CLINICAL APPLICATION OF FFR: EVIDENCE AND PRACTICE

TCT ASIA
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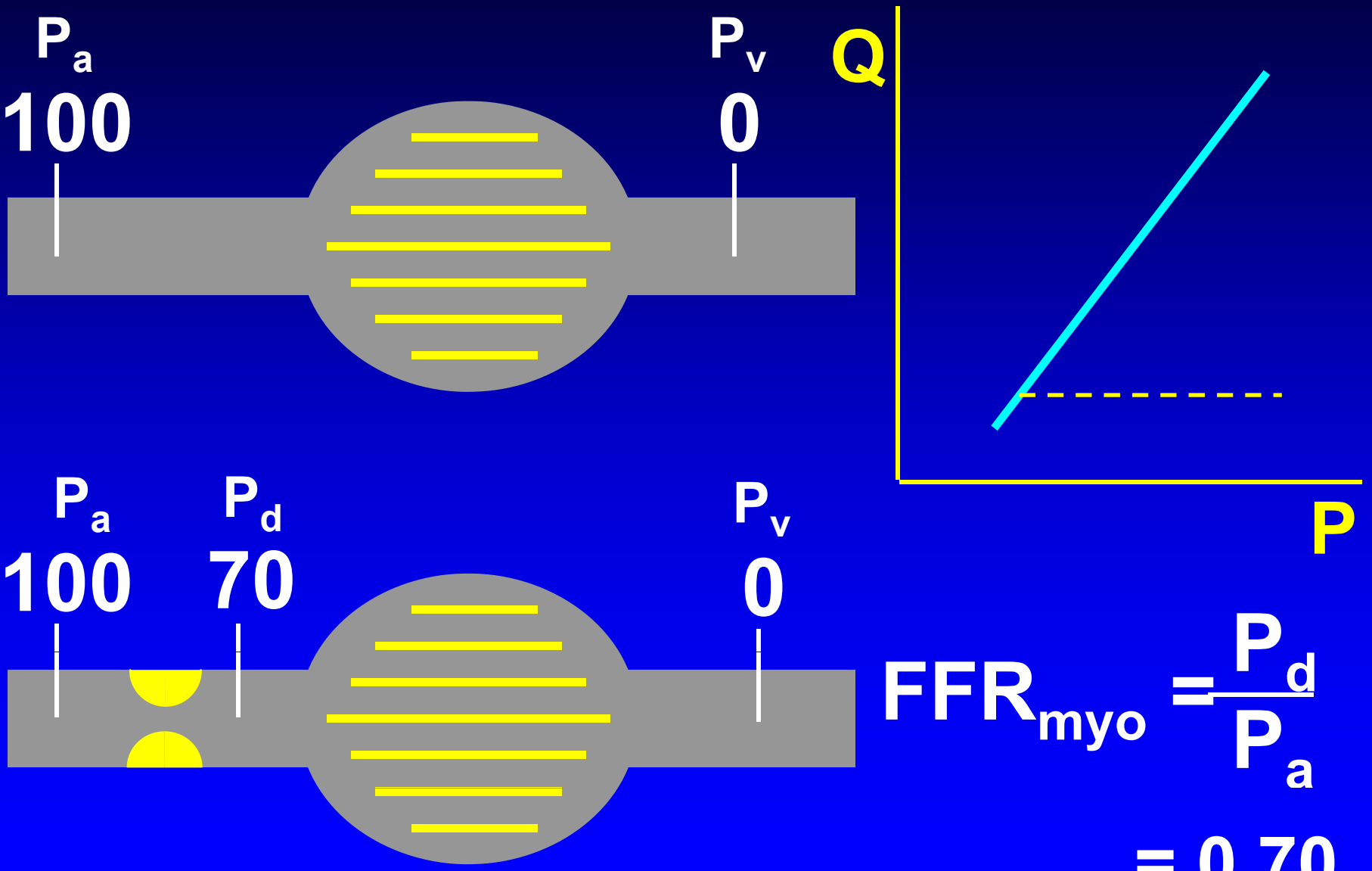
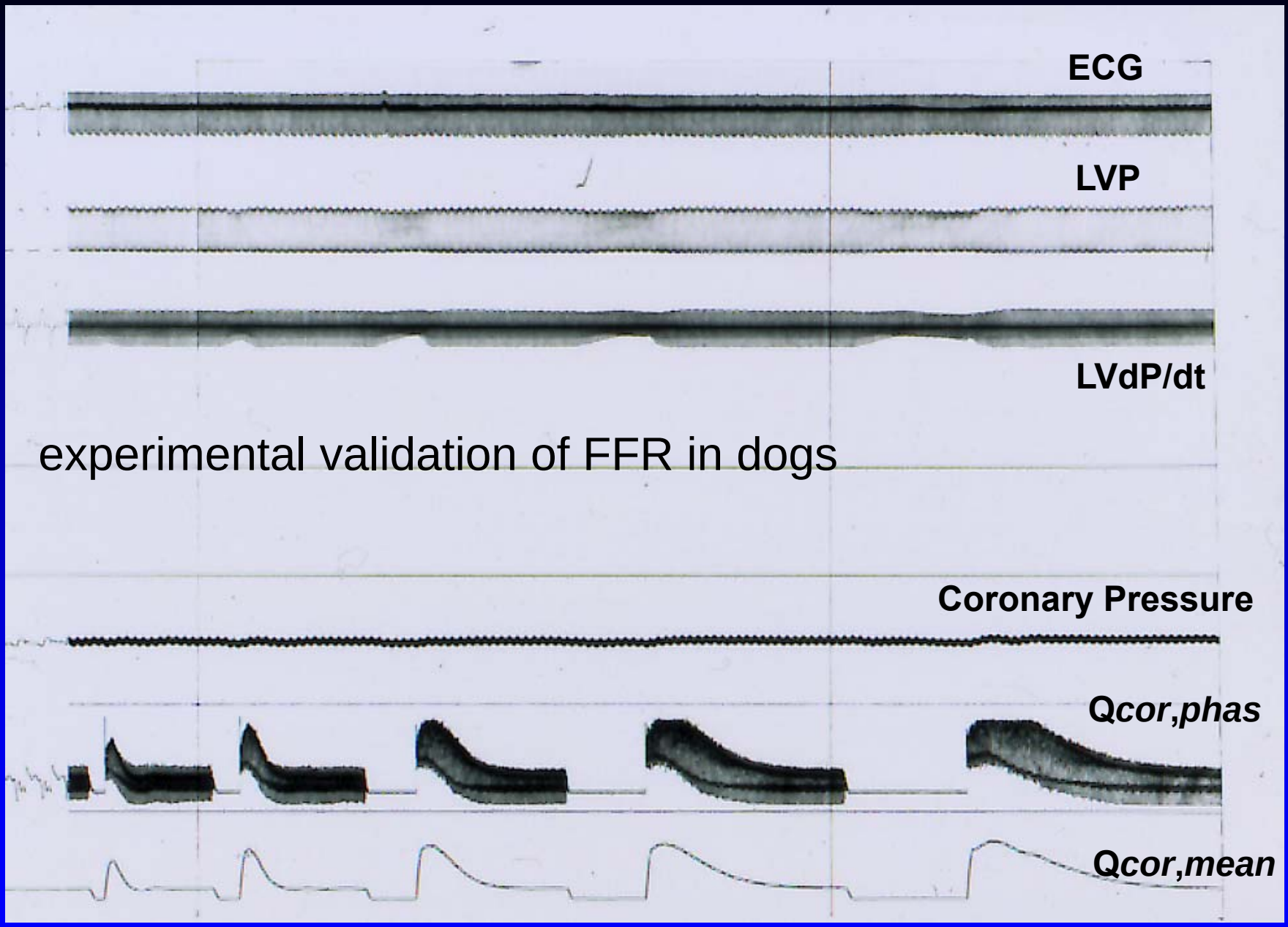
During Maximal Vasodilatation



