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Seoul, Korea
November 21st, 2009

Fractional Flow Reserve and the Results of the FAME Study

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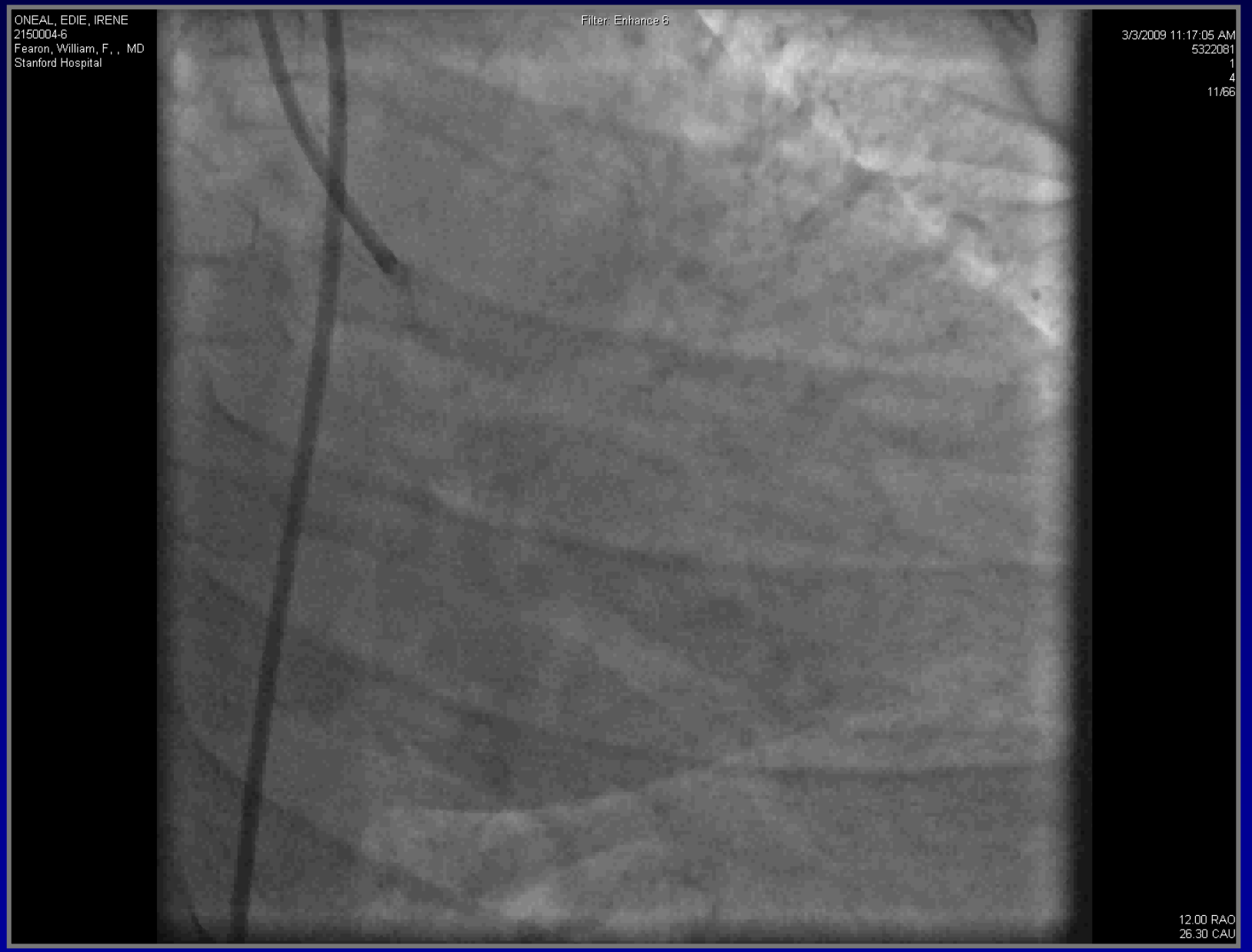
Post FAME Case Example

- 46 year old diabetic woman with HTN and dyslipidemia presents to outside hospital with a NSTEMI in March 2009.
- 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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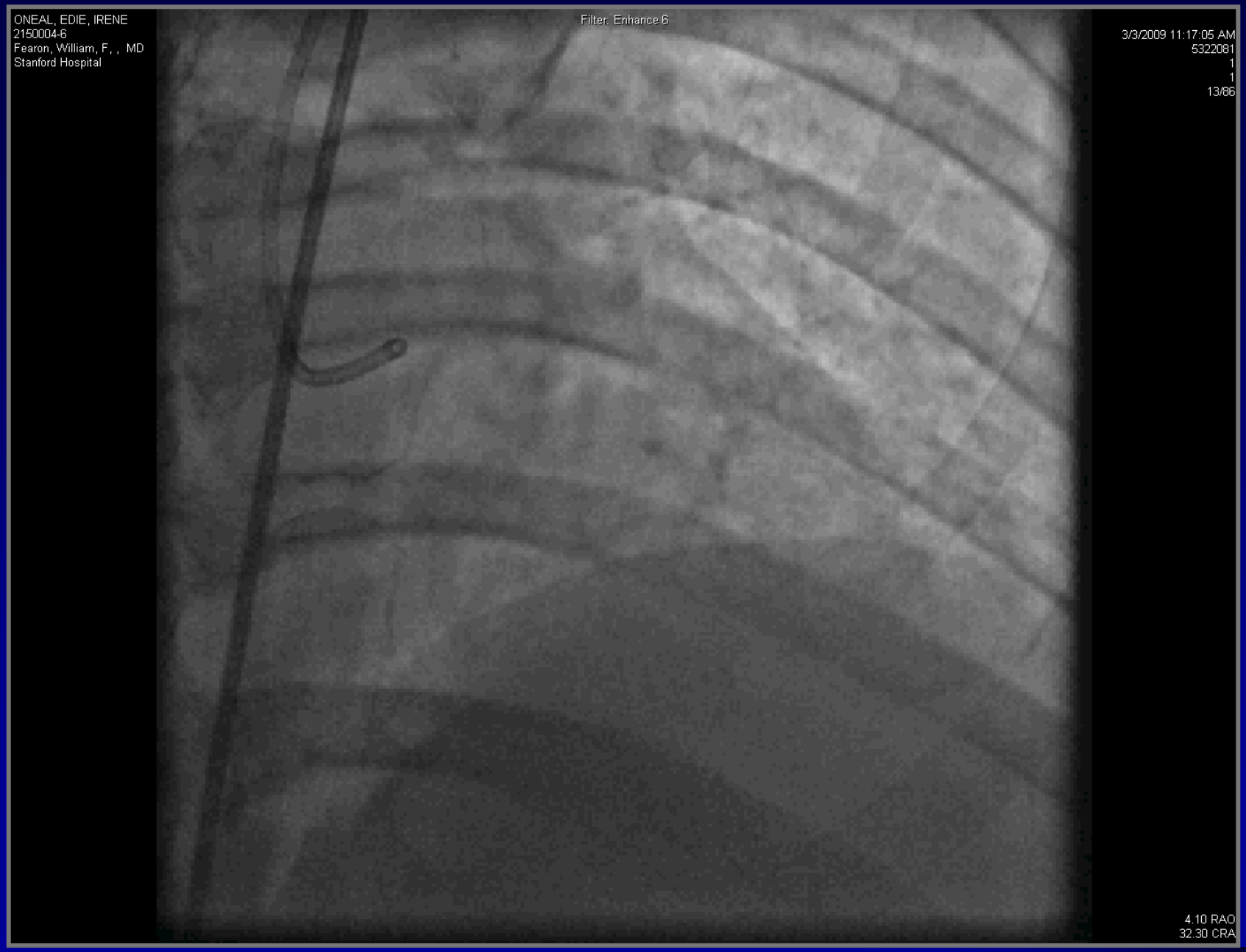
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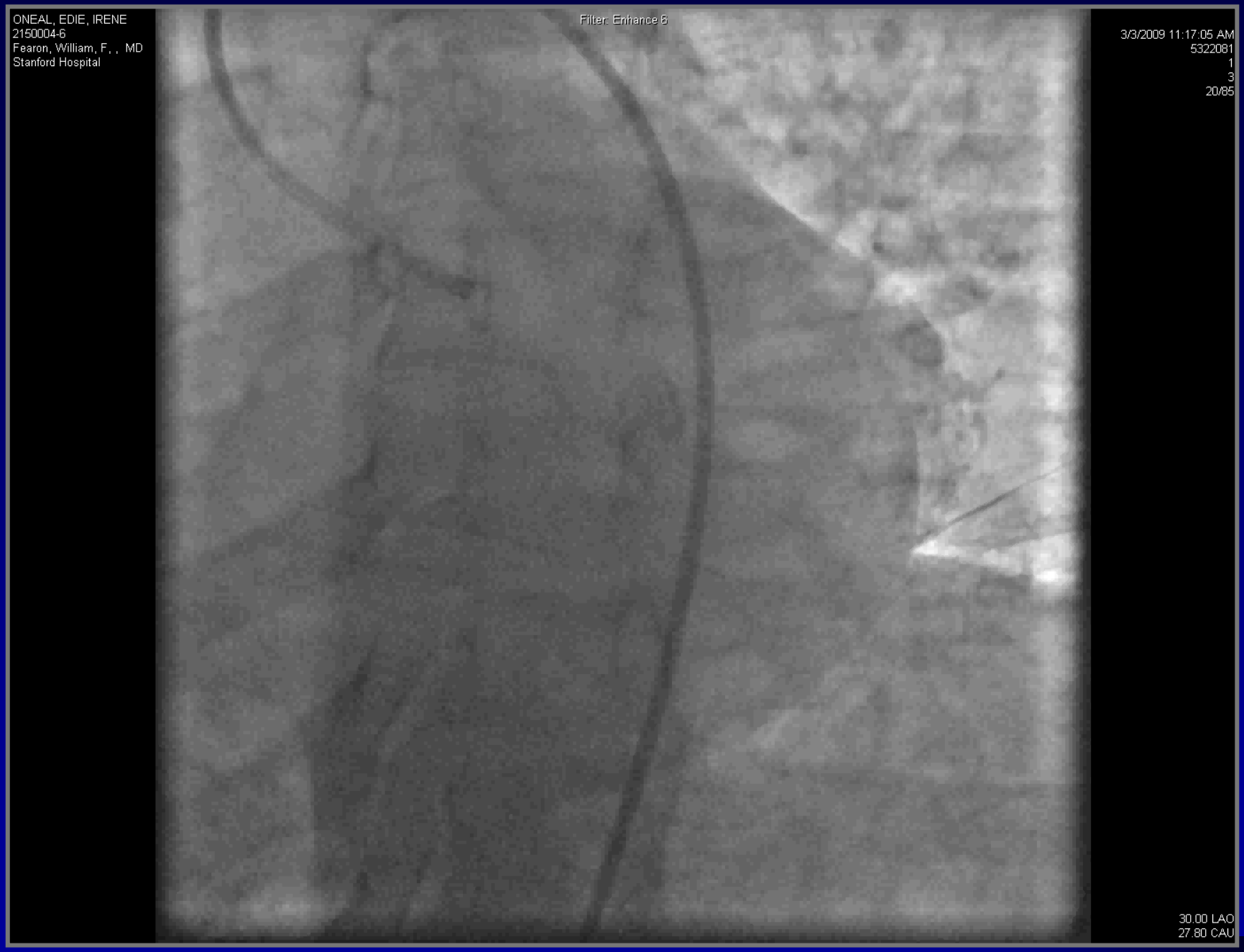
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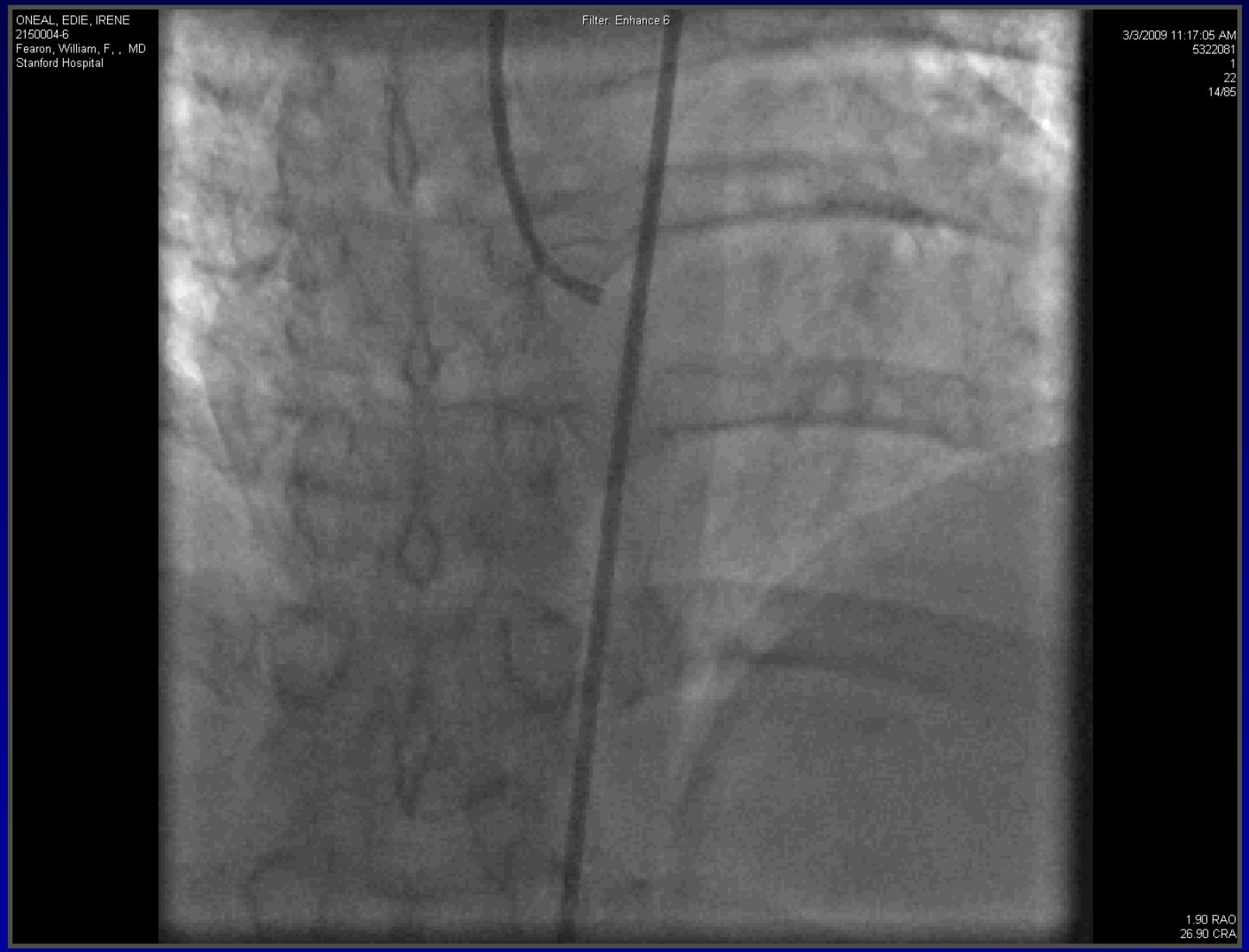
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Frequency of Stress Testing to Document Ischemia Prior to Elective Percutaneous Coronary Intervention

