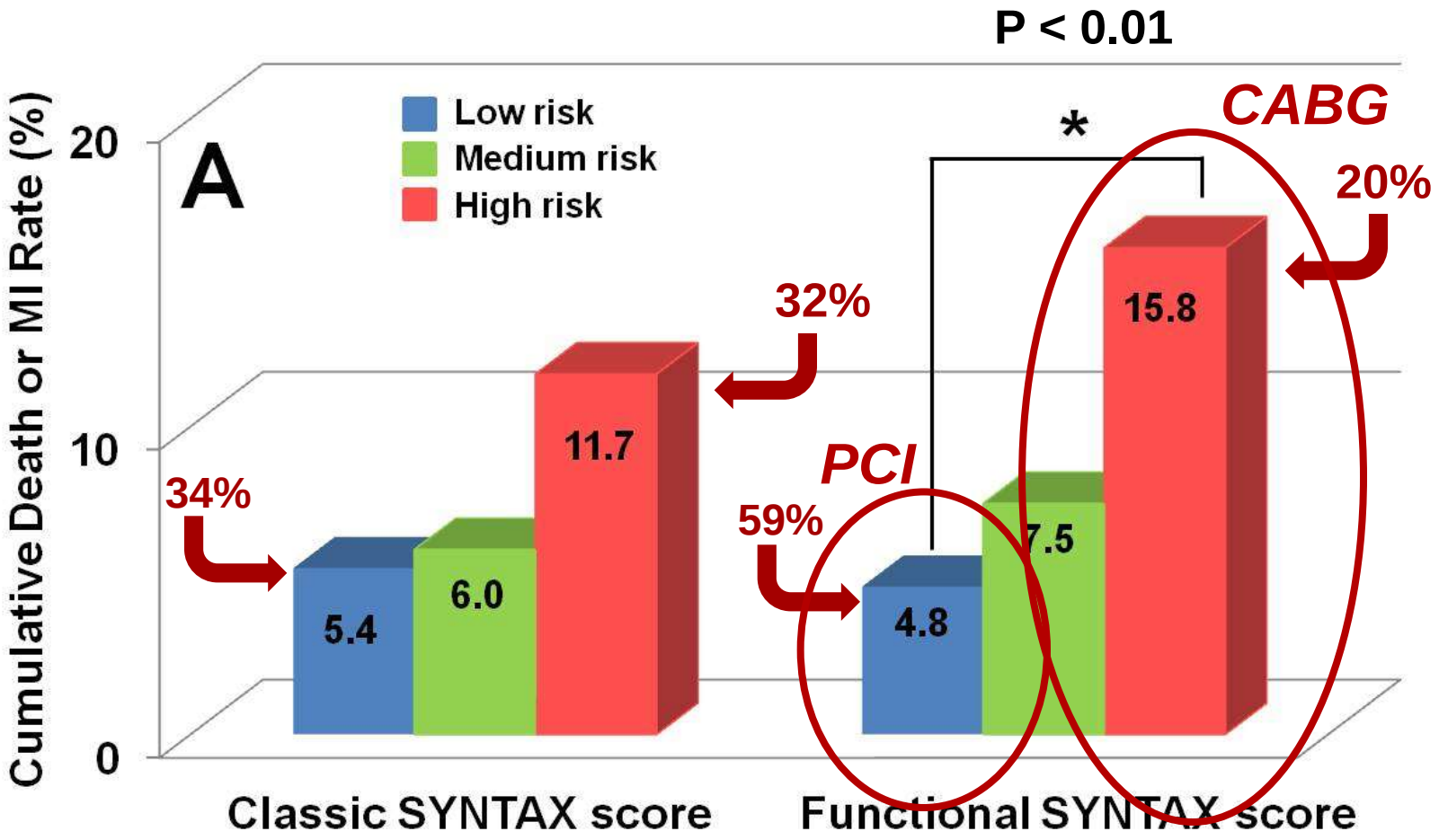
Without FFR



With FFR

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

FSS Discriminates Risk for Death/MI



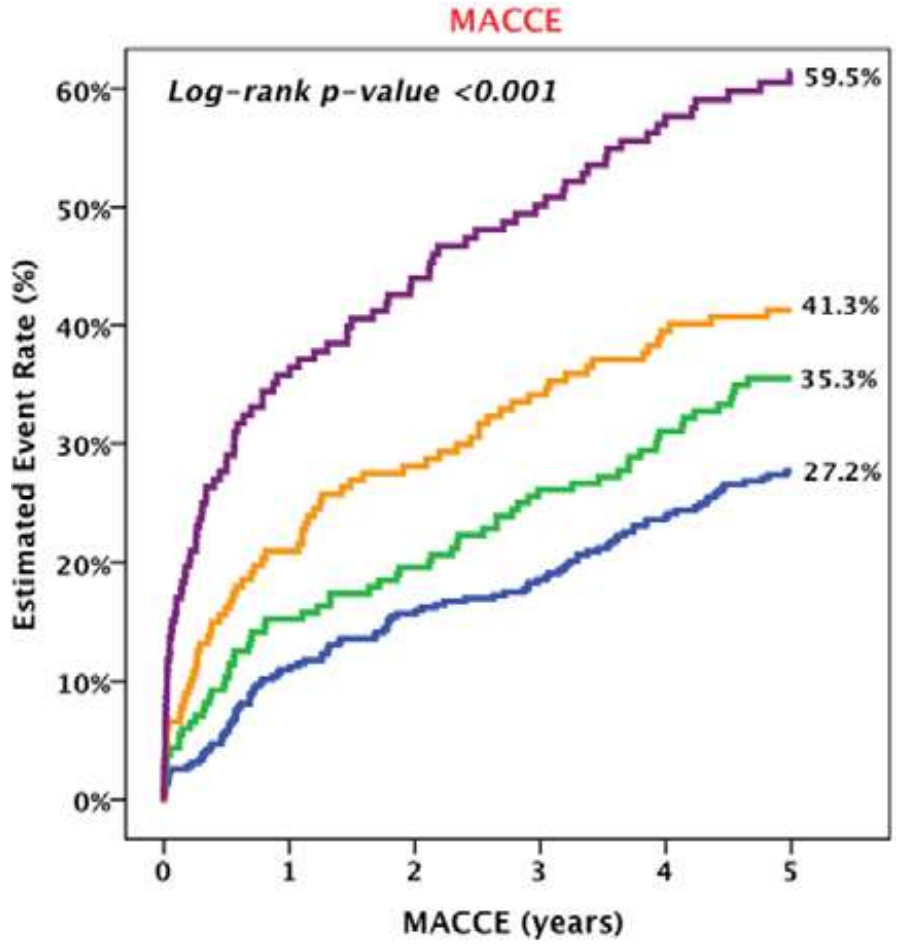
Nam CW, et al. J Am Coll Cardiol 2011;58:1211-8

Residual SYNTAX Score (RSS)

- Calculation of the SYNTAX score after revascularization.
- A reflection of the residual degree of atherosclerosis.
- After angiography-guided revascularization, the RSS predicts future MACE.

