UCSF UC San Francisco Previously Published Works

Title

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.

Permalink

https://escholarship.org/uc/item/54d1n28b

Journal

Journal of the American Heart Association: Cardiovascular and Cerebrovascular Disease, 9(12)

Authors

Ahmad, Yousif Howard, James Arnold, Ahran <u>et al.</u>

Publication Date

2020-06-16

DOI

10.1161/JAHA.119.015263

Peer reviewed

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

Yousif Ahmad D, MRCP; James P. Howard, MRCP; Ahran Arnold, MRCP; Megha Prasad, MD; Henry Seligman, MRCP; Christopher M. Cook, MRCP; Takayuki Warisawa, MD; Matthew Shun-Shun, PhD; Ziad Ali, DPhil, MD; Manish A. Parikh, MD; Rasha Al-Lamee, PhD, MD; Sayan Sen, PhD, MD; Darrel Francis, MD; Jeffrey W. Moses, MD; Martin B. Leon, MD; Gregg W. Stone, MD; Dimitri Karmpaliotis, PhD, MD

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

rimary 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

Correspondence to: Yousif Ahmad, MRCP, Columbia University Medical Center/New York-Presbyterian Hospital, New York, NY. E-mail: ya2431@cumc.columbia. edu

Supplementary Materials for this article are available at https://www.ahajournals.org/doi/suppl/10.1161/JAHA.119.015263

For Sources of Funding and Disclosures, see page 14.

^{© 2020} The Authors. Published on behalf of the American Heart Association, Inc., by Wiley. This is an open access article under the terms of the Creative Commons Attribution License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited. *JAHA* is available at: www.ahajournals.org/journal/jaha

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
--

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

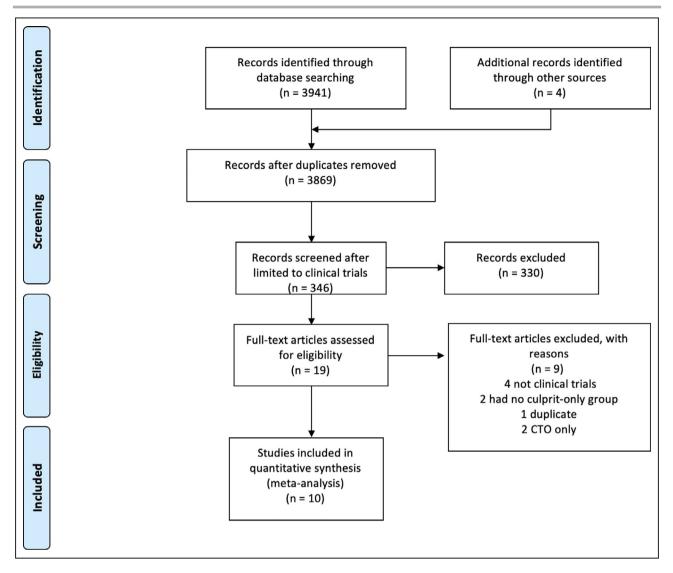


Figure 1. Search strategy and source of included studies. CTO indicates chronic total occlusion.

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

Wade nervo Point Stantin patients Stantin patients Composition Composited Composition	Author	Study Acronym	Year	Region	z	Mean Age [*]	mo [†]	Entry Criteria	Revascularization	Revascularization	Vessel Criteria	Outcomes	Safety Outcomes
 ^a n₁ ^b n₁<	Wald et al ²²	PRAM	2013	Ě	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
NA 2010 All authors' traty, 263 65.2±12.2 30(±17) STEMI in patients angiographically angiographically angiographically in different vessels Ywo arms: (1) staged arrey, (2) PC1 to noncuprit arrey, (2) PC1 to angiographically in different vessels No further arrey, (2) PC1 to angiographically in different vessels >70% stencesis arrey, (2) PC1 to angiographically in different vessels HELPAMI 204 Authors' centers 69 65.3(±7.4) 12 STEMI with angiographically in different vessels Nonculprit artery arrey, (2) PC1 to angiographically in different vessels Nonculprit artery artery, (2) PC1 to angiographically in different vessels >70% stencesis angiographically in different vessels Nonculprit artery artery, (2) PC1 to angiographically in different vessels >70% stencesis angiographically in different vessels >70% stencesis artery, (2) PC1 to angiographically in different vessels >70% stencesis angiographically in different vessels >70% stencesis artery, (2) PC1 to angiographically in different vessels >70% stencesis artery, (2) PC1 to angiographically artery, (2) PC1 to artery, (2) PC1 to arter	Dambrink et al ²³		2010%	Netherlands	121	62 (±10)	e e	STEMI in patients undergoing primary PCI with at least 2 angiographically 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
HELP AMI 2004 Authors' centers 69 65.3 (±7.4) 12 STEMI with angiographically Nonculprit PCI Major vessel are in UK and are in UK and expose angiographically performed during according to (% not stated) traity traity expert angiographically performed during according to (% not stated) traity traity traity expert prior priore angioplasty traity traity traited traited priore priore traited traity traited severe stenosis primary PCI physician's but balloon traity traited severe stenosis primary PCI primary PCI angioplasty traity traited severe stenosis primary PCI primary PCI angioplasty trait traited trait trait procedure discretion based angioplasty trait trait trait trait trait trait trait trait	Politi et al ²⁴	۲ Z	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	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, renospitalization for acute coronary syndrome and repeated coronary revascularization	Contrast-induced nephropathy
vessel also vess	Di Mario et al ²⁵	HELP AMI	2004	Authors' centers are in UK and Italy	S W	65.3 (±7.4)	5	STEMI with angiographically severe stenosis in at least 2 major vessels	Nonculprit PCI performed during primary PCI procedure	Nonculprit PCI according to physician's discretion based on symptoms and ischemia testing	Major vessel (% not stated) but balloon angioplasty allowed in vessel allowed in vessel allowed in vessel allowed in vessel allow frain vessel also stented	Repeat revascularization	MAGE

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

Table 2. Risk of	Risk of Bias of Included Studies	Studies							
Author	Study Acronym	Year	Random Sequence Generation	Allocation Concealment	Blinding of Participants and Personnel	Blinding of Outcome Assessment	Incomplete Outcome Data	Selective Reporting	Other Bias
Mehta et al ^o	COMPLETE	2019	Low risk Computer- generated system	Low risk Computer- generated system	Unclear Not specified	Low risk Events adjudicated by independent committee	Low risk Low drop-out rate	Low risk Pre-specified outcomes reported	Low risk Partly industry- funded but these parties not involved in study design or management
Smits et al ¹⁷	Compare-Acute	2017	Low risk Opaque envelope system	Low risk Opaque envelope system	Unclear Not specified	Low risk Events adjudicated by independent committee	Low risk Low dropout rate	Low risk Prespecified outcomes reported	Low risk Partty industry funded but these parties not involved in study design or management
Hamza et al ¹⁸	NA	2016	Unclear Not specified	Unclear Not specified	Unclear Not specified	Unclear Not specified	Low risk Low dropout rate	High risk Not preregistered and protocol not published	Unclear Source of funding not stated
Zhang et al ¹⁹	NA	2015	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
Engstrøm et al ²⁰	DANAMI-3- PRIMULTI	2015	Low risk Centralized web- based system	Unclear Not specified	High risk Open-label study	Low risk Outcomes adjudicated by independent events committee	Low risk Low dropout rates	Low risk Prespecified outcomes reported	Low risk Funded by independent body
Gerschlick et al ^{10,21}	CVLPRIT	2015	Low risk Interactive voice-response program	Low risk Automated telephone randomisation	High risk Open label	Low risk Outcome adjudication by blinded clinicians	High risk Low dropout rates in both groups but low event rate	Low risk Prespecified outcomes reported	Low risk Funded by independent body
Wald et a ²²	PRAMI	2013	Low risk Computer generated	Unclear Not specified	High risk Open label for participants	Low risk Blinded adjudication	High risk Low dropout rates in both groups but low event rate	Low risk Prespecified outcomes reported	High risk Early termination (significant between groups difference in primary outcome)

J Am Heart Assoc. 2020;9:e015263. DOI: 10.1161/JAHA.119.015263

(Continued)

6

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

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					Relative risk	105% CI
	Events	Ν	Events	Ν	Weight (%)				Relative Har	
Risk of cardiovascular death										
CvLPRIT, 2019 [10]	2	150	7	146	5.1	F			0.28 [0).06, 1.32]
Complete, 2019 [9]	59	2016	64	2025	41.2		⊢æ -1		0.93 [0	0.65, 1.31]
Compare ACUTE, 2017 [17]	3	295	6	590	6.4		,		1.00 [0	0.25, 3.97]
Zhang, 2015 [19]	11	215	14	213	17			4	0.78 [0	0.36, 1.68]
DANAMI 3, 2015 [20]	5	313	9	314	9.8			•	0.56 [0	0.19, 1.64]
PRAMI, 2013 [22]	4	234	10	231	8.9		·		0.39 [0	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 =	5.40, df = 6, p	o for heterog	jeneity = 0.38;	l ² = 21.8%)		•		0.68 [0	0.47, 0.98]
									p for overall effe	ct = 0.037
							-i i	I,		
						0.04	0.2 1	5	25	
					Complet	o rovoco bo	attor - Polativo r	ick > Cult	prit–only revasc. bet	tor

