

Incremental cost-effectiveness of drug-eluting stents compared with a third-generation bare-metal stent in a real-world setting: randomised Basel Stent Kosten Effektivitäts Trial (BASKET)



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Summary

Background No prospective trial-based data are available for incremental cost-effectiveness of drug-eluting stents (DES) compared with bare-metal stents (BMS) in unselected patients, as treated in everyday practice.

Methods The Basel stent cost-effectiveness trial (BASKET) included 826 consecutive patients treated with angioplasty and stenting for 1281 de-novo lesions, irrespective of indication for angioplasty. Patients were randomised to one of two DES (Cypher, n=264; Taxus, n=281) or to a cobalt-chromium-based BMS (Vision, n=281) and followed up for 6 months for occurrence of major adverse cardiac events and costs. Analysis was by intention-to-treat. The primary endpoint was cost-effectiveness after 6 months, with effectiveness defined as reduction of major adverse cardiac events.

Findings Cardiac death, myocardial infarction, or target vessel revascularisation occurred in 39 of 544 (7.2%) patients with DES and 34 of 280 (12.1%) with BMS (odds ratio 0.56, 95% CI 0.35–0.91; p=0.02), without significant differences between the two DES. Total costs at 6 months were higher with DES (mean €10 544, SD 6849) than with BMS (€9639, 9067; p<0.0001); higher stent costs of DES were not compensated for by lower follow-up costs. Incremental cost-effectiveness ratio of DES compared with BMS to avoid one major event was €18 311, and costs per quality-adjusted life-year gained were more than €50 000. Subgroup analyses showed that DES were more cost-effective for elderly patients in specific high-risk groups.

Interpretation In a real-world setting, use of DES in all patients is less cost effective than in studies with selected patients. Use of these stents could be restricted to patients in high-risk groups.

Introduction

The effectiveness of drug-eluting stents (DES) to reduce restenosis compared with bare-metal stents (BMS) has been documented in randomised controlled trials for selected patient groups^{1–6} and compared with an historical control in a real-world setting—ie, in everyday clinical practise.⁷ However, DES are markedly more expensive than BMS. If most stents used were DES it would have an effect on many hospital budgets and lead to difficult discussions among physicians and hospital administrators as to which patients should or could be treated with DES. Indications for use of DES targeted at specific lesions or patients were suggested,⁸ but such targeting might be seen as rationing,⁹ particularly by the patient. Since evidence from controlled studies is absent, local solutions vary widely—on the basis of interpretation of available data, budgets, insurance plans, availability of DES, and beliefs. Additionally, third-generation, bare metal cobalt-chromium stents¹⁰ are now available, but no prospective comparisons of DES with these newer BMS have been published so far.

To address these questions—particularly whether the use of DES relative to BMS is good value for money in an everyday setting—the prospective randomised controlled

Basel stent cost-effectiveness trial (Basel Stent Kosten Effektivitäts Trial, BASKET) was done. The aim was to compare the 6-month clinical effectiveness of the two available DES with that of a third-generation BMS in relation to the incremental costs in all patients treated with percutaneous coronary intervention (PCI) and stenting. The trial should clarify whether unlimited use of DES in all patients is cost-effective to prevent major adverse cardiac events. The two DES used—the sirolimus-coated Cypher stent (Cordis, Johnson and Johnson, Miami Lakes, Florida, USA) and the paclitaxel-coated Taxus stent (Boston Scientific Corporation, Natick, Massachusetts, USA)—were compared with each other, and each was compared with the cobalt-chromium-based Vision stent (Guidant Corporation, Indianapolis, Indiana, USA). Characteristics of lesions and patients with which DES might be more cost-effective were sought.

Methods

Patients and study design

All patients treated with PCI and stenting at the University Hospital of Basel, Switzerland, between May 5, 2003, and May 31, 2004, were included in

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BASKET, irrespective of indication for PCI. The only exclusion criteria were: a target vessel diameter of 4 mm or greater, because the largest DES size available was 3.5 mm (n=23); presence of restenotic lesions, owing to the different causes and outcome of restenotic lesions (n=49); and no consent, mostly because of patients' or referring physicians' preference for DES before angiography and because of patients being unable to give informed consent (n=90). No other stent protocols were allowed during the study period, to avoid angiography-driven repeat interventions. Thus, 826 (84%) of 988 consecutive patients treated with PCI and stenting for 1281 segments were included in BASKET. The operator in charge enrolled all patients being treated with PCI and stenting, and patients were randomised at midnight at the beginning of each day's clinic to one of the three stent types by use of sealed envelopes. Since all PCIs were done in two busy parallel catheterisation laboratories immediately after diagnostic angiography, which was often an emergency or urgent procedure, this randomisation process was the only one compatible with the aim to include every patient being treated with PCI by all operators, even at night and weekends. No patients were sent selectively for PCI. Patients were asked to participate and sign an informed consent form, then they were told which stent they would receive.

Procedures

PCI and stenting was done according to standard procedures, with the final decisions about the appropriate strategy in each individual patient left to the discretion of the operators in charge. In patients with ST elevation myocardial infarction, primary PCI was the treatment of choice. Patients with non-ST elevation myocardial infarction or unstable angina were treated urgently within 24 h of chest pain if possible, mostly with glycoprotein IIb/IIIa blocker therapy. Stent sizes

available for Cypher were 8 mm, 13 mm, 18 mm, 23 mm, and 33 mm at diameters of 2.5 mm, 3.0 mm, and 3.5 mm; for Taxus were 8 mm, 12 mm, 16 mm, 24 mm, and 32 mm at the same diameters as for Cypher; and for Vision were: 8 mm, 12 mm, 18 mm, 24 mm, and 32 mm at diameters of 3.0 mm and 3.5 mm; since Vision stents of 2.5 mm diameter were unavailable at the time of BASKET, Pixel stainless steel stents from the same manufacturer were used.

