SYSTEMATIC REVIEW AND META-ANALYSIS

Complete Revascularization by Percutaneous Coronary Intervention for Patients With ST-Segment–Elevation Myocardial Infarction and Multivessel Coronary Artery Disease: An Updated Meta-Analysis of Randomized Trials

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BACKGROUND: For patients with ST-segment–elevation myocardial infarction (STEMI) and multivessel coronary artery disease, the optimal treatment of the non-infarct-related artery has been controversial. This up-to-date meta-analysis focusing on individual clinical end points was performed to further evaluate the benefit of complete revascularization with percutaneous coronary intervention for patients with STEMI and multivessel coronary artery disease.

METHODS AND RESULTS: We systematically identified all randomized trials comparing complete revascularization with percutaneous coronary intervention to culprit-only revascularization for multivessel disease in STEMI and performed a random-effects meta-analysis. The primary efficacy end point was cardiovascular death analyzed on an intention-to-treat basis. Secondary end points included all-cause mortality, myocardial infarction, and unplanned revascularization. Ten studies (7542 patients) were included: 3664 patients were randomized to complete revascularization and 3878 to culprit-only revascularization. Across all patients, complete revascularization was superior to culprit-only revascularization for reduction in the risk of cardiovascular death (relative risk [RR], 0.68; 95% CI, 0.47–0.98; P=0.037; $I^2=21.8\%$) and reduction in the risk of myocardial infarction (RR, 0.65; 95% CI, 0.54–0.79; P<0.0001; $I^2=0.0\%$). Complete revascularization also significantly reduced the risk of unplanned revascularization (RR, 0.37; 95% CI, 0.28–0.51; P<0.0001; $I^2=64.7\%$). The difference in all-cause mortality with percutaneous coronary intervention was not statistically significant (RR, 0.85; 95% CI, 0.69–1.04; P=0.108; $I^2=0.0\%$).

CONCLUSIONS: For patients with STEMI and multivessel disease, complete revascularization with percutaneous coronary intervention significantly improves hard clinical outcomes including cardiovascular death and myocardial infarction. These data have implications for clinical practice guidelines regarding recommendations for complete revascularization following STEMI.

Key Words: percutaneous coronary intervention
revascularization ST-segment-elevation myocardial infarction

Primary percutaneous coronary intervention (PCI) of the infarct-related artery reduces mortality and myocardial infarction (MI) in patients with ST-segment–elevation MI (STEMI).¹ STEMI patients commonly have multivessel coronary artery disease (CAD)^{1,2} and the presence of multivessel disease confers a worse prognosis.³

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CLINICAL PERSPECTIVE

What Is New?

- Primary percutaneous coronary intervention for patients with ST-segment–elevation myocardial infarction reduces mortality and myocardial infarction.
- For patients with multivessel coronary artery disease, the optimal treatment of the non-in-farct-related artery has been controversial.
- For patients with ST-segment–elevation myocardial infarction and multivessel disease, complete revascularization with percutaneous coronary intervention significantly improves hard clinical outcomes including cardiovascular death and myocardial infarction.

What Are the Clinical Implications?

• Clinical guidelines may need to be updated in light of these findings.

Nonstandard Abbreviations and Acronyms
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CAD	coronary artery disease
FFR	fractional flow reserve
PCI	percutaneous coronary intervention
PPCI	primary percutaneous coronary intervention
STEMI	ST-segment-elevation myocardial infarction

The treatment of non-infarct related arteries in STEMI patients has been controversial, and previously was considered to be a class III indication^{4,5} outside of the setting of cardiogenic shock, largely on the basis of observational studies.⁶ More recently, randomized controlled trials (RCTs) in the field have suggested that complete revascularization with PCI is safe for these patients and may be beneficial. Guidelines now permit PCI to the non-infarct-related artery for STEMI patients but are still somewhat conservative.^{7,8}

The RCTs in the field to date and meta-analyses of them have primarily demonstrated reductions in composite end points (typically major adverse cardiac events, which are defined variably across trials).

With the publication of the largest RCT to date in this field (the COMPLETE [Complete versus Culprit-Only Revascularization Strategies to Treat Multivessel Disease after Early PCI for STEMI] trial⁹) and longerterm follow-up available from another trial,¹⁰ we sought to perform an up-to-date meta-analysis focusing on individual clinical end points to further evaluate the benefit of complete revascularization with PCI for patients with STEMI and multivessel CAD.

METHODS

The data that support the findings of this study are available from the corresponding author on reasonable request.

We carried out a meta-analysis of RCTs that evaluated complete revascularization with PCI for patients with STEMI and multivessel disease. The analysis was conducted in accordance with the published PRISMA guidance¹¹ and was prospectively registered at the PROSPERO (international prospective register of systematic reviews) (CRD42020149243).

Search Strategy

We performed a systematic search of the Medline, Cochrane Central Register of Controlled Trials, and Embase databases from September 2019 to January 2020 for all studies of complete revascularization in STEMI. Our search strings included (*STEMI* or *STsegment myocardial infarction*) AND *multivessel*; and *percutaneous coronary intervention*, respectively. We also hand-searched the bibliographies of relevant selected studies, reviews, and meta-analyses to identify further eligible studies. Abstracts were reviewed for suitability and articles accordingly retrieved. Two independent reviewers performed the search and literature screening (Y.A. and A.A.), with disputes resolved by consensus following discussion with a third author (J.H.).

Inclusion and Exclusion Criteria

We considered all randomized studies of complete revascularization in STEMI. Studies were eligible if they reported clinical outcome data following randomization to complete or culprit-only revascularization. Observational and unpublished studies were not considered.

End Points

The primary efficacy end point was cardiovascular death, and the primary safety end point was risk of major bleeding. We considered MI, all-cause mortality, unplanned revascularization, and contrast-induced nephropathy as secondary end points. All analyses were at the latest available follow-up.

Data Extraction and Analysis

Two authors (Y.A. and A.A.) independently abstracted the data from included trials, verified by a third author (J.H.). Included studies were assessed using the Cochrane Risk of Bias tool.¹² Tests for publication bias would be performed only in the event of \geq 10 trials being included for analysis, and a Funnel plot would be used.¹³



Figure 1. Search strategy and source of included studies. CTO indicates chronic total occlusion.

We analyzed efficacy on an intention-to-treat basis. The primary outcome measure was the relative risk (RR) of cardiovascular death. Random-effects metaanalyses were performed using the restricted maximum likelihood estimator. Additional analyses were performed using fixed effects. All outcomes were assessed as RRs.

As a secondary analysis, we analyzed cardiovascular death, MI, all-cause mortality, and unplanned revascularization as hazard ratios when the trials reported these data. We extracted the hazard ratios with their associated 95% CIs and *P* values. A random-effects meta-analysis was performed of the natural logarithm of the hazard ratios and their associated standard errors using the restricted maximum likelihood estimator. The standard error was calculated by dividing the difference between the natural logarithms of the upper and lower 95% CIs by 2 times the appropriate normal score (1.96). Where the lower 95% CI level approached zero, the standard error was calculated using only the difference between the natural logarithm of the upper 95% CI level and the natural logarithm of the point estimate.

We used the I² statistic to assess heterogeneity.¹⁴ Low or mild heterogeneity was defined as 0% to 30%; moderate heterogeneity was defined as 31% to 60%; and >60% was defined as substantial heterogeneity. Mean values are expressed as mean±SD unless otherwise stated. Statistical significance was set at *P*<0.05. The statistical programming environment R¹⁵ with the *metafor* package¹⁶ was used for all statistical analysis.

Subgroups

We specified the timing of complete revascularization (immediate or staged) as a subgroup

	Safety Outcomes	Major bleeding, contrast-associated acute kidney injury	Net adverse clinical events, death from any cause or MI, any bleeding, hospitalization for heart failure, unstable angina r chest pain, revascularization, stent thrombosis	Major bleeding, contrast-induced nephropathy	Hospitalizations	Periprocedural MI, bleeding requiring transfusion or surgery, contrast-induced nephropathy, stroke	Cardiovascular death, stroke, major bleeding, contrast-induced nephropathy
	Primary Efficacy Outcomes	Composite of cardiovascular death, new MI. Composite of cardiovascular death, new MI, ischemia-driven revascularization	Composite of all- cause mortality, nonfatal MI, any revascularization, cerebrovascular events	Composite of all- cause mortality, recurrent MI, ischemia-driven revascularization	All cause mortality, cardiovascular death, MI	Composite of all- cause mortality, reinfarction, or ischemia- driven (subjective or objective) revascularization	Composite of all- cause mortality, recurrent MI, heart failure, revascularization
	Non-Culprit- Vessel Criteria	At least 70% stenosis or 50%-69% stenosis with FFR ≤0.80	>50% stenosis in major artery or branch vessel >2 mm diameter, FFR s0.80	80% stenosis of vessel	75%-90% stenosis	>50% stenosis in vessel >2 mm diameter, FFR ≤0.80	>70% diameter stenosis in 1 plane or >50% in 2 planes in major/branch vessel >2 mm diameter
	Culprit-Only Revascularization	No further revascularization unless protocol criteria for crossover met	FFR measurement without revascularization but planned revascularization within 45 d could occur (without knowledge of FFR)	Not specifically stated	PCI to nonculprit lesions if evidence of ischemia (symptoms, ECG changes, nuclear study)	No further revascularization planned	No further revascularization planned
	Complete Revascularization	Staged PCI of all nonculprit lesions either during admission or after discharge, ≤45 d from randomization	FFR measurement: if ≤0.80, nonculprit revascularization during index admission preferably within 72 h	PCI to all nonangiographically culprit lesions either at time of primary PCI or within 72 h	Staged PCI to nonculprit vessels 7-10 d after primary PCI	Staged PCI to nonculprit artery if FFR ≤0.80, 2 d after initial PCI	PCI to nonculprit artery during primary PCI procedure
	Entry Criteria	STEMI with culprit primary PCI and at least 1 nonculprit angiographically significant lesion significant able to be randomized within 72 h of culprit-lesion PCI	STEMI with culprit primary PCI and at least 1 nonculprit artery amenable to PCI	STEMI in patients with diabetes melitus undergoing primary PCI with nonculprit stenosis	STEMI in patients undergoing primary PCI with nonculprit stenoses	STEMI in patients undergoing primary PCI with >50% stenosis in nonculprit artery	STEMI in patients undergoing primary PCI with nonculprit artery with angiographically significant stenosis
	Follow-Up, mo [†]	35.8 (IQR, 27.6-44.3)	30	Q	AN .	27 (12–24)	66 (0-87)
	Mean Age [•]	61.6 (±10.7)	62 (±10)	56.4 (±11.5)	NA	63 (34–92)	64.6 (±11.2)
	z	4041	885	100	428	627	296
tudies	Region	31 countries across North America, Europe, Asia and Africa [‡]	24 centers in Europe and Asia	Not stated (authors' centers are Egypt and USA)	Not stated (authors' centers are in China)	Denmark	Š
of Included Si	Year	2019	2017	2016	2015	2015	2015
aracteristics (Study Acronym	COMPLETE	Compare-Acute	Ч Ч	Å	PRIMULTI	CVLPRIT
Table 1. Chi	Author	Mehta et a ^{lo}	Smits et al ¹⁷	Hamza et a ¹⁸	Zhang et a ^{te}	Engstrøm et al ²⁰	Gerschlick et al ^{10,21}

Author	Study Acronym	Year	Region	z	Mean Age [*]	Follow-Up, mo [†]	Entry Criteria	Complete Revascularization	Culprit-Only Revascularization	Non-Culprit- Vessel Criteria	Primary Efficacy Outcomes	Safety Outcomes	
Wald et al ²²	PRAMI	2013	хn	465	62 (32–92)	53	STEMI in patients undergoing primary PCI with nonculprit artery with angiographically significant stenosis	PCI to nonculprit artery during primary PCI procedure	PCI to residual stenoses only if refractory angina and objective ischemia test positive	>50% stenosis in nonculprit artery	Composite of cardiovascular death, nonfatal MI, refractory angina	Noncardiovascular death, repeated revascularisation were secondary outcomes	
Dambrink et al ²³	n/a	2010 ⁵	Netherlands	121	62 (±10)	39	STEMI in patients undergoing primary PCI with at least 2 anglographically significant stenoses in different vessels (or branch plus vessel)	PCI to nonculprit artery before discharge if FFR positive	Ischemia-guided additional revascularization if symptomatic (exercise testing, dobutamine stress echocardiography, or myocardial scintigraphy)	>50% stenosis in >2.5 mm vessel if FFR ≤0.75	Ejection fraction	MACE	
Politi et al ²⁴	۲ ۲	2010	All authors' centers are in Italy	263	65.2±12.2	30 (±17)	STEMI in patients undergoing primary PCI with at least 2 angiographically significant stenoses in different vessels in different vessels	Two arms: (1) staged PCI to nonculprit artery, (2) PCI to nonculprit artery during primary PCI procedure	No further revascularization planned	>70% stenosis	Composite of cardiac or noncardiac death, in-hospital death, reinfarction, rendraction for acute coronary syndrome and repeated coronary revascularization	Contrast-Induced nephropathy	
Di Mario et al ²⁵	HELP AMI	2004	Authors' centers are in UK and Italy	69	65.3 (±7.4)	12	STEMI with angiographically severe stenosis in at least 2 major vessels	Nonculprit PCI performed during procedure	Nonculprit PCI according to physician's discretion based on symptoms and ischemia testing	Major vessel (% not stated) but balloon angioplasty allowed in vessel <2.5 mm if at least i main vessel also stented	Repeat revascularization	MACE	
Compare Acu Early PCI for STE	te indicates Fracti MI; CvLPRIT, Con	onal Flow Reser	-ve-Guided Multiv sion-Only Primary	/essel A / PCI triɛ	ngioplasty in I al; DANAMI 3F	Myocardial Infa PRIMULTI, Cor	arction; COMPLETE	E, Complete versus C ation versus treatment	ulprit-Only Revascu t of the culprit lesion	Ilarization Strate	gies to Treat Multiv with ST-segment e	essel Disease after levation myocardial	_

¹Mean follow-up duration, where stated, in months (±SD where provided) except for COMPLETE and CVLPRIT, where median and IQR are provided, and Compare-Acute, Hamza et al¹⁸, and HELP AMI, where Mean age, where stated, in years (±SD) or median age (interquartile range) except for PRAMI, where mean (range) is provided; value for complete revascularization group provided where values differ between groups. infarction and multivessel disease; FFR, fractional flow reserve; HELP-AMI, Hepacoat for Culprit or Multivessel Stenting for Acute Myocardial Infarction; IQR, interquartile range; MACE, major adverse cardiac events; MI, myocardial infraction; NA, not available; PCI, primary catheter intervention; PRAMI, Preventive Angioplasty in Acute Myocardial Infraction; and STEMI, ST-segment-elevation myocardial infraction. follow-up duration was specified; value for complete revascularization group provided where values differ between groups. [‡]Majority of patients recruited in Canada and United Kingdom (2293, 56%).

Table 1. Continued

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	Other E	Low ri Partiy ind funded these pa not involv study des manager	Low ri Partiy ind funded these pa not involv study des manager	Uncle Source of f not stai	Uncle Source of f not sta	Low ri Fundec indepen body	Low ri Fundec indepen body	High ri Early term (signific between g
	Selective Reporting	tew risk e-specified outcomes reported	Low risk respecified outcomes reported	High risk preregistered 1 protocol not published	High risk preregistered 1 protocol not published	Low risk respecified outcomes reported	Low risk respecified outcomes reported	Low risk respecified outcomes reported
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	Incomplete Outcome Dat	Low risk Low drop-out rate	Low risk Low dropout ra	Low risk Low dropout ra	Unclear Not specified	Low risk Low dropout rates	High risk Low dropout rates in both groups but lov event rate	High risk Low dropout rates in both groups but lov
	Blinding of Outcome Assessment	Low risk Events adjudicated by independent committee	Low risk Events adjudicated by independent committee	Unclear Not specified	Unclear Not specified	Low risk Outcomes adjudicated by independent events committee	Low risk Outcome adjudication by blinded clinicians	Low risk Blinded adjudication
	Blinding of Participants and Personnel	Unclear Not specified	Unclear Not specified	Unclear Not specified	Unclear Not specified	High risk Open-label study	High risk Open label	High risk Open label for participants
	Allocation Concealment	Low risk Computer- generated system	Low risk Opaque envelope system	Unclear Not specified	Unclear Not specified	Unclear Not specified	Low risk Automated telephone randomisation	Unclear Not specified
	Random Sequence Generation	Low risk Computer- generated system	Low risk Opaque envelope system	Unclear Not specified	Unclear Not specified	Low risk Centralized web- based system	Low risk Interactive voice-response program	Low risk Computer generated
Studies	Year	2019	2017	2016	2015	2015	2015	2013
Bias of Included	Study Acronym	COMPLETE	Compare-Acute	ΨZ	ΨZ	DANAMI-3- PRIMULTI	GVLPRIT	PRAMI
Table 2. Risk of	Author	Mehta et al ⁹	Smits et al ¹⁷	Hamza et al ¹⁸	Zhang et al ¹⁹	Engstrøm et al ²⁰	Gerschlick et al ^{10,21}	Wald et al ²²

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(Continued)

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			Random Sequence	Allocation	Blinding of Participants	Blinding of Outcome	Incomplete	Selective	
Author	Study Acronym	Year	Generation	Concealment	and Personnel	Assessment	Outcome Data	Reporting	Other Bias
Dambrink et al ²³	n/a	2010	Low risk Computer-based randomization	Unclear Not specified	Unclear Not specified	Unclear Not specified for primary outcomes	Low risk Low rates of dropout	High risk Not preregistered and protocol not published	High risk Early termination (due to slow enrollment), source of funding not stated
Politi et al ²⁴	п/а	2010	Low risk Computerized randomization	Unclear Not specified	Unclear Not specified	Unclear Not specified	Unclear Not specified	High risk Not preregistered and protocol not published	Unclear Source of funding not stated
Di Mario et al ²⁵	HELP AMI	2009	Unclear Not specified	Unclear Not specified	Unclear Not specified	Unclear Not specified	Unclear Not specified	High risk Not preregistered and protocol not published	Unclear Source of funding not stated

Multivessel PCI for STEMI

analysis. Interactions between subgroups were assessed with metaregression using a mixed-effects model.

