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# Cost Effectiveness of Paclitaxel-Eluting Stents for Patients Undergoing Percutaneous Coronary Revascularization

## Results From the TAXUS-IV Trial

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**OBJECTIVES** This study sought to compare aggregate medical care costs for patients undergoing percutaneous coronary intervention with paclitaxel-eluting stents (PES) and bare-metal stents (BMS) and to formally evaluate the incremental cost effectiveness of PES for patients undergoing single-vessel percutaneous coronary intervention.

**BACKGROUND** Although the cost effectiveness of SES has been studied in both clinical trials and decision-analytic models, few data exist on the cost effectiveness of alternative drug-eluting stent (DES) designs. In addition, no clinical trials have specifically examined the cost effectiveness of DES among patients managed without mandatory angiographic follow-up.

**METHODS** We performed a prospective economic evaluation among 1,314 patients undergoing percutaneous coronary revascularization randomized to either PES (N = 662) or BMS (N = 652) in the TAXUS-IV trial. Clinical outcomes, resource use, and costs (from a societal perspective) were assessed prospectively for all patients over a 1-year follow-up period. Cost effectiveness was defined as the incremental cost per target vessel revascularization (TVR) event avoided and was analyzed separately among cohorts assigned to mandatory angiographic follow-up (n = 732) or clinical follow-up alone (n = 582).

**RESULTS** The PES reduced TVR by 12.2 events per 100 patients treated, resulting in a 1-year cost difference of $572 per patient with incremental cost-effectiveness ratios of $4,678 per TVR avoided and $47,798/quality-adjusted life year (QALY) gained. Among patients assigned to clinical follow-up alone, the net 1-year cost difference was $97 per patient with cost-effectiveness ratios of $760 per TVR event avoided and $5,105/QALY gained.

**CONCLUSIONS** In the TAXUS-IV trial, treatment with PES led to substantial reductions in the need for repeat revascularization while increasing 1-year costs only modestly. The cost-effectiveness ratio for PES in the study population compares reasonably with that for other treatments that reduce coronary restenosis, including alternative drug-eluting stent platforms. (J Am Coll Cardiol 2006;48:253–61) © 2006 by the American College of Cardiology Foundation

Over the past 5 years, both sirolimus-eluting stents (SES) and paclitaxel-eluting stents (PES) have been shown to substantially reduce rates of angiographic and clinical restenosis after percutaneous coronary intervention (PCI) compared with conventional bare-metal stents (BMS) (1–3). In addition to improved clinical outcomes, economic analyses based on both decision-analytic models as well as patient-level data from clinical trials have shown that drug-eluting stents (DES) are reasonably cost effective compared with other generally accepted medical interventions, at least for patients at moderate to high risk of restenosis after single-vessel PCI (4,5). Based on these data, most third-party payers, including the Center for Medicare and Medicaid Services, have provided incremental reimbursement for DES, and these devices have been rapidly incorporated into standard clinical practice.

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Nonetheless, several important questions regarding the cost effectiveness of DES remain unanswered. First, all of the published economic analyses to date are based on data for SES. Whether these analyses apply similarly to PES is unknown. Moreover, the data derived from the SES trials

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**Abbreviations and Acronyms**

BMS = bare-metal stent
CI = confidence interval
DES = drug-eluting stent
DRG = diagnosis-related group
ICU = intensive care unit
PCI = percutaneous coronary intervention
PES = paclitaxel-eluting stent
QALY = quality-adjusted life year
SES = sirolimus-eluting stent
TVR = target vessel revascularization

have important limitations. In particular, rates of clinical restenosis in the control arms of these trials were somewhat higher than previous reports would have suggested (6,7). To some extent, this increase may relate to selection of patients at higher-than-average risk of restenosis for inclusion in the study (2,8). More importantly, however, the vast majority of patients in these studies were assigned to undergo mandatory angiographic follow-up—a process that is known to increase the need for repeat revascularization compared with clinical follow-up alone (9,10). Thus, the extent to which DES reduce the need for follow-up cardiovascular procedures and costs among patients in routine clinical practice is unknown.

To address these unresolved issues, we performed a prospective economic substudy as part of the randomized TAXUS-IV trial. The goals of the study were: 1) to define the net 1-year cost of care for patients undergoing PCI with either PES or conventional BMS; 2) to formally evaluate the cost effectiveness of PES versus BMS for patients undergoing single-vessel PCI, from a societal perspective; and 3) to examine the impact of mandatory angiographic follow-up versus clinical follow-up alone on the cost effectiveness of PES.

## METHODS

**Patient population and treatment protocol.** Between March 29 and July 8, 2002, 1,314 patients undergoing PCI were enrolled in the TAXUS-IV trial at 73 U.S. centers. Details of the study design have been described previously (3). Briefly, patients were eligible if they were undergoing planned PCI to a de novo lesion 10 to 28 mm in length, located in a native coronary artery with a reference vessel diameter 2.5 to 3.75 mm (by visual estimate). Patients who required concurrent PCI of a lesion in a vessel separate from the study lesion were allowed to be enrolled after successful treatment of the nontarget lesion with an approved BMS. The study protocol was approved by the institutional review board at each site, and each patient provided informed consent before enrollment.

