

CLINICAL CONSEQUENCES OF THE FAME STUDY

TCT ASIA

Seoul, Korea, april 26 th, 2012



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GUIDELINES ESC SEPTEMBER 2010

FFR UPGRADED TO LEVEL I A INDICATION

10 – Procedural aspects of PCI

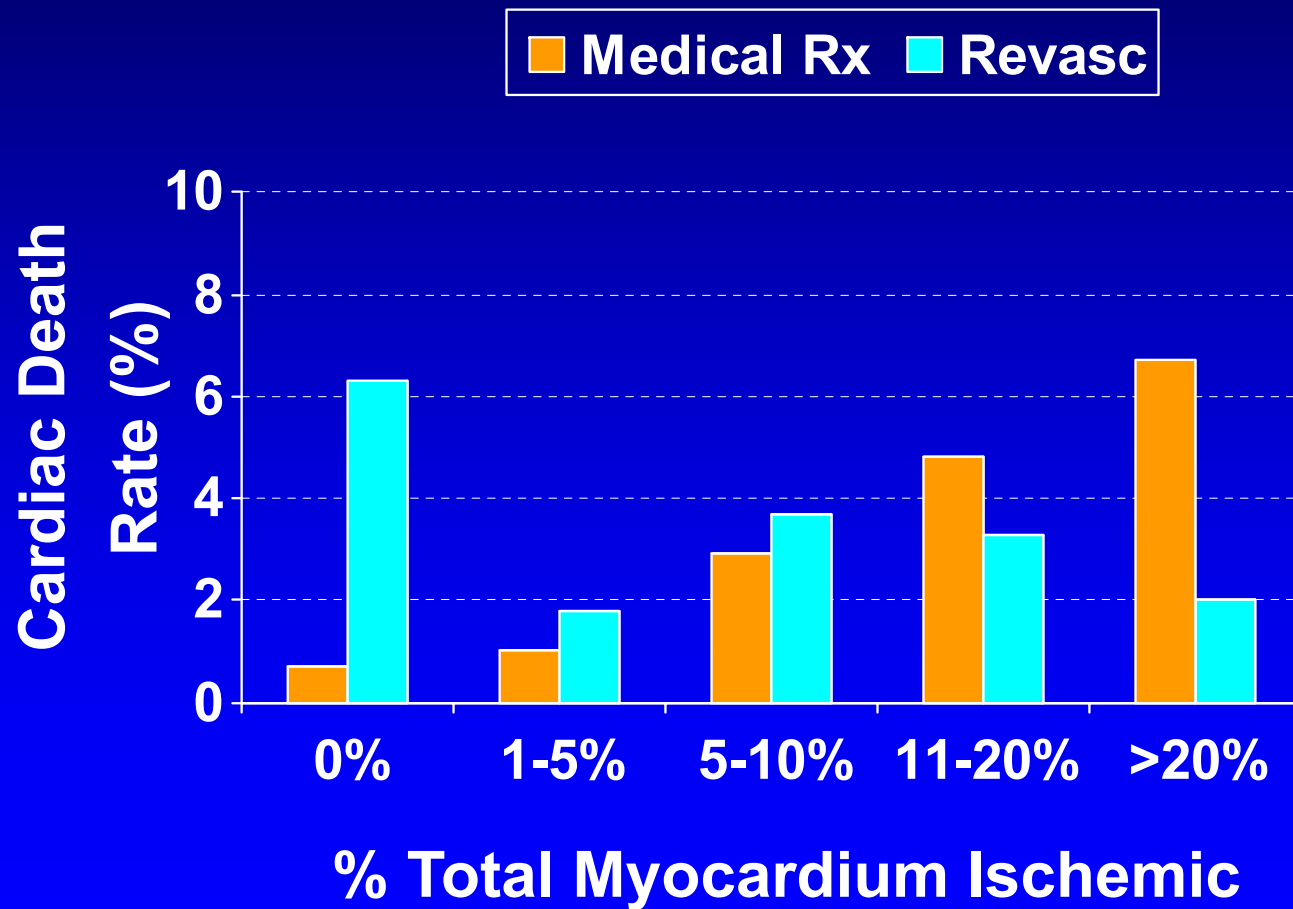
Table 28: Specific PCI devices and pharmacotherapy

| | Class | Level |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------|----------|
| FFR-guided PCI is recommended for detection of ischemia-related lesion(s) when objective evidence of vessel-related ischemia 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 |

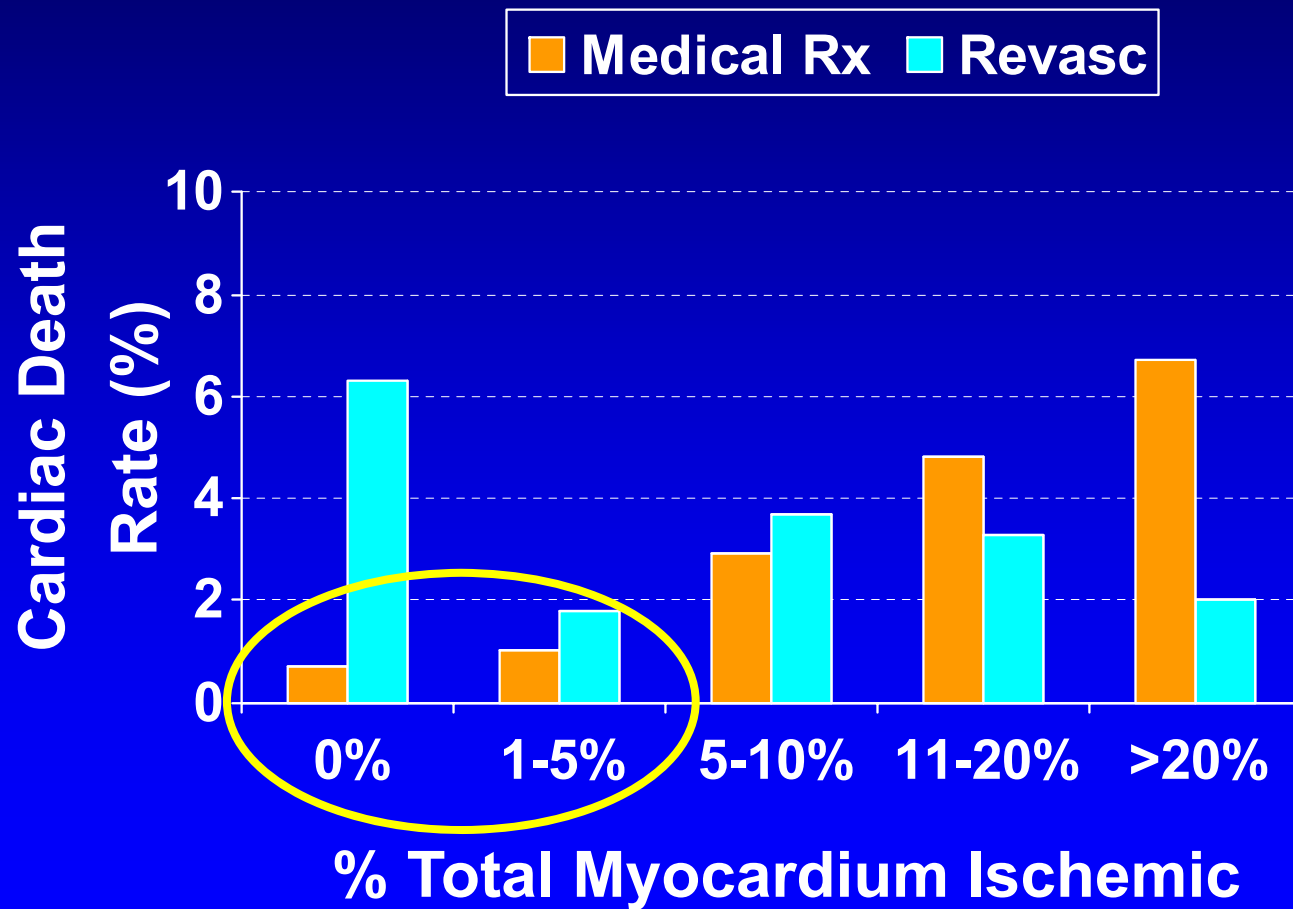
***Risk to die or experience myocardial infarction
in the next 5 years related to a coronary stenosis:***

