COMPLETE TRIAL

A randomized, comparative effectiveness study of complete versus culprit-only revascularization strategies to treat multivessel disease after early percutaneous coronary intervention for ST-segment elevation myocardial infarction

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on behalf of the COMPLETE Trial Executive & Steering Committees and Investigators

Population Health Research Institute
HEALTH THROUGH KNOWLEDGE

Hamilton Health Sciences

McMaster University HEALTH SCIENCES

Disclosures

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Hamilton, Canada

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Background

- Patients undergoing primary PCI to the culprit lesion for STEMI are often found to have multivessel CAD, with 1 or more angiographically significant non-culprit lesions.

- There is uncertainty on how best to manage these non-culprit lesions:
  - *Routinely revascularize them with PCI?*
  - *Manage them conservatively with guideline-directed medical therapy alone?*

- Prior RCT's have shown non-culprit lesion PCI reduces revascularization but none were powered to detect moderate reductions in hard clinical outcomes such as CV death or MI. [1-4]

- Meta-analyses have suggested a possible reduction in CV death or MI, but this result is fragile and no single RCT has been adequately powered to confirm this.[5]

The COMPLETE trial was designed to address this evidence gap.

1. Wald et al. *N Engl J Med* 2013;369:1115-23.
2. Gershlick et al. *J Am Coll Cardiol* 2015;65:963-72.
3. Engstrom et al. *Lancet* 2015;386:665-71.
4. Smits et al. *N Engl J Med* 2017;376:1234-44.
5. Bainey et al. *Can J Cardiol* 2016;32:1542-51.

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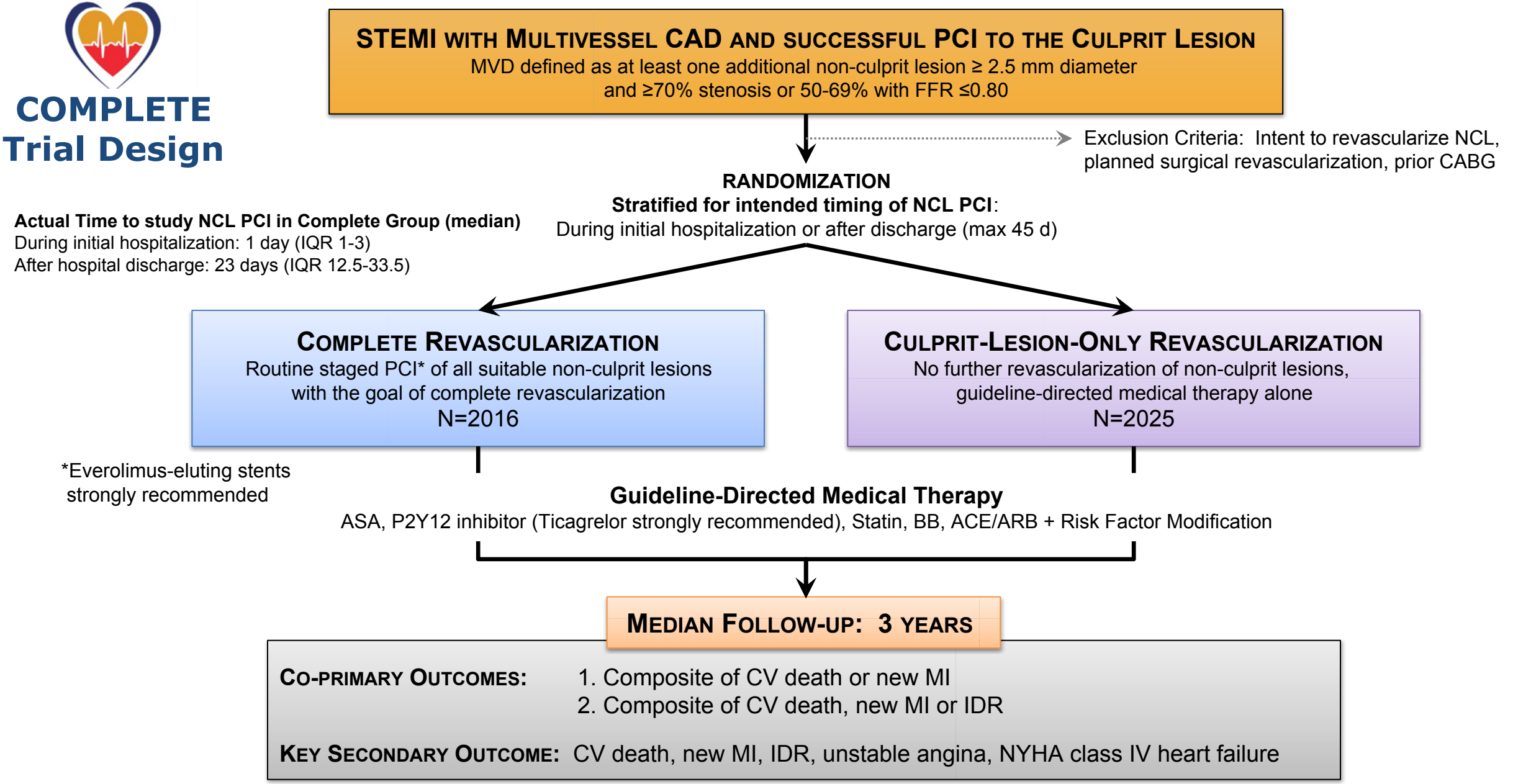
Primary Objective

