Relations of Interest

- Consulting Fees on my behalf go to the Cardiovascular Research Center Aalst
- Contracted Research between the Cardiovascular Research Center Aalst and several pharmaceutical and device companies, including StJude, HeartFlow, Opsense, Volcano
- Ownership Interest: Co-founder and Board member of Argonauts, Genae and Cardio^{3}BioSciences (cell-based regeneration cardiovascular therapies)
- Chairman of PCR
- Co-Chairman of AfricaPCR
- Co-Chairman of EuroPCR, the annual Course of EAPCI

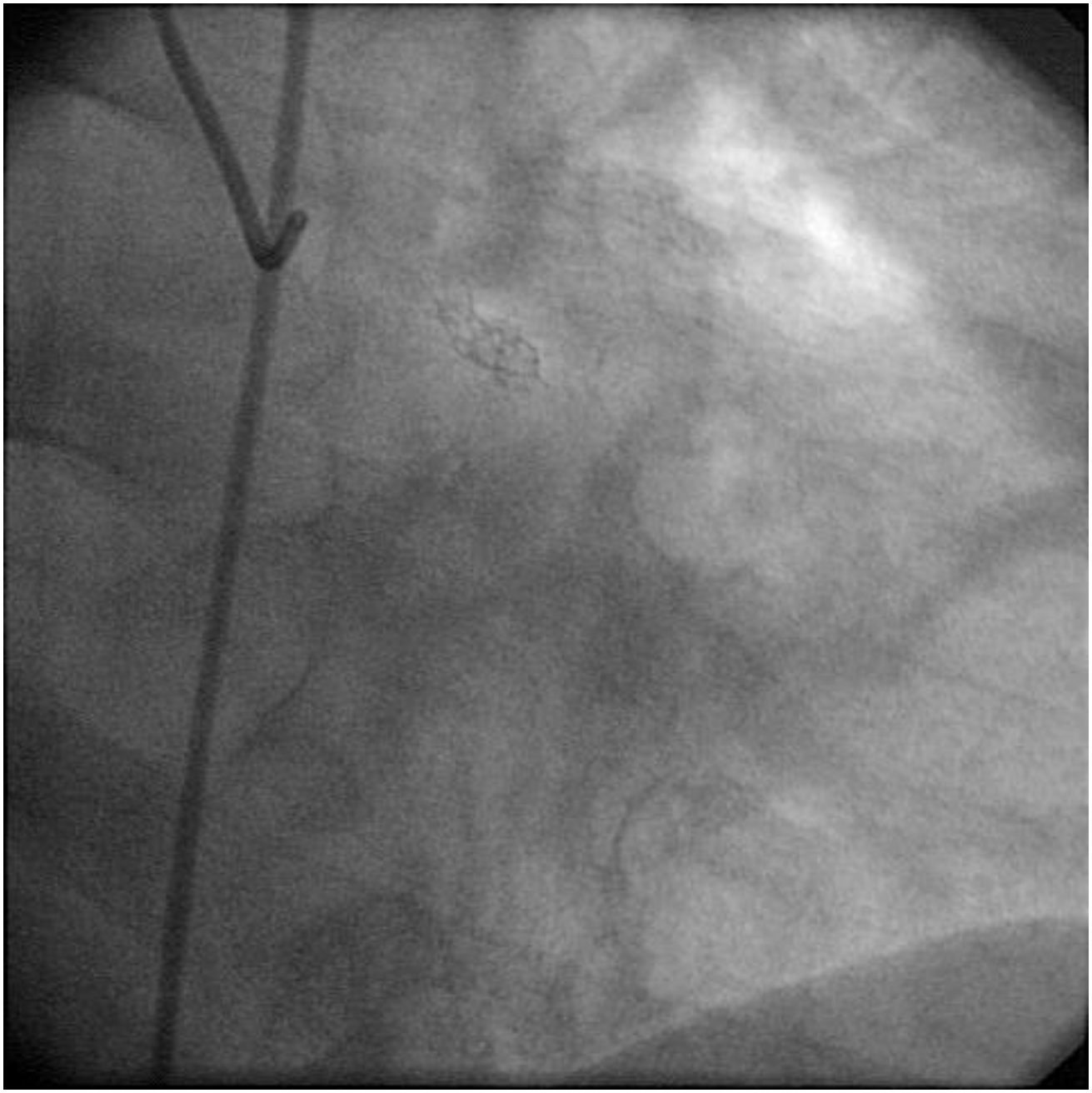
21st Cardiology Update
February 11, 2015

Is FFR essential to guide PCI?

William Wijns

Aalst, B

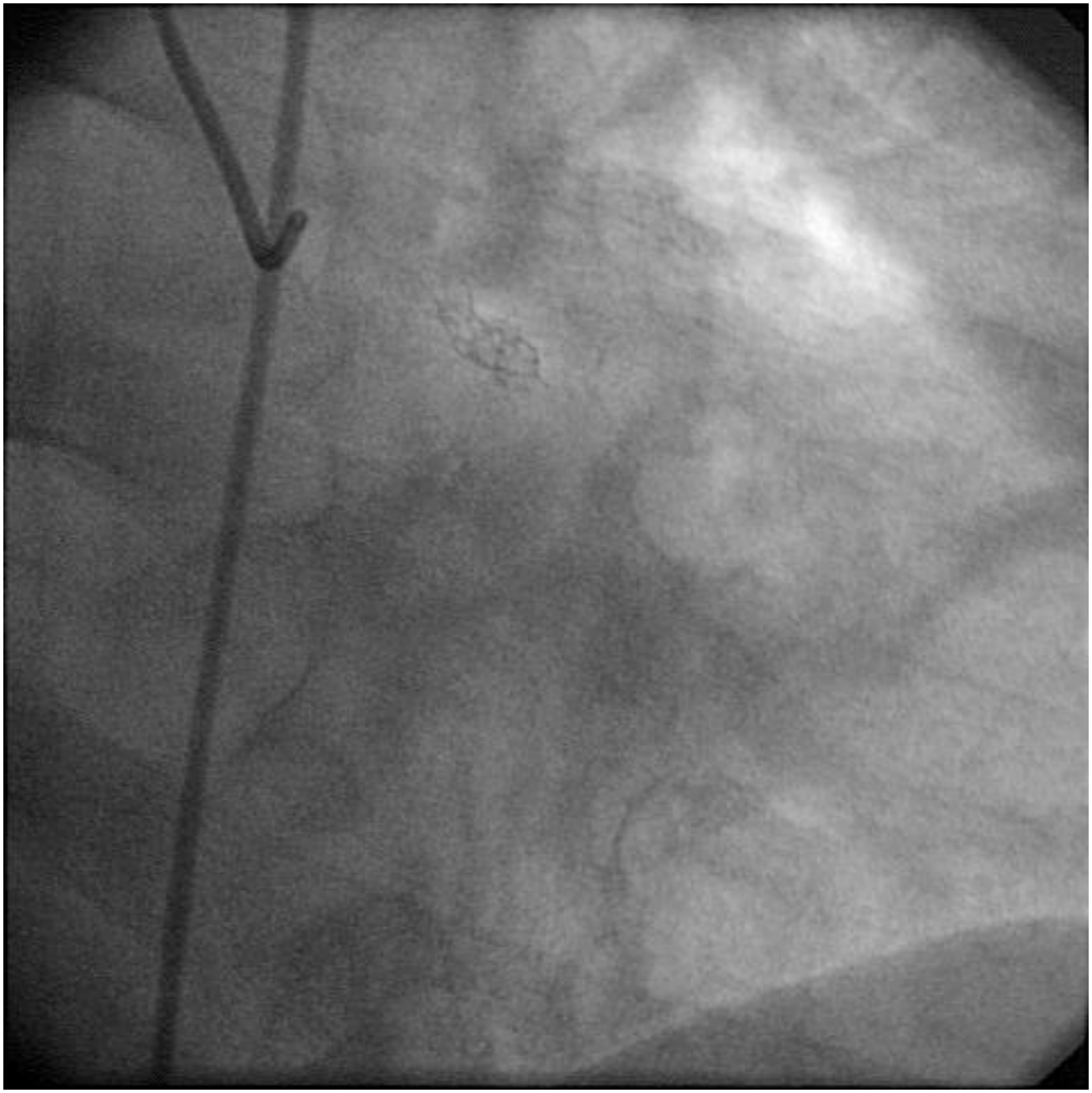
Percutaneous Interventions



Is FFR essential to guide PCI?