Grace A. Lin, MD, MAS
R. Adams Dudley, MD, MBA
F. L. Lucas, PhD
David J. Malenka, MD
Eric Vittinghoff, PhD
Rita F. Redberg, MD, MSc

Context Guidelines call for documenting ischemia in patients with stable coronary artery disease prior to elective percutaneous coronary intervention (PCI).

Objective To determine the frequency and predictors of stress testing prior to elective PCI in a Medicare population.

Design, Setting, and Patients Retrospective, observational cohort study using claims data from a 20% random sample of 2004 Medicare fee-for-service beneficiaries aged 65 years or older who had an elective PCI (N=23 887).

Main Outcome Measures Percentage of patients who underwent stress testing within 90 days prior to elective PCI; variation in stress testing prior to PCI across 306 hospital referral regions; patient, physician, and hospital characteristics that predicted the appropriate use of stress testing prior to elective PCI.

Results In the United States, 44.5% (n=10 629) of patients underwent stress testing within the 90 days prior to elective PCI. There was wide regional variation among the hospital referral regions with stress test rates ranging from 22.1% to 70.6% (national mean, 44.5%; interquartile range, 39.0%-50.9%). Female sex (adjusted odds ratio [AOR], 0.91; 95% confidence interval [CI], 0.86-0.97), age of 85 years or older (AOR, 0.83; 95% CI, 0.72-0.95), a history of congestive heart failure (AOR, 0.85; 95% CI, 0.79-0.92), and prior cardiac catheterization (AOR, 0.45; 95% CI, 0.38-0.54) were associated with a decreased likelihood of prior stress testing. A history of chest pain (AOR, 1.28; 95% CI, 1.09-1.54) and black race (AOR, 1.26; 95% CI, 1.09-1.46) increased the likelihood of stress testing prior to PCI. Patients treated by physicians performing 150 or more PCIs per year were less likely to have stress testing prior to PCI (AOR, 0.84; 95% CI, 0.77-0.93). No hospital characteristics were associated with receipt of stress testing.

Conclusion The majority of Medicare patients with stable coronary artery disease do not have documentation of ischemia by noninvasive testing prior to elective PCI.

JAMA. 2008;300(15):1765-1773 www.jama.com

In the United States, percutaneous coronary intervention (PCI) has become a common treatment strategy for patients with stable coronary artery disease (CAD) and such patients now account for the majority of PCIs performed.[1,2] However, multiple studies have established that some important outcomes for patients with stable CAD (death and risk of future myocardial infarction) do not differ between patients treated with PCI plus optimal medical therapy and patients treated with optimal medical therapy alone.[3-10] The addition of PCI does offer quicker relief of angina than medical therapy alone but also carries an increased risk of repeat revascularization, late-stent thrombosis, and a decreased

JAMA 2008;300:1765

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Limitations of Noninvasive Imaging:

143 Patients with angiographically significant 3 vessel disease (> 70% diameter stenosis)

Nuclear Scan Finding	% Patients
No Defect	18%
Single Vessel Pattern	36%
Two Vessel Pattern	36%
Three Vessel Pattern	10%

Lima et al. J Am Coll Cardiol 2003;42:63-70

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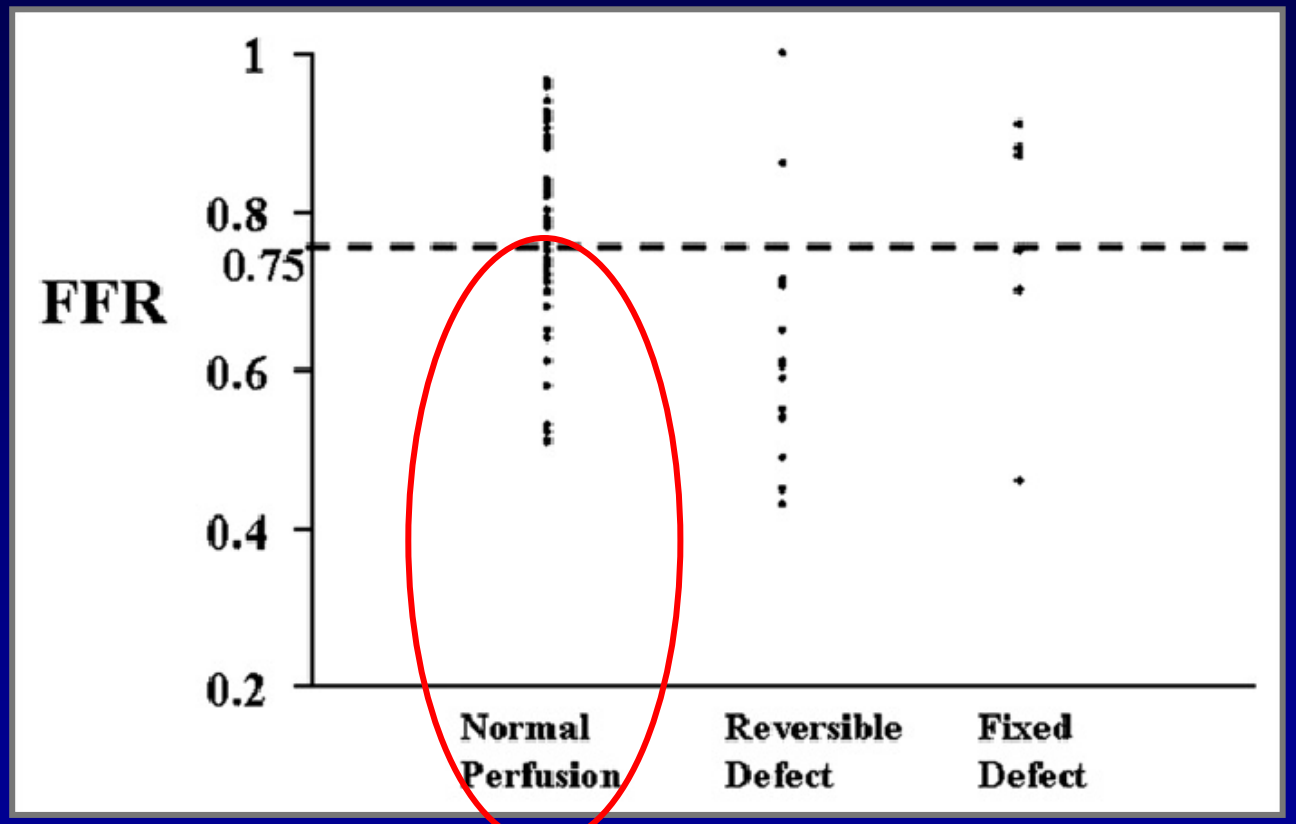
FFR vs. Nuclear Perfusion Scan in MVD

36 patients with multivessel CAD



Discordance occurred in 31% of vessels / territories, predominantly because of a low FFR and normal nuclear result

Ragosta et al. Am J Cardiol 2007;99:896-902

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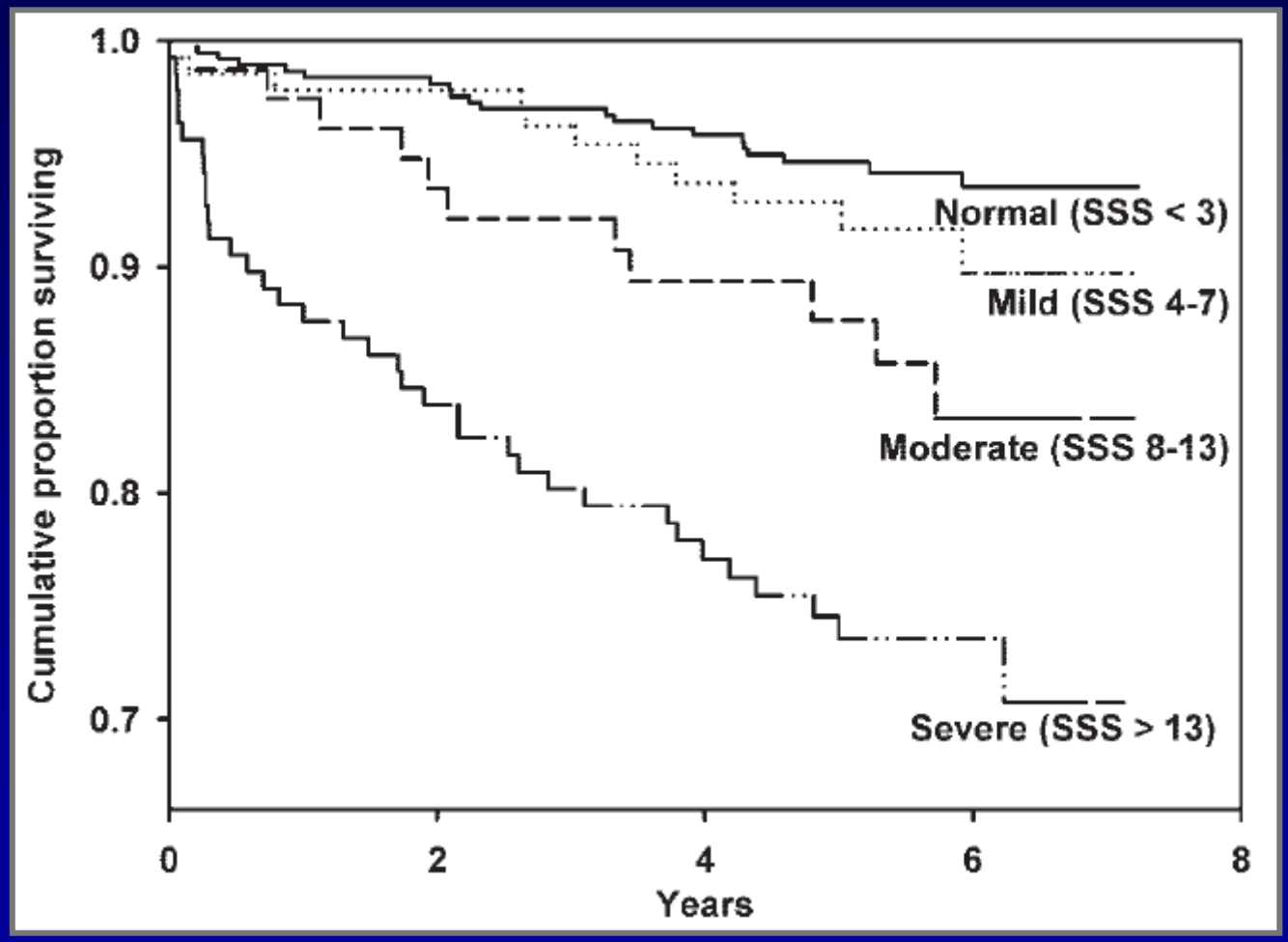
Prognostic Importance of Ischemia

