# In-Hospital and 1-Year Outcomes Among Unselected Percutaneous Coronary Intervention Patients Treated With Either Sirolimus- or Paclitaxel-Eluting Stents

## Results From the EVENT (Evaluation of Drug Eluting Stents and Ischemic Events) Registry

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**Objectives** The aim of this study was to compare outcomes among unselected patients undergoing percutaneous coronary intervention (PCI) with either sirolimus-eluting (SES) or paclitaxel-eluting stents (PES).

**Background** Although the benefits of both SES and PES are well-established, studies comparing these stents directly have yielded conflicting results.

**Methods** We used data from the EVENT (Evaluation of Drug Eluting Stents and Ischemic Events) registry to compare in-hospital and 1-year outcomes among unselected patients undergoing non-emergent PCI with either SES or PES implantation.

**Results** Between July 2004 and June 2006, 6,035 patients underwent PCI with either SES (n = 3,443) or PES (n = 2,592) at 47 U.S. centers. Baseline clinical and angiographic characteristics were generally similar for the 2 stent types. At 1-year, there were no differences in the primary end point of cardiac death or myocardial infarction (MI) between the SES and PES groups (9.1% vs. 10.0%, p = 0.11) or in any individual end points including cardiac death, nonfatal MI, or stent thrombosis. In unadjusted analyses, target lesion revascularization (TLR) was slightly more common with SES than with PES (4.4% vs. 3.3%, p = 0.048), but this difference was no longer apparent after adjusting for baseline characteristics as well as site-related factors (adjusted hazard ratio: 1.09, 95% confidence interval: 0.78 to 1.50).

**Conclusions** Among unselected patients undergoing PCI, adjusted rates of both ischemic complications as well as clinically important restenosis were similar for SES and PES. The unexpected finding that TLR was influenced by site characteristics suggests that the correlation between TLR and angiographic restenosis might be weaker than previously described and warrants further study.   (J Am Coll Cardiol Intv 2009;2:767–75) © 2009 by the American College of Cardiology Foundation

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By reducing neointimal hyperplasia after vascular injury, drug-eluting (coronary) stents (DES) decrease late luminal loss and angiographic restenosis, as compared with bare-metal stents (BMS) (1,2). The first 2 DES approved for clinical use, a polymer-encapsulated stent releasing sirolimus (SES) (Cypher, Cordis, Johnson & Johnson, Miami, Florida) and a polymer-based, paclitaxel-eluting stent (PES) (Taxus, Boston Scientific, Natick, Massachusetts) have been shown to reduce the rates of angiographic and clinical restenosis in several randomized trials (1,2).

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Although the therapeutic benefits of SES and PES over BMS are well-established, there might be differences between the 2 devices. Randomized clinical trials comparing SES with PES directly have demonstrated divergent results. In some studies, the 2 stents were found to be comparable in terms of clinical outcomes (3,4), whereas others have demonstrated superior outcomes with SES—especially in terms of repeat revascularization (5,6).

Although randomized clinical trials remain the "gold standard" for therapeutic comparisons and are the most reliable means to eliminate confounding, randomized trials are not without limitations. Compared with registries, the patient population enrolled in randomized trials is often smaller, limiting statistical power to resolve small but potentially important differences—particularly for rare outcomes. In addition, most clinical trials restrict enrollment to selected patients, thus limiting the generalizability of their findings. Finally, randomized trials (particularly those conducted for regulatory purposes) often incorporate routine angiographic follow-up, which can influence the rates of subsequent clinical end points via the "oculostenotic reflex" (7–9). Although certain of these limitations might be overcome by observational study designs (in particular, issues related to sample size and generalizability), in many cases observational studies lack sufficient clinical or angiographic detail to perform adequate

**Abbreviations and Acronyms**

**ACS** = acute coronary syndrome

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

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

**DM** = diabetes mellitus

**HR** = hazard ratio

**MI** = myocardial infarction

**PCI** = percutaneous coronary intervention

**PES** = paclitaxel-eluting stent(s)

**SES** = sirolimus-eluting stent(s)

**TLR** = target lesion revascularization

risk-adjustment—particularly when the data are collected mainly for administrative purposes.

The EVENT (Evaluation of Drug Eluting Stents and Ischemic Events) registry is a multicenter, observational study of unselected patients undergoing percutaneous coronary intervention (PCI) with planned implantation of Food and Drug Administration–approved intracoronary stents (10). The EVENT registry collects detailed data regarding sociodemographic, clinical, angiographic, and procedural factors, and all patients undergo clinical follow-up at 6 and 12 months. By design, the EVENT registry includes a broad geographic representation of hospitals and practice settings (public/private, academic, and so forth) and therefore provides a cross-sectional "snapshot" of the practice of PCI in the U.S. In this study, we used data from the EVENT registry to assess contemporary U.S. practice with regard to stent selection and to compare the 1-year outcomes of patients after nonemergent PCI with either PES or SES implantation in a large, unselected patient population.

