

Percutaneous coronary intervention versus coronary artery bypass grafting in patients with three-vessel or left main coronary artery disease: 10-year follow-up of the multicentre randomised controlled SYNTAX trial

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ABSTRACT

Background

The Synergy between PCI with Taxus and Cardiac Surgery (SYNTAX) trial was a non-inferiority trial that compared percutaneous coronary intervention (PCI) using first-generation paclitaxel-eluting stents with coronary artery bypass grafting (CABG) in patients with de-novo three-vessel and left main coronary artery disease, and reported results up to 5 years. We now report 10-year all-cause death results.

Methods

The SYNTAX Extended Survival (SYNTAXES) study is an investigator-driven extension of follow-up of a multicentre, randomised controlled trial done in 85 hospitals across 18 North American and European countries. Patients with de-novo three-vessel and left main coronary artery disease were randomly assigned (1:1) to the PCI group or CABG group. Patients with a history of PCI or CABG, acute myocardial infarction, or an indication for concomitant cardiac surgery were excluded. The primary endpoint of the SYNTAXES study was 10-year all-cause death, which was assessed according to the intention-to-treat principle. Prespecified subgroup analyses were performed according to the presence or absence of left main coronary artery disease and diabetes, and according to coronary complexity defined by core laboratory SYNTAX score tertiles. This study is registered with ClinicalTrials.gov, NCT03417050.

Findings

From March, 2005, to April, 2007, 1800 patients were randomly assigned to the PCI (n=903) or CABG (n=897) group. Vital status information at 10 years was complete for 841 (93%) patients in the PCI group and 848 (95%) patients in the CABG group. At 10 years, 248 (28%) patients had died after PCI and 212 (24%) after CABG (hazard ratio 1.19 [95% CI 0.99–1.43], $p = 0.066$). Among patients with three-vessel disease, 153 (28%) of 546 had died after PCI versus 114 (21%) of 549 after CABG (hazard ratio 1.42 [95% CI 1.11–1.81]), and among patients with left main coronary artery disease, 95 (27%) of 357 had died after PCI versus 98 (28%) of 348 after CABG (0.92 [0.69–1.22], $p_{\text{interaction}} = 0.023$). There was no treatment-by-subgroup interaction with diabetes ($p_{\text{interaction}} = 0.60$) and no linear trend across SYNTAX score tertiles ($p_{\text{trend}} = 0.20$).

Interpretation

At 10 years, no significant difference existed in all-cause death between PCI using first-generation paclitaxel-eluting stents and CABG. However, CABG provided a significant survival benefit in patients with three-vessel disease, but not in patients with left main coronary artery disease.

Funding

German Foundation of Heart Research (SYNTAXES study, 5–10-year follow-up) and Boston Scientific Corporation (SYNTAX study, 0-5-year follow-up).

INTRODUCTION

Several randomised trials¹⁻⁸ have compared coronary artery bypass grafting (CABG) versus percutaneous coronary intervention (PCI) with simple balloon angioplasty, bare metal stents, or drug-eluting stents for the treatment of multivessel or left main coronary artery disease, but no significant differences in survival were demonstrated. Results from a pooled analysis of individual patient data⁹ from 11 trials and 11 518 patients suggested that all-cause death was significantly lower after CABG versus PCI at 5-year follow-up (9.2% vs 11.2%; hazard ratio [HR] 1.20 [95% CI 1.06–1.37], $p=0.0038$). However, the mean age of the patient population was 65 years, and thus the overall life expectancy of most patients exceeded this follow-up time. Longer-term follow-up beyond 5 years is required to determine the relative effectiveness of PCI versus CABG. The Synergy between PCI with Taxus and Cardiac Surgery (SYNTAX) trial compared PCI with paclitaxel-eluting stents versus CABG in 1800 patients with de-novo three-vessel disease and left main coronary artery disease, and reported similar survival among patients in the PCI and CABG groups after 5 years of follow-up (13.9% all-cause death in the PCI group vs 11.4% all-cause death in the CABG group, $p=0.10$).^{5,10,11} This study, the SYNTAX Extended Survival (SYNTAXES) study, examined all-cause death after 10 years of follow-up in patients randomly assigned to PCI or CABG in the SYNTAX trial.

Research in context

Evidence before this study

We searched PubMed for articles published in English between database inception and July 24, 2019, with the following search terms: “percutaneous coronary intervention”, “stents”, “coronary artery bypass grafting”, and “random*”. Randomised controlled trials and meta-analyses comparing percutaneous coronary intervention (PCI) using stents versus coronary artery bypass grafting (CABG) in patients with three-vessel or left main coronary artery disease were included. An individual patient data meta-analysis reported that mortality outcomes favoured CABG over PCI at 5-year follow-up in patients with multivessel disease, particularly those with diabetes and more complex coronary artery disease, whereas no significant difference was identified in patients with left main coronary artery disease. It was concluded that longer-term follow-up would be required to better define mortality differences between revascularisation strategies. In our search, we only found two randomised controlled trials reporting survival outcomes at 10 years after PCI versus CABG. In the MASS II trial, patients with multivessel disease had a 10-year all-cause death rate of 24.9% after PCI versus 25.1% after CABG ($p=0.089$). However, PCI was done

with bare metal stents and about 40% of patients had two-vessel disease, and no patients with left main coronary artery disease were included. In the LE MANS trial, which included only patients with left main coronary artery disease ($n=105$), 10-year all-cause death was 21.6% after PCI versus 30.2% after CABG ($p=0.41$). However, the sample size was small and only 35% of PCI procedures were performed with (first-generation) drug-eluting stents. The search did not identify studies reporting outcomes in patients with de-novo three-vessel and left main coronary artery disease randomly assigned to PCI with drug-eluting stents or CABG.

Added value of this study

The current study is the first randomised trial that reports complete 10-year data on all-cause death in patients with de-novo three-vessel and left main coronary artery disease after PCI with drug-eluting stents versus CABG. It provides important insights into the relative effectiveness of PCI versus CABG regarding the most robust and clinically relevant outcome—all-cause death. At 10 years, no significant difference was found in all-cause death between PCI using first-generation paclitaxel-eluting stents and CABG. However, CABG provided a significant survival benefit in patients with three-vessel disease, but not in patients with left main coronary artery disease. These findings can aid decision making for patients with coronary artery disease who require PCI or CABG, accounting for differences in cardiovascular risk factors, coronary lesion complexity (eg, SYNTAX score), and the presence of three-vessel or left main coronary artery disease.

Implications of all the available evidence

Patients with complex, three-vessel coronary artery disease who require revascularisation should undergo CABG as it results in significantly lower all-cause death than PCI. In selected patients with left main coronary artery disease, PCI is a suitable alternative to CABG and provides similar 10-year survival.

METHODS

Study design and patients

The SYNTAX trial (NCT00114972) was a multicentre, randomised controlled trial done in 85 hospitals across 18 North American and European countries, with the aim of assessing non-inferiority of PCI with paclitaxel-eluting stents versus CABG in patients with de-novo three-vessel disease and left main coronary artery disease for the primary endpoint of major adverse cardiac or cerebrovascular events at 1 year. The rationale, design, and 1-year primary endpoint results of the SYNTAX trial

have been published previously, as well as results at prolonged 3-year and 5-year follow-ups.^{1,5,12}

The SYNTAX trial completed follow-up at 5 years and was reinitiated as the SYNTAXES study to evaluate survival up to 10 years (the protocol and CONSORT checklist are available in the appendix pp 26–58). Patients aged 21 years or older with de-novo three-vessel disease and left main coronary artery disease were enrolled with the following exclusion criteria: a history of PCI or CABG, acute myocardial infarction, or an indication for concomitant cardiac surgery (see appendix pp 56–58 for the complete list of inclusion and exclusion criteria).

The SYNTAXES study is registered at ClinicalTrials.gov as an investigator-driven extension of follow-up of the SYNTAX trial. Medical Ethical Committee approval for this study was granted at the institution of the principal investigators (Erasmus University Medical Centre, Rotterdam, Netherlands, reference: MEC-2016-716). Informed consent to obtain information on 10-year vital status was waived, and follow-up was performed in accordance with local law and regulations of each participating site and complied with the Declaration of Helsinki. Survival data were obtained by (electronic) health-care record review and national death registry checks.

Randomisation and masking

Randomisation and masking for the SYNTAXES study was the same as for the SYNTAX study. Briefly, patients who were assessed as equally suitable for CABG or PCI were randomly assigned (1:1) to one of the two treatments, as described in detail in previous publications.^{1,5,12}

Procedures

Procedures were done according to local practice with the intention to accomplish complete revascularisation of any vessel at least 1.5 mm in diameter with stenosis of 50% or more, identified during pre-procedural heart team meetings.¹ CABG could be performed with or without cardiopulmonary bypass and the use of arterial grafts was strongly recommended yet not mandatory. PCI could be performed using a radial, femoral, or brachial approach. Staged PCI procedures were allowed when performed within 72 h of the initial treatment and during the same hospital stay. Every patient was prescribed life-long aspirin, and adherence to contemporaneous guideline- directed medical treatment was highly recommended.¹³

Outcomes

The prespecified primary endpoint of the SYNTAXES study was all-cause death at 10 years in patients randomly assigned to PCI with drug-eluting stents versus CABG. The secondary endpoint was all-cause death at maximum available follow-up in patients randomly assigned to PCI with drug-eluting stents versus CABG.

The left main coronary artery disease subgroup consisted of patients with any left main disease, either isolated, or in combination with single-vessel, two-vessel, or three-vessel coronary artery disease. The three-vessel disease subgroup consisted of patients with coronary artery disease involving all three vessels in the absence of left main coronary artery disease.^{5,12} The anatomical complexity of coronary artery disease was graded according to the SYNTAX score during prerandomisation heart team meetings, with higher SYNTAX scores indicating more complex coronary artery disease.¹⁴ SYNTAX scores, according to core laboratory analyses, were defined according to tertiles, with scores of 22 or lower defined as low, 23–32 as intermediate, and 33 or higher as high.^{1,6} The European System for Cardiac Operative Risk Evaluation (EuroSCORE) was used to assess operative risk. Diabetes was defined as patients requiring treatment with oral hypoglycaemic agents or insulin. Incomplete revascularisation was determined post-procedurally by correlating the revascularised lesions to those lesions identified during the preoperative heart team meeting.