RESULTS

Ten studies^{9,17-25} enrolling 7542 patients met the inclusion criteria (Figure 1). Of those, 3664 patients were randomized to complete revascularization and 3878 to culprit-only revascularization, with a weighted mean follow-up of 31.4 months.

Across all studies, the mean age was 62 years. The full characteristics of included studies including follow-up duration, inclusion criteria, and end points are shown in Table 1, and important differences are highlighted below.

There was some variation in study design between the included trials. The timing of non-culprit vessel PCI in the complete revascularization arms of the trials varied between nonculprit PCI during the primary PCI procedure, staged PCI before discharge from the index admission, staged PCI after discharge, or combinations of these strategies. PRAMI (Preventive Angioplasty in Acute Myocardial Infarction), CvPLRIT (Complete Versus Lesion-Only Primary PCI) trial and HELP-AMI (Hepacoat for Culprit or Multivessel Stenting for Acute Myocardial Infarction) all included an arm in which nonculprit PCI was specified to occur during the index primary PCI procedure, whereas COMPLETE allowed staged PCI after discharge up to 45 days after the index procedure. The location, degree, and index vessel diameter thresholds for coronary stenoses to achieve angiographic significance also varied between included studies: PRAMI was the least restrictive, permitting 50% visual stenosis to be an appropriate nonculprit lesion, whereas Hamza et al¹⁸ required 80% stenosis. Compare Acute (Fractional Flow Reserve-Guided Multivessel Angioplasty in Myocardial Infarction), DANAMI-3-PRIMULTI (complete revascularisation versus treatment of the culprit lesion only in patients with ST-segment elevation myocardial infarction and multivessel disease), and Dambrink et al²³ all required fractional flow reserve (FFR) assessment of the stenosis. Definitions of clinical end points used in each trial are shown in Table S1.

Trial quality was assessed using the Cochrane riskof-bias tool and is shown in Table 2. Given the inherent difficulty in sham-blinding nonculprit PCI, none of the trials adequately blinded the patient or the operator to treatment allocation. However, most outcomes assessed, such as all-cause mortality, cardiovascular death, and nonfatal MI, are relatively bias-resistant in this regard, with the exception of unplanned revascularization. There was no evidence of publication bias as assessed by the funnel plot (P=0.669; see Figure S1).

A summary of stent types used in the included trials is shown in Data S1.

Continued

Fable 2.

Study and Year	Act	ive	Con	trol	Weight (%)		Relative risk [95% CI]
	Events	N	Events	IN	weight (78)		
Risk of cardiovascular death	r						
CvLPRIT, 2019 [10]	2	150	7	146	5.1	·	0.28 [0.06, 1.32]
Complete, 2019 [9]	59	2016	64	2025	41.2	⊢ ∰-1	0.93 [0.65, 1.31]
Compare ACUTE, 2017 [17]	З	295	6	590	6.4		1.00 [0.25, 3.97]
Zhang, 2015 [19]	11	215	14	213	17	⊢ ∎–	0.78 [0.36, 1.68]
DANAMI 3, 2015 [20]	5	313	9	314	9.8	<u> </u>	0.56 [0.19, 1.64]
PRAMI, 2013 [22]	4	234	10	231	8.9	·	0.39 [0.13, 1.24]
Politi, 2010 [24]	6	130	10	84	11.7	·	0.39 [0.15, 1.03]
RE Model for All Studies (Q =	6.40, df = 6, p	o for heterog	eneity = 0.38;	l ² = 21.8%	»)	-	0.68 [0.47, 0.98]
							p for overall effect = 0.037
						r i	
						0.04 0.2 1	5 25
					Comple	ete revasc. better < Relative risk >	Culprit-only revasc. better

Figure 2. Effect of complete revascularization on cardiovascular death.

Compare Acute indicates Fractional Flow Reserve–Guided Multivessel Angioplasty in Myocardial Infarction; COMPLETE, Complete versus Culprit-Only Revascularization Strategies to Treat Multivessel Disease after Early PCI for STEMI; CvLPRIT, Complete Versus Lesion-Only Primary PCI trial; DANAMI 3 PRIMULTI, Complete revascularisation versus treatment of the culprit lesion only in patients with ST-segment–elevation myocardial infarction and multivessel disease; PRAMI, Preventive Angioplasty in Acute Myocardial Infarction.

Efficacy of Complete Versus Culprit-Only Revascularization *Cardiovascular Death*

Complete revascularization with PCI resulted in a significant reduction in the risk of cardiovascular death (RR, 0.68; 95% CI, 0.47–0.98; P=0.037; Figure 2). There was low heterogeneity (I²=21.8%).

Myocardial Infarction

Complete revascularization with PCI resulted in a significant reduction in the risk of MI (RR, 0.65; 95% Cl, 0.54–0.79; P<0.0001; Figure 3). There was no heterogeneity (l²=0.0%). This result was unchanged by restricting the inclusion to patients with spontaneous MI (RR, 0.58; 95% Cl, 0.46–0.73; P<0.001; l²=0.0%; Figure S2).

All-Cause Mortality

The effect of complete revascularization with PCI on all-cause mortality was an RR of 0.85 (95% CI, 0.69– 1.04; P=0.108; Figure 4). There was no heterogeneity (l^2 =0.0%).

Unplanned Revascularization

Complete revascularization with PCI resulted in a significant reduction in the risk of unplanned revascularization (RR, 0.37; 95% CI, 0.28–0.51;

P<0.0001; Figure 5). There was significant heterogeneity (I²=64.7%).

Safety of Complete Revascularization

The effect of complete revascularization with PCI on major bleeding was an RR of 1.12 (95% CI, 0.78–1.62; P=0.540; Figure 6). There was minimal heterogeneity (I²=3.9%). The effect of complete revascularization with PCI on contrast-induced nephropathy was an RR of 1.42 (95% CI, 0.88–2.30; P=0.152; I²=0.0%; Figure S3).

Impact of Timing of Complete Revascularization

Six trials^{16,17,20,21,23,24} reported outcomes for all-cause mortality, MI, and unplanned revascularization in patients who underwent immediate complete revascularization. Four trials^{16,20,21,23} reported outcomes for cardiovascular death in patients who underwent immediate revascularization. Five trials^{9,18,19,22,23} reported outcomes for all-cause mortality, MI, and unplanned revascularization in patients who underwent staged complete revascularization. Four trials^{9,18,19,22,23} reported outcomes for cardiovascularization. Four trials^{9,18,19,22,23} reported outcomes for all-cause mortality, MI, and unplanned revascularization in patients who underwent staged complete revascularization. Four trials^{9,18,19,23} reported outcomes for cardiovascular death in patients who underwent staged revascularization. Staged complete revascularization was performed within a wide temporal interval, from during the index admission up to 45 days after the initial PCI procedure.

Study and Year	Act Events	ive N	Con Events	trol N	Weight (%)				Relative risk	[95% CI]
Risk of MI										
CvLPRIT, 2019 [10]	6	150	12	146	4.1		— •		0.49 [0	.19, 1.26]
Complete, 2019 [9]	109	2016	160	2025	66.8		H 		0.68 [0	.54, 0.87]
Compare ACUTE, 2017 [17]	7	295	28	590	5.6		—		0.50 [0	.22, 1.13]
Hamza, 2016 [18]	1	50	2	50	0.7				0.50 [0	.05, 5.34]
Zhang, 2015 [19]	9	215	14	213	5.6		—		0.64 [0	.28, 1.44]
DANAMI 3, 2015 [20]	15	313	16	314	7.9		 -1		0.94 [0	.47, 1.87]
PRAMI, 2013 [22]	7	234	20	231	5.2		⊢		0.35 [0	.15, 0.80]
Dambrink, 2012 [23]	4	79	0	40	0.4		F		→ 4.61 [0.	25, 83.61]
Politi, 2010 [24]	6	130	7	84	3.3		,		0.55 [0	.19, 1.59]
Help-AMI, 2009 [25]	1	52	1	17	0.5	-			0.33 [0	.02, 4.95]
RE Model for All Studies (Q =	6.35, df = 9, p	o for heterog	geneity = 0.70;	l ² = 0.0%)			•		0.65 [0 p for overall effe	.54, 0.79] ct < 0.001
							- <u>i</u> -i-	1		
						0.04	0.2 1	5	25	
					Comple	te revasc. be	etter < Relative risk	> Culp	rit–only revasc. bet	ter

Figure 3. Effect of complete revascularization on myocardial infarction.

Compare Acute, Fractional Flow Reserve–Guided Multivessel Angioplasty in Myocardial Infarction; COMPLETE, Complete versus Culprit-Only Revascularization Strategies to Treat Multivessel Disease after Early PCI for STEMI; CvLPRIT, Complete Versus Lesion-Only Primary PCI trial; DANAMI 3 PRIMULTI, Complete revascularisation versus treatment of the culprit lesion only in patients with ST-segment–elevation myocardial infarction and multivessel disease; HELP-AMI, Hepacoat for Culprit or Multivessel Stenting for Acute Myocardial Infarction; PRAMI, Preventive Angioplasty in Acute Myocardial Infarction.

Subgroup analysis did not demonstrate evidence of a significant interaction between the timing of complete revascularization and reduction in cardiovascular death (P=0.15; Figure 7).

Subgroup analysis did not demonstrate evidence of a significant interaction between the timing of complete revascularization and the reduction of unplanned revascularization (P=0.86). Subgroup analysis also did not demonstrate evidence of a significant interaction between the timing of complete revascularization and the reduction of MI, but the P value was borderline (0.05). These plots are shown in Figures S4 and S5.

Impact of Revascularization Guided by FFR

Three trials^{16,19,22} reported outcomes for all-cause mortality, MI, and unplanned revascularization in patients who underwent complete revascularization guided by FFR. Two trials^{16,19} reported outcomes for cardiovascular death in patients who underwent complete revascularization guided by FFR. Seven trials^{9,17,18,20,21,23,24} reported outcomes for all-cause mortality, MI, and unplanned revascularization in patients who underwent complete revascularization guided by angiography. Five trials^{9,18,20,21,23} reported outcomes for cardiovascular death in patients who underwent complete revascularization guided by angiography. The COMPLETE trial was regarded as using an angiographic-guided approach because only a very small proportion (0.8%) of patients had treatment guided by FFR.

Subgroup analysis did not demonstrate evidence of a significant interaction between the FFR versus angiography-guided revascularization for any of the end points. Forest plots for each of these end points are shown in Figures S6 through S9.

Hazard Ratio Analysis

We performed a secondary analysis looking at the efficacy end points using hazard ratios, which is more appropriate for time-to-event data but is limited by the reporting of the individual trials. Five trials reported hazard ratios for cardiovascular death, all-cause mortality, MI, and unplanned revascularization. The results are consistent with the main RR analysis for the end points of MI and unplanned revascularization, and the effect sizes were very similar for cardiovascular death, although they failed to reach statistical significance in light of the smaller sample size. These plots are shown in Figures S10 through S13.

Fixed-Effects Analyses

We performed an additional analysis looking at fixedeffects analyses for all our main end points, the results

Study and Year	Acti	ive	Con	trol	W_=====+ (0/)				Relative risk [95% Cl	1
	Events	N	Events	N	weight (%)					_
Risk of death										
CvLPRIT, 2019 [10]	9	150	15	146	6.7		—		0.58 [0.26, 1.29)]
Complete, 2019 [9]	96	2016	106	2025	58		H a hi		0.91 [0.70, 1.19)]
Compare ACUTE, 2017 [17]	4	295	10	590	3.2		·		0.80 [0.25, 2.53	3]
Hamza, 2016 [18]	1	50	4	50	0.9	4			0.25 [0.03, 2.16	5]
Zhang, 2015 [19]	13	215	15	213	8.2				0.86 [0.42, 1.76	5]
DANAMI 3, 2015 [20]	15	313	11	314	7.2			-	1.37 [0.64, 2.93	3]
PRAMI, 2013 [22]	12	234	16	231	8		·•		0.74 [0.36, 1.53	3]
Dambrink, 2012 [23]	2	79	0	40	0.5	⊢			2.56 [0.13, 52.14	4]
Politi, 2010 [24]	10	130	13	84	7				0.50 [0.23, 1.08	3]
Help-AMI, 2009 [25]	1	52	0	17	0.4				1.02 [0.04, 23.91]
BE Model for All Studies (O -	6.34 df – 9 n	o for heteror	ieneity – 0.71.	$l^2 = 0.0\%$					0.85 [0.69 1.04	
	0.04, ui = 0, p		jonony = 0.71,	1 = 0.0707					n for overall effect = 0.104	.] 8
										5
									1	
						0.04 0.	.2 1	5	25	
					Comple	te revasc. better	< Relative risk	> Culp	rit-only revasc. better	

Figure 4. Effect of complete revascularization on all-cause mortality.

Compare Acute, Fractional Flow Reserve–Guided Multivessel Angioplasty in Myocardial Infarction; COMPLETE, Complete versus Culprit-Only Revascularization Strategies to Treat Multivessel Disease after Early PCI for STEMI; CvLPRIT, Complete Versus Lesion-Only Primary PCI trial; DANAMI 3 PRIMULTI, Complete revascularisation versus treatment of the culprit lesion only in patients with ST-segment–elevation myocardial infarction and multivessel disease; HELP-AMI, Hepacoat for Culprit or Multivessel Stenting for Acute Myocardial Infarction; PRAMI, Preventive Angioplasty in Acute Myocardial Infarction.

of which are consistent with our random-effects analyses, and the plots are shown in Figures S14 through S18.

Sensitivity Analyses

We performed a sensitivity analysis including only trials assessed as being at low risk of bias. The results are consistent with the main analysis. These plots (for cardiovascular death, MI, all-cause mortality, and unplanned revascularization) are available in Figures S19 through S22.

We also performed sensitivity analyses excluding trials with low use of drug-eluting stents (defined as <50% of the total trial population). These results are shown in Figures S23 through S27 and are consistent with the main analysis.

We performed a further *jackknife* or *leave one out* sensitivity analysis, excluding each individual included trial in turn. These plots (for cardiovascular death, MI, all-cause mortality, and unplanned revascularization) are available in Figures S28 through S64.

DISCUSSION

In this study we have shown (1) that for patients with STEMI and multivessel disease, the risk of cardiovascular death is reduced by complete revascularization (RR, 0.68; 95% CI, 0.47–0.98; P=0.037), and (2) that this reduction in cardiovascular death is may partially be driven by a reduction in MI, which has a similar pooled point estimate (RR, 0.65; 95% CI, 0.54–0.79; P<0.0001).

Superiority of Complete Revascularization to Culprit-Only Revascularization

The individual trials included in this meta-analysis have shown reduction in unplanned revascularization with a strategy of complete revascularization after STEMI. This finding is intuitive because all patients in the culpritonly arm, by eligibility criteria, had angiographically severe stenoses amenable to PCI, and cardiologists were not blinded to their allocation to the culprit-only arms. Some trials also demonstrated a reduction in MI, including the most recent COMPLETE trial,⁹ which is the largest trial in the field to date. In the current era of contemporary pharmacotherapy and continued advances in stent technology and implantation techniques, hard event rates are low. This makes it difficult for any individual trial in the field of STEMI to show benefits in terms of mortality end points. Consequently, we must turn to meta-analysis to synthesize all available trial data.

