Timing of complete revascularization in patients with ACS and MVD

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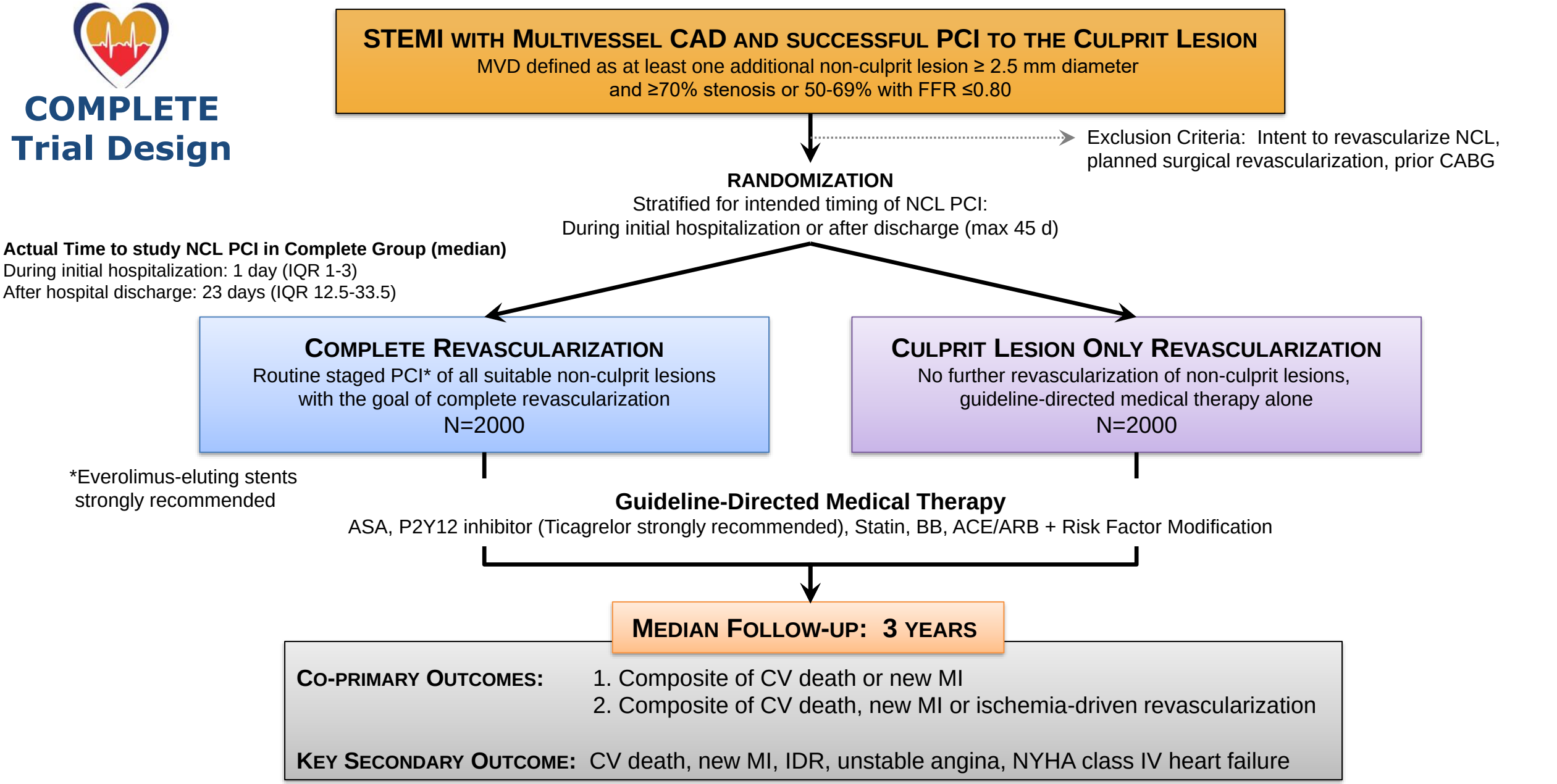
COMPLETE Trial Design

