

# FRACTIONAL FLOW RESERVE *versus* ANGIOGRAPHY FOR GUIDING PCI IN PATIENTS WITH MULTIVESSEL CORONARY ARTERY DISEASE

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on behalf of the *FAME investigators*

# ***FAME study: disclosure***



To perform the FAME study, an unrestricted institutional research grant was obtained from RADI Medical Systems

I have no further conflict of interest to declare

**F**ractional Flow Reserve

*versus*

**A**ngiography for

**M**ultivessel

**E**valuation



**FRACTIONAL FLOW RESERVE  
*versus* ANGIOGRAPHY  
FOR GUIDING PCI IN PATIENTS WITH  
MULTIVESSEL CORONARY ARTERY DISEASE**

# ***FAME study: BACKGROUND (1)***



- Stenting of non-ischemic stenoses has no benefit compared to medical treatment only
- Stenting of ischemia-related stenoses improves symptoms and outcome
- In multivessel coronary disease (MVD), identifying which stenoses cause ischemia is difficult:

*Non-invasive tests are often unreliable in MVD and coronary angiography often results in both under- or overestimation of functional stenosis severity*

# ***FAME study: BACKGROUND (2)***



- **Fractional Flow Reserve (FFR)**, is the most accurate and selective index to indicate whether a particular stenosis is responsible for inducible ischemia
- FFR can be easily determined in the cathlab just prior to stenting

## ***Therefore:***

- ***FFR guidance of PCI in patients with multivessel disease may improve outcome***



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

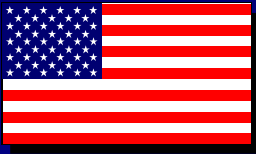


**Randomized multicenter study in 1000 patients undergoing DES-stenting for multivessel disease in 20 US and European centers**

- 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**



# Participating Centers



## USA (6)

Stanford University  
(*William F. Fearon*)

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

University of Louisville  
(*Massoud Leesar*)

St Louis University  
(*Michael Lim*)

University Hospital Virginia  
(*Michael Ragosta*)

University of South Carolina  
(*Eric Powers*)

## EUROPE (14)

King's College Hospital, London)  
(*Ph. MacCarthy*)

Cardiovascular Center Aalst (*B. De Bruyne*)

Catharina Hospital Eindhoven (*N. Pijls*)

Rigshospitalet, Copenhagen (*T. Engstrom*)

Klinikum der Universität München (*V. Klauss*)

Aarhus University Hospital (*Ole Frobert*)

University Hospital Bergmannsheil  
(*Waldemar Bojara*)

Sodersjukhuset, Stockholm (*I Herzfeld*)

Helsingborgs Lasarett (*F Schersten*)

Klinikum Darmstadt (*Gerald Werner*)

Bristol Royal Infirmary (*A. Baumbach*)

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

Glasgow Western Infirmary (*Keith Oldroyd*)

Royal Victoria Hospital, Belfast (*Ganesh Manoharan*)

# ***FAME study***



## ***Steering Committee:***

Nico H.J. Pijls, Eindhoven, Netherlands (PI)

William F. Fearon, Stanford, CA, USA (PI)