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		Con							Rel	ative risk [95% CI]
	Events	Ν	Events	Ν	Weight (%)						
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 B 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			-	i		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						0.94 [0.47, 1.87]
PRAMI, 2013 [22]	7	234	20	231	5.2		H				0.35 [0.15, 0.80]
Dambrink, 2012 [23]	4	79	0	40	0.4						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	6.35, df = 9, p	o for heterog	eneity = 0.70;	l ² = 0.0%)				•			0.65 [0.54, 0.79]
										p for ov	verall effect < 0.001
						[1	i	1		
						0.04	0.2	1	5	25	
					Complet	e revasc. be	tter < Re	elative risk	> Culp	rit–only re	evasc. better

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	Act Events	ive N	Con Events	trol N	Weight (%)					Re	lative risk [95% CI]
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			0.91 [0.70, 1.19]
Compare ACUTE, 2017 [17]	4	295	10	590	3.2		-		-		0.80 [0.25, 2.53]
Hamza, 2016 [18]	1	50	4	50	0.9	-					0.25 [0.03, 2.16]
Zhang, 2015 [19]	13	215	15	213	8.2		ŀ				0.86 [0.42, 1.76]
DANAMI 3, 2015 [20]	15	313	11	314	7.2				-		1.37 [0.64, 2.93]
PRAMI, 2013 [22]	12	234	16	231	8		F				0.74 [0.36, 1.53]
Dambrink, 2012 [23]	2	79	0	40	0.5		·		•		2.56 [0.13, 52.14]
Politi, 2010 [24]	10	130	13	84	7			•			0.50 [0.23, 1.08]
Help-AMI, 2009 [25]	1	52	0	17	0.4	·					1.02 [0.04, 23.91]
RE Model for All Studies (Q = 6	6.34, df = 9, p	o for heterog	eneity = 0.71;	; I ² = 0.0%)				•			0.85 [0.69, 1.04]
										p for c	verall effect = 0.108
						[1	<u> </u>	1		
						0.04	0.2	1	5	25	
					Complet	te revasc. be	etter < Re	elative risk	> Culp	orit–onlv r	evasc. 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 Events	ive N	Con Events	trol N	Weight (%)					Rela	tive risk [95% Cl
Risk of unplanned revascula	risation										
CvLPRIT, 2019 [10]	8	150	16	146	7.7		<u>н</u>	•			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	-					0.17 [0.02, 1.33]
Zhang, 2015 [19]	27	215	62	213	13		H	н			0.43 [0.29, 0.65]
DANAMI 3, 2015 [20]	17	313	52	314	11.4		⊢-∎	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			, ⊢∎ ,			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 = 2	27.33, df = 9,	p for hetero	ogeneity = 0.00); I ² = 64.7	%)		•	•		n for ov	0.37 [0.28, 0.51]
											erall effect < 0.00*
						0.04	0.2	1	5	25	
					Complet	e revasc. be					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 Events		Con	trol N	Weight (%)			Relative risk [95% Cl
	Events	Ν	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		F	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	4.71, df = 6, j	p for heterog	eneity = 0.58;	l ² = 3.9%)			*	1.12 [0.78, 1.62
								p for overall effect = 0.54
						–	тіт	
						0.04	0.2 1 5	25
					Comple	a ravaec he	etter < Relative risk > Cu	Inrit_only revised 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	Active Events	N	Con Events	trol N	Weight (%)					Rela	tive risk [95% Cl
Immediate revascularisation	– risk of CV de	eath									
Politi-Immediate, 2010 [24]	4	65	10	84	8.9		i	• • •			0.52 [0.17, 1.57
PRAMI, 2013 [22]	4	234	10	231	8.5						0.39 [0.13, 1.24
Compare ACUTE, 2017 [17]	3	295	6	590	6.1						1.00 [0.25, 3.97
CvLPRIT, 2019 [10]	2	150	7	146	4.9						0.28 [0.06, 1.32
Random effects model for imm $Q = 1.68$, df = 3, p for heteroge)					-			0.49 [0.26, 0.93
Staged revascularisation – r	isk of CV death	r									
Politi-Staged, 2010 [24]	2	65	10	84	5.3	-	-				0.26 [0.06, 1.14
DANAMI 3, 2015 [20]	5	313	9	314	9.3			• • •			0.56 [0.19, 1.64
Zhang, 2015 [19]	11	215	14	213	16.3		F				0.78 [0.36, 1.68
Complete, 2019 [9]	59	2016	64	2025	40.8			H B H			0.93 [0.65, 1.31
Random effects model for stag $Q = 3.30$, df = 3, p for heteroge								•			0.82 [0.60, 1.12
Evidence of an immediate vers	sus staged mode	erating eff	ect: p = 0.15								
						0.04	0.2	1	5	25	
					Complet	e revasc. be	tter < R	elative risk	> Culpr	it–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.

ARTICLE INFORMATION

Received November 11, 2019; accepted May 4, 2020.

Affiliations

From the Columbia University Medical Center/New York-Presbyterian Hospital, New York, NY (Y.A., M.P., Z.A., M.A.P., J.W.M., M.B.L., D.K.); National Heart and Lung Institute, Imperial College London, London, United Kingdom (Y.A., J.P.H., A.A., H.S., C.M.C., T.W., M.S.-S., R.A.-L., S.S., D.F.); Cardiovascular Research Foundation, New York, NY (G.W.S.); The Zena and Michael A. Wiener Cardiovascular Institute, Icahn School of Medicine at Mount Sinai, New York, NY (G.W.S.).

Sources of Funding

None.

Disclosures

Dr Cook and Dr Al-Lamee have conducted teaching sessions supported by Volcano Corp. Dr Sen has attended and conducted teaching sessions supported by Volcano Corp, St Jude Medical, Medtronic, Pfizer, and AstraZeneca; has received research grant support from Philips, AstraZeneca, Medtronic, and Pfizer; and has received speaking honoraria from Pfizer and Volcano-Philips. Manish A. Parikh: Speakers bureau—Medtronic, Boston Scientific, Abbott Vascular, CSI; advisory board—Philips, Abbott Vascular, Medtronic. A. Kirtane: Institutional funding to Columbia University and/or Cardiovascular Research Foundation from Medtronic, Boston Scientific, Abbott Vascular, Abiomed, CSI, CathWorks, Siemens, Philips, ReCor Medical; personal: conference honoraria and travel/meal reimbursements only. Ziad A. Ali: institutional research grants to Columbia University from St. Jude Medical, and Cardiovascular Systems Inc. Consultant to St Jude Medical, ACIST. Dimitri Karmpaliotis: Speaker's bureau - Abbott Vascular, Boston Scientific, Medtronic; consultant - Vascular Solutions. The remaining authors have no disclosures to report.

Supplementary Materials

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

REFERENCES

- Keeley EC, Boura JA, Grines CL. Primary angioplasty versus intravenous thrombolytic therapy for acute myocardial infarction: a quantitative review of 23 randomised trials. *Lancet.* 2003;361:13–20.
- Rasoul S, Ottervanger JP, de Boer M-J, Dambrink J-HE, Hoorntje JCA, Marcel Gosselink AT, Zijlstra F, Suryapranata H, van 't Hof AWJ; Zwolle Myocardial Infarction Study Group. Predictors of 30-day and 1-year mortality after primary percutaneous coronary intervention for STelevation myocardial infarction. *Coron Artery Dis.* 2009;20:415–421.
- Sorajja P, Gersh BJ, Cox DA, McLaughlin MG, Zimetbaum P, Costantini C, Stuckey T, Tcheng JE, Mehran R, Lansky AJ, et al. Impact of multivessel disease on reperfusion success and clinical outcomes in patients undergoing primary percutaneous coronary intervention for acute myocardial infarction. *Eur Heart J.* 2007;28:1709–1716.

