

# Impact of Drug-Eluting Stents Among Insulin-Treated Diabetic Patients

## A Report From the National Heart, Lung, and Blood Institute Dynamic Registry

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**Objectives** This study sought to evaluate the safety and efficacy of drug-eluting stents (DES) compared with bare-metal stents (BMS) in patients with insulin- and noninsulin-treated diabetes.

**Background** Diabetes is a powerful predictor of adverse events after percutaneous coronary interventions (PCI), and insulin-treated diabetic patients have worse outcomes. The DES are efficacious among patients with diabetes; however, their safety and efficacy, compared with BMS, among insulin-treated versus noninsulin-treated diabetic patients is not well established.

**Methods** Using the National Heart, Lung, and Blood Institute Dynamic Registry, we evaluated 1-year outcomes of insulin-treated (n = 817) and noninsulin-treated (n = 1,749) patients with diabetes who underwent PCI with DES versus BMS.

**Results** The use of DES, compared with BMS, was associated with a lower risk for repeat revascularization for both noninsulin-treated patients (adjusted hazard ratio [HR] = 0.59, 95% confidence interval [CI] 0.45 to 0.76) and insulin-treated subjects (adjusted HR = 0.63, 95% CI 0.44 to 0.90). With respect to safety in the overall diabetic population, DES use was associated with a reduction of death or myocardial infarction (adjusted HR = 0.75, 95% CI 0.58 to 0.96). However, this benefit was confined to the population of noninsulin-treated patients (adjusted HR = 0.57, 95% CI 0.41 to 0.81). Among insulin-treated patients, there was no difference in death or myocardial infarction risk between DES- and BMS-treated patients (adjusted HR = 0.95, 95% CI 0.65 to 1.39).

**Conclusions** Drug-eluting stents are associated with lower risk for repeat revascularization compared with BMS in treating coronary artery disease among patients with either insulin- or noninsulin-treated diabetes. In addition, DES use is not associated with any significant increased safety risk compared with BMS. These findings suggest that DES should be the preferred strategy for diabetic patients. (J Am Coll Cardiol Intv 2008;1:139–47) © 2008 by the American College of Cardiology Foundation

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Diabetes mellitus is a risk factor for cardiovascular disease (1). Although intracoronary stenting is routinely used to treat coronary disease, clinical and angiographic outcomes for diabetic patients compared with nondiabetic individuals are worse. Diabetes remains a strong predictor of adverse prognoses in patients undergoing percutaneous coronary intervention (PCI) (2,3). The clinical efficacy of drug-eluting stents (DES), by reducing the need for repeat revascularization, has resulted in their widespread use (4,5).

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Within the diabetic population, the use of insulin therapy is associated with a worse cardiovascular prognosis than found in those patients treated with oral hypoglycemic drugs or diet (6-9). Restenosis rates and mortality after PCI are higher among insulin-treated patients than among noninsulin-treated diabetic patients (9,10). Although DES are effective for the prevention of restenosis, their efficacy among insulin-treated patients has not been fully elucidated

(11,12). Moreover, despite their short-term efficacy, several recent reports suggest that DES are associated with late stent thrombosis, and diabetes mellitus is itself a risk factor for this (13-15). However, the safety of DES, in relation to bare-metal stents (BMS), among insulin-treated diabetic patients has not been reported.

Therefore, we investigated the safety and efficacy of DES compared with BMS among diabet-

ics according to whether or not insulin treatment was part of their therapy. We used the National Heart, Lung, and Blood Institute (NHLBI) Dynamic Registry to evaluate 1-year outcomes of insulin- and noninsulin-treated patients with diabetes who underwent percutaneous coronary intervention with DES versus those who received BMS.

## Methods

**NHLBI Registry design.** The Registry, coordinated at the University of Pittsburgh, includes 23 sites across North America that enrolled consecutive patients undergoing PCI at several periods of time or waves. Recruitment of 10,962 patients into the 5 waves occurred as follows: Wave 1 (July 1997 to February 1998,  $n = 2,524$ ), Wave 2 (February 1999 to June 1999,  $n = 2,105$ ), Wave 3 (October 2001 to March 2002,  $n = 2,047$ ), Wave 4 (February 2004 to May 2004,  $n = 2,112$ ), and Wave 5 (February 2006 to August 2006,  $n = 2,174$ ). The sirolimus-eluting stent was approved by the U.S. Food

and Drug Administration (FDA) in March 2003 and was available at all Registry sites by the time Wave 4 began. The paclitaxel-eluting stent was approved by the FDA in April 2004 and was available at all sites at that time.