Bernard De Bruyne, Aalst, Belgium

Pim A.L. Tonino, Eindhoven, Netherlands

## ***Data analysis:***

Uwe Siebert, Boston, MA, USA and Hall, A

Rafaele Gothe and Bernard Bornschein, Hall, Austria

## ***Clinical Events Committee:***

Eric Eeckhout, Lausanne, Switzerland

Morton Kern, Irvine, CA, USA

Mamdouh El Gamal, Eindhoven, NL

John Hodgson, Phoenix, AZ, USA

Emanuele Barbato, Naples, Italy

# **FAME study: Study Population**



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

## **Inclusion criteria:**

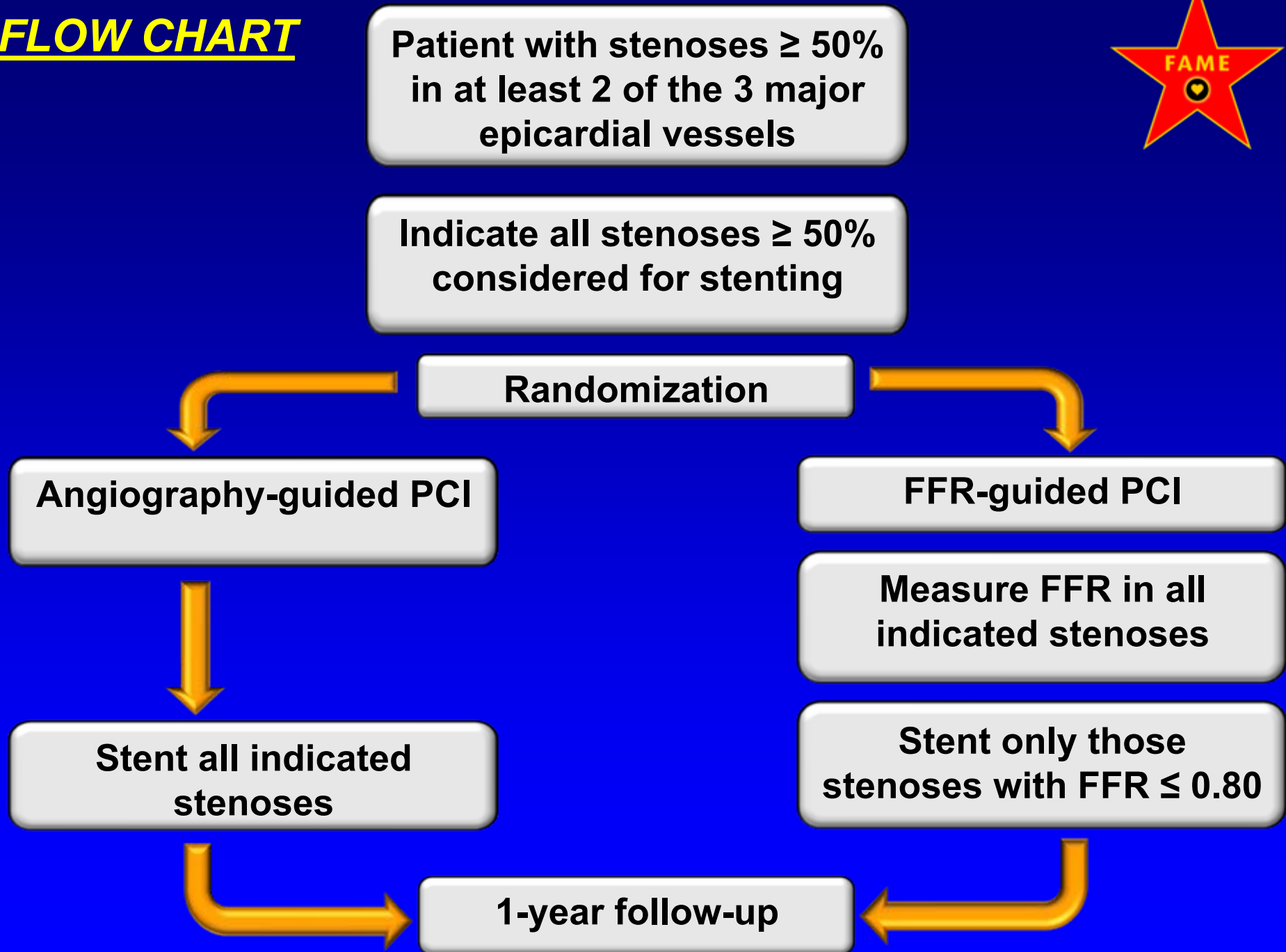
- **ALL** patients with multivessel disease
- At least 2 stenoses  $\geq 50\%$  in 2 or 3 major epicardial coronary artery disease, amenable for stenting

## **Exclusion criteria:**

- Left main disease or previous bypass surgery
- ST-elevation MI with CK  $> 1000$  U/l within last 5 days
- extremely tortuous or calcified coronary arteries