By doing so, we are now able to observe, for the first time, a statistically significant benefit to complete revascularization in STEMI for the end point of cardiovascular

Study and Year	Act	ive	Con	trol						Rela	tive rick [95%	CII
	Events	Ν	Events	N	Weight (%)					Tiola		
Risk of unplanned revascula	arisation											
CvLPRIT, 2019 [10]	8	150	16	146	7.7		⊢	-			0.49 [0.21, 1	.10]
Complete, 2019 [9]	29	2016	160	2025	13.3		⊢∎⊣				0.18 [0.12, 0	.27]
Compare ACUTE, 2017 [17]	18	295	103	590	12		⊢∎⊣				0.35 [0.22, 0	.57]
Hamza, 2016 [18]	1	50	6	50	1.9	-	-	<u> </u>			0.17 [0.02, 1	.33]
Zhang, 2015 [19]	27	215	62	213	13		⊢∎→				0.43 [0.29, 0	.65]
DANAMI 3, 2015 [20]	17	313	52	314	11.4		⊢∎→				0.33 [0.19, 0	.55]
PRAMI, 2013 [22]	16	234	46	231	11.2		⊢∎→				0.34 [0.20, 0	.59]
Dambrink, 2012 [23]	27	79	15	40	11.7		F	- -			0.91 [0.55, 1	.51]
Politi, 2010 [24]	14	130	28	84	10.6		⊢				0.32 [0.18, 0	.58]
Help-AMI, 2009 [25]	9	52	6	17	7.2		·	÷			0.49 [0.20, 1	.18]
RE Model for All Studies (Q =	27.33, df = 9,	p for hetero	geneity = 0.00	D; I ² = 64.7	%)		+			p for ov	0.37 [0.28, 0 erall effect < 0.	.51] 001
							1	-i	1			
						0.04	0.2	1	5	25		
					Comple	te revasc. be	tter < Rela	tive risk	> Culpi	rit–only re	vasc. better	

Figure 5. Effect of complete revascularization on unplanned revascularization.

Compare Acute, Fractional Flow Reserve–Guided Multivessel Angioplasty in Myocardial Infarction; COMPLETE, Complete versus Culprit-Only Revascularization Strategies to Treat Multivessel Disease after Early PCI for STEMI; CvLPRIT, Complete Versus Lesion-Only Primary PCI trial; DANAMI 3 PRIMULTI, Complete revascularisation versus treatment of the culprit lesion only in patients with ST-segment–elevation myocardial infarction and multivessel disease; HELP-AMI, Hepacoat for Culprit or Multivessel Stenting for Acute Myocardial Infarction; PRAMI, Preventive Angioplasty in Acute Myocardial Infarction.

death. The mechanism of this reduction in cardiovascular death might be driven by a reduction in MI, particularly as the effect size is similar for these 2 end points. Other possible mechanisms include reduction in ischemiadriven arrhythmias and heart failure, but no definitive causation can be determined from this analysis.

Our analysis did not demonstrate a statistically significant benefit for complete revascularization with PCI in terms of all-cause mortality (RR, 0.84; 95% CI, 0.69–1.04; P=0.113). This may be due to insufficient power, and future trials in the field may help to identify a benefit in terms of all-cause mortality, which is the most bias-resistant end point. There was no heterogeneity for this outcome, and in fact heterogeneity was also low or absent for MI and cardiac death. This implies consistent findings across the included studies and strengthens the conclusions of our analysis.

Implications for Clinical Practice

It is important that the results of these trials, and the current analysis, are not conflated with the treatment of stable angina, for which PCI should still generally be offered with the goal of alleviating symptoms.²⁵ Moreover, this analysis serves to further illustrate the marked differences between patients who have had STEMI and those who have stable angina or stable

CAD. The 2 entities are pathophysiologically and biologically distinct and therefore require distinct therapeutic strategies.

Clinicians treating patients with STEMI and multivessel disease have, broadly, 3 different management strategies to choose from: stenting the infarcted artery only and leaving all residual disease to medical therapy (culprit-only PCI), treating all appropriate stenoses at the time of STEMI (immediate complete revascularization), and treating the infarct-related artery at the time of STEMI and tackling the residual disease during another procedure (staged complete revascularization).

We sought to investigate whether the timing of complete revascularization had an impact on clinical outcomes. Subgroup analyses did not demonstrate evidence of a significant interaction between the timing of intervention in our analysis; that is, there was a consistent treatment effect for complete revascularization versus infarct-related artery PCI, regardless of the timing when complete revascularization was achieved. Furthermore, the largest RCT in the field to date (COMPLETE) had no immediate PCI arm (patients underwent PCI to achieve complete revascularization in a staged procedure, either during the hospital admission or as an outpatient within 45 days). A further analysis from the COMPLETE trial, initially presented at Transcatheter Therapeutics 2019 and published

Study and Year	Act	ive	Con	trol	Weight (%)		Relative risk [95% Cl]
	Events	N	Events	N	weight (%)		
Risk of bleeding							
CvLPRIT, 2019 [10]	4	150	7	146	8.9	·	0.56 [0.17, 1.86]
Complete, 2019 [9]	58	2016	44	2025	65.7	- ∎-1	1.32 [0.90, 1.95]
Compare ACUTE, 2017 [17]	3	295	8	590	7.5	·	0.75 [0.20, 2.81]
Hamza, 2016 [18]	0	50	0	50	0.9		▶ 1.00 [0.02, 49.44]
DANAMI 3, 2015 [20]	1	313	4	314	2.8		0.25 [0.03, 2.23]
PRAMI, 2013 [22]	7	234	6	231	11.2	·	1.15 [0.39, 3.38]
Dambrink, 2012 [23]	5	79	1	40	3	,	2.53 [0.31, 20.95]
RE Model for All Studies (Q =	4.71, df = 6, p	o for heterog	jeneity = 0.58;	l ² = 3.9%)			1.12 [0.78, 1.62] p for overall effect = 0.540
						0.04 0.2 1	5 25
					Comple	e revasc. better < Relative risk >	Culprit-only revasc. better

Figure 6. Effect of complete revascularization on major bleeding.

Compare Acute, Fractional Flow Reserve–Guided Multivessel Angioplasty in Myocardial Infarction; COMPLETE, Complete versus Culprit-Only Revascularization Strategies to Treat Multivessel Disease after Early PCI for STEMI; CvLPRIT, Complete Versus Lesion-Only Primary PCI trial; DANAMI 3 PRIMULTI, Complete revascularisation versus treatment of the culprit lesion only in patients with ST-segment–elevation myocardial infarction and multivessel disease; PRAMI, Preventive Angioplasty in Acute Myocardial Infarction.

subsequently,²⁶ did not demonstrate a difference between complete revascularization during the index admission (median, 1 day), or after discharge from the hospital (median, 23 days), with a P value for interaction of 0.62 for the outcome of cardiac death or new MI.

It is unlikely that a group in that trial undergoing immediate complete revascularization with PCI would have had better outcomes than a group undergoing staged PCI a median of 1 day after the index procedure. We suggest that achieving complete revascularization, rather than timing of it, is the most important determination of clinical outcomes for these patients. This is also supported by the fact we did not observe a significant interaction whether complete revascularization was guided by FFR or angiography.

Our analysis has not suggested any safety concerns regarding complete revascularization. There was no significant increase in major bleeding or acute kidney injury. These data are reassuring, but treating clinicians must weigh the benefits of complete revascularization (reduction in cardiac death, myocardial infarction, and future revascularization) against potential risks (both short and long term) on an individual case-by-case basis. Our analysis demonstrates a reduction in MI with complete revascularization. The ISCHEMIA trial presentation has suggested that in stable CAD, invasive therapy leads to greater procedural MI but less spontaneous MI. This cannot necessarily be extrapolated to the patient population studied in this analysis, but future trials may wish to separately report periprocedural and spontaneous MI in all patients to permit a more nuanced interpretation of the results and to better advise patients on potential risks and benefits.

Implications for Clinical Practice Guidelines

PCI of the non-infarct-related artery was previously given a class III recommendation in guideline documents, but as further RCTs emerged, guideline recommendations were updated.

European guidelines from 2017⁷ now give a lla recommendation (level of evidence, A) and state that "routine revascularization of non-infarct-related artery lesions should be considered in STEMI patients with multivessel disease before hospital discharge." American College of Cardiology and American Heart Association guidelines from 2015⁵ give a llb recommendation (level of evidence, B-R) and state that "PCI of a non-infarct artery may be considered in selected patients with STEMI and multivessel disease who are hemodynamically stable, either at the time of primary PCI or as a planned procedure."

On the basis of the totality of the randomized trial data and this analysis, guidelines should be updated to give a class I recommendation for complete revascularization in appropriate STEMI patients.

Study and Year	Acti Events	ve N	Cor Events	ntrol N	Weight (%)					Rela	tive risk [95% CI]
Immediate revascularisation	– risk of CV	death									
Politi–Immediate, 2010 [24] PRAMI, 2013 [22] Compare ACUTE, 2017 [17] CvLPRIT, 2019 [10] Random effects model for imme Q = 1.68, df = 3, p for heteroge	4 4 3 2 ediate studies eneity = 0.64;	65 234 295 150 s (p = 0.028) $I^2 = 0.0\%$	10 10 6 7	84 231 590 146	8.9 8.5 6.1 4.9	Ŀ			-		0.52 [0.17, 1.57] 0.39 [0.13, 1.24] 1.00 [0.25, 3.97] 0.28 [0.06, 1.32] 0.49 [0.26, 0.93]
Staged revascularisation – ri	isk of CV dea	ath									
Politi–Staged, 2010 [24] DANAMI 3, 2015 [20] Zhang, 2015 [19] Complete, 2019 [9]	2 5 11 59	65 313 215 2016	10 9 14 64	84 314 213 2025	5.3 9.3 16.3 40.8	Ŀ					0.26 [0.06, 1.14] 0.56 [0.19, 1.64] 0.78 [0.36, 1.68] 0.93 [0.65, 1.31]
Random effects model for stag Q = 3.30, df = 3, p for heteroge	ed studies (p eneity = 0.35;	= 0.203) I ² = 2.6%						•			0.82 [0.60, 1.12]
Evidence of an immediate vers	us staged mo	oderating eff	ect: p = 0.15			·			-1		
					Comple	0.04 ete revasc. bet	0.2 ter < Re	1 lative risk :	5 > Culprit	25 –only re	vasc. better

Figure 7. Effect of timing of complete revascularization on cardiovascular (CV) death.

Compare Acute, Fractional Flow Reserve–Guided Multivessel Angioplasty in Myocardial Infarction; COMPLETE, Complete versus Culprit-Only Revascularization Strategies to Treat Multivessel Disease after Early PCI for STEMI; CvLPRIT, Complete Versus Lesion-Only Primary PCI trial; DANAMI 3 PRIMULTI, Complete revascularisation versus treatment of the culprit lesion only in patients with ST-segment–elevation myocardial infarction and multivessel disease; PRAMI, Preventive Angioplasty in Acute Myocardial Infarction.

Prior Work in the Field

Our meta-analysis differs from previous analyses in several ways. First, and most obviously, it includes the COMPLETE trial, which is by some margin the largest study in the field; we have also included long-term follow-up from the CvLPRIT trial. Second, we used individual end points rather any composite measures such as major adverse cardiac events. The use of composite measures for such an analysis is problematic. If the hazard ratios are synthesized for major adverse cardiac events or the primary composite end point, as it is defined in each individual trial, this will be hampered by the varying definitions seen in each trial. Essentially, disparate data will be meta-analyzed. If events from individual clinical end points counting and combined to assess major adverse cardiac events or another composite, then there is a risk of counting events twice when the trial is providing time-to-event data. Third, we included an analysis of hazard ratios where these data were available, which is the most appropriate analysis for time-to-event data.27

Limitations

We could only report the available data. Subgroup analyses based on factors such as location of MI, diabetes mellitus, left ventricular function, location, and complexity of residual CAD was not possible because trials did not uniformly report these data, and if they did, it was only for the primary outcome measure, which differed across each trial. The individual trials also had other differences in methodology and reporting, but this problem is common to all metaanalyses. It would benefit clinical trialists to attempt to harmonize their definitions of events and their outcome measures to facilitate more accurate synthesis of their results.

The majority of trials did not routinely report postprocedure elevations in cardiac enzymes, so it was not possible to analyze them. The DANAMI trial reported 2 periprocedural MIs in the complete revascularization group but without any details on enzyme elevations; the trial by Dambrink et al²³ reported 4 periprocedural MIs in the complete revascularization group.

Sicker, higher risk patients were generally excluded from these trials. Consequently, our results cannot be extrapolated to patients with cardiogenic shock or those with left main CAD or chronic total occlusions.

Time-to-event data are best analyzed using hazard ratios or survival plots. When we performed this analysis, the benefit of complete revascularization remained for MI and revascularization but was not statistically significant for cardiac death. This is likely due to the reduced sample size because not all trials provided hazard ratios or survival plots. If hazard ratios were available for all included studies, the primary end point may have reached statistical significance using hazard ratios, but these data were not available.

CONCLUSIONS

For patients with STEMI and multivessel disease, complete revascularization with PCI significantly improves hard clinical outcomes including cardiovascular death and MI. These data have implications for clinical practice guidelines regarding recommendations for complete revascularization following STEMI.

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Supplementary Materials

Data S1 Table S1 Figures S1–S64 References 9, 16–24

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SUPPLEMENTAL MATERIAL

Data S1.

Summary of use of stent types in included trials:

In the COMPLETE trial, 86.4% of patients in the complete revascularization arm and 86.1% of the culprit-only arm received a drug-eluting stent during the index procedure. A breakdown of different drug-eluting stent types was not provided.

In the COMPARE-ACUTE trial, 95.4% in the complete revascuarization arm received a DES, and in the culpritonly arm 96.1% received DES. In the complete arm, this was broken down to 227 Xience (72.8%), 6 Promus (1.9%), 79 Other DES (25.3%); and in the culprit arm this was broken down to 442 Xience (71.3%), 20 Promus (3.2%), 158 Other DES (25.5%).

In the CvLPRIT trial, 95.9% of patients in the complete revascularization arm and 90.7% of the culprit-only arm received a drug-eluting stent. A breakdown of different drug-eluting stent types was not provided.

In the DAMBRINK trial, 22.5% in the complete revascularization arm and 17.1% in the culprit-only arm received a drug-eluting stent.

In the DANAMI trial, 93% in the complete revascularization arm and 95% in culprit-only arm received a drugeluting stent.

In the Hamza trial, drug-eluting stents were used in all patients.

In the HELP-AMI trial, the heparin-coated Bx velocity stents were used in all patients.

In the Politi trial, 16.9% in the complete revascularization arm and 11.9% in culprit-only arm received a drugeluting stent.

In the PRAMI trial, 63% in the complete revascularization arm and 58% in the culprit-only arm received a drugeluting stent.

Table S1. Endpoint definitions.

Author	Study	Definition of CV Death	Definition of MI	Definition of IDR
	Acronym			
Mehta <i>et al</i> ⁹	COMPLETE	Clear CV or unknown	Abnormal troponin + one of new symptoms, new ST-T change / LBBB / Q waves, new	All of the following: 1) CCS class ≥ 2
		cause of death.	RWMA / non-viable myocardium on imaging or autopsy/angiographic intra-	angina despite GDMT, 2) PCI / CABG
		Documented non-CV	coronary/stent thrombus. Cardiac death with symptoms and ST-T change / LBBB but	of culprit lesion (within 5mm of
		deaths classified as non-	death prior to troponin measurement. Peri-PCI MI: troponin >35x ULN / CK-MB >5x ULN	stented segment) or non-culprit elsion
		CV (e.g. cancer)	+ one of new symptoms, new ST-T change / LBBB, new RWMA / non-viable myocardium	that resulted in trial eligibility, 3) one
			on imaging or evidence of PCI complication. Peri-CABG: troponin >70x ULN / CK-MB	of: positive functional study
			>10x ULN + one of new q waves / LBBB, new graft/native vessel occlusion or new	demonstrating reversible ischaemia,
			RWMA / non-viable myocardium on imaging.	new ischaemic ECG changes
				consistent with a coronary territory or
				FFR ≤ 0.8.
Smits et	Compare-	CV death not reported	Rise and fall of troponin / CK-MB + one of symptoms, q waves, ST elevation /	Any revascularisation (not IDR)
al. ¹⁶	Acute		depression. Q waves without CK-MB rise. Confirmed MI without Q waves.	
			Peri-PCI MI: rise of CK-MB >3x ULN within 48 hours.	
			Peri-CABG PCI: rise of CK-MB >5x ULN within 7 days.	
			If peak CK/CK-MB from index infarct not reached: chest pain >20 minutes, or new ecg	
			changes, with peak CK/CK-MB 24 hours later \ge 50% higher. If CK/CK-MB falling or	
			normalised within 24 hours of index PCI: new rise >2x ULN if normalised or >50% nadir	
			if falling.	
Hamza <i>et</i>	n/a	CV death not reported.	Not stated	Not stated
a ¹⁷				
Zhang <i>et</i>	n/a	Not translated	Not translated	Revascularisation not reported.
al ¹⁸				
Engstrøm <i>et</i>	DANAMI-3-	Not stated	Not stated	ischaemia-driven (subjective or
al. ¹⁹	PRIMULTI			objective) revascularisation of lesions
				in non-infarct related arteries

Gerschlick	CvLPRIT	Any cardiac causes, or	Type 1: Spontaneous re-MI: Recurrent angina symptoms or new ECG changes occurring	Target lesion re-interventions: inside
et al.20		other vascular causes	before PCI or <48 hours from PCI compatible with re-MI with an elevation of CK-MB,	or within 5 mm of stent. Target vessel
		(e.g. pulmonary	troponin, or total CK above ULN and 20% higher than previous value.	revascularisation: repeated
		embolism, aortic	Type 4a: CK-MB or total CK >3 times the ULN within 48 hours following PCI. If the pre-	interventions in the same vessel by
		dissection)	PCI CK-MB or total CK level > ULN, also: either falling CK-MB or total CK level prior to	PCI/CABG. PCI to lesions not
			the onset of the suspected event, or a peak of biomarker $\ge 20\%$ above the previous	identified previously. CABG for new
			value. With appropriate clinical presentation or new ischemic ECG changes (ST	symptoms or complications of PCI.
			elevation/depression or new Q waves/LBBB).	
			Type 4b: MI associated with stent thrombosis on angiography/autopsy as well as	
			fulfilling the criteria of spontaneous MI (Type 1)	
Wald et	PRAMI	Not stated	Symptoms of cardiac ischemia and a troponin > ULN. For patients with a recurrent MI	Repeat revascularisation was a
al. ²¹			within 14 days after randomization, the definition required new ST change or LBBB	secondary outcome (not IDR).
			with angiographic evidence of coronary-	
			artery occlusion	
Dambrink <i>et</i>	n/a	Not reported	New Q-waves or a new CK and CK-MB rise > ULN (including peri-procedural MI)	Additional unplanned
al. ²²				revascularisations reported (not IDR)
Politi <i>et</i>	n/a	Not stated	Not stated	Not stated
al. ²³				
Di Mario et	HELP AMI	Not stated	Not Stated	Not Stated
al. ²⁴				

CV - cardiovascular, MI - myocardial infarction, RWMA - regional wall motion abnormality, LBBB - left bundle branch block, IDR - ischaemia driven revascularisation, PCI - percutaneous catheter intervention, CABG - Coronary Artery Bypass Grafting, CCS - Canadian Cardiovascular Society, GDMT - guideline directed medical therapy

Figure S1. Funnel plot for publication bias.



