Modelling the cost-effectiveness of cardiac interventions: the case of sirolimus-eluting stents

NEIL HAWKINS, MARK SCULPHER, MARTIN ROTHMAN

Abstract

This article aims to provide a primer on decision modelling to assess the cost-effectiveness of interventions in cardiology. The paper uses a cost-effectiveness model developed to compare alternative coronary stents. This decision analytic model assesses costs to the UK health service and health benefits in terms of quality-adjusted life-years (QALYs). Data were taken from a range of sources, including 12-month follow-up data from three important double-blind randomised controlled trials: RAVEL, SIRIUS and E-SIRIUS. Methods are employed to show the uncertainty in cost-effectiveness.

Sirolimus-eluting stents were compared to 'bare metal' stents in constructing this decision model. The patients included were those individuals with stable coronary disease randomised to the three trials.

The main outcome measures were: mean QALYs, mean health service costs, incremental cost per additional QALY, and the probability that sirolimus-eluting stents are more cost-effective than bare metal stents.

Mean QALY gains per patient from the sirolimus-eluting stent range from 0.011 to 0.017 over 12 months. Although the list price of the sirolimus-eluting stent is £617 more than the bare metal stent, its additional total mean cost per patient including 'cost offsets' from a lower rate of subsequent events, ranges from £53 to £166. The incremental cost of the sirolimus-eluting stent per additional QALY ranges from £3,181 to £15,198. The probability that the sirolimus-eluting stent is less costly than the bare metal stent ranges from 0.13 to 0.34. If the health service is willing to pay up to £40,000 per additional QALY, the probability of the newer stent being the more cost-effective ranges between 0.8 and 1.0. These results are sensitive to assumptions about the price differential between the two forms of stent.

Cost-effectiveness analyses based on models are used increasingly as a basis for decision making. It is essential that these models are developed with clinical input regarding appropriate assumptions and interpretation of evidence.

Key words: decision analysis, cost-effectiveness, quality-adjusted life years, coronary stents.

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Introduction

Healthcare systems in most developed countries are increasingly interested in whether new healthcare interventions represent value for money, as well as improve patients' health. The National Institute for Health and Clinical Excellence (NICE) in England and Wales is an example of an organisation charged with assessing the cost-effectiveness, as well as clinical effectiveness, of healthcare technologies.[1] In the field of cardiology, new medical technologies are rapidly developing, and it is to be expected that healthcare systems will look closely at their effectiveness and cost-effectiveness. NICE has considered a number of cardiac interventions, including coronary stents and implantable cardioverter defibrillators, as well as pharmaceutical products in the field such as the glycoprotein IIb/IIIa receptor antagonists and clopidogrel (see www.nice.org.uk).

Technology assessments undertaken for bodies such as NICE often have limited evidence to draw upon. For some technologies (e.g. new diagnostic tests), there may be no trial data upon which to base an assessment. For the purpose of addressing issues of cost-effectiveness, trials that were designed to assess the efficacy and safety of interventions often have limitations. These include short follow-up, which precludes the estimation of changes in quality-adjusted life expectancy, failure to compare directly the new technology against current clinical practice and the absence of the measurements necessary for a full economic assessment, including impact on health-related quality of life and costs.[2] These features of the evidence base relating to new inter-

ventions have resulted in the use of decision modelling techniques to estimate cost-effectiveness. Such methods incorporate a wide range of existing data rather than relying solely on information from clinical trials. Decision models represent the various clinical pathways along which patients may pass following alternative treatments and quantify the probability of a patient following each pathway. Conditional on a patient following a given pathway, the range of possible costs and health-related outcomes that a patient may experience is defined. In analysing the model, the objective is to calculate the expected (equivalent to mean) costs and health outcome of competing interventions together with the uncertainty in those estimates. Detailed introductions to decision modelling can be found elsewhere.[3]

