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

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Summary

Background In patients presenting with acute coronary syndromes and multivessel coronary artery disease, the question of whether to undertake a strategy of complete revascularisation in cases in which percutaneous coronary intervention (PCI) is performed routinely on non-culprit lesions (in addition to the culprit lesion) or whether to restrict PCI only to the culprit lesion is a common dilemma. The Complete Revascularisation Trialists' Collaboration aimed to determine, based on the totality of data from randomised trials, the effect of a complete revascularisation strategy on major cardiovascular events and whether it reduces cardiovascular death.

Methods In this individual patient data meta-analysis, trials were included if they enrolled at least 250 patients, compared a complete revascularisation strategy (with PCI) to a culprit lesion-only PCI strategy, and enrolled patients presenting with acute ST-segment elevation myocardial infarction or non-ST-segment elevation myocardial infarction. To ensure that no trials were overlooked, we searched Ovid MEDLINE, Embase, and the Cochrane Central Register of Controlled Trials (CENTRAL) for randomised controlled trials published between 1996 and Sept 15, 2025. The primary outcomes were the composite of cardiovascular death or new myocardial infarction and cardiovascular death alone. Hierarchical testing of cardiovascular death alone was planned contingent on reduction in cardiovascular death or new myocardial infarction based on the prespecified alpha level of 0·04. A one-stage individual patient data meta-analysis was performed using a Cox frailty model. All-cause death was the secondary outcome; non-cardiovascular death and new myocardial infarction were additional outcomes. All analyses included all randomly assigned patients. The meta-analysis was registered in PROSPERO, CRD420251124098.

Findings Six randomised controlled trials involving 8836 individuals were included. The median age was 65·8 years (IQR 57·0–76·0), and 2088 (23·6%) patients were female and 6748 (76·4%) were male. Overall, 7768 (87·9%) patients presented with ST-segment elevation myocardial infarction and 1068 (12·1%) with non-ST-segment elevation myocardial infarction. At a median follow-up of 36·0 months (IQR 30·6–48·0), cardiovascular death or new myocardial infarction occurred in 382 (9·0%) of 4259 patients in the complete revascularisation group compared with 528 (11·5%) of 4577 patients in the culprit lesion-only group (hazard ratio [HR] 0·76 [95% CI 0·67–0·87], p<0·0001). There were 155 (3·6%) cardiovascular deaths in the complete revascularisation group compared with 209 (4·6%) in the culprit lesion-only group (HR 0·76 [95% CI 0·62–0·93], p=0·0091). All-cause death occurred in 308 (7·2%) patients in the complete revascularisation group compared with 370 (8·1%) patients in the culprit lesion-only group (HR 0·85 [95% CI 0·73–0·99], p=0·039). Non-cardiovascular death was similar between the groups (153 [3·6%] in the complete revascularisation group *vs* 161 [3·5%] in the culprit lesion-only group; HR 0·98 [95% CI 0·78–1·22], p=0·85). Complete revascularisation reduced new myocardial infarctions compared with culprit lesion-only PCI (255 [6·0%] *vs* 357 [7·8%]; HR 0·76 [95% CI 0·65–0·90], p=0·0011).

Interpretation In patients presenting with acute myocardial infarction and multivessel disease, complete revascularisation reduced the composite of cardiovascular death or new myocardial infarction as well as cardiovascular death alone compared with a culprit lesion-only PCI strategy. In addition, all-cause death was lower with complete revascularisation. These data provide the strongest and most robust evidence to date that complete revascularisation improves important cardiovascular clinical outcomes.

Funding None.

Research in context

Evidence before this study

Several randomised trials of patients with acute myocardial infarction and multivessel coronary artery disease have addressed the important question of whether to routinely undertake a strategy of complete revascularisation in cases in which percutaneous coronary intervention (PCI) is performed routinely on non-culprit-lesions (in addition to the culprit lesion) or whether to manage the non-culprit lesions conservatively by restricting PCI only to the culprit lesion. Most, but not all, of the randomised trials have shown that a complete revascularisation strategy reduces non-fatal events, but the robustness of this benefit based on the totality of evidence from randomised trials and whether complete revascularisation also reduces cardiovascular death are uncertain. To answer this question, we performed a collaborative individual patient data meta-analysis of the randomised trials, which has greater statistical power than any single trial to detect moderate reductions in these clinically important events. To ensure that no trials were overlooked, we searched Ovid MEDLINE, Embase, and the Cochrane Central Register of Controlled Trials from inception to Sept 15, 2025, using terms including "myocardial infarction","multivessel disease", "complete revascularisation", "metaanalysis", and "individual patient data". We found several aggregate data meta-analyses, but no previous individual patient data meta-analyses addressing this question.

Added value of this study

To our knowledge, this is the first individual patient data meta-analysis to assess a complete revascularisation strategy compared with a culprit lesion-only PCI strategy in patients of all ages with acute ST-segment elevation or non-ST-segment elevation myocardial infarction. The large size of this meta-analysis, with 8836 individuals from six randomised controlled trials, allowed for much greater statistical power than any single trial to detect moderate reductions in important clinical outcomes. A complete revascularisation strategy robustly reduced the composite of cardiovascular death or new myocardial infarction, with narrow CIs compared with culprit lesion-only PCI. In addition, complete revascularisation reduced cardiovascular death alone, a new finding that extends the benefit of complete revascularisation to include this important outcome. Furthermore, complete revascularisation reduced all-cause death. As expected, complete revascularisation had no effect on non-cardiovascular death. The benefit of complete revascularisation was consistent in men and women, patients younger than 65 years, and those aged 65 years or older, as well as those presenting with ST-segment elevation and non-ST-segment elevation myocardial infarction and when either an angiography-guided or a physiology-guided PCI strategy was used for non-culprit lesion PCI.