In patients presenting with STEMI and multi-vessel coronary artery disease who have undergone culprit-lesion PCI, the objective is:

To determine whether a strategy of routine, staged non-culprit lesion PCI with the goal of complete revascularization is superior to a strategy of culprit lesion-only PCI in reducing the composite of CV death or new MI.

COMPLETE Trial Design



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

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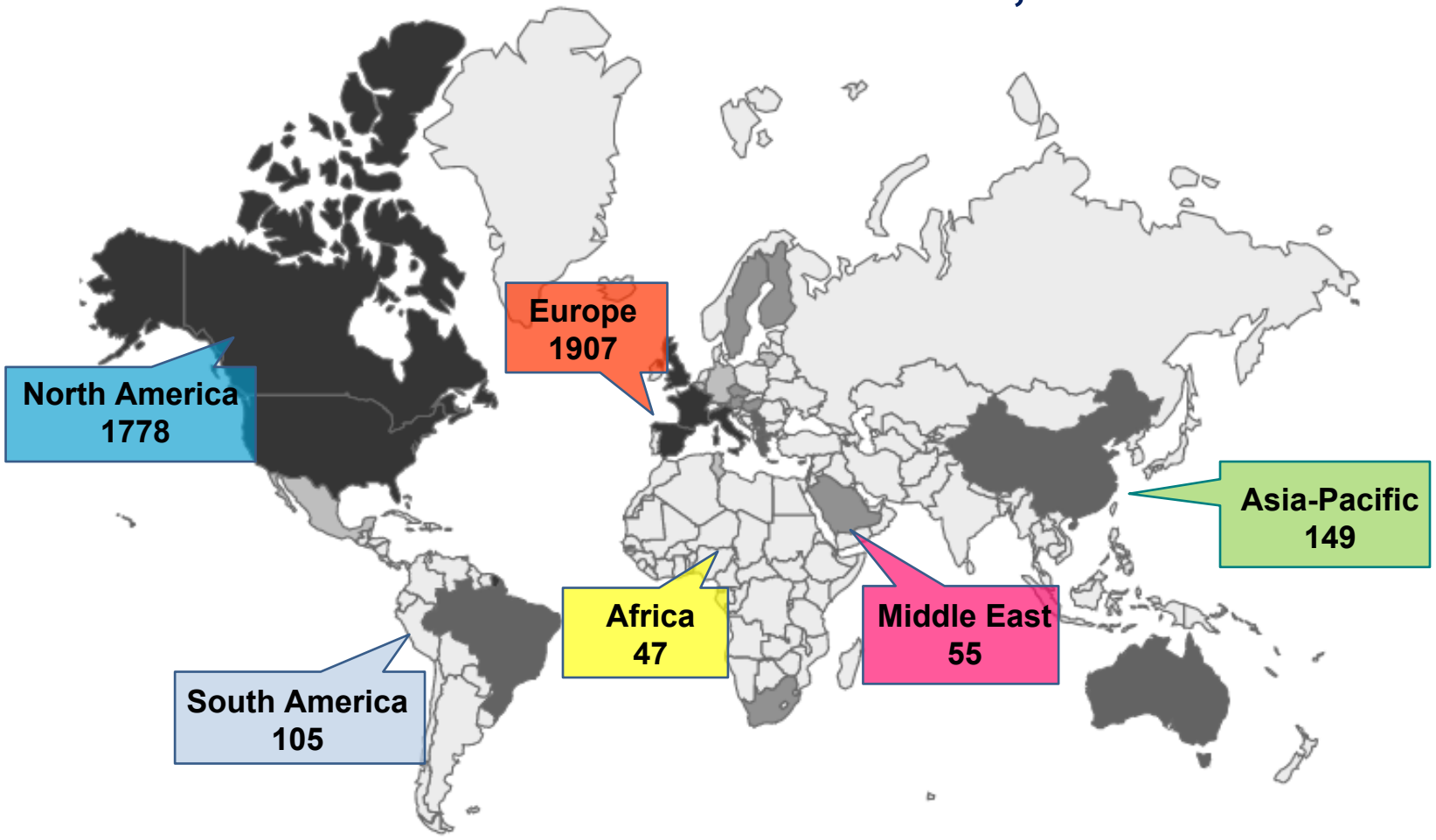
Global Recruitment