A growing number of modelling studies are being undertaken on cardiac interventions to inform decisions about their value for money.[4,5] It is important that these analyses characterise the clinical issues associated with the alternative treatments as accurately as possible, so it is crucial for clinicians to be fully involved in their development. This requires an understanding of the methods used in these studies. The aim of the paper is to provide insight into how decision models are developed and, in particular, how the results and the uncertainty surrounding them are presented. The paper uses a cost-effectiveness model developed to compare sirolimus-eluting stents versus 'bare metal' stents using data from a range of sources including three important double-blind randomised controlled trials: the randomised study with the sirolimus-eluting Bx Velocity™ balloon expandable stent (Cypher®) in the treatment of patients with *de novo* coronary artery lesions (RAVEL),[6] the sirolimus-eluting stent in *de novo* native coronary artery lesions trial (SIRIUS)[7] and the European multi-centre, randomised, double-blind study of the sirolimus-coated Bx Velocity™ balloon-expandable stent in the treatment of patients with *de novo* coronary artery lesions (E-SIRIUS).[8] These trials provide strong evidence that sirolimus-eluting stents reduce revascularisation rates relative to bare metal stents, but are they cost-effective given their additional acquisition cost?

Methods

Study question

The purpose of the model is to assess the differential impact of sirolimus-eluting and bare metal stents on costs to the UK health service and on patients' survival duration, adjusted for their health-related quality of life (HRQL). In 'base-case' analysis, separate sets of results are presented relating to three relevant patient groups. The groups are defined according to the trials from which the clinical data are largely taken.

The characteristics of these three trials, and of their patients, are summarised in table 1. It can be seen that, in terms of mean age and sex, the trials are similar. There are, however, some differences between the studies: RAVEL had a smaller proportion of diabetics and patients with, on average, shorter lesions; in SIRIUS there was a higher proportion of diabetic patients and, on average, patients had larger diameter vessels and longer lesions; and in E-SIRIUS patients had a combination of characteristics of both RAVEL and SIRIUS, with small vessels and longer lesions.

Table 1. Details of the randomised controlled trials of sirolimus-eluting versus standard stents used to provide data for the cost-effectiveness model. Data relate to all patients in the trials

Trial characteristic	RAVEL[6]	E-SIRIUS[8]	SIRIUS[7]
Sample size	238	352	1,058
Age in years (mean ± SD)	60.7±10.4	62.3±10.9	62.3±11.1
Men (%)	76	71	71
Diabetes mellitus (%)	19	23	26
Multi-vessel disease (%)	30	36	42
Diameter of reference vessel (mm, mean ± SD)	2.62±0.53	2.55±0.37	2.80±0.47
Length of lesion (mm, mean ± SD)	9.58±3.25	15.0±6.0	14.4±5.8

Defining benefits and costs

For the base case analysis, it is assumed that the two types of stent do not differ in their effect on mortality. This can be justified on the basis that coronary restenosis is not *per se* predictive of increased risk of death. This has been shown in randomised trials comparing coronary artery bypass grafting (CABG) and balloon angioplasty[9] where, despite the significantly increased rate of restenosis following the angioplasty, there is no commensurate elevated mortality risk. Furthermore, Weintraub *et al*. found no differences in six-year mortality between patients with and without restenosis.[10] The model also assumes that differential effects of the alternative stents on further revascularisation, mortality and myocardial infarction (MI) only occur during the period of measurement in the relevant trial in which the effects are estimated (i.e. 12 months).

The measure of health benefit used is quality-adjusted life years (QALYs). Given the assumption of no differential effect on mortality, these will reflect the decrement to HRQL associated with the symptoms that prompt further revascularisation. To implement this, only further revascularisations driven by patients' symptoms (rather than by angiography alone) are included to reflect the occurrence of such revascularisation in routine clinical practice. It is assumed that, at the onset of symptoms, patients will have to wait before they undergo further revascularisation and, during this period, they will experience the HRQL decrement. After their procedure, they will return to an average HRQL associated with successful revascularisation. HRQL is measured on a 'utility' scale which runs from 0, representing the value of health states considered equivalent to death, to 1, representing good health.[11]

