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Percutaneous coronary invervention versus coronary artery bypass grafting: A meta-analysis

Yolba Smit, MD, MSc,[a] Joan Vlayen, MD,[b] Hetty Koppenaal, MD, MPH,[c] Frank Eefting, MD,[d] Arie Pieter Kappetein, MD, PhD,[e] and Massimo A. Mariani, MD, PhD[f]

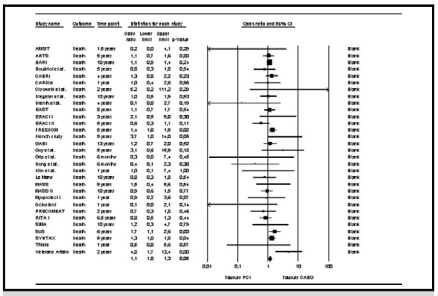
ABSTRACT

Objective: To compare the effectiveness of percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG) in patients with coronary artery disease.

Methods: MEDLINE, Embase, and Cochrane Central were searched, and randomized controlled trials were included. Outcomes were assessed at maximum available follow-up.

Results: This meta-analysis includes 31 trials with 15,004 patients. As regards death, more patients died after PCI compared with CABG across all types of patients (odds ratio [OR], 1.1; 95% confidence interval [CI], 1.0-1.3; $P = .05$) as well as in patients with multivessel disease (OR, 1.2; 95% CI, 1.0-1.4; $P = .02$) or diabetes (OR, 1.6; 95% CI, 1.2-2.1; $P < .01$). Myocardial infarction occurred as frequently after PCI (OR, 1.2; 95% CI, 0.9-1.5; $P = .28$). Repeat revascularization was more common after PCI (OR, 4.5; 95% CI, 3.5-5.8; $P < .01$), with a progressive decline in ORs from the pre-stent era (OR, 7.0; 95% CI, 5.1-9.7; $P < .01$), to the bare metal stent era (OR, 4.5; 95% CI, 3.6-5.5; $P < .01$), and to the drug-eluting stent era (OR, 2.5; 95% CI, 1.8-3.4; $P < .01$). Stroke was more common after CABG (OR, 0.7; 95% CI, 0.5-0.9; $P = .01$).

Conclusions: Compared with PCI, CABG had a lower risk of death in multivessel disease or diabetes patients eligible for either intervention, a lower risk of repeat revascularization, but a higher risk of stroke. (J Thorac Cardiovasc Surg 2015;149:831-8)



Meta-analysed odds ratio for death after PCI or CABG at the latest available follow-up.

Central Message

We conducted a meta-analysis comparing the effectiveness of PCI to CABG in 31 trials on 15,004 patients. Compared to PCI, CABG had a lower risk of death in patients with multivessel disease or diabetes, and a lower risk of repeat revascularization and a higher risk of stroke in all patients.

Author Perspective

This paper supports current thoughts in myocardial revascularization directed to reconsider the role of surgical myocardial revascularization in patients with extensive coronary artery disease, particularly when affected by diabetes. On the other hand, this paper confirms that additional effort should be put in lowering the risk of perioperative neurologic complications in surgical myocardial revascularization because stroke is a rare but devastating and invalidating complication. Off-pump and aortic "no-touch" techniques may play a role in this perspective.

See Editorial Commentary pages 839-40.

Supplemental material is available online.

Revascularization for coronary artery disease can be performed with coronary artery bypass grafting (CABG) or percutaneous coronary intervention (PCI). For more than 20 years, trials have compared the effectiveness and safety of PCI versus CABG. The first trials compared balloon angioplasty to CABG. Improved technology has made it possible to treat increasingly complex lesions with PCI. At the same time, the outcome of CABG has improved because of better perioperative care and extended use of arterial revascularization. After the introduction of bare metal stents, several trials compared PCI with CABG in patients with multivessel disease. More recently, data from randomized trials of drug-eluting stents have shown significant reductions in the rate of repeat interventions with respect to bare metal stents. The latest trials therefore focused on PCI with drug-eluting stents versus CABG.

Earlier meta-analyses of randomized controlled trials (RCTs) comparing PCI versus CABG have been undertaken

From Independent Researcher,[a] Leuth, The Netherlands; ME-TA,[b] Rotselaar, Belgium; Independent Researcher,[c] Vlissingen, The Netherlands; Department of Cardiology,[d] St Antonius Hospital, Nieuwegein, The Netherlands; Department of Cardiothoracic Surgery,[e] Erasmus Medisch Centrum, Rotterdam, The Netherlands; and Department of Cardiothoracic Surgery,[f] University Medical Centre Groningen, University of Groningen, Groningen, The Netherlands.

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Address for reprints: Massimo A. Mariani, MD, PhD, Department of Cardiothoracic Surgery, University Medical Center Groningen, University of Groningen, P.O. Box 30.001, 9700 RB Groningen, The Netherlands (E-mail: m.mariani@umcg.nl).

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Abbreviations and Acronyms

AMIST = Angioplasty versus Minimally Invasive Surgery Trial
ARTS = Arterial Revascularization Therapies Study
AWESOME = Angina With Extremely Serious Operative Mortality Evaluation
BARI = Bypass Angioplasty Revascularization Investigation
CABG = coronary artery bypass grafting
CABRI = Coronary Angioplasty versus Bypass Revascularisation Investigation
CAD = coronary artery disease
CARDia = Coronary Artery Revascularization in Diabetes
CI = confidence interval
EAST = Emory Angioplasty versus Surgery Trial
EXCEL = Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization
ERACI I = Argentine Randomized Trial of Percutaneous Transluminal Coronary Angioplasty Versus Coronary Artery Bypass Surgery in Multivessel Disease
ERACI II = Argentine Randomized Trial of Coronary Angioplasty With Stenting Versus Coronary Bypass Surgery in Patients with Multiple Vessel Disease trial
FREEDOM = Future REvascularization Evaluation in patients with Diabetes mellitus: Optimal management of Multivessel disease
GABI = German Angioplasty Bypass Surgery Investigation
LAD = left anterior descending coronary artery
LMCA = left main coronary artery
MASS = Medicine, Angioplasty, or Surgery Study
OR = odds ratio
PCI = percutaneous coronary intervention
PRECOMBAT = Premier of Randomized Comparison of Bypass Surgery versus Angioplasty Using Sirolimus-Eluting Stent in Patients with Left Main Coronary Artery Disease
RCT = randomized controlled trial
RITA = Randomised Intervention Treatment of Angina
SIMA = Stenting versus Internal Mammary Artery grafting trial
SYNTAX = Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery

with the purpose of evaluating both treatment modalities. These meta-analyses either are now outdated[E1-E3] or present only part of the picture, as they looked at particular disease categories,[E4-E10] specific types of surgery or PCI,[E1,E7,E11] or specific patients.[E12] Individual patient data meta-analyses have the advantage that time-to-event curves can be produced, and analyses of effects in clinically important subgroups can be estimated. However, they are limited by the willingness and/or ability of research groups to participate and share data.[E13-E15]

The present meta-analysis aims to compare the effectiveness and safety of PCI and CABG in patients for whom coronary revascularization is clinically indicated.

METHODS

Search Strategies

We used Cochrane systematic review methods to identify RCTs that met the inclusion criteria. MEDLINE, Embase, and Cochrane Central were searched on December 18, 2013, using text words and medical subheadings. Searches were limited to studies published from 1996 onwards, published in English, and undertaken in humans. Because of continuous improvement of techniques, devices, and medical treatment, studies published before 1996 were considered too old to have policy implications for current clinical practice. References of meta-analyses, reviews, and selected articles were scanned for additional RCTs. The websites www.controlled-trials.com and clinicaltrial.gov were searched for running and unpublished trials, and when such trials were found, the Internet was searched for preliminary or early results. Two databases (Database of Abstracts of Reviews of Effects and the Health Technology Assessment database) were searched via http://www.crd.york.ac.uk/crdweb/.

Inclusion Criteria

Studies were included if they concerned an RCT comparing PCI (with or without stenting) to CABG and if the trial participants were adults with stable or unstable angina, and had single-vessel or multivessel coronary disease.

Study Selection and Quality Criteria

Two reviewers (YS and HK or JV) independently selected the studies; discrepancies were resolved by consensus. Selected trials were assessed for their methodological quality (adequacy of randomization, adequacy of the allocation concealment, the potential for selection bias after allocation and the adequacy of masking) by 2 reviewers (YS and HK or JV) using a scheme based on Schulz et al, which was used in Cochrane reviews on CABG and PCI.[E1,E16,E17]

Data Extraction

Data were extracted by one reviewer (YS) and checked by a second (HK or JV). Events of interest included the primary outcome measures (all-cause death, myocardial infarction, repeat revascularization, and stroke), secondary outcome measures (cardiac death and angina-free survival), general characteristics of the included studies, and data on study participants (eg, type of

vessel involvement). For outcomes, the numerator was the number of events reported; the denominator was the number of patients assigned to a treatment arm (intention-to-treat principle). For myocardial infarction, the number of nonfatal infarctions was taken and, when not available, the number of nonfatal Q-wave infarctions, myocardial infarctions, or myocardial Q-wave infarctions was taken (in that order). For repeat revascularization, the number of procedures was taken and, when not available, the number of patients with a repeat revascularization was taken. When the number of repeat revascularizations was not available, the number of repeat target vessel revascularizations was taken. For angina-free survival, either the number of patients reported to be angina-free was taken or the number of patients with angina was subtracted from the total number of patients minus the dead. For stroke, the number of patients with a nonfatal stroke at follow-up was taken. If not available, the number of patients with a stroke was taken. Data were extracted separately for all reported time points of follow-up (eg, at 1, 2, and 5 years of follow-up), and for the clinical significant subgroup of patients with diabetes.