Statistical analysis

The sample size of the SYNTAXES study was based on the sample size considerations for the original trial, which was powered for a non-inferiority comparison of major adverse cardiac and cerebrovascular events at 12 months between PCI and CABG (a complete description of the sample size calculation is provided in the appendix p 6).¹ Sample sizes were calculated for each of the left main coronary artery disease and three-vessel disease subgroups and overall. After allowing for an expected attrition rate of 3.5%, the overall sample size of 1800 patients (900 per group) resulted in 96% power to detect non-inferiority at a noninferiority margin of 6.6% and a one-sided a level of 5%.

All analyses were according to the intention-to-treat principle. Patients with missing follow-up data were included in the analysis and censored at the time they were lost to follow-up or at 5 years if their recruiting hospital did not participate in the 10-year follow-up. We analysed the primary endpoint of 10-year all-cause death using Kaplan-Meier curves, with a log-rank p value to test between-group differences at a two-sided a value of 0.05. We used Cox proportional hazards models to estimate HRs with 95% CIs comparing PCI with CABG. We did landmark analyses in the overall

population and in prespecified subgroups, setting the landmark point at 5 years to distinguish the results of the 5-year analysis in the SYNTAX trial from the extended follow-up in the SYNTAXES study. Landmark analyses were accompanied by a test for interaction between treatment effect and time (first 5 years versus subsequent period). We did a sensitivity analysis of the primary endpoint using a multivariable Cox model with stepwise forward selection of covariates. Prespecified subgroup analyses were done in a hierarchical manner. For the primary subgroup analysis according to the presence or absence of left main coronary artery disease, we used a prespecified Bonferroni correction, which allowed for the treatment-by-subgroup interaction to be tested at a two-sided α value of 0.025 (0.05/2) in addition to comparing the primary endpoint between PCI and CABG in the overall population. For the secondary subgroup analyses according to presence or absence of diabetes and complexity of coronary artery disease defined by ordered SYNTAX score tertiles, we used an additional Bonferroni correction, which allowed for the interaction and the trend of log HRs across ordered SYNTAX score tertiles to be tested at a two-sided α value of 0.0125 (0.05/4). As this approach allowed, without requiring a significant test of the primary endpoint at the prespecified α level before proceeding with treatment-by-subgroup interaction tests, it mitigated the inflation of the type I error rate considerably when performing multiple subgroup analyses, but did not fully control it. Prespecified subgroup analyses of the primary endpoint by age, sex, and ordered SYNTAX score tertiles in left main coronary artery disease and three-vessel disease subgroups were considered exploratory. Additional post-hoc exploratory analyses in the left main coronary artery disease subgroup were performed according to the presence or absence of additional vessel disease (ie, isolated left main coronary artery disease, or left main coronary artery disease in combination with one-vessel, two-vessel, or three-vessel disease). All subgroup analyses were done in unadjusted and adjusted manners (the statistical analysis plan is available in the appendix pp 59–66). The secondary endpoint of all-cause death at maximum follow-up was analysed identically, including post-hoc subgroup analyses. Baseline characteristics of patients with and without availability of 10-year follow-up were compared to address the potential for attrition bias. Analyses were performed using Stata, version 15, and SPSS Statistics software, version 24. This study is registered with ClinicalTrials.gov, NCT03417050.

Role of the funding source

The funders had no role in the SYNTAXES study design, data collection, data analyses, interpretation of the data, or writing of the report. The corresponding author, and APK, MM, BRdC, PJ, and SJH, had full access to the data in the study and had final responsibility for the decision to submit for publication.

RESULTS

From March, 2005, to April, 2007, 1800 patients were randomly assigned to undergo PCI with paclitaxel-eluting stents (n=903) or CABG (n=897: figure 1). Clinical and angiographic characteristics were well matched between groups (table 1). Further details about the procedural characteristics of the patients included in this study have been published previously^{1,5} and are included in the appendix (p 8).

Information on 10-year survival was collected between March 1, 2017, and June 17, 2019. Two hospitals, which included five patients, elected not to participate in the SYNTAXES study. Information on vital status at 10-year follow-up was complete in 841 (93%) patients in the PCI group and 848 (95%) patients in the CABG group. Baseline characteristics of patients with versus without vital status at 10 years are provided in the appendix (p 9). The median duration of follow-up was 11.2 years (IQR 7.7–12.1) overall and 11.9 years (11.2–12.3) in survivors.

Table 1. Baseline clinical and angiographic characteristics

	PCI group (n=903)	CABG group (n=897)
Age, years	65.2 (9.7)	65.0 (9.8)
Sex		
Women	213 (24%)	189 (21%)
Men	690 (76%)	708 (79%)
Body-mass index, kg/m ²	28.1 (4.8)	27.9 (4.5)
Diabetes		
Requiring oral medications or insulin	231 (26%)	221 (25%)
Requiring insulin	89 (10%)	93 (10%)
Metabolic syndrome	339/737 (46%)	317/696 (46%)
Ever smoked	167 (18%)	196/890 (22%)
Previous myocardial infarction	285/893 (32%)	300/887 (34%)
Previous stroke	35/899 (4%)	43/890 (5%)
Previous transient ischaemic attack	39/901 (4%)	45/888 (5%)
Hypertension (≥130/85 mm Hg)	622 (69%)	574 (64%)
Congestive heart failure	36/898 (4%)	47/880 (5%)
Previous carotid artery disease	73 (8%)	75 (8%)
Hyperlipidaemia	705/896 (79%)	686/889 (77%)

Table 1. Baseline clinical and angiographic characteristics (*continued*)

	PCI group (n=903)	CABG group (n=897)
Angina		
Stable	514 (57%)	513 (57%)
Unstable	262 (29%)	251 (28%)
Ejection fraction <30%	12/891 (1%)	22/875 (3%)
EuroSCORE value	3.8 (2.6)	3.8 (2.7)
Parsonnet score	8.5 (7.0)	8.4 (6.8)
SYNTAX score*	28.4 (11.5)	29.1 (11.4)
Number of lesions	4.3 (1.8)	4.4 (1.8)
Total occlusion	217/897 (24%)	198/897 (22%)
Bifurcation lesion	649/897 (72%)	651/890 (73%)
Three-vessel disease	546 (60%)	549 (61%)
Left main coronary artery disease, any	357 (40%)	348 (39%)
Isolated	42/357 (12%)	49/348 (14%)
Plus one-vessel disease	67/357 (19%)	71/348 (20%)
Plus two-vessel disease	112/357 (31%)	106/348 (30%)
Plus three-vessel disease	136/357 (38%)	122/348 (35%)

Data are mean (SD), n (%), or n/N (%), unless otherwise noted. Percentages might not sum to 100% as a result of rounding. Data are reported according to the intention-to-treat principle. CABG=coronary artery bypass grafting. EuroSCORE=European System for Cardiac Operative Risk Evaluation. PCI=percutaneous coronary intervention. *SYNTAX scores are reported according to core laboratory analysed data.

The primary endpoint of all-cause death at 10 years occurred in 248 (28%) of 903 patients after PCI and 212 (24%) of 897 patients after CABG (HR 1.19 [95% CI 0.99–1.43, $p=0.066$; figure 2A). Landmark analysis between 5-year and 10-year follow-up identified that all-cause death occurred in 122 (14%) patients after PCI and in 107 (12%) patients after CABG (HR 1.17 [95% CI 0.91–1.52]; figure 2B). At maximum follow-up, PCI was associated with higher all-cause death than was CABG (303 [34%] vs 265 [29%], HR 1.18 [95% CI 1.00–1.39]; appendix p 15).

There was a treatment-by-subgroup interaction according to presence or absence of left main coronary artery disease ($p_{\text{interaction}}=0.023$). In the three-vessel disease subgroup, all-cause death at 10 years occurred in 153 (28%) of 546 patients after PCI compared with 114 (21%) of 549 patients after CABG (HR 1.42 [95% CI 1.11–1.81]; figure 3A). In the left main coronary artery disease subgroup, all-cause death at 10 years occurred in 95 (27%) of 357 patients after PCI versus 98 (28%) of 348 patients after CABG (HR 0.92 [95% CI 0.69–1.22]; figures 3B, 4). There was no treatment-by-subgroup interaction according to diabetes status ($p_{\text{interaction}}=0.60$; figures 3C, 3D, 4) and ordered SYNTAX score tertiles ($p_{\text{trend}}=0.20$; figures 4, 5). Results were similar

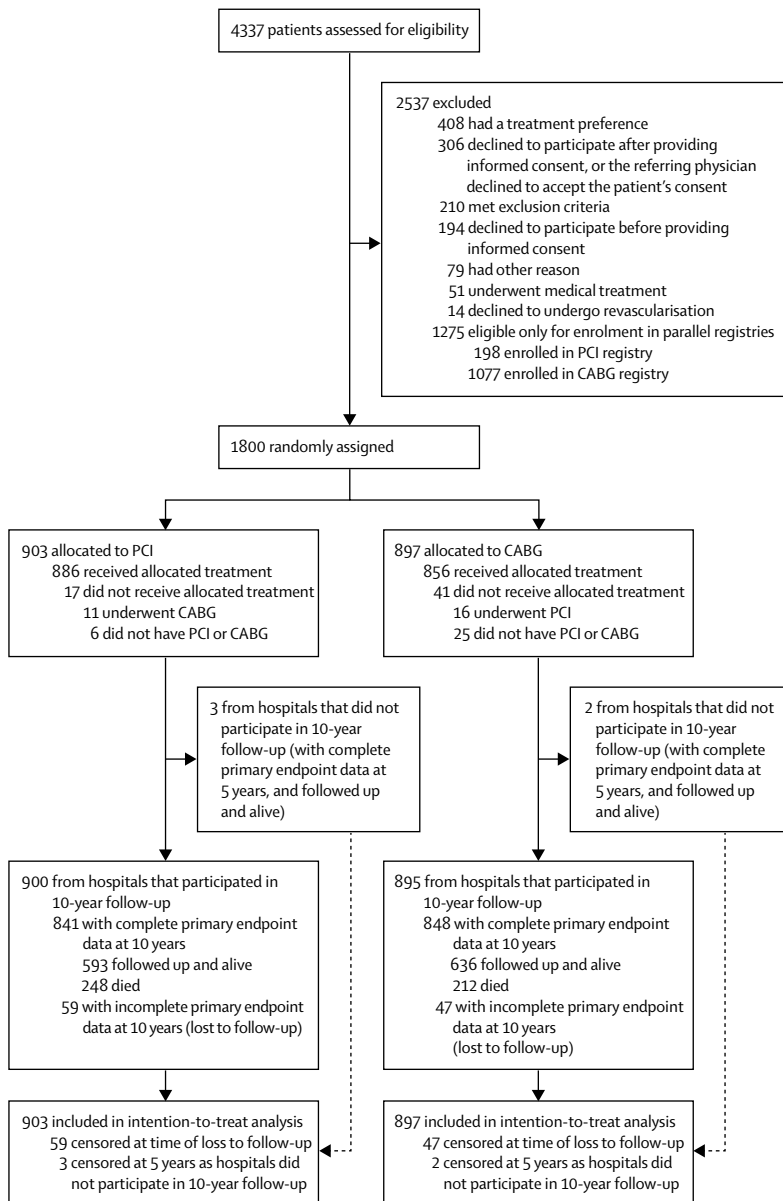


Figure 1. Trial profile Patient flow through the SYNTAX trial (0–5 years of follow-up) and the SYNTAX Extended Survival study (up to 10 years of follow-up). CABG=coronary artery bypass grafting. PCI=percutaneous coronary intervention.

in adjusted subgroup analyses at 10 years and in subgroup analyses at maximum follow-up (appendix pp 16–24). Additional exploratory analyses and the prespecified sensitivity analysis are provided in the appendix (pp 11–14, 25).