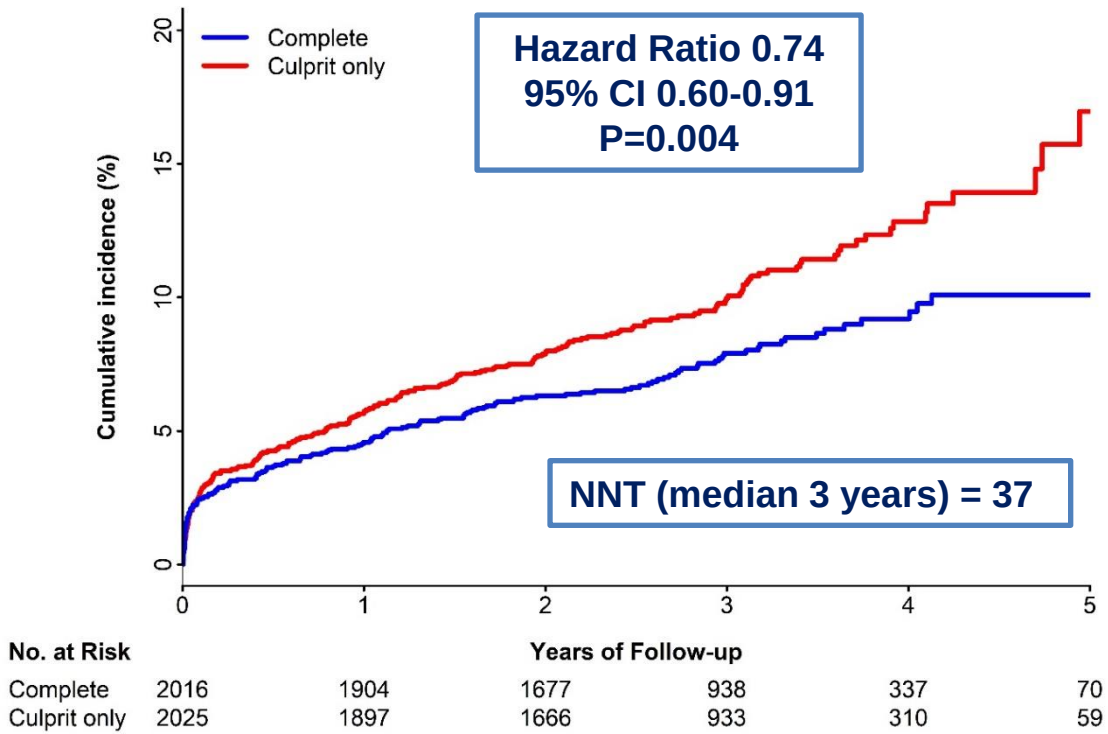


Mehta SR et al. *Am Heart J* 2019; 215:157-166.

COMPLETE Trial: Primary Outcomes

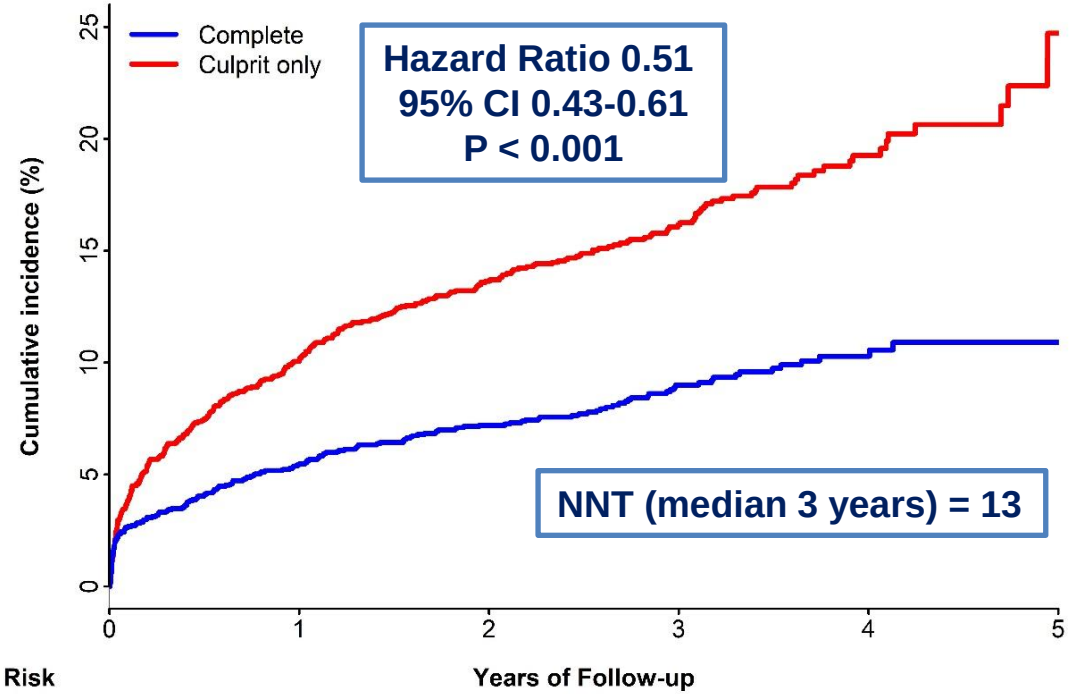
Multivessel vs Culprit Lesion-only PCI for STEMI and muti-vessel CAD