Data Analysis

Medians were calculated as the middle number in a list of ordered numbers, as a summary statistic for the proportion of screened patients (patients assessed for eligibility) that were included in trials, the proportion of patients lost to follow-up, and the proportion of off-pump CABG in trials that used a mix of on-pump and off-pump techniques. Meta-analyzed outcomes were assessed at maximum available follow-up, unless otherwise specified. Outcomes were presented as odds ratios (ORs) with the corresponding 95% confidence intervals (CIs). A *P* value of .05 or smaller was considered statistically significant. A continuity correction of 0.5 was applied in case of zero events in 1 treatment arm. Meta-analyzed results were described using a random effects model. Heterogeneity was assessed with the χ^2 Q statistic, and the I^2 metric with its 95% CIs.[E18] Values of I^2 $\geq$75% suggest very large heterogeneity beyond chance, in which case meta-regression (method of moments) was applied to explore reasons for heterogeneity. Outcomes were also meta-analyzed according to the type of PCI that was evaluated: the pre-stent era (no stents used in the majority of patients, up to 1993); the bare metal stent era (bare metal stents used in the majority of patients, 1994-2001); and the drug-eluting stent era (drug-eluting stents used in the majority of patients, from 2002 onwards). We performed sensitivity analyses excluding studies in which a substantial minority (10% or more) of patients received a different type of PCI, for example, in a trial in the bare metal stent era 90% of patients were treated with bare metal stents and 10% of patients were treated with drug-eluting stents. Although CABG has evolved as well across these time periods—with a greater use of arterial conduits, off-pump surgery, and minimally invasive surgical techniques—this evolvement is not captured as unequivocal in different eras. In addition, meta-analysis of outcomes at time periods of 6 months, 1 year, 1.5 to 2 years, 2.5 to 3 years, 4 years, and 5 years of follow-up was performed for the primary outcomes. Meta-analyses of primary outcomes were performed separately for trials reporting on different types of vessel disease and for trials using either off-pump or on-pump CABG exclusively. For the subgroup analyses of off-pump versus on-pump CABG, we excluded trials from the pre-stent era, as none of these trials used off-pump CABG. In addition, we performed meta-analyses of primary outcomes for diabetes patients (either trials that exclusively included patients with diabetes or trials that reported on subgroups of patients with diabetes). Funnel plots were constructed and the Duval and Tweedie's trim and fill test was applied to examine publication bias. We undertook sensitivity analyses of subgroups with different quality assessment scores. Analyses were performed using Comprehensive Meta-Analysis software, version 2.0 (Biostat, Englewood, NJ). Stata, version 10.0 (StataCorp, College Station, Tex) was used to calculate 95% CI for frequencies not provided in original publications and the 95% CI of I^2.[E19] Microsoft Office Excel 2007 was used for graphs picturing meta-analyzed ORs per time period of follow-up. The ORs given are always for PCI versus CABG.

Role of the Funding Source

The sponsor of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

RESULTS

A total of 4837 records were screened out of which 302 articles were selected for full text review. From these 302 articles, 31 RCTs were selected for inclusion, and data from 91 articles pertaining to these trials were used in the meta-analyses.[E20-E110] If multiple articles were available on a single study, we would only use the most recent or most comprehensive article, unless data for different time periods of follow-up or for different subgroups of patients were not reported in these articles. A flow diagram in Appendix E1 shows the search and selection process. The Angina With Extremely Serious Operative Mortality Evaluation (AWESOME) trial was excluded because patients with medically refractory unstable ischemia and a high risk of adverse outcomes were involved,[E111-E117] whereas the 31 selected RCTs had strict exclusion criteria for patients with a recent myocardial infarction, a previous PCI or CABG, low left ventricular ejection fraction, or serious comorbidity.

Characteristics

The 31 RCTs included a total of 15,004 randomized patients (Table 1). One more trial of drug-eluting stents versus CABG is running at present, the Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization (EXCEL) trial, but its results have not been published to date.[E118] Nine trials (5200 patients) were conducted in the pre-stent era, 14 trials (4276 patients) in the bare metal stent era, and 8 trials (5528 patients) in the drug-eluting stent era. Mixed PCI treatments did not occur in the pre-stent era. However, in 5 out of 14 trials conducted in the bare metal stent era, more than 10% of patients randomized to PCI were treated with either angioplasty alone (13% of patients randomized to PCI in the Arterial Revascularization Therapies Study [ARTS] trial, 30% in the Argentine Randomized Trial of Coronary Angioplasty With Stenting Versus Coronary Bypass Surgery in Patients with Multiple Vessel Disease [ERACI II] trial, 28% in the Medicine, Angioplasty, or Surgery Study [MASS] II trial, and 22% in the Stent or Surgery [SoS] trial) or with drug-eluting stents (35% of patients randomized to PCI in the le Mans trial). In the Coronary Artery Revascularization in Diabetes (CARDia) trial, 31% of patients randomized to PCI were treated with bare metal stents and 69% with drug-eluting stents (this trial was categorized in the drug-eluting stent era). PCI and CABG were compared in patients with multivessel disease (n = 12), proximal left anterior descending coronary artery (LAD) stenosis (n = 11), patients with main stem stenosis (n = 4), a combination of patients with single- or multivessel disease (n = 2), or 3-vessel or left main coronary artery stenosis (n = 2). Trials included a median of 7.8% of screened patients (range, 2.0%-61%). Follow-up was available from

TABLE 1. Characteristics of 31 PCI versus CABG trials, per treatment era

Trial name (references used)	Trial characteristics	Enrolment period	Number of patients included	% Of screened patients enrolled	% Loss to follow-up	Latest follow-up available (y)	Main patient characteristic	% Off-pump CABG	Data on diabetes patients
Pre-stent era			5200						
BARI[E20-E28]	Multicenter, United States and Canada	1988-1991	1829	7.3	2.8	10	Multivessel CAD	0	Yes
CABRI[E29-E32]	Multicenter, Europe	1988-1992	1054	na	0.4	4	Multivessel CAD	0†	Yes
EAST[E33-E36]	Single-center, United States	1987-1990	392	7.7	0	8	Multivessel CAD	0	Yes
ERACI I[E37,E38]	Single-center, Argentina	1988-1990	127	17.0	1.6	3	Multivessel CAD	0	No
French Monocentric Study[E39]	Single-center, France	1989-1993	152	7.8	na	5	Multivessel CAD	0	No
GABI[E40,E41]	Multicenter, Germany	1986-1991	359	4.0	0.5	13	Multivessel CAD	0	No
Goy et al[E42,E43]‡	Single-center, Switzerland	1989-1993	134	2.6	na	5	Proximal LAD stenosis	0	No
MASS I[E44,E45]	Single-center, Brazil	1988-1991	142	na	na	5	Proximal LAD stenosis	0	No
RITA I[E46-E50]	Multicenter, United Kingdom	1988-1991	1011	4.4	0	6.5	Single- or multivessel CAD	0†	Yes
Bare metal stent era			4276						
AMIST[E51]§	Multicenter, United Kingdom	1999-2001	100	9.2	8.0	1.5	Proximal LAD stenosis	100	No
ARTS[E52-E59]‖	Multicenter, international	1997-1998	1205	na	1.7	5	Multivessel CAD	0	Yes
Cisowski et al[E60,E61]	Single-center, Poland	2000-2001	100	na	0	2	Proximal LAD stenosis	100	No
Diegeler et al[E62-E64]	Single-center, Germany	1997-2001	220	na	3.6	10	Proximal LAD stenosis	100	No
Drenth et al[E65-E68]	Single-center, The Netherlands	1997-1999	102	na	0	4	Proximal LAD stenosis	100	No
ERACI II[E69,E70]¶	Multicenter, Argentina	1996-1998	450	16.3	0	5	Multivessel CAD	0†	Yes
Grip et al[E71]	Single-center, Sweden	2001	53	na	0	0.5	Proximal LAD stenosis	100	No
Kim et al[E72]	Single-center, South Korea	2000-2001	100	na	na	1	Proximal LAD stenosis	100	No
Le Mans[E73,E74]#	Multicenter, Poland	2001-2004	105	30.3	0	10	Main stem stenosis	0	No
MASS II[E75-E80]**	Single-center, Brazil	1995-2000	408	2.0	0	10	Multivessel CAD	0	Yes
Myoprotect[E81]	Single-center, Germany	1998-2001	44	na	na	1	Main stem stenosis††	19	No
Octostent[E82-E84]	Multicenter, The Netherlands	1998-2000	280	na	na	7.5	Single- or multivessel CAD	100	No
SIMA[E85,E86]	Multicenter, Europe	1994-1998	121	na	0	10	Proximal LAD stenosis	10	No
SoS[E87-E90]‡‡	Multicenter, Canada and Europe	1996-1999	988	na	0.8	6	Multivessel CAD	3	Yes
Drug-eluting stent era			5528						
Boudriot et al[E91,E92]	Multicenter, Germany	2003-2009	201	46.7	0.5	5	Main stem stenosis	46	No
CARDia[E93]§§	Multicenter, United Kingdom and Ireland	2002-2007	510	na	3.9	1	Diabetes patients with multivessel CAD	31	Yes
FREEDOM[E94-E96]	Multicenter, international	2005-2010	1900	5.8	±1	5	Diabetes patients with multivessel CAD	18.5	Yes
Hong et al[E97]	Single-center, South Korea	2003	189	na	0.8	0.5	Proximal LAD stenosis	100	No
PRECOMBAT[E98]	Multicenter, South Korea	2004-2009	600	41.3	0	2	Main stem stenosis	64	No
SYNTAX[E99-E108]	Multicenter, international	2005-2007	1800	41.5	0.7	5	3-vessel or LMCA stenosis	15	Yes
Thiele et al[E109]‖‖	Single-center, Germany	2003-2007	130	61.0	0	1	Proximal LAD stenosis	100	No
Veterans Affairs[E110]	Multicenter, United States	2006-2010	198	3	na	2	Diabetes patients with severe CAD¶¶	na	Yes