The cost side of the evaluation includes the additional cost of the sirolimus-eluting stents in the initial procedure, and the full cost of any further percutaneous coronary intervention (PCI) or CABG. The cost of further revascularisation procedures incorporates the cost of a prior angiography, the procedure, drug use

Table 2. Inputs into the cost-effectiveness model taken from the specific trials. Unless otherwise stated, data are events / those at risk (probabilities)*

Input	RAVEL[6]		E-SIRIUS[8]		SIRIUS[7]	
	Sirolimus	Bare metal	Sirolimus	Bare metal	Sirolimus	Bare metal
Stents implanted (mean)†	1.03	1.04	1.22	1.19	1.30	1.30
All deaths	2/120 (0.017)	2/118 (0.017)	2/175 (0.011)	1/177 (0.006)	7/533 (0.013)	4/525 (0.008)
Cardiac deaths	0/120 (0.000)	1/118 (0.008)	1/175 (0.006)	1/177 (0.006)	3/533 (0.006)	2/525 (0.004)
Target vessel revascularisation with‡:						
- PCI	1/120 (0.008)	18/118 (0.153)	8/175 (0.046)	42/177 (0.237)	40/533 (0.075)	130/525 (0.248)
- CABG	1/120 (0.008)	0/118 (0.000)	1/175 (0.006)	4/177 (0.023)	8/533 (0.015)	16/525 (0.030)
Myocardial infarction	4/120 (0.033)	6/118 (0.051)	8/175 (0.046)	4/177 (0.023)	16/533 (0.030)	18/525 (0.034)

Key: * Where patients experience more than one event, all events are reported here; † These mean stent numbers are based on currently available stent lengths rather than those in the trials. This has been estimated using mean lesion lengths in the trials, so no standard errors are presented; ‡ Clinically-driven events only; PCI = percutaneous coronary intervention; CABG = coronary artery bypass graft

Table 3. Inputs in the cost-effectiveness model taken from non-trial sources and used in all analyses

Input	Value	Source
Unit costs (2003 prices)		
Sirolimus-eluting stent	£1,762*	Cypher™, Cordis Ltd
Bare metal stent	£1,145*	Bx Velocity™, Cordis Ltd
Angiography	£372	NHS Reference Costs[12]
PCI	£2,984	NHS Reference Costs[12]
CABG	£6,450	NHS Reference Costs[12]
Myocardial infarction	£1,055	NHS Reference Costs[12]
Quality of life weights (mean ± standard deviation)		
Without symptoms	0.84±0.16	ARTS Trial[13]
With symptoms	0.69±0.20	ARTS Trial[13]
Waiting times for revascularisation (Days)	196†	Target maximum waiting time in the NHS National Service Framework[14]

Key: * Including value added tax (VAT); † Referral from GP to consultant appointment = four weeks, decision to investigate to angiography = three months, decision to do procedure to revascularisation = three months; PCI = percutaneous coronary intervention; CABG = coronary artery bypass graft

and hospitalisation. The cost of MI is also incorporated into the analysis.

Data inputs

As with most decision models, the data inputs into the model are taken from several sources (tables 2 and 3). Inputs relating to the number of stents used in the initial procedure are estimated based on the lesions in trial patients and the lengths of stents currently available. Data on the rate of further revascularisations and MIs are taken directly from the RAVEL, E-SIRIUS and SIRIUS trials and based on data collected up to 12-month follow-up (table 2). For trial patients who experienced more than one event, all events are included. All three trials showed a marked reduction in revascularisation rates with sirolimus-eluting stents, although rates of death and MI are relatively low.

Unit costs are used to estimate the monetary cost of clinical events (table 3). The costs of the two forms of stent are taken from a manufacturer's 2003 list prices. In practice, hospitals may pay lower prices, and sensitivity analysis is used to explore the implications of price discounts for cost-effectiveness. All other costs are taken from routine NHS sources.

