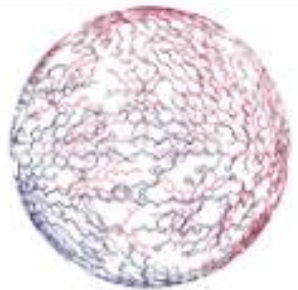


Percutaneous coronary intervention in acute coronary syndrome should be physiology-guided:

PRO

Gianluca Campo

University Hospital of Ferrara



ESC CONGRESS
2026 MUNICH



Visit us <https://elementrials.org>

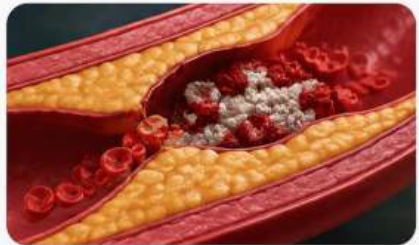
Background

- **ACS (STEMI + NSTEMI) represents the largest part of contemporary PCI practice**
- **Patients are older and more complex. Frailty, comorbidities and bleeding risk increasingly shape decisions**
- **Multivessel disease is frequent. In 50–70% of ACS patients, the culprit is only part of the story**

The drawback - Unclear culprit lesion

Physiology measures flow limitation, not plaque instability.

FAMOUS-NSTEMI: in the FFR arm, 4 of 10 spontaneous MACE occurred after initially planned culprit-vessel PCI was deferred based on $\text{FFR} > 0.80$.



- 1 **Microvascular dysfunction**
Flow indices may be unreliable in the acute culprit territory.
- 2 **Plaque instability**
Rupture, erosion or thrombus may be active even without severe flow limitation.



2023 ESC Guidelines for the management of acute coronary syndromes

Invasive epicardial functional assessment of non-culprit segments of the IRA is not recommended during the index procedure.

III

C

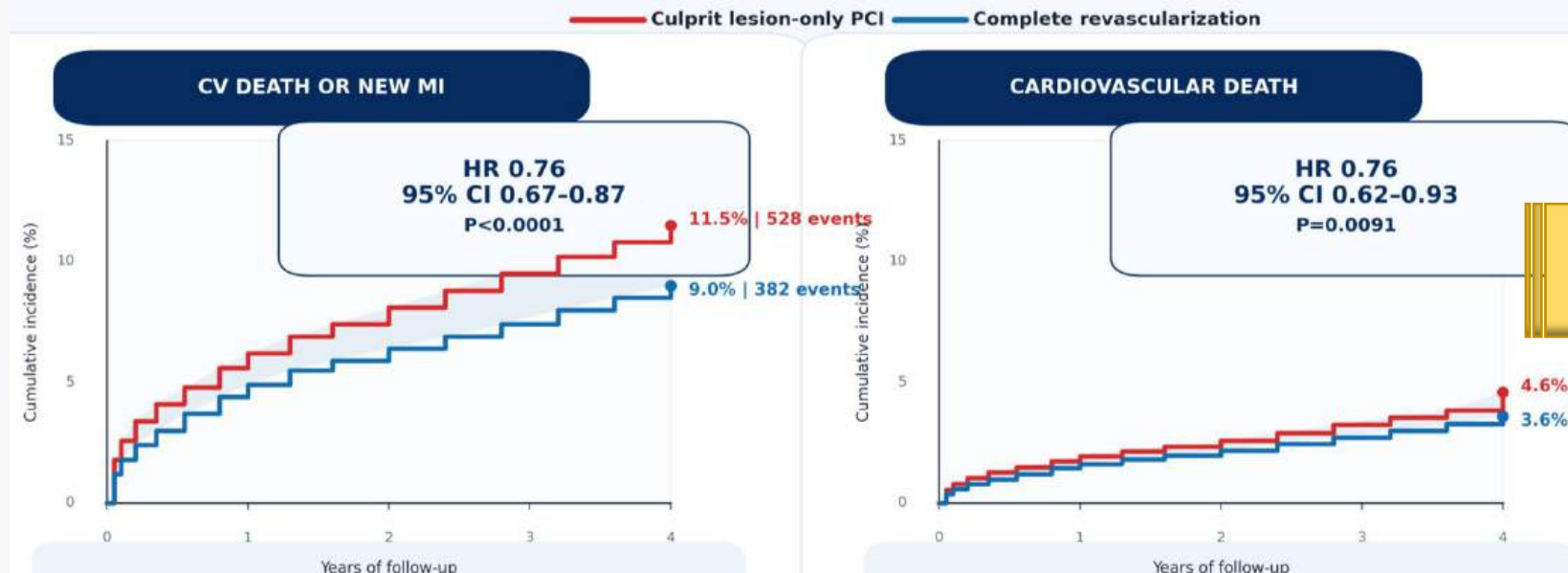
Invasive epicardial functional assessment of ~~non-culprit segments of~~ the IRA is not recommended during the index procedure.

