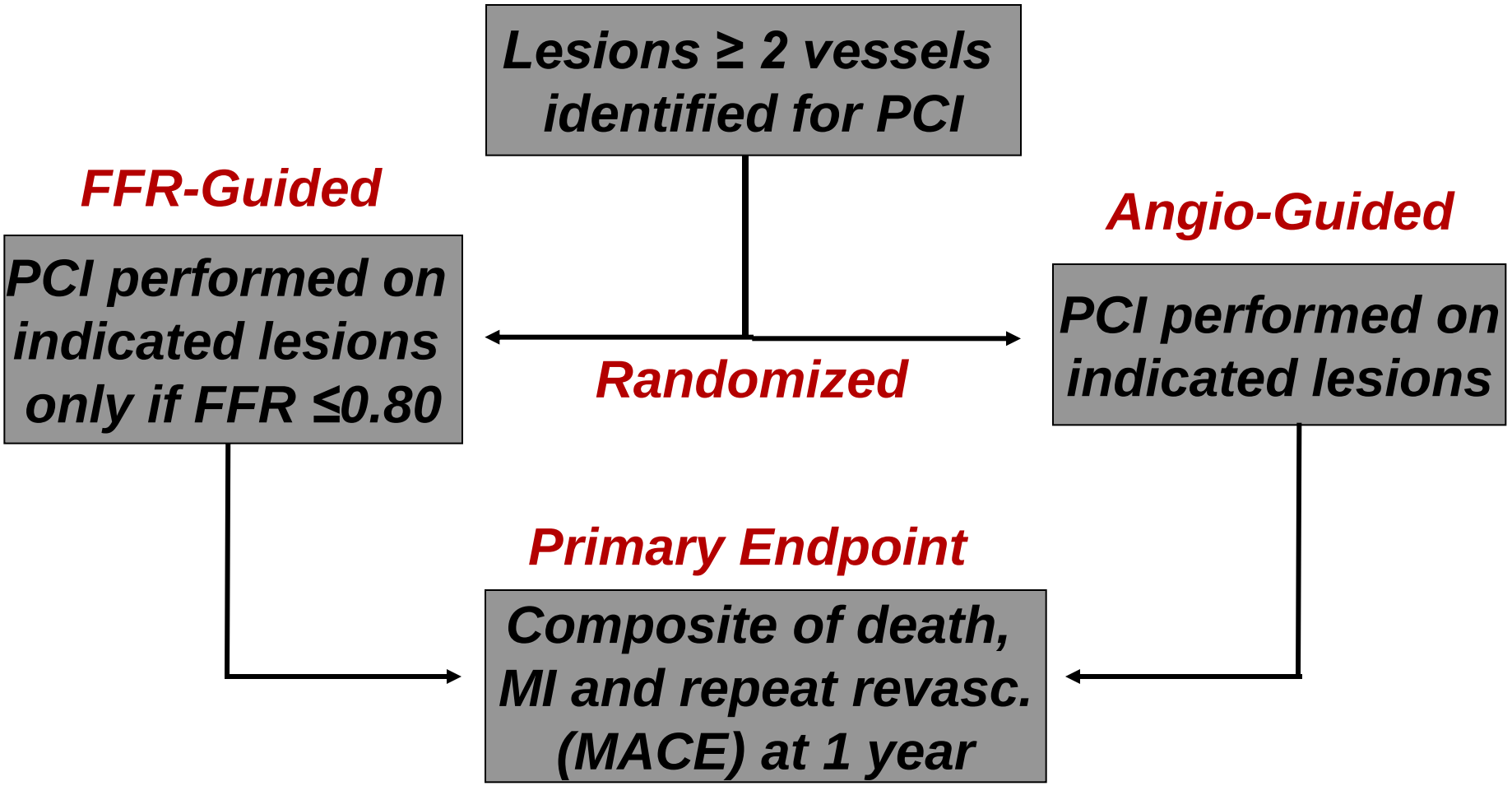
Benefit of Performing PCI Based on FFR

William F. Fearon, MD
Associate Professor
Director, Interventional Cardiology
Stanford University Medical Center

Benefit of FFR-Guided PCI

- FFR-Guided PCI vs. Angiography-Guided PCI
- Functional SYNTAX Score (FSS)
- FFR-Guided PCI vs. Medical Therapy in patients with stable CAD

FAME Trial:



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

FFR Case Example:

- 46 year old diabetic woman with HTN and dyslipidemia presents to outside hospital with a NSTEMI.
- Cath reveals 3 vessel CAD and the patient is transferred to Stanford for CABG.
- Cardiac surgeon reviews angiogram and asks for a second opinion.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Fearon, William, F, , MD
Stanford Hospital
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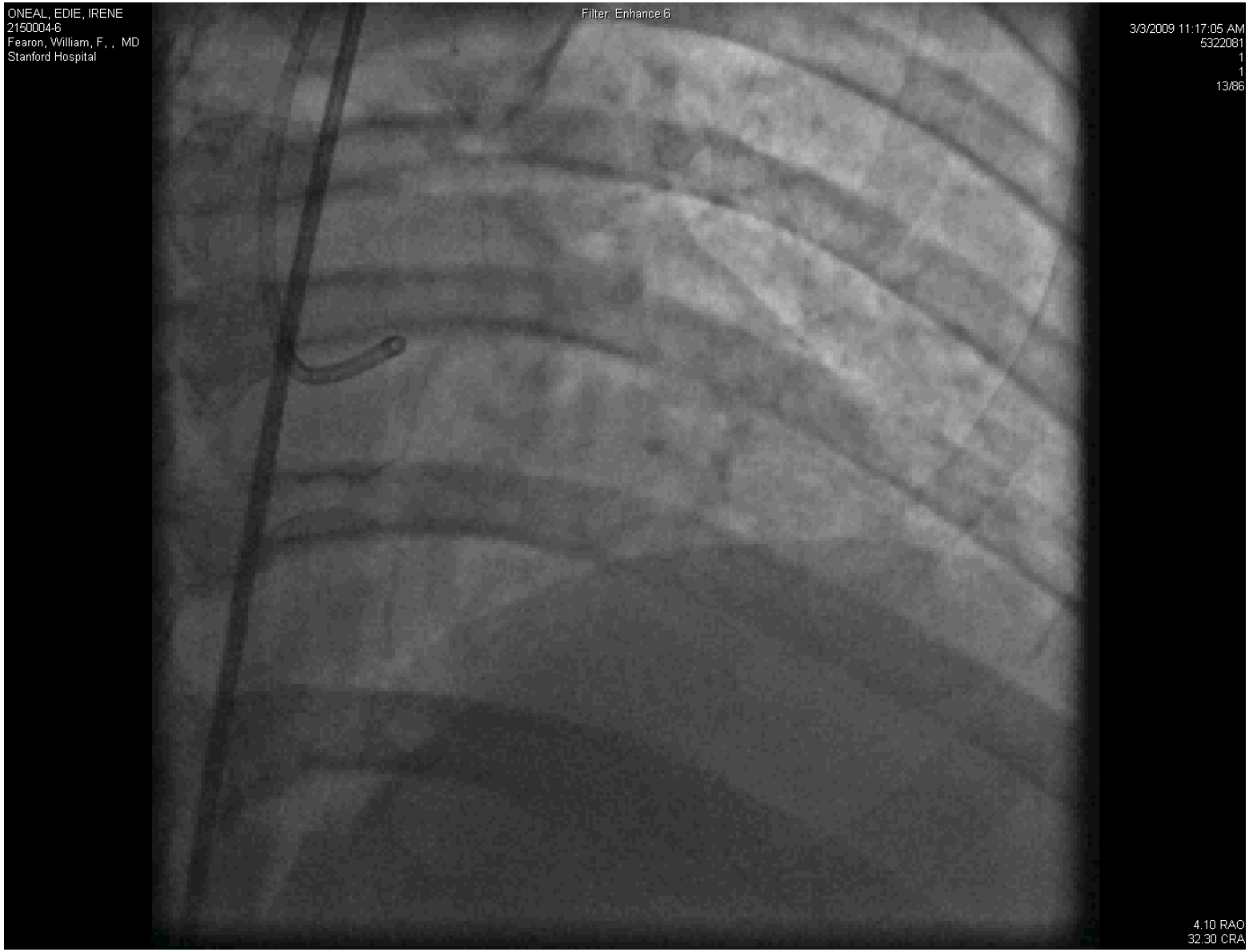
3/3/2009 11:17:05 AM
5322081
1
4
11/66
12.00 RAO
26.30 CAU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1
1
13/86
4.10 RAO
32.30 CRA


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Fearon, William, F, , MD
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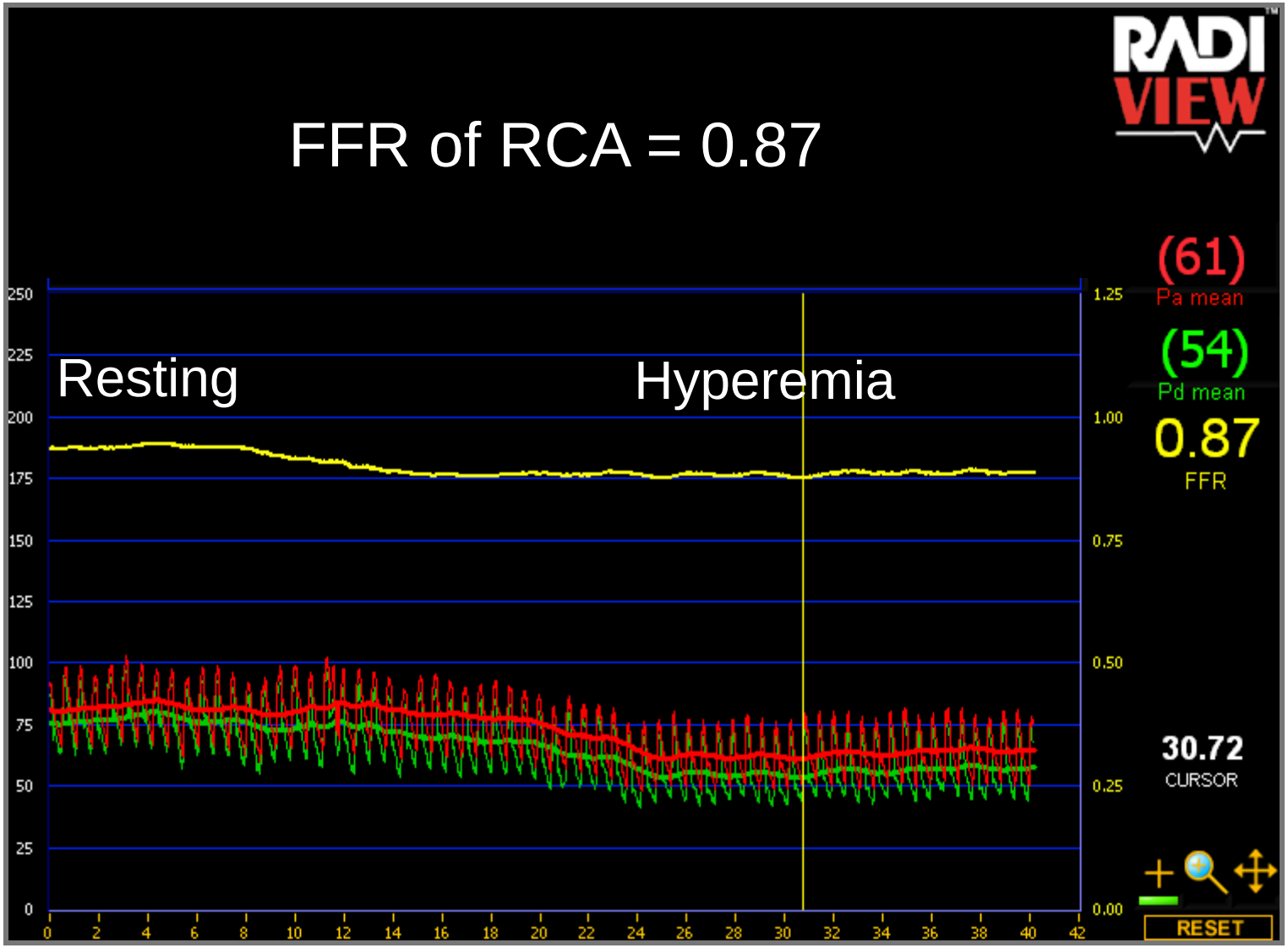
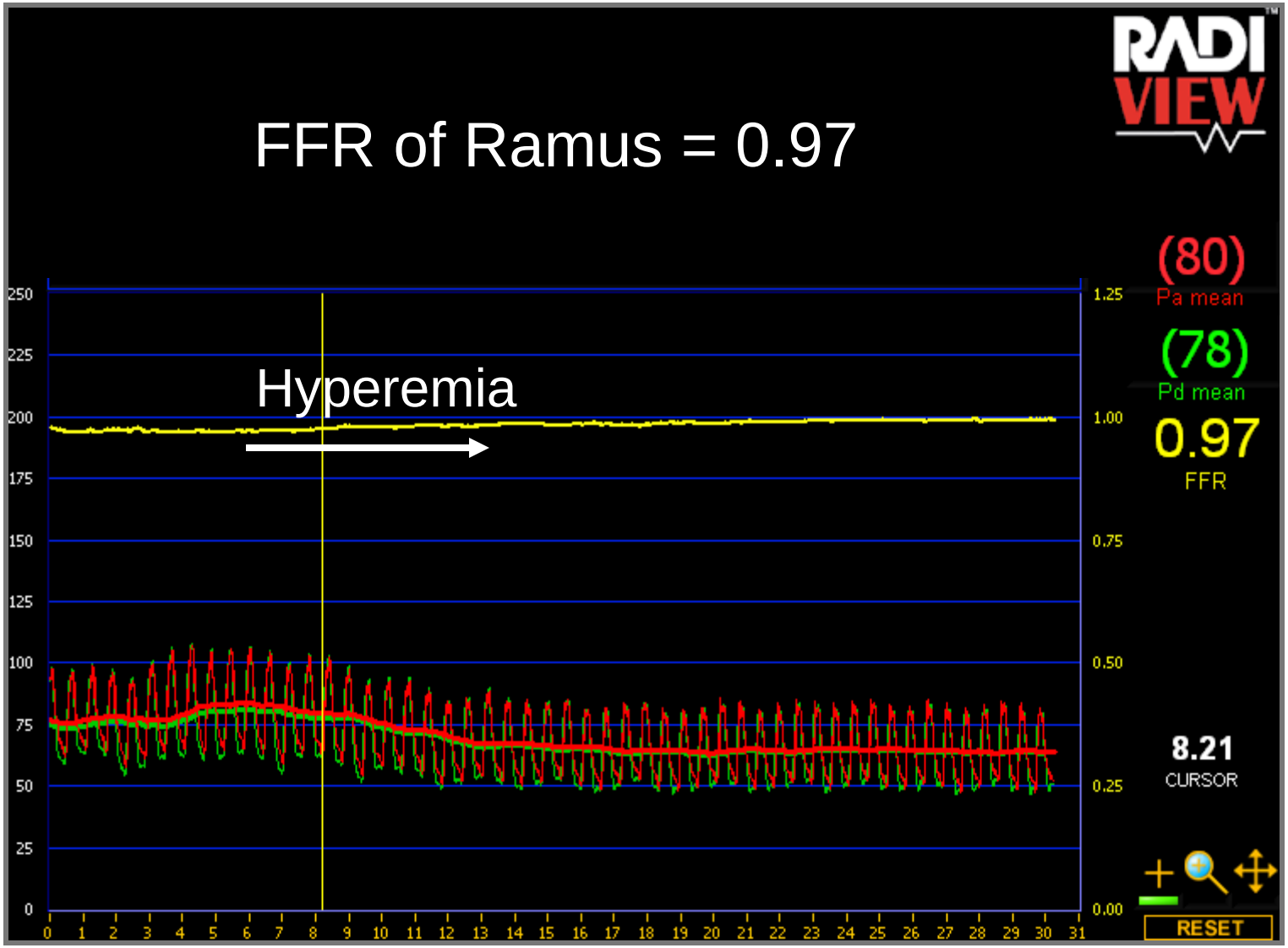
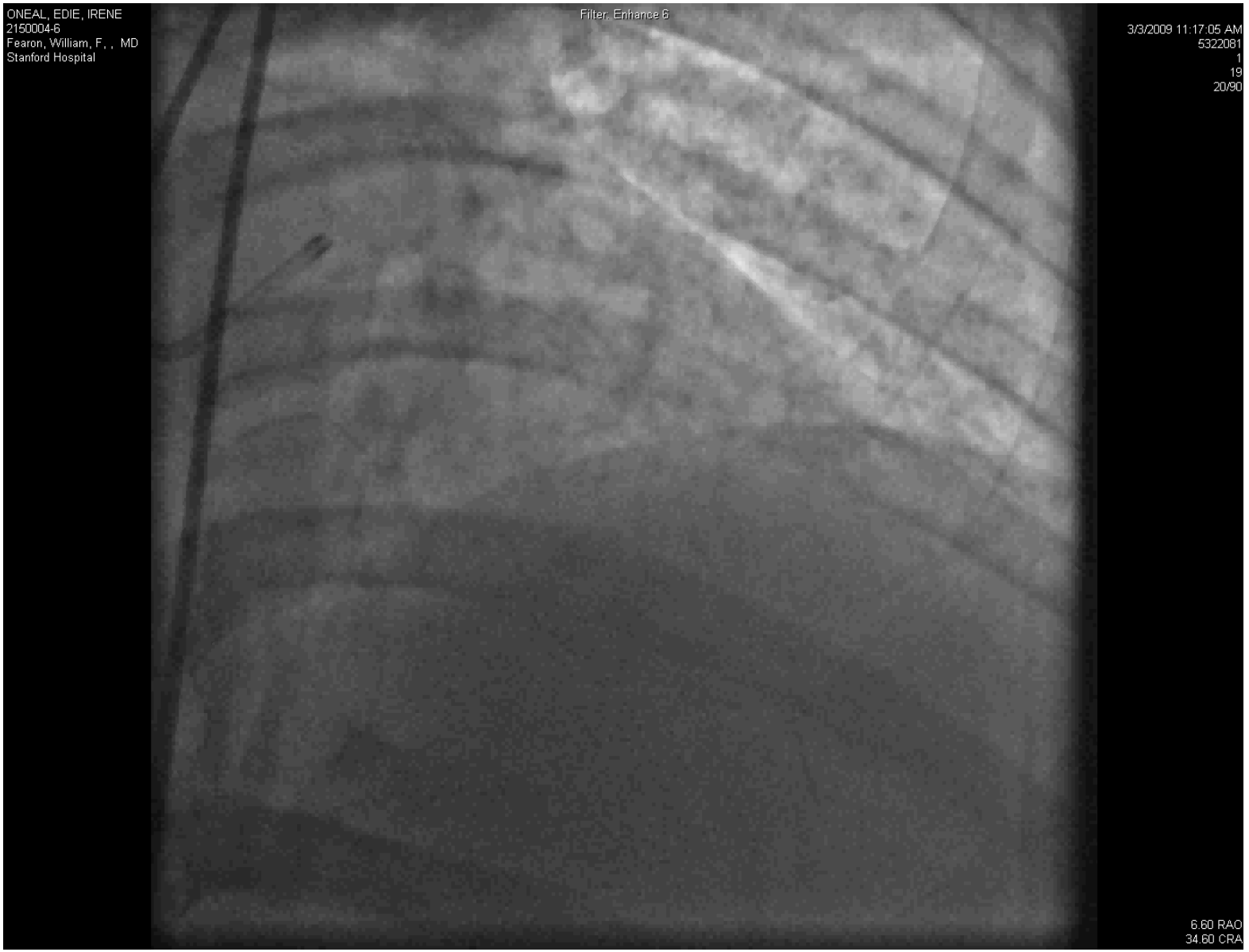
1
22
14/65
1.90 RAO
26.90 CRA

