HERZZENTRUM LEIPZIG

Leipzig Heart Institute LHI

UNIVERSITÄT LEIPZIG

CULPRIT-SHOCK

CULPRIT-SHOCK: Culprit Lesion Only PCI versus Multivessel PCI in Cardiogenic Shock – 1-Year Results

Holger Thiele

on behalf of the CULPRIT-SHOCK Investigators

ESC Congress Munich 2018

Disclosure Statement of Financial Interest

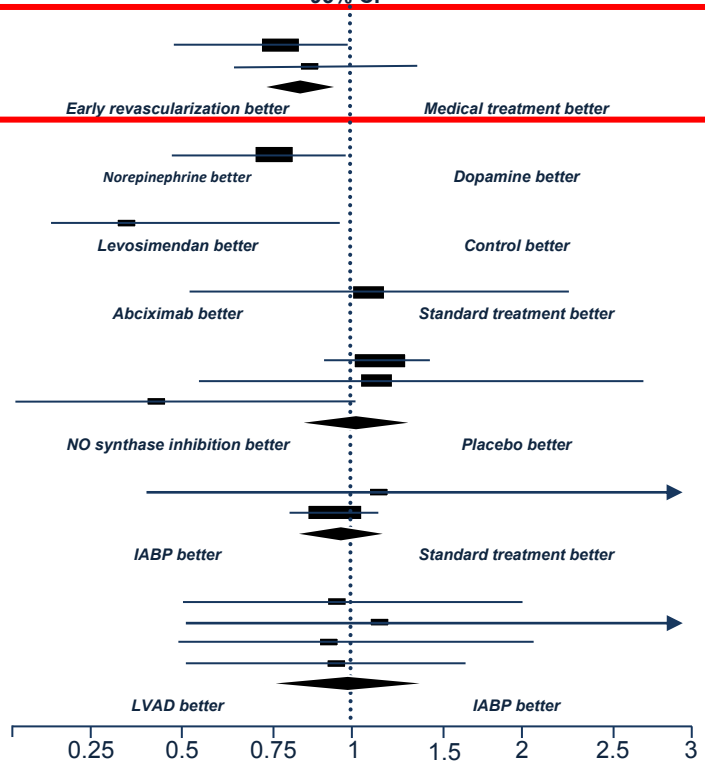
Within the past 12 months, I have had a financial interest/arrangement or affiliation with the organization(s) listed below.

Affiliation/Financial Relationship	Company
• Grant/Research Support	• European Union, German Cardiac Society German Heart Research Foundation
• Consulting Fees/Honoraria	• None
• Major Stock Shareholder/Equity	• None
• Royalty Income	• None
• Ownership/Founder	• None
• Intellectual Property Rights	• None
• Other Financial Benefit	• None

Randomized Trials Cardiogenic Shock

CULPRIT-SHOCK

	Follow-up	n/N	n/N	Relative Risk Mortality 95% CI	Relative Risk 95% CI
Revascularization					
SHOCK	1 year	81/152	100/150		0.72 (0.54;0.95)
SMASH	30 days	22/32	18/23		0.87 (0.66;1.29)
Total		***103/184***	***118/173***		***0.82 (0.69;0.97)***
Vasopressors					
SOAP-2 (CS subgroup)	28 days	64/145	50/135		0.75 (0.55;0.93)
Inotropes					
Unverzagt et al.	30 days	5/16	10/16		0.33 (0.11;0.97)
Glycoprotein IIb/IIIa inhibitors					
PRAGUE-18	In-hospital	15/40	13/40		1.15 (0.59;2.27)
NO synthase inhibitors					
TRIUMPH	30 days	97/201	76/180		1.14 (0.91;1.45)
SHOCK II	30 days	24/59	7/20		1.16 (0.59;2.69)
Cotter et al.	30 days	4/15	10/15		0.40 (0.13;1.05)
Total		***125/275***	***93/215***		***1.05 (0.85;1.29)***
IABP					
IABP-SHOCK I	30 days	7/19	6/21		1.28 (0.45;3.72)
IABP-SHOCK II	30 days	119/300	123/298		0.96 (0.79;1.17)
Total		***126/319***	***129/319***		***0.98 (0.81;1.18)***
LVAD					
Thiele et al.	30 days	9/21	9/20		0.95 (0.48;1.90)
Burkhoff et al.	30 days	9/19	5/14		1.33 (0.57;3.10)
ISAR-SHOCK	30 days	6/13	6/13		1.00 (0.44;2.29)
IMPRESS in Severe Shock	30 days	11/24	12/24		0.92 (0.51;1.66)
Total		***35/77***	***32/71***		***1.01 (0.70;1.44)***



ESC Congress Munich 2018

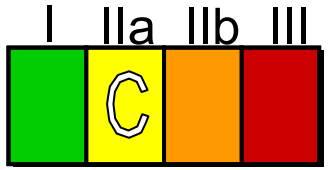
Thiele et al. Eur Heart J 2015;36:1223-1230