The HRQL associated with and without symptoms is taken from the Arterial Revascularisation Therapies Study (ARTS) Group trial.[13] This trial used the EuroQol (EQ)-5D instrument at baseline and follow-up. The EQ-5D asks patients to categorise their health, using one of three levels (no problems, moderate problems and severe problems) on five dimensions – mobility, self-care, ability to undertake usual activities, pain and depression/anxiety – thereby defining themselves in one of 245 possible health states.[15] Each of these states has been scored as a utility based on interviews with 3,395 members of the UK public.[16] The mean HRQL score associated with symptoms (0.69) is assumed to apply throughout the period the patient waits for revascularisation. This is taken to be 196 days, which is the NHS' target waiting time and does not distinguish between initial and repeat procedures.[14] When not in need of revascularisation (i.e. when without symptoms), patients' HRQL is assumed to be the same as the mean HRQL in patients undergoing PCI in the ARTS trial one month after revascularisation (0.84).[13]

Analysis

The expected cost of managing a patient with one of the two types of stent is calculated in a series of steps. The first step involves defining the alternative events that a patient may experience: MI, further revascularisation with PCI and further revascularisation with CABG. The second step is to attach a probability and a cost to each of these events (tables 2 and 3). The probabilities detailed in table 2 allow for the fact that some patients may have two revascularisation procedures. The third step is to

Table 4. The cost-effectiveness of sirolimus-eluting versus standard stents: base-case results using data from the three trials

Input	RAVEL[6]		E-SIRIUS[8]		SIRIUS[7]	
	Sirolimus	Bare metal	Sirolimus	Bare metal	Sirolimus	Bare metal
Total cost	£5,282	£5,116	£5,746	£5,692	£6,033	£5,920
Difference in costs	£166		£53		£113	
Total reduction in QALYs	-0.001	-0.012	-0.004	-0.021	-0.007	-0.022
Difference in QALYs	0.011		0.017		0.015	
ICER	£15,198		£3,181		£7,461	

Key: ICER = incremental cost-effectiveness ratio; QALYs = quality-adjusted life-years

sum the cost of each event weighted by the probability of it occurring. This expected cost is analogous to a mean cost from sampled data and provides the best estimate of the cost that a patient will incur. The expected QALYs associated with the two forms of stent are calculated on a similar basis. Given the base-case assumption of equal mortality with both devices, differential QALYs are simply the difference in quality-adjusted time spent with symptoms.

An important aspect of decision models is how the uncertainty in the estimates of clinical inputs and costs going into the model are reflected in the results. To handle this 'parameter uncertainty', probabilistic sensitivity analysis is undertaken, which involves defining the model inputs as probability distributions rather than as point estimates.[17] This reflects the imprecision of the model inputs which is usually reflected, for example, in terms of confidence intervals. A process known as Monte Carlo simulation is used: this effectively re-runs the model a large number of times, each time randomly picking from the probability distributions representing the parameter uncertainty. In effect, this produces a large number of sets of results. The means of these alternative results are the 'best' (expected) estimate of differential costs and QALYs between the stents. These are used to establish whether one type of stent 'dominates' the other; that is, whether it has higher expected QALYs and lower expected costs. If neither stent dominates, then the incremental cost per additional QALY of the more effective stent – that is, the additional cost divided by the additional QALYs – is calculated. This ratio represents the extra amount the health service would have to pay to generate an additional unit of health for the relevant population. Organisations such as NICE make a judgement regarding whether, compared to other uses of resources, this incremental cost-effectiveness ratio (ICER) represents good value for money.

The variation around that mean result is also important as it shows the uncertainty in cost-effectiveness. This uncertainty is presented using a cost-effectiveness acceptability curve.[18] In our model, the curve shows the probability that sirolimus-eluting stents are more cost-effective than standard stents for a range of levels that the health service might be willing to pay for an additional QALY. NICE has indicated that it is willing to pay £20,000–£40,000 for an additional QALY associated with the technologies it appraises.[19] Finally, to assess how results might change if the differential price of the stents were different, the model is re-run under alternative price assumptions.

