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Cardiovascular Center OLV Aalst

Madrid Microcirculation Meeting

Madrid November 29-30, 2023 9th - 10th 2023

MMM Madrid Microcirculation Meeting - 4th Edition -

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From FAME to ORBITA 2

Bernard De Bruyne, MD, PhD

Cardiovascular Center Aalst, Belgium
and University Hospital Lausanne, Switzerland

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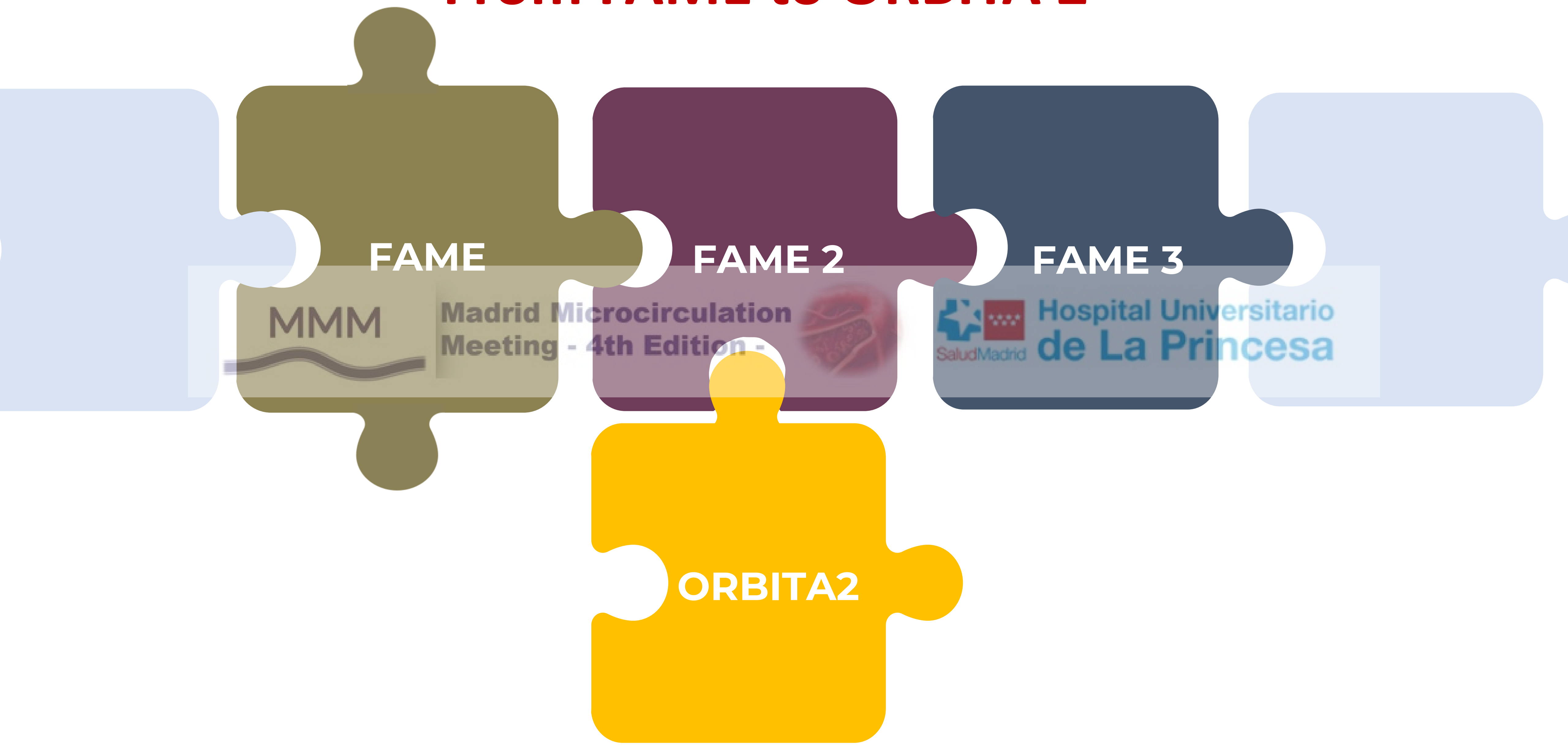

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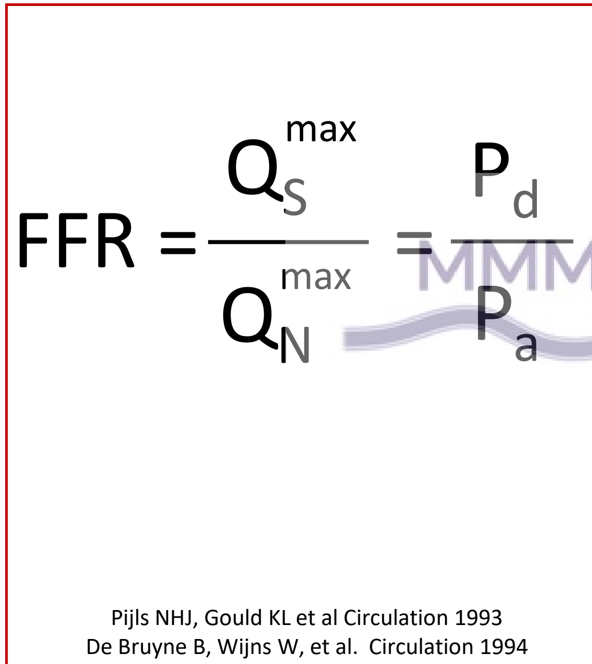
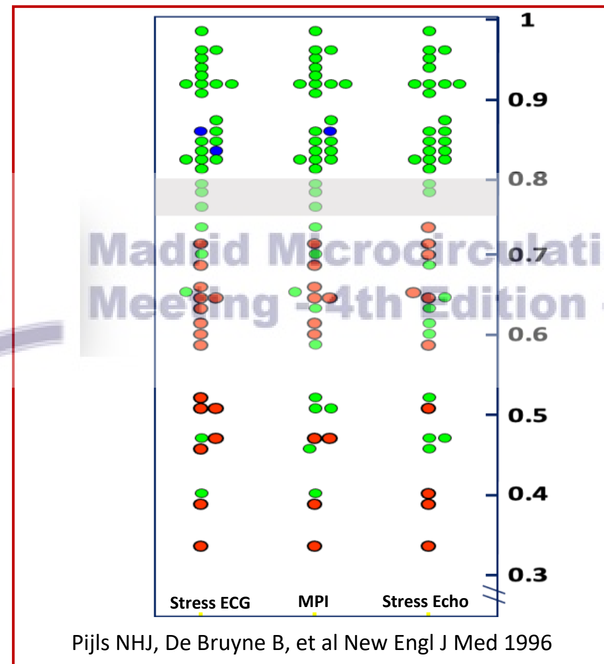
FAME studies