Methods of data collection, quality assurance, and definition of terms have been previously described (16,17). Data collected included baseline demographic, clinical, angiographic, and procedural characteristics, during the index PCI, as well as the incidence of death, myocardial infarction (MI), and the need for coronary artery bypass graft (CABG) surgery during hospitalization. In-hospital and 12-month follow-up data were collected by research coordinators using standardized report forms, guided by a manual of operations. Medical records were reviewed for patients requiring repeat hospitalization. Follow-up coronary angiography was obtained only if clinically indicated.

**Study population.** The analyses evaluate the course of all diabetics within Waves 1 to 5 who underwent PCI, categorized by the type of stents received (BMS versus DES) and by diabetes treatment (insulin- vs. noninsulin-treated). To minimize selection bias, for those patients enrolled during Waves 4 and 5 (i.e., when both DES and BMS were available), only diabetic patients who received a DES were included in the analysis, whereas Wave 4 and 5 patients treated with BMS were excluded ( $n = 297$ ). Analyses of the Wave 4 and 5 patients who received a BMS suggest that these subjects were of higher clinical risk than the BMS-treated patients from earlier waves and were thus not included in these analyses. Use of DES across U.S. sites was relatively uniform. The Dynamic Registry identified study patients with diabetes according to the use of oral hypoglycemic agents, diet, or treatment with insulin. Patients on both insulin and oral therapy were categorized into the insulin-treated group. Seventy-two patients who received a combination of DES and BMS were included in the DES group. Analyses were performed both by including and excluding such patients. Angiograms were analyzed by visual estimates of lesion stenosis, lesion length, and diameter stenosis.

**Clinical outcomes.** Patients were followed up prospectively for 12 months to ascertain death, MI, CABG surgery, repeat PCI, and repeat revascularization (PCI/CABG). The primary outcomes were analyzed as time to event, with the follow-up time measured in days from study entry (index PCI) to the date of the first event among death, MI, CABG, or repeat PCI. Those who were event-free were censored 12 months after study entry. Stent thrombosis was not tracked during Waves 1 to 3 and thus was not specifically included in this analysis.

**Statistical analysis.** Patient characteristics pertaining to the index PCI, including demographics, medical history, cardiac presentation, periprocedural medications, procedural characteristics, and outcomes, were compared by Student  $t$  tests and chi-square tests (asymptotic or Fisher

### Abbreviations and Acronyms

**BMS** = bare metal stent(s)

**CABG** = coronary artery bypass graft

**CI** = confidence interval

**DES** = drug-eluting stent(s)

**HR** = hazard ratio

**MI** = myocardial infarction

**PCI** = percutaneous coronary intervention

exact test) for categorical variables for comparisons by diabetes treatment and by stent received. One-year cumulative incidence rates of clinical outcomes (e.g., death, MI, repeat PCI, and CABG) and composite outcomes (e.g., repeat PCI/CABG, death/MI) were estimated by the Kaplan-Meier method and tested by the log-rank statistic. Multivariable Cox proportional hazards regression was used with cardiac events as the outcome with BMS as the referent category. Fully adjusted 1-year outcome models were fit that included demographic characteristics, clinical variables, and procedural and lesion characteristics as explanatory variables for adjustment. Covariates were selected by forward stepwise methods and those considered to be biologically relevant.

## Results

**Baseline patient characteristics.** A total of 9,170 (84%) patients received stents, and the 1-year rate of follow-up was 96%. Among those receiving stents, 817 (8.9%) were insulin-treated diabetic patients, and 1,749 (19.1%) were noninsulin-treated diabetic patients. Within the insulin-treated group, 373 (45.7%) were patients treated with DES and 444 (54.3%) were patients treated with BMS, whereas the noninsulin-treated group consisted of 779 (44.5%) patients treated with DES and 970 (55.5%) patients treated with BMS. Table 1 lists the baseline characteristics. There was no significant difference in age, but the insulin-treated patients were more likely to be female, to be nonwhite, and