Patients were randomized in a double-blind fashion to implantation of either the slow-release, polymer-based PES (Taxus, Boston Scientific, Natick, Massachusetts; n = 662) or a visually indistinguishable BMS (Express, Boston Scientific, n = 652) stratified by clinical site, target vessel diameter (<3.0 vs. ≥3.0 mm), and the presence of diabetes mellitus. Stent implantation was performed using standard techniques. Postprocedure, all patients received aspirin indefinitely and clopidogrel (300 mg loading dose followed by 75 mg daily) for at least 6 months. At the time of study enrollment, patients were assigned to either mandatory angiographic follow-up at 9 months (n = 732) or clinical follow-up alone (n = 582).

Case report forms documenting baseline patient characteristics, procedural details (including resource use), and clinical outcomes during the initial hospitalization and 1-year follow-up period were completed by a trained research coordinator. All end points (death, myocardial infarction, repeat revascularization) were reviewed by an independent clinical events committee who was blinded to treatment assignment. Repeat revascularization was considered clinically driven if there was evidence of active myocardial ischemia by symptoms, provocative testing, or both.

**Determination of medical care costs.** The primary analytic perspective of our study was societal, consistent with guidelines from the U.S. Panel on Cost Effectiveness in Health and Medicine (11). For this analysis, medical care costs for the initial hospitalization and the 1-year follow-up period were estimated using a combination of resource-based costs and hospital billing data as previously described (12,13). Although some studies have used diagnosis-related group (DRG) payments as a proxy for cost from a societal perspective, we thought that in the case of a relatively new procedure such as DES, a more detailed approach that specifically accounted for variability in procedural as well as hospital resource utilization would more accurately represent opportunity cost.

CARDIAC CATHETERIZATION LABORATORY COSTS. Detailed resource use was recorded for each procedure, and the cost of each item was estimated on the basis of the mean hospital acquisition cost for the item in 2004. The costs of BMS and PES were set at $800 and $2,700 per stent, respectively, based on average hospital acquisition costs for each as of April 2004 (when PES were approved for commercial sale in the U.S.) (14). Costs of additional supplies, overhead, and depreciation for the cardiac catheterization laboratory and nonphysician personnel were estimated on the basis of the average cost per procedure at Beth Israel Deaconess Medical Center in 2004 and adjusted for actual procedure duration.

OTHER HOSPITAL COSTS. All other hospital costs were estimated using hospital billing data and department-level cost-to-charge ratios as previously described (13). For 460 randomly selected patients, itemized bills were obtained for the initial hospitalization and any subsequent cardiovascular hospitalizations during follow-up. Hospital costs were then

estimated by multiplying itemized hospital charges by the cost-center specific cost-to-charge ratio obtained from the hospital's Medicare cost report. Previous studies from our group and others have shown this method to correlate well with data from detailed cost-accounting systems, particularly for the purposes of group comparisons (13,15). All costs were converted to 2004 dollars based on the medical care component of the consumer price index.

For the remaining patients, nonprocedural hospital costs were estimated based on a linear regression model developed using the hospital admissions for which complete billing information was available. Independent variables for this model included length of stay, intensive care unit (ICU) length of stay, bleeding complications, and revascularization procedures. For the purposes of our study, only those target vessel revascularization (TVR) procedures that were determined by the clinical events committee to have been clinically driven were included in the economic analysis so as to limit contamination by angiographically driven procedures or revascularization events unrelated to the study stent.

**OTHER COSTS.** Physician services for inpatient procedures and daily care were assigned costs based on the Medicare fee schedule. Outpatient services and medications (with the exception of thienopyridine treatment) were not tracked during the study and were therefore excluded from the economic analysis. Although both treatment groups received 6 months of clopidogrel, the primary analysis assigned patients in the control group a cost for only 1 month of clopidogrel to reflect as closely as possible standard practice after BMS implantation at the time of the study.

**OTHER ANALYTIC PERSPECTIVES.** Secondary analyses were performed in which costs were assessed from both a hospital perspective and a third-party payer (Medicare) perspective. For the hospital perspective analysis, hospitalization-related costs were assessed as previously described and were balanced against mean Medicare reimbursement rates; all other costs, including physician payments and outpatient medications, were excluded. For the analysis from the perspective of the Medicare program, mean 2004 Medicare reimbursement rates were assigned to each hospitalization based on the underlying DRG as determined by an expert coder who was blinded to treatment assignment. Physician costs were assigned using the 2004 Medicare fee schedule, and costs for outpatient medications (including clopidogrel) were excluded because outpatient medications were not covered by Medicare in 2004.