Ffr Assessment for Multivessel Evaluation

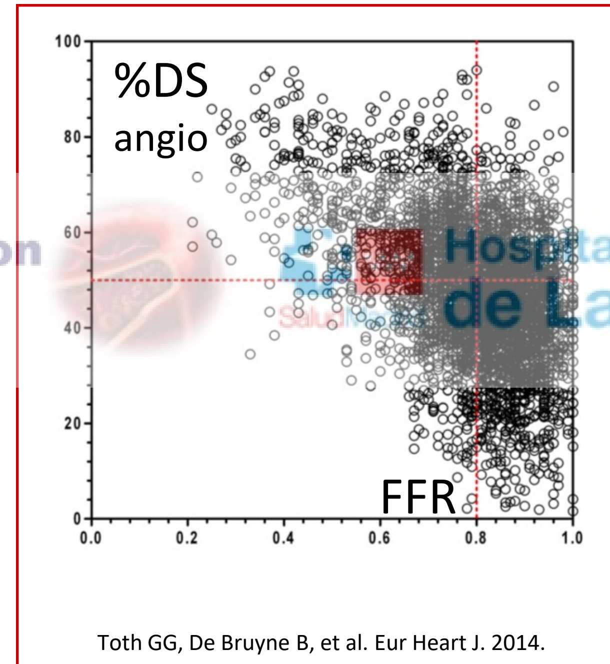
Background



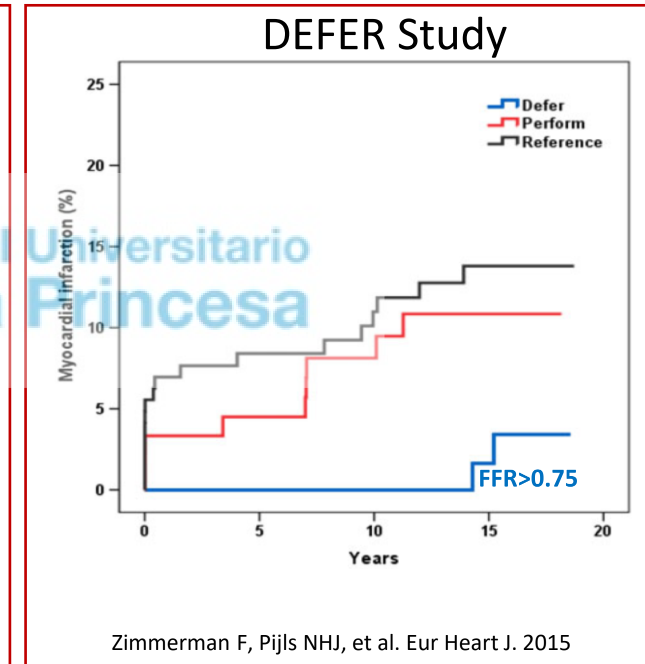
Pijls NHJ, Gould KL et al Circulation 1993
De Bruyne B, Wijns W, et al. Circulation 1994



Pijls NHJ, De Bruyne B, et al New Engl J Med 1996



Toth GG, De Bruyne B, et al. Eur Heart J. 2014.



Zimmerman F, Pijls NHJ, et al. Eur Heart J. 2015

A *flow* index
derived from
pressure measurements

Poor correlation
With
Non-invasive testing

Poor correlation
With
Angiography

Hemodynamically mild
Stenoses do very well
With OMT

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FAME 1

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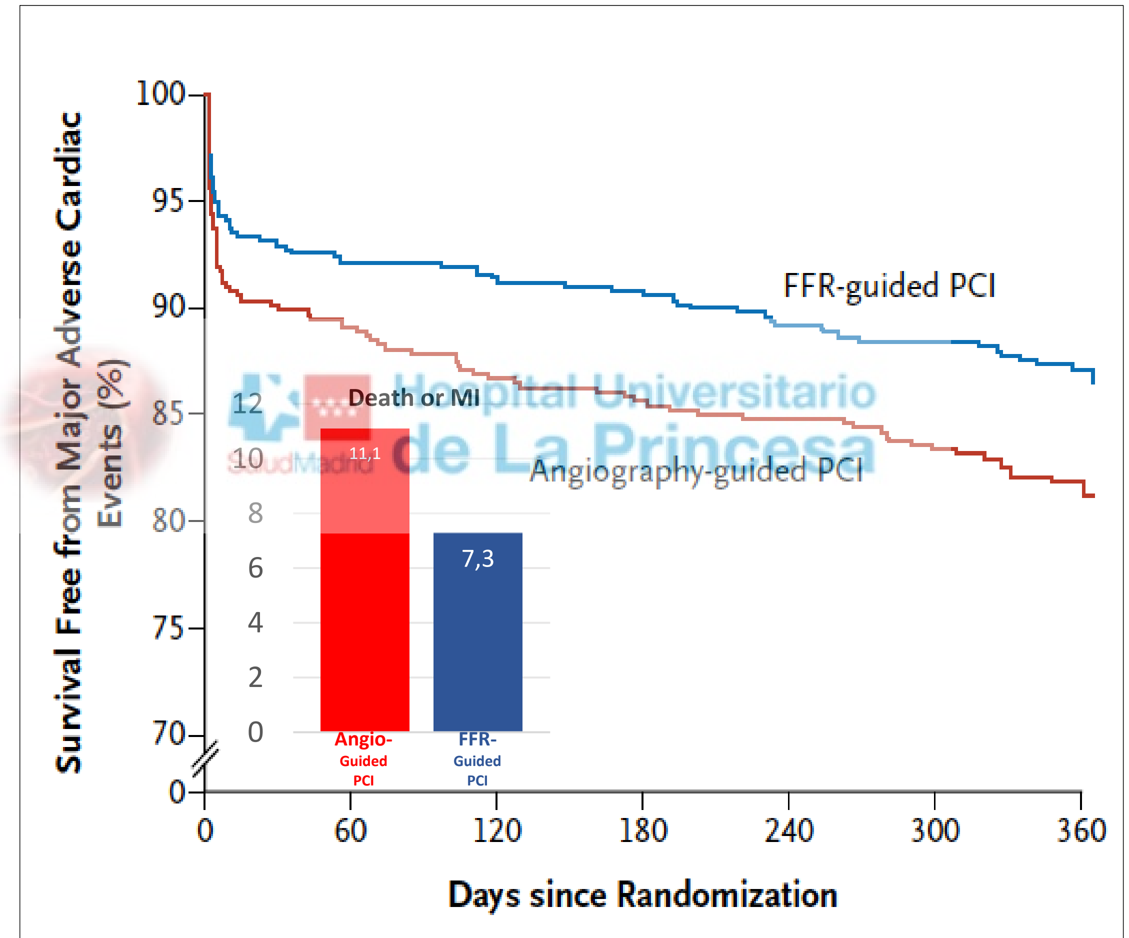
- Concept of FFR-guidance

"FFR B4 U PTCA" *Robert F Wilson, MD*

- Safety of deferring mild stenosis

(AMI in 1/523 deferred lesions at 2 years)



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Tonino PAL, De Bruyne B, NHJ Pijls et al. N Engl J Med 2009

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FIRE Trial

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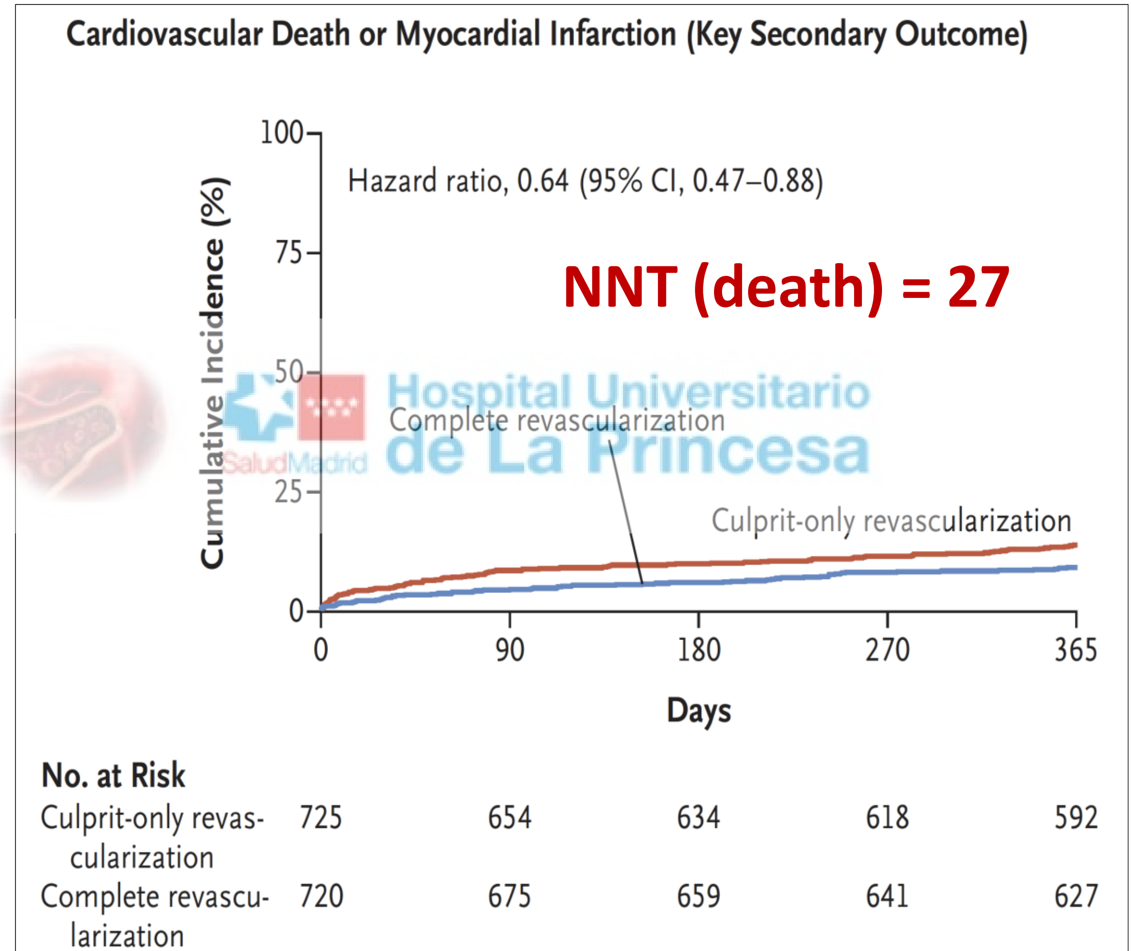
- Physiology-guided revascularization better than culprit only

