Coronary Revascularization in Diabetic Patients

A Systematic Review and Bayesian Network Meta-analysis

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Background: The optimal revascularization technique in diabetic patients is an important unresolved question.

Purpose: To compare long-term outcomes between the revascularization techniques of percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG).

Data Sources: English-language publications in PubMed, the Cochrane Central Register of Controlled Trials, Ovid, and EMBASE between 1 January 1990 and 1 June 2014.

Study Selection: Two investigators independently reviewed randomized, controlled trials comparing PCI (with drug-eluting or bare-metal stents) with CABG in adults with diabetes with multivessel or left main coronary artery disease.

Data Extraction: Study design, quality, patient characteristics, length of follow-up, and outcomes were extracted. For duplicate publications, outcomes were obtained from the publication with the longest follow-up.

Data Synthesis: 40 studies were combined using a Bayesian network meta-analysis that accounted for the variation in stent choice. The primary outcome, a composite of all-cause mortality, nonfatal myocardial infarction, and stroke, increased with PCI (odds ratio [OR], 1.33 [95% credible interval {CrI}, 1.01 to 1.65]). Percutaneous coronary intervention resulted in increased mortality (OR, 1.44 [CrI, 1.05 to 1.91]), no change in the number of myocardial infarctions (OR, 1.33 [CrI, 0.86 to 1.95]), and fewer strokes (OR, 0.56 [CrI, 0.36 to 0.88]).

Limitations: Study design and length of follow-up were heterogeneous, and results were driven primarily by a single study. Costs and nonvascular complications of the interventions were not examined.

Conclusion: Coronary artery bypass grafting seems to be the preferred revascularization technique in diabetics, especially if long-term survival is anticipated. However, because of residual uncertainties and increased risk for stroke with CABG, clinical judgment is required when choosing a revascularization technique in patients with diabetes.

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Diabetes currently affects 300 to 400 million persons worldwide, and that number is projected to increase dramatically over the next 2 decades (1). Cardiovascular disease accounts for more than one half of deaths among diabetics (2) and is at least 2-fold more common in this population than in nondiabetics (3). Thus, diabetic patients account for more than 25% of referrals for coronary revascularization (4) and have poorer outcomes, especially those with multivessel or left main coronary artery disease (CAD) (5, 6).

With more than 1 million revascularization procedures done annually in the United States alone (7), assessing the risks and benefits of these techniques in this subgroup is a public health priority. In particular, deciding on an optimal revascularization strategy is a crucial element of clinical decision making. This review explores the advantages and additional insights that a network meta-analysis provides into the choice of revascularization technique for diabetic patients with multivessel or left main CAD by comparing percutaneous coronary intervention (PCI) with bare-metal stents (BMSs) or drug-eluting stents (DESs) versus coronary artery bypass grafting (CABG).

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Methods

This review was done using a predefined protocol and in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.

Data Sources and Searches

PubMed, the Cochrane Central Register of Controlled Trials, Ovid, and EMBASE were searched for English-language, randomized, controlled trials published between 1 January 2000 and 1 June 2014 about PCI-DES versus CABG in diabetic patients with left main CAD or multivessel disease. The complete search strategy is detailed in **Supplement 1** (available at www.annals.org). Similar searches were done comparing PCI-BMS versus CABG and PCI-BMS versus PCI-DES published between 1 January 1990 and 1 June 2014 and 1 January 2000 and 1 June 2014, respectively.

We also searched established clinical trial registry databases (ClinicalTrials.gov and www.trialresultscenter.org) and proceedings from cardiology conferences (the American Heart Association, American College of Cardiology, Transcatheter Cardiovascular Therapeutics, and European Society of Cardiology congresses). We examined previously published meta-analyses (8–11) for any missing randomized, controlled trials. We searched the references from all

identified articles and did additional PubMed and Google Scholar searches for the senior author of all abstracted articles to obtain any other relevant publications—specifically, updated outcome publications or a diabetic subgroup analysis. Lastly, we contacted authors of selected trials when unpublished data were desired.

Study Selection

The study population comprised diabetic patients with stable or unstable angina in whom angiographically proven multivessel or left main CAD was considered amenable to PCI and CABG. We included all prospective clinical trials with concurrent or historical control groups comparing CABG with PCI in which outcome data had been collected prospectively. The pooled results from the ENDEAVOUR (Randomized, Controlled Trial of the Medtronic Endeavor Drug [ABT-578] Eluting Coronary Stent System Versus the Taxus Paclitaxel-Eluting Coronary Stent System in De Novo Native Coronary Artery Lesions) trial (12–14) contained 15% nonrandomized data, but we included it because of its small contribution and our inability to exclude the nonexperimental data subset. We excluded studies that involved patients with acute myocardial infarction (MI) or duplicate publications, did not contain an experimental comparator group, did not include an extractable diabetic population with clinical outcomes, or had fewer than 9 months of follow-up.

Data Extraction and Risk-of-Bias Assessment

Citations retrieved by the search strategy were screened and subjected to full-text review by 2 investigators using the predetermined selection criteria. Disagreements were resolved by consensus with a third investigator. **Supplement 2** (available at www.annals.org) presents details, including clinical design characteristics, selection criteria, active publication years, relevant population demographic characteristics, follow-up length, and outcome definitions. We extracted outcomes at the longest follow-up where diabetic subgroup data were available. Intention-to-treat sample size (n) and Kaplan–Meier percentage estimates were used when available and converted to an adjusted number of events. Where necessary, we reconstructed outcomes by using methods detailed in **Supplement 3** (available at www.annals.org). Our primary end point, as defined in most studies, was a composite of all-cause mortality, nonfatal MI, and cerebrovascular accident. Our secondary end points included each outcome individually and repeated revascularizations.

We used the Cochrane Collaboration risk-of-bias tool for randomized trials (15). We assessed and classified each study as having high, low, or unclear risk of bias for each of the 7 domains in the Cochrane tool. **Supplement 4** (available at www.annals.org) shows the details of this evaluation for each study.

Data Synthesis and Analysis

We used Bayesian methods that allow more realistic and flexible statistical modeling, including direct and indirect comparisons (16). The primary outcome for each trial was modeled as a binomial distribution with hierarchical modeling accounted for between-study variability in baseline characteristics and treatment effects (16). We included indirect evidence from trials that compared PCI-BMS with PCI-DES or CABG by using a Bayesian (random-effects) network meta-analysis model (17). For studies with more than 2 treatment groups, the random effects were modeled as correlated (bivariate normal distribution) (18).

We assumed a common SD for both random effects (18), implying a correlation coefficient of 0.05. We used an independent random effect to model differences in the baseline odds among studies. We used a vague half-normal prior to estimate the between-study SD (19). Other priors and the length of follow-up were considered in sensitivity analyses. Convergence of Markov chain Monte Carlo samplers was checked by Brooks–Gelman–Rubin diagnostics (20), as implemented in the coda package, version 0.16-1, in R, version 3.0.1 (R Foundation for Statistical Computing) (21), using 4 independent chains. Model adequacy was assessed using node-based residual analysis (17) with consistency model estimates assessed by the "node-splitting" method (22).