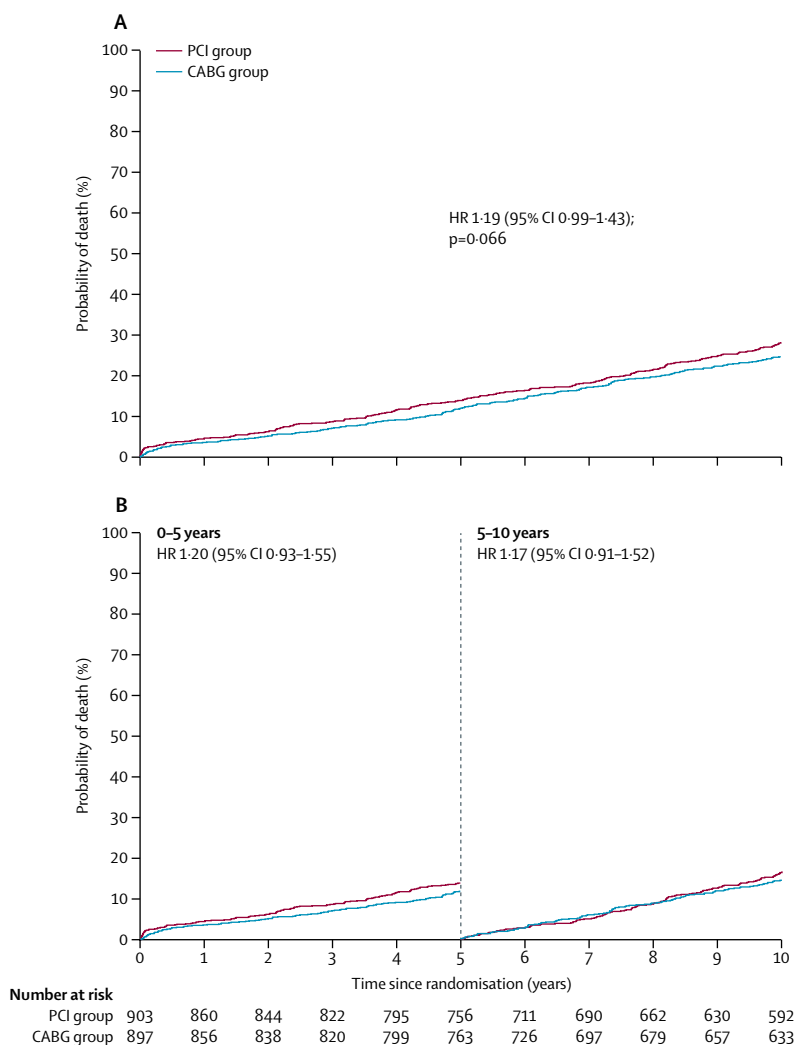


Figure 2. Kaplan-Meier curves for primary analysis of 10-year all-cause death (intention-to-treat population) The probability of all-cause death in PCI versus CABG up to 10 years of follow-up (A) and landmark analysis according to a landmark point at 5 years (B). Because the widths of 95% CIs were not adjusted for multiple comparisons in the landmark analysis, these intervals should not be used for inference about between-group differences. CABG=coronary artery bypass grafting. HR=hazard ratio. PCI=percutaneous coronary intervention.

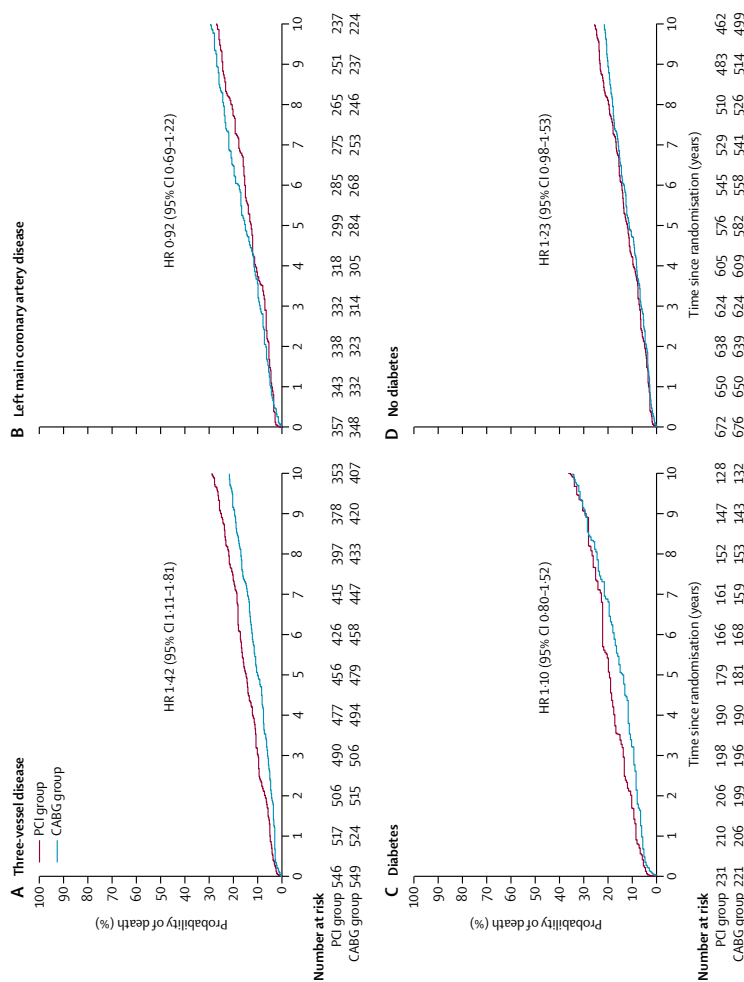


Figure 3. Kaplan-Meier curves for prespecified subgroup analysis of 10-year all-cause death (intention-to-treat population) The probability of all-cause death in PCI versus CABG up to 10 years of follow-up in prespecified subgroups of patients with three-vessel disease (A), with left main coronary artery disease (B), with diabetes (C), and without diabetes (D). p value for interaction for three-vessel disease versus left main coronary artery disease was 0.023, and p value for interaction for diabetes versus no diabetes was 0.60. Because the widths of 95% CIs were not adjusted for multiple comparisons, these intervals should not be used for inference about between-group differences. CABG=coronary artery bypass grafting. HR=hazard ratio. PCI=percutaneous coronary intervention.

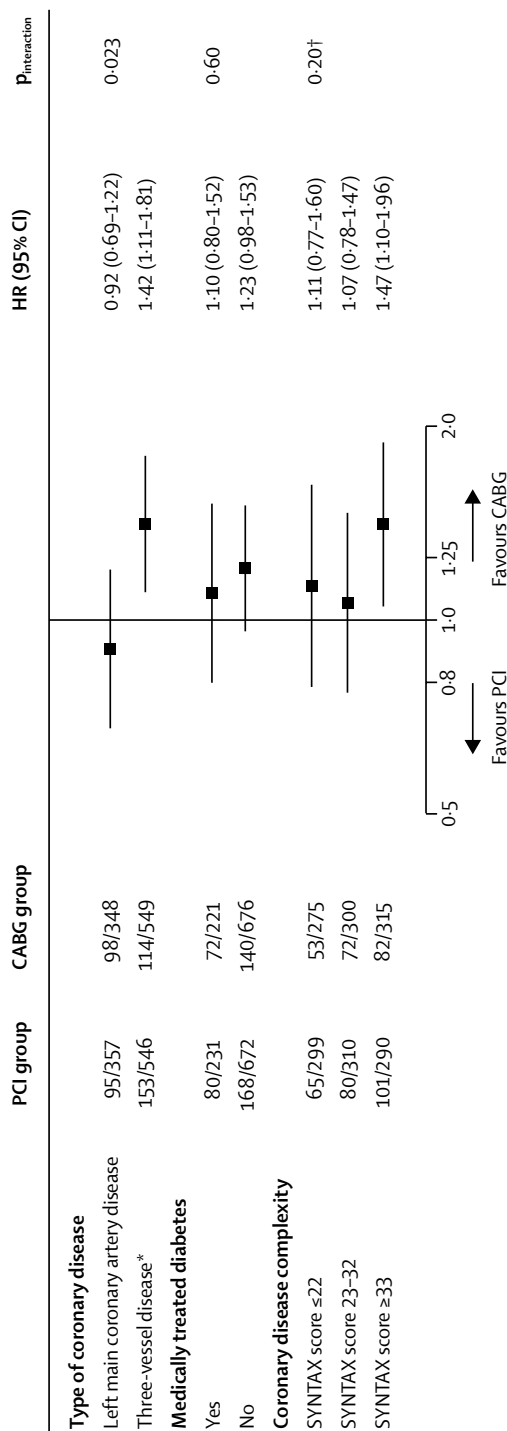


Figure 4. Forest plot of prespecified subgroup analyses of 10-year all-cause death (intention-to-treat population) All-cause death after PCI versus CABG at 10-year follow-up in prespecified unadjusted subgroup analyses according to baseline characteristics. Because the widths of 95% CIs were not adjusted for multiple comparisons, these intervals should not be used for inference about between-group differences. CABG=coronary artery bypass grafting. HR=hazard ratio. PCI=percutaneous coronary intervention. *Patients with coronary artery disease involving all three vessels in the absence of left main coronary artery disease. †p value for trend of log HRs across SYNTAX score tertiles for subgroup analysis according to lesion complexity.