All patients were treated with clopidogrel for 6 months (300 mg periprocedurally, maintenance dose 75 mg per day) irrespective of stents used. Otherwise, patients received usual standard of care—ie, aspirin 100 mg daily and a statin, and other drugs, including glycoprotein IIb/IIIa blockers, were used as clinically indicated.

Patients were prospectively seen on an outpatient basis after 6 months for primary endpoint assessment, and all patients not seen personally were contacted by mail, and by telephone if no response was received.

The primary endpoint was cost-effectiveness after 6 months, with effectiveness defined as reduction of major adverse cardiac events—ie, cardiac death, non-fatal myocardial infarction, and target vessel revascularisation. Mortality from other causes was also analysed, but these events were not included as primary endpoints. Non-fatal myocardial infarction apart from the index intervention was diagnosed on the basis of a typical rise (and fall) of cardiac enzyme concentration, typical chest pain, and new pathological Q-waves or ischaemic ST-T wave changes, or both, in the electrocardiogram, according to current guidelines.¹¹ Since no routine measurements of cardiac enzymes were done after PCI, peri-interventional or repeat myocardial infarction after an acute intervention was a clinical diagnosis based on new chest pain with typical increases in enzymes, electrocardiographic changes, or both. Target vessel revascularisation was defined as intervention (PCI or bypass surgery) driven by a lesion in the same epicardial vessel as initially treated. All events were adjudicated by an independent Critical Events Committee blind to the stent type used.

Costs were ascertained on the basis of procedures, stents used, and days spent in hospital at baseline and during follow-up, based on the Swiss medical tariff TARMED and list prices for stents used in Switzerland converted to €. ¹² The cost estimates used were: hospital stay 1 day €420, intensive care 1 day €1935, coronary angiography €1810, PCI €3095, coronary bypass surgery €7095; one stent (official list prices): Cypher €2380 (until Nov 23, 2003), €2145 (Nov 24, 2003, onwards), Taxus €1935, Vision €1260, Pixel €1130. Costs for medications were not included since prescriptions were identical for all stent types. Private physician's visits costs not related to the intervention and other medications and rehabilitation services were not included, since they followed usual standard care practices and were equally distributed in all patient groups. In view of the short

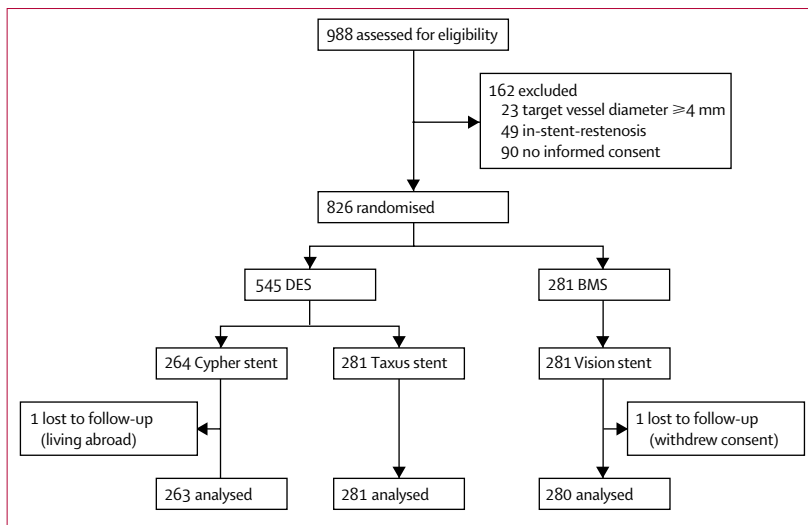


Figure 1: Trial profile

duration of this study, costs and benefits were not discounted. All costs were determined from the perspective of a third party payer. To assess quality-of-life-adjusted life-years (QALYs) gained, we analysed data for the 515 patients (62%) for whom complete data were available from the self-administered EQ-5D questionnaire, including the visual analogue scale from baseline and after 6 months.^{13,14}

The BASKET protocol was approved by the Ethics Committee of the States of Basel, Switzerland. All patients gave written informed consent.

Statistical analysis

The study was planned, undertaken, and analysed according to the intention-to-treat principle, with the primary aim to compare the incremental cost-effectiveness of DES compared with BMS in a 2:1 randomisation including all patients with PCI. This design was based on the assumption that the rate of major adverse cardiac events with DES would be lower, but DES costs higher than those of BMS with an unknown incremental cost-effectiveness ratio. Since differences in effectiveness and costs between the two DES would be small, only exploratory secondary subgroup analyses between the three different stent groups were planned. At the time when the study was conceived, no data on the direct comparison of BMS and DES in a real-world setting were available, but some information on expected event rates had been presented. Therefore, we based the sample size calculation on event rates: considering a 1-year rate of major adverse cardiac events in more than 20% of patients with BMS in the first two direct comparisons with DES in randomised controlled trials^{1,2} and preliminary data from the Rapamycin-Eluting Stent Evaluation At Rotterdam Cardiology Hospital (RESEARCH) trial, which was published later,⁷ we estimated a 6-month event rate of 12% in the BMS group and a 50% reduction with the use of DES. The ability to find a significant reduction in risk is a prerequisite for obtaining conclusive results on cost-effectiveness. Because we wanted to include both available DES we chose a 2:1 randomisation. Thus, at an α level of 0.05 and a power of 80%, 280 patients needed to be included in each of the three groups.¹⁵