**Table 1. Baseline Clinical Characteristics and Risk Factors by Diabetes Treatment**

	Insulin-Treated			Noninsulin-Treated			p Value Insulin-Treated Versus Noninsulin-Treated
	BMS (n = 444)	DES (n = 373)	p Value BMS Versus DES	BMS (n = 970)	DES (n = 779)	p Value BMS Versus DES	
Mean age, yrs	63.9	63.0	0.39	64.4	64.0	0.39	0.15
Female, %	53.4	45.3	0.02	41.6	35.4	0.008	<0.001
Race, %			0.03			0.002	<0.001
White	71.3	62.5		71.5	69.4		
Black	17.6	26.1		12.5	16.7		
Hispanic	7.9	6.7		8.8	10.2		
Asian	2.9	4.0		6.6	3.6		
Other	0.2	0.5		0.6	0.1		
Mean body mass index (kg/m <sup>2</sup> )	31.0	32.2	0.01	30.3	31.4	<0.001	0.06
Prior PCI, %			0.008			<0.001	0.006
None	65.5	58.4		70.1	60.1		
1	21.2	20.1		20.1	24.5		
>1	13.3	21.4		9.8	15.5		
Prior CABG			0.59			0.56	<0.001
None	72.3	69.2		82.4	81.6		
1	25.0	28.2		15.1	16.5		
>1	2.7	2.7		2.5	1.9		
Prior myocardial infarction	38.9	31.2	0.02	33.4	27.3	0.006	0.02
Concomitant diseases, %							
Severe noncardiac comorbidity	52.6	59.1	0.06	39.6	40.1	0.83	<0.001
Cerebrovascular	10.4	11.7	0.56	8.8	7.8	0.43	0.03
Renal	16.3	29.0	<0.001	6.8	11.0	0.002	<0.001
Peripheral vascular disease	18.5	13.6	0.06	8.8	9.8	0.46	<0.001
Pulmonary	13.3	10.0	0.15	9.0	8.5	0.73	0.02
Cancer	7.2	9.2	0.30	6.8	7.6	0.52	0.40
Other	17.2	21.1	0.15	12.6	13.2	0.73	<0.001
Congestive heart failure, %	23.9	20.9	0.32	16.1	12.0	0.02	<0.001
Hypertension, %	80.8	88.8	0.002	77.4	88.7	<0.001	0.21
Hypercholesterolemia, %	73.8	85.1	0.001	68.4	86.2	<0.001	0.16
Smoking, %			0.76			0.66	0.09
Never	39.7	42.2		37.3	35.2		
Current	17.0	16.8		18.8	19.9		
Former	43.4	41.0		43.9	44.9		

BMS = bare-metal stent; CABG = coronary artery bypass graft; PCI = percutaneous coronary intervention; DES = drug-eluting stent.

to present with more cardiovascular comorbidities, including prior revascularization, cerebrovascular disease, renal insufficiency, peripheral vascular disease, and congestive heart failure. Those receiving DES, compared with BMS, were more likely to have hypertension, hypercholesterolemia, and concomitant renal insufficiency, but were less likely to have a history of congestive heart failure. As shown in Table 2, the insulin-treated patients had a greater extent of atherosclerotic burden. In comparing DES versus BMS, there were no important differences in angiographic characteristics, except that the DES groups had longer lesion lengths.

**Procedural and lesion characteristics.** Table 3 illustrates the procedural and lesion characteristics. The lesions intervened on in the insulin-treated patients were more likely to be complex and calcified. Among the entire cohort, patients receiving BMS were more likely to have unstable angina and angiographic evidence of thrombus within treated lesions compared with those who received DES, who were more likely to be present with stable symptoms. However, there were no significant differences observed relating to setting of the procedure (i.e., elective, urgent, or emergent). There was greater use of glycoprotein IIb/IIIa inhibitors in the noninsulin-treated

group treated with BMS. Mean stented length was longer among the DES-treated patients by 3.5 mm.

**Clinical outcomes.** There were no significant differences in 30-day outcomes of death, MI, or repeat revascularization by diabetes regimen or use of DES versus BMS (data not shown). Table 4 shows the 1-year event rates in each of the 4 groups. The risk of repeat revascularization among the entire diabetic cohort was significantly lower with DES compared with BMS (13.7% vs. 21%,  $p < 0.001$ ). Among all DES-treated diabetic patients, there were no significant differences (data not shown) in 1-year death, MI, or repeat revascularization when comparing sirolimus-eluting stents ( $n = 752$ ) versus paclitaxel-eluting stents ( $n = 364$ ). As seen in Table 4 and in Figure 1, there were significant differences in revascularization outcomes between the insulin- and noninsulin-treated diabetic patients. Compared with BMS, the use of DES was associated with significantly lower rates of 1-year need for repeat PCI among noninsulin-treated patients (11.2% vs. 15.6%,  $p = 0.008$ ), but not among the insulin-treated diabetic patients (14.1% vs. 18.1%,  $p = 0.17$ ). The 1-year cumulative rate of repeat revascularization was statistically significantly lower in the DES-treated patients among the noninsulin-treated diabetic group