Results

Expected mean results

The expected costs and QALY reductions are shown in table 4, based on data from the three trials. The QALY reductions are based on estimates of decrements in HRQL during the time spent waiting for further revascularisation. As such, they are directly proportional to the subsequent revascularisation rates observed in the trials, which were always lower in patients randomised to sirolimus-eluting stents. The greater QALY advantage for sirolimus-eluting stent patients based on E-SIRIUS data reflects the higher baseline revascularisation rate (i.e. the rate with bare metal stents) in that trial compared with RAVEL, and the greater relative reduction in revascularisations compared with both RAVEL and SIRIUS.

Table 4 also shows that sirolimus-eluting stents result in an additional overall cost to the health service compared to standard stents. This incremental cost ranges from £54, based on E-SIRIUS data, to £166 using data from RAVEL. These added costs are less than the additional acquisition cost of the sirolimus-eluting stent itself because, in each of the trials, the new stent, on average, results in 'downstream' cost savings due to a lower incidence of further revascularisation. The extent of the cost saving with the sirolimus-eluting stent in the three trials is again directly proportional to the reduction in subsequent revascularisations.

Given the higher overall costs but QALY gains associated with sirolimus-eluting stents, it is appropriate to calculate the incremental costs per extra QALY associated with the new stent, and these are also shown in table 4. The lower additional cost and greater QALY gain associated with data from E-SIRIUS results in the incremental cost-effectiveness ratio being lower (£3,181) than those based on SIRIUS (£7,461) and RAVEL (£15,198).

Uncertainty

The expected costs and QALYs in table 4 are, however, measured imprecisely. Figure 1 shows how the uncertainty in cost-effectiveness can be represented in terms of cost-effectiveness accept-

Table 5. Results of the sensitivity analysis exploring the implications of alternative price differentials between bare metal and the sirolimus-eluting stent

Stent price differential	Incremental cost-effectiveness ratio	Probability that sirolimus-eluting stent is more cost-effective than bare metal stent when the health service is willing to pay:			
		£0 per additional QALY	£20,000 per additional QALY	£30,000 per additional QALY	£40,000 per additional QALY
E-SIRIUS trial					
£500	Cypher® dominates	0.69	0.97	0.99	1.0
£800	£16,486	0.04	0.58	0.80	0.91
SIRIUS trial					
£500	Cypher® dominates	0.65	0.99	1.0	1.0
£800	£23,179	0.0	0.35	0.74	0.92
RAVEL trial					
£500	£4,233	0.36	0.78	0.87	0.92
£800	£32,349	0.0	0.24	0.43	0.60

ability curves (CEACs). For each trial, these curves show the probability that each type of stent will be the more cost-effective, depending on the amount the health service is willing to pay for an additional QALY in these patients.

When that willingness to pay is zero, cost-effectiveness is defined only in terms of whether the stent reduces costs: the curves show a probability of 0.10, 0.34 and 0.13 for sirolimus-eluting stents based on data from RAVEL, E-SIRIUS and SIRIUS, respectively. At the extreme right of the CEACs, the amount the health service is willing to pay for additional QALYs is very high, so the high probability of the sirolimus-eluting stent generating more QALYs outweighs its additional cost, which means it has a high probability of being considered cost-effective.

Points in between these two extremes show how the probability depends on how much the health service is willing to pay for an extra QALY. At a willingness to pay £40,000 per additional QALY, for example, these probabilities are 0.8, 0.99 and 1.0 based on data from RAVEL, E-SIRIUS and SIRIUS, respectively. The point on the horizontal axis at which the curves for the two stents cross will roughly equate with the incremental cost-effectiveness ratios shown in table 4.

Table 5 provides details of a sensitivity analysis to assess the implications for cost-effectiveness of alternative price differentials between the two stents. In the base-case analysis, the difference between the list price of the two stents is £617. The table shows the results of the model, based on the three alternative trials, when that differential ranges between £500 and £800. At the lower price differential, the sirolimus-eluting stent either dominates or has an ICER below £5,000. At the higher price differential, the ICER ranges between £16,486 (based on E-SIRIUS) and £32,349 (based on RAVEL).