- 4. Authors/Task Force members, Windecker S, Kolh P, Alfonso F, Collet J-P, Cremer J, Falk V, Filippatos G, Hamm C, Head SJ, Jüni P, et al. 2014 ESC/EACTS guidelines on myocardial revascularization: the Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS). Developed with the special contribution of the European Association of Percutaneous Cardiovascular Interventions (EAPCI). *Eur Heart J*. 2014;35:2541–2619.
- O'Gara PT, Kushner FG, Ascheim DD, Casey DE, Chung MK, de Lemos JA, Ettinger SM, Fang JC, Fesmire FM, Franklin BA, et al.; American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2013;127:e362–e425.
- Ahmad Y, Cook C, Shun-Shin M, Balu A, Keene D, Nijjer S, Petraco R, Baker CS, Malik IS, Bellamy MF, et al. Resolving the paradox of randomised controlled trials and observational studies comparing multivessel angioplasty and culprit only angioplasty at the time of STEMI. *Int J Cardiol*. 2016;222:1–8.
- Ibanez B, James S, Agewall S, Antunes MJ, Bucciarelli-Ducci C, Bueno H, Caforio ALP, Crea F, Goudevenos JA, Halvorsen S, et al.; ESC Scientific Document Group. 2017 ESC guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: the Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). *Eur Heart J*. 2018;39:119–177.
- Levine GN, Bates ER, Blankenship JC, Bailey SR, Bittl JA, Cercek B, Chambers CE, Ellis SG, Guyton RA, Hollenberg SM, et al. 2015 ACC/ AHA/SCAI focused update on primary percutaneous coronary intervention for patients with ST-elevation myocardial infarction: an update of the 2011 ACCF/AHA/SCAI guideline for percutaneous coronary intervention and the 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction. *Circulation*. 2016;133:1135–1147.
- Mehta SR, Wood DA, Storey RF, Mehran R, Bainey KR, Nguyen H, Meeks B, Di Pasquale G, López-Sendón J, Faxon DP, et al. Complete revascularization with multivessel PCI for myocardial infarction. N Engl J Med. 2019;381:1411–1421.
- Gershlick AH, Banning AS, Parker E, Wang D, Budgeon CA, Kelly DJ, Kane PO, Dalby M, Hetherington SL, McCann GP, et al. Long-term follow-up of complete versus lesion-only revascularization in STEMI and multivessel disease: the CvLPRIT Trial. J Am Coll Cardiol. 2019;74:3083–3094.
- Moher D, Liberati A, Tetzlaff J, Altman DG; PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Ann Intern Med.* 2009;151:264–269.
- Higgins JPT, Altman DG, Gøtzsche PC, Jüni P, Moher D, Oxman AD, Savovic J, Schulz KF, Weeks L, Sterne JAC; Cochrane Bias Methods Group, Cochrane Statistical Methods Group. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJ*. 2011;343:d5928.
- Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA (editors). Cochrane Handbook for Systematic Reviews of Interventions version 6.0 (updated July 2019). Cochrane, 2019. Available at: www.training.cochrane.org/handbook.
- Higgins JPT, Thompson SG. Quantifying heterogeneity in a metaanalysis. Stat Med. 2002;21:1539–1558.
- R Core Team. R: A Language and Environment for Statistical Computing [Internet]. Vienna, Austria: R Foundation for Statistical Computing; 2016. Available at: https://www.R-project.org/. Accessed January 1, 2019.
- Viechtbauer, W. Conducting meta-analyses in R with the metafor package. *Journal of Statistical Software*. 2010;36:1–48. DOI: http://dx.doi. org/10.18637/jss.v036.i03.
- Smits PC, Abdel-Wahab M, Neumann F-J, Boxma-de Klerk BM, Lunde K, Schotborgh CE, Piroth Z, Horak D, Wlodarczak A, Ong PJ, et al. Fractional flow reserve-guided multivessel angioplasty in myocardial infarction. *N Engl J Med.* 2017;376:1234–1244.
- Hamza M, Mahmoud AN, Elgendy IY. A randomized trial of complete versus culprit-only revascularization during primary percutaneous coronary intervention in diabetic patients with acute ST elevation myocardial infarction and multi vessel disease: complete versus culprit revascularization in STEMI diabetic patients. *J Interv Cardiol.* 2016;29:241–247.
- Zhang J, Wang Q, Yang H, Ma L, Fu X, Hou W, Feng J, Liu X. [Evaluation of different revascularization strategies for patients with acute myocardial infarction with lesions of multiple coronary arteries after primary

percutaneous coronary intervention and its economic evaluation]. Zhonghua Wei Zhong Bing Ji Jiu Yi Xue. 2015;27:169–174.

- Engstrøm T, Kelbæk H, Helqvist S, Høfsten DE, Kløvgaard L, Holmvang L, Jørgensen E, Pedersen F, Saunamäki K, Clemmensen P, et al. Complete revascularisation versus treatment of the culprit lesion only in patients with ST-segment elevation myocardial infarction and multivessel disease (DANAMI-3—PRIMULTI): an open-label, randomised controlled trial. *Lancet*. 2015;386:665–671.
- Gershlick AH, Khan JN, Kelly DJ, Greenwood JP, Sasikaran T, Curzen N, Blackman DJ, Dalby M, Fairbrother KL, Banya W, et al. Randomized trial of complete versus lesion-only revascularization in patients undergoing primary percutaneous coronary intervention for STEMI and multivessel disease. J Am Coll Cardiol. 2015;65:963–972.
- Wald DS, Morris JK, Wald NJ, Chase AJ, Edwards RJ, Hughes LO, Berry C, Oldroyd KG. Randomized trial of preventive angioplasty in myocardial infarction. *N Engl J Med*. 2013;369:1115–1123.
- Dambrink J-H, Debrauwere J, van 't Hof A, Ottervanger J-P, Gosselink AT, Hoorntje J, de Boer M-J, Suryapranata H. Non-culprit lesions detected during primary PCI: treat invasively or follow the guidelines? *EuroIntervention*. 2010;5:968–975.

- Politi L, Sgura F, Rossi R, Monopoli D, Guerri E, Leuzzi C, Bursi F, Sangiorgi GM, Modena MG. A randomised trial of target-vessel versus multi-vessel revascularisation in ST-elevation myocardial infarction: major adverse cardiac events during long-term follow-up. *Heart*. 2010;96:662–667.
- 25. Di Mario C, Mara S, Flavio A, Imad S, Antonio M, Anna P, Emanuela P, Stefano DS, Angelo R, Stefania C, et al. Single vs multivessel treatment during primary angioplasty: results of the multicentre randomised HEpacoat[™] for cuLPrit or multivessel stenting for Acute Myocardial Infarction (HELP AMI) Study. *Int J Cardiovasc Intervent*. 2004;6:128–133.
- Wood DA, Cairns JA, Wang J, Mehran R, Storey RF, Nguyen H, Meeks B, Kunadian V, Tanguay JF, Kim HH, et al. Timing of staged nonculprit artery revascularization in patients with ST-segment elevation myocardial infarction: COMPLETE trial. J Am Coll Cardiol. 2019;74:2713–2723.
- Ahmad Y, Howard JP, Arnold A, Shin MS, Cook C, Petraco R, Demir O, Williams L, Iglesias JF, Sutaria N, et al. Patent foramen ovale closure vs. medical therapy for cryptogenic stroke: a meta-analysis of randomized controlled trials. *Eur Heart J*. 2018;39:1638–1649.

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.

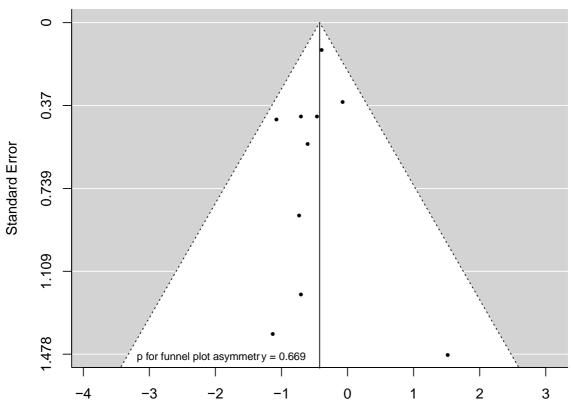
Table S1. Endpoint definitions.

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 et	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 et	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 <i>et</i>	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		Con	trol						Relative risk [95%	% CII
Study and Tear	Events	N	Events	N	Weight (%)					Relative risk [33]	/a Cij
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, 2	25.36]
Help-AMI, 2009	1	52	1	17	0.7	-			1	0.33 [0.02,	4.95]
RE Model for All Studies (Q	= 3.01, df = 6, j	p for heterog	geneity = 0.81	; I ² = 0.0%))		•	•		0.58 [0.46,	0.73]
										p for overall effect < 0	0.001
						Γ	1	i	1		
						0.04	0.2	1	5	25	

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

Study and Year	Act	ive	Con	trol		Relative risk [95% CI]
Study and Tear	Events	Ν	Events	Ν	Weight (%)	
Risk of contrast induced ne	ephropathy					
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	
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	o for heterog	eneity = 0.53;	; I 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	Activ Events	ve N	Cont Events	rol N	Weight (%)				Relative risk [95% Cl
Immediate revascularisati	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	⊢			0.37 [0.08, 1.72
PRAMI, 2013	7	234	20	231	5.2		·		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		<u> </u>		0.50 [0.22, 1.13
CvLPRIT, 2019	6	150	12	146	4		H		0.49 [0.19, 1.26
Random effects model for in	nmediate studies	; (p < 0.001)				-		0.43 [0.27, 0.68
Q = 0.55, df = 5, p for hetero	geneity = 0.99;	$l^2 = 0.0\%$							
Staged revascularisation -	- risk of MI								
Politi-Staged, 2010	4	65	7	84	2.6		⊢	-	0.74 [0.23, 2.4
Dambrink, 2012	4	79	0	40	0.4				4.61 [0.25, 83.6
DANAMI 3, 2015	15	313	16	314	7.8		H		0.94 [0.47, 1.8]
Zhang, 2015	9	215	14	213	5.5		H		0.64 [0.28, 1.44
Complete, 2019	109	2016	160	2025	66.2		HEH		0.68 [0.54, 0.8]
Random effects model for in	nmediate studies	(p = 0.001)				•		0.71 [0.58, 0.8
Q = 2.41, df = 4, p for hetero	geneity = 0.66;	$l^2 = 0.0\%$							
Evidence of an immediate v	ersus staged mo	derating ef	fect: p = 0.05						
									1
								_	-
						0.04	0.2 1	5 2	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 Events	tive N	Cor Events	ntrol N	Weight (%)			Rela	ative risk [95% CI]
Immediate revascularisati	on – risk of ur	planned re	vascularisati	on					
Help-AMI, 2009	9	52	6	17	6.7		⊢ i		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		⊢∎→		0.35 [0.22, 0.57]
CvLPRIT, 2019	8	150	16	146	7.2		⊢ ∎ 1		0.49 [0.21, 1.10]
Random effects model for ir	nmediate studi	es (p < 0.001)				•		0.36 [0.27, 0.48]
Q = 1.96, df = 5, p for heter	ogeneity = 0.85	$5; I^2 = 0.0\%$							
Politi-Staged, 2010	8	65	28	84	8.3		⊢ ∎		0.37 [0.18, 0.76
-	8	65	28	84	8.3		⊢ ∎−−1		
Dambrink, 2012	27	79	15	40	11.1		⊢ ∎-1		0.91 [0.55, 1.51]
DANAMI 3, 2015	17	313	52	314	10.8				0.33 [0.19, 0.55]
	27	215	62	213	12.4				
Zhang, 2015 Complete, 2019	29	2016	160	2025	12.7		⊢∎⊣		
Complete, 2019				2025	12.7		₩		0.18 [0.12, 0.27]
Complete, 2019 Random effects model for ir	nmediate studi	es (p < 0.001)	2025	12.7		•		0.18 [0.12, 0.27]
Complete, 2019 Random effects model for ir	nmediate studi	es (p < 0.001)	2025	12.7		•		0.18 [0.12, 0.27]
Complete, 2019 Random effects model for in Q = 25.63, df = 4, p for hete	nmediate studi rogeneity = 0.0	es (p < 0.001 00; I ² = 82.8%)		12.7		*		0.18 [0.12, 0.27]
	nmediate studi rogeneity = 0.0	es (p < 0.001 00; I ² = 82.8%)		12.7		₩		0.18 [0.12, 0.27
Complete, 2019 Random effects model for ir Q = 25.63, df = 4, p for hete	nmediate studi rogeneity = 0.0	es (p < 0.001 00; I ² = 82.8%)		12.7		₩		0.18 [0.12, 0.27]
Complete, 2019 Random effects model for in Q = 25.63, df = 4, p for hete	nmediate studi rogeneity = 0.0	es (p < 0.001 00; I ² = 82.8%)		12.7		₩		0.43 [0.29, 0.65] 0.18 [0.12, 0.27] 0.38 [0.23, 0.65]