RSS after Angio-guided PCI

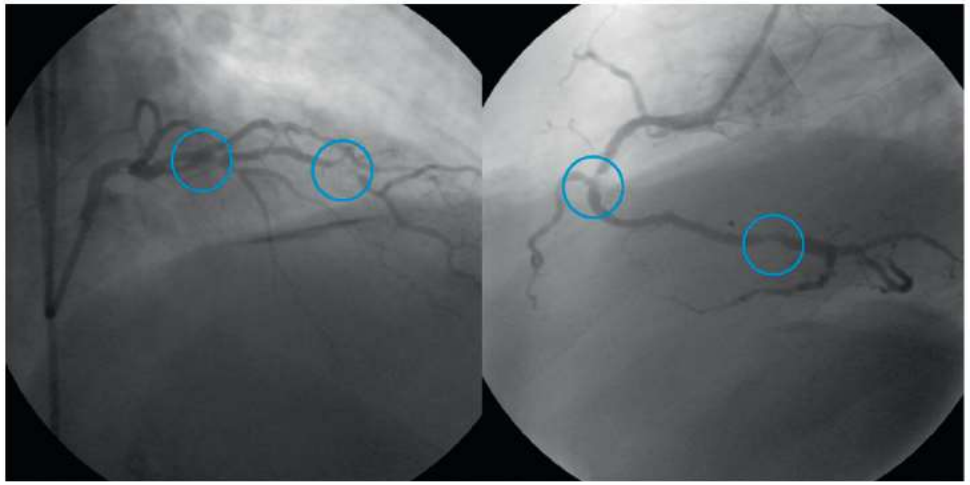
RSS was strongly correlated with outcome in the SYNTAX trial.



Farooq, V et al. Circulation 2013;128(2):141-51

RSS after FFR-guided PCI

Residual SYNTAX Score calculated after FFR-guided PCI in 427 patients in FAME 1



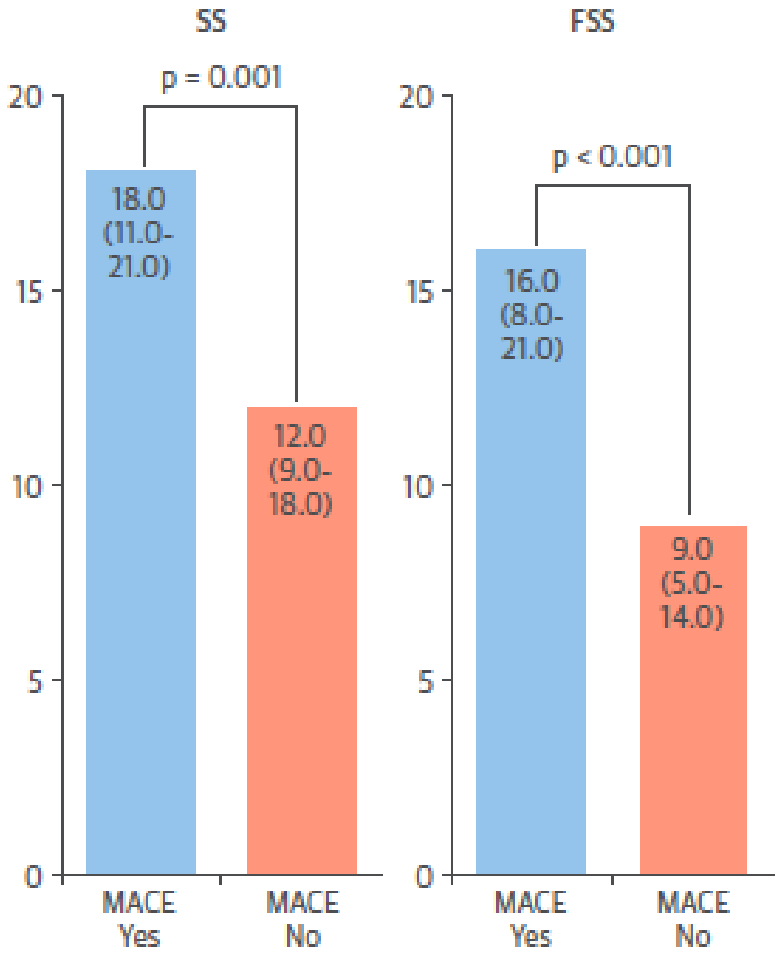
<u>Case 1</u>
SYNTAX Score (SS) = 16
Functional SS = 16
Residual SS = 0

<u>Case 2</u>
SYNTAX Score (SS) = 16
Functional SS = 8
Residual SS = 8

Kobayashi, et al. J Am Coll Cardiol 2016;67:1701-11.

