

# Functional versus Culprit-only Revascularization in Elderly Patients with Myocardial Infarction and Multivessel Disease



## The FIRE trial

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*on behalf of the FIRE trial Investigators*

# Background

- Older patients (75+) are poorly represented in conventional randomized controlled trials
- The risk of periprocedural complications is higher and prognostically impactful in older patients<sup>1</sup>
- The benefit of complete revascularization in older MI patients has been recently questioned<sup>2</sup>

# Research question

**To investigate whether, in older patients (75+ years) with MI and multivessel disease, complete revascularization based on coronary physiology is superior to a culprit-only revascularization strategy**

# Organization

**3 countries:** Italy, Spain, Poland

**34 centers**

**Study PI:** Simone Biscaglia

**Study Chair:** Gianluca Campo

**Executive Committee:** Javier Escaned, Dariusz

Dudek, Raul Moreno, Matteo Tebaldi, Emanuele Barbato



**CEC:** Rita Pavasini, Paolo Cimiglia

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**Stats:** Elisa Maietti, Anna Zanetti, Nicola Pesenti 

**CROs:** AdvicePharma, Impulsae Consulting, KCRI



**Investigator-driven trial**



Università  
degli Studi  
di Ferrara

## Contributors



# Inclusion & Exclusion Criteria



## Inclusion

- **75+ years old**
- **MI (STEMI or NSTEMI)**
- **Multivessel disease**
- **Successful PCI of culprit lesion**

## Exclusion

- **Non culprit lesion on left main**
- **Unclear culprit lesion**
- **Life expectancy <1 year**
- **Prior CABG**
- **Planned surgical revasc**

# Design

All comers, prospective, randomized, multicenter, open-label trial with blinded adjudicated evaluation of outcomes (PROBE).

Pts  $\geq 75$  ys hospitalized for MI (STE or NSTE) with indication to invasive management

