

TCT Asia Pacific 2017

FFR GUIDED PCI IMPROVES OUTCOME

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Potential conflicts of interest

Speaker's name: NICO H J PIJLS

I have the following potential conflicts of interest to report:

- Research contracts : St Jude Medical
- Consulting: St Jude Medical, Opsens
- Employment in industry
- Stockholder of a healthcare company: Philips, GE, ASML, Heartflow
- Owner of a healthcare company
- Other(s):

I do not have any potential conflict of interest



*From a patient's point of view , the wind tunnel
for any index to be used in clinical medicine,
is its **influence on outcome***

FFR and Clinical Outcome:

3 important questions:

- 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 ?

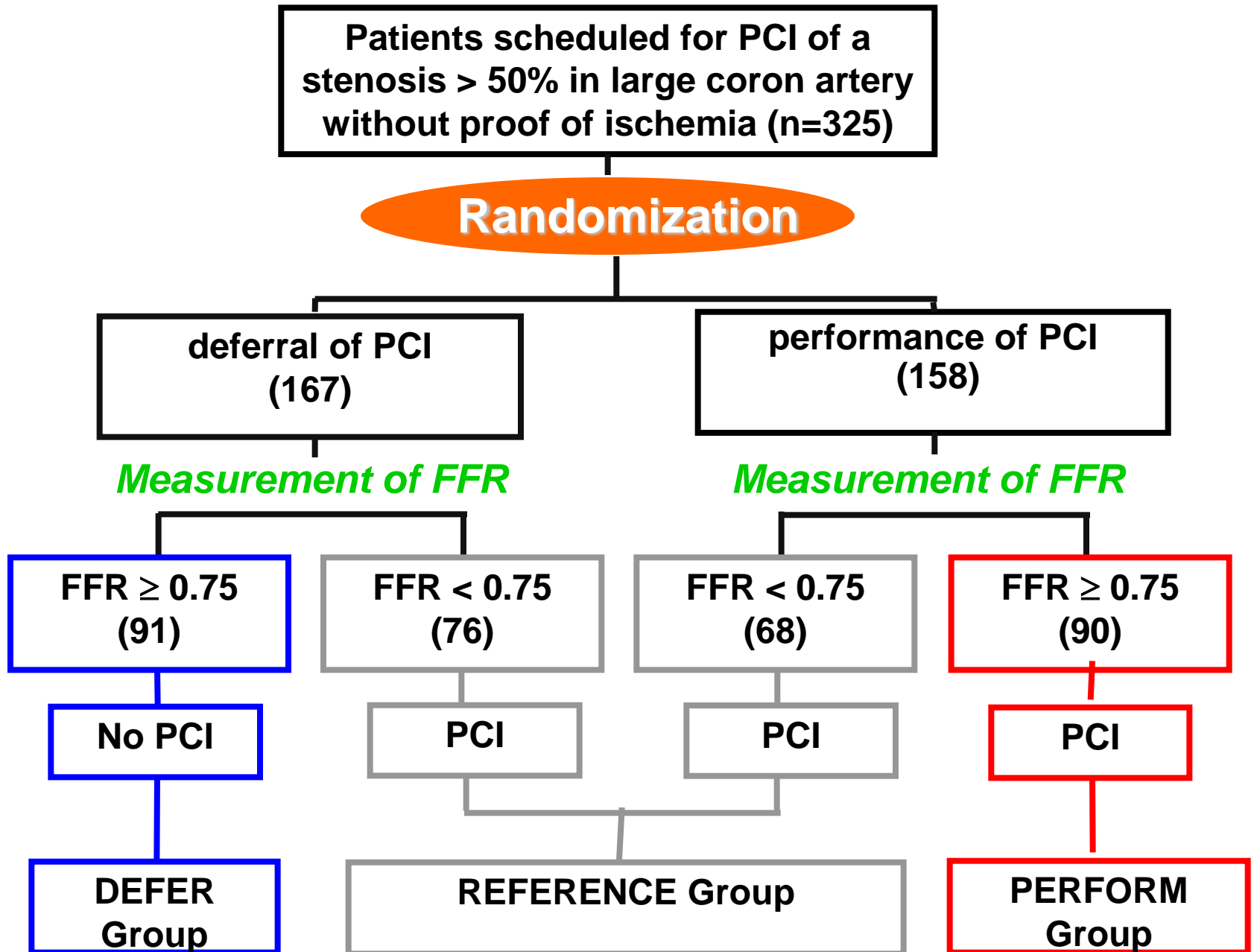
DEFER study

Primary objective

To test safety of deferring PCI of non-ischemic stenosis as indicated by $FFR \geq 0.75$

First randomized controlled trial using FFR with longest follow-up ever (17 years)

