Economic evaluation of drug eluting stents

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Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
Two types of drug-eluting stent (DES) were examined. These were sirolimus-eluting stents and paclitaxel-eluting stents.

Type of intervention
Secondary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised a hypothetical cohort of patients with coronary vessel disease.

Setting
The setting was a tertiary care hospital. The economic study was carried out in Canada.

Dates to which data relate
The effectiveness evidence came from a study published in 2004. No dates for resource consumption were explicitly reported. The costs were presented in 2002 to 2003 values.

Source of effectiveness data
The effectiveness evidence was derived from a synthesis of completed studies and authors' opinions.

Modelling
A decision analytic model was constructed to simulate the clinical outcomes and resource consumption of a patient population treated with DES (sirolimus, paclitaxel or combined) or BMS implantation. The model was based on clinical trial data and commonly accepted treatment approaches for coronary heart disease. Patients undergoing a percutaneous coronary intervention could have several clinical outcomes. Specifically, no event, myocardial infarction (MI), TLR or death. If in-stent restenosis occurred and was focal, it was treated using a repeat percutaneous coronary intervention procedure, with or without the use of a cutting balloon or an additional stent. If the pattern of in-stent restenosis was more diffuse, then brachytherapy, implantation of a DES inside the original stent, or coronary artery bypass graft surgery were treatment options. The clinical pathway was confirmed through interviews with three cardiologists. The time horizon of the model was one year. A simplified version of the model was reported.

Outcomes assessed in the review
The outcomes estimated from the literature were the rates of death, MI, TLR, major adverse cardiac events (MACE) and adverse events with DES and BMS.
Study designs and other criteria for inclusion in the review
The clinical data were derived from a published systematic review of 11 clinical trials (1998 - 2003). Extensive information on the baseline characteristics of the primary trials was provided. The authors carried out a further search but the results were identical to those of the published systematic review.

Sources searched to identify primary studies
The authors search was conducted using MEDLINE, Google and the TCTMD websites.

Criteria used to ensure the validity of primary studies
The use of clinical trials should ensure a high internal validity.

Methods used to judge relevance and validity, and for extracting data
Not stated.

Number of primary studies included
A single study (pooling 11 trials) provided the data.

Methods of combining primary studies
The results of each trial were pooled using a meta-analysis based on a hierarchical Bayesian random-effects model, with pre-specified stratification according to drug and carrier type.

Investigation of differences between primary studies
Not reported.

Results of the review
When pooled estimates of sirolimus trials were considered:

the rate of death was 1% with DES and 0.7% with BMS;
the rates of MI (Q wave and non-Q wave) were 3.2% in both groups;
the rate of TLR was 3.5% with DES and 18.5% with BMS; and
the rate of MACE was 6.8% with DES and 21.0% with BMS.

When pooled estimates of paclitaxel trials were considered:

the rate of death was 0.9% with DES and 1.0% with BMS;
the rate of MI (Q wave and non-Q wave) was 3.3% with DES and 4.0% with BMS;
the rate of TLR was 3.3% with DES and 12.2% with BMS; and
the rate of MACE was 8.7% with DES and 16.7% with BMS.

When pooled estimates of sirolimus and paclitaxel trials were considered:

the rate of death was 0.9% with DES and 0.9% with BMS;
the rate of MI (Q wave and non-Q wave) was 2.7% with DES and 2.9% with BMS;
the rate of TLR was 4.8% with DES and 14.2% with BMS; and
the rate of MACE was 8.5% with DES and 17.4% with BMS.
Thus, the results from the meta-analysis showed that there were no differences in MI or death rates between BMS and DES, but the use of DES was associated with significantly less TLR than BMS.
In terms of adverse events, when pooled estimates of sirolimus trials were considered:
the rates of stent thrombosis were 0.6% for both DES and BSM;
the rate of edge restenosis was 3.6% with DES and 1.3% with BSM; and
the rate of late incomplete stent apposition was 13.3% with DES and 1.9% with BSM.
When pooled estimates of paclitaxel trials were considered:
the rate of stent thrombosis was 0.7% with DES and 0.5% with BSM;
the rate of edge restenosis was 2.9% with DES and 2.5% with BSM; and
the rate of late incomplete stent apposition was 8.6% with DES and 6.9% with BSM.
When pooled estimates of sirolimus and paclitaxel trials were considered:
the rate of stent thrombosis was 0.7% with DES and 0.5% with BSM;
the rate of edge restenosis was 3.0% with DES and 1.9% with BSM; and
the rate of late incomplete stent apposition was 8.5% with DES and 5.1% with BMS.

Methods used to derive estimates of effectiveness
The authors made some assumptions about patient management.