Multivessel PCI in Cardiogenic Shock
European and American Recommendations 2017

Multivessel coronary artery disease present in up to 80% → higher mortality

Guidelines

ESC



ACC/AHA/SCAI

No recommendation

Appropriate Use Criteria

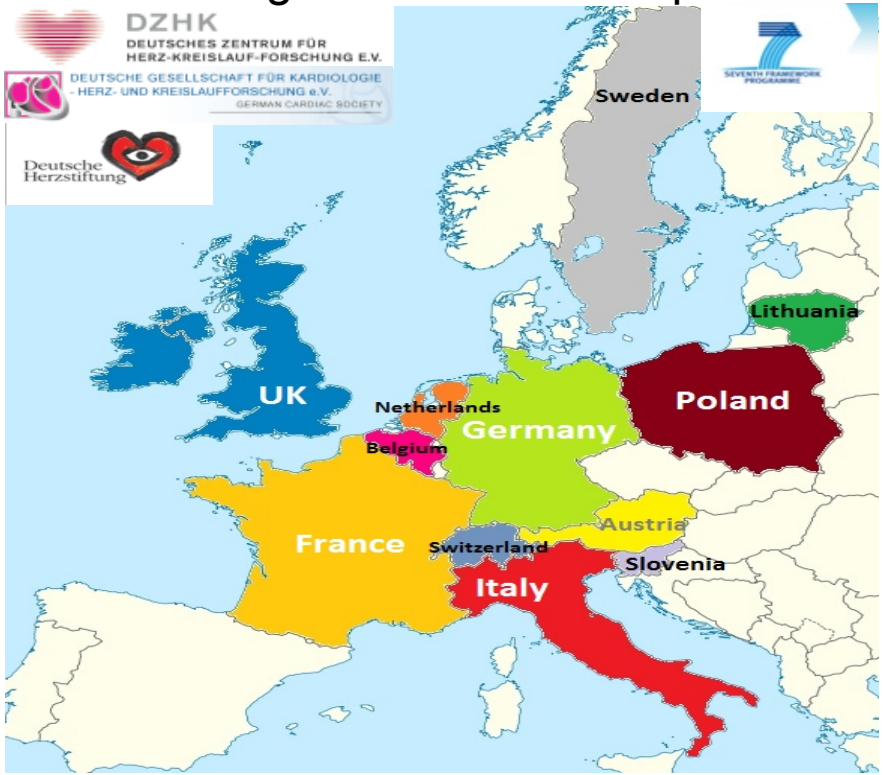
ACC/AATS/AHA/ASE/ASNC/SCAI/SCCT/STS

A (9)

Ibanez et al. Eur Heart J 2018;39:119-177
Levine et al. J Am Coll Cardiol 2016;67:1235-1250
Patel et al. J Am Coll Cardiol 2017;69:570-591

CULPRIT-SHOCK Trial

Investigator-initiated European multicenter trial; 1:1 randomization



PI + Coordination:
Holger Thiele
Co-PI:
Uwe Zeymer
Steffen Desch

National Coordinators (83 centers):

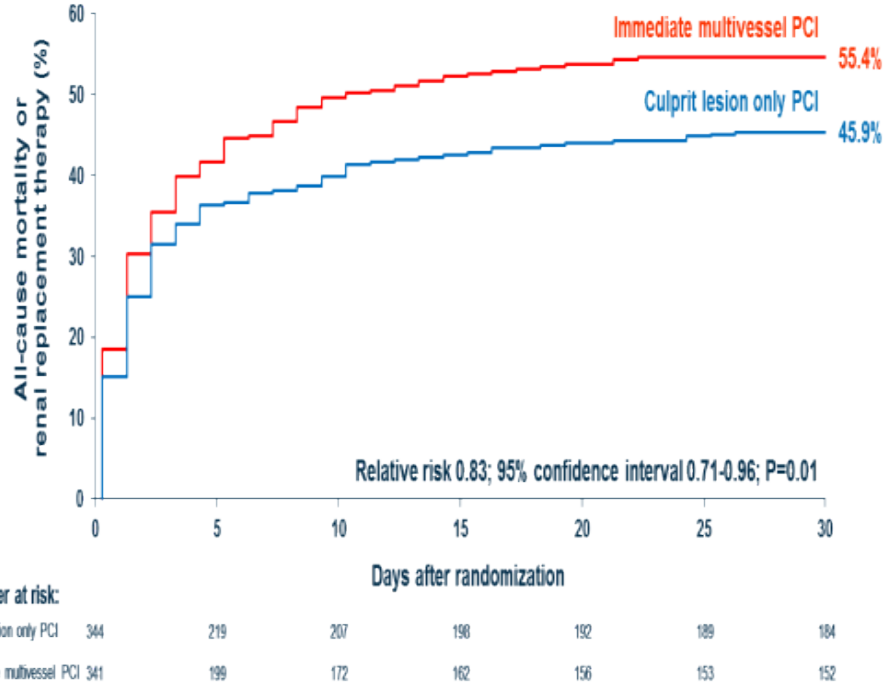
- Kurt Huber
- Gilles Montalescot
- Jan Piek
- Holger Thiele
- Pranas Serpytis
- Janina Stepinska
- Christiaan Vrints
- Marko Noc
- Keith Oldroyd
- Stefan Windecker
- Stefano Savonitto

Thiele et al. Am Heart J. 2016;172:160-169

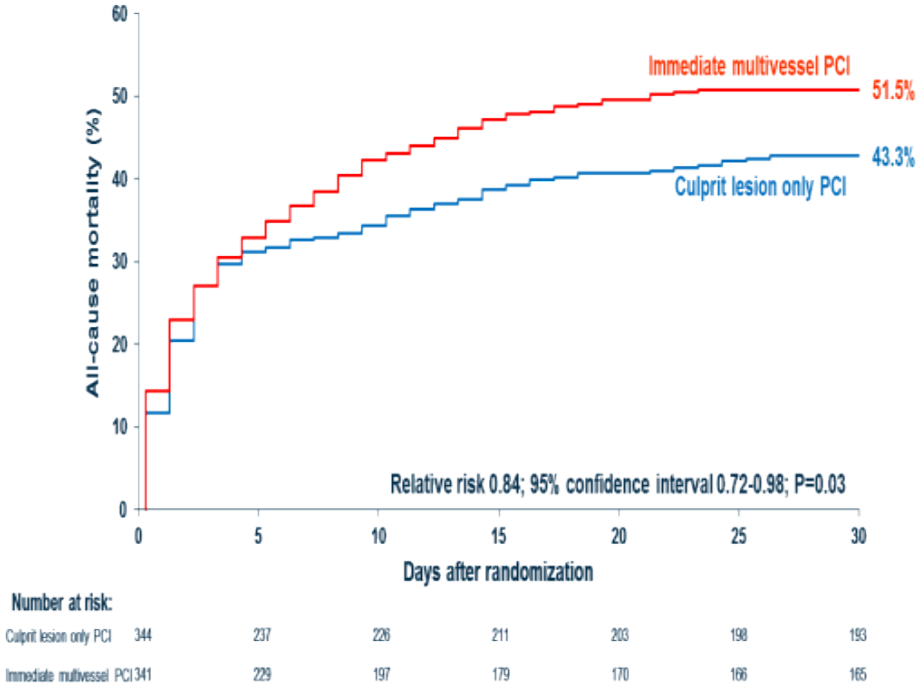
CULPRIT-SHOCK Trial – 30-Day Results

Primary study endpoint – 30 days

All-cause mortality or renal replacement therapy



All-cause mortality – 30 days



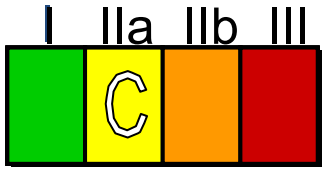
Thiele et al. NEJM 2017; 377:2419-2432

Multivessel PCI in Shock - Guideline Evolution

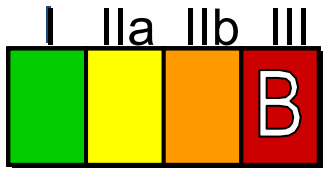
ESC STEMI Guidelines 2017 → Revascularization Guidelines 2018

STEMI (NSTEMI), Cardiogenic Shock

2017



2018



Ibanez et al. Eur Heart J 2018;39:119-177
Neumann et al. Eur Heart J 2018;epub 25.08.2018

Multivessel PCI in Cardiogenic Shock?