**Statistical analysis.** Discrete data are reported as frequencies, and continuous data are reported as mean ± SD. Cost data are reported as both mean and median values. Discrete variables were compared using the Fisher exact test. Normally distributed continuous variables were compared by the Student *t* test. Cost and other non-normally distributed data (length of stay, procedure duration) were compared by the Wilcoxon rank-sum test. Given their non-normal distributions, confidence intervals for cost differences were estimated using bootstrap resampling. All statistical analyses and cost-effectiveness analyses were performed according to the intention-to-treat principle.

**Cost-effectiveness analyses.** Because the major clinical benefit of the PES was a reduction in the incidence of clinical restenosis requiring repeat revascularization, the primary end point for the cost-effectiveness analysis was the incremental cost per repeat revascularization event avoided over the 1-year follow-up period. This disease-specific cost-effectiveness ratio was calculated by dividing the 1-year difference in mean medical care costs by the 1-year difference in the frequency of TVR between the PES and BMS groups (5). The use of TVR events avoided in the denominator of the cost-effectiveness ratio is based on previous studies, which have shown that patients who require TVR have an impaired quality of life over the first year of follow-up compared with patients who avoid such events (16,17).

We also performed a secondary cost-effectiveness analysis using the standard metric of cost per quality-adjusted life year (QALY) gained. Because quality of life was not assessed in the TAXUS-IV trial, quality-adjusted life expectancy for each patient was estimated on the basis of previous data from the Stent-PAMI (Stent Primary Angioplasty in Myocardial Infarction) trial (18). In that study, the EuroQoL health status instrument was administered to 771 patients at 1, 6, and 12 months after initial revascularization, and population-level utilities were assigned to each patient based on a published regression model (19). Weighted averages of utility values at the 3 time points were used to estimate a mean quality-adjusted life expectancy for patients with and without repeat revascularization during follow-up (0.78 vs. 0.86, $p < 0.001$), which were applied to the TAXUS-IV study population, along with a short-term disutility "toll" for patients who required bypass surgery (20,21). As in previous cost-utility analyses (5,22), we assumed that there would be no differences in long-term survival or quality of life beyond the first year of follow-up, because previous studies have shown no association between coronary restenosis and long-term mortality (23). To estimate the uncertainty surrounding cost-effectiveness ratios, we calculated bias-corrected confidence intervals for each cost-effectiveness ratio by the bootstrap method, using 5,000 repeat samplings of the study population.

**Sensitivity and subgroup analyses.** To estimate the cost effectiveness of PES in the real world without distortion by protocol-driven angiographic follow-up, we performed a prespecified analysis among the 582 patients assigned to clinical follow-up alone. Additional prespecified subgroup analyses were performed in which patients were stratified by the presence or absence of treated diabetes mellitus and according to vessel size and lesion length (as determined by the angiographic core laboratory).

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

| | Paclitaxel Group (n = 662) | Control Group (n = 652) |
|---|---|---|
| Age, yrs | 63 ± 11 | 62 ± 11 |
| Gender, % male | 71.8 | 72.4 |
| Diabetes mellitus, % | 23.4 | 25.0 |
| Current smoker, % | 23.4 | 20.1 |
| Previous myocardial infarction, % | 30.5 | 29.9 |
| Nontarget vessel treated, % | 19.8 | 17.0 |
| Ejection fraction, % | 55 ± 10 | 55 ± 10 |
| Assigned to follow-up angiography, % | 56.6 | 54.8 |
| Lesion location | | |
| Left anterior descending, % | 40.0 | 41.4 |
| Circumflex, % | 28.9 | 26.6 |
| Right coronary artery, % | 31.1 | 32.0 |
| Lesion length (mm) | 13.4 ± 6.3 | 13.4 ± 6.2 |
| Lesion length >15 mm, % | 30.5 | 30.6 |
| Reference diameter (mm) | 2.75 ± 0.47 | 2.75 ± 0.49 |
| Reference diameter ≤2.5 mm, % | 30.8 | 32.6 |

p = NS for all comparisons.

## RESULTS

**Patient population.** For the overall study population, baseline clinical and angiographic characteristics were well matched between the PES and BMS groups (Table 1). The mean age was 62 years, and approximately 24% had diabetes. By quantitative angiography, the mean lesion length was 13 mm; the mean reference vessel diameter was 2.75 mm; and 32% of patients had reference vessel diameters ≤2.5 mm.

**Initial treatment costs and resource use.** Table 2 summarizes resource use and costs for the index revascularization procedures. Not surprisingly (given the blinded nature of the study), procedural resource use was virtually identical for the two treatment groups. An average of 1.1 study stents and 0.3 nonstudy stents per patient were implanted for both treatment groups, and 57% of patients received a glycoprotein IIb/IIIa receptor antagonist at the time of their index procedure. The difference in initial procedural costs was $1,988 (95% confidence interval [CI] $1,738 to $2,238) and was driven almost entirely by the higher acquisition cost for PES compared with BMS. Similarly, there were no significant differences in initial hospital complications or resource use between the 2 treatment groups (Table 3). Thus, total costs for the index hospitalization were $2,028 per patient higher for the PES group compared with the control group (95% CI $1,731 to $2,325).