Quantitative variables were presented as mean and SD. Median and IQR were indicated for quantitative variables assessed during follow-up. Categorical variables were described by their distribution. Two group comparisons were done with Fisher's exact test for categorical variables and with the unpaired *t* test or Mann-Whitney *U* test for quantitative variables. The associations between the odds of having a major adverse cardiac event during follow-up and baseline predictors (eg, sex, age, diabetes, CAD presentation, vessel disease, lesion type, number, length and diameter of segments treated, residual stenosis) were tested and odds ratios of significant predictors are reported. In a second step,

	Overall	DES		BMS
	(n=826)	Cypher (n=264)	Taxus (n=281)	(n=281)
Male, n (%)	650 (79%)	209 (79%)	218 (78%)	223 (79%)
Mean age, years (SD)	64 (11)	64 (12)	64 (11)	64 (11)
Diabetes, n (%)	153 (19%)	41 (16%)	52 (19%)	60 (21%)
Hypertension, n (%)	544 (67%)	169 (65%)	185 (66%)	190 (68%)
Hypercholesterolemia, n (%)	620 (75%)	196 (74%)	213 (76%)	211 (75%)
Current smoking, n (%)	235 (28%)	76 (29%)	73 (26%)	86 (31%)
Previous MI, n (%)	226 (27%)	73 (28%)	78 (28%)	75 (27%)
Previous PCI, n (%)	133 (16%)	44 (17%)	47 (17%)	42 (15%)
Previous CABG, n (%)	105 (13%)	37 (14%)	33 (12%)	35 (12%)
STEMI, n (%)*	176 (21%)	64 (24%)	51 (18%)	61 (22%)
Unstable, n (%)*	301 (36%)	96 (36%)	104 (37%)	101 (36%)
Stable, n (%)*	349 (42%)	104 (39%)	126 (45%)	119 (42%)
Glycoprotein IIb/IIIa blockers, n (%)	212 (26%)	74 (28%)	67 (24%)	71 (25%)
Multivessel disease, n (%)	566 (69%)	172 (65%)	199 (71%)	195 (69%)
Left main, n (%)*	9 (1%)	1 (0%)	3 (1%)	5 (2%)
LAD, n (%)*	428 (52%)	139 (53%)	146 (52%)	143 (51%)
LCX, n (%)*	260 (31%)	80 (30%)	90 (32%)	90 (32%)
RCA, n (%)*	292 (35%)	93 (35%)	106 (38%)	93 (33%)
Bypass graft, n (%)*	47 (6%)	22 (8%)	12 (4%)	13 (5%)
Number of lesions	1281	415	433	433
Patients with type A lesion, n (%)	119 (14%)	32 (12%)	42 (15%)	45 (16%)
Patients with type B lesion, n (%)	658 (80%)	214 (81%)	231 (82%)	213 (76%)
Patients with type C lesion, n (%)	198 (24%)	70 (27%)	60 (21%)	68 (24%)
Stented segments, n (SD)	1.5 (0.7)	1.5 (0.7)	1.5 (0.7)	1.7 (0.7)
Stents per segment, n (SD)	1.3 (0.5)	1.2 (0.5)	1.3 (0.5)	1.3 (0.5)
Implanted stents, n (SD)	1.9 (1.1)	1.9 (1.1)	1.9 (1.0)	1.9 (1.0)
Total stent length, mm (SD)	34 (20)	36 (21)	33 (20)	32 (20)
≥ 1 stented segments, n (%)	49 (6%)	14 (5%)	12 (4%)	23 (8%)
≥ 1 stents ≤ 2.5mm, n (%)	229 (28%)	79 (30%)	81 (29%)	69 (25%)
Only stents ≥ 3.5mm, n (%)	210 (25%)	63 (24%)	74 (26%)	73 (26%)
Lesions with angiographic success, n (%)	1241 (97%)	406 (98%)	421 (97%)	414 (96%)

MI=myocardial infarction. CABG=coronary artery bypass grafting. STEMI=ST-elevation myocardial infarction. LAD=left anterior descending. LCX=left circumflex. RCA=right coronary artery. *Clinical presentation. †Treated vessels.

Table 1: Baseline and procedural characteristics

these predictors were included in a multiple logistic regression model and the statistical significance of the respective effect estimates was assessed using the

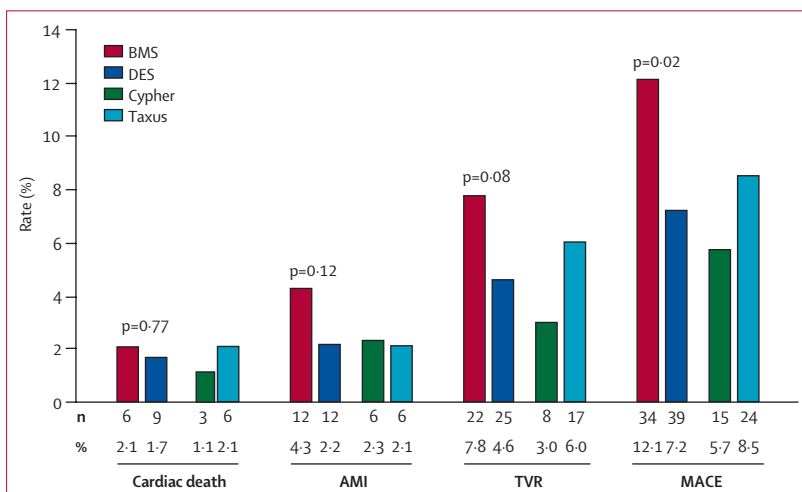


Figure 2: 6-month rates of major adverse cardiac events in DES compared with BMS groups, and in the two subgroups of DES. p values relate to differences between DES and BMS. AMI=acute myocardial infarction. TVR=target lesion revascularisation. MACE=major adverse cardiac events.