- **non-ischemic stenosis: < 1% per year ***
(NUCLEAR studies, DEFER, FAME, PROSPECT, CCTA)
- **ischemic stenosis, if left untreated: 5-10% per year**
(Many historical registries, ACIP, etc)
- **stented stenosis: 2-3% per year**
*(e.g DEFER, FAME, SYNTAX, many large studies
and registries)*

Hachamovitch et al.

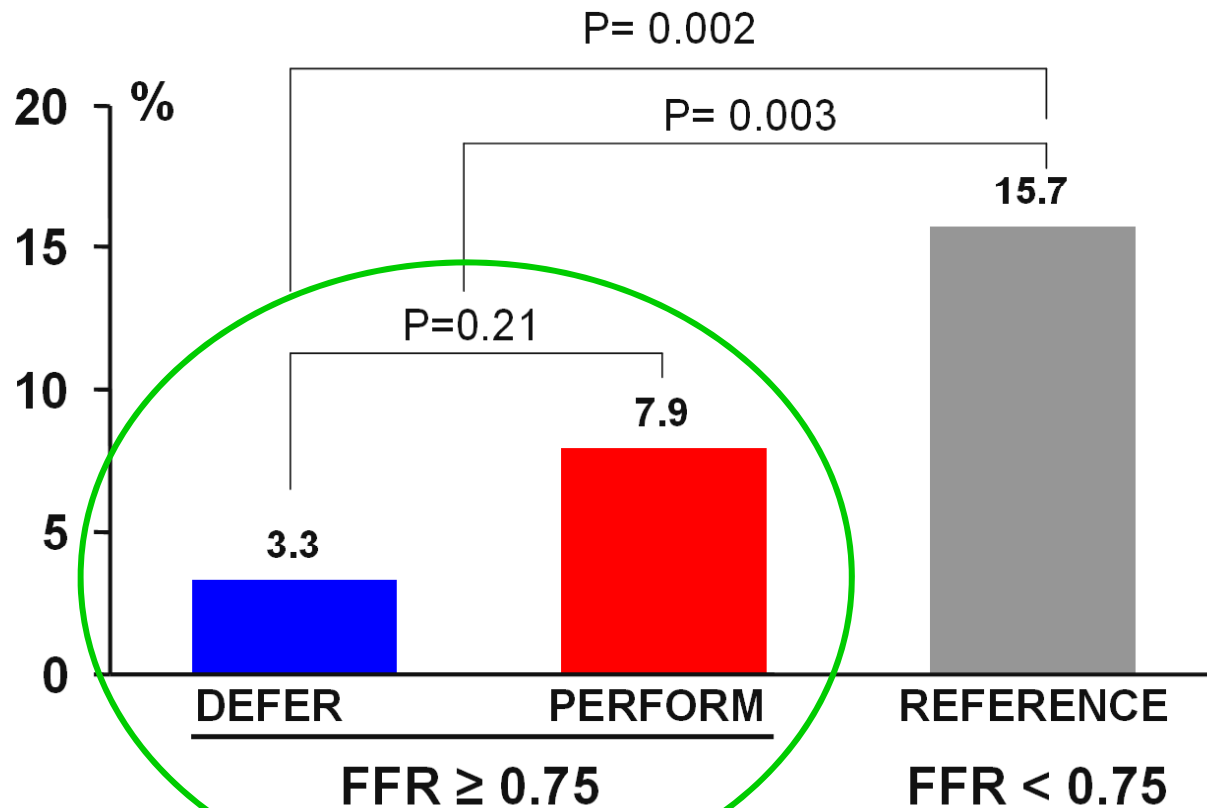


Hachamovitch et al.



Cardiac Death And Acute MI After 5 Years

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





What is the Fate of Mild Stenoses ?