For comparison, frequentist random-effects meta-analyses (DerSimonian–Laird method [23]) were also done; however, by conditioning on the estimate of the between-study variability, the uncertainty may be underestimated. Frequentist meta-analysis was done using the meta package in R, version 3.0.1 (21). Bayesian Markov chain Monte Carlo analysis was done using JAGS software, version 3.2.0 (R Foundation for Statistical Computing) (24).

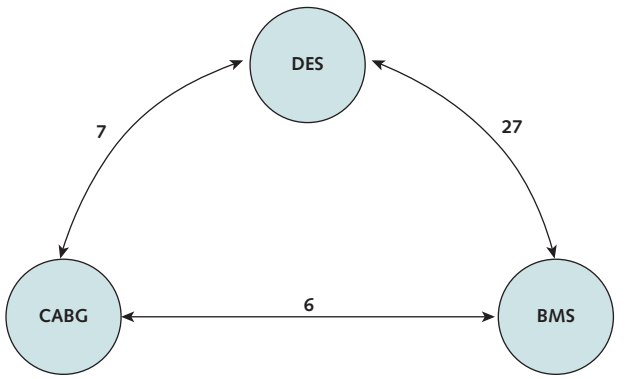
Role of the Funding Source

The Fonds de recherche du Québec-Santé had no role in the conceptualization, searches, data collection, analysis, or interpretation of findings.

RESULTS

Our literature search retained 7 trials that compared PCI-DES with CABG, 6 that compared PCI-BMS with CABG, and 27 that compared PCI-BMS with PCI-DES. **Appendix Figures 1** to **3** (available at www.annals.org) show the evidence search and selection. **Figure 1** shows the network map of comparisons of coronary revascularization techniques. Studies varied with respect to primary end point measures, inclusion or exclusion criteria, and maximum follow-up length (from 9 months to 6 years). All trials included were of high quality—no study scored more than 2 "high risks" out of the 7 domains of the Cochrane risk-of-bias tool. **Supplement 4** shows details of individual studies. As summarized in **Figure 2**, the overall risk of study bias was low.

Figure 1. **Network meta-analysis schematic.**



BMS = bare-metal stent; CABG = coronary artery bypass grafting; DES = drug-eluting stent.

Direct Comparisons

The 7 trials that compared PCI-DES with CABG involved exclusively diabetic populations (the FREEDOM [Future Revascularization Evaluation in Patients with Diabetes Mellitus: Optimal Management of Multivessel Disease [25, 26] and CARDIA [Coronary Artery Revascularisation in Diabetes] [27–30] trials and VA CARDS [Veterans Affairs Coronary Artery Revascularization in Diabetes Study] [31]) or diabetic subgroup analyses (ARTS-I and ARTS-II [Arterial Revascularization Therapy Study I and II] [32–35], ERACI II and III [Argentine Randomized Trial of Percutaneous Transluminal Coronary Angioplasty Versus Coronary Artery Bypass Surgery in Multivessel Disease II and III] [36–38], and the SYNTAX [Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery] [39–42] and PRECOMBAT [Premier of Randomized Comparison of Bypass Surgery Versus Angioplasty Using Sirolimus-Eluting Stent in Patients with Left Main Coronary Artery Disease] trials [43]). **Supplement 2** presents the details of these 7 trials encompassing a total of 3516 diabetic patients and their outcomes.

The primary outcome for most studies was death, MI, or stroke. The Bayesian statistical model showed an increase in the primary end point with PCI-DES versus CABG (odds ratio [OR], 1.40 [95% credible interval {CrI}, 1.08 to 1.73]) (**Figure 3**). Although individual trials were underpowered for isolated clinical outcomes, the pooled analysis of the 6 trials reporting mortality as an end point showed a statistically significant increase in mortality with PCI (OR, 1.65, [CrI, 1.22 to 2.18]) (**Figure 4**). In contrast, isolated MI did not significantly increase with PCI versus CABG (OR, 1.43 [CrI, 0.88 to 2.13]) (**Appendix Figure 4**, available at www.annals.org).

Repeated revascularization rates increased with PCI (OR, 2.65 [CrI, 1.90 to 3.42]) (**Appendix Figure 5**, available at www.annals.org). Compared with CABG, PCI was also associated with a 44% reduction in stroke (OR, 0.56 [CrI, 0.36 to 0.88]) (**Appendix Figure 6**, available at www.annals.org). The combined outcome of death, MI, stroke, or need for revascularization also increased with PCI (OR, 1.97 [CrI, 1.61 to 2.38]) (**Appendix Figure 7**, available at www.annals.org). Analyses using conventional non-Bayesian random-effects models generally gave similar point estimates but narrower CIs, because the uncertainty pertaining to between-study variability was ignored.

In a meta-regression model, we found no statistically significant change in effect size for the primary composite end point, all-cause mortality, or stroke as a function of length of follow-up. However, the effect for MI and repeated revascularization increased over time. For MI, the pooled OR at 2-year follow-up was 0.98 (CrI, 0.58 to 1.60]) compared with 2.0 (CrI, 1.23 to 2.93) at 5 years. For revascularization, the pooled OR at 2 years was 1.59 (CrI, 1.03 to 2.48) compared with 3.16 (CrI, 2.42 to 4.33) at 5 years.