CABG, Coronary artery bypass graft; *BARI*, Bypass Angioplasty Revascularization Investigation; *CAD*, coronary artery disease; *CABRI*, Coronary Angioplasty versus Bypass Revascularisation Investigation; *na*, not available; *EAST*, Emory Angioplasty versus Surgery Trial; *ERACI I*, Argentine Randomized Trial of Percutaneous Transluminal Coronary Angioplasty Versus Coronary Artery Bypass Surgery in Multivessel Disease; *GABI*, German Angioplasty Bypass Surgery Investigation; *LAD*, left anterior descending coronary artery; *MASS*, Medicine, Angioplasty, or Surgery Study; *RITA*, Randomised Intervention Treatment of Angina; *AMIST*, Angioplasty versus Minimally Invasive Surgery Trial; *ARTS*, Arterial Revascularization Therapies Study; *ERACI II*, Argentine Randomized Trial of Coronary Angioplasty With Stenting Versus Coronary Bypass Surgery in Patients with Multiple Vessel Disease; *SIMA*, Stenting versus Internal Mammary Artery grafting trial; *SoS*, Stent or Surgery Trial; *CARDia*, Coronary Artery Revascularization in Diabetes; *FREEDOM*, Future REvascularization Evaluation in patients with Diabetes mellitus: Optimal management of Multivessel disease; *PRECOMBAT*, Premier of Randomized Comparison of Bypass Surgery versus Angioplasty Using Sirolimus-Eluting Stent in Patients with Left Main Coronary Artery Disease; *SYNTAX*, Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery; *LMCA*, left main coronary artery. †Not reported, assumed to be 0%. ‡3% of patients randomized to PCI were treated with a bare metal stents. §2% of patients randomized to PCI were treated with angioplasty. ‖13% of patients randomized to PCI were treated with angioplasty. ¶30% of patients randomized to PCI were treated with angioplasty. #35% of patients randomized to PCI were treated with drug-eluting stents. **28% of patients randomized to PCI were treated with angioplasty. ††Main stem or main stem equivalent lesions. Main-stem-equivalent lesions were defined as a leading proximal LAD stenosis or stenosis of an LAD bypass (≥75%) with a concomitantly documented proximal occlusion of the right coronary artery and/or the left circumflex artery. ‡‡22% of lesions of patients randomized to PCI were treated with angioplasty. §§Drug-eluting stents used in 69% of patients randomized to PCI and bare metal stents in 31% of patients. ‖‖Bare metal stents used in 5% of patients randomized to PCI. ¶¶Either multivessel disease including the left anterior descending coronary artery or isolated proximal left anterior descending coronary artery disease.

TABLE 2. Meta-analyzed ORs for outcomes at the latest available follow-up and per era, PCI versus CABG

Outcome	OR (95% CI)	*P* value	n	I^2 (95% CI), %	*P* value heterogeneity
Mortality	1.1 (1.0-1.3)	.05	31	21.4 (0-50)	.15
Pre-stent era	1.2 (1.0-1.3)	.06	9	0 (0-65)	.48
Bare metal stent era	1.0 (0.8-1.3)	.95	14	12.5 (0-51)	.32
Drug-eluting stent era	1.2 (0.9-1.7)	.21	8	43.8 (0-75)	.09
Myocardial infarction	1.2 (0.9-1.5)	.28	28	59.1 (38-73)	<.01
Pre-stent era	1.2 (0.8-1.8)	.43	7	49.8 (0-79)	.06
Bare metal stent era	0.9 (0.6-1.4)	.78	13	29.9 (0-64)	.15
Drug-eluting stent era	1.4 (0.9-2.4)	.18	8	65.0 (25-84)	<.01
Repeat revascularization	4.5 (3.5-5.8)	<.01*	31	78.3 (70-84)	<.01
Pre-stent era	7.0 (5.1-9.7)	<.01	9	69.6 (39-85)	<.01
Bare metal stent era	4.5 (3.6-5.5)	<.01	14	11.1 (0-49)	.33
Drug-eluting stent era	2.5 (1.8-3.4)	<.01	8	47.1 (0-76)	.07
Stroke	0.7 (0.5-0.9)	.01	12	0 (0-58)	.67
Pre-stent era	1.0 (0.1-15.8)	.98	1	0†	1.00
Bare metal stent era	0.9 (0.6-1.4)	.59	5	0 (0-79)	.42
Drug-eluting stent era	0.6 (0.4-0.8)	<.01	6	0 (0-75)	.84
Cardiac mortality	1.2 (0.9-1.6)	.13	15	27.3 (0-61)	.16
Pre-stent era	1.2 (0.9-1.5)	.18	6	0 (0-75)	.81
Bare metal stent era	1.1 (0.7-1.7)	.82	6	35.0 (0-74)	.17
Drug-eluting stent era	1.3 (0.6-3.2)	.50	3	63.7 (0-90)	.06
Angina-free survival	0.7 (0.6-0.9)	.01	16	60.9 (33-77)	<.01
Pre-stent era	0.7 (0.6-0.9)	<.01	4	8.2 (0-86)	.35
Bare metal stent era	0.7 (0.5-1.0)	.03	10	68.9 (40-84)	<.01
Drug-eluting stent era	1.2 (0.8-1.7)	.40	2	0†	.47

OR, Odds ratio; *CI*, confidence interval; *n*, number of studies included in the analysis. *<.00000001. †95% CI for I^2 cannot be calculated for a meta-analysis of 1 or 2 studies.

0.5 to 13 years (median, 5 years) with a median loss to follow-up of 0.5% (range, 0%-8.0%). Arterial conduits were used ranging from 37% to 100% of all grafts. Thirteen trials exclusively used on-pump operating techniques; 9 trials exclusively used off-pump operating techniques; and 8 trials used a mix of on- and off-pump operating techniques, with a median of 18.8% (range, 3%-64%) off-pump use across these trials. For 1 trial, information on the operating technique was not available.

Trial Quality

All trials randomized patients; 12 out of 31 trials specifically mentioned the use of computer-generated random numbers or random number tables. The other 19 trials did not mention the sequence-generation method. Fourteen out of 31 trials reported adequate procedures to conceal allocation. Twenty-nine out of 31 studies had few exclusions after randomization, whereas none of the trials was triple blind (with blinding of participants, health care providers, and outcome assessors). In 9 of the 31 trials, the outcome assessors were blinded; in 22 of the 31 trials, no blinding at all occurred. Trial quality is presented in detail in a table in Appendix E1.

Meta-Analysis of Outcomes Across All 31 Selected Trials, per Era and per Time Period of Follow-up

Table 2 gives an overview of the outcomes at the latest available follow-up (forest plots are shown in Appendix E1). The odds for mortality were higher for PCI compared to CABG across all studies (OR, 1.1; 95% CI, 1.0-1.3; $P = .05$), but not in each era separately. The odds for myocardial infarction did not differ significantly (OR, 1.2; 95% CI, 0.9-1.5; $P = .28$) across all studies and eras, nor in each era separately. Repeat revascularization was more common across all eras (OR, 4.5; 95% CI, 3.5-5.8; $P < .01$) and in each era separately. The large heterogeneity across all eras ($I^2 = 78.3\%$) was due to a decline in the ORs for repeat revascularization, with progressively less difference in ORs from the pre-stent era to the drug-eluting stent era (in meta-regression, there was interaction between the year of the study's start and the OR for repeat revascularization (coefficient, −0.06 (95% CI, −0.08 to −0.03; $P < .01$). The odds for stroke were lower after PCI compared to CABG across all eras (OR, 0.7; 95% CI, 0.5-0.9; $P = .01$) and in the drug-eluting stent era (OR, 0.6; 95% CI, 0.4-0.8; $P < .01$), but not in the bare metal stent era (only 1 trial provided data on the outcome stroke in the pre-stent era). Cardiac mortality was as common after PCI across all eras (OR, 1.2; 95% CI, 0.9-1.6; $P = .13$). Angina-free survival was less common after PCI (OR, 0.7; 95% CI, 0.6-0.9; $P = .01$) across all eras and in the pre-stent and stent eras, but not in the drug-eluting stent era.

We found no evidence of publication bias for the main outcomes across all studies, neither on visual inspection nor by using Duval and Tweedie's trim and fill test. Sensitivity analyses did not give evidence of a differential

TABLE 3. Meta-analyzed ORs for outcomes in patients with different types of vessel disease at the latest available follow-up across all eras, PCI versus CABG

Outcome	OR (95% CI)	*P* value	n	I^2 (95% CI), %	*P* value heterogeneity
Mortality					
Multivessel disease	1.2 (1.0-1.4)	.02	12	18.3 (0-58)	.26
Proximal LAD stenosis	1.0 (0.7-1.6)	.95	11	0 (0-60)	.61
Main stem stenosis	0.8 (0.5-1.2)	.27	4	0 (0-85)	.99
Myocardial infarction					
Multivessel disease	1.1 (0.8-1.6)	.6	10	71.2 (45-85)	<.01
Proximal LAD stenosis	1.2 (0.6-2.4)	.55	10	35 (0-69)	.13
Main stem stenosis	1.4 (0.5-3.7)	.48	4	0 (0-85)	.58
Repeat revascularization					
Multivessel disease	5.6 (4.2-7.4)	<.01	12	77.3 (61-87)	<.01
Proximal LAD stenosis	5.7 (3.5-9.1)	<.01	11	10.1 (0-50)	.39
Main stem stenosis	2.8 (1.7-4.5)	<.01	4	0 (0-85)	.63
Stroke					
Multivessel disease	0.6 (0.4-1.1)	.11	4	46.9 (0-82)	.13
Proximal LAD stenosis	1.2 (0.2-6.9)	.83	3	0 (0-90)	.47
Main stem stenosis	0.4 (0.1-1.8)	.23	3	0 (0-90)	.87

OR, Odds ratio; *CI*, confidence interval; *n*, number of studies included in the analysis; *LAD*, left anterior descending coronary artery.

effect in studies with different quality scores in the domains of randomization, concealment, and blinding, nor was there a differential effect when studies in which 10% or more of patients were treated with a different type of PCI were excluded (data not shown).

In the analyses of the main outcomes at different time points of follow-up, at 5 years of follow-up, significantly fewer patients died after CABG, compared to PCI (OR, 1.3; 95% CI, 1.1-1.5; $P < .01$) (see Appendix E1 for figures of the primary outcomes meta-analyzed at 0.5, 1, 1.5-2, 2.5-3, 4, and 5 years). At 1 to 4 years of follow-up, the ORs for death were hovering around 1; at 6 months, the OR for death was 0.6 (95% CI, 0.2-1.7; $P = .31$). After 4 and 5 years of follow-up, significantly fewer CABG patients got a myocardial infarction, compared to PCI patients (OR, 2.4; 95% CI, 1.6-3.6; $P < .01$; and OR, 1.6; 95% CI, 1.1-2.3; $P = .01$, respectively). At each time point of follow-up, there were significantly fewer repeat revascularizations after CABG ($P \leq .01$ at each time point). At a time period of 1-year follow-up, stroke was significantly less frequent in the PCI group (OR, 0.5; 95% CI, 0.3-0.7; $P < .01$) but not at the other time periods of follow-up.