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

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

Study and Year	Acti Events	ve N	Con Events	trol N	Weight (%)					Rela	ative risk [95% CI]
FFR-guided revascularisa	tion – risk of C	V 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	FR-guided studi	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			;			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 ar	ngiography-guid	led studies	(p = 0.055)				-	-			0.64 [0.40, 1.01]
Q = 5.93, df = 4, p for hetero	geneity = 0.20;	l ² = 37.6%									
Evidence of an FFR-guided	versus angiogra	aphy-guide	d moderating	effect: p =	0.73						
						[i			
						0.04	0.2	1	5	25	

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

Study and Year	Acti Events	ve N	Cor Events	ntrol N	Weight (%)					Rel	ative risk [95% Cl
FFR-guided revascularisa	tion – risk of d	eath									
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 FI Q = 0.83, df = 2, p for hetero Angiograpgy-guided reva	geneity = 0.66;	$l^2 = 0.0\%$						-			1.20 [0.65, 2.24
Help-AMI, 2009	scularisation -			47							1.02 [0.04, 23.91
Politi, 2010	1	52	0	17	0.4						0.50 [0.23, 1.08
PRAMI, 2013	10 12	130 234	13 16	84 231	7 8						0.74 [0.36, 1.53
Zhang, 2015	12	234	15	231	° 8.2						0.86 [0.42, 1.76
Hamza, 2016	1	50	4	50	0.2	_					0.25 [0.03, 2.16
Complete, 2019	96	2016	106	2025	58		_				0.91 [0.70, 1.19
CvLPRIT, 2019	9	150	15	146	6.7		⊢				0.58 [0.26, 1.29
Random effects model for ar $Q = 4.13$, df = 6, p for hetero	geneity = 0.66;	l ² = 5.6%						•			0.79 [0.62, 1.01
Evidence of an FFR-guided	versus angiogra	aphy-guide	d moderating	effect: p =	0.54						
							1	İ			
						0.04	0.2	1	5	25	

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

Study and Year	Activ Events	/e N	Cor Events	ntrol N	Weight (%)					Rela	ative risk [95% Cl
FFR-guided revascularisa	tion – risk of MI	,									
Dambrink, 2012	4	79	0	40	0.4				-	•	4.61 [0.25, 83.61
DANAMI 3, 2015	15	313	16	314	7.9						0.94 [0.47, 1.87
Compare ACUTE, 2017	7	295	28	590	5.6						0.50 [0.22, 1.13
Random effects model for FI Q = 2.87, df = 2, p for hetero Angiograpgy-guided reva	ogeneity = 0.24; I	² = 16.0%	99)					-			0.77 [0.42, 1.41
Help-AMI, 2009	1	52	1	17	0.5	-	-				0.33 [0.02, 4.95
Politi, 2010	6	130	7	84	3.3						0.55 [0.19, 1.59
PRAMI, 2013	7	234	20	231	5.2		·				0.35 [0.15, 0.80
Zhang, 2015	9	215	14	213	5.6		· –				0.64 [0.28, 1.44
Hamza, 2016	1	50	2	50	0.7						0.50 [0.05, 5.34
Complete, 2019	109	2016	160	2025	66.8			н			0.68 [0.54, 0.87
CvLPRIT, 2019	6	150	12	146	4.1						0.49 [0.19, 1.26
Random effects model for ar $Q = 3.03$, df = 6, p for hetero			(p = 0.000)					•			0.62 [0.48, 0.79
Evidence of an FFR-guided	versus angiogra	iphy-guide	d moderating	effect: p =	0.68						
						l – – – – – – – – – – – – – – – – – – –	1	i	1		
						0.04	0.2	1	5	25	

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

FFR-guided revascularisation -	risk of u	nnlannod r							tive risk [95% C
Dambrink 2012		npianneu re	e vasculariza	tion					
Bambring 2012	27	79	15	40	11.7				0.91 [0.55, 1.5 ⁻
DANAMI 3, 2015	17	313	52	314	11.4				0.33 [0.19, 0.5
Compare ACUTE, 2017	18	295	103	590	12				0.35 [0.22, 0.5]
Random effects model for FFR-gu			23)				-		0.47 [0.25, 0.90
Q = 9.90, df = 2, p for heterogenei	ity = 0.01;	l ² = 79.9%							
Angiograpgy–guided revascula	risation –	risk of unp	lanned re va	sc					
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		H -		0.43 [0.29, 0.6
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, 0.2]
CvLPRIT, 2019	8	150	16	146	7.7		⊢		0.49 [0.21, 1.10
Random effects model for angiogr	aphy-quid	ded studies (p = 0.000)				-		0.33 [0.24, 0.46
							-		0.00 [0.2 1, 0.1
CvLPRIT, 2019 Random effects model for angiogr Q = 12.34, df = 6, p for heterogene	8 aphy-guid	150 ded studies (16 p = 0.000)				•		0.49

Figure S10. Freedom from cardiovascular death.

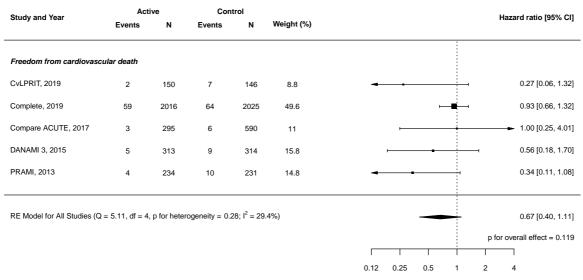


Figure S11. Freedom from myocardial infarction.

Study and Year	Act	ive	Con	trol			Hazard ratio [95% CI]
Study and Teal	Events	Ν	Events	N	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	F	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	%)	-	0.63 [0.49, 0.81]
						р	for overall effect < 0.001
						0.12 0.25 0.5 1 2	4

Figure S12. Freedom from all-cause death.

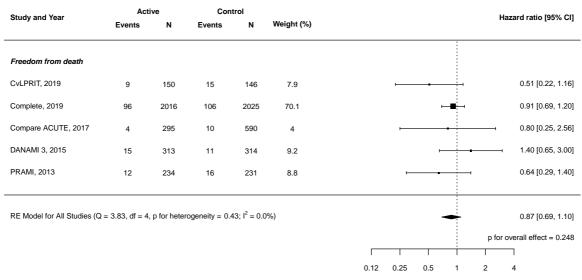


Figure S13. Freedom from unplanned revascularization.

Study and Year	Act	ive	Con				Hazard ratio [95% CI]
-	Events	N	Events	N	Weight (%)		
Freedom from unplanned	revascularisa	ation					
CvLPRIT, 2019	8	150	16	146	11	۱ <u>ــــ</u>	0.46 [0.20, 1.08]
Complete, 2019	29	2016	160	2025	29.8	← ∎	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	F	0.30 [0.16, 0.56]
RE Model for All Studies (Q	= 6.77, df = 4	, p for heter	ogeneity = 0.	15; I ² = 42.	.1%)	-	0.28 [0.20, 0.38]
							p for overall effect < 0.001
						0.12 0.25 0.5	2 4