**Follow-up resource use and costs.** Over the 1-year follow-up period, use of PES was associated with substantial reductions in follow-up resource use and related health-care costs (Table 4). In particular, the need for 1 or more repeat TVR procedures was reduced by 60% in the PES group compared with the BMS group (6.6% vs. 16.6%, $p < 0.001$), with significant reductions in the need for bypass surgery and repeat PCI procedures. The absolute reduction in the number of TVR procedures performed during follow-up was 12.2 events per 100 patients treated (95% CI 8.1 to 16.4).

In the overall study population, mean follow-up medical care costs were $1,456 per patient lower in the paclitaxel group compared with the control group (95% CI $559 to $2,323) (Fig. 1). These cost savings were driven primarily by reductions in the costs for repeat revascularization procedures and their associated hospitalizations, but there were modest reductions in physician fees as well. Mean 1-year medical care costs for the PES group were $14,583, as compared with $14,011 for the control BMS group—a difference of $572 per patient (95% CI $346 less to $1,478 more).

**Cost-effectiveness analyses.** In our base case analysis, the disease-specific incremental cost-effectiveness ratio was $4,678 per TVR avoided (Table 5). Bootstrap simulation showed that this cost-effectiveness ratio remained <$10,000 per TVR avoided in 86.0% of simulations (Fig. 2A). Our secondary analysis showed an incremental cost-utility ratio of $47,798/QALY gained, with 14.8% of bootstrap replicates showing economic dominance (i.e., lower costs and improved quality-adjusted life expectancy) and 56.8% of the results <$50,000/QALY gained (Table 5).

**Results from the nonangiographic subgroup.** Among the prespecified subgroup of patients assigned to clinical follow-up alone, use of PES was associated with an initial

**Table 2.** Procedural Resource Use and Cost

| | Paclitaxel Group (n = 662) | Control Group (n = 652) | p Value |
|---|---|---|---|
| Procedure duration, min | 51 ± 27 | 51 ± 28 | 0.94 |
| Balloon catheters | 2.9 ± 2.4 | 2.8 ± 2.4 | 0.46 |
| Stents (all) | 1.3 ± 0.7 | 1.3 ± 0.8 | 0.70 |
| Stents (study) | 1.1 ± 0.3 | 1.1 ± 0.3 | 0.81 |
| Stents (nonstudy) | 0.3 ± 0.7 | 0.3 ± 0.8 | 0.76 |
| Glycoprotein IIb/IIIa inhibitor used | 58% | 57% | 0.74 |
| Resource costs | | | |
| Medications | $387 ± 1,481 [$104] | $442 ± 1,853 [$104] | 0.16 |
| Balloons/stents | $3,966 ± 1,363 [$3,380] | $1,924 ± 1,193 [$1,440] | <0.001 |
| Additional procedural costs | $1,972 ± 401 [$1,892] | $1,969 ± 426 [$1,814] | 0.63 |
| Total procedural cost | $6,324 ± 2,188 [$5,740] | $4,336 ± 2,427 [$3,852] | <0.001 |

Values in brackets are medians.

**Table 3.** Initial Hospital Events, Resource Use, and Costs

| | Paclitaxel Group (n = 662) | Control Group (n = 652) | p Value |
|---|---|---|---|
| Death, % | 0.0 | 0.3 | 0.25 |
| Myocardial infarction, % | 2.4 | 2.1 | 0.85 |
| Repeat PCI, % | 0.3 | 0.2 | 1.0 |
| Coronary artery bypass surgery, % | 0.0 | 0.2 | 0.50 |
| Diagnostic catheterization, % | 1.2 | 0.3 | 0.11 |
| Vascular complications, % | 0.2 | 0.5 | 0.37 |
| Transfusion, % | 1.4 | 1.4 | 1.0 |
| Length of stay, days | 2.0 ± 2.0 [1] | 1.9 ± 2.1 [1] | 0.74 |
| Postprocedure length of stay, days | 1.3 ± 0.9 [1] | 1.3 ± 1.6 [1] | 0.51 |
| Medical costs | | | |
| Initial procedure | $6,324 ± 2,188 [$5,740] | $4,336 ± 2,427 [$3,852] | <0.001 |
| Hospital room/ancillary/nursing | $2,882 ± 1,858 [$2,497] | $2,849 ± 1,960 [$2,497] | 0.35 |
| Professional fees | $1,889 ± 340 [$1,749] | $1,883 ± 586 [$1,749] | 0.18 |
| Total | $11,096 ± 3,195 [$10,165] | $9,067 ± 3,387 [$8,230] | <0.001 |

Values in brackets are medians.
PCI = percutaneous coronary intervention.

procedural cost increase of $2,069/patient. At 1-year follow-up, randomization to PES was associated with a 62% relative reduction in TVR (5.2% vs. 13.9%, $p < 0.001$), with an absolute reduction of 12.7 events per 100 patients treated, and a corresponding $1,894 per patient reduction in follow-up costs (95% CI $538 to $3,275). Thus, the 1-year net cost of PES versus BMS in the nonangiographic cohort was $97 per patient, with an associated incremental cost-effectiveness ratio of $760 per TVR avoided and $5,105/QALY gained (Table 5). Bootstrap simulation showed that the disease-specific cost-effectiveness ratio was <$10,000 per TVR event avoided in 90.0% of simulations (Fig. 2B), and the cost-utility ratio was <$50,000/QALY gained in 76.3%.