III

A

Multivessel Disease

In multivessel disease, complete revascularization is strongly evidence-based



8836 STEMI patients from 6 RCTs complete vs culprit-only revasc
Complete revasc was in 50% of the cases angio-guided, the other 50% was physio-guided



Multivessel disease in haemodynamically stable STEMI patients undergoing PPCI

Complete revascularization is recommended either during the index PCI procedure or within 45 days.^{508-511,531}

I

A

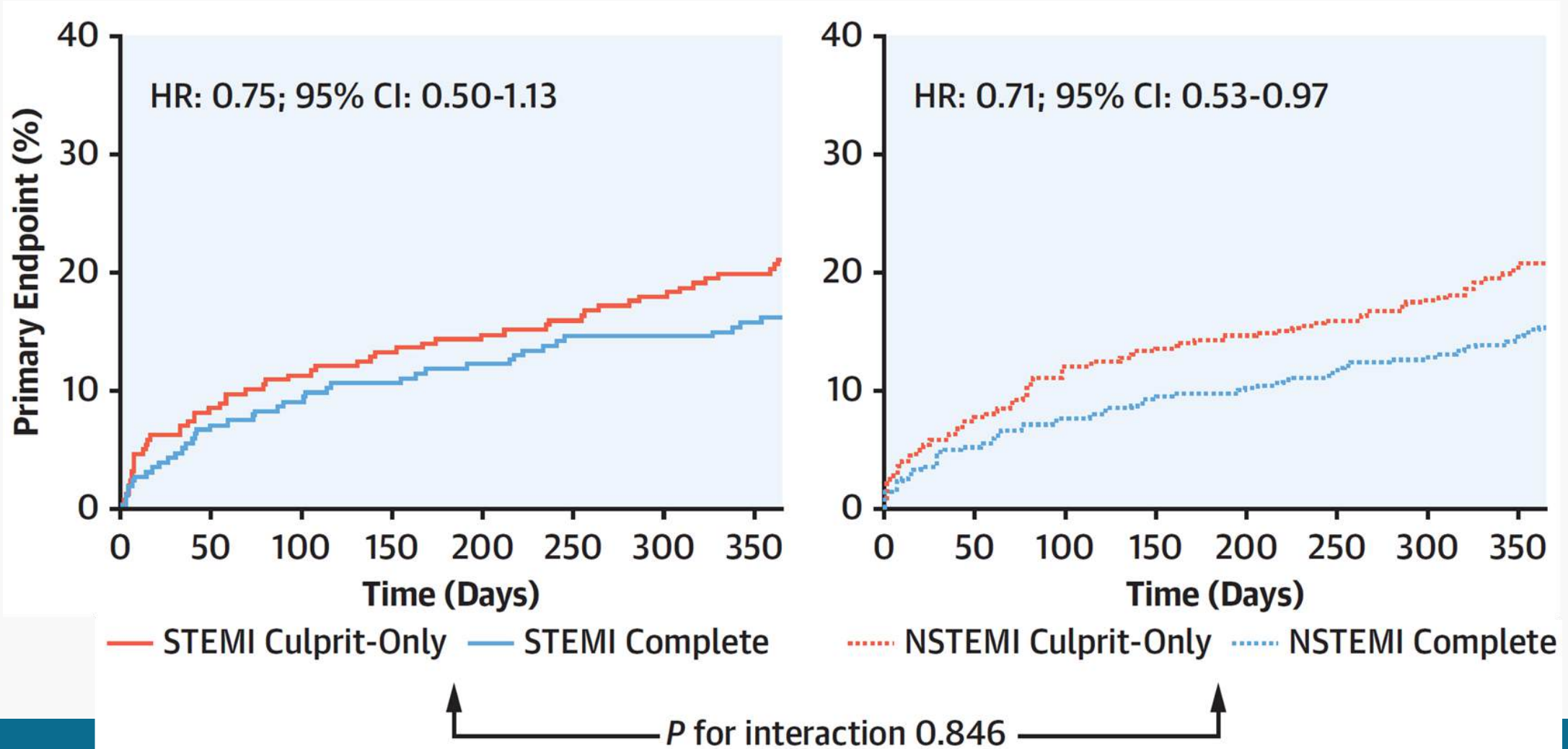


Recommendations for Management of Multivessel CAD in STEMI
Referenced studies that support recommendations are summarized in the Evidence Table.

COR	LOE	Recommendations
1	A	1. In selected, hemodynamically stable patients with STEMI and multivessel disease (MVD), after successful PCI of the infarct-related artery, PCI of significantly stenosed* noninfarct-related arteries is recommended to reduce the risk of death or MI and improve angina-related quality of life (QOL).† ¹⁻⁹

STEMI vs. NSTEMI: no difference

Complete revascularization works in both clinical settings



Nonculprit lesions

How to select non-culprit lesions remains the key debate.