Nuclear perfusion scans in 718 patients followed for 5 years



Leslie, et al. J Nucl Med 2005;46:204-11

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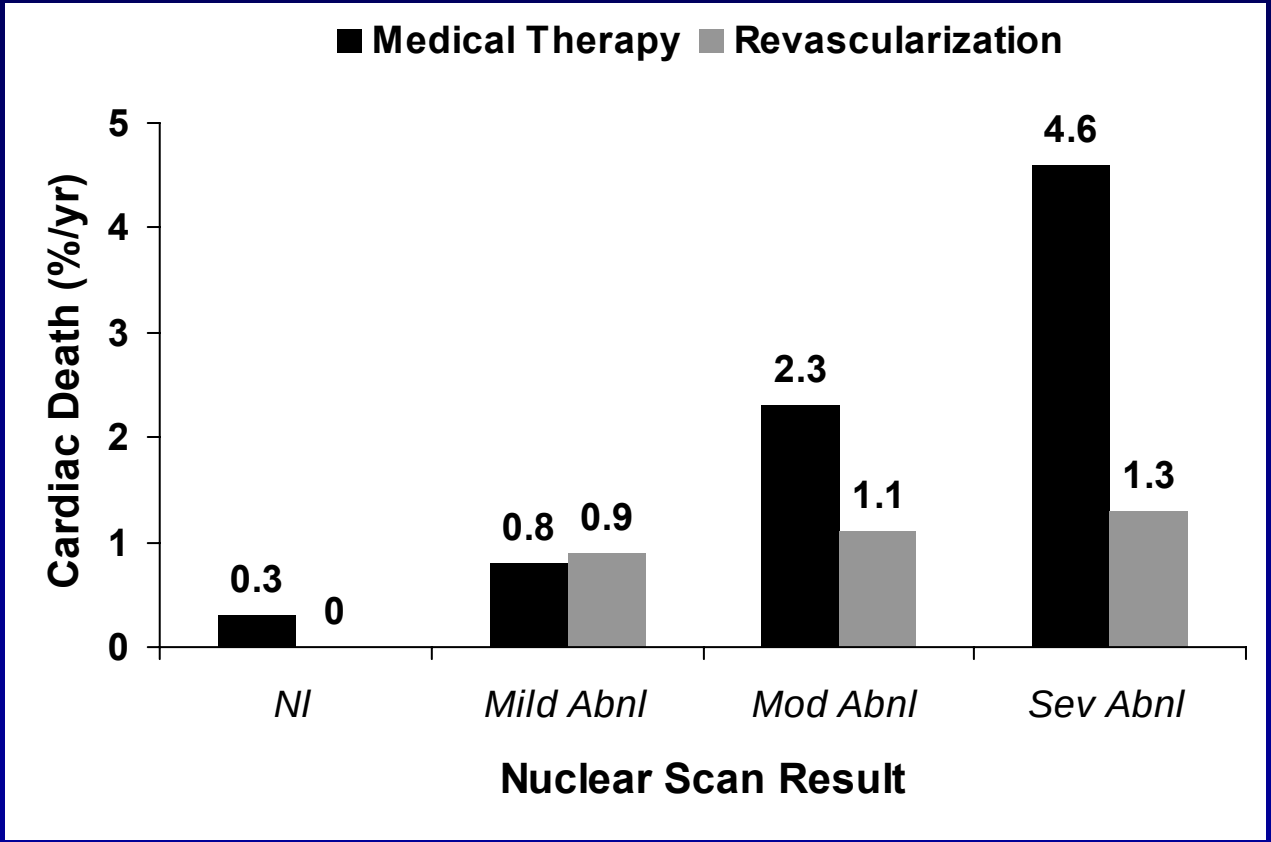
Importance of Revascularization when Ischemia is Present

Nuclear perfusion scans performed in > 5000 patients



Hachamovitch et al. Circulation 1998;97:535-543

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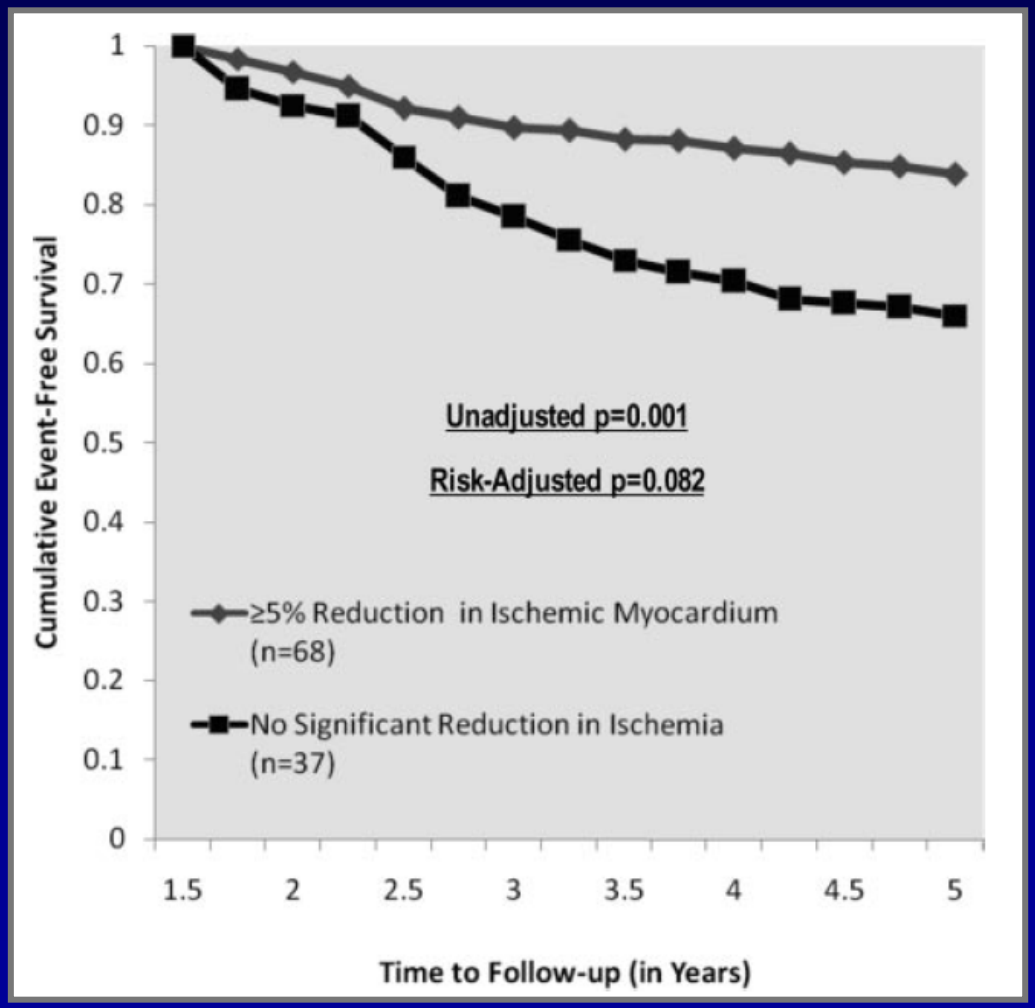
COURAGE Nuclear Substudy

Comparison of death/MI in patients with mod-severe pre-treatment ischemia



Shaw et al. Circulation 2008;117:1283

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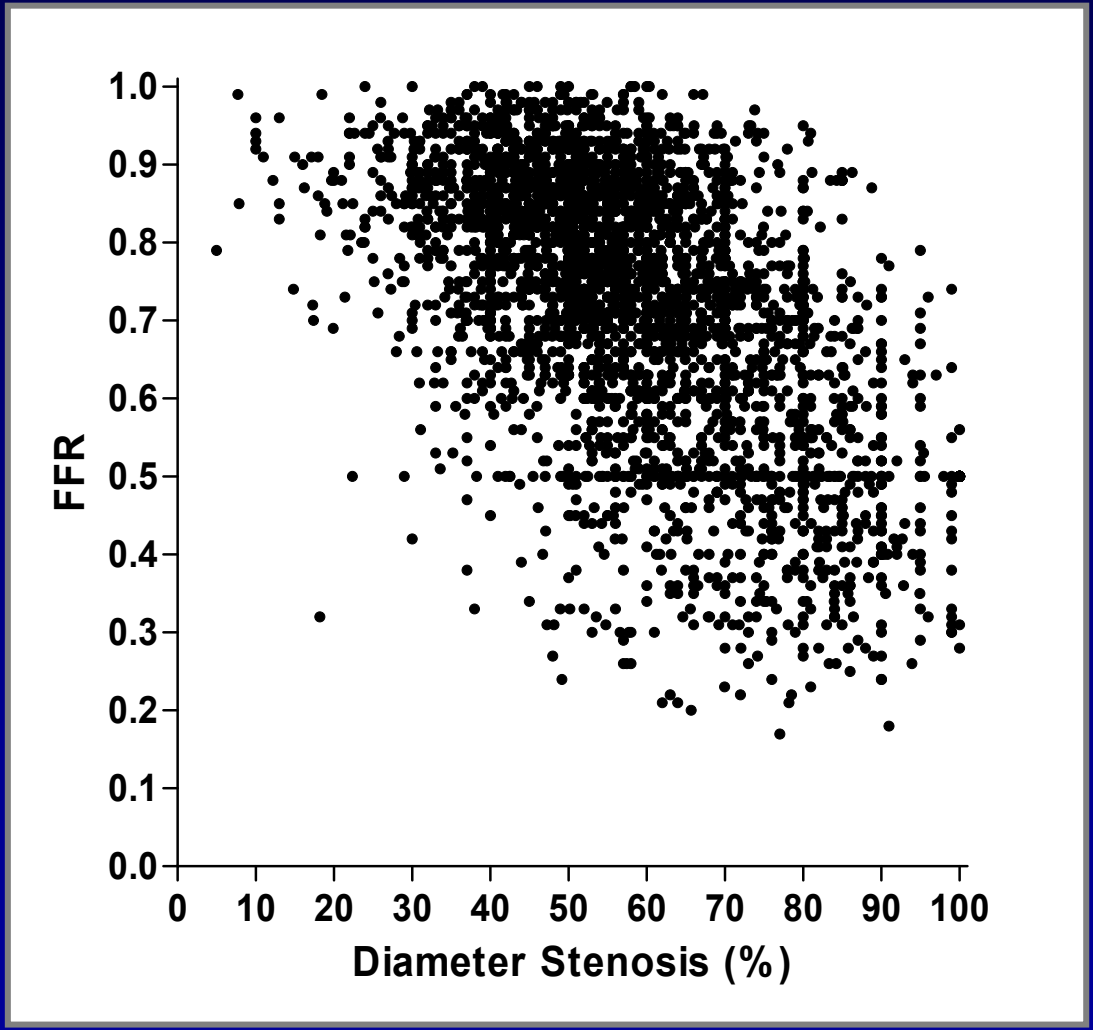
Limitation of Angiography

