Impact of diabetes on outcome with drug-coated balloons versus drug-eluting stents: The BASKET-SMALL 2 trial

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Structured Abstract

Objectives: To evaluate the impact of diabetes mellitus on 3-year clinical outcome in patients undergoing drug-coated balloon (DCB) or drug-eluting stent (DES) treatment for de-novo lesions.

Background: For treatment of de-novo coronary small vessel disease DCB are non-inferior to DES.

Methods: In this prespecified analysis of a multicenter, randomized, non-inferiority trial, including 758 patients with de-novo lesions in coronary vessels <3mm who were randomized 1:1 to DCB or DES and followed over 3 years for major adverse cardiac events (MACE: cardiac death, non-fatal myocardial infarction [MI], and target-vessel revascularization [TVR]), outcome was analyzed regarding the presence or absence of diabetes mellitus.

Results: In non-diabetic patients (n=506) rates of MACE (DCB 13.0% vs. DES 11.5%, hazard ratio [HR] 1.24, 95% confidence interval [CI] 0.73-2.09, p=0.43), cardiac death (2.8% vs. 2.9%, HR 0.97, 95%CI 0.32-2.92, p=0.96), non-fatal MI (5.1% vs. 4.8%, HR 1.00, 95%CI 0.44-2.28, p=0.99), and TVR (8.8% vs. 6.1%, HR 1.64, 95%CI 0.83-3.25, p=0.16) were similar. In diabetic patients (n=252) rates of MACE (19.3% vs. 22.2%, HR 0.82, 95%CI 0.45-1.48, p=0.51), cardiac death (8.8% vs. 5.9%, HR 2.01, 95%CI 0.76-5.31, p=0.16), non-fatal MI (7.1% vs. 9.8%, HR 0.55, 95%CI 0.21-1.49, p=0.24) were similar in DCB and DES. TVR was significantly lower with DCB versus DES (9.1% vs. 15.0%, HR 0.40, 95%CI 0.17-0.94, p=0.036, p=0.011 for interaction).

Conclusions: The rates of MACE are similar in DCB and DES in de-novo coronary lesions of diabetic and non-diabetic patients. In diabetic patients need for TVR was significantly lower with DCB versus DES.

Key Words:

Drug-coated balloon

Drug-eluting stent

Target vessel revascularization

Small vessel disease

Diabetes mellitus

Condensed Abstract

We evaluated the impact of diabetes mellitus in this multicenter, randomized, non-inferiority trial including 758 patients with de-novo lesions in coronary vessels <3mm randomized 1:1 to drug-coated balloons (DCB) or drug-eluting stents (DES). In non-diabetic patients (n=506, 67%) rates of major adverse cardiac events, cardiac death, non-fatal myocardial infarction and target vessel revascularization (TVR) were similar in DCB and DES. In diabetic patients (n=252) rates of MACE, cardiac death, and non-fatal myocardial infarction were similar in DCB and DES, while TVR was significantly lower with DCB compared to DES (9.1% vs. 15.0%, HR 0.40, 95%CI 0.17-0.94, p=0.036, p=0.011 for interaction).

Abbreviations

ACS	Acute coronary syndrome
CAD	Coronary artery disease
CI	Confidence interval
DCB	Drug-coated balloon
DES	Drug-eluting stent
HR	Hazard ratio
MACE	Major adverse cardiac events
MI	Myocardial infarction
PCI	Percutaneous coronary intervention
TVR	Target vessel revascularization

Introduction

The use of drug-eluting stents (DES) for the treatment of de-novo lesions in small coronary arteries is associated with a higher rate of restenosis and stent thrombosis as compared to lesions in larger vessels. Drug-coated balloons (DCB) are an interesting alternative treatment option for patients with de-novo coronary artery disease. DCBs are associated with an antirestenotic efficacy which is associated with the potential for late lumen enlargement (1,2). Since there is no permanent vascular implant the risk of late or very late stent thrombosis is eliminated and the need for dual antiplatelet therapy (DAPT) in patients without acute coronary syndromes (ACS) can be limited to 4 weeks (3) reducing the bleeding risk. Recently, the randomized Basel Kosten Effektivitäts Trial–Drug-Coated Balloons versus Drug-eluting Stents in Small Vessel Interventions (BASKET-SMALL) 2 trial demonstrated in 758 patients a similar efficacy and safety of DCB versus DES in the treatment of de-novo coronary small vessel disease up to 3 years (3,4) with similar rates of cardiac death, non-fatal myocardial infarction and target vessel revascularization (TVR). In addition, rates of vessel thrombosis and major bleeding were numerically lower with use of DCB versus DES.

In patients with diabetes mellitus the occurrence of major adverse cardiac events (MACE) is higher compared to non-diabetic patients (5-7). Especially the risk of restenosis, myocardial infarction and stent thrombosis is increased in diabetic compared to non-diabetic patients. Studies comparing the use of DCB vs. DES in diabetic patients with de-novo coronary artery disease are limited. In a recent meta-analysis (8) including 378 diabetic patients with de-novo lesions use of DCB was associated with similar outcomes regarding MACE and a trend towards a lower rate

of target lesion revascularization (TLR) compared to DES during a mean follow-up of 17 months.

In this pre-specified subgroup analysis of the BASKET-SMALL 2 trial we evaluated the impact of diabetes mellitus on outcome of DCB versus DES in patients with de-novo lesions in small coronary arteries.

Methods

Study design

BASKET-SMALL 2 (9) is an investigator-initiated, randomized, open-label non-inferiority trial demonstrating a similar efficacy and safety for DCB compared with DES within 12 months (4) and 3 years follow-up in 758 patients with de-novo lesions in coronary vessels <3mm (3). This prespecified subgroup-analysis (9) compares the efficacy and safety within 1, 2 and 3 years between patients with and without diabetes mellitus. The trial was performed in 14 centers in Switzerland, Austria and Germany during the years 2012-2017 in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines and was approved by the ethics committees in all participating centers.

Study population and randomization

Patients were eligible for the study when they had an indication for percutaneous coronary intervention (PCI), i.e., an acute coronary syndrome, stable angina pectoris, or silent ischemia, and a suitable angiographic anatomy in a small coronary vessel with a diameter between 2 and 3 mm. Successful predilatation of the lesion, i.e., absence of higher grade dissections (National Heart, Lung, and Blood Institute grade C to F) (10), decreased blood flow (thrombolysis in myocardial infarction score ≤2), or

residual stenosis >30% was mandatory (11). Diabetes mellitus was defined as history of the disease or specific treatment. Exclusion criteria included a concomitant PCI of lesions ≥3 mm in diameter in the same epicardial coronary artery, PCI of in-stent restenosis, life expectancy of <12 months, pregnancy, enrollment in another randomized trial, or inability to give informed consent. Patients were selected 1:1 to be treated by either DCB or DES.

Procedures

Patients randomized to DCB were treated with the paclitaxel-coated SeQuent Please balloon (B. Braun Melsungen AG, Melsungen, Germany), while patients randomized to DES were treated with either the everolimus-eluting Xience stent (Abbott Vascular, Santa Clara, CA, USA) or the paclitaxel-eluting Taxus Element stent (Boston Scientific, Natick, MA, USA) (4,9). The strut thickness of both DES is 81 µm. The DCB needed to be 2 to 3 mm longer on each side than the predilatation balloon to avoid geographical mismatch, and was inflated at nominal pressure for at least 30 sec, as recommended in current guidelines (11). When there were flow-limiting dissections after DCB treatment despite an acceptable result after lesion preparation, stent implantation was performed. After PCI, DAPT was given using acetylsalicylic acid (100 mg per day) and either clopidogrel (75 mg per day), prasugrel (10 mg per day), or ticagrelor (90 mg twice per day); DAPT was continued in stable patients for 4 weeks for DCB or 6 months for DES and in patients with acute coronary syndromes for 12 months. In patients with oral anticoagulation, current guidelines were followed (12), irrespective of DCB or DES treatment. Follow-up was done after 12, 24 and 36 months with structured clinical questionnaires or phone calls to assess clinical events and medication. Patients were followed for median 3 years.

Outcomes

The primary endpoint of this analysis is major adverse cardiac events (MACE) defined as the composite of cardiac death, non-fatal myocardial infarction, and target vessel revascularization (TVR). Cardiac death was defined as any death without a clear cardiac reason, and myocardial infarction was defined according to current guidelines (13). Secondary endpoints were the single components of the primary endpoint according to the Academic Research Consortium definition (14). An independent critical events committee adjudicated all endpoints.

Statistical analysis

All statistical analyses were performed according to the intention-to-treat principle, i.e., all patients were analyzed on the basis of the treatment they were randomly allocated to. All analyses were conducted with the statistical software package R, using “two-sided” statistical tests and confidence intervals, without correction for multiple testing. Categorical data are presented as frequencies and percentages (with the difference between study arms analyzed by Pearson’s chi-squared test). For numerical variables, the mean and standard deviation, or the median and interquartile range are presented, as appropriate, with the difference between study arms analyzed by Student’s t-test or Wilcoxon–Mann–Whitney test, respectively. For each endpoint, treatment effects on the times to event were tested by Cox regressions (with study center as a stratifying factor to account for differences in baseline hazards between study centers). The Kaplan–Meier estimates of the event rates in both study arms are reported along with the corresponding hazard ratios (HR) and 95% confidence intervals (CI). The proportional hazards assumption of the Cox models and the homogeneity of the treatment effects among study centers were

checked by testing the correlation of the scaled Schoenfeld residuals with time and the interaction of the stratifying factor study center with treatment in the Cox models, respectively. Endpoints of patients not experiencing an event were considered as censored on the last observation date.