FRACTIONAL FLOW RESERVE:

- has a sound scientific basis
- has been well validated experimentally
- is the only functional parameter which has been validated clinically versus a true gold standard
- facilitates decision-making in PCI
- and improves outcome of angioplasty



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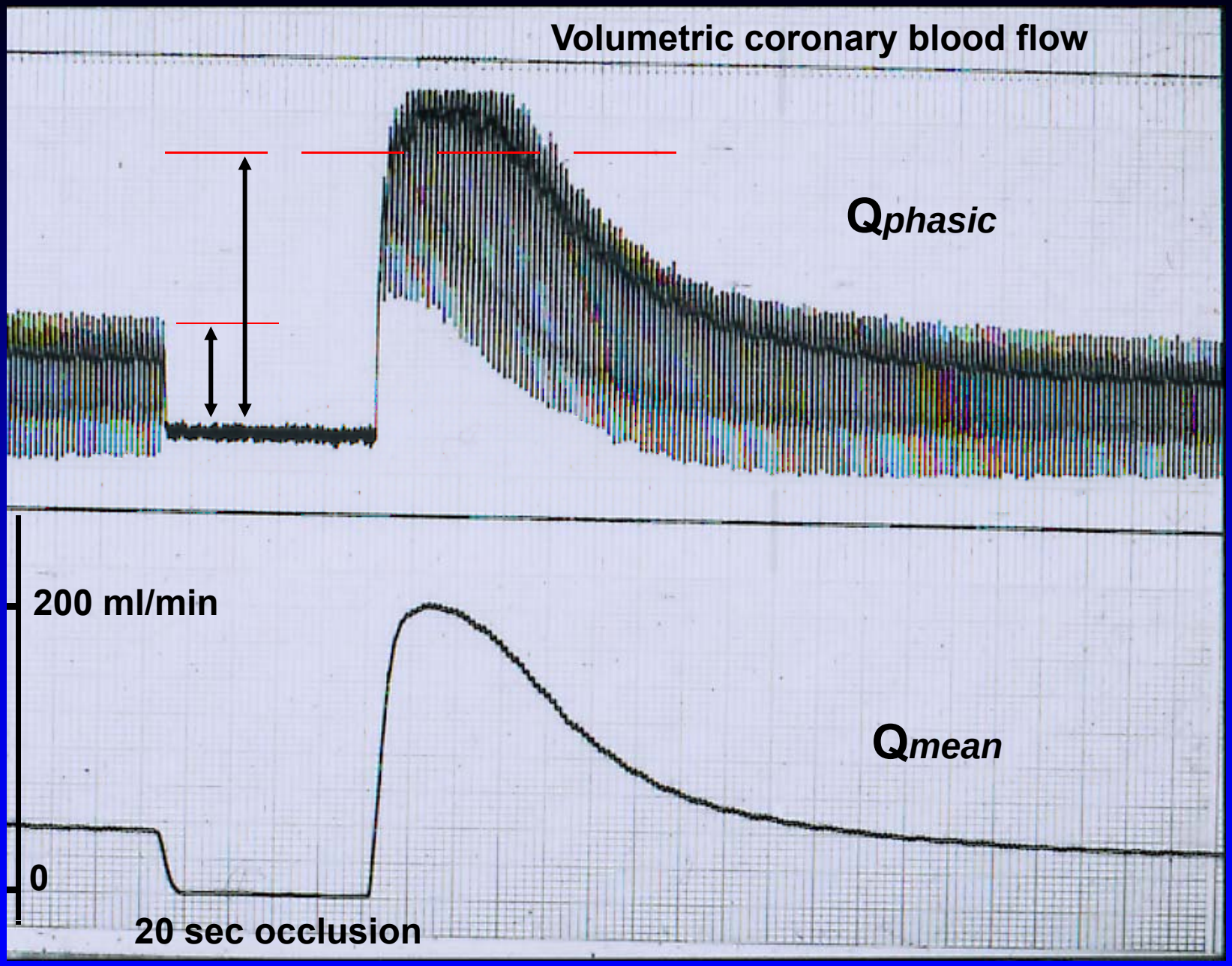
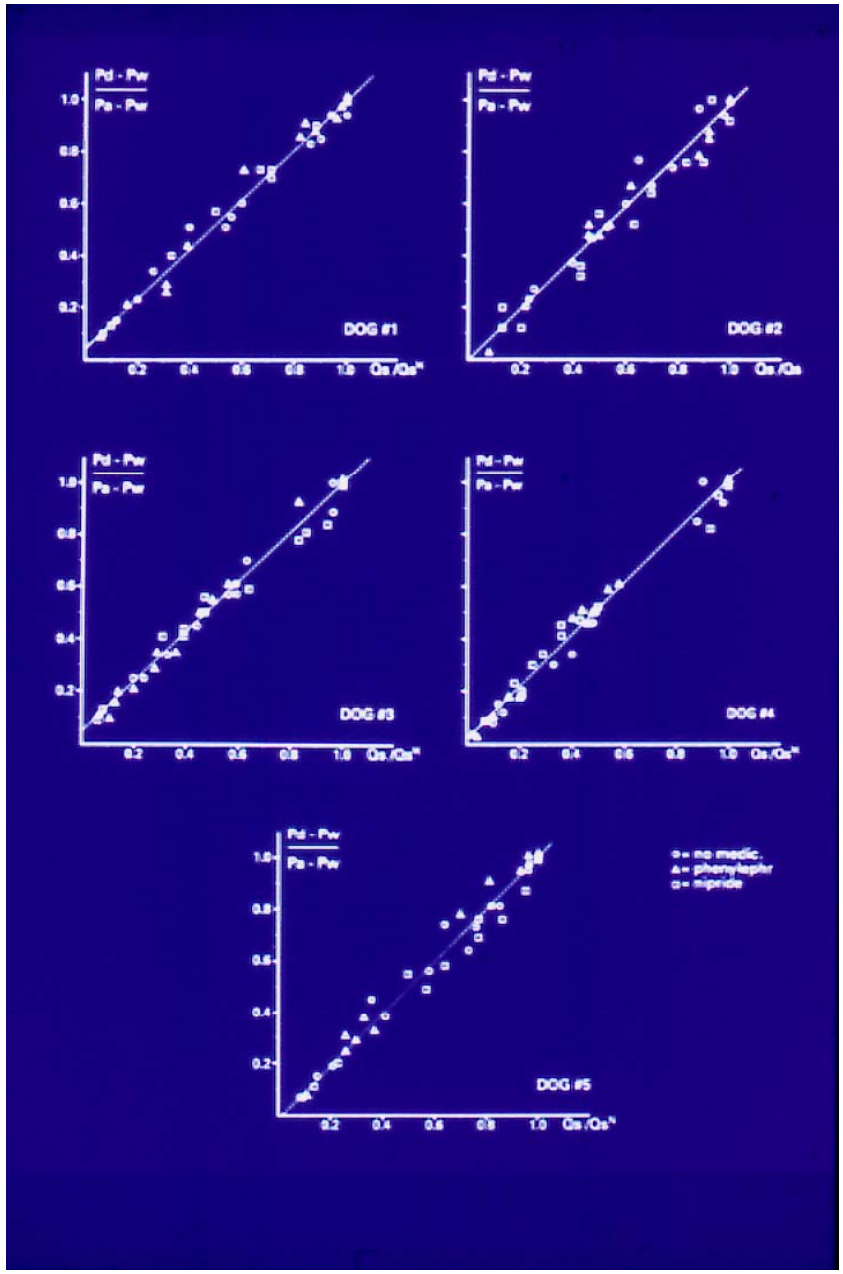