(in ≥ 75-y-o + AMI + MVD)

"FFR B4 U PTCA" *Robert F Wilson, MD*



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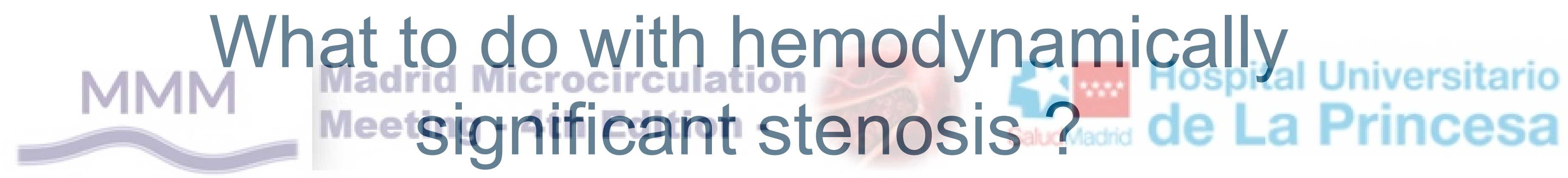
Biscaglia S, Campo G, et al. N Engl J Med 2023

What to do with hemodynamically significant stenosis ?



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From FAME to ORBITA 2

FAME

FAME 2

FAME 3

ORBITA2

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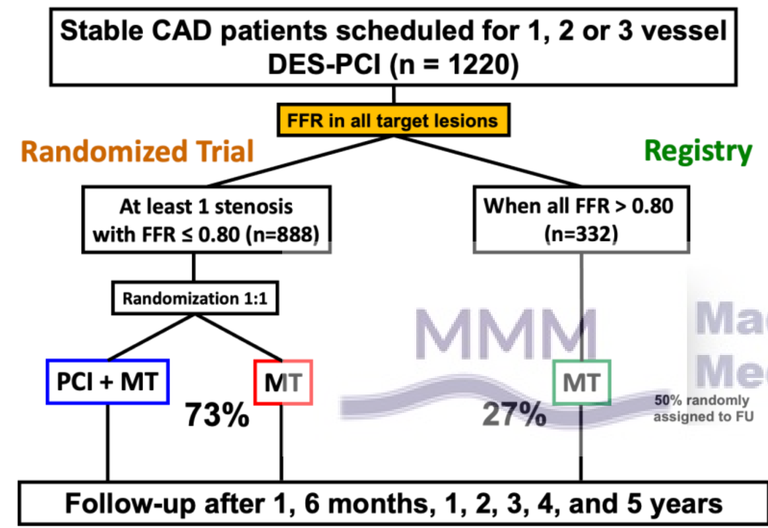

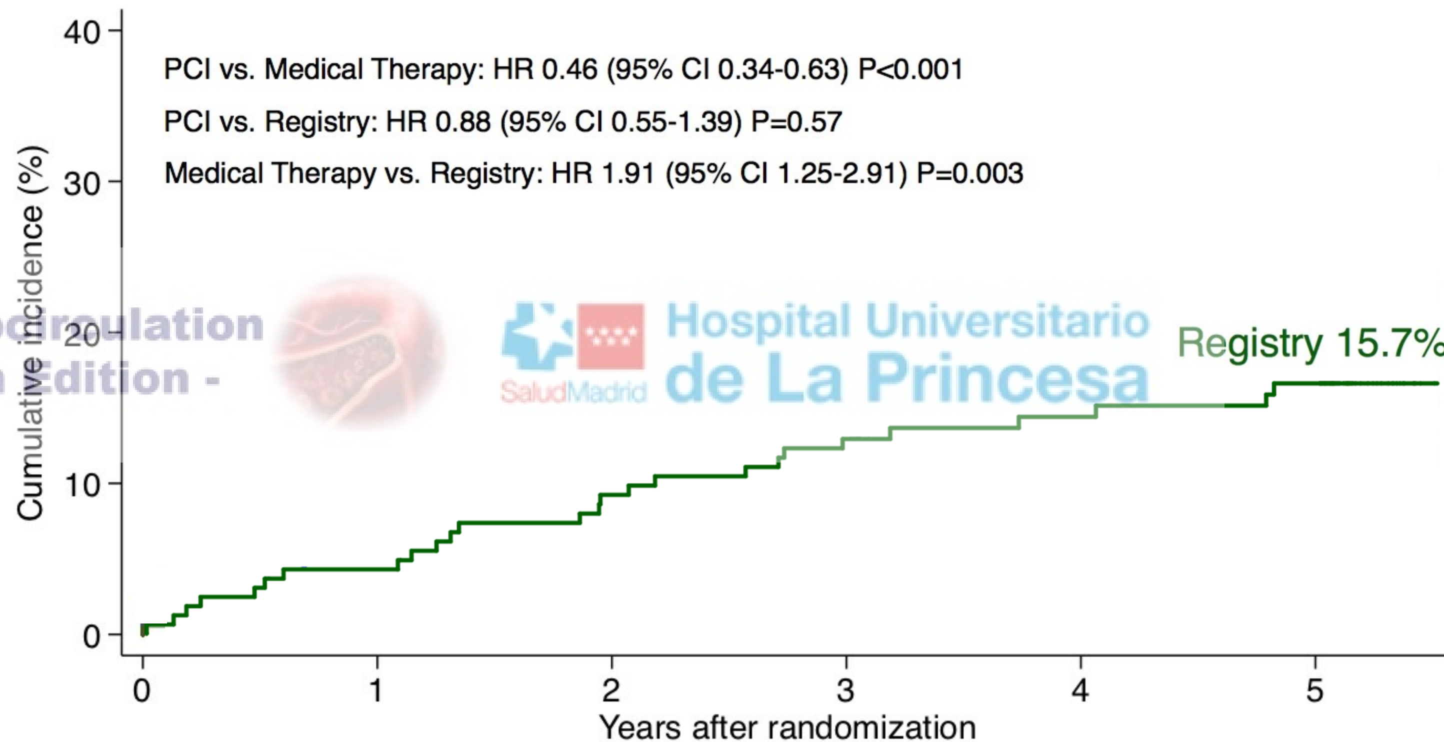

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No. at risk	0	1	2	3	4	5
Medical Therapy	441	360	349	337	271	258
PCI	447	416	403	391	334	321
Registry	166	156	147	141	116	113

De Bruyne B, Pijls NHJ, Fearon WJ et al. NEJM 2012
De Bruyne B, Fearon WF, Jüni P, et al. NEJM 2009
Xaplanteris P, Fournier S, De Bruyne B, et al NEJM 2018