Comparison of QCA to FFR in over 3,000 lesions



Courtesy of Bernard De Bruyne, MD, PhD

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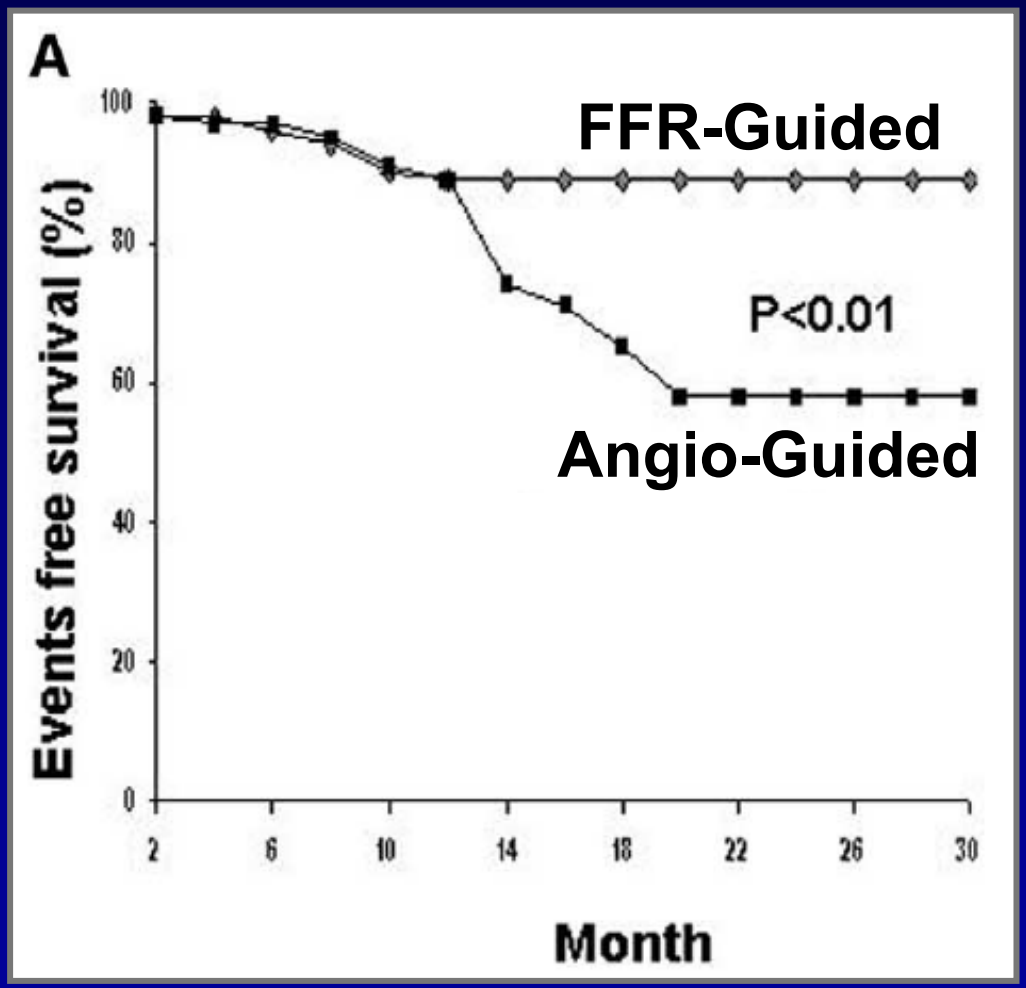
FFR-Guided PCI in MVD

137 Patients, Non-Randomized



Wongpraparut et al. Am J Cardiol 2005;96:877-884.

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Fractional Flow Reserve

versus

Angiography for

Multivessel

Evaluation

New Engl J Med 2009;360:213-24

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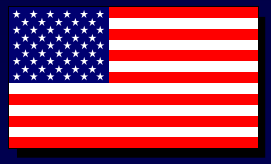
HYPOTHESIS

FFR – guided Percutaneous Coronary Intervention (PCI) in multivessel disease is superior to current angiography – guided PCI

Participating Centers



EUROPE (14)

Cardiovascular Center Aalst *(B. De Bruyne)*

Catharina Hospital Eindhoven *(N.Pijls)*

Rigshospitalet, Copenhagen (*T.Engstrom*)

Klinikum der Universitat Munchen *(V.Klauss)*

Aarhus University Hospital *(O. Frobert)*

University Hosp Bergmannsheil *(W. Bojara)*

Sodersjukhhuset, Stockholm *(I Herzfeld)*

Helsingborgs Lasarett *(F Schersten)*

Klinikum Darmstadt *(Gerald Werner)*

Bristol Royal Infirmary *(A.Baumbach)*

Staedt. Krankenhaus, Bogenhausen *(G.Riess)*

Glasgow Western Infirmary *(K Oldroyd)*

Royal Victoria Hosp, Belfast *(G. Manoharan)*

King´s College Hosp, London *(P.MacCarthy)*

USA (6)

Northeast Cardiology, Bangor, Maine
(Peter N. Ver Lee)

Stanford University
(William F. Fearon)

St Louis University
(Michael Lim)

University of Louisville
(Massoud Leesar)

University of South Carolina
(Eric Powers)

University of Virginia
(Michael Ragosta)

Study Population

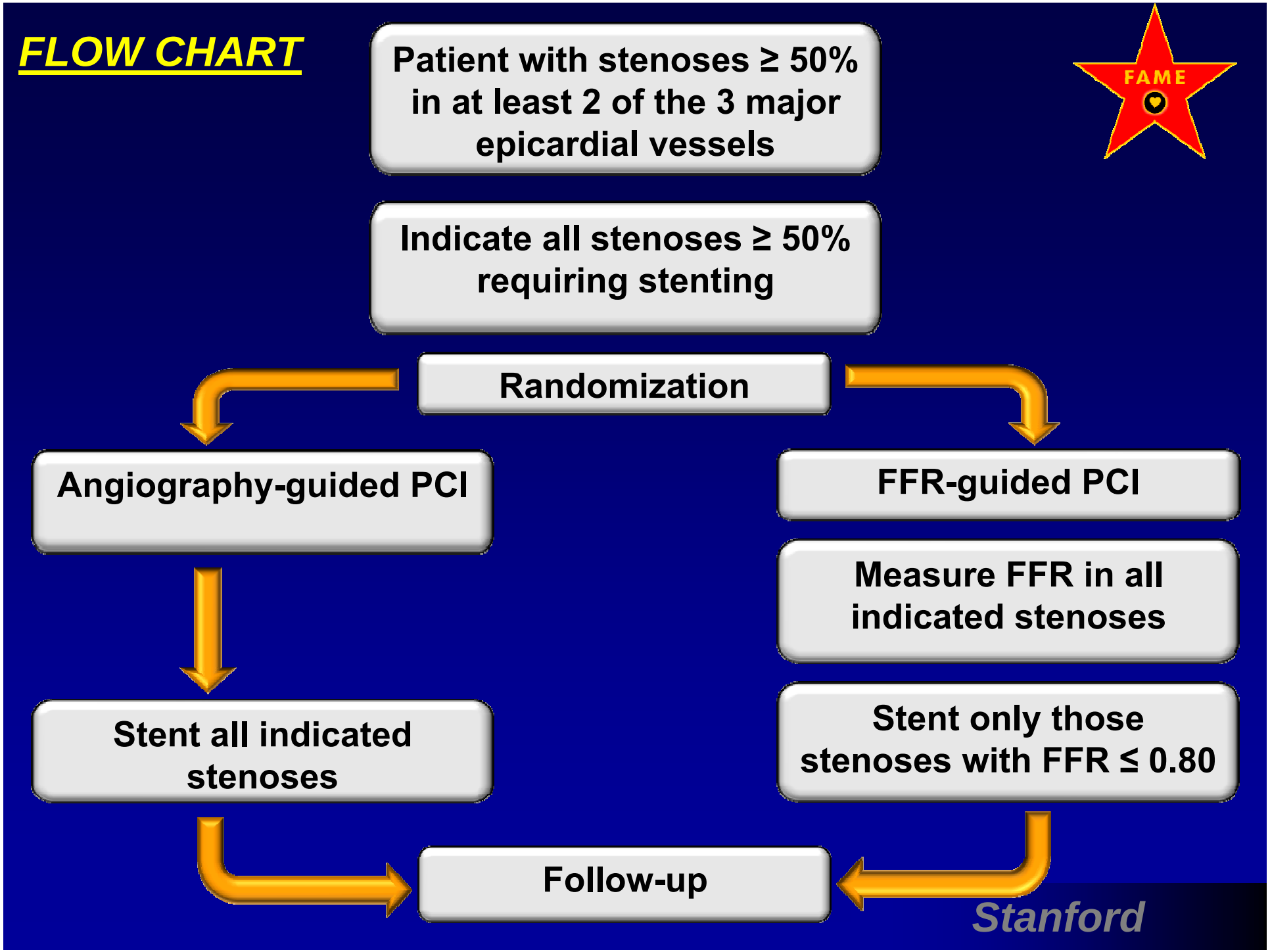
The FAME study was designed to ***reflect daily practice*** in performing PCI in patients ***with multivessel disease***

Inclusion criteria:

- ***ALL*** patients with multivessel disease
- At least 2 stenoses ≥ 50% in 2 or 3 major epicardial coronary artery disease, amenable for stenting

Exclusion criteria:

- Left main disease or previous bypass surgery
- Acute STEMI
- Extremely tortuous or calcified coronary arteries


FLOW CHART
Patient with stenoses ≥ 50% in at least 2 of the 3 major epicardial vessels
FAME
Indicate all stenoses ≥ 50% requiring stenting
Randomization
Angiography-guided PCI
FFR-guided PCI
Measure FFR in all indicated stenoses
Stent all indicated stenoses
Stent only those stenoses with FFR ≤ 0.80
Follow-up
Stanford

PRIMARY ENDPOINT

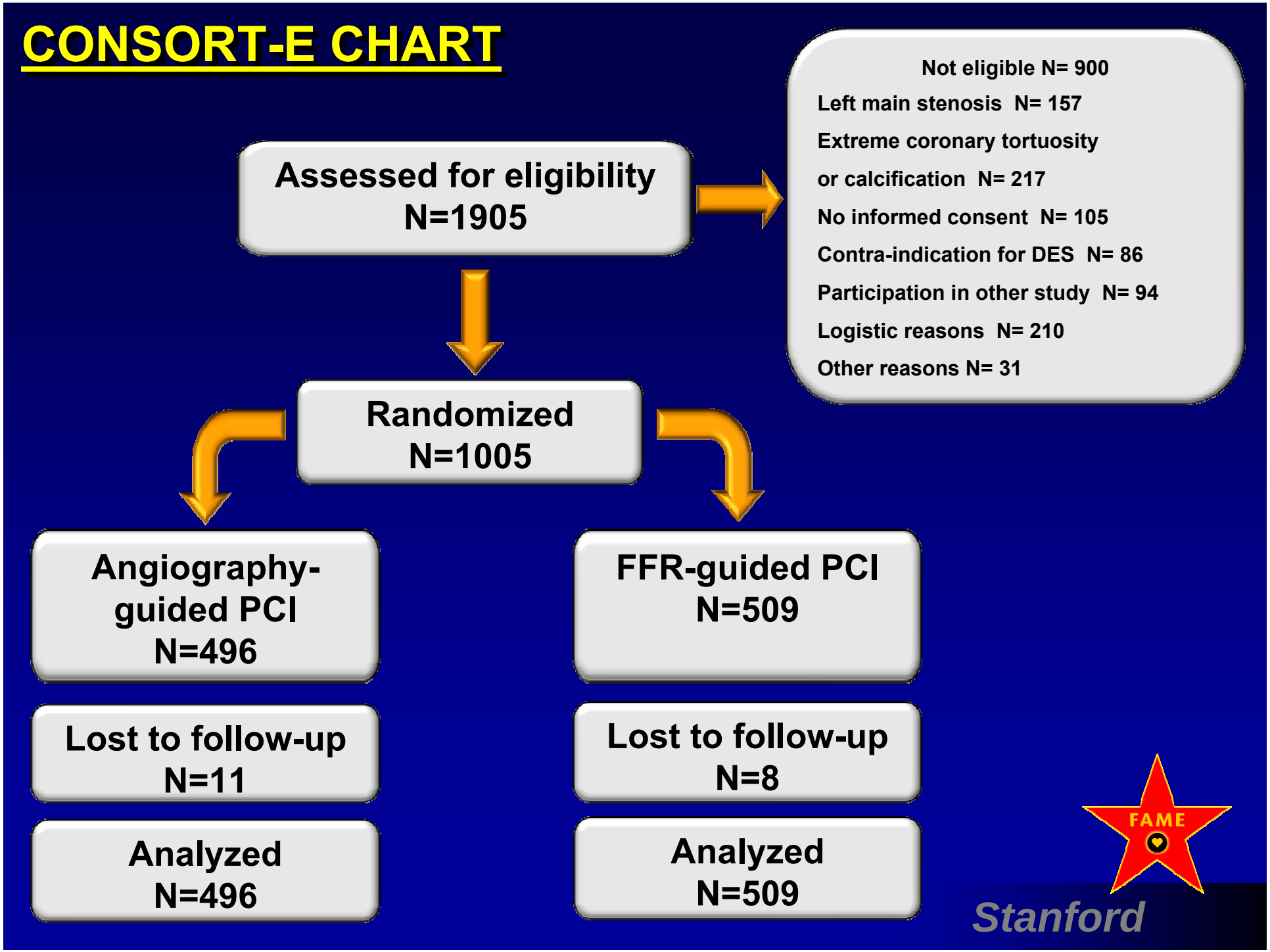
Composite of death, myocardial infarction, or repeat revascularization ("MACE") at 1 year