## Methods

**Patient population.** The design of the EVENT registry has been described elsewhere (10,11). Briefly, the registry is designed to include consecutive, unselected patients undergoing nonemergent PCI at multiple centers within the U.S. Enrollment has been performed in 4 discrete intervals ("waves") of approximately 2,500 patients each in order to assess changes in contemporary interventional practice over time. The current analysis includes patients enrolled in the first 3 waves of the registry, which occurred between July 2004 and June 2006.

Data concerning patient characteristics, clinical presentation, and treatment were collected prospectively at each study site with standardized case report forms and submitted to the data coordinating center. Patients were contacted by study personnel at 6 and 12 months after the index PCI to assess the occurrence of pre-specified clinical end points including death, myocardial infarction (MI), repeat revascularization, and stent thrombosis. When events were suspected, the local study coordinator attempted to obtain supporting medical records to document the event. For the present analysis we included all patients who underwent PCI for reasons other than acute ST-segment elevation MI and received at least 1 commercially available DES (SES or PES). Patients in whom both types of DES were deployed were excluded from the analysis, whereas patients in whom both DES and BMS were used were analyzed according to DES type. The study protocol was approved by ethical review committees at all participating

institutions, and all patients provided written informed consent.

**Definitions, adjudication of events, and study outcomes.** The primary end point was the composite of cardiac death or MI at 1 year. To ensure uniform ascertainment of ischemic events, the study protocol specified that total creatine kinase and creatine kinase-myocardial band (CK-MB) would be collected at baseline and a minimum of 8 and 16 h after the procedure until a peak was observed. The enzymatic criterion for MI was elevation of CK-MB $\geq 3\times$ the local upper limit of normal; if the baseline CK-MB value was elevated, the peak value was required to be at least $2\times$ the baseline level as well (10). Secondary end points included the individual components of the primary end point; target lesion revascularization (TLR); and stent thrombosis (definite or probable according to the Academic Research Consortium classification) (12) at 1-year and cardiac death or MI during the index hospital stay. Target lesion revascularization was site-reported and was defined as any revascularization procedure performed because of a stenosis within the original stented lesion or within 5 mm of the stent margins (1).

**Statistical methods.** Normally distributed continuous variables are presented as mean $\pm$ SD and were compared by Student *t* test. Non-normally distributed continuous variables are presented as median values and interquartile ranges and were compared by the Mann-Whitney test. Discrete variables were compared by the chi-square test or Fisher's exact test when appropriate. Estimated 12-month rates of the primary and secondary end points were determined with the Kaplan-Meier method and compared with the log-rank statistic.

To adjust for differences between the stent groups, we used multiple logistic regression for the analysis of in-hospital outcomes and Cox proportional hazards regression models for the 12-month end points. Adjustment for potential covariates was performed in a sequential manner. First, each comparison was adjusted for baseline clinical and demographic characteristics: age, sex, diabetes, history of bypass surgery, ejection fraction (divided into 4 groups: <25%, 25% to 35%, 36% to 50%, >50%), weight, estimated glomerular filtration rate (based on the Cockroft-Gault formula) (13), and acute coronary syndrome as the indication for PCI. Next, we added adjustments for angiographic factors: number of diseased vessels, number of lesions, angiographic thrombus, treatment of a bifurcation lesion, treatment of a left anterior descending artery lesion, treatment of a totally occluded lesion, and vessel diameter (assessed by maximal balloon diameter). Finally, procedural characteristics were introduced: planned use of a glycoprotein IIb/IIIa inhibitor or bivalirudin, total stent length, use of overlapping stents, and pre-procedural clopidogrel loading. To avoid model overfitting, at each step of our sequential analysis, we used forward stepwise regression to identify potential significant predictors ($p < 0.10$) for

retention in the model; and DES type (SES vs. PES) was forced into the resulting model. Proportionality of the hazard associated with type of DES was verified by assessing the interaction term between the time-log and the stent type.

Finally, because stent selection might be associated with certain practice characteristics, we investigated the impact of stent preference at the site level on clinical outcomes. This was done by dividing the sites into approximately equal-sized groups on the basis of the proportion of DES implanted during the study period that were SES (<50%, 50% to 80%, >80%). This 3-level categorical variable and its interaction with treatment group were included as potential covariates in the final stage of our analysis (14).

## Results

Between July 2004 and June 2006, 7,593 patients were enrolled in Waves 1, 2, and 3 of the EVENT registry. We excluded 584 patients who were undergoing primary PCI for ST-segment elevation MI, 824 patients with no DES deployed, and 150 patients who received both SES and PES. Of the 6,035 patients eligible for inclusion in the current analysis, SES were deployed in 3,443 (57.1%) and PES were deployed in 2,592 (42.9%). Hospital discharge data were available for all patients, and 1-year follow-up was obtained in 5,890 (97.6%). The proportion of SES implanted ranged from 0% to 93% over the 47 sites (Fig. 1). Overall, the proportion of SES use was 51.9% in Wave 1, 60.8% in Wave 2, and 58.4% in Wave 3.