Constant pressure **R ~ 1 / Flow**



Experimental basis of FFR

Horizontal axis:
FFR measured by true flow

Vertical axis:
FFR measured by
Hyperemic pressure ratio

Pijls et al, Circulation 1993

Threshold value of FFR to detect significant stenosis in humans

FFR is the ***only*** functional index which has ever been validated versus a **true gold standard**.
(Prospective multi-testing Bayesian methodology)

ALL studies ever performed in a wide variety of clinical & angiographic conditions, found threshold between 0.75 and 0.80

Sensitivity : 90%
Specificity : 100%

N Engl J Med 1996; 334:1703-1708
Circulation 2010

FFR has been validated in almost all clinical and Angiographic conditions:

- multivessel disease
- left main and ostial stenosis
- diffuse disease
- bifurcation lesions
- tandem lesions
- unstable angina, NSTEMI
- previous myocardial infarction
- etc….

- ….*but not to be used in acute STEMI*

(more than 1500 publications)

FFR and Clinical Outcome:
Evidence from randomised controlled trials

- Is it safe to defer PCI if FFR is negative ?
- Is it indicated to perform PCI if FFR is positive ?
- Does systematic use of FFR improve outcome of PCI ?

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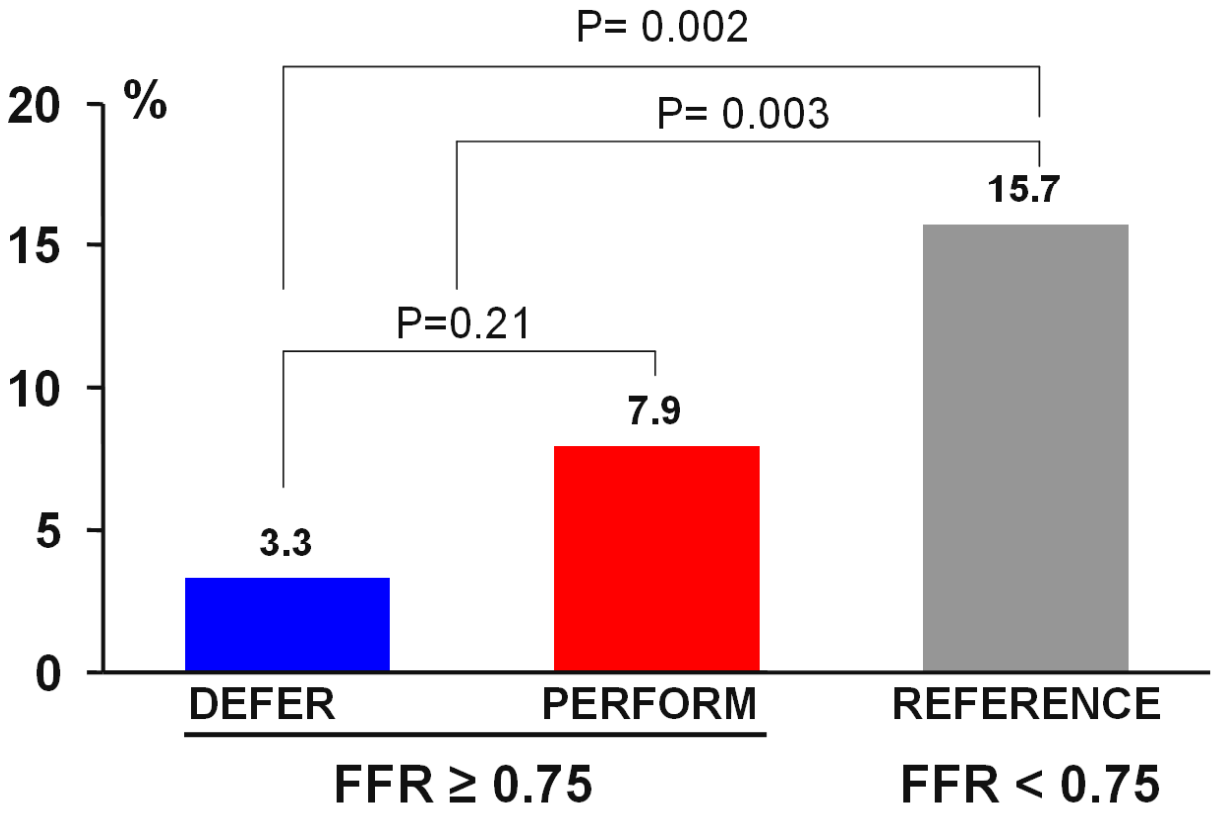
DEFER: Cardiac Death And Acute MI After 5 Years

non-ischemic stenosis, R/x
non-ischemic stenosis, R/x + stent
ischemic stenosis, R/x + stent