FFR of RCA = 0.87



FFR of Ramus = 0.97

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Fearon, William, F, , MD
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5322081
1
19
20/90
6.60 RAO
34.60 CRA

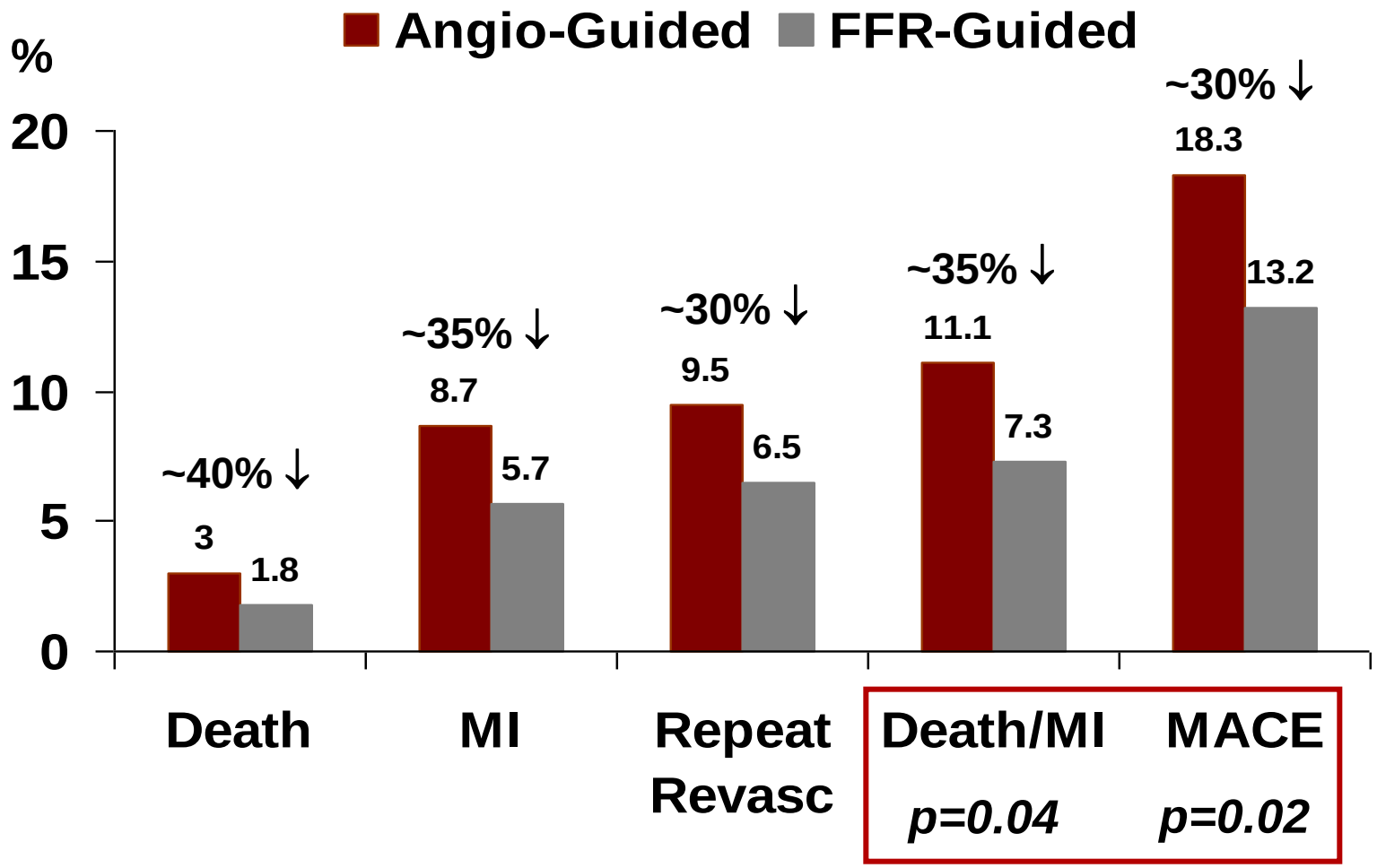
Summary of Case

- Anatomic 3V CAD, functional 1V CAD
- Successfully treated with single stent
- 130 cc contrast, < 1 hour procedure
- Remained event free at > 12 months

	Angio-Guided n = 496	FFR-Guided n = 509	P Value
Indicated lesions / patient	2.7±0.9	2.8±1.0	0.34
Stents / patient	2.7 ± 1.2	1.9 ± 1.3	<0.001

	Angio-Guided n = 496	FFR-Guided n = 509	P Value
Indicated lesions / patient	2.7±0.9	2.8±1.0	0.34
Stents / patient	2.7 ± 1.2	1.9 ± 1.3	<0.001
Procedure time (min)	70 ± 44	71 ± 43	0.51
Contrast agent used (ml)	302 ± 127	272 ± 133	<0.001
Equipment cost (US $)	6007	5332	<0.001
Length of hospital stay (days)	3.7 ± 3.5	3.4 ± 3.3	0.05

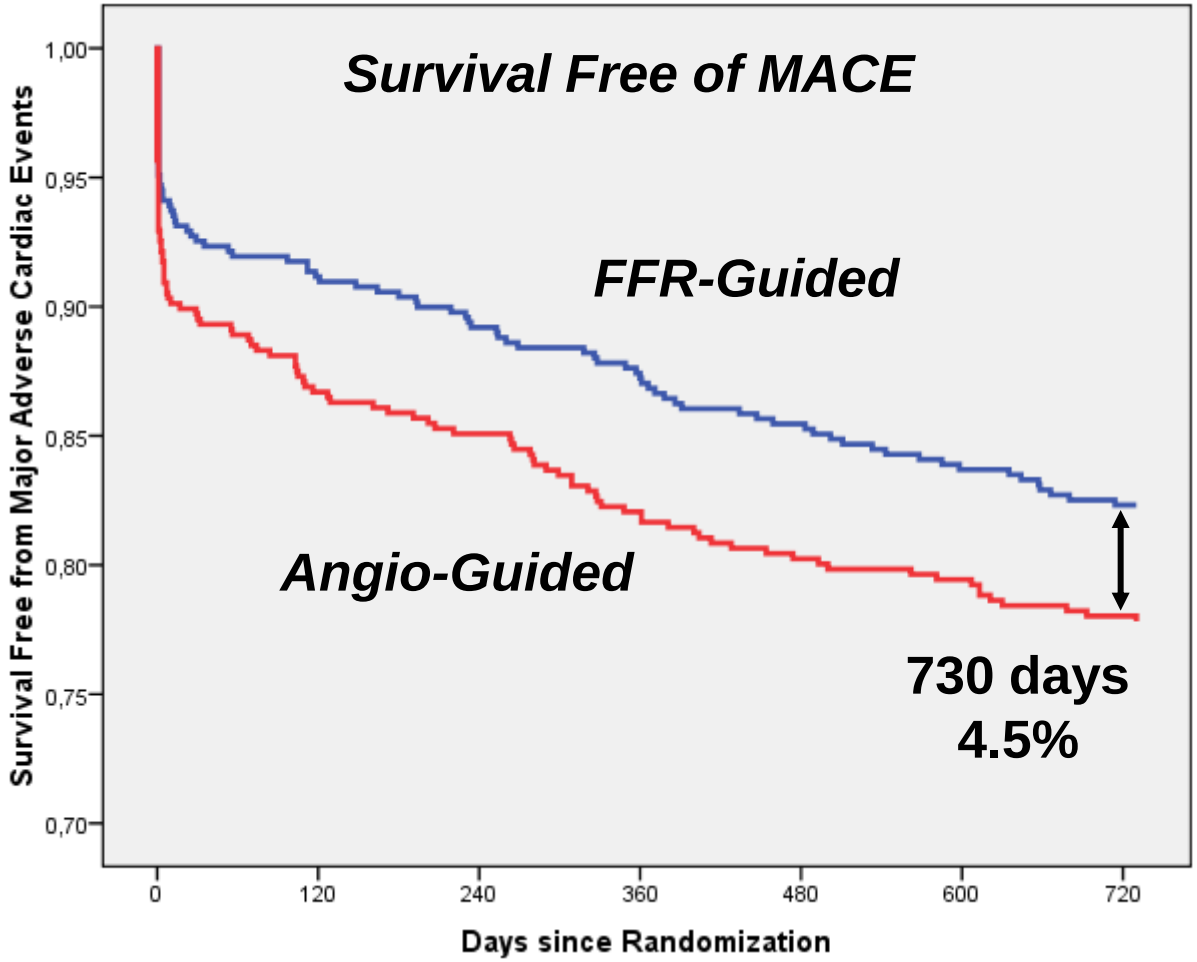
FAME Trial: One Year Outcomes



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

FAME Study: Two Year Outcomes

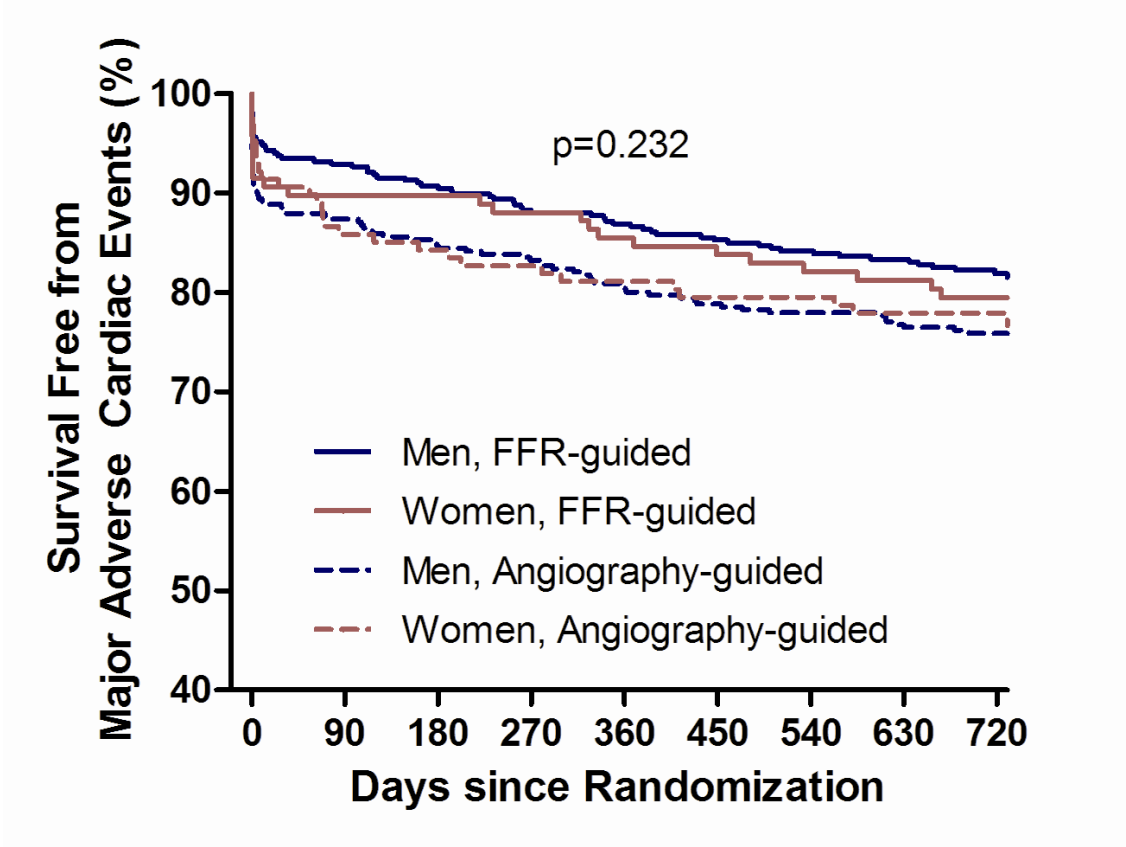
Death/MI was significantly reduced from 12.9% to 8.4% (p=0.02)



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

Sex Differences in the FAME Study

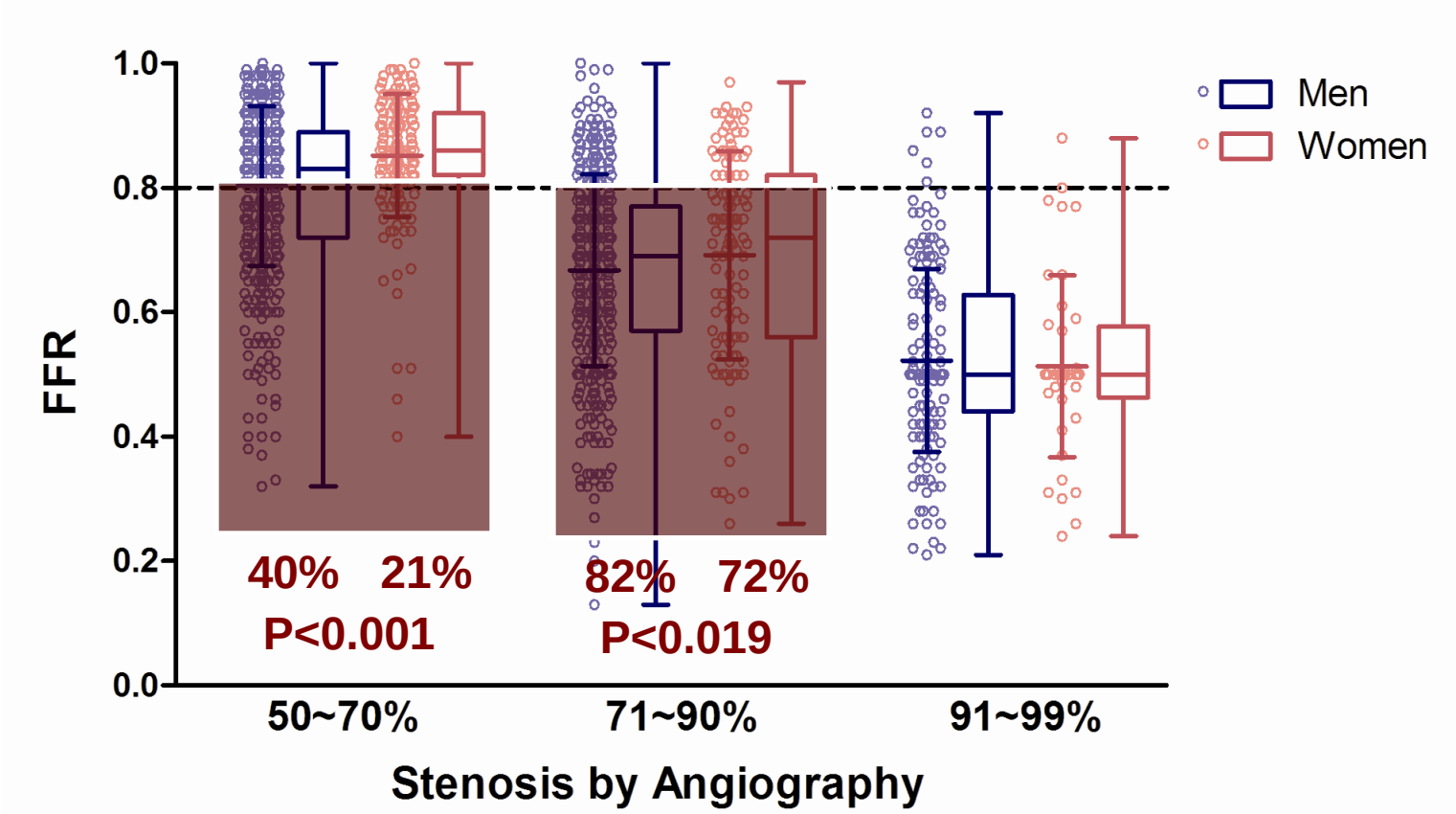
261 of the 1,005 patients in FAME were women



Kim HS, et al. J Am Coll Cardiol 2012;5:1037-42.