Prospect Study Results at 3 Years

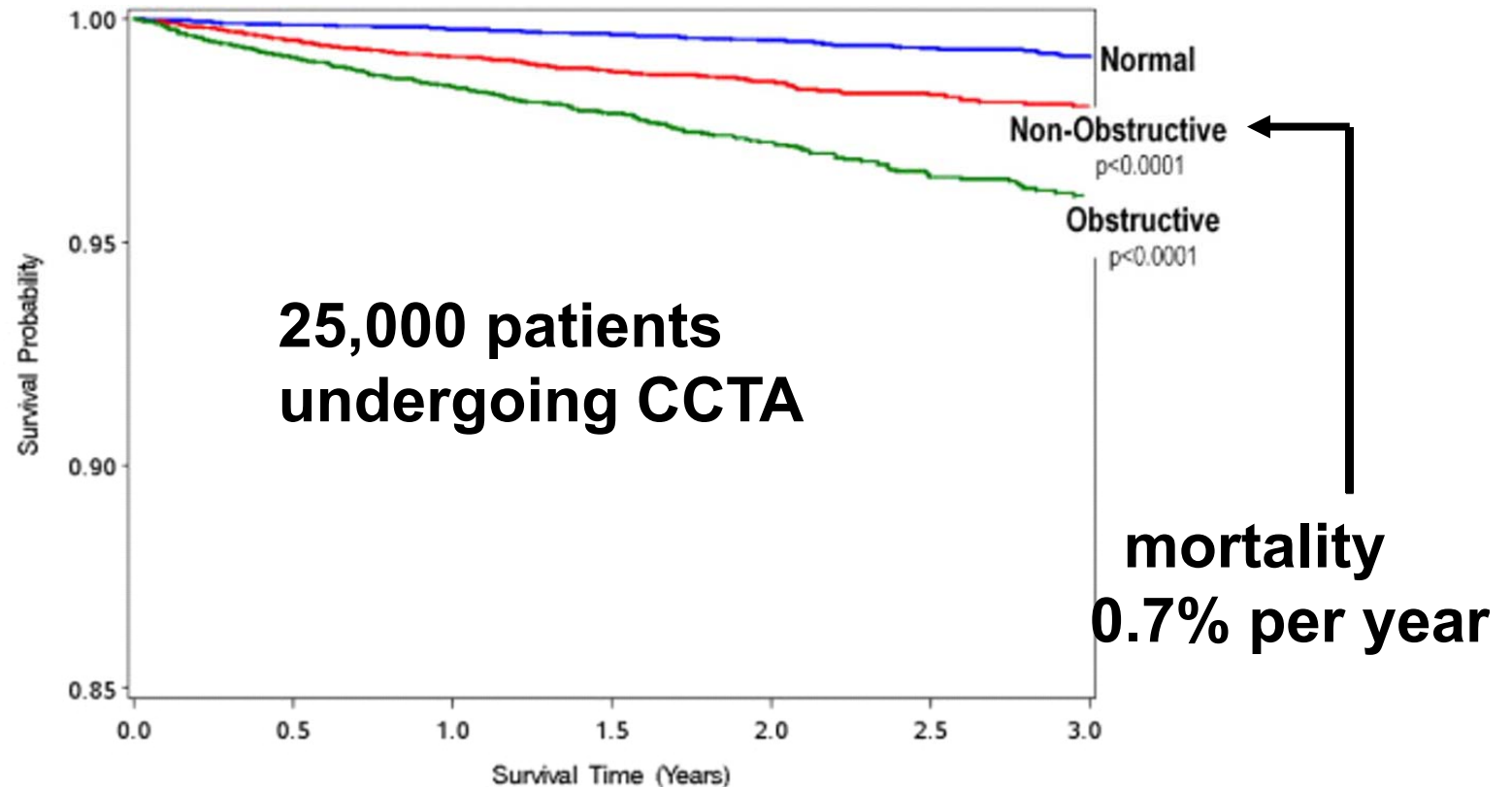
700 pts with ACS

(1812 angiographically visible but untreated lesions)

| | All | Culprit lesion related | Non culprit lesion related | Indeterminate |
|----------------------|-----------|------------------------|----------------------------|---------------|
| Cardiac death | 1.9% (12) | 0.2% (1) | 0% (0) | 1.8% (11) |
| Cardiac arrest | 0.5% (3) | 0.3% (2) | 0% (0) | 0.2% (1) |
| MI (STEMI or NSTEMI) | 3.3% (21) | 2.0% (13) | 1.0% (6) | 0.3% (2) |

www.cardio-vasc.be

Unadjusted All-Cause 3-Year Kaplan-Meier Survival by the Maximal Per-Patient Presence of None, Nonobstructive, and Obstructive CAD



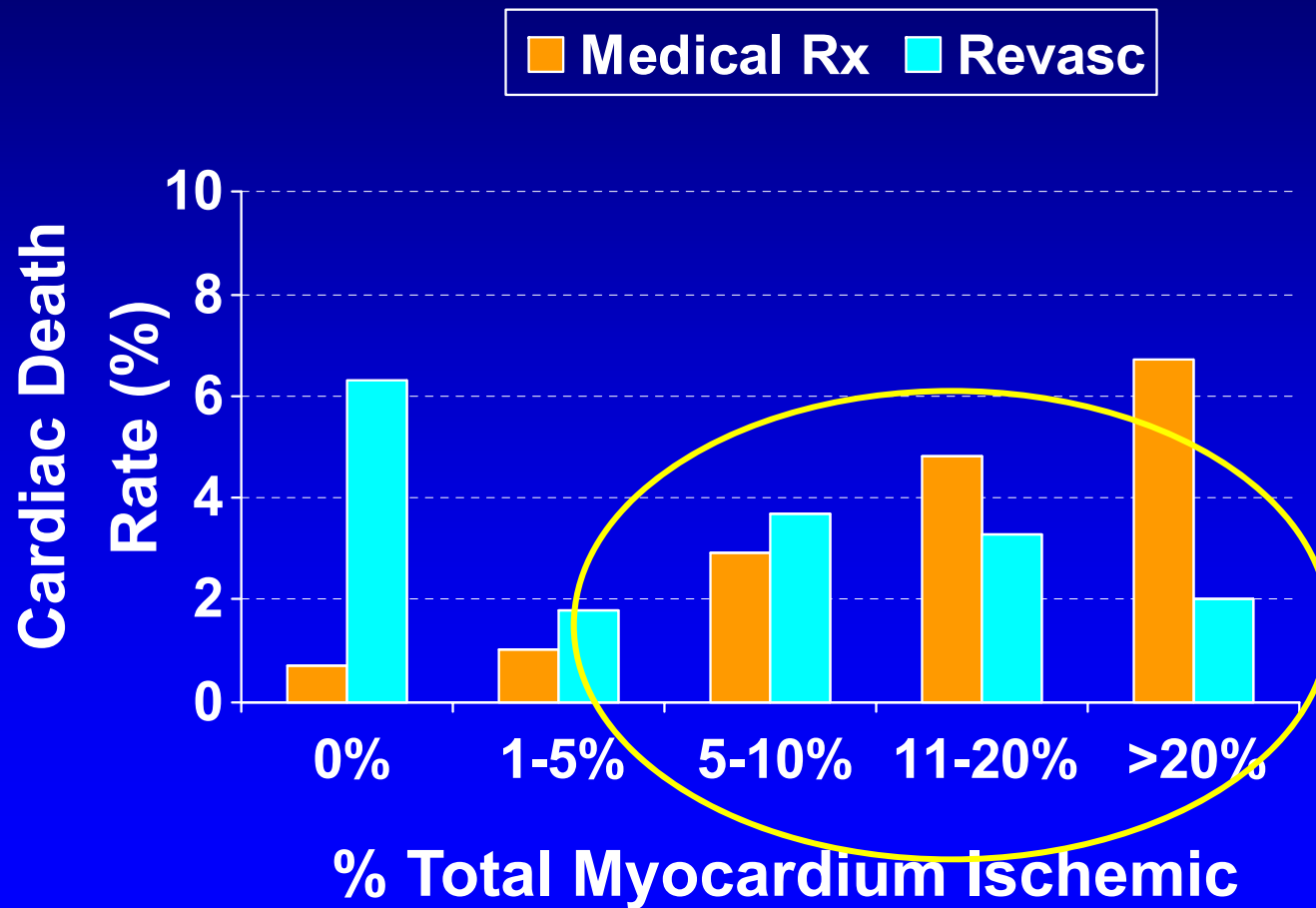
| At Risk | Year 0 | Year 1 | Year 2 | Year 3 |
|-----------------------------|--------|--------|--------|--------|
| Normal | 10146 | 9357 | 5800 | 2907 |
| Non-Obstructive (1-49%) | 8114 | 7437 | 4081 | 1930 |
| Obstructive ($\geq 50\%$) | 5594 | 5135 | 3153 | 1430 |

