Coronary Physiology In The Cathlab

FAME STUDY: 2-year Follow-Up & CLINICAL SUBGROUP ANALYSIS

Educational Training Program ESC
European Heart House
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Nico H.J.Pijls, MD, PhD
Catharina Hospital, Eindhoven
The Netherlands,

FAME study: HYPOTHESIS

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

FAME study: DESIGN

Randomized multicenter study in 1005 patients undergoing DES-stenting for multivessel disease in 20 US and European centers

- independent core-lab
- independent data analysis
- blinded adverse event committee

Multivessel disease:
Stenoses of > 50% in at least 2 of the 3 major coronary arteries

FAME study: 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

Note: patients with previous PCI were not excluded

FLOW CHART

Patient with stenoses ≥ 50% in at least 2 of the 3 major epicardial vessels

Indicate all stenoses ≥ 50% considered for stenting

Randomization

Angiography-guided PCI

Stent all indicated stenoses

FFR-guided PCI

Measure FFR in all indicated stenoses

Stent only those stenoses with FFR ≤ 0.80

follow-up at 1,2,5 year

FAME study: PRIMARY ENDPOINT

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

FAME study: SECONDARY ENDPOINTS

- MACE at 2 and 5 years
- Individual components of MACE at 1,2,5 years
- 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

FAME study: Treatment

- PCI according to local routine
- Only drug-eluting stents (DES)
- FFR measured by Pressure Wire
  (***Certus wire, RADI Medical Systems***)
- Hyperemia induced by i.v. adenosine 140 µg/kg/min in femoral vein
- Follow-up visits at 1and 6 months and 1,2, and 5 years

FAME study: Baseline Characteristics (1)

	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

FAME study: Baseline Characteristics (2)

	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)**	-
90-99% narrowing, No (%)	**207 (15)**	**202(14)**	-
Total occlusion, No (%)	**40 (3)**	**58 (4)**	-
Patients with ≥1 total occlusion (%)	**7.5**	**10.6**	0.08
Patients with prox LAD involved, No (%)	**186 (38)**	**210 (41)**	0.39
% lesions in segment 1,2,6,7,or 11	**960 (71)**	**1032 (73)**	0.42

FAME study: 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
FFR results			
Lesions succesfully measured, No (%)	-	**1329 (98%)**	-
Lesions with FFR ≤ 0.80 ,No (%)	-	**874 (63%)**	-
Lesions with FFR > 0.80 ,No (%)	-	**513 (37%)**	-
Stents per patient	**2.7 ± 1.2**	**1.9 ± 1.3**	<0.001
Lesions succesfully stented (%)	**92%**	**94%**	-
DES, total, No	**1359**	**980**	-

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

FAME study: 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 (18.4)**	**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
Total no. of MACE	**113**	**76**	0.02
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**	