RSS after FFR-guided PCI

Residual SYNTAX Score calculated after FFR-guided PCI in 427 patients in FAME 1



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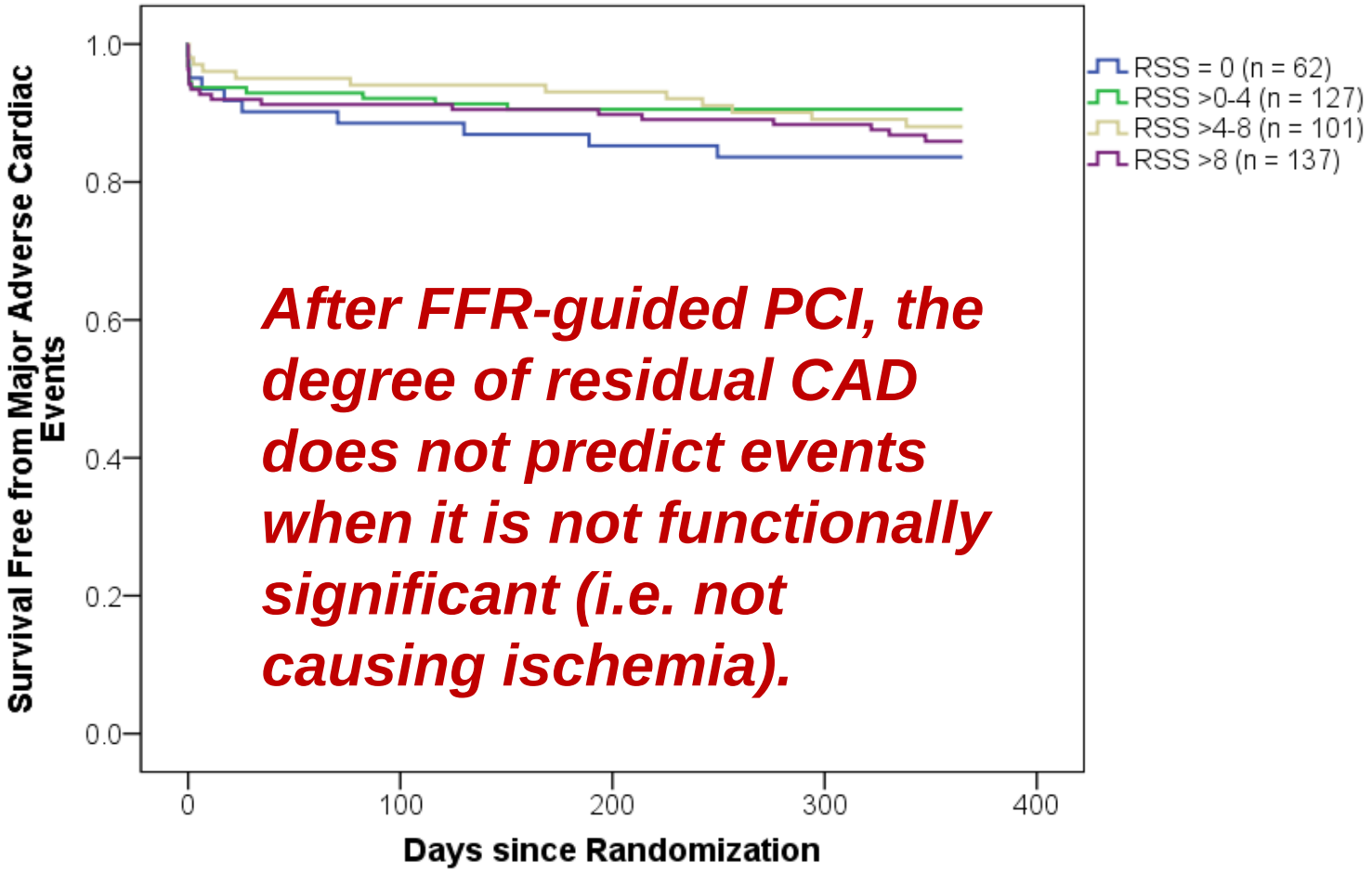
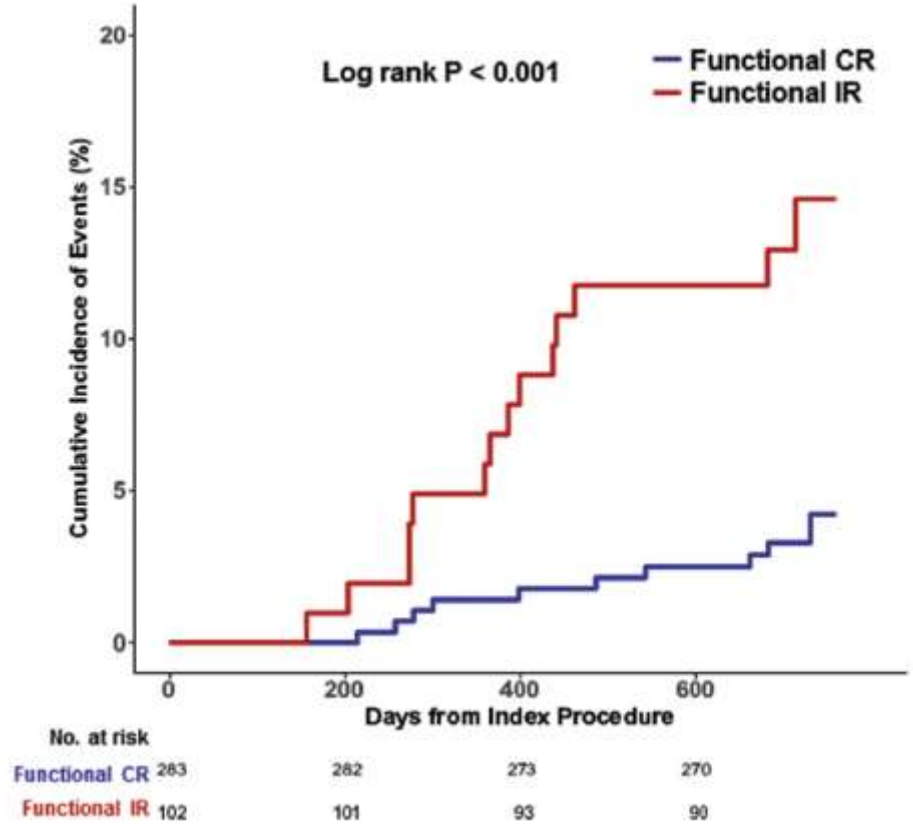


After FFR-guided PCI, the degree of residual CAD does not predict events when it is not functionally significant (i.e. not causing ischemia).

Kobayashi, et al. J Am Coll Cardiol 2016;67:1701-11.

Residual Functional SYNTAX Score

385 patients underwent 3 vessel FFR and PCI. Functionally complete revascularization (residual functional SYNTAX score<1) was compared with functionally incomplete revascularization (rFSS≥1)



Choi, et al. J Am Coll Cardiol Intv 2018;11:237-45.

Residual Functional SYNTAX Score

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	Functional CR	Functional IR
Major adverse cardiac events*	10 (4.2)	14 (14.6)
Cardiac death or myocardial infarction	2 (0.8)	5 (6.2)
Cardiac death	0 (0)	1 (1.0)
All-cause death	4 (1.4)	1 (1.0)
Myocardial infarction	2 (0.8)	4 (5.2)
Ischemia-driven revascularization	10 (4.2)	13 (13.7)

Choi, et al. J Am Coll Cardiol Intv 2018;11:237-45.

Residual Functional SYNTAX Score

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Independent Predictors of MACE

Model 1*		
Functional IR	4.17 (1.85-9.44)	<0.001
Acute coronary syndrome	1.37 (0.60-3.10)	0.452
Diabetes mellitus	0.79 (0.32-1.94)	0.600
Age (per year)	1.02 (0.97-1.06)	0.424
Model 2†		
rFSS (as a continuous value)	1.09 (1.02-1.18)	0.018
Acute coronary syndrome	1.40 (0.62-3.12)	0.413
Diabetes mellitus	0.83 (0.33-2.09)	0.697
Age (per year)	1.02 (0.97-1.06)	0.453

