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Complete Revascularization Trialists' Collaboration Final Results

An individual patient data meta-analysis of randomized trials comparing complete versus culprit lesion-only revascularisation for acute myocardial infarction:

THE COMPLETE REVASCULARISATION TRIALISTS' COLLABORATION

Shamir R. Mehta, Denise TW Tiong, Felix Böhm, Chinthanie Ramasundarahettige, Simone Biscaglia, Gianluca Campo, Stefan James, Pieter C Smits, Daniele Giacoppo, Gerry P McCann, Amerjeet Banning, Dan Eik Høfsten, Gianni Casella, Faith R Kirabo, Helen Nguyen, David A Wood, John A Cairns, Thomas Engstrøm

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Background

- Patients undergoing PCI of the culprit lesion for ACS are often found to have multivessel CAD, with 1 or more non-culprit lesions.
- RCT's have evaluated whether to routinely perform complete revascularisation (multi-vessel PCI of all non-culprit lesions, in addition to the culprit lesion) or manage the non-culprit lesions conservatively (culprit lesion-only PCI).
- Most (but not all), RCT's have shown that complete revascularization reduces non-fatal events, *but there remains uncertainty regarding:*
  1. the robustness of this benefit when considering the totality of RCT data
  2. whether complete revascularization reduces cardiovascular death

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Objective

To perform a collaborative individual patient data meta-analysis to determine the robustness of the effect of complete revascularization on CV death or new MI and CV death alone, based on the totality of data from RCT's

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Outcomes

Primary Outcomes

- CV death or New MI
- CV death alone

Secondary Outcome

- All-cause death

Other Outcomes

- New MI
- Non-CV death

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Methods

Inclusion Criteria: RCT's enrolling at least 250 patients with STEMI or NSTEMI comparing complete revascularisation strategy (with PCI) with either an angiography-guided or physiology guided strategy to a culprit lesion-only PCI strategy

Exclusion: Trials enrolling patients with cardiogenic shock or stable coronary artery disease

Search Strategy: Embase, Ovid MEDLINE and the Cochrane Central Register of Controlled Trials (CENTRAL) from 1996 to 2025 September 15

Analysis: ITT population, data pooled and analyses using a Cox Frailty Model with clustering of trials using a random effect.
The first primary outcome evaluated pre-specified α=0.04. If statistically significant, the α was considered "unused" and transferred to the second primary outcome, which was then tested at the full 0.05 level. If the first primary outcome was not significant, the second primary outcome was tested at α=0.01.

Sensitivity Analysis: 2-Stage analysis with PRAMI included

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Included Trials

TRIAL	N	INVESTIGATORS
Compare-Acute	885	P. Smits, D. Giacoppo
DANAMI-3 PRIMULTI	627	T. Engstrøm, D.E. Høfsten
Cvlprit	296	A. Banning, G. McCann
COMPLETE	4041	S. Mehta, D. Wood, J. Cairns
FIRE	1445	S. Biscaglia, G. Casella, G. Campo
FULL REVASC	1542	F. Böhm, S. James
Total	8836	

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Baseline Characteristics

	Complete N=4,259	Culprit-only N=4,577
Median Age, years	**65.5 (56.8, 76.0)**	**66 (57.0,76.0)**
Male sex	77.3%	75.5%
Female sex	**22.7%**	**24.5%**
Diabetes	19.5%	20.1%
Chronic renal insuff.	12.8%	11.9%
Clinical Presentation		
STEMI	**87.4%**	**88.4%**
NSTEMI	**12.6%**	**11.6%**
Previous MI	8.7%	8.8%
Current smoker	34.7%	34.5%
Hypertension	53.6%	54.8%
Dyslipidaemia	36.9%	36.6%
Previous PCI	8.9%	8.9%
Killip class ≥II	11.8%	11.6%

	Complete N=4,259	Culprit-only N=4,577
Symptom onset to index PCI		
<6 hr	72.3%	72.4%
6-12 hr	15.9%	15.9%
>12 hr	11.8%	11.6%
Medications at discharge		
Aspirin	98.6%	98.4%
P2Y12 Inhibitor		
Any	97.7%	98.2%
Ticagrelor	**59.0%**	**57.0%**
Prasugrel	**11.9%**	**12.9%**
Clopidogrel	26.9%	28.3%
Beta blocker	85.9%	86.1%
ACEi/ARB	81.0%	80.4%
Statin	**97.7%**	**96.7%**

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Procedural/Angiographic Characteristics

	Complete N=4,259	Culprit-only N=4,577
Radial access	79.5%	73.5%
Culprit lesion location*		
LM	44/3831 (1.1%)	46/4167 (1.1%)
LAD	1408/3831 (36.7%)	1520/4167 (36.5%)
Circ	731/3831 (19.0%)	741/4167 (17.8%)
RCA	1655/3831 (43.2%)	1870/4167 (44.9%)
No. of NCL vessels		
1	73.7%	73.3%
≥2	26.3%	26.6%
NCL diameter stenosis*		
50-<70%	743/5273 (14.1%)	736/4895 (15.0%)
70-<90%	3098/5273 (58.8%)	2929/4895 (59.8%)
90-<100%	1145/5273 (21.7%)	960/4895 (19.6%)
100%	287/5273 (5.4%)	270/4895 (5.5%)

	Complete N=4,259	Culprit-only N=4,577
Non-culprit lesion location*		
Left main	13/4888 (0.3%)	7/5089 (0.1%)
LAD	1961/4888 (40.1%)	2190/5089 (43.0%)
Proximal LAD	514/4888 (10.5%)	543/5089 (10.7%)
Mid LAD	739/4888 (15.1%)	857/5089 (16.8%)
Circumflex	1832/4888 (37.5%)	1914/5089 (37.6%)
Prox Circ	897/4888 (18.4%)	964/5089 (18.9%)
Distal Circ/PLV	330/4888 (6.8%)	366/5089 (7.2%)
RCA	1174/4888 (24.0%)	1173/5089 (23.0%)