**Note:** patients with previous PCI were not excluded

# FLOW CHART



# *FAME study: PRIMARY ENDPOINT*



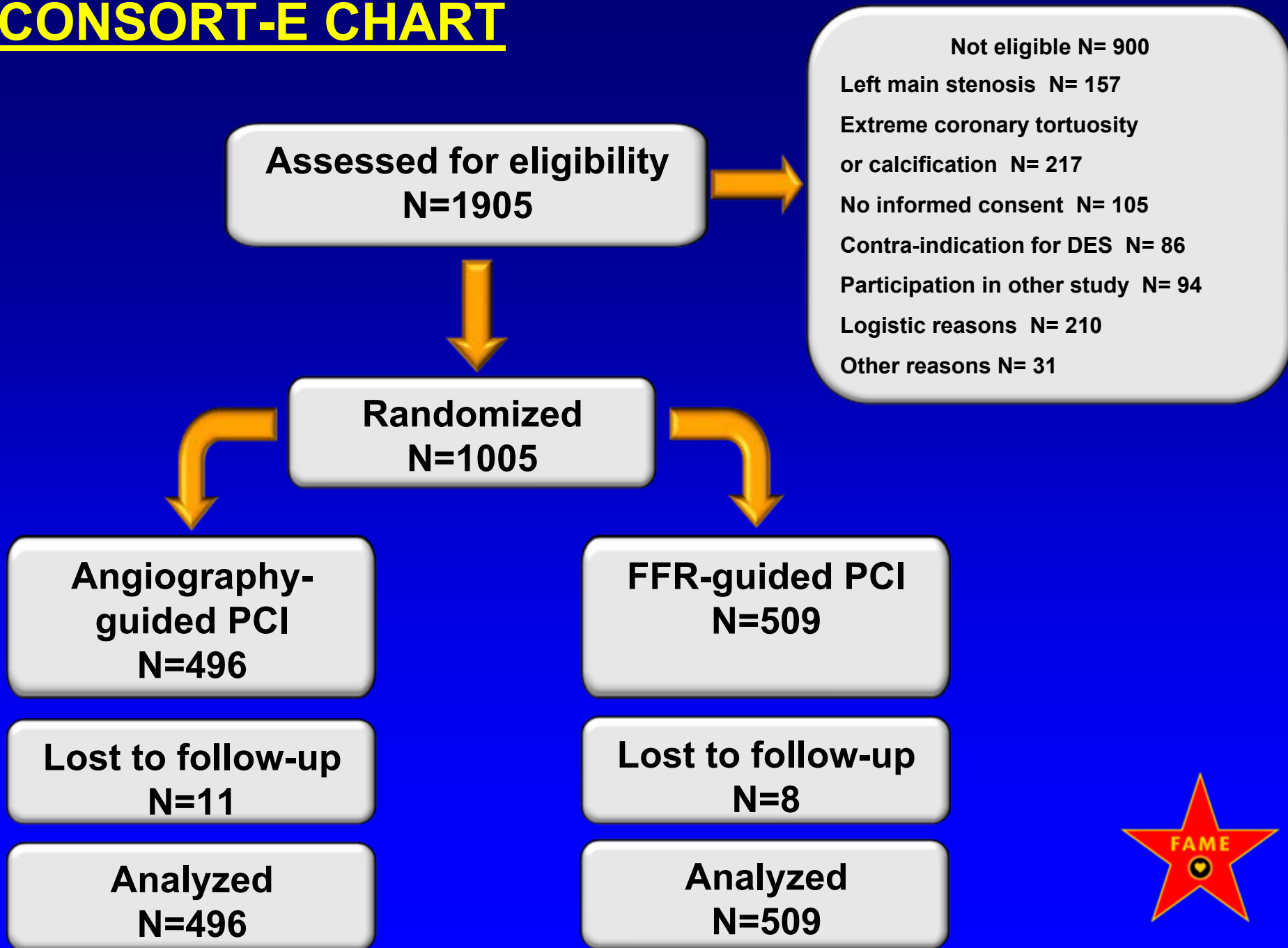
*Composite of death, myocardial infarction,  
or repeat revascularization (“MACE”)  
at 1 year*

# *FAME study: **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





# ***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
- EKG, CK, CK-MB, etc during hospital stay
- Follow-up at 1 month, 6 months, 1 year
- ***Also in case of repeat-procedure , strictly adherence to initial randomization***

# 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
<i># indicated lesions per patient</i>	2.7±0.9	2.8±1.0	0.34

# FAME study: Baseline Characteristics (2)



	ANGIO-group N=496	FFR-group N=509	P-value
<i># indicated lesions per patient</i>	2.7±0.9	2.8±1.0	0.34
Reference diameter (mm)	2.5±0.6	2.5±0.7	0.81
% stenosis severity	61±17	60±18	0.24
MLD (mm)	1.0±0.4	1.0±0.5	0.35

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% stenosis severity	61±17	60±18	0.24
MLD (mm)	1.0±0.4	1.0±0.5	0.35
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



# FAME study: Procedural Results (1)

	ANGIO-group N=496	FFR-group N=509	P-value
<b># indicated lesions per patient</b>	<b>2.7 ± 0.9</b>	<b>2.8 ± 1.0</b>	<b>0.34</b>
<b>FFR results</b>			
Lesions successfully measured, No (%)	-	<b>1329 (98%)</b>	-
Lesions with FFR ≤ 0.80 ,No (%)	-	<b>874 (63%)</b>	-
Lesions with FFR > 0.80 ,No (%)	-	<b>513 (37%)</b>	-
FFR in ischemic lesions	-	<b>0.60 ± 0.14</b>	-
FFR in non-ischemic lesions	-	<b>0.88 ± 0.05</b>	-



# FAME study: Procedural Results (1)

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Lesions with FFR ≤ 0.80 ,No (%)	-	<b>874 (63%)</b>	-
Lesions with FFR > 0.80 ,No (%)	-	<b>513 (37%)</b>	-
<b>stents per patient</b>	<b>2.7 ± 1.2</b>	<b>1.9 ± 1.3</b>	<b>&lt;0.001</b>
Lesions successfully stented (%)	<b>92%</b>	<b>94%</b>	-
DES, total, No	<b>1359</b>	<b>980</b>	-



# ***FAME study: Procedural Results (2)***

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



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Materials used at procedure (US \$)	<b>6007</b>	<b>5332</b>	<b>&lt;0.001</b>
Length of hospital stay (days)	<b>3.7 ± 3.5</b>	<b>3.4 ± 3.3</b>	<b>0.05</b>