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FAME 2

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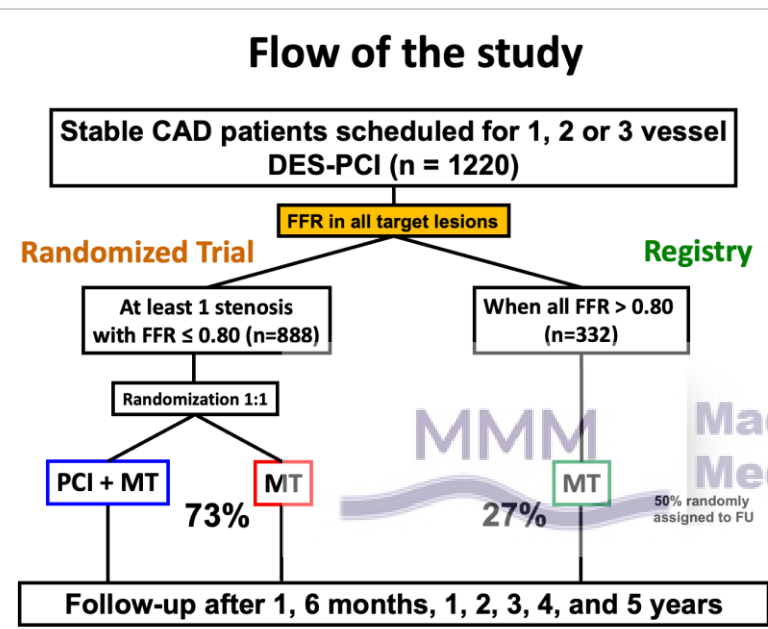

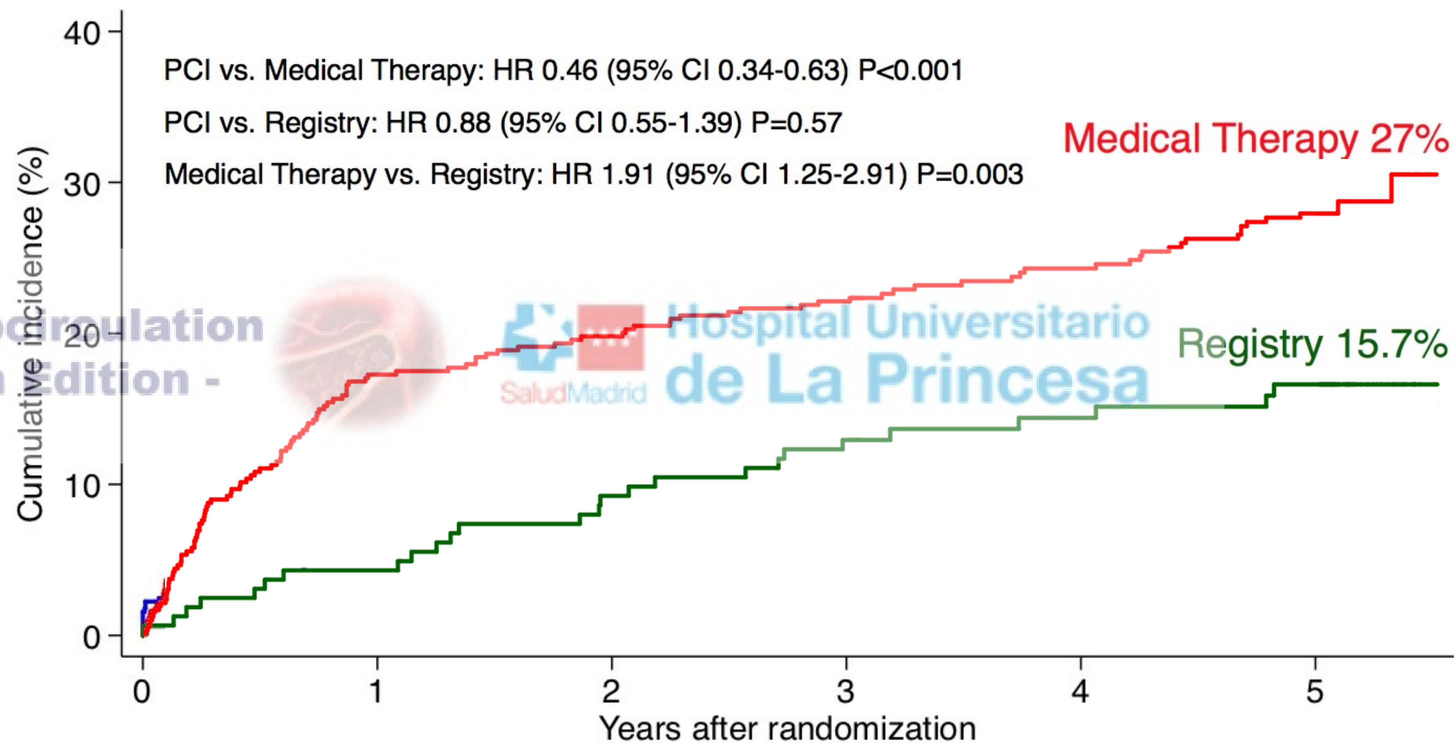

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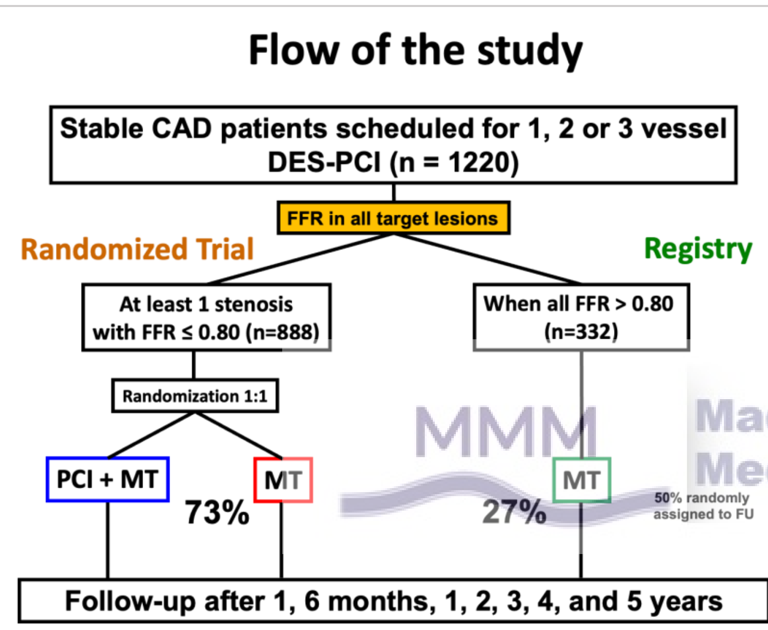
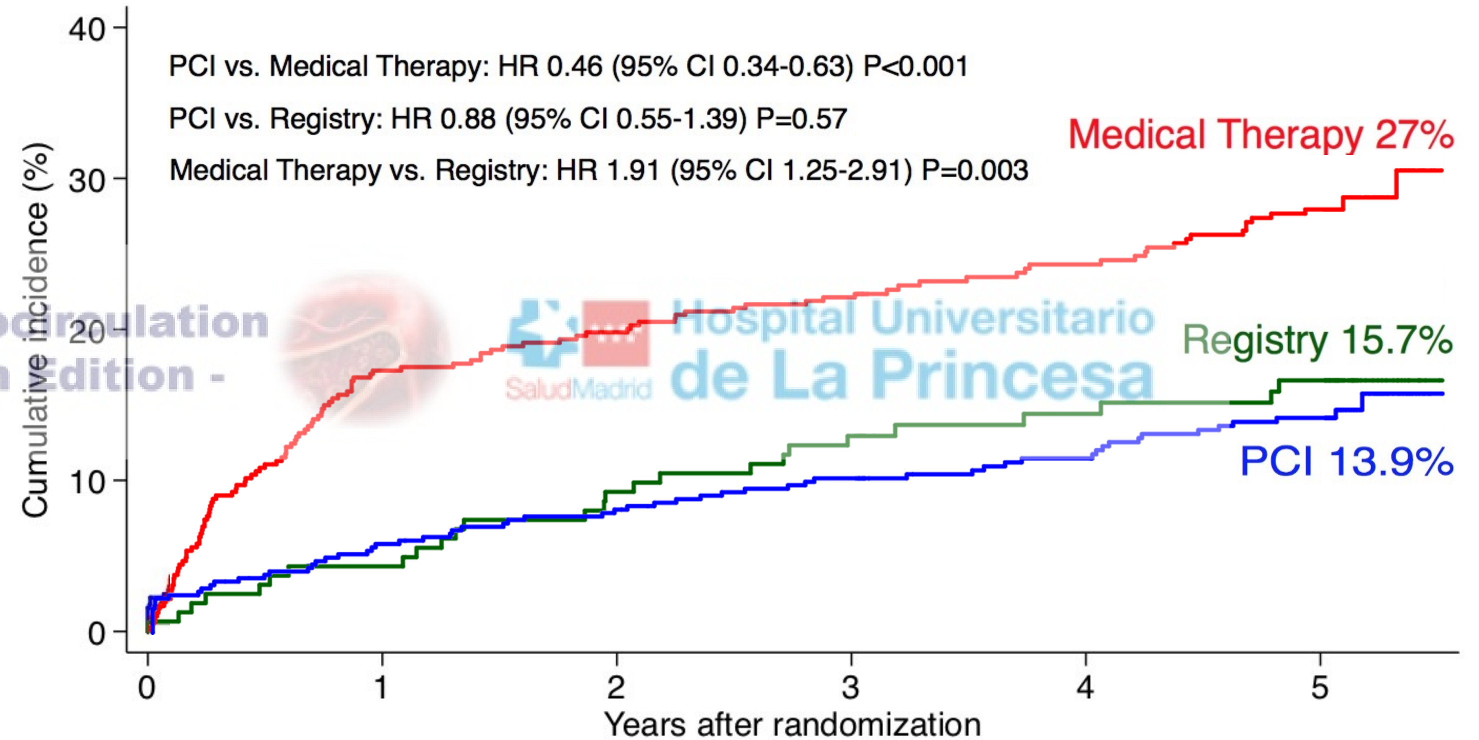
FAME 2





