Number 9

Effective Health Care

Comparative Effectiveness of Percutaneous Coronary Interventions and Coronary Artery Bypass Grafting for Coronary Artery Disease

Executive Summary

Background

Atherosclerosis develops in a patchy, discontinuous fashion within coronary arteries. Therefore, it is possible to treat the discrete areas of obstruction that most impede coronary blood flow to the myocardium. The mechanical approaches to coronary revascularization fall broadly into two categories: coronary artery bypass grafting surgery (CABG) and catheter-based percutaneous coronary interventions (PCI). Together, these coronary revascularization methods are among the most common major medical procedures performed in North America and Europe.

Coronary bypass surgery and coronary angioplasty (with or without stents) are alternative approaches to mechanical coronary revascularization, so their comparative effectiveness in terms of patient outcomes has been of great interest. The comparative effectiveness of bypass surgery and angioplasty is an open question primarily for those patients for whom either procedure would be technically feasible and whose coronary disease is neither too limited nor too extensive.

Effective Health Care Program

The Effective Health Care Program was initiated in 2005 to provide valid evidence about the comparative effectiveness of different medical interventions. The object is to help consumers, health care providers, and others in making informed choices among treatment alternatives. Through its Comparative Effectiveness Reviews, the program supports systematic appraisals of existing scientific evidence regarding treatments for high-priority health conditions. It also promotes and generates new scientific evidence by identifying gaps in existing scientific evidence and supporting new research. The program puts special emphasis on translating findings into a variety of useful formats for different stakeholders, including consumers.

The full report and this summary are available at **www.effectivehealthcare.ahrq.gov/reports/final.cfm**

AHRQ
Agency for Healthcare Research and Quality
Advancing Excellence in Health Care • www.ahrq.gov

Effective Health Care

CABG is generally preferred for patients with left main coronary artery disease or severe triple-vessel disease with reduced left ventricular function because it has been previously shown in randomized trials to improve survival compared with medical therapy. In contrast, PCI is generally preferred for patients with most forms of single-vessel disease when symptoms warrant coronary revascularization, in light of its lower procedural risk and the evidence that PCI reduces angina and myocardial ischemia in this subset of patients.

The choice between PCI and CABG is most relevant for patients whose coronary artery disease (CAD) lies in between these extremes, namely patients with single-vessel disease of the proximal left anterior descending artery (LAD), most forms of double-vessel CAD, and less extensive forms of triple-vessel CAD. Most randomized controlled clinical trials (RCTs) of angioplasty and surgery have been conducted in this middle segment of the patient population with CAD.

The purpose of this report is to evaluate the evidence for the comparative effectiveness of PCI and CABG in this population of patients with CAD. Specifically, the report addresses the following key questions:

Key Question 1a. In patients with ischemic heart disease and angiographically proven single or multi-vessel disease, what is the effectiveness of PCI compared with CABG in reducing the occurrence of adverse objective outcomes and improving subjective outcomes?

Key Question 1b. Over what period of time are the comparative benefits of PCI and CABG sustained?

Key Question 2. Is there evidence that the comparative effectiveness of PCI and CABG varies based on:

a. Age, sex, race, or other demographic risk factors?

b. Coronary disease risk factors, diabetes, or other comorbid disease?

c. Angiographic-specific factors including, but not limited to, the number of diseased vessels amenable to bypass or stenting, vessel territory of stenoses (e.g., left main or anterior descending coronary arteries, right coronary artery, circumflex coronary artery), diffuse vs. focal stenoses, left ventricular function, or prior revascularization procedures?

d. CABG-specific factors including, but not limited to, cardiopulmonary bypass mode (normothermic vs. hypothermic), type of cardioplegia used (blood vs. crystalloid), or use of saphenous vein grafts, single or bilateral internal mammary artery grafts, or other types of bypass grafts?

e. Clinical presentation (e.g., stable angina or unstable angina based on New York Heart Association functional class I-IV, acute coronary syndrome, cardiogenic shock, acute myocardial infarction with or without ST elevation, or silent ischemia)?

f. Adjunctive medical therapies, such as short-term intravenous or oral antiplatelet drugs, or long-term use of oral antiplatelet drugs?

g. Process characteristics such as provider volume, hospital volume, and setting (e.g., academic vs. community)?

h. Prior PCI or CABG revascularization procedures?

Conclusions

We identified 23 RCTs of PCI vs. CABG that enrolled a total of 9,963 patients. (Descriptions and full names of RCTs are shown in Tables A and B.) The early studies (patient entry 1987-1993) principally used balloon angioplasty as the PCI technique, and the recent studies (1994-2002) principally used stents as the PCI technique. Only one small trial of PCI vs. CABG used drug-eluting stents (Seoul-Hong). The demographic characteristics and cardiac risk factor profiles of trial participants were typical of patients with coronary disease, although only 27 percent of trial patients were women and few trials included patients age 75 and over. Patients with either left main disease, single-vessel disease other than in the proximal LAD, prior CABG, or poor left ventricular function were generally excluded. Among PCI-assigned patients, use of stents and adjunctive medical therapy (e.g., dual antiplatelet therapy) was common in the recent studies but not in the earlier trials conducted when balloon angioplasty was standard. Arterial grafting with the left internal mammary artery was frequently employed in CABG-assigned patients, especially in more recent trials. The quality of most trials was high; all but two trials included randomization methods that were sound and clearly explained, their dropout rates were low, and they performed intention-to-treat analyses.

To assess the extent to which the RCT results are generalizable to the wider population of patients presenting with CAD, we evaluated the results of 96 articles reporting on patients who received either PCI or CABG and were followed in 10 large registries. Overall the quality of the observational studies was high because each enrolled large numbers of subjects who had good followup and adequate descriptions of most key subject characteristics. Among the registries, patients with single-vessel disease were more likely to be selected for PCI, whereas patients with left main or extensive triple-vessel disease or total coronary occlusions were more likely to be selected for CABG.

Short-term/procedural outcomes

For consistency, throughout this document, we present results in the positive frame (e.g., survival rather than mortality, freedom from strokes rather than strokes). We present PCI-CABG survival differences and PCI-CABG differences in freedom from myocardial infarction (MI), stroke, angina, and repeat revascularization such that positive numbers favor PCI and negative numbers favor CABG. Similarly, we present PCI/CABG odds ratios such that ratios greater than 1.0 favor PCI and ratios less than 1.0 favor CABG. In this section, we present the short-term/procedural outcomes which were reported either as "in hospital," "procedural," or "within 30 days" of the procedure. Results were statistically homogeneous unless otherwise noted.