Min, J. K. et al. J Am Coll Cardiol 2011;58:849-860

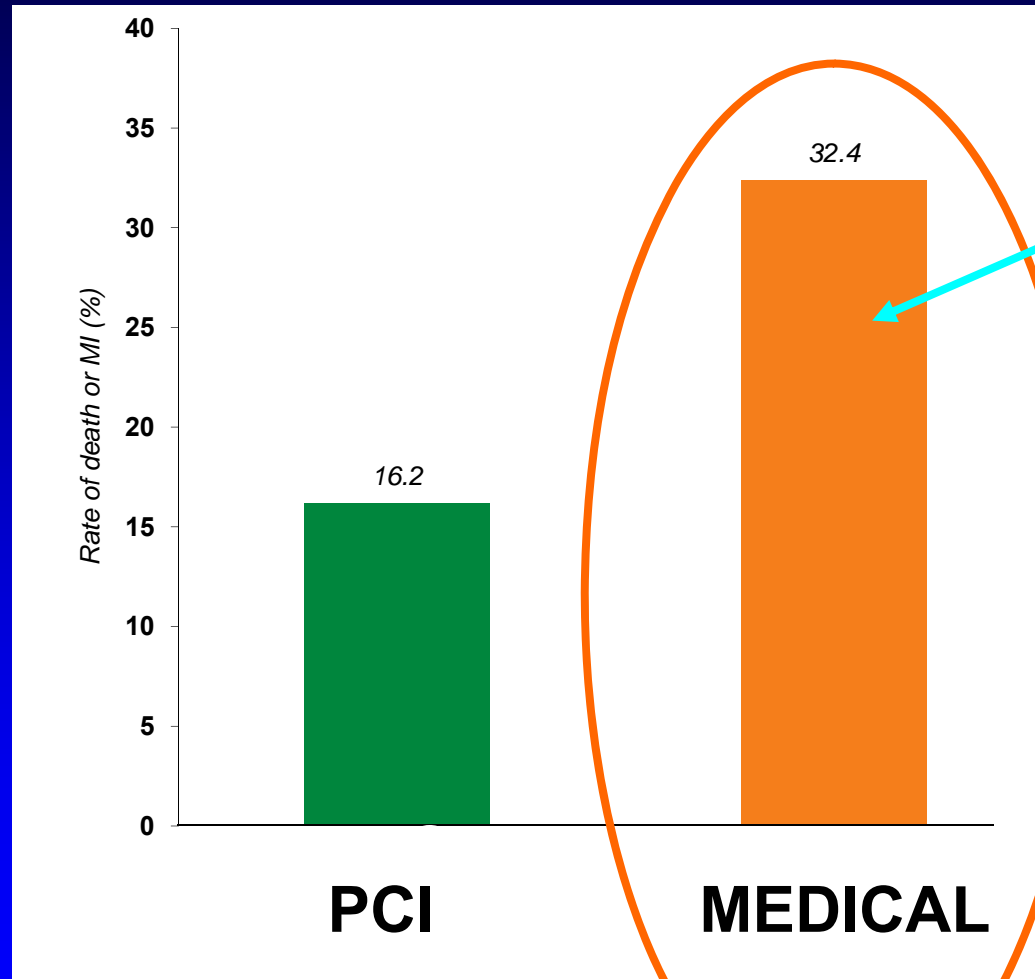
***Risk to die or experience myocardial infarction
in the next 5 years related to a coronary stenosis:***

- **non-ischemic stenosis: < 1% per year ***
(NUCLEAR studies, DEFER, FAME, PROSPECT, CCTA)
 - **No ischemia**
excellent outcome with medical treatment
no need for mechanical revascularization
- **ischemic stenosis, if left untreated, or treated medically: 5-10% per year**
(Many historical registries, ACIP, etc)
- **stented stenosis: 2-3% per year**

Hachamovitch et al.



Death & MI 5 during 5 years of follow-up after PCI vs Medical Treatment in **ISCHEMIC** stenosis

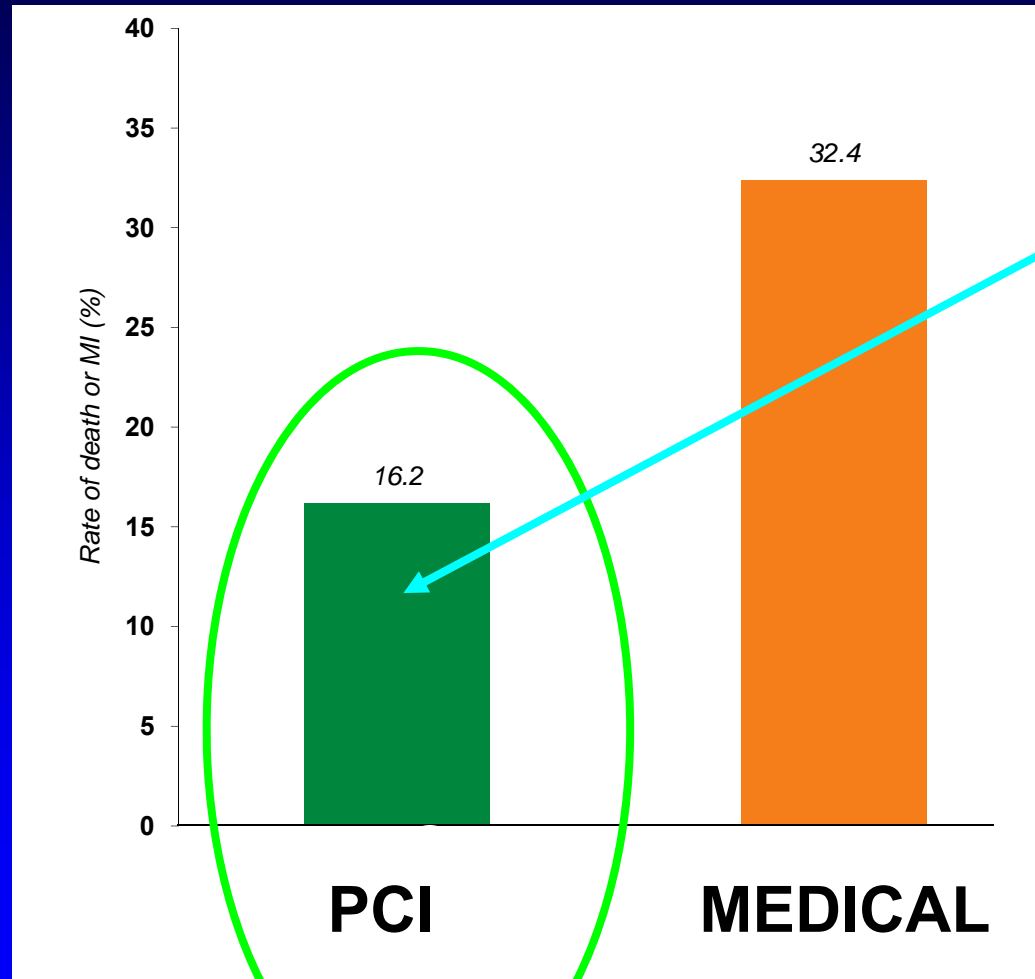


**Death + AMI
6.5 % per year
with OMT**

P=0.001

*Shaw et al,
Circulation 2008*

Death & MI 5 during 5 years of follow-up after PCI vs Medical Treatment in **ISCHEMIC** stenosis