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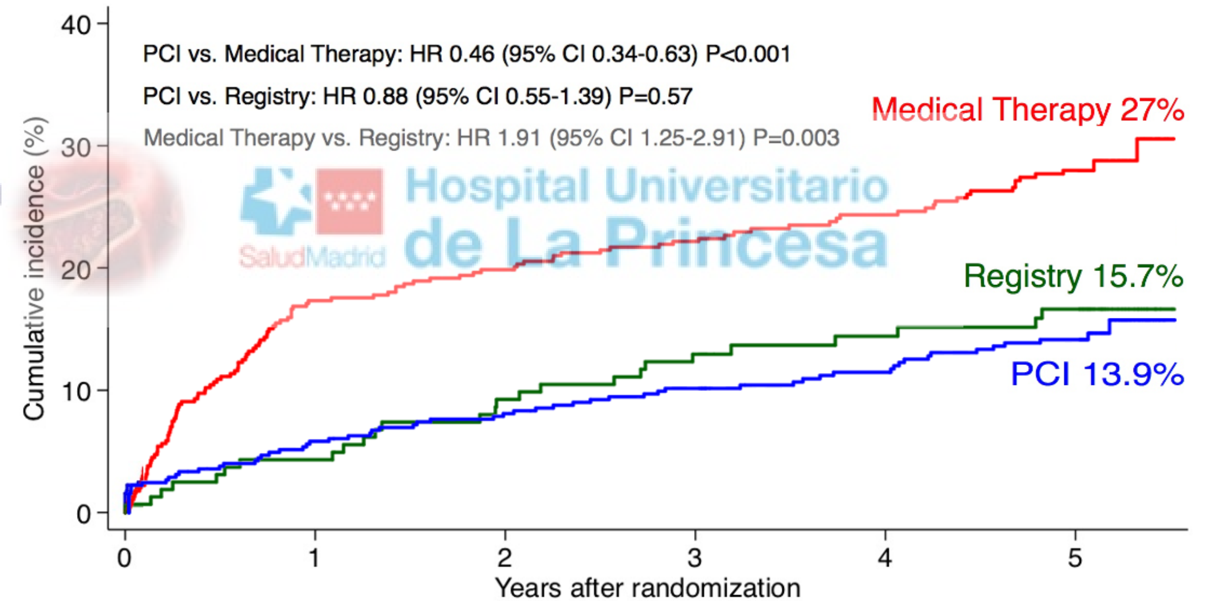
De Bruyne B, Fearon WF, Jüni P, et al. NEJM 2009
Xaplanteris P, Fournier S, De Bruyne B, et al NEJM 2018

FAME 2

- *FFR-guided* PCI is superior to OMT in CCS patients (MACE)
- Safety of deferring mild stenosis
- Only patients with FFR+ lesions
- Ischemia is 'innocent bystander'



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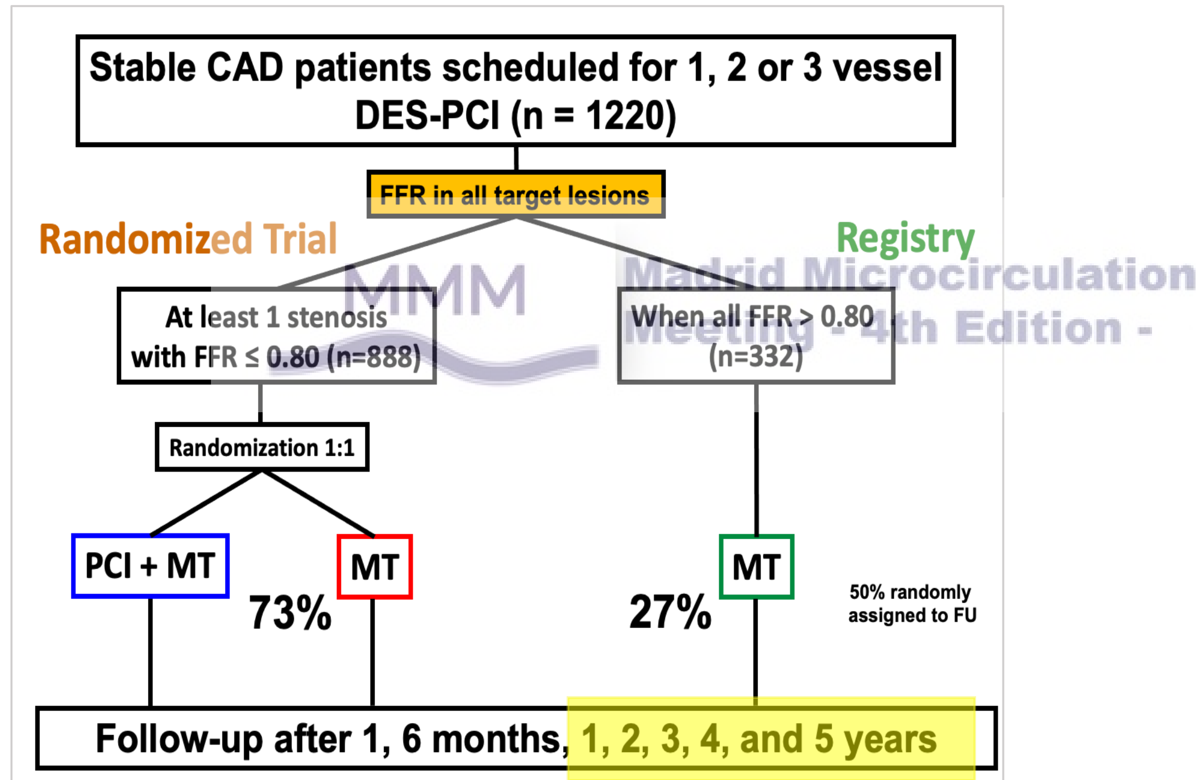
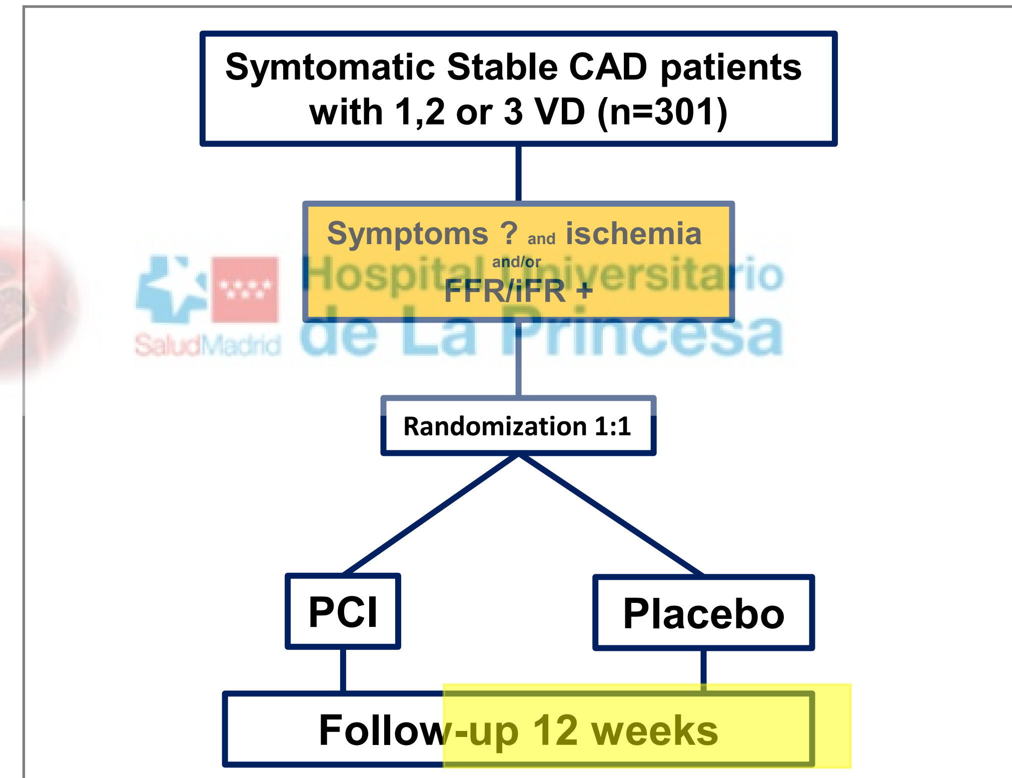
FAME 2