Procedural survival. In randomized trials, procedural survival was high for both procedures and did not differ significantly: PCI-CABG procedural survival difference was 0.1 percent (95-percent confidence interval (CI): -0.3 to +0.6 percent) and PCI/CABG odds ratio for survival of 1.4 (CI: 0.98 to 1.97). There were no significant differences in procedural survival when trials were subdivided into balloon-era and stent-era studies or into single-vessel-disease and multi-vessel-disease patient populations.

In large registries, procedural survival has increased significantly over time. Short-term procedural survival after PCI generally exceeded that of CABG in both earlier and more recent time intervals, however, even after controlling for differences in clinical characteristics.

Freedom from procedural strokes. Freedom from procedural stroke (reported by 16 randomized trials) was significantly higher after PCI than after CABG: PCI-CABG difference in freedom from procedural stroke of 0.6 percent (CI: 0.2 to 1.0 percent, p=0.002) and PCI/CABG odds ratio for freedom from procedural stroke 1.96 (CI: 1.16, 3.3, p=0.01).

Freedom from procedural myocardial infarctions. Freedom from procedural MI was not assessed in a consistent fashion across trials of PCI and CABG, and there was significant heterogeneity in this outcome among the randomized trials. The pooled PCI-CABG difference in freedom from procedural MI was small and not statistically significant.

Long-term outcomes

Survival. Long-term survival across all randomized trials between 1 and 5 years of followup was similar in CABG-assigned and PCI-assigned patients, with less than 1-percent absolute PCI-CABG survival difference at each time point. (PCI/CABG odds ratios ranged from 0.94 to 1.13.) None of the differences was statistically significant.

The long-term survival difference between PCI and CABG was significantly different in the older trials that relied on balloon angioplasty, but not in the more recent trials that employed coronary stents. The 5-year survival was higher after CABG in balloon-era trials (PCI-CABG survival difference -2.1 percent, CI: -4.1 to -0.1 percent, p=0.04), whereas 5-year survival did not differ between the procedures in stent-era trials (PCI-CABG survival difference 1.1 percent, CI: -1.4 to +3.7 percent). Stent-era trials included more patients with single-vessel disease, however, and had shorter followup than balloon-era trials.

In large clinical registries, comparative survival after PCI or CABG varied significantly according to the extent of coronary disease. Survival was significantly better after PCI in patients with single-vessel disease that did not involve the proximal LAD, and survival was significantly better after CABG in patients with extensive triple-vessel or left main disease. In analyses from large clinical registries of patients with middle spectrum CAD severity, there was no difference in survival after PCI or CABG.

Freedom from angina. Freedom from angina was significantly greater after CABG than after PCI in randomized trials between 1 and 5 years post-procedure. (PCI-CABG difference in freedom from angina ranged from -5.0 percent to -8.0 percent; PCI/CABG odds ratio ranged from 0.50 to 0.66, $p<0.0001$ at 1, 3, and 5 years.)

Freedom from repeat revascularization. Freedom from repeat coronary revascularization was significantly greater after CABG than after PCI. (PCI-CABG difference in freedom from repeat revascularization ranged from -23 to -33 percent, PCI/CABG odds ratios ranged from 0.11 to 0.13; $p <0.0001$ at 1 and 5 years.) The gap between PCI and CABG in repeat revascularization procedures narrowed in more recent trials that used coronary stents. Nevertheless, patients undergoing PCI with stents required repeat procedures significantly more often than patients undergoing CABG.

Freedom from myocardial infarction. The PCI-CABG difference in freedom from MI was small, less than 1 percent (PCI/CABG odds ratios ranged from 0.87 to 0.92), between 1 and 5 years after the procedure and did not achieve statistical significance at any time point.

Quality of life. Eleven randomized trials reported quality-of-life data using a variety of different measures. In general, quality-of-life scores improved to a significantly greater extent after CABG than after PCI between 6 months and 3 years of followup but equalized thereafter. The degree of improvement in quality of life was correlated with relief of angina.

Cost. The methods of cost determination varied among trials and countries, yet 9 of the 10 RCTs found that the initially lower cost among PCI-assigned patients narrowed substantially over followup. In medium- to long-term followup, PCI-assigned patients had only modestly lower costs (roughly 5 percent) than CABG-assigned patients. This pattern of progressively narrowing cost differences was evident both in trials employing balloon angioplasty and in trials using coronary stents.

Comparative effectiveness by patient demographics

In contrast to the fairly robust evidence concerning overall clinical outcomes, there was much less evidence from randomized trials to gauge whether the comparative effectiveness of CABG and PCI varies according to patient or provider characteristics. Most clinical trials have not reported outcomes in key subgroups, and most have reported only survival, not other outcomes. The most extensively examined subgroup (patients with diabetes) was reported by only 7 of 23 randomized trials. Furthermore, the selection of patients and providers to participate in trials narrowed the range of clinical characteristics and reduced the statistical power to detect variations. For example, most patients in RCTs had preserved left ventricular function, so variations in the efficacy of PCI and CABG according to ventricular function would be difficult to detect. Nevertheless, some conclusions can be drawn from the evidence provided by randomized trials and large registries.

Age. Older patients had more procedural complications from both PCI and CABG, especially stroke. Patients aged 65 years and older had lower long-term survival compared with younger patients. The survival difference between PCI and CABG at 7 years in the BARI trial did not significantly favor CABG in the older patients (-4.7 percent PCI-CABG survival difference) to a greater extent than in the younger patients (-2.8 percent PCI-CABG survival difference). Older patients had more freedom from angina, however, and more freedom from repeat revascularization procedures. The randomized trials enrolled very few patients 75 years of age and over, so conclusions about the comparative effectiveness of PCI and CABG cannot be made for very old patients.

Gender. Roughly 27 percent of the patients in randomized trials were women, and their outcomes were similar to those among men in the trials that examined outcomes by gender. In the BARI trial, women had lower overall survival than men with each procedure, but the PCI-CABG survival difference in women was similar to that in men. In the pooled data from four stent-era trials (ARTS, ERACI-II, MASS-II, SoS), women had clinical outcomes relatively similar to those of men.

Race. Outcomes after PCI and CABG according to race were analyzed only by the BARI trial and registry, which found African-American patients had significantly lower overall survival, irrespective of treatment with PCI or CABG.