likelihood ratio test. Non-parametric bootstrap was used to estimate 95% CI for differences in average costs and for the incremental cost-effectiveness ratios presented (each of these simulations using 50000 bootstrap samples drawn from the original data set),¹⁶ and also to assess the shape of the joint sampling distribution of the differences in average individual costs and effects between the two treatment groups (with 5000 bootstrap samples per simulation). The presentation of cost-effectiveness results as cost-effectiveness ratios with 95% CI is inappropriate, since confidence intervals of costs (ie, the numerator of the cost-effectiveness ratio) and effects (ie, the denominator of the cost-effectiveness ratio) are multiplied, and it is also insufficient, since the interpretation of cost-effectiveness ratios depends on the quadrants of the cost-effectiveness plane into which incremental costs and effects fall.¹⁷ For example, in the assessment of a less efficient, but cheaper new treatment strategy (represented in the lower left quadrant of the cost-effectiveness plane), a numerically high cost-effectiveness ratio would be favourable, whereas in the familiar situation of a more expensive, but more efficient strategy (upper right quadrant), the opposite is true.¹⁷ The remaining quadrants represent situations where the evaluated strategy is more expensive and less effective (dominated; upper left quadrant) or less expensive and more effective (dominant; lower right quadrant). This is taken into account by an additional graphical representation of the bootstrapping results in the cost-effectiveness plane, with 95% and 50% confidence ellipses describing their degree of uncertainty. In our analysis, we calculated the cost-effectiveness ratio by dividing the difference in average net costs between DES and BMS by its net benefit expressed as difference in the proportion of major adverse cardiac events. For calculation of a cost-utility ratio of QALYs, the denominator of this equation was replaced by the difference in QALYs between the two groups. Since quality of life questionnaires could not be obtained at the time of events in most patients, quality of life data at baseline and follow-up were judged as previously described.¹²

Role of the funding source

The funding source of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

Figure 1 shows the trial profile. Follow-up was complete for all but two patients. Baseline characteristics are shown in table 1. Patients were predominantly male. Ages ranged from 26 years to 93 years. Patients had high rates of previous myocardial infarction, previous revascularisation, and risk factors for coronary artery disease. Three fifths of the patients presented with

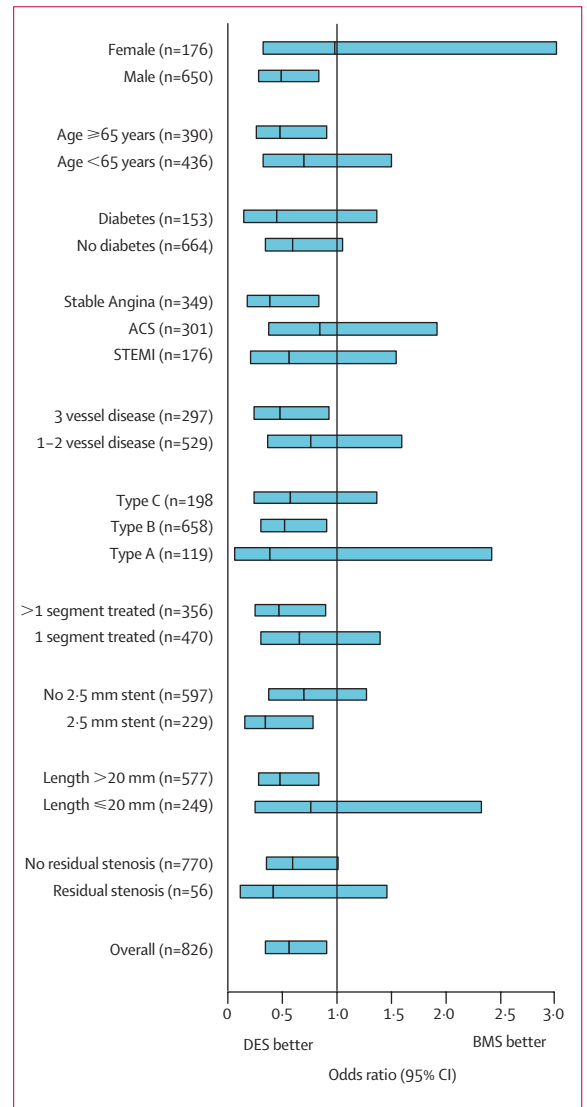


Figure 3: Effectiveness of DES compared with BMS in subgroups
ACS=acute coronary syndrome. STEMI=ST-elevation myocardial infarction.

acute coronary syndromes and more than two thirds had multi-vessel coronary artery disease. On average, patients were treated with nearly two stents with a total stent length of more than 30 mm per patient. Angiographic success was high. Notably, these parameters did not differ between the three stent groups.

During a median hospital stay of 6 days (IQR 2–13) at baseline, six patients died (mortality 0.7%; one non-cardiac death due to aortic aneurysm rupture, cardiac death: two Cypher, two Taxus, one BMS). 12 patients had a myocardial infarction (three Cypher, one Taxus, eight BMS; p=0.03 for comparison of BMS with DES, Fisher’s exact test) and ten needed early target vessel revascularisation (three Cypher, three Taxus, and four BMS). Subacute stent thrombosis occurred in eight patients (1%; three Cypher, three Taxus, and two BMS).