**Additional subgroup and sensitivity analyses.** Stratified analyses according to additional patient characteristics are summarized in Figure 3. In general, these analyses were similar to the overall trial results, with cost-effectiveness ratios consistently <$10,000 per repeat revascularization avoided. Paclitaxel-eluting stents were less attractive, however, for patients with reference vessel diameters ≥3.0 mm (C/E ratio ~$25,000 per TVR avoided), whereas they were economically dominant in patients with reference vessel diameters <2.5 mm and in patients with diabetes mellitus.

The results of our analysis were substantially improved if we assumed that all patients would receive 12 months of postprocedure clopidogrel treatment, regardless of stent type (Table 5). In the overall trial population, this assumption reduced the 1-year cost difference from $572 to $122, with resulting cost-effectiveness and cost-utility ratios of $997 per TVR avoided and $10,183/QALY gained, respectively. Among the subgroup assigned to clinical follow-up alone, the assumption of equal clopidogrel duration changed PES implantation from a cost-effective to an economically dominant strategy, with 1-year cost savings of $353 per patient compared with BMS implantation.

**Table 4.** Follow-Up Events, Resource Use, and Costs

| | Paclitaxel Group (n = 662) | Control Group (n = 652) | Difference (95% Confidence Interval) | p Value |
|---|---|---|---|---|
| Death, % | 2.1 | 1.4 | 0.7 (−0.7 to 2.1) | 0.40 |
| Myocardial infarction, % | 1.1 | 2.5 | −1.4 (−2.8 to 0.0) | 0.06 |
| Repeat TVR, % | 6.6 | 16.6 | −9.9 (−13.3 to −6.5) | <0.001 |
| CABG | 1.7 | 3.8 | −2.2 (−3.9 to −0.4) | 0.02 |
| PCI | 5.1 | 13.3 | −8.2 (−11.3 to −5.1) | <0.001 |
| Repeat cardiovascular hospitalization, % | 18.6 | 26.4 | −7.8 (−12.3 to −3.3) | <0.001 |
| Number of TVR events (per 100 patients) | 6.9 | 19.2 | −12.2 (−16.4 to −8.1) | <0.001 |
| CABG | 1.7 | 3.8 | −2.2 (−3.9 to −0.4) | 0.02 |
| PCI | 5.3 | 15.3 | −10.0 (−13.8 to −6.3) | <0.001 |
| Hospital admissions (per 100 patients) | 26.4 | 38.0 | −11.6 (−19.8 to −3.4) | 0.01 |
| Hospital days (per 100 patients) | 71.3 | 104.9 | −33.6 (−64.9 to −2.3) | 0.03 |
| Follow-up costs | | | | |
| Hospitalizations | $2,241 [$0] | $3,749 [$0] | −$1,508 (−2,226 to −797) | <0.001 |
| Outpatient services/medications | $814 [$540] | $414 [$90] | $400 (327 to 475) | <0.001 |
| Physician fees | $432 [$0] | $780 [$0] | −$349 (−492 to −179) | 0.001 |
| Total follow-up costs | $3,487 [$540] | $4,944 [$90] | −$1,456 (−2,323 to −559) | <0.001 |
| Aggregate 1-yr costs | $14,583 [$11,699] | $14,011 [$9,540] | $572 (−346 to 1,478) | <0.001 |

Values in brackets are medians.
CABG = coronary artery bypass graft surgery; PCI = percutaneous coronary intervention; TVR = target vessel revascularization.