Comparative effectiveness by comorbidities

Diabetes. Survival at 1 and 5 years in patients with diabetes was reported by six trials (Figure A). The BARI trial reported a significant survival advantage for patients with diabetes assigned to CABG: 5-year survival of 80 percent with CABG vs. 65 percent with PCI. None of the other trials found as dramatic a difference in survival between patients with and without diabetes. In the EAST trial, for example, the 59 patients with treated diabetes had slightly better survival in the PCI arm at 3 years, equivalent survival at 5 years, and slightly better survival in the CABG arm at 8 years. Among the 62 patients with diabetes in the RITA trial, however, only 2 of the 29 PCI patients died, compared with 8 of the 33 CABG patients. Overall, the survival difference between PCI and CABG was not significantly different among patients with diabetes (Figure A); the pooled PCI-CABG survival difference was -0.8 percent at 5 years, but the confidence limits were very wide, from -8.3 to +6.6 percent (PCI/CABG odds ratio 0.87; CI: 0.51 to 1.49).

Obesity. In general, obesity was not consistently associated with significant differences in comparative effectiveness of PCI and CABG in the two trials that reported outcomes by body mass index. Overall rates of survival, freedom from MI, and freedom from stroke were not affected by body mass index in the ARTS trial. Survival in the BARI trial was decreased in patients with either a very low (<20) or a very high (≥35) body mass index.

Other comorbidities. Outcomes according to hypertension, tobacco use, renal dysfunction, and vascular disease were not generally reported by randomized trials.

Comparative effectiveness by angiographic factors

Extent of disease. There was no significant difference in the comparative survival benefit when randomized trials were subdivided into those enrolling patients with single-vessel proximal LAD disease and those enrolling patients with multi-vessel disease (Figure B). In the RITA trial, the survival difference between PCI and CABG was comparable in patients with single-vessel disease and multi-vessel disease (mostly two-vessel disease).

In the randomized trials that enrolled patients with multi-vessel disease, the survival difference between CABG and PCI was greater among patients with three-vessel disease than among patients with two-vessel disease but did not achieve statistical significance. The randomized trials generally excluded patients with extensive coronary disease. Accordingly, comparative efficacy of CABG and PCI according to variations in coronary anatomy could not be fully tested.

In large clinical registries, comparative survival after PCI or CABG varied significantly with the extent of coronary disease, with better survival after PCI in patients with the least extensive coronary disease and better survival after CABG in patients with the most extensive disease.

Left ventricular function. Most trials comparing PCI and CABG randomized patients with relatively preserved left ventricular function and a low prevalence of heart failure. The limited range of ejection fractions within the trials precludes a stringent test of whether the comparative effectiveness of PCI and CABG varies according to left ventricular function. Only the BARI and AWESOME trials reported specific analyses: they found no significant differences in the comparative efficacy of PCI and CABG according to the level of left ventricular function.

Comparative effectiveness by CABG-specific factors

Use of minimally invasive techniques. "Minimally invasive" surgery, which is performed through a small throracotomy incision on a beating heart, was compared with PCI in eight small randomized trials. These trials enrolled patients with single-vessel proximal LAD disease (predominantly or exclusively) and generally used PCI with stents as the comparator. These trials showed no significant differences in survival between PCI and CABG over a relatively short followup period.

Use of internal mammary arteries. Standard CABG was used in all trials that enrolled patients with multivessel disease, with variable use of left internal mammary grafting, ranging from a low of 37 percent in the early GABI study to over 90 percent in the more recent ARTS, MASS-II, and SoS studies. In a meta-regression, the 1-year survival advantage for CABG vs. PCI increased along with the proportion of internal mammary artery grafts used, but this trend was not statistically significant and not evident at 5 years.

Comparative effectiveness by clinical presentation

Three randomized trials (ARTS, BARI, and SoS) examined the outcomes of patients according to their clinical presentation. Comparative survival after PCI and CABG was not consistently different between patients with stable or unstable angina. The randomized trials generally excluded patients with acute myocardial infarction, severe congestive heart failure, or cardiogenic shock, so no conclusions about the comparative efficacy of PCI and CABG can be drawn for these patient subgroups.

Comparative effectiveness and use of adjunctive medical therapies

The RCTs did not report comparative effectiveness data based on the use of adjunctive medical therapy for PCI or CABG. It is uncertain whether patients who have undergone CABG are as likely as patients who have undergone PCI to comply with recommendations for long-term use of aspirin, beta-blockers, angiotensin-converting enzyme inhibitors, and statins. There is relatively little evidence on this question from randomized trials; however, the Duke Database, a large observational registry of patients receiving both procedures, reports relatively similar use of evidence-based therapies after PCI and CABG.

Comparative effectiveness and volume-outcome relationship

There was considerable evidence that procedural outcomes of both CABG and PCI were significantly worse in low-volume hospitals and with low-volume operators. This relationship remained significant for PCI, even as procedural risk has been reduced by the availability of coronary stents and adjunctive therapy. While none of these studies were randomized and causality is uncertain, these findings are consistent with a large body of literature demonstrating a relationship between the volume of patients treated and short-term survival for a wide variety of procedures. The magnitude of association of procedural outcomes with volume of PCI and CABG may be only modest, however, at least among sufficiently experienced centers and operators.

Comparative effectiveness and prior revascularization

Most randomized trials excluded patients with prior CABG, but one randomized trial and several clinical registries have compared PCI with re-do CABG in patients with a prior CABG. In the AWESOME trial, 142 patients with prior CABG were randomized to either re-do CABG (75 patients) or PCI (67 patients). While procedural survival was significantly lower in the patients assigned to CABG (92 vs. 100 percent), 3-year survival did not differ significantly. A similar pattern has been reported by large clinical registry studies from Cleveland, Emory, and Kansas City: procedural mortality was higher for re-do CABG than for PCI, but survival at 5 to 6 years of followup did not differ significantly.

Remaining Issues

This comprehensive review of the comparative effectiveness of PCI and CABG identified numerous gaps in evidence that would be suitable for future research. The paucity of published analyses of PCI and CABG outcomes according to patient characteristics strongly suggests the value of a collaborative pooling of individual patient-level data from the randomized trials to (a) enhance statistical power to identify subgroup effects and (b) reduce publication bias by including data from all trials. A collaboration of four stent trials (ARTS, ERACI-II, MASS-II, and SoS) has pooled 1-year outcomes and provided useful short-term analysis in key subgroups. The planned extension of this collaborative pooling to include 5-year followup data should be very informative.