*Per Lesion

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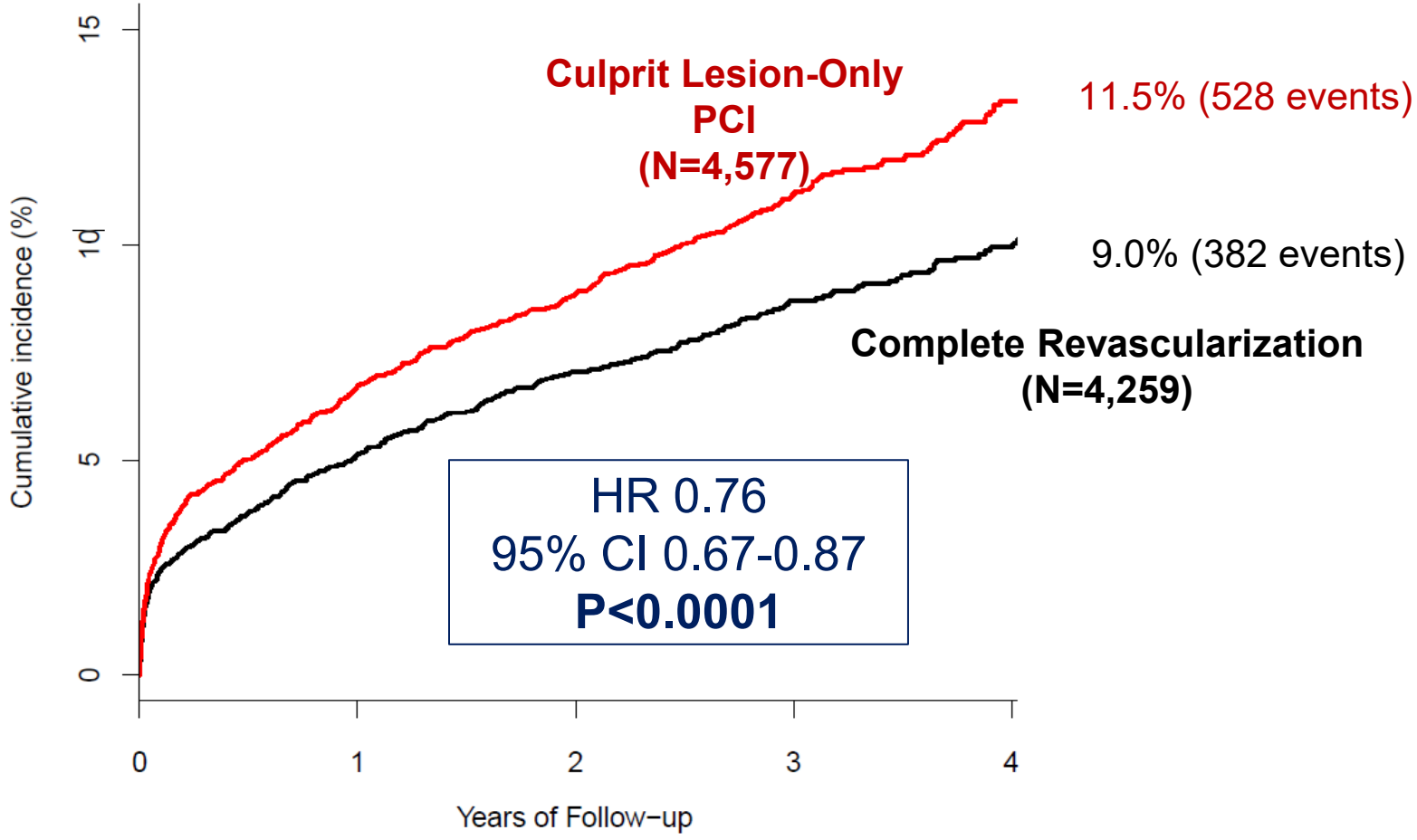
Primary Outcome: CV Death or New MI



No. at Risk (number censored)

Complete Revas.	4259(2)	3964(5)	3532(14)	2564(595)	1061(597)
Culprit-only PCI	4577(0)	4202(7)	3757(13)	2684(556)	1016(561)

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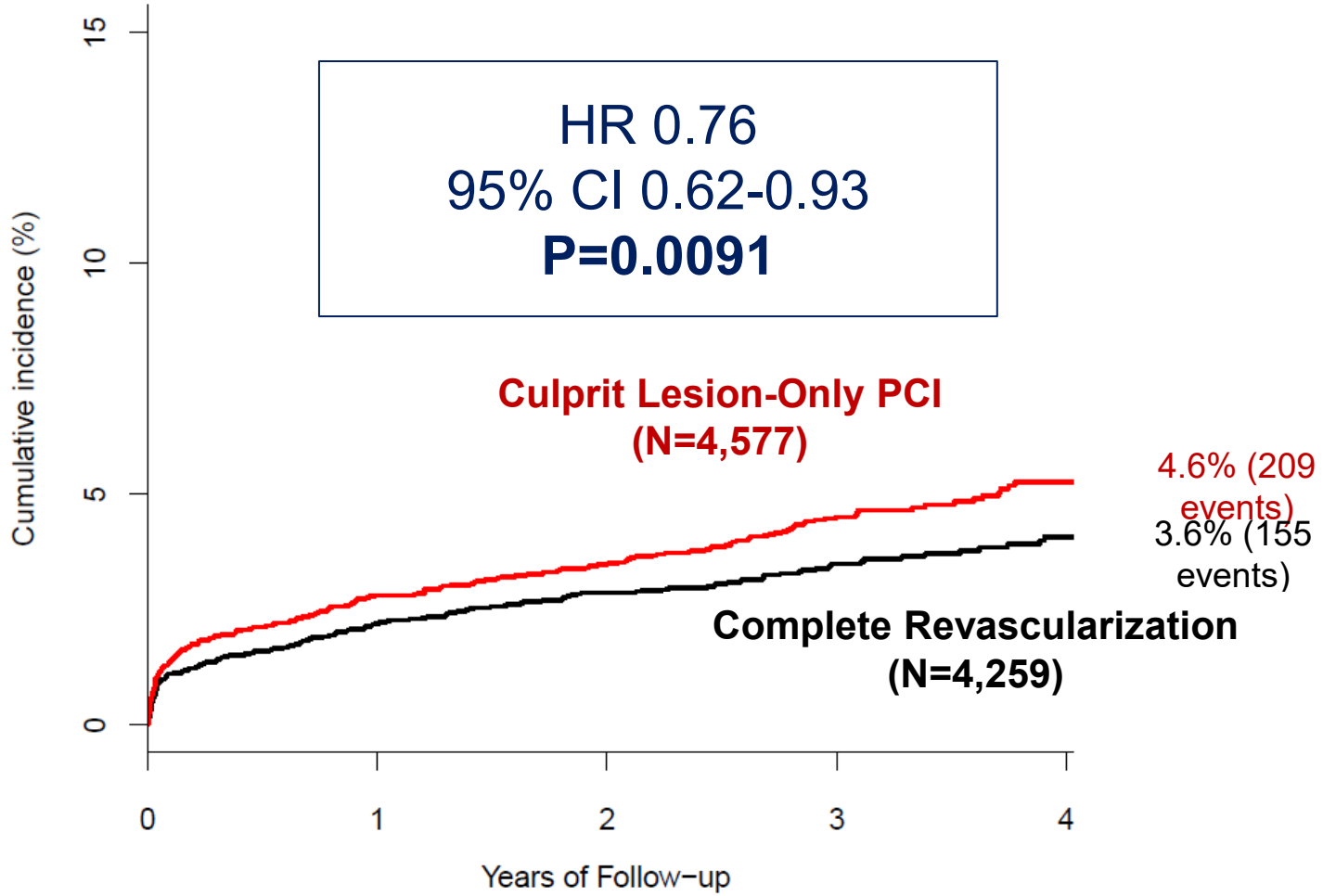
Primary Outcome: CV Death