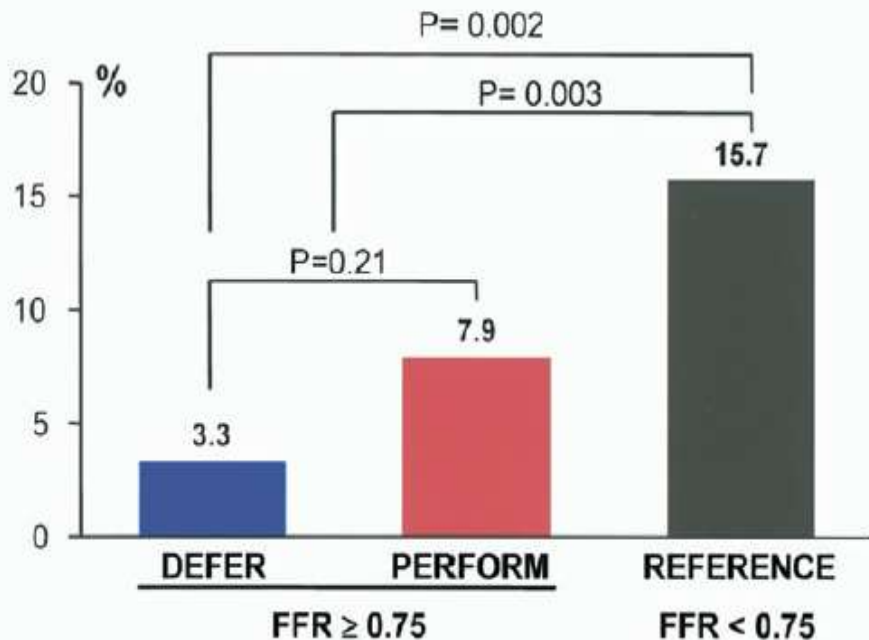
The *DEFER* Study: Flow Chart



5-year follow-up

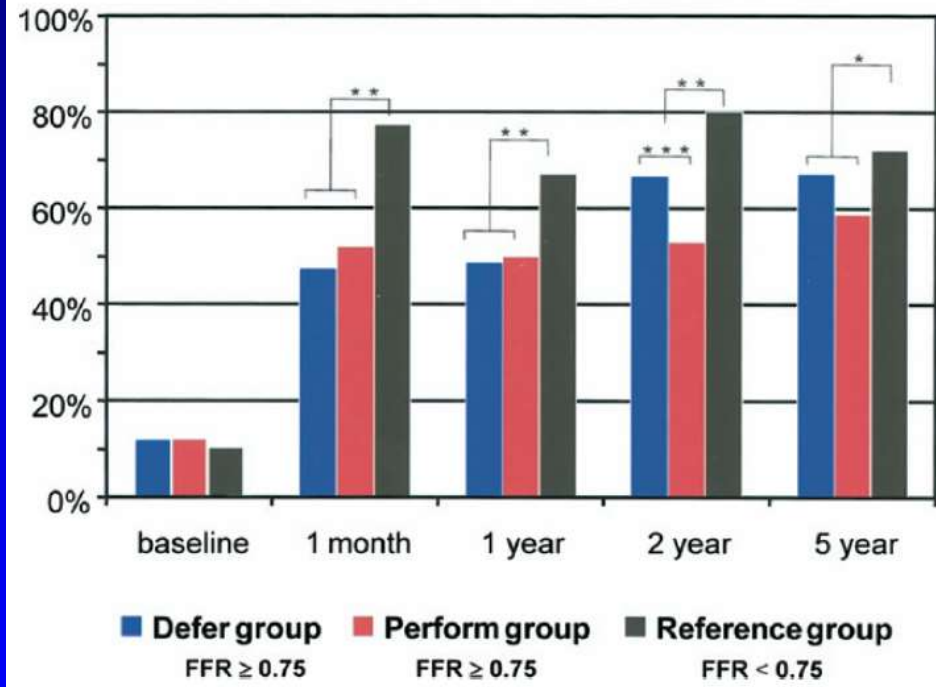
Outcome

Cardiac Death and Acute MI after 5 Years

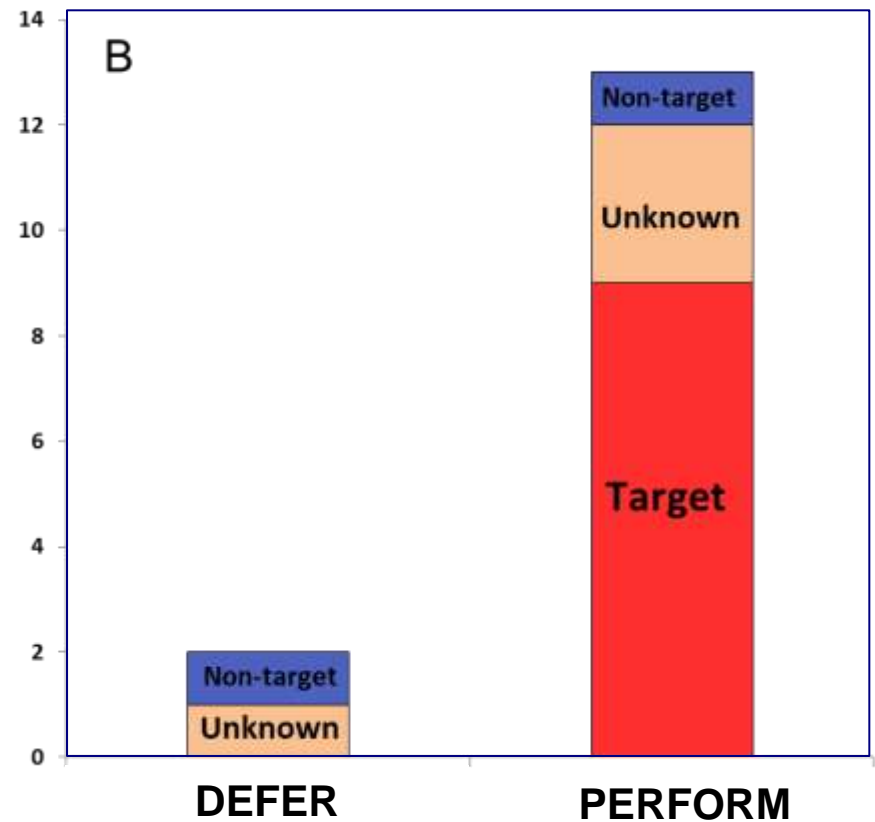
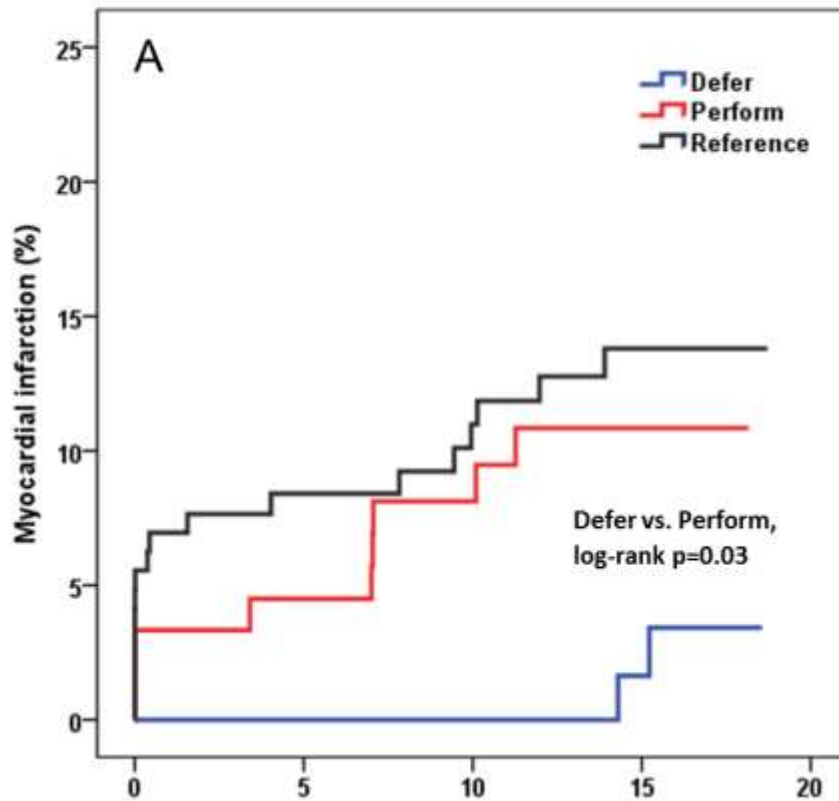