A more extensive collaborative study to pool individual patient data from both balloon-era and stent-era trials would provide additional advantages. First, the number of patients and outcome events would be greatly increased, thereby improving statistical power even

further in patient subgroups. Second, more direct assessments of the impact of stents on the comparative effectiveness of PCI and CABG would be feasible, as well as assessment of whether relative efficacy changes over extended followup.

Further research on the association of procedure volume with outcome should examine additional outcome measures, both short term (e.g., nonfatal myocardial infarction, completeness of revascularization) and long term (e.g., survival, angina relief, freedom from repeat procedures), preferably in large patient cohorts using contemporaneous CABG and PCI and applying the same analytic methods. Development of evidence-based process measures for PCI and CABG would facilitate efforts to improve quality of care and might provide better performance measures than procedure volume. However, research is required to understand the relative ability of structural measures (e.g., volume) and process measures to predict institutions or physicians with low-quality CABG and PCI outcomes.

Further clinical trials are also needed to assess whether the availability of drug-coated stents has affected the comparative efficacy of PCI and CABG. Such trials are particularly warranted, as pooled studies suggest that rates of survival and MI are not different between bare metal stents and drug-coated stents over medium-term followup. Recent safety concerns about drug-coated stents emphasize the need for extended followup and trials large enough to detect clinically meaningful differences in outcomes. Furthermore, the procedural risk of CABG in large registries has also declined progressively over time, indicating that both CABG and PCI methods continue to evolve. Several trials to compare contemporary CABG with PCI using drug-coated stents, including the large FREEDOM (NCT 00086540) and SYNTAX trials (NCT 00114972), are currently underway and should be complete in 2012.[1]

[1] NCT numbers are National Clinical Trial numbers, which the National Institutes of Health assigns to trials for tracking purposes.

Full Report

This executive summary is part of the following document: Bravata DM, McDonald KM, Gienger AL, Sundaram V, Perez MV, Varghese R, Kapoor JR, Ardehali R, McKinnon MC, Stave CD, Owens DK, Hlatky MA. Comparative Effectiveness of Percutaneous Coronary Interventions and Coronary Artery Bypass Grafting for Coronary Artery Disease. Comparative Effectiveness Review No. 9. (Prepared by Stanford-UCSF Evidence-based Practice Center under Contract No. 290-02-0017.) Rockville, MD: Agency for Healthcare Research and Quality. October 2007. Available at: www.effectivehealthcare.ahrq.gov/reports/final.cfm.

For More Copies

For more copies of Comparative Effectiveness of Percutaneous Coronary Interventions and Coronary Artery Bypass Grafting for Coronary Artery Disease: Executive Summary. No. 9 (AHRQ Pub. No. 08-EHC002-1), please call the AHRQ Clearinghouse at 1-800-358-9295 or e-mail ahrqpubs@ahrq.gov.

Table A. Brief overview of reviewed randomized controlled trials

AMIST—Angioplasty versus Minimally Invasive Surgery Trial A small United Kingdom trial of 100 patients with single-vessel proximal LAD disease conducted 1999-2001. Reeves BC, Angelini GD, Bryan AJ, et al. A multi-centre randomised controlled trial of minimally invasive direct coronary bypass grafting versus percutaneous transluminal coronary angioplasty with stenting for proximal stenosis of the left anterior descending coronary artery. Health Technol Assess 2004 Apr;8(16):1-43.
ARTS—Arterial Revascularization Therapies Study A large European trial of 1,205 patients with MVD that used bare metal stents. One of four trials that participated in the pooling project of stent trials. Serruys PW, Unger F, Sousa JE, et al. Comparison of coronary-artery bypass surgery and stenting for the treatment of multivessel disease. N Engl J Med 2001 Apr 12;344(15):1117-24.
AWESOME—Angina With Extremely Serious Operative Mortality Evaluation A medium-sized U.S Department of Veterans Affairs trial of 454 patients with medically refractory angina, high procedural risk, and single- or multi-vessel disease. Morrison DA, Sethi G, Sacks J, et al. Percutaneous coronary intervention versus coronary artery bypass graft surgery for patients with medically refractory myocardial ischemia and risk factors for adverse outcomes with bypass: a multicenter, randomized trial. Investigators of the Department of Veterans Affairs Cooperative Study #385, the Angina With Extremely Serious Operative Mortality Evaluation (AWESOME). J Am Coll Cardiol 2001 Jul;38(1):143-9.
BARI—Bypass Angioplasty Revascularization Investigation Large U.S.-Canadian trial of 1,829 patients that used balloon angioplasty and reported extensively on outcomes in patient subgroups. Extended followup to 10 years has been reported. The Bypass Angioplasty Revascularization Investigation (BARI) Investigators. Comparison of coronary bypass surgery with angioplasty in patients with multivessel disease. N Engl J Med 1996 Jul 25;335(4):217-25.
CABRI—Coronary Angioplasty versus Bypass Revascularisation Investigation Large European trial of 1,054 patients with MVD that used balloon angioplasty and had limited followup. CABRI Trial Participants. First-year results of CABRI (Coronary Angioplasty versus Bypass Revascularisation Investigation). Lancet 1995 Nov 4;346(8984):1179-84.
EAST—Emory Angioplasty versus Surgery Trial A medium-sized, single-center U.S. trial of 392 patients with MVD that used balloon angioplasty and reported extended followup to 8 years. King SB, 3rd, Lembo NJ, Weintraub WS, et al. A randomized trial comparing coronary angioplasty with coronary bypass surgery. Emory Angioplasty versus Surgery Trial (EAST). N Engl J Med 1994 Oct 20;331(16):1044-50.
ERACI-I—Argentine Randomized Trial of PTCA versus CABG in Multi-Vessel Disease A small Argentine trial of 127 patients with MVD that used balloon angioplasty and had limited followup. Rodriguez A, Boullon F, Perez-Balino N, et al. for ERACI Group. Argentine randomized trial of percutaneous transluminal coronary angioplasty versus coronary artery bypass surgery in multivessel disease (ERACI): in-hospital results and 1-year follow-up. J Am Coll Cardiol 1993;22(4):1060-7.
ERACI-II—Second Argentine Randomized Trial of PTCA versus CABG in Multi-Vessel Disease A medium-sized trial of 450 patients with MVD conducted by the same Argentine group that organized ERACI-I. The trial used bare metal stents and was one of four trials that participated in the primary data pooling project. Rodriguez A, Bernardi V, Navia J, et al. for ERACI II Investigators. Argentine Randomized Study: Coronary Angioplasty with Stenting versus Coronary Bypass Surgery in Patients with Multiple-Vessel Disease (ERACI II): 30-day and one-year follow-up results. J Am Coll Cardiol 2001 Jan;37(1):51-8.