Results

Out of 758 randomized patients 252 (33%) were diabetic and 506 (67%) non-diabetic. Baseline characteristics are depicted in Table 1. Patients with compared to patients without diabetes mellitus were significantly older and suffered significantly more often from cardiovascular risk factors such as hypercholesterolemia, hypertension, higher body mass index and renal dysfunction, while other parameters such as previous MI, previous PCI or coronary bypass graft surgery, target vessel or antiplatelet therapy were well balanced between the groups.

Table 2 shows the Kaplan-Meier estimates of event rates between the two study arms (DES versus DCB) within each subgroup (patients with versus without diabetes mellitus) for each single endpoint.

In the population without diabetes mellitus, rates of MACE, cardiac death, non-fatal MI, TVR and all-cause death were statistically not different between patients treated with DCB or DES up to three years of follow-up. In the population with diabetes mellitus, the rates of MACE, non-fatal MI and all-cause death were statistically not different between patients treated with DCB or DES up to three years of follow-up. In diabetic patients cardiac death was significantly more frequent within 12 months in patients treated with DCB compared to patients treated with DES while results were statistically not different after two (DES versus DCB 4.1% vs. 7.8%, p=0.10) and three years (DES versus DCB 5.9% vs. 8.8%, p=0.16). In contrast, TVR occurred

significantly more frequent in diabetic patients treated with DES compared to patients treated with DCB after 2 (DES vs. DCB 13.1% vs. 5.6%, p=0.037) and 3 years of follow-up (DES vs. DCB 15.0% vs. 9.1%, p=0.036). Figure 1 details the Kaplan-Meier estimates of the cumulative probabilities of MACE (panel A), non-fatal MI (panel B), TVR (panel C) and all-cause death (panel D) during three years in the four combinations of subgroups (diabetic or non-diabetic) and study arms (DCB or DES). Events occurred numerically more often in diabetic patients. Rates of MACE, non-fatal MI and TVR were higher in patients with diabetes mellitus treated with DES (Figure 1).

Cox regression analysis stratified by study center and adjusted for diabetic status with interaction of treatment showed that the interaction between diabetic status and randomized treatment (DCB or DES) was significant regarding TVR for all follow-up timepoints (Table 2).

In addition we performed additional analyses comparing DCB with PES (n=93) and EES (Supplement Table 1-3). Baseline characteristics were not different between the three groups except for renal dysfunction being lower in the PES group (Supplement table 1). Kaplan-Meier estimates of event rates at 1, 2 and 3 years in patients without diabetes mellitus showed similar event rates except for MACE at 2 years and TVR at 2 and 3 years being significantly lower with EES (Supplement Table 2). Kaplan-Meier estimates of event rates in patients with diabetes mellitus showed similar event rates except for TVR at 2 years and non-fatal MI at 2 years being significantly higher with PES (Supplement Table 2). Interaction testing (Supplement Table 3) demonstrated significant interactions for EES and diabetic status for MACE at 2 years and TVR at 1, 2 and 3 years with higher hazard ratios.

Discussion

In this pre-specified subgroup analysis of the randomized BASKET-SMALL 2 trial we were able to demonstrate that 1) the risk of MACE, death, non-fatal MI, and TVR is significantly higher in patients with diabetes mellitus compared to non-diabetic patients up to three years of follow-up; 2) in patients both with and without diabetes mellitus, rates of MACE, death, and non-fatal MI are similar for DCB and DES; and 3) the rate of TVR in diabetic patients is significantly lower after DCB versus DES up to three-years follow-up, while rates of MACE, non-fatal MI or TVR are numerically highest in diabetic patients treated with DES.

Different randomized trials assessed the efficacy and safety of DCB in de-novo small vessel disease. BASKET-SMALL 2 was the largest trial with the longest follow-up comparing efficacy and safety of DCB versus DES in de-novo lesions of small coronary vessels (<3mm). For the total study group the rate of MACE, TVR, non-fatal MI and cardiac death was similar between DCB and DES (3,4). In this trial, about one third of patients had diabetes mellitus. In the randomized Balloon Elution and Late Loss Optimization (BELLO) study 182 patients with de-novo lesions in small coronary arteries (<2.8mm by visual estimation) were randomized to DCB (In-Pact Falcon paclitaxel DCB) or DES (Taxus Liberté, Boston Scientific, Marlborough, USA) (15). After 3 years follow-up the Kaplan-Meier analysis demonstrated a significantly lower MACE rate for DCB compared to DES (14.4% vs. 30.4%, p=0.015). Rates of diabetes mellitus were 43.3% in DCB and 38% in DES. In the Drug Eluting Balloon Efficacy for Small Coronary Vessel Disease Treatment (PICCOLETO) II trial 232 patients were randomized to DCB (Elutax SV, Aachen Resonance, Germany) or everolimus eluting EES. One-year MACE rate was statistically not different with 7.5% for DES and 5.6% for DCB (p=0.55) (16). Frequency of patients with diabetes

mellitus was 38%. In the randomized RESTORE Small Vessel Disease China trial 230 patients (vessel diameter <2.75mm) were randomized to DCB (RESTORE, Cardionovum, Bonn, Germany) or DES (RESOLUTE integrity, Medtronic, Minneapolis, Minnesota, USA). Target lesion failure (TLF; 5.2% vs. 3.7%, p=0.75) and TLR (5.2% vs. 2.8%, p=0.50) were statistically not different between DCB and DES (17). Frequency of patients with diabetes mellitus was 46% and 48% for DCB and DES, respectively.

The amount of neointimal proliferation and the rate of restenosis increase with decreasing reference vessel diameter. Thus, lesions in small coronary arteries are associated with a higher risk of restenosis, need for repeat revascularization and stent thrombosis compared to lesions in larger coronary arteries. In addition, the frequency of diabetes mellitus is high in patients with coronary lesions in small vessels. The presence of diabetes mellitus was associated with a larger amount of neointimal thickness demonstrated by optical coherence tomography (18) and a higher risk of all-cause mortality and new Q-wave myocardial infarction at 2 years after PCI compared to non-diabetic patients (19). A recent patient-level analysis based on 6 prospective randomized trials evaluated the occurrence of TLF (cardiac death, TLR, target vessel MI) after DES implantation up to 5 years (20). With 10.072 patients included in the analysis reference vessel diameter was the only lesion-related predictor at 5 years (p=0.003). The presence of diabetes mellitus was a strong clinical predictor of TLF both between 30 days and 1 year (p<0.01) and between 1 and 5 years (p=0.002). Thus, patients with lesions in small coronary arteries suffering from diabetes mellitus have a high risk for MACE. In our study cardiac death after one year was significantly lower with DES, while there was no difference after 2 and 3 years of follow-up. In a meta-analysis including 4590 patients

the use of PES for treatment of coronary artery disease was associated with numerically lower mortality rates within 3 years of follow-up (21).

Data comparing the outcome of DCB versus DES in diabetic patients with small coronary arteries are limited. In the SeQuent Please World-Wide Registry (22) 491 patients with de-novo coronary artery disease were included in small vessels with a mean reference diameter of 2.6 mm. Rates of MACE (2.6%) and TVR (1.0%) were low with no presence of vessel thrombosis, while the presence of diabetes mellitus was a significant predictor for TLR (p=0.023). In the randomized BELLO study 74 patients suffered from diabetes mellitus and 108 patients were non-diabetic (23). In patients with diabetes mellitus, angiographic restenosis and in-segment late loss were significantly lower with DCB as compared to DES (respectively, 6.3% vs. 25.0%; p=0.039 and -0.013±0.39 vs. 0.25±0.53; p=0.023), with no differences noted in nondiabetic patients. The cumulative MACE rate at 1 year was similar between DCB and DES in both the diabetic (13.2% vs. 25%, p=0.194) and nondiabetic groups (11.8% vs. 14.3%, p=0.699). In a recent meta-analysis including 378 diabetic patients with de-novo lesions the use of DCB was associated with similar outcomes regarding MACE (odds ratio 0.63, 95% CI 0.36-1.12, p=0.11) and a trend towards a lower rate of TLR (odds ratio 0.51, 95% CI 0.25-1.06, p=0.07) compared to DES (8) during a mean follow-up of 17 months. The use of EES was superior to PES for de-novo coronary artery disease in patients without (24) and with (25) diabetes mellitus. Our DES population consisted of PES and EES with an identical strut thickness of 81 µm. In consistence with previous data (25) exploratory analysis showed significantly higher Kaplan-Meier estimates for TVR and non-fatal MI at 2 years with PES.