HR 0.76
95% CI 0.62-0.93
P=0.0091



No. at Risk (number censored)					
Complete Revas.	4259(2)	4087(5)	3689(14)	2708(629)	1118(631)
Culprit−only PCI	4577(0)	4380(7)	3976(14)	2885(598)	1094(603)

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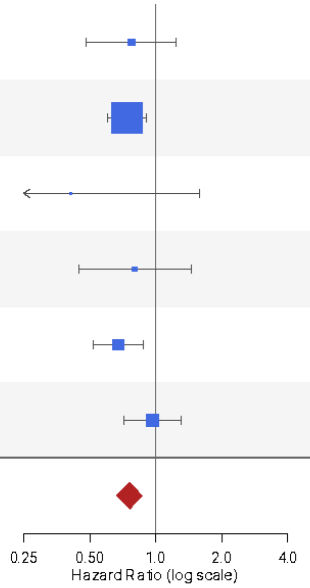
Primary Outcomes Forest Plots

CV Death or New MI

Study	Complete Event/Total (%/yr*)	Culprit Event/Total (%/yr*)	Hazard Ratio (95% CI)
COMPARE-ACUTE	24/295 (2.86)	61/590 (3.72)	0.77 (0.48 -1.24)
COMPLETE	158/2016 (2.69)	213/2025 (3.67)	0.74 (0.60 -0.91)
CvLPRIT	3/150 (0.37)	7/146 (0.99)	0.41 (0.11 -1.59)
DANAMI3-PRIMULTI	20/314 (3.02)	25/313 (3.74)	0.80 (0.45 -1.45)
FIRE	92/720 (4.97)	132/725 (7.48)	0.67 (0.52 -0.88)
FULL REVASC	85/764 (2.60)	90/778 (2.68)	0.97 (0.72 -1.30)
One stage IPD analysis	-	-	**0.76 (0.67 -0.87) p = <0.0001**

P heterogeneity=0.49

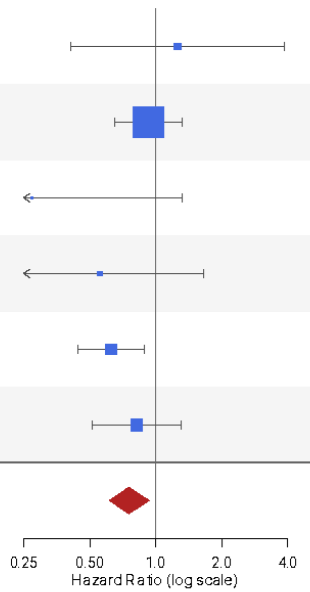


*Event rate per 100 person-years

CV Death

Study	Complete Event/Total (%/yr*)	Culprit Event/Total (%/yr*)	Hazard Ratio (95% CI)
COMPARE-ACUTE	5/295 (0.57)	8/590 (0.46)	1.26 (0.41 -3.85)
COMPLETE	59/2016 (0.97)	64/2025 (1.05)	0.93 (0.65 -1.32)
CvLPRIT	2/150 (0.25)	7/146 (0.96)	0.27 (0.06 -1.32)
DANAMI3-PRIMULTI	5/314 (0.73)	9/313 (1.30)	0.56 (0.19 -1.66)
FIRE	52/720 (2.70)	81/725 (4.33)	0.63 (0.44 -0.89)
FULL REVASC	32/764 (0.93)	40/778 (1.14)	0.82 (0.51 -1.30)
One stage IPD analysis	-	-	**0.76 (0.62 -0.93) p = 0.0091**