Table A. Brief overview of reviewed randomized controlled trials (continued)

GABI—German Angioplasty Bypass Surgery Investigation A medium-sized German trial of 359 patients with MVD that used balloon angioplasty and has reported the longest followup of any PCI-CABG trial (13 years). Hamm CW, Reimers J, Ischinger T, et al. A randomized study of coronary angioplasty compared with bypass surgery in patients with symptomatic multivessel coronary disease. German Angioplasty Bypass Surgery Investigation (GABI). N Engl J Med 1994 Oct 20;331(16):1037-43.
Groningen A small, single-center Dutch study of 100 patients with single-vessel proximal LAD disease randomized to either stent implantation or minimally invasive bypass surgery. Drenth DJ, Veeger NJGM, Winter JB, et al. A prospective randomized trial comparing stenting with off-pump coronary surgery for high-grade stenosis in the proximal left anterior descending coronary artery: three-year follow-up. J Am Coll Cardiol 2002 Dec 4;40(11):1955-60.
Lausanne A small, single-center Swiss trial of 134 patients with single-vessel proximal LAD disease that used balloon angioplasty. Goy JJ, Eeckhout E, Burnand B, et al. Coronary angioplasty versus left internal mammary artery grafting for isolated proximal left anterior descending artery stenosis. Lancet 1994;343(8911):1449-53.
Leipzig A small, single-center German study of 220 patients with single-vessel proximal LAD disease that compared bare-metal stents with minimally invasive CABG. Diegeler A, Thiele H, Falk V, et al. Comparison of stenting with minimally invasive bypass surgery for stenosis of the left anterior descending coronary artery. N Engl J Med 2002 Aug 22;347(8):561-6.
MASS-I—Medicine, Angioplasty, or Surgery Study A small, single-center Brazilian trial that used three treatment options for patients with single-vessel proximal LAD disease. (Only outcomes in patients assigned to PCI or CABG were used in this report.) Hueb WA, Bellotti G, de Oliveira SA, et al. The Medicine, Angioplasty, or Surgery Study (MASS): a prospective, randomized trial of medical therapy, balloon angioplasty or bypass surgery for single proximal left anterior descending artery stenoses. J Am Coll Cardiol 1995;26(7):1600-5.
MASS-II—Second Medicine, Angioplasty, or Surgery Study A medium-sized Brazilian trial of 408 patients with MVD conducted by the same investigators as the MASS-I trial. This study used bare-metal stents and was one of four trials that contributed to the primary data pooling project for stent trials. Hueb W, Soares PR, Gersh BJ, et al. The Medicine, Angioplasty, or Surgery Study (MASS-II): a randomized, controlled clinical trial of three therapeutic strategies for multivessel coronary artery disease: one-year results. J Am Coll Cardiol 2004 May 19;43(10):1743-51.
Myoprotect I A small, single-center German trial of 44 high-risk patients with left main or left main equivalent disease randomized to PCI supported by retroinfusion of the anterior cardiac vein or to bypass surgery. Pohl T, Giehrl W, Reichart B, et al. Retroinfusion-supported stenting in high-risk patients for percutaneous intervention and bypass surgery: results of the prospective randomized Myoprotect I study. Catheter Cardiovasc Interv 2004;62(3):323-30.
Octostent A medium-sized Dutch trial of 280 patients with single-vessel or multi-vessel disease comparing coronary stents with off-pump bypass surgery. Eefting F, Nathoe H, van Dijk D, et al. Randomized comparison between stenting and off-pump bypass surgery in patients referred for angioplasty. Circulation 2003 Dec 9;108(23):2870-6.

Table A. Brief overview of reviewed randomized controlled trials (continued)

Poland A small, single-center Polish trial of 100 patients with single-vessel proximal LAD disease, comparing coronary stenting with minimally invasive direct coronary bypass grafting. Cisowski M, Drzewiecki J, Drzewiecka-Gerber A, et al. Primary stenting versus MIDCAB: preliminary report – comparison of two methods of revascularization in single left anterior descending coronary artery stenosis. Ann Thorac Surg 2002;74(4):S1334-9.
RITA—Randomised Intervention Treatment of Angina A large United Kingdom trial of 1,011 patients with single-vessel or multi-vessel disease comparing balloon angioplasty with bypass surgery. Henderson RA, Pocock SJ, Sharp SJ, et al. Long-term results of RITA-1 trial: clinical and cost comparisons of coronary angioplasty and coronary-artery bypass grafting. Randomised Intervention Treatment of Angina. Lancet 1998 Oct 31;352(9138):1419-25.
Seoul-Hong A small, single-center Korean trial of 189 patients with proximal LAD disease comparing treatment with DES to MIDCAB. Hong SJ, Lim D-S, Seo HS, et al. Percutaneous coronary intervention with drug-eluting stent implantation vs. minimally invasive direct coronary artery bypass (MIDCAB) in patients with left anterior descending coronary artery stenosis. Catheter Cardiovasc Interv 2005 Jan;64(1):75-81.
Seoul-Kim A small, single-center Korean trial of 100 patients with proximal LAD disease comparing treatment with BMS to MIDCAB. Kim JW, Lim DS, Sun K, et al. Stenting or MIDCAB using ministernotomy for revascularization of proximal left anterior descending artery? Int J Cardiol 2005 Mar 30;99(3):437-41.
SIMA—Stenting versus Internal Mammary Artery study A small European trial of 123 patients with isolated proximal LAD disease comparing coronary stenting with MIDCAB. Goy JJ, Kaufmann U, Goy-Eggenberger D, et al. A prospective randomized trial comparing stenting to internal mammary artery grafting for proximal, isolated de novo left anterior coronary artery stenosis: the SIMA trial. Mayo Clin Proc 2000;75(11):1116-23.
SoS—Stent or Surgery A large European-Canadian trial of 988 patients with MVD comparing coronary stenting with CABG. One of four trials that contributed to the individual data pooling project for stent trials. SoS Investigators. Coronary artery bypass surgery versus percutaneous coronary intervention with stent implantation in patients with multivessel coronary artery disease (the Stent or Surgery trial): a randomised controlled trial. Lancet 2002 Sep 28;360(9338):965-70.
Toulouse A small, single-center French study of 152 patients with single-vessel proximal LAD disease comparing balloon angioplasty with bypass surgery. Carrie D, Elbaz M, Puel J, et al. Five-year outcome after coronary angioplasty versus bypass surgery in multivessel coronary artery disease: results from the French Monocentric Study. Circulation 1997;96(9 Suppl):II-1-6.