PHYSIOLOGY OR ANGIOGRAPHY?

LET'S EXPLORE



PHYSIOLOGY-GUIDED
Function first



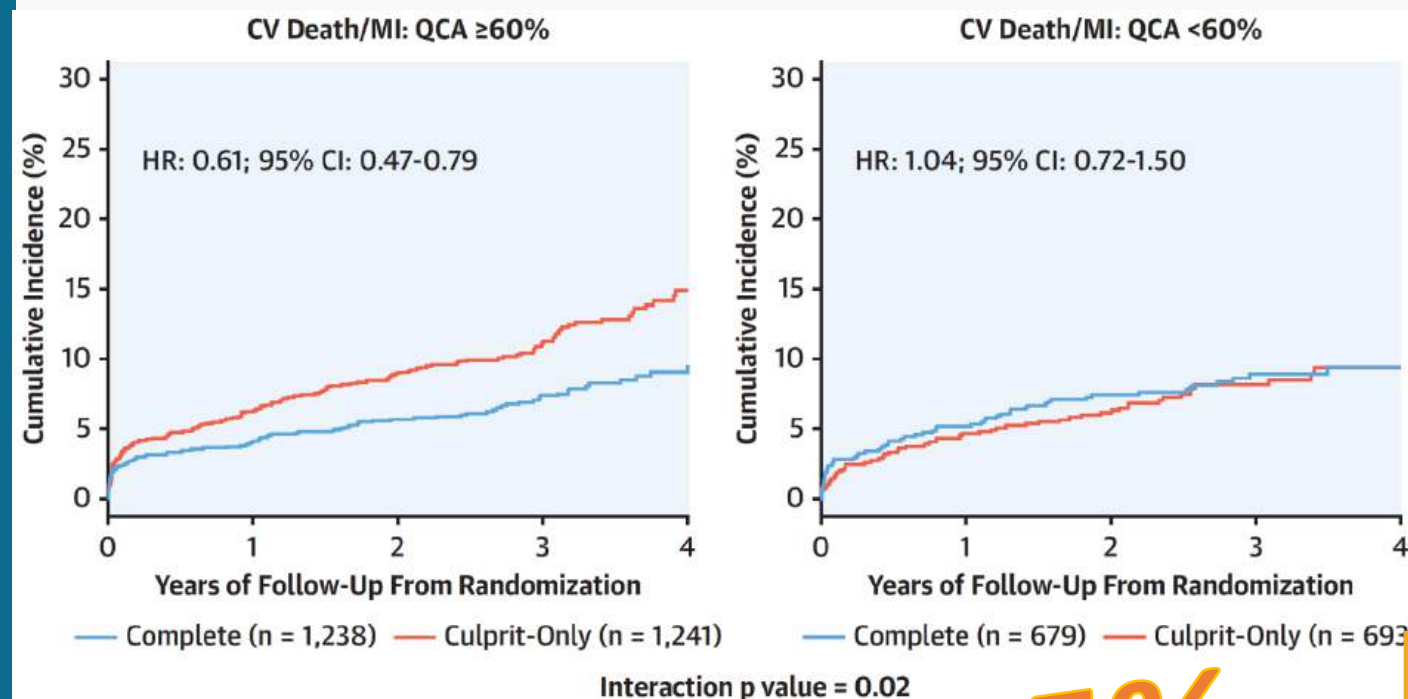
ANGIOGRAPHY-GUIDED
Anatomy first



The Achilles' heel of angio-guided

Angio-guided complete revasc is effective but associated with overtreatment.

Some lesions are treated without benefit, exposing patients to unnecessary events.