Multivessel disease at coronary artery angiography

Culprit lesion clearly identifiable and successfully treated



**Physiology-guided Complete Revascularization**

**Culprit-only Revascularization**

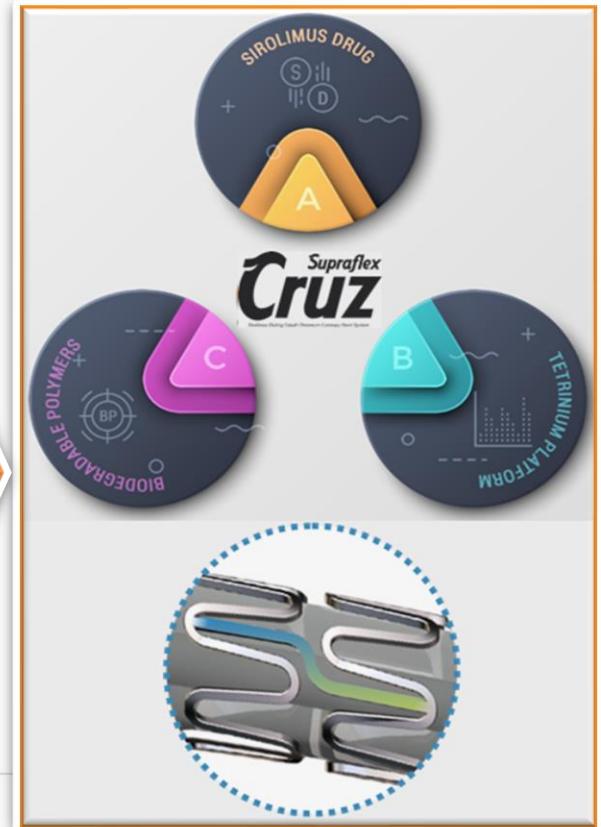
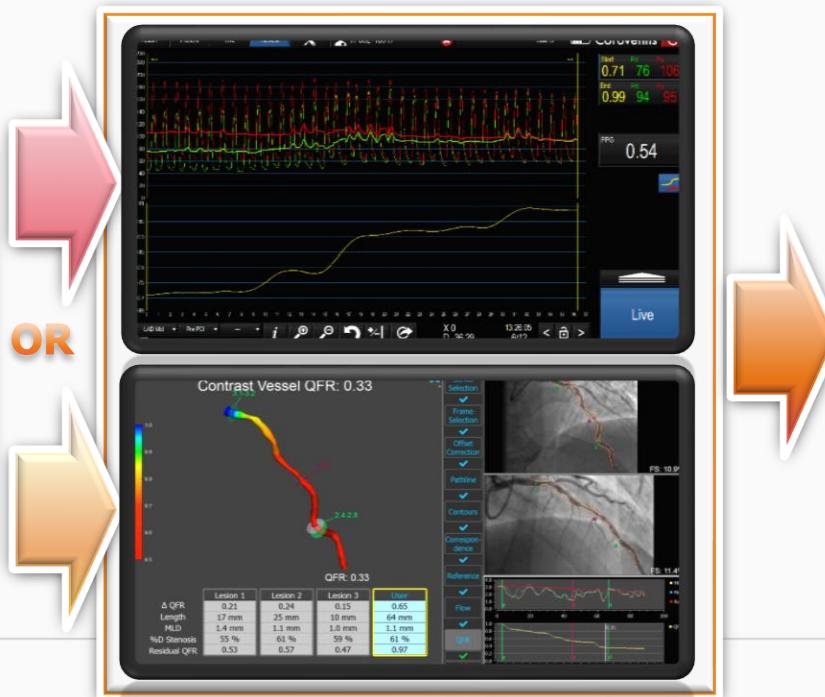
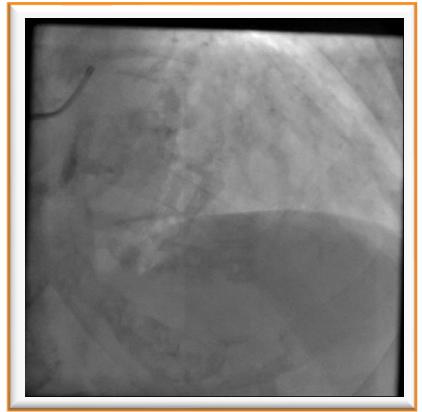
**1-, 3-, and 5-year follow-up**



We estimated a conservative **15% rate** of the primary endpoint at 1 year in the culprit-only strategy group. Considering that functional assessment should **reduce the primary endpoint of at least 30%**, 1368 patients are required to have a 80% chance of detecting, as significant at the 5% level, a 30% difference in the primary outcome between the two groups.

# Coronary Physiology & Stents

- Non-culprit lesions were assessed with either wire-based FFR, resting index or angiography-derived FFR
- Flow-limiting lesions ( $\text{FFR} \leq 0.80$ , resting  $\leq 0.89$ ) had to be revascularized with biodegradable-polymer sirolimus ultra-thin stent(s)