Estimates of effectiveness and key assumptions
Stent thrombosis always results in acute MI. The consequences of DES thrombosis are the same as those of BMS thrombosis. Edge restenosis has the same clinical features as in-stent restenosis. Only patients with in-stent restenosis will undergo another revascularisation procedure. A stent thrombosis results in another percutaneous transluminal coronary angiography procedure. The average number of stents (1.5) implanted per patient was the same for a DES and a BMS. Only the paclitaxel polymer DES was examined since the non-polymer version was unavailable.

Measure of benefits used in the economic analysis
The summary benefit measure used in was the number of TLRs avoided.

Direct costs
The cost analysis was undertaken from two different perspectives. One perspective was that of a tertiary care hospital, the other was that of a provincial ministry of health. The analysis from a hospital perspective included acquisition costs for stents and drugs, costs for hospitalisation (including the costs of repeat vascularisation) and costs for rehabilitation. The analysis from a provincial payer perspective included all these costs, plus physician fees and charges for laboratory and diagnostic testing. The unit costs were presented separately from the quantities of resources used. Resource use was
based on the opinions of three experts (two interventional cardiologists and one non-interventional cardiologist) who perform angioplasty and stent implantation at health centres across Canada. Primary cost sources included stent manufacturers, the SWCHSC's drug formulary, Ontario Drug Benefit formulary, the Ontario Case Costing Initiative and communication with clinical experts. No discounting was applied because of the short time horizon of the analysis. The price year was 2002/2003.

**Statistical analysis of costs**
The costs were treated deterministically in the base-case.

**Indirect Costs**
The indirect costs were not considered.

**Currency**
Canadian dollars (Can$).

**Sensitivity analysis**
A simple univariate sensitivity analysis was conducted by varying the cost of DES from $608 (the cost of BMS) to the original DES list price of $3,500. The threshold value for DES to be cost-neutral was estimated. Further, a probabilistic sensitivity analysis was undertaken by assigning stochastic distributions to all model inputs and using 5,000 replications. Normal distributions were assigned to cost parameters, while beta and dirichlet distributions were used for probabilities of events. Cost-effectiveness acceptability curves were generated.

**Estimated benefits used in the economic analysis**
Patients receiving DES had a significantly lower rate of TLR than those in the BMS group.

The absolute risk reduction with respect to BMS was:

- 12.5% for sirolimus when data from the SIRIUS trial were used, and 15% when pooled data were used; and
- 8.3% for paclitaxel when data from the TAXUS IV trial were used, and 8.9% when pooled data were used.

**Cost results**
From the hospital perspective, the expected costs during one year ranged from Can$4,350 to Can$4,430 per patient for DES and from Can$1,939 to Can$2,505 for the BMS group, depending on the data used in the model.

From the provincial perspective, the expected costs per patient during one year ranged from Can$4,702 to Can$4,797 for DES and from Can$2,404 to Can$3,072 for the BMS group.

**Synthesis of costs and benefits**
Incremental cost-effectiveness ratios (ICERs; i.e. the cost per TLR avoided) were calculated to combine the costs and benefits of the alternative strategies examined in the study.

Using the hospital perspective, the ICER ranged from Can$12,527 to Can$29,048.

Using the provincial perspective, the ICER ranged from Can$11,133 to Can$27,687.

For sirolimus, there would need to be a Can$750 difference between BMS and DES acquisition costs to obtain an ICER of Can$5,000 per TLR. At a willingness to pay of Can$20,000 per TLR avoided, the difference in acquisition cost could increase to Can$3,000. In contrast, for paclitaxel, there would need to be a Can$445 difference between BMS.
and DES acquisition costs to obtain an ICER of Can$5,000 per TLR. At a willingness to pay of Can$20,000 per TLR avoided, the difference in acquisition cost was Can$1,780.

The probabilistic sensitivity analysis showed that DES were more costly, with an expected incremental cost of Can$1,848 (95% credible interval: 510 - 5,278) and an absolute reduction in TLR of 9.4% (95% credible interval: 7.8 - 11.0). Thus, DES were more costly in 99.94% of replications and led to a reduction in TLRs in 100% of replications. The incremental cost per TLR avoided with DES was Can$19,640 (95% credible interval: 5,177 - 57,420).

The cost-effectiveness acceptability curve indicated that, at a value of Can$50,000 for each TLR avoided, the probability that DES is cost-effective was 93.56%. For values of less than Can$1,000 for each TLR avoided, the probability that DES is cost-effective was less than 10%. However, there is no commonly accepted value for a TLR avoided.

The budget impact analysis showed that, if BMS were replaced by DES in patients at high risk for restenosis (estimated to be 40% of all coronary heart disease patients), the annual budget impact for Canada would be Can$37.9 million, but there would be between 1,169 (8.3%) and 2,113 (15%) fewer revascularisation events.