Based on the current analysis, we are now able to extend this knowledge comparing the outcome of DCB versus DES to 252 diabetic patients and 506 non-diabetic patients included in the BASKET-SMALL 2 trial. Patients were followed for 3 years,

which is an important issue since long-term risk in patients with diabetes mellitus is high. Within this follow-up, the use of DCB or DES in de-novo coronary artery disease was associated with similar outcomes in non-diabetic patients. In contrast, the risk of TVR was significantly higher in patients with versus without diabetes mellitus (hazard ratio 1.93, 95% CI 1.14-3.25, p=0.014) as already signaled by the results of the SeQuentPlease World Wide registry (22), the BELLO trial (23) and in the previously mentioned meta-analysis (8). In addition, the angiographic subgroup analysis of BASKET-SMALL 2 trial demonstrated vessel occlusions only in the DES population but not in the DCB group (26) underscoring the risk of neointimal proliferation in small vessels which is significantly higher after DES implantation in diabetic patients compared with non-diabetic patients (18). The benefit regarding a lower TVR rate in diabetic patients treated with DCB may be explained by the overall benefits of DCB compared with DES: 1) no permanent metallic frame or polymer inducing inflammation, neo-atherosclerosis and neointimal proliferation, 2) no long-term risk of stent thrombosis since with DCB nothing is left behind allowing late lumen enlargement since there is no metallic cage, and 3) the possibility of a shorter treatment with DAPT. The last point might be of special interest in patients with a high bleeding risk. The occurrence of bleeding often leads to a reduction in antiplatelet therapy increasing the risk of thrombotic ischemic events. According to the recent published DCB consensus paper DAPT after DCB in non-ACS patients can be limited to 4 weeks (11), which reduces the risk of bleeding without increasing the risk of vessel thrombosis. Bleeding after PCI is an important clinical problem of contemporary PCI and increases mortality by seven-fold (27). There is a growing need to shorten DAPT in patients at bleeding risk such as in the elderly or those needing anticoagulation. Of note, the hypothesis in the randomized DEBUT trial was that PCI with DCB is non-inferior to PCI with bare-metal stents in patients with de-

novo lesions (2.5-4.0mm vessel size) at risk for bleeding (28). In this trial, MACE rate was significantly lower with 1% after DCB compared to 14% after stent implantation (risk ratio 0.07, 95% CI 0.01-0.52, p<0.0001 for non-inferiority and p=0.00034 for superiority).

The use of DCB in de-novo lesions in small coronary arteries is associated with (at least) similar results compared to DES shown in the large, randomized BASKET-SMALL 2 trial. New data (28, 29) indicate that DCB may be also beneficial in selected patients with de-novo lesions in coronary arteries with vessel size up to 4.0 mm.

Limitation

In this pre-specified analysis of the randomized BASKET-SMALL 2 trial the number of patients in the diabetic population is limited and does not confer enough power to draw definitive conclusions regarding clinical endpoints. However, this study represents the largest population of diabetic patients assessed in a randomized trial in the field. In our study, 28% of patients received paclitaxel-eluting stents, which was not analyzed separately due to the low number of events and the expectedly limited statistical power. Since patients in the study received treatment with paclitaxel-iopromide-coated DCB, these long-term results can only be extrapolated to those who received these devices.

Conclusion

Based on the randomized BASKET SMALL 2 trial with 3 years of follow-up, the rates of MACE, non-fatal MI, need for TVR and cardiac death are similar between DCB and DES in non-diabetic patients. In diabetic patients the need for TVR is significantly lower with DCB compared to DES. The study demonstrates the sustained efficacy and safety of DCB in diabetic patients with de-novo lesions of small coronary vessels up to 3 years compared to DES.

Tables

Table 1: Baseline Characteristics

	overall	% missing	nondiabetic	diabetic	p
n	758		506	252	
age (mean (SD))	67.79 (10.34)	0.0	66.73 (10.60)	69.93 (9.45)	0.0001
sex = male (%)	557 (73.5)	0.0	379 (74.9)	178 (70.6)	0.2435
BMI (mean (SD))	28.29 (4.54)	0.4	27.51 (4.06)	29.84 (5.03)	<0.0001
smoking (%)		2.2			0.0034
current smoker	154 (20.8)		120 (24.3)	34 (13.7)	
former smoker	267 (36.0)		169 (34.3)	98 (39.5)	
no	320 (43.2)		204 (41.4)	116 (46.8)	
hypercholesterolaemia = yes (%)	521 (69.4)	0.9	334 (66.8)	187 (74.5)	0.0379
hypertension = yes (%)	656 (86.8)	0.3	424 (84.1)	232 (92.1)	0.0035
family history = yes (%)	278 (40.3)	9.1	185 (39.7)	93 (41.7)	0.6754
diabetes (%)		0.5			<0.0001
IDDM	95 (12.6)		0 (0.0)	95 (37.7)	
NIDDM	157 (20.8)		0 (0.0)	157 (62.3)	
no	502 (66.6)		502 (100.0)	0 (0.0)	
multi-step proc. = yes (%)	63 (8.3)	0.0	38 (7.5)	25 (9.9)	0.3207
prev. anterior MI = yes (%)	121 (16.0)	0.1	75 (14.9)	46 (18.3)	0.2719
prev. other MI = yes (%)	185 (24.4)	0.0	127 (25.1)	58 (23.0)	0.5897
prev. any MI = yes (%)	293 (38.7)	0.0	194 (38.3)	99 (39.3)	0.8629
prev. PCI = yes (%)	476 (62.8)	0.0	316 (62.5)	160 (63.5)	0.8417
prev. CABG = yes (%)	71 (9.4)	0.0	43 (8.5)	28 (11.1)	0.3026
heart failure = yes (%)	83 (11.0)	0.1	42 (8.3)	41 (16.3)	0.0015
stroke/TIA (%)		0.1			0.3885
stroke	39 (5.2)		23 (4.6)	16 (6.3)	
TIA	27 (3.6)		16 (3.2)	11 (4.4)	
no	691 (91.3)		466 (92.3)	225 (89.3)	
aortic aneurysm = yes (%)	11 (1.5)	0.1	9 (1.8)	2 (0.8)	0.4540
PAOD = yes (%)	53 (7.0)	0.1	32 (6.3)	21 (8.3)	0.3879
COPD = yes (%)	64 (8.4)	0.0	38 (7.5)	26 (10.3)	0.2416
coronary disease (%)		0.0			0.7886
STEMI	15 (2.0)		10 (2.0)	5 (2.0)	
NSTEMI	109 (14.4)		74 (14.6)	35 (13.9)	
unstable	90 (11.9)		64 (12.6)	26 (10.3)	
stable	544 (71.8)		358 (70.8)	186 (73.8)	
acute coronary disease = yes (%)	214 (28.2)	0.0	148 (29.2)	66 (26.2)	0.4262
renal disease (rep.) = yes (%)	113 (14.9)	0.0	45 (8.9)	68 (27.0)	<0.0001
liver disease (rep.) = yes (%)	16 (2.1)	0.0	4 (0.8)	12 (4.8)	0.0009
dementia = yes (%)	1 (0.1)	0.1	1 (0.2)	0 (0.0)	1.0000
renal dysfunction (calc.) = yes (%)	174 (23.0)	0.0	92 (18.2)	82 (32.5)	<0.0001
coronary LM = yes (%)	27 (3.6)	0.0	19 (3.8)	8 (3.2)	0.8430
coronary LAD = yes (%)	616 (81.3)	0.0	402 (79.4)	214 (84.9)	0.0853
coronary LCX = yes (%)	562 (74.1)	0.0	367 (72.5)	195 (77.4)	0.1773
coronary RCA = yes (%)	477 (62.9)	0.0	314 (62.1)	163 (64.7)	0.5315
multi-vessel coronary disease = yes (%)	598 (78.9)	0.0	394 (77.9)	204 (81.0)	0.3753
ejection fraction type (%)		24.7			0.4907
angiography	347 (60.8)		230 (59.7)	117 (62.9)	
echography	217 (38.0)		149 (38.7)	68 (36.6)	
scintigraphy	7 (1.2)		6 (1.6)	1 (0.5)	
ejection fraction perc. (median [IQR])	60.00 [53.00, 62.00]	24.9	60.00 [54.00, 64.00]	60.00 [50.00, 60.00]	0.0233
initial hosp. = out-patient (%)	17 (2.2)	0.0	16 (3.2)	1 (0.4)	0.0306
prev. clopidogrel = yes (%)	205 (27.0)	0.0	140 (27.7)	65 (25.8)	0.6452
prev. ASS = yes (%)	611 (80.6)	0.0	413 (81.6)	198 (78.6)	0.3667
prev. prasugrel = yes (%)	74 (9.8)	0.0	56 (11.1)	18 (7.1)	0.1130
prev. ticagrelor = yes (%)	118 (15.6)	0.0	80 (15.8)	38 (15.1)	0.8767
prev. statin = yes (%)	502 (66.3)	0.1	326 (64.4)	176 (70.1)	0.1393
prev. anticoagulants = yes (%)	64 (8.7)	3.0	38 (7.8)	26 (10.5)	0.2799

Categorical variables are depicted as frequencies and percentages, numerical variables as mean and standard deviation (except for ejection fraction as median and interquartile range); with p-values for the difference between study arms obtained by Pearson's chi-squared test and Student's t-test, respectively (Wilcoxon–Mann–Whitney test for ejection fraction).