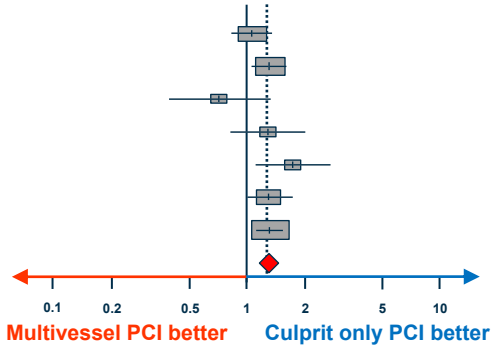
Metaanalysis Mortality – Registry-Data

Short-term follow-up

	MV-PCI		C-PCI		RR	95%CI
	Events	Total	Events	Total		
IABP-SHOCK II	75	167	119	284	1.07	[0.86-1.33]
ALKK	81	173	201	562	1.31	[1.08-1.33]
KAMIR	13	124	56	386	0.72	[0.41-1.28]
Yang et al.	19	60	68	278	1.29	[0.85-1.98]
Cavender et al.	20	43	42	156	1.73	[1.14-2.61]
EHS-PCI	40	82	95	254	1.30	[0.99-1.71]
NCDR	158	433	737	2654	1.31	[1.14-1.51]
Overall	**406**	**1082**	**1318**	**4574**	**1.26**	**[1.12-1.41]**

Heterogeneity: τ^2=0.007, I^2=31.0%, p=0.19

Test for overall effect: p=0.001

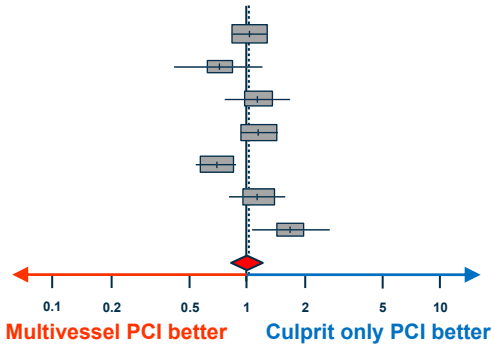


Long-term follow-up

	MV-PCI		C-PCI		RR	95%CI
	Events	Total	Events	Total		
IABP-SHOCK II	91	167	149	284	1.04	[0.87-1.24]
KAMIR	16	124	69	386	0.72	[0.43-1.19]
Yang et al.	21	60	85	278	1.14	[0.78-1.69]
Cavender et al.	32	43	101	156	1.15	[0.93-1.42]
Mylotte et al.	37	66	82	103	0.70	[0.56-0.89]
van der Schaaf et al.	22	37	66	124	1.12	[0.82-1.53]
SHOCK	7	9	26	57	1.71	[1.09-2.67]
Overall	**226**	**506**	**578**	**1387**	**1.03**	**[0.85-1.25]**

Heterogeneity: τ^2=0.043, I^2=67.8%, p=0.005

Test for overall effect: p=0.77



de Waha et al. Eur Heart J Acute Cardiovasc Care. 2018;7:28-37

Statistical Methodology

CULPRIT-SHOCK

Primary Study Endpoint:

- **30-day all-cause mortality or renal replacement therapy**

Secondary Study Endpoints:

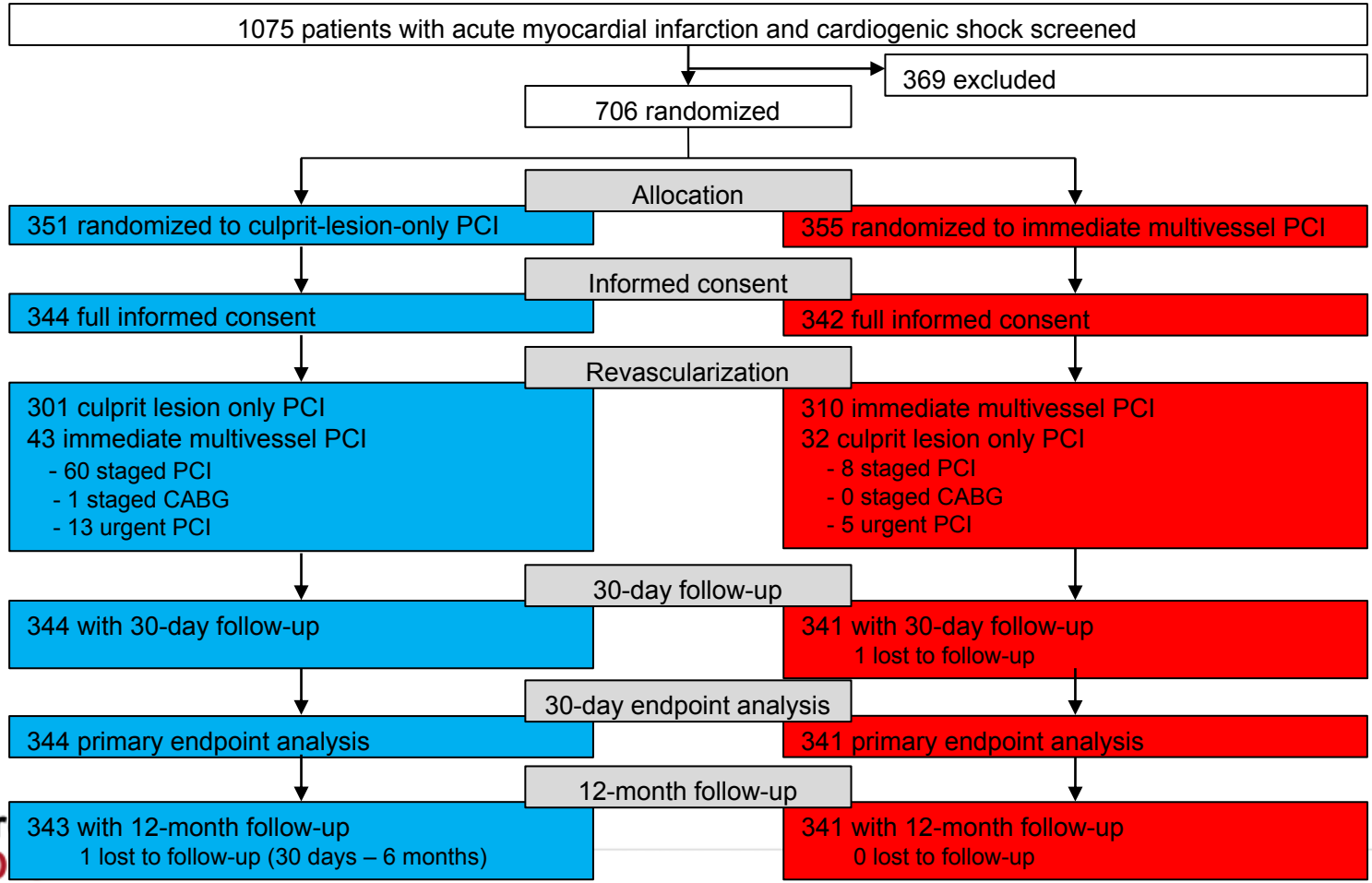
- 30-day all-cause mortality
- Renal failure with requirement of renal replacement therapy
- Time to hemodynamic stabilization
- Duration of catecholamine therapy
- Serial creatinine-clearance
- Length of ICU-stay
- SAPS-II score
- Requirement and length of mechanical ventilation
- All-cause death within 6 and 12 months follow-up
- Recurrent infarction within 30-days, 6 and 12 months follow-up
- Death or recurrent infarction at 6 and 12 months follow-up
- Rehospitalization for congestive heart failure within 30 days, 6-, and 12-months follow-up
- Death/recurrent infarction/rehospitalization for congestive heart failure within 30 days, 6-, and 12-months follow-up
- Need for recurrent revascularization (PCI and/or CABG) within 30 days, 6-, and 12-months follow-up
- Peak creatine kinase, creatine kinase-MB