- Decision to perform PCI is based on global appraisal of the clinical condition, functional evaluation, procedural benefits and risks, and coronary anatomy

- When functional evaluation is not available or inconclusive, FFR can be applied on the spot, with high spatial resolution to inform decision-making



Revascularisation vs Best Medical Therapy

No benefit of PCI

in the **absence** of ischemia

1998: Nuclear imaging studies

2005: Besançon randomised trial*

2007: Defer randomised trial

2012: FAME 2 registry

2013: SJ Park registry**

2013: Mayo Clinic registry ***

* Legalery, Eur Heart J 26:2623

** Eur Heart J 34:3553

*** Lim, Eur Heart J 34:1375-83

DEFER Study Results at 5 years

FFR > 0.75

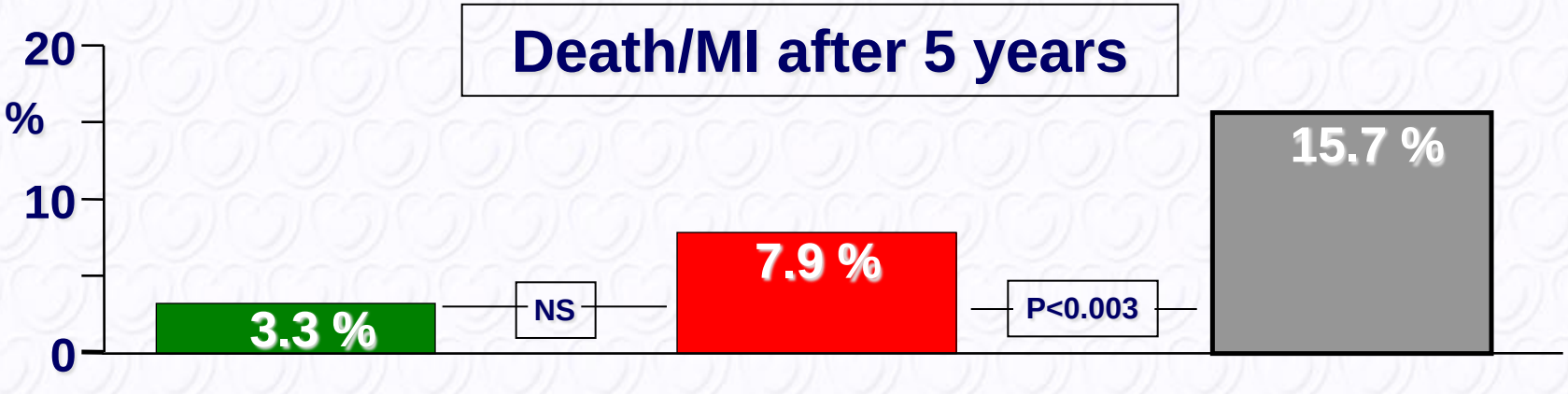
No PCI

PCI

FFR < 0.75

PCI

DEFER | **PERFORM** | **REFERENCE**



When FFR > 0.75 Death and MI rate is < 1% per year

Pijls et al, JACC 2007;49:2105-1.

Revascularisation vs Best Medical Therapy

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in the **absence** of ischemia

