Cost-Effectiveness of Drug-Eluting Stents Versus Bare Metal Stents in Clinical Practice

Pascha E. Schafer, MD; Matthew T. Sacrinty, MPH; David J. Cohen, MD, MSc; Michael A. Kutcher, MD; Sanjay K. Gandhi, MD; Renato M. Santos, MD; William C. Little, MD; Robert J. Applegate, MD

Background—Drug-eluting stents (DES) reduce the need for repeat target revascularization (TVR) compared with bare metal stents (BMS) but are more costly. The objective was to evaluate the cost-effectiveness of DES versus BMS.

Methods and Results—We evaluated clinical outcomes and costs of care over 3 years in 1147 undergoing BMS before the availability of DES and 1247 DES patients at Wake Forest University Baptist Medical Center from 2002 to 2005. Costs for index stenting, TVR, and clopidogrel use were assessed. The 2 groups were well matched for baseline characteristics. Index stenting costs were $1846 higher per patient for DES versus BMS ($1737 more to $1950 more). At 3 years, absolute TVR rates were 15.2 per 100 DES patients and 24.1 per 100 BMS patients, and as a result, cumulative TVR-related costs were $2065 less per patient for DES versus BMS ($3001 less to $1134 less). Including the cost of clopidogrel, the incremental cost-effectiveness ratio per TVR avoided with DES was $4731 through 1 year, $4703 through 2 years, and $6379 through 3 years.

Conclusions—At 3 years, the higher index cost of DES versus BMS was completely offset by lower TVR-related costs. However, because of extended clopidogrel use for DES, the incremental cost-effectiveness ratio per TVR avoided ranged from $4703 to $6379 over 3 years. These unadjusted observational findings provide support for the continued use of DES in routine practice but highlight the important impact of prolonged dual antiplatelet use on the cost-effectiveness of this technology. (Circ Cardiovasc Qual Outcomes. 2011;4:408-415.)

Key Words: health economics ■ stent therapy ■ dual antiplatelet therapy ■ clinical outcomes ■ cost effectiveness
most of the DES used in the study: sirolimus-eluting stents, n=973; paclitaxel-eluting stents, n=262; and both, n=12. Previous studies have demonstrated equivalent TVR outcomes between sirolimus- and paclitaxel-eluting stents; therefore we combined outcomes of both drug-eluting stents in our economic analysis. The study was approved by the Institutional Review Board of Wake Forest University Baptist Medical Center (WFUBMC). These patients were included in previous reports from our aggregate PCI experience.

WHAT IS KNOWN

- Drug-eluting stents are more effective in reducing restenosis than bare metal stents but cost more than bare metal stents.

WHAT THE STUDY ADDS

- This study found that drug-eluting stents reduced the need for target vessel revascularization compared with bare metal stents over the 3-year study period, with an absolute reduction in target vessel revascularization of 8.8 events per 100 patients.
- The increased initial costs of drug-eluting stents compared with bare metal stents were offset by savings from fewer repeat procedures at 3 years.
- The 3-year incremental cost-effectiveness ratios was $6379 per target vessel revascularization avoided, as the result of prolonged use of clopidogrel.

Index Stenting and Clinical Follow-Up

PCI was performed according to standard techniques. Anticoagulation during PCI was accomplished with unfractionated heparin or bivalirudin per standard protocol. Patients received glycoprotein IIb/IIIa receptor inhibition with abciximab or eptifibatide at the discretion of the interventionalist.

Patients also received clopidogrel (300 to 600 mg as a loading dose, given before or immediately after the procedure, followed by 75 mg/d). Clopidogrel was given for a minimum of 1 month in patients who did not have follow-up with either chart or Social Security Death Index review. Events reported to have occurred at 30 days, with complete records from the outside institution. All follow-up was obtained in an additional 18% of patients who did not have follow-up with either chart or Social Security Death Index review. Events reported to have occurred at outside institutions were reviewed and confirmed by obtaining records from the outside institution. All follow-up was obtained retrospectively and was censored at 3 years±30 days, with complete 3-year follow-up available in 96% of BMS patients and 91% of DES patients.

Clinical outcomes were defined per recent guidelines. TVR was defined as the need for either surgical or percutaneous revascularization of the target vessel and included patients who presented with myocardial infarction and stent thrombosis. Any TVR in the follow-up period was included in the cost-estimation analysis but was censored at the first occurrence for the calculation of cumulative incidence rates. Stent thrombosis was defined as presentation with acute coronary syndrome and definite angiographic or pathological evidence of stent thrombosis. Nonfatal myocardial infarction was defined as ischemic symptoms and an elevation of creatine kinase-MB or troponin I above the upper limit of normal, with or without ST elevation or development of Q waves.