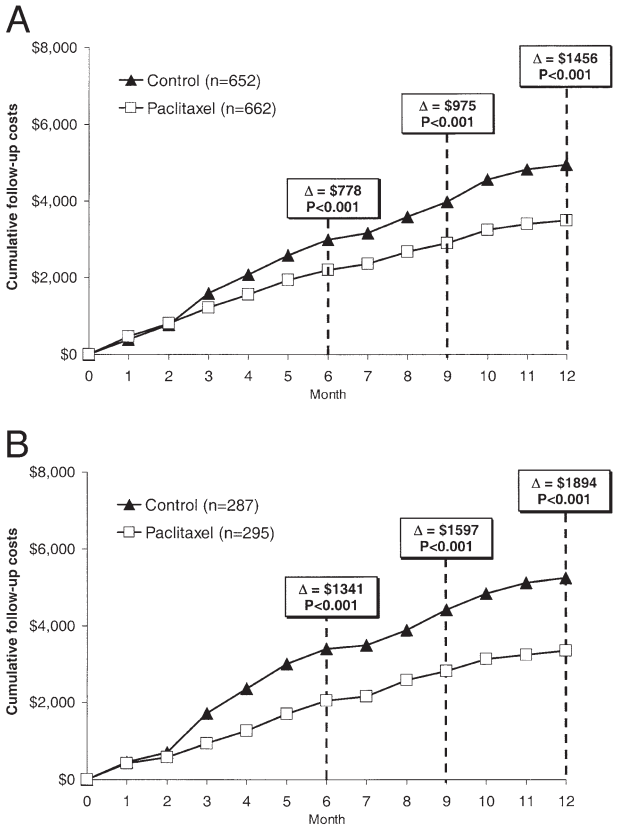


**Figure 1.** Cumulative follow-up costs for the paclitaxel and control stent groups for the overall trial population **(A)** and the subgroup assigned to clinical follow-up alone **(B)**. Mean cost differences at 6, 9, and 12 months are indicated in the **boxes**.

Our findings were also sensitive to the cost of hospitalization for repeat revascularization and to the analytic perspective. If repeat revascularization costs were, on average, 48% lower than observed in our study, the cost-effectiveness ratio for PES would increase to $10,000 per repeat revascularization avoided. On the other hand, if repeat revascularization costs were 43% higher than we observed, initial PES implantation would be a cost-saving strategy. When examined from the perspective of the Medicare system, aggregate 1-year costs were slightly lower for PES than for BMS ($18,818 vs. $19,045; 95% CI for difference $1,374 less to $919 more). In contrast, from the hospital perspective, net profit (i.e., revenue-cost) per patient was actually lower with PES than BMS ($6,605 vs. $7,064; 95% CI $1,120 less to $201 more).

## DISCUSSION

This is the first prospective economic evaluation of coronary PES within the U.S. health care system. Using individual patient-level data from the TAXUS-IV trial, we found that use of PES increased initial hospital costs by more than $2,000 per patient compared with conventional BMS implantation, driven predominantly by the higher acquisition cost of the PES. Nonetheless, over the 1-year follow-up period, use of PES was associated with significant reduc-

**Table 5.** Cost Effectiveness of Paclitaxel-Eluting Stents Under Alternative Assumptions About Adjunctive Medications

| Scenario | Δ Cost (95% CI) | RepRev Procedures Avoided per 100 Patients | C/E Ratio ($/RepRev Avoided) | % <$10,000 per RepRev Avoided* | % Dominant* | C/E Ratio ($/QALY Gained) | % <$50,000/ QALY Gained* | % Dominant* |
|---|---|---|---|---|---|---|---|---|
| Population: overall | | | | | | | | |
| Primary analysis† | $572 (−$346 to $1,478) | 12.2 | $4,678 | 86.0 | 14.8 | $47,798 | 56.8 | 14.8 |
| No difference in duration of clopidogrel | $122 (−$796 to $1,028) | 12.2 | $997 | 96.9 | 40.5 | $10,183 | 82.9 | 40.5 |
| Population: clinical F/U | | | | | | | | |
| Primary analysis† | $97 (−$1,376 to $1,498) | 12.7 | $760 | 90.0 | 46.0 | $5,105 | 76.3 | 46.0 |
| No difference in duration of clopidogrel | −$353 (−$1,826 to $1,048) | 12.7 | Dominant | 96.5 | 66.8 | Dominant | 89.3 | 66.8 |

*Percentages and confidence intervals are based on 5,000 bootstrap simulations of trial results. †Primary analysis = 6 months of dual antiplatelet therapy in paclitaxel-eluting stent group versus 1 month in control group.
C/E = cost-effectiveness; CI = confidence interval; F/U = follow-up; RepRev = repeat revascularization; QALY = quality-adjusted life year.