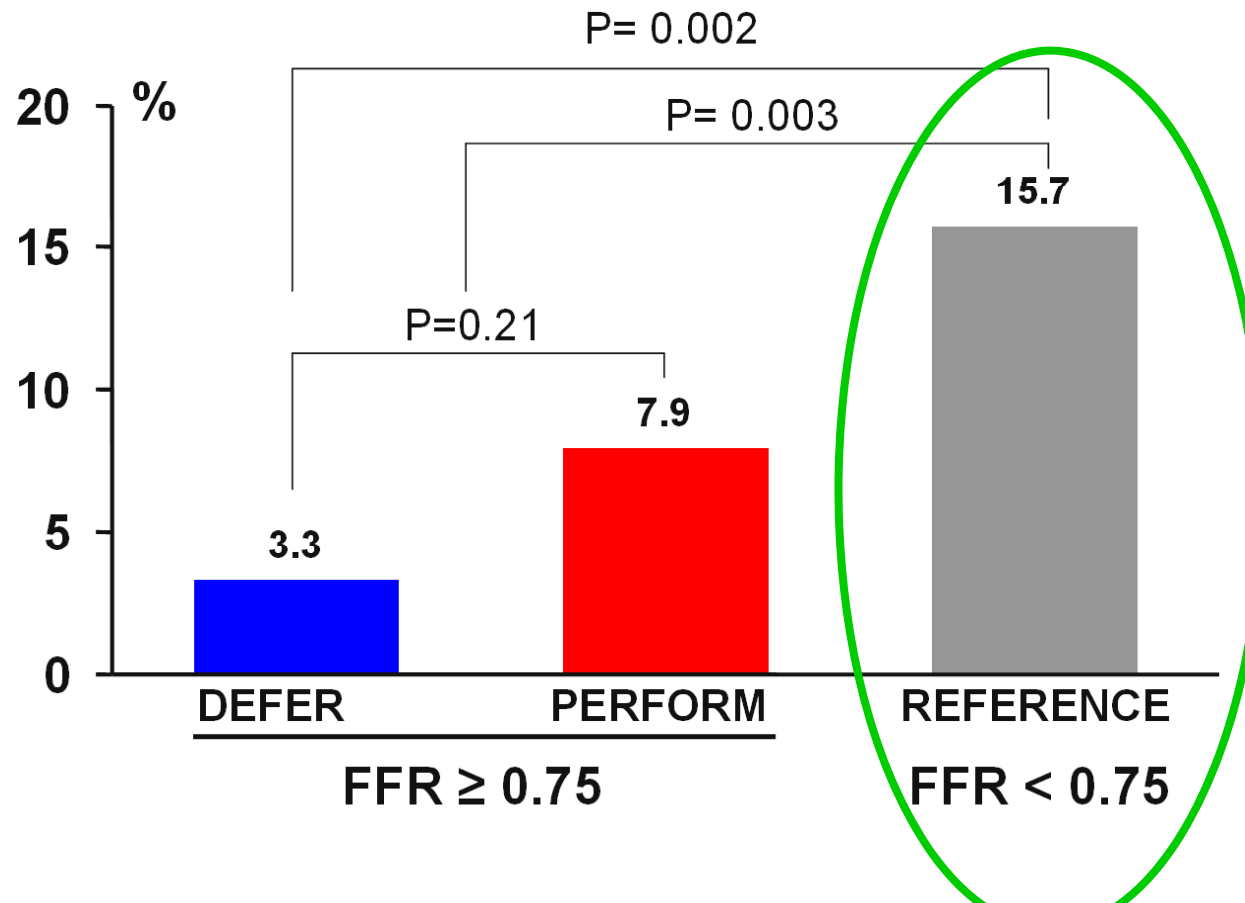
**Death + AMI
3.2 % per year
with stent**

$P=0.001$

*Shaw et al,
Circulation 2008*

Cardiac Death And Acute MI After 5 Years

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



***Risk to die or experience myocardial infarction
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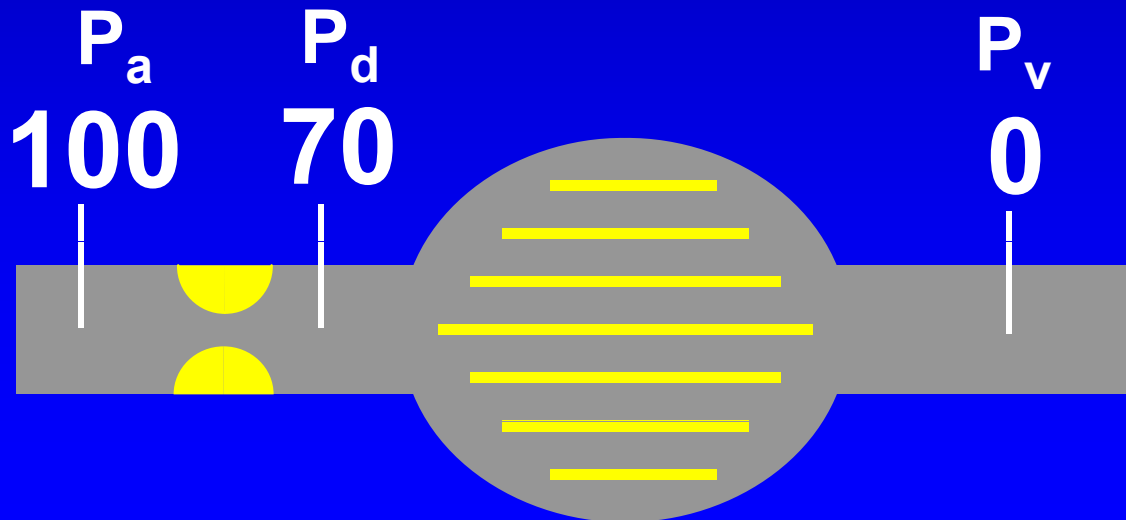
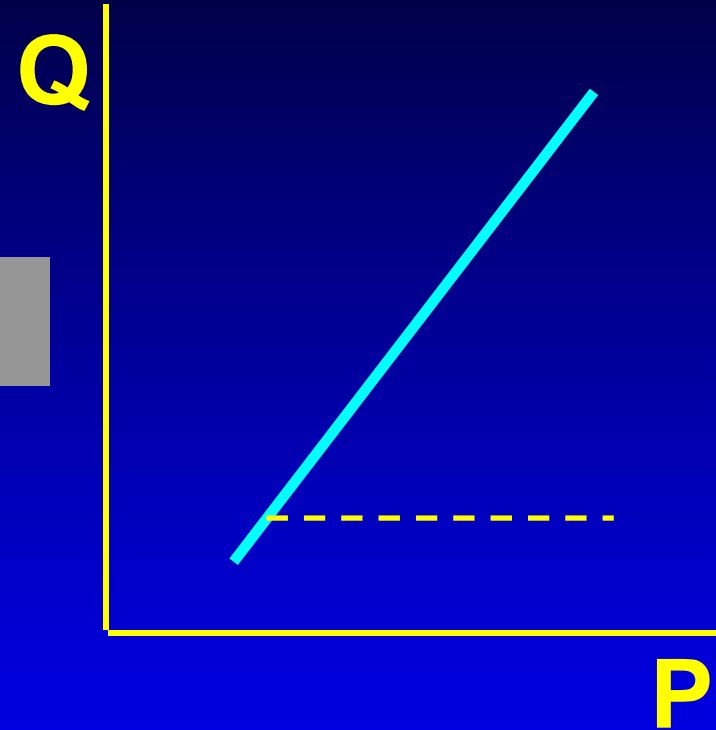
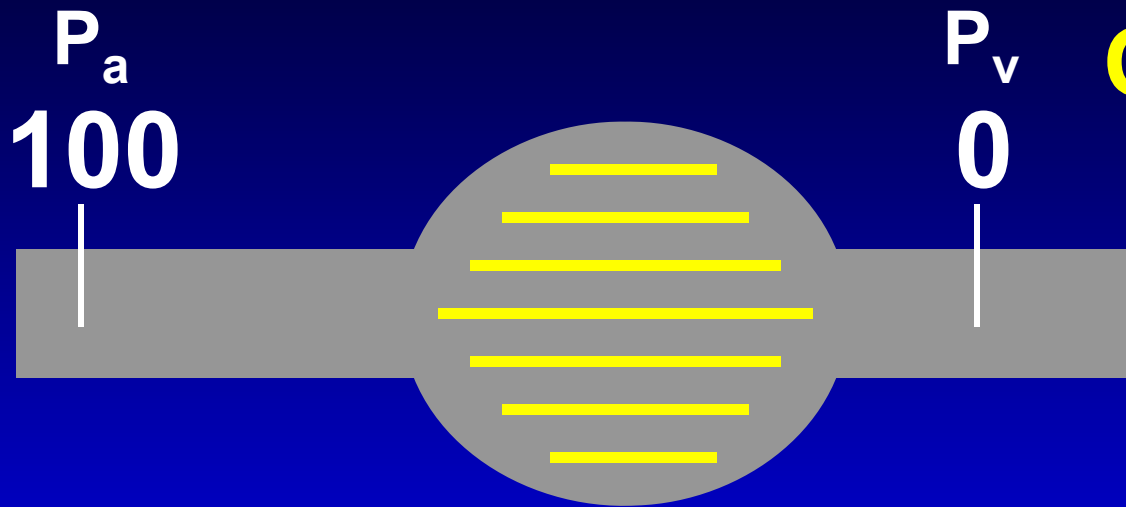
So, at this point it will be clear that *functionally significant (= ischemic) lesions should be revascularized,*