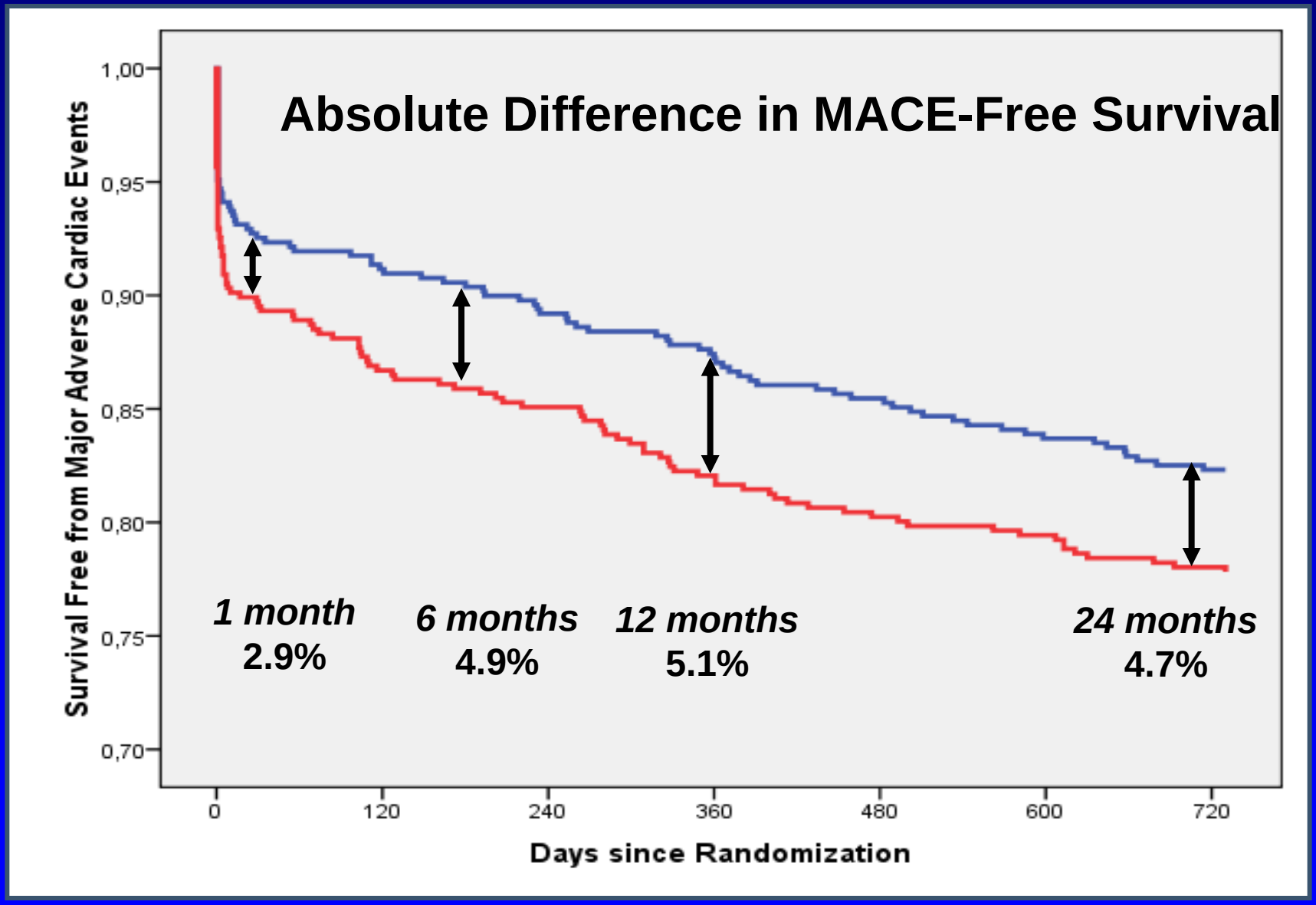
FAME study: Adverse Events at 2 years

Complete follow-up at 2 years in 93,7 % of all patients

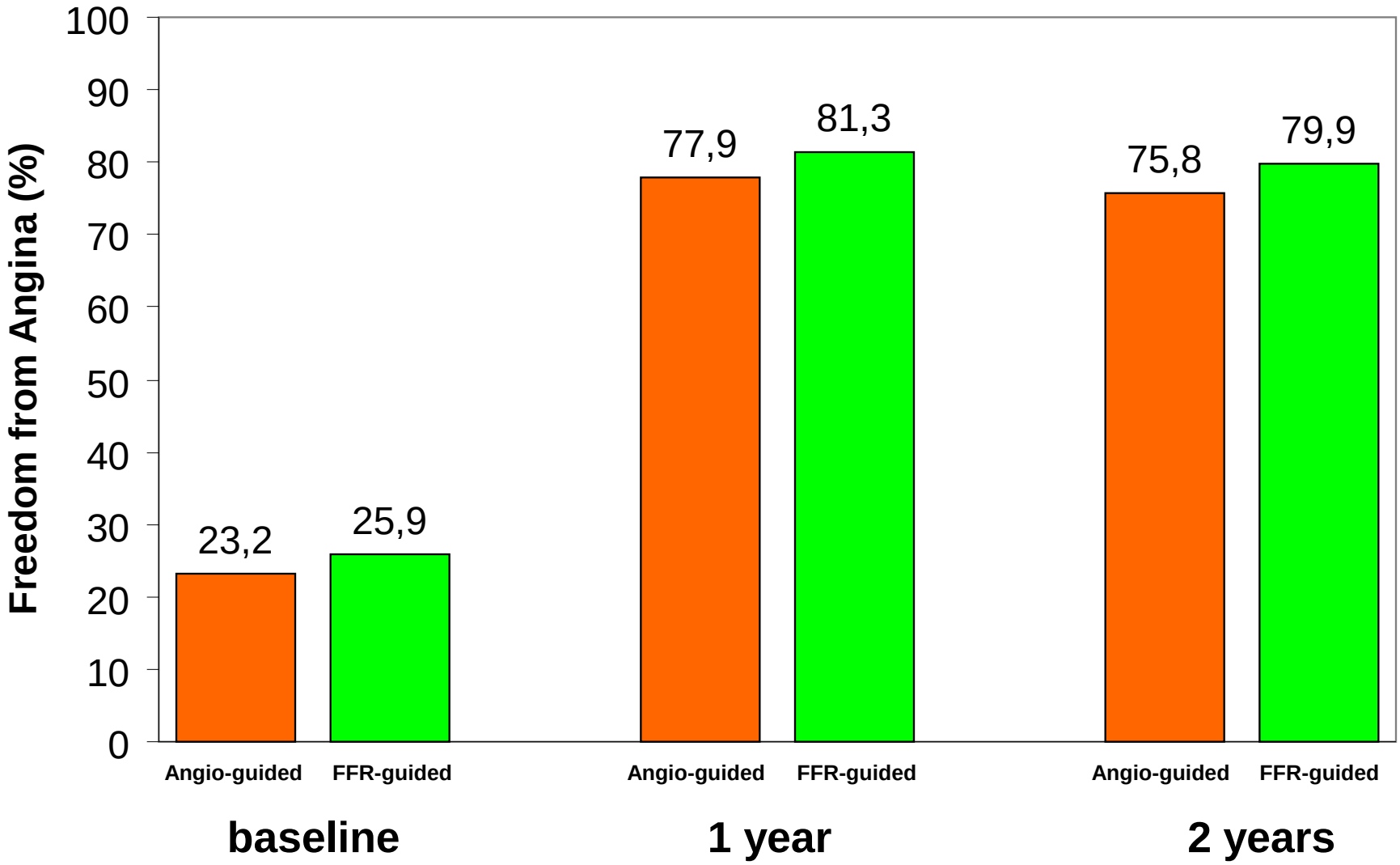
FAME study: Adverse Events at 2 years

	ANGIO-group N=496	FFR-group N=509	P-value
Individual endpoints, No (%)			
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, No(%)			
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
Total No of MACE	**139**	**105**	0.01

FAME study: Event-free Survival 24 months



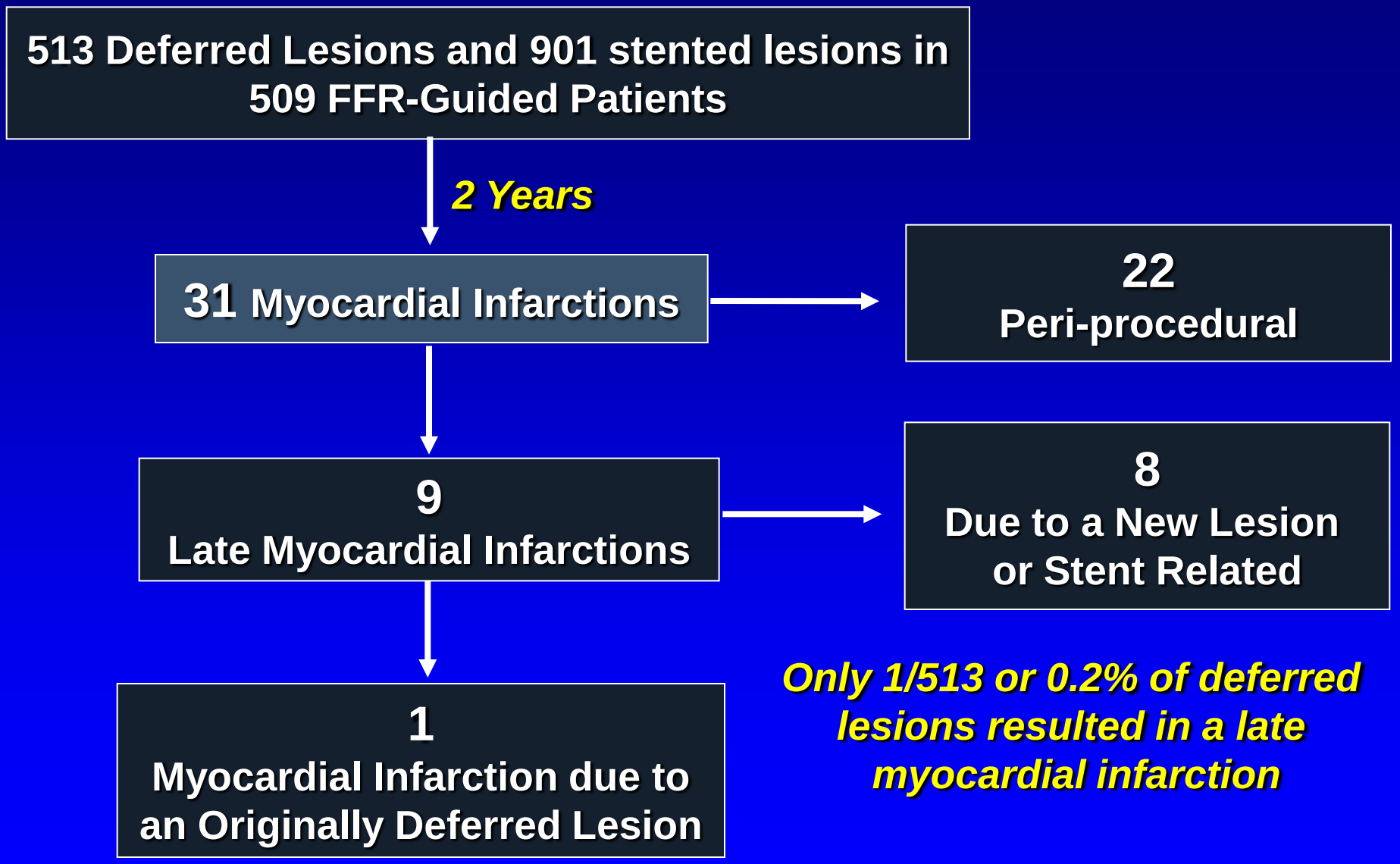
Freedom from Angina



Angio-guided

FFR-guided

Outcome of Deferred Lesions (1):



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

Outcome of Deferred Lesions (2):

513 Deferred Lesions and 901 stented lesions in 509 FFR-Guided Patients

2 Years

53 Repeat Revascularizations → **37** in a New Lesion and/or in a Restenotic One

16 Originally Deferred Lesions → **6** Without FFR or Despite an FFR > 0.80

10 Originally Deferred Lesions with Clear Progression

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

FAME study: Subgroup Analysis

Caveats in Subgroup Analysis:

- subgroup analysis is not trivial
- good study is underpowered for subgroups
- subgroups should be pre-defined beforehand, no “dredging” for subgroups afterwards
- co-variate adjustment & interaction testing
- if results of trial equally apply to all pre-defined subgroups ⟶ corroboration of main study (heterogeneity testing)