CV Death or New MI



No. at Risk						
Complete	2016	1904	1677	938	337	70
Culprit only	2025	1897	1666	933	310	59

CV Death, New MI, or IDR



No. at Risk						
Complete	2016	1886	1659	925	329	66
Culprit only	2025	1808	1559	865	294	57

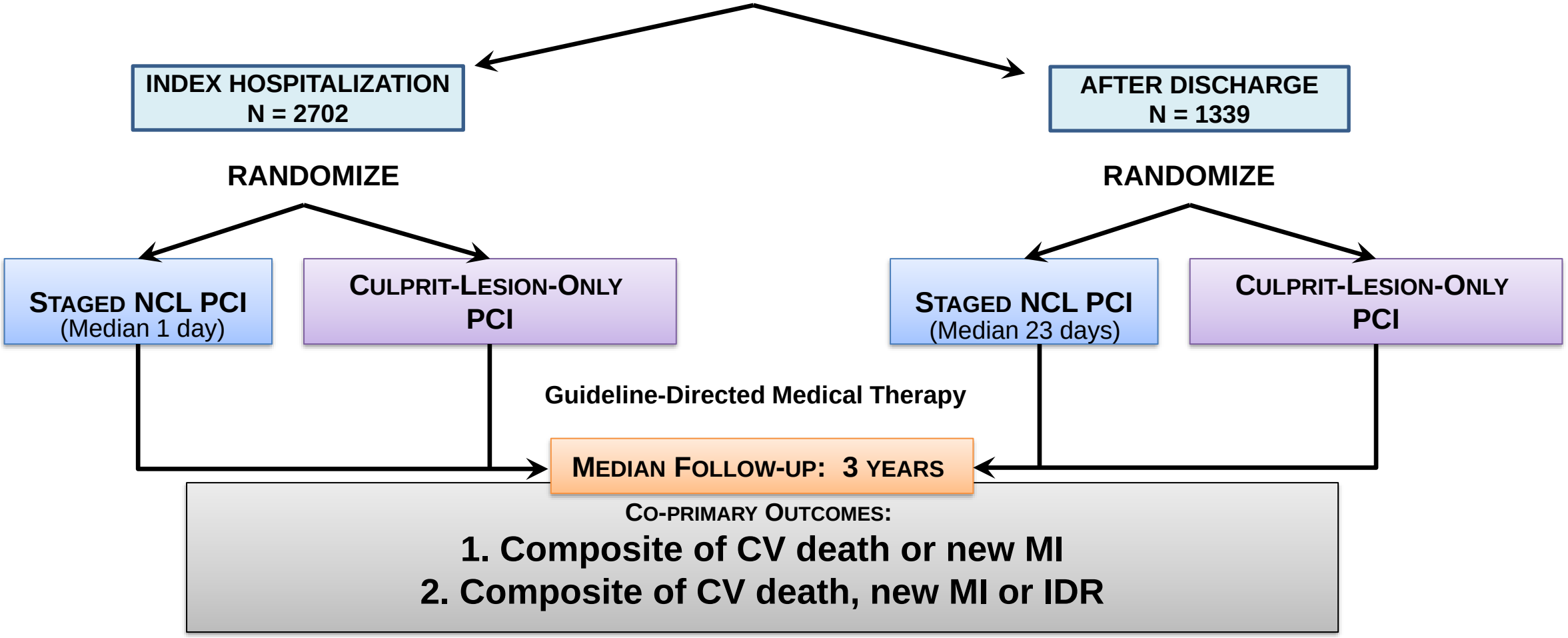
Mehta SR et al. *N Engl J Med* 2019

COMPLETE Timing Analysis

STEMI WITH MULTIVESSEL CAD AND SUCCESSFUL PCI TO THE CULPRIT LESION

STRATIFY

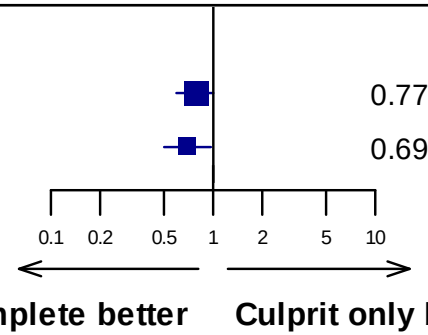
BY INTENDED TIMING OF NON-CULPRIT LESION (NCL) PCI



Timing of Non-Culprit Lesion PCI: During or After Initial Hospitalization

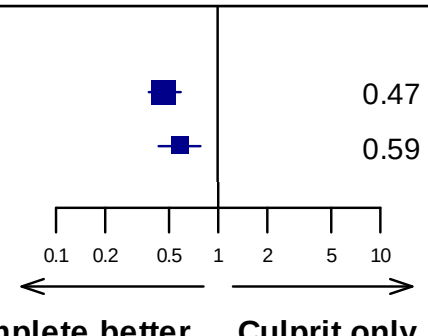
CV death or New MI