Cost Estimation

Costs were assessed from a health care system perspective and are reported in 2005 US dollars. Previous studies have demonstrated that differences in index procedural costs for PCI with comparable BMS and DES cohorts are driven entirely by the cost of stent acquisition. Therefore, cost of the index procedure was estimated by using the actual costs for each stent type in 2005 (bare metal=$975, sirolimus-eluting=$2100, and paclitaxel-eluting=$2550) multiplied by the number of stents placed per procedure. This method of procedural cost estimation accounted for differences in stent acquisition costs only and did not include other hospitalization costs related to the index procedure. The total cost of each follow-up TVR hospitalization was obtained from the WFUBMC accounting databases and converted to 2005 dollars, using the Medical Care component of the Consumer Price Index. Physician fees for TVR hospitalizations were estimated using the NC Medicare Physician Fee Schedule for 2005. To accurately measure the total duration of clopidogrel therapy during the 3-year study period, we reviewed patient medical records to estimate the initial duration of clopidogrel use after index PCI and included additional duration if therapy was restarted at any time during the study period. Using this methodology, actual clopidogrel duration was estimated for 91% of the study patients. For the remaining patients, none of whom had repeat hospitalizations, we assumed that clopidogrel was used for the recommended duration of the time of the study (BMS, 1 month; sirolimus-eluting, 3 months; and paclitaxel-eluting, 6 months) or until death if death occurred before the end of the recommended duration. The cost of clopidogrel therapy was estimated using the average wholesale price of clopidogrel for 2005 ($4.67 per day).

Statistical Analysis

Categorical data are reported as percentages, and continuous data are reported as both means and medians. Variables were compared using the chi-squared or Fisher exact testing where appropriate for categorical variables and Student t test for continuous variables, including cost. Because costs were non-normally distributed, confidence intervals were estimated using the bootstrap method with 1000 repeat samplings of the study population. Consistent with previous analysis in this field, the major benefit observed with drug-eluting stenting compared with bare metal stenting was a reduction in the need for TVR. Therefore, the primary end point for the cost-effectiveness analysis was the incremental cost per repeat TVR avoided over the 3-year study period, in which TVR was considered a surrogate for the incidence of myocardial infarction and death associated with repeat revascularization.

This choice in end points included only those costs and effects that were directly attributable to the type of stent placed at the index PCI. Incremental cost-effectiveness ratios (ICERs) were estimated at yearly intervals by dividing mean cost of DES minus BMS by the absolute number of TVR events avoided per 100 patients at each time point with DES. For the purposes of calculating ICERs past 1 year, costs and effects were discounted at a rate of 3% per annum consistent with current guidelines. To estimate uncertainty surrounding cost estimates, we evaluated the distribution of ICERs estimated from 1000 bootstrap samples of the study population and expressed this uncertainty in terms of a cost-effectiveness acceptability curve.

We also performed a secondary economic analysis using the standard metric of cost per quality-adjusted life-year (QALY) gained. Because quality of life was not assessed directly in this study, quality-adjusted life expectancy was estimated on the basis of previous data from the Stent-PAMI (Stent Primary Angioplasty in Myocardial Infarction) trial. In that study, the EuroQol health status instrument was administered to 771 patients at 1, 6, and 12...
Table 1. Baseline Clinical and Procedural Characteristics by Stent Type

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>DES (n=1247)</th>
<th>BMS (n=1147)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male sex</td>
<td>65%</td>
<td>66%</td>
<td>0.581</td>
</tr>
<tr>
<td>Age, y</td>
<td>63±12</td>
<td>64±12</td>
<td>0.165</td>
</tr>
<tr>
<td>Heart failure class III or IV</td>
<td>16%</td>
<td>15%</td>
<td>0.539</td>
</tr>
<tr>
<td>Current smoker</td>
<td>34%</td>
<td>31%</td>
<td>0.153</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>32%</td>
<td>32%</td>
<td>0.628</td>
</tr>
<tr>
<td>Hypertension</td>
<td>78%</td>
<td>76%</td>
<td>0.304</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>11%</td>
<td>12%</td>
<td>0.442</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>9%</td>
<td>11%</td>
<td>0.330</td>
</tr>
<tr>
<td>History of renal failure</td>
<td>6%</td>
<td>5%</td>
<td>0.224</td>
</tr>
<tr>
<td>Left ventricular ejection fraction, %</td>
<td>50±11</td>
<td>48±16</td>
<td>0.247</td>
</tr>
</tbody>
</table>