Implications of all the available evidence

This individual patient data meta-analysis of randomised trials provides the largest and most comprehensive evidence on the effects of a complete revascularisation strategy compared with a culprit-lesion only PCI strategy. The benefit of complete revascularisation on the composite of cardiovascular death or new myocardial infarction, as well as cardiovascular death and all-cause death alone is clinically relevant and important. Complete revascularisation for patients with acute myocardial infarction and multivessel disease is one of the few clinical indications outside primary PCI for ST-segment elevation myocardial infarction for which a PCI-based strategy reduces important outcomes, including cardiovascular death.

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Introduction

Percutaneous coronary intervention (PCI) of the culprit lesion is the recommended method of reperfusion for patients presenting with acute coronary syndromes.[1,2] About a half of these patients are found to have multivessel coronary artery disease at the time of the index PCI, with additional non-culprit lesions in locations separate from the culprit lesion that caused the acute event.[3] Over the past decade, several randomised trials of haemodynamically stable patients with acute myocardial infarction have addressed the important question of whether to routinely perform complete revascularisation with PCI to these non-culprit lesions in addition to the culprit lesion or to manage them conservatively by restricting PCI to the culprit lesion only.[4–10] The results of most randomised trials and trial-level meta-analyses comparing these strategies demonstrated the benefit of complete revascularisations in reducing composite outcomes driven mainly by non-fatal ischaemic events.[4–9,11,12] Moreover, none of the individual randomised trials were powered to detect moderate reductions in cardiovascular death. To address this gap in the evidence, the Complete Revascularisation Trialists' Collaboration, a multinational collaboration involving the principal investigators of randomised controlled trials (RCTs) evaluating a complete revascularisation strategy versus a culprit lesion-only strategy in patients presenting with acute myocardial infarction and multivessel coronary artery disease, aimed to determine, based on the totality of randomised evidence, the effect of complete revascularisation on the composite outcome of cardiovascular death or new myocardial infarction and on cardiovascular death and all-cause death taken separately.

Methods

Search strategy and selection criteria

In this individual patient data meta-analysis, trials were included if they were randomised trials enrolling at least 250 patients, compared a complete revascularisation strategy (with PCI) to a culprit lesion-only PCI strategy,

and enrolled patients presenting with acute ST-segment elevation myocardial infarction (STEMI) or non-ST-segment elevation myocardial infarction (NSTEMI). Complete revascularisation was defined as a strategy of angiography-guided or physiology-guided PCI to all suitable non-culprit lesions, in addition to PCI of the culprit lesion. A culprit lesion-only strategy was defined as PCI of only the culprit lesion, with no intervention on non-culprit lesions. Trials enrolling patients with cardiogenic shock or stable coronary artery disease were excluded. To ensure that no trials were overlooked, we conducted a comprehensive literature search using the following databases from 1996 to Sept 15, 2025: Embase, Ovid MEDLINE, and the Cochrane Central Register of Controlled Trials (CENTRAL). The search strategy used the following keywords: "ST segment elevation myocardial infarction", "non-ST segment elevation myocardial infarction", "myocardial infarction", "complete revascularisation", "multi-vessel revascularisation", "culprit lesion-only percutaneous coronary intervention", and "non-culprit coronary artery" (the full search strategy is available in the appendix p 2). There was no language restriction, and two investigators (DTWT and SRM) identified eligible studies with disagreements resolved by consensus. The meta-analysis was registered in PROSPERO (CRD420251124098) and conducted and reported in accordance with the PRISMA guidelines (appendix p 11).[13] Quality assessment revealed that all trials were randomised with adequate concealment of treatment allocation and had an open-label design with masked adjudication of outcome events, adequate statistical methods, and complete reporting of outcomes.

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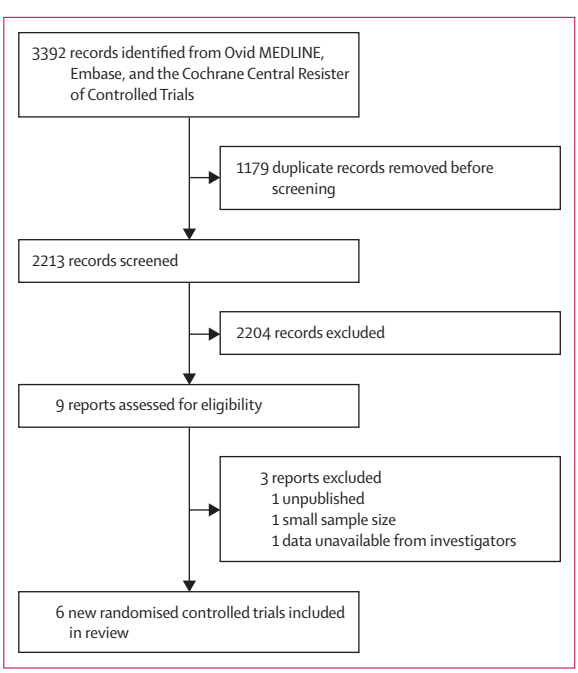

Figure 1: **Study selection**

Principal investigators of eligible trials were invited to collaborate and provide anonymised, patient-level data. The principal investigator of one trial declined to participate and provide data.[4] Each trial was approved by local ethics committees, and all patients in each trial provided informed consent.