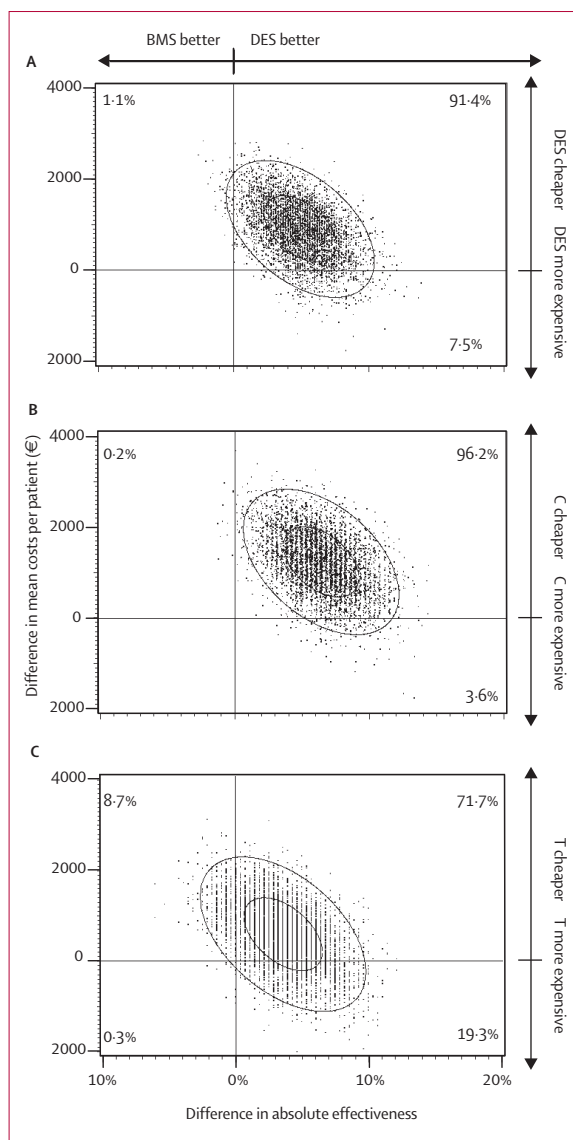


Figure 4: Incremental cost-effectiveness of (A) DES versus BMS, (B) Cypher versus BMS, and (C) Taxus versus BMS

The outer ellipse represents the 95% CI for the true incremental cost-effectiveness of the compared stents. The inner ellipse defines the 50% confidence region. The centre of the ellipse represents the point estimate of incremental effects and costs: for (A) 4.9% major adverse cardiac events prevented with €905 per patient, (B) 6.4% major adverse cardiac events prevented with €1236 per patient, and (C) 3.6% major adverse cardiac events prevented with €593 per patient. Point estimates and corresponding percentages in the upper right quadrant reflect a more effective and more expensive treatment, whereas in the lower right quadrant reflect a more effective but less expensive treatment. Note that the ellipse in (B) is shifted somewhat to the right (more effective) and upwards (more expensive), whereas in (C) it is shifted downwards (less expensive) and to the left (less effective) compared to BMS (differences not significant). C=Cypher. T=Taxus.

Thus, the rate of in-hospital major adverse cardiac events was 2.3% in the Cypher, 1.8% in the Taxus, and 3.6% in the BMS group ($p=0.24$ for comparison of BMS with DES, Fisher's exact test).

	BMS (n=281)	All DES (n=545)	Cypher DES (n=264)	Taxus DES (n=281)
Cost of stents				
Mean (SD)	2259 (1268)	3961 (2254)	4269 (2461)	3617 (2004)
Median (IQR)	2258 (1258)	3871 (2619)*	4284 (2381)	3871 (1935)†
Initial hospital treatment				
Cost, mean (SD)	6194 (7414)	5710 (4811)	5930 (4311)	5505 (5237)
Cost, median (IQR)	5290 (7065)	5532 (6807)	5839 (7065)	4871 (6726)
Mean days in hospital (SD)	7.6 (7.8)	7.3 (7.8)	7.2 (7.7)	7.5 (7.7)
Mean hours in ICU (SD)	37 (61, n=186)	33 (34, n=362)	36 (35, n=183)	30 (32, n=176)
Follow-up				
Cost, mean (SD)	1185 (4487)	873 (4089)	676 (3817)	1058 (4328)
Cost, median (IQR)	0 (0)	0 (0)	0 (0)	0 (0)
Mean days in hospital (SD)	0.9 (4.7, n=21)	0.7 (4.5, n=27)	0.6 (4.5, n=11)	0.7 (4.4, n=16)
Mean hours in ICU (SD)	5 (39, n=12)	3 (20, n=15)	3 (24, n=5)	2 (14, n=10)
Number of angiographies	22	30	10	20
Number of PCI	17	27	9	18
Number of CABG	6	3	1	2
Overall 6-month MACE costs				
Mean (SD)	9639 (9067)	10544 (6849)	10875 (6264)	10233 (7553)
Median (IQR)	7678 (8174)	9187 (7778)*	9810 (7253)	8742 (7855)‡

Number of patients with ICU stay and hospital admission during follow-up are given where applicable. * $p<0.0001$ DES vs BMS (Mann-Whitney U test). † $p<0.0001$ Cypher vs Taxus (Mann-Whitney U test with Bonferroni adjustment). ‡ $p=0.034$ Cypher vs Taxus. ICU=intensive care unit. CABG=coronary artery bypass grafting. MACE=major adverse cardiac event.