SECONDARY ENDPOINTS

- Individual components of MACE at 1 year
- Functional class
- Use of anti-anginal drugs
- Health-related quality of life (EuroQOL-5D)

- Procedure time
- Amount of contrast agent used during procedure
- Cost of the procedure

CONSORT-E CHART



Baseline Characteristics

	ANGIO-group N=496	FFR-group N=509	P-value
Age, mean±SD	64±10	65±10	0.47
Male, %	73	75	0.30
Diabetes, %	25	24	0.65
Hypertension, %	66	61	0.10
Current smoker, %	32	27	0.12
Hyperlipidemia, %	74	72	0.62
Previous MI, %	36	37	0.84
Unstable angina, %	36	29	0.11
Previous PCI , %	26	29	0.34
LVEF, mean±SD	57±12	57±11	0.92
LVEF < 50% , %	27	29	0.47

Procedural Results (1)

	ANGIO-group N=496	FFR-group N=509	P-value
# indicated lesions per patient	**2.7 ± 0.9**	**2.8 ± 1.0**	0.34
50-70% narrowing, No (%)	**550 (41)**	**624 (44)**	-
70-90% narrowing, No (%)	**553 (41)**	**530 (37)**	-
> 90% narrowing, No (%)	**247 (18)**	**260 (18)**	-
Stents per patient	**2.7 ± 1.2**	**1.9 ± 1.3**	<0.001
Lesions succesfully stented (%)	**92%**	**94%**	-
DES, total, No	**1359**	**980**	-

Procedural Results (2)

	ANGIO-group N=496	FFR-group N=509	P-value
Procedure time (min)	70 ± 44	71 ± 43	0.51

Procedural Results (2)

	ANGIO-group N=496	FFR-group N=509	P-value
Procedure time (min)	70 ± 44	71 ± 43	0.51
Contrast agent used (ml)	302 ± 127	272 ± 133	<0.001

Procedural Results (2)

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Procedure time (min)	70 ± 44	71 ± 43	0.51
Contrast agent used (ml)	302 ± 127	272 ± 133	<0.001
Materials used at procedure (US $)	6007	5332	<0.001

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Materials used at procedure (US $)	6007	5332	<0.001
Length of hospital stay (days)	3.7 ± 3.5	3.4 ± 3.3	0.05

Adverse Events at 1 year

	ANGIO-group N=496	FFR-group N=509	P-value
Events at 1 year, No (%)			
Death, MI, CABG, or repeat-PCI			

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Death, MI, CABG, or repeat-PCI	91 (18.3)	67 (13.2)	0.02

Adverse Events at 1 year

	ANGIO-group N=496	FFR-group N=509	P-value
Events at 1 year, No (%)			
Death, MI, CABG, or repeat-PCI	**91 (18.3)**	**67 (13.2)**	**0.02**
Death	**15 (3.0)**	**9 (1.8)**	0.19
Death or myocardial infarction	**55 (11.1)**	**37 (7.3)**	0.04
CABG or repeat PCI	**47 (9.5)**	**33 (6.5)**	0.08

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Total no. of MACE	**113**	**76**	0.02

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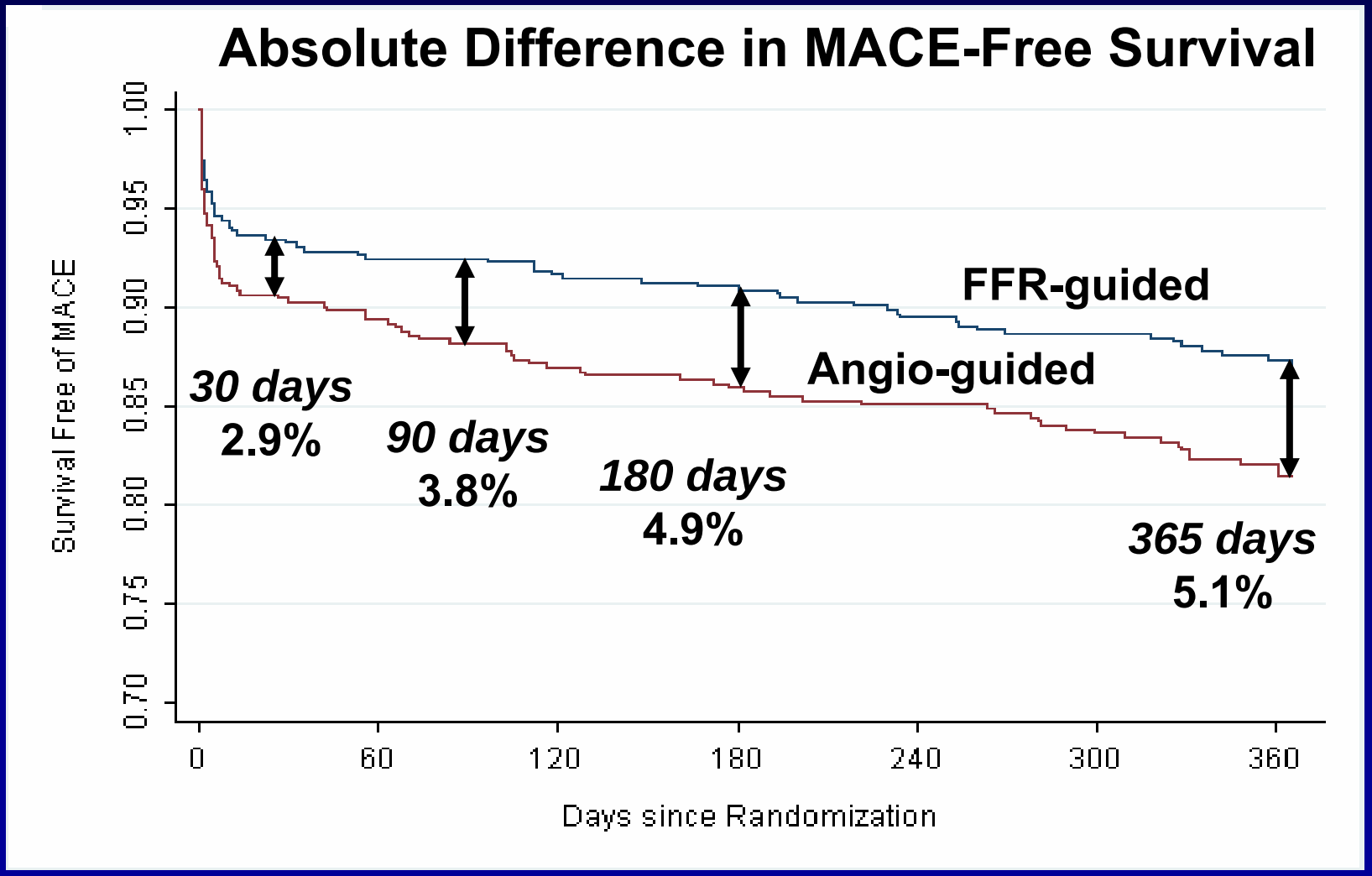
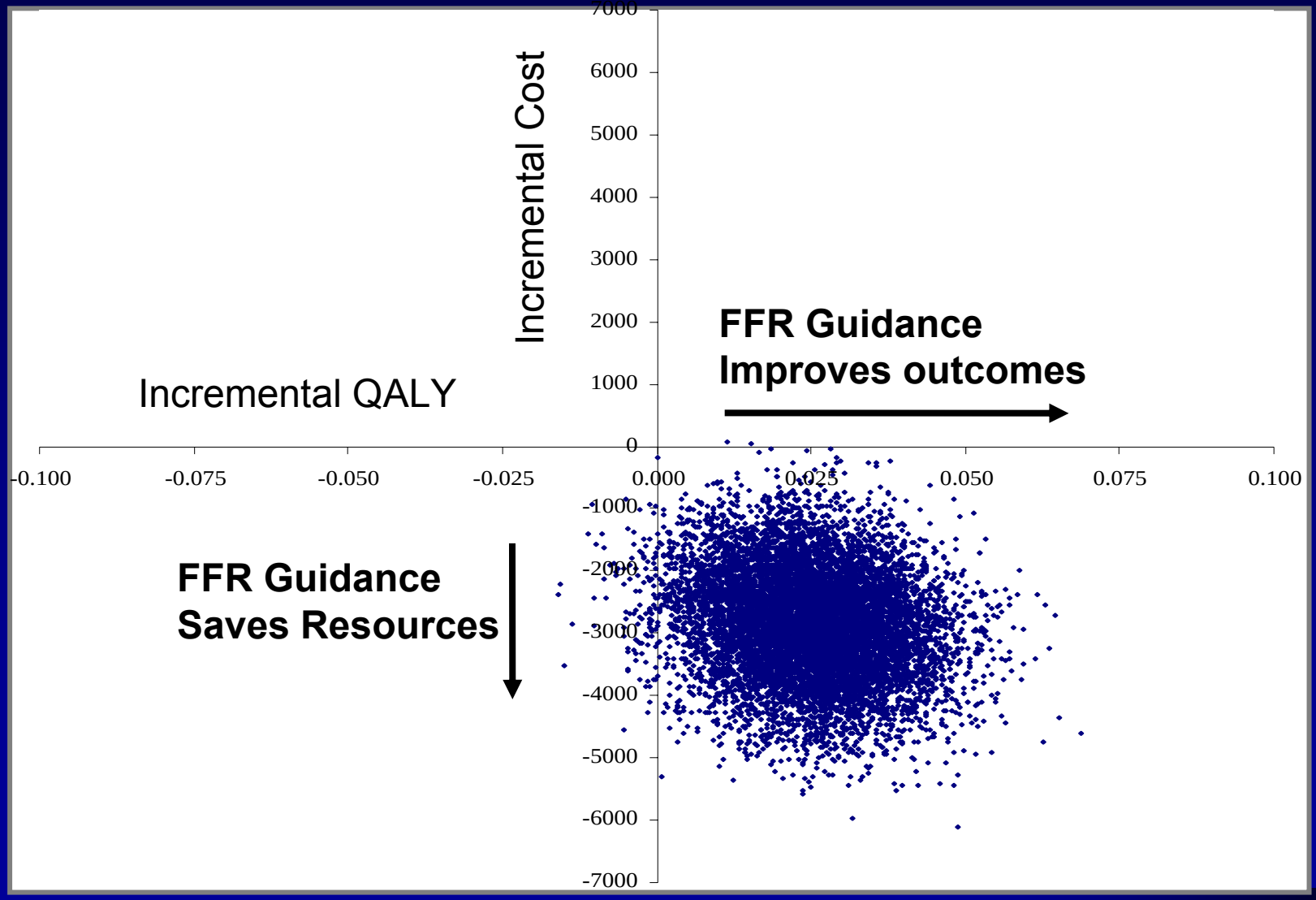
CABG or repeat PCI	**47 (9.5)**	**33 (6.5)**	0.08
Total no. of MACE	**113**	**76**	
Myocardial infarction, specified			
All myocardial infarctions	**43 (8.7)**	**29 (5.7)**	0.07
Small periprocedural CK-MB 3-5 x N	**16**	**12**	
Other infarctions (“late or large”)	**27**	**17**	