1998: Nuclear imaging studies

2005: Besançon randomised trial*

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2012: FAME 2 registry

2013: SJ Park registry**

2013: Mayo Clinic registry ***

Evidence for benefit of PCI

In the **presence** of ischemia

1997: ACIP trial

2003: Nuclear imaging studies

2008: Nuclear substudy COURAGE

2009: Substudy of BARI 2 D

2012: FAME 2 randomised trial

2013: Mayo Clinic registry***

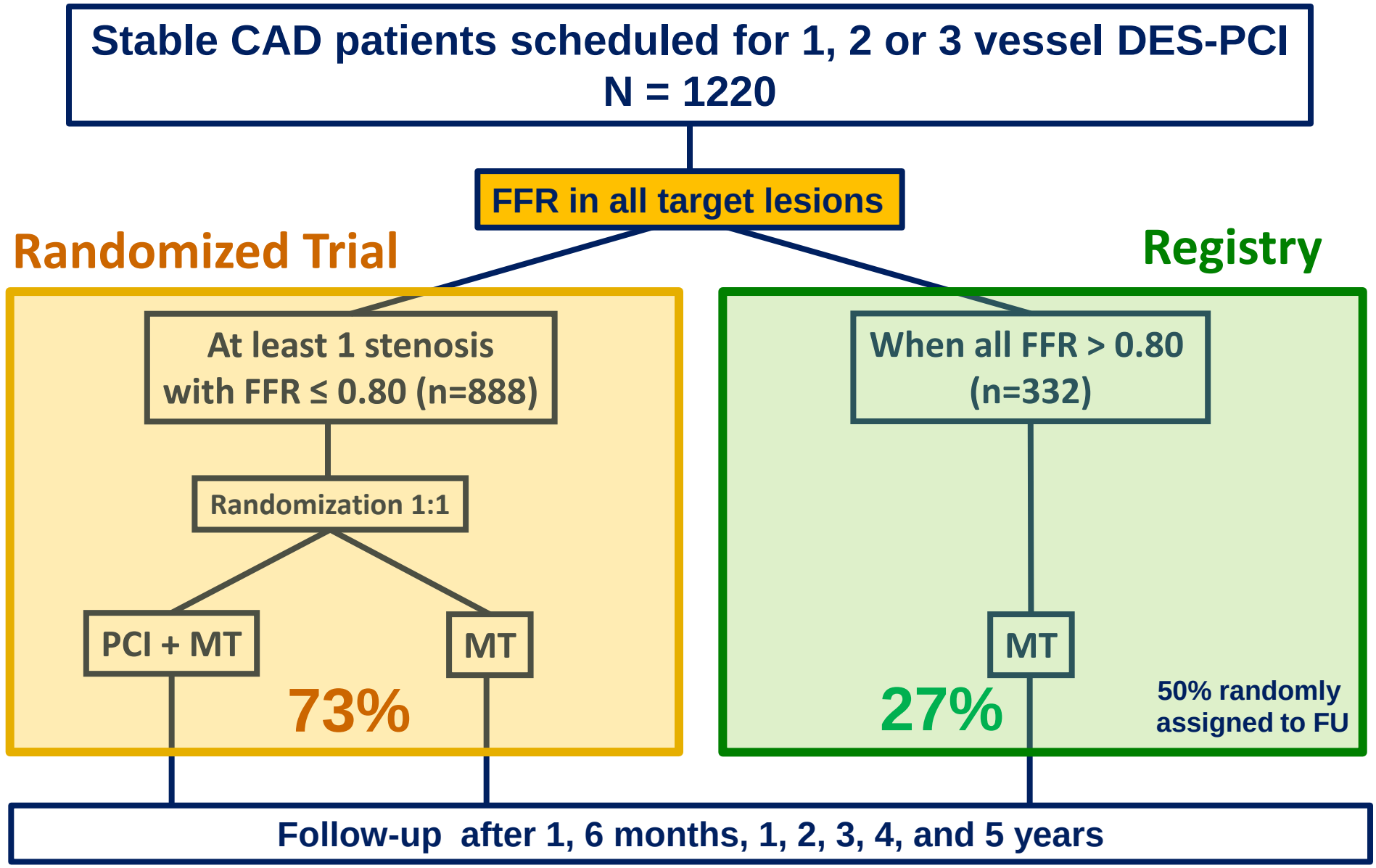
20XX: ISCHEMIA trial

* Legalery, Eur Heart J 26:2623

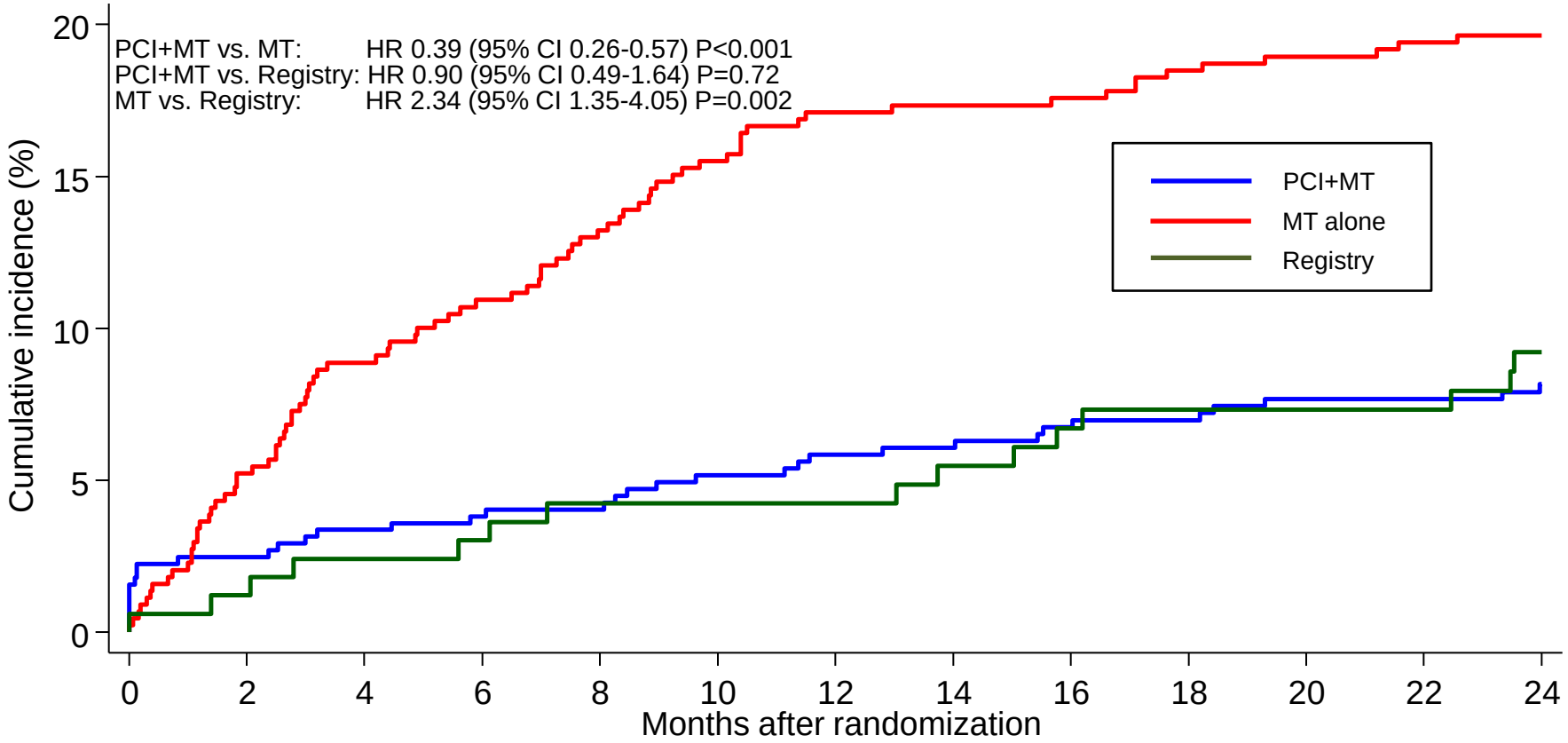
** Eur Heart J 34:3553

*** Lim, Eur Heart J 34:1375-83

FAME 2 Flow Chart



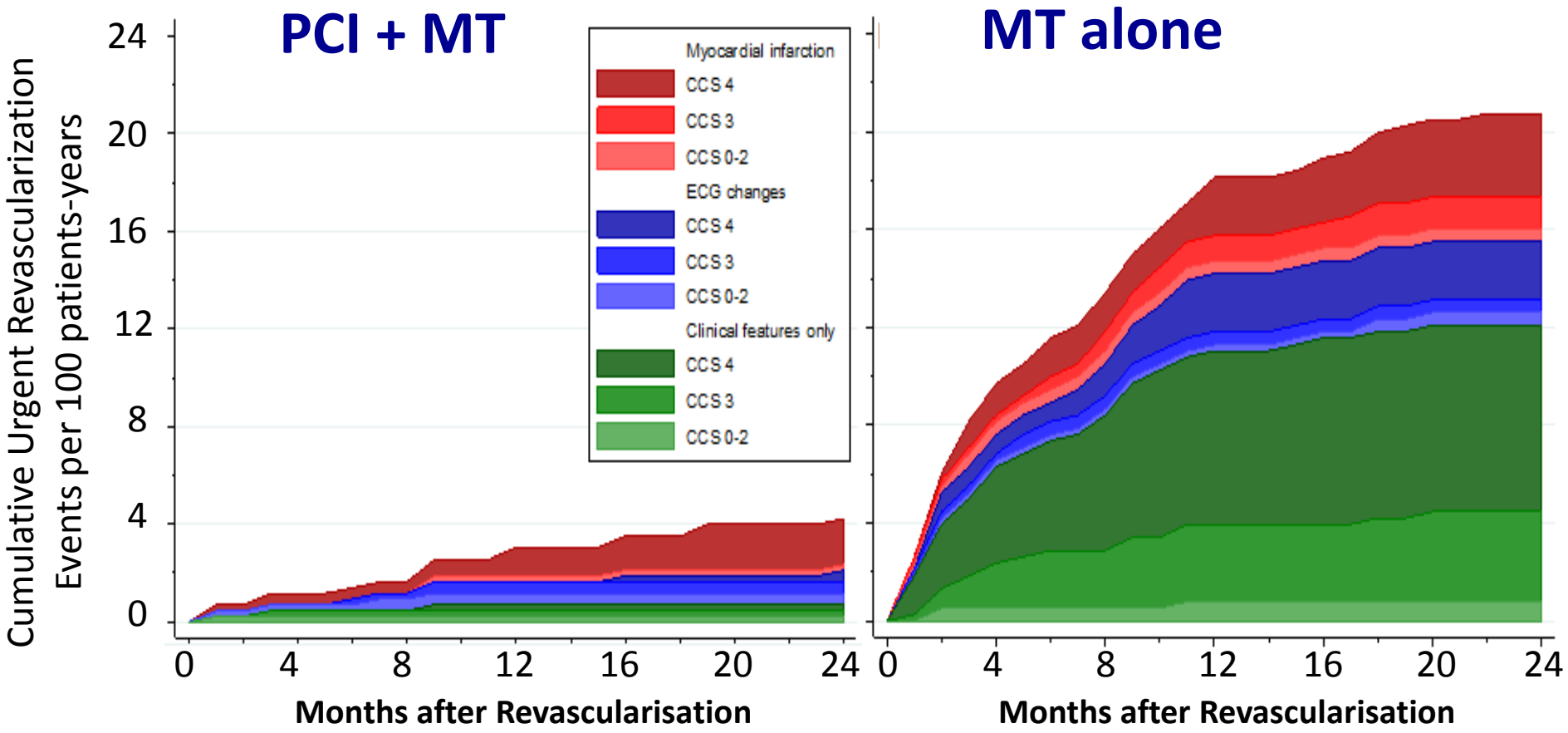
FAME 2 Primary Outcomes



No. at risk

MT	441	417	398	389	379	369	362	360	359	355	353	351	297
PCI+MT	447	434	429	426	425	420	416	414	410	408	405	403	344
Registry	166	164	162	160	157	157	156	153	151	150	150	150	122

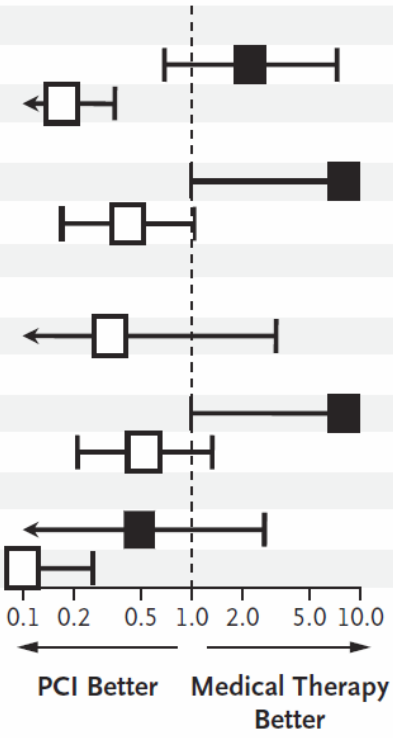
Urgent revascularizations according to different triggers for the revascularization



Urgent revascularization was triggered in >80% by an MI, by dynamic ST changes, or by resting angina