Funnel plot for risk of MI (by standard error)

Log Risk Ratio

Figure S2. Effect of complete revascularization on risk of spontaneous myocardial infarction.

Study and Year	Active		Control							Relative risk [95% CI]
	Events	N	Events	Ν	Weight (%)					
Risk of spontaneous MI										
CvLPRIT, 2019	0	150	2	146	0.6	-				0.19 [0.01, 4.02]
Complete, 2019	83	2016	142	2025	75.3		н	₽		0.59 [0.45, 0.76]
Compare ACUTE, 2017	5	295	17	590	5.4		—	•		0.59 [0.22, 1.58]
DANAMI 3, 2015	13	313	16	314	10.3		⊢			0.82 [0.40, 1.67]
PRAMI, 2013	7	234	20	231	7.4		⊢	-		0.35 [0.15, 0.80]
Dambrink, 2012	0	79	0	40	0.3	-				▶ 0.51 [0.01, 25.36]
Help-AMI, 2009	1	52	1	17	0.7	-				0.33 [0.02, 4.95]
RE Model for All Studies (Q =	3.01, df = 6, p	for heterog	eneity = 0.81;	l ² = 0.0%)			•	•		0.58 [0.46, 0.73]
										p for overall effect < 0.001
						Г	1	-i	I	
						0.04	0.2	1	5	25

Figure S3. Effect of complete revascularization on risk of contrast-induced nephropathy.

Study and Year	Active		Control			Relative risk [95% CI]
Study and real	Events	N	Events	N	Weight (%)	
Risk of contrast induced nep	ohropathy					
CvLPRIT, 2019	2	150	2	146	6.1	0.97 [0.14, 6.82]
Complete, 2019	30	2016	19	2025	70.6	1.59 [0.90, 2.81]
Hamza, 2016	3	50	1	50	4.6	► 3.00 [0.32, 27.87]
DANAMI 3, 2015	4	313	1	314	4.8	► 4.01 [0.45, 35.70]
PRAMI, 2013	1	234	3	231	4.5	• 0.33 [0.03, 3.14]
Politi, 2010	3	130	3	84	9.3	0.65 [0.13, 3.13]
RE Model for All Studies (Q =	4.16, df = 5, p	for heterog	eneity = 0.53;	l ² = 0.0%)		1.42 [0.88, 2.30]
						p for overall effect = 0.152
						0.04 0.2 1 5 25

Figure S4. Effect of timing of complete revascularization on myocardial infarction.

Study and Year	Act Events	live N	Cor Events	ntrol N	Weight (%)			Re	elative risk [95% CI]
Immediate revascularisatio	on – risk of MI								
Help-AMI, 2009	1	52	1	17	0.5	-			0.33 [0.02, 4.95]
Politi-Immediate, 2010	2	65	7	84	1.6	F			0.37 [0.08, 1.72]
PRAMI, 2013	7	234	20	231	5.2		⊢ −−−1		0.35 [0.15, 0.80]
Hamza, 2016	1	50	2	50	0.7				0.50 [0.05, 5.34]
Compare ACUTE, 2017	7	295	28	590	5.5		— ———————————————————————————————————		0.50 [0.22, 1.13]
CvLPRIT, 2019	6	150	12	146	4		⊢−−− −−−1		0.49 [0.19, 1.26]
Random effects model for im	mediate studie	es (p < 0.001)				-		0.43 [0.27, 0.68]
Q = 0.55, df = 5, p for hetero	geneity = 0.99	; I ² = 0.0%							
Staged revascularisation -	risk of MI								
Politi-Staged, 2010	4	65	7	84	2.6		⊢ −− −		0.74 [0.23, 2.42]
Dambrink, 2012	4	79	0	40	0.4		H	>	4.61 [0.25, 83.61]
DANAMI 3, 2015	15	313	16	314	7.8				0.94 [0.47, 1.87]
Zhang, 2015	9	215	14	213	5.5		⊢ −−−		0.64 [0.28, 1.44]
Complete, 2019	109	2016	160	2025	66.2		H		0.68 [0.54, 0.87]
Random effects model for im	nmediate studie	es (p = 0.001)				•		0.71 [0.58, 0.88]
Q = 2.41, df = 4, p for hetero	geneity = 0.66	; I ² = 0.0%							
Evidence of an immediate ve	ersus staged m	oderating ef	fect: p = 0.05	i					
							- i - i		
						0.04	0.2 1	5 25	

Complete revasc. better < Relative risk > Culprit-only revasc. better

Figure S5. Effect of timing of complete revascularization on unplanned revascularization.

Study and Year	Ac	tive	Cor	ntrol					Rela	tive risk [95% Cl
	Events	N	Events	N	Weight (%)					
Immediate revascularisatic	on – risk of ur	planned re	vascularisati	on						
Help-AMI, 2009	9	52	6	17	6.7		—			0.49 [0.20, 1.18
Politi-Immediate, 2010	6	65	28	84	7.2		⊢			0.28 [0.12, 0.63
PRAMI, 2013	16	234	46	231	10.6		⊢	-		0.34 [0.20, 0.59
Hamza, 2016	1	50	6	50	1.8	-	-			0.17 [0.02, 1.33
Compare ACUTE, 2017	18	295	103	590	11.4		H	-		0.35 [0.22, 0.57
CvLPRIT, 2019	8	150	16	146	7.2					0.49 [0.21, 1.10
Random effects model for im	mediate studie	es (p < 0.001)				•			0.36 [0.27, 0.48
Q = 1.96, df = 5, p for hetero	geneity = 0.85	5; $I^2 = 0.0\%$					-			•
Politi-Staged, 2010	8	65	28	84	8.3		⊢	-		0.37 [0.18, 0.7
Politi-Staged, 2010	8	65	28	84	8.3		⊢-■-	-		0.37 [0.18, 0.76
Dambrink, 2012	27	79	15	40	11.1					0.91 [0.55, 1.51
DANAMI 3, 2015	17	313	52	314	10.8		⊢-₩-	-		0.33 [0.19, 0.55
Zhang, 2015	27	215	62	213	12.4		H	н		0.43 [0.29, 0.65
Complete, 2019	29	2016	160	2025	12.7					0.18 [0.12, 0.27
Random effects model for im	mediate studie	es (p < 0.001)				-	-		0.38 [0.23, 0.65
Q = 25.63, df = 4, p for heter	ogeneity = 0.0)0; l ² = 82.8%	, D							
Q = 25.63, df = 4, p for heter	ogeneity = 0.0	00; I ² = 82.8%	5							
Q = 25.63, df = 4, p for heter	rogeneity = 0.0	00; I ² = 82.8%	fect: p = 0.86	ŝ						
Q = 25.63, df = 4, p for heter Evidence of an immediate ve	rogeneity = 0.0	00; I ² = 82.8% noderating ef	fect: p = 0.86	3						
Q = 25.63, df = 4, p for heter Evidence of an immediate ve	ogeneity = 0.0	00; I ² = 82.8%	fect: p = 0.86	6					 	

Complete revasc. better < Relative risk > Culprit-only revasc. better

Figure S6. Effect of FFR-guided revascularization on cardiovascular death.

Study and Year	Activ Events	e N	Con Events	ntrol N	Weight (%)					Rela	ative risk [95% CI]
FFR-guided revascularisa	tion – risk of CV	death									
DANAMI 3, 2015	5	313	9	314	9.8						0.56 [0.19, 1.64]
Compare ACUTE, 2017	3	295	6	590	6.4		⊢				1.00 [0.25, 3.97]
Random effects model for FI	R-guided studie	es (p = 0.4	05)								0.70 [0.30, 1.63]
Q = 0.43, df = 1, p for hetero	geneity = 0.51; I	² = 0.0%									
Angiograpgy-guided reva	scularisation –	risk of CV	' death								
Politi, 2010	6	130	10	84	11.7			i			0.39 [0.15, 1.03]
PRAMI, 2013	4	234	10	231	8.9						0.39 [0.13, 1.24]
Zhang, 2015	11	215	14	213	17		-				0.78 [0.36, 1.68]
Complete, 2019	59	2016	64	2025	41.2			н			0.93 [0.65, 1.31]
CvLPRIT, 2019	2	150	7	146	5.1	⊢					0.28 [0.06, 1.32]
Random effects model for an	ngiography-guide	ed studies	(p = 0.055)				_	-			0.64 [0.40, 1.01]
Q = 5.93, df = 4, p for hetero	geneity = 0.20; I	² = 37.6%									
Evidence of an FFR-quided	versus angiogra	phv-auide	ed moderating	effect: p =	0.73						
5	3 3		5								
						[1		1		
						0.04	0.2	1	5	25	

Figure S7. Effect of FFR-guided revascularization on all-cause mortality.

Study and Year	Active Events	N	Con Events	trol N	Weight (%)					Rel	ative risk [95% CI]
FFR-guided revascularisa	tion – risk of dea	th									
Dambrink, 2012	2	79	0	40	0.5		·			-	2.56 [0.13, 52.14]
DANAMI 3, 2015	15	313	11	314	7.2				-		1.37 [0.64, 2.93]
Compare ACUTE, 2017	4	295	10	590	3.2				-		0.80 [0.25, 2.53]
Random effects model for F Q = 0.83, df = 2, p for hetero	FR-guided studies	(p = 0.50 = 0.0%	63) 45					-			1.20 [0.65, 2.24]
Angiograpgy-guided reva	scularisation – n	sk or dea	ui -								4 00 10 04 00 041
Help-AMI, 2009	1	52	0	17	0.4						1.02 [0.04, 23.91]
Politi, 2010	10	130	13	84	7			-			0.50 [0.23, 1.08]
PRAMI, 2013	12	234	16	231	8		F				0.74 [0.36, 1.53]
Zhang, 2015	13	215	15	213	8.2						0.86 [0.42, 1.76]
Complete 2010	1	00	4	000	0.9						0.25 [0.05, 2.10]
Cyl PRIT 2019	90	2010	100	2025	50						0.58[0.26 1.29]
Random effects model for a $Q = 4.13$, df = 6, p for hetero	ngiography-guideo ogeneity = 0.66; I ²	1 studies = 5.6%	(p = 0.059)	140	0.7			•			0.79 [0.62, 1.01]
Evidence of an FFR-guided	versus angiograp	hy-guide	d moderating	effect: p =	0.54						
						•	•	•			
						0.04	0.2	1	5	25	

Figure S8. Effect of FFR-guided revascularization on myocardial infarction.

Study and Year	Active Events	N	Con Events	trol N	Weight (%)					Rel	ative risk [95% CI]
FFR-guided revascularisa	tion – risk of MI										
Dambrink, 2012 DANAMI 3, 2015 Compare ACUTE, 2017 Random effects model for FI 0 = 2.87. df = 2. p for beterr	4 15 7 FR-guided studies	79 313 295 (p = 0.39	0 16 28 99)	40 314 590	0.4 7.9 5.6				.		4.61 [0.25, 83.61] 0.94 [0.47, 1.87] 0.50 [0.22, 1.13] 0.77 [0.42, 1.41]
Angiograpgy-guided reva	scularisation - ris	sk of MI									
Help-AMI, 2009 Politi, 2010 PRAMI, 2013 Zhang, 2015 Hamza, 2016 Complete, 2019 CvLPRIT, 2019 Random effects model for ar Q = 3.03, df = 6, p for heterc Evidence of an FFR-guided	1 6 7 9 1 109 6 ngiography-guided geneity = 0.81; I ² : versus angiograph	52 130 234 215 50 2016 150 I studies (= 4.7%	1 7 20 14 2 160 12 7p = 0.000)	17 84 231 213 50 2025 146 effect: p =	0.5 3.3 5.2 5.6 0.7 66.8 4.1	•					0.33 [0.02, 4.95] 0.55 [0.19, 1.59] 0.35 [0.15, 0.80] 0.64 [0.28, 1.44] 0.50 [0.05, 5.34] 0.68 [0.54, 0.87] 0.49 [0.19, 1.26] 0.62 [0.48, 0.79]
						[1				
						0.04	0.2	1	5	25	

Figure S9. Effect of FFR-guided revascularization on unplanned revascularization.

Study and Year	Active Events	'n	Contro Events	^{ol} N	Weight (%)					Rela	ative risk [95% CI]
FFR-guided revascularisa	tion – risk of unp	lanned i	e vascularizatio	on							
Dambrink, 2012 DANAMI 3, 2015 Compare ACUTE, 2017	27 17 18	79 313 295	15 52 103	40 314 590	11.7 11.4 12		⊦ ⊢∎⊥ ⊢∎⊥				0.91 [0.55, 1.51] 0.33 [0.19, 0.55] 0.35 [0.22, 0.57]
Random effects model for F $Q = 9.90$, df = 2, p for hetero	FR-guided studie: ogeneity = 0.01; I ²	s (p = 0.0 = 79.9%	23)				-	-			0.47 [0.25, 0.90]
Angiograpgy-guided reva	scularisation – ri	sk of un	planned re vasc	•							
Help-AMI, 2009	9	52	6	17	7.2		⊢				0.49 [0.20, 1.18]
Politi, 2010	14	130	28	84	10.6		⊢ _				0.32 [0.18, 0.58]
PRAMI, 2013	16	234	46	231	11.2		⊢ ∎				0.34 [0.20, 0.59]
Zhang, 2015	27	215	62	213	13			- i			0.43 [0.29, 0.65]
Hamza, 2016	1	50	6	50	1.9	-					0.17 [0.02, 1.33]
Complete, 2019	29	2016	160	2025	13.3		H H H				0.18 [0.12, 0.27]
CvLPRIT, 2019	8	150	16	146	7.7			÷			0.49 [0.21, 1.10]
Random effects model for an Q = 12.34, df = 6, p for heter Evidence of an FFR-guided	ngiography–guide rogeneity = 0.05; l versus angiograp	d studies ² = 50.4% hy-guide	(p = 0.000) % d moderating ef	fect: p =	0.79		•				0.33 [0.24, 0.46]
								'			
						0.04	02	1	5	25	

Figure S10. Freedom from cardiovascular death.



Figure S11. Freedom from myocardial infarction.

Study and Year	Acti	ve	Con	trol			Hazard ratio [95% CI]
	Events	Ν	Events	Ν	Weight (%)		
Freedom from MI							
CvLPRIT, 2019	6	150	12	146	6.2	·	0.43 [0.16, 1.15]
Complete, 2019	109	2016	160	2025	64.9	⊢∎	0.68 [0.54, 0.86]
Compare ACUTE, 2017	7	295	28	590	8.9	·	0.50 [0.22, 1.13]
DANAMI 3, 2015	15	313	16	314	11.7	·	0.94 [0.47, 1.90]
PRAMI, 2013	7	234	20	231	8.2	⊢−−−− +	0.32 [0.14, 0.75]
RE Model for All Studies (Q =	= 4.92, df = 4,	p for heter	ogeneity = 0.3	30; I ² = 9.5	5%)	-	0.63 [0.49, 0.81]
							p for overall effect < 0.001
						0.12 0.25 0.5 1 2	4

Figure S12. Freedom from all-cause death.



Figure S13. Freedom from unplanned revascularization.