P heterogeneity=0.38



*Event rate per 100 person-years

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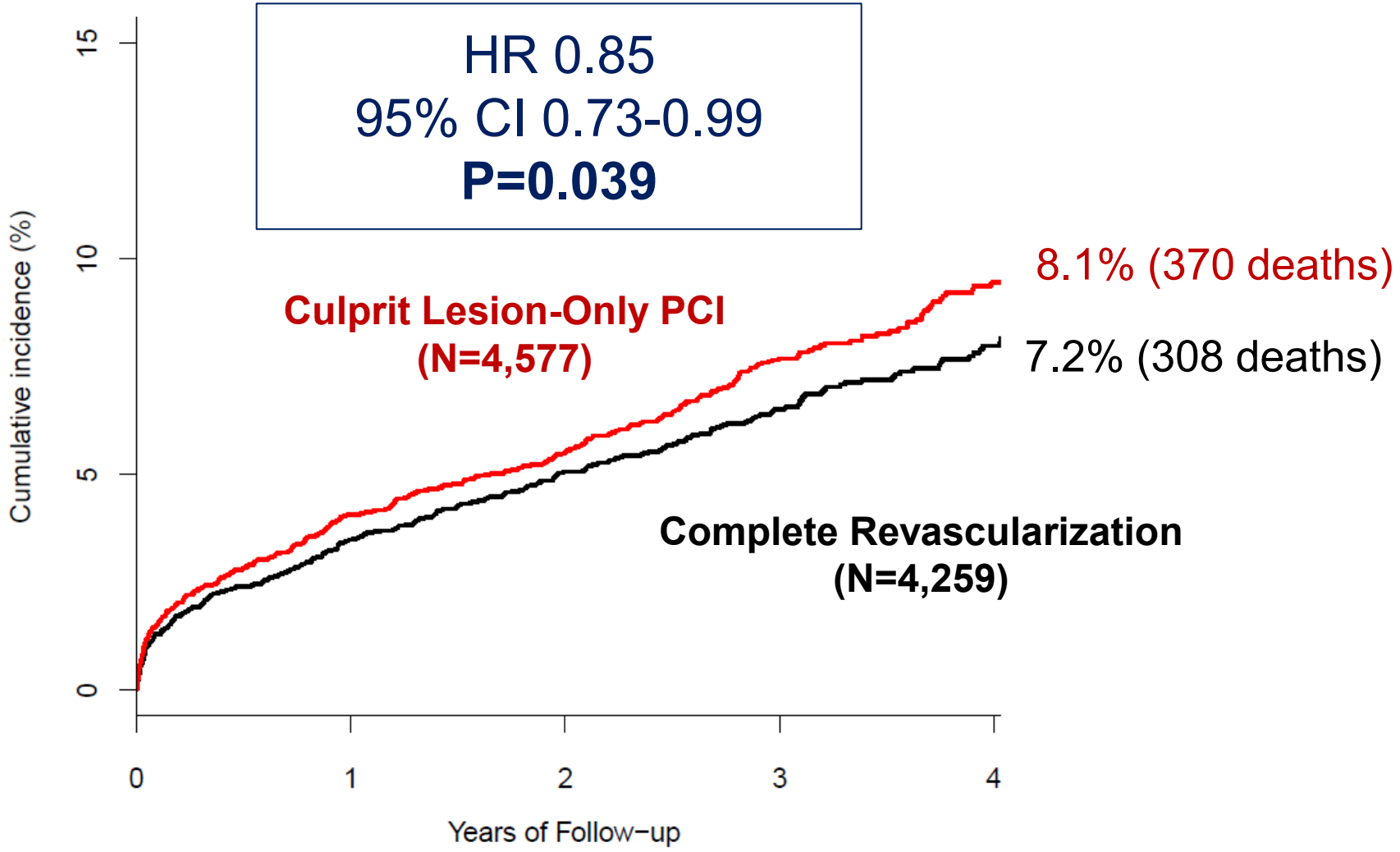
Secondary Outcome
All-cause Death

Median Follow-up 3 years

HR 0.85
95% CI 0.73-0.99
P=0.039



No. at Risk (number censored)					
Complete Revas.	4259(2)	4086(5)	3688(14)	2707(629)	1117(631)
Culprit−only PCI	4577(0)	4379(7)	3975(14)	2884(598)	1093(603)

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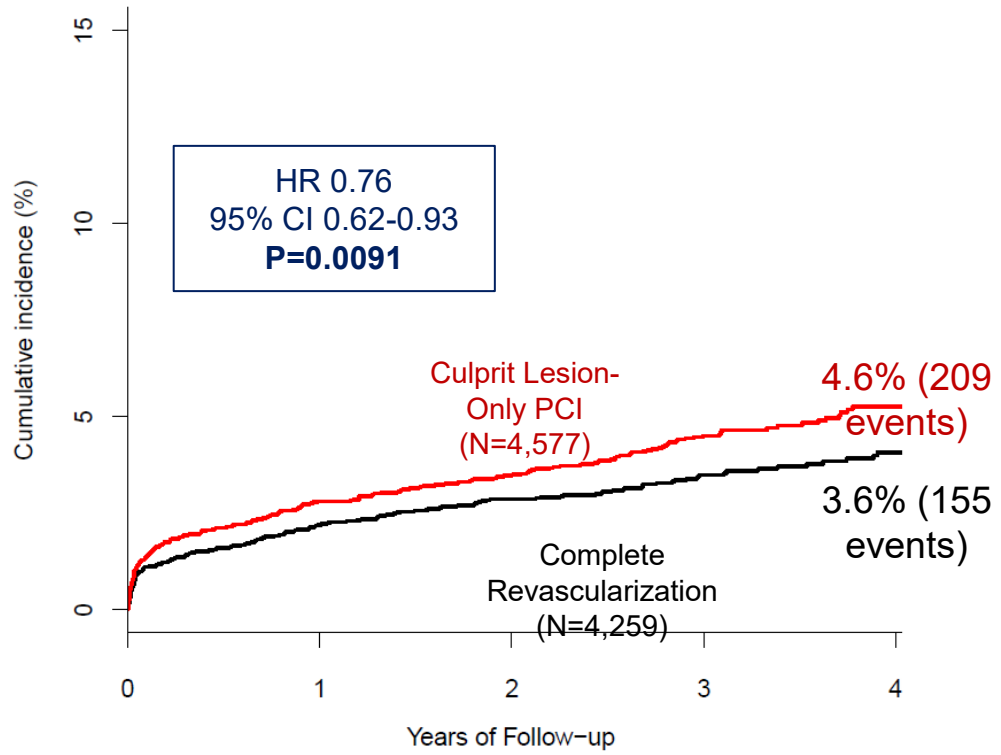
CV Death and Non-CV Death