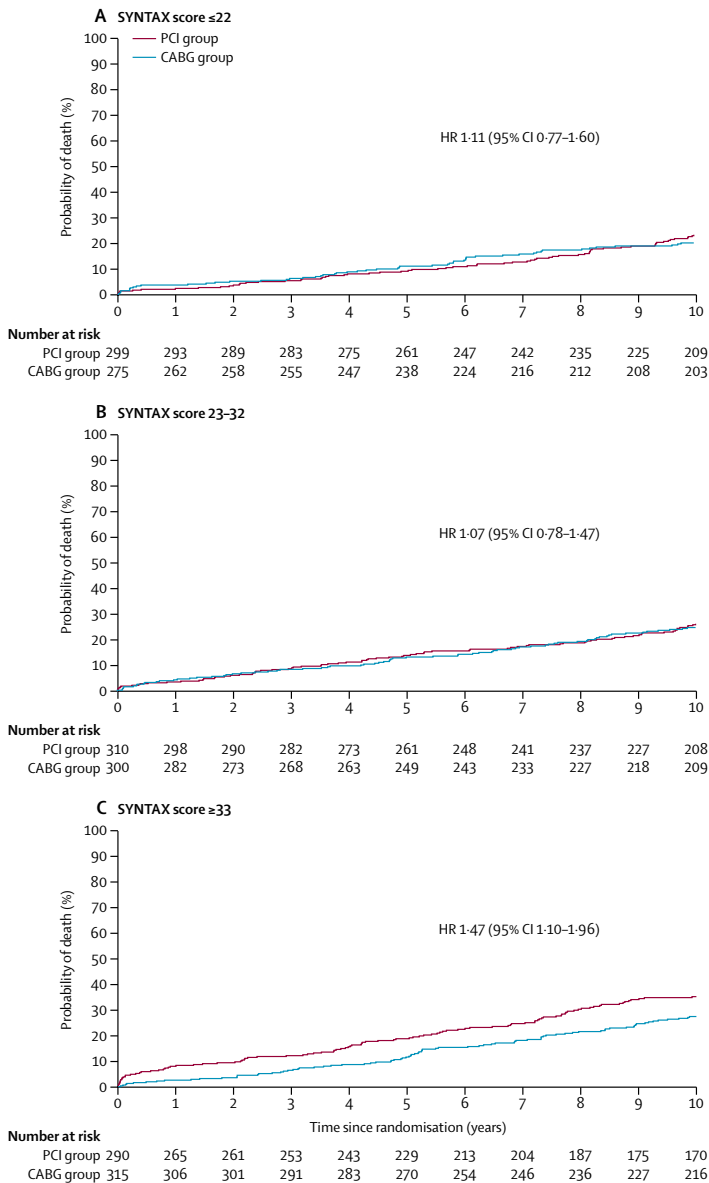


Figure 5. Kaplan-Meier curves for 10-year all-cause death in prespecified SYNTAX score tertile subgroups (intention-to-treat population). The probability of all-cause death in PCI versus CABG up to 10 years of follow-up in prespecified subgroups of patients with low SYNTAX scores (≤ 22 ; A), intermediate SYNTAX scores (23-32; B), and high SYNTAX scores (≥ 33 ; C). p value for trend was 0.30. SYNTAX scores were reported according to core laboratory analysed data. Because the widths of 95% CIs were not adjusted for multiple comparisons, these intervals should not be used for inference about between-group differences. CABG=coronary artery bypass grafting. HR=hazard ratio. PCI=percutaneous coronary intervention.

DISCUSSION

The SYNTAX trial reported similar survival in patients with de-novo three-vessel and left main coronary artery disease randomly assigned to PCI with paclitaxel-eluting stents versus CABG after 5 years of follow-up. The SYNTAXES study is the first study to assess 10-year survival after PCI with drug-eluting stents versus CABG. At 10-year follow-up, the proportions of all-cause deaths between PCI and CABG were similar. Prespecified subgroup analyses identified that CABG resulted in significantly lower all-cause death than did PCI in patients with three-vessel disease, whereas no significant difference between PCI and CABG was identified in patients with left main coronary artery disease. The current study provides unique long-term insights into survival after PCI versus CABG by extending follow-up to 10 years, which could aid in decision making in determining the optimal revascularisation strategy for patients with coronary artery disease. Moreover, the primary endpoint of all-cause death focuses on the most robust endpoint that is clinically relevant for both patients and physicians. In addition, follow-up at 10 years was complete for 94% of randomly assigned patients and equally distributed between CABG and PCI.

In the SYNTAX trial, PCI was performed with first-generation drug-eluting stents that are no longer available. Newer-generation drug-eluting stents have been shown to be associated with significantly improved mid-term (up to 3 years of follow-up) outcomes, including reduction of all-cause death.¹⁵ Moreover, the larger adoption of fractional-flow reserve instead of solely angiography-guided interventions, in combination with the application of intravascular ultrasound, has resulted in improved outcomes after PCI.^{16,17} Indeed, the SYNTAX II study¹⁸ demonstrated that these developments were associated with significant reductions in adverse events during follow-up. Despite these improvements, most recent randomised trials have shown that CABG remained consistently associated with lower rates of repeat revascularisation at mid-term followup compared with PCI, regardless of which type of stent was used.^{2,4} Longer-term follow-up of trials comparing contemporaneous PCI with CABG are therefore warranted to determine the relative effectiveness of PCI versus CABG.

According to our prespecified subgroup analyses, patients with more complex coronary disease (eg, three-vessel disease and those with higher SYNTAX scores) continued to derive a benefit of CABG over PCI beyond the 5-year follow-up. These results underscore the long-term impact of CABG over PCI that might be attributable to two factors. First, coronary bypass surgery offers the advantage of overcoming the overall burden of complex and diffuse atherosclerotic disease by constructing the anastomosis distal to diseased segments, whereas PCI only treats significant

flow-limiting lesions without protecting the distally diseased vessels. Second, CABG is associated with a higher rate of complete revascularisation than achieved with PCI.^{19,21} Particularly in patients with diffuse and complex coronary disease, PCI can be technically challenging and more frequently results in incomplete revascularisation. More incomplete revascularisation is associated with an increased risk of death at 5-year follow-up, whereas minimal incomplete revascularisation is not.^{22,23} In patients with low coronary disease complexity for which complete revascularisation with PCI is achievable, PCI is a suitable alternative to CABG.²⁴ Finally, adherence to guideline-directed medical therapy after revascularisation is important to adequately treat any progression of coronary artery disease.

The FREEDOM Follow-On study²⁵ found significantly fewer deaths with CABG versus PCI at a median followup of 7.5 years in patients with multivessel disease. Typically, patients with diabetes, who have more complex and progressive coronary disease, also benefit from CABG compared with PCI.⁶ The current study, however, found no survival difference between PCI and CABG in patients with diabetes at 10 years. This finding could be due to chance related to the smaller sample size (n=452) as compared with the FREEDOM trial (n=1900). The length of follow-up could also have affected the difference in results of the FREEDOM study (median 7.5 years) and the current study (median 11.2 years), because in our analysis the Kaplan-Meier curves converged further with follow-up prolonging after 7–8 years. Moreover, the inclusion of patients with left main coronary artery disease in the current study could have had an effect on the relative benefit of CABG over PCI in the overall diabetic cohort. In the recent pooled analysis of PCI versus CABG randomised trials, diabetes was an effect modifier in patients with multivessel disease but not in patients with left main coronary artery disease.⁹

Results at the 5-year follow-up provided promising survival outcomes of PCI versus CABG in patients with left main coronary artery disease and was corroborated in the pooled analysis of trials.⁹ It is reassuring that PCI resulted in a similar number of deaths at 10 years compared with CABG, as shown in the current analysis. The LE MANS trial²⁶ also reported similar survival outcomes at 10 years in patients randomly assigned to CABG or PCI with bare metal stents or first-generation drug-eluting stents, but in a smaller cohort (n=105). Similarly, the observational MAIN-COMPARE study²⁷ (n=2240) found no survival difference between PCI with bare metal stents or drug-eluting stents and CABG at 10-year follow-up. PCI for a focal left main lesion—ie, large in diameter with high flow—results in better stent patency and is therefore a suitable alternative to CABG in selected patients with left main coronary artery disease. Nevertheless, 56% of patients with left main coronary artery disease

who underwent PCI in the SYNTAX trial had a distal left main lesion.²⁸ Moreover, in the EXCEL trial,⁴ 80.5% of patients had a distal lesion that involved a bifurcation or trifurcation lesion, and subgroup analyses according to the presence or absence of a distal bifurcation or trifurcation lesion found no significant interaction. These data suggest that PCI can be an alternative to CABG not only in patients with relatively non-complex left main lesions, but also in patients with more complex disease, as also demonstrated in our analyses according to SYNTAX scores. The NOBLE³ and EXCEL⁴ trials might provide important additional insights in long-term outcomes after PCI with second-generation stents versus CABG if follow-up is prolonged to 10 years.

Despite the fact that the SYNTAX score was originally intended to predict major adverse cardiac and cerebrovascular events at the 1-year follow-up,¹⁴ the recent pooled analysis of randomised trials suggested an interaction between SYNTAX score tertiles and death, particularly in patients with multivessel disease and less so in patients with left main coronary artery disease.^{9,29} In patients with left main coronary artery disease, we confirmed the absence of an association between the SYNTAX score and 10-year all-cause death. However, although in the current study the interaction test was negative, the visual interpretation of the interaction in patients with three-vessel disease indicates that patients with advanced coronary artery disease, as reflected by increasing SYNTAX scores, have a benefit with CABG over PCI. Indeed, in the subgroup of patients with three-vessel disease and a high SYNTAX score, PCI resulted in higher 10-year all-cause death than did CABG (HR 1.91 [95% CI 1.25–2.92]; appendix p 21), indicating a significant survival benefit of CABG over PCI. This hypothesis is further corroborated by the reasons for exclusion from randomisation in the SYNTAX trial; the majority of patients were referred to CABG for having very complex coronary artery disease (mean SYNTAX score was 37.8).³⁰

At maximum follow-up, CABG appeared to be associated with a borderline survival benefit compared with PCI. It is important to note that the HR was similar at 10-year and maximum follow-up, but with additional deaths the statistical power was increased at maximum follow-up. The differences in survival outcomes between PCI and CABG at maximum follow-up were identified only in patients with three-vessel disease but not left main coronary artery disease, similar to the 10-year findings. Because of the limited number of patients at risk at maximum follow-up, these results should be interpreted as hypothesis-generating and could be used for sample size calculation in randomised controlled trials comparing PCI with CABG.