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

Study and Year	Active		Control						Relative risk [95% CI]
	Events	N	Events	N	Weight (%)				
Risk of cardiovascular dea	nth								
CvLPRIT, 2019	2	150	7	146	3.1	·			0.28 [0.06, 1.32]
Complete, 2019	59	2016	64	2025	60.8		H H -1		0.93 [0.65, 1.31]
Compare ACUTE, 2017	3	295	6	590	3.9		·		1.00 [0.25, 3.97]
Zhang, 2015	11	215	14	213	12.6		H		0.78 [0.36, 1.68]
DANAMI 3, 2015	5	313	9	314	6.3	٠			0.56 [0.19, 1.64]
PRAMI, 2013	4	234	10	231	5.6	<u> </u>			0.39 [0.13, 1.24]
Politi, 2010	6	130	10	84	7.8	F			0.39 [0.15, 1.03]
FE Model for All Studies (Q =	= 6.40, df = 6, p	o for heterog	eneity = 0.38;	l ² = 6.3%)			•		0.76 [0.58, 0.99]
									p for overall effect = 0.043
							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 Year	Active		Control							Relative risk [95% CI]
	Events	N	Events	N	Weight (%)					Neialive Hak [35 / 01]
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 II 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		۲			0.94 [0.47, 1.87]
PRAMI, 2013	7	234	20	231	5.2		⊢			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]
FE Model for All Studies (Q =	= 6.35, df = 9, p	for heterog	eneity = 0.70;	l ² = 0.0%)				•		0.65 [0.54, 0.79]
										p for overall effect < 0.001
						Γ	1	1	Т	
						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							Po	lative risk [95% CI]
	Events	N	Events	N	Weight (%)					Re	ative fisk [35 /6 Gi]
Risk of death											
CvLPRIT, 2019	9	150	15	146	6.7		—	<u> </u>			0.58 [0.26, 1.29]
Complete, 2019	96	2016	106	2025	58			н			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	-		<u> </u>			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	7.2			·	-		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	—		-		i	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
								-i	1		
						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	Act	ive	Con	trol						Pole	tive risk [95% CI]
Study and Tear	Events	N	Events	Ν	Weight (%)					Neid	luve lisk [95 % Cij
Risk of unplanned revasc	ularisation										
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		⊢∎→				0.35 [0.22, 0.57]
Hamza, 2016	1	50	6	50	0.7	-	-	<u> </u>			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		F	-			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); I ² = 67.1	%)		•				0.36 [0.30, 0.43]
										p for ov	erall effect < 0.001
							1	1	Ι		
						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	Act	ve	Con	trol						Rel	ative risk [95% CI]
	Events	N	Events	N	Weight (%)						
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	-					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		F		-		2.53 [0.31, 20.95]
FE Model for All Studies (Q =	= 4.71, df = 6, p	for heterog	eneity = 0.58;	l ² = 0.0%)				•			1.16 [0.83, 1.60]
										p for o	verall effect = 0.387
							1	i	I		
						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	Act	ive	Con	trol				Relative risk [95% CI]
Study and real	Events	N	Events	N	Weight (%)			Relative flak [35 % OI]
Risk of cardiovascular deat	h							
CvLPRIT, 2019	2	150	7	146	7.5			0.28 [0.06, 1.32]
Complete, 2019	59	2016	64	2025	41.4	н	-	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 =	6.39, df = 5, p	p for heterog	eneity = 0.27;	l ² = 31.4%	b)	-		0.62 [0.39, 0.99]
								p for overall effect = 0.044
							i 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	Act	ive	Con	trol						Po	lative risk [95% CI]
Study and Tear	Events	N	Events	N	Weight (%)					Ne	lative lisk [95 /8 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			⊦∎⊦			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						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	o for heterog	eneity = 0.42	; I ² = 0.0%)				•			0.66 [0.54, 0.80]
										p for c	verall effect < 0.001
								1	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	Act	ive	Con	trol						Pol	ative risk [95% CI]
olddy and real	Events	N	Events	N	Weight (%)					iter	alive hak [35 / 6i]
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		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	7.7			•			0.50 [0.23, 1.08]
RE Model for All Studies (Q	= 5.09, df = 6, p	o for heterog	eneity = 0.53	; l ² = 0.0%)				•			0.85 [0.69, 1.06]
										p for o	verall effect = 0.150
						Γ	1	i	1		
						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	Act	ive	Con	trol						Polativ	e risk [95% Cl]
Study and Teal	Events	N	Events	N	Weight (%)					Relativ	e lisk [95 % Cij
Risk of unplanned revascu	larisation										
CvLPRIT, 2019	8	150	16	146	10.6		-			C	0.49 [0.21, 1.10]
Complete, 2019	29	2016	160	2025	16.6		⊢∎⊣			C	0.18 [0.12, 0.27]
Compare ACUTE, 2017	18	295	103	590	15.2					C	0.35 [0.22, 0.57]
DANAMI 3, 2015	17	313	52	314	14.6					C	0.33 [0.19, 0.55]
PRAMI, 2013	16	234	46	231	14.4		⊢∎	•		C	0.34 [0.20, 0.59]
Dambrink, 2012	27	79	15	40	14.9					C	0.91 [0.55, 1.51]
Politi, 2010	14	130	28	84	13.8		⊢∎	•		C	0.32 [0.18, 0.58]
RE Model for All Studies (Q	= 25.33, df = 6,	p for hetero	geneity = 0.0	0; l ² = 73.5	%)		•			C	0.37 [0.25, 0.54]
										p for overa	II effect < 0.001
							1	i	1		
						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.

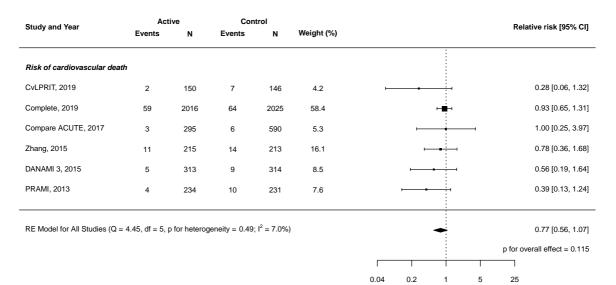


Figure S24. Sensitivity analysis excluding trials with low use of drug-eluting stents for the effect of complete revascularization on risk of myocardial infarction.

Study and Year	Acti	ve	Con	trol					Relative risk [95% CI]
Study and Tear	Events	N	Events	Ν	Weight (%)				Relative risk [55 % Ci]
Risk of MI									
CvLPRIT, 2019	6	150	12	146	4.3			4	0.49 [0.19, 1.26]
Complete, 2019	109	2016	160	2025	69.8		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	for heterog	eneity = 0.64;	; I ² = 0.0%)			•		0.65 [0.53, 0.79] p for overall effect < 0.001
						-	ı 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	Act	ve	Con	trol						Relative risk [95%	4 CII
Study and Teal	Events	Ν	Events	Ν	Weight (%)					Relative hak [337	0.01
Risk of death											
CvLPRIT, 2019	9	150	15	146	7.2					0.58 [0.26, 1	1.29]
Complete, 2019	96	2016	106	2025	63			H		0.91 [0.70, 1	1.19]
Compare ACUTE, 2017	4	295	10	590	3.4			-	-	0.80 [0.25, 2	2.53]
Hamza, 2016	1	50	4	50	1	-				0.25 [0.03, 2	2.16]
Zhang, 2015	13	215	15	213	8.8					0.86 [0.42, 1	1.76]
DANAMI 3, 2015	15	313	11	314	7.9				-	1.37 [0.64, 2	2.93]
PRAMI, 2013	12	234	16	231	8.7		F			0.74 [0.36, 1	1.53]
RE Model for All Studies (Q =	= 3.92, df = 6, p	for heterog	jeneity = 0.69;	; l ² = 0.0%)				•		0.87 [0.71, 1	-
										p for overall effect = 0	0.217
						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 Year	Act	ive	Con	trol						Polat	ive risk [95% CI]
	Events	N	Events	Ν	Weight (%)					Neiat	ive nak [35 /6 OI]
Risk of unplanned revascu	Ilarisation										
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						0.33 [0.19, 0.55]
PRAMI, 2013	16	234	46	231	15.5		⊢-∎ 1				0.34 [0.20, 0.59]
RE Model for All Studies (Q	= 11.55, df = 6,	p for hetero	geneity = 0.07	7; l ² = 48.5	%)		•				0.32 [0.24, 0.43]
										p for ove	erall effect < 0.001
						[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	Act	ive	Con	trol						Relative risk [95% CI]
Study and Tear	Events	Ν	Events	Ν	Weight (%)					Relative fisk [35 % Ci]
Risk of bleeding										
CvLPRIT, 2019	4	150	7	146	11.8		·			0.56 [0.17, 1.86]
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		F			1.15 [0.39, 3.38]
RE Model for All Studies (Q =	= 4.17, df = 5, p	o for heterog	eneity = 0.53;	l ² = 12.6%	5)			-		1.03 [0.67, 1.60]
										p for overall effect = 0.885
							Ι	i	1	
						0.04	0.2	1	5	25

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

Study and Year	Act	ive	Con	trol					Relative risk [95% CI]
Study and Tear	Events	N	Events	Ν	Weight (%)				Relative fisk [35 % CI]
Risk of CV death									
CvLPRIT, 2019	2	150	7	146	6.1				0.28 [0.06, 1.32]
Complete, 2019	59	2016	64	2025	39.9		H B -1		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	—			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	o for heterog	eneity = 0.28	l ² = 30.4%	»)		-		0.64 [0.43, 0.96]
									p for overall effect = 0.032
							i		
						0.04 0.2	1	5	25

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

Acti	ve	Con	trol						Relative risk [95% CI]
Events	N	Events	N	Weight (%)					
2	150	7	146	7.8					0.28 [0.06, 1.32]
3	295	6	590	9.9		—			1.00 [0.25, 3.97]
11	215	14	213	32		-			0.78 [0.36, 1.68]
5	313	9	314	16.1		·	•		0.56 [0.19, 1.64]
4	234	10	231	14.4					0.39 [0.13, 1.24]
6	130	10	84	19.8		⊢			0.39 [0.15, 1.03]
3.07, df = 5, p	o for heterog	geneity = 0.69;	l ² = 0.0%))			•		0.55 [0.36, 0.85]
									p for overall effect = 0.007
					0.04	0.2	1	5	25
	Events 2 3 11 5 4 6	2 150 3 295 11 215 5 313 4 234 6 130	Events N Events 2 150 7 3 295 6 11 215 14 5 313 9 4 234 10 6 130 10	Events N Events N 2 150 7 146 3 295 6 590 11 215 14 213 5 313 9 314 4 234 10 231 6 130 10 84	Events N Events N Weight (%) 2 150 7 146 7.8 3 295 6 590 9.9 11 215 14 213 32 5 313 9 314 16.1 4 234 10 231 14.4	Events N Events N Weight (%) 2 150 7 146 7.8	Events N Events N Weight (%) 2 150 7 146 7.8	Events N Events N Weight (%) 2 150 7 146 7.8 3 295 6 590 9.9 11 215 14 213 32 5 313 9 314 16.1 4 234 10 231 14.4 6 130 10 84 19.8	Events N Events N Weight (%) 2 150 7 146 7.8 3 295 6 590 9.9 11 215 14 213 32 5 313 9 314 16.1 4 234 10 231 14.4 6 130 10 84 19.8