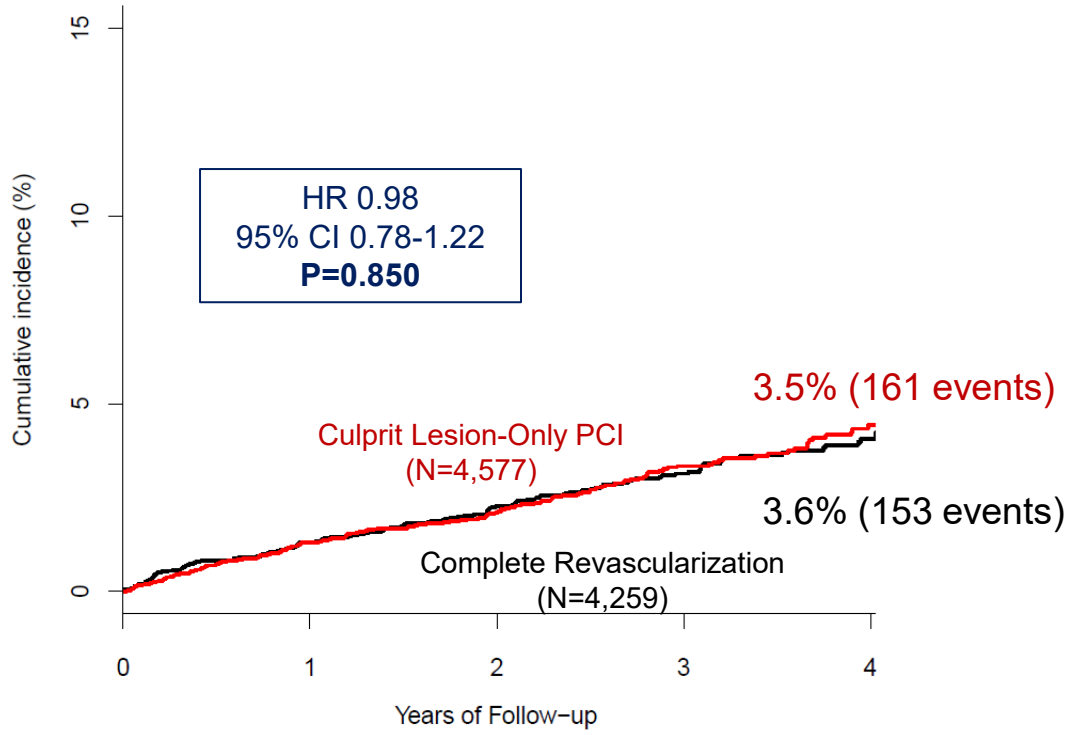
CV Death



No. at Risk (number censored)

Complete Revas.	4259(2)	4087(5)	3689(14)	2708(629)	1118(631)
Culprit-only PCI	4577(0)	4380(7)	3976(14)	2885(598)	1094(603)

Non-CV Death



No. at Risk (number censored)

Complete Revas.	4259(2)	4086(5)	3688(14)	2707(629)	1117(631)
Culprit-only PCI	4577(5)	4379(12)	3975(20)	2884(604)	1093(609)

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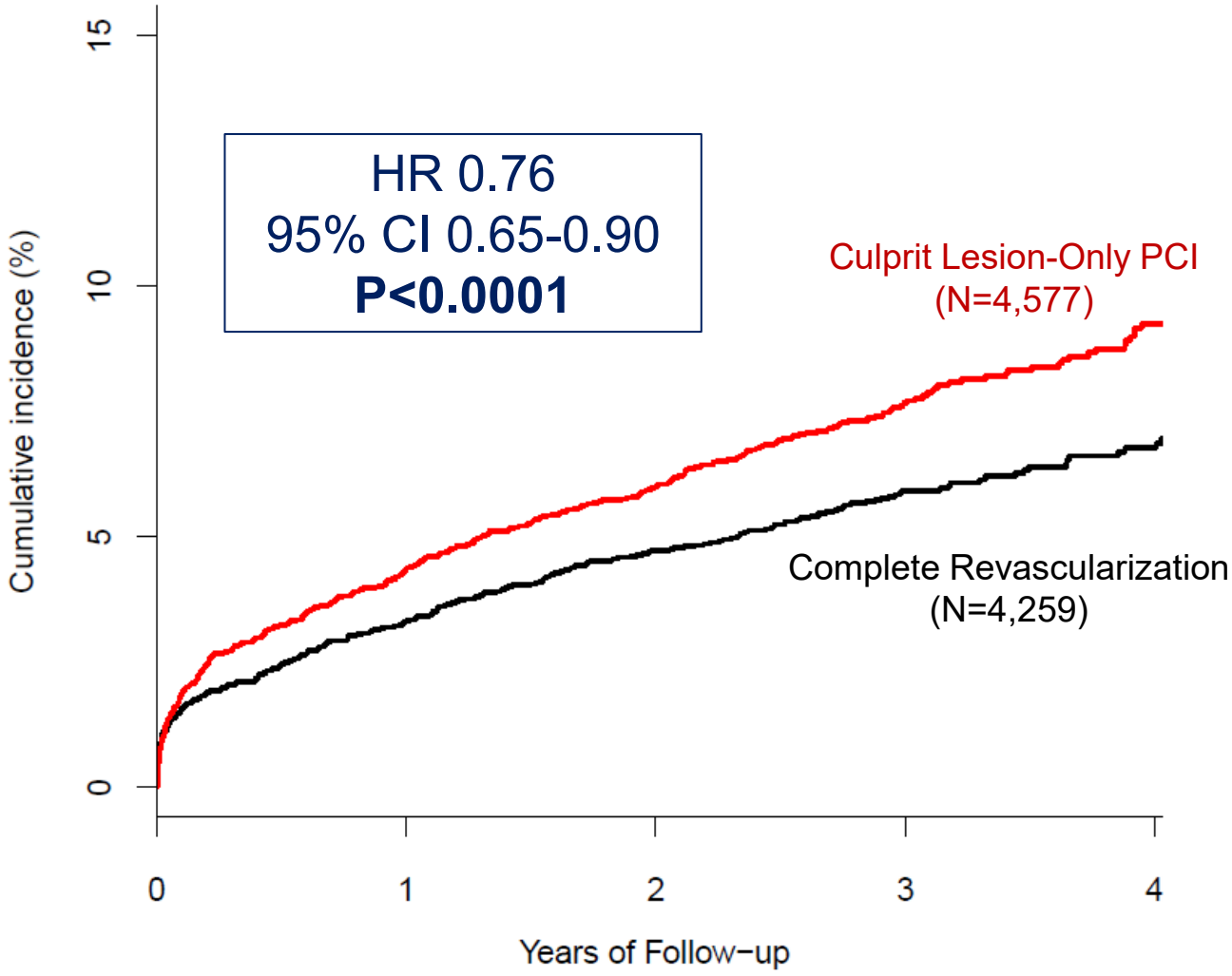
New MI