**Baseline characteristics.** Baseline clinical characteristics were generally similar between the 2 stent groups (Table 1). Patients in the PES group were more likely to have undergone PCI in the setting of an acute coronary syndrome and less likely to have chronic stable angina or a positive stress test as indications for revascularization.
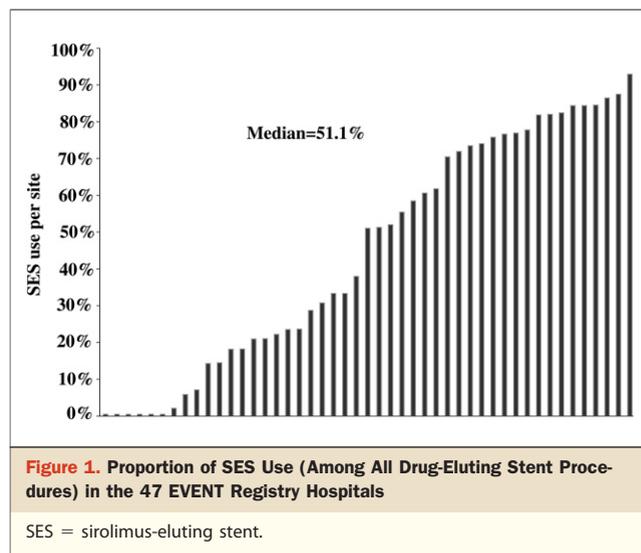


**Figure 1. Proportion of SES Use (Among All Drug-Eluting Stent Procedures) in the 47 EVENT Registry Hospitals**

SES = sirolimus-eluting stent.

**Table 1.** Baseline Demographic and Clinical Characteristics

| | SES Group (n = 3,443) | PES Group (n = 2,592) | p Value |
|---|---|---|---|
| **Demographic** | | | |
| Age, yrs, mean ± SD | 64.2 ± 11.7 | 64.7 ± 11.0 | 0.09 |
| Male | 67.7% | 68.8% | 0.40 |
| **Medical history** | | | |
| Diabetes | 34.7% | 35.2% | 0.69 |
| Hypertension | 79.0% | 79.3% | 0.79 |
| Hyperlipidemia | 76.6% | 73.2% | 0.002 |
| Current smoking | 22.4% | 23.3% | 0.44 |
| Renal dialysis | 1.5% | 1.8% | 0.32 |
| Stroke | 9.0% | 8.8% | 0.78 |
| Congestive heart failure | 9.8% | 10.1% | 0.65 |
| Peripheral arterial disease | 9.7% | 11.1% | 0.07 |
| Previous MI | 33.8% | 34.2% | 0.78 |
| MI within 7 days of PCI | 8.7% | 8.9% | 0.71 |
| Previous PCI | 39.0% | 38.1% | 0.47 |
| Previous CABG | 20.8% | 22.4% | 0.12 |
| **Indication for PCI** | | | <0.001 |
| Acute coronary syndrome | 32.4% | 39.3% | |
| Chronic stable angina or positive stress test | 59.7% | 53.7% | |
| Other | 7.9% | 6.9% | |
| Off-label indication for the PCI* | 53.9% | 49.2% | 0.002 |
| **Ejection fraction** | | | 0.24 |
| <25% | 2.4% | 2.4% | |
| 25%–35% | 6.6% | 5.5% | |
| 36%–50% | 20.1% | 18.7% | |
| >50% | 54.0% | 55.8% | |
| Unknown | 17.0% | 17.7% | |
| **Baseline laboratory data** | | | |
| Creatinine >2.0 mg/dl | 3.6% | 3.1% | 0.25 |
| Estimated creatinine clearance, ml/min† | 87.6 ± 43.6 | 88.7 ± 43.8 | 0.35 |
| **Medications before PCI** | | | |
| Statin | 68.2% | 64.3% | 0.002 |
| Beta blocker | 69.6% | 69.0% | 0.64 |
| ACE inhibitor | 39.3% | 39.2% | 0.92 |
| Angiotensin receptor blocker | 12.0% | 13.4% | 0.13 |
| **Number of diseased vessels** | | | |
| 1 | 49.3% | 51.6% | 0.18 |
| 2 | 30.3% | 27.9% | |
| 3 | 20.5% | 20.5% | |
| Lesions/patient, mean ± SD | 1.36 ± 0.61 | 1.34 ± 0.61 | 0.14 |

*Criteria for off-label use (at least 1 of the following, calculated only for subjects with all data available): >1 lesion treated, total stent length >36 mm, bifurcation lesion, lesion in bypass graft, baseline creatine kinase myocardial band ≥3× upper limit of normal, stenosis pre-procedure = 100%, maximum balloon diameter >4 mm, left ventricular ejection fraction <25%, and unprotected left main artery intervention. †Creatinine clearance was estimated by Cockcroft and Gault equation.