140 centers, 31 countries



Australia	*Lithuania*
Austria	*Macedonia*
Belgium	*Mexico*
Brazil	*Poland*
Canada	*Portugal*
China	*Romania*
Colombia	*Saudi Arabia*
Czech Republic	*Serbia*
Finland	*South Africa*
France	*Spain*
Germany	*Sweden*
Greece	*Switzerland*
Hungary	*Tunisia*
Israel	*United Kingdom*
Italy	*USA*
Kuwait	

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Study Power and Follow-up

- **Study Power:** 80% power for CVD/MI and 89% power for CVD/MI/IDR to detect a 22% HRR.

  To preserve the overall type I error rate of 5% for the testing of both co-primary outcomes, the first co-primary outcome was tested at a P value of 0.045 and the second at a P value of 0.0119*

- **Recruitment Period:** February 1, 2013 – March 6, 2017

- **Angiographic Core Lab:** Central review of all coronary angiograms in the trial

- **Analysis:** Intention-to-treat, Cox proportional hazards model, stratified by intended timing of revascularization, stratified log rank test

- **Follow-up (vital status):** 99.1% in *Complete* group and 99.3% *Culprit-Lesion-only* group

- **Crossover in first 45 days:** From *Complete Revasc* to *Culprit-Lesion-only* = 3.9%
  From *Culprit-Lesion-only* to *Complete Revasc* = 4.7%

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

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Baseline Characteristics

	Complete N=2016	Culprit-only N=2025
Age (yrs)	61.6	62.4
Gender (% male)	80.5	79.1
Diabetes (%)	19.1	19.9
Chronic renal insuff. (%)	2.0	2.3
Prior MI (%)	7.3	7.6
Current smoker (%)	40.6	38.9
Hypertension (%)	48.7	50.7
Dyslipidemia (%)	37.9	39.4
Prior PCI (%)	7.0	7.0
Prior stroke (%)	3.2	3.1
Hemoglobin A1C	6.3	6.3
LDL (mmol/L)	3.1	3.1
Creatinine (µmol/L)	84.7	85.2

	Complete N=2016	Culprit-only N=2025
Sx onset to Culprit PCI (%)		
<6 hours	69.4	67.1
6~12 hours	16.1	17.7
>12 hours	14.5	15.3
Discharge Meds (%)		
ASA	99.8	99.5
P2Y12 Inhibitor	99.4	99.7
Ticagrelor	64.4	63.3
Prasugrel	9.6	8.3
Clopidogrel	25.6	28.2
Beta blocker	88.1	89.1
ACEi/ARB	85.5	84.6
Statin	98.2	97.2

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Procedural Characteristics

	Complete N=2016	Culprit-only N=2025
Index PCI for STEMI		
Primary	**91.9%**	**93.1%**
Pharmaco-invasive	**3.2%**	**3.0%**
Rescue	**4.9%**	**3.9%**
Radial access	**80.8%**	**80.7%**
Residual diseased vessels		
1	**76.1%**	**77.1%**
≥2	**23.9%**	**22.9%**
NCL location		
Left main	**0.4%**	**0.1%**
LAD	**38.0%**	**41.2%**
Proximal LAD	**9.8%**	**10.4%**
Mid LAD	**21.7%**	**23.7%**
Circumflex	**36.4%**	**35.6%**
RCA	**25.3%**	**23.2%**