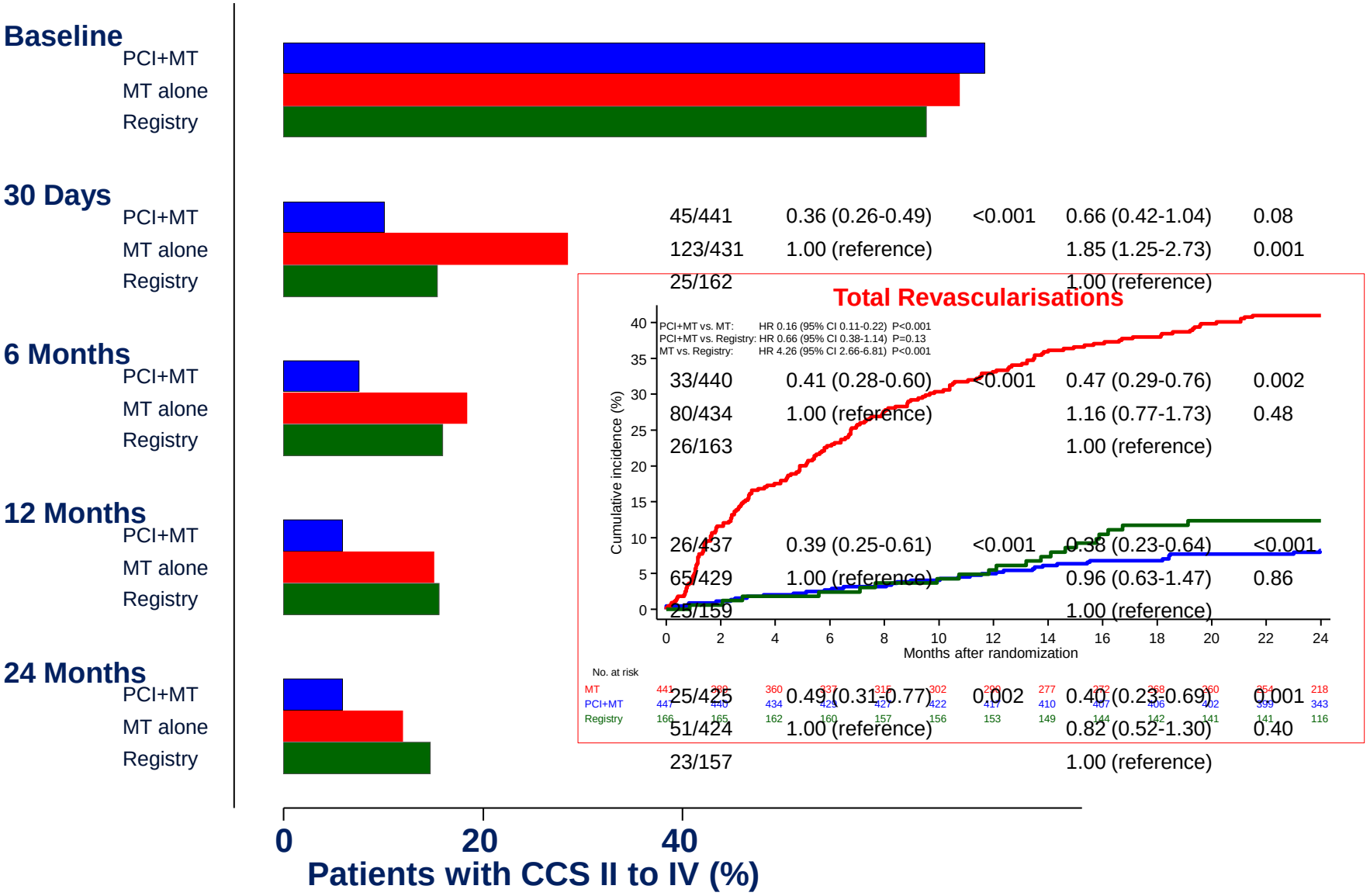
FAME 2 - Landmark Analysis

End Point	PCI	Medical Therapy	Relative Risk (95% CI)	P Value	P Value for Interaction
	no. of events/total no. (%)				
Primary end point					<0.001
≤7 days	9/447 (2.0)	4/441 (0.9)	2.24 (0.69–7.31)	0.17	
8 days to maximum follow-up	10/427 (2.3)	52/428 (12.1)	0.17 (0.09–0.35)	<0.001	
Death or myocardial infarction					0.003
≤7 days	8/447 (1.8)	1/441 (0.2)	7.99 (0.99–64.57)	0.04	
8 days to maximum follow-up	7/428 (1.6)	16/431 (3.7)	0.42 (0.17–1.04)	0.053	
Death					—
≤7 days	0/447	0/441			
8 days to maximum follow-up	1/436 (0.2)	3/432 (0.7)	0.33 (0.03–3.17)	0.37	
Myocardial infarction					0.007
≤7 days	8/447 (1.8)	1/441 (0.2)	7.99 (0.99–64.57)	0.04	
8 days to maximum follow-up	7/428 (1.6)	13/431 (3.0)	0.52 (0.21–1.32)	0.16	
Urgent revascularization					0.09
≤7 days	2/447 (0.4)	4/441 (0.9)	0.49 (0.09–2.70)	0.45	
8 days to maximum follow-up	5/434 (1.2)	45/428 (10.5)	0.10 (0.04–0.26)	<0.001	



N Engl J Med 2012;367:991-1001.

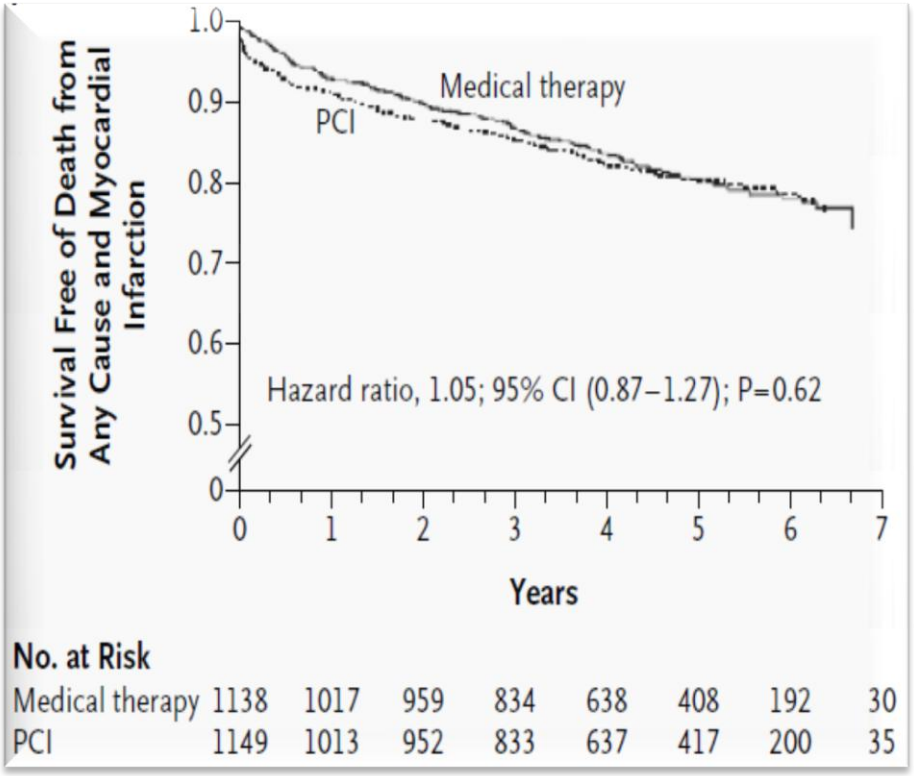
FAME 2 Symptoms



Is FFR essential to guide PCI?

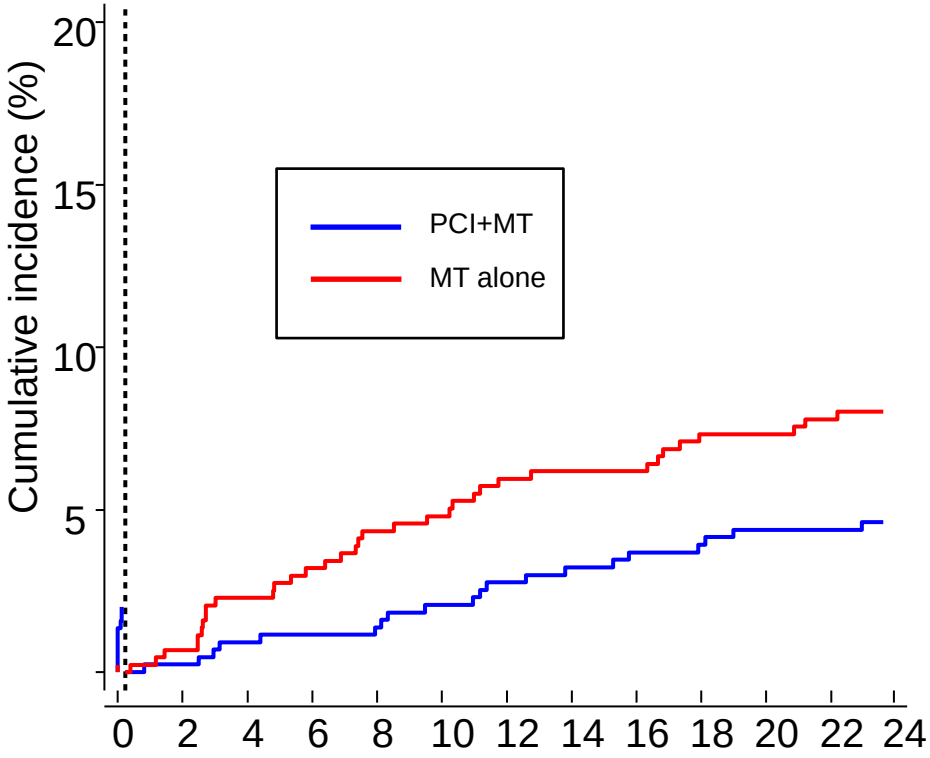
- In order to optimise appropriate use of revascularisation, dual targeting (by anatomy and function) is to be recommended
- Then outcomes are prognostically superior and symptomatically equivalent to those obtained with single targeting (by anatomy only)