Sample Size:

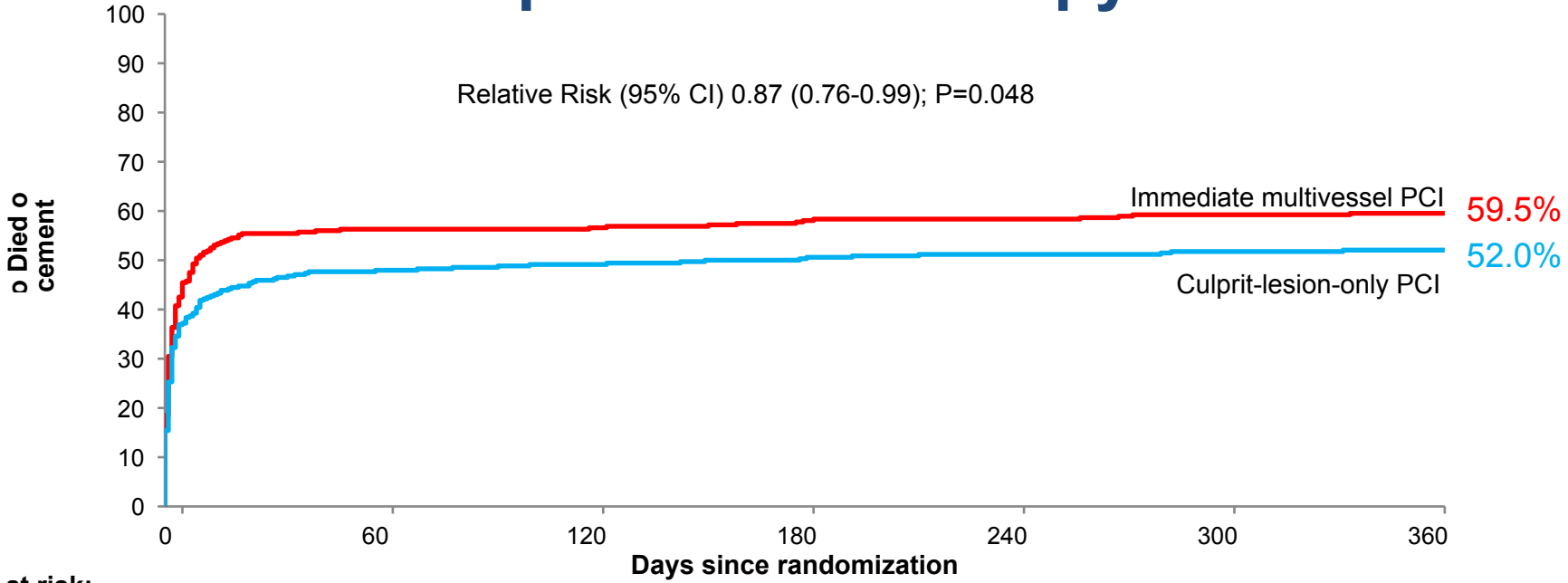
- **Estimated 50% event rate in multivessel PCI versus 38% in culprit lesion only group for primary endpoint**
- **1 interim analysis (50% of patients)**
- 2-sided Chi^2-test; power: 80%, alpha=0.048 for final analysis → **684 patients**
- **To compensate losses in follow-up → 706 patients**

Thiele et al. Am Heart J. 2016;172:160-169

Trial Flow


1075 patients with acute myocardial infarction and cardiogenic shock screened
369 excluded
706 randomized
Allocation
351 randomized to culprit-lesion-only PCI
355 randomized to immediate multivessel PCI
Informed consent
344 full informed consent
342 full informed consent
Revascularization
301 culprit lesion only PCI
43 immediate multivessel PCI
- 60 staged PCI
- 1 staged CABG
- 13 urgent PCI
310 immediate multivessel PCI
32 culprit lesion only PCI
- 8 staged PCI
- 0 staged CABG
- 5 urgent PCI
30-day follow-up
344 with 30-day follow-up
341 with 30-day follow-up
1 lost to follow-up
30-day endpoint analysis
344 primary endpoint analysis
341 primary endpoint analysis
12-month follow-up
343 with 12-month follow-up
1 lost to follow-up (30 days – 6 months)
341 with 12-month follow-up
0 lost to follow-up