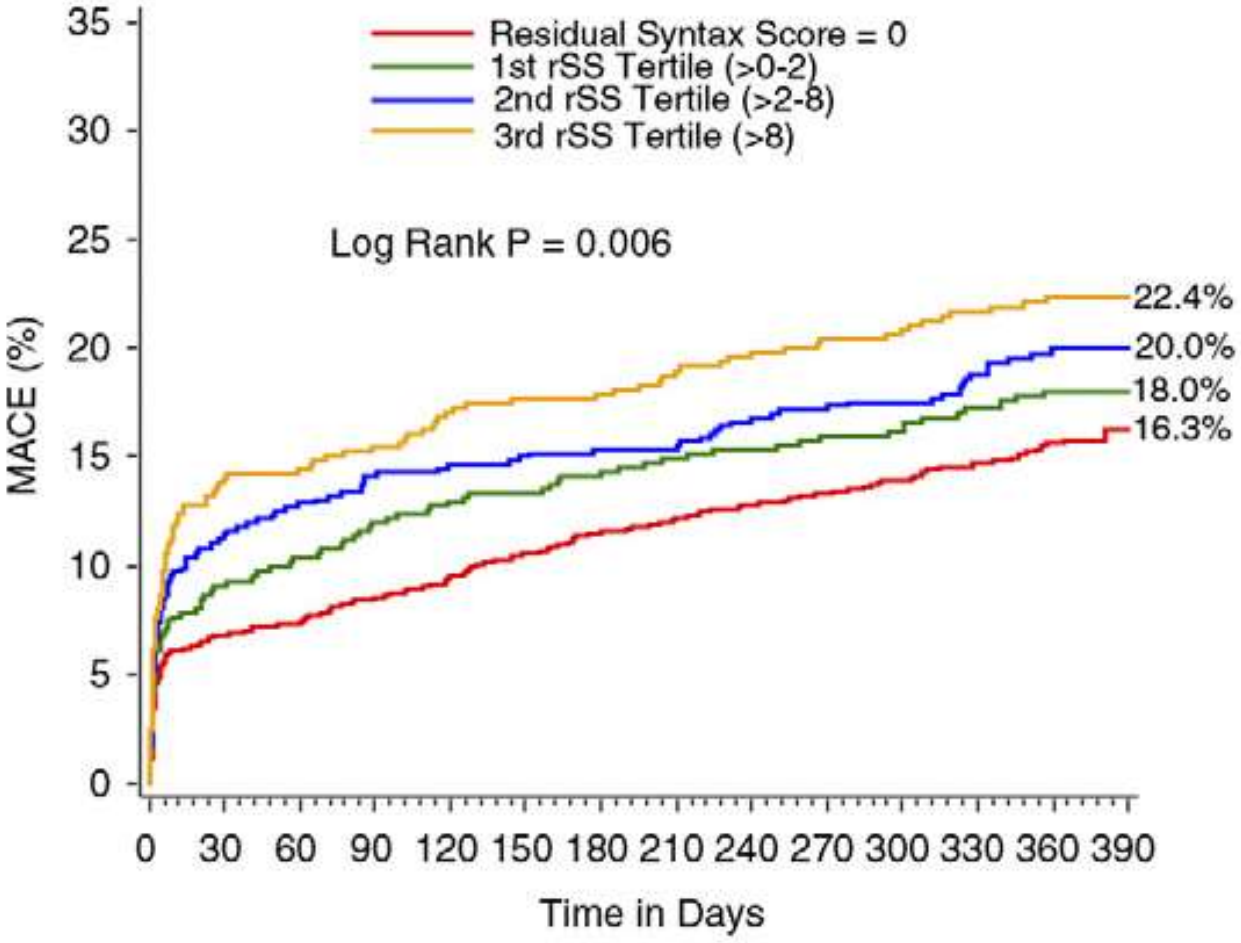
Choi, et al. J Am Coll Cardiol Intv 2018;11:237-45.

What about in ACS?

Are there non-culprit plaques which are biologically active and prone to rupture, even though they may not be functionally significant?

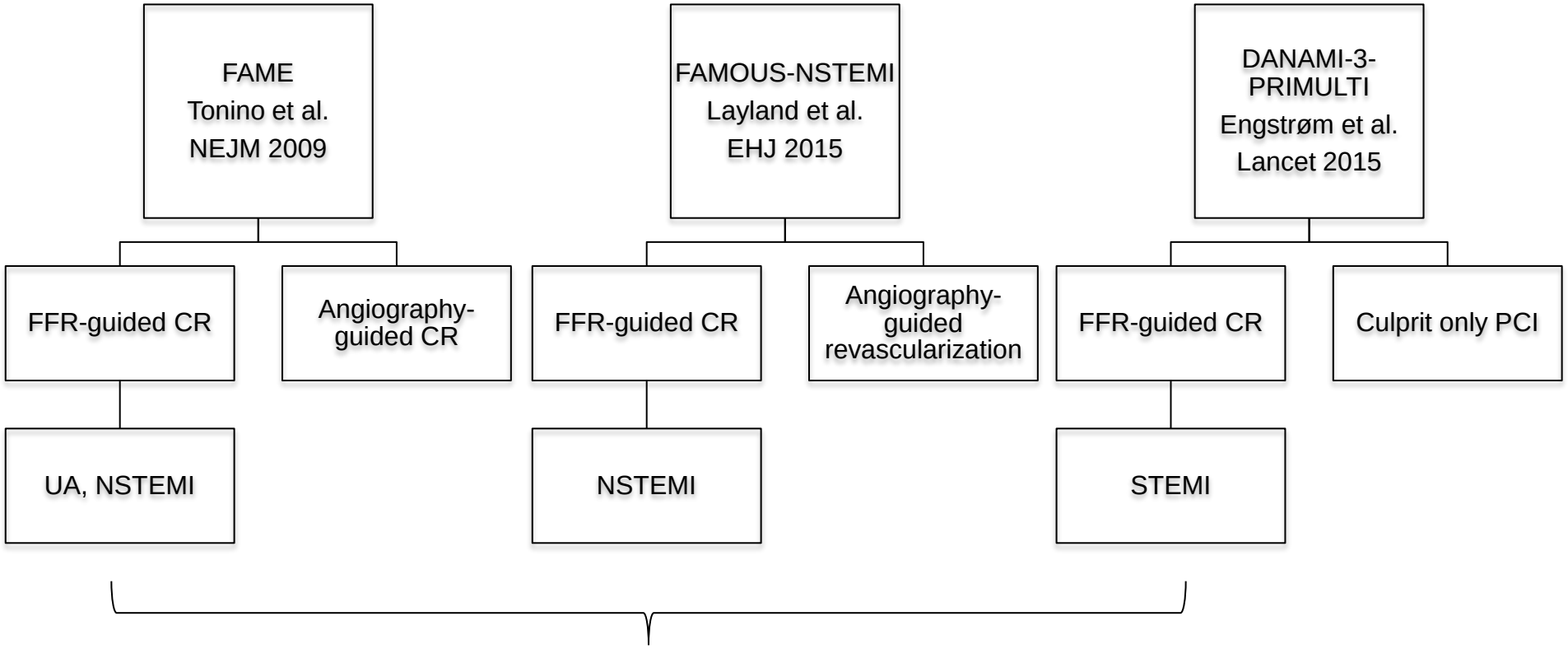
Residual SYNTAX Score in ACS?

Residual SYNTAX Score calculated in ACS patients undergoing angio-guided PCI



Genereux P, et al. J Am Coll Cardiol. 2012;58:2165-74.