Only Angiography



COURAGE
NEJM 2007

Angiography + FFR



FAME 2
NEJM 2014

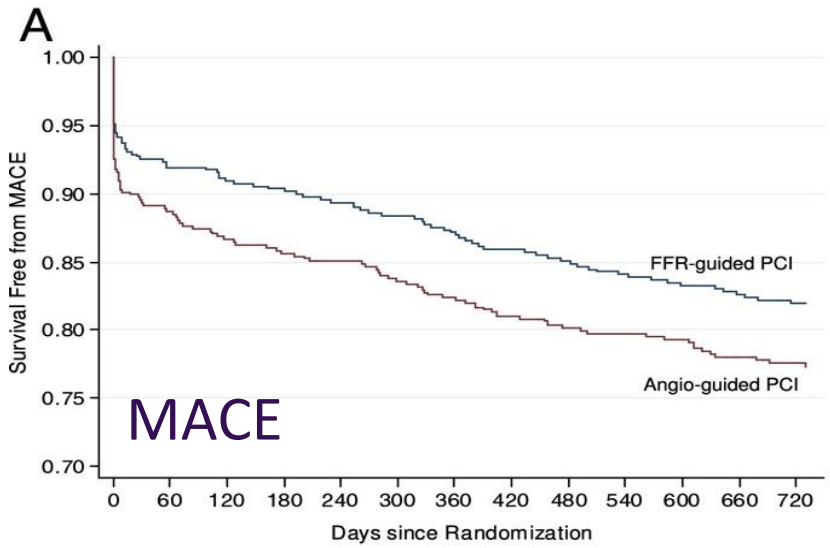
Is FFR essential to guide PCI?

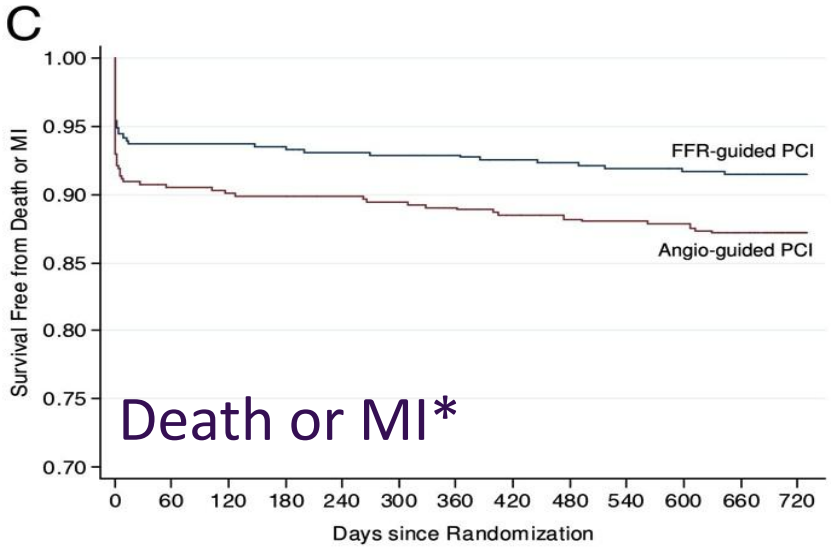
What if the benefit of revascularisation by PCI was confounded by …

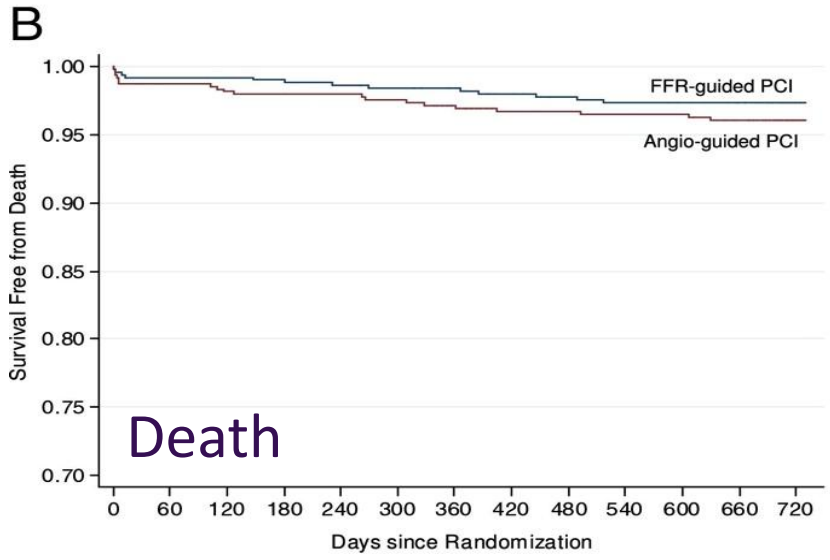
failure to restrict stent implantation to ischemic stenoses (FFR +)

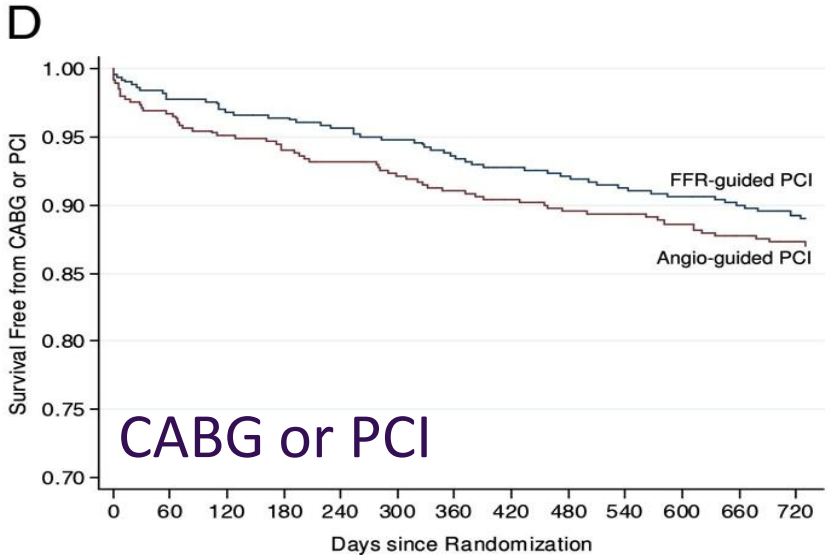
FAME 1 Guidance Randomised Trial

Event-free rates at 2 years



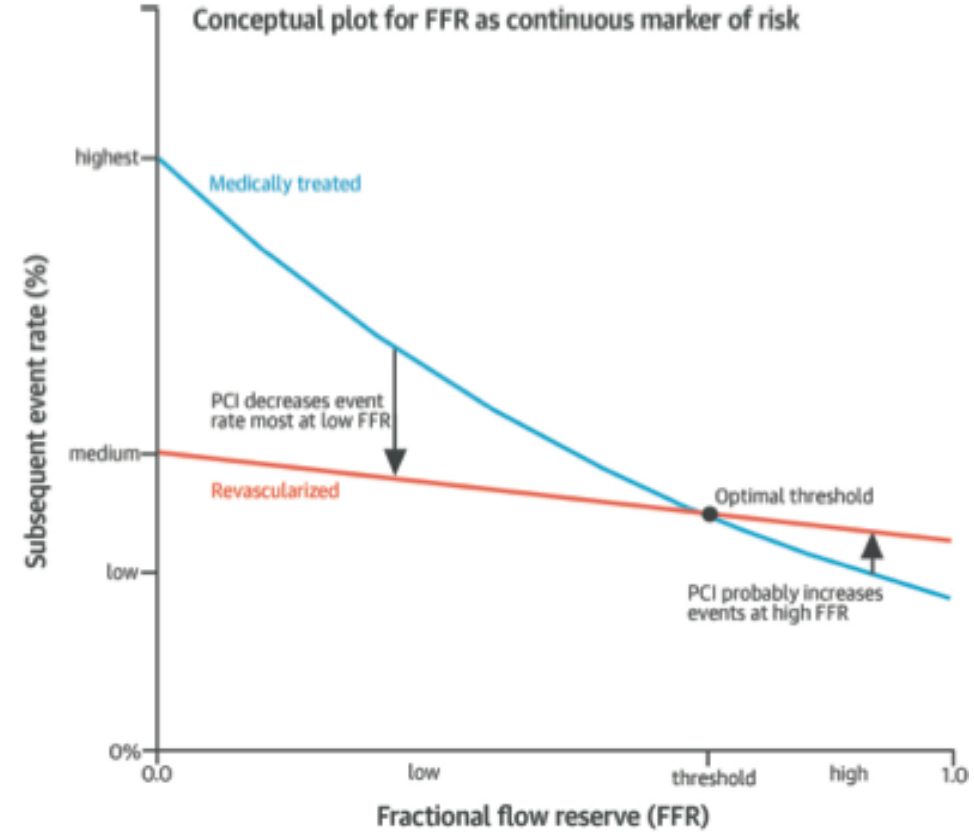






Pijls et al. JACC 2010:56;177

Prognostic Value of Fractional Flow Reserve Linking Physiologic Severity to Clinical Outcomes