DEFER-study, JACC 2007; 49 : 2105-2111

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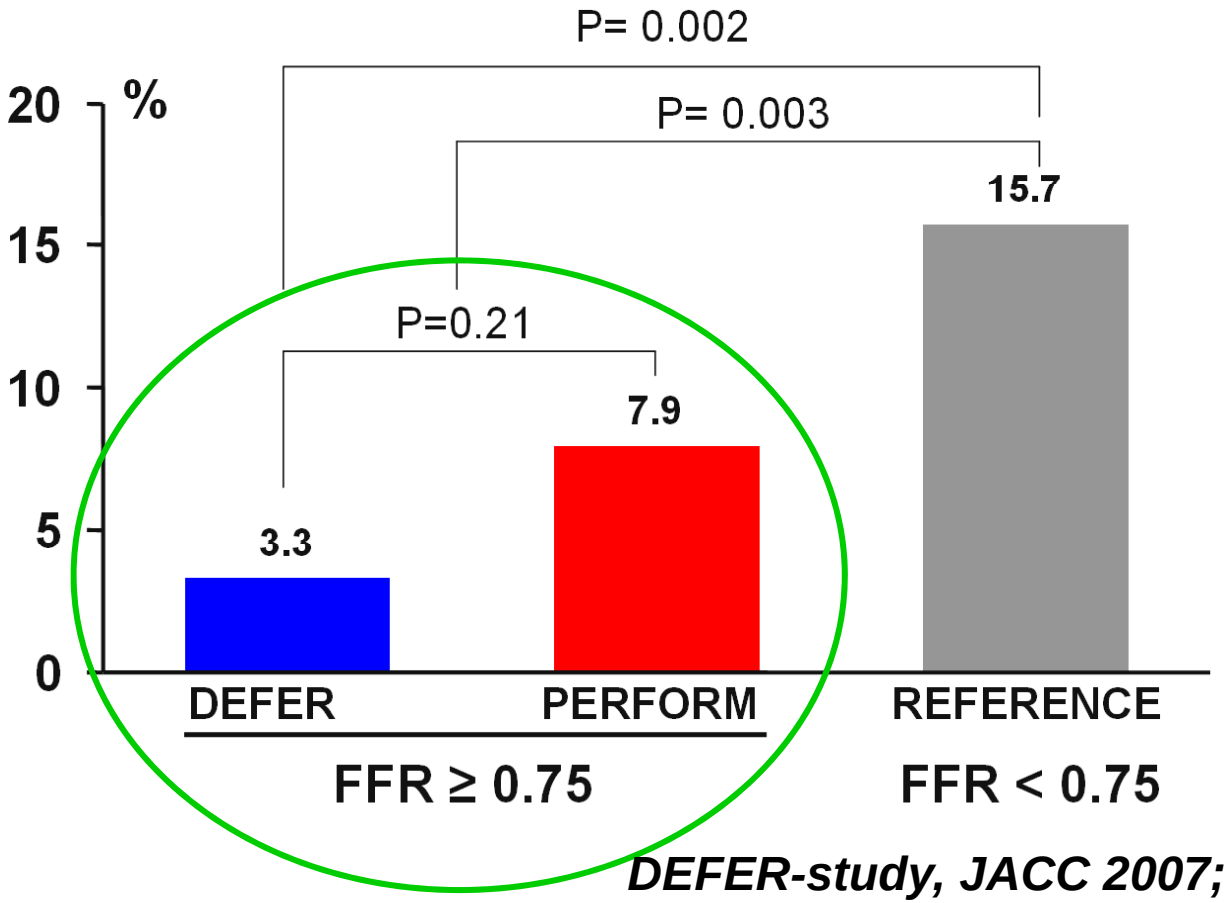

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FUNCTIONALLY *NON*-*SIGNIFICANT* STENOSIS

→ **Stenting a functionally non-significant (FFR-negative) stenosis does NOT make any sense.**

It is unnecessary, expensive, and increases the risk of death and MI without any symptomatic benefit

DEFER, FAME, Nuclear; Prospect

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FUNCTIONALLY *SIGNIFICANT* STENOSIS

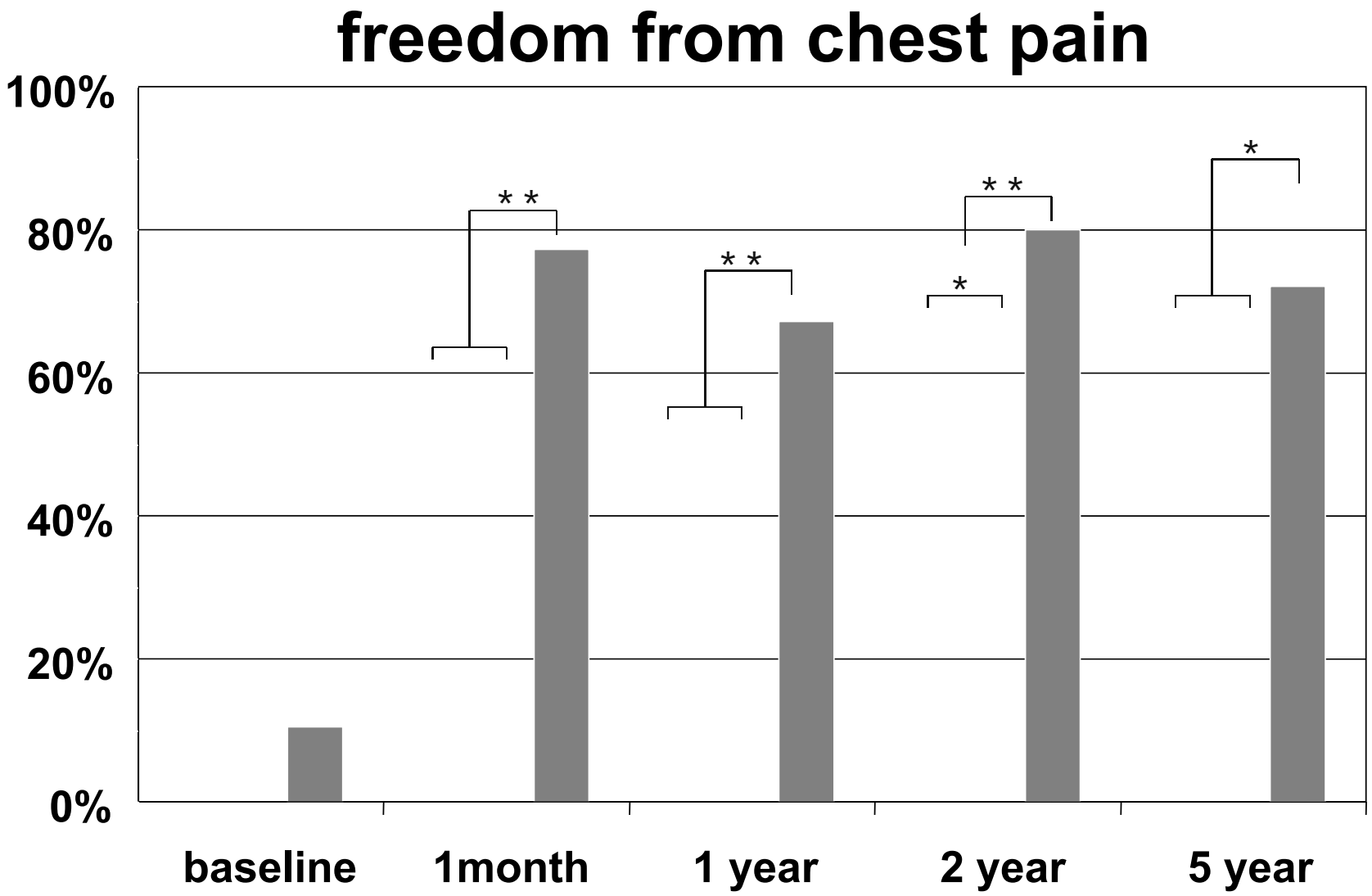
→ **a *functionally significant ("FFR-POSITIVE")* stenosis generally gives symptoms (angina)**
("ischemic" stenosis, hemodynamically significant stenosis)