	Complete	Culprit Only	HR (95% CI)	Interaction P
	no. of events/total no. (%/yr)			
Intent to perform non-culprit lesion PCI				0.62
During initial hospitalization	101/1353 (2.7)	130/1349 (3.5)	0.77 (0.59-1.00)	
After initial hospitalization	57/663 (2.7)	83/676 (3.9)	0.69 (0.49-0.97)	



CV death, New MI, or IDR

	Complete	Culprit Only	HR (95% CI)	Interaction P
	no. of events/total no. (%/yr)			
Intent to perform non-culprit lesion PCI				0.27
During initial hospitalization	113/1353 (3.0)	227/1349 (6.6)	0.47 (0.38-0.59)	
After initial hospitalization	66/663 (3.1)	112/676 (5.4)	0.59 (0.43-0.79)	



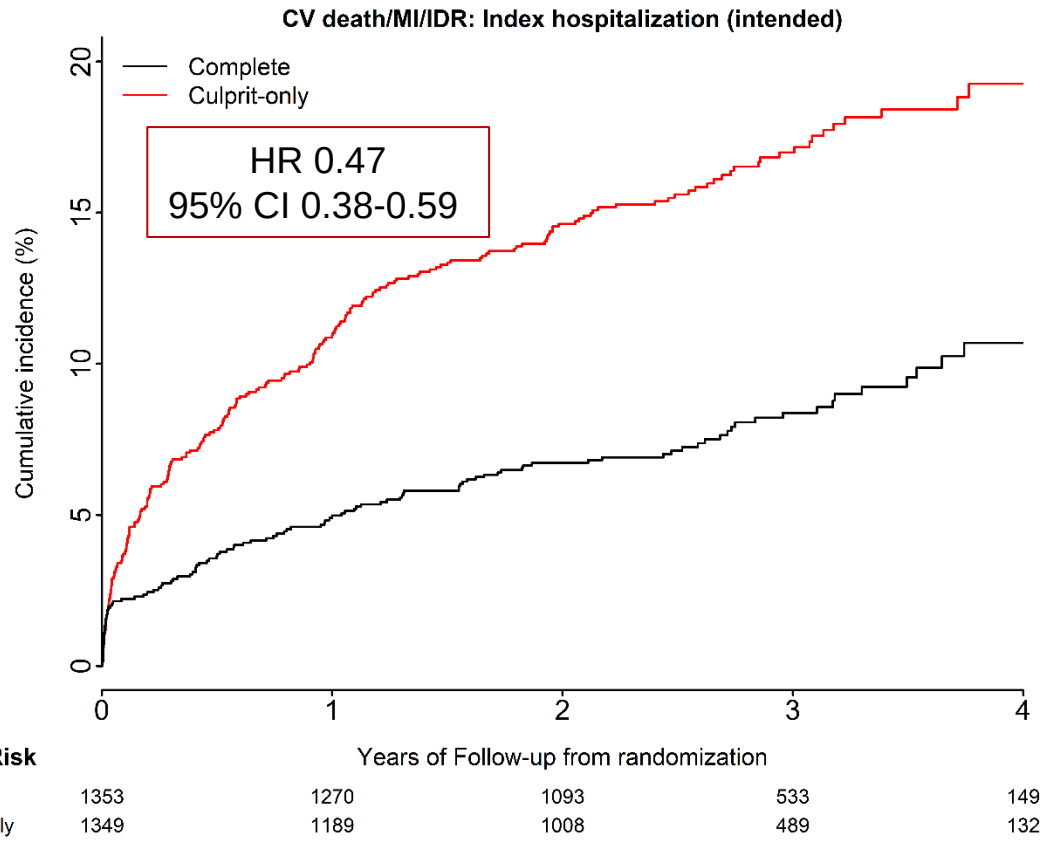
Median Time to study NCL PCI in Complete Group