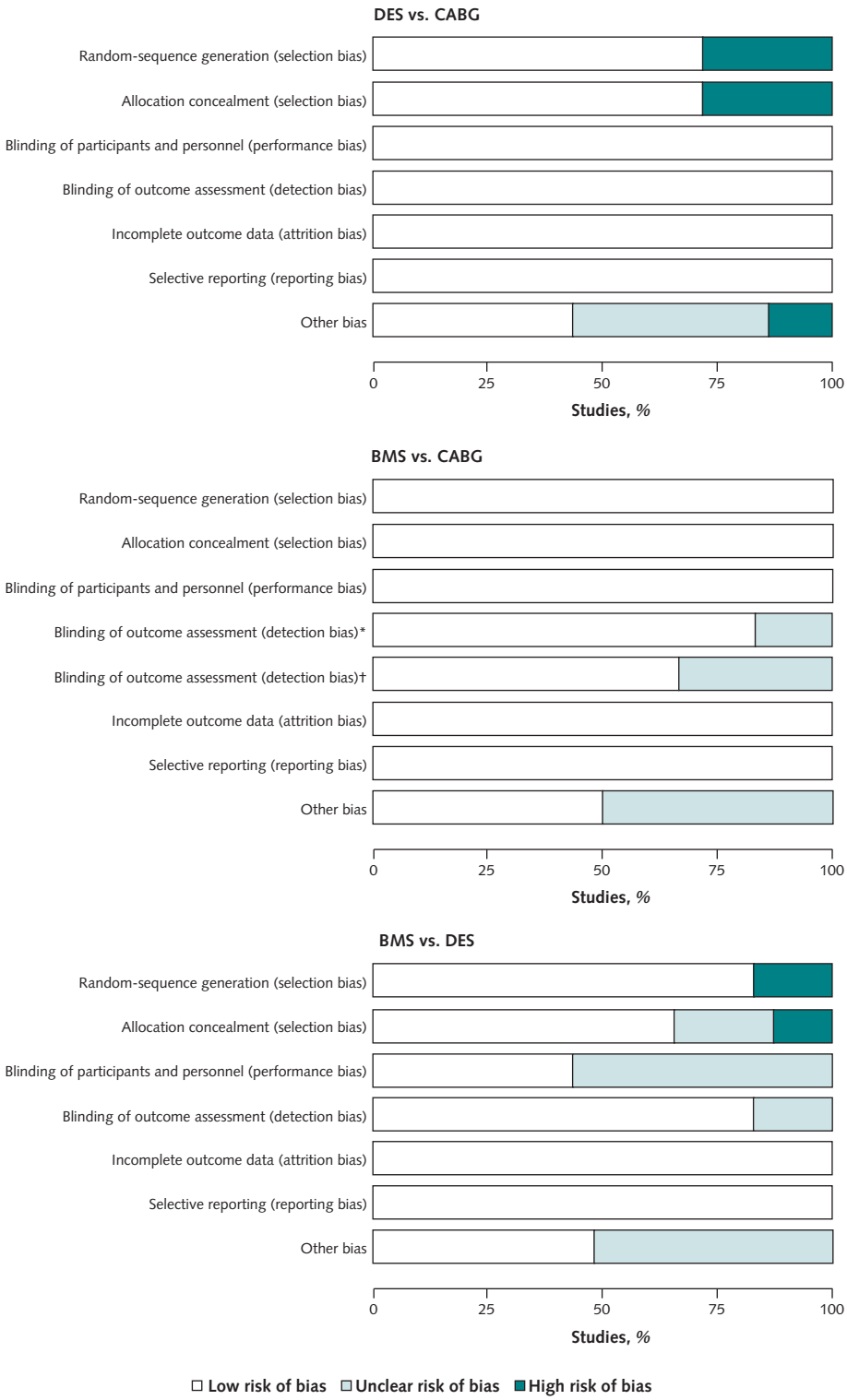
Indirect Comparisons

We identified 6 trials (1011 participants) that compared PCI-BMS with CABG (**Supplement 2**), and these studies reported an increase in the primary composite end point (OR, 1.36 [95% CI, 0.89 to 2.07]) (**Figure 3**). Rather than simply combining studies of PCI-BMS versus CABG with those of PCI-DES versus CABG as has previously been done, we modeled the differences between the 2 comparator groups by considering 27 published randomized studies (3688 participants) comparing PCI-BMS with PCI-DES in diabetic patients (**Supplement 2**).

Studies comparing PCI-BMS with PCI-DES showed an increase in the composite end point (OR, 1.28 [CI, 0.95 to 1.73]) (**Figure 3**) and served as the link that allowed more coherent incorporation of the older studies of the former technique with the more contemporary studies of the latter in the network meta-analysis. Overall, PCI increased the primary composite outcome (OR, 1.33 [CI, 1.01 to 1.65]) (**Figure 3**) and total mortality (OR, 1.44 [CI, 1.05 to 1.91]) (**Figure 4**) when all evidence from the randomized trials in the network meta-analysis was used.

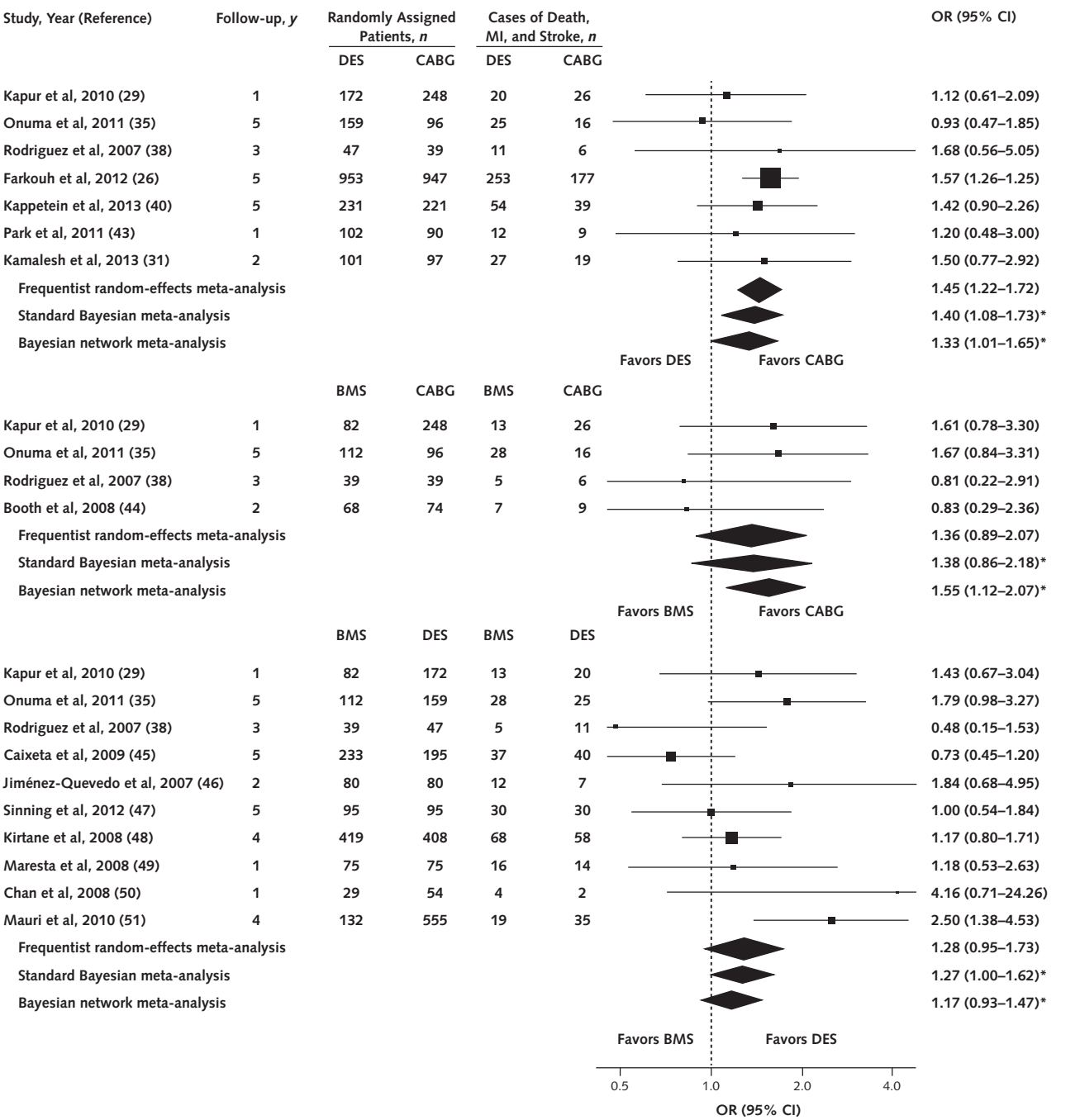
Some inconsistency between the effect estimates obtained through the direct and indirect comparisons was evident. In other cases, the low statistical power of tests of inconsistency was perhaps responsible for statistical significance not being achieved because the point estimates were compatible with clinically meaningful differences (direct and indirect ORs for total mortality, 1.65 and 0.99, respectively; $P = 0.1$ for difference). Sensitivity analyses with noninformative priors had no effect on the point estimates; however, as expected, these perhaps less-realistic priors produced slightly wider CrIs. The **Appendix Table** (available at www.annals.org) presents values for direct, in-