Symptoms

% Patients Free from Chest Pain



Myocardial infarction: 15-year follow up



- **Significant higher infarct rate in perform group ($p < 0.03$)**
- **Most infarctions related to target vessel**

SUMMARY OF DEFER STUDY

Deferral vs Performance of PCI in non-ischemic stenosis
(based upon FFR > 0,75) **gives the following very long term (> 15 years) outcome:**

- **Mortality:**
no difference in mortality
- **(Late) Myocardial Infarction:**
significant advantage in favour of Defer Group
- **Repeated PCI/CABG:**
no differences

Is it safe to defer PCI if FFR is negative ? → YES !!!

Risk for death or MI related to functionally non-significant stenosis:

- **FAME study** : 0.4 % per year (f.u. of 2 years; *NEJM 2009*)
- *FAME -2 study*

Also with other modalities of investigation, outcome of non-significant lesions is excellent:

- **CCTA studies**: 0.7 % per year (*Min, JACC 2011*)
- **Prospect study**: 0.4 % per year (*Stone, NEJM 2011*)

FFR and Clinical Outcome:

3 important questions:

- 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 ?

FAME 2 Flow Chart

Stable CAD patients scheduled for 1, 2 or 3 vessel DES-PCI
N = 1220

FFR in all target lesions

Randomized Trial

Registry

At least 1 stenosis
with $FFR \leq 0.80$ (n=888)

When all $FFR > 0.80$
(n=332)