During initial hospitalization: 1 day (IQR 1-3)

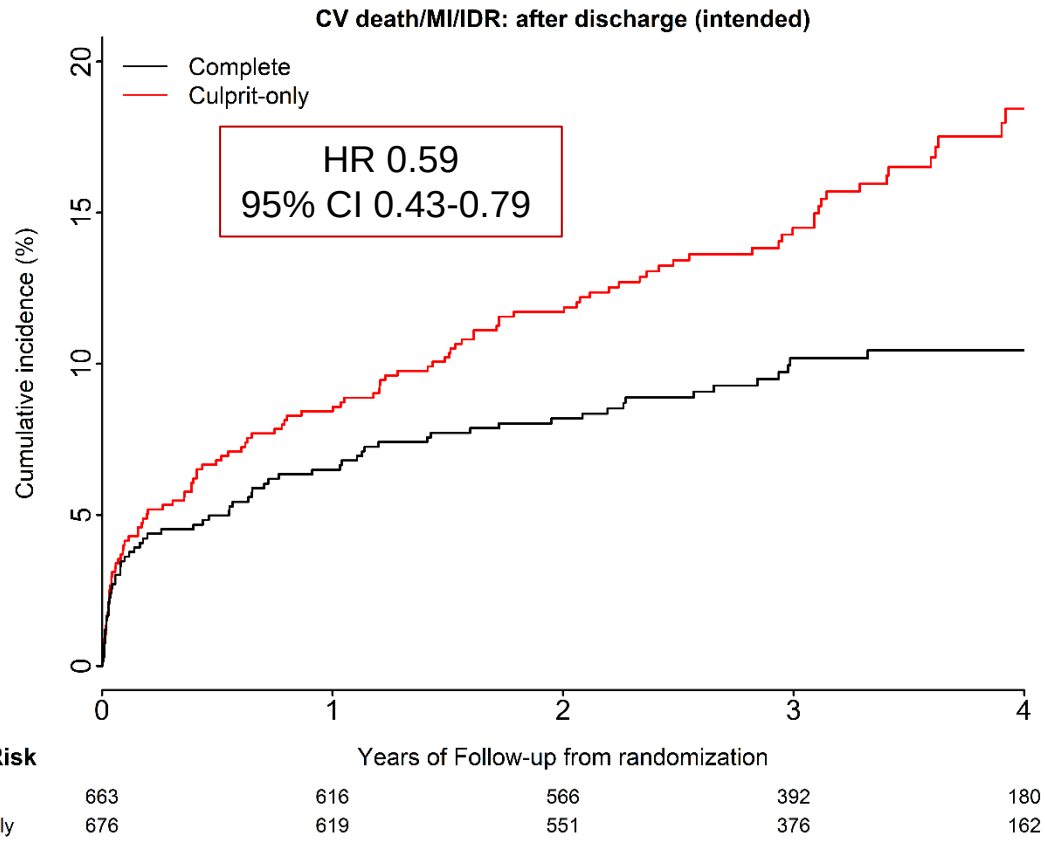
After Hospital Discharge: 23 days (IQR 12.5-33.5)