Outcomes

The primary outcomes were the composite of cardiovascular death or new myocardial infarction and cardiovascular death alone. These outcomes were tested using a hierarchal testing procedure whereby the composite of cardiovascular death or new myocardial infarction was tested first and had to achieve significance (prespecified alpha of 0·04) for cardiovascular death to be tested. The key secondary outcome was all-cause death. Other outcomes were non-cardiovascular death and new myocardial infarction. The duration of follow-up reported in each primary trial paper was used except in two trials, in which longer-term, 3-year data, were reported.[14,15]

Data analysis

All analyses were based on the intention-to-treat population, which was defined as all patients randomly assigned to either complete revascularisation or culprit lesion-only PCI, regardless of the treatment they actually received. Data for each individual participant of each trial were harmonised before statistical analysis and merged into a single dataset to facilitate a one-stage individual patient data meta-analysis. Baseline characteristics were summarised for each study and for the pooled study population. Our primary method of analysis used a one-step approach, as outlined by Riley and colleagues,[16] in which individual participant-level data from all studies are pooled and analysed using a Cox frailty model, with clustering by trial included as a random effect. Assuming a constant treatment effect across studies, the random effects were included for the intercept only. We assessed heterogeneity using the treatment-by-study interaction. We assessed the proportionality assumption by using the supermum test in SAS and using the time interaction variable in the model. For the two primary outcomes, the fallback procedure was applied to determine statistical significance. The first primary outcome was evaluated at a prespecified alpha level of 0·04. If statistically significant, the alpha was considered to be unused and was transferred to the second primary outcome, which was then tested at the full 0·05 level. If the first primary outcome was not significant, the second primary outcome would be tested at an alpha level of 0·01. Results are presented as hazard ratios (HRs) with 95% CIs. For each predefined subgroup (age [<60 years, 60 to <75 years, or ≥75 years], sex [male or female], diabetes [yes or no], type of myocardial infarction [STEMI or NSTEMI], Killip class [<II or ≥II], non-culprit

	Complete revascularisation group (n=4259)	Culprit lesion-only group (n=4577)
Age, years	65·5 (56·8–76·0)	66·0 (57·0–76·0)
Sex		
Male	3293 (77·3%)	3455 (75·5%)
Female	966 (22·7%)	1122 (24·5%)
Diabetes	828/4255 (19·5%)	918/4570 (20·1%)
Chronic renal insufficiency	370/2899 (12·8%)	383/3218 (11·9%)
Clinical presentation		
STEMI	3723 (87·4%)	4045 (88·4%)
NSTEMI	536 (12·6%)	532 (11·6%)
Previous myocardial infarction	370/4252 (8·7%)	402/4569 (8·8%)
Current smoker	1476/4254 (34·7%)	1575/4567 (34·5%)
Hypertension	2279/4255 (53·6%)	2503/4569 (54·8%)
Dyslipidaemia	1569/4250 (36·9%)	1671/4563 (36·6%)
Previous PCI	378/4256 (8·9%)	407/4571 (8·9%)
Previous stroke	160/3709 (4·3%)	176/4017 (4·4%)
Time from symptom onset to index PCI		
<6 h	2526/3493 (72·3%)	2748/3793 (72·4%)
6–12 h	556/3493 (15·9%)	604/3793 (15·9%)
>12 h	411/3493 (11·8%)	441/3793 (11·6%)
Killip class ≥II	497/4218 (11·8%)	527/4528 (11·6%)
Medications at discharge		
Aspirin	4187/4248 (98·6%)	4478/4551 (98·4%)
P2Y12 inhibitor		
Any	4152/4250 (97·7%)	4467/4551 (98·2%)
Ticagrelor	2509/4250 (59·0%)	2596/4551 (57·0%)
Prasugrel	505/4250 (11·9%)	588/4551 (12·9%)
Clopidogrel	1142/4250 (26·9%)	1287/4551 (28·3%)
β-blocker	3647/4247 (85·9%)	3917/4551 (86·1%)
ACE inhibitor or ARB	3441/4248 (81·0%)	3660/4553 (80·4%)
Statin	4149/4246 (97·7%)	4400/4550 (96·7%)
Radial access	3137/3945 (79·5%)	3135/4264 (73·5%)
Culprit lesion location		
Left main coronary artery	44/3831 (1·1%)	46/4167 (1·1%)
Left anterior descending artery	1408/3831 (36·8%)	1520/4167 (36·5%)
Circumflex artery	731/3831 (19·1%)	741/4167 (17·8%)
Right coronary artery	1655/3831 (43·2%)	1870/4167 (44·9%)
Number of residual diseased vessels (core laboratory test)		
1	2835/3846 (73·7%)	3058/4169 (73·4%)
≥2	1011/3846 (26·3%)	1111/4169 (26·6%)
Non-culprit lesion location (core laboratory test)*		
Left main artery	13/4888 (0·3%)	7/5089 (0·1%)
Left anterior descending artery	1961/4888 (40·1%)	2190/5089 (43·0%)
Proximal left anterior descending artery	514/4888 (10·5%)	543/5089 (10·7%)
Mid left anterior descending artery	739/4888 (15·1%)	857/5089 (16·8%)
Circumflex artery	1832/4888 (37·5%)	1914/5089 (37·6%)
Proximal circumflex (includes obtuse marginal and ramus) artery	897/4888 (18·4%)	964/5089 (18·9%)
Distal circumflex and posterior left ventricular arteries	330/4888 (6·8%)	366/5089 (7·2%)
Right coronary artery	1174/4888 (24·0%)	1173/5089 (23·0%)
Non-culprit lesion diameter stenosis (visual)*†		
50% to <70%	743/5273 (14·1%)	736/4895 (15·0%)
70% to <90%	3098/5273 (58·8%)	2929/4895 (59·8%)
90% to <100%	1145/5273 (21·7%)	960/4895 (19·6%)
100%	287/5273 (5·4%)	270/4895 (5·5%)

(Table 1 continues in next column)

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Data are median (IQR), n (%), n/N (%), or mean (SD). ACE=angiotensin-converting enzyme. ARB=angiotensin receptor blocker. NSTEMI=non-ST-segment elevation myocardial infarction. PCI=percutaneous coronary intervention. STEMI=ST-segment elevation myocardial infarction. *Per number of non-culprit lesions. †1231 patients were included in the 50% to <70% culprit lesion category, 4574 in the 70% to <90% category, 1914 in the 90% to <100% category, and 548 in the 100% category.