If DES replaced BMS for all patients who need coronary stents, the budgetary impact would be Can$126.8 million, but there would be between 2,923 (8.3%) and 5,283 (15%) fewer revascularisation events.

**Authors' conclusions**

For hospitals using the paclitaxel drug-eluting stent (DES), the additional cost relative to bare metal stents (BMS) per target lesion revascularisation (TLR) avoided was estimated to be between Can$26,000 and Can$29,000. For the sirolimus DES, it was estimated to be between Can$12,000 and Can$17,000. The corresponding figures from the provincial perspective were Can$25,000 to Can$27,000 for the paclitaxel DES and Can$11,000 to Can$15,000 for the sirolimus DES. However, there is no consensus on an acceptable range of cost per TLR avoided that would be considered cost-effective.

**CRD COMMENTARY - Selection of comparators**

The choice of the comparator (BMS) was appropriate as it reflected the current standard of care in the authors' setting. You should decide whether this is a valid comparator in your own setting.

**Validity of estimate of measure of effectiveness**

The clinical data were derived from a published systematic review of the literature. Extensive information on the baseline characteristics of the primary studies, such as patient demographics, restenosis risk level, lesion length and number of stents implanted, was provided. The validity of the primary estimates was ensured by the inclusion of clinical trials. The method used to combine the primary estimates was reported. Results from two clinical trials (SIRIUS and TAXUS IV) were reported alongside the pooled estimates. Sensitivity analyses were undertaken to address the issue of uncertainty in some data. Assumptions were also made to define some treatment pathways in the decision model. The authors noted that the use of data from trials might limit the applicability of the results of the analysis to a real-world setting, owing to the possible impact of study protocol which might alter typical treatment patterns.

**Validity of estimate of measure of benefit**

The summary benefit measure was specific to the disease considered in the study and would not be comparable with the benefits of other health care interventions. The impact of the technologies examined in the study on quality of life or expected survival was not investigated. The authors stated that, given the lack of statistically significant differences in mortality, life-years were not used as the summary benefit measures. Further, quality-adjusted life-years were difficult to measure.

**Validity of estimate of costs**
The analysis of the costs was carried out satisfactorily. Two perspectives were adopted in the study and it appears that all the relevant categories of costs have been included in the analysis. Extensive information on the unit costs, quantities of resources used, and sources of data was reported, which enhances the possibility of replicating the cost analysis in other settings. The issue of variability in some key cost estimates was explicitly addressed in the sensitivity analysis. Some resource use data were derived using experts' opinions, but alternative values were considered in the sensitivity analysis. The price year (2002 and 2003) was reported, which will facilitate reflation exercises in other settings. A budget impact analysis was also carried out, which might be relevant for decision-makers.

**Other issues**

The authors stated that the use of the "cost per event avoided" limits the possibility of making comparisons with the results of other studies since even other cardiology analyses used the "cost per death avoided". However, comparisons with other studies suggested that the incremental ratio of Can$11,133 to Can$15,192 per TVR avoided for the sirolimus-eluting stent fell within the range of ICERs of other cardiovascular procedures considered to be acceptable by some investigators in the USA. However, the meaning of such a conclusion within the Canadian context was unclear. The results of other cost-effectiveness analyses of DES were reported. The issue of the generalisability of the study results to other settings was implicitly addressed in the sensitivity analysis. However, the authors pointed out that some cost estimates were specific to the context of the study (the hospital or the province), thus caution is required when extrapolating such estimates to other settings. With the use of probabilistic sensitivity analysis, the results were presented as credible ranges of values, which enhance the robustness of the cost-effectiveness ratios. The authors noted that the use of a medium-term time horizon might represent a limitation of the analysis. In fact, it is likely that a longer time-horizon would produce results that were more favourable to the DES because of the avoided future revascularisation events.

**Implications of the study**

The study results showed the cost-effectiveness estimates associated with DES. However, it was highlighted that no consensus on the acceptable cost-effectiveness threshold is available in Canada. The authors stated that the availability of a national cardiovascular database to record procedural data and costs would be helpful given the need for better data collection.

**Source of funding**

CCOHTA is a non-profit organisation funded by the federal, provincial and territorial governments of Canada.

**Bibliographic details**


**Other publications of related interest**


**Indexing Status**

Subject indexing assigned by CRD
MeSH
Canada; Cardiovascular Diseases; Clinical Trials as Topic; Cost-Benefit Analysis; Costs and Cost Analysis; Drug Delivery Systems; Myocardial Revascularization; Paclitaxel; Sirolimus; Stents

AccessionNumber
22005008255

Date bibliographic record published
31/03/2006

Date abstract record published
31/03/2006