Wood DA…Mehta SR, et al. *J Am Coll Cardiol* 2019

Second Co-Primary Outcome
CV death, MI or IDR



Index Hospitalization



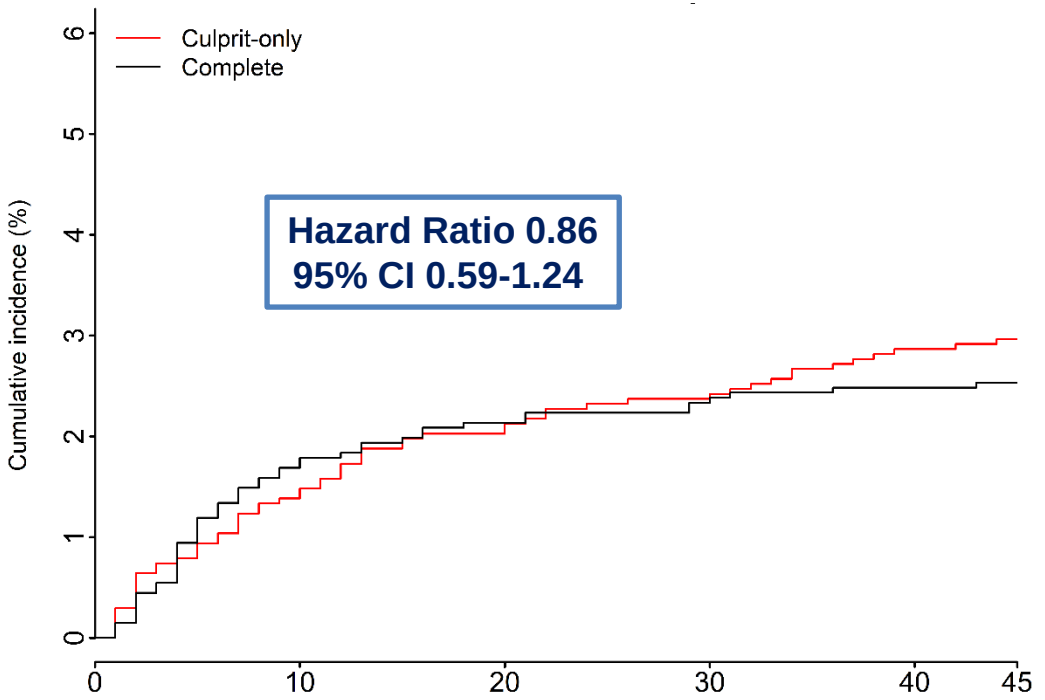
After Discharge

Interaction P=0.27

Wood DA…Mehta SR, et al. *J Am Coll Cardiol* 2019

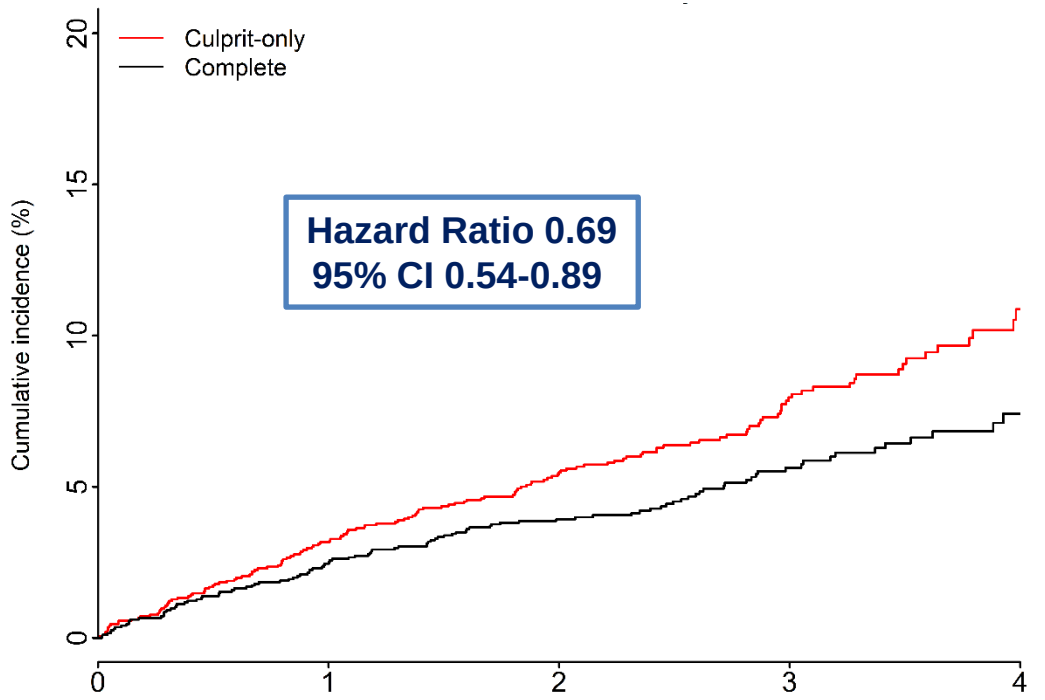
CV Death or New MI: Benefit Emerges Over the Longer Term

Randomization to 45 Days



No. at Risk						
Culprit-only	2025	1995	1982	1975	1964	1961
Complete	2016	1979	1970	1966	1963	1962

>45 days to Study End (Median 3y.)