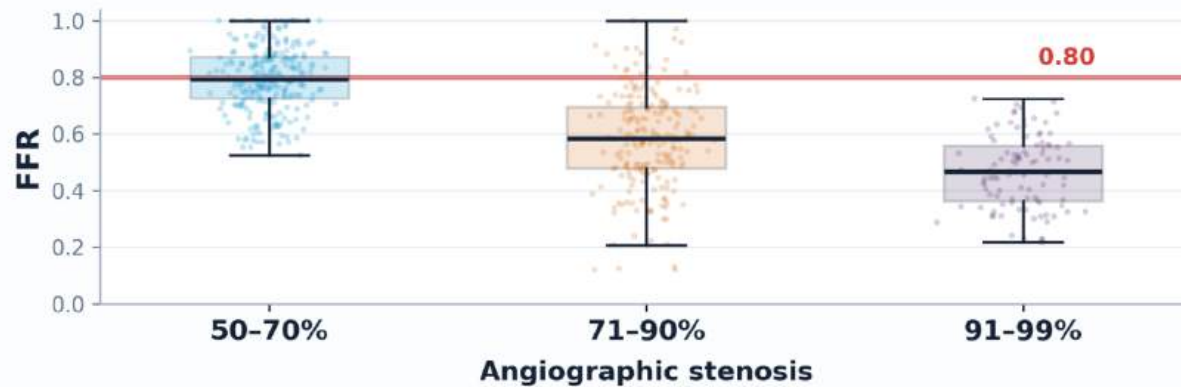
Subgroup	Complete no. of events/total no. (% per person-yr)	Culprit Only no. of events/total no. (% per person-yr)	Hazard Ratio (95% CI)	p Value for Interaction
Co-Primary outcomes				
Cardiovascular death or MI				0.02
QCA $\geq 60\%$	94/1,238 (2.5)	151/1,241 (4.2)	0.61 (0.47-0.79)	
QCA $< 60\%$	57/679 (3.0)	56/693 (2.9)	1.04 (0.72-1.50)	
Other secondary outcomes				
MI				0.02
QCA $\geq 60\%$	65/1,238 (1.8)	114/1,241 (3.2)	0.56 (0.41-0.76)	
QCA $< 60\%$	42/679 (2.2)	41/693 (2.1)	1.04 (0.68-1.61)	
Other outcomes				
Stroke				0.32
QCA $\geq 60\%$	23/1,238 (0.6)	22/1,241 (0.6)	1.05 (0.58-1.88)	
QCA $< 60\%$	11/679 (0.6)	6/693 (0.3)	1.86 (0.69-5.04)	
NYHA functional class IV HF				0.02
QCA $\geq 60\%$	35/1,238 (0.9)	46/1,241 (1.2)	0.76 (0.49-1.18)	
QCA $< 60\%$	21/679 (1.1)	10/693 (0.5)	2.14 (1.01-4.55)	
Stent thrombosis				0.03
QCA $\geq 60\%$	15/1,238 (0.4)	16/1,241 (0.4)	0.94 (0.46-1.90)	
QCA $< 60\%$	10/679 (0.5)	2/693 (0.1)	5.12 (1.12-23.40)	

35%

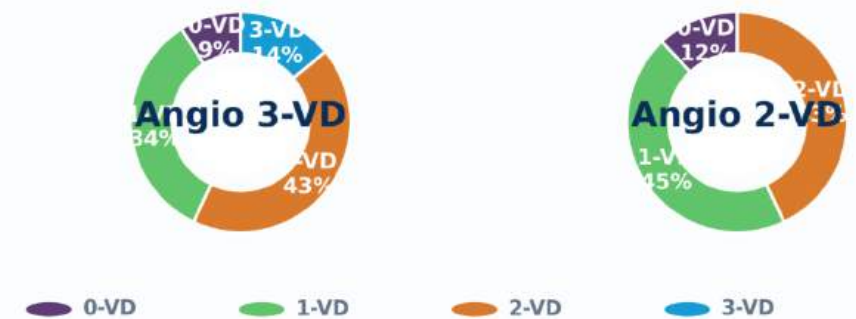
The Achilles' heel of angio-guided

Visual assessment of diameter stenosis fails in the discrimination of flow-limiting coronary lesions

Wide FFR range within each angiographic class



Anatomical MVD reclassified by physiology



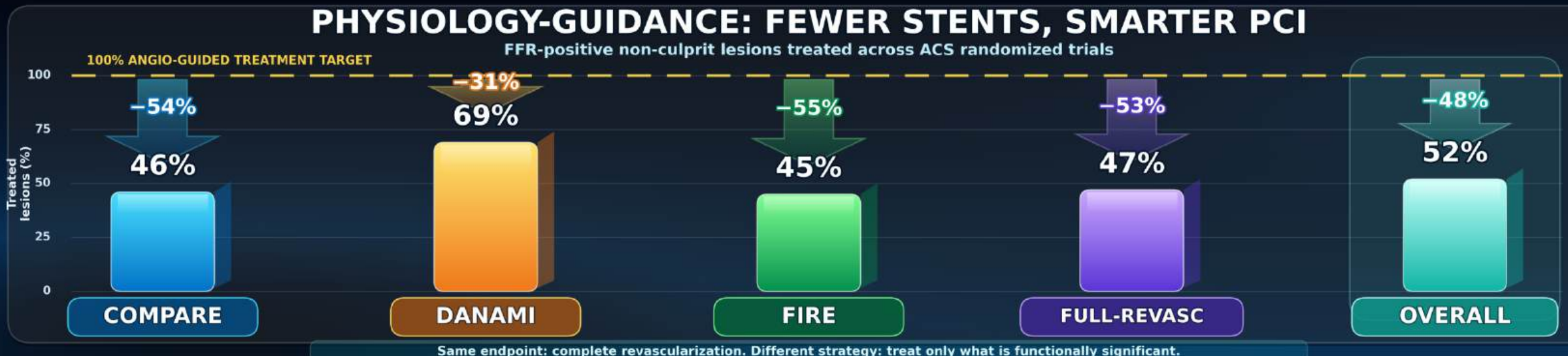
A lesion may look severe without being ischemic — and multivessel disease may not be functionally multivessel.