# ***FAME study: Adverse Events at 1 year***

	<b>ANGIO-group N=496</b>	<b>FFR-group N=509</b>	<b>P-value</b>
<b><i>Events at 1 year, No (%)</i></b> <b>Death, MI, CABG, or repeat-PCI</b>	<b>91 (18.4)</b>	<b>67 (13.2)</b>	<b>0.02</b>



# FAME study: Adverse Events at 1 year

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<b>Death, MI, CABG, or repeat-PCI</b>	<b>91 (18.4)</b>	<b>67 (13.2)</b>	<b>0.02</b>
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



# FAME study: Adverse Events at 1 year

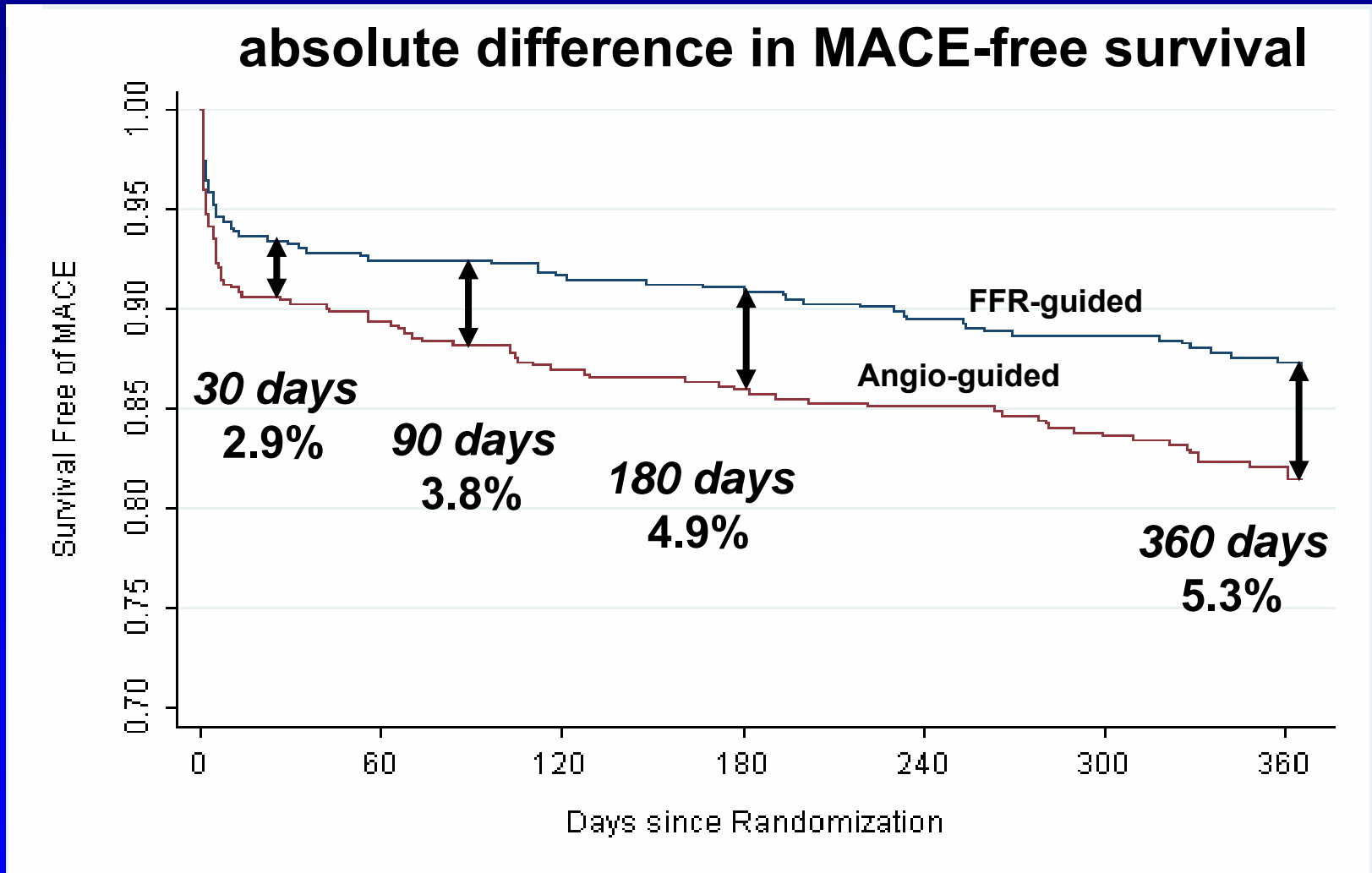
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CABG or repeat PCI	47 (9.5)	33 (6.5)	0.08
Total no. of MACE	113	76	0.02



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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
<b>Myocardial infarction, specified</b>			
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: *Event-free Survival*