**Table 2. Angiographic Characteristics by Diabetes Treatment**

	Insulin-Treated			Noninsulin-Treated			
	BMS (n = 444)	DES (n = 373)	p Value BMS Versus DES	BMS (n = 970)	DES (n = 779)	p Value BMS Versus DES	p Value Insulin-Treated Versus Noninsulin-Treated
Mean left ventricular function, %	48.7	50.0	0.14	51.7	52.0	0.62	0.01
Abnormal left ventricular function, %	41.1	36.7	0.28	34.3	30.3	0.12	0.005
Coronary artery lesion location, %							
Left anterior descending only	15.4	14.5	0.74	18.9	15.1	0.04	0.17
Left circumflex only	5.6	7.5	0.28	6.9	7.9	0.40	0.45
Right coronary only	10.7	6.7	0.05	11.6	8.2	0.02	0.34
Left anterior descending, left circumflex, and right coronary	36.9	40.5	0.30	29.7	35.4	0.01	0.002
Number of vessels diseased, %			0.75			0.03	0.03
Single-vessel	29.3	26.5		35.5	29.3		
Double-vessel	32.1	31.4		32.5	33.2		
Three-vessel	38.1	41.6		31.8	37.0		
Percent with stenoses >50% in diameter							
Left main coronary artery	7.7	7.5	0.94	5.3	6.3	0.36	0.07
Left anterior descending artery	74.8	77.7	0.32	73.9	76.1	0.29	0.50
Left circumflex artery	60.6	65.1	0.18	54.9	62.4	0.002	0.03
Right coronary artery	70.7	69.4	0.69	64.4	66.0	0.50	0.01
Bypass graft	19.8	22.0	0.45	13.2	11.6	0.30	<0.001
Any total occlusions	46.2	45.6	0.87	37.9	37.4	0.80	<0.001
Mean number of significant lesions	3.5	3.8	0.13	3.2	3.3	0.04	<0.001
Amenable to complete revascularization by PCI, %	71.6	83.3	<0.001	78.8	89.6	<0.001	<0.001
Amenable to complete revascularization by CABG, %	75.9	72.6	0.29	81.8	77.3	0.02	0.003

Abbreviations as in Table 1.

**Table 3. Procedural and Lesion Characteristics by Diabetes Treatment and Type of Stent Received**

Procedural	Insulin-Treated			Noninsulin-Treated			p Value Insulin-Treated Versus Noninsulin-Treated
	BMS (n = 444)	DES (n = 373)	p Value BMS Versus DES	BMS (n = 970)	DES (n = 779)	p Value BMS Versus DES	
Reason for revascularization, %							
Asymptomatic coronary artery disease	6.1	12.9	<0.001	5.9	14.1	<0.001	0.76
Stable angina	20.0	17.4	0.34	19.8	22.1	0.24	0.25
Unstable angina	47.1	38.9	0.02	45.8	35.7	<0.001	0.33
Acute myocardial infarction	23.0	22.8	0.95	23.5	23.4	0.96	0.75
Cardiogenic shock	2.9	0.5	0.01	2.6	0.4	0.0003	0.67
Circumstances of procedure, %			0.84			0.18	0.23
Elective	60.8	59.8		57.0	61.1		
Urgent	32.0	31.9		32.4	30.2		
Emergent	7.2	8.3		10.6	8.7		
Glycoprotein IIb/IIIa inhibitor use, %	35.6	34.3	0.70	39.9	33.2	0.004	0.34
Lesions	BMS (n = 656)	DES (n = 527)	p Value BMS Versus DES	BMS (n = 1,458)	DES (n = 1,117)	p Value BMS Versus DES	p Value Insulin-Treated Versus Noninsulin-Treated
ACC/AHA lesion classification, %			0.17			<0.001	0.002
A	13.1	11.5		12.9	9.5		
B1	29.2	27.7		34.2	34.0		
B2	34.2	31.5		34.4	30.8		
C	23.5	29.2		18.5	25.7		
Reference vessel size, mm	3.0	3.0	0.92	3.0	3.0	0.11	0.18
Mean lesion length, mm	12.9	17.5	<0.001	13.2	16.9	<0.001	0.43
Mean diameter stenosis, %	83.1	82.7	0.02	82.8	83.3	0.21	0.63
Evidence of thrombus, %	15.2	12.0	0.12	16.0	10.0	<0.001	0.76
Ulcerated, %	13.0	12.8	0.91	12.1	12.0	0.93	0.45
Bifurcation, %	10.4	8.0	0.17	11.2	9.4	0.15	0.31
Calcified, %	29.2	32.9	0.17	25.1	30.2	0.005	0.03
DES type							
Sirolimus		62.0	N/A		61.2	N/A	0.97
Paclitaxel		31.3	N/A		31.7	N/A	0.57

ACC/AHA = American College of Cardiology/American Heart Association; N/A = not applicable; other abbreviations as in Table 1.