Randomization 1:1

PCI + MT

MT

MT

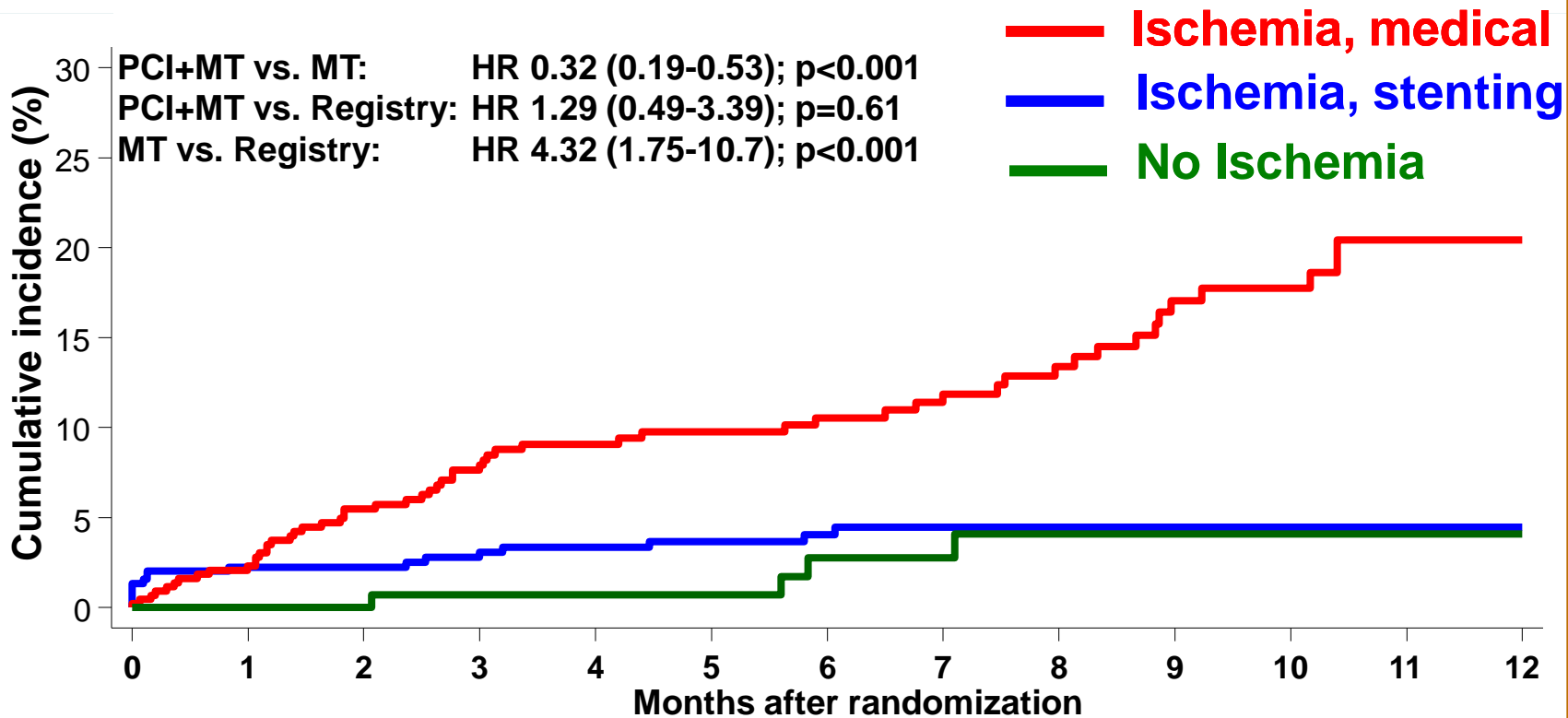
73%

27%

50% randomly
assigned to FU

Follow-up after 1, 6 months, 1, 2, 3, 4, and 5 years

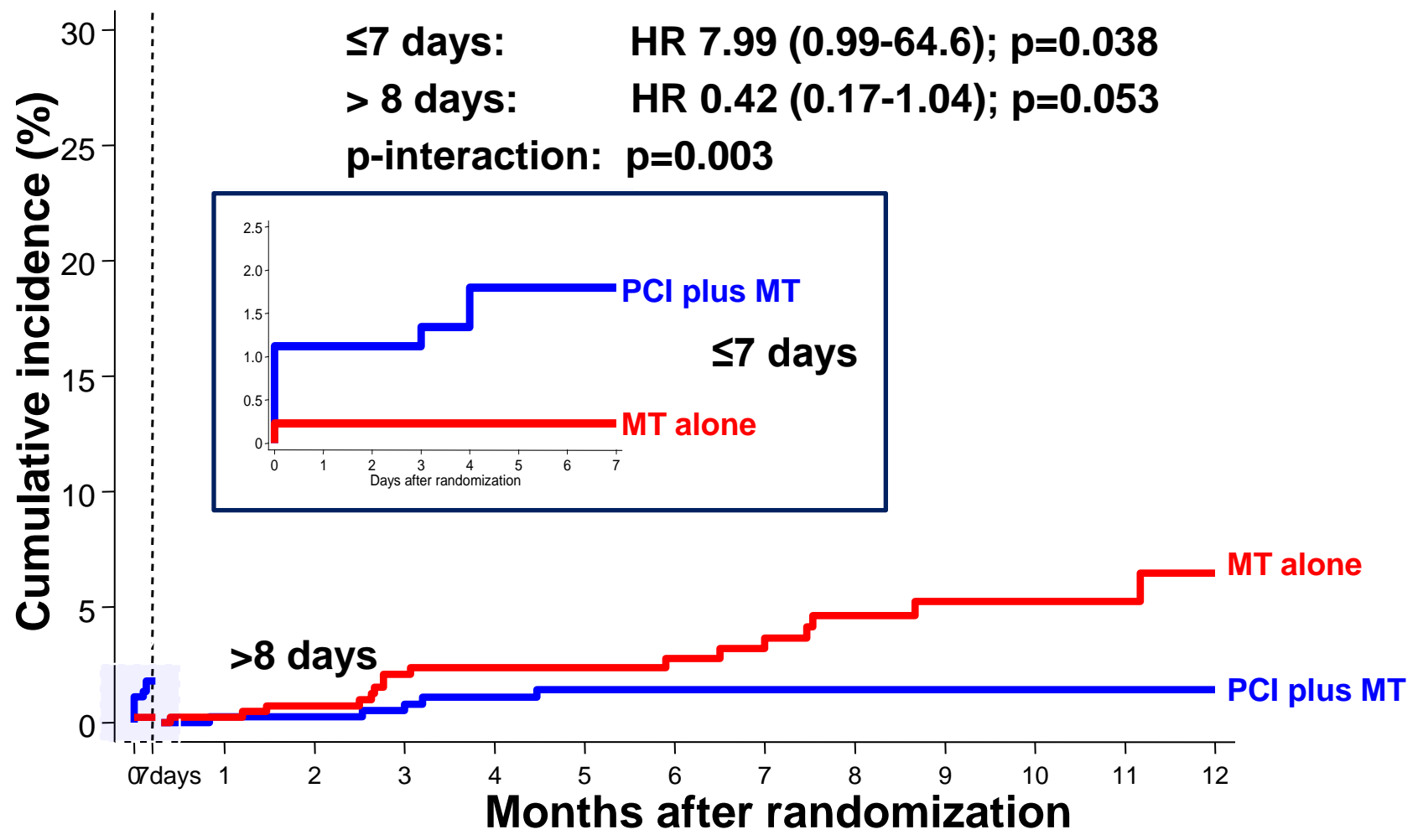
Primary Outcomes (death, AMI, urgent revasc)