# ***FAME study: Functional Class at 1 Year***



	<b>ANGIO-group N=496</b>	<b>FFR-group N=509</b>	<b>P-value</b>
Patients without event and free from angina	<b>326 (68)</b>	<b>360 (73)</b>	<b>0.07</b>
Patients free from angina, No. (%)	<b>374 (78)</b>	<b>399 (81)</b>	<b>0.20</b>
Number of anti-anginal meds, No.	<b>1.2 ± 0.7</b>	<b>1.2 ± 0.8</b>	<b>0.48</b>
EQ-5D visual analogue scale	<b>74 ± 16</b>	<b>75 ± 16</b>	<b>0.65</b>

# *FAME study: Consequences*



- In most recently performed studies to PCI in MVD, PCI was performed on an angiography-guided basis (such as in SYNTAX 3-VD)
- Outcome of PCI in those studies was comparable to outcome in the angiography-guided arm of FAME
- Outcome in the FFR-guided arm of FAME was comparable to outcome of CABG in SYNTAX and much better than, e.g. outcome of medical treatment in COURAGE

# TREATMENT OPTIONS FOR MVD



- Therefore, it might be expected that indications for PCI as treatment of MVD, will expand in 2 directions

**R/x**

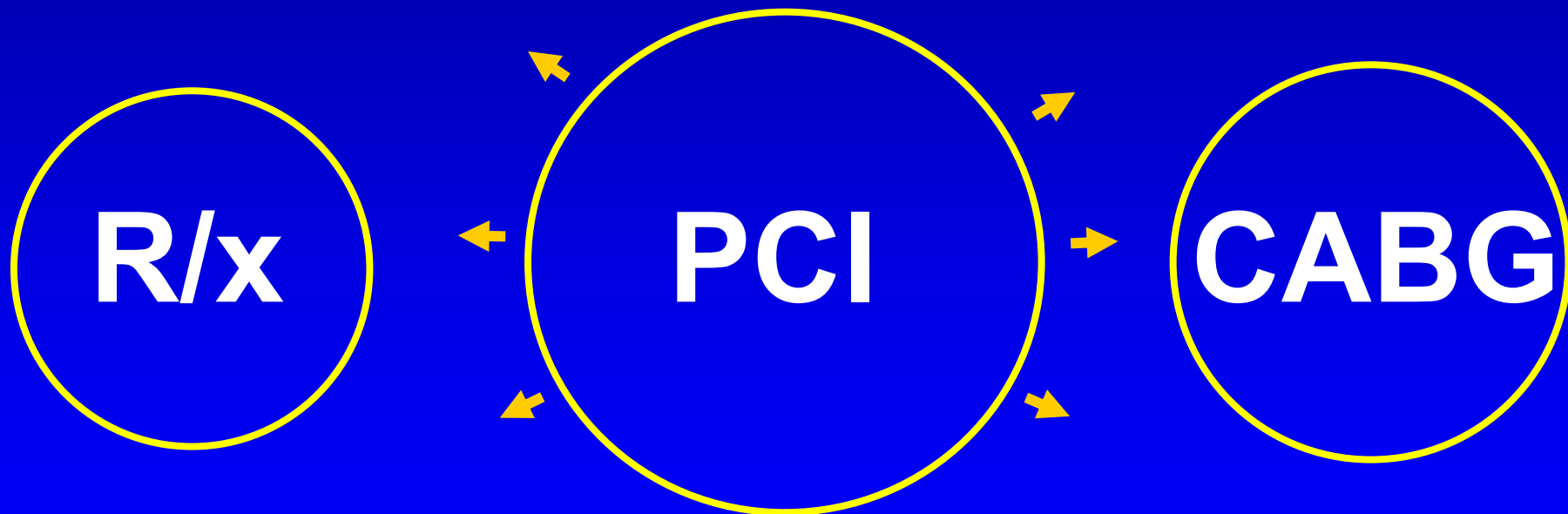
**PCI**

**CABG**

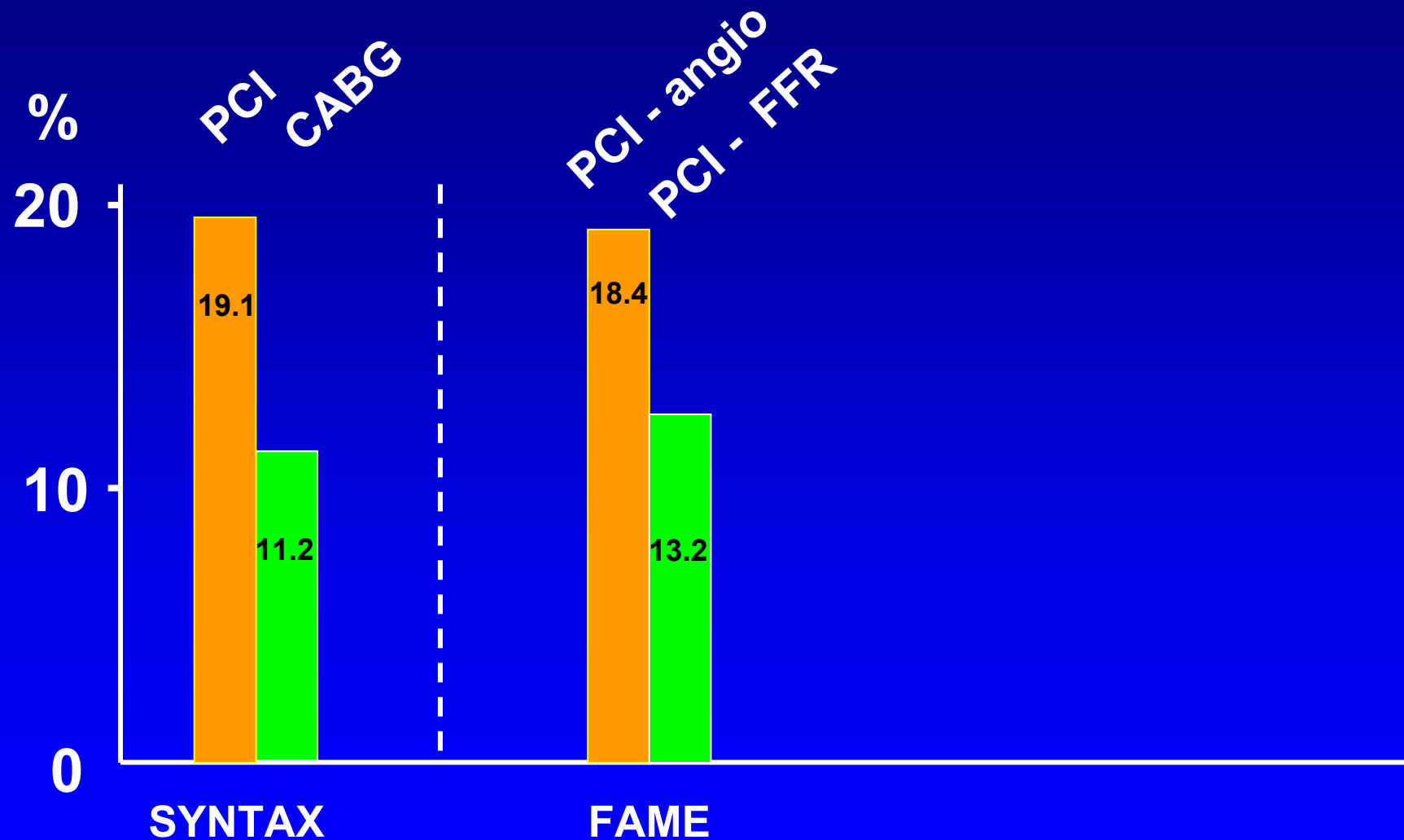
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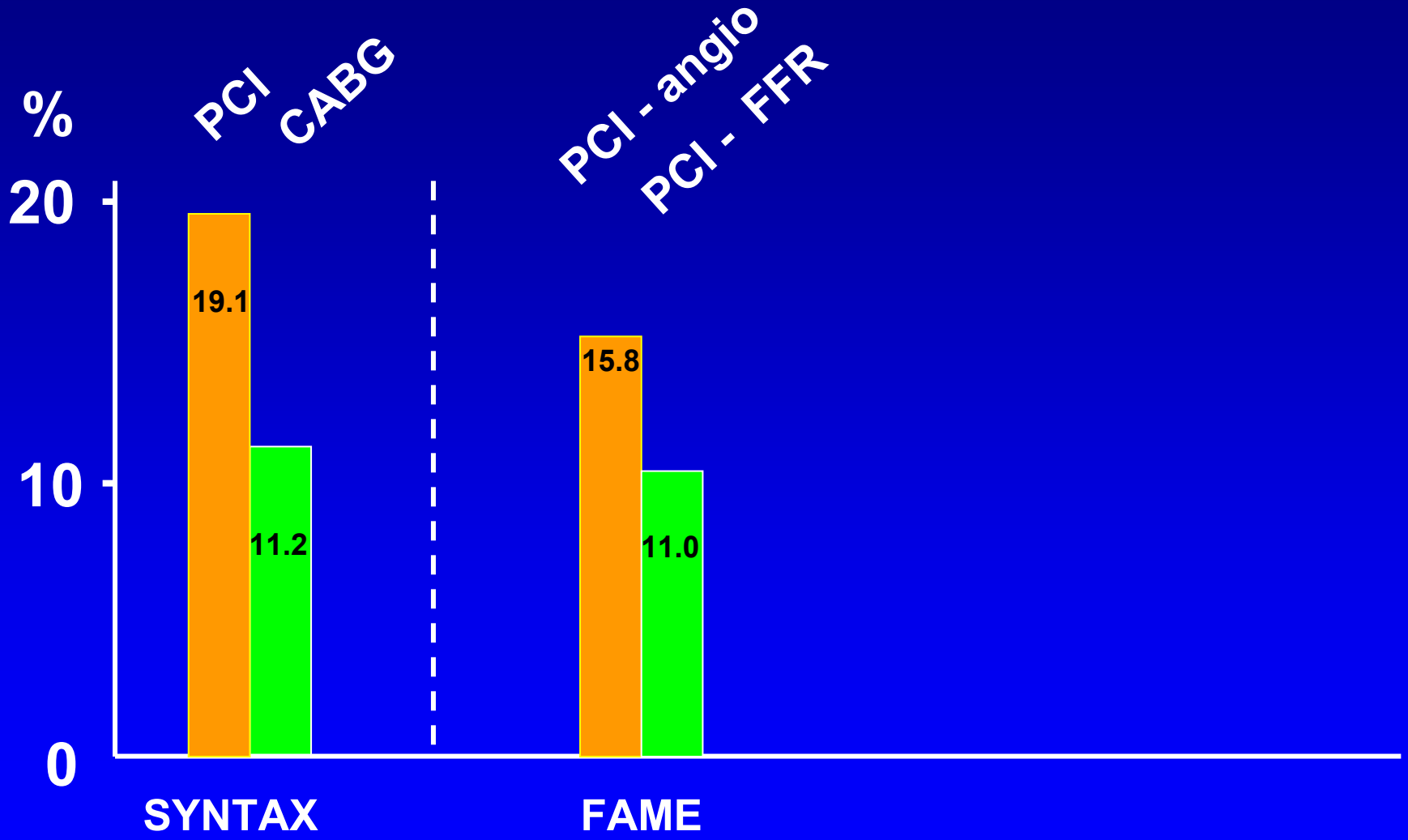