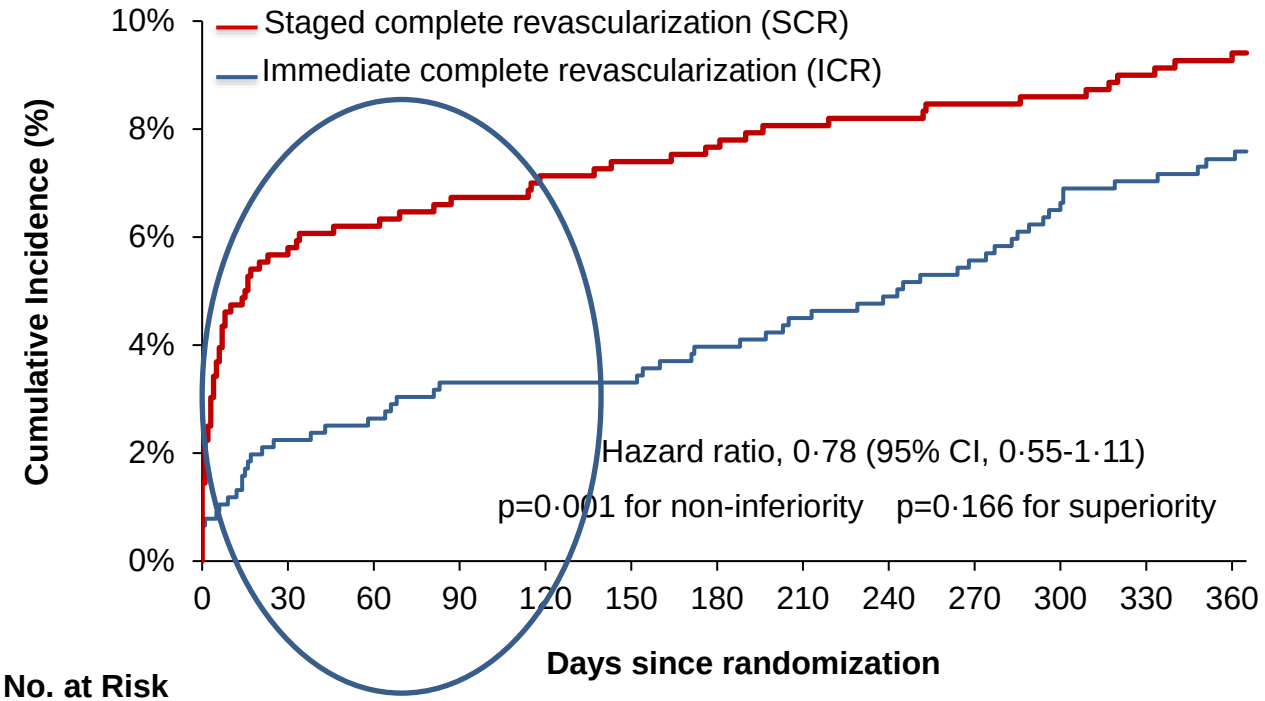


No. at Risk					
Culprit-only	1961	1883	1537	834	244
Complete	1962	1892	1568	842	274

Wood DA, Mehta SR et al, *J Am Coll Cardiol* 2019

Biovasc Trial: Immediate vs Staged Complete Revascularization

Composite of all-cause mortality, myocardial infarction, any unplanned ischemia-driven revascularization and cerebrovascular events



