Economic evaluation of sirolimus-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
Sirolimus-eluting stents were compared with conventional stents in patients undergoing percutaneous coronary intervention (PCI).

Type of intervention
Treatment.

Economic study type
Cost-utility analysis.

Study population
The study population comprised a cohort of 7,334 patients in the Alberta Provincial Project for Outcome Assessment in Coronary Heart Disease (APPROACH) who underwent PCI with implantation of a bare metal stent.

Setting
The study setting was secondary care. The economic study was carried out in Canada.

Dates to which data relate
The APPROACH database provided information on patients undergoing PCI between 1998 and 2000. The effectiveness data were derived from studies published between 2002 and 2004. The price year was 2002.

Source of effectiveness data
All outcomes considered in the analysis were derived from the APPROACH database, a prospective cohort initiative capturing data for all patients undergoing cardiac catheterisation in Alberta. The efficacy of sirolimus-eluting stents was derived from a meta-analysis of data from four randomised controlled trials (RCTs). The authors also supplemented the data with several assumptions of their own.

Modelling
A Markov model was used to estimate the cost and clinical outcomes after PCI with stenting in 6-month intervals. Patients in the model progressed through five health states after an initial PCI:

- alive with no clinical restenosis (i.e. event free);
- clinical restenosis as determined by the need for a subsequent coronary artery bypass graft (CABG);
- clinical restenosis as determined by the need for repeat PCI;
- repeat catheterisation with no subsequent revascularisation procedure (defined as no PCI or CABG in the ensuing 3
months); and death.

Outcomes assessed in the review
The outcomes derived from the APPROACH database were:

- the death rate within 7 days after an initial PCI;
- the rate of repeat catheterisation for restenosis within 12 months after index PCI with or without the revascularisation procedure;
- the death rate within 6 months;
- the death rate within 30 days after patients received CABG or repeat PCI, and for those without a revascularisation procedure;
- the subsequent mortality rate; and
- the EQ-5D utility score for an event and for an event-free health state.

The outcome derived from the review of the literature was the relative risk of clinical restenosis of sirolimus-eluting stents in comparison with conventional stents.

Study designs and other criteria for inclusion in the review
Only RCTs were included in the review of the literature to determine the efficacy of sirolimus-eluting stents.

Sources searched to identify primary studies
Not reported.

Criteria used to ensure the validity of primary studies
Not reported.

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

Number of primary studies included
The APPROACH database was used to derive all outcome data. In addition, four RCTs were included in the review to determine the efficacy of sirolimus-eluting stents.

Methods of combining primary studies
Data from the four trials were pooled in a meta-analysis using a random-effects model (DerSimonian and Laird).

Investigation of differences between primary studies
Differences between the four trials was tested using a chi-squared statistic, (p=0.38).

Results of the review
The outcomes derived from the APPROACH database were as follows:

the death rate within 7 days after the initial PCI was 1.1%;

the rate of repeat catheterisation for restenosis within 12 months after index PCI was 8.2% with a revascularisation procedure and 12.2% without it;

the death rate within 6 months was 1.4%;

the death rate within 30 days after patients received CABG was 3.1%;

the death rate within 30 days after patients received repeat PCI was 1.4%;

the death rate within 30 days was 1.8% for those without a revascularisation procedure;

the subsequent mortality rate was 1.4%; and

the EQ-5D utility score was 0.77 for an event and 0.85 for an event-free health state.

The relative risk of clinical stenosis when sirolimus-eluting stents were compared with conventional stents was 0.23 (95% confidence interval: 0.2 - 0.3).

Methods used to derive estimates of effectiveness
The authors supplemented data from the APPROACH database and the review of the literature with their own assumptions.

Estimates of effectiveness and key assumptions
The authors assumed that restenosis occurred only in the first year after the initial PCI, and that thereafter patients had an ongoing long-term risk of death. The authors reported that this assumption was consistent with the published literature.

Based on the literature, the authors assumed that 49.5% of repeat catheterisations that were not followed by PCI or CABG would have been avoided if sirolimus-eluting stents had been used.

Measure of benefits used in the economic analysis
The measure of benefits used was the QALYs gained. Health-related quality of life (HRQOL) was estimated in 1,954 patients of the APPROACH 1998-2000 cohort from self-reported EuroQol EQ-5D utility scores obtained 1 year after catheterisation. After year 1, HRQOL was assumed to be the same for patients in all of the health states.

Direct costs
The resource quantities and the costs were not reported separately. The direct costs included in the study were those of the health care service. These were for hospital care, ambulatory care, home care, physician claims and medication costs. The cost data were obtained from Alberta Health and Wellness (the sole payer for hospital and physician care in Alberta) for the 1995-1997 APPROACH cohort and were available to March 2001. Discounting was necessary, as the costs were incurred over the lifetime of the patient, and was appropriately undertaken using an annual rate of 3%. The study reported the incremental costs of sirolimus-eluting stents in comparison with conventional stents. Annual costs were converted to 2002 prices by applying a yearly inflation factor. The price year was 2002.

Statistical analysis of costs
The incremental costs were treated as point estimates (i.e. the data were deterministic).
Indirect Costs
The indirect costs were not included.

Currency
Canadian dollars (Can$).

Sensitivity analysis
To examine the impact of the various assumptions required to run the Markov model, the authors conducted several scenario and sensitivity analyses. The authors varied the 30-day mortality rates associated with second procedures (+/-50%) and the probability of receiving CABG, as opposed to PCI (+/- 25%).