No. at Risk (number censored)

Complete Revas.	4259(2)	3964(5)	3532(14)	2564(595)	1061(597)
Culprit−only PCI	4577(5)	4202(12)	3757(19)	2684(562)	1016(567)

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Summary of Main Outcomes

Median Follow-up 3 Years

Outcome	Complete Revasc (N=4259)	Culprit Lesion-only PCI (N=4577)	HR (95% CI)	P-value
Primary Outcome: CV death or new MI	382 (9.0%)	528 (11.5%)	0.76 (0.67-0.87)	<0.0001
Primary Outcome: CV death	155 (3.6%)	209 (4.6%)	0.76 (0.62-0.93)	0.0091
Secondary Outcome: All-cause death	308 (7.2%)	370 (8.1%)	0.85 (0.73-0.99)	0.039
Non-CV death	153 (3.6%)	161 (3.5%)	0.98 (0.78-1.22)	0.85
New MI	255 (6.0%)	357 (7.8%)	0.76 (0.65-0.90)	0.0011

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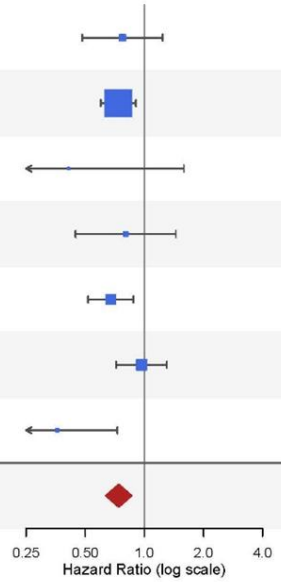
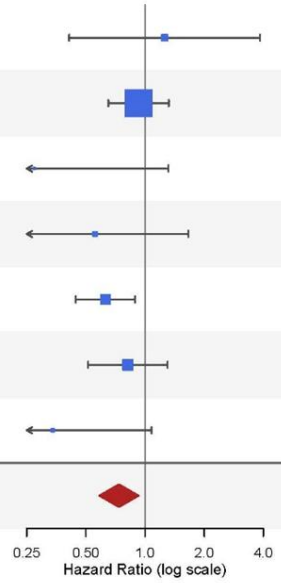
Sensitivity Analysis: Two stage approach including PRAMI

Study	Complete Event/Total (%/yr*)	Culprit Event/Total (%/yr*)	CV Death or New MI	Hazard Ratio (95% CI)
COMPARE−ACUTE	24/295 (2.86)	61/590 (3.72)		0.77 (0.48 −1.24)
COMPLETE	158/2016 (2.69)	213/2025 (3.67)		0.74 (0.60 −0.91)
CvLPRIT	3/150 (0.37)	7/146 (0.99)		0.41 (0.11 −1.59)
DANAMI3−PRIMULTI	20/314 (3.02)	25/313 (3.74)		0.80 (0.45 −1.45)
FIRE	92/720 (4.97)	132/725 (7.48)		0.67 (0.52 −0.88)
FULL REVASC	85/764 (2.60)	90/778 (2.68)		0.97 (0.72 −1.30)
PRAMI	11/234 (NA)	27/231 (NA)		0.36 (0.18 −0.73)
Two stage meta−analysis	–	–		**0.74 (0.64 −0.86) p = <0.001**



Heterogeneity (I^2): 15.8%
**Event rate per 100 person−years; NA − Data not available*

Study	Complete Event/Total (%/yr*)	Culprit Event/Total (%/yr*)	CV Death	Hazard Ratio (95% CI)
COMPARE−ACUTE	5/295 (0.57)	8/590 (0.46)		1.26 (0.41 −3.85)
COMPLETE	59/2016 (0.97)	64/2025 (1.05)		0.93 (0.65 −1.32)
CvLPRIT	2/150 (0.25)	7/146 (0.96)		0.27 (0.06 −1.32)
DANAMI3−PRIMULTI	5/314 (0.73)	9/313 (1.30)		0.56 (0.19 −1.66)
FIRE	52/720 (2.70)	81/725 (4.33)		0.63 (0.44 −0.89)
FULL REVASC	32/764 (0.93)	40/778 (1.14)		0.82 (0.51 −1.30)
PRAMI	4/234 (NA)	10/231(NA)		0.34 (0.11 −1.08)
Two stage meta−analysis	–	–		**0.74 (0.58 −0.93) p = 0.010**



Heterogeneity (I^2): 11.5%
**Event rate per 100 person−years; NA − Data not available*

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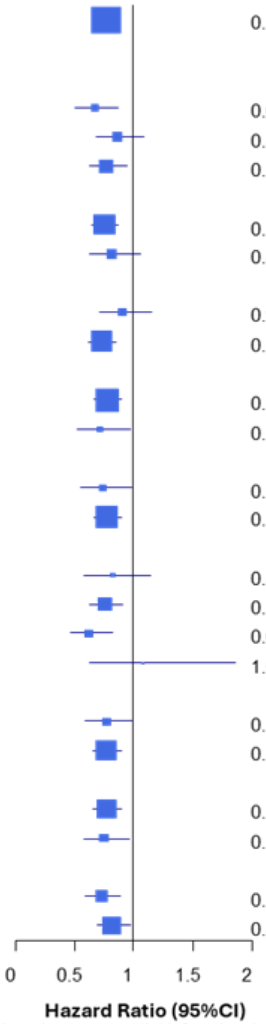
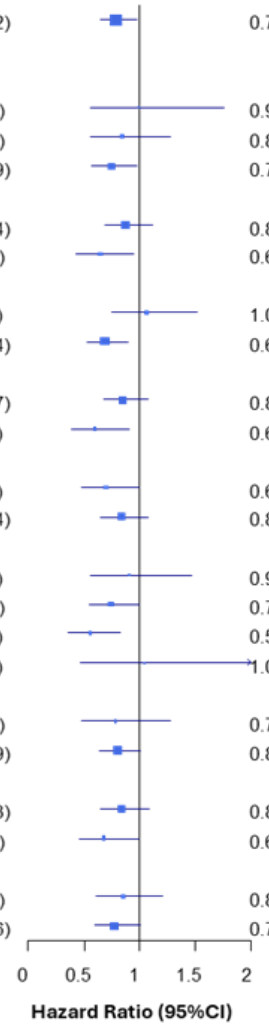
Subgroups