Discussion

The type of results presented here are now routinely used as an important input into decision making – for example, by NICE. But how should they be interpreted by decision makers? One important consideration relates to whether the incremental cost per additional QALY is considered good value for money. In other words, what is the system's willingness to pay for an additional QALY? Because the NHS and many other healthcare systems are having to decide how to allocate a fixed healthcare budget, the correct way of addressing this question is to assess the costs and benefits of those healthcare interventions and programmes which would have to be removed or down-scaled to fund new technologies such as sirolimus-eluting stents. For example, if the least efficient programme currently being funded (inside or outside cardiology) were generating QALYs at a higher cost than sirolimus-eluting stents, then there could be a net gain in QALYs if that programme was removed and the resources released were allocated to the new stents. In other words, the opportunity cost of introducing the new technology would have to be worth incurring. Whether this was possible would also depend on the size of the relevant patient groups because the value of the total resources freed up needs to be at least equal to the additional cost of sirolimus-eluting stents.

The problem facing decision makers such as those in NICE, however, is that they have a very imperfect idea of the costs and benefits of the health care which is currently funded. Therefore, whether existing interventions should be displaced and, if so, which ones, is not clear. This has resulted in decision makers having to judge whether an incremental cost-effectiveness ratio represents good value by following a 'rule of thumb' rather than looking formally at opportunity cost. These 'cost per QALY thresholds' have been suggested by, for example, decision makers in Ontario.[20] New draft guidance from NICE suggests an effective threshold of between £20,000 and £40,000 per QALY,[19] but emphasises that other factors may be taken into consideration. On the basis of these thresholds, sirolimus-eluting stents would probably be considered cost-effective. Evidence on decisions by NICE[21] and the Australian healthcare system[22] suggests

some sort of threshold is emerging but that it does not entirely explain all decisions.

An important element of this paper has been to show the importance of reflecting uncertainty in the cost-effectiveness results, in particular using probabilistic sensitivity analysis. How should this influence decision makers? If the overall objective of decision-making is for the health service to maximise health (QALYs) gain for its population from the finite resources at its disposal, then the focus should be on the best estimates of cost and QALYs, that is their expected values, and how the incremental cost-effectiveness ratio compares with the opportunity cost.[23] In such a situation, the value of presenting the uncertainty in the results, as in figure 1, is that it provides a starting point for considering whether further research should be funded. Formal methods exist to establish the value for money, and appropriate design, of such additional research based on decision analytic models.[2]

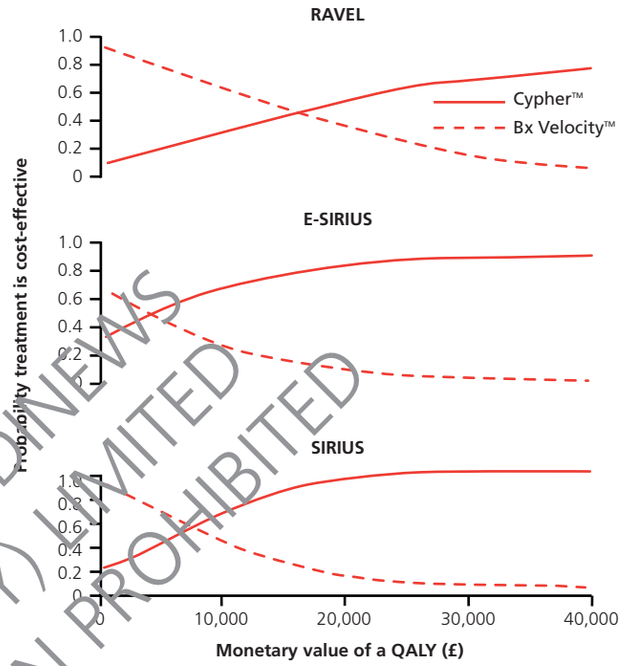
It is also likely that, regardless of the assessment of the need for extra research, decision makers will want to be aware of the probability that, if they recommend that a new technology is funded, this is the wrong decision and, in reality, this will lead to an inefficient use of resources. This decision uncertainty is explicitly shown in the cost-effectiveness acceptability curves in figure 1.