RSS after FFR-guided PCI in ACS

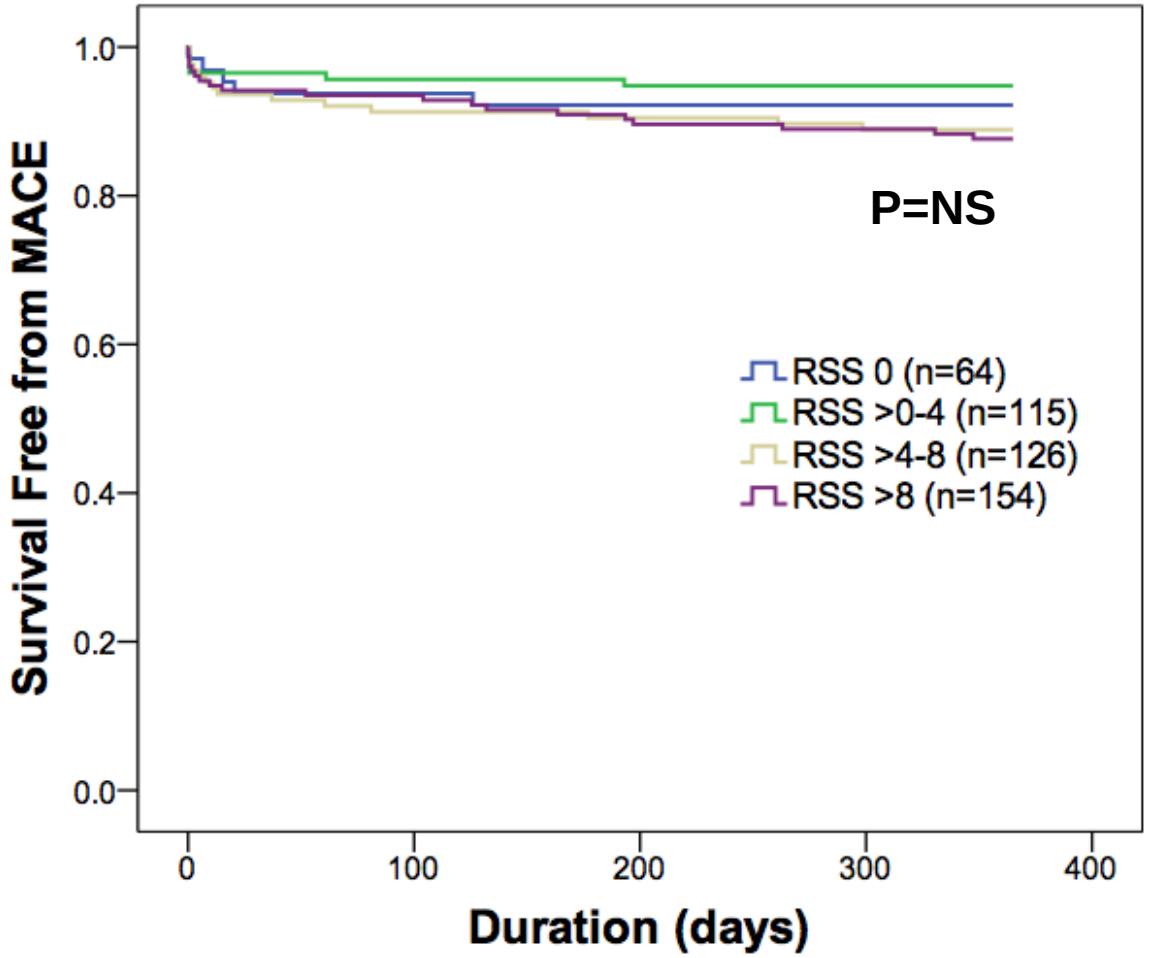


A total of *459 patients presenting with ACS who underwent "functionally" complete revascularization.

*Preliminary data. Final analyses will include higher number of patients.