.....whereas it makes no sense to stent non-ischemic lesions

*Therefore, the **key issue** is to establish if a particular stenosis is associated with reversible ischemia....*

→ Fractional Flow Reserve (FFR)

During Maximal Vasodilatation



$$\text{FFR}_{\text{myo}} = \frac{P_d}{P_a} = 0.70$$

FFR is the most accurate method to indicate or exclude reversible ischemia



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%

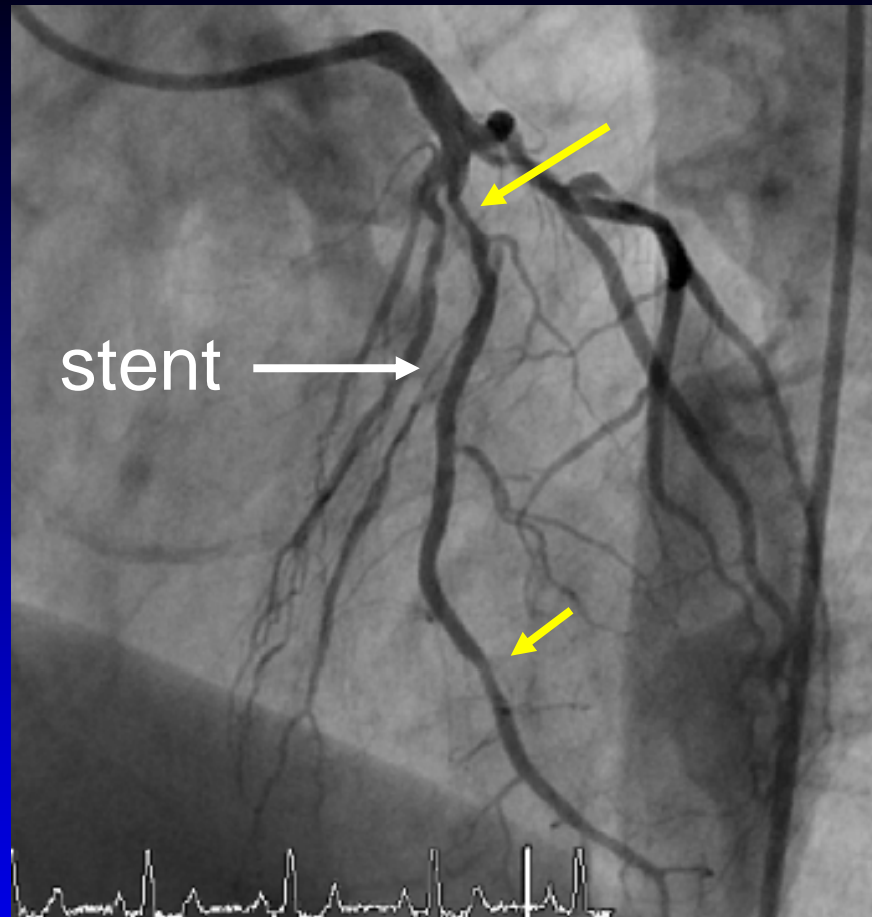
*N Engl J Med 1996; 334:1703-1708
Circulation 2010, many others*



Moreover, FFR has an unequalled spatial resolution to discriminate those spots or segments within a coronary artery which are responsible for ischemia:

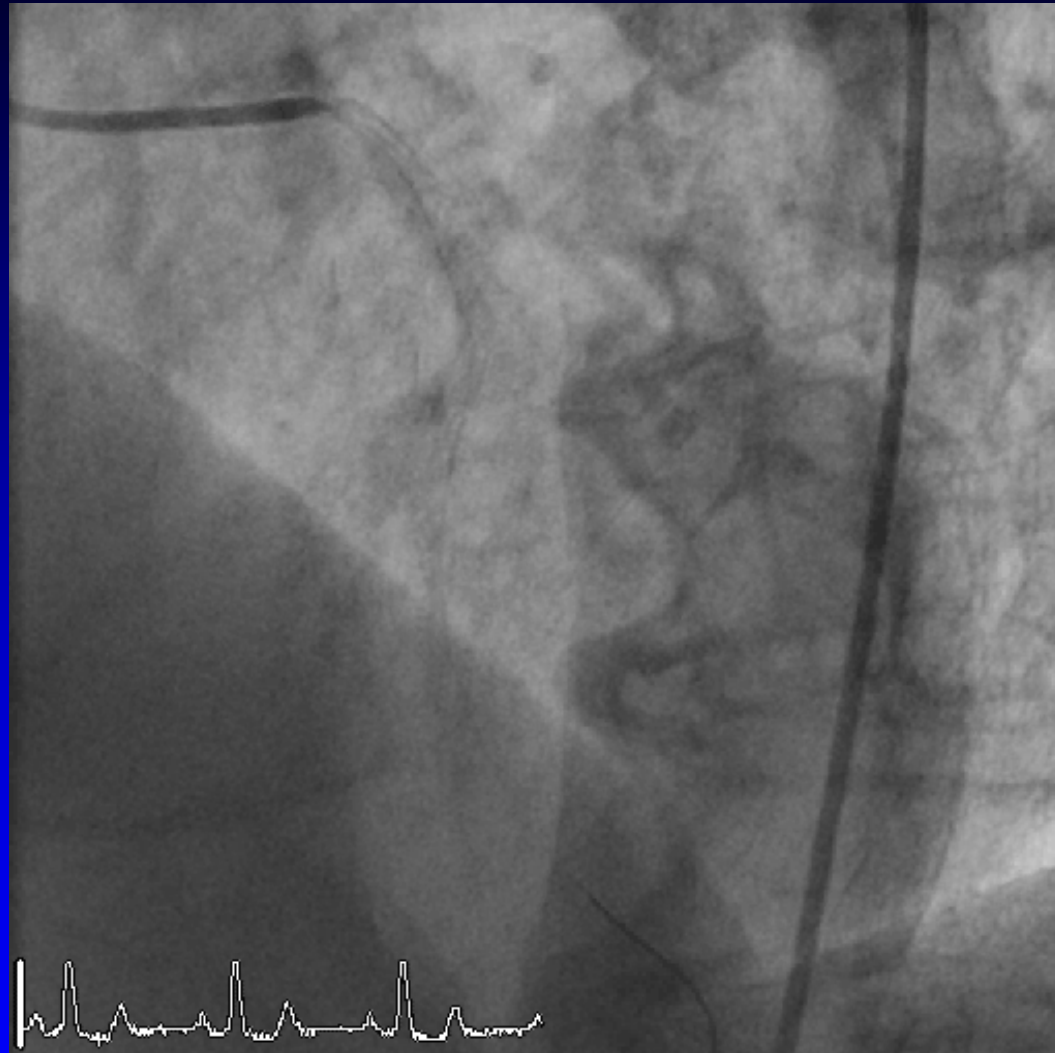
- Exercise testing: ischemia per patient
- MIBI Spect : ischemia per artery
- FFR : ischemia per stenosis/segment