ACE = angiotensin-converting enzyme; CABG = coronary artery bypass grafting; MI = myocardial infarction; PCI = percutaneous coronary intervention; PES = paclitaxel-eluting stent; SES = sirolimus-eluting stent.

Angiographic characteristics including the number of lesions treated as well as high-risk lesion characteristics also tended to be similar between the 2 groups (Table 2). Intervention in left anterior descending artery lesions and totally occluded lesions were more common in the SES group; in contrast, lesions in the PES group were more likely to have reduced flow (Thrombolysis In Myocardial Infarction flow grade 0 to 2) and more likely to have angiographic thrombus.

**Procedural characteristics.** Procedural factors including antithrombotic therapies are summarized in Table 3. Patients in the PES group were more likely to receive a glycoprotein IIb/IIIa inhibitor as part of their antithrombotic regimen

**Table 2. Angiographic Characteristics**

| Per Lesion | SES Group (n = 4,683 Lesions) | PES Group (n = 3,465 Lesions) | p Value |
|---|---|---|---|
| Lesion location | | | 0.018 |
| LAD | 37.6% | 34.7% | |
| Circumflex | 22.3% | 24.6% | |
| RCA | 31.5% | 32.7% | |
| LMCA | 1.6% | 1.2% | |
| SVG | 7.0% | 6.8% | |
| ACC/AHA lesion classification | | | 0.36 |
| A | 11.3% | 11.9% | |
| B1 | 32.5% | 34.1% | |
| B2 | 37.2% | 33.5% | |
| C | 19.1% | 20.4% | |
| Lesion characteristics | | | |
| % stenosis, mean ± SD | 83.5 ± 11.3 | 84.2 ± 11.2 | 0.006 |
| Total occlusion | 5.4% | 3.8% | <0.001 |
| Bifurcation | 11.3% | 10.9% | 0.654 |
| Angiographic thrombus | 6.2% | 9.4% | <0.001 |
| TIMI flow grade | | | <0.001 |
| 0 | 5.4% | 5.2% | |
| 1 | 2.8% | 5.2% | |
| 2 | 6.9% | 10.5% | |
| 3 | 84.9% | 79.1% | |
| Vessel diameter (mm)* | 3.15 ± 0.56 | 3.08 ± 0.49 | <0.001 |
| Lesion length† | 22.99 ± 12.97 | 21.39 ± 11.81 | <0.001 |

Per lesion analysis. *Estimated on the basis of maximum balloon diameter. †Estimated on the basis of total stent length.

ACC/AHA = American College of Cardiology/American Heart Association; LAD = left anterior descending artery; LMCA = left main coronary artery; RCA = right circumflex artery; SVG = saphenous vein graft; TIMI = Thrombolysis In Myocardial Infarction; other abbreviations as in Table 1.

but less likely to have received clopidogrel loading before PCI, consistent with the higher incidence of acute coronary syndromes. Maximum balloon diameter and total stent length were slightly greater for the SES group.

**Procedural and in-hospital outcomes.** The DES deployment was unsuccessful in 0.7% of the lesions attempted with SES and 1.4% with PES (p = 0.001), whereas side branch occlusion was somewhat more frequent with SES vs. PES

**Table 3. Procedural Characteristics**

| | SES Group | PES Group | p Value |
|---|---|---|---|
| Medications during the procedure | | | |
| Heparin | 59.5% | 58.9% | 0.64 |
| Glycoprotein IIb/IIIa inhibitor | 40.6% | 40.0% | 0.62 |
| Direct thrombin inhibitor | 42.1% | 42.6% | 0.72 |
| Other | 4.3% | 4.3% | 0.99 |
| Clopidogrel loading* | 38.0% | 41.8% | 0.003 |
| Stents implanted | | | |
| Mean ± SD | 1.60 ± 0.85 | 1.55 ± 0.86 | 0.043 |
| Median (interquartile range) | 1.00 (1.00–2.00) | 1.00 (1.00–2.00) | |
| More than 1 stent in at least 1 lesion | 21.3% | 18.5% | 0.008 |
| Total stent length, mean ± SD | 30.7 ± 19.7 | 28.2 ± 18.8 | <0.001 |
| Statins at discharge | 83.9% | 76.6% | <0.001 |
| Clopidogrel at discharge† | 95.7% | 96.8% | 0.07 |

Per patient analysis. *Clopidogrel loading defined as chronic therapy (>1 week before treatment); loading dose (≥300 mg) at least 6 h before PCI; or loading dose (≥600 mg) at least 2 h before PCI. †Captured in waves 2 and 3 (3,994 subjects).