Table 2: Costs per patient (€)

Rates of events at 6 months for DES versus BMS are shown in figure 2. Compared with BMS, the use of DES reduced the rate of major adverse cardiac events by 44% (odds ratio [OR] 0.56; 95% CI 0.35–0.91, $p=0.02$) mainly due to a lower rate of target vessel revascularisation (0.57; 0.31–1.02) without significant changes in the rate of cardiac death (0.77; 0.27–2.18), myocardial infarction (0.51; 0.22–1.14) or hospital admissions for acute coronary syndrome (1.16; 0.36–3.81, all Fisher's exact test). There were six additional non-cardiac deaths (three in the BMS, two in the Cypher, and one in the Taxus group). There were no statistically significant differences between the two DES in any of these events. However, the absolute difference between Cypher and BMS was always somewhat larger than that between Taxus and BMS (figure 2). Subgroup analyses showed a uniform trend towards a better outcome with DES, with no significant interactions between subgroups and treatment effect (figure 3). Univariate predictors of major adverse cardiac events were residual stenosis of greater than 50% (OR 3.58, $p=0.0006$), three-vessel disease (2.49, $p=0.0003$), more than one segment treated (2.15, $p=0.003$), age (1.34 per 10 years, $p=0.001$, unpaired t test), total stent length of greater than 20 mm (2.11, $p=0.02$), and use of DES (0.56, $p=0.02$), whereas small stent size (ie 2.5 mm) was of borderline significance (1.61, $p=0.06$; all p values by Fisher's exact test unless otherwise indicated). Independent predictors by multivariate logistic regression analysis were three-vessel disease (OR 2.03, $p=0.006$), residual stenosis greater than 50% (2.38, $p=0.02$), more than one treated segment (1.69, $p=0.05$), and use of DES (0.58, $p=0.03$); importantly, risk reduction of major adverse cardiac events by DES was not affected by patient-related or lesion-related factors.

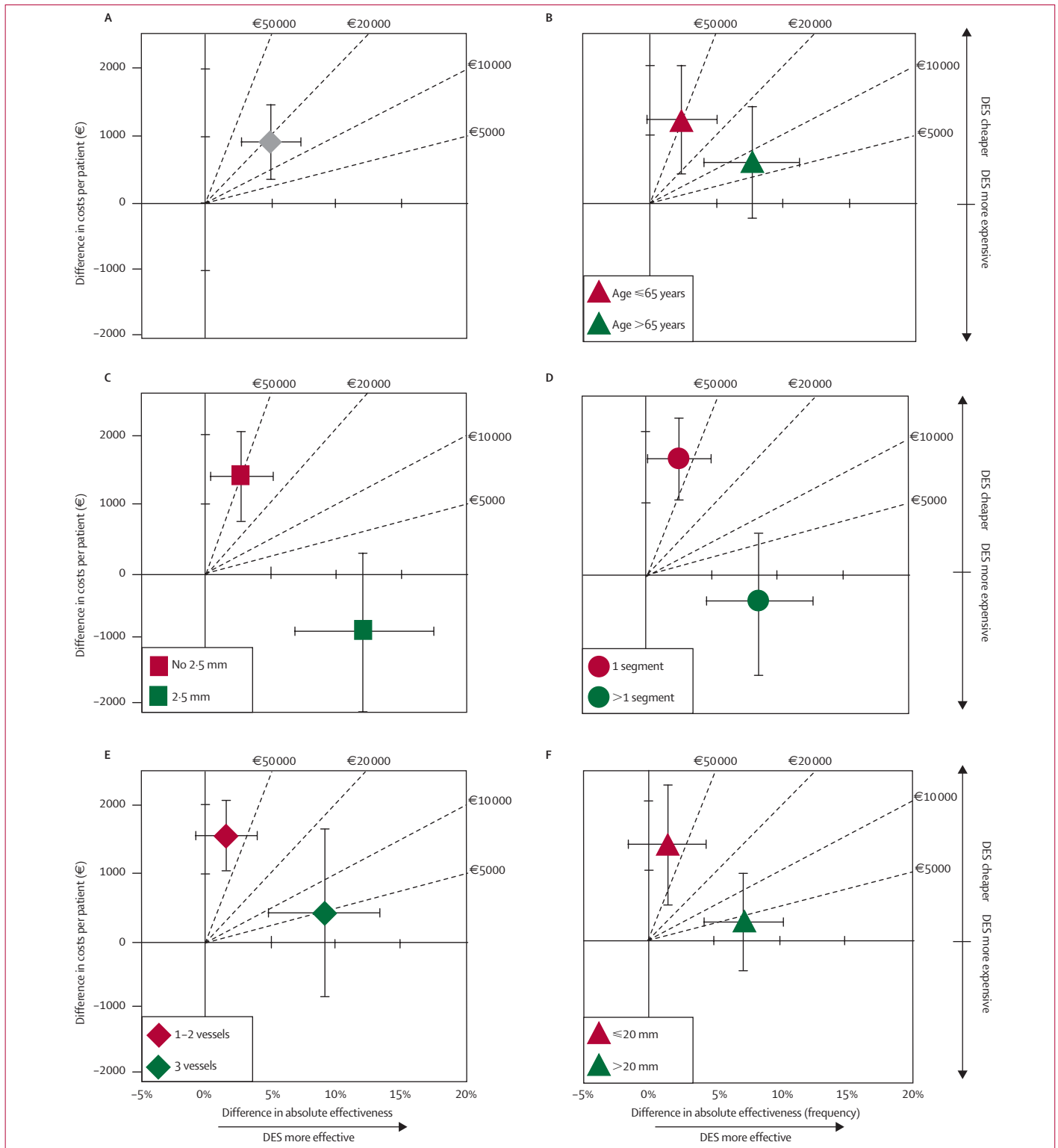


Figure 5: Cost-effectiveness planes presenting differences in effectiveness (frequency) and costs (mean) of DES versus BMS overall and in high-risk and low-risk subgroups
 Bars show SE. Subgroups (red symbols=low-risk, green symbols=high-risk): (B) age, (C) stent size (no 2.5 mm=no stent of 2.5 mm diameter used, 2.5=at least one stent of 2.5 mm diameter used), (D) number of segments treated, (E) number of vessels with significant stenoses, (F) total stent length per patient. Note that high-risk subsets are always more to the right (DES with higher absolute benefit) and downwards (DES costs relatively lower) compared with lower-risk subsets, indicating a more favourable incremental cost-effectiveness ratio compared to BMS. Dotted lines indicate different levels of cost-effectiveness ratios to prevent major adverse cardiac events in one patient.