CENTRAL ILLUSTRATION **Conceptual Relationship Between FFR and Outcomes**

N Johnson, JACC 2014: 64;1641

Prognostic Value of Fractional Flow Reserve Linking Physiologic Severity to Clinical Outcomes

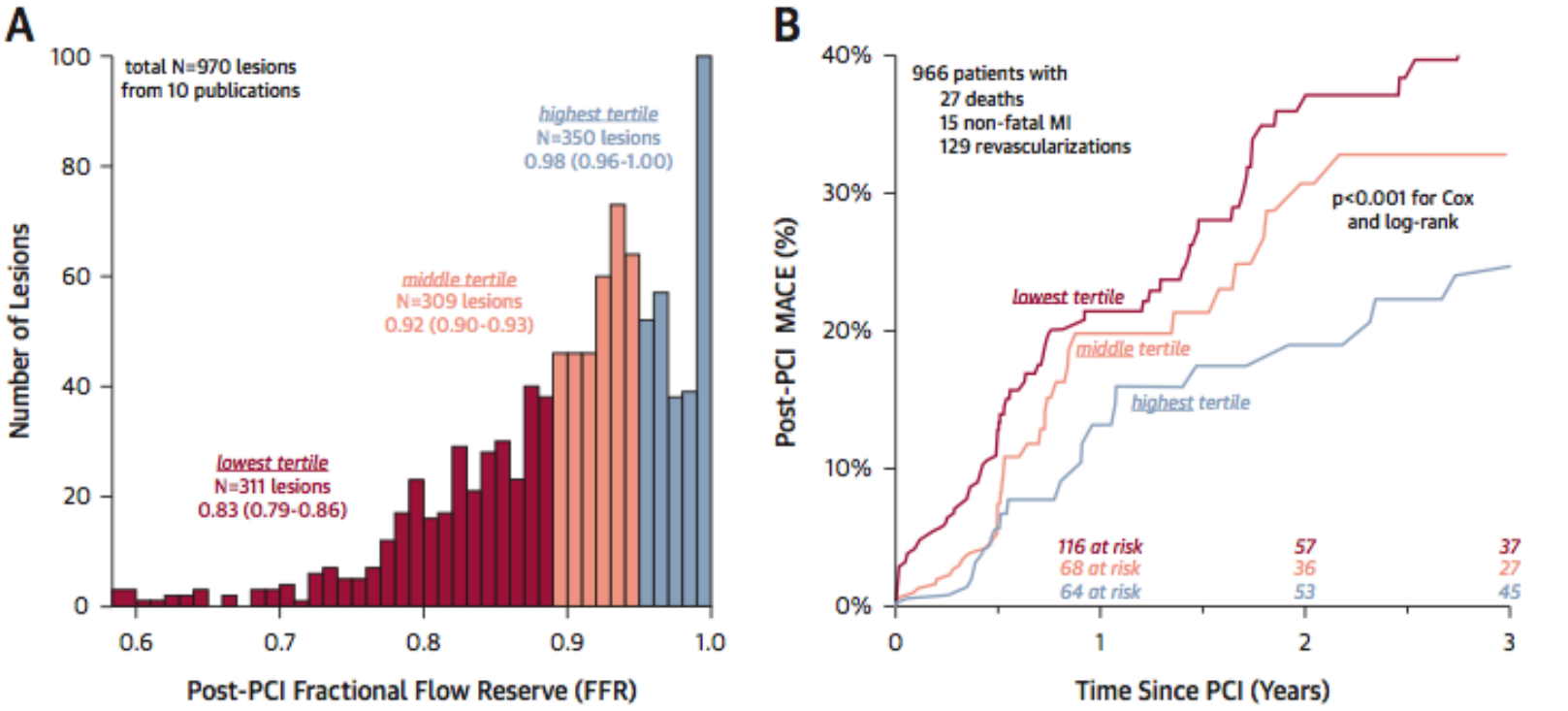
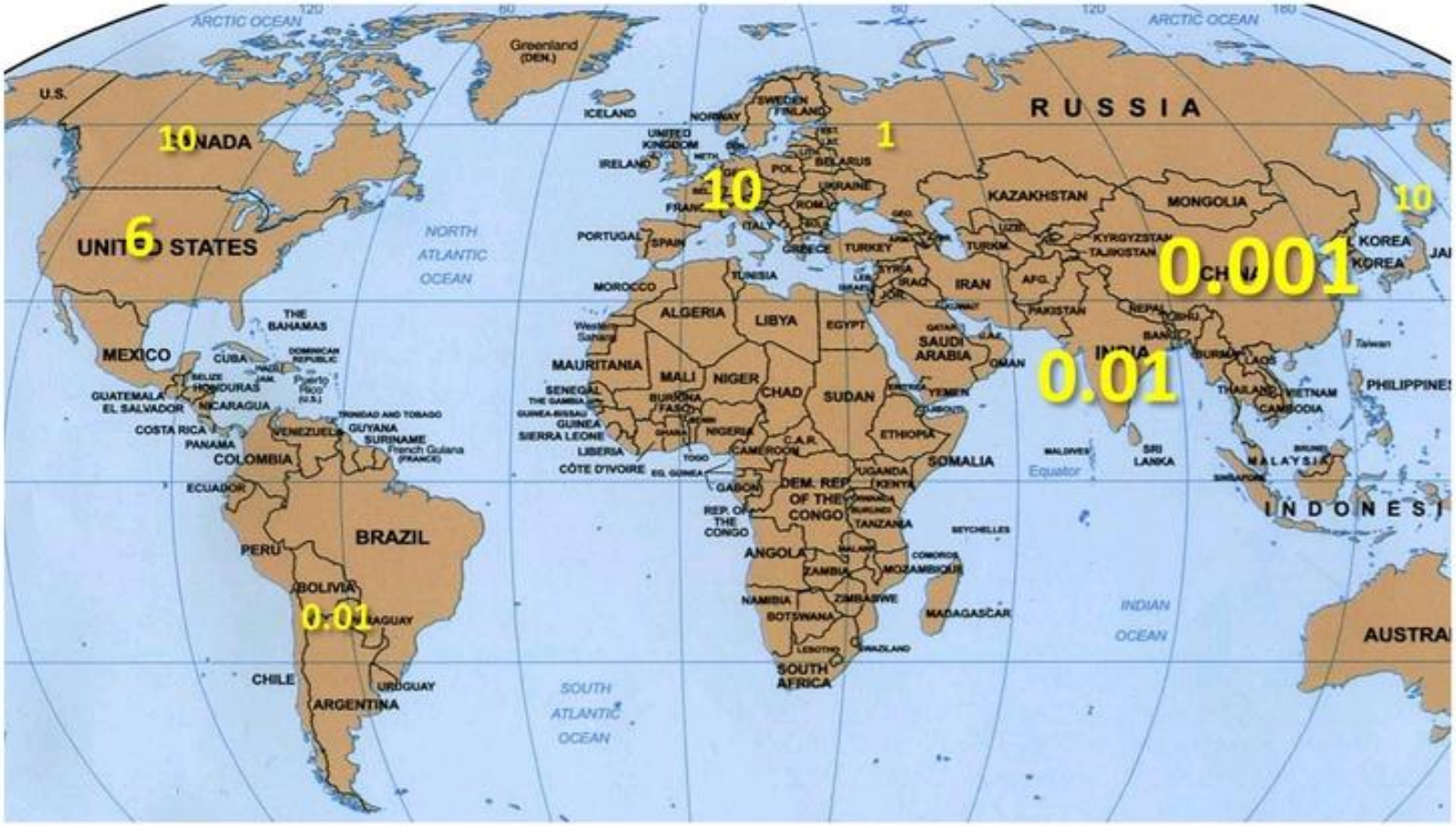


FIGURE 4 **FFR Measurements Made Immediately After PCI**

(A) Histogram. Lesion-level histogram of post-PCI FFR values from the patient-level analysis colored by tertiles **(red, salmon, periwinkle)**. **(B)** Survival curves. Kaplan-Meier event curves for tertiles of post-PCI FFR values (colors match histogram). Both continuous Cox regression and tertile-based log-rank tests demonstrated a significant ($p < 0.001$), inverse relationship between post-PCI FFR and subsequent clinical events. Abbreviations as in Figures 1 and 2.