Results

Baseline Characteristics

For the overall study population, baseline clinical characteristics were similar between the DES and BMS groups (Table 1), with 72% of DES and 70% of BMS patients presenting with acute coronary syndrome (P=0.20). Comorbidities including heart failure, diabetes, and history of renal failure were similar by stent type. Procedural characteristics such as the number of vessels per lesions stented and number of stents placed were similar by stent type (P=NS for all comparisons), with the exception that mean DES length was longer than mean BMS length (24.8±8.0 mm versus 20.1±9.9 mm, P<0.001). In-laboratory use of bivalirudin during the index PCI was slightly higher with DES compared with BMS (13% versus 9%, P=0.002). The average length of stay was similar, 3.6 days for DES and 3.3 days for BMS (P=0.95).

Clinical Outcomes

At the 1-year landmark, clopidogrel use was 47% with DES and 29% with BMS (P<0.001); at 2 years, these values were 38% with DES and 26% with BMS (P<0.001) and at 3 years, 31% with DES and 25% with BMS (P<0.001). The cumulative mean (median) clopidogrel duration over the entire study period was 499 (273) days for DES and 329 (40) days for BMS (P<0.001). Clopidogrel was in use during the first year for 236 (215) days for DES and 139 (31) days for BMS (P<0.001); during the second year for 143 (0) days for DES and 99 (0) days for BMS (P<0.001); and during the third year for 119 (0) days DES and 91 (0) days for BMS (P<0.001). Statin therapy during follow-up was similar, with 85% of DES and BMS patients using 1 or more statins at the 3-year landmark (P=0.702). Over the 3-year follow-up period, DES was associated with reductions in adverse clinical outcomes compared with BMS (Table 2). In particular, DES was associated with a 32% reduction in the need for TVR (12.4% DES versus 18.3% BMS, P<0.001) and a 19% reduction in death from all causes (10.8% DES versus 13.3% BMS, P=0.052). The absolute difference in TVR events observed with DES was 8.8 events per 100 patients treated compared with BMS. The incidence of stent thrombosis was similar at 3 years, 1.3% DES versus 1.0% BMS, P=0.45.

Cost-Effectiveness Analysis

Index stenting costs were $1846 higher per patient with DES compared with BMS (95% confidence interval [CI], $1737 more to $1950 more) (Table 3). Mean cumulative follow-up costs, including hospitalization for TVR and clopidogrel therapy costs, were $5350 with DES and $6625 with BMS, a difference of $1275 less for DES (95% CI, $2288 less to $281 less) (Figure 1). The mean (median) cost of percutaneous revascularization was $23 555 ($17 751), whereas the mean (median) cost of surgical revascularization was $45 312 ($40 011). As a result of the absolute reduction in TVR events observed with DES compared with BMS, the majority of which were hospitalizations for percutaneous revascularization, mean TVR-related costs over 3 years of follow-up were $2065 less with DES compared with BMS (95% CI, $3001 less to $1134 less). The 3-year aggregate mean cost associated with DES was $8741 and for BMS was $8171, a difference of $570 higher for DES compared with BMS (95% CI, $458 less to $1542 more). Incremental cost-effectiveness ratios were $4731 per TVR avoided through 1 year, $4703 per TVR avoided through 2 years, and $6379 per TVR avoided through 3 years. Bootstrap resampling demonstrated that ICERs remained <$10 000 in 82.0% of simulations through 1 year, 77.2% of simulations through 2 years, and 67.4% of simulations through 3 years (Figure 2). We performed a subgroup analysis of single-lesion procedures to determine the effect of length and diameter of the
stented lesion on the cumulative 3-year cost-effectiveness of DES (Figure 3). Within all single-lesion procedures, we observed a 3-year ICER of $2716 per TVR avoided with DES and a cost utility ratio of $37 973 per QALY gained with DES. Among the length and diameter subcategories, DES was economically dominant in lesions ≥18 mm in length and in lesions ≥2.5 mm or ≥3.0 mm in diameter, whereas the 3-year ICER was $13 783 per TVR avoided for lesions ≥18 mm in length and $9272 per TVR avoided for lesions 2.6 to 3.0 mm in diameter.

We also conducted a sensitivity analysis examining the effect of varying durations of clopidogrel use and absolute stent cost differences compared with 2005 costs between DES and BMS on the ICER through 3 years (Table 4). Altering both the potential duration of clopidogrel usage, based on historical and current recommendations, and the absolute difference in stenting costs had a significant impact on the ICER through 3 years, with resulting values ranging from a high of $20 752 per TVR avoided to economic dominance (ie, lower costs and lower TVR incidence with DES).