Abbreviations as in Table 1.

**Table 4.** Clinical Outcomes During the Index Hospital Stay and at 1 Year

|  | SES Group | PES Group | p Value |
|---|---|---|---|
| Procedural outcomes |  |  |  |
| Unsuccessful DES deployment | 0.9% | 1.8% | 0.001 |
| Side branch occlusion | 2.1% | 1.3% | 0.02 |
| No reflow | 0.8% | 0.4% | 0.08 |
| Angiographic success* | 99.2% | 98.9% | 0.30 |
| In hospital |  |  |  |
| Death | 0.1% | 0.1% | 1.00 |
| MI | 6.0% | 7.1% | 0.07 |
| Death or MI | 6.1% | 7.2% | 0.09 |
| At 1 yr† |  |  |  |
| Cardiac death | 1.6% | 1.7% | 0.64 |
| MI | 7.9% | 8.8% | 0.18 |
| Cardiac death or MI | 9.1% | 10.0% | 0.11 |
| Any death | 2.8% | 2.9% | 0.84 |
| TLR | 4.4% | 3.3% | 0.02 |
| Cardiac death, MI, or TLR | 12.3% | 12.4% | 0.78 |
| Stent thrombosis | 0.9% | 1.2% | 0.27 |

*Angiographic success defined as a final diameter stenosis <30% after stent implantation. †One-year rates are based on Kaplan-Meier estimates.

DES = drug-eluting stent(s); TLR = target lesion revascularization, other abbreviations as in Table 1.



**Figure 2.** Kaplan-Meier Survival Curves

Kaplan-Meier survival curves for time to cardiac death or myocardial infarction (MI) **(A)**, time to definite or probable stent thrombosis **(B)**, and time to target lesion revascularization **(C)**. PES = paclitaxel-eluting stent(s); SES = sirolimus-eluting stent(s).

(1.6% vs. 1.0%, p = 0.02). Overall, there was no significant difference in the incidence of angiographic success; the proportion of lesions with a final diameter stenosis >30% after stent implantation was 0.8% for SES and 1.1% for PES stented lesions (p = 0.30). There were no significant differences in in-hospital clinical outcomes between the stent groups, although there was a trend toward slightly more frequent periprocedural MI in the PES group (7.1% vs. 6.0%, p = 0.07).

**One-year clinical outcomes.** At 1 year after the index procedure, there were no differences in the incidence of cardiac death, nonfatal MI, or their composite between the SES and PES groups (Table 4, Fig. 2A). The incidence of Academic Research Consortium definite or probable stent thrombosis was similar between the 2 stent groups as well (0.9% vs. 1.2%, p = 0.27). However, the incidence of TLR at 1 year was slightly higher among the SES group compared with PES group (4.4% vs. 3.3%, p = 0.02).