Event-free Survival

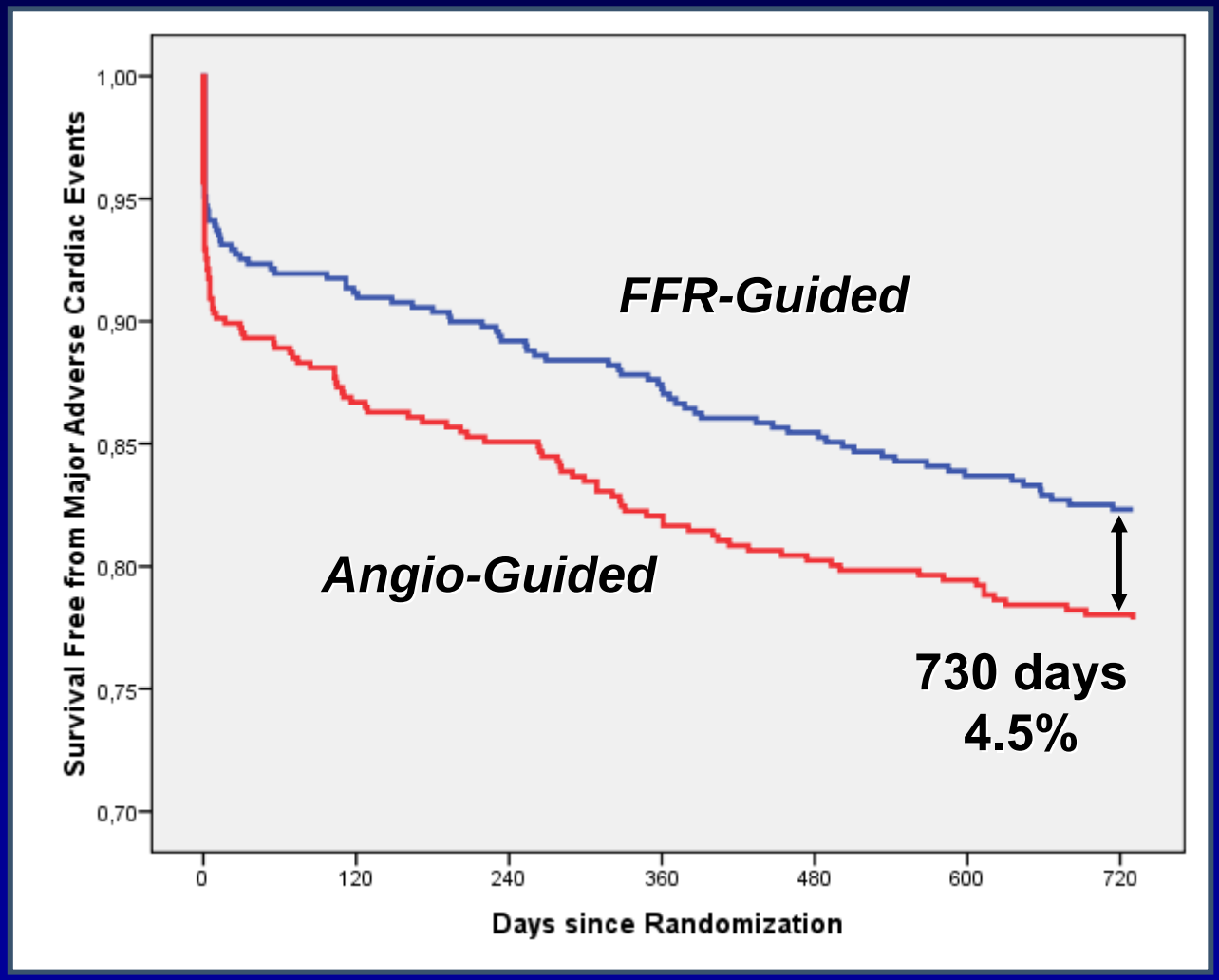


FAME 1 Year Economic Evaluation

Bootstrap Simulation



2 Year Survival Free of MACE



Late Breaking Trial, TCT 2009

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Adverse Events at 2 Years

	Angio-Guided n = 496	FFR-Guided n = 509	P Value
Total no. of MACE	**139**	**105**	
Individual Endpoints			
Death	19 (3.8)	13 (2.6)	0.25
Myocardial Infarction	48 (9.7)	31 (6.1)	0.03
CABG or repeat PCI	61 (12.3)	53 (10.4)	0.35
Composite Endpoints			
Death or Myocardial Infarction	63 (12.7)	43 (8.4)	0.03
Death, MI, CABG, or re-PCI	110 (22.2)	90 (17.7)	0.07

Late Breaking Trial, TCT 2009

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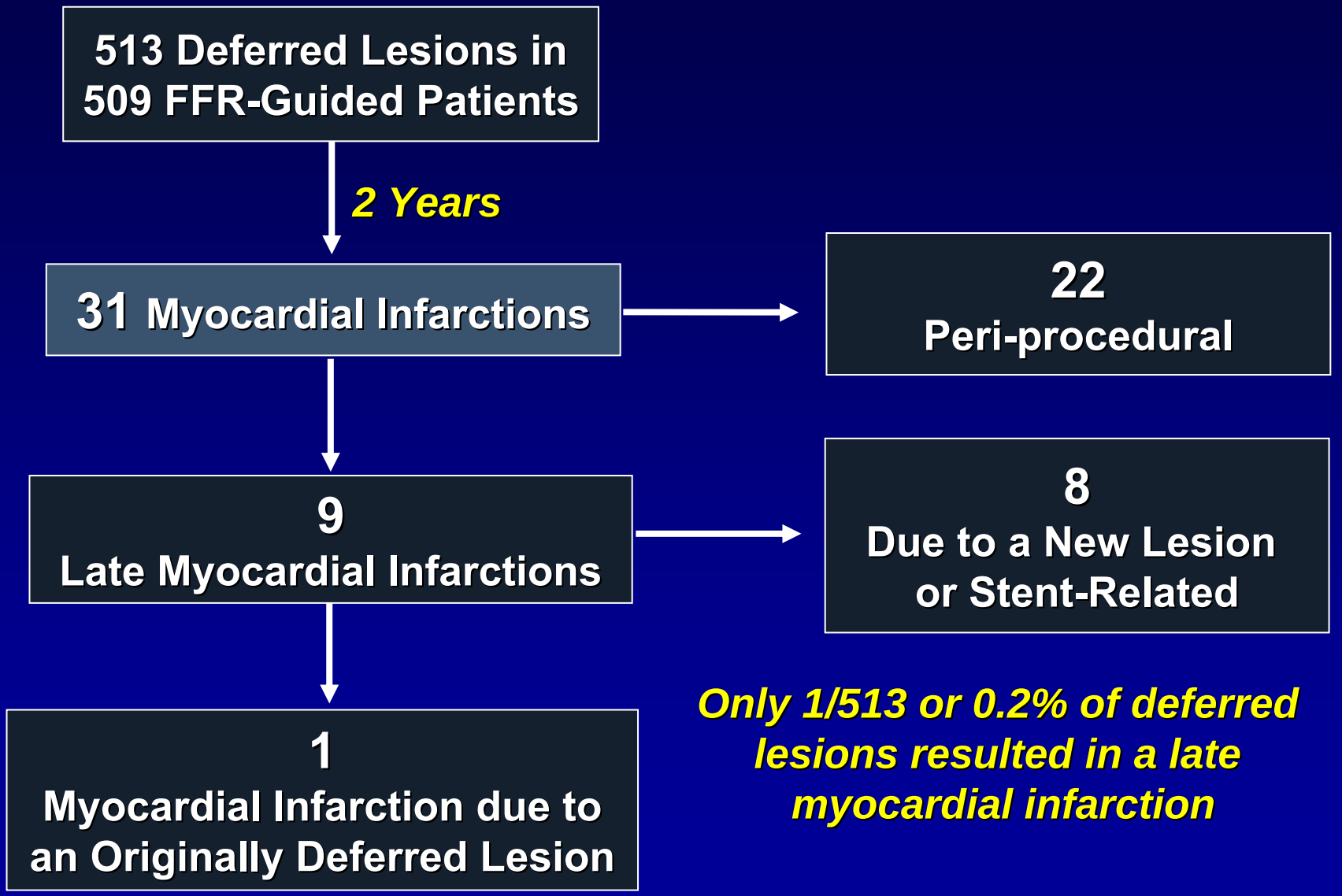
2 Year Outcome of Deferred Lesions



Only 1/513 or 0.2% of deferred lesions resulted in a late myocardial infarction

Late Breaking Trial, TCT 2009

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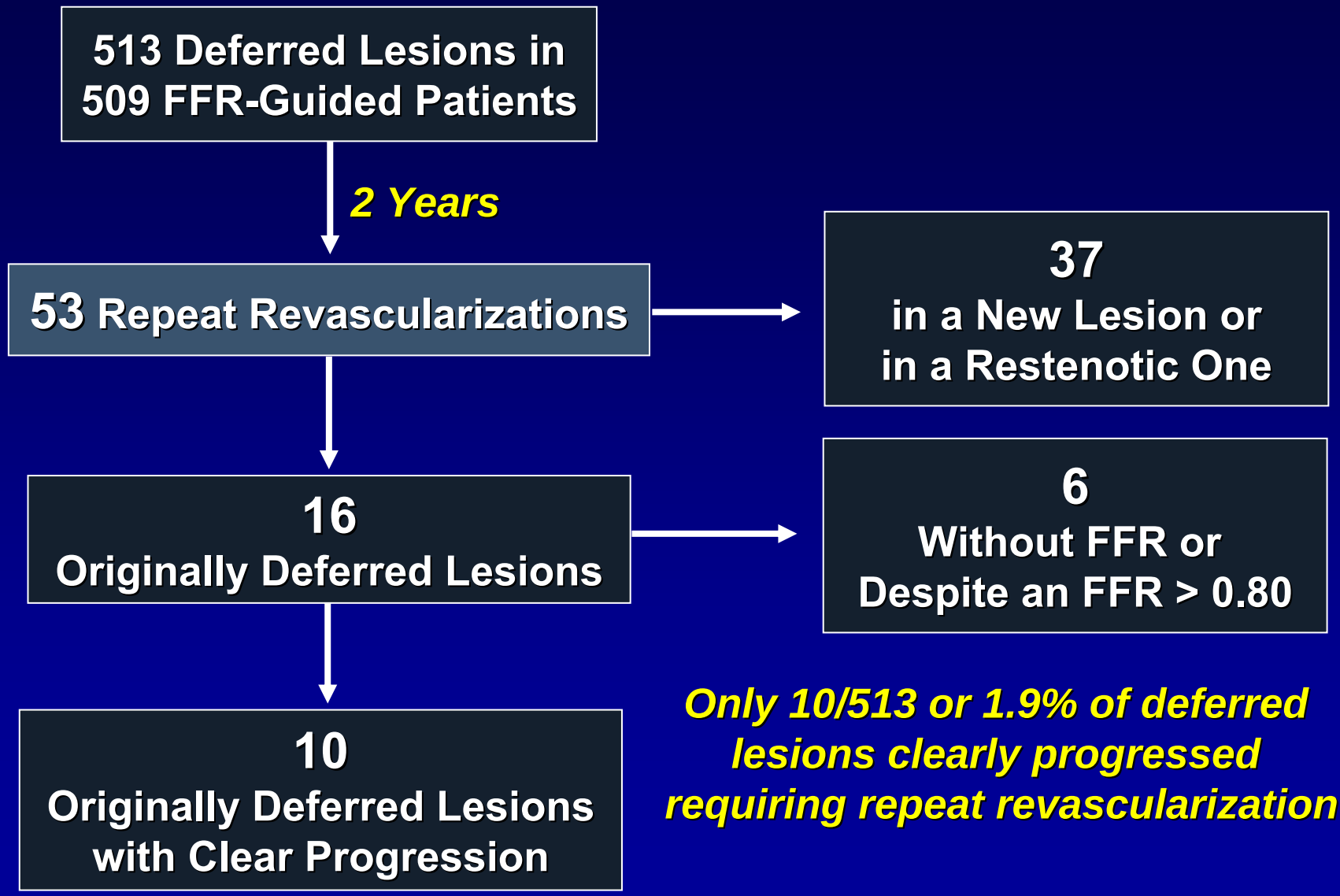
2 Year Outcome of Deferred Lesions