Physio-guided cuts overtreatment

Physiology makes complete revascularization more selective.

Selective PCI means fewer unnecessary stents.

Despite doing less, physiology-guided PCI does better than culprit-only PCI.



Is physiology better than angio?

FLOWER MI

STUDY

n=1163
STEMI + MVD

41
sites

586
FFR arm

577
Angio arm

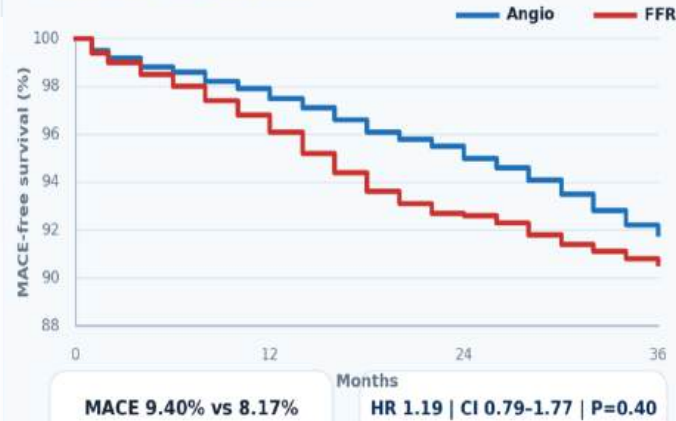
Procedural feature

>95% staged non-culprit PCI
FFR used as treatment gatekeeper

PCI INTENSITY



PRIMARY ENDPOINT



- Low rate of AEs
- 95% staged procedure
- 50% of staged procedure w/o revasc

FRAME AMI

MODERN AMI POPULATION

n=562
AMI + MVD

14
Korean sites

47.2%
STEMI

52.8%
NSTEMI

TIMING



~~60-65% physiology in the index setting
more aligned with contemporary ACS workflow

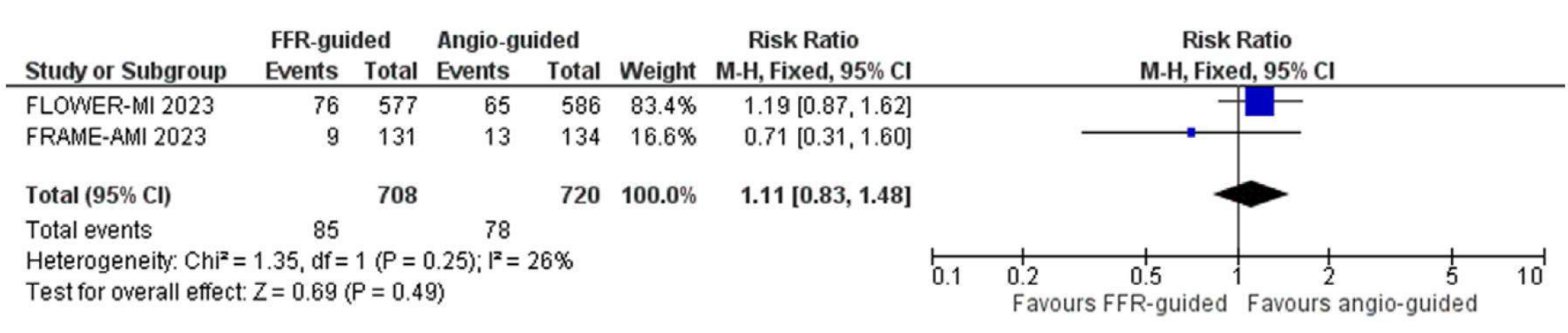
SELECTIVE PCI



PRIMARY ENDPOINT



Is physiology better than angio?



- Same outcomes. Fewer procedures and stents.
- Could outcomes improve if physiology is used at its full potential?

(index procedure, PCI planning, disease pattern definition)

Functional Coronary Angiography to Indicate and Guide Revascularization in STEMI Patients with Multivessel Disease



The AIR-STEMI trial

ORIGINAL ARTICLE

Complete Revascularization Guided by Functional Coronary Angiography in STEMI

S. Biscaglia,¹ A. Erriquez,¹ I. Colaioni,² A. Hakeem,³ F. Mantovani,⁴ M. Menozzi,⁵ M. Barbierato,⁶ M. Ariotti,⁷ G. Bugani,⁸ R. Scarsini,⁹ D. D'Amario,¹⁰ L. Donazzan,¹¹ A. Polimeni,¹² M. Giordan,¹³ G. Benatti,¹⁴ G. Venturi,¹⁵ M. Ruozzi,¹⁶ F. Moretti,¹⁷ A. Monello,¹⁸ E. Moscarella,¹⁹ F. Versaci,² J.A. Shah,³ V. Guiducci,⁴ C. Cavazza,⁵ F. Gallo,⁶ A. Rubboli,⁷ M. Borgi,² A.A. Lakho,³ A. Capecchi,⁸ V. Lanzilotti,⁸ F. Ottani,⁵ G. Casella,⁸ A.M. Leone,²⁰ M. Tebaldi,²¹ R. Pavasini,¹ R. Piccolo,²² J. Farina,¹ D. Martella,²³ and G. Campo,¹ for the AIR-STEMI Trial Investigators*