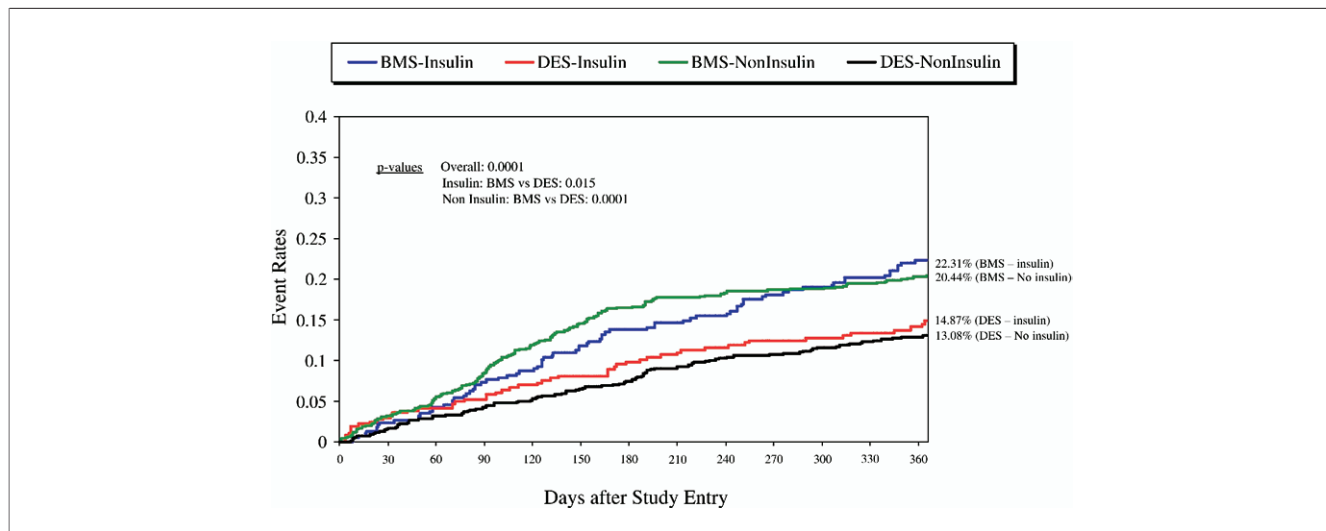
(13.1% vs. 20.4%,  $p < 0.001$ ) as well as the insulin-treated group (14.9% vs. 22.3%,  $p = 0.02$ ). There were no significant changes in these findings when the patients who

received a combination of both DES and BMS were excluded from the analysis. Furthermore, no differences were observed between paclitaxel-eluting stents and

**Table 4. Cumulative Event Rates for 1-Year Follow-Up by Diabetes Treatment and Type of Stent Received**

	All Diabetes Patients			Insulin-Treated			Noninsulin-Treated		
	BMS (n = 1,414)	DES (n = 1,152)	p Value	BMS (n = 444)	DES (n = 373)	p Value	BMS (n = 970)	DES (n = 779)	p Value
Death	8.5	5.4	0.003	9.8	8.4	0.52	7.8	3.9	<0.001
Myocardial infarction	6.6	5.9	0.52	7.8	10	0.29	6	4	0.07
Coronary artery bypass graft	6.5	2.1	<0.001	5.1	1.8	0.02	7.2	2.3	<0.001
Repeat PCI	16.4	12.1	0.003	18.1	14.1	0.17	15.6	11.2	0.008
Death/myocardial infarction	13.8	10.3	<0.001	16	15.8	0.99	12.7	7.6	<0.001
CABG/repeat PCI	21	13.7	<0.001	22.3	14.9	0.02	20.4	13.1	<0.001
Death/MI/repeat PCI/CABG	29.8	20.1	<0.001	32.3	24.5	0.03	28.6	18.5	<0.001

Abbreviations as in Table 1.