	Complete N=2016	Culprit-only N=2025
NCL diameter	**2.8 mm**	**2.9 mm**
Mean NCL stenosis (visual)	**79.3%**	**78.7%**
NCL stenosis (visual)		
50-69% and FFR<0.80	**0.8%**	**0.6%**
70-79%	**41.3%**	**45.1%**
80-89%	**33.5%**	**32.6%**
90-99%	**22.3%**	**19.7%**
100%	**2.1%**	**2.0%**
SYNTAX score (Core Lab)		
Baseline	**16.3**	**16.0**
Culprit lesion specific	**8.8**	**8.6**
Non-culprit lesion specific	**4.5**	**4.5**
Residual (after index PCI)	**7.2**	**7.0**

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Complete revascularization was achieved in 90.1% after NCL PCI (SYNTAX score = 0)

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Mean NCL stenosis (visual)	79.3%	78.7%
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		45.1%
80-89%	33.5%	32.6%
90-99%	22.3%	19.7%
100%	2.1%	2.0%
SYNTAX score (Core Lab)		
Baseline	16.3	16.0
Culprit lesion specific	8.8	8.6
Non-culprit lesion specific	4.5	4.5
Residual (after index PCI)	7.2	7.0

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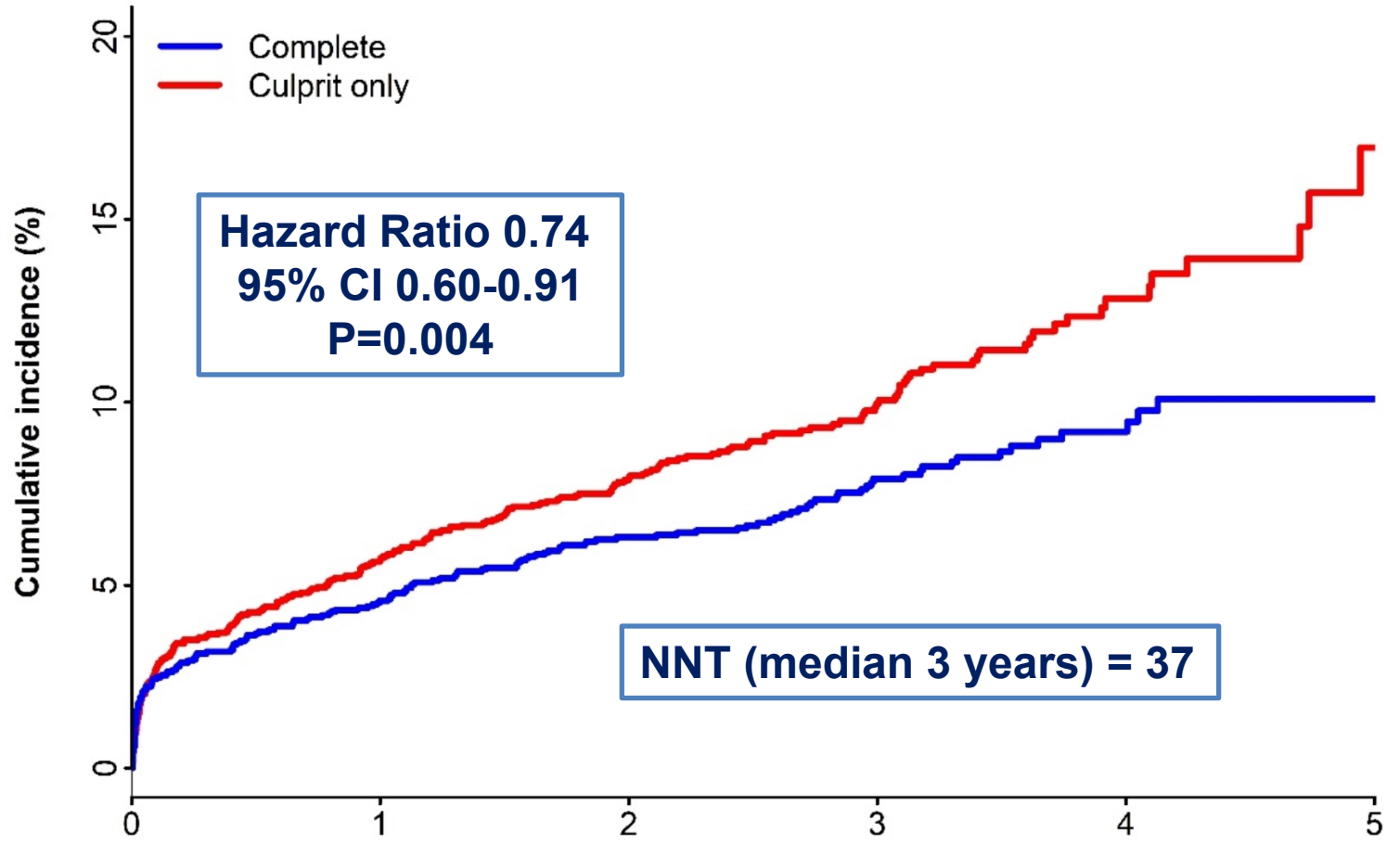
First Co-Primary Outcome: CV Death or New MI