6-month incremental costs of treatment with DES compared with BMS are summarised in table 2. In DES-treated patients, stent costs were significantly higher than in patients treated with BMS (mean €1702 higher per patient), whereas costs of the initial hospital treatment were similar and follow-up costs were relatively small in all groups (mean €312 lower for DES vs BMS) and did not differ significantly between the groups. Thus, overall 6-month costs were still €905 higher in the DES group than in BMS group. Costs for Cypher were slightly greater than those for Taxus.

Based on these findings, an average incremental cost-effectiveness ratio for DES versus BMS of €18 311 to prevent one major adverse cardiac event per patient was calculated (figure 4). This cost-effectiveness ratio was similar for Cypher versus BMS (€19 264) and for Taxus versus BMS (€16 694). Subgroup analyses of parameters predicting major adverse cardiac events regarding cost-effectiveness ratios are shown in figure 5, indicating that DES might be cost-effective in high-risk patients such as those with three-vessel disease, age older than 65 years, more than one segment treated, small stent sizes, or stent length greater than 20 mm. Mean EQ-5D scores increased similarly in both groups (DES from 0.84 [SD 0.21] to 0.91 [0.17], $p < 0.0001$; BMS from 0.83 [0.22] to 0.89 [0.20], $p = 0.004$) whereas the mean visual analogue scale increased more in the DES group (from 68 [23] to 75 [20], $p < 0.0001$) than in the BMS group (from 68 [21] to 70 [20], $p = 0.21$; all Mann-Whitney *U* test). On the basis of these data, the cost-utility ratio for DES versus BMS for each QALY gained was €73 283 when calculated from the EQ-5D index, and €54 546 when calculated from the visual analogue scale.

Discussion

We compared incremental cost-effectiveness of the two available DES with a third-generation BMS in a prospective, randomised trial based on a real-world setting. The findings of BASKET confirm a 44% overall reduction in the rate of major adverse cardiac events with DES compared with BMS use, without significant differences in effectiveness between the two DES stents. Increased costs of DES were not greatly compensated for by reductions in event-related follow-up costs, leaving higher overall costs of DES compared with BMS treatment. The incremental cost-effectiveness ratio for DES versus BMS was close to €20 000 to avoid one major adverse cardiac event per patient, for both types of DES. Corresponding costs per QALY gained were greater than €50 000. In subgroups of high-risk elderly patients with three-vessel disease, treatment of multiple segments, long treated-segments, or small vessels, use of DES was more cost-effective or even cost-saving. Therefore, the use of DES could be restricted to certain high-risk patient subgroups as defined in this study, at least until the prices of DES are reduced.

A recent hierarchical Bayesian meta-analysis of randomised clinical trials of DES, based on 11 trials with 5103 patients, showed that DES are effective at decreasing rates of major adverse cardiac events from 16.4% (BMS) to 7.8% (DES), mainly by reducing rates of target vessel revascularisation, but not of myocardial infarction or death.⁶ DES seemed to be safe in the short-to-medium term, although definitive conclusions were not possible until larger studies with longer follow-up are available. The RESEARCH registry attempted to compare DES with conventional BMS use in a real-world setting.⁷ The results showed that unrestricted use of sirolimus-eluting stents was safe and effective in reducing both repeat revascularisations and major adverse cardiac events at 1 year. However, the study compared two consecutive patient groups with different baseline characteristics, whereas in BASKET, there were no significant differences between patient groups. Our patient population was similar to that described in RESEARCH with slightly higher risk and a slightly higher 6-month rate of major adverse cardiac events.⁷ This trend towards higher risk might, in part, be due to the growing confidence and ease of treating more complex lesions with DES, as noted also in the TAXUS-Stent Evaluated At Rotterdam Cardiology Hospital (T-SEARCH) registry,¹⁸ and reflects a contemporary patient population seen in a tertiary referral hospital, which is also primary care hospital for the city of Basel. Reduction in events by 44% in BASKET was comparable to the 34% reduction shown in RESEARCH. Importantly, the relative reduction of events was independent of lesion-specific and patient-specific factors. Thus, results from BASKET confirm findings from previous studies in selected patient populations and a real-world registry, but BASKET extends these findings to a contemporary unselected population in a prospective randomised manner.

Recently, two randomised comparisons of the two available DES have been presented. Both had large patient subgroups with follow-up angiography, but results remained conflicting: whereas in one study,¹⁸ clinical and angiographic results favoured sirolimus-coated stents, such differences were not found in the other study.¹⁹ As in our study, consecutive series of patients in the published T-SEARCH registry²⁰ showed no significant differences in 1-year outcome in a real-world setting between sirolimus-coated and paclitaxel-coated DES. However, in each of these comparisons there was a trend in favour of sirolimus-coated stents, as noted in a most recent meta-analysis.²¹ Much more detailed scrutiny will be needed to define whether specific subgroups of patients benefit more from one DES compared with the other.