→ Hyperemic pressure pullback recording



Male, born in 1952

Anterior wall MI and stent mid-LAD 1 month earlier
additional 70% stenosis prox LAD



PressureWire in LAD



FFR LAD (i.v. adenosine)



FFR LAD, pull-back & advance across prox segment



LAD hyperemic pullback detail

*The wind tunnel to prove the effectiveness
of any method,
is a prospective and randomized trial.....*

→ **FAME study**



FAME study: HYPOTHESIS



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

FLOW CHART



Patient with stenoses $\geq 50\%$
in at least 2 of the 3 major
epicardial vessels

Indicate all stenoses $\geq 50\%$
considered for stenting

Randomization

Angiography-guided PCI

FFR-guided PCI

Stent all indicated
stenoses

Measure FFR in all
indicated stenoses

Stent only those
stenoses with $FFR \leq 0.80$

follow-up at 1,2,5 year

FAME study: Adverse Events at 2 years



| | ANGIO-group N=496 | FFR-group N=509 | P-value |
|-------------------------------------|----------------------|--------------------|---------|
| <i>Individual endpoints, No (%)</i> | | | |
| 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 |
| <i>Composite endpoints, No(%)</i> | | | |
| 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 |

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Outcome of Deferred (non-ischemic) Lesions:



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

2 Years

9

Late Myocardial Infarctions

8

Due to a New Lesion
or Stent Related

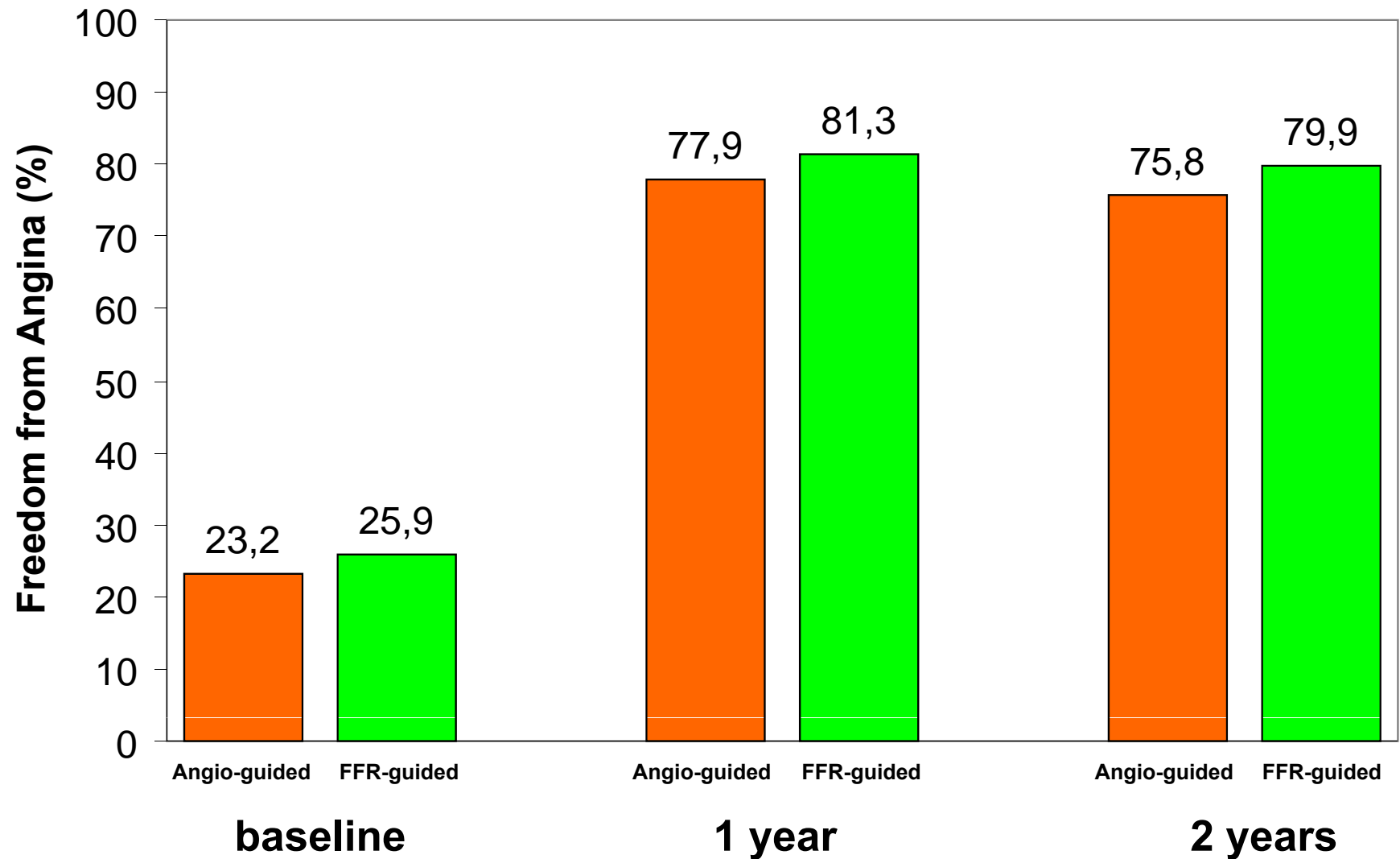
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Myocardial Infarction due to
an Originally Deferred Lesion