# MACE in SYNTAX – 3VD and FAME

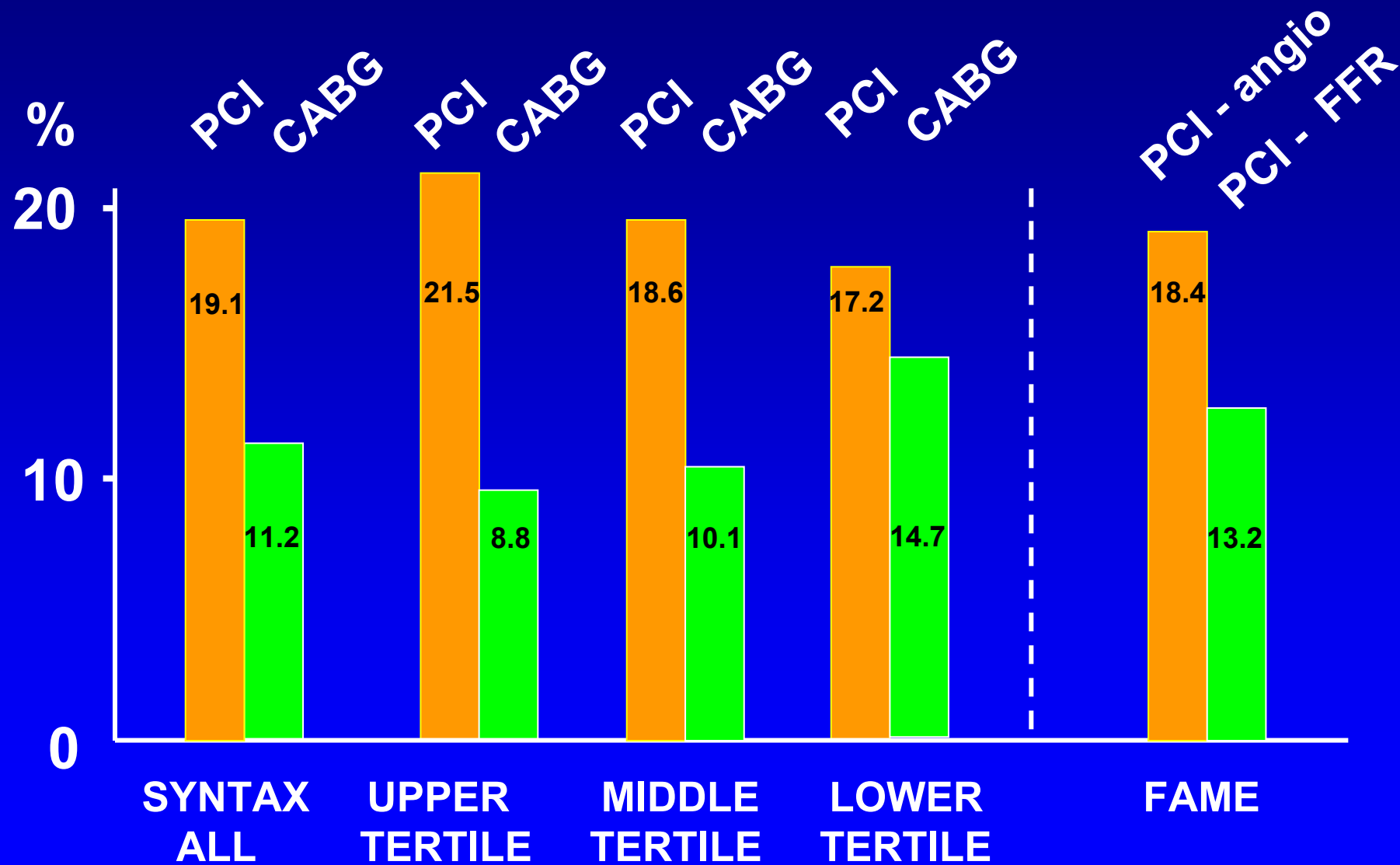


# MACCE in SYNTAX – 3VD and FAME

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

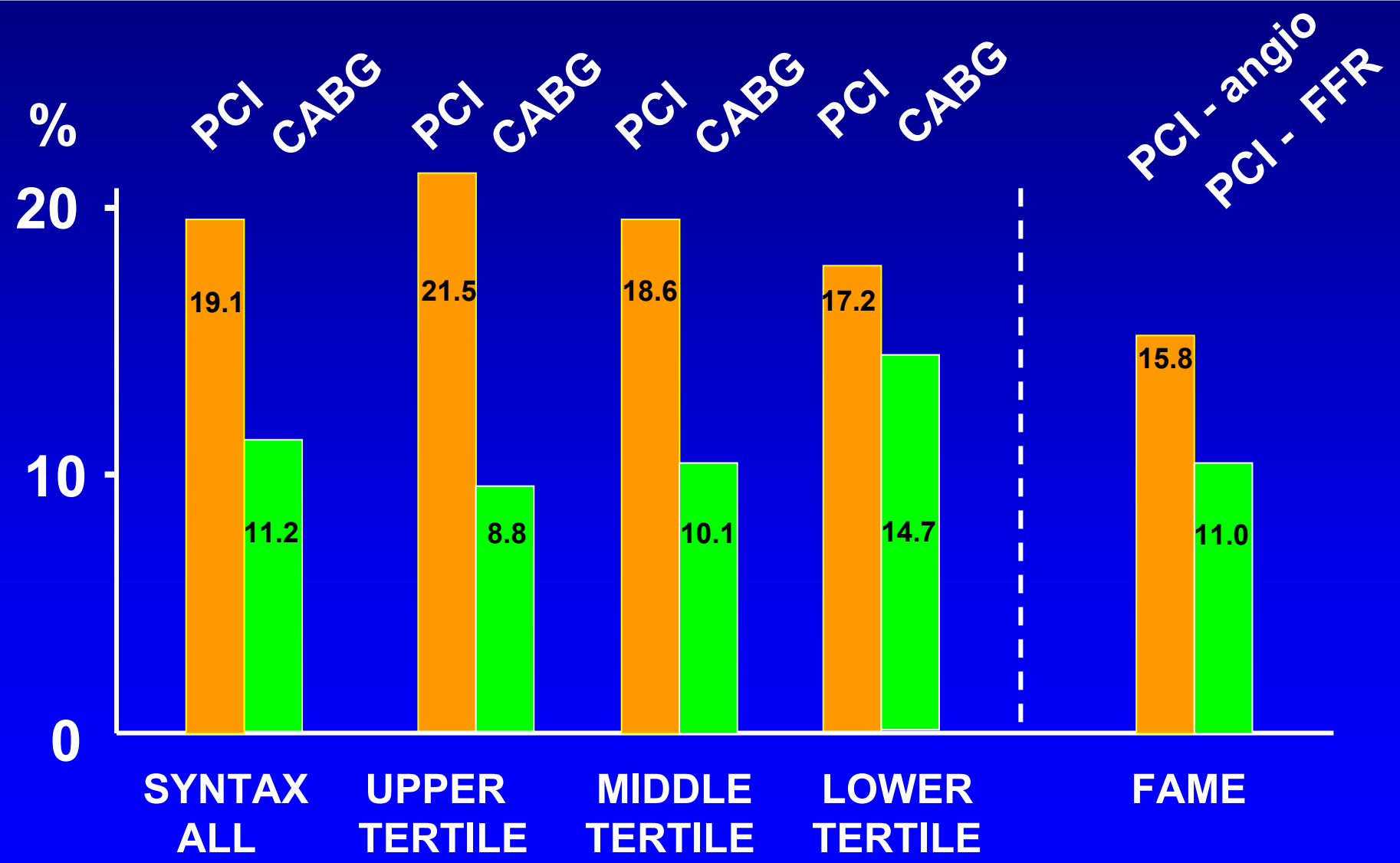


# MACE in SYNTAX – 3VD and FAME



# MACCE in SYNTAX – 3VD and FAME

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



# ***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 year by ~ 30%***
- reduces mortality and myocardial infarction at 1 year by ~ 35 %***

# ***FAME study: CONCLUSIONS (2)***



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

- is cost-saving and does not prolong the procedure***
- reduces the number of stents used***
- decreases the amount of contrast agent used***
- results in a similar, if not better, functional status***

# ***FAME study: CONCLUSIONS (3)***



***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.***