Study and Year	Active		Con	trol			Hazard ratio [05% CI]
Study and Tear	Events	Ν	Events	Ν	Weight (%)		
Freedom from unplanned re	evascularisa	tion					
CvLPRIT, 2019	8	150	16	146	11	⊢ -	0.46 [0.20, 1.08]
Complete, 2019	29	2016	160	2025	29.8	◄-∎ 1	0.18 [0.12, 0.26]
Compare ACUTE, 2017	18	295	103	590	21.3	——	0.32 [0.19, 0.54]
DANAMI 3, 2015	17	313	52	314	20.7	·	0.31 [0.18, 0.53]
PRAMI, 2013	16	234	46	231	17.2	⊢ ,	0.30 [0.16, 0.56]
RE Model for All Studies (Q =	6.77, df = 4,	p for heter	ogeneity = 0.1	15; I ² = 42.	1%)	-	0.28 [0.20, 0.38]
							p for overall effect < 0.001
							i I I
						0.12 0.25 0.5	1 2 4

Figure S14. Fixed effects analysis for effect of complete revascularization on risk of cardiovascular death.

Study and Year	Active		Control							Relative ri	isk [95% Cl]
-	Events	N	Events	N	Weight (%)						
Risk of cardiovascular death											
CvLPRIT, 2019	2	150	7	146	3.1			-		0.28	3 [0.06, 1.32]
Complete, 2019	59	2016	64	2025	60.8			-		0.93	3 [0.65, 1.31]
Compare ACUTE, 2017	3	295	6	590	3.9					1.00	0 [0.25, 3.97]
Zhang, 2015	11	215	14	213	12.6					0.78	3 [0.36, 1.68]
DANAMI 3, 2015	5	313	9	314	6.3					0.56	6 [0.19, 1.64]
PRAMI, 2013	4	234	10	231	5.6			-		0.39	9 [0.13, 1.24]
Politi, 2010	6	130	10	84	7.8		⊢ ∎			0.39	9 [0.15, 1.03]
FE Model for All Studies (Q = 6	.40, df = 6, p	for heterog	eneity = 0.38;	l ² = 6.3%)			•			0.76	6 [0.58, 0.99]
										p for overall e	ffect = 0.043
						[- i		1		
						0.04	0.2 1		5	25	

Figure S15. Fixed effects analysis for effect of complete revascularization on risk of myocardial infarction.

Study and Veer	Active		Control							Beletive	iak [05%/ CI]
Study and rear	Events	Ν	Events	Ν	Weight (%)					Relative	ISK [95% CI]
Risk of MI											
CvLPRIT, 2019	6	150	12	146	4.1					0.49	0.19, 1.26]
Complete, 2019	109	2016	160	2025	66.8			H - H		0.68	8 [0.54, 0.87]
Compare ACUTE, 2017	7	295	28	590	5.6		·			0.50	0 [0.22, 1.13]
Hamza, 2016	1	50	2	50	0.7					0.50	0 [0.05, 5.34]
Zhang, 2015	9	215	14	213	5.6					0.64	[0.28, 1.44]
DANAMI 3, 2015	15	313	16	314	7.9		۲			0.94	[0.47, 1.87]
PRAMI, 2013	7	234	20	231	5.2		·			0.35	5 [0.15, 0.80]
Dambrink, 2012	4	79	0	40	0.4					→ 4.61	[0.25, 83.61]
Politi, 2010	6	130	7	84	3.3					0.55	5 [0.19, 1.59]
Help-AMI, 2009	1	52	1	17	0.5	-				0.33	8 [0.02, 4.95]
FE Model for All Studies (Q =	6.35, df = 9, p	for heterog	eneity = 0.70;	l ² = 0.0%)				•		0.65	5 [0.54, 0.79]
										p for overall e	effect < 0.001
							1	- <u>i</u>			
						0.04	0.2	1	5	25	

Figure S16. Fixed effects analysis for effect of complete revascularization on risk of all-cause mortality.

Study and Year	Active		Control							Pol	ativo rick [05% Cl]
Study and Tear	Events	N	Events	Ν	Weight (%)					Nei	ative risk [95 % Ci]
Risk of death											
CvLPRIT, 2019	9	150	15	146	6.7						0.58 [0.26, 1.29]
Complete, 2019	96	2016	106	2025	58			H H H			0.91 [0.70, 1.19]
Compare ACUTE, 2017	4	295	10	590	3.2			-	•		0.80 [0.25, 2.53]
Hamza, 2016	1	50	4	50	0.9	-					0.25 [0.03, 2.16]
Zhang, 2015	13	215	15	213	8.2		F				0.86 [0.42, 1.76]
DANAMI 3, 2015	15	313	11	314	7.2				-		1.37 [0.64, 2.93]
PRAMI, 2013	12	234	16	231	8		F				0.74 [0.36, 1.53]
Dambrink, 2012	2	79	0	40	0.5		·				2.56 [0.13, 52.14]
Politi, 2010	10	130	13	84	7		·				0.50 [0.23, 1.08]
Help-AMI, 2009	1	52	0	17	0.4						1.02 [0.04, 23.91]
FE Model for All Studies (Q =	6.34, df = 9, p	for heterog	eneity = 0.71;	l ² = 0.0%)				•			0.85 [0.69, 1.04]
										p for o	verall effect = 0.108
							1	i			
						0.04	0.2	1	5	25	

Figure S17. Fixed effects analysis for effect of complete revascularization on risk of unplanned revascularization.

Study and Year	Active		Control							Relat	ive risk [95% Cl]
	Events	N	Events	N	Weight (%)					noidi	
Risk of unplanned revascula	arisation										
CvLPRIT, 2019	8	150	16	146	4.4						0.49 [0.21, 1.10]
Complete, 2019	29	2016	160	2025	19.4		⊢∎⊣				0.18 [0.12, 0.27]
Compare ACUTE, 2017	18	295	103	590	12.8		H				0.35 [0.22, 0.57]
Hamza, 2016	1	50	6	50	0.7	-					0.17 [0.02, 1.33]
Zhang, 2015	27	215	62	213	17.6			-			0.43 [0.29, 0.65]
DANAMI 3, 2015	17	313	52	314	10.7		⊢-∎				0.33 [0.19, 0.55]
PRAMI, 2013	16	234	46	231	10.2			+			0.34 [0.20, 0.59]
Dambrink, 2012	27	79	15	40	11.6						0.91 [0.55, 1.51]
Politi, 2010	14	130	28	84	8.8		⊢ ∎				0.32 [0.18, 0.58]
Help-AMI, 2009	9	52	6	17	3.9		·				0.49 [0.20, 1.18]
FE Model for All Studies (Q =	27.33, df = 9,	p for hetero	geneity = 0.00); l ² = 67.1	%)		•				0.36 [0.30, 0.43]
										p for ove	rall effect < 0.001
							1	-i			
						0.04	0.2	1	5	25	
Figure S18. Fixed effects analysis for effect of complete revascularization on risk of major bleeding.

Study and Year	Active		Control							Polativo risk [05% CI]
oludy and real	Events	N	Events	Ν	Weight (%)					Kelative fisk [35 / 61]
Risk of bleeding										
CvLPRIT, 2019	4	150	7	146	7.4					0.56 [0.17, 1.86]
Complete, 2019	58	2016	44	2025	71.8			⊷∎⊶		1.32 [0.90, 1.95]
Compare ACUTE, 2017	3	295	8	590	6.2			-	-	0.75 [0.20, 2.81]
Hamza, 2016	0	50	0	50	0.7	-		_		▶ 1.00 [0.02, 49.44]
DANAMI 3, 2015	1	313	4	314	2.3	-			I	0.25 [0.03, 2.23]
PRAMI, 2013	7	234	6	231	9.3		⊢			1.15 [0.39, 3.38]
Dambrink, 2012	5	79	1	40	2.4				•	2.53 [0.31, 20.95]
FE Model for All Studies (Q =	4.71, df = 6, p	for heterog	eneity = 0.58;	$I^2 = 0.0\%)$				-		1.16 [0.83, 1.60]
								-		p for overall effect = 0.387
							1	i	1	
						0.04	0.2	1	5	25

Figure S19. Sensitivity analysis for risk of cardiovascular death including only trials at low-risk of bias.

Study and Year	Active		Control							Relative rick [05% CI]
Study and real	Events	Ν	Events	Ν	Weight (%)					Relative lisk [35 % OI]
Risk of cardiovascular death										
CvLPRIT, 2019	2	150	7	146	7.5	F				0.28 [0.06, 1.32]
Complete, 2019	59	2016	64	2025	41.4			H H -1		0.93 [0.65, 1.31]
Compare ACUTE, 2017	3	295	6	590	9.2			-		1.00 [0.25, 3.97]
DANAMI 3, 2015	5	313	9	314	13.6					0.56 [0.19, 1.64]
PRAMI, 2013	4	234	10	231	12.4					0.39 [0.13, 1.24]
Politi, 2010	6	130	10	84	15.8		⊢−−−■ −			0.39 [0.15, 1.03]
RE Model for All Studies (Q = 6	6.39, df = 5, p	for heterog	eneity = 0.27;	l ² = 31.4%	b)		-	-		0.62 [0.39, 0.99]
										p for overall effect = 0.044
						Γ	1	i		
						0.04	0.2	1	5	25

Figure S20. Sensitivity analysis for risk of myocardial infarction including only trials at low-risk of bias.

Study and Year	Active		Control							Rela	ative risk [95% CI]
oludy and rear	Events	Ν	Events	N	Weight (%)					iteit	111VE 113K [35 // CI]
Risk of MI											
CvLPRIT, 2019	6	150	12	146	4.4		·•				0.49 [0.19, 1.26]
Complete, 2019	109	2016	160	2025	71.6		н	H			0.68 [0.54, 0.87]
Compare ACUTE, 2017	7	295	28	590	6		-				0.50 [0.22, 1.13]
DANAMI 3, 2015	15	313	16	314	8.4		F				0.94 [0.47, 1.87]
PRAMI, 2013	7	234	20	231	5.6		· •	-			0.35 [0.15, 0.80]
Dambrink, 2012	4	79	0	40	0.5						4.61 [0.25, 83.61]
Politi, 2010	6	130	7	84	3.6						0.55 [0.19, 1.59]
RE Model for All Studies (Q =	6.05, df = 6, p	for heterog	eneity = 0.42;	l ² = 0.0%)			•	•			0.66 [0.54, 0.80]
										p for ov	erall effect < 0.001
								i	1		
						0.04	0.2	1	5	25	

Figure S21. Sensitivity analysis for risk of all-cause mortality including only trials at low-risk of bias.

Study and Year	Active		Control			Polative risk	105% CII
	Events	Ν	Events	N	Weight (%)		
Risk of death							
CvLPRIT, 2019	9	150	15	146	7.4	0.58 [0.	.26, 1.29]
Complete, 2019	96	2016	106	2025	64.1	0.91 [0.	.70, 1.19]
Compare ACUTE, 2017	4	295	10	590	3.5	0.80 [0.	.25, 2.53]
DANAMI 3, 2015	15	313	11	314	8	1.37 [0.	.64, 2.93]
PRAMI, 2013	12	234	16	231	8.8	0.74 [0.	.36, 1.53]
Dambrink, 2012	2	79	0	40	0.5	 2.56 [0.	13, 52.14]
Politi, 2010	10	130	13	84	7.7	0.50 [0.	.23, 1.08]
RE Model for All Studies (Q =	5.09, df = 6, p	for heterog	eneity = 0.53;	l ² = 0.0%)		0.85 [0.	.69, 1.06]
						p for overall effe	ct = 0.150
						0.04 0.2 1 5 25	

Figure S22. Sensitivity analysis for risk of unplanned revascularization including only trials at low-risk of bias.

Study and Year	Active		Control							Relative risk [95% CI]
	Events	N	Events	N	Weight (%)					
Risk of unplanned revascula	arisation									
CvLPRIT, 2019	8	150	16	146	10.6		⊢	-		0.49 [0.21, 1.10]
Complete, 2019	29	2016	160	2025	16.6		⊢∎⊣			0.18 [0.12, 0.27]
Compare ACUTE, 2017	18	295	103	590	15.2		⊢ ∎			0.35 [0.22, 0.57]
DANAMI 3, 2015	17	313	52	314	14.6		⊢ ∎1			0.33 [0.19, 0.55]
PRAMI, 2013	16	234	46	231	14.4					0.34 [0.20, 0.59]
Dambrink, 2012	27	79	15	40	14.9		⊢	-		0.91 [0.55, 1.51]
Politi, 2010	14	130	28	84	13.8					0.32 [0.18, 0.58]
RE Model for All Studies (Q =	25.33, df = 6,	p for hetero	geneity = 0.00); I ² = 73.5	%)		•			0.37 [0.25, 0.54]
										p for overall effect < 0.001
								i		
						0.04	0.2	1	5	25

Figure S23. Sensitivity analysis excluding trials with low use of drug-eluting stents for the effect of complete revascularization on risk of cardiovascular death.



Figure S24. Sensitivity analysis excluding trials with low use of drug-eluting stents for the effect of complete revascularization on risk of myocardial infarction.

Study and Year	Active		Control							Relative risk [95% CI]
	Events	Ν	Events	Ν	Weight (%)					
Risk of MI										
CvLPRIT, 2019	6	150	12	146	4.3		·			0.49 [0.19, 1.26]
Complete, 2019	109	2016	160	2025	69.8			H - H		0.68 [0.54, 0.87]
Compare ACUTE, 2017	7	295	28	590	5.8		·			0.50 [0.22, 1.13]
Hamza, 2016	1	50	2	50	0.7					0.50 [0.05, 5.34]
Zhang, 2015	9	215	14	213	5.8					0.64 [0.28, 1.44]
DANAMI 3, 2015	15	313	16	314	8.2		,			0.94 [0.47, 1.87]
PRAMI, 2013	7	234	20	231	5.5		-	-		0.35 [0.15, 0.80]
RE Model for All Studies (Q =	4.26, df = 6, p	o for heterog	eneity = 0.64;	l ² = 0.0%)				•		0.65 [0.53, 0.79]
										p for overall effect < 0.001
							1	i	1	
						0.04	0.2	1	5	25

Figure S25. Sensitivity analysis excluding trials with low use of drug-eluting stents for the effect of complete revascularization on risk of all-cause mortality.

Study and Year	Active		Control							Relative risk [95% CI]
	Events	Ν	Events	Ν	Weight (%)					Kelutive Hak [50% of]
Risk of death										
CvLPRIT, 2019	9	150	15	146	7.2					0.58 [0.26, 1.29]
Complete, 2019	96	2016	106	2025	63			H		0.91 [0.70, 1.19]
Compare ACUTE, 2017	4	295	10	590	3.4				-	0.80 [0.25, 2.53]
Hamza, 2016	1	50	4	50	1	-			I	0.25 [0.03, 2.16]
Zhang, 2015	13	215	15	213	8.8		۲			0.86 [0.42, 1.76]
DANAMI 3, 2015	15	313	11	314	7.9					1.37 [0.64, 2.93]
PRAMI, 2013	12	234	16	231	8.7		F			0.74 [0.36, 1.53]
RE Model for All Studies (Q =	3.92, df = 6, p	o for heterog	eneity = 0.69;	l ² = 0.0%)				•		0.87 [0.71, 1.08]
										p for overall effect = 0.217
							1	i		
						0.04	0.2	1	5	25

Figure S26. Sensitivity analysis excluding trials with low use of drug-eluting stents for the effect of complete revascularization on risk of unplanned revascularization.

Study and Vear	Active		Control							Pola	tive rick [95% CI]
Study and Tear	Events	Ν	Events	Ν	Weight (%)					Keia	live lisk [35 / 61]
Risk of unplanned revascul	arisation										
CvLPRIT, 2019	8	150	16	146	9.3		-				0.49 [0.21, 1.10]
Complete, 2019	29	2016	160	2025	20.5		⊢∎⊣				0.18 [0.12, 0.27]
Compare ACUTE, 2017	18	295	103	590	17.3		⊢-∎	•			0.35 [0.22, 0.57]
Hamza, 2016	1	50	6	50	1.9	-					0.17 [0.02, 1.33]
Zhang, 2015	27	215	62	213	19.7			-			0.43 [0.29, 0.65]
DANAMI 3, 2015	17	313	52	314	15.9		H				0.33 [0.19, 0.55]
PRAMI, 2013	16	234	46	231	15.5		⊢∎-				0.34 [0.20, 0.59]
RE Model for All Studies (Q =	11.55, df = 6,	p for hetero	geneity = 0.07	7; I ² = 48.5	%)		+				0.32 [0.24, 0.43]
										p for ove	erall effect < 0.001
							1	—i—	1		
						0.04	0.2	1	5	25	

Figure S27. Sensitivity analysis excluding trials with low use of drug-eluting stents for the effect of complete revascularization on risk of major bleeding.