Figure 2. **Summary of risk of bias using the Cochrane risk-of-bias tool.**



BMS = bare-metal stent; CABG = coronary artery bypass grafting; DES = drug-eluting stent.

Figure 3. **Composite end point of all-cause mortality, MI, and stroke.**



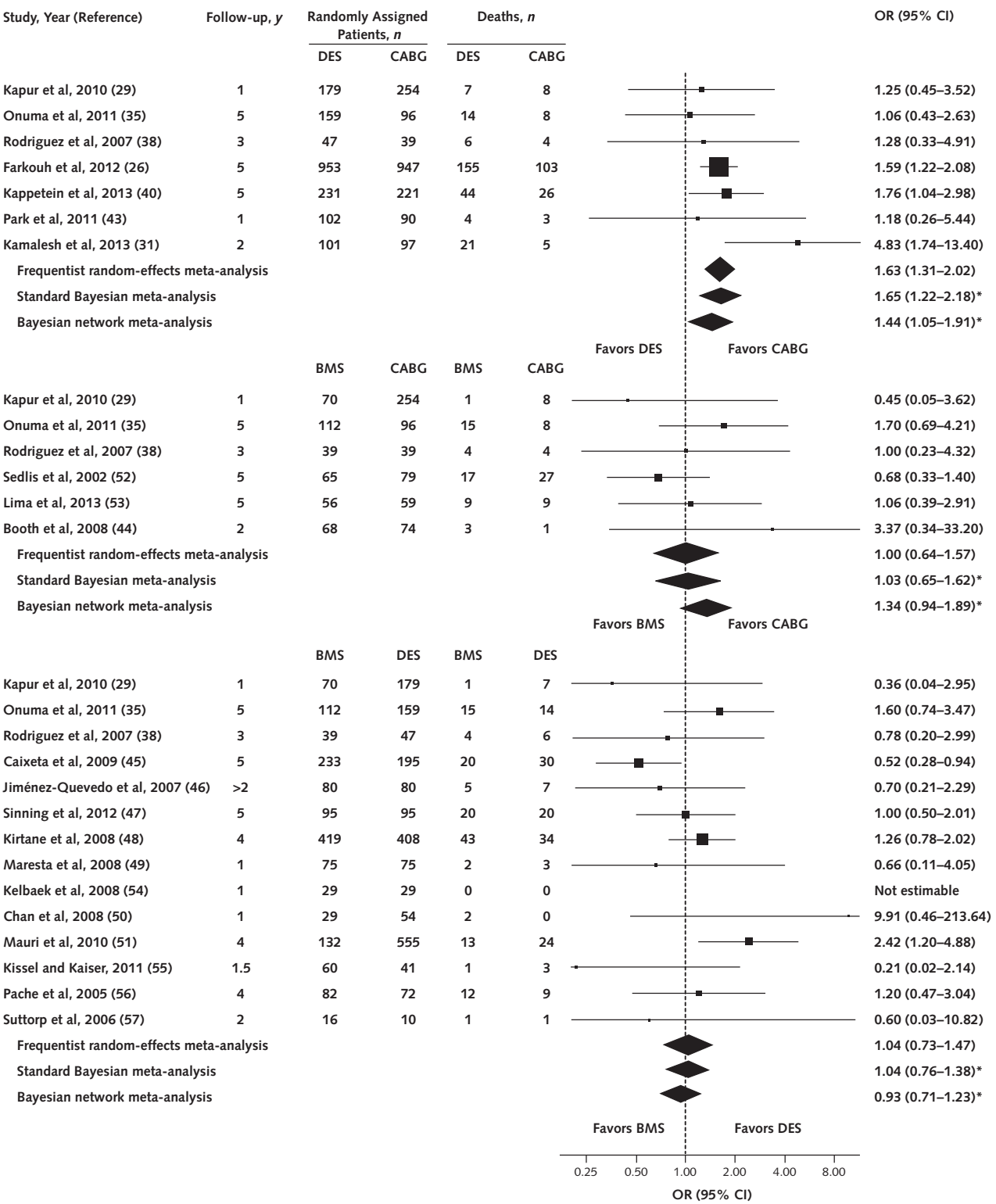
BMS = bare-metal stent; CABG = coronary artery bypass grafting; DES = drug-eluting stent; MI = myocardial infarction; OR = odds ratio.
* OR (95% credible interval).

direct, and network estimates along with results of node-splitting analysis for consistency.

Discussion

This review shows that the randomized evidence comparing the choice of revascularization techniques in diabetic patients is of high quality. The evidence is compatible with increased risk when diabetic patients with multivessel disease or left main CAD undergo PCI compared with CABG. Specifically, the composite outcome of death, nonfatal MI, and stroke increased by a statistically significant 33% with PCI. The individual end points showed a statistically significant 44% increase in mortality, 44% decrease in stroke, and inconclusive results for MI with PCI-DES.

Figure 4. **All-cause mortality.**



BMS = bare-metal stent; CABG = coronary artery bypass grafting; DES = drug-eluting stent; OR = odds ratio.
* OR (95% credible interval).

The need for repeated revascularization increased 137% with PCI.

Although previous studies have found similar results, our analysis allows for a more complete and better appreciation of the statistical and clinical nuances of this evidence base. The most recent meta-analyses (10, 11), which simply combined studies of PCI-BMS and PCI-DES, reported precise and clinically important differences. However, in our review, when previous evidence from studies of PCI-BMS versus CABG was included, the clinical advantages for CABG decreased and the uncertainty around the estimates increased.

The lower end of these CIs approaches unity and underscores that a role remains for individual decision making in the choice of revascularization techniques for patients with diabetes. Therefore, although CABG may generally be preferred, there are individual clinical situations in which PCI may be a reasonable alternative. For example, it might be preferred for patients at high risk for perioperative stroke or whose long-term survival is compromised because of noncardiac factors.