PCI and stenting is extremely effective in relieving symptoms (angina) in such patients

(and much more effective than medical treatment)

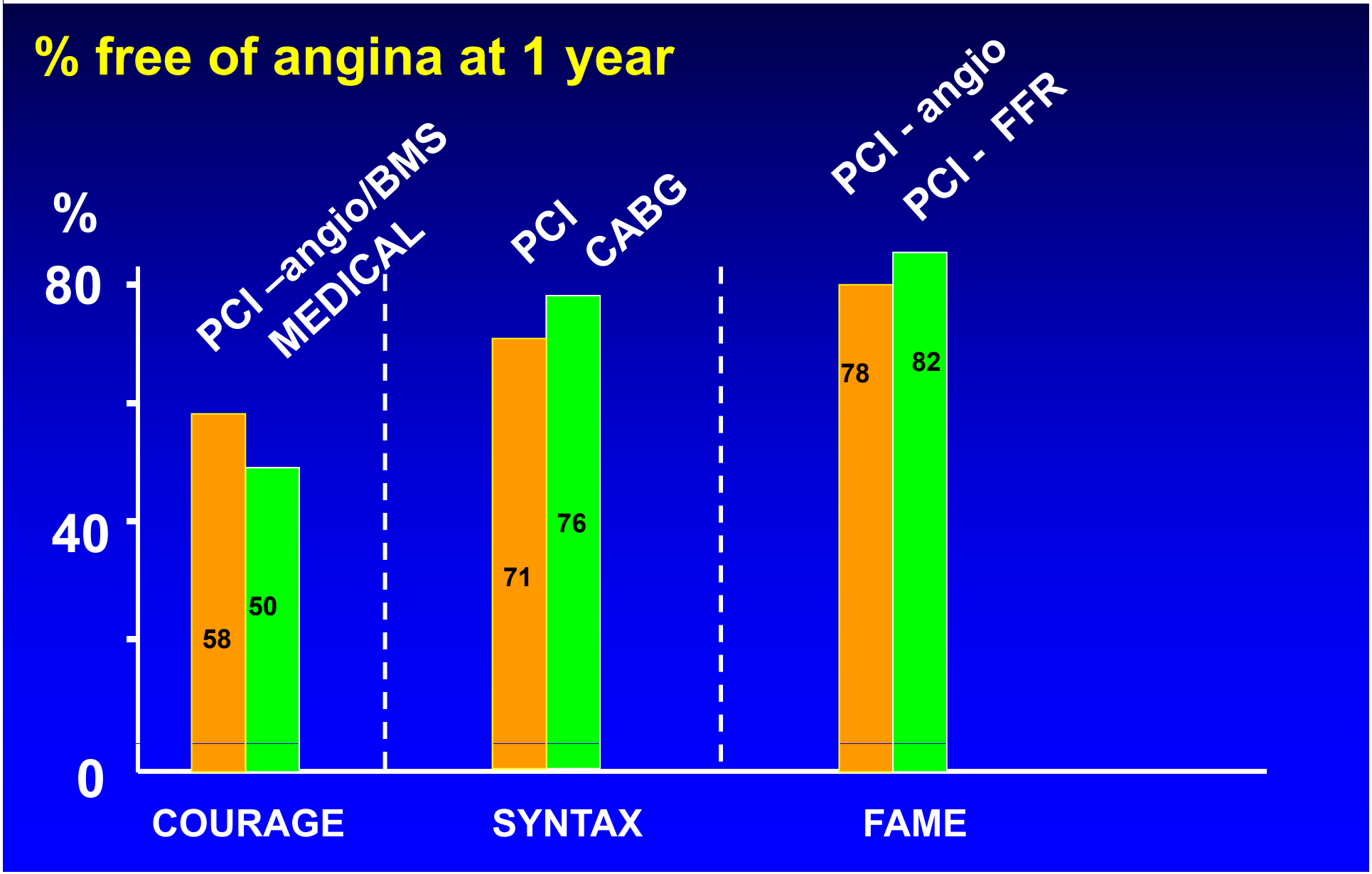
DEFER, COURAGE, SYNTAX, FAME

DEFER-study, JACC 2007; 49 : 2105-2111



Ischemic lesions (FFR < 0.75)
treated by stenting

FUNCTIONAL CLASS in COURAGE - SYNTAX – 3VD and FAME



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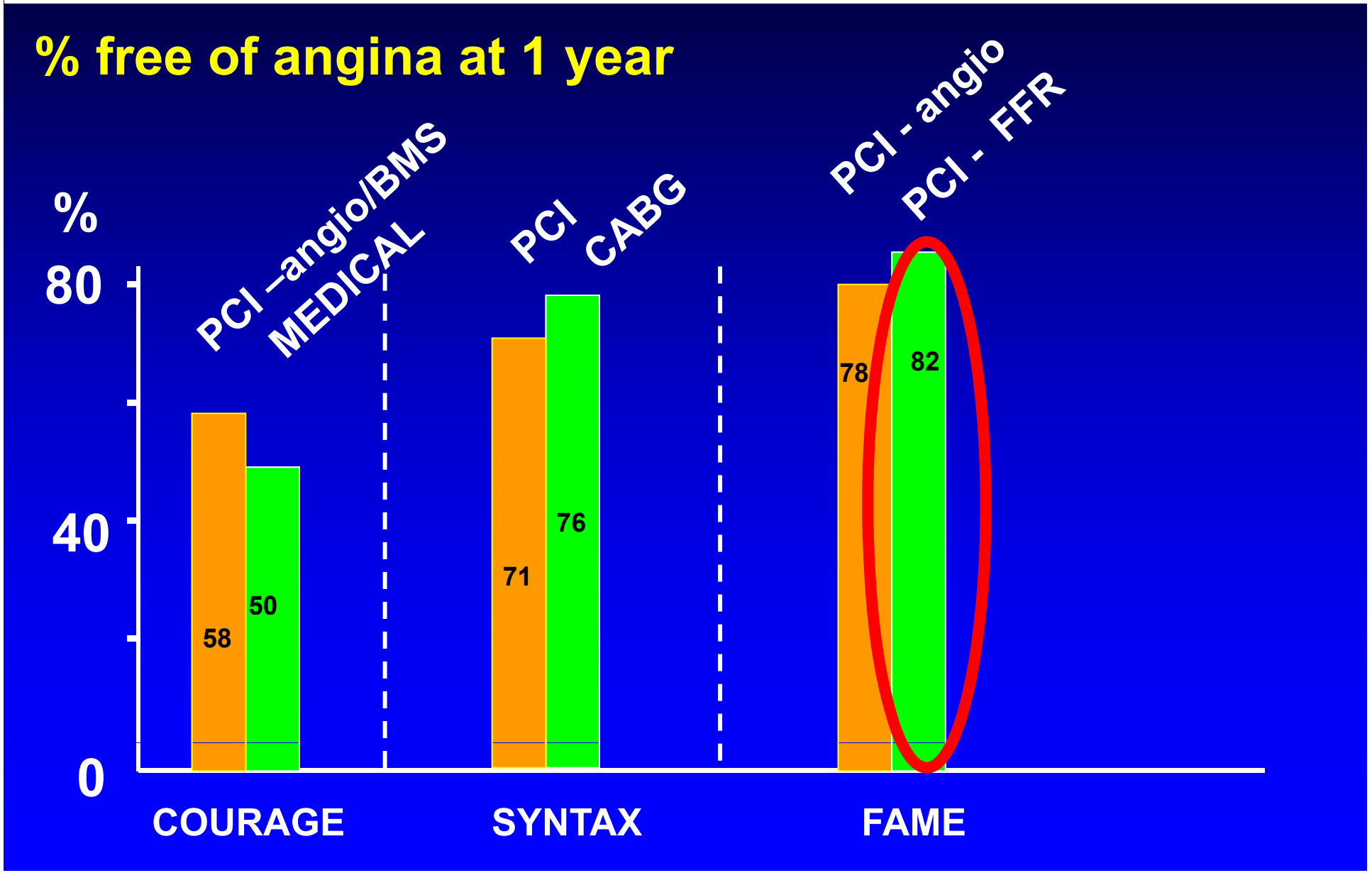