Study and Year	Active		Control			Polative risk [05% Cl
	Events	Ν	Events	Ν	Weight (%)	
Risk of bleeding						
CvLPRIT, 2019	4	150	7	146	11.8	
Complete, 2019	58	2016	44	2025	58.5	1.32 [0.90, 1.95]
Compare ACUTE, 2017	3	295	8	590	10.1	0.75 [0.20, 2.81]
Hamza, 2016	0	50	0	50	1.3	◀ 1.00 [0.02, 49.44
DANAMI 3, 2015	1	313	4	314	3.9	■ 0.25 [0.03, 2.23]
PRAMI, 2013	7	234	6	231	14.5	
RE Model for All Studies (Q =	4.17, df = 5, p	for heterog	eneity = 0.53;	l ² = 12.6%	b)	1.03 [0.67, 1.60
						p for overall effect = 0.885
						0.04 0.2 1 5 25

Figure S28. Sensitivity analysis for risk of cardiovascular death excluding the COMPARE ACUTE trial.

Study and Year	Active		Control							Pola	tive rick [95% CI]
	Events	Ν	Events	Ν	Weight (%)					Reidi	
Risk of CV death											
CvLPRIT, 2019	2	150	7	146	6.1	F					0.28 [0.06, 1.32]
Complete, 2019	59	2016	64	2025	39.9			⊢∎⊣			0.93 [0.65, 1.31]
Zhang, 2015	11	215	14	213	18.8		-				0.78 [0.36, 1.68]
DANAMI 3, 2015	5	313	9	314	11.4		·	•			0.56 [0.19, 1.64]
PRAMI, 2013	4	234	10	231	10.4		, e				0.39 [0.13, 1.24]
Politi, 2010	6	130	10	84	13.4		——	_			0.39 [0.15, 1.03]
RE Model for All Studies (Q =	6.24, df = 5, p	for heterog	eneity = 0.28;	l ² = 30.4%	b)		-	-			0.64 [0.43, 0.96]
										p for ove	erall effect = 0.032
						Γ	1	i	Ι		
						0.04	0.2	1	5	25	

Figure S29. Sensitivity analysis for risk of cardiovascular death excluding the COMPLETE trial.

Study and Year	Active		Control							Relative risk [95% CI]
olddy and real	Events	N	Events	Ν	Weight (%)					
Risk of CV death										
CvLPRIT, 2019	2	150	7	146	7.8	-				0.28 [0.06, 1.32]
Compare ACUTE, 2017	3	295	6	590	9.9			_		1.00 [0.25, 3.97]
Zhang, 2015	11	215	14	213	32		-	-		0.78 [0.36, 1.68]
DANAMI 3, 2015	5	313	9	314	16.1		·•			0.56 [0.19, 1.64]
PRAMI, 2013	4	234	10	231	14.4		·			0.39 [0.13, 1.24]
Politi, 2010	6	130	10	84	19.8					0.39 [0.15, 1.03]
RE Model for All Studies (Q = 3	3.07, df = 5, p f	for heteroge	eneity = 0.69; I	² = 0.0%)				-		0.55 [0.36, 0.85]
										p for overall effect = 0.007
							1	i	Ι	
						0.04	0.2	1	5	25

Figure S30. Sensitivity analysis for risk of cardiovascular death excluding the CVLPRIT trial

Study and Year	Active		Control							Relative risk [95% CI]
otady and real	Events	Ν	Events	N	Weight (%)					
Risk of CV death										
Complete, 2019	59	2016	64	2025	48.2			-		0.93 [0.65, 1.31]
Compare ACUTE, 2017	3	295	6	590	6			_		1.00 [0.25, 3.97]
Zhang, 2015	11	215	14	213	16.9					0.78 [0.36, 1.68]
DANAMI 3, 2015	5	313	9	314	9.3		·			0.56 [0.19, 1.64]
PRAMI, 2013	4	234	10	231	8.4		·			0.39 [0.13, 1.24]
Politi, 2010	6	130	10	84	11.2		·	_		0.39 [0.15, 1.03]
RE Model for All Studies (Q = 4	1.76, df = 5, p	for heterog	eneity = 0.45;	l ² = 16.3%)		-	•		0.73 [0.51, 1.03]
										p for overall effect = 0.073
						Γ	1	i		
						0.04	0.2	1	5	25

Figure S31. Sensitivity analysis for risk of cardiovascular death excluding the DANAMI 3 trial

Study and Year	Activ	ve	Cont	rol						Relative risk [95% CI]
Study and Tear	Events	Ν	Events	Ν	Weight (%)					Relative fisk [35 /6 Olj
Risk of CV death										
CvLPRIT, 2019	2	150	7	146	6.1	F				0.28 [0.06, 1.32]
Complete, 2019	59	2016	64	2025	43.4			H B H		0.93 [0.65, 1.31]
Compare ACUTE, 2017	3	295	6	590	7.5			-		1.00 [0.25, 3.97]
Zhang, 2015	11	215	14	213	19.3					0.78 [0.36, 1.68]
PRAMI, 2013	4	234	10	231	10.3		·			0.39 [0.13, 1.24]
Politi, 2010	6	130	10	84	13.5			_		0.39 [0.15, 1.03]
RE Model for All Studies (Q = 6	6.08, df = 5, p	for heterog	eneity = 0.30;	l ² = 25.9%	5)		-	-		0.68 [0.46, 1.02]
										p for overall effect = 0.062
						Γ	1	i	Ι	
						0.04	0.2	1	5	25

Figure S32. Sensitivity analysis for risk of cardiovascular death excluding the Politi trial

Study and Year	Activ	ve	Cont	rol						Relative risk [95% CI]	
olddy and real	Events	N	Events	N	Weight (%)						
Risk of CV death											
CvLPRIT, 2019	2	150	7	146	4.2	F				0.28 [0.06, 1.32]	
Complete, 2019	59	2016	64	2025	58.4					0.93 [0.65, 1.31]	
Compare ACUTE, 2017	3	295	6	590	5.3		—	_		1.00 [0.25, 3.97]	
Zhang, 2015	11	215	14	213	16.1					0.78 [0.36, 1.68]	
DANAMI 3, 2015	5	313	9	314	8.5		·			0.56 [0.19, 1.64]	
PRAMI, 2013	4	234	10	231	7.6		·			0.39 [0.13, 1.24]	
											_
RE Model for All Studies (Q = 4	1.45, df = 5, p	for heterog	eneity = 0.49;	l ² = 7.0%)				•		0.77 [0.56, 1.07]	
										p for overall effect = 0.115	į
						[1	i			
						0.04	0.2	1	5	25	

Figure S33. Sensitivity analysis for risk of cardiovascular death excluding the PRAMI trial

Study and Year	Activ	ve	Cont	rol						Relativ	ve risk [95% CI]
olddy and real	Events	Ν	Events	N	Weight (%)					Relativ	
Risk of CV death											
CvLPRIT, 2019	2	150	7	146	5						0.28 [0.06, 1.32]
Complete, 2019	59	2016	64	2025	49.7			H B -1			0.93 [0.65, 1.31]
Compare ACUTE, 2017	3	295	6	590	6.3			-			1.00 [0.25, 3.97]
Zhang, 2015	11	215	14	213	17.6						0.78 [0.36, 1.68]
DANAMI 3, 2015	5	313	9	314	9.8						0.56 [0.19, 1.64]
Politi, 2010	6	130	10	84	11.7			_			0.39 [0.15, 1.03]
RE Model for All Studies (Q = 5	5.09, df = 5, p	for heterog	eneity = 0.40;	l ² = 16.0%	5)		-	•			0.73 [0.51, 1.04]
										p for over	all effect = 0.084
						Γ	I	i	1		
						0.04	0.2	1	5	25	

Figure S34. Sensitivity analysis for risk of cardiovascular death excluding the Zhang trial

Study and Year	Activ	ve	Cont	rol						Relative risk [95% CI]
	Events	Ν	Events	N	Weight (%)					
Risk of CV death										
CvLPRIT, 2019	2	150	7	146	7.5					0.28 [0.06, 1.32]
Complete, 2019	59	2016	64	2025	41.4			-		0.93 [0.65, 1.31]
Compare ACUTE, 2017	3	295	6	590	9.2			-	_	1.00 [0.25, 3.97]
DANAMI 3, 2015	5	313	9	314	13.6					0.56 [0.19, 1.64]
PRAMI, 2013	4	234	10	231	12.4					0.39 [0.13, 1.24]
Politi, 2010	6	130	10	84	15.8		⊢∎	-		0.39 [0.15, 1.03]
RE Model for All Studies (O - 6	30 df - 5 n	for beteroo	eneity - 0.27:	1 ² - 31 /%)					0.62 [0.20, 0.00]
	5.55, ui = 5, p	ioi neterog	eneny = 0.27,	1 - 51.470	9					0.02 [0.39, 0.99]
										p for overall effect = 0.044
						Г	1	i		
						0.04	0.2	1	5	25

Figure S35. Sensitivity analysis for risk of myocardial infarction excluding the COMPARE ACUTE trial

Study and Year	Active Control Events N Events N Wei							Relative risk [95% CI]		
	Events	N	Events	N	Weight (%)					
Risk of MI										
CvLPRIT, 2019	6	150	12	146	4.3					0.49 [0.19, 1.26]
Complete, 2019	109	2016	160	2025	70.7			H -		0.68 [0.54, 0.87]
Hamza, 2016	1	50	2	50	0.7					0.50 [0.05, 5.34]
Zhang, 2015	9	215	14	213	5.9					0.64 [0.28, 1.44]
DANAMI 3, 2015	15	313	16	314	8.3		,			0.94 [0.47, 1.87]
PRAMI, 2013	7	234	20	231	5.5		⊢			0.35 [0.15, 0.80]
Dambrink, 2012	4	79	0	40	0.5					4.61 [0.25, 83.61]
Politi, 2010	6	130	7	84	3.5					0.55 [0.19, 1.59]
Help-AMI, 2009	1	52	1	17	0.5	-				0.33 [0.02, 4.95]
RE Model for All Studies (Q =	5.93, df = 8, p	o for heterog	geneity = 0.66;	l ² = 0.0%)				•		0.66 [0.54, 0.81]
										p for overall effect < 0.001
						Γ	1	i		
						0.04	0.2	1	5	25

Figure 36. Sensitivity analysis for risk of myocardial infarction excluding the COMPLETE trial

Study and Year	Active Control Events N Events N Weight (%)				Relative risk [95% CI]						
	Events	N	Events	N	Weight (%)						
Risk of MI											
CvLPRIT, 2019	6	150	12	146	12.3						0.49 [0.19, 1.26]
Compare ACUTE, 2017	7	295	28	590	16.7			L			0.50 [0.22, 1.13]
Hamza, 2016	1	50	2	50	2						0.50 [0.05, 5.34]
Zhang, 2015	9	215	14	213	16.8						0.64 [0.28, 1.44]
DANAMI 3, 2015	15	313	16	314	23.6		F	-			0.94 [0.47, 1.87]
PRAMI, 2013	7	234	20	231	15.8		·				0.35 [0.15, 0.80]
Dambrink, 2012	4	79	0	40	1.3						4.61 [0.25, 83.61]
Politi, 2010	6	130	7	84	10						0.55 [0.19, 1.59]
Help-AMI, 2009	1	52	1	17	1.5	-					0.33 [0.02, 4.95]
RE Model for All Studies (Q =	5.82, df = 8, p	for heterog	geneity = 0.67;	l ² = 0.0%)	I		-	•		p for ov	0.59 [0.42, 0.82] erall effect = 0.002
							1	-i		·	
						0.04	0.2	1	5	25	
					Complet	e revasc. be	tter < Re	lative risk	> Culpr	it-only rev	vasc. better

Figure S37. Sensitivity analysis for risk of myocardial infarction excluding the CvLPRIT trial

Study and Year	Acti Events	ive N	Con Events	trol N	Weight (%)	%) Rela			Relative risk [95% CI]	
	2101110		210110							
Risk of MI										
Complete, 2019	109	2016	160	2025	69.6			H - H		0.68 [0.54, 0.87]
Compare ACUTE, 2017	7	295	28	590	5.8					0.50 [0.22, 1.13]
Hamza, 2016	1	50	2	50	0.7					0.50 [0.05, 5.34]
Zhang, 2015	9	215	14	213	5.8					0.64 [0.28, 1.44]
DANAMI 3, 2015	15	313	16	314	8.2		,			0.94 [0.47, 1.87]
PRAMI, 2013	7	234	20	231	5.5		⊢			0.35 [0.15, 0.80]
Dambrink, 2012	4	79	0	40	0.5					4.61 [0.25, 83.61]
Politi, 2010	6	130	7	84	3.5			•		0.55 [0.19, 1.59]
Help-AMI, 2009	1	52	1	17	0.5	-				0.33 [0.02, 4.95]
RE Model for All Studies (Q =	5.98. df = 8. p	o for heteroa	eneity = 0.65:	$l^2 = 0.0\%$				•		0.66 [0.54 0.80]
	,		,	,				- -		n for everall effect + 0.001
										p for overall effect < 0.001
							I	I	ſ	I
						0.04	0.2	1	5	25

Figure S38. Sensitivity analysis for risk of myocardial infarction excluding the Dambrink trial

Study and Year	Activ	ve	Cont	trol						Relative risk [95% CI]
	Events	N	Events	N	Weight (%)					
Risk of MI										
CvLPRIT, 2019	6	150	12	146	4.1		·			0.49 [0.19, 1.26]
Complete, 2019	109	2016	160	2025	67.1			+		0.68 [0.54, 0.87]
Compare ACUTE, 2017	7	295	28	590	5.6					0.50 [0.22, 1.13]
Hamza, 2016	1	50	2	50	0.7					0.50 [0.05, 5.34]
Zhang, 2015	9	215	14	213	5.6					0.64 [0.28, 1.44]
DANAMI 3, 2015	15	313	16	314	7.9		,			0.94 [0.47, 1.87]
PRAMI, 2013	7	234	20	231	5.3					0.35 [0.15, 0.80]
Politi, 2010	6	130	7	84	3.3					0.55 [0.19, 1.59]
Help-AMI, 2009	1	52	1	17	0.5	-				0.33 [0.02, 4.95]
RE Model for All Studies (Q =	4.59, df = 8, p	for heterog	geneity = 0.80;	$l^2 = 0.0\%$)				•		0.64 [0.53, 0.78]
										p for overall effect < 0.001
						Γ		i	T	
						0.04	0.2	1	5	25

Figure S39. Sensitivity analysis for risk of myocardial infarction excluding the DANAMI 3 trial

Study and Year	Acti Events	ive N	Con Events	trol N	Weight (%)					Rela	ative risk [95% CI]
Risk of MI											
CvLPRIT, 2019	6	150	12	146	4.9		·				0.49 [0.19, 1.26]
Complete, 2019	109	2016	160	2025	69.3			H - H			0.68 [0.54, 0.87]
Compare ACUTE, 2017	7	295	28	590	6.7		·	;			0.50 [0.22, 1.13]
Hamza, 2016	1	50	2	50	0.8	·					0.50 [0.05, 5.34]
Zhang, 2015	9	215	14	213	6.7						0.64 [0.28, 1.44]
PRAMI, 2013	7	234	20	231	6.3		·				0.35 [0.15, 0.80]
Dambrink, 2012	4	79	0	40	0.5						4.61 [0.25, 83.61]
Politi, 2010	6	130	7	84	4						0.55 [0.19, 1.59]
Help-AMI, 2009	1	52	1	17	0.6	-					0.33 [0.02, 4.95]
RE Model for All Studies (Q =	5.15, df = 8, p	for heterog	eneity = 0.74;	l ² = 1.4%)				•		p for ov	0.62 [0.50, 0.77] rerall effect < 0.001
						1	1		1		
						0.04	0.2	1	5	25	
					Complet	e revasc. be	tter < Re	lative risk	> Culpr	rit-only re	vasc. better

Figure S40. Sensitivity analysis for risk of myocardial infarction excluding the Hamza trial

Study and Year	Act	ive	Control Events N Weight (%)				Relative risk [95% CI]
	Events	N	Events	N	Weight (%)		
Risk of MI							
CvLPRIT, 2019	6	150	12	146	4.1	⊢	0.49 [0.19, 1.26]
Complete, 2019	109	2016	160	2025	67.2	⊢ ∎4	0.68 [0.54, 0.87]
Compare ACUTE, 2017	7	295	28	590	5.6		0.50 [0.22, 1.13]
Zhang, 2015	9	215	14	213	5.6		0.64 [0.28, 1.44]
DANAMI 3, 2015	15	313	16	314	7.9		0.94 [0.47, 1.87]
PRAMI, 2013	7	234	20	231	5.3	·	0.35 [0.15, 0.80]
Dambrink, 2012	4	79	0	40	0.4	·	➡ 4.61 [0.25, 83.61]
Politi, 2010	6	130	7	84	3.3	·	0.55 [0.19, 1.59]
Help-AMI, 2009	1	52	1	17	0.5	→	0.33 [0.02, 4.95]
RE Model for All Studies (Q =	6.31, df = 8, p	o for heterog	geneity = 0.61;	; l ² = 0.0%)		•	0.65 [0.54, 0.79]

Complete revasc. better < Relative risk > Culprit-only revasc. better

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0.04 0.2

Figure S41. Sensitivity analysis for risk of myocardial infarction excluding the HELP-AMI trial