Only 10/513 or 1.9% of deferred lesions clearly progressed requiring repeat revascularization

Late Breaking Trial, TCT 2009

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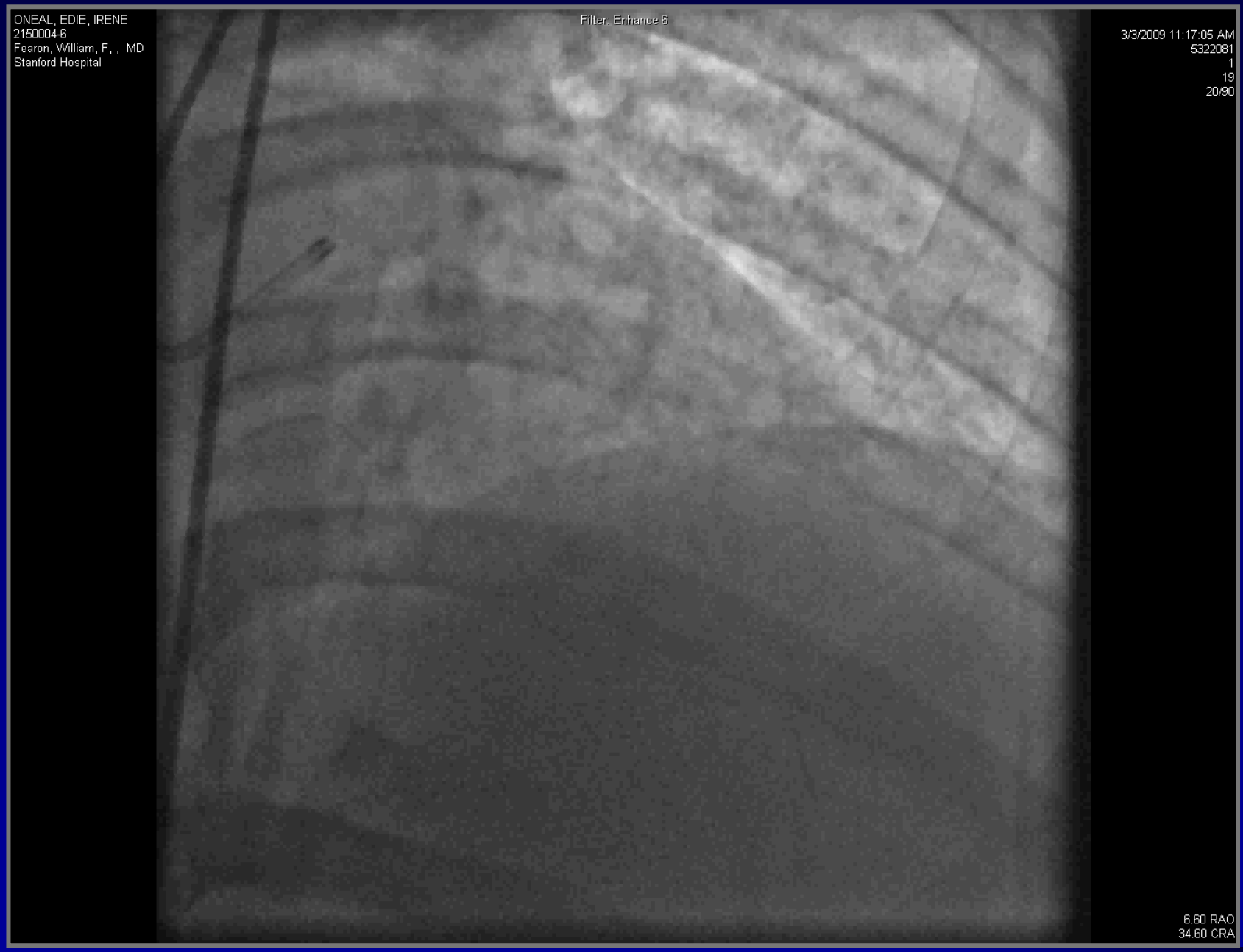
Post FAME Case Example

- 46 year old diabetic woman with HTN and dyslipidemia presents to outside hospital with a NSTEMI in March 2009.
- 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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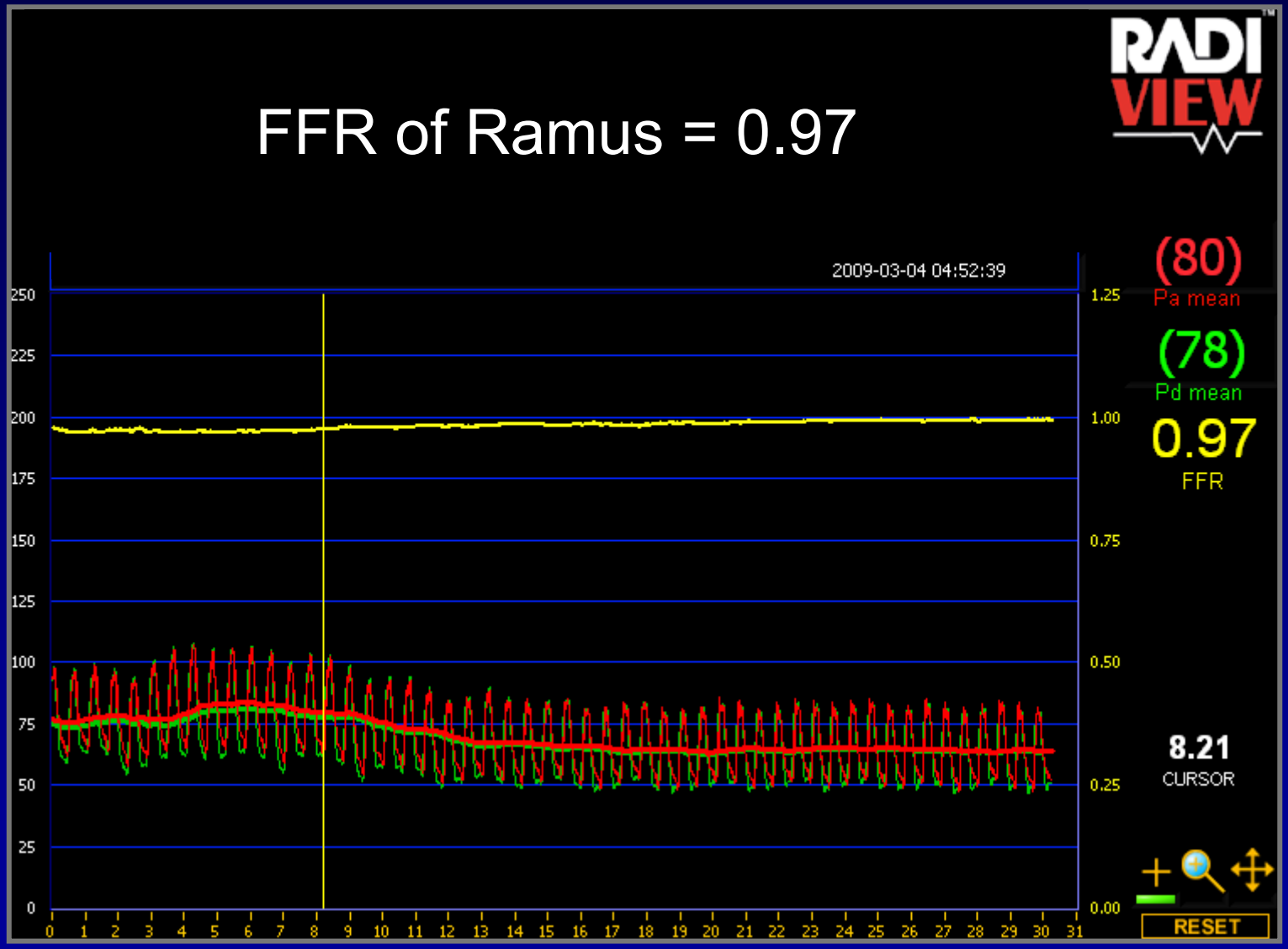
FFR of Ramus = 0.97



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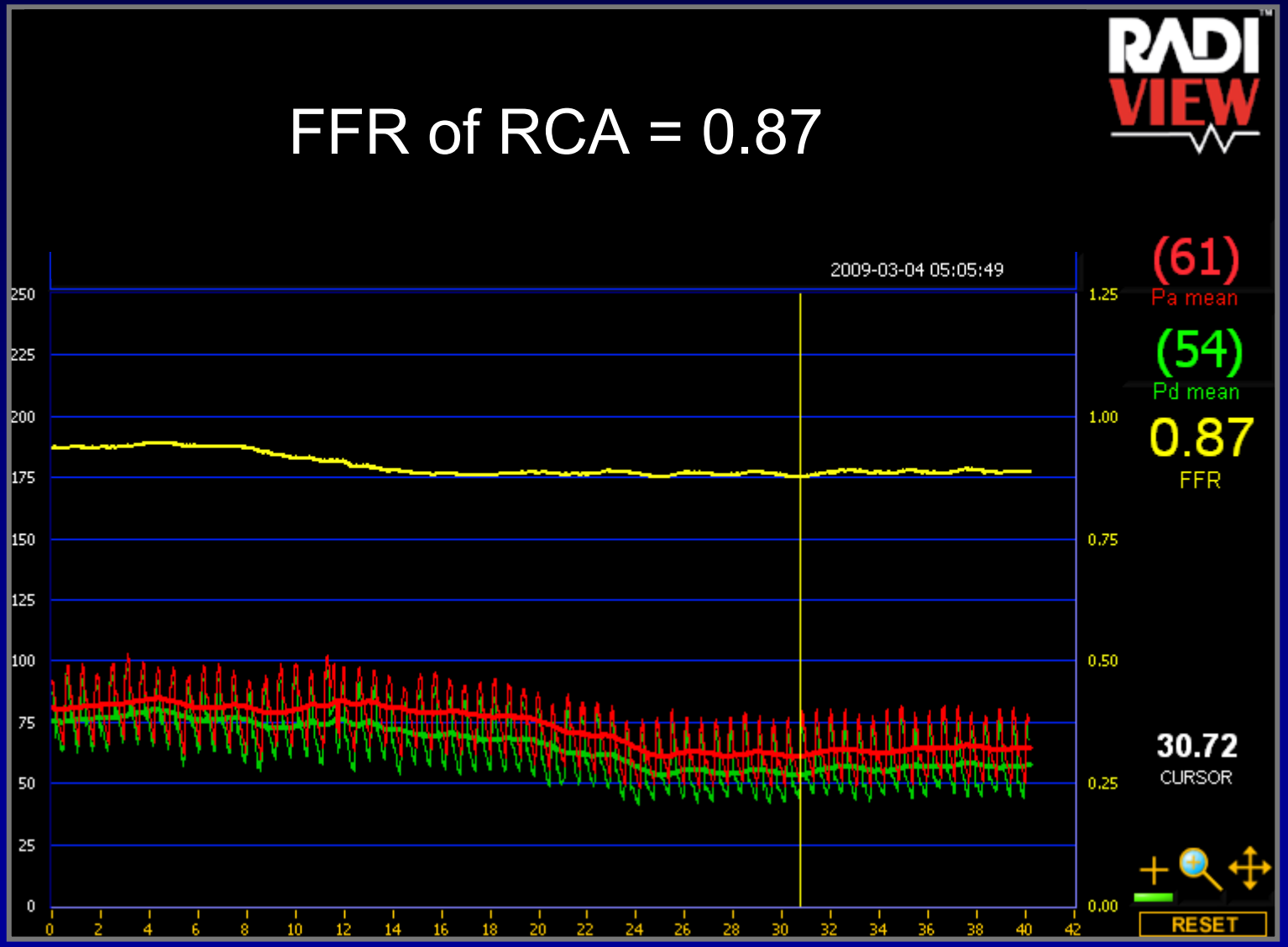
FFR of RCA = 0.87