No. at risk

MT	441	414	370	322	283	253	220	192	162	127	100	70	37
PCI+MT	447	414	388	351	308	277	243	212	175	155	117	92	53
Registry	166	156	145	133	117	106	93	74	64	52	41	25	13

Kaplan-Meier plots of Landmark Analysis of Death or MI



FFR and Clinical Outcome:

3 important questions:

- 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 ?*

FAME study: HYPOTHESIS



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

**FAME 1 study; N= 1006
5 - year follow up presented today
and published in Lancet today
(van Nunen L, Zimmermann F, Tonino P, et al)**



FLOW CHART

(N = 1006)

**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

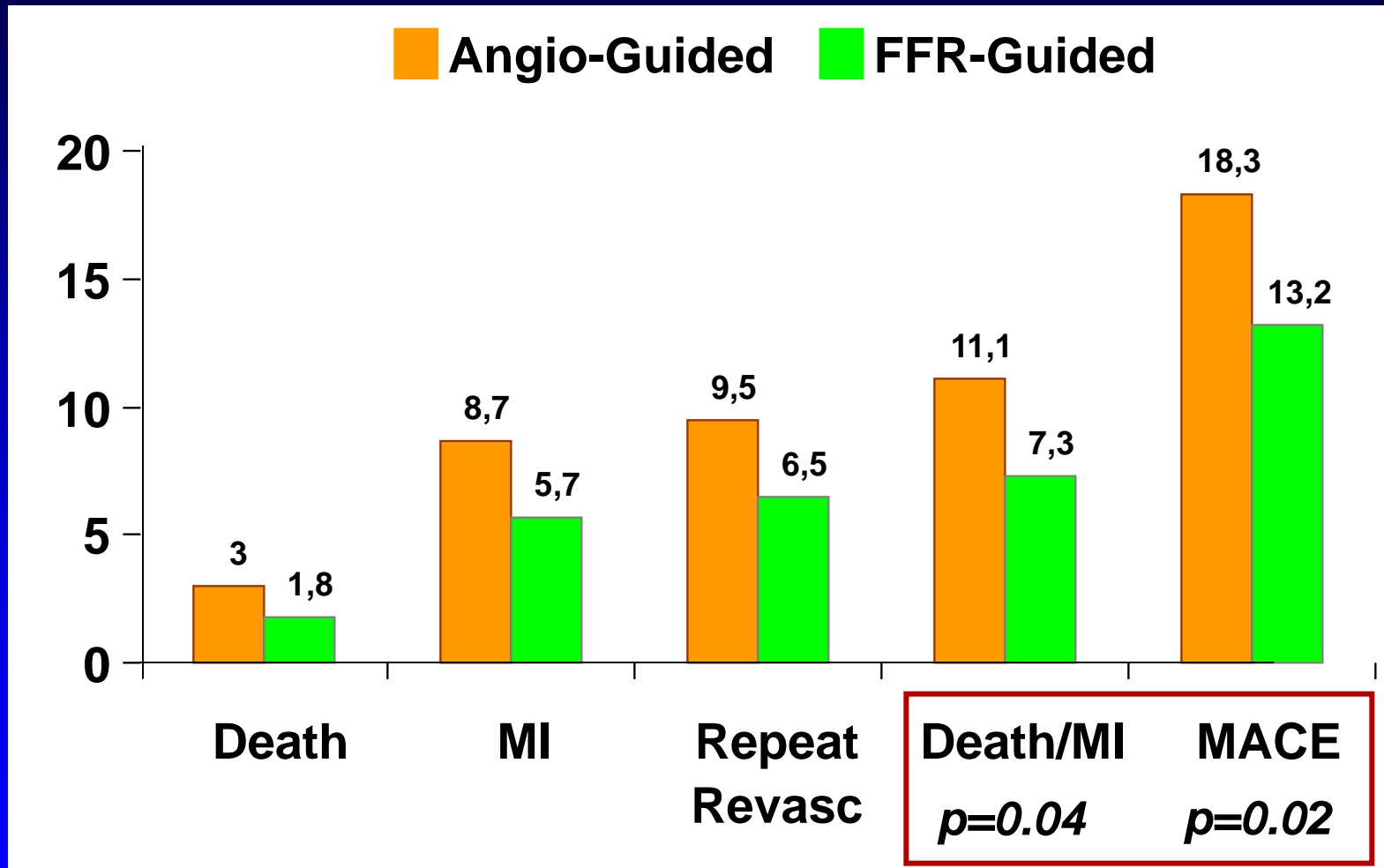
**Stent all indicated
stenoses**

**Measure FFR in all
indicated stenoses**

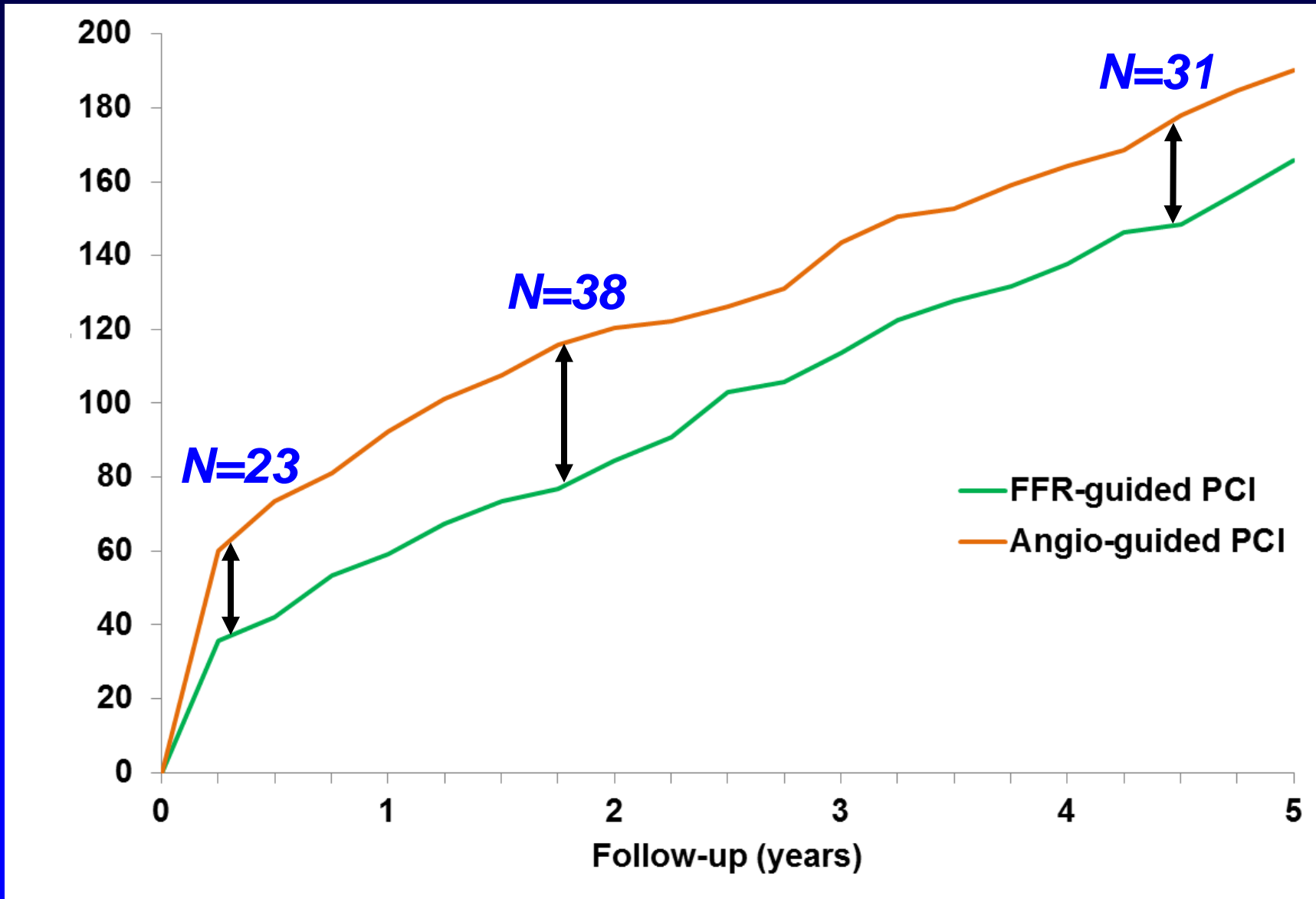
**Stent only those
stenoses with FFR ≤ 0.80**

1, 2, 5-year follow-up

Measuring FFR in Multivessel Disease: FAME Study (N=1005) : One Year Outcomes



FAME study: cumulative events during 5-year follow-up

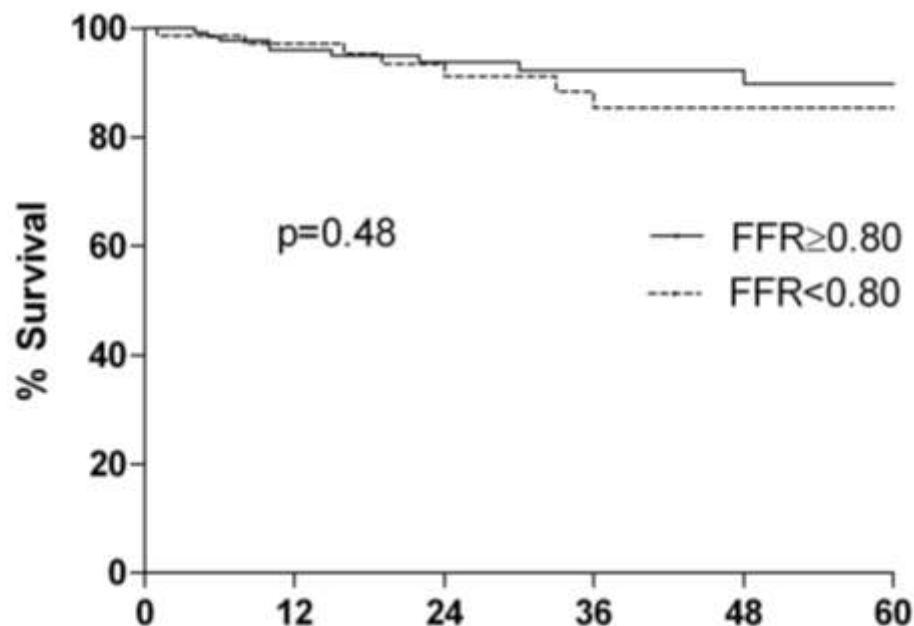


What about Left Main?