Evidence has favored CABG as the revascularization treatment of choice for diabetic patients since the 1997 publication of BARI (Bypass Angioplasty Revascularization Investigation), a randomized trial sponsored by the National Heart, Lung, and Blood Institute. This trial showed that CABG significantly decreased mortality in patients with diabetes at 5 years compared with percutaneous transluminal coronary angioplasty (58). This seminal finding led to the initial guideline recommendations for CABG as the preferred method of revascularization in diabetic patients with multivessel disease (59). However, both techniques improved over the next 2 decades, leading some to reconsider PCI in high-risk patients (60).

Conclusions of recent randomized, controlled trials comparing PCI-DES with CABG have differed. The FREEDOM trial (26) and the prespecified diabetic subgroup analysis of the SYNTAX trial (40) declared CABG superior to PCI-DES, whereas the lower-powered CARDIA (29) and PRECOMBAT (43) trials concluded that PCI-DES was non-inferior to CABG. Other trials, including ARTS-II (35) and ERACI III (38), also suggested that PCI-DES is an acceptable alternative to CABG for diabetic patients with multivessel disease or left main CAD.

Meta-analyses, when appropriate, have a clear role in improving precision. However, it is important that study heterogeneity be properly assessed, which can be difficult with traditional frequentist meta-analysis. The main advantage of our network meta-analysis is its rigorous assessment of the variability among studies, including the evolution of surgical and PCI techniques. The inclusion of this comprehensive body of evidence enables us to learn from experience. Nevertheless, to give equal weight to the older and newer evidence would be inappropriate, particularly because revascularization techniques have improved over time. Therefore, our hierarchical approach determines relative weights by the similarities and differences between the older and newer studies.

The main limitation of our study arises from the difficulty of extracting common outcomes from the differing study protocols. Although misclassification of outcomes may occur, it is likely to be small, nondifferential, and not clinically significant. Inconsistency is another difficulty in a network of evidence, and it occurs when direct and indirect treatment effects are at odds (61). As with heterogeneity in standard 2-way comparison meta-analyses, this difficulty can be the result of genuine diversity (for example, differences in the patient populations being compared) or can arise when studies of different quality, and hence different levels of risk of bias, are combined (62).

In our analysis, we observed some partial incoherence when evaluating the different outcomes. For example, the composite outcome decreased only minimally in studies of PCI-DES versus CABG compared with those of PCI-BMS versus CABG, despite the known and substantial advantages observed in randomized trials of PCI-DES versus PCI-BMS. Similarly, the observed mortality advantage seen in the PCI-DES versus CABG studies is inconsistent with the lack of a mortality difference observed in the trials of PCI-BMS versus CABG and PCI-BMS versus PCI-DES. These inconsistencies probably reflect the dominant role that the single large FREEDOM trial (26) plays in this mortality analysis. They reflect the difficulty of combining different studies without rigorous statistical and clinical expertise and highlight the care that must be taken in accounting for and interpreting between-study variations. If important between-study heterogeneity really does exist, further confirmatory studies are mandatory. Other limitations include our inability to consider costs, nonvascular complications, and the use of subgroup analyses.

In conclusion, our study suggests that CABG provides several superior long-term clinical outcomes in diabetic patients with multivessel disease or left main CAD compared with PCI-DES. Although a statistically significant mortality benefit was observed, the magnitude of this benefit remains uncertain. The largest advantage of CABG is in avoiding repeated revascularization. Of note, although we have included all pertinent randomized studies, 1 large study strongly influenced our results (26). This dependence on 1 study coupled with the increased stroke rate with CABG suggests that, although CABG is the preferred revascularization technique on average, clinical judgment remains important. Specifically, there is a need for further data as these techniques continue to evolve and for a personalized evaluation of the right revascularization technique for the right diabetic patient.

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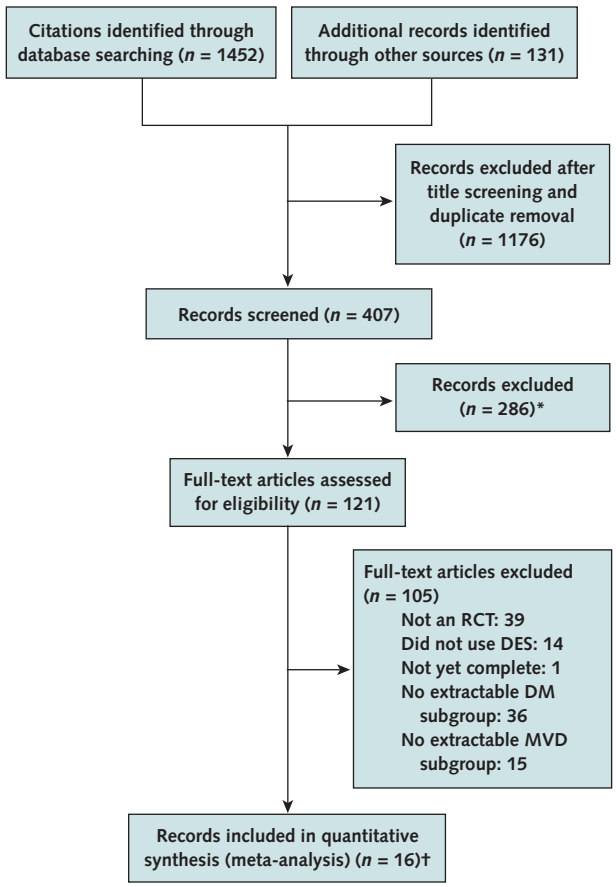
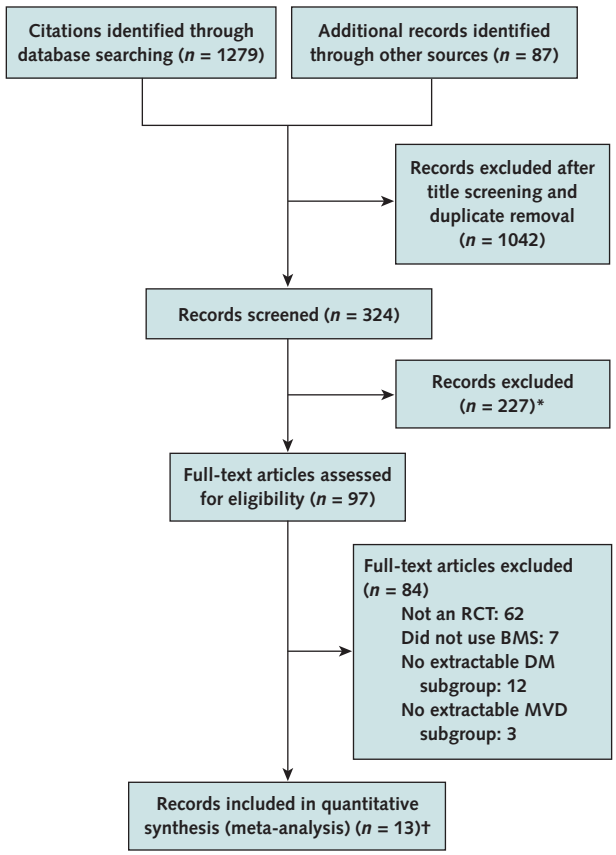
Appendix Figure 1. **Summary of evidence search and selection for PCI-DES versus CABG.**