# Endpoints

## Primary

**Death, any MI, any stroke, or ID-revascularization**

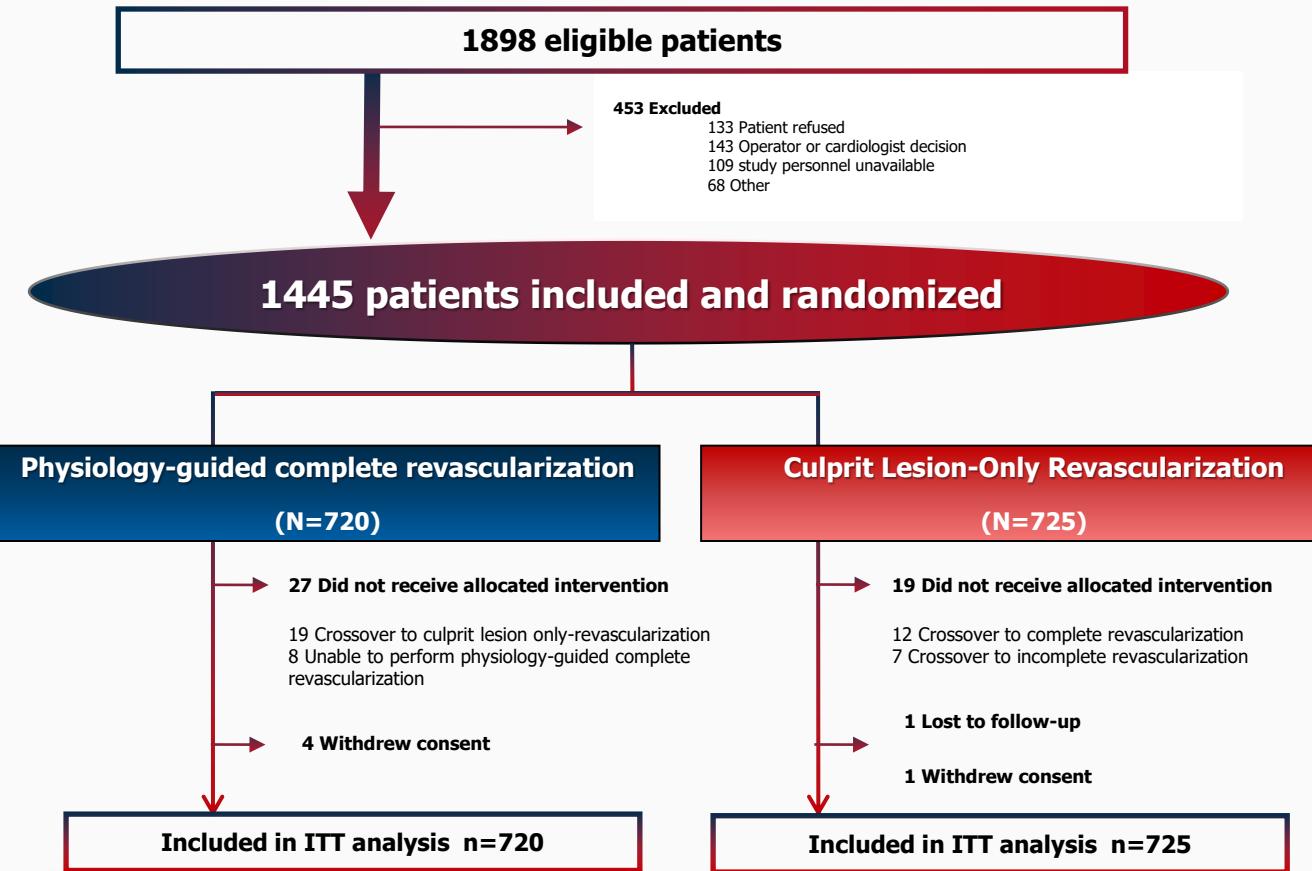
## Key secondary

**Cardiovascular death or MI**

## Safety

**CA-AKI, stroke, or BARC type 3-5 bleeding**

# Flow-chart



- **76% of eligible patients enrolled**
- **2.6% crossover from culprit-only**
- **Follow-up complete in 99.9% of patients**

# Baseline Characteristics

<b>Characteristic</b>	<b>Culprit-Only (N=725)</b>	<b>Physiology-Guided Complete (N=720)</b>	<b>Characteristic</b>	<b>Culprit-Only (N=725)</b>	<b>Physiology-Guided Complete (N=720)</b>
<b>Age (IQR) – yr</b>	80 (77-84)	81 (77-84)	<b>Killip class ≥2</b>	208 (28.7)	204 (28.3)
<b>Female sex</b>	265 (36.6)	263 (36.5)	<b>Hospital LOS</b>	5 (3-7)	6 (4-8)
<b>Comorbidities</b>					
Hypertension	592 (81.7)	593 (82.4)	Aspirin	683 (94.2)	692 (96.1)
Diabetes	233 (32.1)	230 (31.9)	Clopidogrel	358 (49.4)	371 (51.5)
Prior MI	116 (16)	104 (14.4)	Ticagrelor	337 (46.5)	326 (45.3)
eGFR <60 ml/min	332 (45.8)	330 (45.8)	Prasugrel	16 (2.2)	16 (2.2)
PAD	127 (17.5)	122 (16.9)	Vitamin K antagonist	36 (5)	27 (3.8)
<b>Clinical presentation</b>					
STEMI	256 (35.3)	253 (35.1)	NOAC	129 (17.8)	137 (19)
NSTEMI	469 (64.7)	467 (64.9)	ACEi or ARB	552 (76.1)	556 (77.2)
			Statin	661 (91.2)	680 (94.4)