*0.2% of deferred
lesions resulted in a late
myocardial infarction*



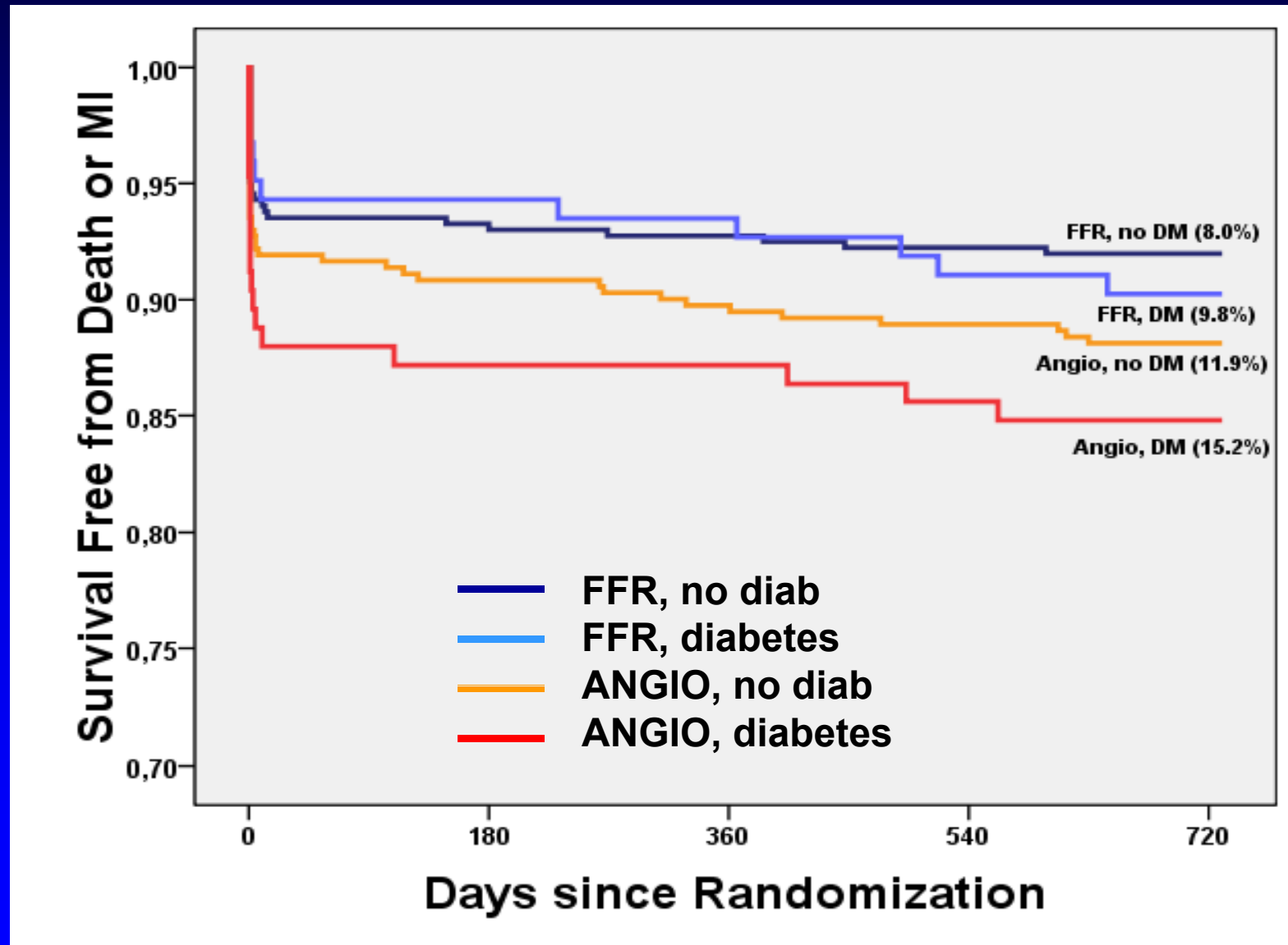
Freedom from Angina in the FAME study



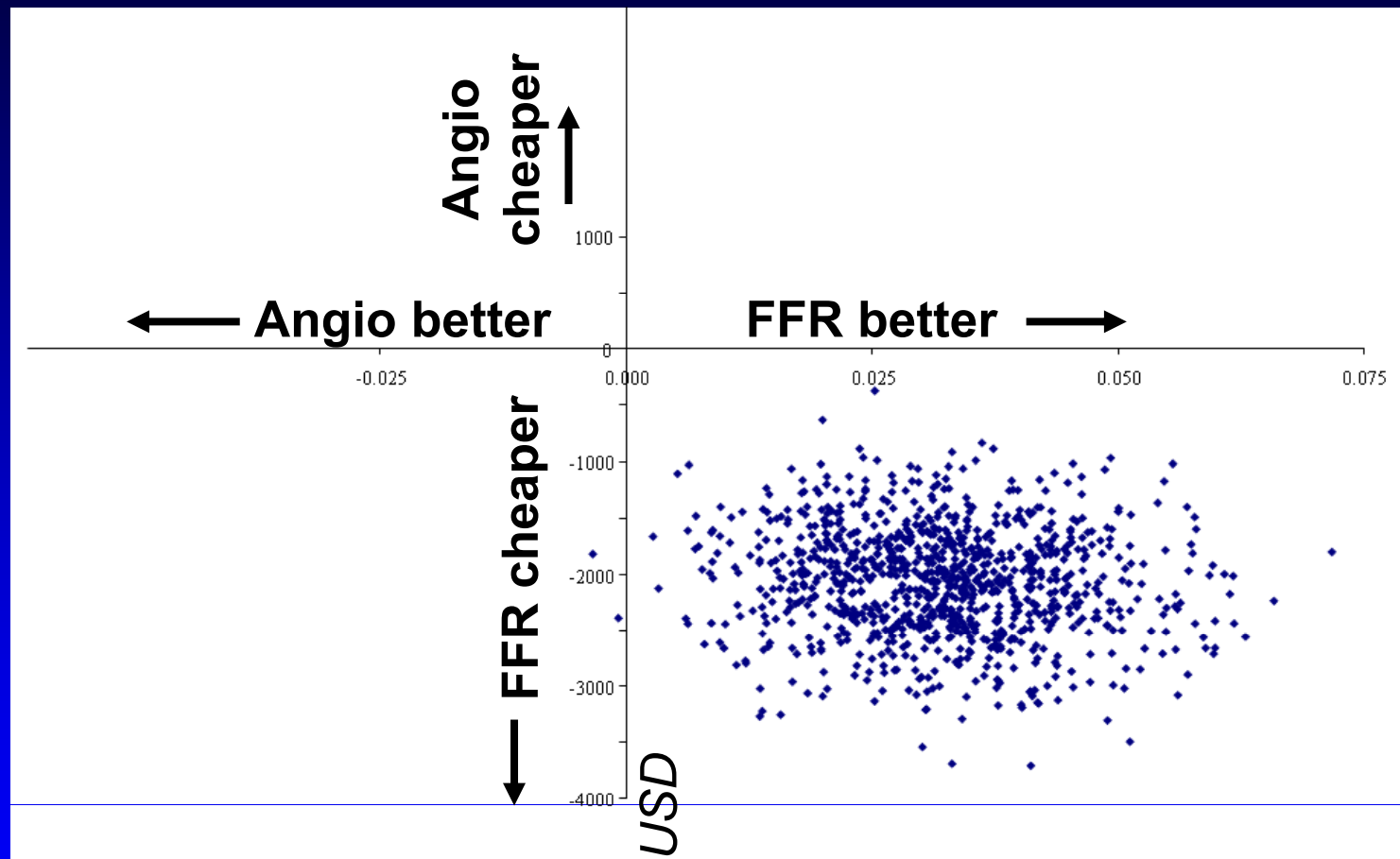
■ Angiography - guided

■ FFR - guided

FAME study: *Diabetes vs Non-Diabetes*



FAME study: Economic Evaluation (1)



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

FFR –guided PCI:



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

→ **New horizons for PCI**

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

TREATMENT OPTIONS FOR MVD



With the use of Fractional Flow Reserve, indications for PCI expand and PCI becomes a better, more effective and cost-saving treatment in a larger proportion of patients with coronary artery disease