	CV death or New MI				CV death			
	Complete (No. of events/ Total no. (%/yr))	Culprit-Lesion only (No. of events/ Total no. (%/yr))	HR (95% CI)	P Interaction	Complete (No. of events/ Total no. (%/yr))	Culprit-Lesion only (No. of events/ Total no. (%/yr))	HR (95% CI)	P Interaction
Overall	382/ 4259 (2.87)	528/ 4577 (3.78)	0.76 (0.67-0.87)		155/ 4259 (1.12)	209/ 4577 (1.42)	0.76 (0.62-0.93)	
Age (years)				**0.38**				**0.65**
<60	90/ 1425 (1.94)	138/ 1486 (2.94)	0.67 (0.51-0.87)		23/ 1425 (0.48)	24/ 1486 (0.49)	0.99 (0.56-1.76)	
60 to <75	131/ 1591 (2.52)	166/ 1731 (2.97)	0.86 (0.68-1.08)		41/ 1591 (0.76)	53/ 1731 (0.90)	0.84 (0.56-1.27)	
≥75	161/ 1243 (4.66)	224/ 1360 (6.09)	0.77 (0.63-0.94)		91/ 1243 (2.52)	132/ 1360 (3.39)	0.74 (0.57-0.97)	
Sex				**0.61**				**0.19**
Male	283/ 3293 (2.71)	386/ 3455 (3.65)	0.75 (0.65-0.88)		116/ 3293 (1.07)	138/ 3455 (1.24)	0.87 (0.68-1.12)	
Female	99/ 966 (3.45)	142/ 1122 (4.21)	0.81 (0.63-1.05)		39/ 966 (1.29)	71/ 1122 (2.01)	0.64 (0.43-0.94)	
Diabetes				**0.13**				**0.05**
Yes	116/ 828 (4.93)	143/ 918 (5.41)	0.91 (0.71-1.16)		59/ 828 (2.36)	62/ 918 (2.20)	1.07 (0.75-1.52)	
No	266/ 3431 (2.43)	385/ 3659 (3.40)	0.72 (0.62-0.84)		96/ 3431 (0.85)	147/ 3659 (1.24)	0.69 (0.53-0.89)	
MI Type				**0.65**				**0.16**
STEMI	314/ 3723 (2.67)	437/ 4045 (3.49)	0.77 (0.67-0.89)		121/ 3723 (0.99)	154/ 4045 (1.17)	0.85 (0.67-1.08)	
NSTEMI	68/ 536 (4.47)	91/ 532 (6.37)	0.71 (0.52-0.98)		34/ 536 (2.14)	55/ 532 (3.63)	0.60 (0.39-0.92)	
Killip class				**0.79**				**0.38**
≥ 2	80/ 497 (5.92)	111/ 527 (8.16)	0.74 (0.55-0.98)		48/ 497 (3.40)	72/ 527 (5.00)	0.69 (0.48-1.00)	
< 2	298/ 3721 (2.53)	411/ 4001 (3.31)	0.77 (0.66-0.89)		107/ 3721 (0.87)	136/ 4001 (1.04)	0.84 (0.65-1.08)	
Non-culprit Lesion Stenosis Severity				**0.28**				**0.34**
50% to <70%	59/ 608 (2.91)	76/ 623 (3.51)	0.81 (0.58-1.14)		31/ 608 (1.48)	36/ 623 (1.59)	0.91 (0.56-1.47)	
70% to <90%	196/ 2289 (2.71)	254/ 2285 (3.57)	0.76 (0.63-0.92)		72/ 2289 (0.96)	97/ 2285 (1.30)	0.74 (0.54-1.00)	
90% to <100%	92/ 1040 (2.87)	119/ 874 (4.76)	0.62 (0.47-0.82)		38/ 1040 (1.14)	56/ 874 (2.12)	0.55 (0.37-0.83)	
100%	28/ 280 (3.79)	25/ 268 (3.53)	1.08 (0.63-1.85)		12/ 280 (1.56)	11/ 268 (1.51)	1.05 (0.46-2.37)	
Proximal/mid LAD nonculpirt				**0.98**				**0.98**
Presence	94/ 1195 (2.41)	135/ 1339 (3.20)	0.76 (0.59-0.99)		28/ 1195 (0.69)	39/ 1339 (0.88)	0.78 (0.48-1.27)	
Absent	268/ 2750 (3.07)	368/ 2925 (4.06)	0.76 (0.65-0.89)		122/ 2750 (1.34)	161/ 2925 (1.69)	0.80 (0.63-1.01)	
Number of residual diseased vessels				**0.87**				**0.35**
1	249/ 2835 (2.72)	343/ 3058 (3.59)	0.77 (0.65-0.90)		105/ 2835 (1.10)	133/ 3058 (1.33)	0.84 (0.65-1.09)	
≥ 2	106/ 1011 (3.31)	154/ 1111 (4.43)	0.75 (0.58-0.96)		40/ 1011 (1.19)	65/ 1111 (1.77)	0.67 (0.45-1.00)	
Complete Revascularization Strategy*				**0.39**				**0.66**
Angiography-guided	161/ 2166 (2.41)	220/ 2171 (3.37)	0.72 (0.59-0.89)		61/ 2166 (0.88)	71/ 2171 (1.04)	0.86 (0.61-1.21)	
Physiology guided	221/ 2093 (3.34)	308/ 2406 (4.14)	0.81 (0.68-0.97)		94/ 2093 (1.36)	138/ 2406 (1.76)	0.78 (0.60-1.01)	