Table 1: **Baseline and procedural characteristics**

	Complete revascularisation group (n=4259)	Culprit lesion-only group (n=4577)	HR (95% CI)	p value
First primary outcome: cardiovascular death or new myocardial infarction	382 (9·0%)	528 (11·5%)	0·76 (0·67–0·87)	<0·0001
Second primary outcome: cardiovascular death	155 (3·6%)	209 (4·6%)	0·76 (0·62–0·93)	0·0091
Secondary outcome: all-cause death	308 (7·2%)	370 (8·1%)	0·85 (0·73–0·99)	0·039
Non-cardiovascular death	153 (3·6%)	161 (3·5%)	0·98 (0·78–1·22)	0·85
New myocardial infarction	255 (6·0%)	357 (7·8%)	0·76 (0·65–0·90)	0·0011

Data are n (%) unless otherwise stated. HR=hazard ratio.

Table 2: **Summary of main outcomes at a median follow-up of 36 months**

lesion stenosis severity [50% to <70%, 70% to <90%, 90% to <100%, or 100%], proximal or mid left anterior descending artery non-culprit lesion [present or absent], number of residual diseased vessels [one or two or more], and complete revascularisation strategy [angiography guided or physiology guided]), interactions were formally tested between strata by the Wald test. A p value of less than 0·05 was considered to be significant. We created time-to-event curves for the main outcomes by adjusting for competing events such that non-cardiovascular death, cardiovascular death, and all-cause death were considered as competing events for cardiovascular death or new myocardial infarction, cardiovascular death, non-cardiovascular death, and new myocardial infarction, respectively. We performed a prespecified sensitivity analysis including the PRAMI

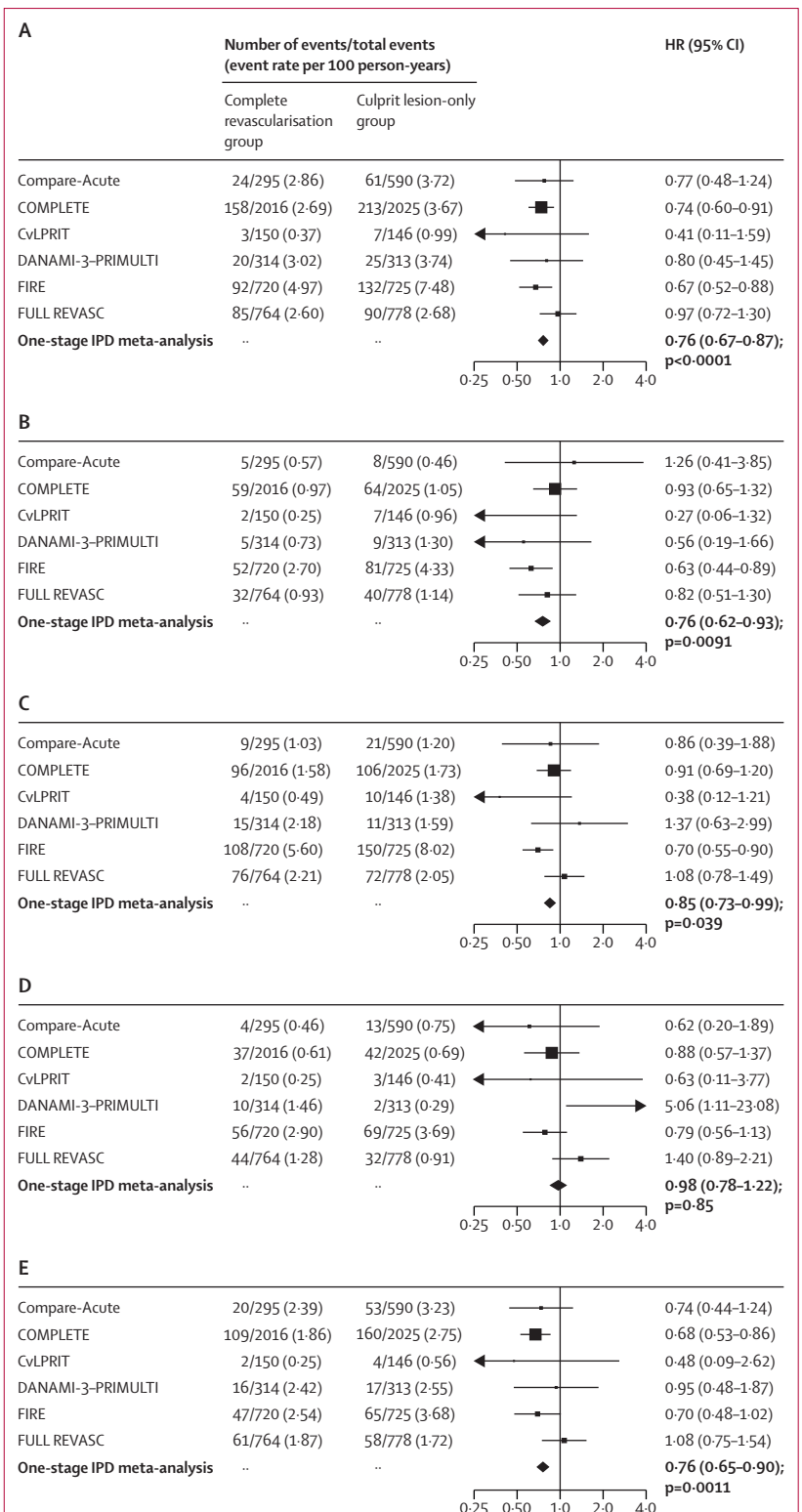

Figure 2: **Effect estimates for main outcomes**
(A) First primary outcome of cardiovascular death or new myocardial infarction. (B) Second primary outcome of cardiovascular death. (C) Secondary outcome of all-cause death. (D) Other outcome of non-cardiovascular death. (E) Other outcome of new myocardial infarction. HR=hazard ratio. IPD=individual patient data.

trial and conducted a two-stage random effects model considering study as a random effect. Heterogeneity for this analysis was assessed using I^2 statistic. All analysis were performed using SAS software for Linux (version 9.4). Figures were produced using R (version 4.5.1).