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

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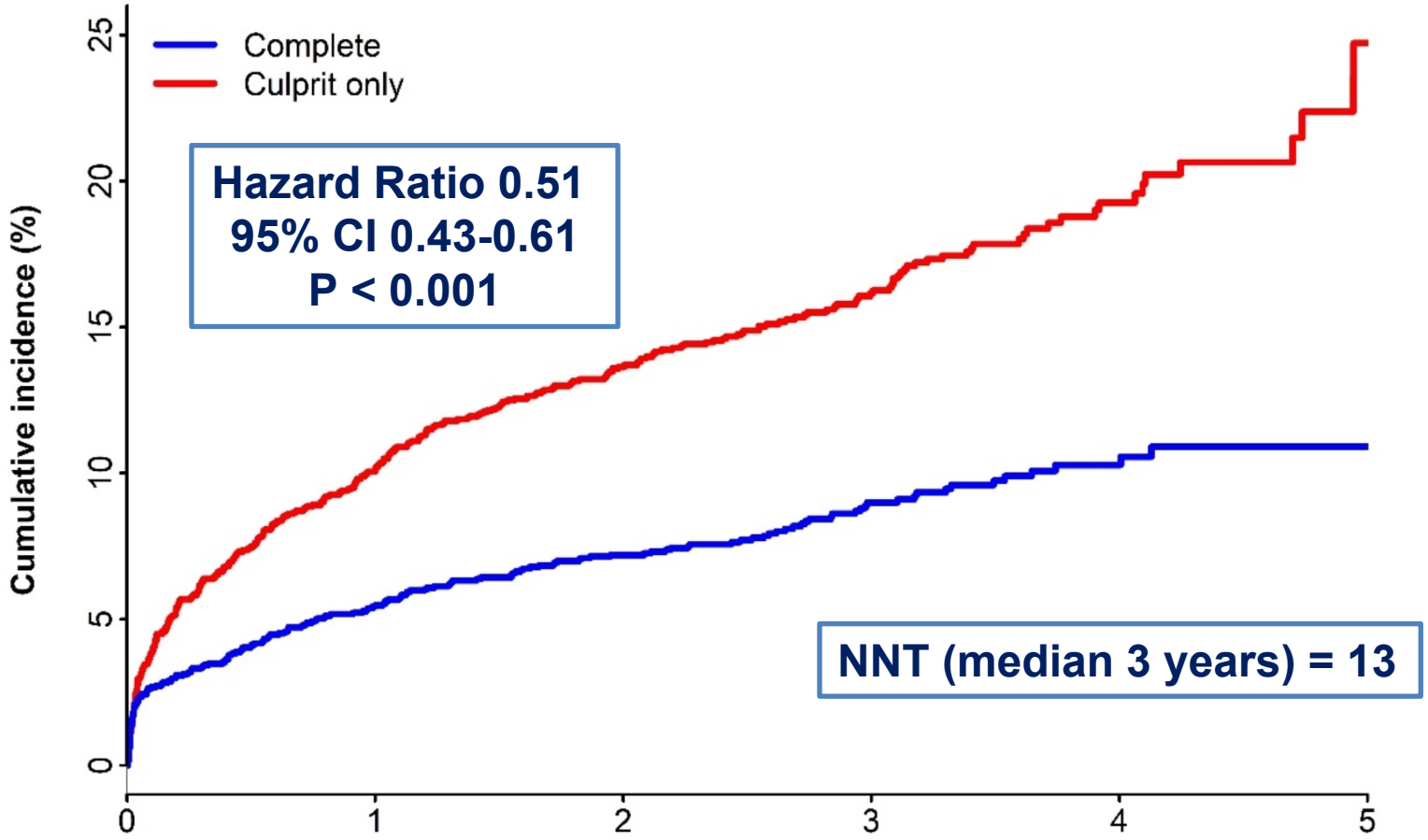
2nd Co-Primary Outcome: CV Death, New MI, or IDR