Sex Differences in the FAME Study

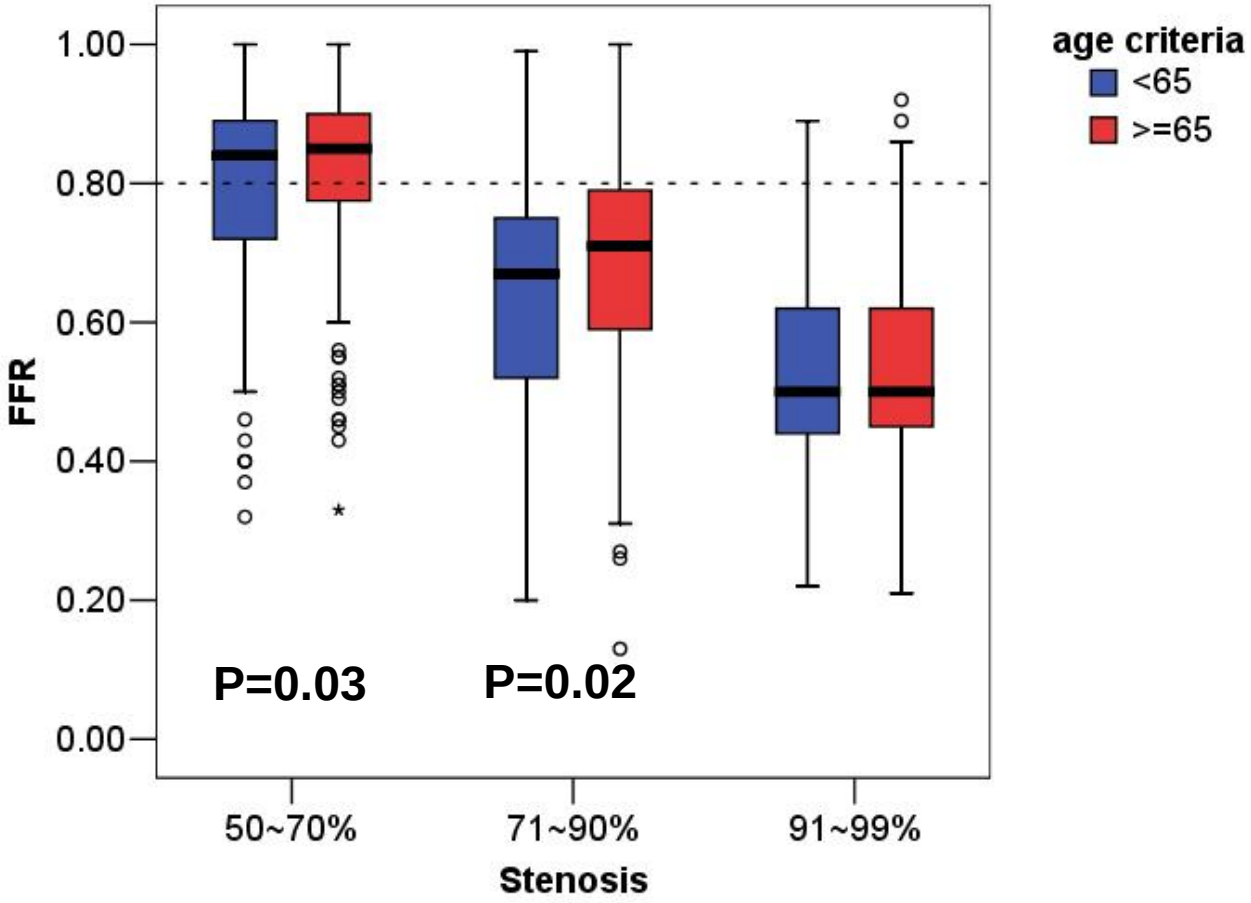
FFR was significantly higher in women than men (0.75±0.18 vs. 0.71±0.17, p=0.001)



Kim HS, et al. JACC Interventions 2012; 5:1037-42.

Age Differences in the FAME Study

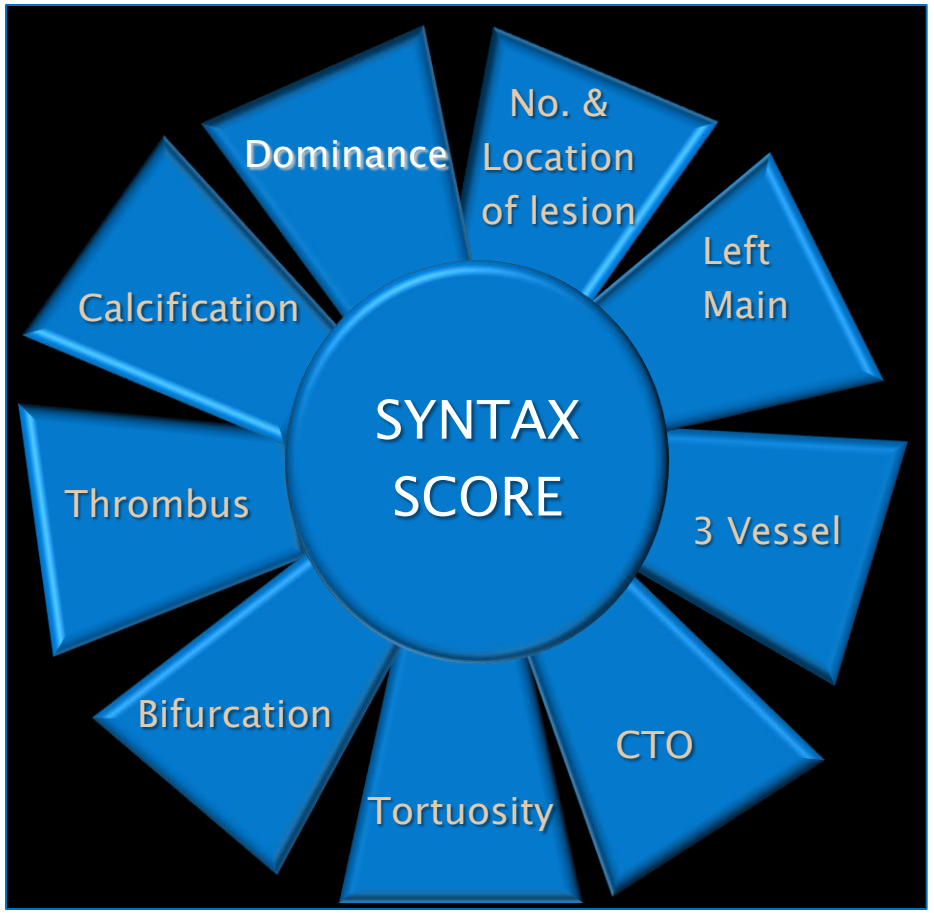
FFR was significantly higher in patients > 65 years old



Unpublished Data

SYNTAX Score

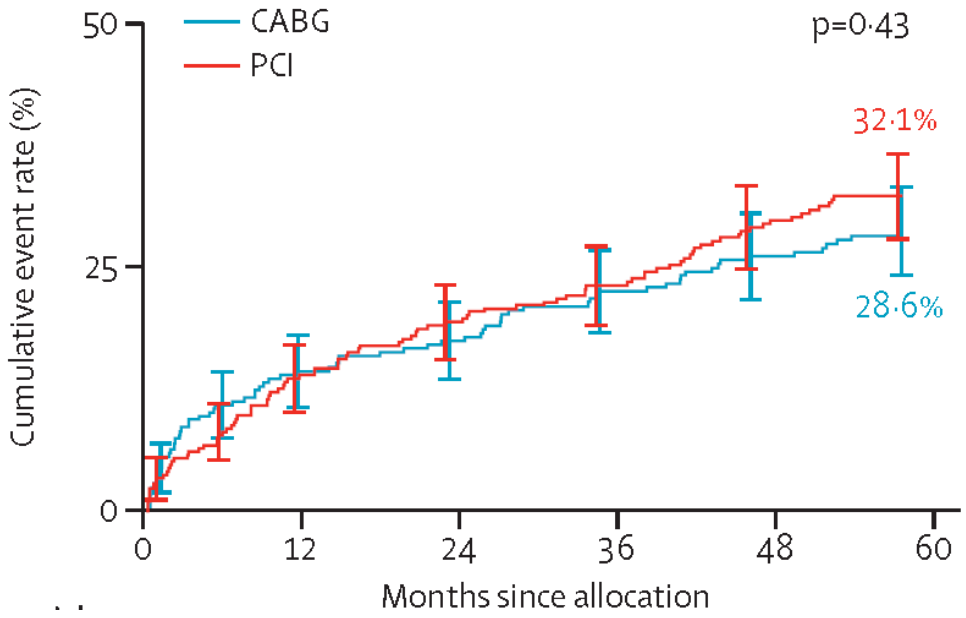
- Angiography-based scoring system aimed at determining coronary lesion complexity
- Because it is angiography-based, it is inherently limited by the accuracy of the coronary angiogram



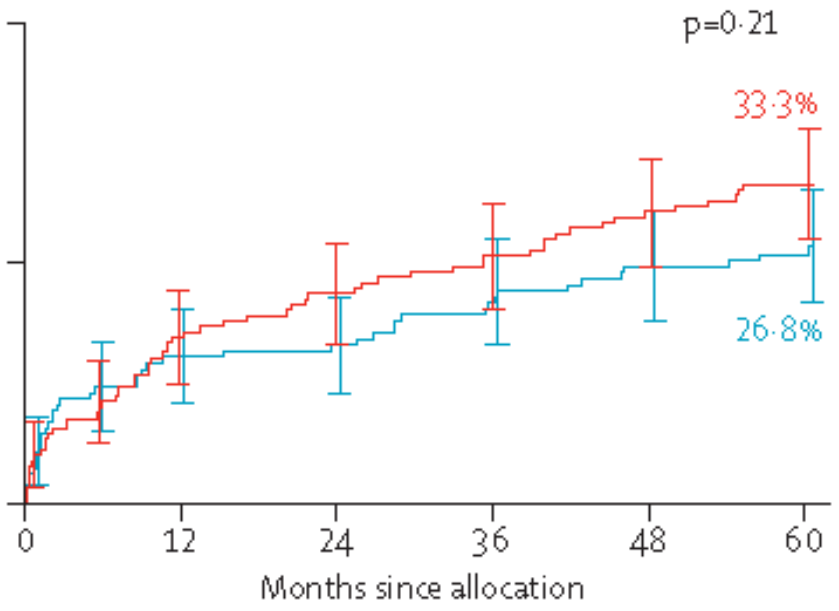
SYNTAX

5 Year Outcomes: Lowest SYNTAX Tertile (0-22)

All Patients



3-Vessel CAD only

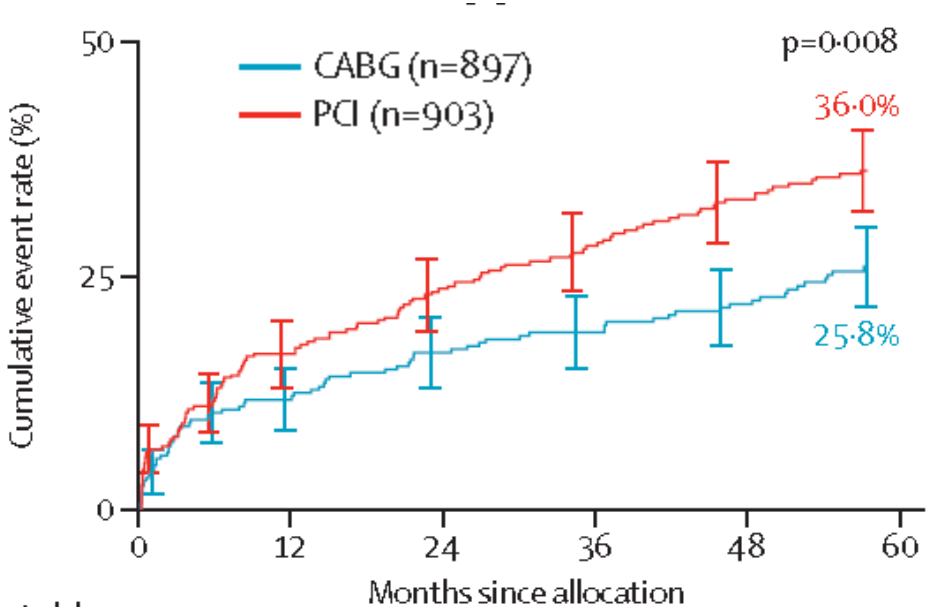


Mohr, et al. Lancet 2013;381:629-38

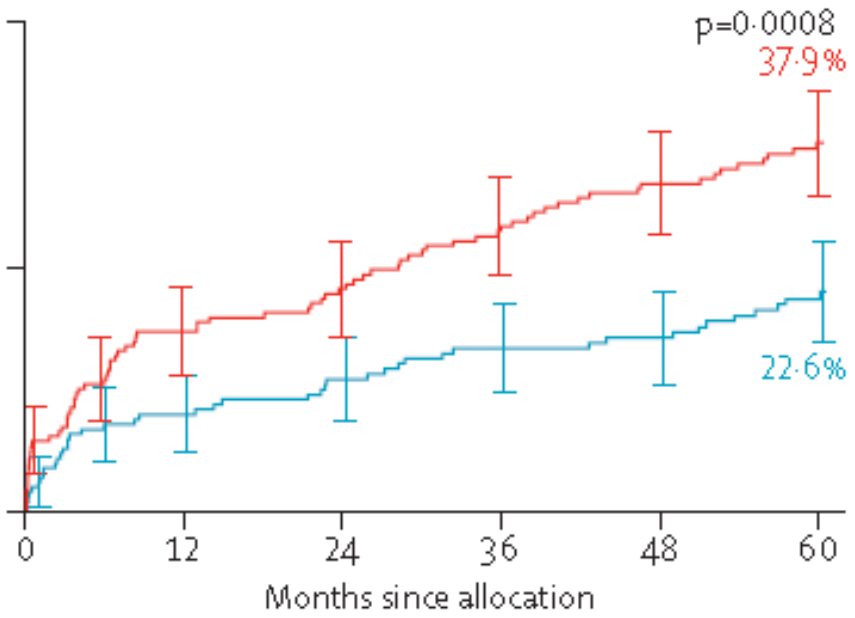
SYNTAX

5 Year Outcomes: Middle SYNTAX Tertile (23-32)

All Patients



3-Vessel CAD only

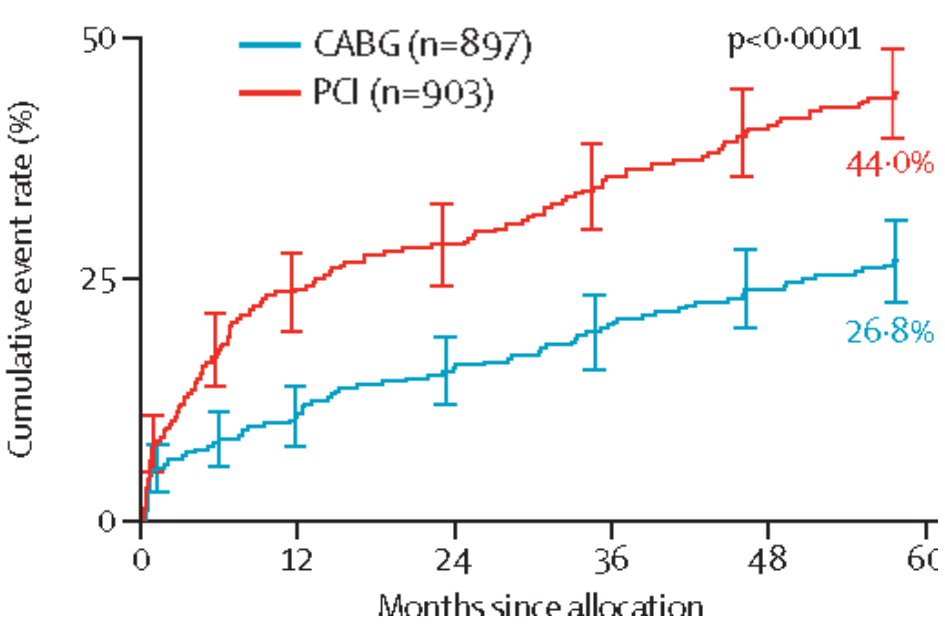


Mohr, et al. Lancet 2013;381:629-38

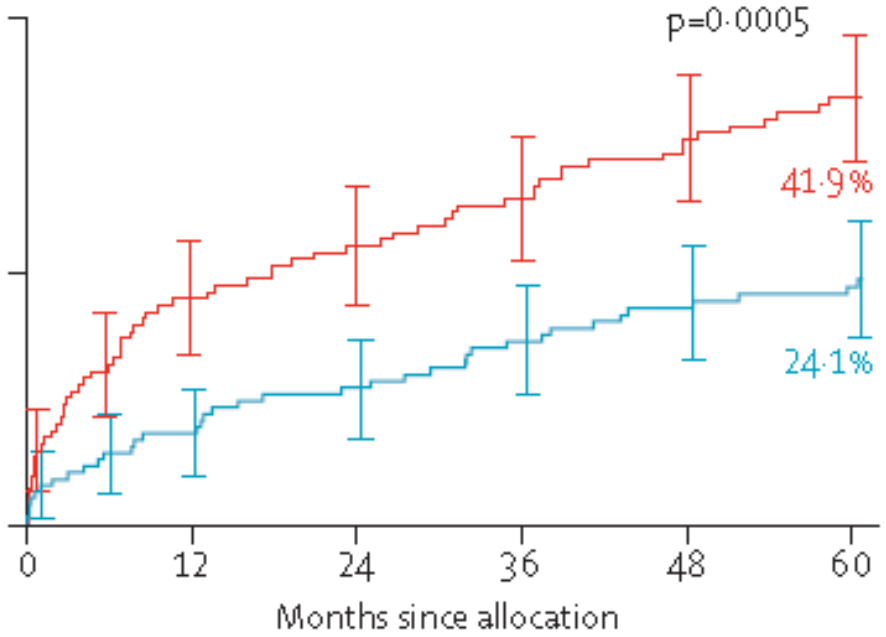
SYNTAX

5 Year Outcomes: Highest SYNTAX Tertile (>32)

All Patients



3-Vessel CAD only



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

Impact of SYNTAX Score on PCI

Recently published Appropriate Use Criteria

	CABG	PCI
Two-vessel CAD with proximal LAD stenosis	A	A
Three-vessel CAD with low CAD burden (i.e., three focal stenosis, low SYNTAX score)	A	A
Three-vessel CAD with intermediate to high CAD burden (i.e., multiple diffuse lesions, presence of CTO, or high SYNTAX score)	A	U
Isolated left main stenosis	A	U
Left main stenosis and additional CAD with low CAD burden (i.e., one to two vessel additional involvement, low SYNTAX score)	A	U
Left main stenosis and additional CAD with intermediate to high CAD burden (i.e., three vessel involvement, presence of CTO, or high SYNTAX score)	A	I