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

Study and Year	Act	ive	Con	trol					Relative risk [95% CI]
Study and Tear	Events	Ν	Events	Ν	Weight (%)				Relative lisk [35% of
Risk of CV death									
RISK OF CV dealin									
Complete, 2019	59	2016	64	2025	48.2		H B H		0.93 [0.65, 1.31]
Compare ACUTE, 2017	3	295	6	590	6	H	-		1.00 [0.25, 3.97]
Zhang, 2015	11	215	14	213	16.9	Ē			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 =	4.76, df = 5, p	o for heterog	eneity = 0.45;	; l ² = 16.3%	6)		•		0.73 [0.51, 1.03]
									p for overall effect = 0.073
							i	1	
						0.04 0.2	1	5	25

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

Study and Year	Act	ive	Con	trol				Relative risk [95% CI]
oludy and real	Events	N	Events	Ν	Weight (%)			Kelative fisk [35% OI]
Risk of CV death								
CvLPRIT, 2019	2	150	7	146	6.1	·		0.28 [0.06, 1.32]
Complete, 2019	59	2016	64	2025	43.4	+ -		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 =	= 6.08, df = 5, p	o for heterog	eneity = 0.30	l ² = 25.9%	b)	-		0.68 [0.46, 1.02]
								p for overall effect = 0.062
							I	
						0.04 0.2 1	5	25

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

Study and Year	Act	ive	Con	trol					Relative risk [95% CI]
Study and Tear	Events	N	Events	Ν	Weight (%)				Kelative fisk [35% OI]
Risk of CV death									
CvLPRIT, 2019	2	150	7	146	4.2				0.28 [0.06, 1.32]
Complete, 2019	59	2016	64	2025	58.4		H B -1		0.93 [0.65, 1.31]
Compare ACUTE, 2017	3	295	6	590	5.3	Ē			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	ı ——			0.39 [0.13, 1.24]
RE Model for All Studies (Q =	= 4.45, df = 5, j	o for heterog	eneity = 0.49	; I ² = 7.0%))		•		0.77 [0.56, 1.07]
									p for overall effect = 0.115
							i	I	
						0.04 0.2	1	5	25

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

Study and Year	Act	ive	Con	trol						Relative risk [95% CI]
	Events	N	Events	Ν	Weight (%)					Kelative fisk [35% OI]
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 -		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 =	5.09, df = 5, j	o for heterog	eneity = 0.40	; I ² = 16.0%	6)			•		0.73 [0.51, 1.04]
										p for overall effect = 0.084
						Γ	I	İ	Ι	
						0.04	0.2	1	5	25

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

Study and Year	Act	ive	Con	trol			Relative risk [95% CI]
Study and Tear	Events	N	Events	Ν	Weight (%)		Relative flak [35 % OI]
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	H	0.93 [0.65, 1.31]
Compare ACUTE, 2017	3	295	6	590	9.2	▶ <u> </u>	1.00 [0.25, 3.97]
DANAMI 3, 2015	5	313	9	314	13.6	⊧ <u></u> i	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 =	= 6.39, df = 5, p	o for heterog	geneity = 0.27	; I ² = 31.4%	6)	-	0.62 [0.39, 0.99]
							p for overall effect = 0.044
						гтіт	
						0.04 0.2 1 5	25

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

Relative risk [95% Cl]					trol	Cor	ive	Act	Study and Year
Kelative fisk [55% Cij				Weight (%)	N	Events	N	Events	Study and Teal
									Risk of MI
0.49 [0.19, 1.26]	-			4.3	146	12	150	6	CvLPRIT, 2019
0.68 [0.54, 0.87]		н		70.7	2025	160	2016	109	Complete, 2019
0.50 [0.05, 5.34]				0.7	50	2	50	1	Hamza, 2016
0.64 [0.28, 1.44]				5.9	213	14	215	9	Zhang, 2015
0.94 [0.47, 1.87]		-		8.3	314	16	313	15	DANAMI 3, 2015
0.35 [0.15, 0.80		·		5.5	231	20	234	7	PRAMI, 2013
4.61 [0.25, 83.61]				0.5	40	0	79	4	Dambrink, 2012
0.55 [0.19, 1.59				3.5	84	7	130	6	Politi, 2010
0.33 [0.02, 4.95]			-	0.5	17	1	52	1	Help-AMI, 2009
0.66 [0.54, 0.81]		•			; l ² = 0.0%)	eneity = 0.66	p for heterog	= 5.93, df = 8,	RE Model for All Studies (C
p for overall effect < 0.001									
5 25	I 5	0.2	0.04						

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

Year	Act	ive	Con	trol					Relative risk [95% CI]
leal	Events	Ν	Events	N	Weight (%)				Relative fisk [95% Ci]
,									
2019	6	150	12	146	12.3		⊢		0.49 [0.19, 1.26]
ACUTE, 2017	7	295	28	590	16.7		⊢		0.50 [0.22, 1.13]
016	1	50	2	50	2	·			0.50 [0.05, 5.34]
15	9	215	14	213	16.8		⊢_∎		0.64 [0.28, 1.44]
, 2015	15	313	16	314	23.6			-	0.94 [0.47, 1.87]
013	7	234	20	231	15.8		⊢_ ∎I		0.35 [0.15, 0.80]
2012	4	79	0	40	1.3				4.61 [0.25, 83.61]
)	6	130	7	84	10		·		0.55 [0.19, 1.59]
2009	1	52	1	17	1.5	-		i	0.33 [0.02, 4.95]
for All Studios (O - 6	5.82, df = 8, j	p for heterog	geneity = 0.67;	l ² = 0.0%)	I		•		0.59 [0.42, 0.82]
IOI All Studies ($Q = C$									
									p for overall effect = 0.002
						Γ			p for overall effect = 0.002

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

Study and Year	Act	ive	Con	trol						Pol	ative risk [95% CI]
Study and Tear	Events	N	Events	Ν	Weight (%)					Rei	alive fisk [95 % Cij
Risk of MI											
Complete, 2019	109	2016	160	2025	69.6			H a 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	4					0.33 [0.02, 4.95]
RE Model for All Studies (Q	= 5.98, df = 8, p	p for heterog	geneity = 0.65	; l ² = 0.0%))			•			0.66 [0.54, 0.80]
										p for ov	verall effect < 0.001
							I	1	Ι		
						0.04	0.2	1	5	25	

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

Study and Year	Act	ive	Con	trol						Relative risk [95% CI]
Study and Tear	Events	N	Events	N	Weight (%)					Relative fisk [95 % Ci]
Risk of MI										
CvLPRIT, 2019	6	150	12	146	4.1		·	<u> </u>		0.49 [0.19, 1.26]
Complete, 2019	109	2016	160	2025	67.1			H a H		0.68 [0.54, 0.87]
Compare ACUTE, 2017	7	295	28	590	5.6			<u> </u>		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	4				0.33 [0.02, 4.95]
RE Model for All Studies (Q	= 4.59, df = 8, j	o for heterog	geneity = 0.80;	; I ² = 0.0%))			•		0.64 [0.53, 0.78]
										p for overall effect < 0.001
							1	i	1	
						0.04	0.2	4	5	25

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

Study and Year	Events	N	Events	Ν	Weight (%)				Relative 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		+=+		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	-		i	0.33 [0.02, 4.95]
RE Model for All Studies (Q = 5.	15, df = 8, p	o for heterog	eneity = 0.74	; l ² = 1.4%)			•		0.62 [0.50, 0.77]
									p for overall effect < 0.001
						-	1	1	