- 3 prospective studies and 8 registries
- together 810 patients
- not a single patient in any of these studies ever died due to a deferred LM lesion with FFR > 0.80

Clinical Outcome Data after FFR-Guided Revascularization in Patients with LM Equivocal LM Stenosis (N=209)

SURVIVAL RATE



No at risk	Months					
	0	12	24	36	48	60
FFR \geq 0.80	136	103	72	52	38	26
FFR < 0.80	73	56	41	30	14	10

Deferring revascularization of 30-70% LM stenosis based upon FFR > 0.80, is extremely safe !!

FFR and Clinical Outcome: 3 important questions:

- Is it safe to defer PCI if FFR is negative ? **→ YES !**
(*Defer study 15-y f.u, Lancet 2015*)
- Is it indicated to perform PCI if FFR is positive ?
→ YES !
(*FAME-2 , NEJM 2012 & 2014*)
- Does systematic use of FFR improve PCI outcome
→ YES !
(*FAME, NEJM 2009, EHJ 2015,*
PRIMULTI, NEJM 2016 and COMPARE ACUTE NEJM 2017)

OUTCOME OF FFR- GUIDED PCI IN ACS / STEMI

ORIGINAL ARTICLE

Fractional Flow Reserve–Guided Multivessel Angioplasty in Myocardial Infarction

Pieter C. Smits, M.D., Ph.D., Mohamed Abdel-Wahab, M.D., Franz-Josef Neumann, M.D., Bianca M. Boxma-de Klerk, Ph.D., Ketil Lunde, M.D., Carl E. Schotborgh, M.D., Zsolt Piroth, M.D., David Horak, M.D., Adrian Wlodarczak, M.D., Paul J. Ong, M.D., Rainer Hambrecht, M.D., Oskar Angerás, M.D., Gert Richardt, M.D., Ph.D., and Elmira Omerovic, M.D., for the Compare-Acute Investigators*

Compare Acute Study:

PPCI in STEMI of infarct-related artery, immediately followed by FFR-guided PCI of remaining lesions

PRIMULTI Study:

PPCI in STEMI of infarct-related artery, followed by FFR-guided PCI of remaining lesions within the same hospital admission

Complete revascularisation versus treatment of the culprit lesion only in patients with ST-segment elevation myocardial infarction and multivessel disease (DANAMI-3—PRIMULTI): an open-label, randomised controlled trial

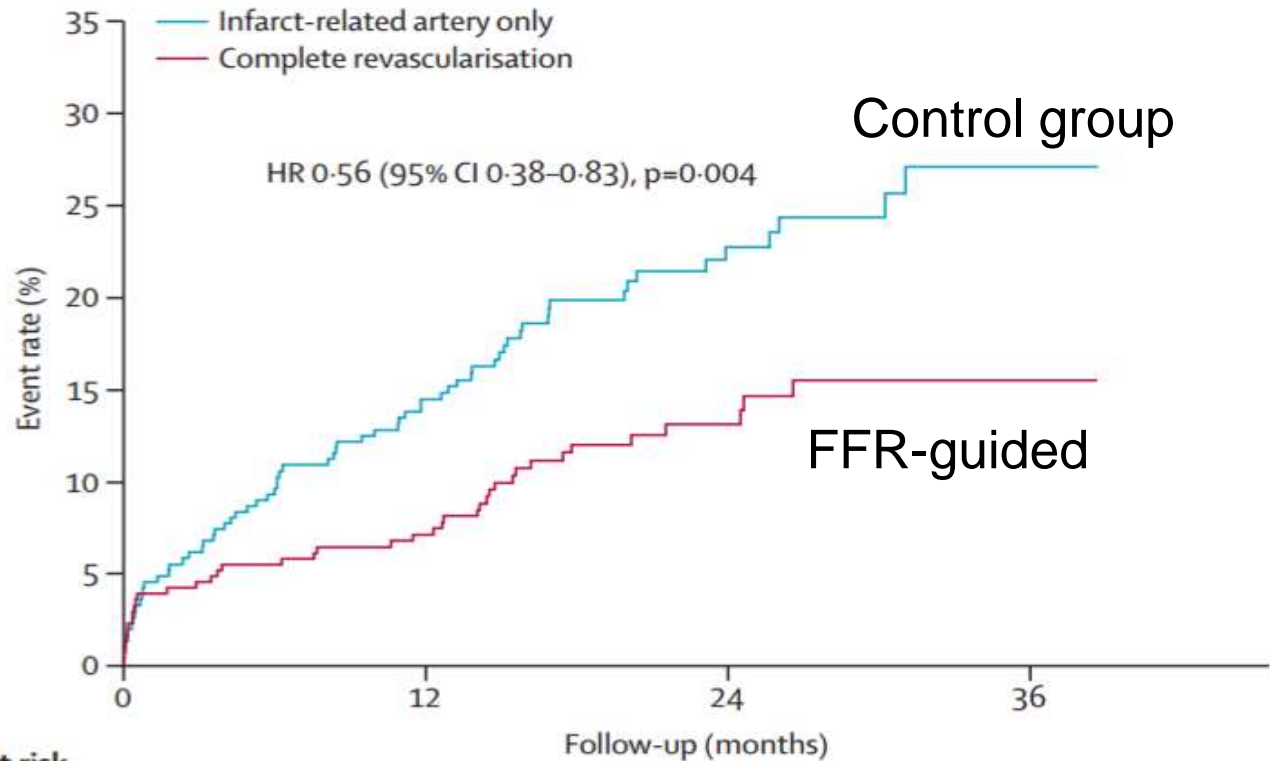


Thomas Engstrom, Henning Kelbak, Steffen Helqvist, Dan Erik Hafsten, Lene Klevgaard, Lene Holmvang, Erik Jørgensen, Frants Pedersen, Kari Saunamäki, Peter Clemmensen, Ole De Backer, Jan Ravkilde, Hans-Henrik Tilsted, Anton Boel Villadsen, Jens Aaroe, Svend Eggert Jensen, Bent Raungaard, Lars Køber, for the DANAMI-3—PRIMULTI Investigators*