Role of the funding source

There was no funding source for this study.

Results

Overall, six controlled randomised trials[5–10] involving 8836 individuals were included: 4259 patients were randomly assigned to complete revascularisation and 4577 to a culprit lesion-only strategy. Results of the search strategy are shown in figure 1. Mean follow-up was 38·7 months (SD 15·0), and the median follow-up was 36·0 months (IQR 30·6–48·0). Median age was 65·8 years (IQR 57·0–76·0), and 2088 (23·6%) patients were female and 6748 (76·4%) were male. Baseline and procedural characteristics by treatment group are shown in table 1. In four trials,[6,7,9,10] complete revascularisation was achieved using a physiology-guided approach and in two trials[5,8] with an angiography-guided approach. In terms of timing, one trial recommended non-culprit lesion PCI during the index procedure,[7] whereas three trials recommended non-culprit lesion PCI as a staged procedure,[6,8,10] and two trials allowed either option.[5,9] Data on race or ethnicity were not collected. At discharge from the index hospitalisation, 8665 (98·5%) of 8799 patients were on aspirin, 8619 (97·9%) of 8801 were on a P2Y12 inhibitor (5105 [58·0%] on ticagrelor, 1093 [12·4%] on prasugrel, and 2429 [27·6%] on clopidogrel), 7564 (86·0%) of 8798 were on a β-blocker, 7101 (80·7%) of 8801 were on an angiotensin-converting enzyme inhibitor or angiotensin receptor blocker, and 8549 (97·2%) of 8796 were on a statin (table 1).

The first primary outcome composite of cardiovascular death or new myocardial infarction occurred in 382 (9·0%) of 4259 patients in the complete revascularisation group compared with 528 (11·5%) of 4577 patients in the culprit lesion-only group (HR 0·76 [95% CI 0·67–0·87], p<0·0001; table 2; figures 2A, 3A), with no evidence of heterogeneity ($p_{heterogeneity}$=0·49). The second primary outcome of cardiovascular death occurred in 155 (3·6%) patients in the complete revascularisation group compared with 209 (4·6%) patients in the culprit lesion-only group (HR 0·76 [95% CI 0·62–0·93], p=0·0091; table 2; figures 2B, 3B), with no evidence for heterogeneity ($p_{heterogeneity}$=0·38). Time-to-event curves adjusted for competing risk showed a similar pattern to the primary analysis (appendix p 22).

The secondary outcome of all-cause death was significantly lower in the complete revascularisation group than in the culprit lesion-only group (308 [7·2%] of 4259 patients *vs* 370 [8·1%] of 4577 patients; HR 0·85 [95% CI 0·73–0·99], p=0·039; table 2;