MACE

De Bruyne B, Pijls NHJ, et al NEJM 2012

ORBITA 2



Angina

Rajkumar CA, Al-Lamee RK, et al NEJM 2023, 10.1056/NEJMoa2310610

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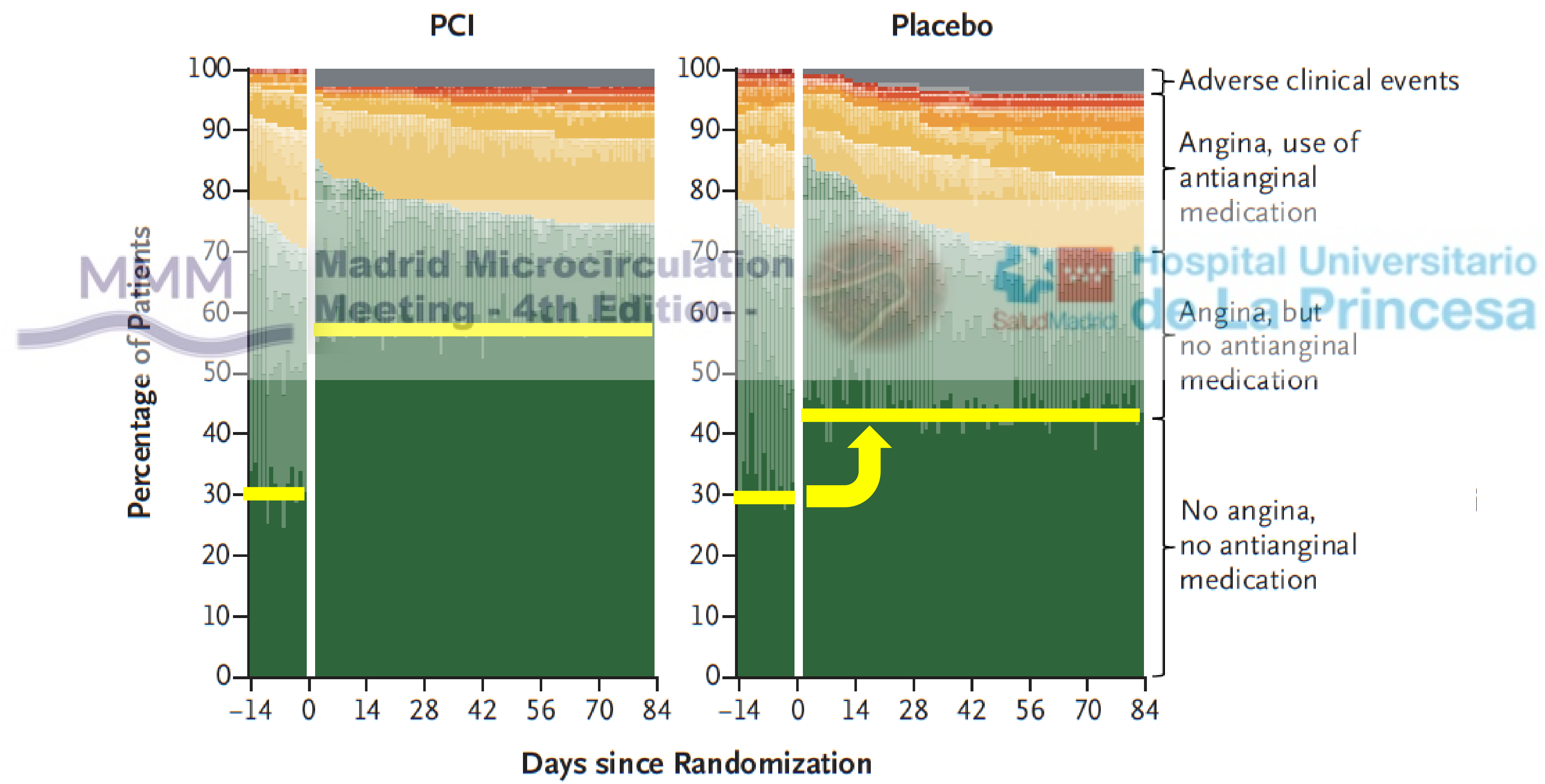

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Rajkumar CA, Al-Lamee RK, et al NEJM 2023, 10.1056/NEJMoa2310610