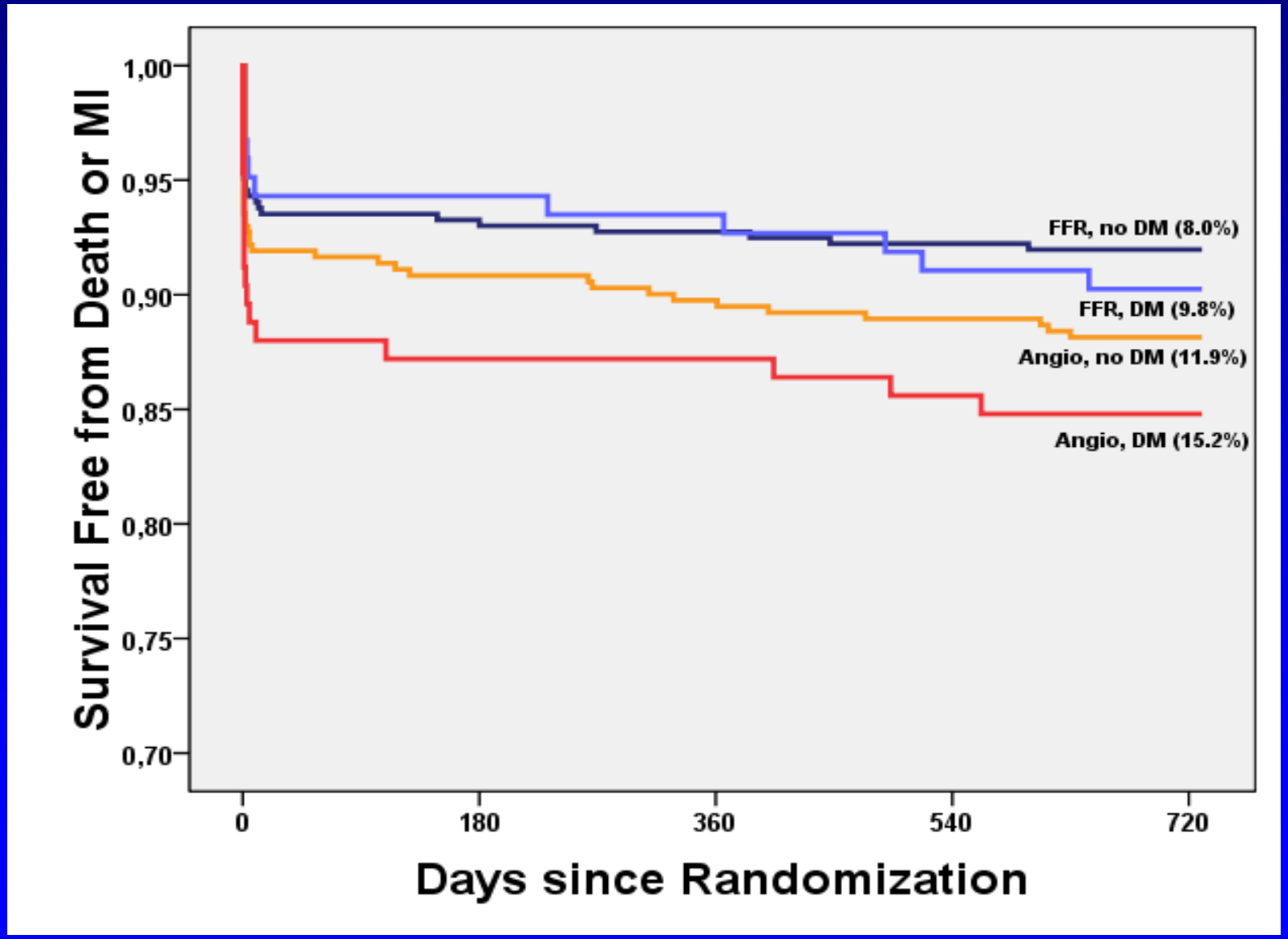
FAME study: Diabetes vs Non-Diabetes

In the FAME study, 248 patients (24.7 %) had *diabetes*:

- **125 in the angio-guided group**
- **123 in the FFR-guided group**

How was outcome in these patients ?

FAME study: Diabetes vs Non-Diabetes



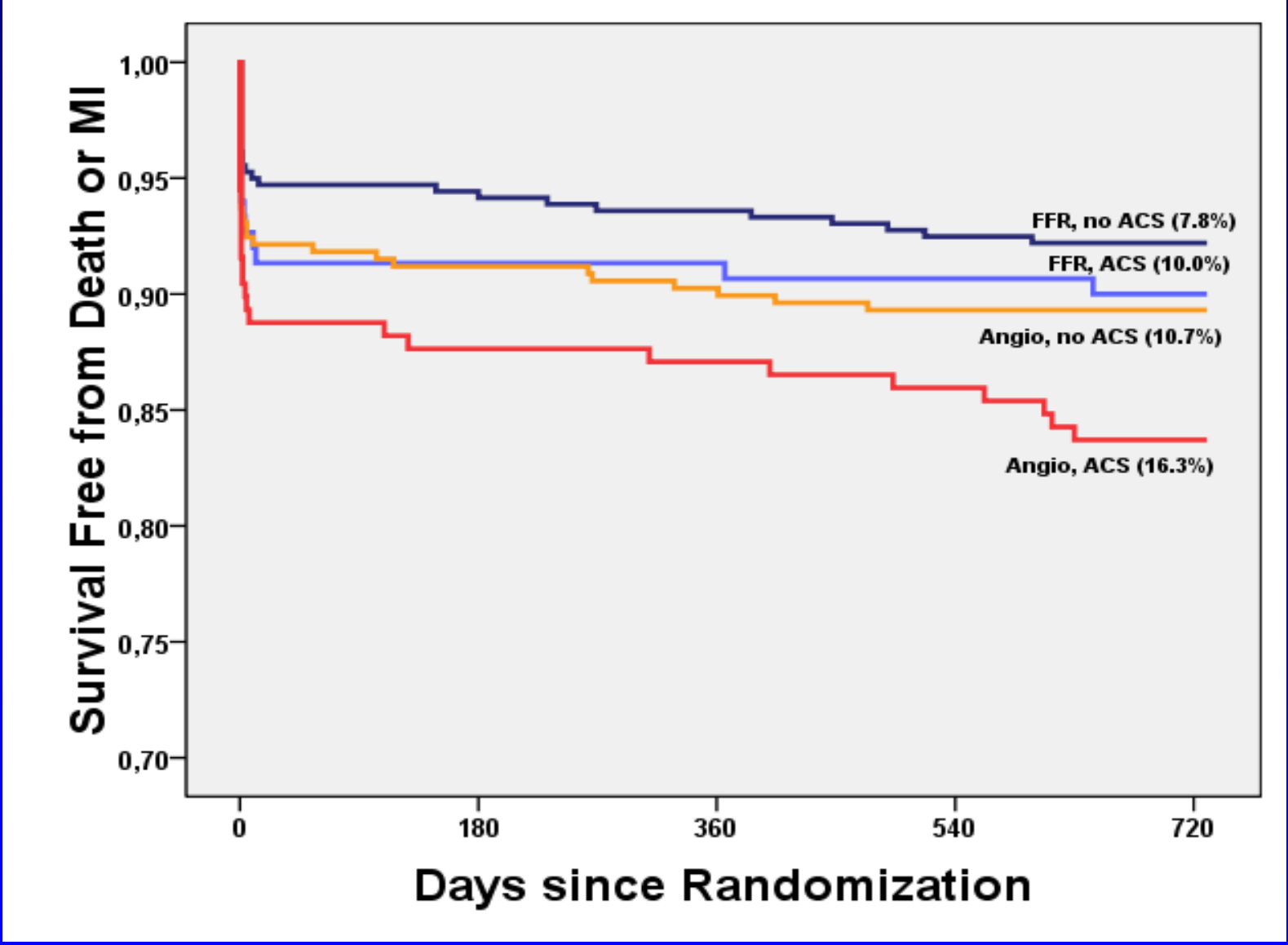
FAME study:Unstable Angina & Non-Stemi

In the FAME study, 328 patients (32.6 %) was admitted because of unstable angina or non-Stemi

- **178 in the angio-guided group**
- **150 in the FFR-guided group**

How was outcome in these patients ?