Recently, four studies²²⁻²⁵ and several commentaries have been published assessing the cost-effectiveness of DES compared with BMS. After adjustment of observed results for consequences of angiographic follow-up, the

authors of the RAndomised study with the sirolimus-eluting Bx VELOCITY stents in the treatment of de novo native coronary artery lesions (RAVEL) analysis calculated a difference in major adverse cardiac event-free survival of 11.1% in favour of DES at an additional 1-year cost of €166.²² Based on the more complex coronary lesions in the SIRoImUS-eluting balloon expandable stent in the treatment of patients with de-novo native coronary artery lesions (SIRIUS) trial, an incremental cost-effectiveness ratio for DES of US\$1650 per repeat revascularisation event avoided or US\$27 540 per QALY gained was calculated, again after adjustment for consequences of angiographic follow-up and imputation for missing quality-of-life data.²³ The authors concluded that although the use of sirolimus-eluting stents was not cost-saving compared to BMS implantation in complex lesions, their use seemed to be reasonably cost-effective within the US health-care system. Canadian investigators pooled the relative reduction of restenosis at 9–12 months from four clinical trials of sirolimus-eluting stents and combined it with measures of resource utilisation and quality of life from the Alberta Provincial Project for Outcome Assessment in Coronary Heart disease (APPROACH) cohort database.²⁴ They calculated a base-case cost-utility ratio of Canadian \$58 721 per QALY gained for DES, and concluded that the use of sirolimus-eluting stents is associated with a cost per QALY that is similar to or higher than that of other accepted medical therapies. They argued that DES might be economically more attractive for patients at higher risk of restenosis or death. Based on a decision-analytic model, US authors calculated a cost-effectiveness ratio of about US\$7000 per repeat revascularisation avoided, assuming a target vessel revascularisation rate of 14% with BMS, an 80% reduction in target vessel revascularisation by DES, an incremental cost of US\$2000 per DES, and a use of 1.3 stents per single vessel procedure.²³ Translated to a UK setting and based on a retrospective analysis of prospectively collected audit data of 2884 patients, however, DES were found not to be cost effective compared with conventional BMS except for 4% of patients at the highest risk.²⁵ Although DES were clearly effective, these authors concluded that general use is not justified unless price premium falls substantially.

Commentaries addressed important limitations of all these analyses,^{8,26–28} particularly the assumptions necessary to correct for angiography-driven revascularisations in studies with angiographic endpoints, the absence of prospectively collected quality-of-life data, and the highly selected patient populations in these studies. All commentaries concluded that relative efficacy and cost-effectiveness of competing stents cannot be defined until data from direct comparisons are available, if possible in unselected real-world settings.

BASKET adds important new data, since we attempted to assess incremental cost-effectiveness and cost-utility of

DES compared with BMS in a prospective randomised study in a real-world setting. The cost difference between DES and third-generation BMS was smaller than previously described, an average of 1.9 stents was used per patient and the rate of target vessel revascularisation with BMS was only 12%, resulting in a less favourable overall cost-effectiveness ratio for DES use in unselected patients. This result, and the finding that DES use seems to be more cost-effective or even cost-saving in high-risk patients, substantiate assumptions based on studies with sirolimus-eluting stents and the APPROACH registry.²⁴

Limitations to such an analysis lie in the difficulty of considering all cost-relevant factors, particularly non-medical costs. We used list prices for stents in our calculations, but actual market prices may be considerably lower and vary substantially; this may be especially true for BMS, even though third-generation BMS are more expensive than stainless-steel stents. Nevertheless, the data provided in this study can be applied to local situations by replacing presented values with local stent costs. In addition, the bootstrap replications depicted in figure 4 reflect the variability of costs and effects. The relatively long baseline hospital stays in this study reflect local practice for patients with acute myocardial infarction and unstable angina, as well as 2–3-day stays for diagnostic testing and PCI in stable situations. Also, we did not consider the implications for clinical practice of increased costs of DES strategy due to treatment of patients at higher risk with more and longer stents, increased use of glycoprotein IIb/IIIa inhibitors, and changes in length of hospital stay. Neither did we assess cost savings due to reduced rates of bypass surgery (–22% during the BASKET experience at the University Hospital of Basel). Extension of interventional treatment to high risk and multivessel situations where DES are particularly cost-effective, obviating the need for bypass surgery with prolonged hospitalisation and rehabilitation stays, will be welcomed by the patients, who will favour interventional cardiologists, hospitals, and reimbursement systems that will be able to offer them such a device.

At the time of BASKET the new cobalt-chromium-based stents were not available in the sizes of 2.5 mm. Despite that, rates of major adverse cardiac events were relatively low for the BMS used in BASKET. Finally, the follow-up period of this report was limited to 6 months—the time when most target vessel revascularisations are expected. The increased revascularisation rate observed at months 7 and 8 in some studies was probably due to protocol-driven angiographic controls, which were not allowed in BASKET. This fact was acknowledged in recent cost-effectiveness analyses of DES.^{20,22–24} To avoid these problems but still capture a possible further delay of the restenotic process by DES beyond even 12 months, the primary endpoint was set at 6 months with a secondary evaluation after 18 months, which is still ongoing.

Contributors

All authors participated in the conception and conduct of the study and contributed to the final manuscript. M Pfisterer, as principal investigator, had the original idea for the study and, together with C Kaiser, was responsible for general trial coordination, did PCIs, and wrote the manuscript. P Bonetti, A Linka, A Bernheim, M Zellweger, and A Zutter did most of the enrolment and follow-up of the patients. H P Brunner-La Rocca was responsible for the statistical analysis and took substantial part in writing the manuscript. P Buser and S Osswald brought in cardiological experience, did PCIs, took part in the interpretation of the data, and helped to finalise the manuscript. L Grize helped with the statistical analysis and interpretation of the results and critically reviewed the final manuscript.

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Conflict of interest statement

We declare that we have no conflict of interest.

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