Study and Year	Act	ive	Con	trol	M(=:=h+ (0/)					Rela	tive risk [95% CI]
	Events	N	Events	N	weight (%)						
Risk of MI											
CvLPRIT, 2019	6	150	12	146	4.1			—			0.49 [0.19, 1.26]
Complete, 2019	109	2016	160	2025	67.1			H - H			0.68 [0.54, 0.87]
Compare ACUTE, 2017	7	295	28	590	5.6						0.50 [0.22, 1.13]
Hamza, 2016	1	50	2	50	0.7	,					0.50 [0.05, 5.34]
Zhang, 2015	9	215	14	213	5.6						0.64 [0.28, 1.44]
DANAMI 3, 2015	15	313	16	314	7.9		٠				0.94 [0.47, 1.87]
PRAMI, 2013	7	234	20	231	5.3						0.35 [0.15, 0.80]
Dambrink, 2012	4	79	0	40	0.4					-	4.61 [0.25, 83.61]
Politi, 2010	6	130	7	84	3.3						0.55 [0.19, 1.59]
RE Model for All Studies (Q =	6.11, df = 8, p	o for heterog	eneity = 0.64;	l ² = 0.0%)				•			0.65 [0.54, 0.79]
										p for ov	erall effect < 0.001
							1	i	1		
						0.04	0.2	1	5	25	
					Complet	te revasc. be	tter < Re	lative risk	> Culpr	it-only re	vasc. better

Figure S42. Sensitivity analysis for risk of myocardial infarction excluding the Politi trial

Study and Year	Act Events	ive N	Con Events	trol N	Weight (%)					Rela	tive risk [95% CI]
Risk of MI											
CvLPRIT, 2019	6	150	12	146	4.2		·				0.49 [0.19, 1.26]
Complete, 2019	109	2016	160	2025	69.1		н	н			0.68 [0.54, 0.87]
Compare ACUTE, 2017	7	295	28	590	5.7						0.50 [0.22, 1.13]
Hamza, 2016	1	50	2	50	0.7						0.50 [0.05, 5.34]
Zhang, 2015	9	215	14	213	5.8		⊢	÷			0.64 [0.28, 1.44]
DANAMI 3, 2015	15	313	16	314	8.1						0.94 [0.47, 1.87]
PRAMI, 2013	7	234	20	231	5.4		·	4			0.35 [0.15, 0.80]
Dambrink, 2012	4	79	0	40	0.5						4.61 [0.25, 83.61]
Help-AMI, 2009	1	52	1	17	0.5	-					0.33 [0.02, 4.95]
RE Model for All Studies (Q =	6.26, df = 8, p	o for heterog	geneity = 0.62;	l ² = 0.0%)			•	•		p for ov	0.65 [0.54, 0.80] erall effect < 0.001
						[1	1	I		
						0.04	0.2	1	5	25	
					Complet	te revasc. bet	ter < Relat	ive risk :	> Culpr	it-only re	vasc. better

Figure S43. Sensitivity analysis for risk of myocardial infarction excluding the PRAMI trial

Study and Year	Acti Events	ve N	Cont Events	trol N	Weight (%)					Relative risk [95% CI]
Risk of MI										
CvLPRIT, 2019	6	150	12	146	4.3		·			0.49 [0.19, 1.26]
Complete, 2019	109	2016	160	2025	70.5			H - H		0.68 [0.54, 0.87]
Compare ACUTE, 2017	7	295	28	590	5.9		·			0.50 [0.22, 1.13]
Hamza, 2016	1	50	2	50	0.7					0.50 [0.05, 5.34]
Zhang, 2015	9	215	14	213	5.9		-			0.64 [0.28, 1.44]
DANAMI 3, 2015	15	313	16	314	8.3					0.94 [0.47, 1.87]
Dambrink, 2012	4	79	0	40	0.5				-	4.61 [0.25, 83.61]
Politi, 2010	6	130	7	84	3.5					0.55 [0.19, 1.59]
Help-AMI, 2009	1	52	1	17	0.5	-			i	0.33 [0.02, 4.95]
RE Model for All Studies (Q =	4.06, df = 8, p	for heterog	geneity = 0.85;	l ² = 0.0%)				•		0.67 [0.55, 0.82]
										p for overall effect < 0.001
						Γ		i	1	
						0.04	0.2	1	5	25

Figure S44. Sensitivity analysis for risk of myocardial infarction excluding the Zhang trial

Study and Year	Acti Events	ve N	Con Events	trol N	Weight (%)					Rela	tive risk [95% CI]
Risk of MI											
CvLPRIT, 2019	6	150	12	146	4.3						0.49 [0.19, 1.26]
Complete, 2019	109	2016	160	2025	70.7			-			0.68 [0.54, 0.87]
Compare ACUTE, 2017	7	295	28	590	5.9		·				0.50 [0.22, 1.13]
Hamza, 2016	1	50	2	50	0.7	·					0.50 [0.05, 5.34]
DANAMI 3, 2015	15	313	16	314	8.3		۲				0.94 [0.47, 1.87]
PRAMI, 2013	7	234	20	231	5.5		·				0.35 [0.15, 0.80]
Dambrink, 2012	4	79	0	40	0.5						4.61 [0.25, 83.61]
Politi, 2010	6	130	7	84	3.5			•			0.55 [0.19, 1.59]
Help-AMI, 2009	1	52	1	17	0.5	-	_				0.33 [0.02, 4.95]
RE Model for All Studies (Q =	6.35, df = 8, p	for heterog	eneity = 0.61;	l ² = 0.0%)				•		p for ov	0.65 [0.53, 0.79] erall effect < 0.001
						Γ	1	i	Ι		
						0.04	0.2	1	5	25	
					Complet	e revasc. be	tter < Re	lative risk	> Culpr	it−only re	vasc. better

Figure S45. Sensitivity analysis for risk of all-cause mortality excluding the COMPARE ACUTE trial

Study and Year	Acti	ve	Con	trol		Relative risk [95% CI]
	Events	N	Events	N	Weight (%)	
Risk of death						
CvLPRIT, 2019	9	150	15	146	6.9	0.58 [0.26, 1.29]
Complete, 2019	96	2016	106	2025	59.9	0.91 [0.70, 1.19]
Hamza, 2016	1	50	4	50	0.9	0.25 [0.03, 2.16]
Zhang, 2015	13	215	15	213	8.4	0.86 [0.42, 1.76]
DANAMI 3, 2015	15	313	11	314	7.5	1.37 [0.64, 2.93]
PRAMI, 2013	12	234	16	231	8.2	0.74 [0.36, 1.53]
Dambrink, 2012	2	79	0	40	0.5	2.56 [0.13, 52.14]
Politi, 2010	10	130	13	84	7.2	0.50 [0.23, 1.08]
Help-AMI, 2009	1	52	0	17	0.4	1.02 [0.04, 23.91]
RE Model for All Studies (Q =	6.33, df = 8, p	for heterog	eneity = 0.61;	l ² = 0.0%)		• 0.85 [0.69, 1.04]
						p for overall effect = 0.117
						0.04 0.2 1 5 25
					Complet	te revasc. better < Relative risk > Culprit-only revasc. better

Figure S46. Sensitivity analysis for risk of all-cause mortality excluding the COMPLETE trial

Study and Year	Activ	/e	Control							Relative risk [95% CI]
	Events	N	Events	N	Weight (%)					
Risk of death										
CvLPRIT, 2019	9	150	15	146	15.9			■		0.58 [0.26, 1.29]
Compare ACUTE, 2017	4	295	10	590	7.6			-	-	0.80 [0.25, 2.53]
Hamza, 2016	1	50	4	50	2.2	-	=			0.25 [0.03, 2.16]
Zhang, 2015	13	215	15	213	19.4		F			0.86 [0.42, 1.76]
DANAMI 3, 2015	15	313	11	314	17.3				-	1.37 [0.64, 2.93]
PRAMI, 2013	12	234	16	231	19		F			0.74 [0.36, 1.53]
Dambrink, 2012	2	79	0	40	1.1		·		-	2.56 [0.13, 52.14]
Politi, 2010	10	130	13	84	16.6		H	∎		0.50 [0.23, 1.08]
Help-AMI, 2009	1	52	0	17	1	·				1.02 [0.04, 23.91]
RE Model for All Studies (Q =	5.66, df = 8, p	for heterog	geneity = 0.69;	l ² = 0.0%)	1			•		0.76 [0.56, 1.05]
										p for overall effect = 0.094
						Γ	1	i	Ι	
						0.04	0.2	1	5	25

Figure S47. Sensitivity analysis for risk of all-cause mortality excluding the CvLPRIT trial

Study and Year	Act Events	ive N	Con Events	trol N	Weight (%)	Relative risk [95% CI]
Risk of death						
Complete, 2019	96	2016	106	2025	62.2	0.91 [0.70, 1.19]
Compare ACUTE, 2017	4	295	10	590	3.4	0.80 [0.25, 2.53]
Hamza, 2016	1	50	4	50	1	
Zhang, 2015	13	215	15	213	8.7	0.86 [0.42, 1.76]
DANAMI 3, 2015	15	313	11	314	7.8	1.37 [0.64, 2.93]
PRAMI, 2013	12	234	16	231	8.5	0.74 [0.36, 1.53]
Dambrink, 2012	2	79	0	40	0.5	– – – – – 2.56 [0.13, 52.14]
Politi, 2010	10	130	13	84	7.5	0.50 [0.23, 1.08]
Help-AMI, 2009	1	52	0	17	0.5	1.02 [0.04, 23.91]
RE Model for All Studies (Q =	5.45, df = 8, p	o for heterog	jeneity = 0.71;	; l ² = 0.0%)		0.87 [0.70, 1.07] p for overall effect = 0.190
						0.04 0.2 1 5 25
					Complet	e revasc. better < Relative risk > Culprit-only revasc. better

Figure S48. Sensitivity analysis for risk of all-cause mortality excluding the Dambrink trial

Study and Year	Acti Events	ve N	Cont Events	trol N	Weight (%)					Relative risk [95% CI]
Risk of death										
CvLPRIT, 2019	9	150	15	146	6.7			•		0.58 [0.26, 1.29]
Complete, 2019	96	2016	106	2025	58.3			H		0.91 [0.70, 1.19]
Compare ACUTE, 2017	4	295	10	590	3.2			-		0.80 [0.25, 2.53]
Hamza, 2016	1	50	4	50	0.9	-				0.25 [0.03, 2.16]
Zhang, 2015	13	215	15	213	8.2		F			0.86 [0.42, 1.76]
DANAMI 3, 2015	15	313	11	314	7.3			·	-	1.37 [0.64, 2.93]
PRAMI, 2013	12	234	16	231	8		⊢			0.74 [0.36, 1.53]
Politi, 2010	10	130	13	84	7					0.50 [0.23, 1.08]
Help-AMI, 2009	1	52	0	17	0.4	·				1.02 [0.04, 23.91]
RE Model for All Studies (Q =	5.82, df = 8, p	o for heterog	eneity = 0.67;	l ² = 0.0%)				•		0.84 [0.68, 1.03]
										p for overall effect = 0.098
							I	i	Τ	
						0.04	0.2	1	5	25

Figure S49. Sensitivity analysis for risk of all-cause mortality excluding the DANAMI 3 trial

Study and Year	Acti Events	ive N	Cont Events	trol N	Weight (%)					Rela	ative risk [95% CI]
Risk of death											
CvLPRIT, 2019	9	150	15	146	7.4						0.58 [0.26, 1.29]
Complete, 2019	96	2016	106	2025	61.5			H			0.91 [0.70, 1.19]
Compare ACUTE, 2017	4	295	10	590	3.5			-	4		0.80 [0.25, 2.53]
Hamza, 2016	1	50	4	50	1	-					0.25 [0.03, 2.16]
Zhang, 2015	13	215	15	213	9		F				0.86 [0.42, 1.76]
PRAMI, 2013	12	234	16	231	8.8		⊢				0.74 [0.36, 1.53]
Dambrink, 2012	2	79	0	40	0.5		H		-		2.56 [0.13, 52.14]
Politi, 2010	10	130	13	84	7.7						0.50 [0.23, 1.08]
Help-AMI, 2009	1	52	0	17	0.5			+			1.02 [0.04, 23.91]
RE Model for All Studies (Q =	4.69, df = 8, p	for heterog	eneity = 0.79;	l ² = 0.6%)				•			0.81 [0.65, 1.01]
										p for ov	verall effect = 0.058
							Ι	i	1		
						0.04	0.2	1	5	25	

Figure S50. Sensitivity analysis for risk of all-cause mortality excluding the Hamza trial

Study and Year	Act Events	ive N	Con Events	trol N	Weight (%)	Relative risk [95% Cl]
Risk of death						
CvLPRIT, 2019	9	150	15	146	6.7	0.58 [0.26, 1.29]
Complete, 2019	96	2016	106	2025	58.6	▶ 0.91 [0.70, 1.19]
Compare ACUTE, 2017	4	295	10	590	3.2	• 0.80 [0.25, 2.53]
Zhang, 2015	13	215	15	213	8.2	0.86 [0.42, 1.76]
DANAMI 3, 2015	15	313	11	314	7.3	1.37 [0.64, 2.93]
PRAMI, 2013	12	234	16	231	8	0.74 [0.36, 1.53]
Dambrink, 2012	2	79	0	40	0.5	► 2.56 [0.13, 52.14]
Politi, 2010	10	130	13	84	7	0.50 [0.23, 1.08]
Help-AMI, 2009	1	52	0	17	0.4	1.02 [0.04, 23.91]
RE Model for All Studies (Q =	5.11, df = 8, p	for heterog	jeneity = 0.75;	l ² = 0.0%)		0.85 [0.70, 1.05] p for overall effect = 0.135
						0.04 0.2 1 5 25
					Complet	ete revasc. better < Relative risk > Culprit-only revasc. better

Figure S51. Sensitivity analysis for risk of all-cause mortality excluding the HELP-AMI trial

Study and Year	Acti Events	ive N	Con Events	trol N	Weight (%)	Relative risk [95% CI]
Risk of death						
CvLPRIT, 2019	9	150	15	146	6.7	0.58 [0.26, 1.29]
Complete, 2019	96	2016	106	2025	58.3	⊷ 0.91 [0.70, 1.19]
Compare ACUTE, 2017	4	295	10	590	3.2	0.80 [0.25, 2.53]
Hamza, 2016	1	50	4	50	0.9	0.25 [0.03, 2.16]
Zhang, 2015	13	215	15	213	8.2	0.86 [0.42, 1.76]
DANAMI 3, 2015	15	313	11	314	7.3	1.37 [0.64, 2.93]
PRAMI, 2013	12	234	16	231	8	0.74 [0.36, 1.53]
Dambrink, 2012	2	79	0	40	0.5	2.56 [0.13, 52.14]
Politi, 2010	10	130	13	84	7	0.50 [0.23, 1.08]
RE Model for All Studies (Q =	6.33, df = 8, p	for heterog	eneity = 0.61;	l ² = 0.0%)		• 0.84 [0.69, 1.04]
						p for overall effect = 0.107
						0.04 0.2 1 5 25
					Complet	ete revasc. better < Relative risk > Culprit-only revasc. better

Figure S52. Sensitivity analysis for risk of all-cause mortality excluding the Politi trial

Study and Year	Act	ive N	Con	trol N	Weight (%)	Relati	ive risk [95% CI]
	Lventa		Lventa	N	Height (70)		
Risk of death							
CvLPRIT, 2019	9	150	15	146	7.2		0.58 [0.26, 1.29]
Complete, 2019	96	2016	106	2025	62.4	F E -1	0.91 [0.70, 1.19]
Compare ACUTE, 2017	4	295	10	590	3.4	F	0.80 [0.25, 2.53]
Hamza, 2016	1	50	4	50	1		0.25 [0.03, 2.16]
Zhang, 2015	13	215	15	213	8.8	⊢	0.86 [0.42, 1.76]
DANAMI 3, 2015	15	313	11	314	7.8	·	1.37 [0.64, 2.93]
PRAMI, 2013	12	234	16	231	8.6	⊢ ∎	0.74 [0.36, 1.53]
Dambrink, 2012	2	79	0	40	0.5	÷	2.56 [0.13, 52.14]
Help-AMI, 2009	1	52	0	17	0.5	· · · · · ·	1.02 [0.04, 23.91]
RE Model for All Studies (Q =	4.42, df = 8, p	o for heterog	jeneity = 0.82;	l ² = 0.0%)		p for ove	0.88 [0.71, 1.09] rall effect = 0.236
						0.04 0.2 1 5 25	
					Complet	te revasc. better < Relative risk > Culprit-only reva	asc. better

Figure S53. Sensitivity analysis for risk of all-cause mortality excluding the PRAMI trial