FUNCTIONALLY *SIGNIFICANT* STENOSIS

→ **stenting a *functionally significant* stenosis is justified , when technically feasible**

DEFER, COURAGE, SYNTAX, FAME

FFR and Clinical Outcome:
Evidence from randomised controlled trials

- Is it safe to defer PCI if FFR is negative ?
- Is it indicated to perform PCI if FFR is positive ?
- ***Does systematic use of FFR improve outcome of PCI ? (decrease of Myocardial Infarction & death)***

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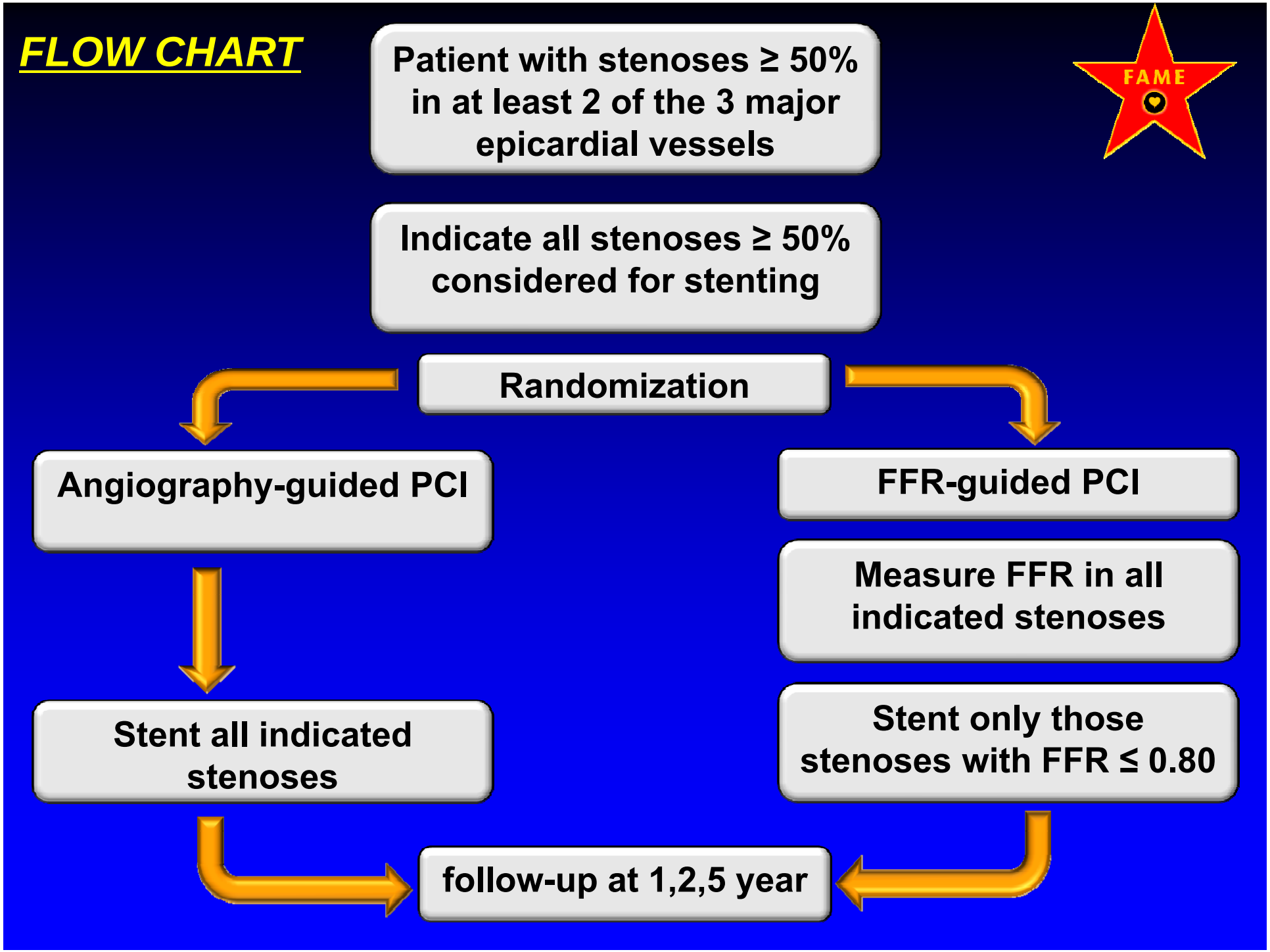
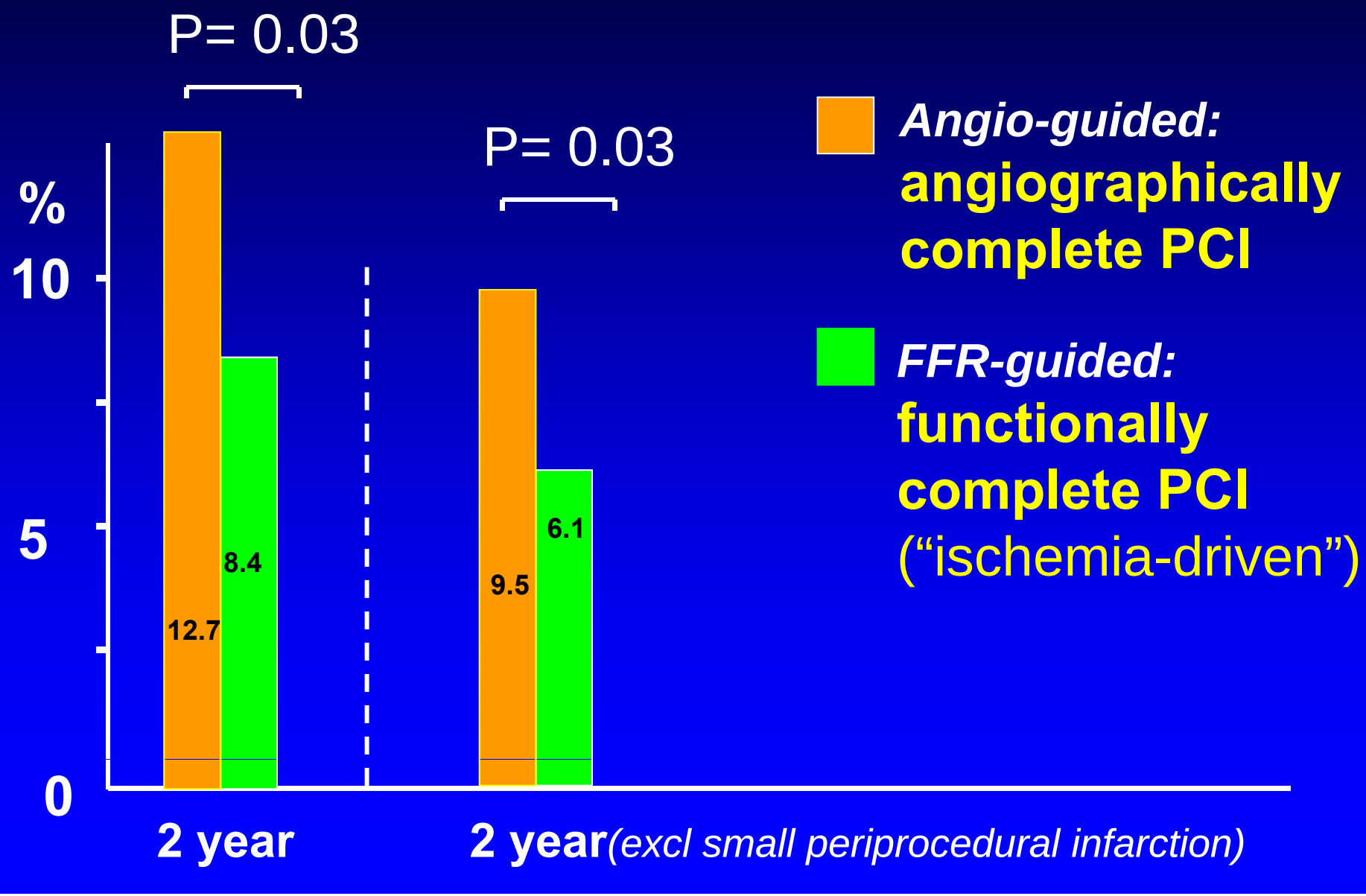
→ **FAME studies**