Organization

Investigator-initiated, multicenter, prospective, superiority, randomized trial

Countries: Italy



Pakistan



21 centers

Study PI:

Simone Biscaglia



Study Chair:

Gianluca Campo



Executive Committee: Abdul Hakeem, Giulia Bugani, Francesca Mantovani, Giampaolo Niccoli, Iginio Colaiori, Elisabetta Moscarella, Rocco Vergallo, Alberto Polimeni, Domenico D'Amario, Giulia Masiero

CEC:

Rita Pavasini, Raffaele Piccolo



DSMB:

Matteo Tebaldi, Antonio M. Leone



Core Lab:

Andrea Erriquez



ARO (University Hospital of Ferrara):



Veronica Lodolini, Alice Santoni, Martina Viola,
Elisa Mosele, Chiara Manzalini

Stats: Donato Martella



Sponsor:



SERVIZIO SANITARIO REGIONALE
EMILIA-ROMAGNA
Azienda Ospedaliero - Universitaria di Ferrara

Supporters:



Ricerca Finalizzata 2021
GR-2021-12372516



Università
degli Studi
di Ferrara



Study Design

Inclusion criteria

- **STEMI**
- **MVD**
- **Successful PPCI**

Pts hospitalized for STEMI with indication to primary PCI

Multivessel disease at coronary artery angiography

Culprit lesion clearly identifiable and successfully treated

Exclusion criteria

- ⊙ **Culprit unclear**
- ⊙ **Prior CABG**
- ⊙ **LM as nonculprit**
- ⊙ **Life exp <1 year**

R

Physiology-guided Complete Revascularization

Angiography-guided Complete Revascularization

BP-SES Supraflex Cruz recommended

Primary endpoint: median follow-up 17.9 months (IQR 12-24 months)

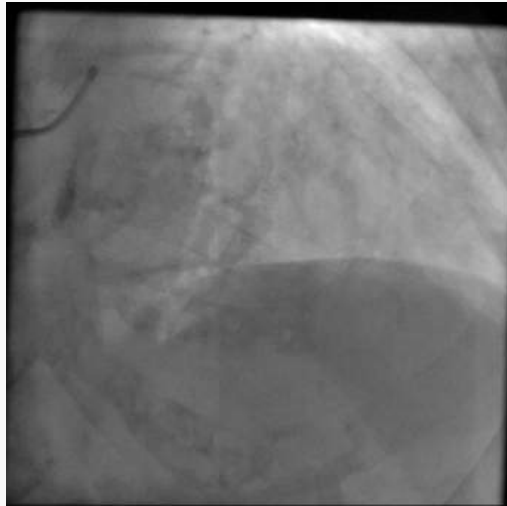
Sample Size

We estimated that **9% of patients in the angiography group** would experience a primary outcome event. Assuming a **relative risk reduction of 35% with the physiology-guided strategy**, we calculated that a sample of 1718 patients would provide 80% power to detect a significant between-group difference at a two-sided alpha level of 0.05. To account for an anticipated 5% attrition rate, the **target sample size was increased to at least 1800 patients**