An important caveat with decision models is that their results are always conditional on their data and assumptions. In terms of data, the results relate only to the mix of patients in the three randomised trials from which data have been drawn. The cost-effectiveness of drug-eluting stents in patients with, for example, multi-vessel and diffuse disease remains to be assessed. Although all models are necessarily simplifications of reality, the model presented here was selected as it was a relatively uncomplicated representation of patients' possible prognoses and, as such, suitable for a primer paper such as this.

An important assumption in the model is that the HRQL benefits from a lower rate of subsequent revascularisation come the avoidance of waiting times for further procedures during which the patient will be symptomatic. This waiting time is assumed to be 196 days, based on the target maximum waiting time in the NHS National Service Framework.[14] In some centres this period might be longer (in which case the incremental cost per QALY gained from the sirolimus-eluting stent will be lower than reported here); in others it will be shorter (and therefore the incremental cost per QALY of the newer stent will be higher). The effect of any over-estimate of this time will be offset by the fact that the direct negative impact of a further revascularisation on HRQL (e.g. pain and time away from usual activities following the procedure) is not included in the model. The reason for not including this effect in the model was that good evidence about this 'convalescence effect' is not available. The absence of this evidence is likely to result in conservative results with respect to sirolimus-eluting stents.

A second assumption is that the model only looks at differences in event rates over the period of 12-month follow-up in the three trials from which clinical evidence is drawn. In reality, those differences are likely to extend further into the future, but the future shape of the relevant time-to-event curves is highly uncertain. Again, the decision to look only at events during trial follow-up is likely to generate conservative estimates of the cost-effectiveness of sirolimus-eluting stents because its advantage over bare metal stents, in terms of rates of subsequent revascularisation, is unlikely to stop immediately.

Figure 1. Uncertainty associated with the cost-effectiveness results based on clinical data from each trial. The diagrams are cost-effectiveness acceptability curves which show the probability of the two types of stent being the more cost-effective for a range of maximum values the health service may be willing to pay for an additional quality-adjusted life-year (QALY)



There is an important role for sensitivity analysis to explore whether changing particular assumptions in the model markedly affects the results. Sensitivity analysis shows that cost-effectiveness is, not surprisingly, sensitive to the price differential between the two types of stent. A differential ranging from £500 to £800 has a marked effect on cost-effectiveness results. The key issue is, however, whether this would change policy-makers' decisions. The maximum ICER of £32,349 (based on RAVEL data) is close to the NICE threshold.[19]

In conclusion, cost-effectiveness analyses based on models are now increasingly used as a basis for decision making by bodies such as NICE. It is essential that these models are developed with clinical input regarding appropriate assumptions and interpretation of evidence.

Conflict of interest

The research described here was funded by Cordis Ltd. MS also

Key messages

- Cost-effectiveness analysis is increasingly used internationally to inform decision making about which health care interventions should be covered/reimbursed
- The analysis indicates that the sirolimus-eluting stent generates more quality-adjusted life years (QALYs) than bare metal stents (0.011 to 0.017 over 12 months)
- The additional acquisition price of sirolimus-eluting stents is £617 based on list prices but its net additional cost over the bare metal stent is less (£53 to £166), reflecting cost savings associated with a lower rate of subsequent revascularisation
- The incremental cost of the sirolimus-eluting stent per additional QALY ranges from £3,181 to £15,198; the probability that the newer stent is less costly ranges from 0.10 to 0.34
- If the health service is willing to pay up to £40,000 per additional QALY, the probability of the newer stent being the more cost-effective ranges between 0.8 and 1.0
- These results are sensitive to assumptions about the price differential between the two forms of stent