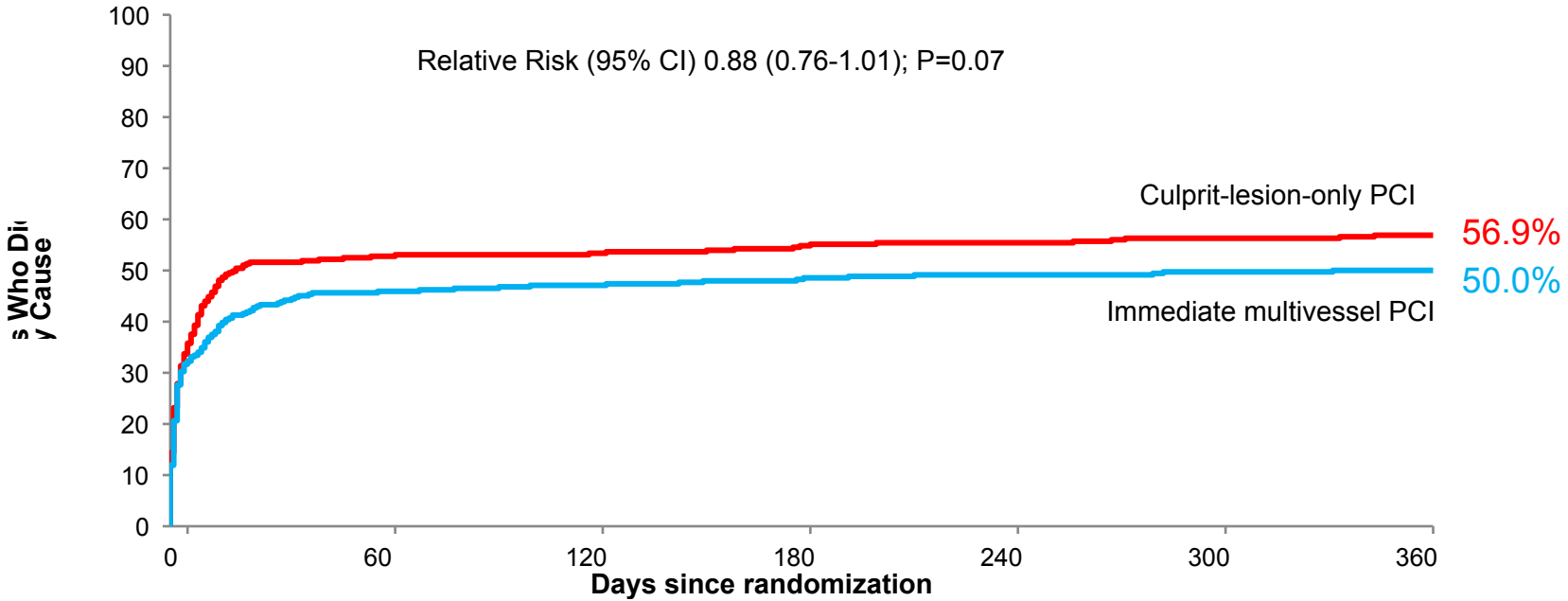
1-Year All-Cause Mortality or Renal Replacement Therapy



Number at risk:

Culprit-lesion-only PCI	344	179	174	171	167	165	142
Immediate multivessel PCI	341	149	149	145	142	139	122

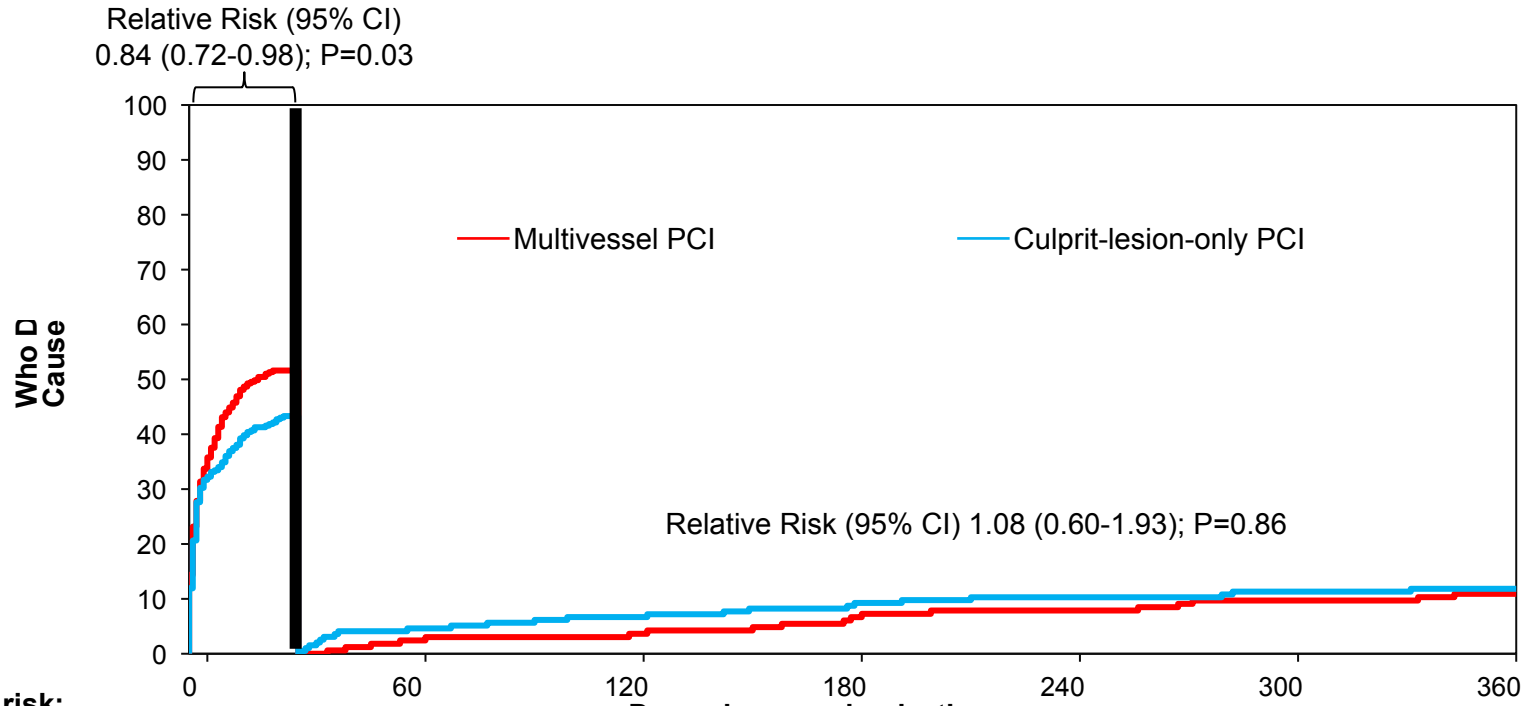
1-Year All-Cause Mortality



Number at risk:

Multivessel PCI	341	161	160	156	152	149	131
Culprit-lesion-only PCI	344	186	181	178	174	172	147

1-Year All-Cause Mortality – Landmark Analysis

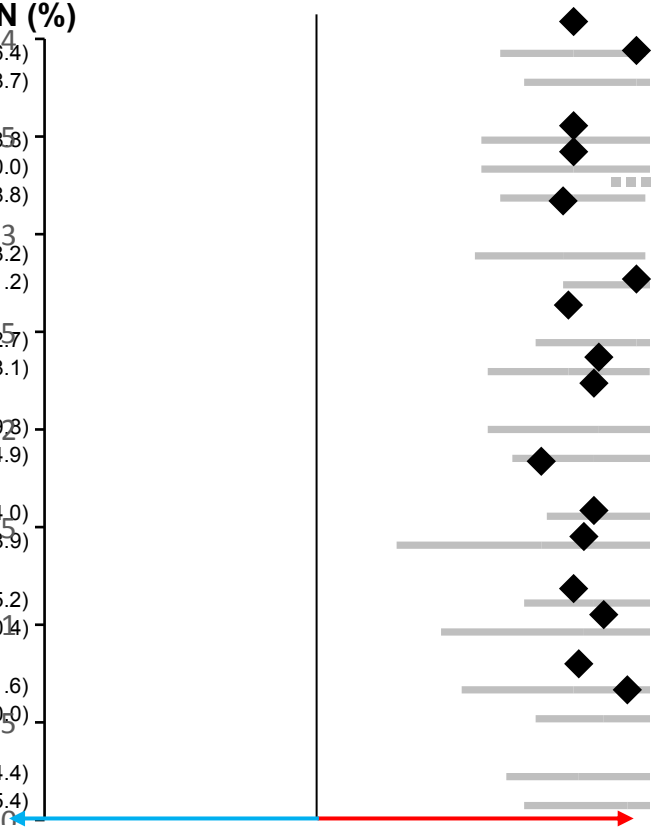


Number at risk:

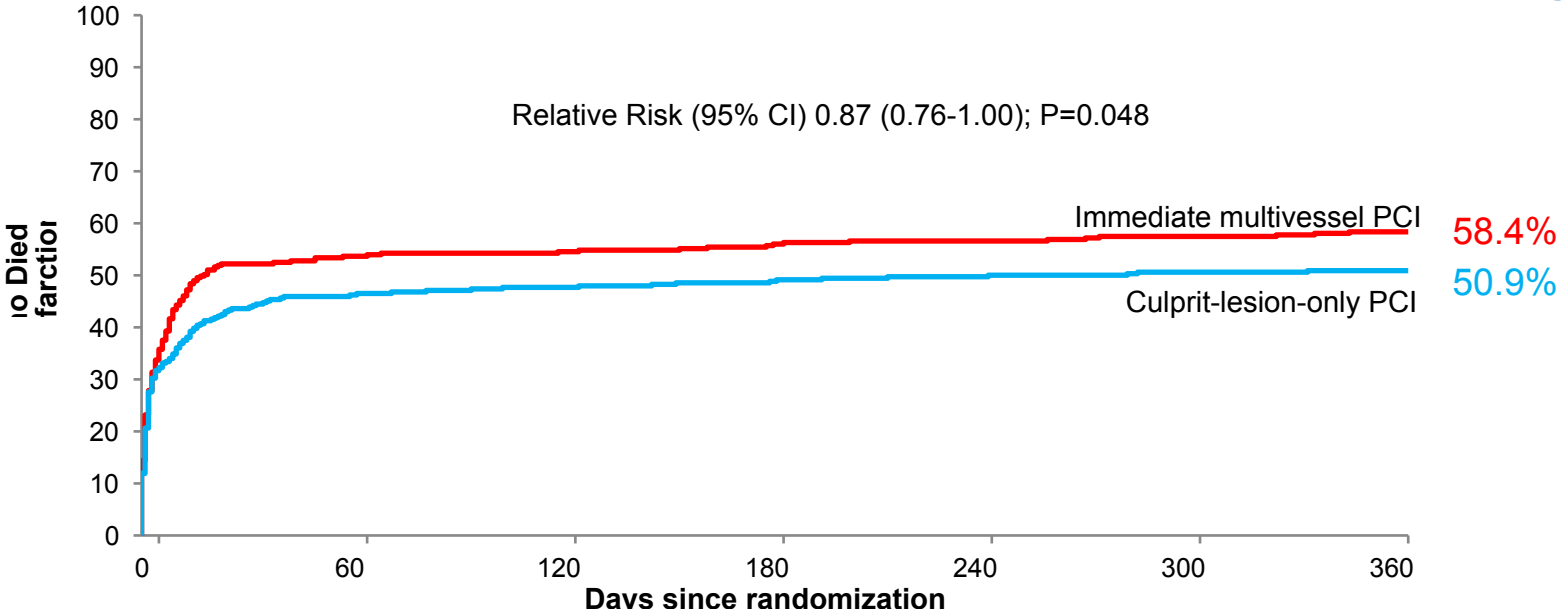
Multivessel PCI	165	161	160	156	152	149	131
Culprit-lesion-only PCI	195	186	181	178	174	172	147