# Procedural Characteristics

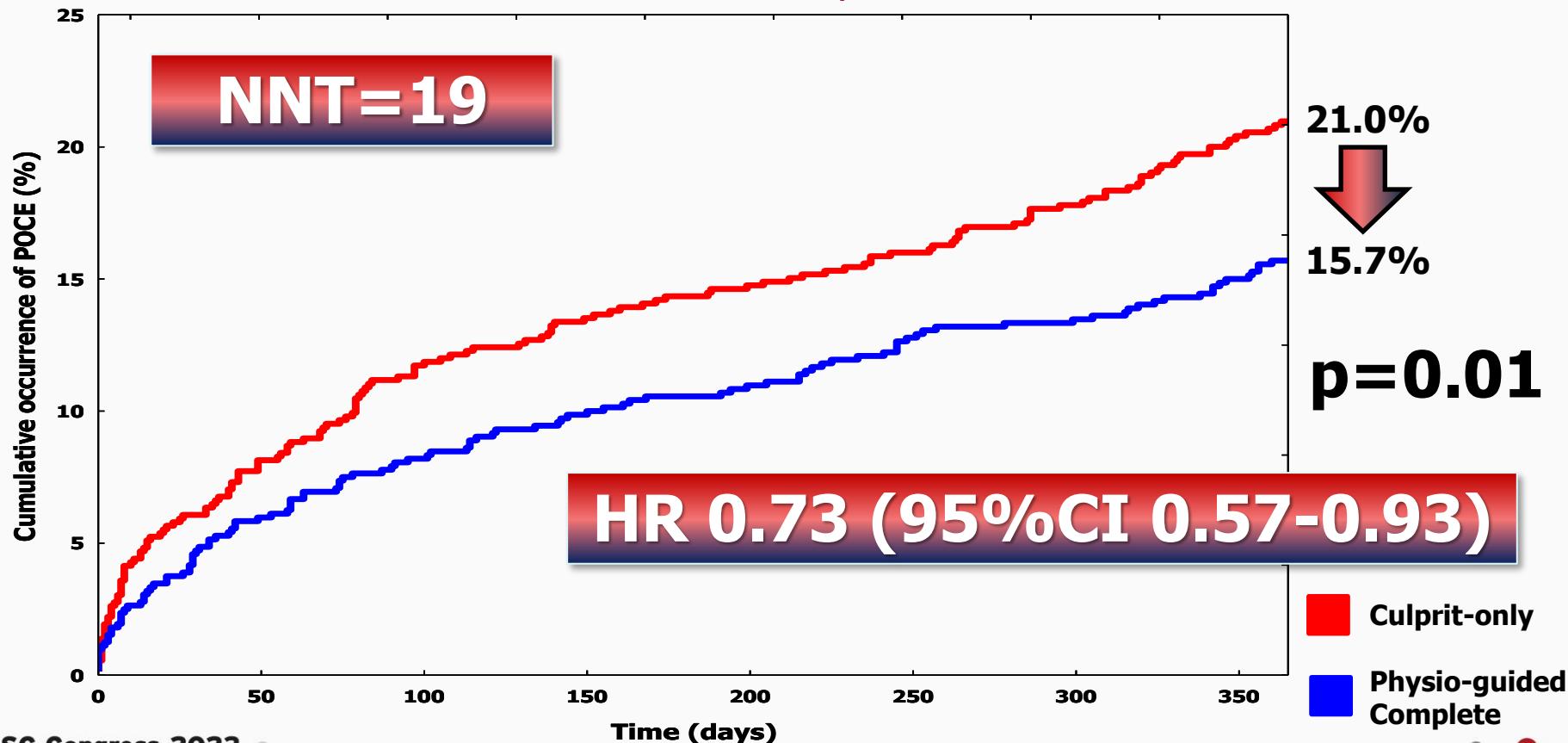


Characteristic	Culprit-Only (n=725)	Physiology-Guided Complete (N=720)
<b>Procedures</b>		
Total number	725	961
Days from index to staged procedures	-	3 (2-4)
Radial access	672 (92.7)	911 (94.8)
<b>Number of non-culprit vessels per patient</b>		
One	510 (70.3)	503 (69.9)
Two or more	215 (29.7)	217 (30.1)
<b>Location of non-culprit vessels</b>		
LAD	291 (30.6)	296 (31.2)
LCX	319 (33.5)	308 (32.5)
RCA	320 (33.6)	310 (32.7)
RI	21 (2.2)	34 (3.6)

Characteristic	Culprit-Only (n=725)	Physiology-Guided Complete (N=720)
<b>RVD</b>	3.0 (2.5-3.0)	3.0 (2.5-3.0)
<b>Diameter stenosis</b>	70 (60-80)	70 (60-80)
<b>Percent diameter stenosis</b>		
50-69%	401 (42.2)	390 (41.1)
70-89%	378 (39.7)	380 (40.1)
90-99%	172 (18.1)	178 (18.8)
<b>Type of physiological assessment</b>		
Wire-based hyperemic	-	451 (49.6)
Wire-based non hyperemic	-	138 (15.2)
Angiography-based index	-	320 (35.2)
<b>Functionally significant NCL</b>	-	425 (44.8)