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

Events N Events N Weight (%) Risk of MI CvLPRIT, 2019 6 150 12 146 4.1	Events			trol			Relative risk [95% CI]
CvLPRIT, 2019 6 150 12 146 4.1		N	Events	N	Weight (%)		
Complete, 2019 109 2016 160 2025 67.2 Image: Compare ACUTE, 2017 0.68 0.68 0.50 0.68 0.50 0.68 0.50 0.50 0.50 0.50 0.50 0.50 0.50 0.64 0.64 0.64 0.64 0.64 0.64 0.64 0.64 0.64 0.50 0.64 0.50 0.35 0.50 0.35 0.50 0.50 0.50 0.50 0.50 0.50 0.50 0.50 0.50 0.50 0.50 0.50 0.50 0.50<							
Compare ACUTE, 2017 7 295 28 590 5.6 	6	150	12	146	4.1	·	0.49 [0.19, 1.26]
Zhang, 2015 9 215 14 213 5.6 0.64 [0.28, 1] DANAMI 3, 2015 15 313 16 314 7.9 0.94 [0.47, 1] PRAMI, 2013 7 234 20 231 5.3 0.35 [0.15, 0] Dambrink, 2012 4 79 0 40 0.4 4.61 [0.25, 83]	109	2016	160	2025	67.2	⊢ ∰4	0.68 [0.54, 0.87]
DANAMI 3, 2015 15 313 16 314 7.9 Image: model 0.94 [0.47, 1] PRAMI, 2013 7 234 20 231 5.3 Image: model 0.35 [0.15, 0] Dambrink, 2012 4 79 0 40 0.4 Image: model 4.61 [0.25, 83]	7	295	28	590	5.6	— <u> </u>	0.50 [0.22, 1.13]
PRAMI, 2013 7 234 20 231 5.3 0.35 [0.15, 0 Dambrink, 2012 4 79 0 40 0.4 4.61 [0.25, 83	9	215	14	213	5.6	⊢	0.64 [0.28, 1.44]
Dambrink, 2012 4 79 0 40 0.4	15	313	16	314	7.9	—	0.94 [0.47, 1.87]
	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	4	79	0	40	0.4	·	4.61 [0.25, 83.61]
	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	1	52	1	17	0.5		0.33 [0.02, 4.95]
	or, ur = 8, p	ioi neterog	eneity = 0.61;	, i = 0.0%)		•	0.65 [0.54, 0.79] p for overall effect < 0.001
Help-AMI, 2009		109 7 9 15 7 4 6 1	109 2016 7 295 9 215 15 313 7 234 4 79 6 130 1 52	109 2016 160 7 295 28 9 215 14 15 313 16 7 234 20 4 79 0 6 130 7 1 52 1	109 2016 160 2025 7 295 28 590 9 215 14 213 15 313 16 314 7 234 20 231 4 79 0 40 6 130 7 84 1 52 1 17	109 2016 160 2025 67.2 7 295 28 590 5.6 9 215 14 213 5.6 15 313 16 314 7.9 7 234 20 231 5.3 4 79 0 40 0.4 6 130 7 84 3.3	109 2016 160 2025 67.2 $\bullet \bullet \bullet$ 7 295 28 590 5.6 $\bullet \bullet \bullet \bullet \bullet$ 9 215 14 213 5.6 $\bullet \bullet \bullet \bullet \bullet \bullet$ 15 313 16 314 7.9 $\bullet \bullet \bullet \bullet \bullet \bullet \bullet$ 7 234 20 231 5.3 $\bullet \bullet \bullet \bullet \bullet \bullet \bullet \bullet \bullet$ 4 79 0 40 0.4 $\bullet \bullet $

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

1 5

٦

25

Г

0.04 0.2

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

Study and Voar	Act	tive	Con	trol						Polativa	risk [95% CI]
Study and Year	Events	Ν	Events	N	Weight (%)					Relative	115K [95 /8 CI]
Risk of MI											
CvLPRIT, 2019	6	150	12	146	4.1					0.4	9 [0.19, 1.26]
Complete, 2019	109	2016	160	2025	67.1		F	•		0.6	8 [0.54, 0.87]
Compare ACUTE, 2017	7	295	28	590	5.6			;		0.5	0 [0.22, 1.13]
Hamza, 2016	1	50	2	50	0.7					0.5	0 [0.05, 5.34]
Zhang, 2015	9	215	14	213	5.6					0.6	4 [0.28, 1.44]
DANAMI 3, 2015	15	313	16	314	7.9		F			0.9	4 [0.47, 1.87]
PRAMI, 2013	7	234	20	231	5.3		·	-		0.3	5 [0.15, 0.80]
Dambrink, 2012	4	79	0	40	0.4				-	→ 4.6	1 [0.25, 83.61]
Politi, 2010	6	130	7	84	3.3		·			0.5	5 [0.19, 1.59]
	= 6.11, df = 8,	p for heterog	geneity = 0.64	; l ² = 0.0%)	1		•	•		0.6	5 [0.54, 0.79]
RE Model for All Studies (Q											
RE Model for All Studies (Q										p for overall	effect < 0.001
RE Model for All Studies (Q						Г <u> </u>	I			p for overall	effect < 0.001

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

Study and Year	Active		Control							Pol	ative risk [95% CI]
	Events	N	Events	N	Weight (%)					Neid	live lisk [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	H .			0.68 [0.54, 0.87]
Compare ACUTE, 2017	7	295	28	590	5.7		·	<u></u>			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		<u> </u>				0.94 [0.47, 1.87]
PRAMI, 2013	7	234	20	231	5.4		·	•			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 for heterog	geneity = 0.62	; l ² = 0.0%))		•	•			0.65 [0.54, 0.80]
										p for ov	erall effect < 0.001
								i –			

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

Study and Year	Active		Con	Control						Relative risk [95% C
Study and Tear	Events	N	Events	Ν	Weight (%)					Relative fisk [95% C
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 II H		0.68 [0.54, 0.8]
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, 1.8]
Dambrink, 2012	4	79	0	40	0.5		·			→ 4.61 [0.25, 83.6 ⁻
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, 4.9
RE Model for All Studies (Q :	= 4.06, df = 8, p	o for heterog	eneity = 0.85	; l ² = 0.0%)				•		0.67 [0.55, 0.82
										p for overall effect < 0.00
						l – – – – – – – – – – – – – – – – – – –	1	i	Τ	
						0.04	0.2	1	5	25

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

Study and Year	Active		Con	trol						Polativ	e risk [95% CI]
Study and Tear	Events	N	Events	N	Weight (%)					Kelativ	e lisk [95 /8 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		н	-		0	.68 [0.54, 0.87]
Compare ACUTE, 2017	7	295	28	590	5.9		·	<u> </u>		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		F			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	4				0	.33 [0.02, 4.95]
RE Model for All Studies (Q	= 6.35, df = 8, j	p for heterog	geneity = 0.61	; l ² = 0.0%)	I		•	•		0	.65 [0.53, 0.79]
										p for overa	ll effect < 0.001
						Γ	1	1	1		
						0.04	0.2	1	5	25	
					Comple	te revasc. be	etter < Rela	itive risk	> Culp	rit-only revas	c. better

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

Relative risk [95% (Control		Active		Study and Year
		/eight (%)	N	Events	Ν	Events	
							Risk of death
0.58 [0.26, 1.2		6.9	146	15	150	9	CvLPRIT, 2019
→ 0.91 [0.70, 1.1		59.9	2025	106	2016	96	Complete, 2019
0.25 [0.03, 2.*	<u>م</u>	0.9	50	4	50	1	Hamza, 2016
0.86 [0.42, 1.7	F	8.4	213	15	215	13	Zhang, 2015
1.37 [0.64, 2.9		7.5	314	11	313	15	DANAMI 3, 2015
0.74 [0.36, 1.5	<u> </u>	8.2	231	16	234	12	PRAMI, 2013
► 2.56 [0.13, 52.1	·	0.5	40	0	79	2	Dambrink, 2012
0.50 [0.23, 1.0	·=	7.2	84	13	130	10	Politi, 2010
1.02 [0.04, 23.9	<u> </u>	0.4	17	0	52	1	Help-AMI, 2009
• 0.85 [0.69, 1.0			; l ² = 0.0%)	eneity = 0.61	o for heterog	= 6.33, df = 8,	RE Model for All Studies (C
p for overall effect = 0.1							

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

Study and Year	Active		Control							Po	lative risk [95% CI]
Study and Teal	Events	N	Events	Ν	Weight (%)					Re	lative lisk [55 % Ci]
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	-			1		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		⊢				0.74 [0.36, 1.53]
Dambrink, 2012	2	79	0	40	1.1		H		-	-	2.56 [0.13, 52.14]
Politi, 2010	10	130	13	84	16.6			•			0.50 [0.23, 1.08]
Help-AMI, 2009	1	52	0	17	1	<u> </u>		-		i	1.02 [0.04, 23.91]
RE Model for All Studies (Q	= 5.66, df = 8, p	for hetero	geneity = 0.69;	$l^2 = 0.0\%$)			•			0.76 [0.56, 1.05]
										p for c	verall effect = 0.094
						-	1	i			
						0.04	0.2	1	5	25	

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

Relative risk [95% C				Control		Active		Study and Year	
Kelative lisk [55 % C			Weight (%)	N	Events	N	Events	Study and Tear	
								Risk of death	
⊢ - 0.91 [0.70, 1.1	H a H		62.2	2025	106	2016	96	Complete, 2019	
	·		3.4	590	10	295	4	Compare ACUTE, 2017	
0.25 [0.03, 2.1	,	-	1	50	4	50	1	Hamza, 2016	
0.86 [0.42, 1.7	·		8.7	213	15	215	13	Zhang, 2015	
1.37 [0.64, 2.9			7.8	314	11	313	15	DANAMI 3, 2015	
0.74 [0.36, 1.5	⊢		8.5	231	16	234	12	PRAMI, 2013	
2.56 [0.13, 52.1	H		0.5	40	0	79	2	Dambrink, 2012	
0.50 [0.23, 1.0	·		7.5	84	13	130	10	Politi, 2010	
1.02 [0.04, 23.9		—	0.5	17	0	52	1	Help-AMI, 2009	
• 0.87 [0.70, 1.0	•			; l ² = 0.0%)	eneity = 0.71	p for heterog	= 5.45, df = 8,	RE Model for All Studies (Q :	
p for overall effect = 0.15									

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

Study and Year	Active		Con	Control				Relative risk [95% CI]
Study and Teal	Events	N	Events	N	Weight (%)			Relative risk [35 % 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]
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, j	p for heterog	geneity = 0.67	; I ² = 0.0%))		•	0.84 [0.68, 1.03]
								p for overall effect = 0.098
							<u> </u>	
						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	Active		Control						Relative risk [
Study and Teal	Events	N	Events	Ν	Weight (%)					Re	iative fisk [95 /0 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 a 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]
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		·		•		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	o for heterog	geneity = 0.79	; l ² = 0.6%)				•			0.81 [0.65, 1.01]
										p for c	verall effect = 0.058
						Г		İ	Ι		
						0.04	0.2	1	5	25	