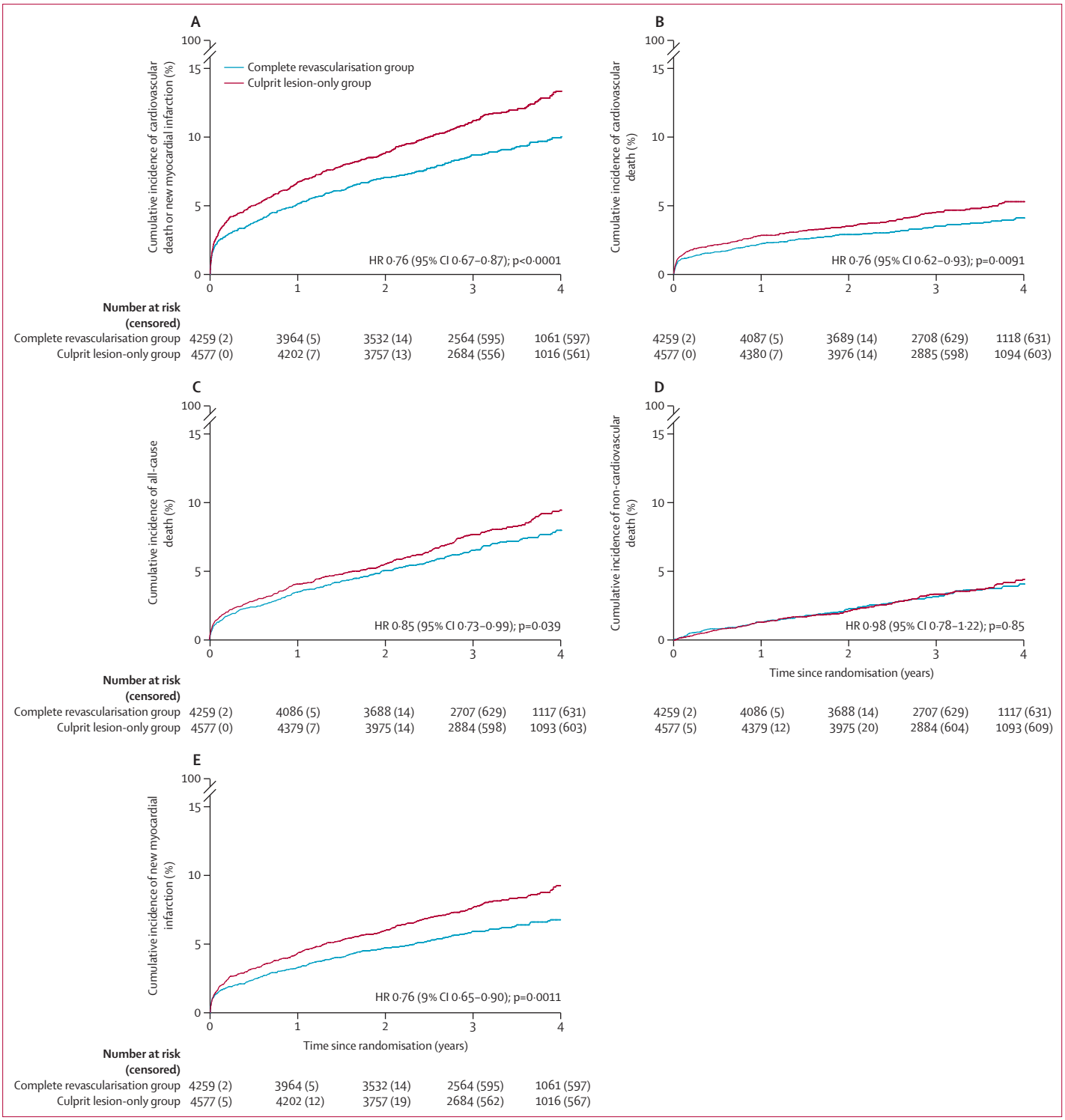

Figure 3: **Cumulative incidence of main outcomes**
(A) First primary outcome of cardiovascular death or new myocardial infarction. (B) Second primary outcome of cardiovascular death. (C) Secondary outcome of all-cause death. (D) Other outcome of non-cardiovascular death. (E) Other outcome of new myocardial infarction. HR=hazard ratio.

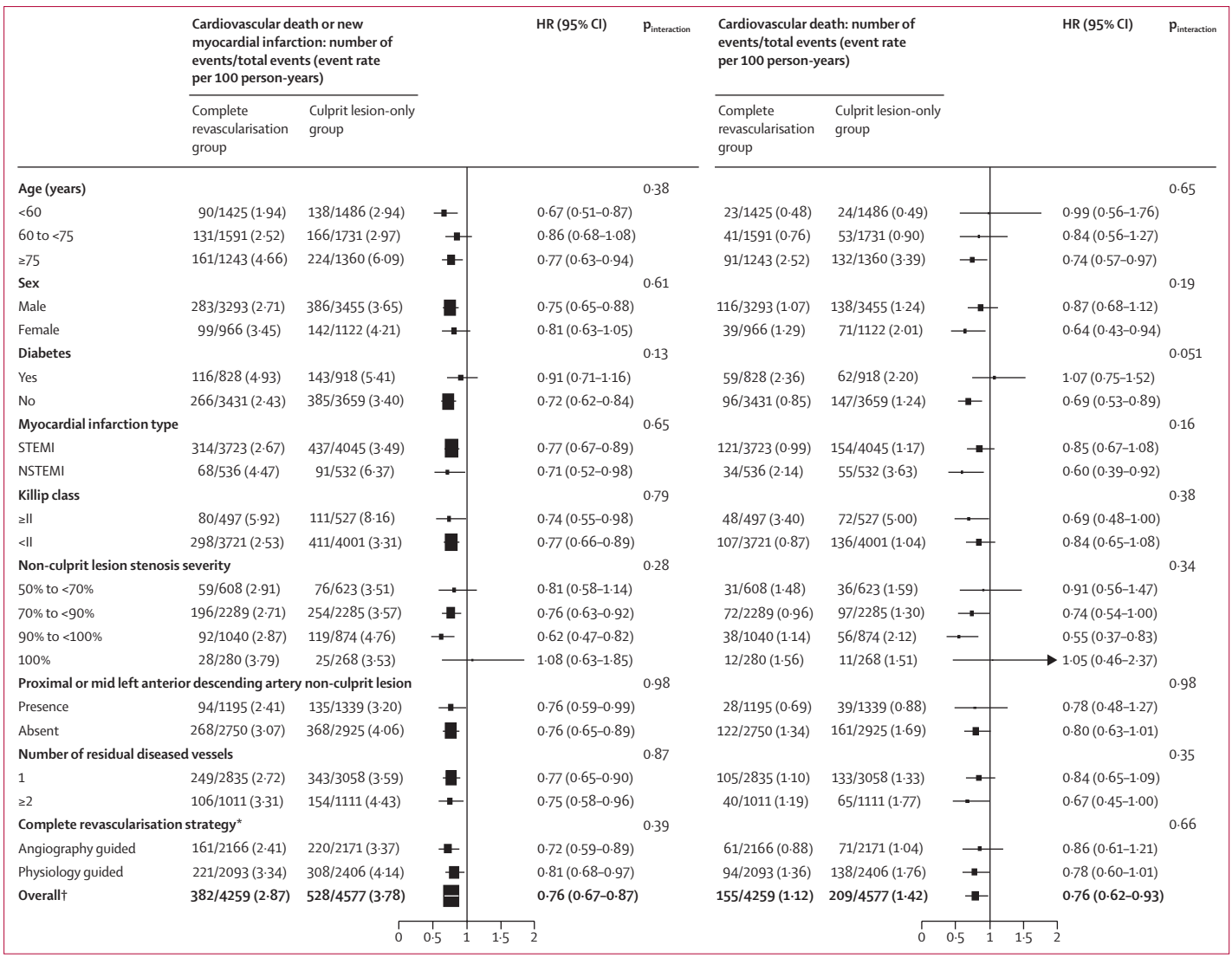

Figure 4: **Subgroup analyses of primary outcomes**
HR=hazard ratio. NSTEMI=non-ST-segment elevation myocardial infarction. STEMI=ST-segment elevation myocardial infarction. *Trial level. †Based on the random effects model.

figures 2C, 3C), with no evidence for heterogeneity ($p_{heterogeneity}$=0·15).