RSS after FFR-guided PCI in ACS

After functionally complete revascularization, RSS was not predictive

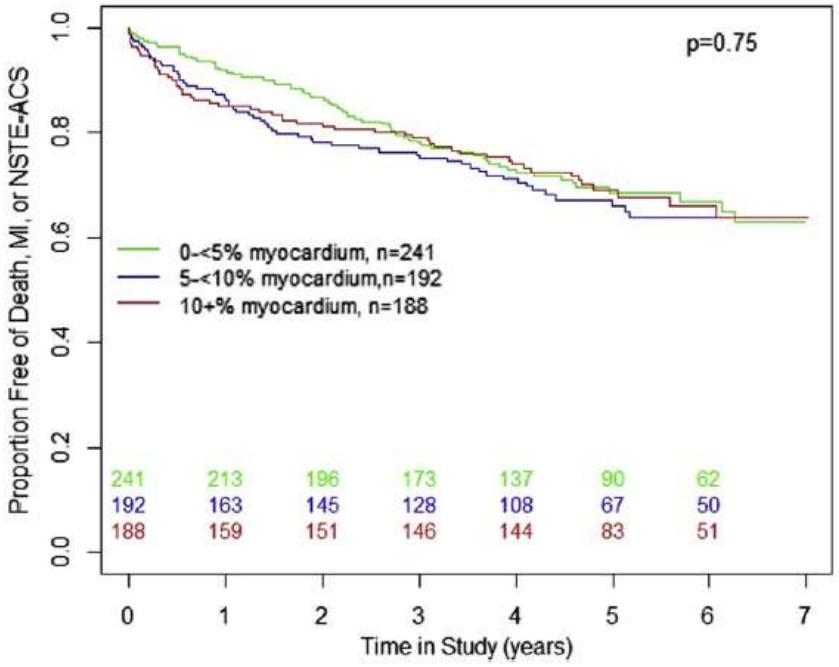


Kobayashi, et al. TCT 2017

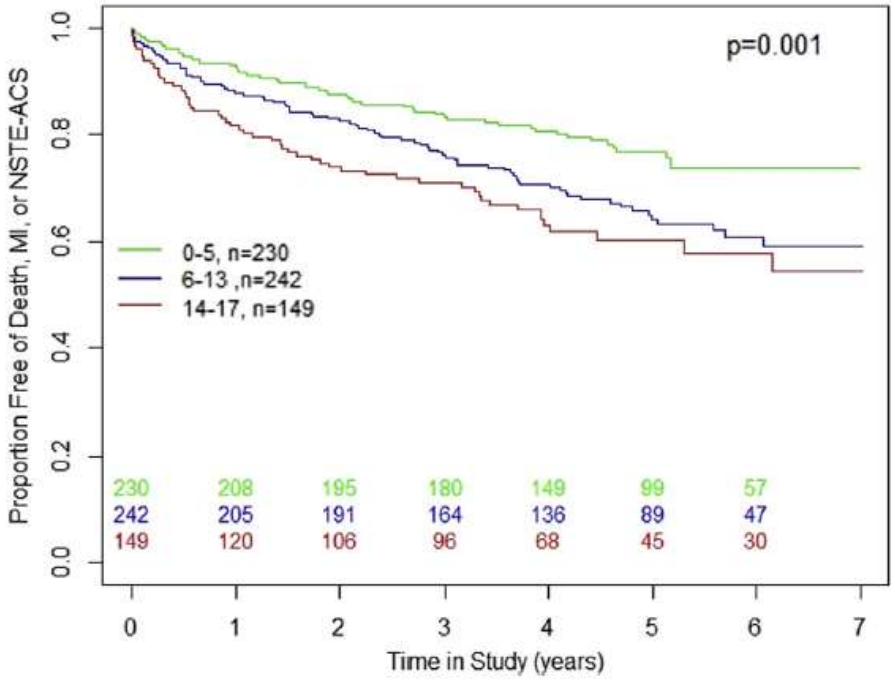
Ischemic vs. Anatomic CAD Burden

621 COURAGE patients with NPS and QCA prior to randomization

Degree of Ischemia



Anatomic Burden of CAD



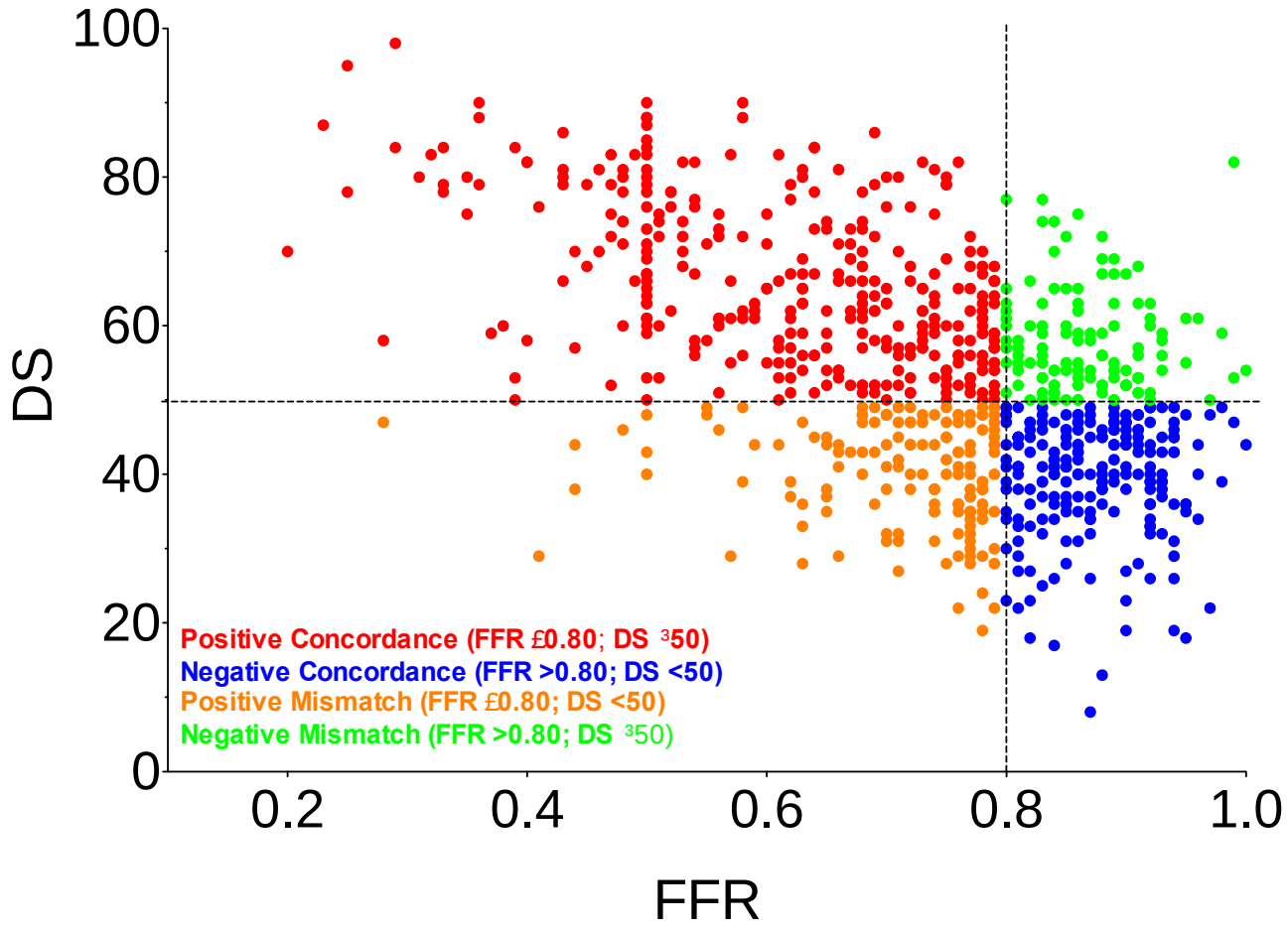
Mancini, et al. J Am Coll Cardiol Interv 2014;7:195-201.

Ischemic vs. Anatomic CAD Burden

- Major limitation of this study:
  - The degree of ischemia was assessed ***before*** the patient was treated with PCI or medical therapy.
  - What we really want to know is what is the degree of ***residual*** ischemia, because this is likely to be more predictive of outcomes than simply the burden of atherosclerosis.

Ischemic vs. Anatomic CAD Burden

1,029 lesions from 607 medically treated patients in FAME 2



Ciccarelli, et al. Circulation 2017;68:in press.

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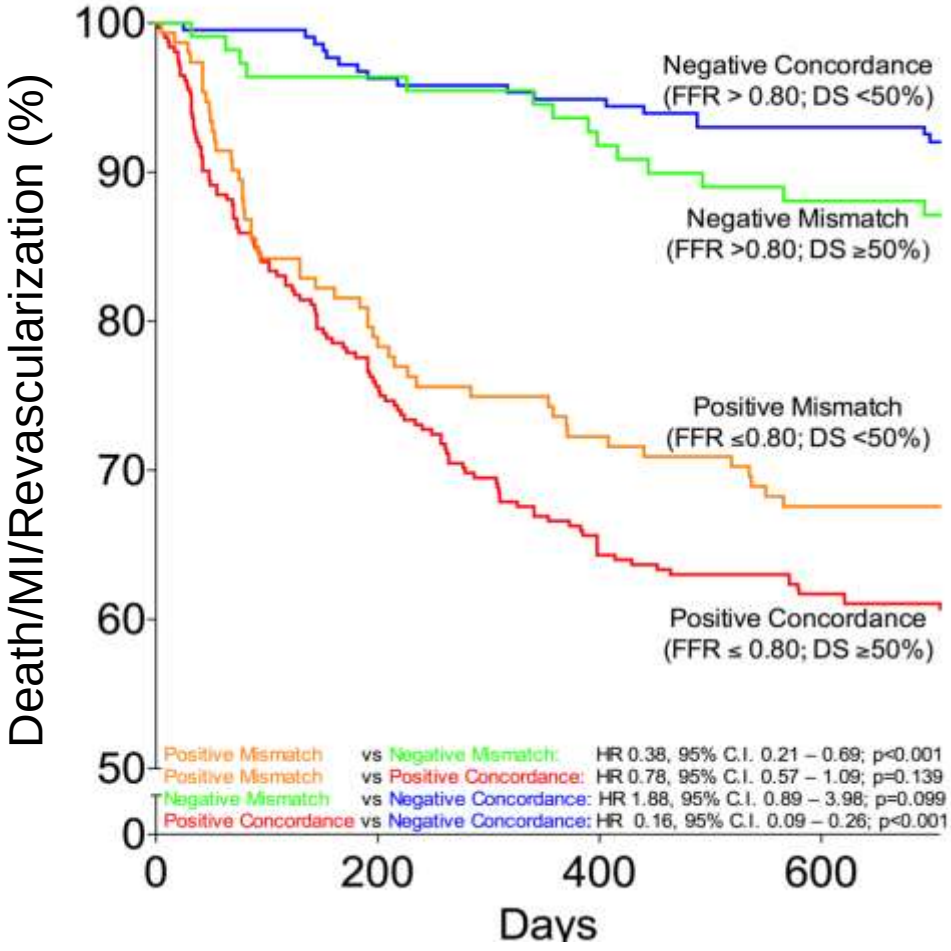
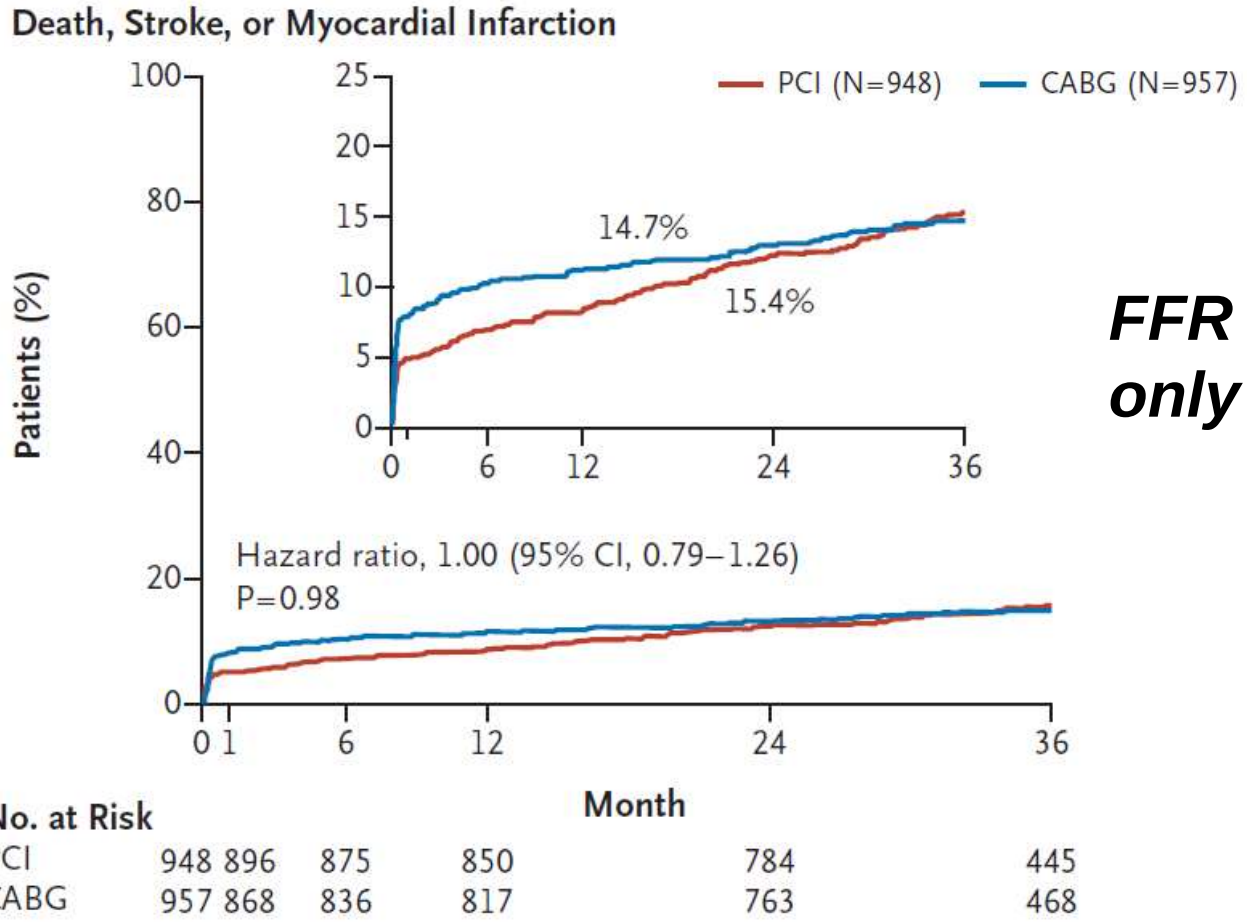