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

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Efficacy Outcomes

	Complete Revasc. N=2016		Culprit Lesion Only N=2025		HR (95% CI)	P value
	N (%)	%/year	N (%)	%/year		
Co-Primary Outcomes						
CV death or MI	**158 (7.8)**	**2.7**	**213 (10.5)**	**3.7**	**0.74 (0.60-0.91)**	**0.004**
CV death, MI or IDR	**179 (8.9)**	**3.1**	**339 (16.7)**	**6.2**	**0.51 (0.43-0.61)**	**<0.001**
Key Secondary Outcome						
CV death, MI, IDR, unstable angina or class IV HF	272 (13.5)	4.9	426 (21.0)	8.1	0.62 (0.53-0.72)	<0.001
Other Secondary Outcomes						
MI	109 (5.4)	1.9	160 (7.9)	2.8	0.68 (0.53-0.86)	0.002
IDR	29 (1.4)	0.5	160 (7.9)	2.8	0.18 (0.12-0.26)	<0.001
Unstable Angina	70 (3.5)	1.2	130 (6.4)	2.2	0.53 (0.40-0.71)	<0.001
CV death	59 (2.9)	1.0	64 (3.2)	1.0	0.93 (0.65-1.32)	0.68
All-cause Death	96 (4.8)	1.6	106 (5.2)	1.7	0.91 (0.69-1.20)	0.51

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Sub-types of MI

	Complete Revasc. N=2016		Culprit Lesion Only N=2025		HR (95% CI)
	N (%)	%/year	N (%)	%/year	
Subtype of MI					
NSTEMI	66 (3.27)	1.11	105 (5.19)	1.78	0.63 (0.46-0.85)
STEMI	43 (2.13)	0.72	53 (2.62)	0.88	0.81 (0.54-1.22)
Universal MI Definition					
Type 1	63 (3.13)	1.05	128 (6.32)	2.17	0.49 (0.36-0.66)
Type 2	16 (0.79)	0.26	13 (0.64)	0.21	1.24 (0.60-2.58)
Type 3	4 (0.20)	0.07	1 (0.05)	0.02	4.04 (0.45-36.17)
Type 4a	16 (0.79)	0.27	8 (0.40)	0.13	2.01 (0.86-4.70)
Type 4b	8 (0.40)	0.13	13 (0.64)	0.21	0.62 (0.26-1.49)
Type 5	1 (0.05)	0.02	1 (0.05)	0.02	1.00 (0.06-15.92)

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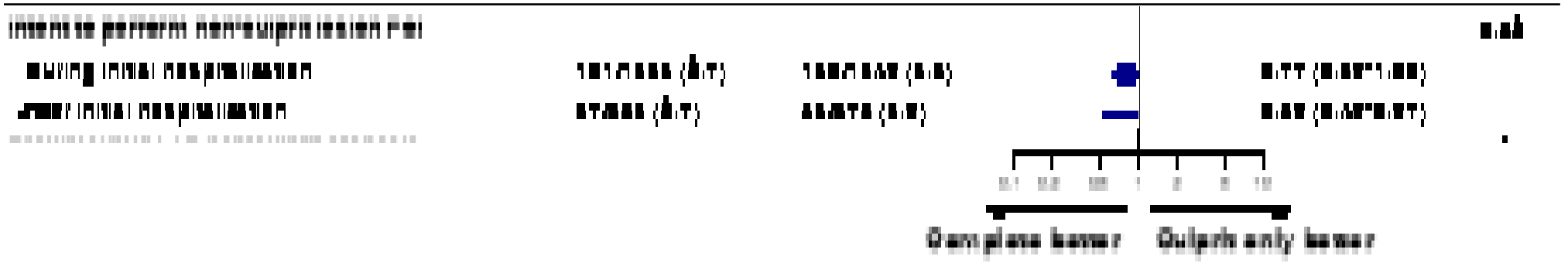
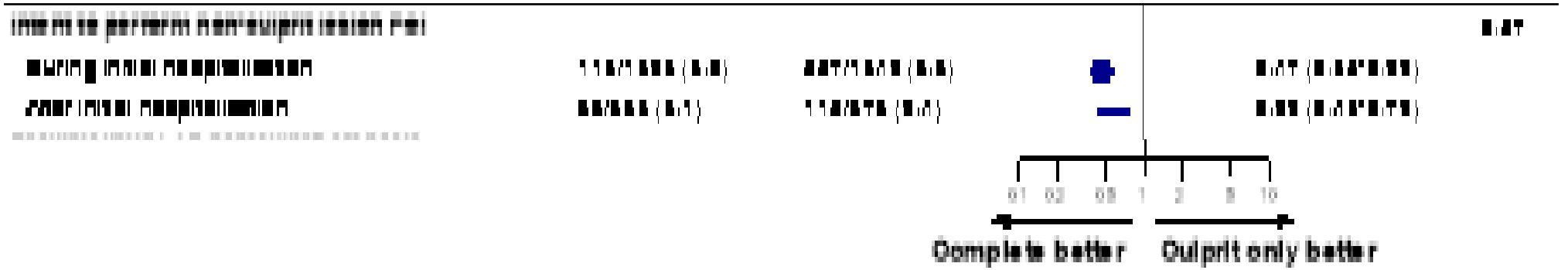
Timing of Non-Culprit Lesion PCI: During or After Index Hospitalization