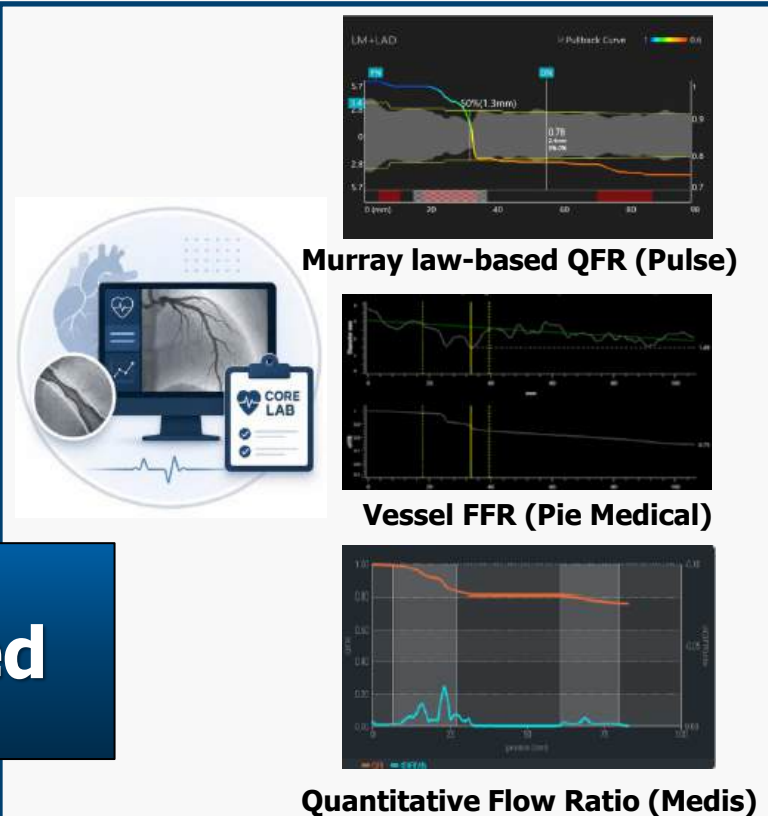
Functional Coronary Angiography

Angiography-guided

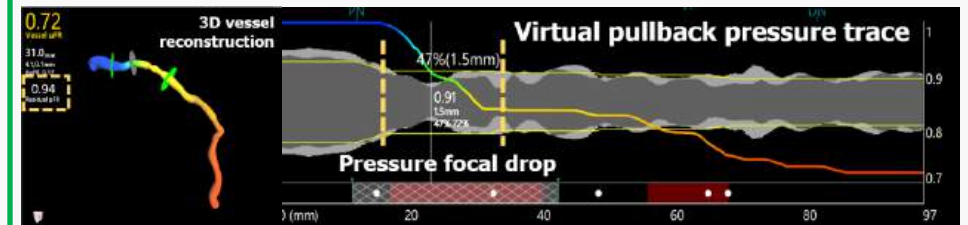
- PCI of all nonculprit lesions with %DS $\geq 50\%$
- During the index or staged procedure (index hospitalization)



Central Core Lab – Functional Coronary Angiography



Positive angio-derived FFR $\rightarrow$ PCI



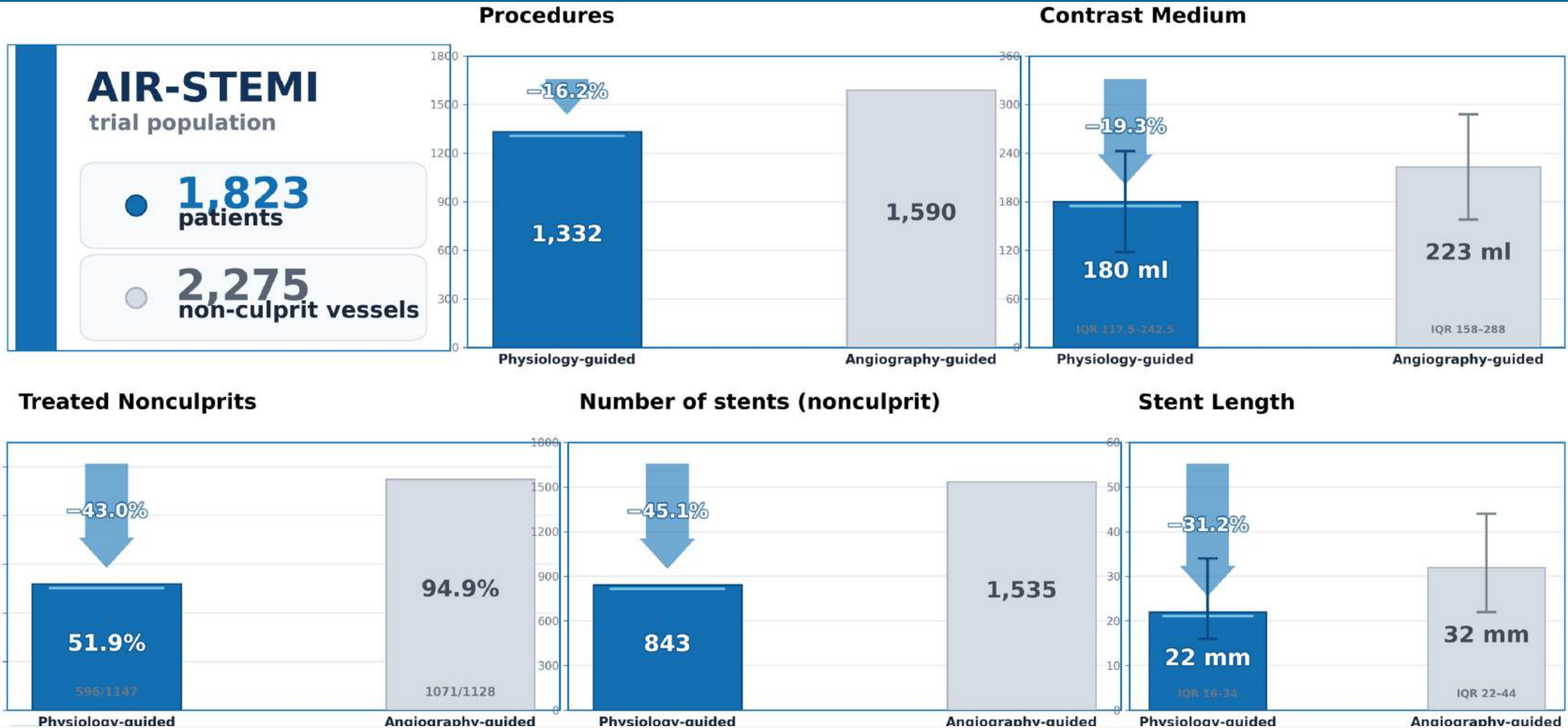
- Distal single point FFR value
- Longitudinal pattern of disease
- Procedural plan / treatment indication