Negative Concordance : FFR >0.80; DS <50%
Negative Mismatch : FFR >0.80; DS ≥50%
Positive Mismatch : FFR ≤0.80; DS <50%
Positive Concordance : FFR ≤0.80; DS ≥50%

Ciccarelli, et al. Circulation 2017;68:in press.

PCI for Left Main Disease

EXCEL Trial: 1,905 patients with left main disease and low to intermediate SYNTAX score randomized to PCI or to CABG

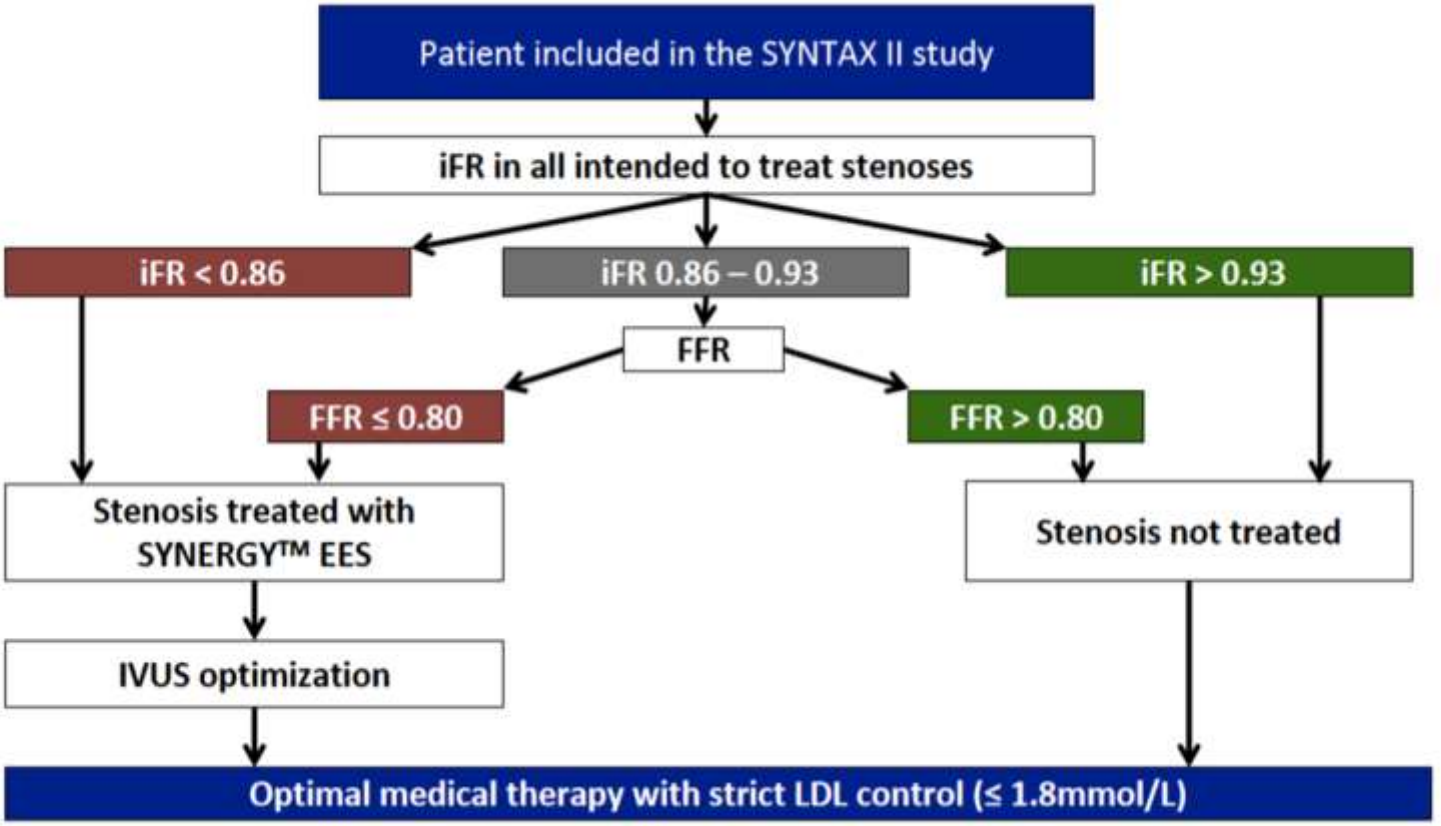


FFR was used in only 9% of cases.

Stone GW, et al. New Engl J Med 2016;375:2223-2235.