Additional limitations should be considered. First, the endpoint was all-cause death only. Although causes of death could have provided additional insights into mechanisms of death that could potentially be related to the revascularisation strategy, it was not feasible to collect those data.³¹ Second, additional outcomes, such as myocardial infarction, stroke, stent thrombosis, and graft occlusion, were not assessed but are important to consider when choosing the most appropriate revascularisation strategy.

In conclusion, no significant differences in all-cause death emerged between PCI with first-generation paclitaxel-eluting stents and CABG at 10 years. Nonetheless, in patients with three-vessel disease, CABG provided a significant survival benefit over PCI, whereas no treatment differences were identified in patients with left main coronary artery disease. The decision to opt for PCI or CABG in patients with three-vessel disease or left main coronary artery disease should be put forward by a multidisciplinary heart team that takes into consideration the presence or absence of mortality differences in patient subgroups. In addition, the overall coronary lesion complexity (eg, SYNTAX score), and other cardiovascular risk factors of an individual patient, such as diabetes and additional comorbidities, together with a patient's preference, should be included in the discussion.

Contributors

DJFMT, APK, PWS, F-WM, M-CM, MJM, DRH, NC, PD, KDD, and SJH designed the SYNTAX trial or SYNTAXES study, enrolled patients, or collected the data. DJFMT, APK, PWS, MM, BRdC, PJ, and SJH analysed and interpreted the data. BRdC and MM were the study statisticians. The analyses were performed in twofold, with one team led by PJ and one team led by SJH and DJFMT, to ensure validity of analyses. DJFMT participated in the study design and oversaw data collection and verification. DJFMT, APK, PJ, and SJH drafted the report, which was critically reviewed by all authors. All authors approved the final version of the manuscript for submission.

Declaration of interests

APK is Chief Medical Officer, Vice President at Medtronic. PWS reports personal consultancy fees from Abbott Laboratories, Biosensors, Cardialysis, Medtronic, Micell, Sino Medical Sciences Technology, Philips/Volcano, Xeltis, and Heartflow. MJM reports non-financial support from Edwards Lifesciences, Medtronic, and Abbott, outside the submitted work. NC reports grants from Boston Scientific Corporation, Haemonetics, and HeartFlow; personal fees from Boston Scientific Corporation, Abbott, Haemonetics, and Heartflow; education grant from Volcano Phillips; and non-financial support from Haemonetics, Heartflow, Biosensors, and Edwards,

outside the submitted work. KDD is the chief medical officer of Shockwave Medical Inc and 4Tech Cardio Ireland, and is also on the Board of Directors of Avicena LLC, JenaValve Technology Inc, and InnovHeart srl, and is a senior adviser to Conformal Medical Inc. PJ reports grants from Canadian Institutes of Health Research, AstraZeneca, Biotronik, Biosensors International, Eli Lilly, and The Medicines Company, outside the submitted work; reports honoraria to the institution for participation in advisory boards from Amgen unrelated to the submitted work, but has not received personal payments by any pharmaceutical company or device manufacturer; serves as unpaid member of the steering group of trials funded by AstraZeneca, Biotronik, Biosensors, St Jude Medical, and The Medicines Company; and is a Tier 1 Canada Research Chair in Clinical Epidemiology of Chronic Diseases funded by the Canadian Institutes of Health Research. SJH is Global Clinical Evidence Director at Medtronic. All other authors declare no competing interests.

Data sharing

The SYNTAX Extended Survival study hereby declares that no data will be made available to others.

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SUPPLEMENTARY APPENDIX

Ten-Year Survival After Percutaneous Coronary Intervention versus Coronary Artery Bypass Grafting in Patient with Three-Vessel and Left Main Coronary Artery Disease: A Multicentre, Randomized Controlled Trial

The SYNTAX Extended Survival (SYNTAXES) study

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This appendix has been provided by the authors to give readers additional information about their work.

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II. SAMPLE SIZE CALCULATION

The sample size of the SYNTAX Extended Survival study was based on the sample size considerations for the original trial. The original SYNTAX trial was powered for a noninferiority comparison of major adverse cardiac and cerebrovascular events (MACCE) at 12 months between CABG and PCI. The trial was powered separately for patients with 3VD and patients with LMCAD, so that each would have 80% power for a non-inferiority comparison of MACCE between PCI and CABG. For the subgroup of patients with 3VD only, the expected MACCE rates were 12% for both CABG and PCI. With a noninferiority margin of 5% and a one-sided alpha of 5%, 1050 patients were needed to have 80% power for the analysis. After allowing for an expected attrition rate of 3.5%, 1090 patients (545 per group) were needed for the 3VD comparison. For the subgroup of patients with LMCAD, the expected MACCE rates were 15% for CABG and 17% for PCI. With a noninferiority margin of 9% and a one-sided alpha of 5%, 684 patients were needed to have 80% power for the analysis. After allowing for an expected attrition rate of 3.5%, 710 patients (355 per group) were needed for the LMCAD comparison. After allowing for an expected attrition rate of 3.5%, the overall sample size of 1800 patients (900 per group) resulted in 96% power to detect noninferiority at a noninferiority margin of 6.6% (weighted average of 5.0% for the 3VD subgroup and 9.0% for LMCAD subgroup) and a one-sided alpha of 5%.

III. EXPLORATORY ANALYSES AND PRE-SPECIFIED SENSITIVITY ANALYSIS

Results from additional exploratory analyses and sensitivity analyses are provided below in Table 2 to Table 5, and in Figures S4 to S10.

IV. SUPPLEMENTARY TABLES

Table S1. Procedural characteristics of the randomized SYNTAX patients.

Characteristics	PCI (n = 903)	CABG (n = 897)
Revascularization presentation – no. (%)		
Urgent	4.1 (37/896)	3.8 (33/870)
Emergent	1.8 (16/896)	3.9 (34/870)
Elective	94.1 (843/896)	92.3 (803/870)
Off-pump surgery – no. (%)	-	15.0 (128/853)
Graft revascularization – no. (%)		
≥ 1 arterial graft	-	97.3 (831/854)
Bilateral internal thoracic arteries	-	27.6 (236/854)
Complete arterial revascularization	-	18.9 (161/854)
Venous graft only	-	2.6 (22/854)
Grafts per patient – mean ± SD	-	2.8 ± 0.7
Distal anastomoses – mean ± SD	-	3.2 ± 0.9
Staged procedure – (%)	14.1 (125/885)	-
Bi/trifurcation lesions treated – no. (%)	24.8 (790/3180)	-
Lesions treated - mean ± SD	3.6 ± 1.6	-
Stents implanted - mean ± SD	4.6 ± 2.3	-
Total length implanted - mean ± SD, mm	86.1 ± 47.9	-
Range, mm	8.0 – 324.0	-
Long stenting (>100 mm) – no. (%)	33.2 (291/877)	-
Complete revascularization [#] – no. %	56.7 (508/896)	63.2 (550/870)
Post procedural hospital stay [#] – days	3.4 ± 4.5	9.5 ± 8.0

Supplementary Appendix Table S1. Values are shown as mean ± SD (standard deviation) or frequencies in percentages and (n), unless otherwise noted. [#]Both differed significantly between PCI versus CABG (P=0.005). Abbreviations used: CABG; coronary artery bypass grafting, PCI; percutaneous coronary intervention.

Table S2. Baseline Clinical and Angiographic Characteristics of the patients with and without vital status up to 10-year follow-up.

Characteristics	With 10-year follow-up (n=1689)	Without 10-year follow-up (n=111)	P-value
Age (years)	65.1 ± 9.7	65.1 ± 9.6	0.23
Female sex – no. (%)	370 (21.9)	32 (28.8)	0.09
Body mass index (kg/m ²) - mean ± SD	28.0 ± 4.6	29.0 ± 5.1	0.32
Diabetes – no. (%)			
Requiring oral medications or insulin	417 (24.6)	35 (31.5)	0.11
Requiring insulin	173 (10.2)	13 (11.7)	0.62
Metabolic syndrome – no. (%)	615 (45.7)	41 (46.6)	0.87
Prior nicotine abuse – no. (%)	1090 (64.8)	71 (64.5)	0.96
Prior myocardial infarction – no. (%)	556/1673 (33.2)	29/107 (27.1)	0.19
Prior stroke – no. (%)	75/1679 (4.5)	3/110 (2.7)	0.39
Prior transient ischemic attack – no. (%)	82/1679 (4.9)	2/110 (1.8)	0.14
Hypertension (≥130/85mmHg) – no. (%)	1109 (65.7)	87 (78.4)	0.006
Congestive heart failure – no. (%)	82/1673 (4.9)	1/105 (1.0)	0.06
Prior carotid artery disease – no. (%)	137 (8.1)	11 (9.9)	0.50
Hyperlipidaemia – no. (%)	1314/1674 (78.5)	77 (69.4)	0.03
Angina – no. (%)			
Stable	969 (57.4)	58 (52.3)	0.29
Unstable	478 (28.3)	35 (31.5)	0.47
Ejection fraction <30% – no. (%)	29/1661 (1.7)	3 (2.7)	0.46
EuroSCORE value - mean ± SD	3.8 ± 4.6	3.5 ± 2.9	0.06
Parsonnet score - mean ± SD	8.5 ± 7.0	8.4 ± 5.7	0.07
SYNTAX score [∞] – mean ± SD	28.8 ± 11.4	27.5 ± 11.6	0.76
No. of lesions – mean ± SD	4.0 ± 1.7	4.1 ± 7.8	0.38
Total occlusion – no. (%)	387/1676 (23.1)	28 (25.2)	0.61
Bifurcation lesion – no. (%)	1221/1676 (72.9)	79 (71.2)	0.70
Three-vessel disease	1029 (60.9)	66 (59.5)	0.76
Left main disease, any	660 (39.1)	45 (40.5)	0.76

Table S2. This table reports the baseline characteristics of those patients with 10-year all-cause death follow-up (PCI n=841, CABG n=848) versus those without 10-year follow-up (PCI n=62; including 3 patients from not-participating SYNTAXES sites, CABG n=49; including 2 patients from not-participating SYNTAXES sites). Values are shown as mean ± SD (standard deviation) or frequencies in percentages and (n), unless otherwise noted. [∞]SYNTAX scores reported according to core-lab analysed data. Abbreviations used: CABG; coronary artery bypass grafting, PCI; percutaneous coronary intervention.