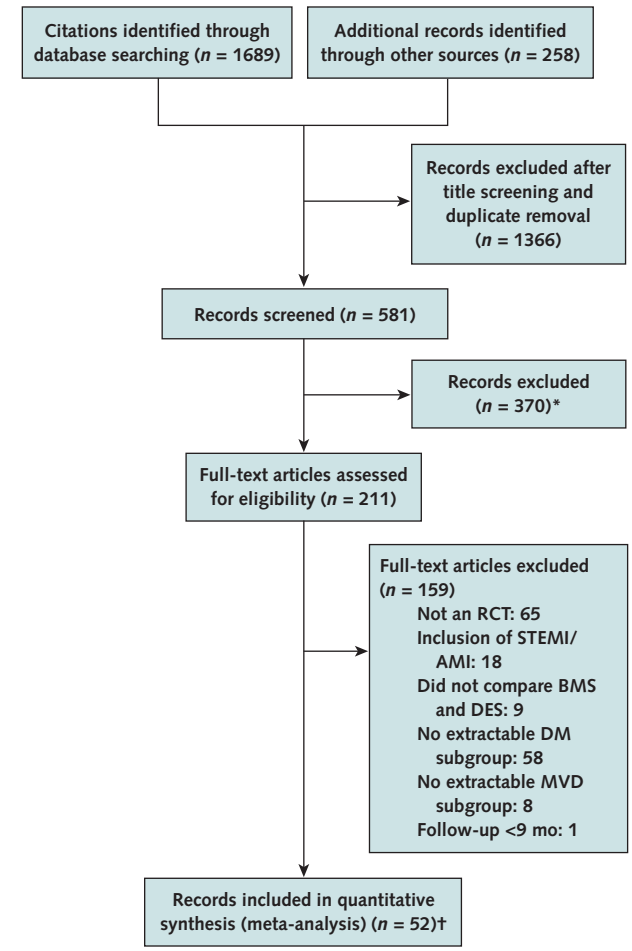
CABG = coronary artery bypass grafting; DES = drug-eluting stent; DM = diabetes mellitus; MVD = multivessel disease; PCI-DES = percutaneous coronary intervention with drug-eluting stents; RCT = randomized, controlled trial.
* Not an RCT.
† 7 studies.

Appendix Figure 2. **Summary of evidence search and selection for PCI-BMS versus CABG.**



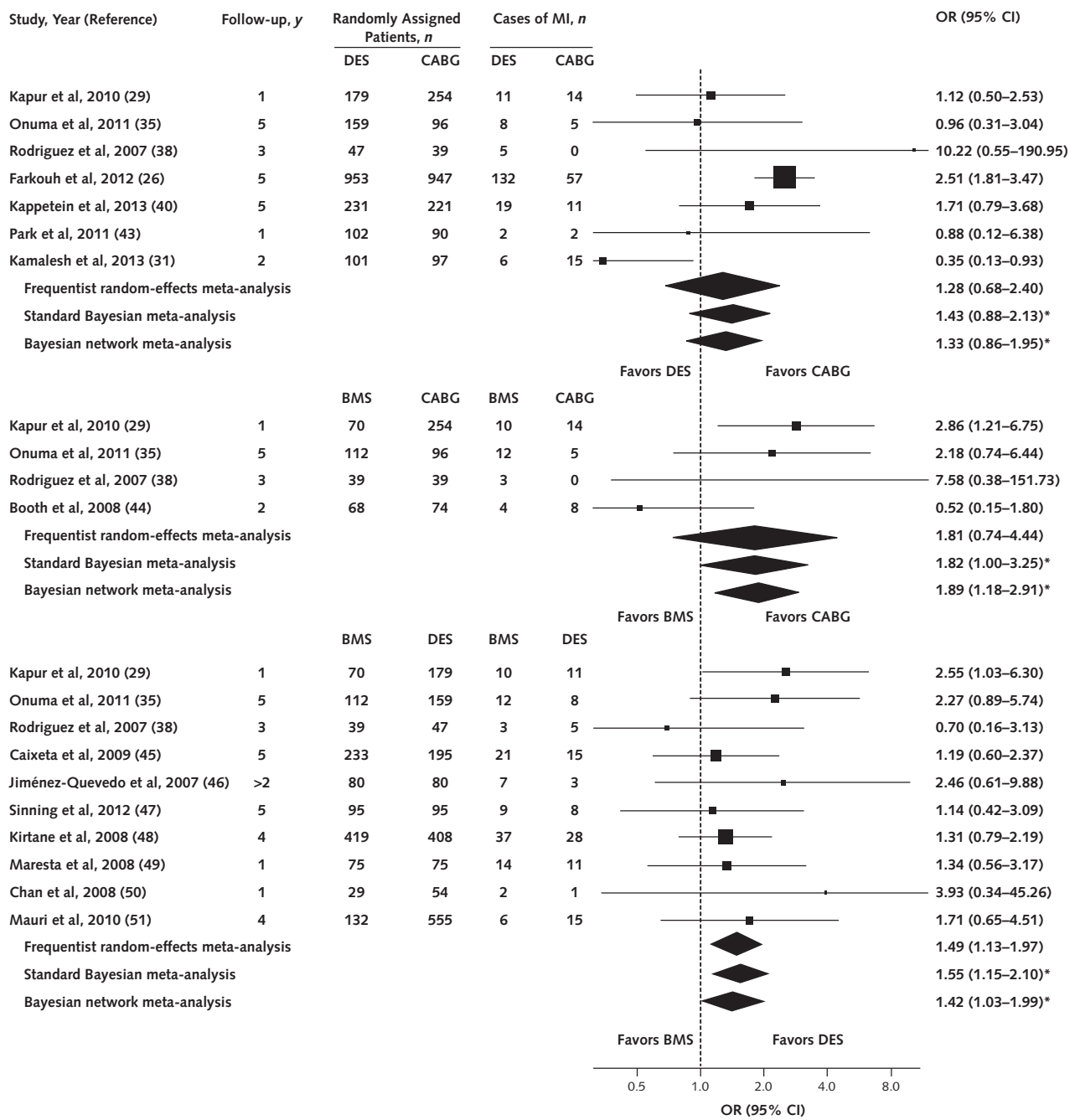
BMS = bare-metal stent; CABG = coronary artery bypass grafting; DM = diabetes mellitus; MVD = multivessel disease; PCI-BMS = percutaneous coronary intervention with bare-metal stents; RCT = randomized, controlled trial.
* Not an RCT.
† 6 studies.