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

Study and Year	Active		Control					Relative ris	105% CI1
study and real	Events	N	Events	N	Weight (%)			Relative HS	[93 % Ci]
Risk of death									
CvLPRIT, 2019	9	150	15	146	6.7		·	0.58 [0	.26, 1.29]
Complete, 2019	96	2016	106	2025	58.6		+ H +	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		⊢− ∎−−1	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, I	p for heterog	jeneity = 0.75;	; I ² = 0.0%))		•	0.85 [0	.70, 1.05]
								p for overall effe	ct = 0.135

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

Study and Year	Active		Con	Control					Relative risk [95% CI]
Study and Tear	Events	N	Events	Ν	Weight (%)				Relative fisk [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, j	p for heterog	geneity = 0.61;	; l ² = 0.0%)	1		•		0.84 [0.69, 1.04]
									p for overall effect = 0.107
							- i - i	I	

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

Study and Year	Active		Control				Relative risk [95% CI]
Study and Tear	Events	N	Events	Ν	Weight (%)		Relative lisk [55 % Ci]
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	H H 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	8.8	⊢	0.86 [0.42, 1.76]
DANAMI 3, 2015	15	313	11	314	7.8	► <u>+</u> =	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	geneity = 0.82;	; l ² = 0.0%)		•	0.88 [0.71, 1.09]
							p for overall effect = 0.236
						0.04 0.2 1	5 25
					Comple	e revasc. better < Relative risk > 0	Culprit-only revasc. better

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

Study and Year	Act	Active		Control			Relative risk [95% CI]
	Events	N	Events	N	Weight (%)		
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 E 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	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 =	= 6.20, df = 8, p	o for heterog	eneity = 0.62	; I ² = 0.0%))	•	0.85 [0.69, 1.06]
							p for overall effect = 0.150

 0.04
 0.2
 1
 5
 25

 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	Act	Active		Control			Relative risk [95% CI]
	Events	N	Events	N	Weight (%)		Relative has [50% of]
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	⊢∎ -I	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	·	▶ 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	o for heterog	geneity = 0.61	; l ² = 0.0%)		•	0.84 [0.68, 1.05]
							p for overall effect = 0.120

 0.04
 0.2
 1
 5
 25

 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	Act	Active		Control						Pol	ative risk [95% CI]
Study and Tear	Events	N	Events	N	Weight (%)					Rei	alive fisk [95 % Ci]
Risk of unplanned reva	scularisation										
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		H	-			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 = 0.0	D; I ² = 67.7	%)		•	-			0.38 [0.27, 0.54]
										p for ov	verall effect < 0.001
								1	I		
						0.04	0.2	1	5	25	

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

Study and Year	Acti	ive	Con	trol						Polati	ve risk [95% Cl]
Study and Teal	Events	N	Events	N	Weight (%)					Relati	ve lisk [95 % Ci]
Risk of unplanned revascu	larisation										
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		F	-			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 heter	ogeneity = 0.12	2; I ² = 41.4	%)		•				0.42 [0.32, 0.55]
										p for over	rall effect < 0.001
						Γ	1	i	Ι		
						0.04	0.2	1	5	25	

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

Study and Year	Act	Active		Control						Pol	ative risk [95% CI]
	Events	N	Events	N	Weight (%)					Kei	ative fisk [55 % Ci]
Risk of unplanned revasc	ılarisation										
Complete, 2019	29	2016	160	2025	14.3		⊢∎⊣				0.18 [0.12, 0.27]
Compare ACUTE, 2017	18	295	103	590	13			-			0.35 [0.22, 0.57]
Hamza, 2016	1	50	6	50	2.2	-		<u> </u>			0.17 [0.02, 1.33]
Zhang, 2015	27	215	62	213	14		H	-			0.43 [0.29, 0.65]
DANAMI 3, 2015	17	313	52	314	12.3		⊢∎-	-			0.33 [0.19, 0.55]
PRAMI, 2013	16	234	46	231	12.1		H	-			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 [0.18, 0.58]
Help-AMI, 2009	9	52	6	17	7.9			-			0.49 [0.20, 1.18]
RE Model for All Studies (Q	= 26.79, df = 8,	p for hetero	ogeneity = 0.0	0; I ² = 68.1	%)		•				0.37 [0.26, 0.51]
										p for o	verall effect < 0.001
							1	i	I		
						0.04	0.2	1	5	25	

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

Study and Year	Act	Active		Control						Pol	ative risk [95% CI]
Study and Tear	Events	N	Events	Ν	Weight (%)					Rei	ative fisk [55 % Ci]
Risk of unplanned revascu	larisation										
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						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	verall effect < 0.001
						-	1	i	Ι		
						0.04	0.2	1	5	25	

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

Study and Year	Act	Active		Control						Pol	ative risk [95% CI]
Study and Tear	Events	N	Events	N	Weight (%)					Rei	alive risk [95% Ci]
Risk of unplanned revascu	larisation										
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		H	H			0.43 [0.29, 0.65]
PRAMI, 2013	16	234	46	231	12.6		H	-			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]
Help-AMI, 2009	9	52	6	17	8.4		—	•			0.49 [0.20, 1.18]
RE Model for All Studies (Q	= 27.20, df = 8,	, p for hetero	geneity = 0.0	0; l ² = 67.8	%)		-	•			0.38 [0.27, 0.54]
										p for o	verall effect < 0.001
							1	i	1		
						0.04	0.2	1	5	25	

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

Study and Year	Act	ive	Cor	trol			Relative risk [95% CI]
olddy and real	Events	N	Events	N	Weight (%)		Kelative fisk [35 % Ci]
Risk of unplanned revasc	ularisation						
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	H -	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	⊢ ∎→	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	ogeneity = 0.0	0; I ² = 67.6	%)	•	0.38 [0.28, 0.52]
							p for overall effect < 0.001

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

1 5

٦

25

Г

0.04

0.2

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

Study and Year	Act	Active		Control						Pol	ative risk [95% CI]
Study and Tear	Events	N	Events	N	Weight (%)					Rei	auve nsk [95 % Ci]
Risk of unplanned revascu	larisation										
CvLPRIT, 2019	8	150	16	146	8.5						0.49 [0.21, 1.10]
Complete, 2019	29	2016	160	2025	14.2		⊢∎⊣				0.18 [0.12, 0.27]
Compare ACUTE, 2017	18	295	103	590	12.9						0.35 [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 [0.29, 0.65]
DANAMI 3, 2015	17	313	52	314	12.2		H				0.33 [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 [0.18, 0.58]
RE Model for All Studies (Q	= 26.84, df = 8,	p for hetero	geneity = 0.0	D; I ² = 68.2	%)		+				0.37 [0.26, 0.51]
										p for ov	rerall effect < 0.001
								i	1		
						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	Control						Pola	tive risk [95% C
Study and Tear	Events	N	Events	Ν	Weight (%)				Reid	luve HSK [95 /8 C
Risk of unplanned revascu	ılarisation									
CvLPRIT, 2019	8	150	16	146	8.9		·			0.49 [0.21, 1.1
Complete, 2019	29	2016	160	2025	14.6		⊢∎⊣			0.18 [0.12, 0.2
Compare ACUTE, 2017	18	295	103	590	13.3		⊢∎⊣			0.35 [0.22, 0.5
Hamza, 2016	1	50	6	50	2.4	-	-			0.17 [0.02, 1.3
Zhang, 2015	27	215	62	213	14.3		⊢∎-			0.43 [0.29, 0.6
DANAMI 3, 2015	17	313	52	314	12.7		⊢∎⊣			0.33 [0.19, 0.5
PRAMI, 2013	16	234	46	231	12.5					0.34 [0.20, 0.5
Dambrink, 2012	27	79	15	40	13		F	-		0.91 [0.55, 1.5
Help-AMI, 2009	9	52	6	17	8.3					0.49 [0.20, 1.1
RE Model for All Studies (Q =	= 27.19, df = 8	, p for hetero	geneity = 0.0	0; I ² = 68.1	%)		•			0.38 [0.27, 0.5
								1	p for ov	erall effect < 0.00
									 p for ov	erall effect < 0.00

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

Study and Year	Act	ive	Control							Pol	tive risk [95% CI]
Study and Teal	Events	N	Events	Ν	Weight (%)					Neid	luve lisk [95 % Cij
Risk of unplanned revascu	larisation										
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		H	-			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			-			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 = 0.0	D; I ² = 68.1	%)		•				0.38 [0.27, 0.54]
										p for ov	erall effect < 0.001
						Г	Ι	1	Ι		
						0.04	0.2	1	5	25	

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

Study and Year	Act	ive	Control				Relative risk [95% CI]
olddy and real	Events	N	Events	N	Weight (%)		Relative hak [35% Ci]
Risk of unplanned revasc	ularisation						
CvLPRIT, 2019	8	150	16	146	9.2	• • ••••	0.49 [0.21, 1.10]
Complete, 2019	29	2016	160	2025	14.9	⊢∎→	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	⊢ ∎→	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	⊢∎	0.91 [0.55, 1.51]
Politi, 2010	14	130	28	84	12.2	⊢ ∎→	0.32 [0.18, 0.58]
Help-AMI, 2009	9	52	6	17	8.5	⊢_ ∎i	0.49 [0.20, 1.18]
RE Model for All Studies (Q	= 26.42, df = 8,	, p for heterc	ogeneity = 0.0	0; 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

1 5

٦

25

Г

0.04

0.2