There was no difference in non-cardiovascular death between the groups (153 [3·6%] of 4259 patients in the complete revascularisation group *vs* 161 [3·5%] of 4577 patients in the culprit lesion-only group; HR 0·98 [95% CI 0·78–1·22], p=0·85; table 2; figures 2D, 3D), with no evidence of heterogeneity ($p_{heterogeneity}$=0·092). New myocardial infarction was reduced in the complete revascularisation group compared with the culprit lesion-only group (255 [6·0%] *vs* 357 [7·8%]; HR 0·76 [95% CI 0·65–0·90], p=0·0011; table 2; figures 2E, 3E), with no evidence of heterogeneity ($p_{heterogeneity}$=0·37).

We found consistent results for the two primary outcomes in all prespecified subgroups (figure 4). Specifically, there was no evidence of interaction in treatment effect according to age, sex, diabetes status, myocardial infarction type (STEMI *vs* NSTEMI), non-culprit lesion stenosis severity, presence versus absence of a proximal or mid left anterior descending artery non-culprit lesion, and one versus two residual non-culprit lesion vessels. There was also no evidence of interaction in trials using predominantly an angiography-guided versus a physiology-guided strategy (figure 4).

Discussion

This individual patient data meta-analysis involving 8836 patients from six multicentre randomised trials provides the largest and most comprehensive evidence on the effects of complete revascularisation versus a culprit

lesion-only PCI strategy in patients presenting with acute myocardial infarction and multivessel coronary artery disease. We found that a strategy of complete revascularisation reduced the composite of cardiovascular death or new myocardial infarction by about a quarter compared with a culprit lesion-only PCI strategy. In addition, we found that complete revascularisation reduced cardiovascular death alone by a similar relative magnitude and that complete revascularisation also reduced all-cause death. As expected, complete revascularisation had no effect on non-cardiovascular death.

With a relatively long follow-up of more than 3 years, we observed more than 900 cardiovascular deaths or new myocardial infarctions, which means that our individual patient data meta-analysis had much higher statistical power than in any single randomised trial to detect moderate differences between the groups. The results are robust for cardiovascular death or new myocardial infarction, with the HR of 0·76 having narrow 95% CIs. Moreover, with more than 350 cardiovascular deaths, our individual patient data meta-analysis was also able to detect clinically relevant reductions in this important outcome. Even the COMPLETE trial,[8] the largest randomised trial with more than 4000 patients, was underpowered to detect differences in cardiovascular death.[8] The one-quarter reduction in cardiovascular death is a new finding that extends the benefit of complete revascularisation to include this important outcome. Complete revascularisation for patients presenting with myocardial infarction is now one of the few clinical indications outside primary PCI for STEMI[17] for which a PCI-based strategy reduces cardiovascular mortality. The proportional HR reductions translate into a number needed to treat of 41 patients (95% CI 27–85) to prevent one cardiovascular death or new myocardial infarction and 99 patients (95% CI 53–593) to prevent one cardiovascular death over a period of 3 years. In addition to these benefits, we found a reduction in all-cause death favouring complete revascularisation.

The time-to-event curves show increasing divergence for all the main outcome events, including all-cause death, during 4 years of follow-up. This finding suggests that the treatment effect of complete revascularisation is durable and seems to increase with time. This benefit might have been due to the robust reduction in new myocardial infarctions, which includes both periprocedural and spontaneous infarctions. Similar long-term benefit of revascularisation was observed in the early trials of coronary artery bypass graft surgery versus medical management.[18] By design, the trials in this individual patient data meta-analysis were open label, making non-fatal outcomes potentially subject to reporting bias.[19,20] The reduction in all-cause death, the most objective of outcomes, is therefore reassuring. Furthermore, the benefit observed is in addition to guideline-directed medical therapy, including a high proportion of patients discharged on dual antiplatelet therapy, statins, angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, or β-blockers.

The larger sample size in this individual data meta-analysis also provided greater confidence in evaluating the effect of complete revascularisation for consistency in important subgroups. With regard to age, our data extend results from previous studies[21] and an individual patient data meta-analysis in patients aged 75 years or older,[22] showing consistent benefit across the full age range, including in patients younger than 60 years. Our data also gave us greater statistical power to show consistent treatment effects between sexes, a reassuring finding as women are systematically under-represented in clinical trials, generally comprising less than 25% of patients. The benefit of complete revascularisation was consistent among patients with STEMI and NSTEMI, with sparse data for NSTEMI available from randomised trials.[23] The benefit of complete revascularisation was consistent for patients with, compared with those without, a non-culprit proximal or mid left anterior descending artery lesion, similar to what was observed in at least one trial.[24]

The trials in this analysis included immediate and staged non-culprit lesion PCI timing, each compared with a culprit lesion-only PCI strategy, rather than direct comparisons according to timing. In the COMPLETE trial, randomisation was stratified for the intended timing of non-culprit lesion staged PCI, and consistent benefits of complete revascularisation were observed regardless of timing.[25] Three trials have directly compared immediate versus staged non-culprit lesion PCI, with two trials finding non-inferiority of a staged procedure with immediate non-culprit lesion PCI[26,27] and a third more recent trial finding no difference.[28] Importantly, none of the trials demonstrated differences in cardiovascular death according to timing of non-culprit lesion PCI.