The authors also assessed the effect of varying the rate of clinical restenosis seen with conventional stents to reflect the restenosis rates reported in the individual trials and other clinical settings. They also varied the clinical restenosis rate by up to 100%. The authors conducted a scenario analysis, by evaluating a scenario in which (1) sirolimus-eluting stents would not prevent catheterisations (relative risk 1.0), and (2) all catheterisations were potentially preventable with the use of sirolimus-eluting stents. To assess the assumption that HRQOL was applied for the first year after the initial PCI, the authors evaluated scenarios in which either the HRQOL decrement was sustained or no HRQOL decrement was associated with this procedure. The authors evaluated the impact of varying the cost of sirolimus-eluting stents by 25% or 50%.

Estimated benefits used in the economic analysis
The incremental gain using sirolimus-eluting stents over conventional stents was 0.04 QALYs.

Cost results
The incremental costs of using sirolimus-eluting stents over conventional stents was Can$2,600.

Synthesis of costs and benefits
The costs and benefits were combined using an incremental cost-utility ratio (i.e. the additional cost required for every QALY gained). The cost per QALY gained by implanting a sirolimus-eluting stent rather than a conventional stent was Can$58,721.

The authors found that their analysis was robust to plausible alternative scenarios. However, when they considered a scenario in which sirolimus-eluting stents did not reduce the frequency of repeat catheterisation with no revascularisation procedure, the cost per QALY gained rose to Can$108,340.

The sensitivity analyses showed that the results were sensitive to plausible variations in the cost of stents and the estimate of the effectiveness of sirolimus-eluting stents.

Authors’ conclusions
The use of sirolimus-eluting stents was associated with a cost per quality-adjusted life-year (QALY) similar to, or higher than that of other accepted medical forms of therapy. It was also associated with a significant incremental cost.

CRD COMMENTARY - Selection of comparators
The use of conventional stents as the comparator was justified as these represented current practice in the authors’ setting. You should decide if this represents current practice in your own setting.

Validity of estimate of measure of effectiveness
The authors did not report that a systematic review of the literature was undertaken to identify all relevant research and minimise biases. However, the authors included four RCTs to derive effectiveness estimates, with these being appropriately combined in a meta-analysis. Further, the authors investigated differences between the four trials using appropriate statistical techniques, and found the studies to be homogeneous. The authors also supplemented data from the literature with their own assumptions, which were appropriately tested in the sensitivity analysis.

Validity of estimate of measure of benefit
The estimation of benefits (QALYs) was modelled using a Markov model, which was appropriate. The utility scores were obtained using the EQ-5D and the cohort of patients undertaking the APPROACH study. The use of QALYs facilitates comparisons across different health care programmes.

Validity of estimate of costs
All the categories of cost relevant to the health care service perspective adopted were included in the analysis, as were all relevant cost for each category. The costs and the quantities were not reported separately, which will limit the generalisability of the authors’ results. The costs were derived from 1,812 patients in the APPROACH database who underwent an initial PCI. Appropriate sensitivity analyses of the prices were conducted. Since the costs were incurred over the lifetime of the patient, discounting was necessary and was appropriately performed. The authors inflated the prices using inflation indices. However, it was unclear if the inflation index used was a general one, or a health care one. This is important as health care prices tend to increase faster than general prices. The price year was reported, which will aid any future inflation exercises.

Other issues
The authors did not compare their findings with those from other studies. The issue of generalisability to other settings was addressed in the sensitivity analysis. The authors do not appear to have presented their results selectively, and their conclusions reflected the scope of the analysis. The authors reported no limitations to their study.

Implications of the study
The authors reported that if sirolimus-eluting stents were to be introduced in the absence of health care budget increases, additional resources would be required from other health care sectors, owing to the elevated incremental cost.

Source of funding
Supported by the Canada Institute of Health Research, and the Alberta Heritage Foundation for Medical Research, the Heart and Stroke Foundation of Canada, the Libin Trust Fund, the W Garfield Weston Foundation, the Heart and Stroke Foundation of Alberta, Alberta Health and Wellness, Merck Frosst Canada Ltd., Monsanto Canada Inc-Searle, Eli Lilly Canada Inc., Guidant Corporation, Boston Scientific Ltd, Hoffmann-LaRoche Ltd. and Johnson & Johnson-Cordis Corporation.

Bibliographic details
Shrive F M, Manns B J, Galbraith P D, Knudtson M L, Ghali W A. Economic evaluation of sirolimus-eluting stents. CMAJ: Canadian Medical Association Journal 2005; 172(3): 345-351

PubMedID
15684117

DOI
10.1503/cmaj.1041062

Other publications of related interest
Weaver WD, Reisman MA, Griffin JJ, et al. Optimum percutaneous transluminal coronary angioplasty compared with
routine stent strategy trial (OPUS-1): a randomised trial. Lancet 2000;355:2199-203.

Morie MC, Serruys PW, Sousa JE, et al. A randomized comparison of a sirolimus-eluting stent with a standard stent for coronary revascularization. New England Journal of Medicine 2002;346:1773-80.

Moses JW, Leon MB, Popma JJ, et al. Sirolimus-eluting stents versus standard stents in patients with stenosis in a native coronary artery. New England Journal of Medicine 2003;349:1315-23.

**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Age Factors; Aged; Angioplasty, Balloon, Coronary /economics /mortality; Cohort Studies; Coronary Disease /economics /mortality /therapy; Coronary Restenosis; Cost-Benefit Analysis; Diabetes Complications; Female; Humans; Immunosuppressive Agents /administration & dosage /economics; Male; Markov Chains; Middle Aged; Quality-Adjusted Life Years; Risk; Sirolimus /administration & dosage /economics; Stents /economics

**AccessionNumber**
22005008070

**Date bibliographic record published**
31/10/2005

**Date abstract record published**
31/10/2005