**Figure 1. Repeat Revascularization Event Rates**

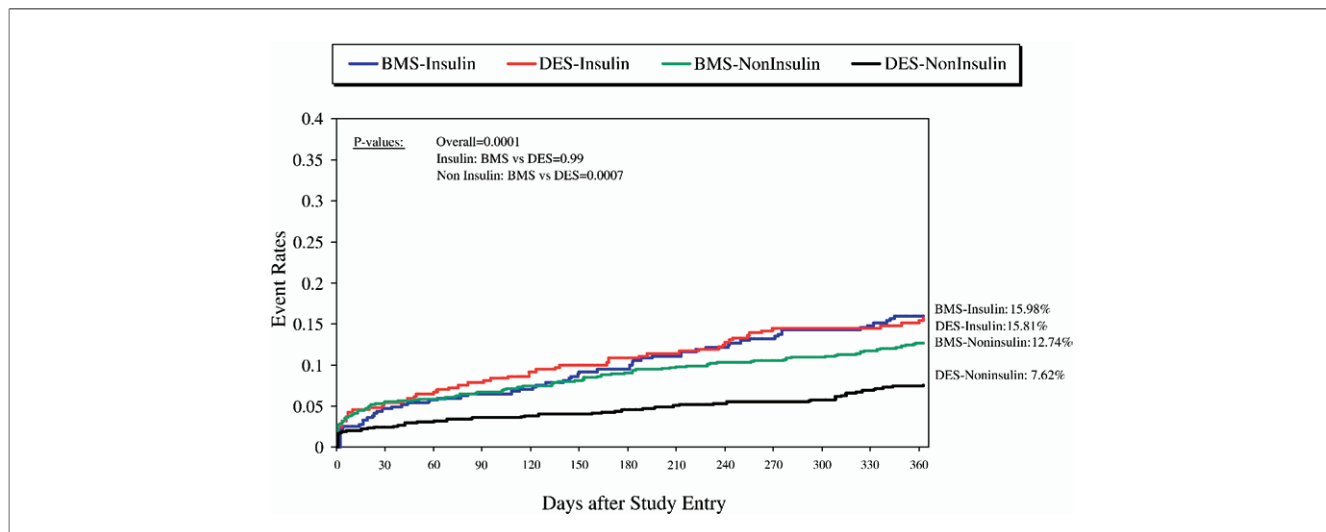
Kaplan-Meier 1-year curves of the incidence of the composite endpoint of post-discharge repeat percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG) by diabetes treatment regimen and use of drug-eluting stent (DES) versus bare-metal stent (BMS).

sirolimus-eluting stents within either the insulin- or noninsulin-treated populations.

Overall, as seen in Table 4, among the entire diabetic population studied, the hazard ratio (HR) of death and MI at 1 year was significantly lower among the DES-treated patients compared with the BMS-treated patients (10.3% vs. 13.8%,  $p < 0.001$ ). However, as seen in Figure 2, this benefit was only observed in the population of noninsulin-treated patients (7.6% vs. 12.7%,  $p < 0.001$ ), whereas among insulin-treated patients, there was no difference in death or MI risk between DES- and BMS-treated patients

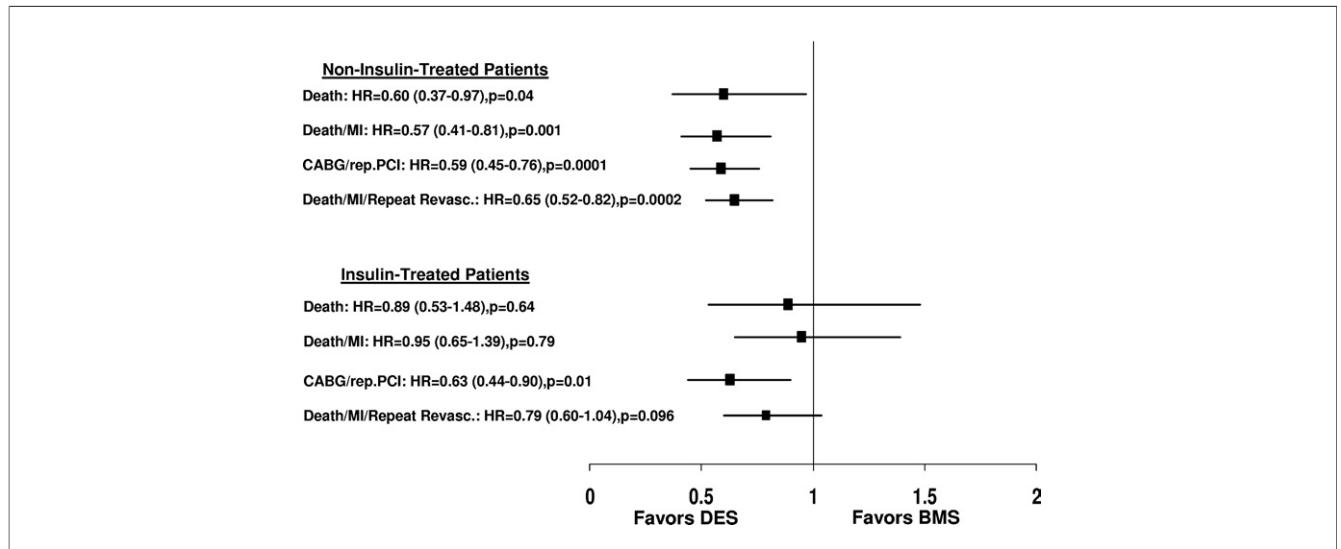
(15.8% vs. 16%,  $p = 0.99$ ). In evaluating the entire diabetic cohort, there was a reduction in the combined outcome of death, MI, and repeat revascularization with DES compared with BMS (20.1% vs. 29.8%,  $p < 0.001$ ). This benefit was appreciated in both the insulin- and noninsulin-treated subjects (Table 4).