Two trials in this meta-analysis used predominantly an angiography-guided strategy[5,8] and four trials used a physiology-guided strategy employing fractional flow reserve (FFR).[6,7,9,10] We found consistent benefit for both strategies on the primary outcomes. Although each strategy has shown benefit compared with a culprit lesion-only PCI strategy,[11] there remains uncertainty as to which of these strategies is the preferred approach.[29] Two trials[30,31] have directly compared angiography-guided and physiology-guided complete revascularisation strategies, with mixed results. A physiology-guided strategy avoids unnecessary PCI in about 40–50% of patients, thereby improving outcomes.[32] However, a substantial proportion of non-culprit lesions are thin-capped fibroatheromas,[33] a plaque phenotype that is more prone to future plaque rupture resulting in clinical events,[34,35] even in FFR-negative lesions.[36] The COMPLETE-2 trial (NCT05701358) is comparing these strategies in a large-scale, multinational trial involving more than 5000 patients, including use of optical coherence tomography to characterise non-culprit lesion plaque phenotype in 1500 of these patients. In the

meantime, on the basis of the results of this individual patient data meta-analysis, both physiology-guided and angiography-guided non-culprit lesion PCI strategies are reasonable options.

Limitations of our study merit consideration. We had to exclude one modest-sized trial because the principal investigator declined to participate.[4] This trial reported 14 cardiovascular deaths (four in the complete revascularisation group and ten in the culprit lesion-only group) and 27 myocardial infarctions (seven in the complete revascularisation group and 20 in the culprit lesion-only group). We performed a sensitivity analysis including this trial, and it demonstrated consistent results with our primary analysis (appendix p 4). Second, the definition of myocardial infarction differed slightly in individual trials. Because all trials were randomised and had adjudication committees masked to treatment allocation, the risk of bias was low. Importantly, we also found reductions in cardiovascular death and all-cause death, events that are less subject to bias. Third, although fewer patients with NSTEMI (n=1068) were included than those with STEMI (n=7768), the results were consistent showing reductions in both primary outcomes in both groups. Nevertheless, additional trials in patients with NSTEMI are warranted.

In summary, the results of this individual patient data meta-analysis showed that, compared with culprit lesion-only PCI, complete revascularisation reduced both the composite of cardiovascular death or new myocardial infarction, and most importantly that of cardiovascular death alone, each by about a quarter. In addition, complete revascularisation reduced all-cause death. These data provide the strongest and most robust evidence to date that complete revascularisation improves important clinical outcomes in patients with acute myocardial infarction and multivessel coronary artery disease.

Contributors

SRM, FB, SB, GCam, PCS, and TE conceived the study. SRM and CR supervised the study. SRM wrote the first draft of the manuscript. All authors contributed to methodology, and review, and editing of the manuscript. DTWT performed the search strategy, wrote the first draft of the protocol, and performed study quality review. DTWT and SRM selected the studies. SRM, DTWT, and HN contributed to project administration. Data curation and validation was performed by SRM (COMPLETE trial), FB (Complete Revascularisation Trialists' Collaboration individual patient data meta-analysis), SB (FIRE trial), GCam (FIRE trial), SJ (FULL REVASC trial), PCS (Compare-Acute trial), DG (Compare-Acute trial), GPM (CvLPRIT trial), AB (CvLPRIT trial), DEH (DANAMI-3–PRIMULTI trial), CR (Complete Revascularisation Trialists' Collaboration individual patient data meta-analysis), DAW (COMPLETE trial), HN (Complete Revascularisation Trialists' Collaboration individual patient data meta-analysis), JAC (COMPLETE trial), and TE (DANAMI-3–PRIMULTI trial). CR and FRK performed statistical analyses. CR and FRK accessed and verified the data. All authors had access to all the included data and the corresponding author had final responsibility for the decision to submit to publication.

Declaration of interests

SRM has received an institutional grant from Abbott and consulting fees from Amgen, Janssen, Merck, Novartis, and Novo Nordisk, outside of the submitted work. GPM has received research grants from the British Heart Foundation and the UK National Institute for Health and Care Research, and research support from Circle CVI, outside of the submitted work. GCam has received research grants from Sahajanand Medical Technologies (SMT), Abbott, and Siemens, and honoraria from Menarini, Daichii, Amgen, Abbott, and Sanofi, as well as support for attending meetings from Menarini, Abbott, and Daichii, outside of the submitted work. PCS has received research grants from Abbott Vascular and SMT, consulting fees from Abbott Vascular, Microport, and Terumo, and lecture fees from SMT and Elixer Medical Corporation, outside of the submitted work; is a data safety monitoring board (DSMB) member for the LEGACY and PROCTOR trials, outside of the submitted work; and is a minor share holder of CERC, outside of the submitted work. FB has received institutional research grants from Abbott and Boston Scientific for the FULL REVASC trial and is Chairman of the Swedish Coronary Angiography and Angioplasty Registry, outside of the submitted work. SJ has received institutional research grants from Amgen, Novo Nordisk, Merck, AstraZeneca, Elixir, Medtronic, and Edwards, and honoraria from Medtronic, outside of the submitted work. JAC has received research grants from Edwards Laboratories and participated as a DSMB member for the ASPIRE-AF, CLARITY, CODE-MI, EpiROC, LAAOS IV, and OCEAN trials, outside of the submitted work. SB has received research grants from SMT, Siemens, and Abbott, and honoraria from SMT and Medis, outside of the submitted work. TE has received speaker fees from Novo Nordisk, Abbott Vascular, and Boston Scientific, and served on advisory boards for Novo Nordisk and Abbott Vascular, outside of the submitted work. All other authors declare no competing interests.

Data sharing

Requests for data sharing will be considered pending review and approval of the Complete Revascularisation Trialists' Collaboration steering committee and the principal investigators of the included trials. Requests for data should be made to the corresponding author.

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