Table 2: Comparison of event numbers and Kaplan-Meier estimated of event rates between the two study arms within each subgroup for all endpoints

type of event	subgroup	study arm	1-y events (rate)	1-y HR [95% CI]	2-y events (rate)	2-y HR [95% CI]	3-y events (rate)	3-y HR [95% CI]
MACE	nondiabetic	DES	12 (5.01%)	1 —reference—	18 (7.59%)	1 —reference—	26 (11.46%)	1 —reference—
		DCB	16 (6.22%)	1.37 [0.64, 2.91] (p=0.418)	26 (10.27%)	1.53 [0.83, 2.80] (p=0.172)	32 (12.98%)	1.24 [0.73, 2.09] (p=0.427)
	diabetic	DES	16 (12.68%)	1 —reference—	23 (18.50%)	1 —reference—	27 (22.15%)	1 —reference—
		DCB	12 (10.23%)	0.83 [0.38, 1.80] (p=0.630)	16 (13.93%)	0.79 [0.41, 1.52] (p=0.474)	21 (19.29%)	0.82 [0.45, 1.48] (p=0.505)
	Interaction			0.56 [0.19, 1.65] (p=0.294)		0.47 [0.19, 1.16] (p=0.101)		0.63 [0.29, 1.40] (p=0.259)
cardiac death	nondiabetic	DES	2 (0.83%)	1 —reference—	4 (1.69%)	1 —reference—	6 (2.87%)	1 —reference—
		DCB	4 (1.55%)	1.64 [0.30, 9.04] (p=0.568)	5 (1.95%)	1.03 [0.27, 3.86] (p=0.965)	7 (2.78%)	0.97 [0.32, 2.92] (p=0.958)
cardiac death	diabetic	DES	3 (2.40%)	1 —reference—	5 (4.08%)	1 —reference—	7 (5.93%)	1 —reference—
		DCB	8 (6.86%)	3.85 [1.02, 14.60] (p=0.047)	9 (7.79%)	2.49 [0.83, 7.49] (p=0.103)	10 (8.83%)	2.01 [0.76, 5.31] (p=0.161)
	interaction			2.35 [0.27, 20.39] (p=0.439)		2.48 [0.44, 13.83] (p=0.301)		2.04 [0.47, 8.90] (p=0.341)
non-fatal MI	nondiabetic	DES	5 (2.08%)	1 —reference—	8 (3.39%)	1 —reference—	11 (4.75%)	1 —reference—
		DCB	3 (1.19%)	0.61 [0.15, 2.60] (p=0.508)	9 (3.65%)	1.08 [0.41, 2.82] (p=0.873)	12 (5.12%)	1.00 [0.44, 2.28] (p=0.999)
non-fatal MI	diabetic	DES	8 (6.31%)	1 —reference—	11 (8.88%)	1 —reference—	12 (9.82%)	1 —reference—
		DCB	3 (2.55%)	0.27 [0.06, 1.18] (p=0.082)	5 (4.57%)	0.43 [0.14, 1.35] (p=0.148)	7 (7.05%)	0.55 [0.21, 1.49] (p=0.243)
	interaction			0.47 [0.06, 3.54] (p=0.466)		0.45 [0.11, 1.93] (p=0.283)		0.63 [0.18, 2.23] (p=0.472)
TVR	nondiabetic	DES	7 (2.94%)	1 —reference—	10 (4.25%)	1 —reference—	14 (6.08%)	1 —reference—
		DCB	10 (3.94%)	1.55 [0.59, 4.11] (p=0.375)	17 (6.82%)	2.00 [0.91, 4.41] (p=0.085)	21 (8.75%)	1.64 [0.83, 3.25] (p=0.156)
TVR	diabetic	DES	10 (7.99%)	1 —reference—	16 (13.13%)	1 —reference—	18 (15.02%)	1 —reference—
		DCB	3 (2.58%)	0.27 [0.07, 1.01] (p=0.053)	6 (5.56%)	0.36 [0.14, 0.94] (p=0.037)	9 (9.12%)	0.40 [0.17, 0.94] (p=0.036)
	interaction			0.63 [0.18, 2.23] (p=0.472)		0.16 [0.05, 0.56] (p=0.004)		0.25 [0.08, 0.72] (p=0.011)
all-causes death	nondiabetic	DES	4 (1.64%)	1 —reference—	7 (2.92%)	1 —reference—	12 (5.39%)	1 —reference—
		DCB	6 (2.32%)	1.30 [0.36, 4.64] (p=0.691)	7 (2.72%)	0.86 [0.30, 2.47] (p=0.780)	11 (4.37%)	0.78 [0.34, 1.79] (p=0.564)
all-causes death	diabetic	DES	5 (3.93%)	1 —reference—	10 (7.97%)	1 —reference—	15 (12.20%)	1 —reference—
		DCB	11 (9.29%)	2.92 [1.00, 8.52] (p=0.051)	15 (12.91%)	1.74 [0.76, 3.97] (p=0.187)	17 (14.85%)	1.41 [0.69, 2.90] (p=0.346)
	interaction			2.17 [0.41, 11.46] (p=0.363)		2.02 [0.53, 7.71] (p=0.301)		1.77 [0.59, 5.29] (p=0.305)

Cox regression stratified by study center, MACE=major adverse cardiac events, MI=myocardial infarction, TVR=target vessel revascularization, HR=hazard ratio, CI=confidence intervals. Rates are Kaplan-Meier rates at each landmark time. Interaction is presented for diabetes mellitus and randomized treatment strategy.

Figure legends:

Figure 1A: Kaplan-Meier estimates of the cumulative probabilities of major adverse cardiac events (MACE) during three years in the four combinations of subgroups and study arms (DES=drug eluting stent, DCB=drug coated balloon)

Figure 1B: Kaplan-Meier estimates of the cumulative probabilities of non-fatal myocardial infarction during three years in the four combinations of subgroups and study arms (DES=drug eluting stent, DCB=drug coated balloon)

Figure 1C: Kaplan-Meier estimates of the cumulative probabilities of target vessel revascularization (TVR) during three years in the four combinations of subgroups and study arms (DES=drug eluting stent, DCB=drug coated balloon)

Figure 1D: Kaplan-Meier estimates of the cumulative probabilities of all-cause death during three years in the four combinations of subgroups and study arms (DES=drug eluting stent, DCB=drug coated balloon)

Central illustration: BASKET SMALL 2 TRIAL - Event rates with DCB and DES in de-novo coronary lesions of diabetic and non-diabetic patients.

PERSPECTIVES

What Is Known? Treatment of de-novo lesions in small coronary arteries (vessel diameter <3mm) with drug-coated balloons (SeQuent Please, B.Braun, Melsungen, Germany) is non-inferior to drug-eluting stents regarding the occurrence of major adverse cardiac events, cardiac death, non-fatal myocardial infarction and target vessel revascularization up to 3 years of clinical follow-up.

What Is New? Outcome of non-diabetic patients treated with DCB is similar to DES with respect to MACE, non-fatal MI, TVR and cardiac death. In diabetic patients rates of MACE, non-fatal MI and cardiac death are similar between DCB and DES while need for TVR is significantly lower up to 3 years.

What Is Next? These results generate the hypothesis that use of DCB for treatment of de-novo lesions in small coronary vessels is superior to DES with respect to TVR, which needs to be studied in a separate trial.