In risk-adjusted analyses, there were no significant differences in the composite outcome of cardiac death or MI or in-stent thrombosis at 1 year, and the adjusted hazard ratios (HRs) remained virtually unchanged from the univariate results (Figs. 3A and 3B). The adjusted HR for TLR remained higher with SES after adjustment for clinical, angiographic, and procedural characteristics. After adjusting for site-level stent selection (i.e., high/intermediate/low SES use), however, this difference was markedly attenuated and no longer statistically significant (fully adjusted HR: 1.09, 95% confidence interval: 0.79 to 1.51). There were
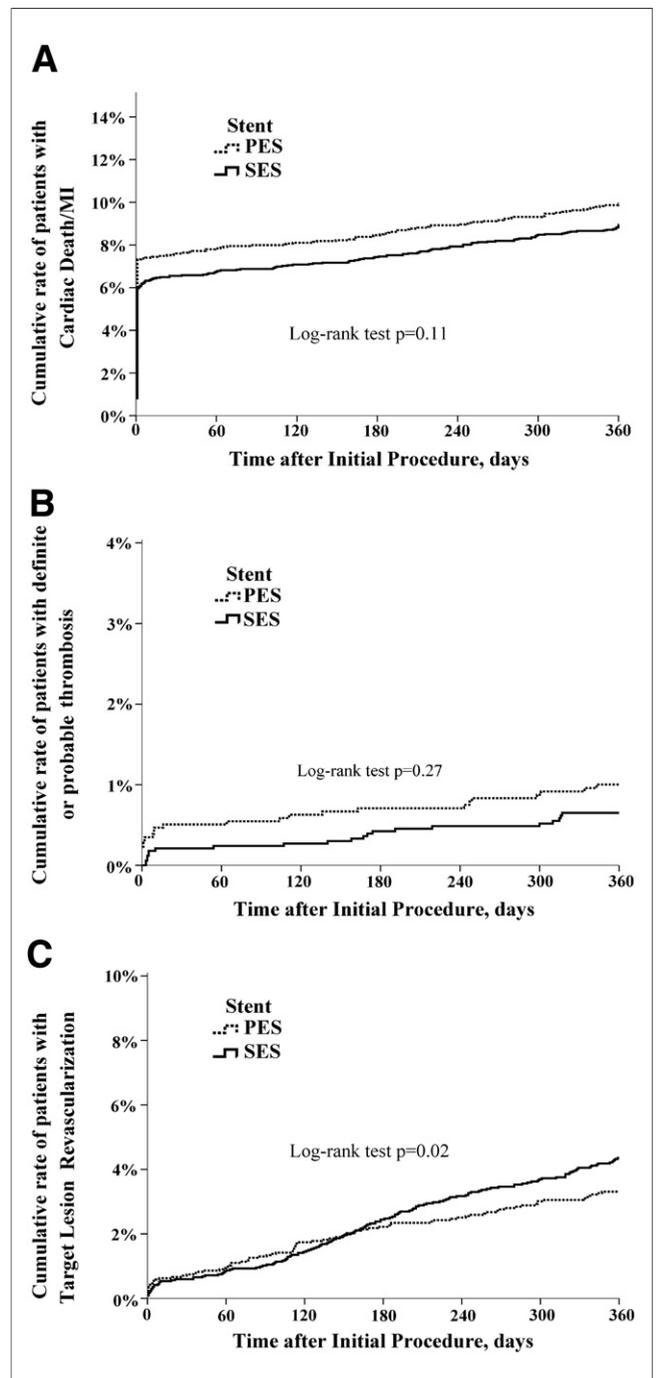
also no significant differences in risk-adjusted ischemic (cardiac death or MI) or restenosis-related (TLR) outcomes by stent type over a broad range of subgroups, including patients with or without diabetes, acute coronary syndrome, multivessel disease, or off-label DES use (Figs. 4A and 4B).
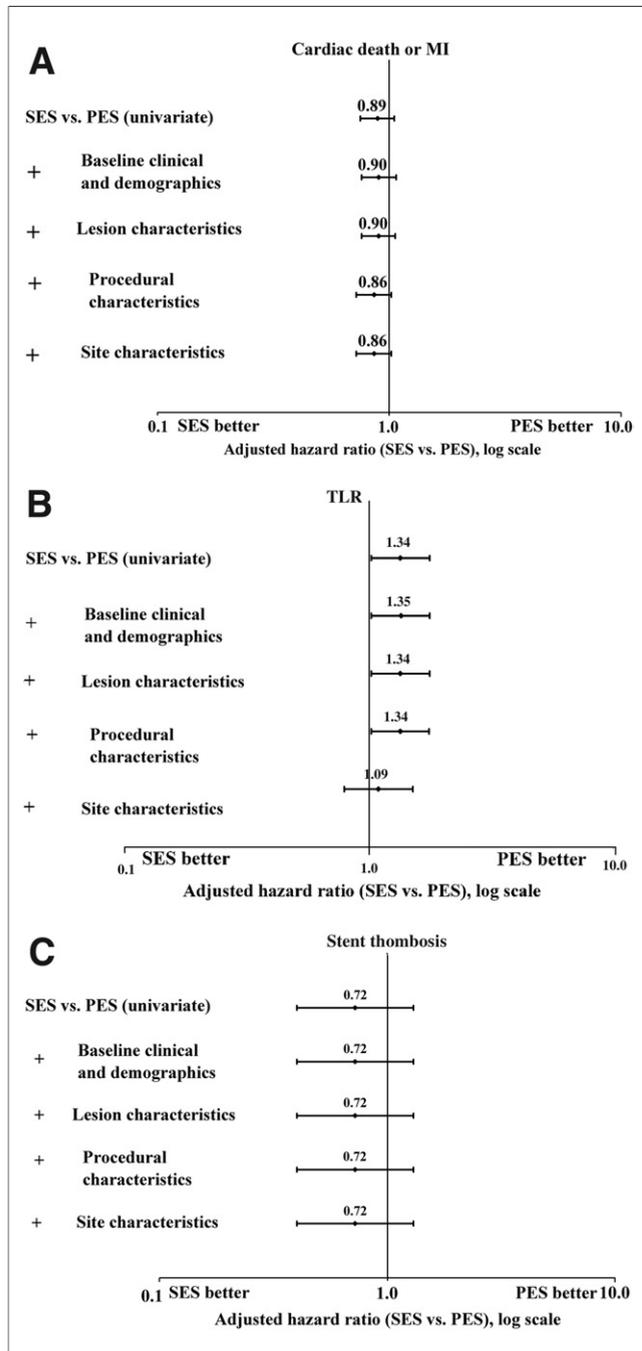
**Figure 3. Cox Proportional Hazard Regression Derived Hazard Ratios**

Cox proportional hazard regression derived hazard ratios comparing SES versus PES for the end points of cardiac death or MI **(A)**, target lesion revascularization **(B)**, and stent thrombosis **(C)** at 12 months (with 95% confidence interval). Hazard ratios are derived from risk-adjustment models with sequential inclusion of baseline clinical characteristics, lesion characteristics, procedural characteristics, and site characteristics as described in the Methods section. Abbreviations as in Figure 2.