Control groups:

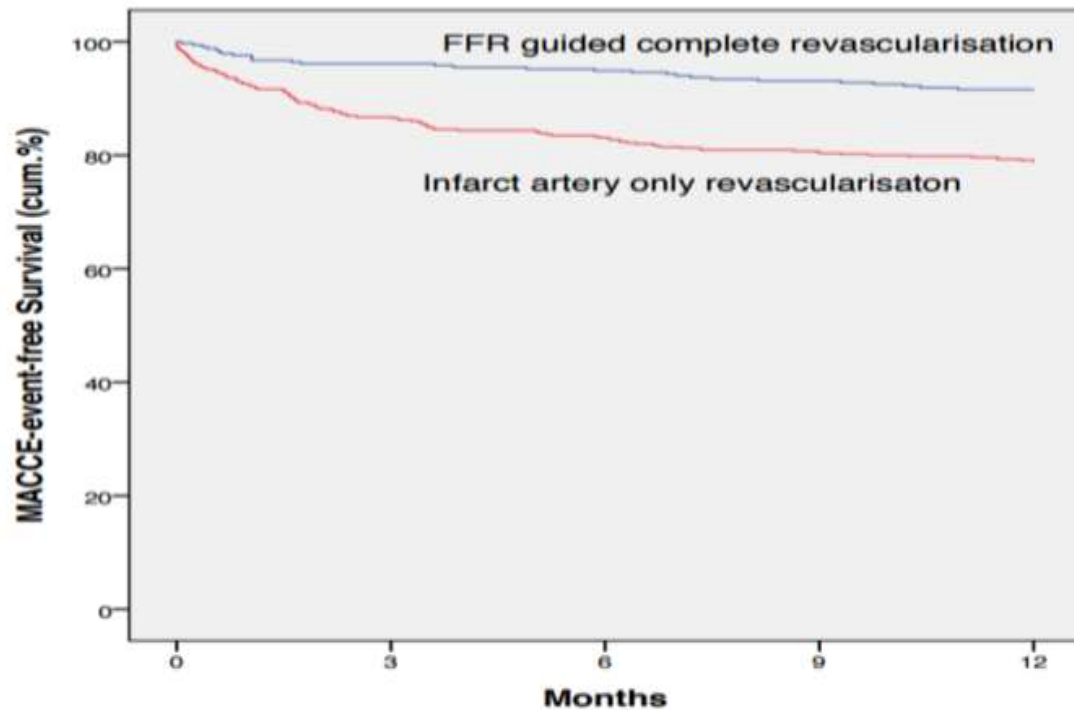
PPCI in STEMI of infarct-related artery only, and clinically-driven or non-invasive testing-driven revascularization of other lesions later on

MACE rate



Number at risk		Follow-up (months)			
	0	12	24	36	
Infarct-related artery only	313	271	142	53	
Complete revascularisation	314	291	159	55	

Primulti trial : superiority of FFR-guided complete revascularisation in STEMI, *performed within the same hospital admission*



No. at risk					
FFR guided complete	287	279	276	259	212
Culprit lesion only	589	511	491	456	370

COMPARE ACUTE trial : superiority of FFR-guided complete revascularisation in STEMI, *performed within the same session*

FFR IN STEMI: WHAT IS THE BOTTOMLINE.....!!!

- **In STEMI with multivessel disease (*lesions in non-infarct vessel*) you can NOT leave the other lesions just untreated**
- **Both FFR-guided PCI of the “other” lesions in the acute session (Compare-Acute), as well as shortly thereafter (Primulti) ,improves outcome**
- ***Whether you choose for “all-in-one” or for a staged procedure within the same admission, does not really matter, as long as you do it !***

WHAT ABOUT RESTING INDICES (iFR, Pd/Pa at rest)

Recent studies suggest that in some (low risk) populations, **iFR** may be non-inferior to FFR
(DEFINE-FLAIR & SWEDE-HEART studies)

CAVEAT:

- **both studies were underpowered**
(as iFR and FFR yield similar decision in 80% of all patients, the power is made by the remaining 20% only. This weakens a non-inferior design and would strengthen a superiority design)
- **had (very) low risk populations**
*1.4 lesion per patient vs 2.8 in FAME;
0.7 stent per patient vs 1.9 in FAME;
45 % of patients no PCI at all vs 11% in FAME*
- **and a large non-inferiority margin (> 50% of event rate)**
All of which issues favour showing non-inferiority a-priori

Define-Flair, Swede-Heart studies (NEJM 2017)

Worrying finding in meta-analysis of both studies:

- ***strong trend to increased mortality with iFR ($p < 0.09$)***

- ***Be careful in extrapolating these results in low risk population to the average, more complex populations in present-day cathlabs.***
- ***iFR has only be compared to FFR and never proved direct superiority above standard treatment in any study***

CONCLUSION

The *superiority* of FFR-guided PCI to improve outcome has been *directly* demonstrated now in *many RCT's* in almost all clinical and angiographic conditions:

- *from single to complex multivessel disease*
- *Left Main disease*
- *Proximal LAD disease*
- *ACS and STEMI*
- *Bifurcations*
- *and many others*