Outcomes in Patients With Different Types of Diseased Vessels

Twelve trials evaluated patients with multivessel disease, 11 trials analyzed patients with proximal LAD stenosis and 4 trials analyzed patients with left main stenosis (Table 3). All-cause death was higher after PCI compared to surgery in multivessel disease (OR, 1.2; 95% CI, 1.0-1.4; $P = .02$), but not in proximal LAD stenosis or left main stenosis. Myocardial infarction did not occur significantly more often after PCI compared to CABG in patients with multivessel disease, proximal LAD stenosis, or left main stenosis. Repeat revascularization favored CABG in multivessel disease, proximal LAD stenosis, and main stem stenosis patients. The OR for repeat revascularization

TABLE 4. Meta-analyzed ORs for outcomes in patients with on- and off-pump surgery at the latest available follow-up, in the bare metal stent and drug-eluting stent eras, PCI versus CABG

Outcome	OR (95% CI)	*P* value	n	I^2 (95% CI), %	*P* value heterogeneity
Mortality					
On-pump surgery	0.9 (0.7-1.2)	.40	4	0 (0-85)	.50
Off-pump surgery	0.8 (0.5-1.3)	.34	9	0 (0-65)	.52
Myocardial infarction					
On-pump surgery	1.0 (0.6-1.9)	.94	4	58.8 (0-86)	.06
Off-pump surgery	0.8 (0.4-1.6)	.13	8	18.9 (0-62)	.28
Repeat revascularization					
On-pump surgery	5.3 (3.8-7.3)	<.01	4	26.4 (0-72)	.25
Off-pump surgery	3.2 (2.2-4.7)	<.01	9	0 (0-65)	.67
Stroke					
On-pump surgery	0.8 (0.5-1.4)	.54	3	10.8 (0-91)	.33
Off-pump surgery	1.4 (0.1-20.6)	.82	2	32.8*	.22

OR, Odds ratio; *CI*, confidence interval; *n*, number of studies included in the analysis. *95% CI for I^2 cannot be calculated for a meta-analysis of 1 or 2 studies.

TABLE 5. Meta-analyzed ORs for outcomes in diabetes patients at the latest available follow-up across all eras, PCI versus CABG

Outcome	OR (95% CI)	*P* value	n	I^2 (95% CI), %	*P* value heterogeneity
Mortality	1.6 (1.2-2.1)	<.01	12	27.4 (0-63)	.18
Pre-stent era	1.5 (0.8-2.8)	.26	4	49.6 (0-83)	.11
Bare metal stent era	1.6 (1.0-2.5)	.07	4	0.3 (0-85)	.39
Drug-eluting stent era	1.7 (1.1-2.6)	.02	4	51.6 (0-84)	.10
Myocardial infarction	1.2 (0.8-2.0)	.33	7	64.4 (20-84)	.01
Pre-stent era	1.1 (0.6-1.9)	.75	1	0*	1.00
Bare metal stent era	1.0 (0.3-2.7)	.93	2	44.5*	.18
Drug-eluting stent era	1.4 (0.7-2.6)	.34	4	74.0 (28-91)	<.01
Repeat revascularization	3.4 (2.1-5.7)	<.01	6	72.0 (35-88)	<.01
Pre-stent era	—	—	0	—	—
Bare metal stent era	6.3 (3.3-11.8)	<.01	2	0*	.89
Drug-eluting stent era	2.7 (1.5-4.9)	<.01	4	67.0 (0-90)	<.01
Stroke	0.5 (0.3-0.8)	.01	4	0 (0-85)	.60
Pre-stent era	—	—	0	—	—
Bare metal stent era	—	—	0	—	—
Drug-eluting stent era	0.5 (0.3-0.8)	.01	4	0 (0-85)	.60

OR, Odds ratio; *CI*, confidence interval; *n*, number of studies included in the analysis. *95% CI for I^2 cannot be calculated for a meta-analysis of 1 or 2 studies.

was around twice as high for multivessel disease (OR, 5.6; 95% CI, 4.2-7.4) and proximal LAD stenosis patients (OR, 5.7; 95% CI, 3.5-9.1), compared to patients with main stem stenosis (OR, 2.8; 95% CI, 1.7-4.5). Differences in stroke rate were not significant in either patient group.

Outcomes in Off-Pump Versus On-Pump Surgery

We excluded all trials from the pre-stent era, as in none of these studies off-pump surgery was used. In the bare metal stent and drug-eluting stent eras, 4 trials used on-pump surgery exclusively, whereas 9 trials used off-pump surgery exclusively. There was no significant difference between CABG and PCI in mortality, myocardial infarction, and stroke when off-pump surgery was used, or even when on-pump surgery was used (Table 4). The meta-analyzed primary outcomes did not differ between off-pump and on-pump surgery. Only 2 (Drenth and Kim) out of 9 trials that used off-pump surgery exclusively reported on stroke as an outcome. Stroke was not more common after CABG in these 2 studies (OR, 1.4; 95% CI, 0.1-20.6; $P = .82$).

Outcomes in (Subgroups of) Patients With Diabetes

Twelve trials provided data on patients with diabetes separately, usually as a subgroup except for the CARDia, Future REvascularization Evaluation in patients with Diabetes mellitus: Optimal management of Multivessel disease (FREEDOM), and Veterans Affairs trials that included patients with diabetes exclusively. The OR for death favored CABG at the latest available follow-up across all 12 studies (OR, 1.6; 95% CI, 1.2-2.1; $P < .01$), as well as in the drug-eluting stent era (OR, 1.7; 95% CI, 1.1-2.6, $P = .01$) (Table 5). Myocardial infarctions did not differ significantly. Repeat revascularization in patients with diabetes occurred more frequently after PCI compared to CABG (OR, 3.4; 95% CI, 2.1-5.7; $P < .01$). Data on stroke in patients with diabetes were only available for the drug-eluting stent era and occurred less frequently after PCI (OR, 0.5; 95% CI, 0.3-0.8; $P = .01$). Effect sizes were similar—though differences were not always statistically significant—if only randomized data on patients with diabetes were meta-analyzed (ie, subgroup data were left out of the meta-analysis) with an OR for death of 1.8 (95% CI, 0.8-3.8; $P = .14$); myocardial infarction 1.2 (95% CI, 0.5-3.0; $P = .65$); repeat revascularization 2.6 (95% CI, 1.0-6.4; $P = .05$); and stroke 0.5 (95% CI, 0.3-0.8; $P = .01$). In patients without diabetes (data from subgroups only), there was no difference in mortality (OR, 1.0; 95% CI, 0.9-1.2; $P = .74$) or myocardial infarction (OR, 1.0; 95% CI, 0.7-1.5; $P = .95$). Only 8 trials provided data on subgroups of patients without diabetes. All these 8 trials were from the pre-stent era (5 trials) or the bare metal stent era (3 trials). Only 2 of them provided data on repeat revascularization; therefore, we did not meta-analyze repeat revascularization for patients without diabetes, and none of them provided stroke data.

DISCUSSION

To our knowledge, this meta-analysis is the most up-to-date and complete overview of the effectiveness of PCI versus CABG as revascularization strategies for patients with coronary artery disease. This meta-analysis includes 31 trials with 15,004 patients. Our main findings are that CABG led to a small survival benefit over PCI. This survival difference benefits patients with multivessel disease and patients with diabetes, respectively. In addition, repeat revascularization was less common after CABG, though PCI is narrowing the gap over time. Stroke was more common after CABG.

Composite endpoints of major adverse cardiac and cerebrovascular events were not used. First, composite

endpoints are not uniformly defined across trials, which leads to loss of information if only a subset of composite endpoints can be meta-analyzed. Second, when included in a composite endpoint, repeat revascularization dominates the other composites as they occur at a much higher rate. Third, there is now evidence that from a patient's perspective the components of composite endpoints are not equally important. Patients found the risk of death to be the most important outcome (relative weight 0.23), followed by stroke (0.18), potential increased longevity and recovery time (each 0.17), myocardial infarction (0.14), and risk of repeat revascularization (0.11).[E119]

Our study is limited by the fact that we did not have access to individual patient data, and analyzed patients at group level. It is more difficult to unravel the complex interactions of different patient-related factors (type of PCI or CABG, type of vessel involvement, time of follow-up, subgroups involved) that influence outcomes, when less detailed information is available. Therefore, results should be interpreted with caution. For example, that we found a (nonsignificant) higher myocardial infarction rate after PCI in the drug-eluting stent era may be confounded by diabetes, as 3 of the 8 trials in the drug-eluting stent era were in patients with diabetes exclusively. In addition, subgroup analyses may have been underpowered; many trials did not provide data on subgroups of interest. Subgroup analyses may best be seen as hypothesis generating as patients were usually not randomized according to the subgroups of interest. As an example, the difference in mortality between PCI and CABG is not apparent when studies that used off-pump or on-pump CABG exclusively were analyzed separately. In addition, we tested a lot of hypotheses, which makes the chance of a spurious finding higher. As a remedy, a stricter cut-off for statistical significance (eg, 0.01) might be used. If we had used a cut-off of 0.01 the higher all-cause death after PCI compared to surgery in multivessel disease would be nonsignificant.

Another limitation is that only few studies (12 of 31 trials) provided data on stroke. Notably, only 2 of 9 trials that used off-pump surgery exclusively provided stroke data. As the risk of stroke is lower after off-pump CABG, compared to on-pump CABG,[E120] the difference in stroke risk in our meta-analysis may have been overestimated in favor of PCI.

Heterogeneous definitions of myocardial infarction and stroke further complicate the interpretation of our findings.