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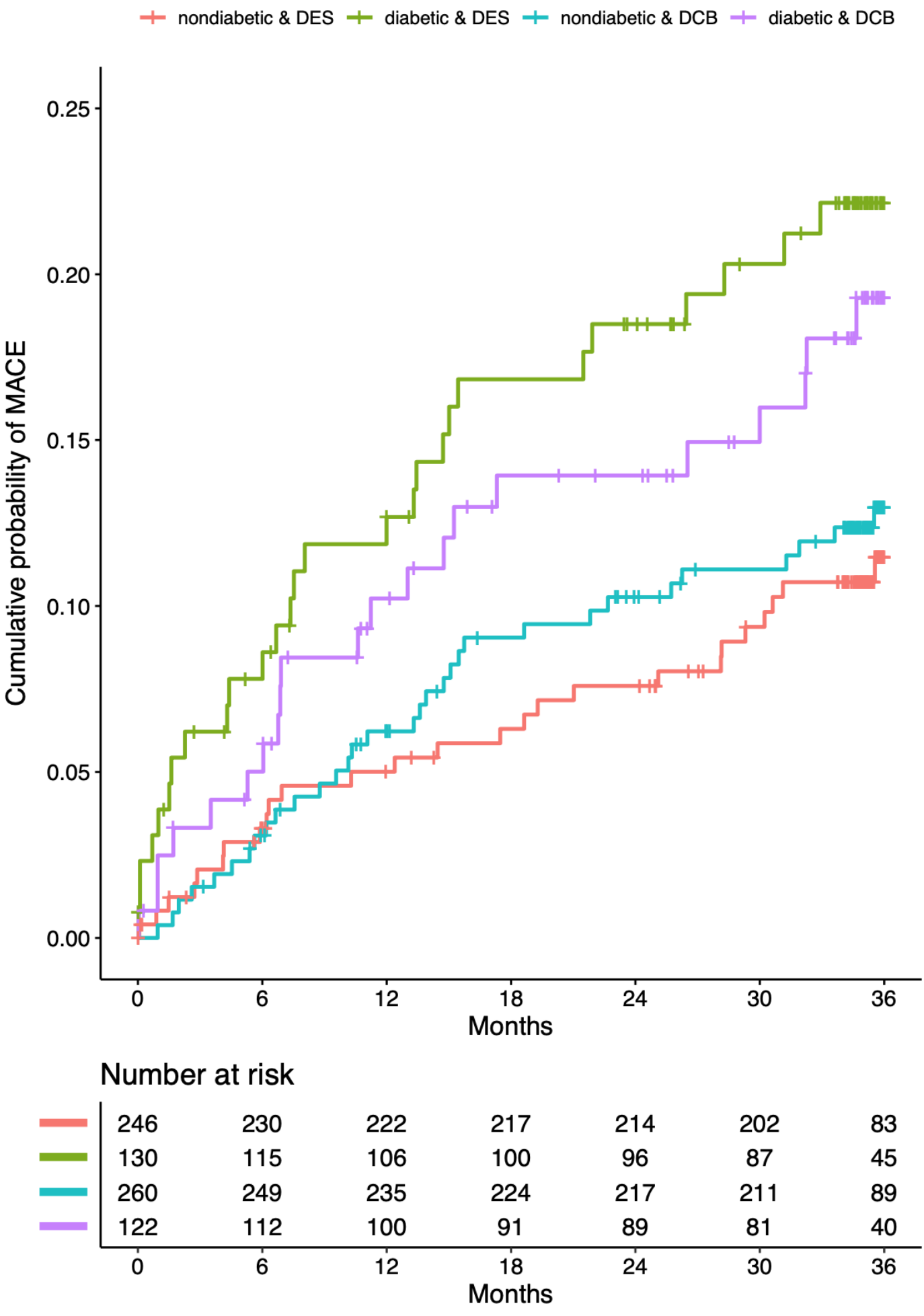
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diabetic & DES
nondiabetic & DCB
diabetic & DCB
Cumulative probability of MACE
0.25
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Months
Number at risk
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260 249 235 224 217 211 89
122 112 100 91 89 81 40
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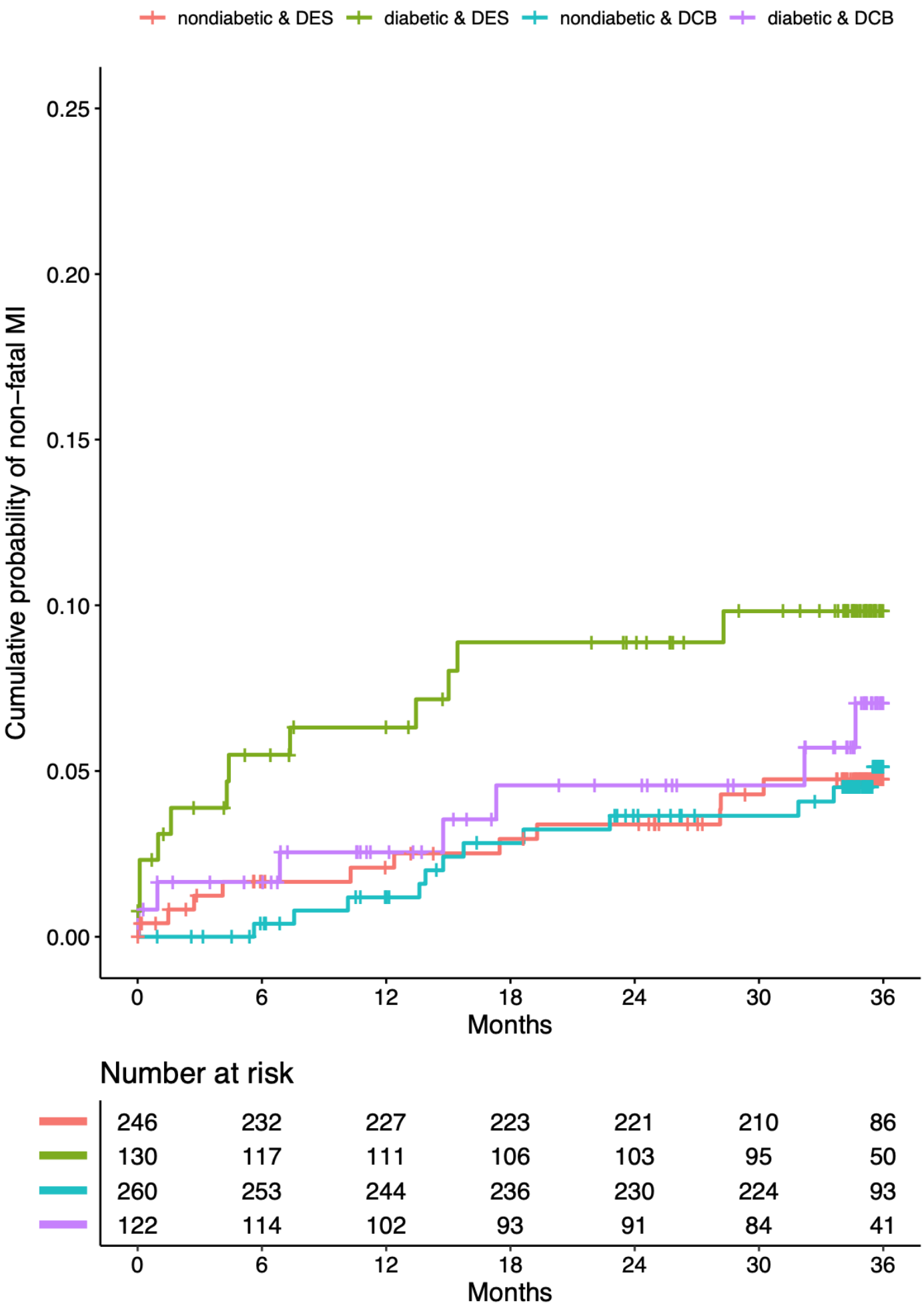
nondiabetic & DES
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diabetic & DCB
Cumulative probability of non−fatal MI
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Months
Number at risk
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122 114 102 93 91 84 41
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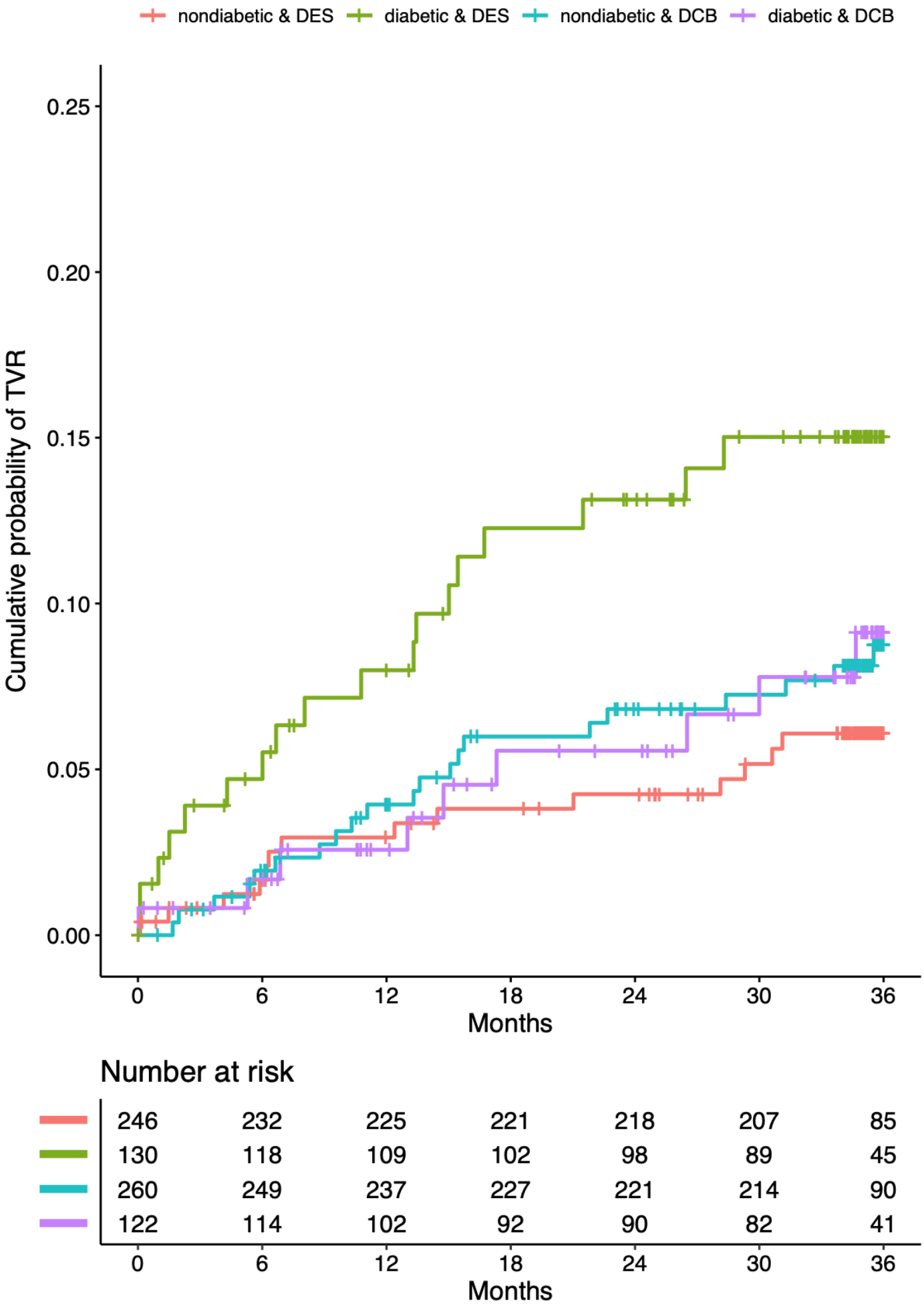
nondiabetic & DES
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diabetic & DCB
Cumulative probability of TVR
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Months
Number at risk
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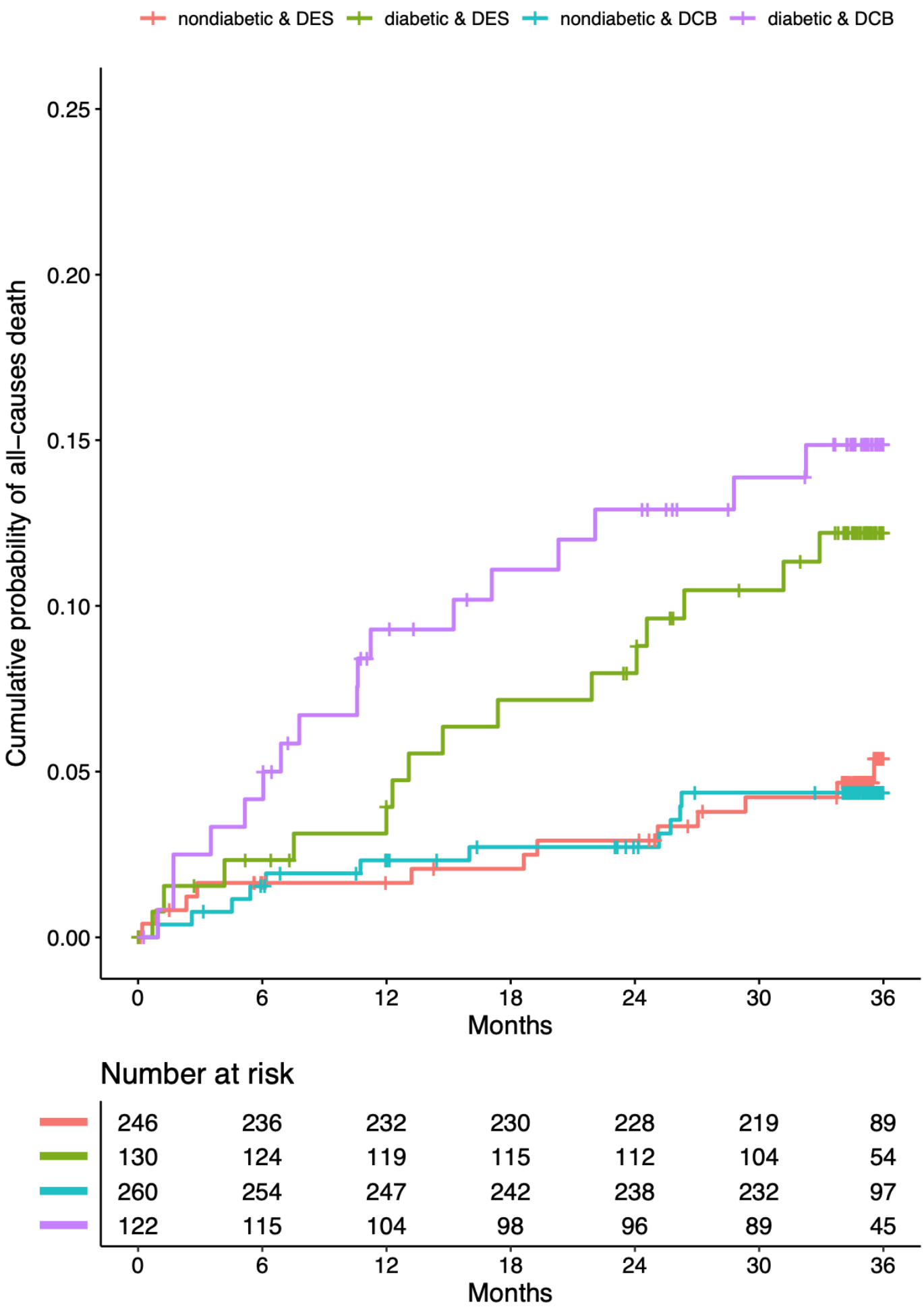
nondiabetic & DES
diabetic & DES
nondiabetic & DCB
diabetic & DCB
Cumulative probability of all−causes death
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Months
Number at risk
246 236 232 230 228 219 89
130 124 119 115 112 104 54
260 254 247 242 238 232 97
122 115 104 98 96 89 45
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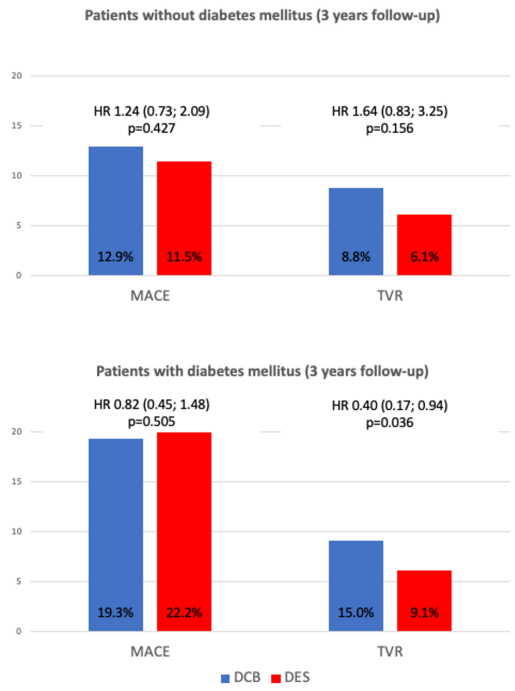
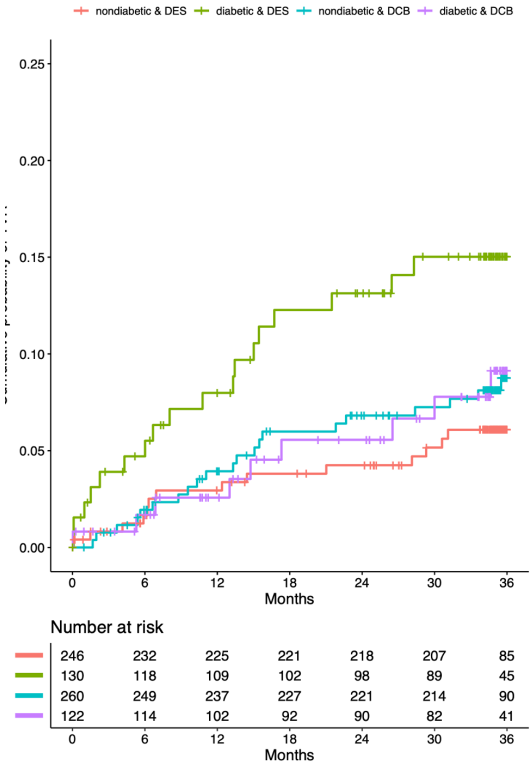
Months