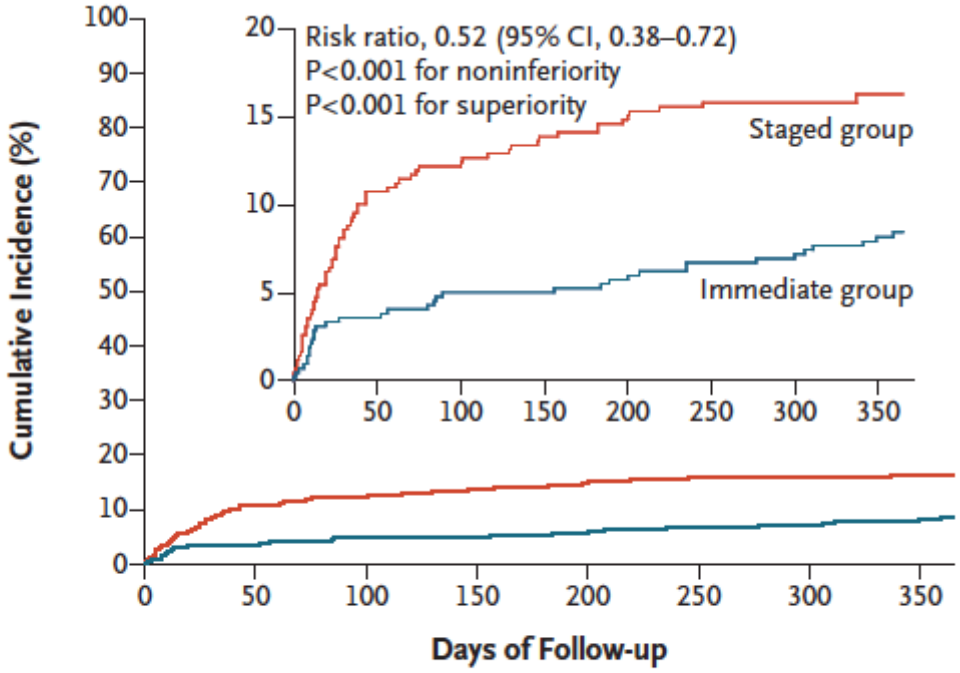
No. at Risk

ICR	764	736	733	728	728	728	723	718	714	709	701	695	650
SCR	761	712	705	701	698	696	694	691	690	687	686	681	638

Diletti R. Lancet 2023

MULTISTARS Trial

Immediate multivessel PCI or PCI of the culprit lesion followed by staged multivessel PCI of nonculprit lesions within **19 to 45 days after the index procedure** (staged group).



No. at Risk

Staged group	422	376	366	360	354	351	350	345
Immediate group	418	403	397	396	392	390	387	369

Table 3. Primary and Secondary End Points.*

End Point	Immediate Group (N=418)	Staged Group (N=422)	Treatment Effect (95% CI)
Primary end point at 1 yr			
Death from any cause, nonfatal myocardial infarction, stroke, unplanned ischemia-driven revascularization, or hospitalization for heart failure — no. (%)	35 (8.5)	68 (16.3)	0.52 (0.38–0.72)†
Secondary end points at 1 yr‡			
Death from any cause — no. (%)	12 (2.9)	11 (2.6)	1.10 (0.48–2.48)§
Nonfatal myocardial infarction — no. (%)	8 (2.0)	22 (5.3)	0.36 (0.16–0.80)§
Stroke — no. (%)	5 (1.2)	7 (1.7)	0.72 (0.23–2.26)§
Unplanned ischemia-driven revascularization — no. (%)	17 (4.1)	39 (9.3)	0.42 (0.24–0.74)§

Stahli BE. et al. NEJM 2023

BIOVASC and MULTISTARS

1. **Only a minority of patients (40%) in BIOVASC had. The clinical relevance of NCL PCI timing differs substantially in STEMI vs NSTEMI.**
   - STEMI is a medical emergency and goal is to restore TIMI 3 flow to the culprit. NCL PCI in STEMI setting can be risky if there is a complication.
   - NSTEMI patients are more stable, without ongoing ischemia, the culprit lesion is usually patent. MV PCI is much safer

2. **There is a potential bias in the ascertainment of new MI between the 2 randomized groups and we cannot exclude the possibility that the early difference is an artifact of new MI diagnosis in the acute setting vs later**
   - Soon after primary PCI, new MI is almost impossible to diagnose (biomarkers are rising). By contrast in the staged PCI group, it is much easier as troponin has plateaued, decreased or normalized allowing detection of a re-elevation of biomarkers.

Timing of NCL PCI in STEMI and NSTEMI

STEMI

In hospital staged NCL PCI is still the most common choice in most centers

- Advantages are patient is more stable and free of ischemia
- Facilitates complex PCI of NCL's
- Easier to perform physiology and imaging to guide PCI

In selected patients with STEMI, immediate NCL PCI is not unreasonable in hemodynamically stable patients with simple NCL's

NSTEMI

Either immediate or staged MV PCI depending are reasonable options

COMPLETE-2 Study Design

COMPLETE-2

STEMI or NSTEMI with Multivessel Coronary Artery Disease

At least one additional non-culprit lesion ≥2.5 mm diameter and ≥50% stenosis

N=5100

Randomization

Stratified by STEMI or NSTEMI and NCL PCI Timing

Physiology-Guided NCL PCI

Routine PCI of all physiological positive lesions with the goal of complete revascularization

n=2550

Angiography-Guided NCL PCI

Routine PCI of all angiographical suitable lesions with the goal of complete revascularization

n=2550

COMPLETE-2 OCT

Primary Objective: Whether vulnerable plaque (lipid-rich plaque and thin cap fibroatheroma) as identified by OCT imaging predicts CV death, new MI, TLR, or unstable angina (related to a non-stented lesion)

N=1510

Median Follow-Up: 3.5 Years

Primary Outcomes

Efficacy: Time to first occurrence of the composite of CV death, new MI, or ischemia-driven revascularization

Safety: Time to first occurrence of the composite of clinically significant bleeding, stroke, stent thrombosis, or contrast-associated acute kidney injury