Rates of clopidogrel use were similar among SES and PES recipients at 6 months (88.1% vs. 89.1%, p = 0.21) but slightly higher among SES recipients at 12 months (83.1%

vs. 80.3%, p = 0.01). Rates of statin use were slightly higher among SES versus PES recipients at both 6 and 12 months (95.5% vs. 94.2% and 96.1% vs. 94.3%, respectively; p < 0.05 for both comparisons). Inclusion of 6-month clopidogrel and statin use as additional covariates in our multivariable analysis had no major impact on the adjusted HRs for the 1-year outcome comparisons.

The incidence of each clinical outcome at 1 year, stratified by both DES type and site-level stent preference (by tertile) is displayed in Table 5. For the end points of cardiac death/MI and stent thrombosis, there was no evidence of a site level effect on clinical outcomes. For TLR, however, sites that used >80% SES had significantly higher rates than those sites with either 50% to 80% or <50% SES use (5.3% vs. 3.2% vs. 3.5%, respectively; p < 0.001). Nonetheless, there was no evidence of a significant interaction between site-level stent use and the impact of DES type on any of the clinical outcomes.
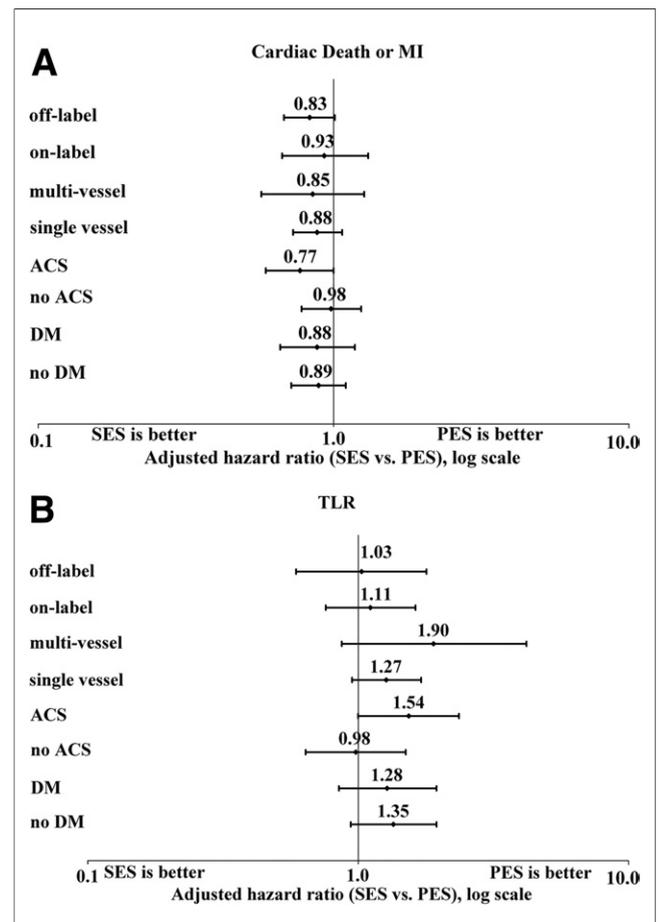


**Figure 4. Adjusted Hazard Ratios (SES vs. PES) for Cardiac Death or MI and TLR**

Adjusted hazard ratios (SES vs. PES) for cardiac death or MI **(A)** and TLR **(B)** among pre-specified subgroups. ACS = acute coronary syndrome; DM = diabetes mellitus; TLR = target lesion revascularization; other abbreviations as in Figure 2.

**Table 5.** Association Between Site-Level Stent Preference, DES Type, and 1-Year Clinical Outcomes

| | SES Proportion | | | | | | |
| | <50% | | 50%–80% | | >80% | | |
| | SES | PES | SES | PES | SES | PES | p Value for Interaction* |
|---|---|---|---|---|---|---|---|
| Cardiac death or MI (%) | 11.6% | 10.2% | 7.7% | 10.2% | 9.8% | 9.3% | 0.67 |
| Stent thrombosis (%) | 1.5% | 1.2% | 0.8% | 1.2% | 1.0% | 0.7% | 0.34 |
| TLR (%) | 5.1% | 3.1% | 3.1% | 3.0% | 5.4% | 4.8% | 0.98 |

*p value for interaction between the stent type and SES proportion derived from the final Cox survival model.

Abbreviations as in Table 4.