Table S3. Landmark analysis for the overall cohort and according to pre-specified subgroups of patients with three-vessel disease, left main coronary artery disease, diabetes, without diabetes and according to SYNTAX score tertiles.

Time period of landmark analysis	HR (95% CI)	P for interaction
All patients		0.99
0-5 years	1.20 (0.93 to 1.55)	
>5-10 years	1.17 (0.91 to 1.52)	
Three-vessel disease		0.59
0-5 years	1.52 (1.08 to 2.14)	
>5-10 years	1.33 (0.95 to 1.87)	
Left main coronary artery disease		0.58
0-5 years	0.85 (0.57 to 1.27)	
>5-10 years	1.00 (0.67 to 1.49)	
Diabetes		0.082
0-5 years	1.48 (0.93 to 2.34)	
>5-10 years	0.83 (0.53 to 1.31)	
No diabetes		0.23
0-5 years	1.07 (0.78 to 1.46)	
>5-10 years	1.41 (1.02 to 1.95)	
Syntax score 0-22		0.097
0-5 years	0.81 (0.48 to 1.36)	
>5-10 years	1.51 (0.90 to 2.54)	
Syntax score 23-32		0.92
0-5 years	1.05 (0.68 to 1.62)	
>5-10 years	1.09 (0.68 to 1.74)	
Syntax score ≥33		0.23
0-5 years	1.76 (1.16 to 2.67)	
>5-10 years	1.23 (0.82 to 1.85)	

Table S3. HR: hazard ratio; CI: confidence interval. A HR below 1 favours Percutaneous Coronary Intervention, and above 1 favours Coronary Artery Bypass Graft. The p-values for interaction are for the time-by-treatment interactions based on a cut-off at 5 years to distinguish between the period up to 5 years and the subsequent follow-up up to 10 years.

Table S4. Multivariable Cox proportional hazard model – Sensitivity analysis

Characteristics	HR (95% CI)	P for interaction
Overall cohort	1.24 (1.02 – 1.48)	
Type of Coronary Artery Disease		0.022
Left Main Disease	0.96 (0.72 – 1.27)	
Three-Vessel Disease	1.48 (1.16 – 1.89)	

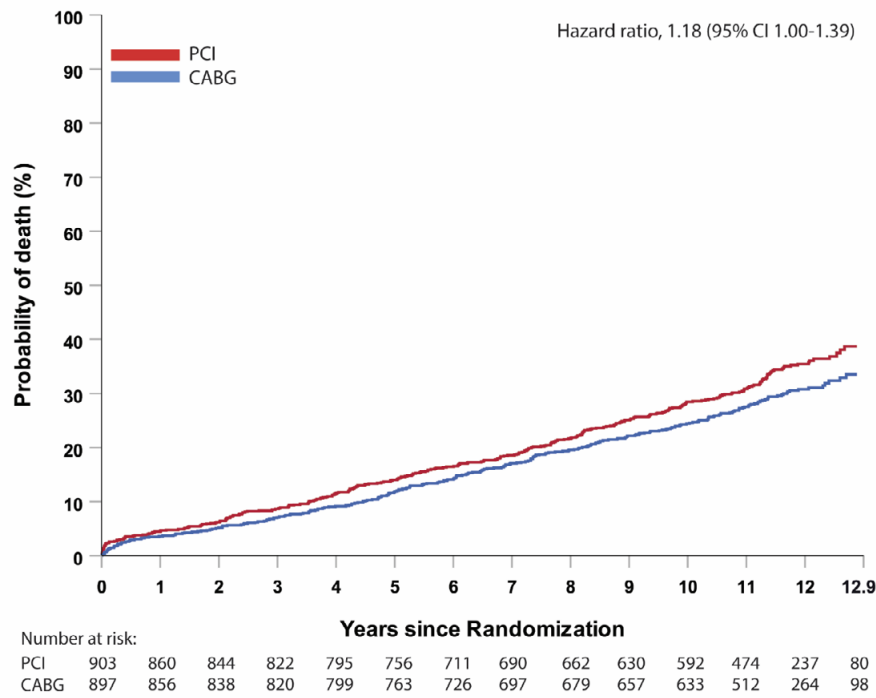
Supplementary Appendix Table S4. The model included all 1800 randomized patients and was constructed using stepwise forward selection. Significance levels of 0.10 for both addition and removal from the model were used, considering all baseline variables listed Table 1 and forcing the allocated treatment and the variables used for stratification of randomization (LMCAD and diabetes) into the model. Subgroup specific estimates of the hazard ratios of the primary endpoint in the LMCAD and 3VD subgroups were derived by appropriate linear combinations of coefficients representing treatment and the interaction between treatment and subgroup (LMCAD versus 3VD). Abbreviations used: CI; confidence interval, HR; hazard ratio.

Table S5. Multivariable Cox proportional hazard model – Included Variables.

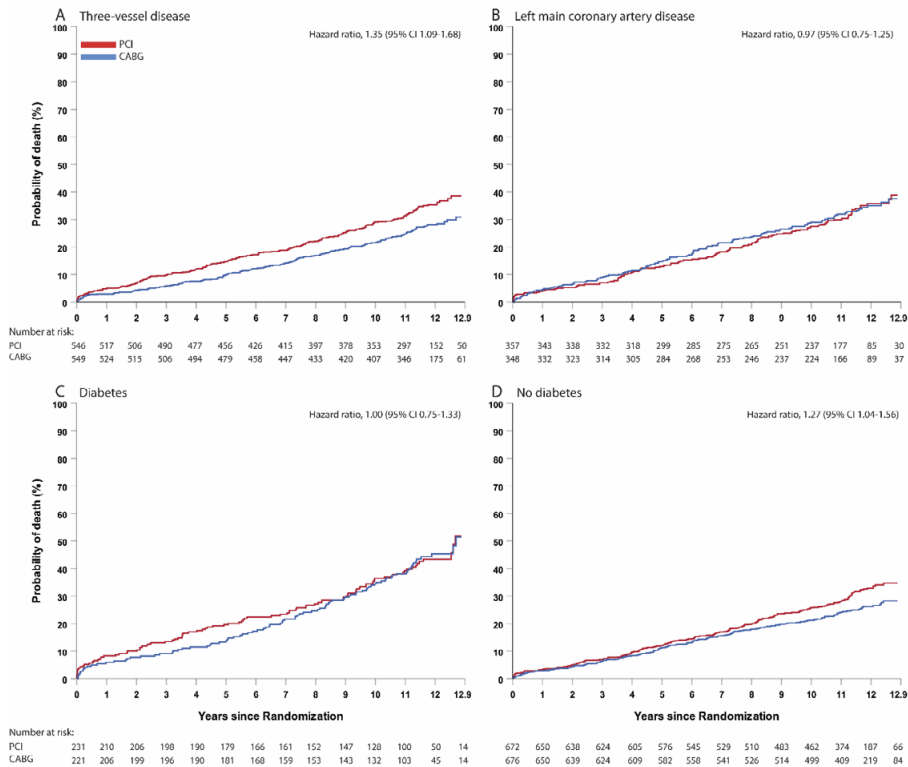
Characteristics	HR (95% CI)
Allocated treatment (PCI versus CABG)	1.23 (1.02 – 1.48)
Age, years	1.04 (1.03 – 1.05)
Bifurcation lesion	1.18 (0.95 – 1.47)
Congestive heart failure	1.34 (1.15 – 1.56)
Diabetes	1.40 (1.14 – 1.72)
EuroSCORE	1.16 (1.11 – 1.21)
Left Main Disease	1.14 (0.94 – 1.37)
Metabolic syndrome	1.39 (1.13 – 1.71)
Nicotine abuse at time of enrolment	1.46 (1.20 – 1.79)

Supplementary Appendix Table S5. The model included all 1800 randomized patients and was constructed using stepwise forward selection. This table represents the individual variables, with hazard ratios and 95% confidence intervals, that were included in the final model. Abbreviations used: CI; confidence interval, HR; hazard ratio.

V. SUPPLEMENTARY FIGURES



Supplementary Appendix Figure S1. All-cause death at maximum follow-up of patients randomized to PCI versus CABG (intention-to-treat population). Kaplan-Meier curves describing the probability of death in PCI versus CABG up to 12.9 years of follow-up. Curves were truncated at 12.9 years when only 10% of patients were at risk to avoid visual misinterpretation. Because the widths of 95% confidence intervals were not adjusted for multiple comparisons, these intervals should not be used for inference about between-group differences. Abbreviations used: CABG; coronary artery bypass grafting, CI; confidence interval, PCI; percutaneous coronary intervention.



Supplementary Appendix Figure S2. All-cause death at maximum follow-up of patients randomized to PCI versus CABG with 3VD, LMCAD, diabetes and without diabetes (intention-to-treat population). Kaplan-Meier curves describing the probability of death in PCI versus CABG up to 12.9 years of follow-up in pre-specified subgroups of patients with three-vessel disease (Panel A), left main coronary artery disease (Panel B), with diabetes (Panel C) and without diabetes (Panel D). Curves were truncated at 12.9 years when only 10% of patients were at risk to avoid visual misinterpretation. Because the widths of 95% confidence intervals were not adjusted for multiple comparisons, these intervals should not be used for inference about between-group differences. Abbreviations used: CABG; coronary artery bypass grafting, CI; confidence interval, PCI; percutaneous coronary intervention.