FAME study: Unstable Angina & Non-STEMI



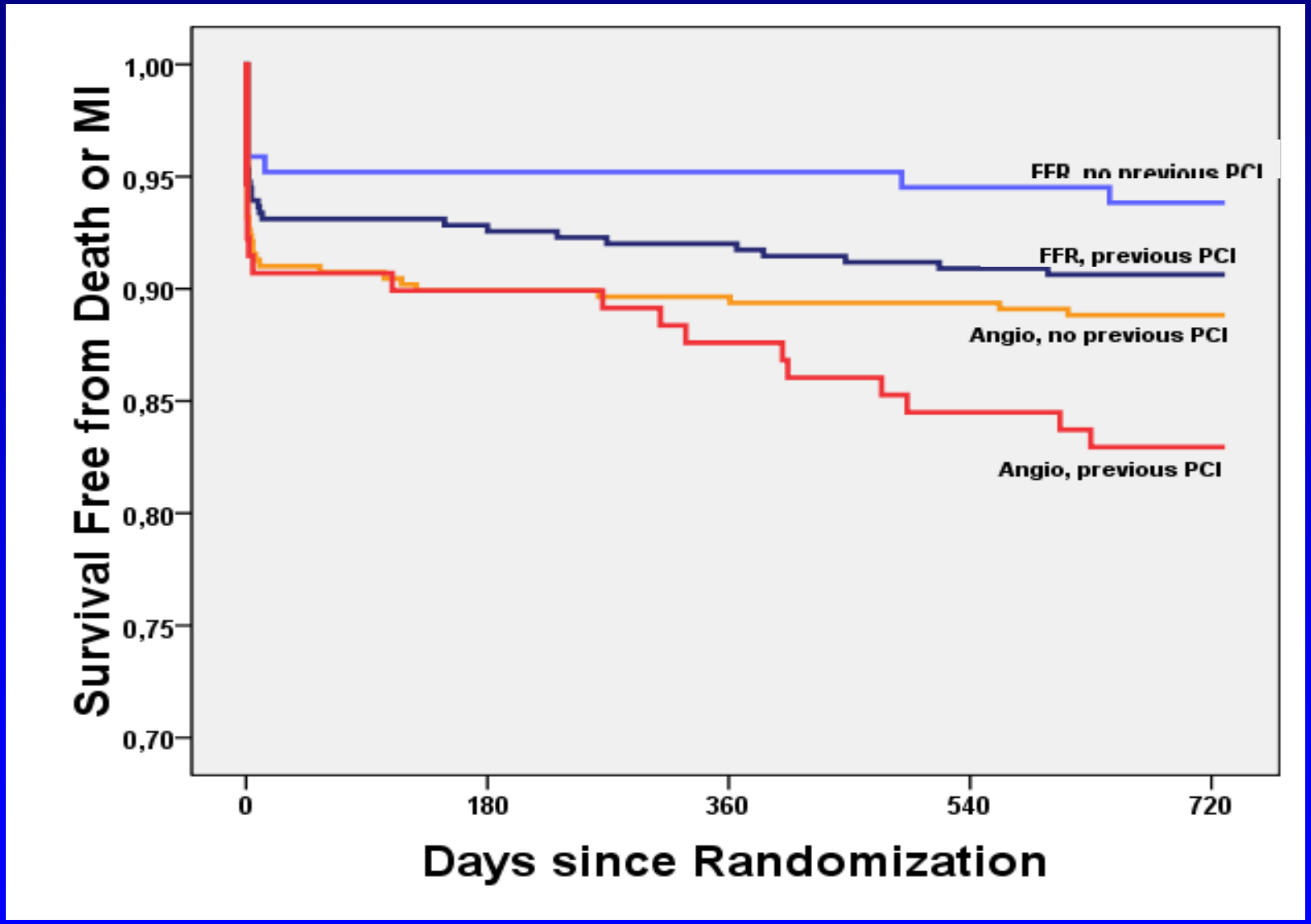
FAME study: Previous PCI

In the FAME study, 275 patients (27.9 %) had *Previous PCI*:

- **180 in the angio-guided group**
- **187 in the FFR-guided group**

How was outcome in these patients ?

FAME study: Patients with Previous PCI



FAME study: CONCLUSIONS (1)

Routine measurement of FFR during PCI with DES in patients with multivessel disease, when compared to current angiography guided strategy

- ***Reduces the rate of the composite endpoint of death, myocardial infarction, re-PCI and CABG at 1 and 2 years by ~ 30%***

- ***Reduces mortality and myocardial infarction at 1 and 2 years by ~ 35 %***

- ***These effects were of equal order in all predefined subgroups without significant heterogeneity***

FAME study: Clinical Consequence

Routine measurement of FFR during DES-stenting in patients with multivessel disease is superior to current angiography guided treatment.

It improves outcome of PCI significantly

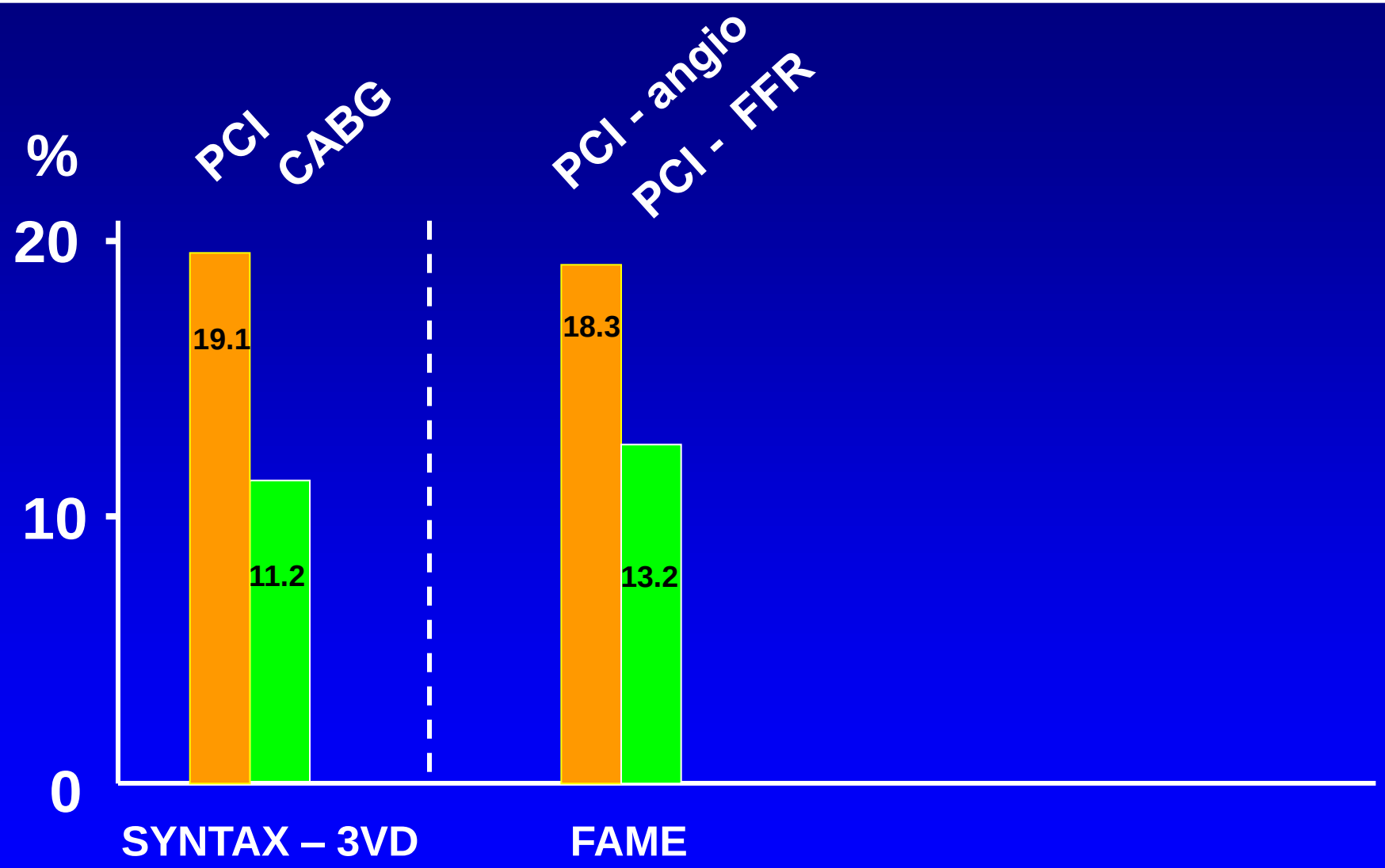
It supports the evolving paradigm of

"Functionally Complete Revascularization", i.e. stenting of ischemic lesions and medical treatment of non-ischemic ones.