Negative angio-derived FFR $\rightarrow$ OMT



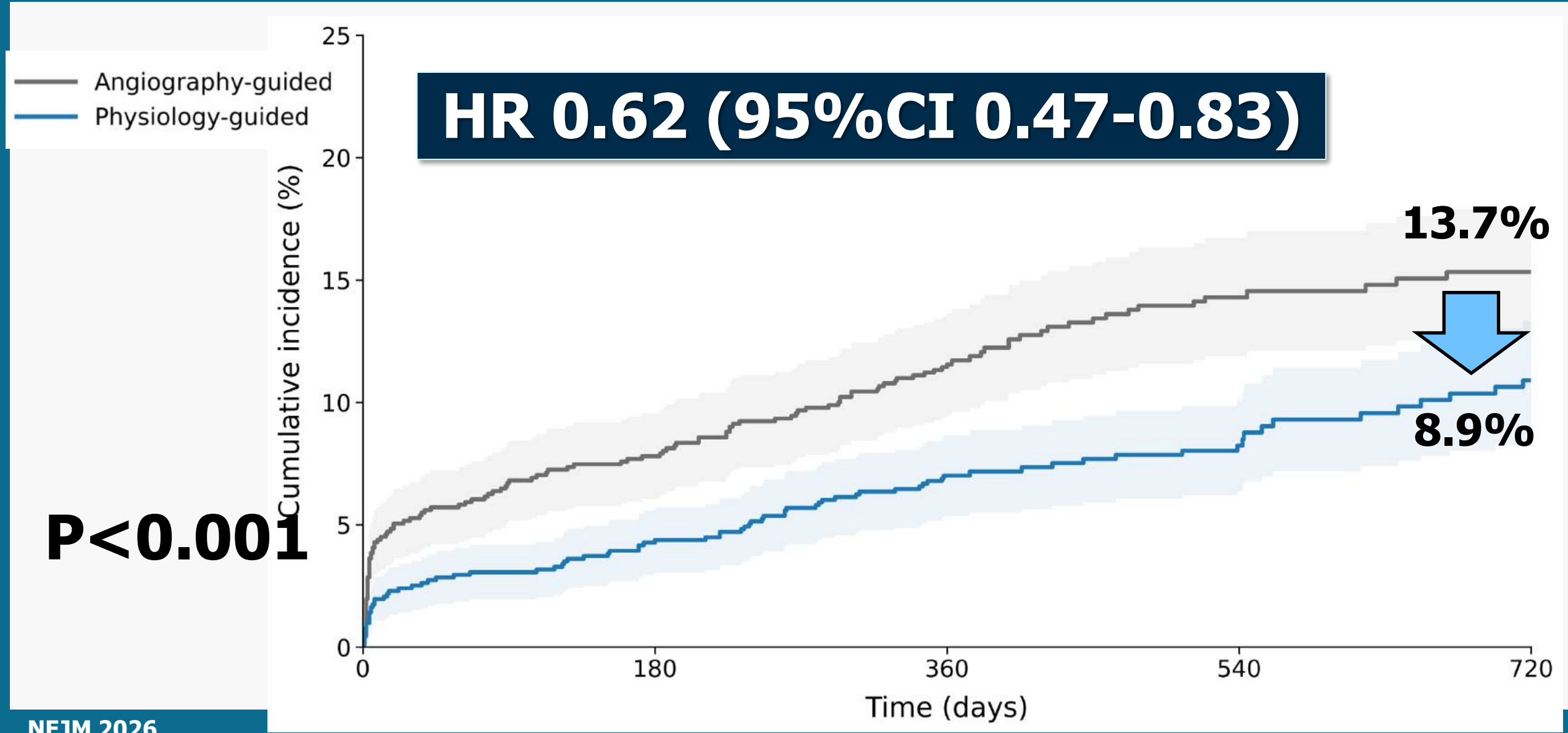
Physiology-guided

Procedural Data





Primary Endpoint (death, MI, CVA, ID-revasc)



Conclusions

- **The culprit lesion remains an angiographic and/or clinical decision.**
- **Beyond the culprit, physiology is the best tool we have to decide where — and how — to revascularize.**