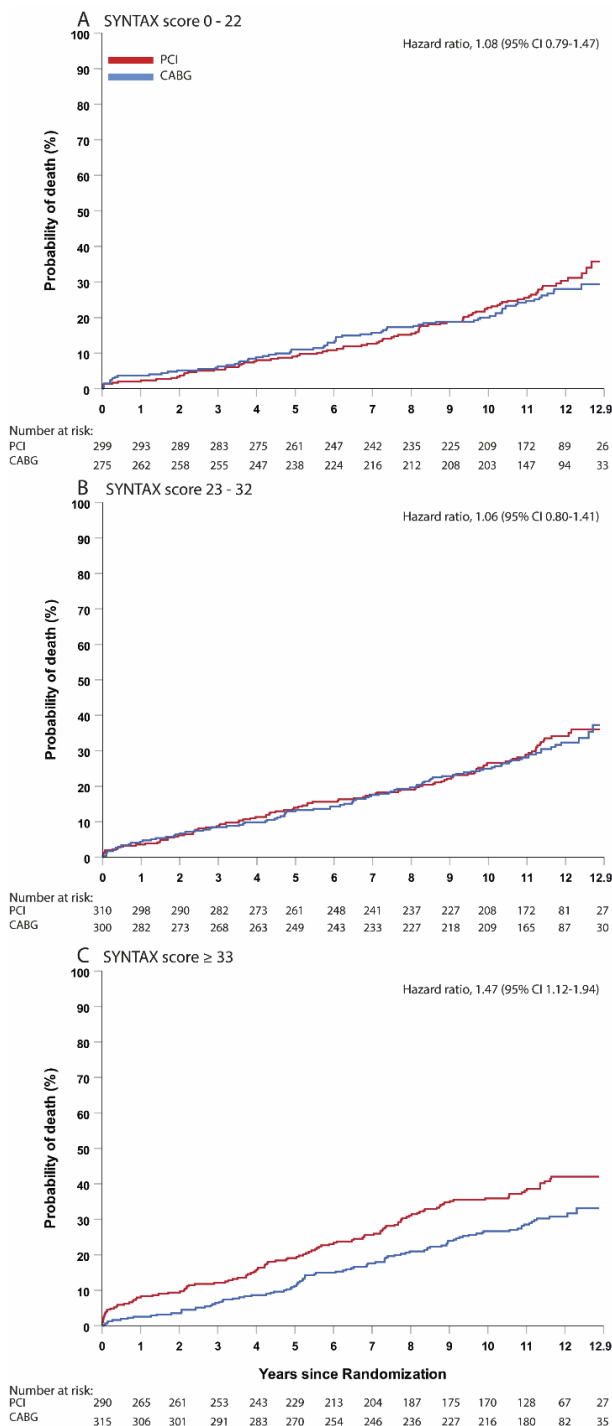
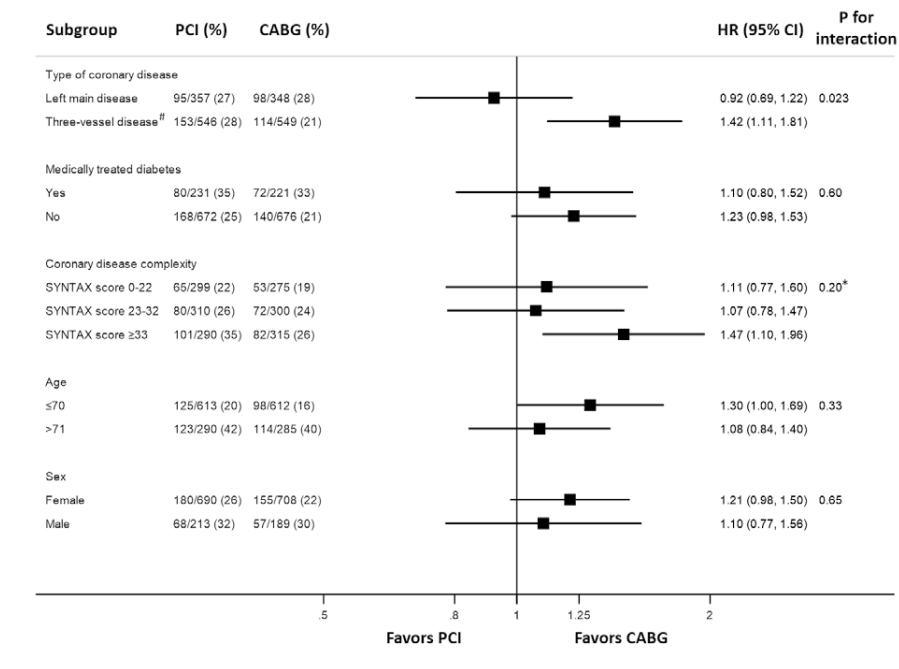
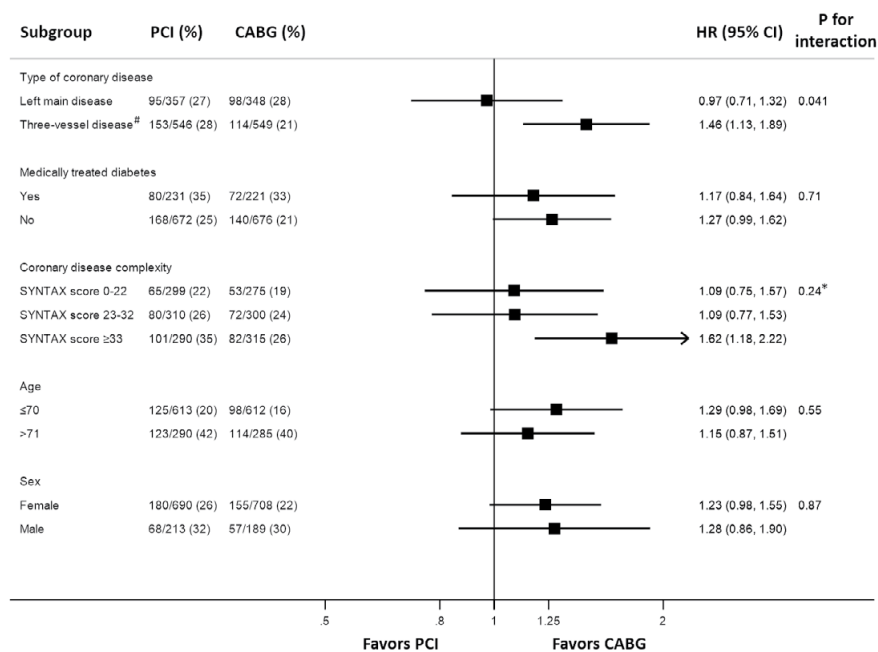


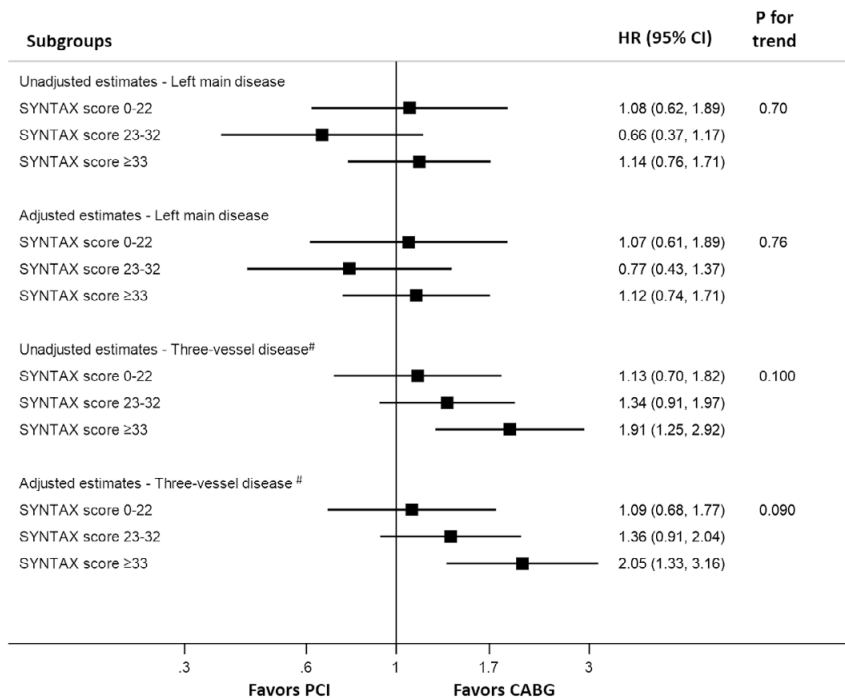
Figure S3. All-cause death at maximum follow-up of patients randomized to PCI versus CABG with low, intermediate and high SYNTAX scores (intention-to-treat population). Kaplan-Meier curves describing the probability of death in PCI versus CABG up to 12.9 years of follow-up in pre-specified subgroups of patients with low SYNTAX scores (0-22; panel A), intermediate SYNTAX scores (23-32; Panel B), and high SYNTAX scores (≥ 33 ; Panel C). SYNTAX scores were reported according to core-lab analysed data. Curves were truncated at 12.9 years when only 10% of patients were at risk to avoid visual misinterpretation. Because the widths of 95% confidence intervals were not adjusted for multiple comparisons, these intervals should not be used for inference about between-group differences. Abbreviations used: CABG; coronary artery bypass grafting, CI; confidence interval, PCI; percutaneous coronary intervention.



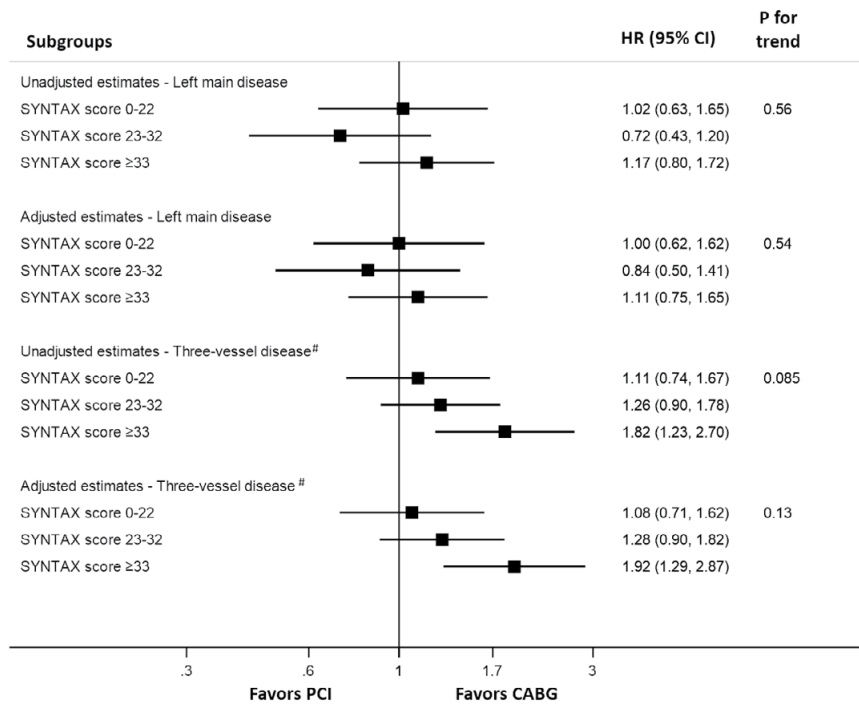
Supplementary Appendix Figure S4. Unadjusted subgroup analyses on 10-year all-cause death in patients randomized to PCI and CABG (intention-to-treat population). All-cause death after PCI versus CABG during 10-year follow-up in pre-specified unadjusted subgroup analyses according to baseline characteristics. Outcomes according to age and sex were considered exploratory. *P value for trend of log HRs across SYNTAX tertiles for subgroup analysis according to lesion complexity. Because the widths of 95% confidence intervals were not adjusted for multiple comparisons, these intervals should not be used for inference about between-group differences. [#]Patients with coronary artery disease involving all three vessels in the absence of left main disease. Abbreviations used: CABG; coronary artery bypass grafting, CI; confidence interval, HR; hazard ratio, PCI; percutaneous coronary intervention.