Figure 3 shows adjusted relative risks for adverse outcomes for the 4 groups, with variables adjusted for detailed in the figure legend. Overall, the use of DES was efficacious and safe in both the insulin- and noninsulin-treated groups. In noninsulin-treated patients, the use of



**Figure 2. Death or Myocardial Infarction Event Rates**

Kaplan-Meier 1-year curves of the incidence of the composite end point of death or myocardial infarction (MI) by diabetes treatment regimen and use of DES versus BMS. Abbreviations as in Figure 1.



**Figure 3. Relative Benefit of DES Over BMS for Safety and Efficacy**

Adjusted hazard ratios (solid squares) and 95% confidence intervals (horizontal lines) for safety and efficacy outcomes at 1-year comparing DES-treated versus BMS-treated (referent category) patients, stratified by diabetes treatment regimen. Variables adjusted for included age, vessel disease, history of congestive heart failure, hypertension, prior coronary intervention, peripheral vascular disease, history of hypercholesterolemia, number of significant lesions, renal disease, presence of total occlusion, tortuous lesion, unstable angina, acute myocardial infarction, cardiogenic shock, emergency procedure, urgent procedure, attempted an ostial lesion, attempted a class C lesion, attempted lesion receiving collaterals, attempted thrombus, and discharge medication (i.e., presence of at least 2 of the following: beta-blockers, calcium blocker, long-acting nitrates, angiotensin-converting enzyme inhibitors, statins, clopidogrel/ticlopidine). Abbreviations as in Figure 1.

DES was associated with an estimated 35% lower risk of repeat PCI (adjusted HR = 0.65, 95% confidence interval [CI] 0.49 to 0.87,  $p = 0.003$ ), 41% lower risk of repeat revascularization (adjusted HR = 0.59, 95% CI 0.45 to 0.76,  $p = 0.0001$ ), and 43% lower risk of death or MI (adjusted HR = 0.57, 95% CI 0.41 to 0.81,  $p = 0.001$ ). Among insulin-treated patients, the adjusted relative risk estimates related to use of DES for repeat PCI among the insulin-treated group showed a trend toward significance with a 24% lower risk for repeat PCI (adjusted HR = 0.76, 95% CI 0.52 to 1.11,  $p = 0.15$ ) and a 37% lower risk for repeat revascularization (adjusted HR = 0.63, 95% CI 0.44 to 0.90,  $p = 0.01$ ). There was virtually no difference in the adjusted risk of death or MI with DES use (adjusted HR = 0.95, 95% CI 0.65 to 1.39,  $p = 0.79$ ). With respect to the combined outcome of death, MI, and repeat revascularization, after adjustment, DES use was associated with a significant decrease in event rates in the noninsulin-treated group (adjusted HR 0.65, 95% CI 0.52 to 0.82,  $p < 0.001$ ) but not in the insulin-treated group (adjusted HR 0.79, 95% CI 0.60 to 1.04,  $p = 0.1$ ). Tests for interactions between stent type and treatment (insulin- vs. noninsulin-treated) showed no significant effect.

## Discussion

This study is among the first to focus exclusively on the safety and efficacy of DES among patients with diabetes

mellitus stratified by insulin therapy. The primary finding is the beneficial effect of DES in reducing the need for repeat revascularization in both insulin- and noninsulin-treated diabetic patients as compared with BMS. Several studies have documented the benefit of DES over BMS among noninsulin-treated diabetic patients (5). Our results confirm these observations and extend this benefit to insulin-treated patients as well, without evidence of increased hazard. This benefit in the insulin-treated population is particularly noteworthy given the baseline differences between the groups. Compared with the BMS-treated patients, those who received DES had higher rates of hypertension, hypercholesterolemia, and renal insufficiency, and had longer lesion lengths. Despite the fact that these characteristics portend worse outcomes, DES was still found to be beneficial over BMS.