Abbreviations: BMS=bare-metal stent; CABG=coronary artery bypass grafting; DES=drug-eluting stent; LAD=left anterior descending artery; MIDCAB=minimally invasive direct coronary artery bypass grafting; PCI=percutaneous coronary intervention; PTCA=percutaneous transluminal coronary angioplasty.

Table B. Summary of comparative effectiveness data for PCI vs. CABG

Key Questions and outcomes	Strength of evidence[a]	Summary, conclusions, and comments
Key Question 1a. Comparative effectiveness objective outcomes and subjective outcomes		
Short-term outcomes		
Procedural survival	Acceptable	- Reported by 23 RCTs. - Procedural survival was slightly but not significantly higher in PCI patients (PCI-CABG survival difference 0.1%; 95% CI: -0.3 to +0.6%). - Procedural survival in RCTs was higher than that reported by large administrative databases and clinical registries.
Freedom from procedural stroke	Acceptable	- Reported by 14 RCTs. - Freedom from procedural strokes was significantly more common after PCI (PCI-CABG difference in freedom from procedural stroke 0.6%; CI: 0.2 to 1.0%; p=0.01).
Freedom from procedural MI	Weak	- Reported by 20 RCTs. - Definition of MI varied across trials; results were heterogeneous. - Freedom from procedural MI was slightly but not significantly lower after CABG.
Long-term outcomes		
Survival	Robust	- Overall survival in RCTs was slightly higher after CABG than after PCI between 1 and 5 years of followup, but the absolute PCI-CABG survival difference was small at each time point (less than 1%) and not statistically significant. - 5-year survival was significantly higher after CABG in balloon-era trials (PCI-CABG survival difference -2.1%; CI: -4.1 to -0.1%). However, in stent-era trials, 5-year survival was not significantly different (PCI-CABG survival difference 1.1%; CI: -1.4 to +3.7%). - There was no significant difference in the PCI-CABG survival difference according to extent of disease.
Freedom from angina	Robust	- Reported by 12 RCTs at 1 year and 7 RCTs at 3 and 5 years. - Freedom from angina was significantly greater after CABG (PCI-CABG difference in freedom from angina ranges from -5% to -8%; p value <0.0001 at 1, 3, and 5 years).
Freedom from repeat revascularization	Robust	- Reported by 11 RCTs at 1 year and 9 RCTs at 5 years - Patients assigned to PCI required 24% more repeat procedures than patients assigned to CABG at 1 year (p <0.0001) and 33% more at 5 years (p<0.0001).
Freedom from myocardial infarction	Acceptable	- 10 RCTs reported followup data. - There was no difference in freedom from MI between PCI and CABG.

Table B. Summary of comparative effectiveness data for PCI vs. CABG (continued)

Key Questions and outcomes	Strength of evidence[a]	Summary, conclusions, and comments
Long-term outcomes (continued)		
Quality of life	Acceptable	- Reported by 11 RCTs using a variety of different measures. - Quality-of-life scores improved significantly more after CABG than after PCI between 1 and 3 years. - Quality-of-life scores were correlated with the presence and severity of angina.
Cost	Robust	- Reported by 10 RCTs using a variety of methods. - 9 RCTs found significantly lower initial costs for PCI than for CABG, but this difference narrowed substantially over subsequent followup.
Key Question 1b. Sustainability of comparative effectiveness		
Survival	Acceptable	- 11 trials (including 77% of all randomized patients) reported 5 or more years of followup. - The PCI-CABG survival difference in these 11 trials did not change significantly between 1 and 5 years. - 4 trials with longer followup showed no major changes in the PCI-CABG survival difference between 5 and 7 to 8 years of followup.
Freedom from angina	Acceptable	- The initial significant advantage of CABG over PCI in freedom from angina grew progressively smaller between 1 year and 5 years of followup.
Key Question 2a. Comparative effectiveness by demographic factors		
Age	Acceptable	- Outcomes by age reported by 3 studies. - There were more procedural complications, especially stroke, in the older patients. - Patients aged 65 years and older had lower overall survival. - The RCTs enrolled very few patients age 75 and over, limiting conclusions about the comparative effectiveness of PCI and CABG in this population.
Gender	Acceptable	- Outcomes by gender reported by 3 studies. - Women had lower overall survival, but the survival difference between PCI and CABG was similar to that in men. - Women had lower quality of life at baseline but improved to a similar degree with CABG and PCI.
Race	Weak	- Outcomes by race reported by only 1 study. - African-American patients had a lower survival regardless of PCI or CABG treatment.

Table B. Summary of comparative effectiveness data for PCI vs. CABG (continued)

Key Questions and outcomes	Strength of evidence[a]	Summary, conclusions, and comments
Long-term outcomes (continued)		
Key Question 2b. Comparative effectiveness by comorbidities		
Diabetes	Acceptable	- Survival at 1 and 5 years in patients with diabetes was reported by 6 RCTs. - The BARI trial found significantly better survival for patients with diabetes assigned to CABG (5-year survival of 80% vs. 65%). - None of the other five reports found a significant difference in survival between PCI and CABG for patients with diabetes. - The pooled data from all trials showed no significant difference in survival after PCI vs. after CABG (PCI-CABG survival difference -0.8%; CI: -8.3 to +6.6%).
Obesity	Weak	- Obesity did not consistently alter the comparative effectiveness of PCI and CABG.
Other comorbidities	Weak	- There was no evidence suggesting that hypertension, tobacco use, renal dysfunction, and vascular disease increased risk differently among PCI and CABG recipients.
Key Question 2c. Comparative effectiveness by angiographic factors		
Extent of disease	Acceptable	- There was no significant difference by extent of disease among patients assigned to PCI or CABG. - In clinical registries, patients with extensive disease had improved survival with CABG, whereas patients with minimal disease had improved survival with PCI. (Interaction test was highly significant.)
Left ventricular function	Weak	- Few patients with poor left ventricular function were enrolled in RCTs. - There was no evidence that the PCI-CABG survival difference was modified by the degree of left ventricular dysfunction.
Use of stents	Acceptable	- 10 trials used bare-metal stents, 11 used balloon angioplasty, and only the Seoul trial used drug-eluting stents. - Survival at 5 years was significantly better after CABG in balloon-era trials, but there was no difference in survival in stent-era trials.
Key Question 2d. Comparative effectiveness by CABG-specific factors		
Use of minimally invasive techniques	Weak	- "Minimally invasive" surgery has been compared with PCI in 7 small RCTs. - These trials showed similar outcomes after PCI and CABG over a relatively short followup period.
Use of mammary arteries	Weak	- Internal mammary artery use increased over time.