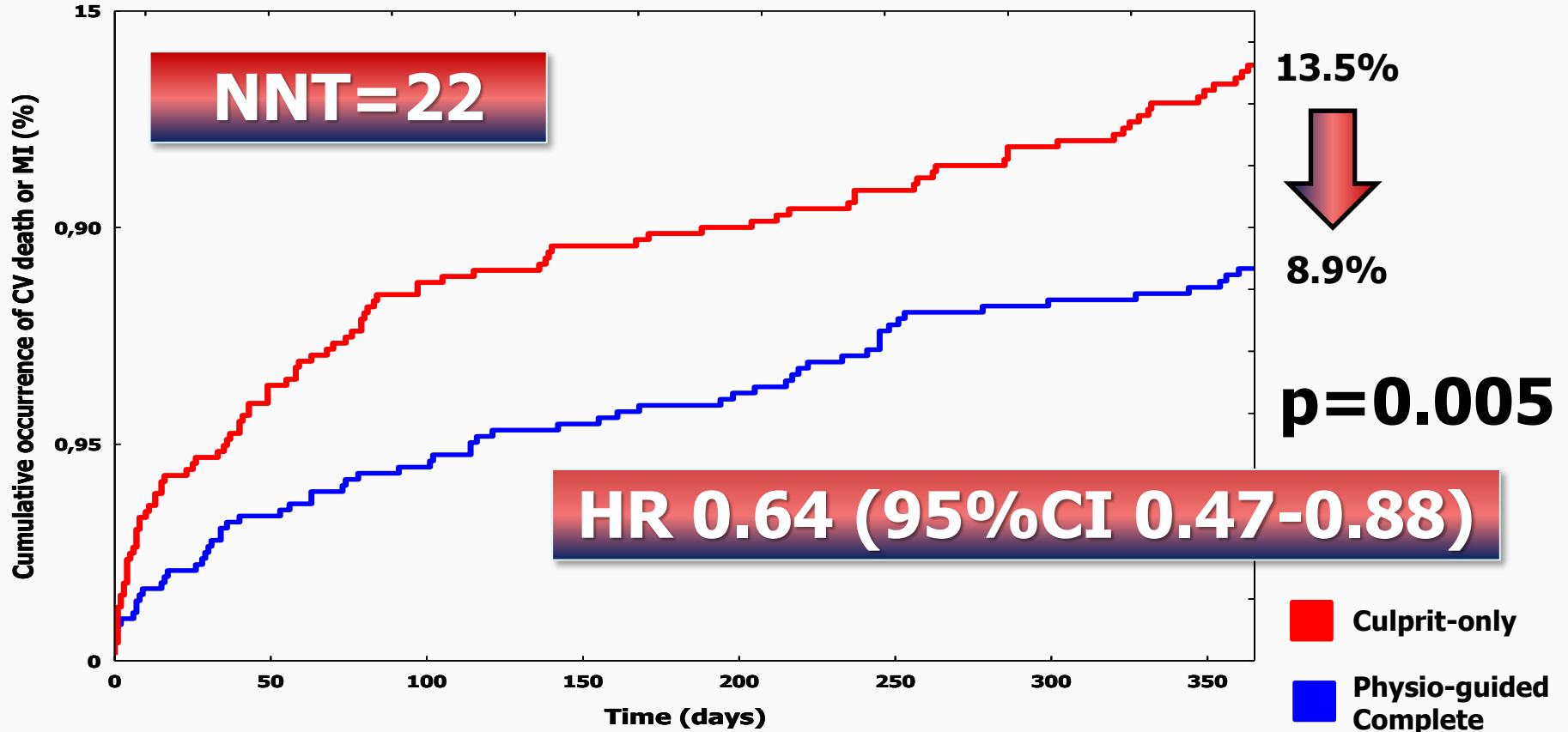
# Primary endpoint

All-cause death, any MI,  
stroke, or ID-revascularization



# Key secondary endpoint

CV death or MI



# Safety and Secondary Endpoints



Outcome	Culprit-Only (n=725)	Complete (n=720)	Hazard Risk (95% CI)	P
	no. (%)	no. (%)		
<b>Death</b>	93 (12.8)	66 (9.2)	<b>0.70 (0.51-0.96)</b>	<b>0.027</b>
<b>Cardiovascular death</b>	56 (7.7)	36 (5)	<b>0.64 (0.42-0.97)</b>	<b>0.034</b>
<b>Non-cardiovascular death</b>	37 (5.1)	30 (4.2)	0.82 (0.50-1.32)	0.40
<b>Stroke</b>	7 (1.0)	12 (1.7)	1.73 (0.68-4.40)	0.25
<b>Myocardial infarction</b>	51 (7.0)	32 (4.4)	<b>0.62 (0.40-0.97)</b>	<b>0.035</b>
<b>ID-revascularization</b>	49 (6.8)	31 (4.3)	<b>0.63 (0.40-0.98)</b>	<b>0.041</b>
<b>Safety endpoint*</b>	148 (20.4)	162 (22.5)	1.11 (0.89-1.37)	0.37

# Limitations

- Open label study
- Our results may not apply to:
  - Complete revascularization outside index hospitalization
  - Complete revascularization guided by conventional angiography
  - Patients not treated with biodegradable-polymer sirolimus eluting stent

# Conclusions



**Among patients aged 75 years or older with MI and multivessel disease, physiology-guided complete revascularization, as compared to a culprit-only revascularization strategy, reduced**

- **Composite of death, MI, stroke, or ID-revascularization**
- **Cardiovascular death or MI**



ORIGINAL ARTICLE

## Complete or Culprit-Only PCI in Older Patients with Myocardial Infarction

S. Biscaglia, V. Guiducci, J. Escaned, R. Moreno, V. Lanzilotti, A. Santarelli, E. Cerrato, G. Sacchetta, A. Jurado-Roman, A. Menozzi, I. Amat Santos, J.L. Díez Gil, M. Ruozzi, M. Barbierato, L. Fileti, A. Picchi, V. Lodolini, G. Biondi-Zocca, E. Maietti,\* R. Pavasini, P. Cimaglia, C. Tumscitz, A. Erriquez, C. Penzo, I. Colaiori, G. Pignatelli, G. Casella, G. Iannopollo, M. Menozzi, F. Varbella, G. Caretta, D. Dudek, E. Barbato, M. Tebaldi, and G. Campo,  
for the FIRE Trial Investigators†

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