Patel, et al. JACC 2012;59:857-881

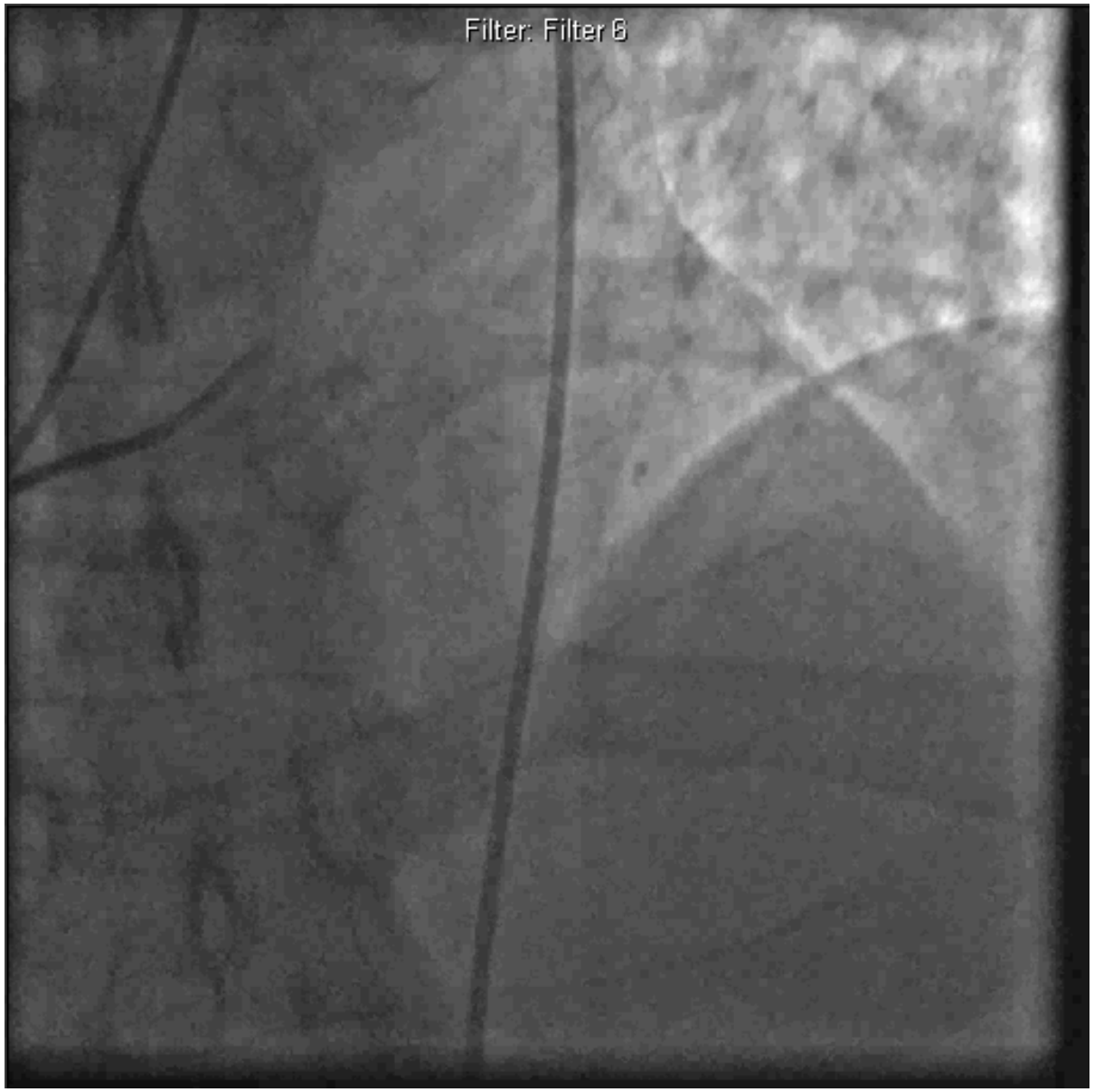
Can we enhance the SYNTAX Score?

- By incorporating FFR into the SYNTAX score, termed “Functional SYNTAX Score” (FSS), can we:
  - Convert high/medium risk SYNTAX score patients to a lower risk group?
  - Improve our risk stratification of patients with multivessel CAD undergoing PCI?

Functional SYNTAX Score Case:

"Mr. H."

- 79 year old retired physicist with angina
- Risk factors include HTN and dyslipidemia
- Stress echo revealed anteroseptal and apical ischemia
- Referred for coronary angiography…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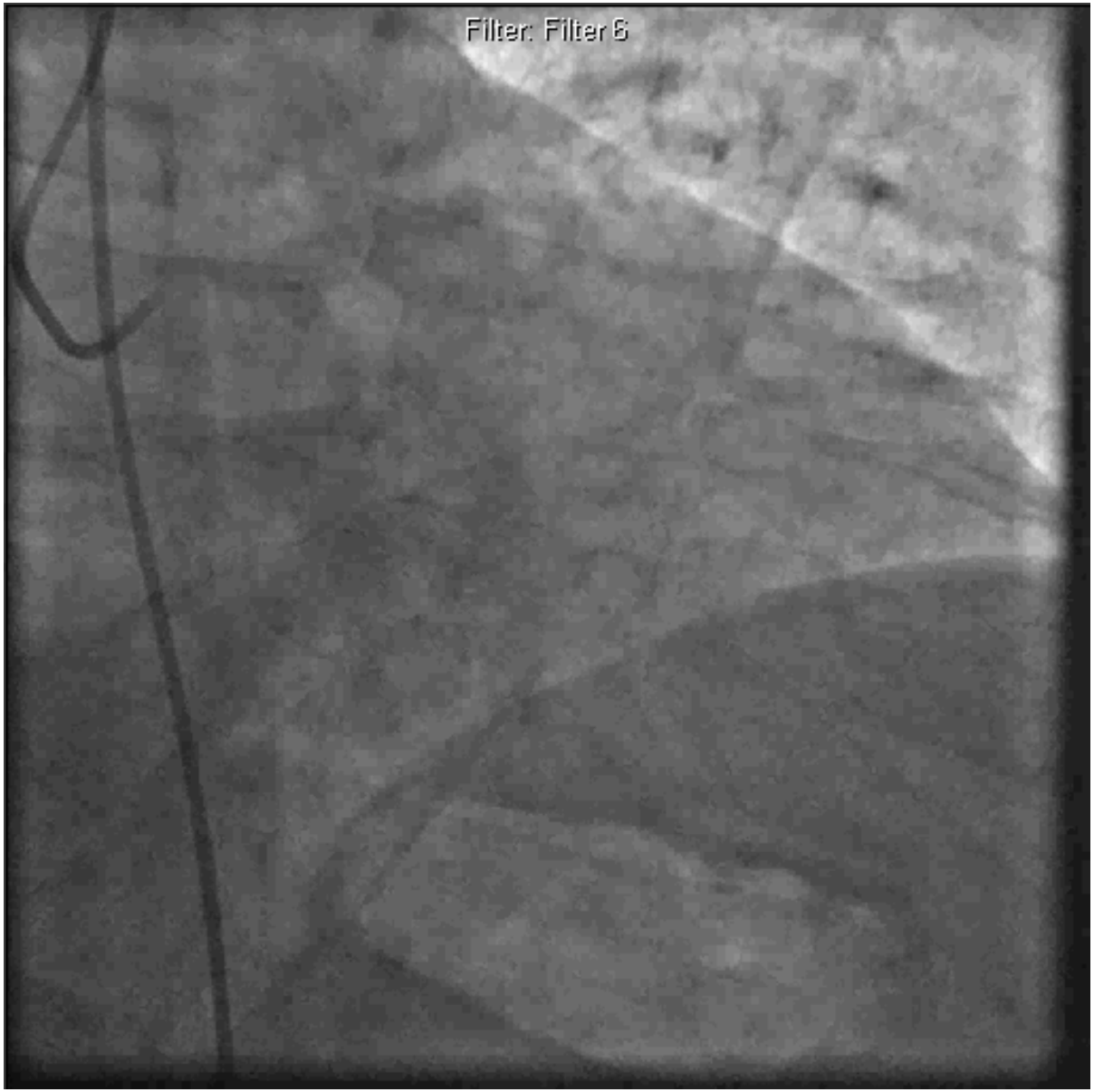
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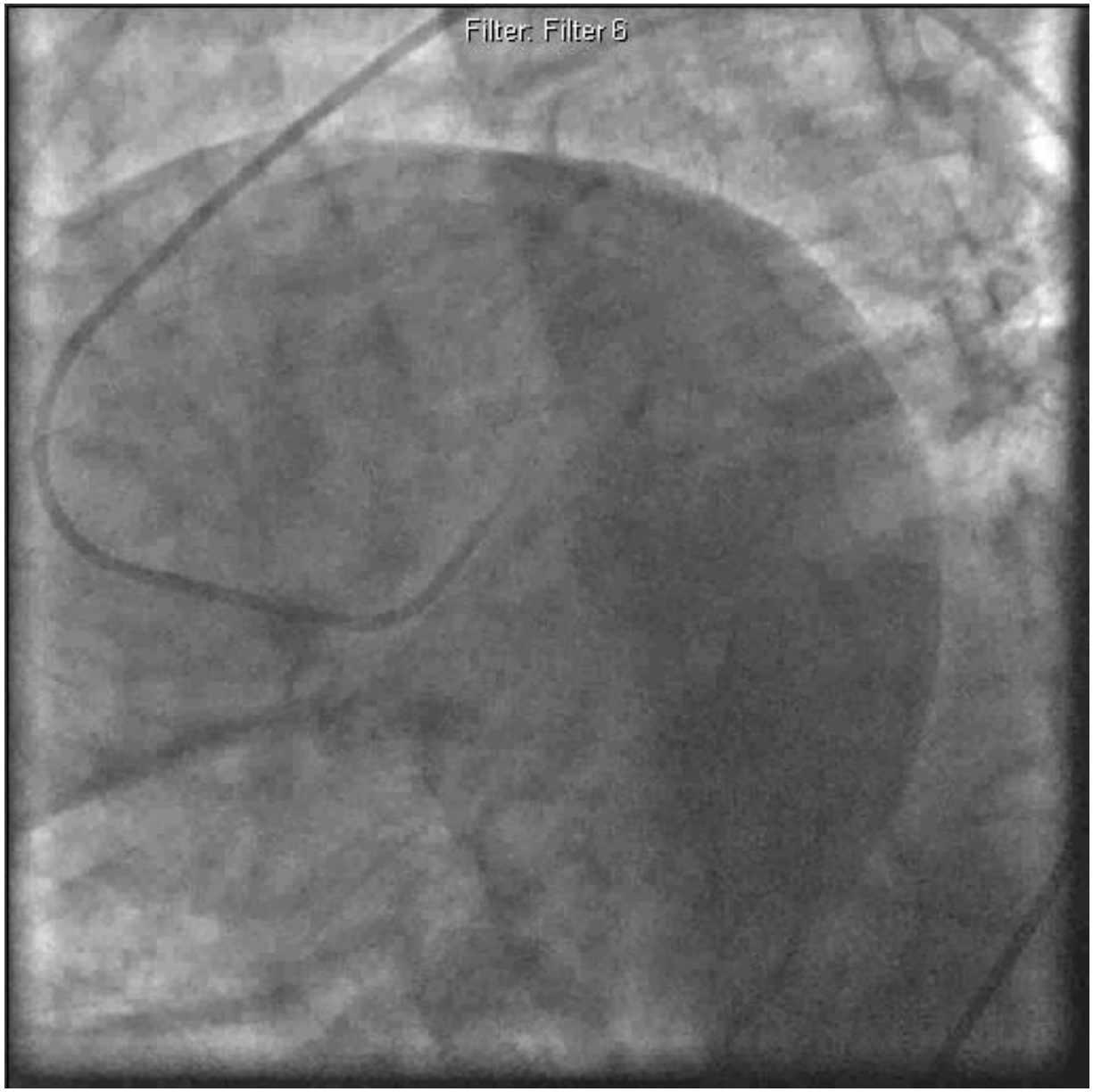
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SYNTAX Score = 25

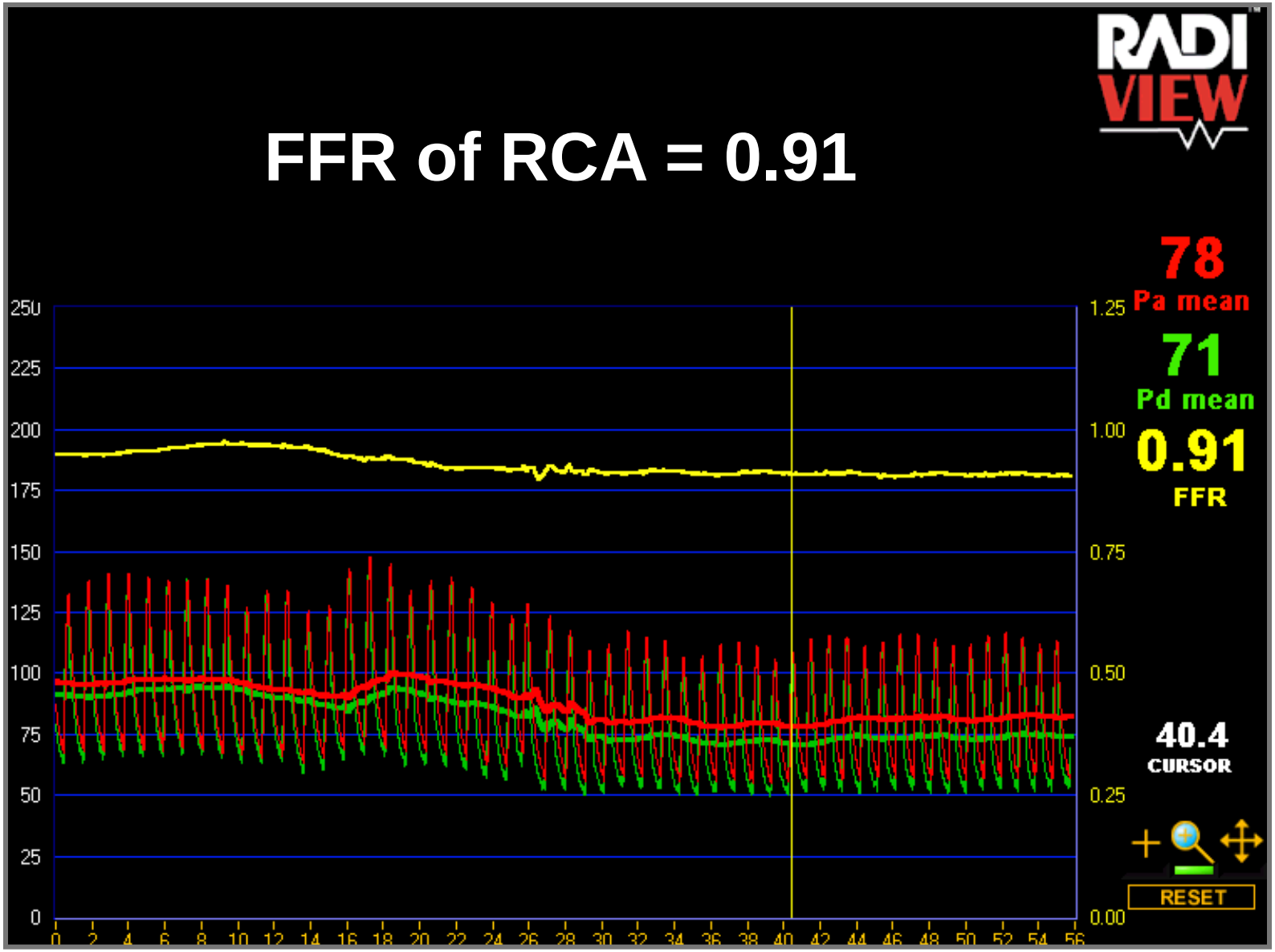
Impact of SYNTAX Score on PCI

European guidelines for revascularization

Subset of CAD by anatomy	Favours CABG	Favours PCI
1VD or 2VD - non-proximal LAD	IIb C	I C
1VD or 2VD - proximal LAD	I A	IIa B
3VD simple lesions, full functional revascularization achievable with PCI, SYNTAX score ≤22	I A	IIa B
3VD complex lesions, incomplete revascularization achievable with PCI, SYNTAX score >22	I A	III A
Left main (isolated or 1VD, ostium/shaft)	I A	IIa B
Left main (isolated or 1VD, distal bifurcation)	I A	IIb B
Left main + 2VD or 3VD, SYNTAX score ≤32	I A	IIb B
Left main + 2VD or 3VD, SYNTAX score ≥33	I A	III B

Wijns W, Kolh P, et al. Eur Heart J 2010;31:2501-55

FFR of RCA = 0.91



How should we handle this case?