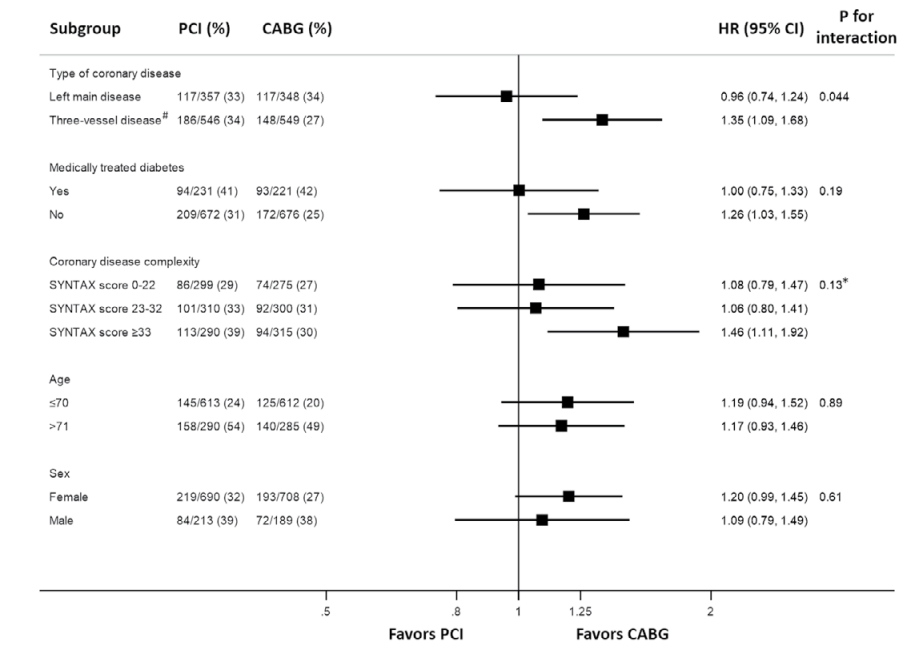
Supplementary Appendix Figure S5. Adjusted subgroup analyses on 10-year all-cause death in patients randomized to PCI and CABG (intention-to-treat population). All-cause death after PCI versus CABG during 10-year follow-up in pre-specified adjusted subgroup analyses according to baseline characteristics. *P value for trend of log HRs across SYNTAX tertiles for subgroup analysis according to lesion complexity. Because the widths of 95% confidence intervals were not adjusted for multiple comparisons, these intervals should not be used for inference about between-group differences. [#]Patients with coronary artery disease involving all three vessels in the absence of left main disease. Abbreviations used: CABG; coronary artery bypass grafting, CI; confidence interval, HR; hazard ratio, PCI; percutaneous coronary intervention.



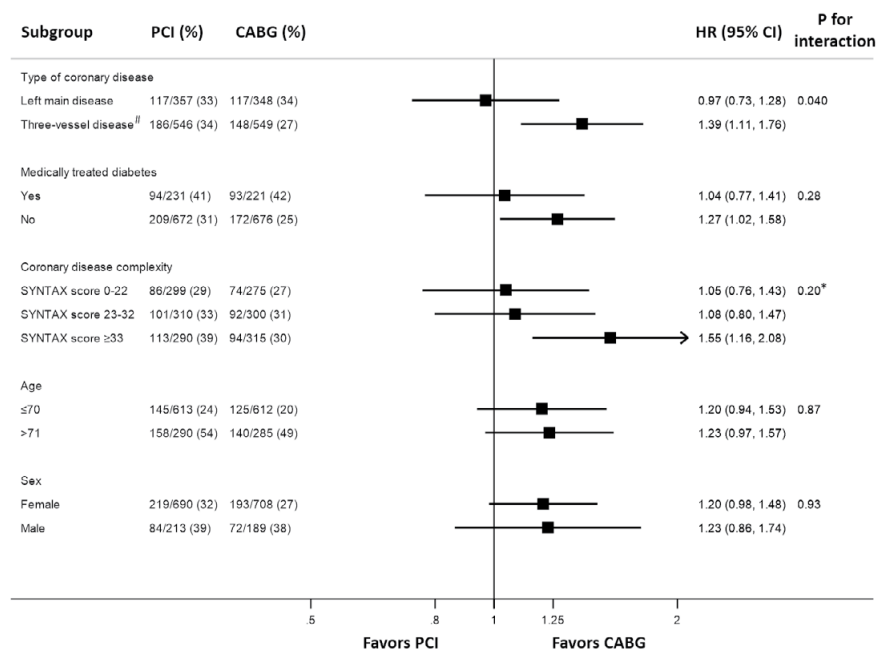
Supplementary Appendix Figure S6. Subgroup analyses according to SYNTAX score tertiles in 3VD and LMCAD subgroups at 10 year follow-up (intention-to-treat population). PCI versus CABG 10-year all-cause death (unadjusted and adjusted) hazard ratios in the overall cohort and pre-specified subgroups of patients 3VD and LMCAD according to low SYNTAX scores (0-22), intermediate SYNTAX scores (23-32) and high SYNTAX scores (≥33). [#]Patients with coronary artery disease involving all three vessels in the absence of left main disease. Because the widths of 95% confidence intervals were not adjusted for multiple comparisons, these intervals should not be used for inference about between-group differences. Abbreviations used: CABG; coronary artery bypass grafting, CI; confidence interval, HR; hazard ratio, PCI; percutaneous coronary intervention.



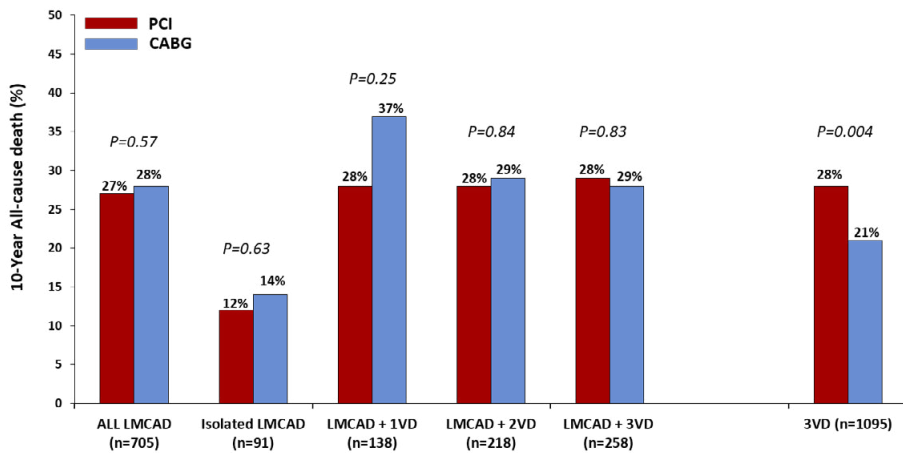
Supplementary Appendix Figure S7. Subgroup analyses according to SYNTAX score tertiles in 3VD and LMCAD subgroups at maximum follow-up (intention-to-treat population). PCI versus CABG 10-year all-cause death (unadjusted and adjusted) hazard ratios in the overall cohort and pre-specified subgroups of patients 3VD and LMCAD according to low SYNTAX scores (0-22), intermediate SYNTAX scores (23-32) and high SYNTAX scores (≥33). Because the widths of 95% confidence intervals were not adjusted for multiple comparisons, these intervals should not be used for inference about between-group differences. [#]Patients with coronary artery disease involving all three vessels in the absence of left main disease. Abbreviations used: CABG; coronary artery bypass grafting, CI; confidence interval, HR; hazard ratio, PCI; percutaneous coronary intervention.



Supplementary Appendix Figure S8. Unadjusted subgroup analyses at maximum follow-up in patients randomized to PCI and CABG (intention-to-treat population). All-cause death after PCI versus CABG during maximum follow-up in pre-specified adjusted subgroup analyses according to baseline characteristics. *P value for trend of log HRs across SYNTAX tertiles for subgroup analysis according to lesion complexity. Because the widths of 95% confidence intervals were not adjusted for multiple comparisons, these intervals should not be used for inference about treatment effects. Because the widths of 95% confidence intervals were not adjusted for multiple comparisons, these intervals should not be used for inference about between-group differences. [#]Patients with coronary artery disease involving all three vessels in the absence of left main disease. Abbreviations used: CABG; coronary artery bypass grafting, CI; confidence interval, HR; hazard ratio, PCI; percutaneous coronary intervention.



Supplementary Appendix Figure S9. Adjusted subgroup analyses at maximum follow-up in patients randomized to PCI and CABG (intention-to-treat population). All-cause death after PCI versus CABG during maximum follow-up in pre-specified adjusted subgroup analyses according to baseline characteristics. *P value for trend of log HRs across SYNTAX tertiles for subgroup analyses according to lesion complexity. Because the widths of 95% confidence intervals were not adjusted for multiple comparisons, these intervals should not be used for inference about between-group differences. [#]Patients with coronary artery disease involving all three vessels in the absence of left main disease. Abbreviations used: CABG; coronary artery bypass grafting, CI; confidence interval, HR; hazard ratio, PCI; percutaneous coronary intervention.



Supplementary Appendix Figure S10. PCI versus CABG 10-year all-cause death outcomes between PCI and CABG in pre-specified subgroups of patients three-vessel and left main coronary artery disease; with any additional coronary artery disease (intention-to-treat population). All LMCAD (PCI n=357, CABG n=348), isolated (PCI n=42, CABG n=49), LMCAD + 1VD (PCI n=67, CABG n=71), LMCAD + 2VD (PCI n=112, CABG n=106), LMCAD + 3VD (PCI n=136, CABG n=122), 3VD (PCI n=546, CABG n=549). P values, to determine potential differences between PCI versus CABG, were derived from a log rank test. Abbreviations used: CABG; coronary artery bypass grafting, PCI; percutaneous coronary intervention, LMCAD: left main coronary artery disease, 1VD: one-vessel disease, 2VD: two-vessel disease, 3VD: three-vessel disease.