Because we did not perform a survival analysis, the meta-analyzed ORs for myocardial infarction and repeat revascularization might be overestimated. We did not estimate the numbers at risk for each time point of follow-up or a time-to event analysis. If we wanted to meta-analyze hazard ratios, we would have to leave out several trials for each outcome, as not all trials performed time-to-event analyses. For example, of the 7 trials with a follow-up of 8 years or longer, 4 trials had information missing that was needed to calculate hazard ratios for some outcomes, including 2 trials where such information was missing for the outcome death. However, because the number of deaths was small, especially in those studies with a follow-up of <5 years, and because the loss to follow-up was small at a median of 0.5%, we feel that the method used is sound.

The generalizability of our findings is limited by the fact that only a very small proportion (median, 7.8%) of screened patients were randomized. Exclusion criteria were usually very strict; for example, patients with a recent myocardial infarction, a low left ventricular ejection fraction, or a prior PCI/CABG procedure could not participate. The range of patients that is included in the RCTs is also limited because patients have to be eligible for both PCI and CABG. In real life, many patients with coronary artery disease will not be eligible for both procedures as, for example, PCI is not technically feasible or because they have contraindications for CABG. Fortunately, the most recent trials included a much higher proportion of screened patients, with trials on drug-eluting stents including a median of 41% of screened patients (range, 3%-61%).

The Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery (SYNTAX) score has the potential to further refine the optimal treatment strategy for individual patients. Today, knowledge on the best treatment strategy in view of individual SYNTAX scores stems from the SYNTAX study only, and needs to be further elucidated. The ongoing EXCEL trial is designed to further evaluate one of the outstanding questions the SYNTAX trial raised: Do patients with left main disease and a SYNTAX score $\leq$32 benefit more from PCI than from CABG?

CONCLUSIONS

Compared with PCI, CABG had a lower risk of death or repeat revascularization but a higher risk of stroke. The smaller risk of death favors patients with multivessel disease or with diabetes.

Our findings are valid in settings and in patients comparable to those of the original PCI versus CABG trials: high-volume, state-of-the-art cardiac centers where patient treatment is discussed and decided upon by a team of interventional cardiologists and cardiac surgeons, and in highly selective patients eligible for either intervention. The results do not necessarily apply to other settings or patients.

Conflict of Interest Statement

Massimo A. Mariani reports consulting fees from Sorin and lecture fees from Sorin and Maquet. All other authors have nothing to disclose with regard to commercial support.

We would like to thank Gerry Ligtenberg, Carina Parmentier, and Desiree Welten for their constructive comments in various stages of our research.

APPENDIX E1

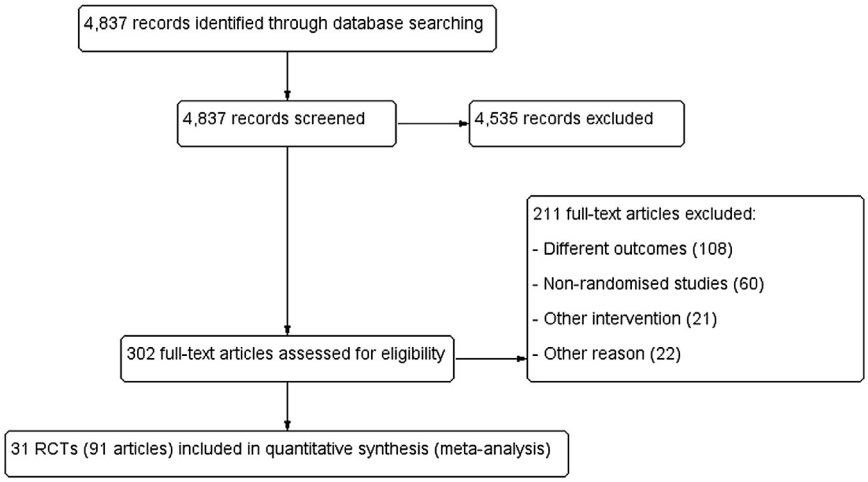


FIGURE E1. Flow diagram of the search and selection process. *RCT*, Randomized controlled trial.

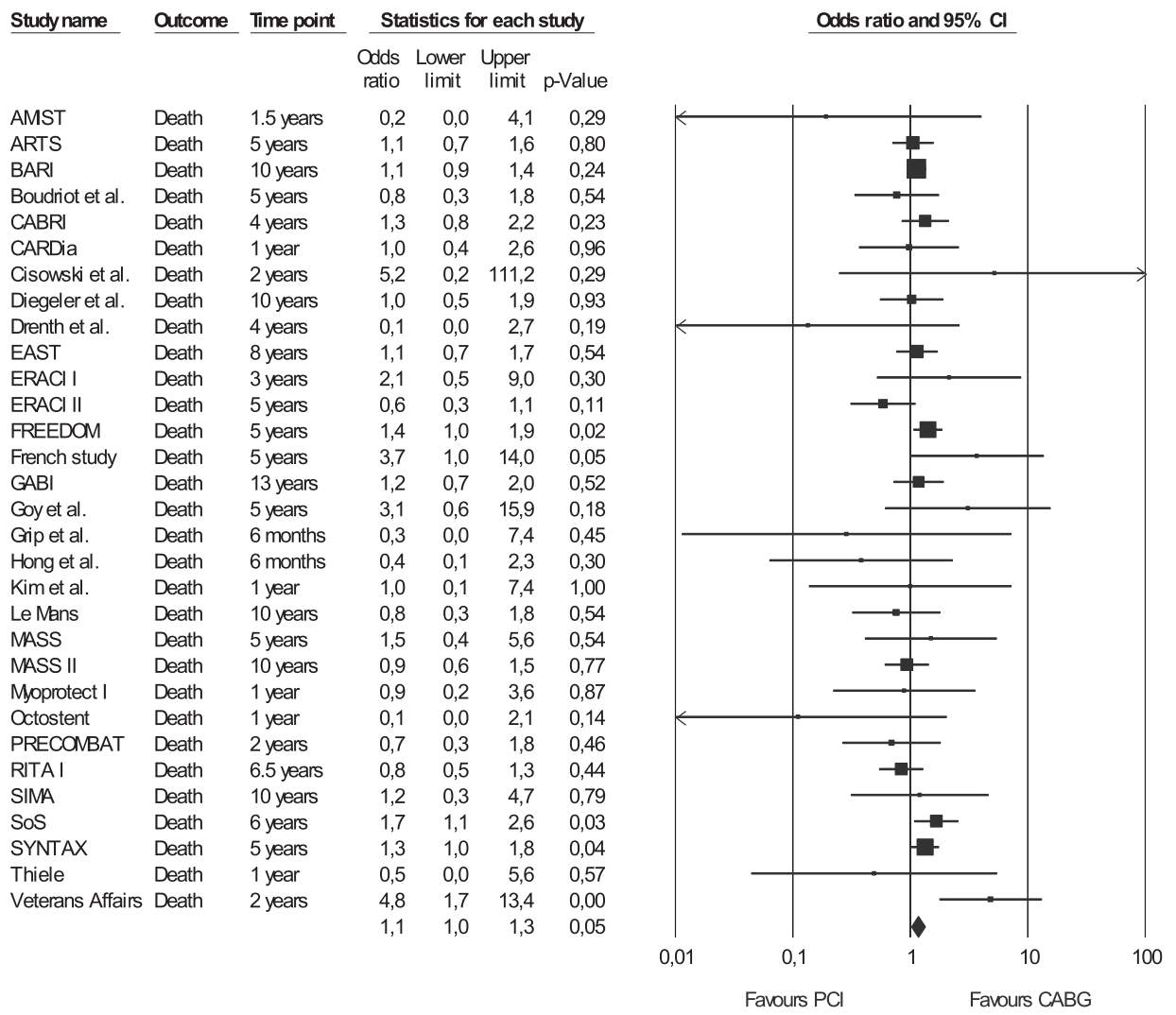


FIGURE E2. Meta-analyzed odds ratios for death after PCI or CABG at the latest available follow-up. *PCI*, Percutaneous coronary intervention; *CABG*, coronary artery bypass grafting; *CI*, confidence interval; *AMIST*, Angioplasty versus Minimally Invasive Surgery Trial; *ARTS*, Arterial Revascularization Therapies Study; *BARI*, Bypass Angioplasty Revascularization Investigation; *CABRI*, Coronary Angioplasty versus Bypass Revascularisation Investigation; *EAST*, Emory Angioplasty versus Surgery Trial; *ERACI I*, Argentine Randomized Trial of Percutaneous Transluminal Coronary Angioplasty Versus Coronary Artery Bypass Surgery in Multivessel Disease; *GABI*, German Angioplasty Bypass Surgery Investigation; *MASS*, Medicine, Angioplasty, or Surgery Study; *RITA*, Randomised Intervention Treatment of Angina; *ERACI II*, Argentine Randomized Trial of Coronary Angioplasty With Stenting Versus Coronary Bypass Surgery in Patients with Multiple Vessel Disease; *SIMA*, Stenting versus Internal Mammary Artery grafting trial; *SoS*, Stent or Surgery Trial; *CARDia*, Coronary Artery Revascularization in Diabetes; *FREEDOM*, Future REvascularization Evaluation in patients with Diabetes mellitus: Optimal management of Multivessel disease; *PRECOMBAT*, Premier of Randomized Comparison of Bypass Surgery versus Angioplasty Using Sirolimus-Eluting Stent in Patients with Left Main Coronary Artery Disease; *SYNTAX*, Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery.