1-Year All-Cause Mortality – Subgroups

Baseline Variable	Culprit-lesion-only PCI	Multivessel PCI	Relative Risk (95% CI)	P for Interaction
	1-year all-cause mortality n/N (%)			
Sex				
Male	122/257 (47.5)	150/266 (56.4)	0.84 (0.71-0.99)	0.42
Female	49/86 (57.0)	44/75 (58.7)	0.97 (0.75-1.26)	
Age				
<50 years	7/17 (41.2)	3/16 (18.8)	2.20 (0.68-7.06)	0.11
50-75 years	89/212 (42.0)	113/226 (50.0)	0.84 (0.68-1.03)	
>75 years	76/115 (66.1)	78/99 (78.8)	0.84 (0.71-0.99)	
Diabetes				
No	102/235 (43.4)	116/218 (53.2)	0.82 (0.67-0.99)	0.22
Yes	63/102 (61.8)	71/116 (61.2)	1.01 (0.82-1.25)	
Hypertension				
No	71/139 (51.1)	68/129 (52.7)	0.97 (0.77-1.22)	0.28
Yes	96/200 (48.0)	119/205 (58.1)	0.83 (0.69-1.00)	
Type of infarction				
NSTEMI	52/98 (53.1)	58/97 (59.8)	0.89 (0.69-1.14)	0.99
STEMI	114/237 (48.1)	128/233 (54.9)	0.88 (0.73-1.04)	
STEMI type				
Anterior infarction	59/108 (54.6)	61/113 (54.0)	1.01 (0.79-1.29)	0.24
Non-anterior infarction	37/97 (38.1)	45/92 (48.9)	0.78 (0.56-1.08)	
Previous infarction				
No	136/279 (48.8)	155/281 (55.2)	0.88 (0.75-1.04)	0.82
Yes	31/60 (51.7)	32/53 (60.4)	0.86 (0.62-1.19)	
Coronary artery disease				
2-vessel disease	53/122 (43.4)	64/124 (51.6)	0.84 (0.65-1.10)	0.78
3-vessel disease	118/218 (54.1)	129/215 (60.0)	0.90 (0.77-1.06)	
Chronic total occlusion				
No	123/265 (46.4)	143/263 (54.4)	0.85 (0.72-1.01)	0.64
Yes	49/79 (62.0)	51/78 (65.4)	0.95 (0.75-1.20)	



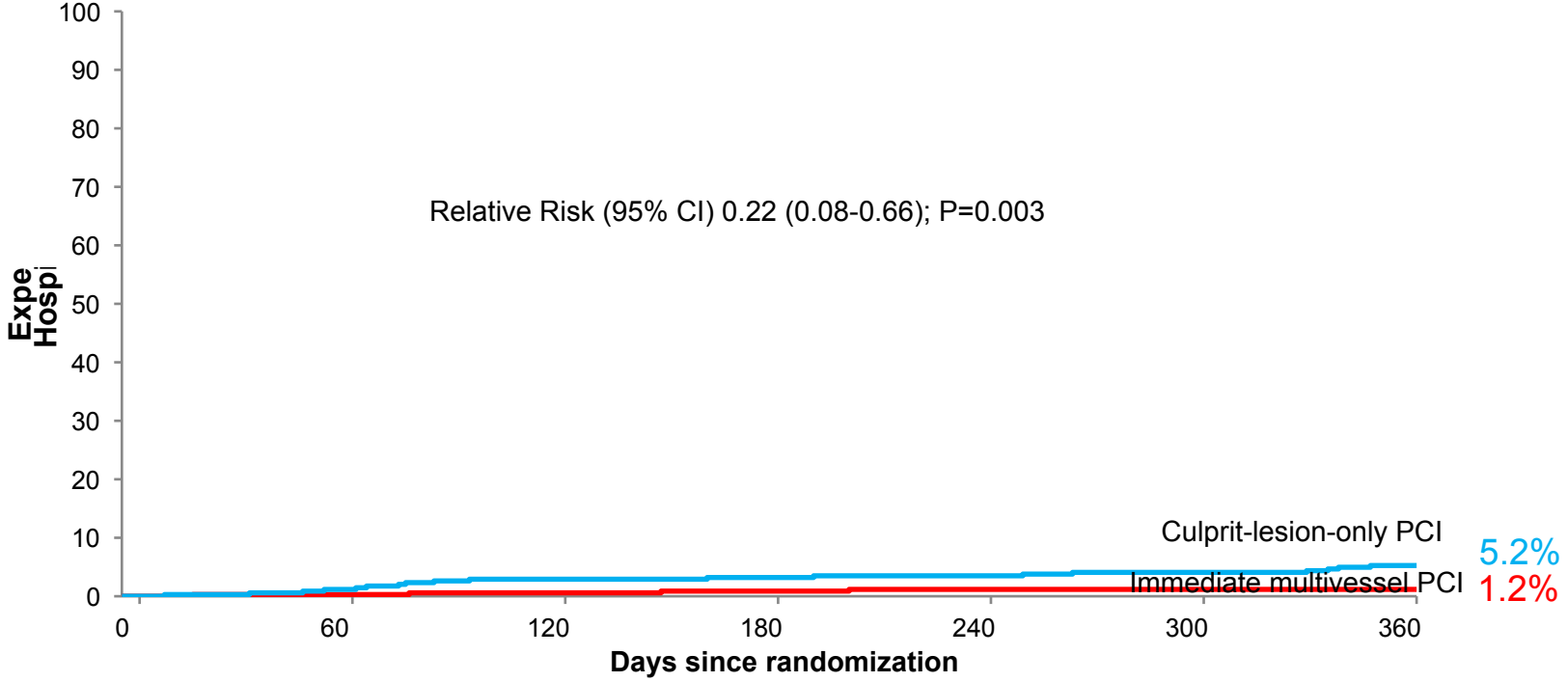
1-Year All-Cause Mortality or Reinfarction



Number at risk:

Multivessel PCI	341	158	156	152	148	145	126
Culprit-lesion-only PCI	344	185	179	176	172	169	145