European guidelines for revascularization

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Left main (isolated or 1VD, distal bifurcation)	I A	IIb B
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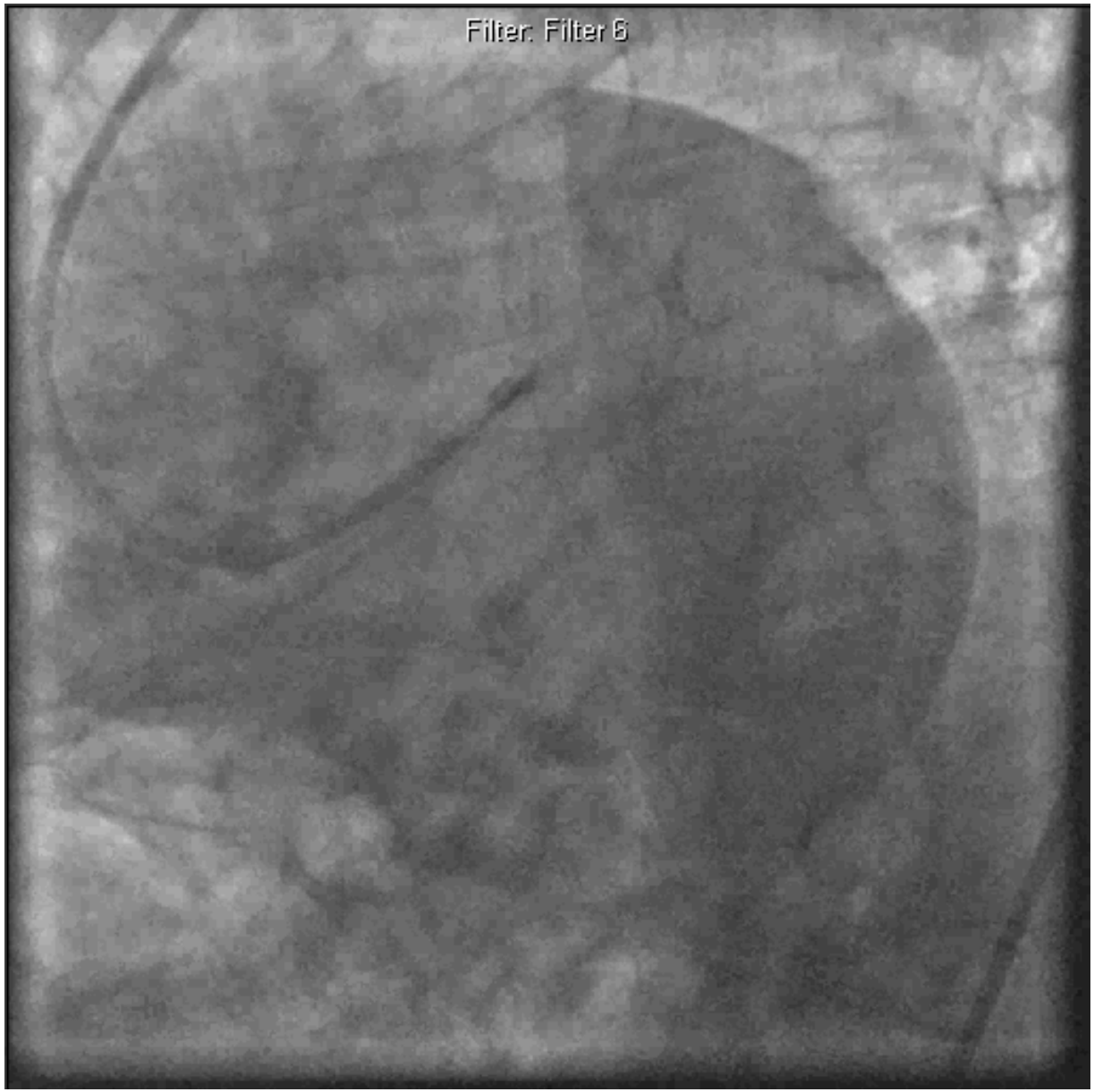
Left main + 2VD or 3VD, SYNTAX score ≥33	I A	III B

Functional SYNTAX score after FFR = 18.5

Wijns W, Kolh P, et al. Eur Heart J 2010;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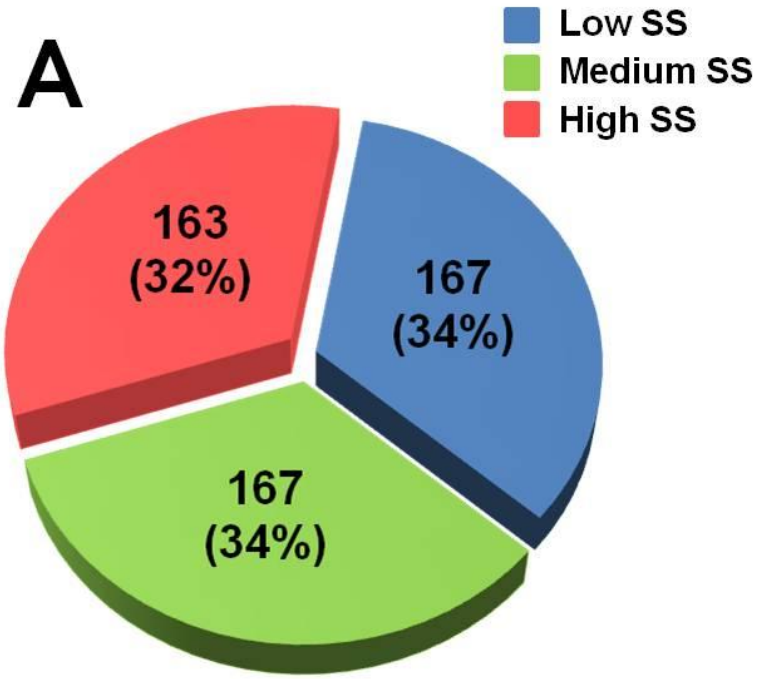
Functional SYNTAX Score

Reclassifies > 30% of Cases

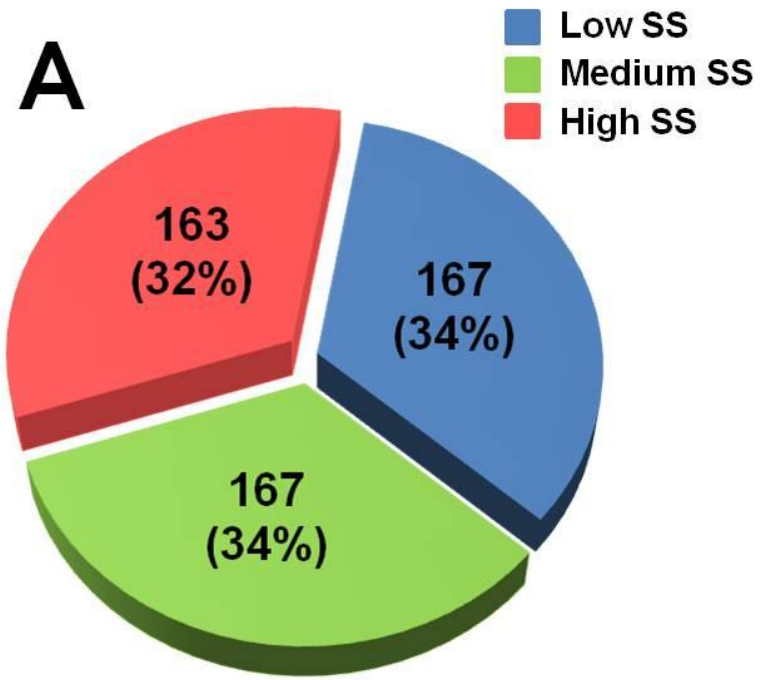


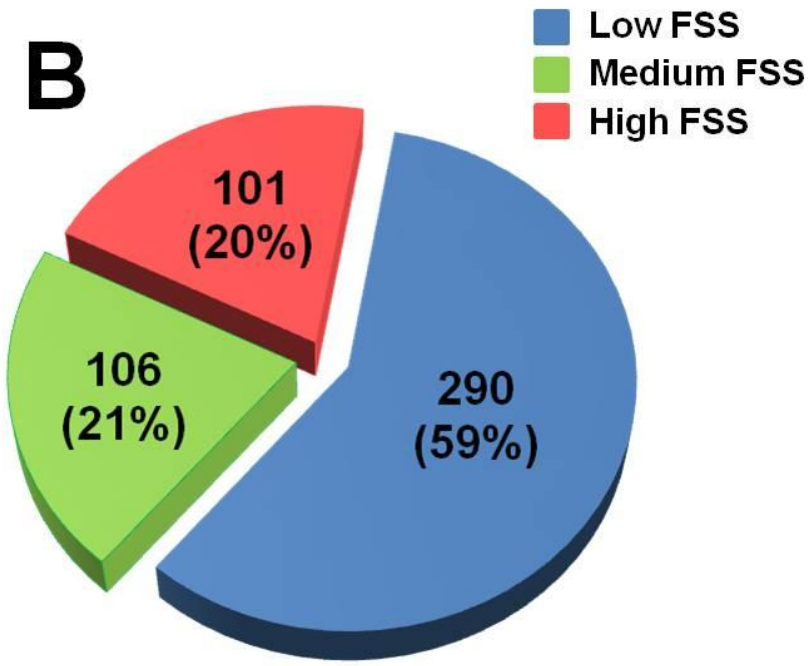
Without FFR

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

Functional SYNTAX Score

Reclassifies > 30% of Cases





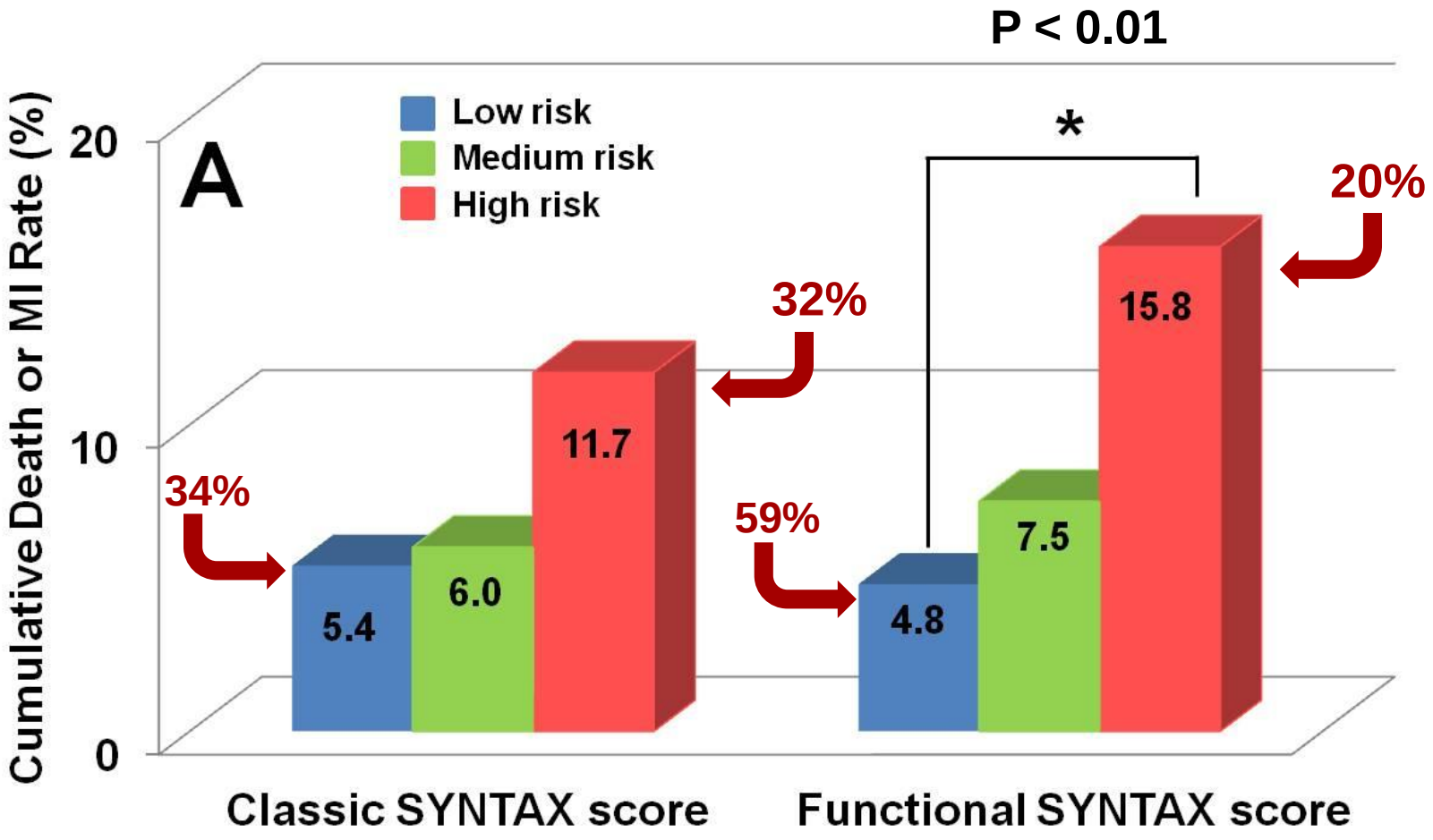
Without FFR

With FFR

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

Functional SYNTAX Score

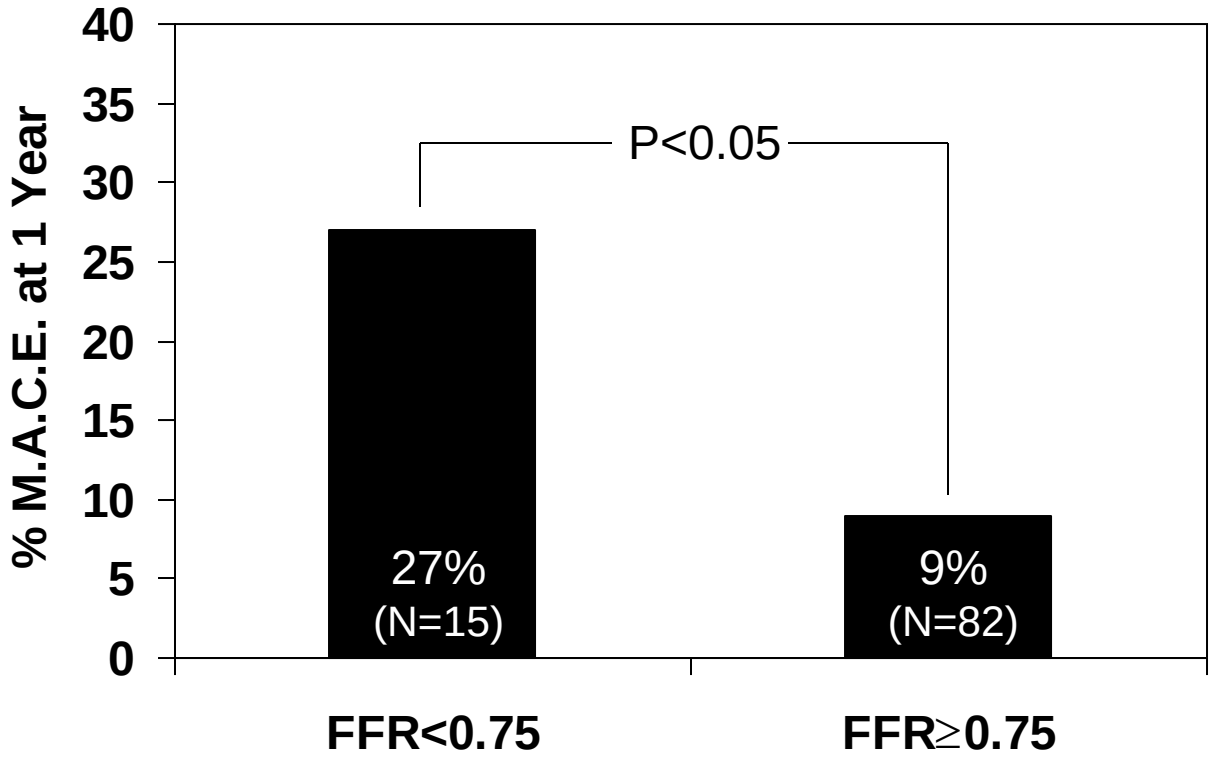
Discriminates Risk for Death/MI



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

Danger of Deferring PCI if FFR < 0.75

97 patients with intermediate lesions treated medically



Chamuleau et al. Am J Cardiol 2002;89:377-380

Danger of not Heeding FFR Result

71 patients in whom FFR was ignored:

34 deferred despite FFR < 0.80

37 stented despite FFR > 0.80

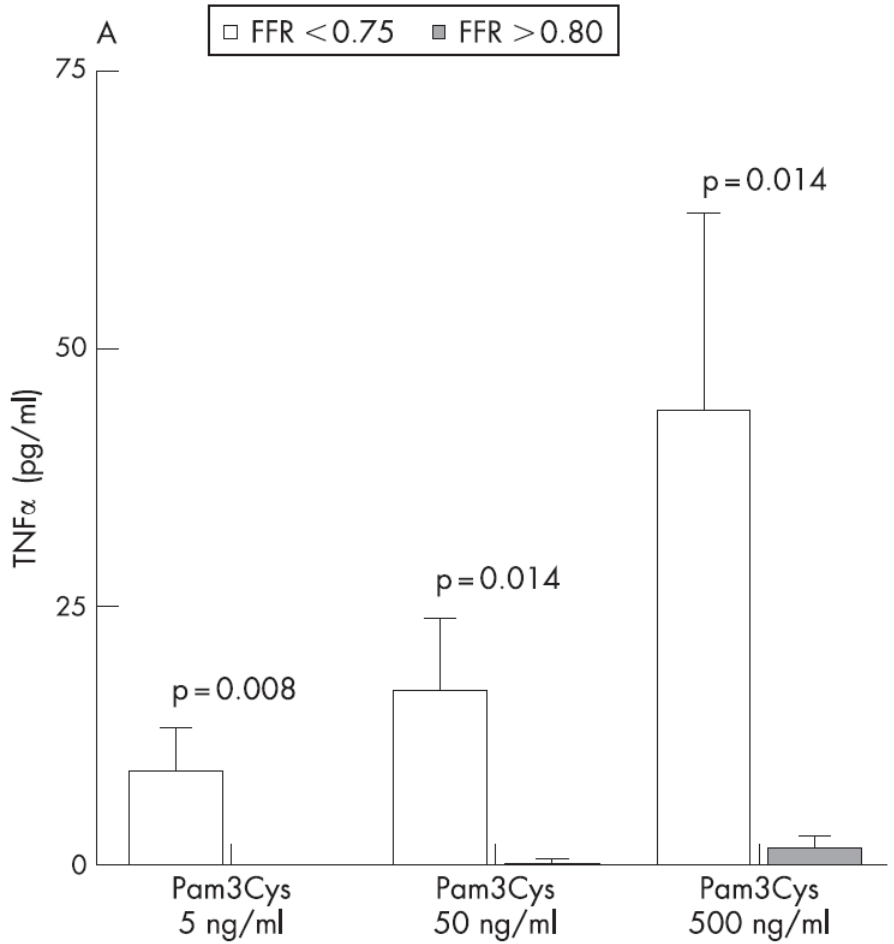
	Non-compliance group ($n = 71$)		Compliance group ($n = 336$)	
	No revasc ($n = 34$)	Revasc ($n = 37$)	No revasc ($n = 237$)	Revasc ($n = 99$)
Clinical events	7/34 (21%)	4/37 (11%)	14/237 (7%)	6/99 (6%)
Death	2/34 (6%)	1/37 (3%)	3/237 (1%)	0/99
Acute coronary syndromes	2/34 (6%)	1/31 (3%)	2/237 (1%)	0/99
Vessel revascularization	3/34 (9%)	2/37 (5)	9/237 (4%)	6/99 (6%)

P=0.01

Legalery et al. Eur Heart J 2005;26:2623-2629

Why might ischemia-producing lesions lead to “vulnerability”?