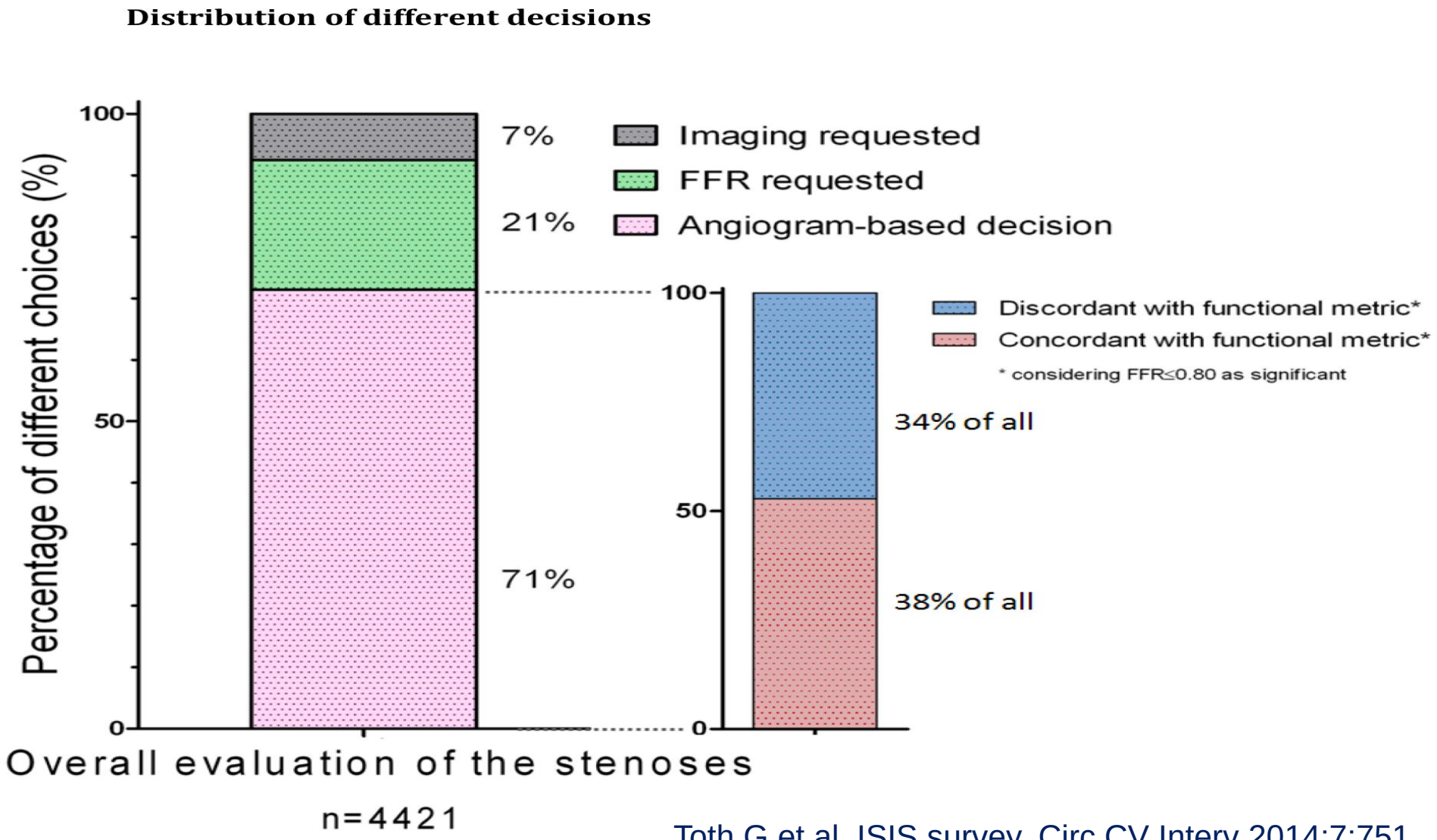
N Johnson, JACC 2014: 64;1641

Global Adoption of FFR remains limited



Rough estimate of FFR adoption in different regions of the world.
Figures show % of FFR adoption in clinical practice (not p values!)

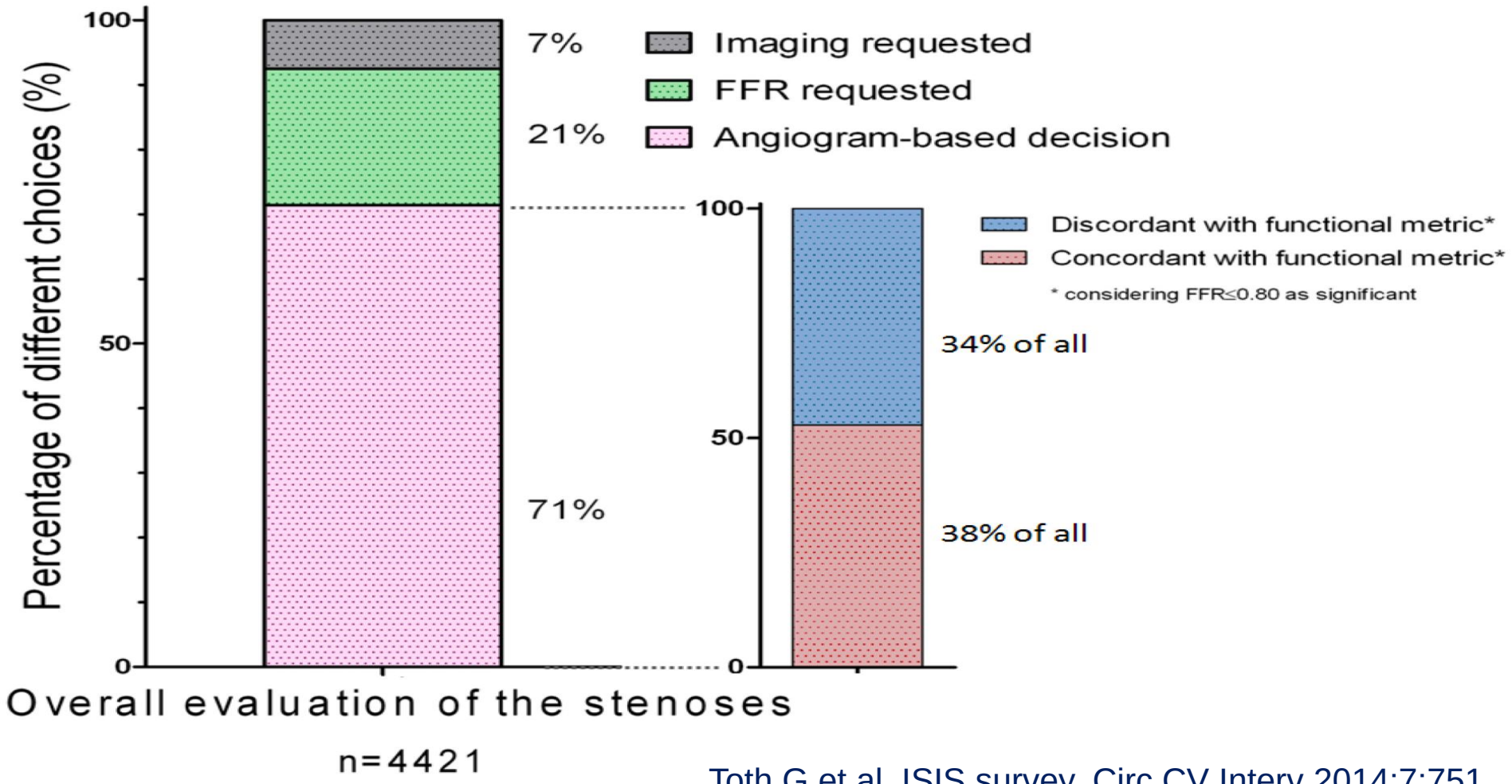
FFR to identify appropriate targets for PCI