Overall- Based on random effects model ** - Trial level*

STEMI=ST-segment elevation myocardial infarction, NSTEMI=Non-ST-segment elevation myocardial infarction, LAD=Left aneterior descending;

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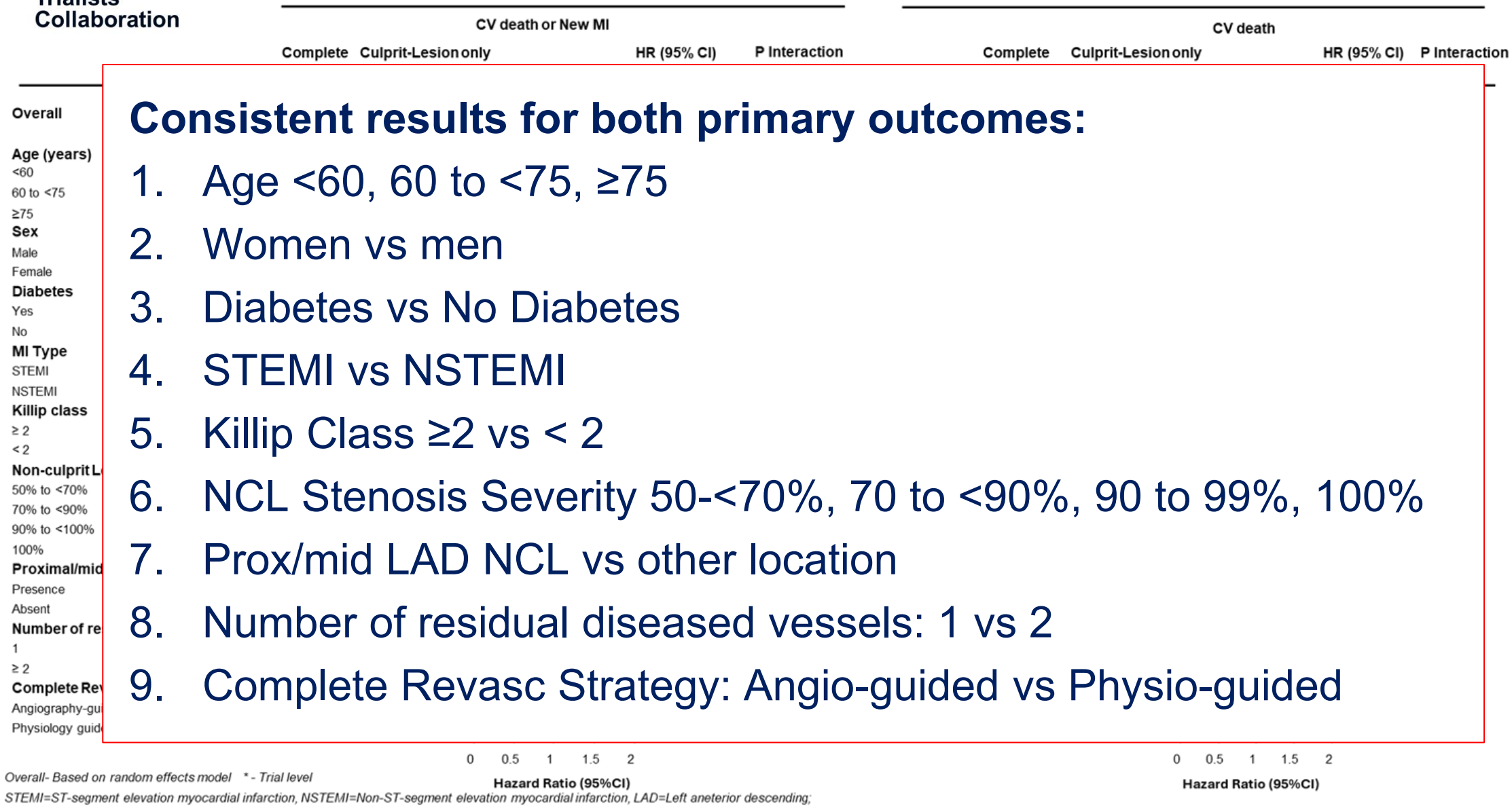
Subgroups



Consistent results for both primary outcomes:

1. Age <60, 60 to <75, ≥75
2. Women vs men
3. Diabetes vs No Diabetes
4. STEMI vs NSTEMI
5. Killip Class ≥2 vs < 2
6. NCL Stenosis Severity 50-<70%, 70 to <90%, 90 to 99%, 100%
7. Prox/mid LAD NCL vs other location
8. Number of residual diseased vessels: 1 vs 2
9. Complete Revasc Strategy: Angio-guided vs Physio-guided

*Overall- Based on random effects model * - Trial level*
STEMI=ST-segment elevation myocardial infarction, NSTEMI=Non-ST-segment elevation myocardial infarction, LAD=Left aneterior descending;

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Conclusions

This IPD involving 8,836 patients from 6 multicentre randomized trials demonstrated that, compared with culprit lesion-only PCI, **complete revascularisation:**

- **Reduced CV death or new MI** by 24% (P<0.0001)
- **Reduced CV death alone** by 24% (P=0.0091)
- **Reduced all-cause death** by 15% P=0.039)
- **Reduced new MI** by 24% (P=0.0011)
- **Had no effect on Non-CV Death**

This benefit was consistent in all subgroups studied, including:

- **Women and men**
- **Younger and older patients**
- **STEMI and NSTEMI**
- **Physiology-guided and angiography-guided NCL PCI strategies**

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Implications

- These data provide the strongest evidence that complete revascularisation improves important clinical outcomes in patients with acute MI and multivessel CAD

- The number needed to treat to prevent 1 CV death or new MI is 41 patients and to prevent 1 CV death is 99 over 3 years.

- Data from the IPD establish complete revascularization for patients with acute MI as one of the few clinical indications where a PCI-based strategy reduces cardiovascular and all-cause death

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Complete versus culprit lesion-only revascularisation for acute myocardial infarction (Complete Revascularisation Trialists' Collaboration): an individual patient data meta-analysis of randomised trials

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