Study and Year	Acti	ve	Con	trol			Relative risk [95% CI]
orady and real	Events	N	Events	N	Weight (%)		Kelutre Hak [0070 el]
Risk of death							
CvLPRIT, 2019	9	150	15	146	7.2	⊢	0.58 [0.26, 1.29]
Complete, 2019	96	2016	106	2025	63.1	H ≣ →	0.91 [0.70, 1.19]
Compare ACUTE, 2017	4	295	10	590	3.4		0.80 [0.25, 2.53]
Hamza, 2016	1	50	4	50	1		0.25 [0.03, 2.16]
Zhang, 2015	13	215	15	213	8.9	⊢−	0.86 [0.42, 1.76]
DANAMI 3, 2015	15	313	11	314	7.9		1.37 [0.64, 2.93]
Dambrink, 2012	2	79	0	40	0.5	·	→ 2.56 [0.13, 52.14]
Politi, 2010	10	130	13	84	7.6		0.50 [0.23, 1.08]
Help-AMI, 2009	1	52	0	17	0.5	<u>بــــــــــــــــــــــــــــــــــــ</u>	1.02 [0.04, 23.91]
RE Model for All Studies (Q =	6.20, df = 8, p	for heterog	geneity = 0.62;	l ² = 0.0%)		•	0.85 [0.69, 1.06]
							p for overall effect = 0.150

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 Complete revasc. better

 Relative risk >
 Culprit-only revasc. better
Figure S54. Sensitivity analysis for risk of all-cause mortality excluding the Zhang trial

Study and Year	Acti	ve	Cont	rol			
	Events	N	Events	N	Weight (%)		
Risk of death							
CvLPRIT, 2019	9	150	15	146	7.3		0.58 [0.26, 1.29]
Complete, 2019	96	2016	106	2025	63.2	H	0.91 [0.70, 1.19]
Compare ACUTE, 2017	4	295	10	590	3.5		0.80 [0.25, 2.53]
Hamza, 2016	1	50	4	50	1		0.25 [0.03, 2.16]
DANAMI 3, 2015	15	313	11	314	7.9		1.37 [0.64, 2.93]
PRAMI, 2013	12	234	16	231	8.7		0.74 [0.36, 1.53]
Dambrink, 2012	2	79	0	40	0.5	H	▶ 2.56 [0.13, 52.14]
Politi, 2010	10	130	13	84	7.6	⊢	0.50 [0.23, 1.08]
Help-AMI, 2009	1	52	0	17	0.5	·	1.02 [0.04, 23.91]
RE Model for All Studies (Q =	6.34, df = 8, p	for heterog	geneity = 0.61;	l ² = 0.0%)		•	0.84 [0.68, 1.05]
							p for overall effect = 0.120

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 Complete revasc. better

 Relative risk >
 Culprit-only revasc. better

Figure S55. Sensitivity analysis for risk of unplanned revascularization excluding the COMPARE ACUTE trial

Study and Year	Acti	ve	Con	trol						Rela	tive risk [95% CI]
	Events	N	Events	N	Weight (%)					Reid	
Risk of unplanned revascula	arisation										
CvLPRIT, 2019	8	150	16	146	9.1		-				0.49 [0.21, 1.10]
Complete, 2019	29	2016	160	2025	14.8		⊢∎⊣				0.18 [0.12, 0.27]
Hamza, 2016	1	50	6	50	2.4	-					0.17 [0.02, 1.33]
Zhang, 2015	27	215	62	213	14.5		⊢∎-	-			0.43 [0.29, 0.65]
DANAMI 3, 2015	17	313	52	314	12.9						0.33 [0.19, 0.55]
PRAMI, 2013	16	234	46	231	12.7		⊢∎				0.34 [0.20, 0.59]
Dambrink, 2012	27	79	15	40	13.2						0.91 [0.55, 1.51]
Politi, 2010	14	130	28	84	12.1						0.32 [0.18, 0.58]
Help-AMI, 2009	9	52	6	17	8.5		⊢ — ■				0.49 [0.20, 1.18]
RE Model for All Studies (Q =	27.32, df = 8,	p for hetero	geneity = 0.00); I ² = 67.7	%)		-				0.38 [0.27, 0.54]
										p for ove	erall effect < 0.001
						[Ι	i	1		
						0.04	0.2	1	5	25	

Figure S56. Sensitivity analysis for risk of unplanned revascularization excluding the COMPLETE trial

Study and Year	Activ	ve	Cont	rol						Polativo rick [05% CI]
olddy and real	Events	N	Events	N	Weight (%)					Relative hak [35 / 61]
Risk of unplanned revascula	arisation									
CvLPRIT, 2019	8	150	16	146	7.6		·			0.49 [0.21, 1.10]
Compare ACUTE, 2017	18	295	103	590	14.7					0.35 [0.22, 0.57]
Hamza, 2016	1	50	6	50	1.5	-				0.17 [0.02, 1.33]
Zhang, 2015	27	215	62	213	16.9		⊷∎-	-		0.43 [0.29, 0.65]
DANAMI 3, 2015	17	313	52	314	13.4					0.33 [0.19, 0.55]
PRAMI, 2013	16	234	46	231	13					0.34 [0.20, 0.59]
Dambrink, 2012	27	79	15	40	14		,	-		0.91 [0.55, 1.51]
Politi, 2010	14	130	28	84	12		·			0.32 [0.18, 0.58]
Help-AMI, 2009	9	52	6	17	6.9					0.49 [0.20, 1.18]
RE Model for All Studies (Q =	12.84, df = 8,	p for hetero	geneity = 0.12	; l ² = 41.4	%)		•			0.42 [0.32, 0.55]
										p for overall effect < 0.001
								i		
						0.04	0.2	1	5	25

Figure S57. Sensitivity analysis for risk of unplanned revascularization excluding the CvLPRIT trial

Study and Year	Acti	ve	Con	trol						Relative risk [95% CI]	
	Events	N	Events	N	Weight (%)						
Risk of unplanned revascula	arisation										
Complete, 2019	29	2016	160	2025	14.3		⊢∎⊣			0.18 [0.12, 0.27]	l
Compare ACUTE, 2017	18	295	103	590	13		⊢ ∎			0.35 [0.22, 0.57]	l
Hamza, 2016	1	50	6	50	2.2	-				0.17 [0.02, 1.33]	J
Zhang, 2015	27	215	62	213	14		∎	-		0.43 [0.29, 0.65]	J
DANAMI 3, 2015	17	313	52	314	12.3		- 			0.33 [0.19, 0.55]	J
PRAMI, 2013	16	234	46	231	12.1		⊢∎			0.34 [0.20, 0.59]	J
Dambrink, 2012	27	79	15	40	12.6					0.91 [0.55, 1.51]	J
Politi, 2010	14	130	28	84	11.5		H			0.32 [0.18, 0.58]	J
Help-AMI, 2009	9	52	6	17	7.9					0.49 [0.20, 1.18]	I
RE Model for All Studies (Q =	26.79, df = 8,	p for hetero	geneity = 0.00); I ² = 68.1	%)		*			0.37 [0.26, 0.51]	
										p for overall effect < 0.001	
							Ι	i			
						0.04	0.2	1	5	25	

Figure S58. Sensitivity analysis for risk of unplanned revascularization excluding the Dambrink trial

Study and Year	Acti	ve	Con	trol						Rela	tive risk [95% CI]
	Events	N	Events	N	Weight (%)					Reid	
Risk of unplanned revascula	arisation										
CvLPRIT, 2019	8	150	16	146	7.1						0.49 [0.21, 1.10]
Complete, 2019	29	2016	160	2025	17.3		⊢∎⊣				0.18 [0.12, 0.27]
Compare ACUTE, 2017	18	295	103	590	14.2						0.35 [0.22, 0.57]
Hamza, 2016	1	50	6	50	1.4	-					0.17 [0.02, 1.33]
Zhang, 2015	27	215	62	213	16.6			-			0.43 [0.29, 0.65]
DANAMI 3, 2015	17	313	52	314	12.9		⊢-∎				0.33 [0.19, 0.55]
PRAMI, 2013	16	234	46	231	12.5			•			0.34 [0.20, 0.59]
Politi, 2010	14	130	28	84	11.5		⊢				0.32 [0.18, 0.58]
Help-AMI, 2009	9	52	6	17	6.4			<u>-</u>			0.49 [0.20, 1.18]
RE Model for All Studies (Q =	12.54, df = 8,	p for hetero	geneity = 0.13	3; I ² = 39.9	%)		+				0.33 [0.26, 0.42]
										p for ov	erall effect < 0.001
							1	i	I		
						0.04	0.2	1	5	25	

Figure S59. Sensitivity analysis for risk of unplanned revascularization excluding the DANAMI 3 trial

Study and Year	Acti	ve	Con	trol						Relative risk [95% Cl	n
	Events	N	Events	N	Weight (%)						u .
Risk of unplanned revascula	arisation										
CvLPRIT, 2019	8	150	16	146	9		⊢			0.49 [0.21, 1.10)]
Complete, 2019	29	2016	160	2025	14.7		⊢∎→			0.18 [0.12, 0.27	7]
Compare ACUTE, 2017	18	295	103	590	13.4		⊢-■			0.35 [0.22, 0.57	']
Hamza, 2016	1	50	6	50	2.4	-				0.17 [0.02, 1.33	3]
Zhang, 2015	27	215	62	213	14.4			-		0.43 [0.29, 0.65	5]
PRAMI, 2013	16	234	46	231	12.6		⊢			0.34 [0.20, 0.59)]
Dambrink, 2012	27	79	15	40	13.1			-		0.91 [0.55, 1.51]
Politi, 2010	14	130	28	84	12		⊢			0.32 [0.18, 0.58	3]
Help-AMI, 2009	9	52	6	17	8.4					0.49 [0.20, 1.18	3]
RE Model for All Studies (Q =	27.20, df = 8,	p for hetero	geneity = 0.00); I ² = 67.8	%)		•			0.38 [0.27, 0.54	4]
										p for overall effect < 0.00	1
						Γ	1	i			
						0.04	0.2	1	5	25	

Figure S60. Sensitivity analysis for risk of unplanned revascularization excluding the Hamza trial

Study and Year	Acti	ive	Con	trol			Polativo rick [05% CI]
Study and Tear	Events	Ν	Events	Ν	Weight (%)		Relative hak [35 % OI]
Risk of unplanned revascul	arisation						
CvLPRIT, 2019	8	150	16	146	7.9	·	0.49 [0.21, 1.10]
Complete, 2019	29	2016	160	2025	13.6	⊷∎→	0.18 [0.12, 0.27]
Compare ACUTE, 2017	18	295	103	590	12.2	⊢ ∎i	0.35 [0.22, 0.57]
Zhang, 2015	27	215	62	213	13.3	⊷∎→	0.43 [0.29, 0.65]
DANAMI 3, 2015	17	313	52	314	11.6		0.33 [0.19, 0.55]
PRAMI, 2013	16	234	46	231	11.4	⊢ ∎→	0.34 [0.20, 0.59]
Dambrink, 2012	27	79	15	40	11.9	⊢ ∎1	0.91 [0.55, 1.51]
Politi, 2010	14	130	28	84	10.8	⊢ ∎→	0.32 [0.18, 0.58]
Help-AMI, 2009	9	52	6	17	7.3	⊢	0.49 [0.20, 1.18]
RE Model for All Studies (Q =	26.80, df = 8,	p for hetero	geneity = 0.00); l ² = 67.6	%)	•	0.38 [0.28, 0.52]
							p for overall effect < 0.001

Complete revasc. better < Relative risk > Culprit-only revasc. better

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Figure S61. Sensitivity analysis for risk of unplanned revascularization excluding the HELP-AMI trial

Study and Year	Acti Events	ve N	Cont Events	trol N	Weight (%)					Relative ri	sk [95% CI]
Risk of unplanned revascula	arisation										
CvLPRIT, 2019	8	150	16	146	8.5		⊢			0.49	0.21, 1.10]
Complete, 2019	29	2016	160	2025	14.2		⊢∎⊣			0.18	8 [0.12, 0.27]
Compare ACUTE, 2017	18	295	103	590	12.9		·			0.35	5 [0.22, 0.57]
Hamza, 2016	1	50	6	50	2.2	-				0.17	[0.02, 1.33]
Zhang, 2015	27	215	62	213	13.9			-		0.43	8 [0.29, 0.65]
DANAMI 3, 2015	17	313	52	314	12.2		⊢ ∎			0.33	8 [0.19, 0.55]
PRAMI, 2013	16	234	46	231	12					0.34	[0.20, 0.59]
Dambrink, 2012	27	79	15	40	12.6					0.91	[0.55, 1.51]
Politi, 2010	14	130	28	84	11.5		⊢-∎			0.32	2 [0.18, 0.58]
RE Model for All Studies (Q =	26.84, df = 8,	p for hetero	geneity = 0.00); I ² = 68.2	%)		•			0.37	7 [0.26, 0.51]
										p for overall ef	ffect < 0.001
							I	Ì	I		
						0.04	0.2	1	5	25	

Figure S62. Sensitivity analysis for risk of unplanned revascularization excluding the Politi trial

Study and Year	Act	ive	Con	trol	Weight (%)					Rela	tive risk [95% CI]
	Events	N	Events	N	Weight (76)						
Risk of unplanned revascula	arisation										
CvLPRIT, 2019	8	150	16	146	8.9			ц.			0.49 [0.21, 1.10]
Complete, 2019	29	2016	160	2025	14.6		⊢∎⊣				0.18 [0.12, 0.27]
Compare ACUTE, 2017	18	295	103	590	13.3			-			0.35 [0.22, 0.57]
Hamza, 2016	1	50	6	50	2.4	-					0.17 [0.02, 1.33]
Zhang, 2015	27	215	62	213	14.3		⊢∎	-			0.43 [0.29, 0.65]
DANAMI 3, 2015	17	313	52	314	12.7		⊢-■	4			0.33 [0.19, 0.55]
PRAMI, 2013	16	234	46	231	12.5		⊢-■	-			0.34 [0.20, 0.59]
Dambrink, 2012	27	79	15	40	13						0.91 [0.55, 1.51]
Help-AMI, 2009	9	52	6	17	8.3			<u> </u>			0.49 [0.20, 1.18]
RE Model for All Studies (Q =	27.19, df = 8,	p for hetero	geneity = 0.00); I ² = 68.1	%)		+				0.38 [0.27, 0.54]
										p for ov	erall effect < 0.001
								1	1		
						0.04	0.2	1	5	25	
					Complet	e revasc. be	tter < Re	lative risk	> Culpr	it-only rev	/asc. better

Figure S63. Sensitivity analysis for risk of unplanned revascularization excluding the PRAMI trial

Study and Year	Acti Events	ve N	Cont Events	trol N	Weight (%)					Relat	tive risk [95% CI]
Risk of unplanned revascula	arisation										
CvLPRIT, 2019	8	150	16	146	9						0.49 [0.21, 1.10]
Complete, 2019	29	2016	160	2025	14.7		⊢∎⊣				0.18 [0.12, 0.27]
Compare ACUTE, 2017	18	295	103	590	13.4		⊢∎→				0.35 [0.22, 0.57]
Hamza, 2016	1	50	6	50	2.4	-					0.17 [0.02, 1.33]
Zhang, 2015	27	215	62	213	14.4			4			0.43 [0.29, 0.65]
DANAMI 3, 2015	17	313	52	314	12.8		⊢∎⊸				0.33 [0.19, 0.55]
Dambrink, 2012	27	79	15	40	13.1		٠				0.91 [0.55, 1.51]
Politi, 2010	14	130	28	84	12		⊢ ∎				0.32 [0.18, 0.58]
Help-AMI, 2009	9	52	6	17	8.4						0.49 [0.20, 1.18]
RE Model for All Studies (Q =	27.30, df = 8,	p for hetero	geneity = 0.00); I ² = 68.1	%)		+				0.38 [0.27, 0.54]
										p for ove	erall effect < 0.001
						Γ	I	i	I		
						0.04	0.2	1	5	25	

Figure S64. Sensitivity analysis for risk of unplanned revascularization excluding the Zhang trial

Study and Year	Acti	ve	Con	trol			Relative risk [95% CI]
Study and Tear	Events	Ν	Events	Ν	Weight (%)		
Risk of unplanned revascula	arisation						
CvLPRIT, 2019	8	150	16	146	9.2	·	0.49 [0.21, 1.10]
Complete, 2019	29	2016	160	2025	14.9	⊢ ∎1	0.18 [0.12, 0.27]
Compare ACUTE, 2017	18	295	103	590	13.6	⊢ ∎	0.35 [0.22, 0.57]
Hamza, 2016	1	50	6	50	2.4		- 0.17 [0.02, 1.33]
DANAMI 3, 2015	17	313	52	314	13	⊢∎ 1	0.33 [0.19, 0.55]
PRAMI, 2013	16	234	46	231	12.8	⊢ ∎→	0.34 [0.20, 0.59]
Dambrink, 2012	27	79	15	40	13.3	⊷∎	
Politi, 2010	14	130	28	84	12.2	⊢ ∎	0.32 [0.18, 0.58]
Help-AMI, 2009	9	52	6	17	8.5	⊢∎	- 0.49 [0.20, 1.18]
RE Model for All Studies (Q =	26.42, df = 8,	p for hetero	geneity = 0.00	D; I ² = 66.3	%)	+	0.37 [0.26, 0.52]
							p for overall effect < 0.001

Complete revasc. better < Relative risk > Culprit-only revasc. better

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