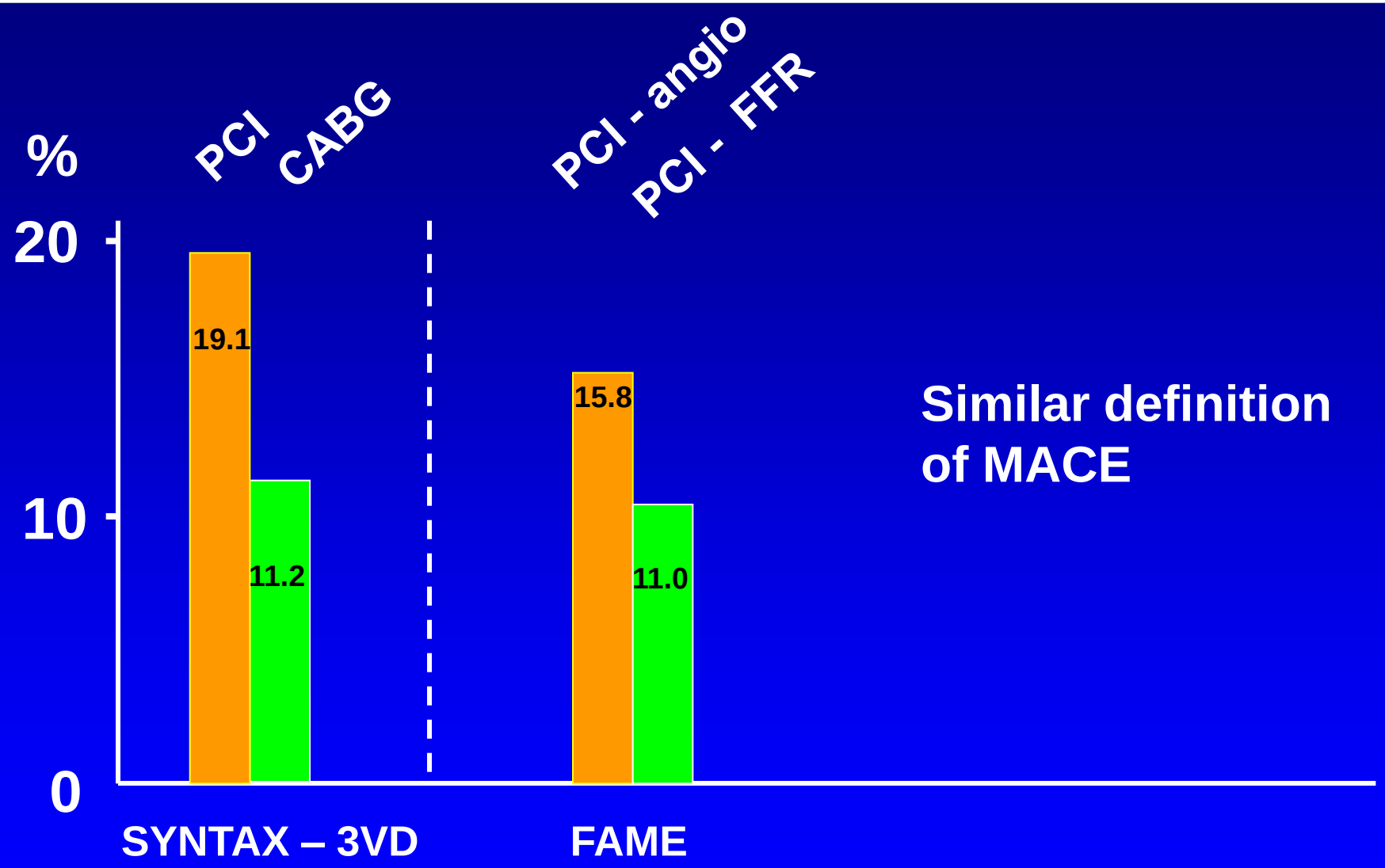
BACK UP SLIDES

How does FAME fit with other recently performed RCT's to (DES) stenting in Multivessel Disease