Appendix Figure 3. **Summary of evidence search and selection for PCI-BMS versus PCI-DES.**



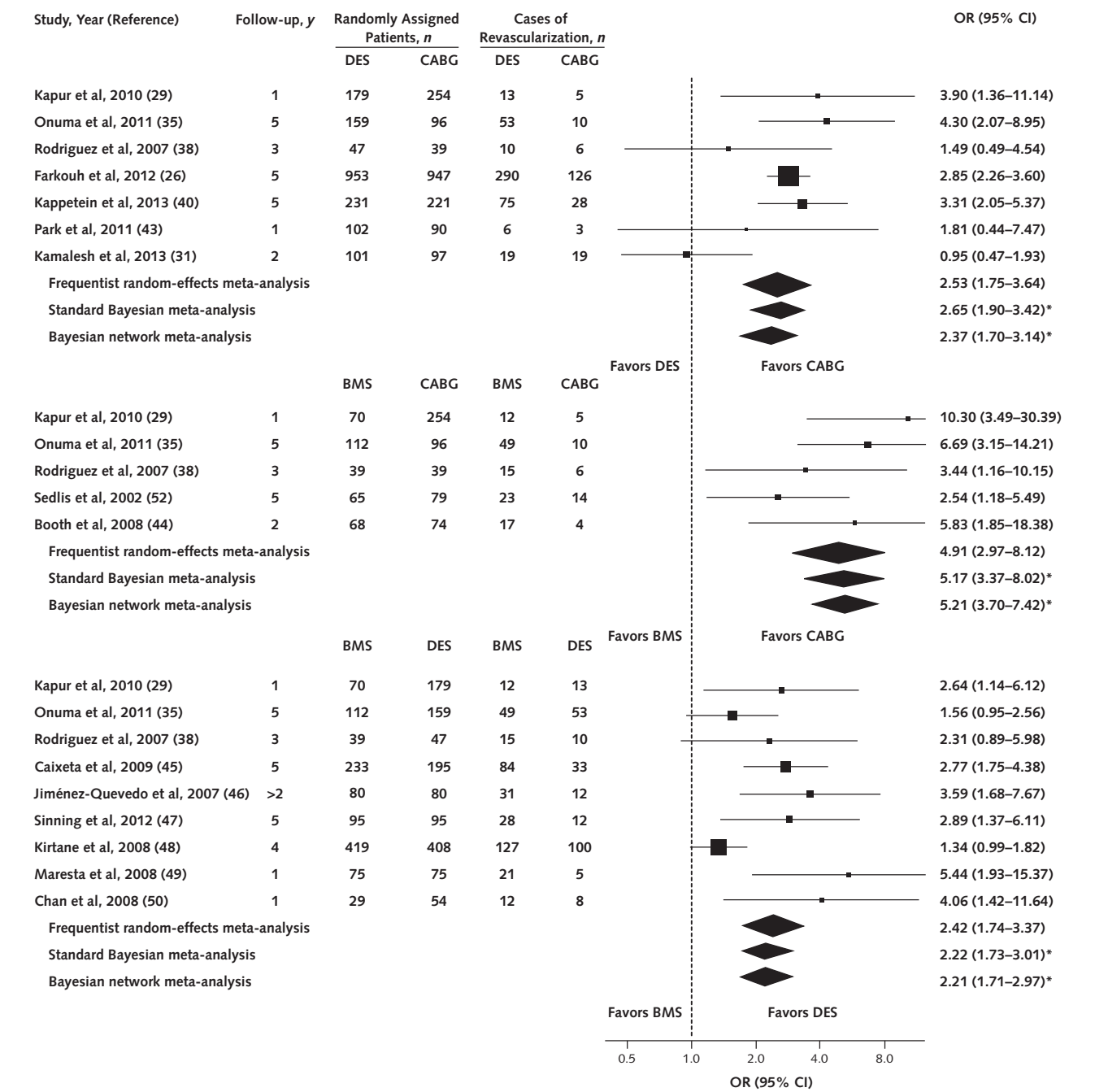
AMI = acute myocardial infarction; BMS = bare-metal stent; DES = drug-eluting stent; DM = diabetes mellitus; MVD = multivessel disease; PCI-BMS = percutaneous coronary intervention with bare-metal stents; PCI-DES = percutaneous coronary intervention with drug-eluting stents; RCT = randomized, controlled trial; STEMI = ST-segment elevation myocardial infarction.
* Not an RCT.
† 27 studies.

Appendix Figure 4. **Cases of MI.**



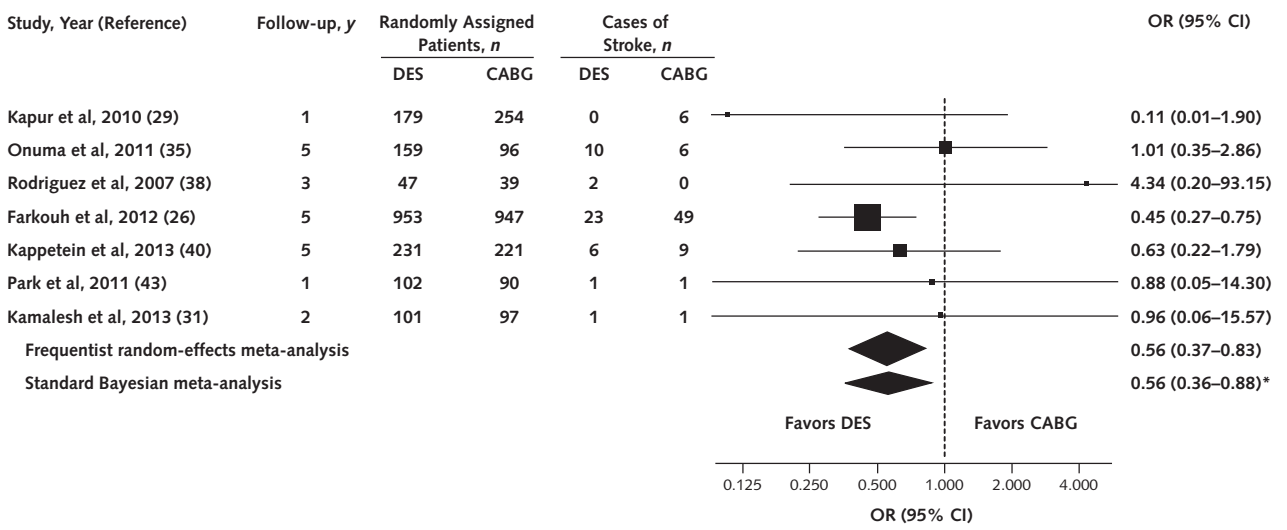
BMS = bare-metal stent; CABG = coronary artery bypass grafting; DES = drug-eluting stent; MI = myocardial infarction; OR = odds ratio.
* OR (95% credible interval).

Appendix Figure 5. **Cases of revascularization.**



BMS = bare-metal stent; CABG = coronary artery bypass grafting; DES = drug-eluting stent; OR = odds ratio.
* OR (95% credible interval).