## Discussion

Although both SES and PES have been available for more than 5 years, there is still controversy as to the relative clinical utility of these 2 devices. Given the large volume of PCI procedures performed annually (nearly 1 million in the U.S. alone), most of which involve placement of DES, the issue of stent selection continues to have important public health implications. In this study, we used data from a large, prospective multicenter registry conducted at 47 diverse U.S. centers to examine this issue.

The main result of our study was that, among unselected patients undergoing PCI between 2004 and 2006 (the period of maximum DES penetration in U.S. practice), SES and PES were quite similar in terms of both ischemic complications (cardiac death, MI, stent thrombosis) as well as clinical restenosis (TLR) at 1 year after nonemergent revascularization. Moreover, we found no important differences in clinical outcomes across a broad range of patient subgroups.

**Comparison with previous studies.** Most early clinical trials (including those that incorporated routine angiographic follow-up) have tended to favor the SES in terms of both TLR and stent thrombosis (3,6,15–17). More recently, clinical trials without angiographic follow-up (4) as well as registry studies (18,19) have found few, if any, differences in clinical outcomes between the 2 types of DES. The most likely explanation for the difference in stent performance between the randomized trials and the registry-based studies relates to the fact that most randomized trials to date have incorporated routine angiographic follow-up in either a majority (3,15,16) or at least a substantial proportion of the study participants (5). Because SES have consistently been found to result in superior angiographic outcomes to PES, it seems that the performance of angiographic follow-up results in a greater tendency toward revascularization of borderline stenoses among PES-treated patients. The results of the SORT OUT II (Danish Organization on Randomized Trials with Clinical Outcome), which demonstrated comparable rates of TLR among more than 2,000 patients randomized to SES or PES and did not undergo

routine angiographic follow-up (4), provides the most compelling evidence to date of this differential bias.

Our study both confirms the results of these previous studies and extends them in several important ways. First, our study is 1 of the largest studies to date to compare alternative DES designs and incorporates a larger number of study sites and broader geographic representation than any previous study. Moreover, the all-inclusive nature of the EVENT registry allowed us to perform comparisons of clinical outcomes between PES and SES over a broad range of patient and lesion types. The complexity of the population included in our study is demonstrated by the high proportions of patients with multi-lesion procedures (18.5%), chronic total occlusions (4.7%), saphenous vein graft (7.0%), bifurcation lesions (11.1%), and thrombotic lesions (7.5%). In addition, among registry studies, the EVENT registry is the only 1 that incorporates routine assessment of cardiac enzymes and adjudication of all suspected MIs. Thus, our study provides strong evidence that the safety of PES and SES are comparable, both in terms of stent thrombosis as well as periprocedural infarction. Finally, the use of clinical data—as opposed to administrative datasets—allows for more thorough risk-adjustment as well as assessment of more specific mechanistic end points such as stent thrombosis and TLR.

**Impact of site-level factors.** Our study is the first to suggest that site-specific characteristics might play a role in determining clinical outcomes of PCI—particularly for end points related to repeat revascularization. In contrast to previous studies that generally demonstrated either similar or lower rates of clinically significant restenosis with SES compared with PES, in the EVENT registry we found that the 1-year incidence of TLR was actually slightly higher with SES than PES (4.4% vs. 3.3%, p = 0.02)—a difference that persisted even after adjustment for clinical, angiographic, and procedural differences. However, after controlling for site stent preference, the HR was markedly attenuated and the difference was no longer statistically significant.

In light of the well-documented superior angiographic performance of SES compared with PES, these findings suggest that factors other than angiographic restenosis

might play an important role in determining rates of clinical surrogates for restenosis, including TLR. Although it is not possible to determine the specific factors responsible for this phenomenon in this study, 1 possible explanation is that sites that are more aggressive about screening for restenosis might preferentially choose to implant SES or that such sites might have different thresholds for performing repeat revascularization. Further study of surveillance patterns after PCI might provide additional insight into this novel finding. In the interim, these findings suggest that analyses of registry data to compare rates of revascularization should be certain to adjust for potential site effects.

**Study limitations.** This study has several important limitations. As in any observational study, it is likely that our findings are impacted to some degree by unmeasured confounding. However, we believe that selection of a DES, in contrast to many clinical decisions, might be driven by factors beyond the operator's control (such as hospital contracting and availability of product) and thus less likely to be influenced by patient characteristics. In addition, although we did attempt to adjust for a broad range of angiographic factors, these were determined on the basis of self-reported data rather than an objective, angiographic core laboratory. Finally, despite including more than 6,000 patients, our study had only modest power to detect differences in rare events such as stent thrombosis.

## Conclusions

In this multicenter registry of nonemergent PCI with 2 types of DES, we found that adjusted 1-year rates of both ischemic complications (death, MI, stent thrombosis) as well as clinically important restenosis (TLR) were comparable for SES and PES across a broad range of patient and lesion characteristics. The finding that TLR seemed to be related to site characteristics suggests that the correlation between TLR and angiographic restenosis might be weaker than previously suggested and warrants further study.

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