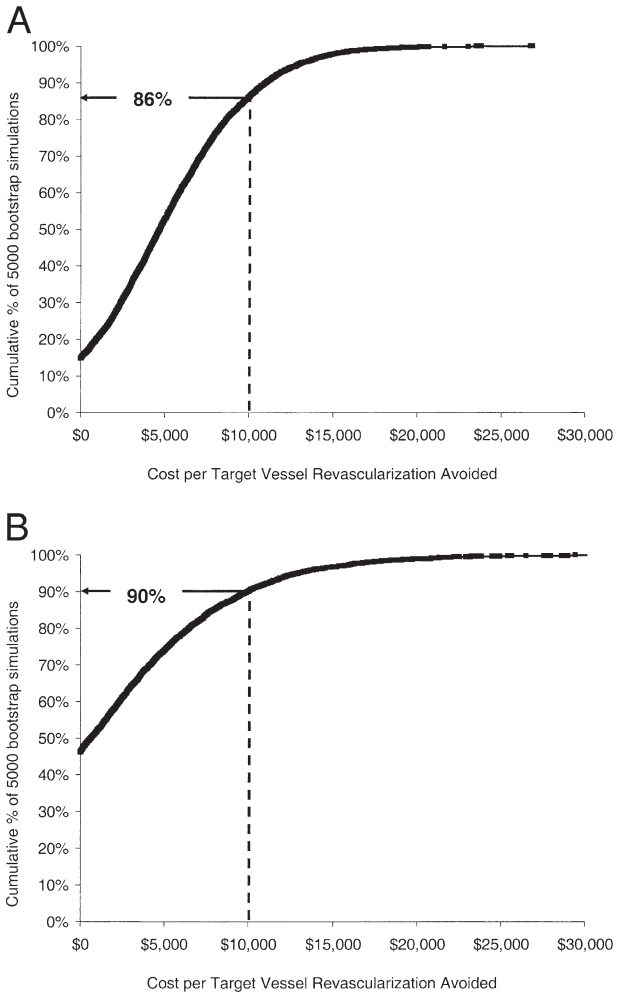


**Figure 2.** Cumulative distribution plot of the incremental cost-effectiveness ratio for paclitaxel-eluting stent compared with bare-metal stent based on bootstrap analysis of the primary TAXUS-IV trial results among the overall study population **(A)** and the subgroup assigned to clinical follow-up alone **(B)**. As indicated by the **arrow**, 86% of the resulting cost-effectiveness ratios were <$10,000 per target vessel revascularization event avoided for the overall population, and 90% were less than this threshold for the clinical follow-up cohort.

tions in a variety of morbid events, including rehospitalization (12 fewer events per 100 patients treated), repeat PCI (10 fewer events per 100 patients treated), and bypass surgery (2 fewer events per 100 patients treated). In addition to these clinical benefits, use of PES was associated with a reduction in follow-up medical care costs of ~$1,500 per patient.

Although these cost savings were insufficient to fully offset the higher initial treatment costs, the overall results of our economic analysis nonetheless suggest that use of PES may be reasonably cost-effective from a societal perspective over a broad range of patient and lesion characteristics. Indeed, the incremental cost-effectiveness ratio of $4,700 per TVR event avoided for PES compares favorably with the cost effectiveness of several other devices that have been shown to reduce coronary restenosis, including BMS (vs. balloon angioplasty) (9,24) and vascular brachytherapy (22). Moreover, this cost-effectiveness ratio is also substantially lower than empirically derived willingness-to-pay thresholds for PCI patients in the U.S. (25). The relative attractiveness of PES is also corroborated by our cost-utility analysis, which showed that for the overall TAXUS-IV population, the cost-utility ratio for PES implantation was <$50,000/QALY gained—a commonly cited benchmark for the U.S. health care system (26).

**Comparison with previous studies.** The only previous study to examine the cost effectiveness of DES in the U.S. health care system was performed alongside the SIRIUS (Sirolimus-Eluting Balloon Expandable Stent in the Treatment of Patients with De Novo Native Coronary Lesions) trial (5). In that study, use of SES compared with BMS was associated with a net 1-year cost of ~$300 per patient and a reduction of 19 revascularization events per 100 patients treated, with an incremental cost-effectiveness ratio of $1,650 per repeat revascularization avoided and $27,540/QALY gained. It is important to recognize that even though both the TAXUS-IV and the SIRIUS trials compared DES with an approved BMS, the ability to perform meaningful indirect economic comparisons between the 2 trials is limited. In particular, the BMS used in each study differed in a number of important characteristics, including stent geometry and strut thickness. Moreover, the 1-year rate of TVR in the control population differed substantially between the 2 studies. Thus, it is not possible to directly compare the cost effectiveness of these alternative DES designs based on the current data. Ongoing studies involving direct comparisons of alternative DES systems may be helpful in this regard.

An additional difference between the 2 trials was the duration of dual antiplatelet therapy after stent implantation. In the SIRIUS trial, patients in the DES arm were required to receive 3 months of dual antiplatelet therapy, whereas 6 months of dual antiplatelet therapy were prescribed in the TAXUS-IV trial. In both trials, the excess duration of dual antiplatelet therapy (at a cost of ~$100/month) accounted for nearly all of the net cost of DES placement at 1 year. Thus, if one were to assume that all patients would receive 1 year of dual antiplatelet therapy after stent placement (as supported by the CREDO [Clopidogrel for the Reduction of Events During Observation] trial) (27), use of both SES and PES would have been nearly cost neutral in their respective trials. On the other hand, if one assumes that standard practice is to prescribe only 1 month of dual antiplatelet therapy after BMS implantation, the shorter duration of therapy prescribed with the SES may represent a relative economic advantage of this platform.