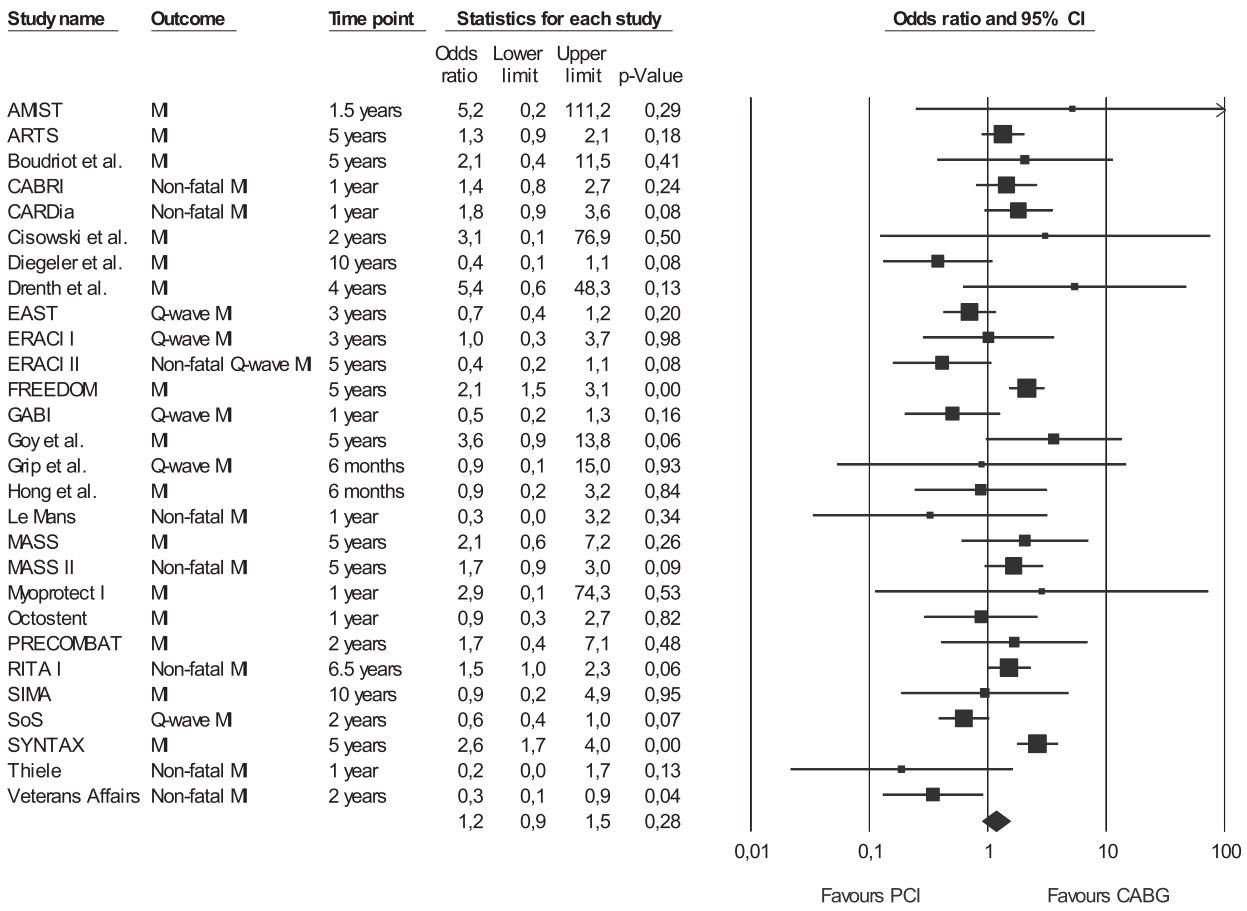


FIGURE E3. Meta-analyzed odds ratios for myocardial infarction after PCI or CABG at the latest available follow-up. *PCI*, Percutaneous coronary intervention; *CABG*, coronary artery bypass grafting; *CI*, confidence interval; *MI*, myocardial infarction; *AMIST*, Angioplasty versus Minimally Invasive Surgery Trial; *ARTS*, Arterial Revascularization Therapies Study; *CABRI*, Coronary Angioplasty versus Bypass Revascularisation Investigation; *EAST*, Emory Angioplasty versus Surgery Trial; *ERACI I*, Argentine Randomized Trial of Percutaneous Transluminal Coronary Angioplasty Versus Coronary Artery Bypass Surgery in Multivessel Disease; *GABI*, German Angioplasty Bypass Surgery Investigation; *MASS*, Medicine, Angioplasty, or Surgery Study; *RITA*, Randomised Intervention Treatment of Angina; *ERACI II*, Argentine Randomized Trial of Coronary Angioplasty With Stenting Versus Coronary Bypass Surgery in Patients with Multiple Vessel Disease; *SIMA*, Stenting versus Internal Mammary Artery grafting trial; *SoS*, Stent or Surgery Trial; *CARDia*, Coronary Artery Revascularization in Diabetes; *FREEDOM*, Future REvascularization Evaluation in patients with Diabetes mellitus: Optimal management of Multivessel disease; *PRECOMBAT*, Premier of Randomized Comparison of Bypass Surgery versus Angioplasty Using Sirolimus-Eluting Stent in Patients with Left Main Coronary Artery Disease; *SYNTAX*, Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery.

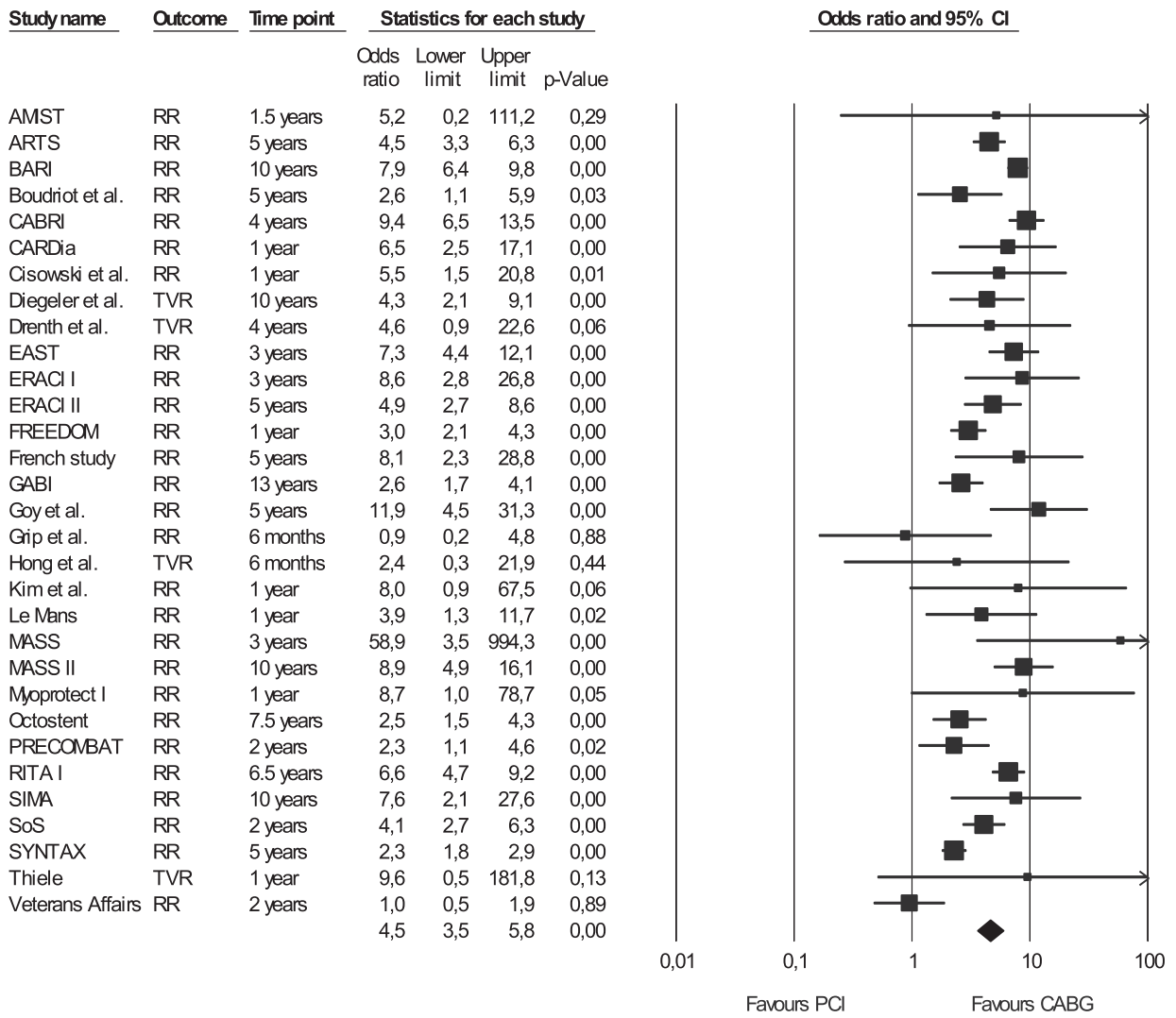


FIGURE E4. Meta-analyzed odds ratios for repeat revascularization after PCI or CABG at the latest available follow-up. *PCI*, Percutaneous coronary intervention; *CABG*, coronary artery bypass grafting; *CI*, confidence interval; *RR*, repeat revascularization; *TVR*, target vessel revascularization; *AMIST*, Angioplasty versus Minimally Invasive Surgery Trial; *ARTS*, Arterial Revascularization Therapies Study; *BARI*, Bypass Angioplasty Revascularization Investigation; *CABRI*, Coronary Angioplasty versus Bypass Revascularisation Investigation; *EAST*, Emory Angioplasty versus Surgery Trial; *ERACI I*, Argentine Randomized Trial of Percutaneous Transluminal Coronary Angioplasty Versus Coronary Artery Bypass Surgery in Multivessel Disease; *GABI*, German Angioplasty Bypass Surgery Investigation; *MASS*, Medicine, Angioplasty, or Surgery Study; *RITA*, Randomised Intervention Treatment of Angina; *ERACI II*, Argentine Randomized Trial of Coronary Angioplasty With Stenting Versus Coronary Bypass Surgery in Patients with Multiple Vessel Disease; *SIMA*, Stenting versus Internal Mammary Artery grafting trial; *SoS*, Stent or Surgery Trial; *CARDia*, Coronary Artery Revascularization in Diabetes; *FREEDOM*, Future REvascularization Evaluation in patients with Diabetes mellitus: Optimal management of Multivessel disease; *PRECOMBAT*, Premier of Randomized Comparison of Bypass Surgery versus Angioplasty Using Sirolimus-Eluting Stent in Patients with Left Main Coronary Artery Disease; *SYNTAX*, Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery.