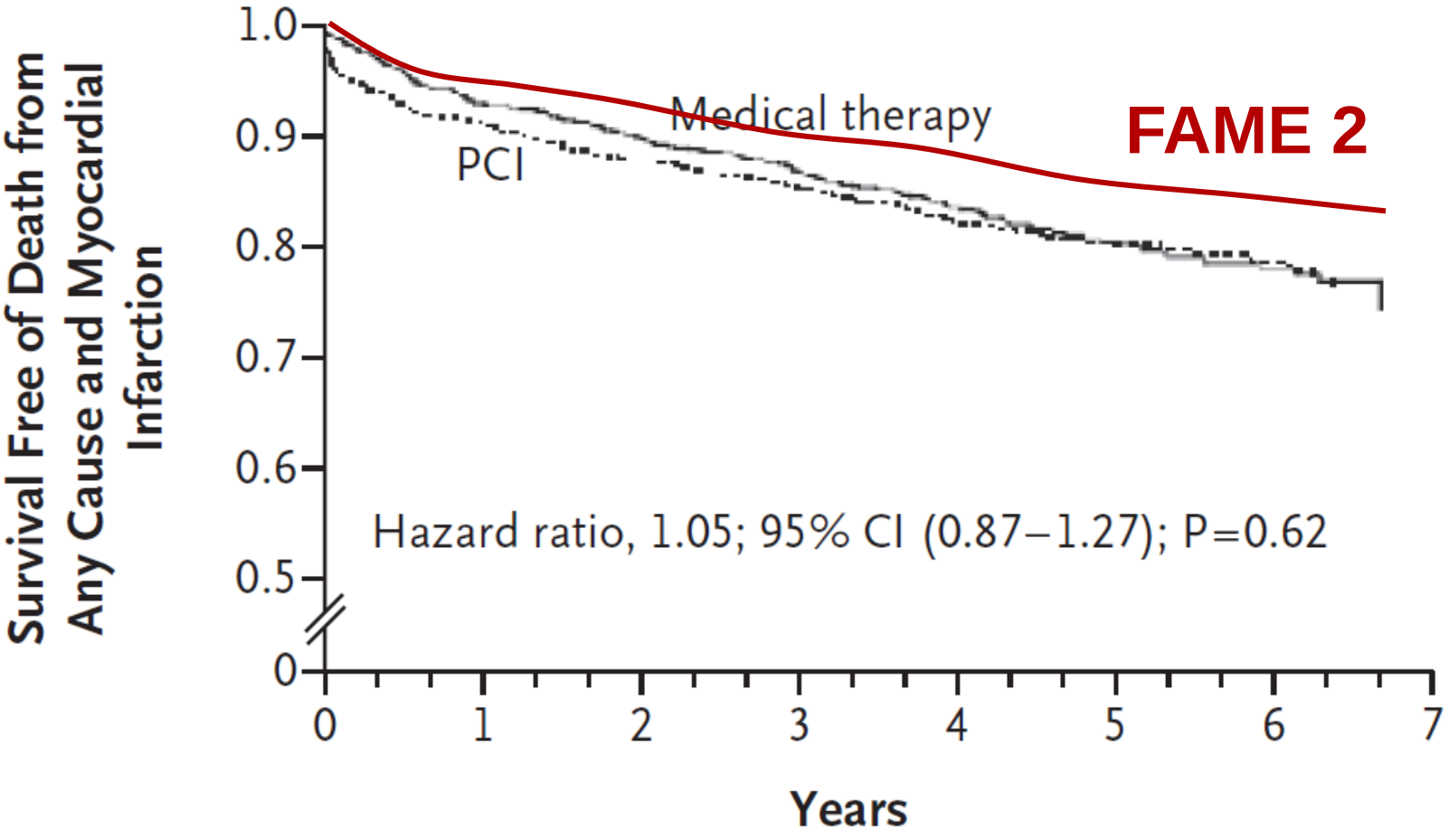
Increased production of TNF-α correlates with fractional flow reserve measured in 70 patients referred for PCI



Versteeg, et al. Heart 2008;94:770

Implications of FAME

Death and MI in the COURAGE study



Boden et al., New Engl J Med 2007;356:1503-16.

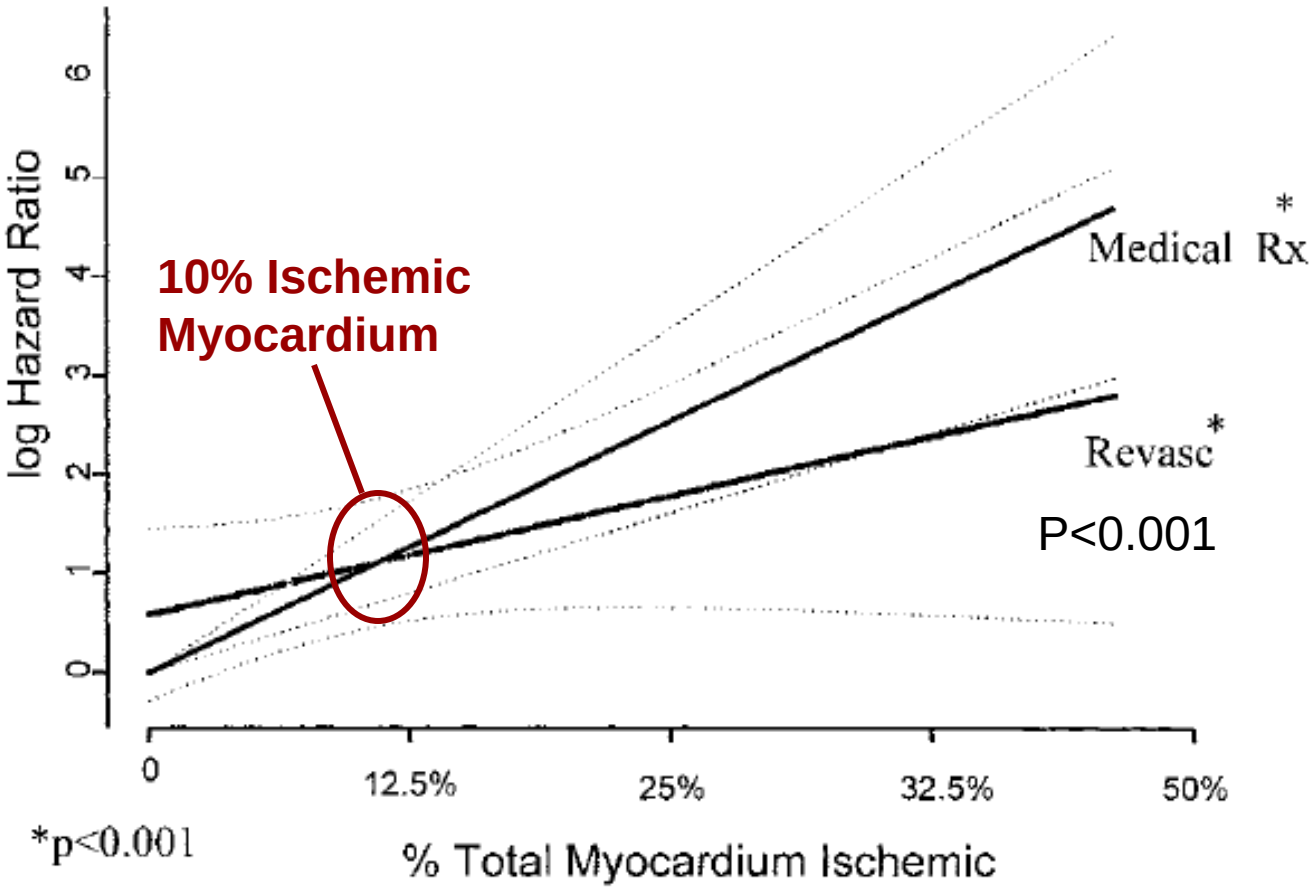
Degree of Ischemia in COURAGE

	PCI+OMT (n=159)			OMT (n=155)			Difference by Treatment	
	Pretreatment	6 to 18 Months	*P*	Pretreatment	6 to 18 Months	*P*	*P*	*P*
Rest TPD	6.4±7	3.4±6	<0.0001	6.1±7	3.3±6	<0.0001	0.70	0.83
Stress TPD	14.6±10	8.9±8	<0.0001	14.7±11	11.4±10	<0.0001	0.87	0.018
Territory								
Right coronary artery	2.5±3	1.4±2	<0.0001	2.7±4	2.1±3	<0.0001	0.60	0.012
Left anterior descending artery	5.8±5	3.6±4	<0.0001	5.9±5	4.8±5	<0.0001	0.97	0.021
Left circumflex artery	5.3±4	3.6±4	<0.0001	5.3±5	4.2±4	<0.0001	0.96	0.26
% Ischemia			<0.0001			<0.0001	0.40	0.019
0 to 4.9%	43.0%	53.4%		37.9%	46.0%			
5% to 9.9%	26.0%	30.9%		29.1%	27.0%			
≥10%	31.0%	15.8%		33.0%	27.0%			
Left ventricular ejection fraction								
Rest	57.0±11	57.0±9	0.97	57.0±9	57.7±6	0.30	0.97	0.14
Poststress	51.0±11	54.8±10	0.001	53.4±10	54.2±12	0.38	0.09	0.49
End-diastolic volume								
Rest	103.2±40	105.2±38	0.41	100.0±30	102.6±32	0.43	0.26	0.30
Poststress	112.7±40	111.0±38	0.44	102.3±33	105.9±35	0.21	0.13	0.33
End-systolic volume								
Rest	47.6±29	47.9±28	0.84	45.2±23	45.0±25	0.88	0.13	0.30
Poststress	57.2±29	52.5±29	0.02	49.5±23	49.8±24	0.88	0.33	0.49

Shaw, et al. Circulation 2008;117:1283-91.

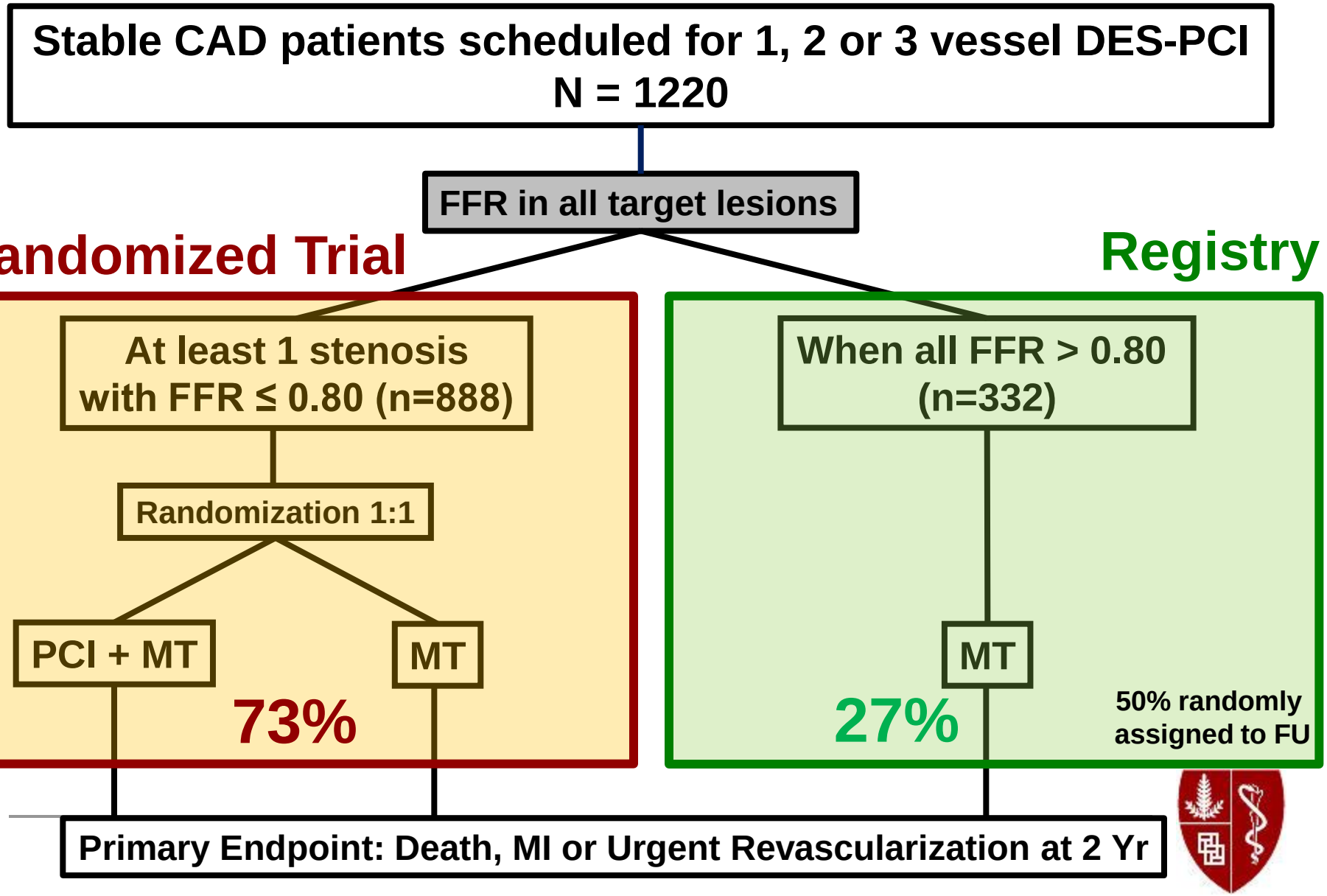
Importance of Ischemia

With greater degrees of ischemia, there is a survival benefit for revascularization



Hachamovitch, et al. Circulation 2003;107:2900-06.

FAME 2


Stable CAD patients scheduled for 1, 2 or 3 vessel DES-PCI
N = 1220
FFR in all target lesions
Randomized Trial
Registry
At least 1 stenosis with FFR ≤ 0.80 (n=888)
Randomization 1:1
PCI + MT
MT
73%
When all FFR > 0.80 (n=332)
MT
27%
50% randomly assigned to FU
Primary Endpoint: Death, MI or Urgent Revascularization at 2 Yr

Baseline Characteristics

	Randomized Trial		Registry	p
Patients, N	PCI+MT=447	MT=441	with FU=166	
Demographic				
Age (y)	63.5±9.3	63.9±9.6	63.6±9.8	0.90
Male sex - (%)	79.6	76.6	68.1	0.005
BMI	28.3±4.3	28.4±4.6	27.8±3.9	0.14
Risk factors for CAD				
Positive family history CAD - (%)	48.3	46.9	45.8	0.65
Smoking - (%)	19.9	20.4	21.1	0.79
Hypertension - (%)	77.6	77.8	81.9	0.23
Hypercholesterolemia - (%)	73.9	78.9	71.1	0.15
Diabetes mellitus - (%)	27.5	26.5	25.3	0.65
Insulin requiring diabetes - (%)	8.7	8.8	6.0	0.24