In addition to extending our previous findings regarding the cost effectiveness of SES to a second DES system, the current study adds to our understanding of the optimal application of these devices in several ways. Stratified analyses of the overall trial population show that implantation of PES is cost saving for several patient subgroups,

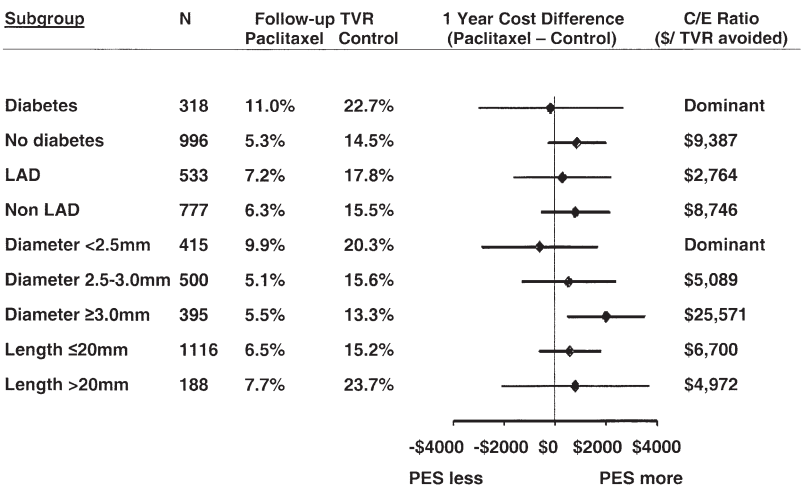


**Figure 3.** Subgroup analyses of rates of target vessel revascularization (TVR) and 1-year medical care cost differences between the paclitaxel and control stent groups along with the associated cost-effectiveness ratios for paclitaxel-eluting stent (PES) versus bare-metal stent implantation. Dominant indicates those subgroups for which PES implantation was economically dominant (i.e., lower overall costs and better clinical outcomes). LAD = left anterior descending coronary artery.

including patients with diabetes and lesions located in vessels with a reference diameter <2.5 mm. These findings are not surprising given that both smaller reference vessel diameters and diabetes are associated with higher rates of clinical and angiographic restenosis after BMS implantation (28). On the other hand, for patients with reference vessel diameters ≥3.0 mm, our analysis suggests that even though use of PES results in significant reductions in restenosis, at current stent prices the cost-effectiveness ratio exceeds $20,000 per repeat revascularization avoided. Thus, in health care systems with constrained resources, use of PES for such patients might be considered economically unattractive at current stent prices.

Finally and most importantly, this study is the first to specifically evaluate the cost effectiveness of DES among patients undergoing clinical follow-up alone. Several previous studies have shown that rates of repeat revascularization are increased substantially when patients are subject to mandatory angiographic follow-up because of the "oculostenotic reflex" (9,10). Thus, economic analyses derived from clinical trials that incorporate angiographic follow-up in a high proportion of patients may overestimate both the clinical and the economic benefits of DES compared with those that would be observed in routine clinical practice. In the TAXUS-IV trial, analysis of the prespecified subgroup assigned to clinical follow-up alone showed a net 1-year cost of $97 per patient for the PES group with a highly favorable incremental cost-effectiveness ratio of <$1,000 per TVR avoided. It is interesting to note that the 1-year follow-up cost offset with PES in the nonangiographic cohort was greater than that observed in the angiographic cohort ($1,894 per patient vs. $1,104 per patient). It is possible that these somewhat counterintuitive results reflect the fact that repeat revascularization procedures in the nonangiographic cohort were more challenging and resource-intensive compared with those procedures driven by angiographic findings alone. Regardless of the underlying mechanism, the fact that the cost-effectiveness ratio remained <$10,000 per TVR avoided in more than 90% of bootstrap replicates provides substantial confidence in the cost effectiveness of PES for real-world PCI patients similar to the TAXUS-IV trial population.

**Study limitations.** Our study has several important limitations. Given the multicenter nature of the trial, it was not possible to obtain cost data from the internal accounting systems of each participating center. Consequently, our estimates of catheterization laboratory costs (other than devices and medications) were based on data from a single hospital. We do not believe that this approach detracts substantially from our findings, however, because most procedural costs were estimated using national average price-weights, and the remainder accounted for only 13% of total costs at 1 year. In addition, we only collected detailed billing data on a subset of study participants. It is unlikely that we substantially underestimated hospital costs for the other participants, however, because our imputation model accounted for both ICU and non-ICU length of stay—the major determinants of hospital cost.

As with any clinical trial, the results of our study should be considered specific to the trial population and may not be applicable to the full spectrum of PCI patients. In particular, our findings cannot be extrapolated directly to populations for whom the incremental cost of DES would be substantially greater than in the TAXUS-IV trial, such as very long lesions or patients undergoing multivessel revascularization. Moreover, our analysis was limited to a 1-year follow-up period. If future studies show a significant excess of late events (either stent thrombosis or restenosis) with PES, the cost effectiveness of PES would be less favorable than suggested by our current data. Finally, quality of life data were not directly available in this trial. As a result, our cost-utility analysis was based on extrapolated utility weights from U.S. stent patients enrolled in a previous study (17). In this regard, it is reassuring

that our utility weights for patients with and without clinical restenosis were comparable to those recently reported from a similar analysis of Canadian patients (29).

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