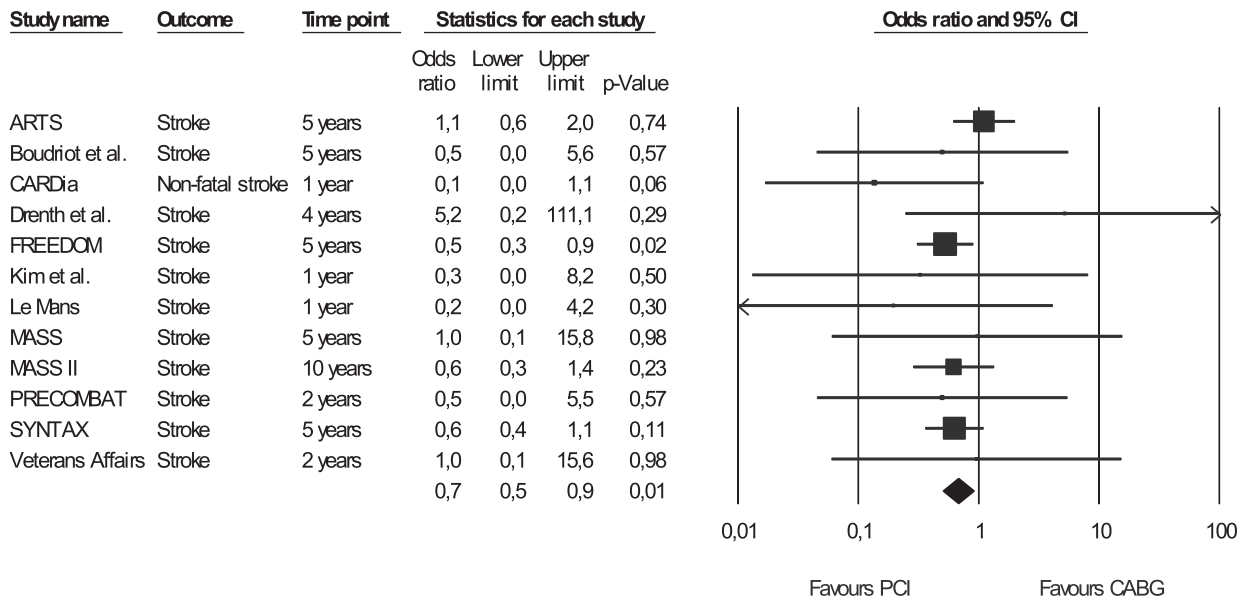


FIGURE E5. Meta-analyzed odds ratios for stroke after PCI or CABG at the latest available follow-up. *PCI*, Percutaneous coronary intervention; *CABG*, coronary artery bypass grafting; *CI*, confidence interval; *ARTS*, Arterial Revascularization Therapies Study; *CARDia*, Coronary Artery Revascularization in Diabetes; *FREEDOM*, Future REvascularization Evaluation in patients with Diabetes mellitus: Optimal management of Multivessel disease; *MASS*, Medicine, Angioplasty, or Surgery Study; *PRECOMBAT*, Premier of Randomized Comparison of Bypass Surgery versus Angioplasty Using Sirolimus-Eluting Stent in Patients with Left Main Coronary Artery Disease; *SYNTAX*, Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery.

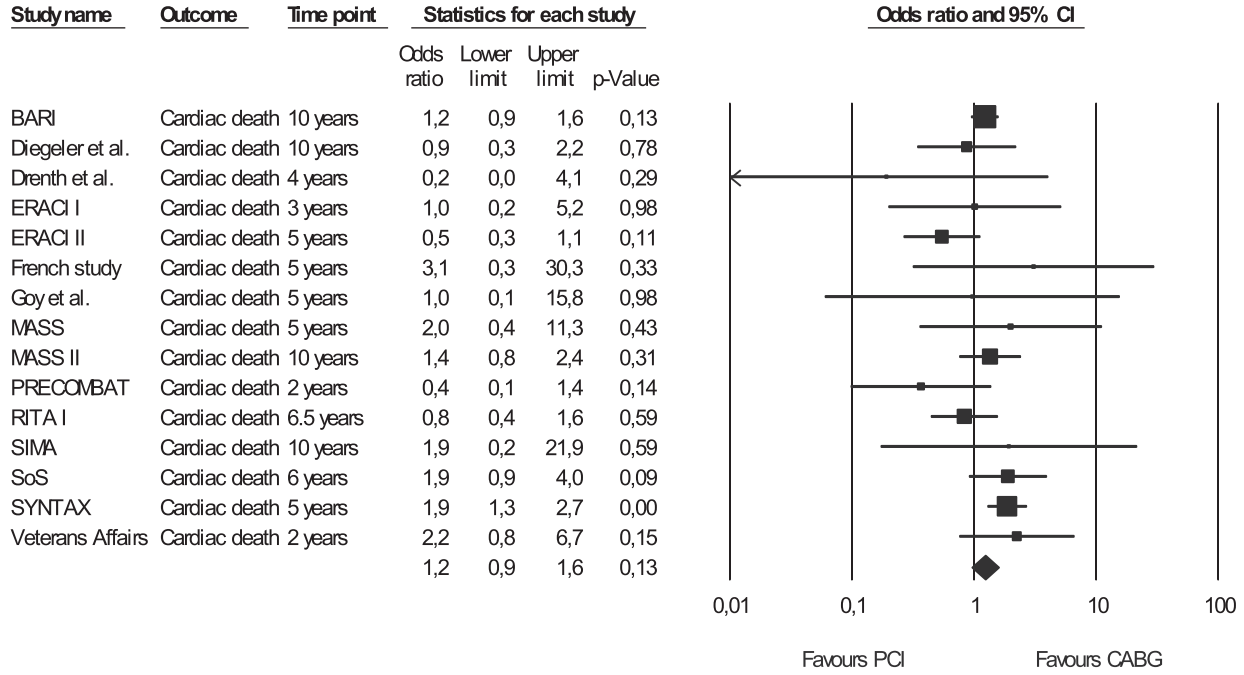


FIGURE E6. Meta-analyzed odds ratios for cardiac death after PCI or CABG at the latest available follow-up. *PCI*, Percutaneous coronary intervention; *CABG*, coronary artery bypass grafting; *CI*, confidence interval; *BARI*, Bypass Angioplasty Revascularization Investigation; *ERACI I*, Argentine Randomized Trial of Percutaneous Transluminal Coronary Angioplasty Versus Coronary Artery Bypass Surgery in Multivessel Disease; *ERACI II*, Argentine Randomized Trial of Coronary Angioplasty With Stenting Versus Coronary Bypass Surgery in Patients with Multiple Vessel Disease; *MASS*, Medicine, Angioplasty, or Surgery Study; *PRECOMBAT*, Premier of Randomized Comparison of Bypass Surgery versus Angioplasty Using Sirolimus-Eluting Stent in Patients with Left Main Coronary Artery Disease; *RITA*, Randomised Intervention Treatment of Angina; *SIMA*, Stenting versus Internal Mammary Artery grafting trial; *SoS*, Stent or Surgery Trial; *SYNTAX*, Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery.

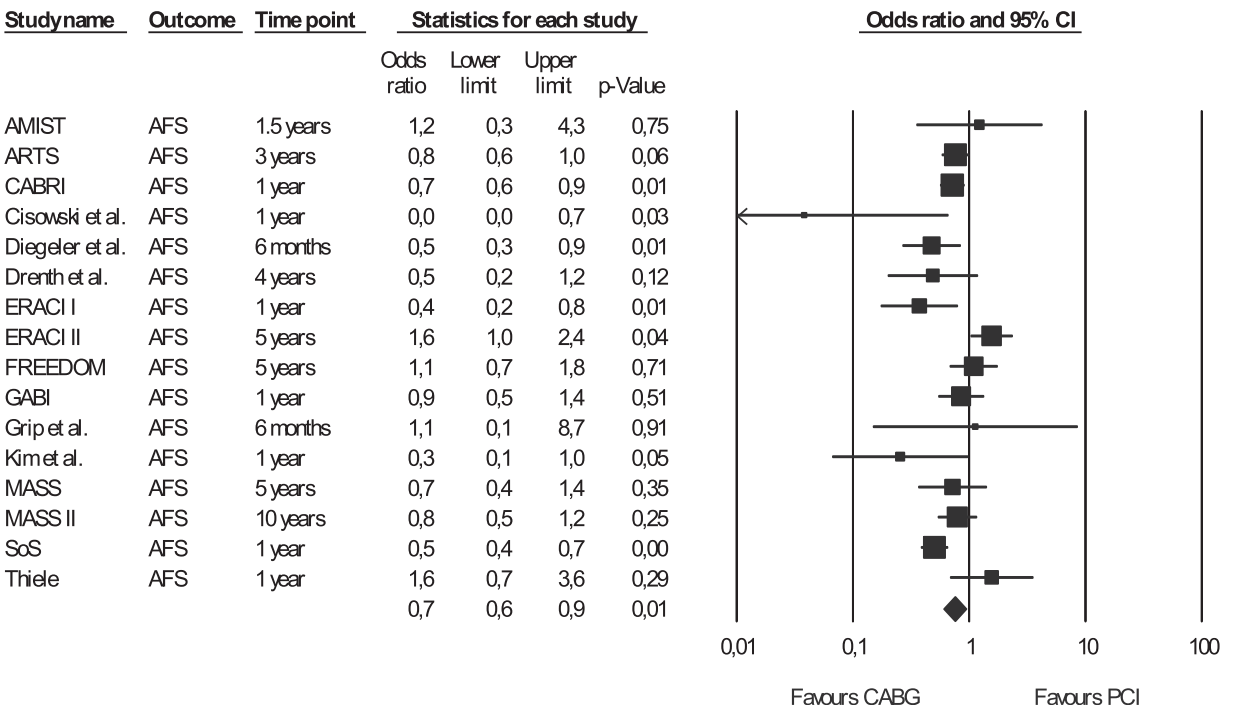
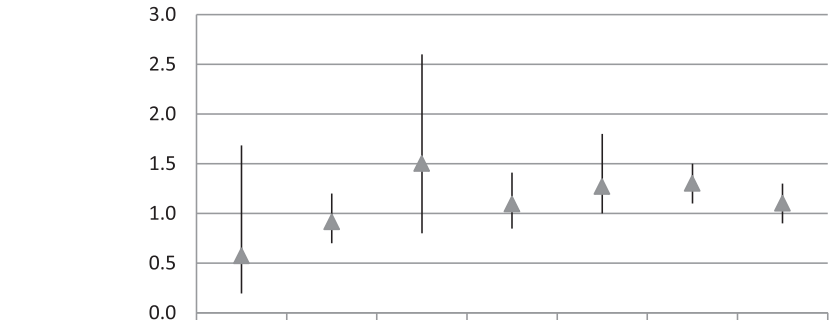