Actual 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)

CV death or New MI



CV death, New MI, or IDR



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Main Pre-Defined Subgroup Analyses

CV death/MI

Subgroup	Complete	Culprit only	HR (95% CI)	P value for interaction
	no. of events/total no. (%/yr)			
Overall	168/2016 (2.7)	213/2026 (3.7)	0.74 (0.60-0.91)	
Main pre-defined:				
Proximal/mid LAD non-culprit stenosis				0.2
Presence	64/820 (2.7)	78/849 (3.1)	0.86 (0.62-1.20)	
Absence	87/1097 (2.7)	129/1085 (4.2)	0.65 (0.49-0.85)	
Non-culprit stenosis severity ≥ 80% visual or ≥ 60% core lab				0.033
Presence	127/1668 (2.6)	183/1631 (3.9)	0.67 (0.53-0.84)	
Absence	31/346 (3.2)	29/392 (2.6)	1.23 (0.74-2.04)	
Residual SYNTAX score				0.32
<6(median)	60/885 (2.3)	90/870 (3.6)	0.65 (0.47-0.90)	
≥ 6(median)	91/1033 (3.0)	117/1070 (3.8)	0.80 (0.61-1.05)	

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Safety and Other Outcomes

	Complete Revasc. N=2016		Culprit Lesion Only N=2025		HR (95% CI)	P value
	N (%)	%/year	N (%)	%/year		
Stroke	38 (1.9)	0.6	29 (1.4)	0.5	1.31 (0.81-2.13)	0.27
Stent thrombosis	26 (1.3)	0.4	19 (0.9)	0.3	1.38 (0.76-2.49)	0.28
All cause death or new MI	194 (9.6)	3.3	251 (12.4)	4.3	0.77 (0.64-0.93)	0.006
Major bleeding	58 (2.9)	1.0	44 (2.2)	0.7	1.33 (0.90-1.97)	0.15
Contrast-associated acute kidney injury*	30 (1.5)	-	19 (0.9)	-	1.59 (0.89-2.84)	0.11
NYHA class IV heart failure	58 (2.9)	1.0	56 (2.8)	0.9	1.04 (0.72-1.50)	0.83
Clinically non-significant bleeding	32 (1.6)	0.5	27 (1.3)	0.4	1.19 (0.71-1.99)	0.50

* There were 7 vs 0 patients with AKI associated with complete revasc during index hospitalization

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Conclusions

In patients with STEMI and multi-vessel coronary artery disease:

- Compared with culprit-lesion-only PCI, routine non-culprit lesion PCI with the goal of complete revascularization:
  - **Reduced CV death or new MI by 26%** (P=0.004), NNT = 37
  - **Reduced CV death, new MI or IDR by 49%** (P<0.001), NNT = 13
- The benefit of complete revascularization was similar in those undergoing non-culprit lesion PCI during the index hospitalization (median 1 day) and several weeks after hospital discharge (median 3 weeks)
- There were no significant differences in bleeding, stent thrombosis, AKI or stroke

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Acknowledgments

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ORIGINAL ARTICLE

Complete Revascularization with Multivessel PCI for Myocardial Infarction

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