MACE in SYNTAX – 3VD and FAME

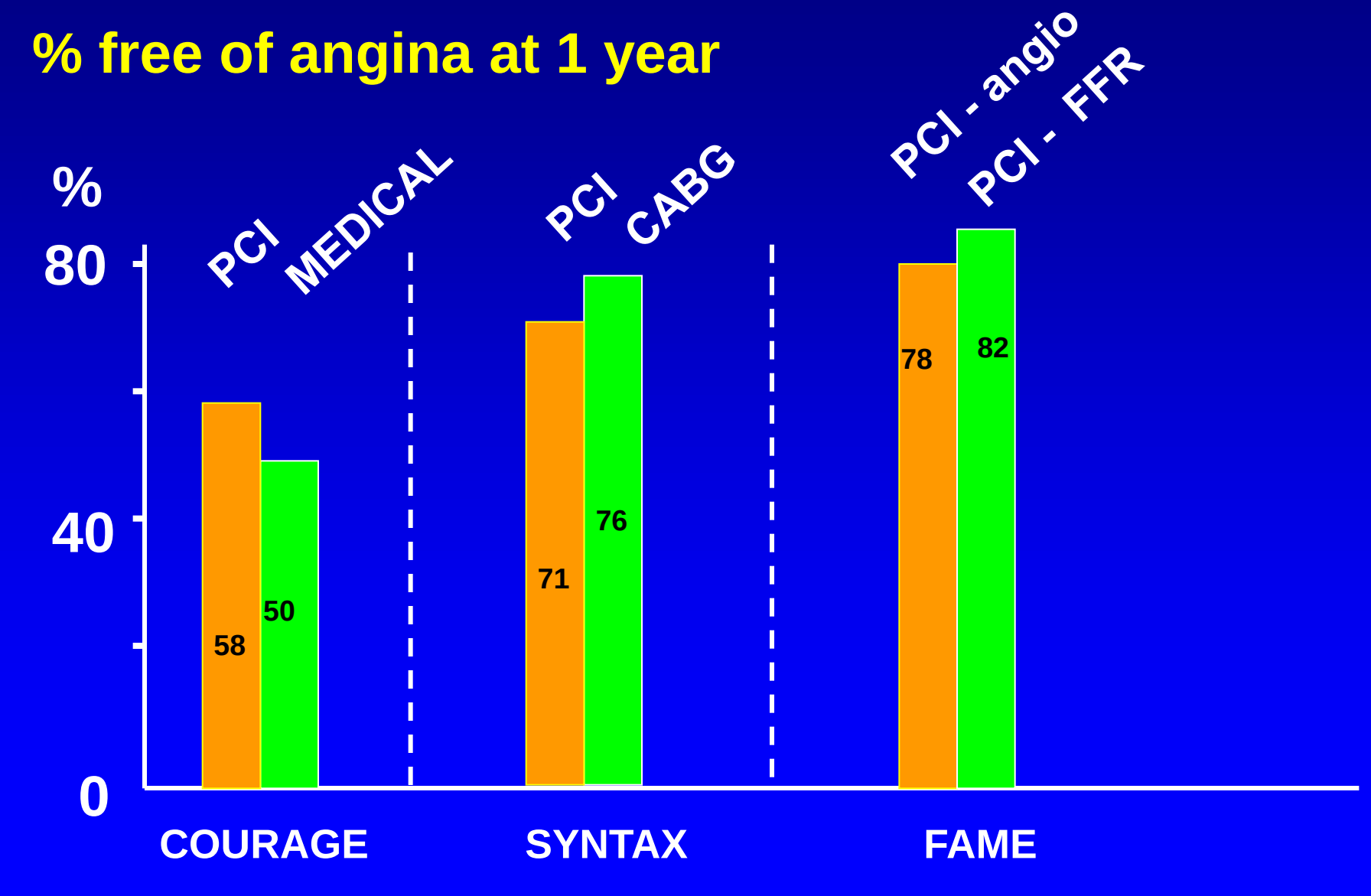


MACE in SYNTAX – 3VD and FAME



Similar definition of MACE

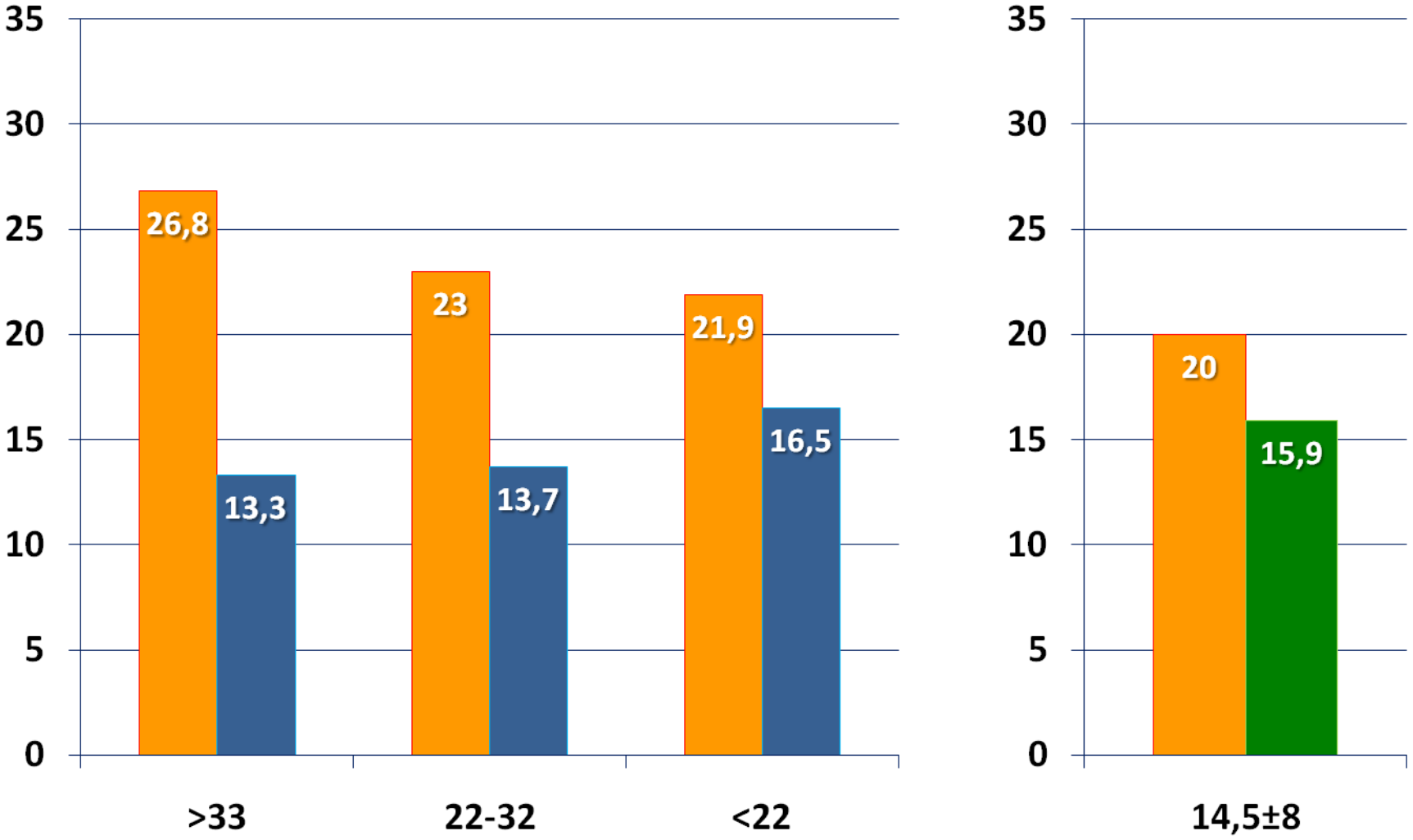
FUNCTIONAL CLASS in COURAGE - SYNTAX – 3VD and FAME