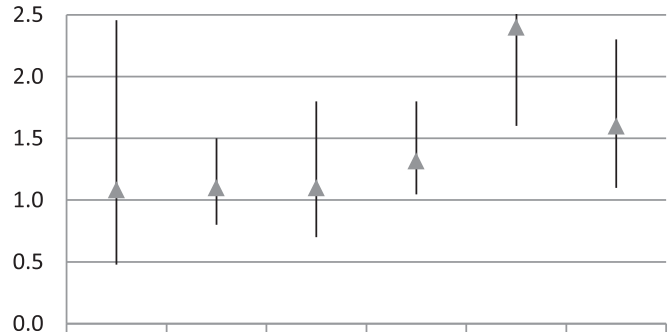
FIGURE E7. Meta-analyzed odds ratios for angina-free survival after PCI or CABG at the latest available follow-up. *PCI*, Percutaneous coronary intervention; *CABG*, coronary artery bypass grafting; *AFS*, angina-free survival; *CI*, confidence interval; *AMIST*, Angioplasty versus Minimally Invasive Surgery Trial; *ARTS*, Arterial Revascularization Therapies Study; *CABRI*, Coronary Angioplasty versus Bypass Revascularisation Investigation; *ERACI I*, Argentine Randomized Trial of Percutaneous Transluminal Coronary Angioplasty Versus Coronary Artery Bypass Surgery in Multivessel Disease; *ERACI II*, Argentine Randomized Trial of Coronary Angioplasty With Stenting Versus Coronary Bypass Surgery in Patients with Multiple Vessel Disease; *FREEDOM*, Future REvascularization Evaluation in patients with Diabetes mellitus: Optimal management of Multivessel disease; *GABI*, German Angioplasty Bypass Surgery Investigation; *MASS*, Medicine, Angioplasty, or Surgery Study; *SoS*, Stent or Surgery Trial.

ACD



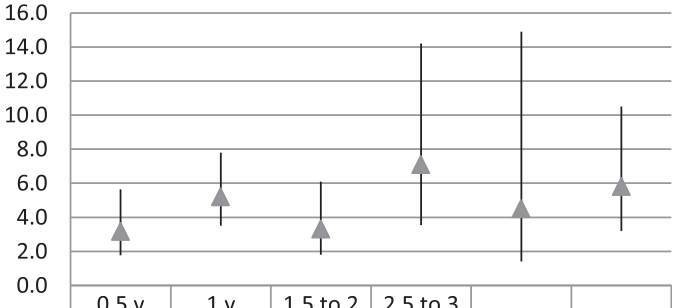
	0.5 y (n=5)	1 y (n=17)	1.5 to 2 y (n=8)	2.5 to 3 y (n=8)	4 y (n=3)	5 y (n=13)	10 y (n=5)
▲ meta-analysed OR	0.6	0.9	1.5	1.1	1.3	1.3	1.1
95% lower	0.2	0.7	0.8	0.8	1.0	1.1	0.9
95% upper	1.7	1.2	2.6	1.4	1.8	1.5	1.3

FIGURE E8. Meta-analyzed odds ratios for death per time period of follow-up, PCI versus CABG. *OR*, Odds ratio; *n*, number of studies meta-analyzed; *y*, years of follow-up.



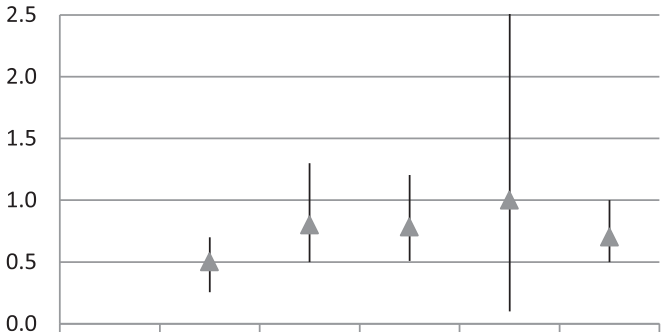
	0.5 y (n=5)	1 y (n=18)	1.5 to 2 y (n=8)	2.5 to 3 y (n=8)	4 y (n=2)	5 y (n=9)
▲ meta-analysed OR	1.1	1.1	1.1	1.3	2.4	1.6
95% lower	0.5	0.8	0.7	1.0	1.6	1.1
95% upper	2.5	1.5	1.8	1.8	3.6	2.3

FIGURE E9. Meta-analyzed odds ratios for myocardial infarction per time period of follow-up, PCI versus CABG. *OR*, Odds ratio; *n*, number of studies meta-analyzed; *y*, years of follow-up.



	0.5 y (n=5)	1 y (n=19)	1.5 to 2 y (n=6)	2.5 to 3 y (n=8)	4 y (n=3)	5 y (n=9)
▲ meta-analysed OR	3.2	5.2	3.3	7.1	4.5	5.8
95% lower	1.8	3.5	1.8	3.5	1.4	3.2
95% upper	5.6	7.8	6.1	14.2	14.9	10.5

FIGURE E10. Meta-analyzed odds ratios for repeat revascularization per time period of follow-up, PCI versus CABG. *OR*, Odds ratio; *n*, number of studies meta-analyzed; *y*, years of follow-up.



		1 y (n=9)	1.5 to 2 y (n=4)	2.5 to 3 y (n=3)	4 y (n=2)	5 y (n=5)
▲ meta-analysed OR		0.5	0.8	0.8	1.0	0.7
95% lower		0.3	0.5	0.5	0.1	0.5
95% upper		0.7	1.3	1.2	6.9	1.0

FIGURE E11. Meta-analyzed odds ratios for stroke per time period of follow-up, PCI versus CABG. *OR*, Odds ratio; *n*, number of studies meta-analyzed; *y*, years of follow-up.

TABLE E1. Quality assessment of 31 included trials studying PCI versus CABG

Study	Adequate randomization*	Adequate concealment†	Selection bias‡	Adequate masking§
AMIST	A	A	A	C
ARTS	A	A	A	C
BARI	A	A	A	C
Boudriot	A	A	A	B
CABRI	A	A	A	C
CARDia	A	A	A	B
Cisowski et al	B	B	A	B
Diegeler et al	A	A	A	C
Drenth et al	B	B	A	C
EAST	B	B	A	B
ERACI I	B	B	A	C
ERACI II	A	A	A	C
FREEDOM	B	A	B	C
French Monocentric Study	B	B	A	C
GABI	B	B	A	C
Goy et al	B	B	A	C
Grip et al	B	B	A	C
Hong et al	B	B	A	C
Kim et al	B	B	A	C
Le Mans	B	B	A	C
MASS I	B	B	A	C
MASS II	B	B	A	C
Myoprotect	B	B	A	C
Octostent	A	A	A	B
PRECOMBAT	A	B	A	B
RITA	A	A	A	B
SIMA	B	B	A	C
SoS	A	A	A	C
SYNTAX	B	A	B	B
Thiele	B	B	A	C
Veterans Affairs	B	A	B	B

AMIST, Angioplasty versus Minimally Invasive Surgery Trial; *ARTS*, Arterial Revascularization Therapies Study; *BARI*, Bypass Angioplasty Revascularization Investigation; *CABRI*, Coronary Angioplasty versus Bypass Revascularisation Investigation; *CARDia*, Coronary Artery Revascularization in Diabetes; *EAST*, Emory Angioplasty versus Surgery Trial; *ERACI I*, Argentine Randomized Trial of Percutaneous Transluminal Coronary Angioplasty Versus Coronary Artery Bypass Surgery in Multivessel Disease; *ERACI II*, Argentine Randomized Trial of Coronary Angioplasty With Stenting Versus Coronary Bypass Surgery in Patients with Multiple Vessel Disease; *FREEDOM*, Future REvascularization Evaluation in patients with Diabetes mellitus: Optimal management of Multivessel disease; *GABI*, German Angioplasty Bypass Surgery Investigation; *MASS*, Medicine, Angioplasty, or Surgery Study; *PRECOMBAT*, Premier of Randomized Comparison of Bypass Surgery versus Angioplasty Using Sirolimus-Eluting Stent in Patients with Left Main Coronary Artery Disease; *RITA*, Randomised Intervention Treatment of Angina; *SIMA*, Stenting versus Internal Mammary Artery grafting trial; *SoS*, Stent or Surgery Trial; *SYNTAX*, Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery. *Adequacy of the randomization process: *A*, adequate sequence generation is reported (such as computer-generated random numbers or random number tables); *B*, did not specify one of the adequate reported methods in (A) but mentioned randomization method; *C*, other methods of allocation that appear to be unbiased; *D*, did not specify one of the adequate reported methods in (A) but mentioned randomization method. †Adequacy of the allocation concealment process: *A*, adequate measures to conceal allocations. Concealment will be deemed adequate where randomization is centralized or pharmacy controlled, or where the following are used: serially numbered containers, on-site computer-based systems where assignment is unreadable until after allocation, other methods with robust methods to prevent foreknowledge of the allocation sequence to clinicians and patients; *B*, unclear concealed trials, in which the authors either did not report allocation concealment approach at all or reported an approach that did not fall into one of the categories in (A); *C*, inadequately concealed trials, in which method of allocation is not concealed. Inadequate approaches will include the use of alternation, case record numbers, days of the week, open random number lists, and serially numbered envelopes, even opaque. ‡Potential for selection bias after allocation: *A*, studies where an intention to treat analysis is possible and few exclusions (with adequate reporting of these exclusions); *B*, studies that reported exclusions as reported in (A), but exclusions were less than 10%; *C*, no reporting of exclusions; exclusions of 10% or more or wide differences in exclusions between groups. §Adequacy of masking: *A*, double (or triple) blind; *B*, single-blind; *C*, nonblind; *D*, unclear.

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