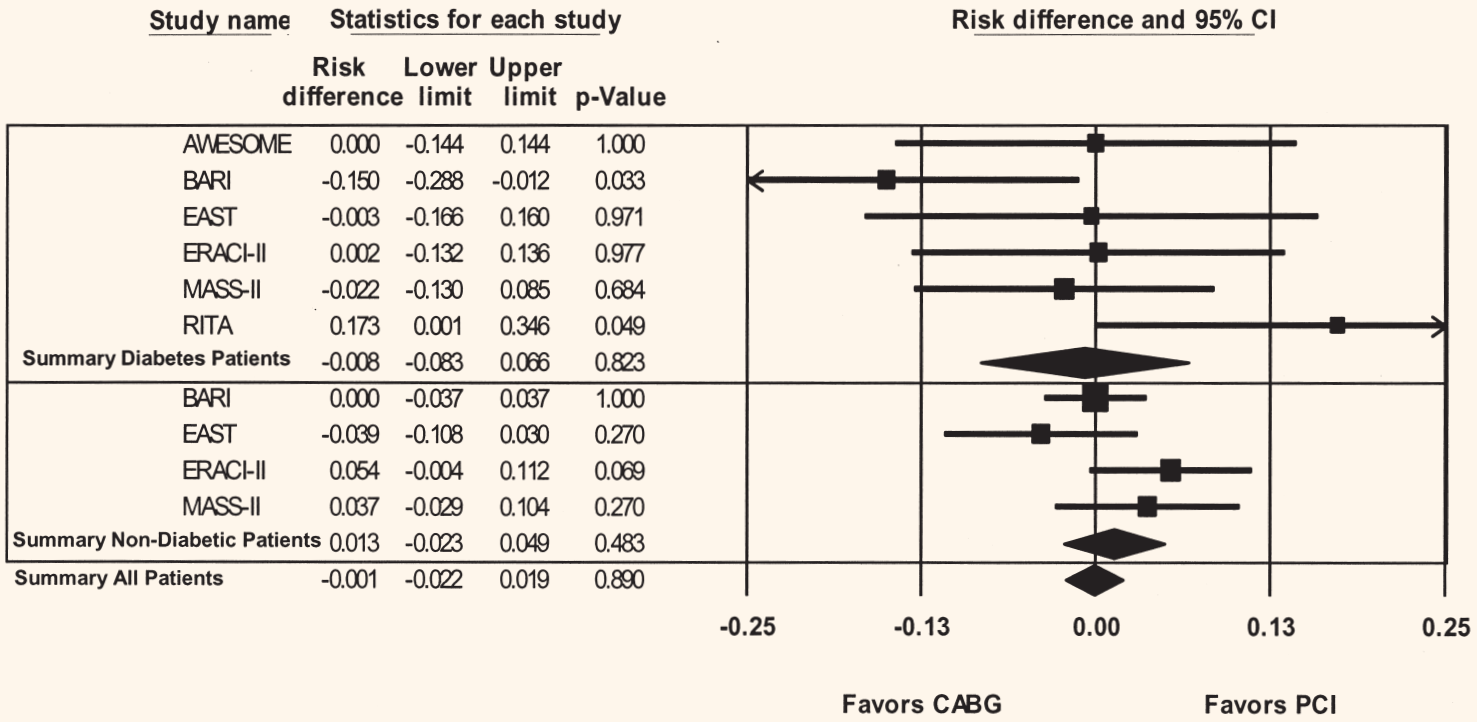
Table B. Summary of comparative effectiveness data for PCI vs. CABG (continued)

Key Questions and outcomes	Strength of evidence[a]	Summary, conclusions, and comments
Long-term outcomes (continued)		
Key Question 2e. Comparative effectiveness by clinical presentation		
Clinical presentation	Acceptable	- Reported by 3 RCTs. - Comparative survival after PCI and CABG was not consistently different between patients with stable or unstable angina.
Key Question 2f. Comparative effectiveness by adjunctive therapies		
Adjunctive therapies	Weak	- RCTs did not provide comparative effectiveness data based on the use of adjunctive medical therapy for PCI or CABG.
Key Question 2g. Comparative effectiveness by process characteristics		
Process characteristics	Robust	- Short-term procedural risk of both CABG and PCI increased significantly in low-volume hospitals and with low-volume operators.
Key Question 2h. Comparative effectiveness by prior revascularization		
Prior revascularization	Weak	- 1 RCT and several clinical registries have compared PCI with re-do CABG in patients with a prior CABG. - Procedural risk was considerably higher in CABG patients assigned to CABG, but there is no difference in late survival.

[a] Strength of evidence was based on predefined criteria, as defined by the GRADE methodology.

Abbreviations: CABG=coronary artery bypass grafting; CI=confidence interval; MI=myocardial infarction; PCI=percutaneous coronary intervention; RCT=randomized controlled trial.

Figure A. Comparison of survival among patients with and without diabetes at 5 years

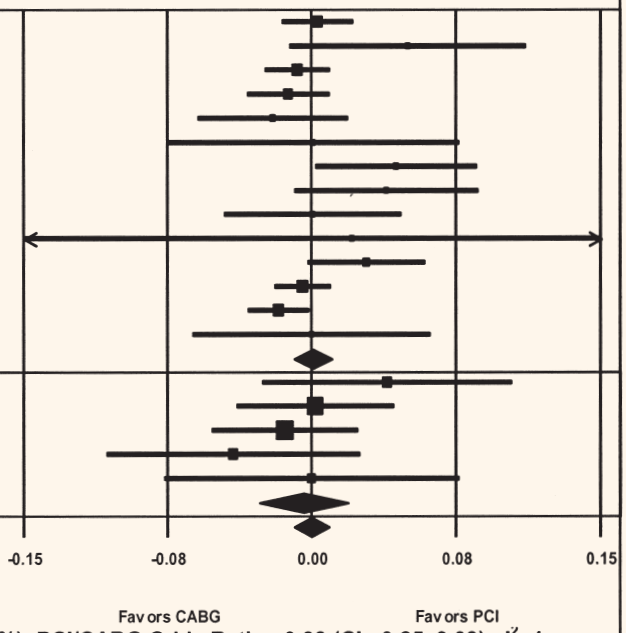


Patients with diabetes: Heterogeneity statistics: Q=8.4; p-value = 0.14; I^2=40. PCI/CABG odds ratio: 0.87 (CI: 0.51, 1.49; p=0.6).
Patients without diabetes: Heterogeneity statistics: Q=5.0; p-value = 0.2; I^2=40. PCI/CABG odds ratio: 1.16 (CI: 0.75, 1.78; p=0.5).