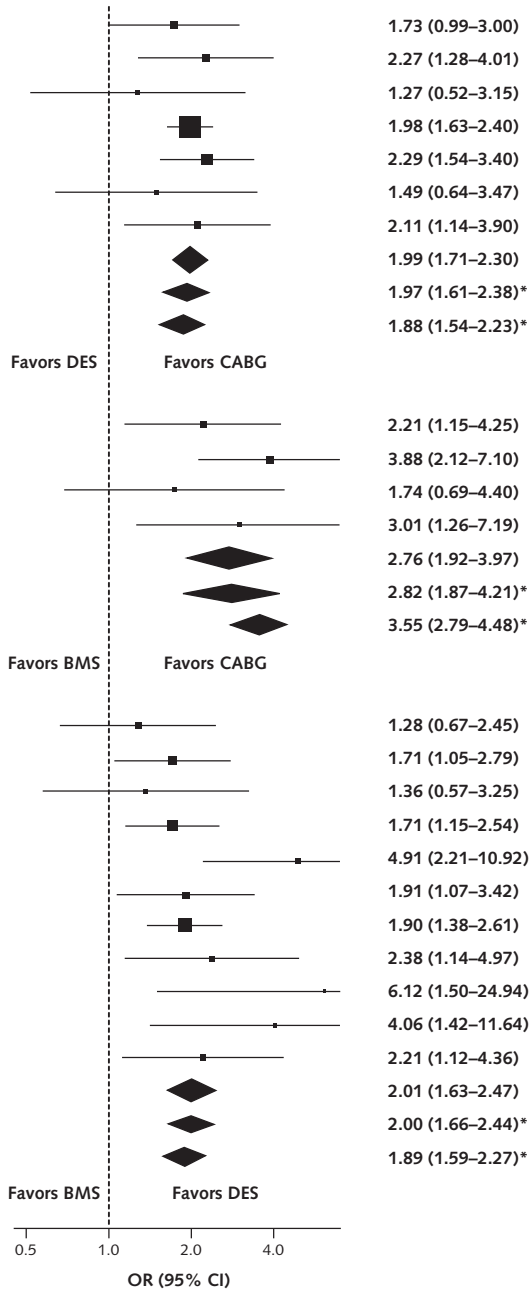
Appendix Figure 6. **Cases of stroke.**



CABG = coronary artery bypass grafting; DES = drug-eluting stent; OR = odds ratio.
* OR (95% credible interval).

Appendix Figure 7. **Cases of MACCEs.**

Study, Year (Reference)	Follow-up, *y*	Randomly Assigned Patients, *n*		MACCEs, *n*		OR (95% CI)
		DES	CABG	DES	CABG	
Kapur et al, 2010 (29)	1	172	248	31	28	1.73 (0.99–3.00)
Onuma et al, 2011 (35)	5	159	96	64	22	2.27 (1.28–4.01)
Rodriguez et al, 2007 (38)	3	47	39	17	12	1.27 (0.52–3.15)
Farkouh et al, 2012 (26)	5	953	947	402	255	1.98 (1.63–2.40)
Kappetein et al, 2013 (40)	5	231	221	105	59	2.29 (1.54–3.40)
Park et al, 2011 (43)	2	102	90	16	10	1.49 (0.64–3.47)
Kamalesh et al, 2013 (31)	2	101	97	40	23	2.11 (1.14–3.90)
Frequentist random-effects meta-analysis						1.99 (1.71–2.30)
Standard Bayesian meta-analysis						1.97 (1.61–2.38)*
Bayesian network meta-analysis						1.88 (1.54–2.23)*
		BMS	CABG	BMS	CABG	
Kapur et al, 2010 (29)	1	82	248	18	28	2.21 (1.15–4.25)
Onuma et al, 2011 (35)	5	112	96	60	22	3.88 (2.12–7.10)
Rodriguez et al, 2007 (38)	3	39	39	17	12	1.74 (0.69–4.40)
Booth et al, 2008 (44)	2	68	74	20	9	3.01 (1.26–7.19)
Frequentist random-effects meta-analysis						2.76 (1.92–3.97)
Standard Bayesian meta-analysis						2.82 (1.87–4.21)*
Bayesian network meta-analysis						3.55 (2.79–4.48)*
		BMS	DES	BMS	DES	
Kapur et al, 2010 (29)	1	82	172	18	31	1.28 (0.67–2.45)
Onuma et al, 2011 (35)	5	112	159	60	64	1.71 (1.05–2.79)
Rodriguez et al, 2007 (38)	3	39	47	17	17	1.36 (0.57–3.25)
Caixeta et al, 2009 (45)	5	233	195	106	64	1.71 (1.15–2.54)
Jiménez-Quevedo et al, 2007 (46)	>2	80	80	33	10	4.91 (2.21–10.92)
Sinning et al, 2012 (47)	5	95	95	49	34	1.91 (1.07–3.42)
Kirtane et al, 2008 (48)	4	419	408	134	81	1.90 (1.38–2.61)
Maresta et al, 2008 (49)	1	75	75	28	15	2.38 (1.14–4.97)
Kelbaek et al, 2008 (54)	3	29	29	12	3	6.12 (1.50–24.94)
Chan et al, 2008 (50)	1	29	54	12	8	4.06 (1.42–11.64)
Mehilli et al, 2011 (63)	1	107	111	29	16	2.21 (1.12–4.36)
Frequentist random-effects meta-analysis						2.01 (1.63–2.47)
Standard Bayesian meta-analysis						2.00 (1.66–2.44)*
Bayesian network meta-analysis						1.89 (1.59–2.27)*



BMS = bare-metal stent; CABG = coronary artery bypass grafting; DES = drug-eluting stent; MACCE = major adverse cardiovascular and cerebrovascular event; OR = odds ratio.
* OR (95% credible interval).

Appendix Table. **PCI-DES Versus CABG Study Design Characteristics**

End Point	Network Meta-analysis		Direct Estimate		Indirect Estimate		Inconsistency Estimate		*P* Value
	Log OR	SD	Log OR	SD	Log OR	SD	Change in Log OR	SD	
Primary outcome	0.279	0.125	0.315	0.128	0.080	0.247	0.235	0.246	0.337
Death*	0.363	0.149	0.461	0.159	−0.008	0.271	0.469	0.286	0.099
MACCE	0.626	0.094	0.679	0.094	0.211	0.194	0.468	0.194	0.014
MI	0.279	0.210	0.316	0.217	0.136	0.335	0.180	0.340	0.590
Repeated revascularization	0.854	0.157	0.913	0.167	0.604	0.267	0.309	0.273	0.246

CABG = coronary artery bypass grafting; PCI-DES = percutaneous coronary intervention with drug-eluting stents; MACCE = major adverse cardiovascular and cerebrovascular event; MI = myocardial infarction; OR = odds ratio.
* All causes.