ORBITA 2

PCI

Placebo

Percentage of Patients

100
90
80
70
60
50
40
30
20
10
0

–14 0 14 28 42 56 70 84

–14 0 14 28 42 56 70 84

Days since Randomization

Adverse clinical events

Angina, use of antianginal medication

Angina, but no antianginal medication

No angina, no antianginal medication

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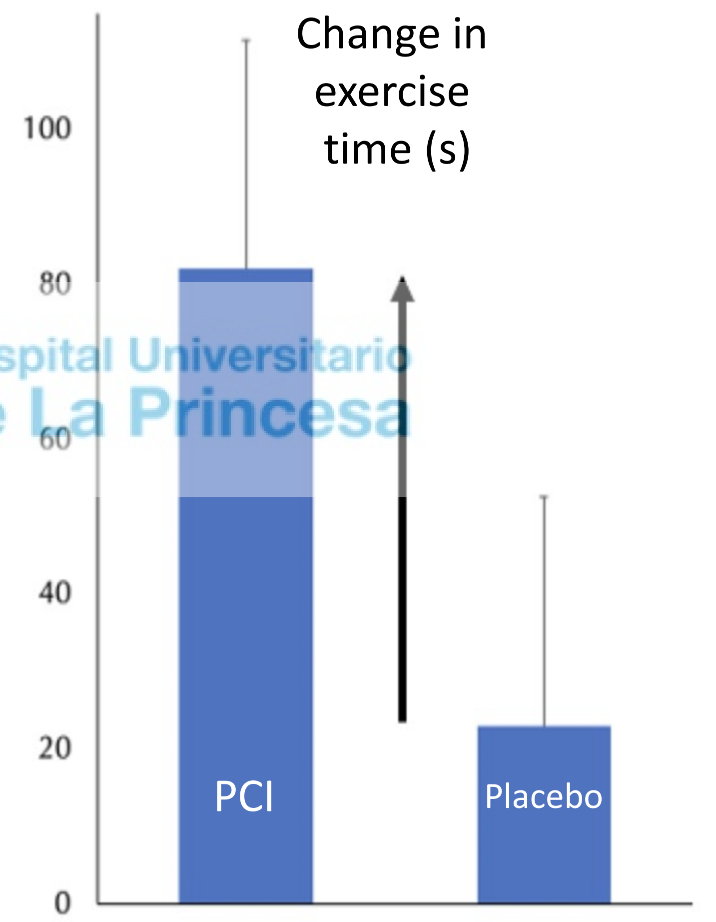

Rajkumar CA, Al-Lamee RK, et al NEJM 2023, 10.1056/NEJMoa2310610

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FAME 2

- *FFR-guided* PCI is superior (MACE) to OMT in CCS patients
- Safety of deferring mild stenosis
- After 5 years

MACE

De Bruyne B, Fearon WF, Jüni P, et al. NEJM 2009
De Bruyne B, Pijls NHJ, Fearon WJ et al. NEJM 2012
Xaplanteris P, Fournier S, De Bruyne B, et al. NEJM 2018

ORBITA 2

- *FFR-guided* PCI is superior (Angina) to ‘nothing’ in CCS pts
- Signal about MACE’s
- After 12 weeks

Angina

Rajkumar CA, Al-Lamee RK, et al NEJM 2023, 10.1056/NEJMoa2310610

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From FAME to ORBITA 2

FAME

FAME 2

FAME 3

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ORBITA2

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CABG versus FFR-guided PCI for 3-VD

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FAME 3

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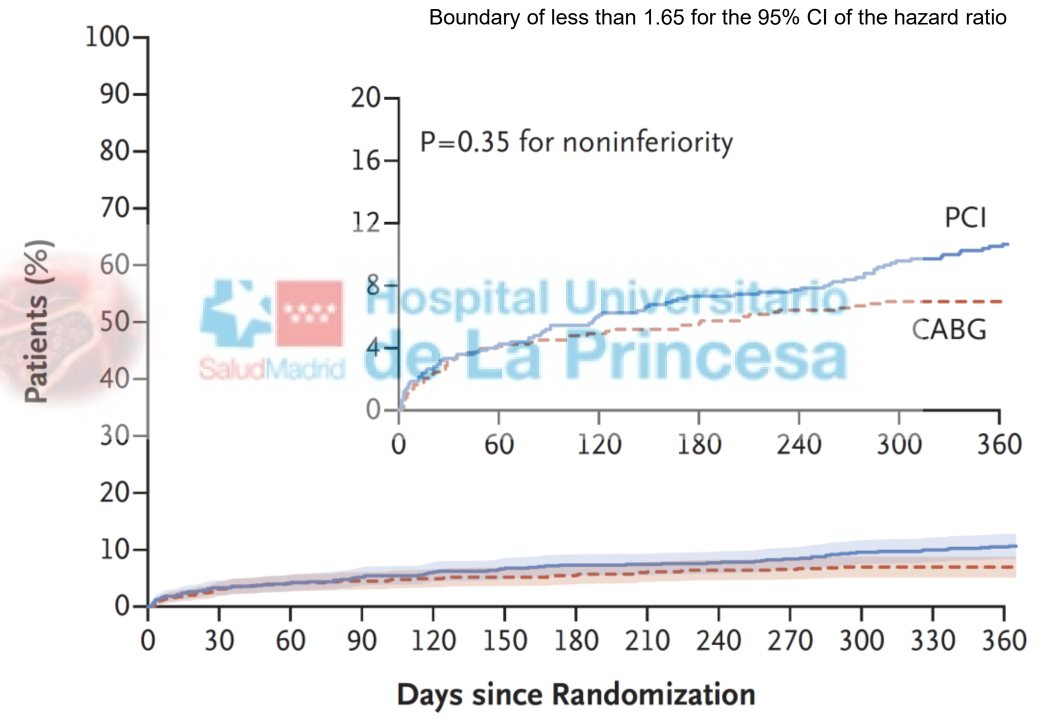
- Overall, in patients with angiographic 3-VD, CABG is superior to FFR-guided PCI



No. at Risk													
PCI	757	728	721	713	707	702	697	696	693	687	678	674	670
CABG	743	709	701	698	695	693	691	686	683	682	679	679	679

Fearon WF, Zimmermann FM, De Bruyne B, et al NEJM 2022

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FAME 3

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Influence of Functional SYNTAX Score (≤22)

- Overall, in patients with angiographic 3-VD, CABG is superior to FFR-guided PCI
- FFR measurements (and functional SYNTAX score) identify 50% of patients in whom PCI and CABG provide similar results

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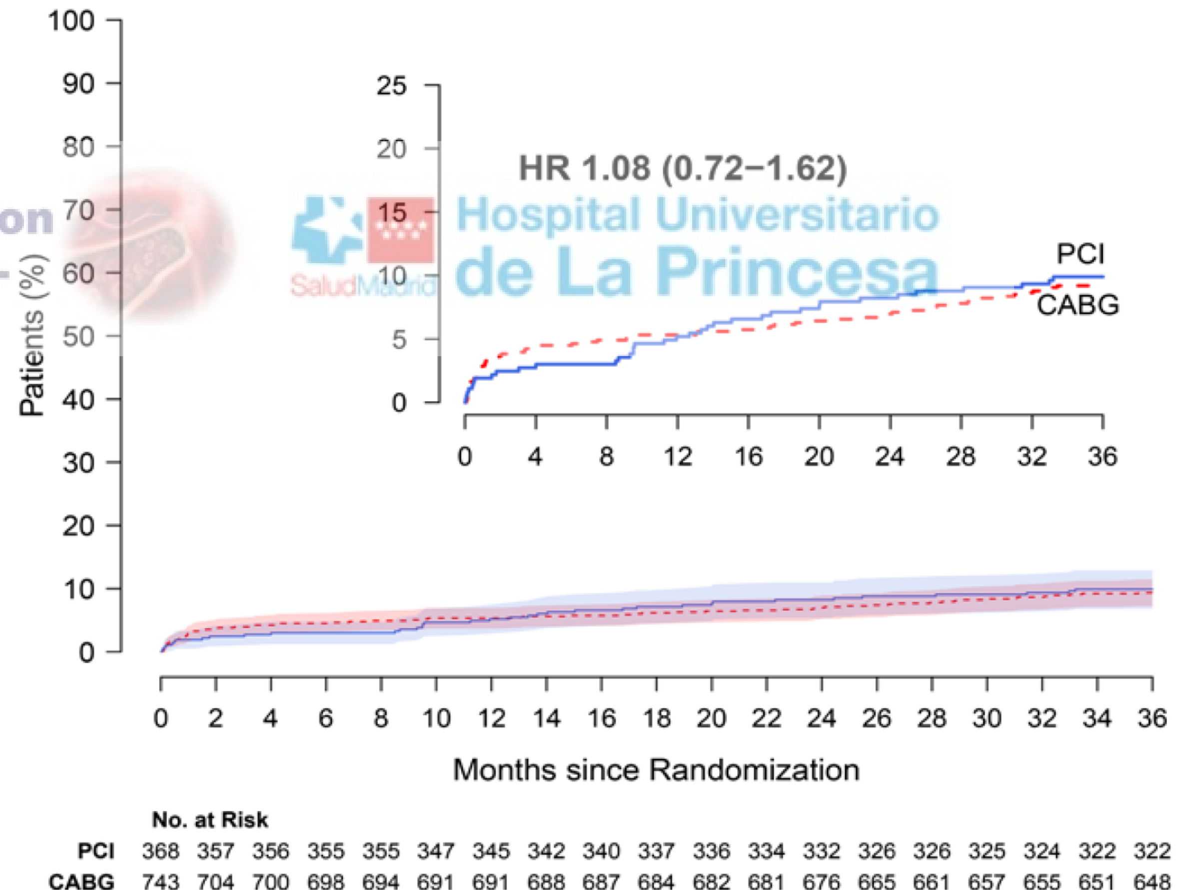