Central illustration: BASKET SMALL 2 TRIAL - Event rates with DCB and DES in de-novo coronary lesions of diabetic and non-diabetic patients.





Impact of diabetes on outcome with drug-coated balloons versus drug-eluting stents: The BASKET-SMALL 2 trial

Supplemental Material

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Supplement table 1: Baseline characteristics

	overall	% missing	DCB	PES	EES	p
n	716		367	93	256	
age (mean (SD))	67.71 (10.24)	0.0	67.03 (10.23)	67.24 (9.59)	68.87 (10.40)	0.0776
sex = male (%)	525 (73.3)	0.0	283 (77.1)	64 (68.8)	178 (69.5)	0.0627
BMI (mean (SD))	28.30 (4.59)	0.3	28.42 (4.58)	27.28 (4.21)	28.50 (4.70)	0.0726
smoking (%)		2.2				0.1657
current smoker	145 (20.7)		79 (22.0)	20 (21.7)	46 (18.5)	
former smoker	251 (35.9)		138 (38.4)	34 (37.0)	79 (31.7)	
no	304 (43.4)		142 (39.6)	38 (41.3)	124 (49.8)	
hypercholesterolaemia = yes (%)	493 (69.5)	1.0	253 (69.1)	65 (72.2)	175 (69.2)	0.8388
hypertension = yes (%)	620 (86.8)	0.3	313 (85.3)	80 (87.0)	227 (89.0)	0.3993
family history = yes (%)	260 (40.1)	9.4	141 (41.6)	34 (40.0)	85 (37.8)	0.6637
diabetes (%)		0.6				0.4312
IDDM	91 (12.8)		46 (12.6)	10 (10.9)	35 (13.8)	
NIDDM	147 (20.6)		68 (18.6)	18 (19.6)	61 (24.0)	
no	474 (66.6)		252 (68.9)	64 (69.6)	158 (62.2)	
multi-step proc. = yes (%)	61 (8.5)	0.0	26 (7.1)	9 (9.7)	26 (10.2)	0.3661
prev. anterior MI = yes (%)	115 (16.1)	0.1	58 (15.8)	18 (19.4)	39 (15.3)	0.6452
prev. other MI = yes (%)	174 (24.3)	0.0	101 (27.5)	18 (19.4)	55 (21.5)	0.1103
prev. any MI = yes (%)	277 (38.7)	0.0	152 (41.4)	33 (35.5)	92 (35.9)	0.3056
prev. PCI = yes (%)	449 (62.7)	0.0	223 (60.8)	60 (64.5)	166 (64.8)	0.5425
prev. CABG = yes (%)	64 (8.9)	0.0	34 (9.3)	11 (11.8)	19 (7.4)	0.4221
heart failure = yes (%)	82 (11.5)	0.1	47 (12.8)	7 (7.5)	28 (10.9)	0.3373
stroke/TIA (%)		0.1				0.7867
stroke	37 (5.2)		16 (4.4)	5 (5.4)	16 (6.2)	
TIA	25 (3.5)		11 (3.0)	4 (4.3)	10 (3.9)	
no	653 (91.3)		339 (92.6)	84 (90.3)	230 (89.8)	
aortic aneurysm = yes (%)	11 (1.5)	0.0	4 (1.1)	2 (2.2)	5 (2.0)	0.6037
PAOD = yes (%)	49 (6.8)	0.0	26 (7.1)	10 (10.8)	13 (5.1)	0.1725
COPD = yes (%)	61 (8.5)	0.0	29 (7.9)	5 (5.4)	27 (10.5)	0.2581
coronary disease (%)		0.0				0.4750
STEMI	15 (2.1)		12 (3.3)	1 (1.1)	2 (0.8)	
NSTEMI	101 (14.1)		49 (13.4)	14 (15.1)	38 (14.8)	
unstable	88 (12.3)		47 (12.8)	11 (11.8)	30 (11.7)	
stable	512 (71.5)		259 (70.6)	67 (72.0)	186 (72.7)	
acute coronary disease = yes (%)	204 (28.5)	0.0	108 (29.4)	26 (28.0)	70 (27.3)	0.8452
renal disease (rep.) = yes (%)	109 (15.2)	0.0	54 (14.7)	7 (7.5)	48 (18.8)	0.0332
liver disease (rep.) = yes (%)	16 (2.2)	0.0	6 (1.6)	3 (3.2)	7 (2.7)	0.5181
dementia = yes (%)	1 (0.1)	0.1	0 (0.0)	0 (0.0)	1 (0.4)	0.4075
renal dysfunction (calc.) = yes (%)	167 (23.3)	0.0	92 (25.1)	13 (14.0)	62 (24.2)	0.0713
coronary LM = yes (%)	25 (3.5)	0.0	11 (3.0)	2 (2.2)	12 (4.7)	0.3967
coronary LAD = yes (%)	579 (80.9)	0.0	300 (81.7)	76 (81.7)	203 (79.3)	0.7283
coronary LCX = yes (%)	528 (73.7)	0.0	281 (76.6)	63 (67.7)	184 (71.9)	0.1571
coronary RCA = yes (%)	446 (62.3)	0.0	222 (60.5)	59 (63.4)	165 (64.5)	0.5862