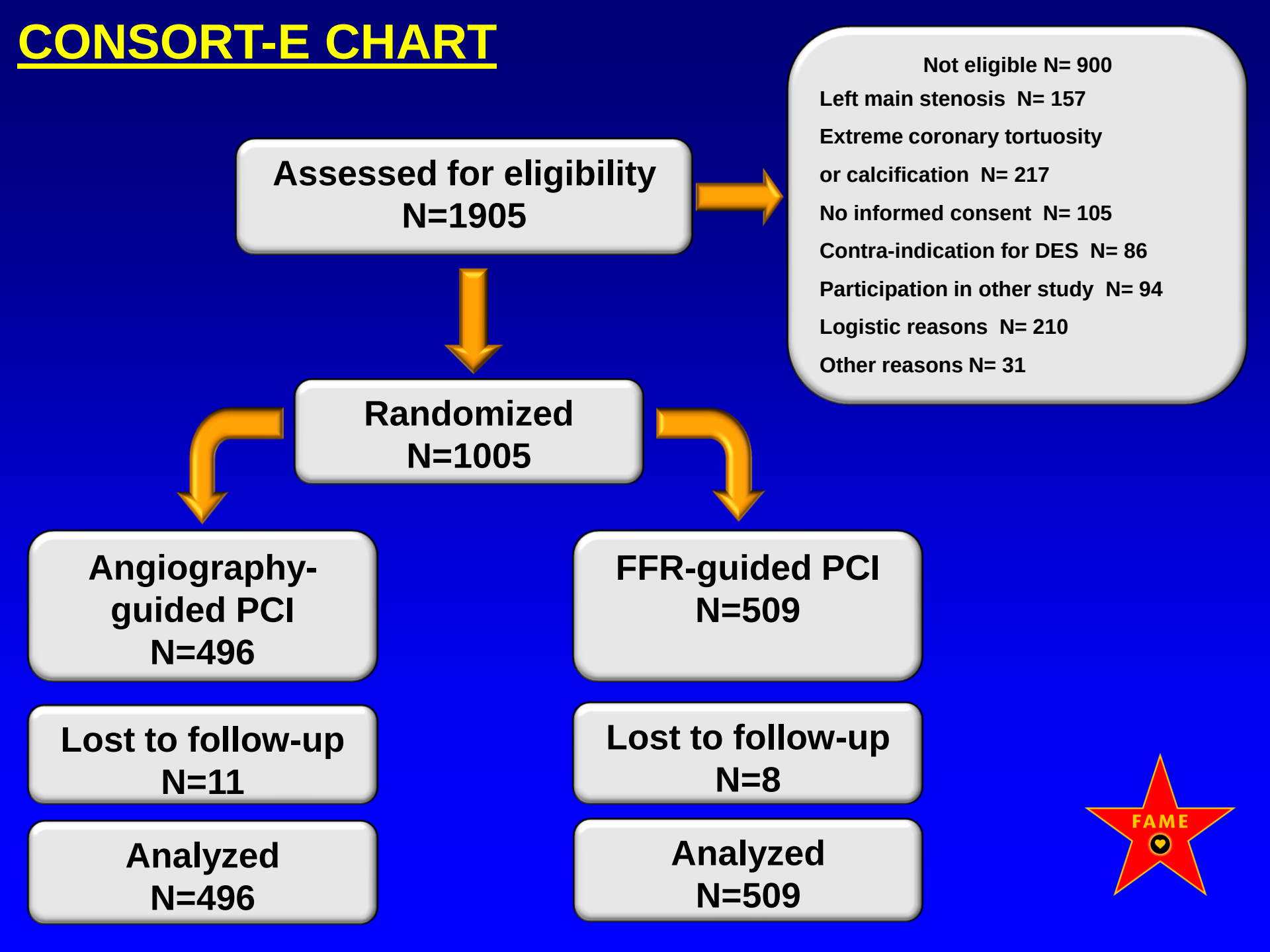
FAME and SYNTAX in Perspective

2-Year MACE rate in SYNTAX 3VD versus FAME

Identical Definition of MACCE: i.e. Including CVA and Excluding CK-MB 3-5 x N

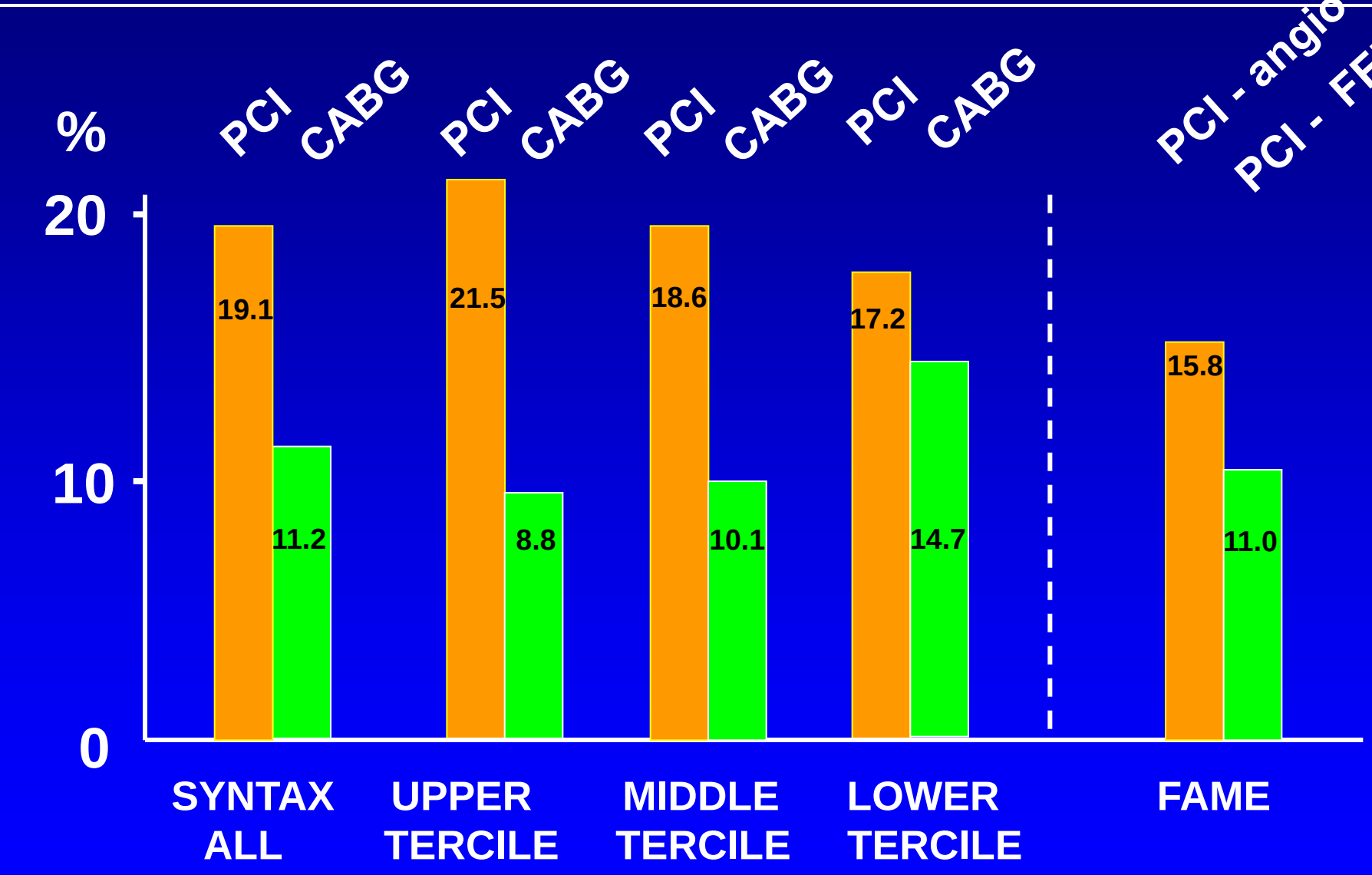


CONSORT-E CHART



MACCE in SYNTAX – 3VD and FAME

similar definition of MACCE, including CVA and excluding CKMB 3-5 x N



Catharina Hospital, Eindhoven, The Netherland

"FUNCTIONAL CLASS IS A SOFT ENDPOINT" ??

<u>*You are 50 years* old and have "stable angina" cl 2 :</u>

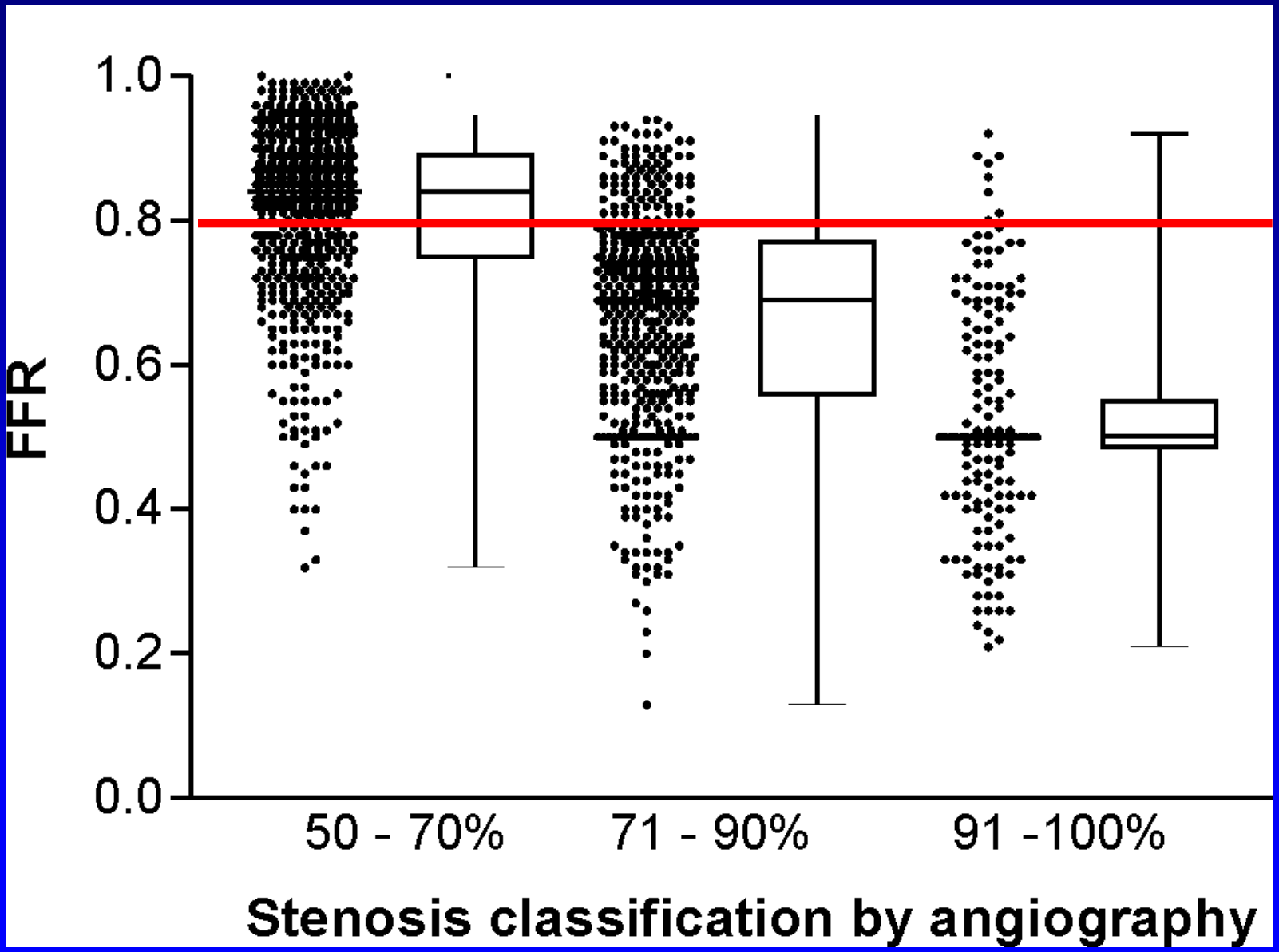
- *When playing tennis,you have to stop after 15 minutes*
- *When running 2 stairs in a hurry, you feel your chest or has to take nitro*
- *You are reminded twice a week that you are heart patient*

And now there is a highly effective sophisticated method, FFR-guided PCI , that not only decreases event rate but makes you forget about your heart troubles !