De Bruyne, et al. New Engl J Med 2012;367:991-1001

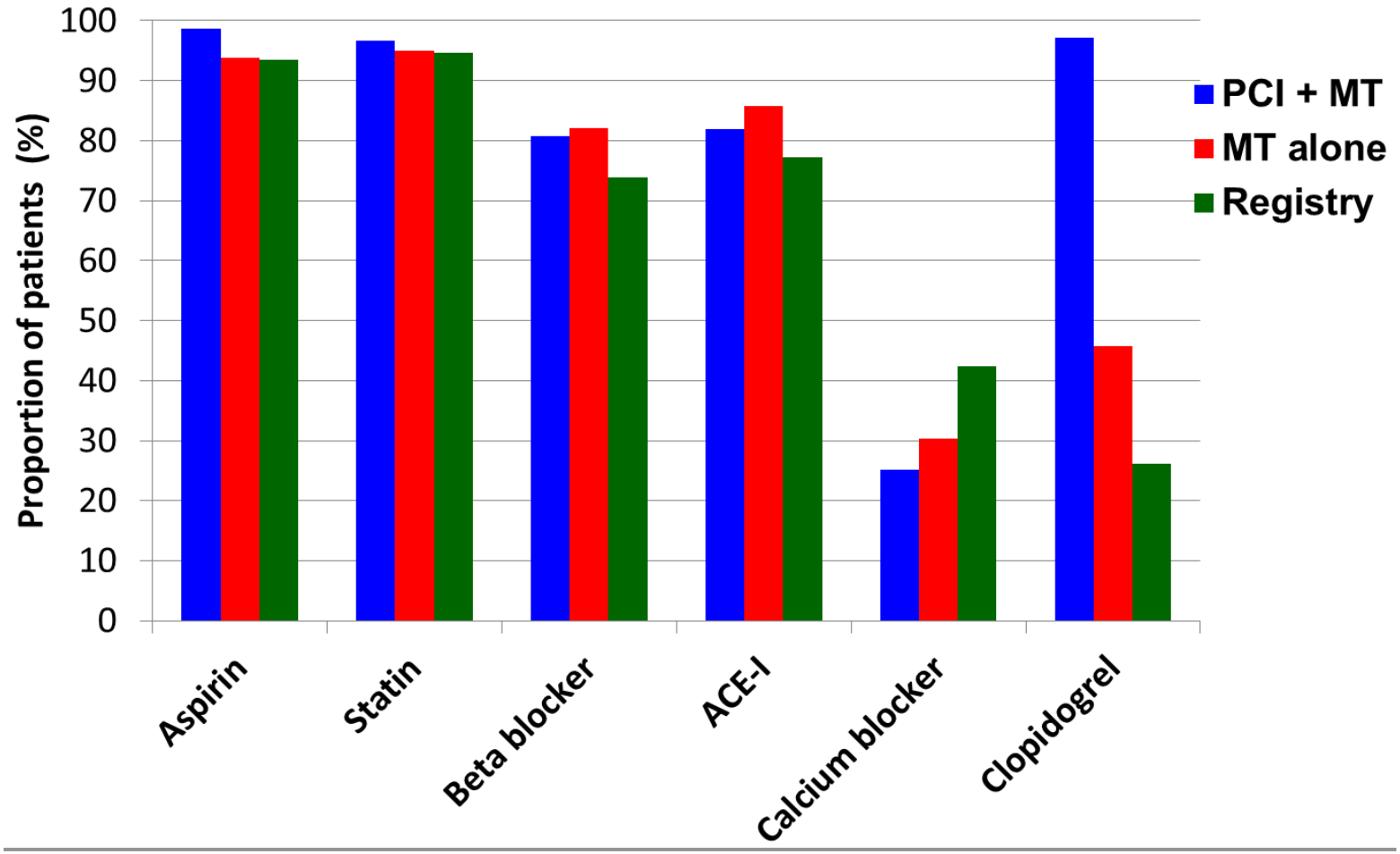
Angiographic Characteristics

	Randomized trial N=888		Registry N=322	P*
Patients, N	**PCI+MT=447**	**MT=441**	**with FU=166**	
Angiographically significant stenoses - no. per patient	**1.87±1.05**	**1.73±0.94**	**1.32±0.59**	**<0.001**
No of vessels with ≥ 1 significant stenoses - (%)				**<0.001**
1	**56.2**	**59.2**	**81.9**	
2	**34.9**	**33.1**	**15.7**	
3	**8.9**	**7.7**	**2.4**	
Prox- or mid- LAD stenoses - (%)	**65.1**	**62.6**	**44.6**	**<0.001**

De Bruyne, et al. New Engl J Med 2012;367:991-1001

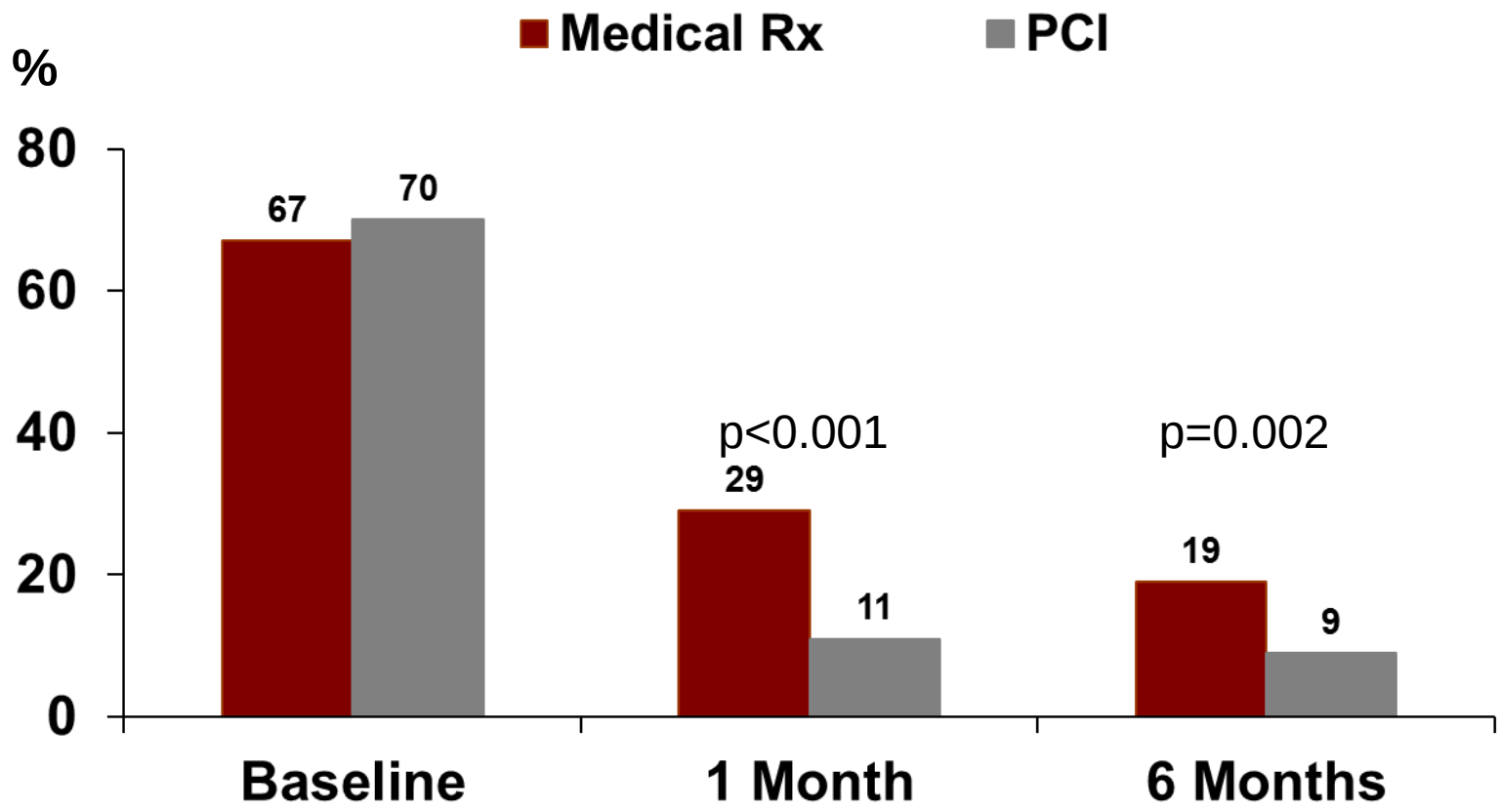
FAME 2 Trial

Medications at 6 Month Follow-Up



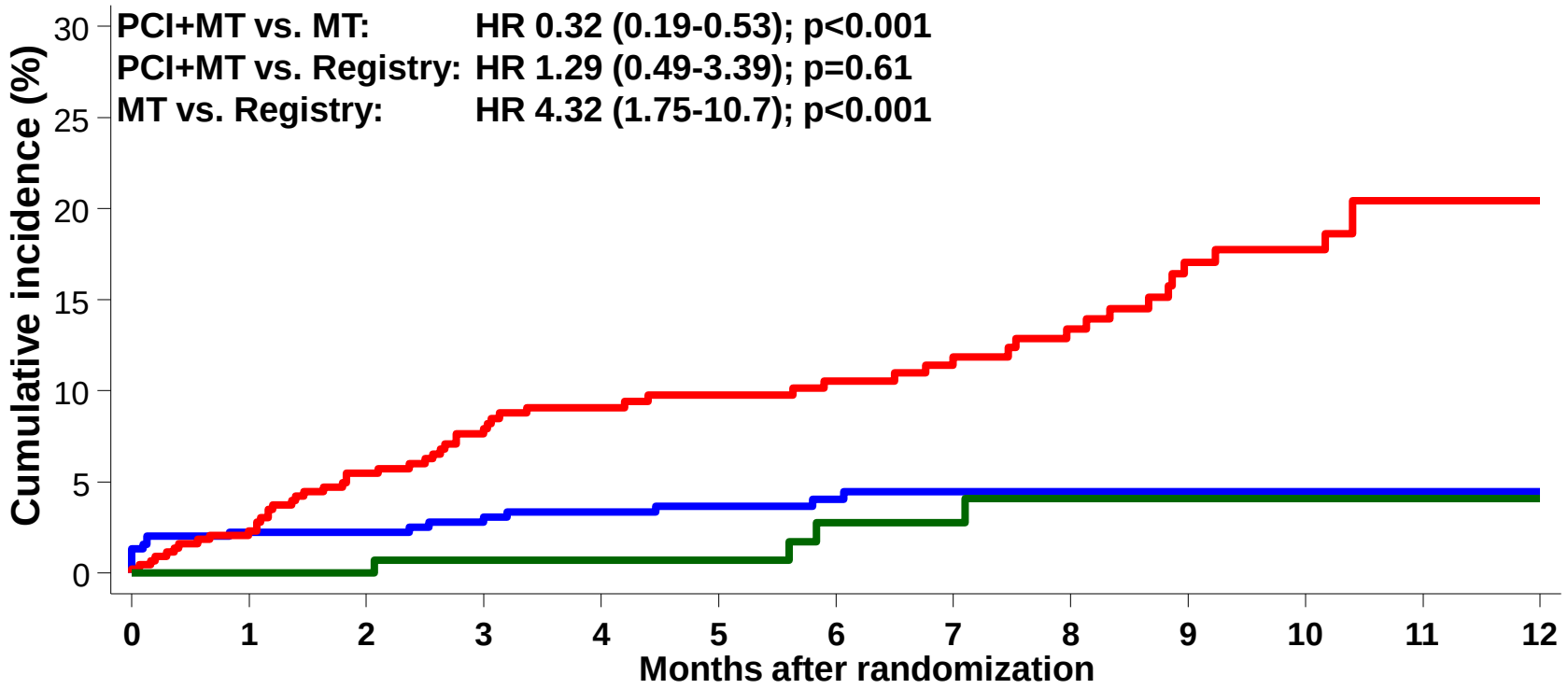
De Bruyne, et al. New Engl J Med 2012;367:991-1001

Patients with Angina Class II to IV



De Bruyne, et al. New Engl J Med 2012;367:991-1001

Primary Endpoint: *Death, MI, Urgent Revasc*



No. at risk

MT	441	414	370	322	283	253	220	192	162	127	100	70	37
PCI+MT	447	414	388	351	308	277	243	212	175	155	117	92	53
Registry	166	156	145	133	117	106	93	74	64	52	41	25	13

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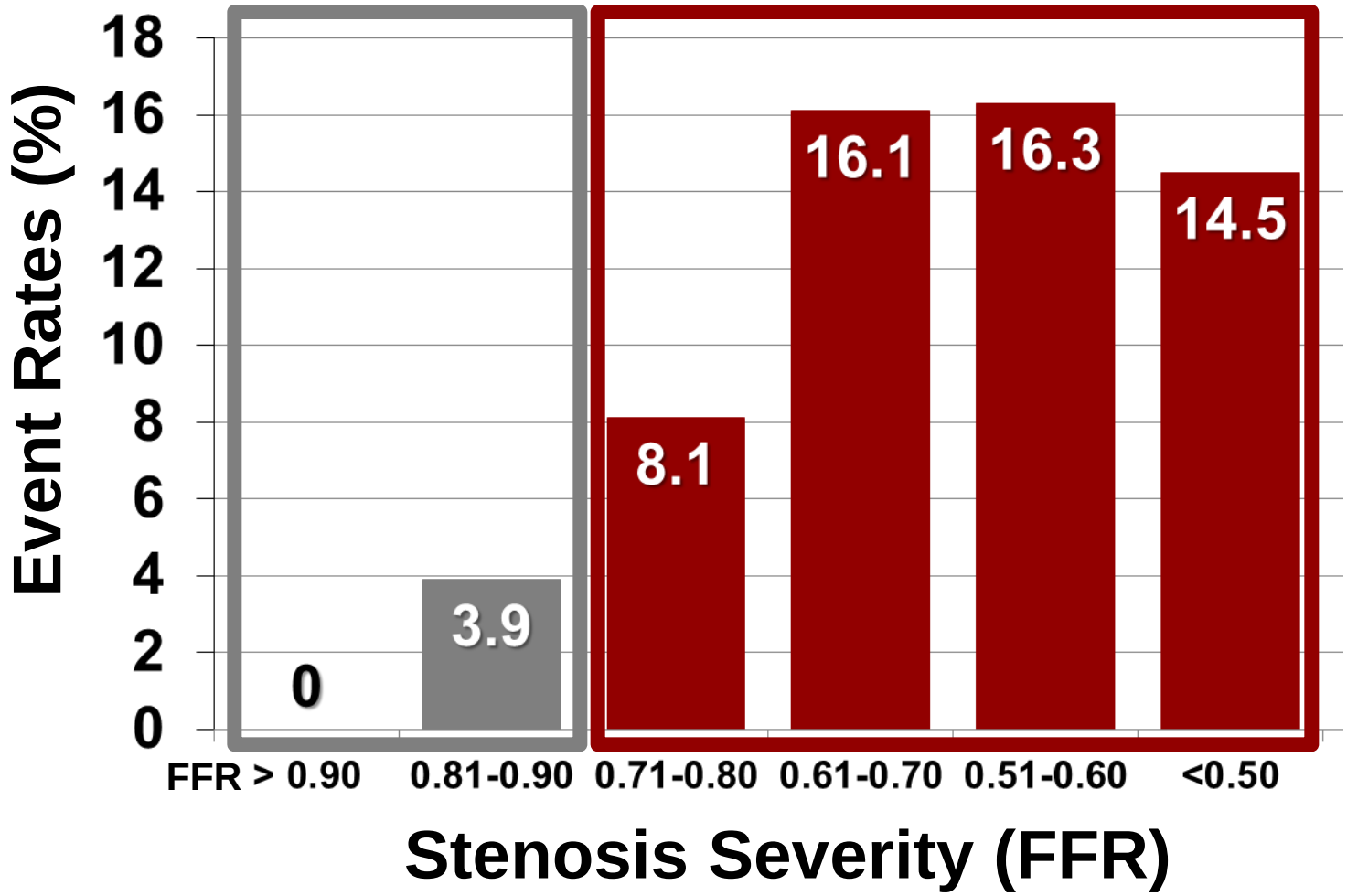
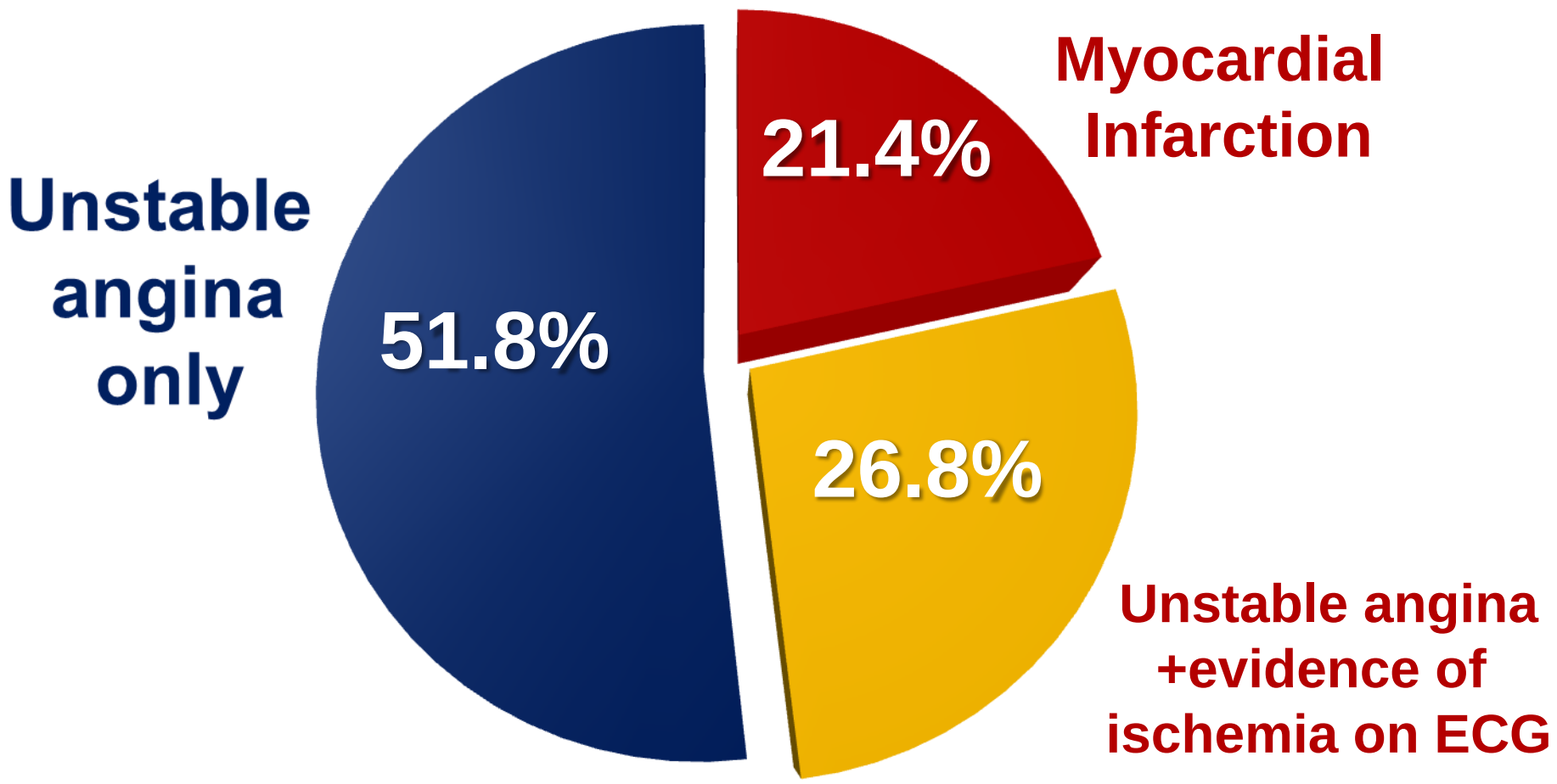
Relationship Between FFR and Outcomes