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Summary of Case

- Anatomic 3V CAD, functional 1V CAD
- Successfully treated with single stent
- 130 cc contrast, < 1 hour procedure
- Remains event free at 8 months

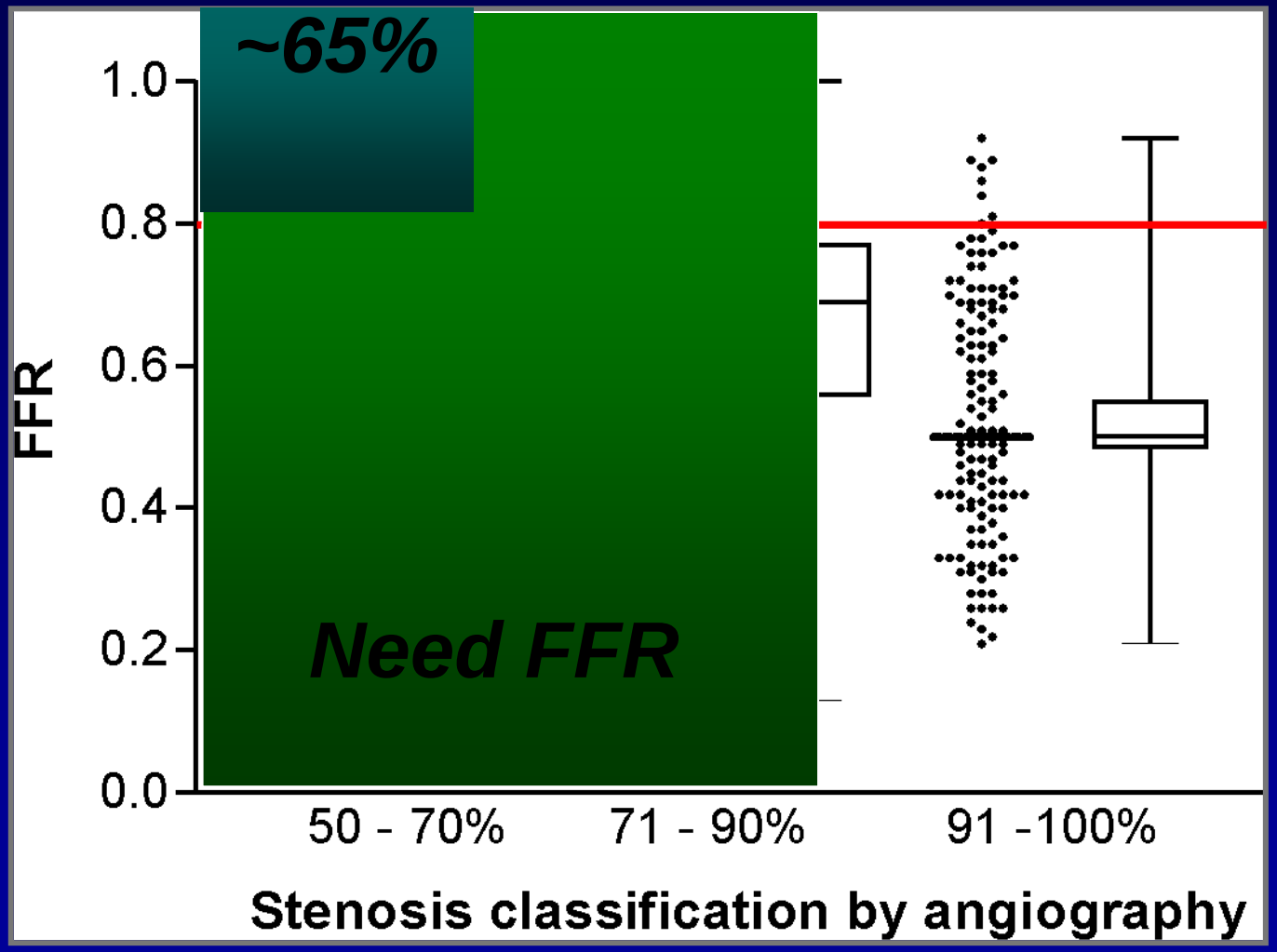
Anatomic vs. Functional CAD

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

Tonino et al., JACC 2009 (submitted)

Which Lesions Need FFR?

1329 lesions in the FFR-guided arm



Tonino et al., JACC 2009 (submitted)

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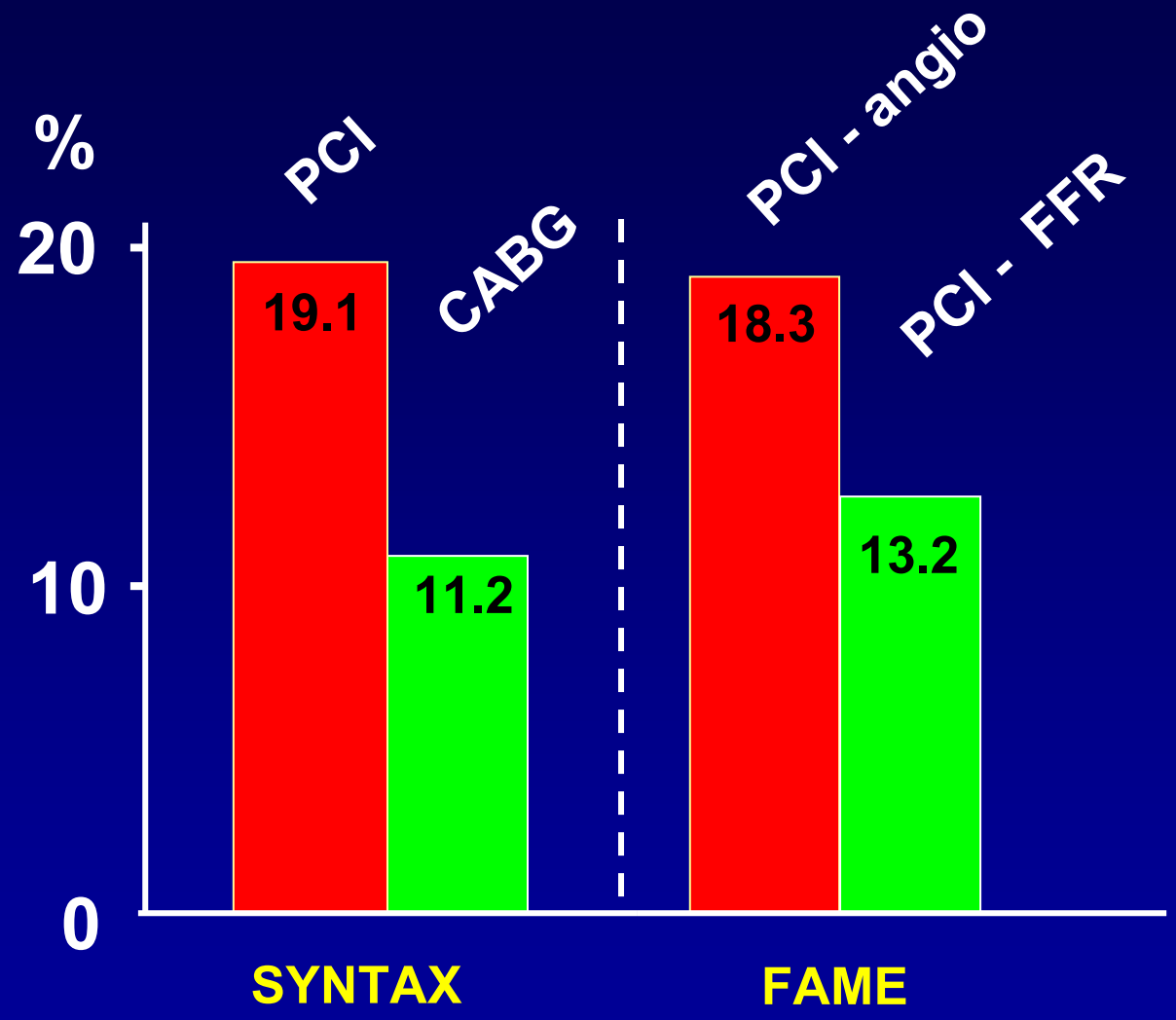
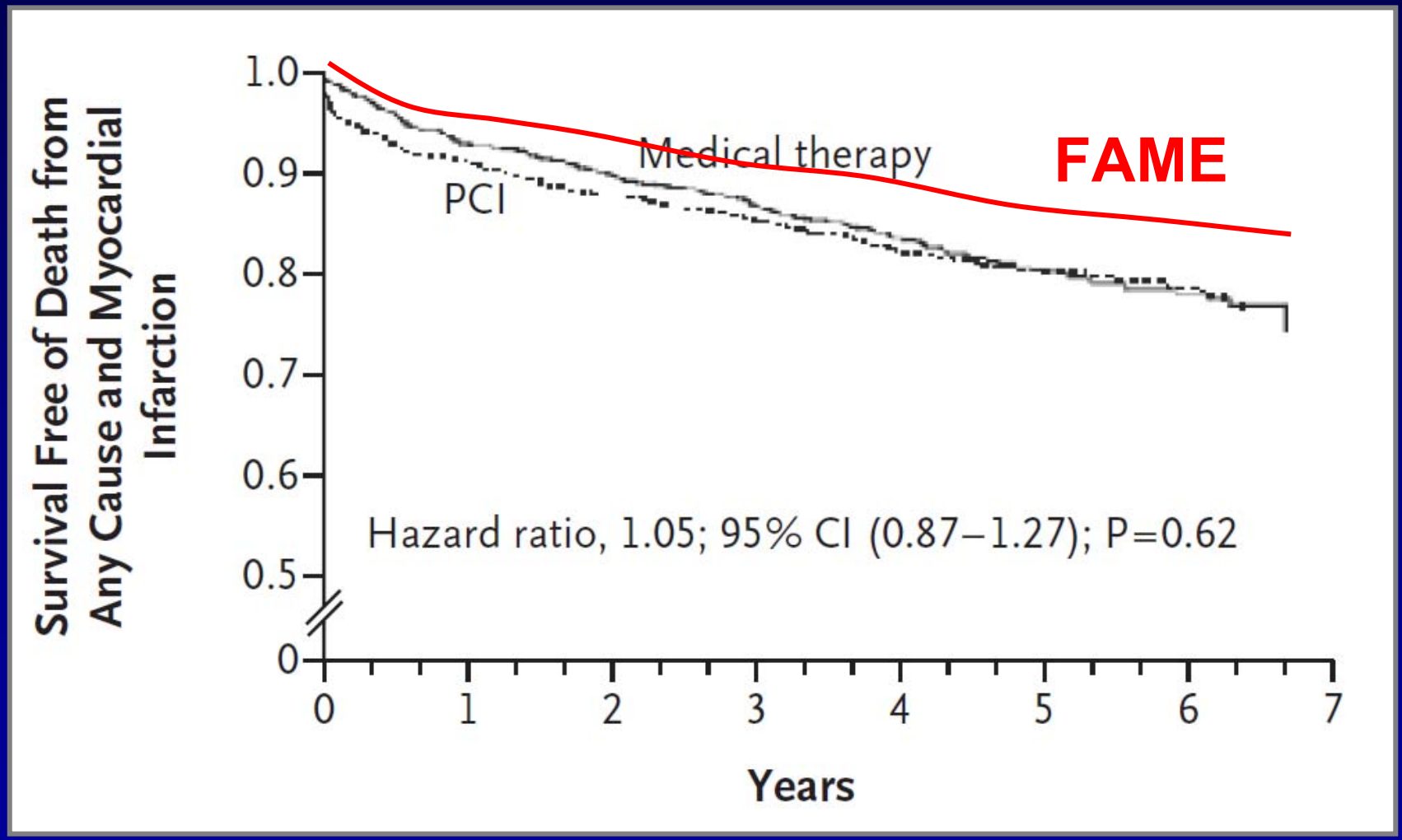
Implications of FAME



1 year MACE Rates

Implications of FAME

Death and MI in the COURAGE study



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

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Conclusion:

- FFR-guided PCI in patients with multi-vessel CAD compared to angio-guided PCI:
  - Improves outcomes at 1 year
  - Saves money
  - Simplifies the procedure
  - Is durable out to two years with excellent outcomes in the deferred lesions