Our secondary analysis of the effects of TVR on quality-adjusted life expectancy showed incremental cost-utility ratios of $65 052 per QALY gained through 1 year, $63 426 per QALY gained through 2 years, and $87 705 per QALY gained through 3 years. Bootstrap resampling demonstrated that cost-utility ratios remained ≥$50 000 per QALY gained in 39.2% of simulations through 1 year, 41.8% of simulations through 2 years, and 36.0% of simulations through 3 years; these probabilities increased to 65.8%, 65.0%, and 55.4% when a threshold of $100 000 per QALY gained was considered.

Table 3. Cumulative 3-Year Costs

<table>
<thead>
<tr>
<th>Variable</th>
<th>DES (n=1247)</th>
<th>BMS (n=1147)</th>
<th>Difference (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Index stenting cost, $</td>
<td>3392±1732</td>
<td>1546±921</td>
<td>1846 (1737 to 1950)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Follow-up costs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Repeat revascularization cost, $</td>
<td>3021±10075</td>
<td>5087±12994</td>
<td>−2065 (−3001 to −1134)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Clopidogrel therapy cost, $</td>
<td>2328±2017</td>
<td>1538±2038</td>
<td>790 (626 to 946)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Aggregate 3-y cost, $</td>
<td>8741±10890</td>
<td>8171±13675</td>
<td>570 (−458 to 1542)</td>
<td>0.262</td>
</tr>
</tbody>
</table>

Values in brackets are medians.

Figure 1. Cumulative revascularization costs. A, Cumulative clopidogrel therapy costs; B, cumulative follow-up costs; and C, revascularization and clopidogrel costs.
This unadjusted observational study with 3-year landmark follow-up examined the cost-effectiveness of DES versus BMS in terms of avoidance of the need for repeat revascularization procedures in a "real-world" setting. Our analysis assessed actual differences in baseline stent costs, costs of hospitalization (including associated physician fees) at the time of any repeat procedure, and costs for actual clopidogrel usage. As expected, DES reduced the need for TVR compared with BMS over the 3-year study period, with an absolute reduction in TVR of 8.8 events per 100 patients. As a result, we observed cost savings of $2065 per patient with DES over the 3-year follow-up period, which completely offset the $1846 initial excess stent cost. However, we also observed a $790 excess cost of extended clopidogrel therapy associated with DES implantation, resulting in ICERs for DES compared with BMS of $4731 per TVR avoided through 1 year and $6379 per TVR avoided through 3 years. These observations provide some of the first insights into the cost-effectiveness of DES compared with BMS in routine clinical practice and highlight the importance of prolonged dual antiplatelet therapy use in this setting.

Previous studies examining the cost-effectiveness of DES versus BMS have been based on clinical outcomes data from Food and Drug Administration–approved clinical trials restricted to “on-label” use of DES.4,5 Cost-effectiveness analysis of paclitaxel-eluting stents, based on clinical results from the TAXUS-IV trial, demonstrated an ICER of $4678 per TVR event avoided at 1 year,4 whereas a cost-effectiveness analysis of sirolimus-eluting stents, based on clinical results from the SIRIUS trial, demonstrated an ICER of $1650 per TVR avoided at 1 year. The ICER of DES versus BMS in our study at 1 year was $4731 and comparable to these randomized trials despite our inclusion of a broader range of patient and lesion subgroups than were evaluated in these other studies. Our 1-year cost-utility ratio calculated to only include the effects of TVR was $65 052 per QALY gained, which was higher than those estimated in TAXUS-IV ($47 798/QALY gained) and SIRIUS ($27 540/QALY gained). Several key differences between the randomized trials and our current study that could have accounted for the observed differences in cost utility ratios warrant further discussion. First, 89% of the BMS control cohort in our current study consisted of newer generation, thin-strutted BMS in contrast to the older-generation, thick-strut BX Velocity stent used in SIRIUS, which could have resulted in a lower absolute TVR difference for DES compared with BMS in our study.21,22 Additionally, the lack of routine angiographic follow-up in our study probably resulted in lower absolute differences in TVR between DES and BMS compared with the SIRIUS and TAXUS-IV trials, in which a majority of the patients underwent trial-mandated angiographic follow-up.23 Finally, both the SIRIUS and TAXUS-IV trials had inclusion criteria focusing on patients who were at increased risk of restenosis (eg, small reference vessel diameter), which may have further accentuated cost and TVR-effect differences between DES and BMS compared with our “all-comers” study population. Previous economic analysis of coronary interventions have indicated that quality-adjusted life expectancy may not fully capture the transient benefits of a therapy associated with significantly reduced risk of restenosis and the patient’s willingness to pay for this benefit.24 Thus, our analysis should be reassuring that DES are cost-effective compared with BMS in routine care.