FAME 2: Patients with angiographically significant stenoses treated with OMT



Courtesy of: Bernard De Bruyne, MD, PhD

Patients with urgent revascularization

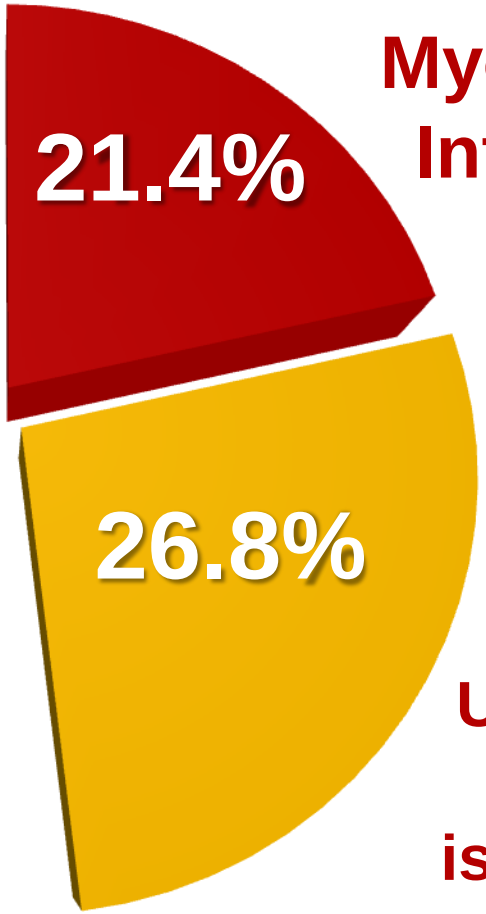


Patients with urgent revascularization

Urgent revascularization driven by MI or unstable angina with ECG changes

FFR-Guided PCI + MT		MT
0.9%	vs.	5.2%

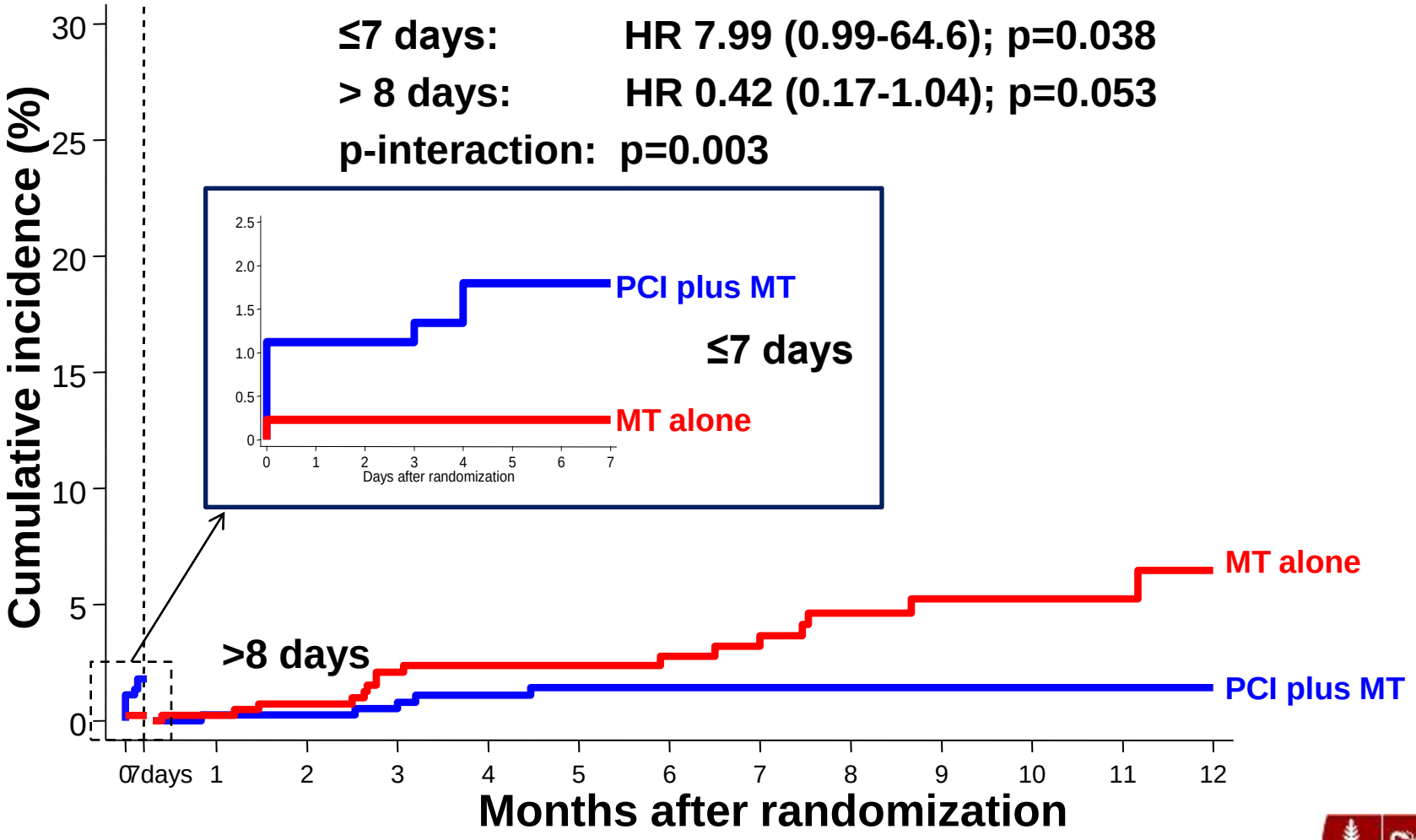
p<0.001
83% Relative Risk Reduction



Myocardial Infarction

Unstable angina +evidence of ischemia on ECG

Landmark Analysis for Death/MI



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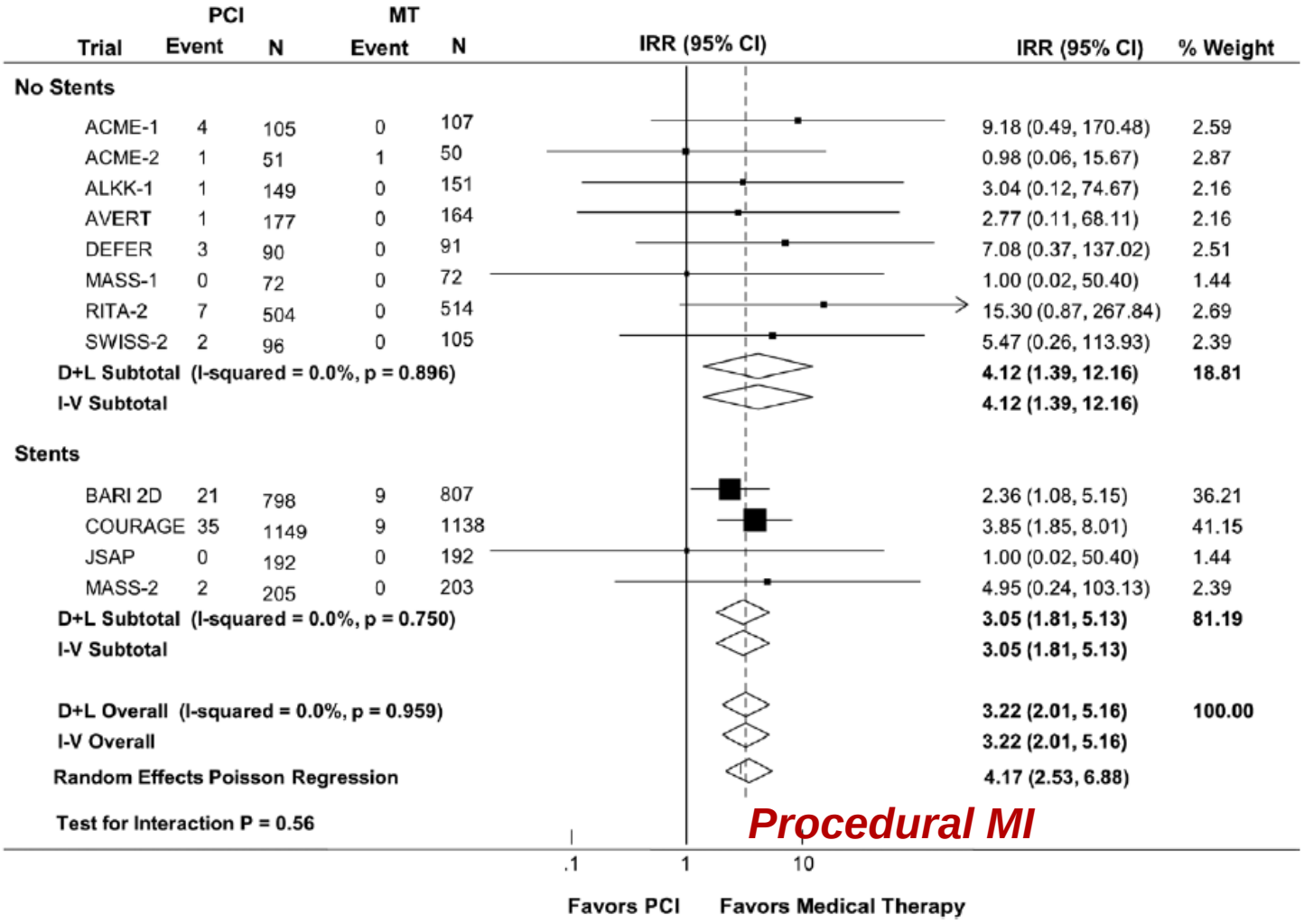
Spontaneous vs. Procedural MI

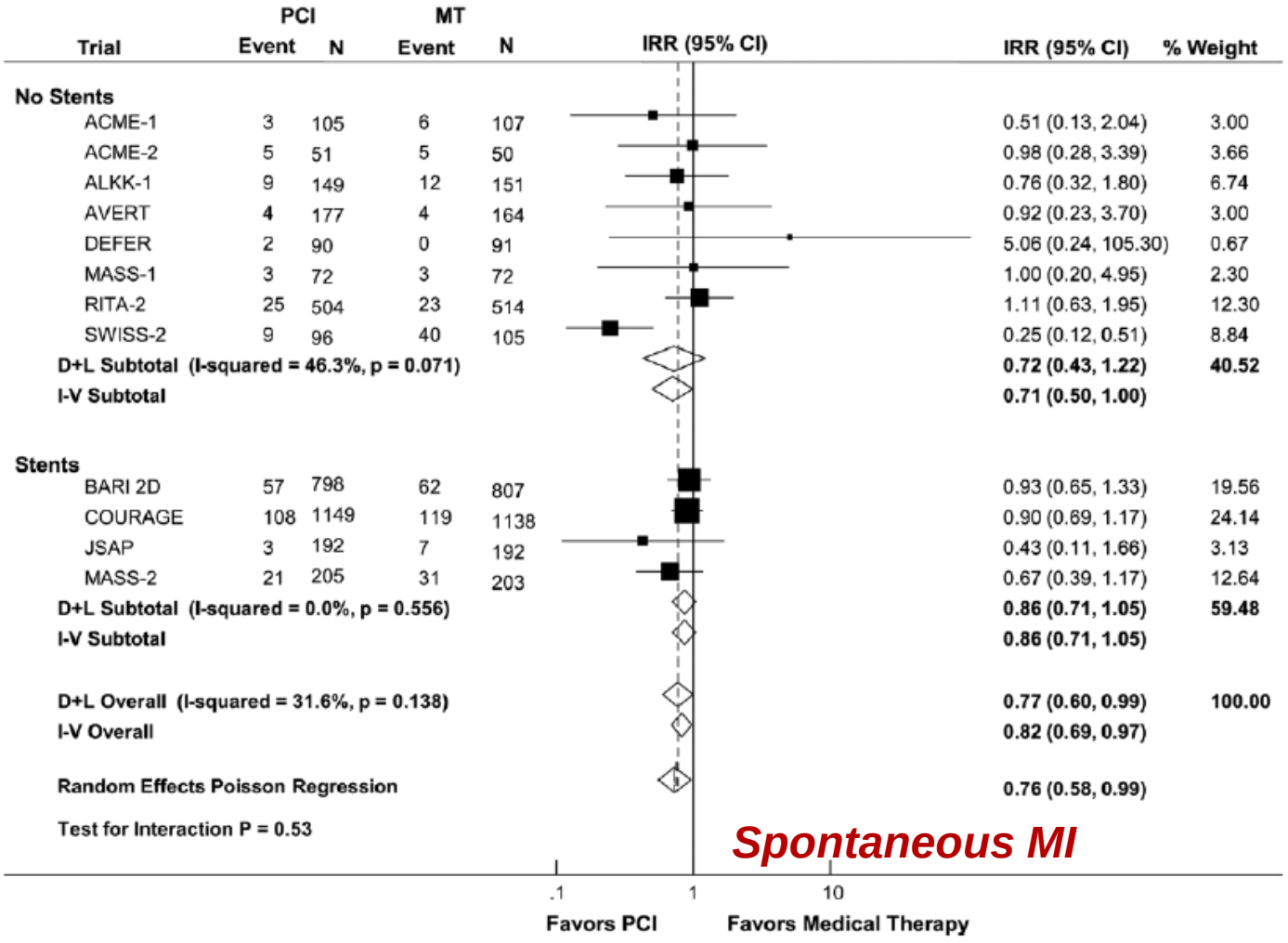
Meta-analysis of 12 randomized trials comparing PCI to OMT



Bangalore, et al. Circulation 2013;127:769-781

Spontaneous vs. Procedural MI

Meta-analysis of 12 randomized trials comparing PCI to OMT



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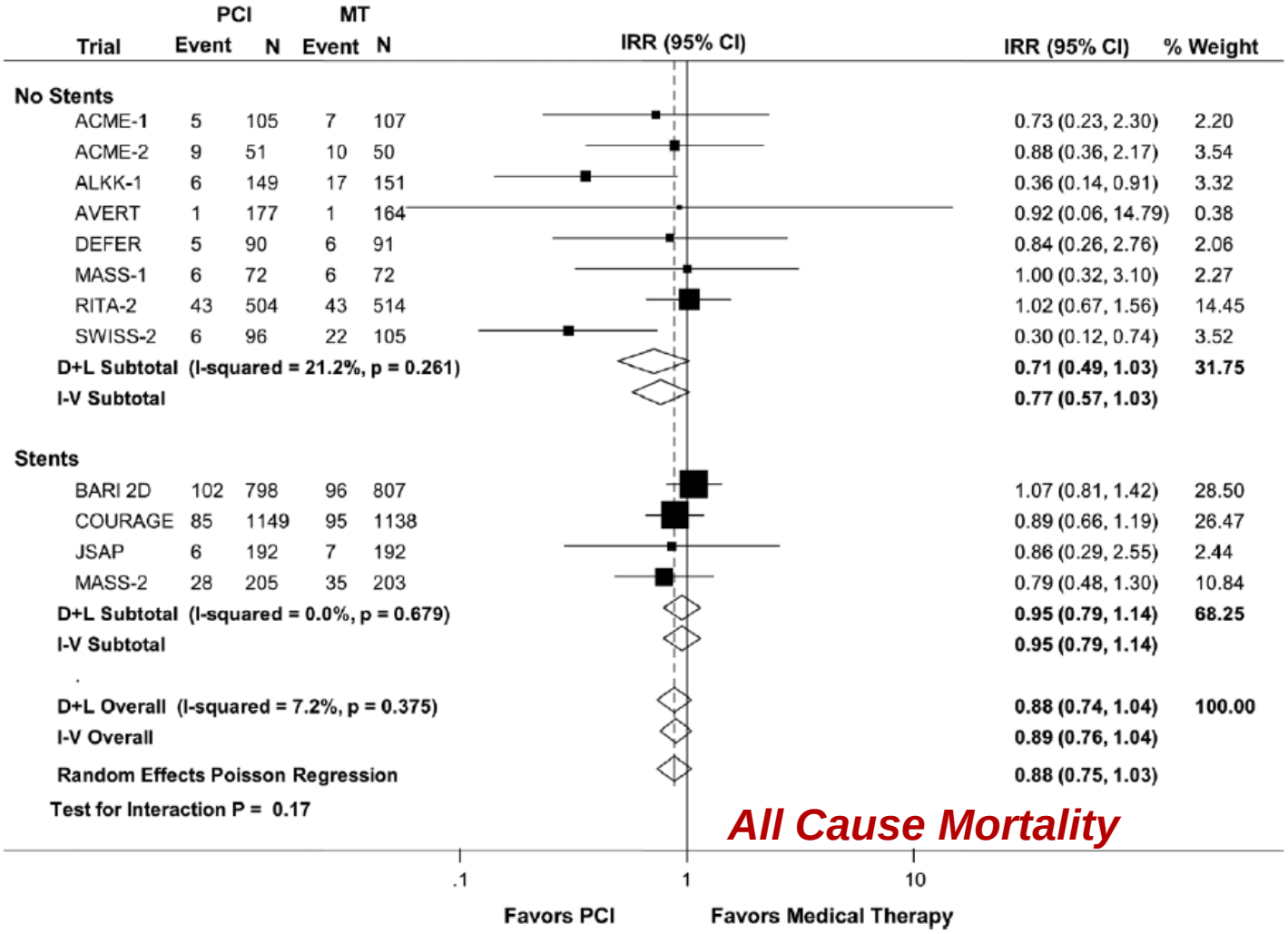

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Conclusion:

- FFR-Guided PCI
  - Improves outcomes compared to angio-guidance
  - Simplifies PCI in patients with multivessel disease and may convert patients from CABG to PCI
  - Improves outcomes compared to medical therapy in patients with stable CAD