multi-vessel coronary disease = yes (%)	563 (78.6)	0.0	300 (81.7)	69 (74.2)	194 (75.8)	0.1084
ejection fraction type (%)		24.4				0.0127
angiography	328 (60.6)		169 (59.7)	56 (78.9)	103 (55.1)	
echography	206 (38.1)		110 (38.9)	15 (21.1)	81 (43.3)	
scintigraphy	7 (1.3)		4 (1.4)	0 (0.0)	3 (1.6)	
initial hosp. = out-patient (%)	17 (2.4)	0.0	11 (3.0)	3 (3.2)	3 (1.2)	0.2862
prev. clopidogrel = yes (%)	191 (26.7)	0.0	98 (26.7)	23 (24.7)	70 (27.3)	0.8877
prev. ASS = yes (%)	579 (80.9)	0.0	286 (77.9)	82 (88.2)	211 (82.4)	0.0592
prev. prasugrel = yes (%)	70 (9.8)	0.0	36 (9.8)	11 (11.8)	23 (9.0)	0.7312
prev. ticagrelor = yes (%)	111 (15.5)	0.0	53 (14.4)	13 (14.0)	45 (17.6)	0.5163
prev. statin = yes (%)	475 (66.4)	0.1	238 (64.9)	65 (69.9)	172 (67.5)	0.5975
prev. anticoagulants = yes (%)	62 (8.9)	3.2	30 (8.5)	3 (3.6)	29 (11.3)	0.0885

Categorical variables are depicted as frequencies and percentages, numerical variables as mean and standard deviation (except for ejection fraction as median and interquartile range); with p-values for the difference between study arms obtained by Pearson’s chi-squared test and Student’s t-test, respectively (Wilcoxon–Mann–Whitney test for ejection fraction).

Supplement table 2: Comparison of event numbers and Kaplan–Meier estimates of event rates between devices within each subgroup for all endpoints.

type of event	subgroup	device	1-y events (rate)	1-y HR [95% CI] (p-value)	2-y events (rate)	2-y HR [95% CI] (p-value)	3-y events (rate)	3-y HR [95% CI] (p-value)
MACE	nondiabetic	DCB	15 (6.00%)	1 —reference—	24 (9.73%)	1 —reference—	30 (12.51%)	1 —reference—
		Taxus	8 (12.31%)	2.00 [0.82, 4.91] (p=0.130)	10 (15.50%)	1.49 [0.69, 3.20] (p=0.307)	13 (20.44%)	1.68 [0.85, 3.31] (p=0.133)
		Xience	3 (1.96%)	0.30 [0.09, 1.03] (p=0.055)	7 (4.64%)	0.42 [0.18, 0.99] (p=0.046)	10 (7.29%)	0.50 [0.24, 1.03] (p=0.062)
MACE	diabetic	DCB	10 (9.10%)	1 —reference—	14 (13.10%)	1 —reference—	19 (18.95%)	1 —reference—
		Taxus	4 (14.29%)	1.89 [0.57, 6.24] (p=0.299)	6 (21.43%)	1.86 [0.69, 4.99] (p=0.216)	6 (21.43%)	1.28 [0.50, 3.29] (p=0.602)
		Xience	11 (11.95%)	1.19 [0.48, 2.93] (p=0.703)	16 (17.67%)	1.21 [0.57, 2.56] (p=0.612)	19 (21.40%)	1.16 [0.59, 2.28] (p=0.661)
cardiac death	nondiabetic	DCB	4 (1.59%)	1 —reference—	5 (2.00%)	1 —reference—	7 (2.86%)	1 —reference—
		Taxus	1 (1.54%)	1.20 [0.12, 11.99] (p=0.877)	1 (1.54%)	0.99 [0.11, 9.06] (p=0.991)	1 (1.54%)	0.69 [0.08, 5.86] (p=0.731)
		Xience	0 (0.00%)	0.00 [0.00, Inf] (p=0.999)	2 (1.34%)	0.68 [0.13, 3.52] (p=0.643)	4 (3.28%)	0.97 [0.28, 3.33] (p=0.958)
cardiac death	diabetic	DCB	6 (5.49%)	1 —reference—	7 (6.49%)	1 —reference—	8 (7.63%)	1 —reference—
		Taxus	0 (0.00%)	0.00 [0.00, Inf] (p=0.999)	0 (0.00%)	0.00 [0.00, Inf] (p=0.998)	0 (0.00%)	0.00 [0.00, Inf] (p=0.998)
		Xience	2 (2.18%)	0.26 [0.05, 1.32] (p=0.104)	4 (4.48%)	0.51 [0.14, 1.80] (p=0.296)	6 (6.99%)	0.68 [0.23, 2.03] (p=0.490)
non-fatal MI	nondiabetic	DCB	3 (1.22%)	1 —reference—	9 (3.75%)	1 —reference—	12 (5.26%)	1 —reference—
		Taxus	3 (4.64%)	3.49 [0.65, 18.79] (p=0.146)	4 (6.26%)	1.64 [0.48, 5.58] (p=0.431)	5 (7.90%)	1.69 [0.57, 5.02] (p=0.344)
		Xience	2 (1.31%)	0.98 [0.16, 5.94] (p=0.983)	4 (2.65%)	0.69 [0.21, 2.25] (p=0.538)	5 (3.36%)	0.67 [0.24, 1.92] (p=0.460)
non-fatal MI	diabetic	DCB	3 (2.72%)	1 —reference—	5 (4.87%)	1 —reference—	7 (7.56%)	1 —reference—
		Taxus	3 (10.71%)	4.92 [0.94, 25.64] (p=0.058)	5 (17.86%)	5.00 [1.34, 18.61] (p=0.017)	5 (17.86%)	3.11 [0.94, 10.32] (p=0.064)
		Xience	5 (5.44%)	2.28 [0.49, 10.71] (p=0.297)	6 (6.63%)	1.20 [0.34, 4.22] (p=0.780)	7 (7.91%)	1.13 [0.37, 3.44] (p=0.835)
TVR	nondiabetic	DCB	9 (3.65%)	1 —reference—	15 (6.18%)	1 —reference—	19 (8.16%)	1 —reference—
		Taxus	6 (9.33%)	2.29 [0.78, 6.69] (p=0.130)	7 (10.95%)	1.36 [0.54, 3.41] (p=0.515)	10 (15.96%)	1.73 [0.78, 3.82] (p=0.177)
		Xience	1 (0.65%)	0.16 [0.02, 1.29] (p=0.085)	3 (1.98%)	0.28 [0.08, 0.96] (p=0.044)	3 (1.98%)	0.23 [0.07, 0.79] (p=0.019)
TVR	diabetic	DCB	3 (2.76%)	1 —reference—	6 (5.93%)	1 —reference—	9 (9.77%)	1 —reference—
		Taxus	3 (10.71%)	3.52 [0.70, 17.71] (p=0.126)	6 (21.43%)	3.80 [1.20, 12.04] (p=0.023)	6 (21.43%)	2.56 [0.89, 7.34] (p=0.080)
		Xience	7 (7.72%)	3.49 [0.88, 13.90] (p=0.076)	10 (11.25%)	2.15 [0.76, 6.09] (p=0.151)	11 (12.54%)	1.85 [0.74, 4.66] (p=0.190)
all-causes death	nondiabetic	DCB	6 (2.39%)	1 —reference—	7 (2.80%)	1 —reference—	11 (4.48%)	1 —reference—
		Taxus	1 (1.54%)	0.66 [0.08, 5.69] (p=0.704)	1 (1.54%)	0.57 [0.07, 4.76] (p=0.603)	2 (3.15%)	0.82 [0.17, 3.82] (p=0.795)
		Xience	2 (1.27%)	0.59 [0.12, 2.94] (p=0.518)	5 (3.24%)	1.25 [0.39, 3.95] (p=0.708)	8 (5.81%)	1.24 [0.50, 3.10] (p=0.645)
all-causes death	diabetic	DCB	9 (8.13%)	1 —reference—	13 (12.03%)	1 —reference—	15 (14.14%)	1 —reference—
		Taxus	0 (0.00%)	0.00 [0.00, Inf] (p=0.998)	1 (3.57%)	0.30 [0.04, 2.38] (p=0.256)	1 (3.57%)	0.25 [0.03, 1.91] (p=0.180)
		Xience	4 (4.27%)	0.39 [0.11, 1.32] (p=0.130)	7 (7.61%)	0.57 [0.22, 1.51] (p=0.262)	12 (13.33%)	0.79 [0.35, 1.79] (p=0.578)

Cox regression stratified by study center, MACE=major adverse cardiac events, MI=myocardial infarction, TVR=target vessel revascularization, HR=hazard ratio, CI=confidence intervals. Rates are Kaplan-Meier rates at each landmark time. Interaction is presented for diabetes mellitus and randomized treatment strategy.