There are several factors that may influence the cost-effectiveness of DES compared with BMS. As the acquisition cost of DES relative to BMS may vary significantly among
institutions, we calculated ICERs under alternative assumptions of the absolute differences in stent costs. Compared with the $1846 average excess procedural costs of DES versus BMS in our study, reducing this difference by $500 would have decreased the ICER in our study by more than 50%. Thus, stent costs have a significant impact on the cost-effectiveness. We also observed differences in DES cost-effectiveness within lesion length and diameter stratifications. Within all single-lesion procedures, DES was most economically attractive compared with BMS in longer-lesion lengths (>18 mm) and small (<2.5 mm) or large (>3.0 mm) lesion diameter. An interesting observation from this study is that even though savings resulting from avoidance of repeat revascularization procedures fully offset the higher initial cost of DES, the net 3-year cost of DES treatment remained higher than that for BMS because of the greater duration of dual antiplatelet therapy prescribed in routine practice. Whether such extended therapy beyond current guidelines is warranted is unknown. Nonetheless, our study demonstrates that such prolonged therapy has the potential to substantially alter the cost-effectiveness of DES therapy. For example, when we assumed dual antiplatelet therapy duration equal to that recommended at the time of our study (2004), the ICER for DES decreased from $6379 to only $1746 per TVR event avoided. Conversely, assuming all patients in our study took clopidogrel for the minimum current recommendations (1 year for DES, 1 month for BMS), the ICER for DES increased to $15 070 per TVR event avoided. Because a majority of our patients received stent therapy as part of an acute coronary syndrome, guidelines for dual antiplatelet therapy in these patients, particularly for those receiving BMS, may be of greater duration than recommended for stents in elective patients. Thus, a contemporary estimate of the ICER for DES probably falls somewhere in between our actual results and those assumed under current clopidogrel therapy guidelines. As cost-effectiveness of stent therapy is scrutinized more closely in the coming years, the issue of concomitant drug therapy must be addressed in a consistent manner.

The use of cost-effectiveness information such as the observations from this study will depend on the perspective one takes. From a societal perspective, a treatment strategy (ie, DES) that improves patient outcomes by reducing morbid events (ie, TVR) at a cost less than $10 000 per event avoided has in general viewed favorably. For an individual hospital, the higher upfront costs of DES, however, may not be fully covered by reimbursement rates, especially if multiple stents are required during the procedure. Use of this kind of data may be most beneficial in identifying specific patient and lesion subsets with either very favorable, or unfavorable, incremental cost-effectiveness ratios. For example, Cohen et al observed that treatment of vessels <2.5 mm in diameter with sirolimus-eluting stents compared with BMS was associated with a dominant ICER, whereas Bakhai et al observed that treatment of vessels ≥3.0 mm with PES compared with BMS increased the ICER from $4678 overall to $25 571 per TVR avoided. As cost assessment of therapies become more commonplace, subgroup analyses such as these probably will become more common if not required by payors/participants in health care.

**Limitations**

This economic analysis was conducted from a health care system perspective at a single US institution and therefore
may not accurately reflect the cost-effectiveness profile of DES compared with BMS in other settings. We included only physician fees associated with percutaneous or surgical revascularization specifically and did not include other professional costs such as anesthesia costs associated with surgical procedures or daily hospital care, which may have resulted in a small bias against DES. Additionally, we used unadjusted outcomes instead of adjusted outcomes, although the 2 populations were well matched with respect to baseline clinical and angiographic characteristics. However, unmeasured differences in concomitant medical therapy between the consecutive DES and BMS cohorts could have accounted for some of the observed differences in outcomes. Finally, quality-of-life data were not directly available in this study; therefore, our cost-utility analysis was based on extrapolated utility weights from US stent patients enrolled in a previous study.

**Conclusion**

The present study is one of the first to examine cost-effectiveness of DES compared with BMS in routine clinical practice. At 1 year, the ICER was $4731 per TVR event avoided, which was only slightly higher than that observed in a similar analysis from the TAXUS-IV trial, despite the presence of off-label characteristics in >70% of our patients. At 3 years, the higher cost of DES at the index procedure was completely offset by lower costs of TVR, yet the 3-year ICER was $6379 per TVR avoided as the result of prolonged use of clopidogrel. These findings provide support for the continued use of DES in today’s health care environment and also demonstrate the importance of determining the optimal duration of dual antiplatelet therapy after DES implantation to more accurately define the long-term value of this technology.

**Disclosures**

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**References**


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