SYNTAX II

Single arm study comparing physiology guided PCI to historical control



Escaned J, et al. Eur Heart J. 2018; in press

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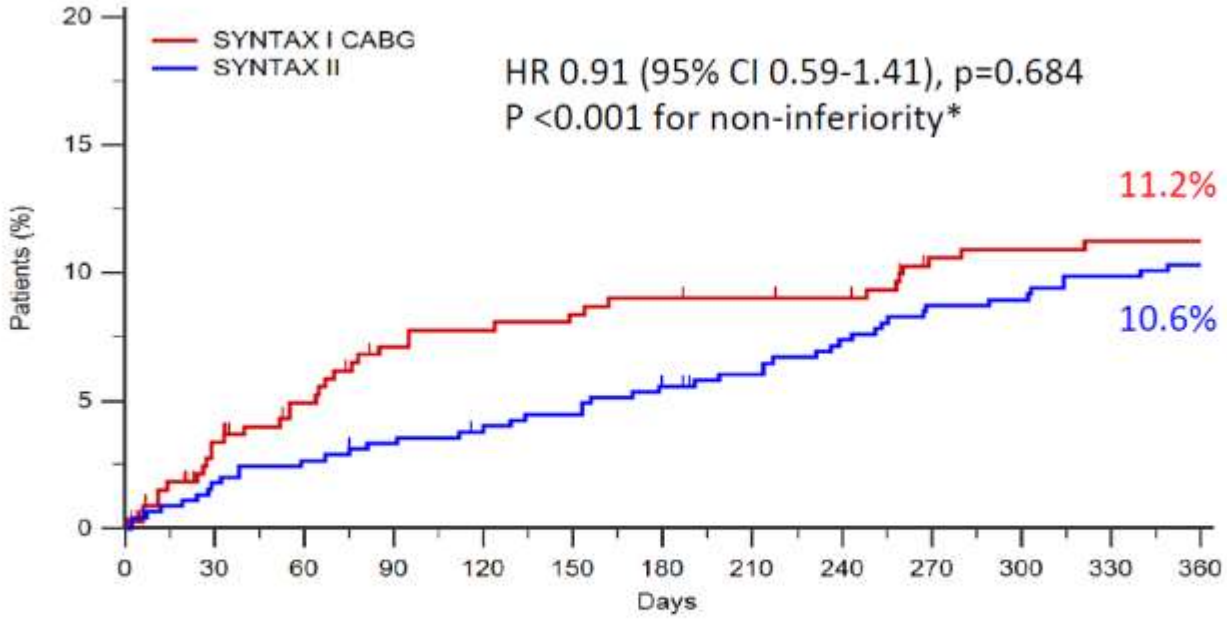
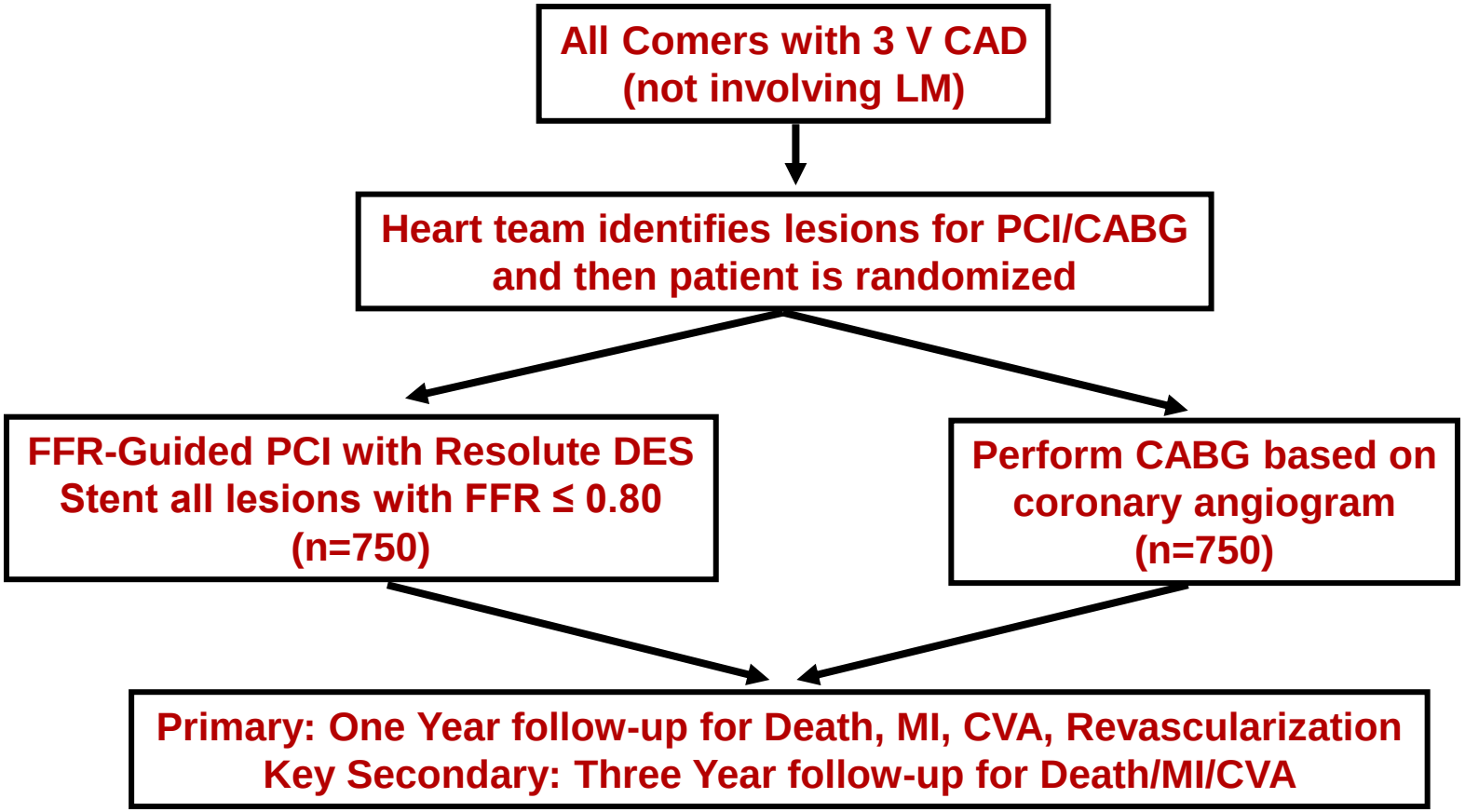


SYNTAX I CABG	334	313	304	295	293	291	289	288	287	279	278	277	277
SYNTAX II	450	441	437	433	429	427	421	417	411	405	404	400	398

*Non-inferiority margin of 5% with a one-sided alpha of 5%

Escaned J, et al. Eur Heart J. 2018; in press

FAME 3 Trial



Non-inferior Design

Zimmermann, et al. Am H J 2015;170:619-26.

NCT02100722

Conclusions

- After functionally complete revascularization, the residual, functionally insignificant lesions do not increase the risk for MACE, even in ACS patients.
- Functional significance is a stronger predictor of cardiac events than angiographic appearance.
- The Functional SYNTAX Score is being tested prospectively in the FAME 3 trial comparing FFR-guided PCI to CABG.