Zimmermann FM, Fearon WF, et al Circulation 2023

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FAME 3

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Influence of diabetes

- Overall, in patients with angiographic 3-VD, CABG is superior to FFR-guided PCI
- FFR measurements (and functional SYNTAX score) identify 50% of patients in whom PCI and CABG provide similar results
- Also in diabetic patients…

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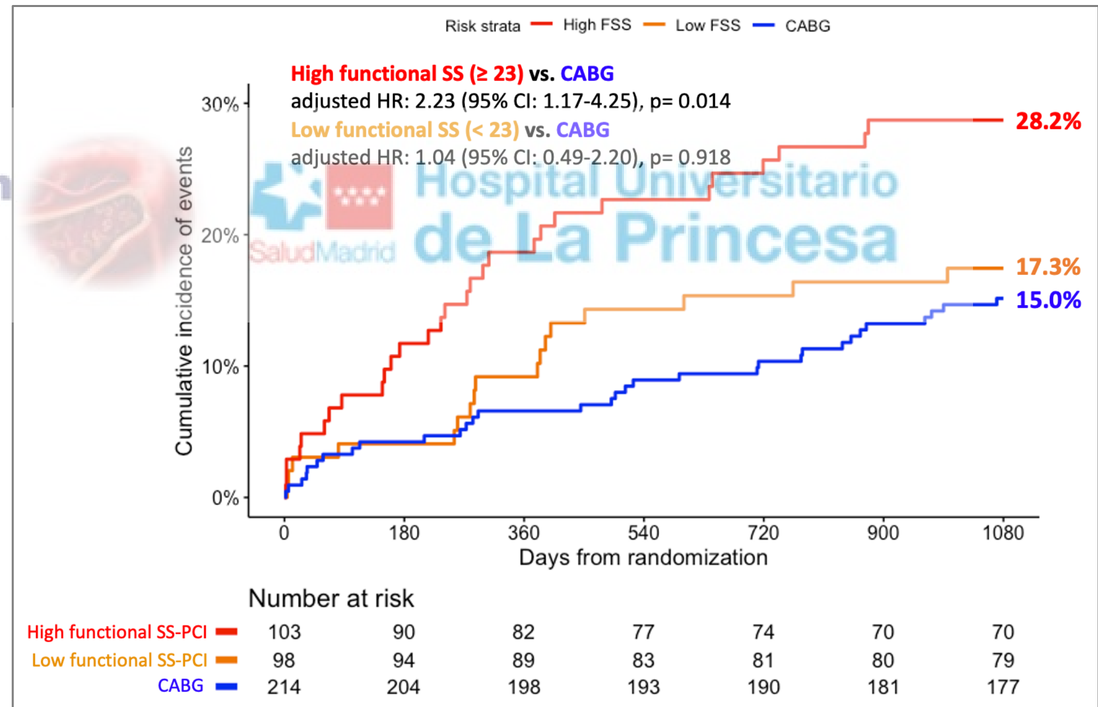

Takahashi K, Fearon WF, et al under review

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FAME 3

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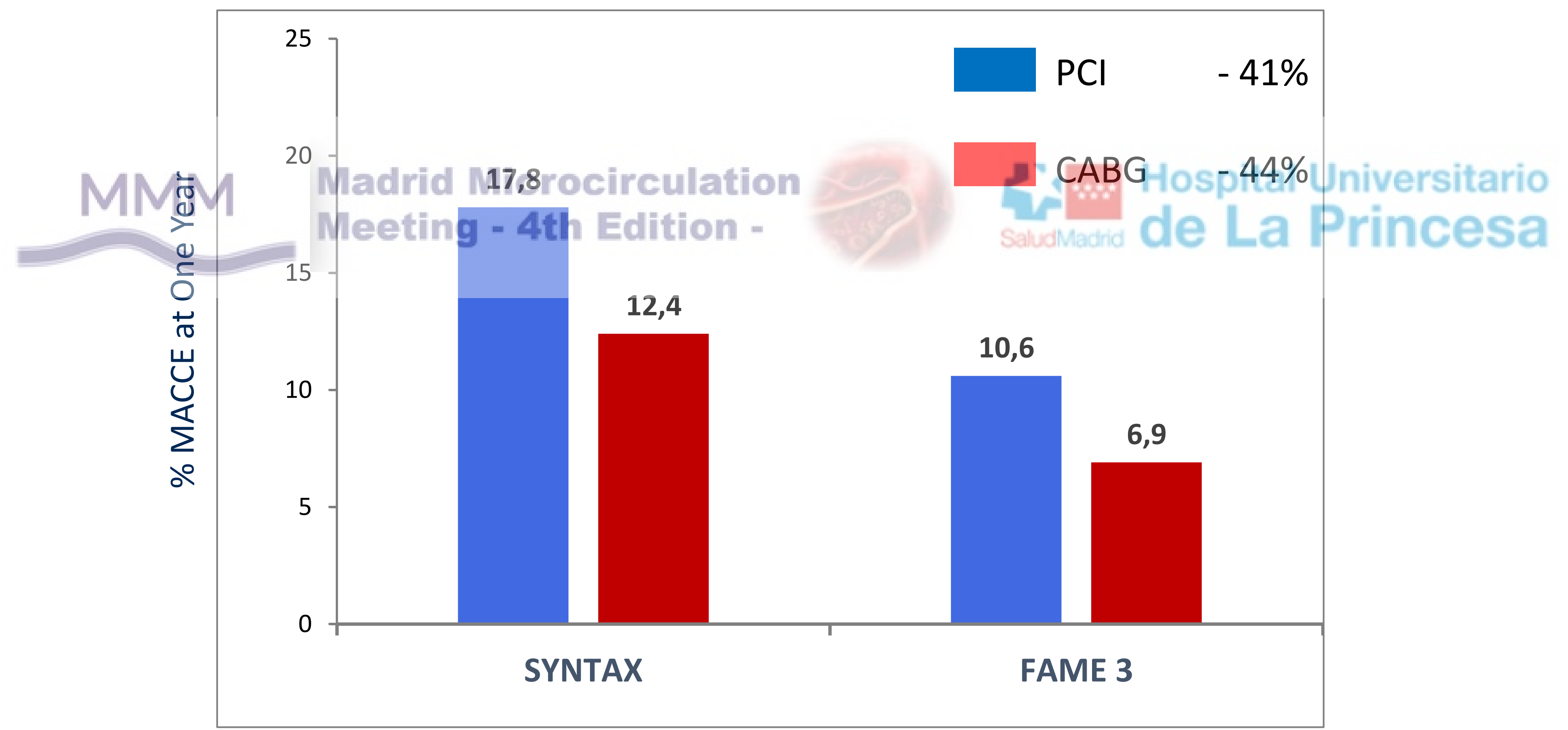

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Serruys PW et al. NEJM 2009
Fearon WF et al. NEJM 2021

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Conclusive Remarks

1. Applied, wire-based, coronary physiology has changed our understanding of CIHD and of its treatment.

2. When performed in a standardized manner, these measurements are safe, simple, largely operator independent, accurate, and precise.

3. Imaging-derived physiology should not come at the cost of accuracy and precision.

4. Epicardial disease is only part of the problem

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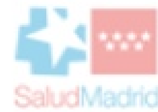

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