Supplement Table 3: Cox regressions stratified by study center and adjusted for diabetic status(with and without interaction with device).

type of event	variable	1-y HR [95% CI] (p-value)	2-y HR [95% CI] (p-value)	3-y HR [95% CI] (p-value)
MACE	device: Taxus vs DCB	2.02 [0.99, 4.09] (p=0.052)	1.73 [0.95, 3.15] (p=0.072)	1.59 [0.93, 2.74] (p=0.091)
	device: Xience vs DCB	0.76 [0.39, 1.48] (p=0.418)	0.82 [0.48, 1.39] (p=0.458)	0.80 [0.50, 1.27] (p=0.341)
	subgroup: diabetic vs nondiabetic	2.11 [1.19, 3.74] (p=0.010)	1.91 [1.20, 3.04] (p=0.006)	1.85 [1.22, 2.79] (p=0.004)
MACE	device: Taxus vs DCB	1.97 [0.97, 4.00] (p=0.061)	1.69 [0.93, 3.07] (p=0.088)	1.58 [0.92, 2.71] (p=0.100)
	device: Xience vs DCB	0.50 [0.21, 1.22] (p=0.128)	0.65 [0.35, 1.20] (p=0.170)	0.67 [0.40, 1.14] (p=0.143)
	subgroup: diabetic vs nondiabetic	2.53 [1.32, 4.85] (p=0.005)	2.05 [1.25, 3.37] (p=0.004)	1.98 [1.28, 3.05] (p=0.002)
	interaction: diabetic & Taxus	0.84 [0.20, 3.63] (p=0.818)	1.13 [0.33, 3.82] (p=0.850)	0.76 [0.24, 2.38] (p=0.639)
	interaction: diabetic & Xience	4.41 [0.96, 20.29] (p=0.057)	3.16 [1.03, 9.72] (p=0.045)	2.36 [0.89, 6.26] (p=0.084)
cardiac death	device: Taxus vs DCB	0.55 [0.07, 4.59] (p=0.583)	0.36 [0.04, 2.81] (p=0.326)	0.28 [0.04, 2.14] (p=0.219)
	device: Xience vs DCB	0.20 [0.04, 0.95] (p=0.043)	0.57 [0.21, 1.55] (p=0.270)	0.79 [0.35, 1.79] (p=0.572)
	subgroup: diabetic vs nondiabetic	3.40 [1.07, 10.82] (p=0.038)	2.48 [0.97, 6.33] (p=0.057)	2.14 [0.97, 4.73] (p=0.061)
cardiac death	device: Taxus vs DCB	—perfect separation—	1.05 [0.12, 9.33] (p=0.962)	0.70 [0.08, 5.87] (p=0.746)
	device: Xience vs DCB	—perfect separation—	0.61 [0.19, 1.98] (p=0.413)	0.85 [0.35, 2.09] (p=0.726)
	subgroup: diabetic vs nondiabetic	—perfect separation—	2.81 [1.07, 7.39] (p=0.037)	2.35 [1.05, 5.27] (p=0.037)
	interaction: diabetic & Taxus	—perfect separation—	0.00 [0.00, 3.35] (p=0.473)	0.00 [0.00, 4.20] (p=0.504)
	interaction: diabetic & Xience	—perfect separation—	0.74 [0.09, 5.80] (p=0.773)	0.69 [0.13, 3.55] (p=0.657)
non-fatal MI	device: Taxus vs DCB	4.04 [1.27, 12.85] (p=0.018)	2.60 [1.10, 6.14] (p=0.030)	2.11 [0.96, 4.63] (p=0.062)
	device: Xience vs DCB	1.63 [0.53, 5.01] (p=0.391)	0.89 [0.39, 2.05] (p=0.783)	0.81 [0.39, 1.69] (p=0.574)
	subgroup: diabetic vs nondiabetic	3.75 [1.43, 9.79] (p=0.007)	2.29 [1.12, 4.69] (p=0.023)	2.04 [1.07, 3.87] (p=0.029)
non-fatal MI	device: Taxus vs DCB	3.64 [1.08, 12.25] (p=0.037)	2.30 [0.92, 5.71] (p=0.074)	1.98 [0.88, 4.47] (p=0.100)
	device: Xience vs DCB	1.33 [0.36, 4.84] (p=0.668)	0.85 [0.35, 2.06] (p=0.712)	0.77 [0.35, 1.69] (p=0.513)
	subgroup: diabetic vs nondiabetic	3.52 [1.23, 10.11] (p=0.019)	2.07 [0.97, 4.42] (p=0.061)	1.97 [1.01, 3.84] (p=0.047)
	interaction: diabetic & Taxus	1.56 [0.16, 15.46] (p=0.704)	2.74 [0.48, 15.59] (p=0.255)	1.82 [0.38, 8.79] (p=0.454)
	interaction: diabetic & Xience	2.25 [0.22, 23.41] (p=0.497)	1.69 [0.31, 9.24] (p=0.546)	1.54 [0.34, 6.92] (p=0.573)
TVR	device: Taxus vs DCB	2.50 [1.04, 5.98] (p=0.040)	2.12 [1.05, 4.29] (p=0.036)	2.00 [1.07, 3.75] (p=0.030)
	device: Xience vs DCB	1.05 [0.43, 2.57] (p=0.919)	0.93 [0.47, 1.87] (p=0.846)	0.74 [0.39, 1.41] (p=0.361)
	subgroup: diabetic vs nondiabetic	1.73 [0.81, 3.70] (p=0.159)	1.99 [1.10, 3.60] (p=0.024)	1.92 [1.12, 3.28] (p=0.018)
TVR	device: Taxus vs DCB	2.51 [1.04, 6.07] (p=0.041)	1.99 [0.97, 4.09] (p=0.060)	1.94 [1.03, 3.63] (p=0.039)
	device: Xience vs DCB	0.48 [0.11, 2.05] (p=0.321)	0.61 [0.25, 1.49] (p=0.279)	0.46 [0.19, 1.10] (p=0.080)
	subgroup: diabetic vs nondiabetic	2.30 [0.81, 6.50] (p=0.118)	2.17 [1.07, 4.37] (p=0.031)	2.41 [1.27, 4.58] (p=0.007)
	interaction: diabetic & Taxus	1.52 [0.22, 10.34] (p=0.668)	2.44 [0.57, 10.49] (p=0.229)	1.43 [0.39, 5.25] (p=0.588)
	interaction: diabetic & Xience	22.33 [1.86, 268.43] (p=0.014)	9.09 [1.80, 46.01] (p=0.008)	8.31 [1.81, 38.08] (p=0.006)
all-causes death	device: Taxus vs DCB	0.30 [0.04, 2.37] (p=0.256)	0.37 [0.09, 1.62] (p=0.188)	0.45 [0.14, 1.52] (p=0.201)
	device: Xience vs DCB	0.47 [0.18, 1.22] (p=0.121)	0.74 [0.36, 1.54] (p=0.425)	0.92 [0.50, 1.67] (p=0.777)
	subgroup: diabetic vs nondiabetic	2.68 [1.12, 6.41] (p=0.026)	3.08 [1.52, 6.25] (p=0.002)	2.55 [1.42, 4.56] (p=0.002)

all-causes death	device: Taxus vs DCB	0.80 [0.09, 6.88] (p=0.839)	0.45 [0.09, 2.17] (p=0.320)	0.53 [0.16, 1.80] (p=0.309)
	device: Xience vs DCB	0.50 [0.16, 1.55] (p=0.229)	0.91 [0.40, 2.09] (p=0.826)	1.02 [0.52, 1.97] (p=0.959)
	subgroup: diabetic vs nondiabetic	2.93 [1.18, 7.31] (p=0.021)	2.90 [1.39, 6.05] (p=0.005)	2.39 [1.29, 4.40] (p=0.005)
	interaction: diabetic & Taxus	0.00 [0.00, 4.06] (p=0.499)	0.49 [0.03, 9.13] (p=0.631)	0.33 [0.03, 4.14] (p=0.389)
	interaction: diabetic & Xience	0.79 [0.11, 5.83] (p=0.814)	0.48 [0.11, 2.14] (p=0.337)	0.64 [0.19, 2.14] (p=0.471)