FAME: FFR-guided PCI in MVD is Superior to Standard Angiography-guided PCI

Tonino et al, NEJM 2009; Pijls et al, JACC 2010


FLOW CHART
Patient with stenoses ≥ 50% in at least 2 of the 3 major epicardial vessels
FAME
Indicate all stenoses ≥ 50% considered for 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 at 1,2,5 year

DEATH & MI in the FAME study after 2 years



FFR –guided PCI:

- improves outcome
- improves quality of live
- is cost-saving
- reduces radiation and contrast exposure
- does not prolong time of procedure

Tonino et al, NEJM 2009; Pijls et al, JACC 2010

FAME-2: FFR-guided PCI in Coronary Artery Disease is Superior to Optimum Medical Therapy

Multivessel PCI vs Medical Treatment:

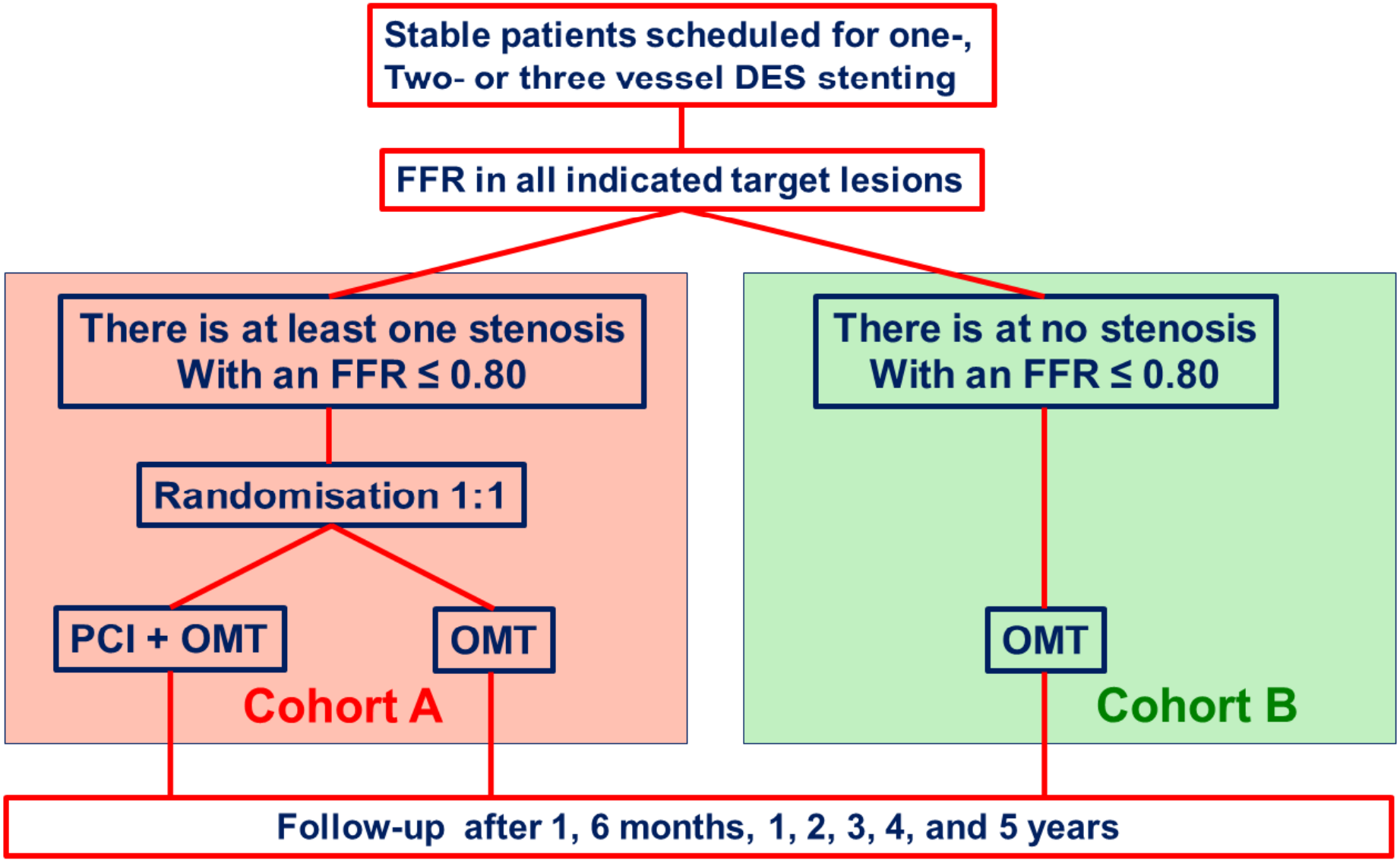
COURAGE study:

Negative bias for PCI in COURAGE trial:

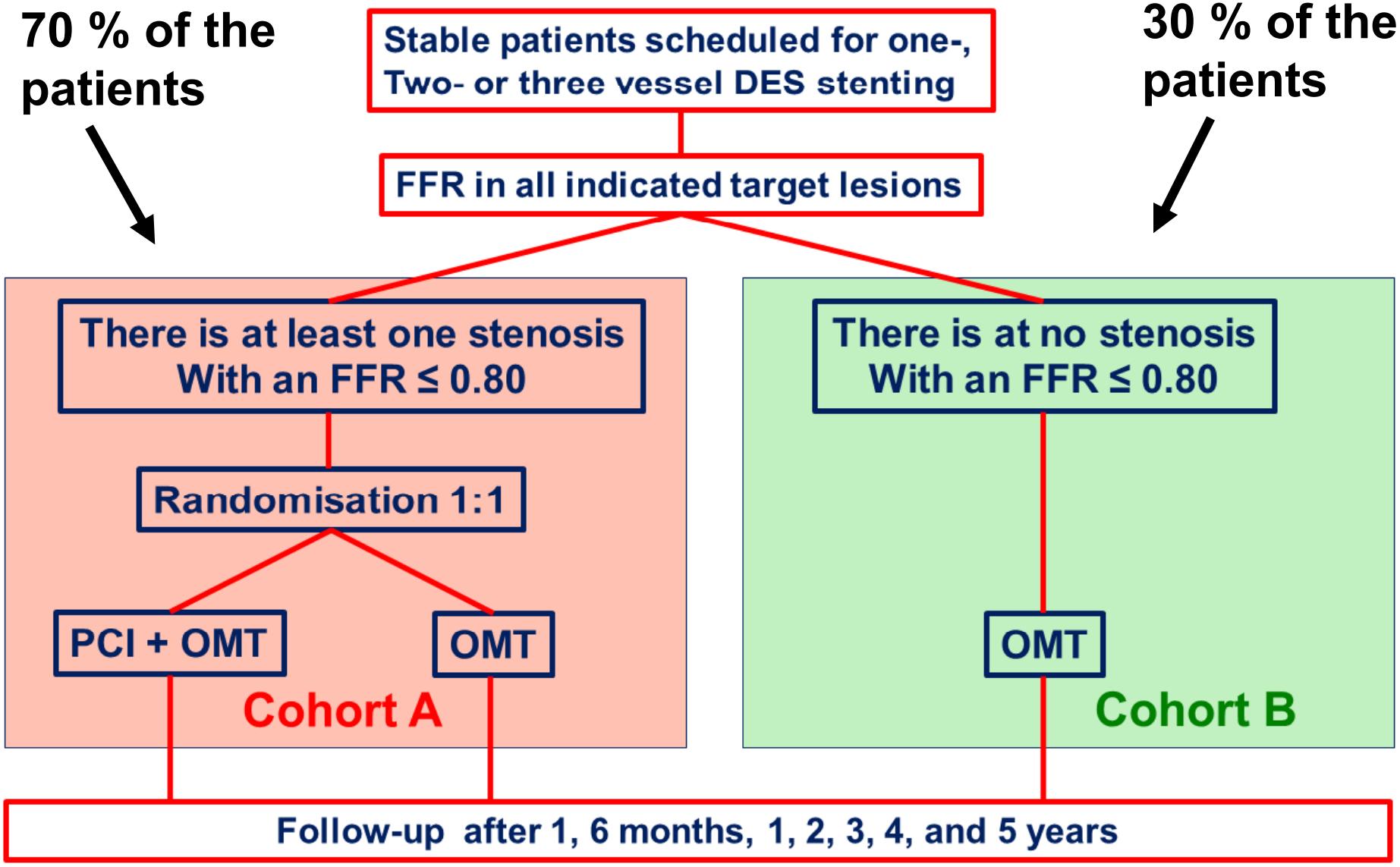
1. PCI was angio-guided, not FFR-guided
2. A number of ischemic lesions were not treated, because they were angiographically mild
3. And a number of non-ischemic lesion were unnecessarily treatred because they looked angiographically more severe

→ **FAME – 2 Study**

FAME 2 Trial Flow Chart



FAME 2 Trial Flow Chart



FAME 2 Trial Primary End-Points

The primary end-point of the FAME 2 trial is the 24-month major adverse cardiac event rate defined as:

- All cause death
- Myocardial infarction
- Unplanned hospitalisation leading to urgent revascularisation

as adjudicated by the Clinical Event Committee (CEC)

On recommendation of the independent Data and Safety Monitoring Board enrollment was halted on January 15, 2012 due to a significantly increased patient risk of major adverse cardiac events (MACE) among patients randomized to OMT alone compared to patients randomized to OMT plus FFR-guided PCI

Timeline of results of FAME-2:

- *PCR may 2012 Paris: preliminary results of cohort A*
- *ESC aug 2012 Munich: late-breaking trial*
- *publication of the study : september 2012*
- *TCT oct 2012 Miami: large perspective of study*

In summary:

EVIDENCE FROM RANDOMIZED TRIALS:

FFR guidance of PCI facilitates decision making whether to stent or not to stent and where to stent

FFR-guided PCI is superior to guidance by angiography alone ***AND*** superior to optimal medical treatment,
both with respect to improving symptoms but also with respect to decreasing myocardial infarction rate and death

Use of FFR makes PCI to a better treatment modality of CAD and will further expand the patient populations in whom PCI is a benificial treatment

GUIDELINES ESC SEPTEMBER 2010

FFR UPGRADED TO LEVEL I A INDICATION

10 – Procedural aspects of PCI

Table 28: Specific PCI devices and pharmacotherapy

	Class	Level
FFR-guided PCI is recommended for detection of ischemia-related lesion(s) when objective evidence of vessel-related ischamia is not available	I	A
DES* are recommended for reduction of restenosis/reocclusion, if no contraindication to extended DAPT	I	A
Distal embolic protection is recommended during PCI of SVG disease to avoid distal embolisation of debris and prevent MI	I	B
Rotablation is recommended for preparation of heavily calcified or severely fibrotic lesions that cannot be crossed by a balloon or adequately dilated before planned stenting	I	C

ESC-EACTS Guidlines for Myocardial Revascularisation, August 30, 2010