The rates of repeat revascularization observed in our study are consistent with findings from prior studies. In the first ARTS I (Arterial Revascularization Therapy Study), the 1-year rate of repeat revascularization for BMS in the diabetic patient subgroup was 22.3%, which is similar to our findings with rates of 20.4% and 22.3% among noninsulin- and insulin-treated patients, respectively (18). Similarly, in the ARTS II trial, 12.6% of DES-treated diabetic patients required repeat revascularization by 1 year (18). In our study, the DES-treated groups had repeat revascularization rates of 13.1% and 14.9% among noninsulin- and insulin-treated patients, respectively.

Our results support those from the DIABETES (Diabetes and Sirolimus-Eluting Stent) study, in which the beneficial impact of DES over BMS in reducing repeat PCI was compatible in both insulin- and noninsulin-treated diabetic patients (5). However, in the SIRIUS (Sirolimus-Eluting Stent in De Novo Coronary Lesions) study, those who were on insulin therapy did not have a significant benefit of DES against target lesion revascularization (19), but our study had greater numbers of patients. In a trial comparing sirolimus-eluting versus paclitaxel-eluting stents, the 2 stents had similar outcomes in all diabetic patients; however, among insulin-treated patients, paclitaxel-eluting stents were associated with lower adverse event rates (20,21). We found no differences between the 2 DES stents currently approved by the FDA.

Recently, there has been a focus on the safety of DES for off-label indications. The FDA has noted that at least 60% of DES use is off-label for indications including in-stent restenosis, long lesions, CABG, and the use of overlapping and multiple stents in a single vessel (22). Our group has also confirmed the widespread use of DES for off-label indications (23). These characteristics are frequently seen among diabetes patients; therefore, there is interest in the safety profile of DES in this group. Moreover, the safety of DES has recently come into question with studies suggesting that sirolimus-eluting stents are associated with increased mortality in the diabetic population (24).

We showed no short-term (1-year) adverse safety issue as it pertains to the outcome of death or MI among insulin-treated diabetic patients treated with DES compared with BMS. After statistical adjustment, there was no difference in mortality among insulin-treated patients regardless of the stent used. However, it is notable that although an overall reduction in death or MI was seen in the DES-treated diabetic patients (compared with the BMS-treated diabetic subjects), this was limited only to the noninsulin-treated subjects. This finding may represent a real phenomenon in that there are several reports of restenosis resulting in increased mortality, especially among diabetic patients (25). Therefore, it is plausible that DES, by prevention of restenosis, may be associated with lower rates of death or MI. Still, our results should be cautiously interpreted because it seems unlikely that there is an interaction between DES, noninsulin treatment, and mortality. There were important baseline differences between the BMS- and DES-treated groups within this population. The BMS-treated patients were more likely to present with unstable angina and with angiographic evidence for thrombus, both characteristics that may predispose them to worse clinical outcomes, especially in the presence of diabetes mellitus (26). Furthermore, despite our efforts to statistically adjust for several different variables, it is still possible that there are confounding variables that are unaccounted for and that can partially explain some of these findings.

The higher rate of mortality among the insulin-treated patients is consistent with other studies showing a higher mortality risk among insulin-requiring patients (27,28). Overall, however, the safety of DES versus BMS in the high-risk diabetic population is consistent with a recent meta-analysis that showed a similar safety profile of DES in these patients (29). The safety of DES in insulin-treated patients is an important finding given several recent reports from other registries suggesting that diabetes, particularly insulin-treated diabetes, is an independent predictor of stent thrombosis (30,31). Although we did not specifically track stent thrombosis in our study, the lack of significant differences in mortality and MI between the DES-treated and BMS-treated patients suggests that the 1-year safety profile is favorable.

**Study limitations.** The Dynamic Registry is not a randomized trial. The number of insulin-treated patients treated with DES was relatively modest; nonetheless, we were able to identify significant differences. There may be residual confounding not fully accounted for in the multivariable analyses; however, the large cohort of patients and the relative similarity in baseline variables between the DES and the BMS groups argue in favor of the validity of the results. Another limitation is that we may not be able to account for the precise effect of changing patterns in pharmacologic therapy of atherosclerosis and diabetes. We could not account for the duration or degree of control of diabetes. Despite this, our results regarding rates of repeat revascularization among insulin-treated and noninsulin-treated patients mimic those from other studies.

## Conclusions

Our results show the efficacy of DES over BMS in reducing the need for repeat revascularization in insulin-treated as well as noninsulin-treated diabetic patients. In addition, DES use is not associated with any significant increased safety risk compared with BMS. These findings suggest that DES should be the preferred strategy for patients with diabetes.

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