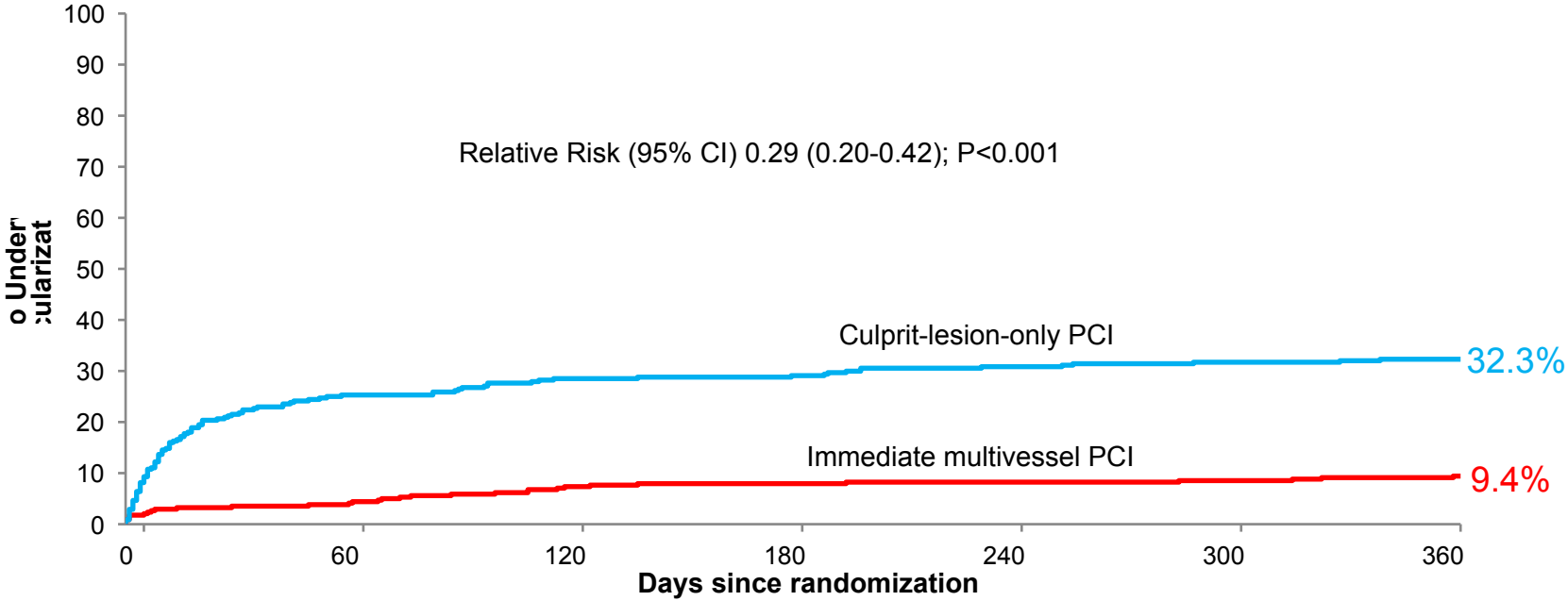
1-Year Rehospitalization Congestive Heart Failure



Number at risk:

Culprit-lesion-only PCI	344	339	333	332	331	329	301
Multivessel PCI	341	340	339	338	337	337	321

1-Year Repeat Revascularization



Number at risk:

Culprit-lesion only PCI	344	256	245	244	237	234	223
Multivessel PCI	341	327	316	313	312	311	293

1-Year Clinical Endpoints and Safety

CULPRIT-SHOCK

	Culprit-lesion-only PCI (n=344)	Multivessel PCI (n=341)	Relative Risk	95% CI	P-Value
All-cause mortality; n/total (%)	172/344 (50.0)	194/341 (56.9)	0.88	0.76–1.01	0.07
Renal replacement therapy; n/total (%)	40/344 (11.6)	56/341 (16.4)	0.71	0.49–1.03	0.07
Reinfarction; n/total (%)	6/344 (1.7)	7/341 (2.1)	0.85	0.29–2.50	0.77
Death/reinfarction; n/total (%)	175/344 (50.9)	199/341 (58.4)	0.87	0.76–1.00	0.048
Rehospitalization for congestive heart failure; n/total (%)	18/344 (5.2)	4/341 (1.2)	4.46	1.53–13.04	0.003
Death/reinfarction/rehospitalization for congestive heart failure; n/total (%)	190/344 (55.2)	203/341 (59.5)	0.87	0.93–1.06	0.87
Repeat revascularization; n/total (%)	111/344 (32.3)	32/341 (9.4)	3.44	2.39-4.95	<0.001
Repeat PCI; n/total (%)	107/344 (31.1)	29/341 (8.5)	3.66	2.50–5.36	
Repeat CABG; n/total (%)	4/344 (1.2)	3/341 (0.9)	1.32	0.30–5.86	
All-cause mortality or renal replacement therapy; n/total (%)	179/344 (52.0)	203/341 (59.5)	0.87	0.76–0.99	0.048
Stroke; n/total (%)	15/344 (4.4)	14/341 (4.1)	1.06	0.52–2.17	0.87
Bleeding (BARC 2, 3 or 5); n/total (%)	65/344 (18.9)	79/341 (23.2)	0.82	0.61–1.09	0.82
Any bleeding event; n/total (%)	75/344 (21.8)	86/341 (25.2)	0.86	0.66–1.13	0.86

Summary and Conclusions

CULPRIT-SHOCK

- In patients with acute myocardial infarction and cardiogenic shock culprit-lesion-only PCI - with possible staged revascularization - compared with immediate multivessel PCI is associated with a reduction in all-cause death or renal replacement therapy at 30 days.
- This effect in the composite endpoint is persistently observed at 12 months follow-up.
- The 30-day difference in all-cause mortality is attenuated over time. However, there is no increase in mortality after 30-days until 1-year follow-up.
- Culprit-lesion-only PCI is possibly associated with a higher incidence of heart failure hospitalizations and more frequent repeat revascularization at 1-year.
- The 1-year results of CULPRIT-SHOCK support the recent change in ESC guideline recommendations.

www.nejm.org

The NEW ENGLAND JOURNAL of MEDICINE

CULPRIT-SHOCK

ORIGINAL ARTICLE

One-Year Outcomes after PCI Strategies in Cardiogenic Shock

H. Thiele, I. Akin, M. Sandri, S. de Waha-Thiele, R. Meyer-Saraei, G. Fuernau, I. Eitel, P. Nordbeck, T. Geisler, U. Landmesser, C. Skurk, A. Fach, A. Jobs, H. Lapp, J.J. Piek, M. Noc, T. Goslar, S.B. Felix, L.S. Maier, J. Stepinska, K. Oldroyd, P. Serpytis, G. Montalescot, O. Barthelemy, K. Huber, S. Windecker, L. Hunziker, S. Savonitto, P. Torremante, C. Vrints, S. Schneider, U. Zeymer, and S. Desch, for the CULPRIT-SHOCK Investigators*