Note: All studies reporting comparative effectiveness data for patients with diabetes were included in this analysis, not just the studies reporting comparative outcomes for patients with and without diabetes.
Abbreviations: CABG=coronary artery bypass grafting; CI=confidence interval; PCI=percutaneous coronary intervention.

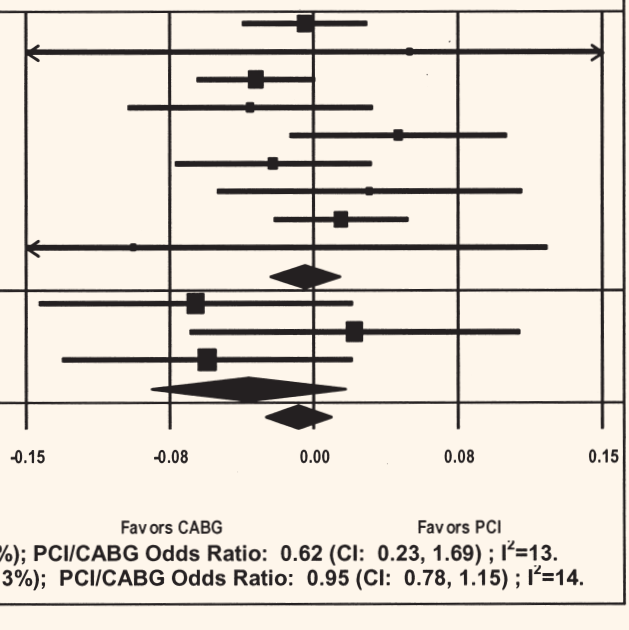
Figure B. Comparison of single (SVD) with multi-vessel (MVD) survival at 1 and 5 years

Study name	Risk difference	Lower limit	Upper limit	p-Value	PCI	CABG
ARTS	0.003	-0.015	0.022	0.731	570 / 585	571 / 588
AWESOME	0.050	-0.012	0.112	0.111	189 / 208	175 / 203
BARI*	-0.007	-0.024	0.010	0.408	879 / 915	884 / 914
CABRI	-0.012	-0.034	0.010	0.278	511 / 532	491 / 505
EAST	-0.020	-0.059	0.019	0.318	181 / 191	184 / 190
ERACI	0.001	-0.075	0.077	0.984	59 / 62	58 / 61
ERACI II	0.044	0.002	0.086	0.041	216 / 223	196 / 212
GABI	0.039	-0.009	0.087	0.111	151 / 155	130 / 139
MASS-II	0.001	-0.046	0.047	0.980	183 / 194	181 / 192
Myoprotect	0.021	-0.239	0.281	0.874	16 / 21	14 / 19
Octostent	0.029	-0.002	0.059	0.068	138 / 138	136 / 140
RITA*	-0.005	-0.019	0.010	0.547	497 / 506	489 / 495
SoS	-0.017	-0.033	-0.001	0.037	464 / 476	492 / 496
Toulouse*	-0.000	-0.062	0.062	0.999	70 / 73	68 / 71
MVD Overall	0.000	-0.009	0.010	0.936	4126 / 4279	4071 / 4225
Groningen	0.039	-0.026	0.104	0.238	51 / 51	47 / 49
Leipzig*	0.002	-0.039	0.043	0.925	107 / 110	103 / 106
MASS	-0.014	-0.052	0.024	0.476	70 / 71	70 / 70
Poland	-0.041	-0.107	0.025	0.227	47 / 49	50 / 50
Seoul-Kim	0.000	-0.077	0.077	1.000	48 / 50	48 / 50
SVD Overall	-0.004	-0.027	0.018	0.705	323 / 331	318 / 325
1-year Overall	-0.000	-0.009	0.009	0.940	4450 / 4610	4389 / 4550



1-Year: SVD PCI-CABG Survival Difference: -0.4% (CI: -3.0%, 2.0%); PCI/CABG Odds Ratio: 0.88 (CI: 0.25, 3.08) ; I^2<1.
MVD PCI-CABG Survival Difference: 0.04% (CI: -0.9%, 1.0%); PCI/CABG Odds Ratio: 1.03 (CI: 0.76, 1.4) ; I^2=32.

Study name	Risk difference	Lower limit	Upper limit	p-Value	PCI	CABG
ARTS	-0.005	-0.037	0.028	0.780	504 / 552	513 / 559
AWESOME	0.050	-0.166	0.266	0.649	30 / 38	19 / 26
BARI	-0.030	-0.061	0.001	0.059	727 / 842	768 / 860
EAST	-0.033	-0.097	0.031	0.312	153 / 174	161 / 177
ERACI II	0.044	-0.013	0.101	0.128	194 / 209	176 / 199
GABI*	-0.021	-0.072	0.030	0.421	161 / 173	148 / 156
MASS-II	0.029	-0.050	0.108	0.475	149 / 177	139 / 171
RITA	0.014	-0.021	0.049	0.428	455 / 494	438 / 483
Toulouse	-0.094	-0.309	0.121	0.393	21 / 31	27 / 35
MVD Overall	-0.005	-0.023	0.013	0.587	2393 / 2690	2390 / 2666
Lausanne	-0.062	-0.143	0.020	0.141	59 / 65	63 / 65
Leipzig	0.021	-0.065	0.107	0.629	95 / 106	91 / 104
MASS	-0.056	-0.131	0.020	0.151	65 / 71	67 / 69
SVD Overall	-0.034	-0.085	0.016	0.180	219 / 242	221 / 238
5-year Overall	-0.008	-0.025	0.009	0.335	2612 / 2932	2611 / 2904



5-Years: SVD PCI-CABG Survival Difference: -3% (CI: -9.0%, 2.0%); PCI/CABG Odds Ratio: 0.62 (CI: 0.23, 1.69) ; I^2=13.
MVD PCI-CABG Survival Difference: -0.5% (CI: -2.3%, 1.3%); PCI/CABG Odds Ratio: 0.95 (CI: 0.78, 1.15) ; I^2=14.

Note: Trial names followed by an asterisk indicate that the survival data were abstracted from Kaplan-Meier curves.
Abbreviations: CABG=coronary artery bypass grafting; CI=confidence interval; PCI=percutaneous coronary intervention.