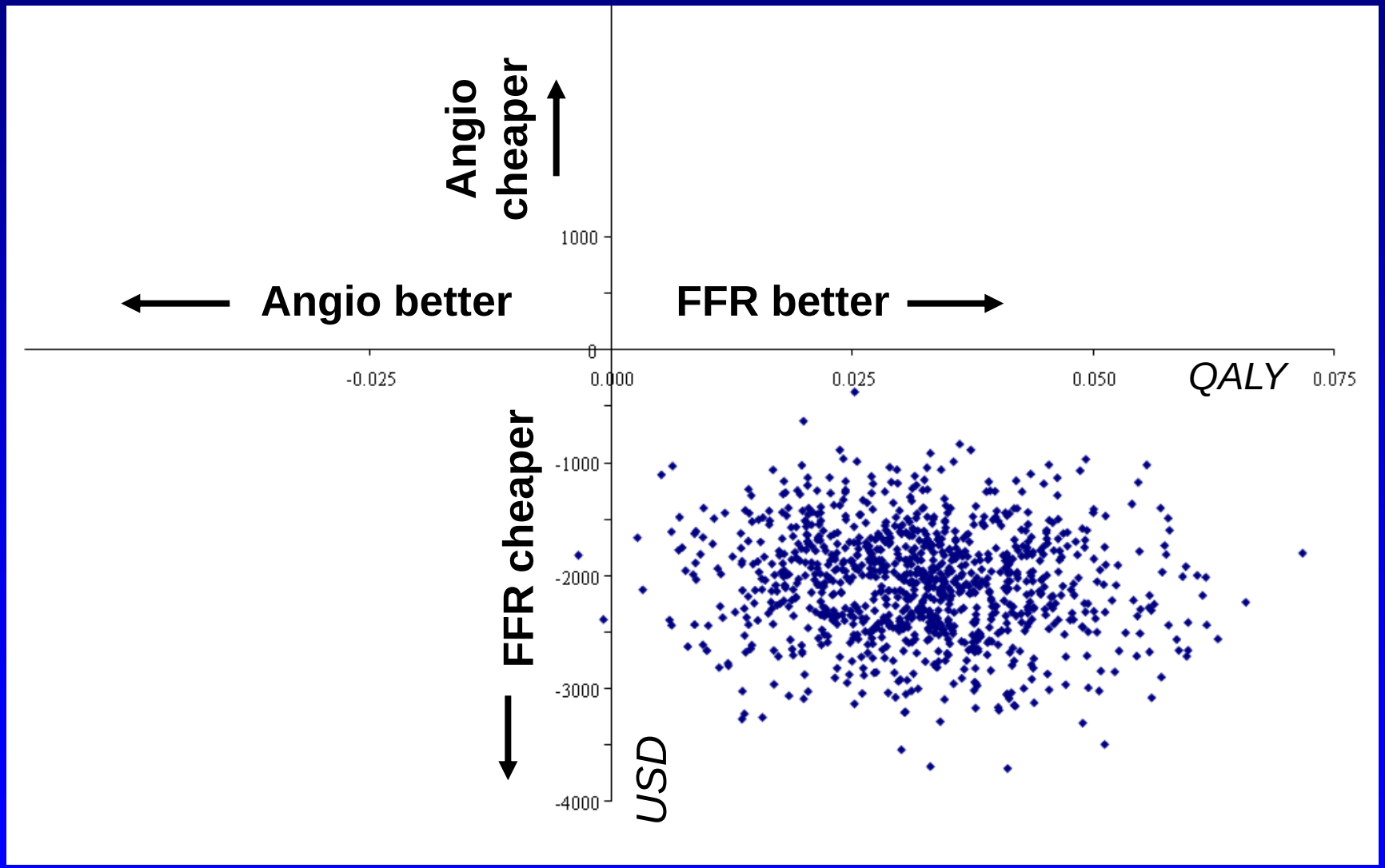
Quality of Life <u>is</u> important in todays world !!!

“I do not stent lesions of 50-70%”

Ischemic threshold 0.80



FAME study: Economic Evaluation (1)



FAME study: Economic Evaluation

Incremental health care costs in first year

Angio-guided PCI: USD 14,357

FFR – guided PCI : USD 12,291

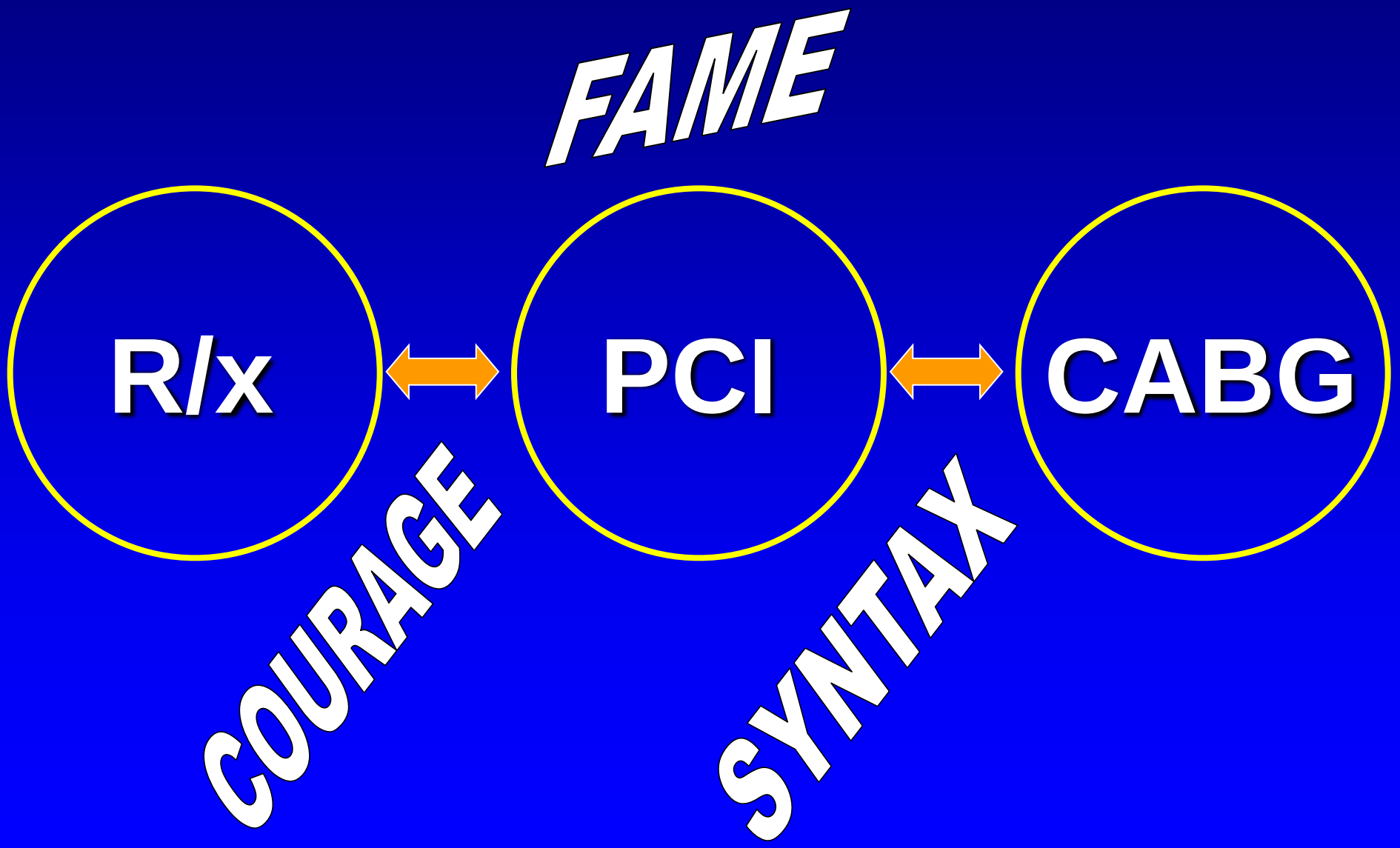
An FFR-guided strategy to multivessel PCI is one of those rare situations in medicine in which a new innovative treatment not only improves outcome but is also cost-saving

Fearon et al, Circulation 2010

TREATMENT OPTIONS FOR MVD

What are the consequences of the FAME study for the treatment of patients with multivessel disease ?

TREATMENT OPTIONS FOR MVD



TREATMENT OPTIONS FOR MVD