Toth G et al, ISIS survey, Circ CV Interv 2014:7;751

FFR to identify appropriate targets for PCI

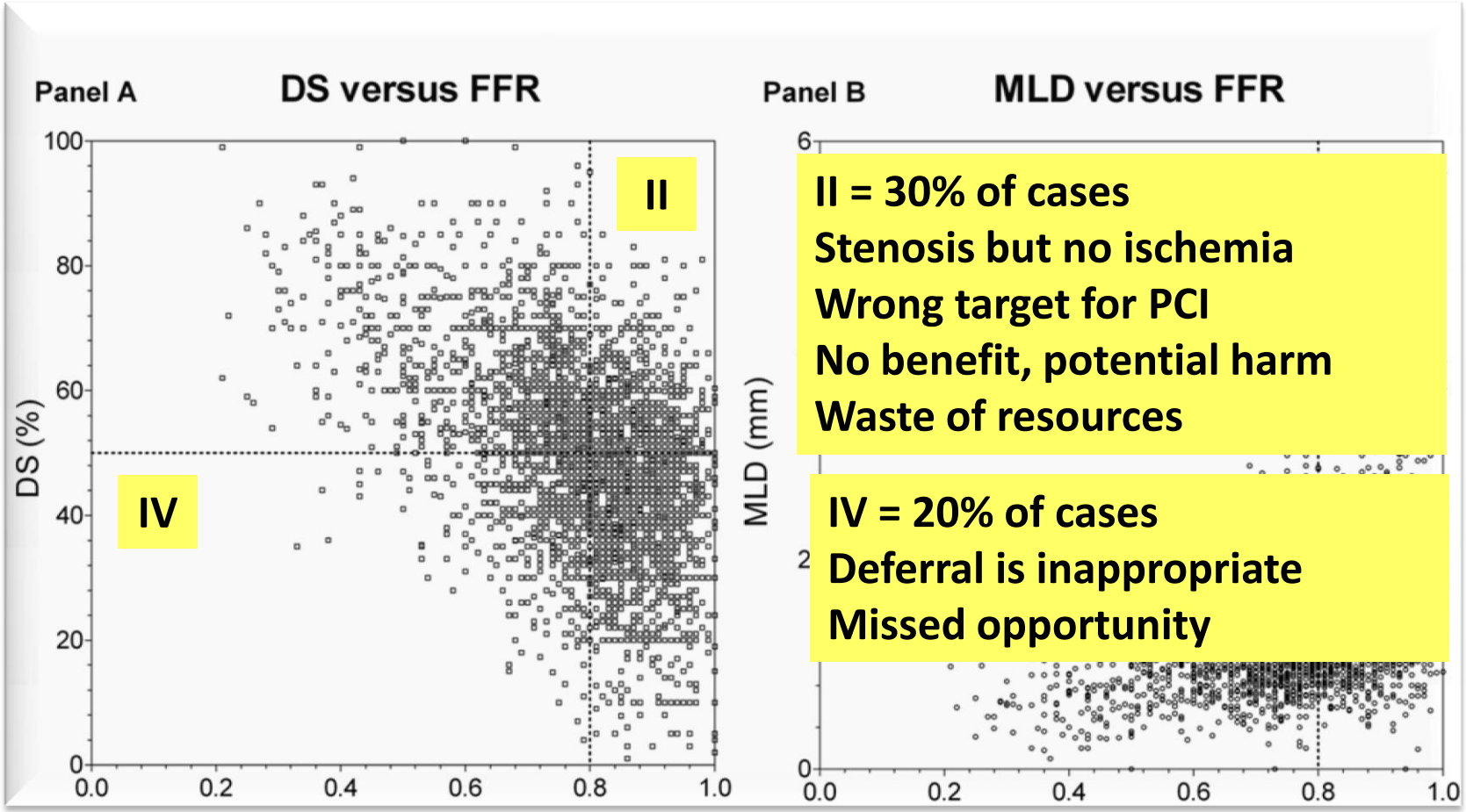
No perceived need for FFR



Toth G et al, ISIS survey, Circ CV Interv 2014:7;751

gulf PCR 2013

Why apply functional indices?



II = 30% of cases
Stenosis but no ischemia
Wrong target for PCI
No benefit, potential harm
Waste of resources

IV = 20% of cases
Deferral is inappropriate
Missed opportunity

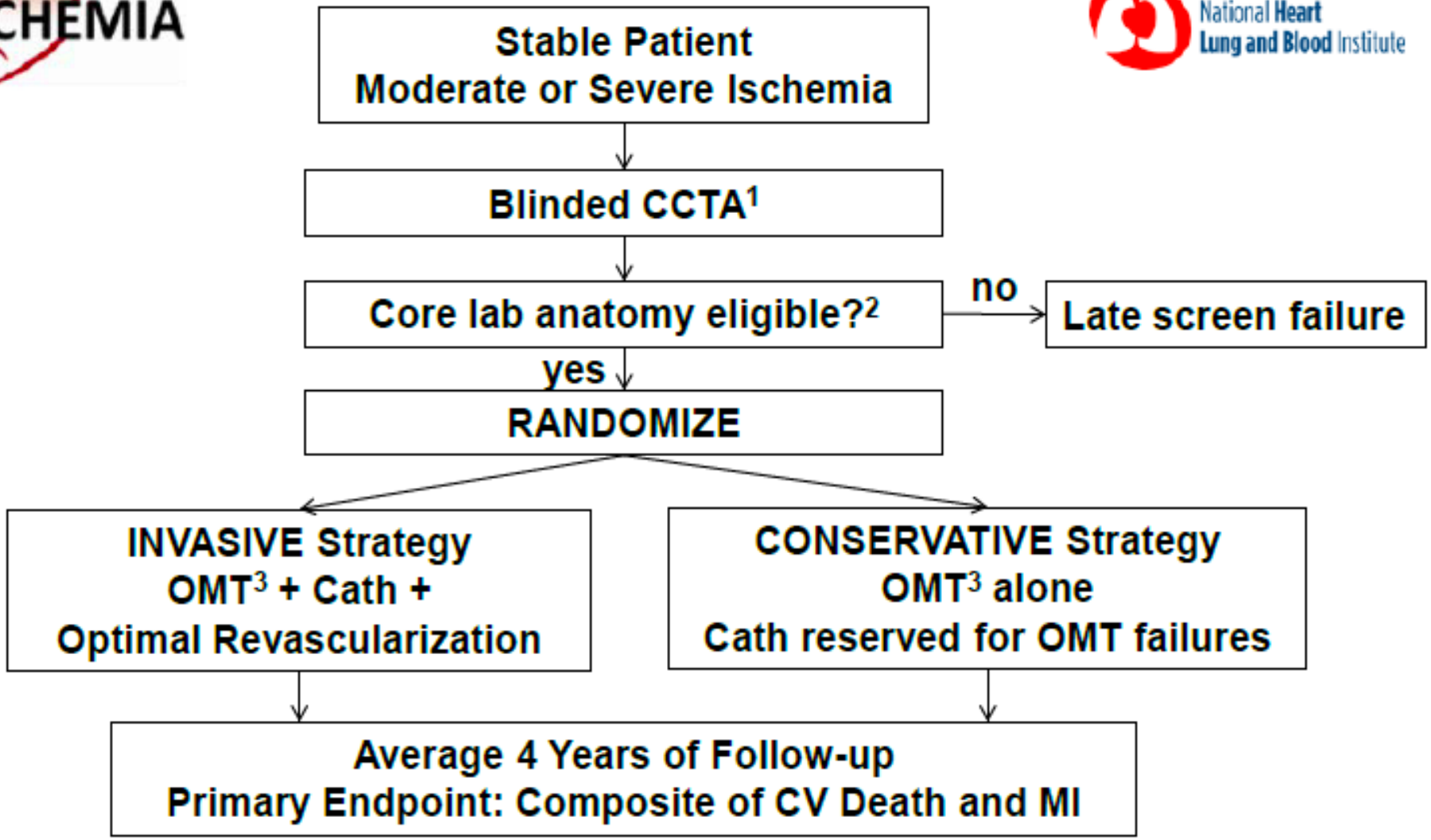
Angiographic guidance to revascularization results in inappropriate intervention in ~50% of cases

Is FFR essential to guide PCI?

Evaluation of ischemia is essential to guide revascularisation by PCI (and CABG)

ISCHEMIA

National Heart Lung and Blood Institute



[1]CCTA will be performed in all patients with eGFR ≥60 mL/min
[2]Exclude patients with LM disease or no obstructive disease
[3]OMT=Optimal medical therapy