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References

1. National Institute for Clinical Excellence. Technical guidance for manufacturers and sponsors on making a submission to a technology appraisal: (http://www.nice.org.uk), 2001.
2. Claxton K, Sculpher M, Drummond M. A rational framework for decision making by the National Institute for Clinical Excellence. *Lancet* 2002; **360**:711-15.
3. Hunink M, Glaziou P, Siegel J *et al. Decision making in health and medicine. integrating evidence and values.* Cambridge: Cambridge University Press, 2001.
4. Kuntz KM, Fleishmann KE, Hunink MGM, Douglas PS. Cost-effectiveness of diagnostic strategies for patients with chest pain. *Ann Int Med* 1999;**130**:709-18.
5. Cohen DJ. Evaluation of the cost-effectiveness of coronary stenting: a societal perspective. *Am Heart J* 1999;**137**:133-7.
6. Morice M-C, Serruys PWS, Sousa JE *et al.* A randomised controlled comparison of a sirolimus-eluting stent with a standard stent for coronary revascularisation. *N Eng J Med* 2002;**346**:1773-9.
7. Moses JW, Leon MB, Popma JJ *et al.* Sirolimus-eluting stents versus standard stents in patients with stenosis in a native coronary artery. *N Eng J Med* 2003;**349**:1315-23.
8. Schofer J, Schluter M, Gershlick AH *et al.* Sirolimus-eluting stents for treatment of patients with long atherosclerotic lesions in small coronary arteries: double-blind, randomised controlled trial (E-SIRIUS). *Lancet* 2003;**362**:1093.
9. Pocock SJ, Henderson RA, Rickards AF *et al.* Meta-analysis of randomised trials comparing coronary angioplasty with bypass surgery. *Lancet* 1995;**346**:1184-9.
10. Weintraub WS, Ghazzal ZM, Douglas JSJ *et al.* Long-term clinical follow-up in patients with angiographic restudy after successful angioplasty. *Circulation* 1993;**87**:831-40.
11. Drummond MF, Sculpher MJ, Torrance GW, O'Brien B, Stoddart GL. *Methods for the economic evaluation of healthcare programmes.* 3rd ed. Oxford: Oxford University Press, 2005.
12. NHS Executive. *The New NHS – 2003 Reference Costs*. www.doh.gov.uk/nhsexec/refcosts.htm. London: NHS Executive, 2003.
13. Serruys PW, Unger F, Sousa JE *et al.* Comparison of coronary-artery bypass surgery and stenting for the treatment of multivessel disease. *N Engl J Med* 2001;**344**:1117-24.
14. Department of Health. *National Service Frameworks for Coronary Heart Disease*. London: Department of Health, 2000.
15. Kind P. The EuroQol instrument: an index of health-related quality of life. In: Spilker B, (ed). *Quality of life and pharmacoeconomics in clinical trials.* 2nd ed. Philadelphia: Lippincott-Raven, 1996.
16. Dolan P, Gudex C, Kind P, Williams A. A social tariff for EuroQol: results from a UK general population survey. Centre for Health Economics Discussion Paper 138. Centre for Health Economics, University of York: CHE, 1995.
17. Briggs AH, Goeree R, Blackhouse G, O'Brien BJ. Probabilistic analysis of cost-effectiveness models: choosing between treatment strategies for gastroesophageal reflux disease. *Med Decis Making* 2002;**22**:290-308.
18. Van Hout BA, Al MJ, Gordon GS, Rutten FFH. Costs, effects and c/e-ratios alongside a clinical trial. *Health Economics* 1994;**3**:309-19.
19. National Institute for Clinical Excellence (NICE). *Guide to the methods of technology appraisal*. London: NICE, 2004.
20. Laupacis A, Feeny D, Detsky AS, Tugwell PX. How attractive does a new technology have to be to warrant adoption and utilization? Tentative guidelines for using clinical and economic evaluations. *Can Med Assoc J* 1992;**146**:473-81.
21. Raftery J. NICE: faster access to modern treatments? Analysis of guidance on health technologies. *BMJ* 2001;**323**:1300-03.
22. George B, Harris A, Mitchell A. Cost-effectiveness analysis and the consistency of decision making. *Pharmacoeconomics* 2001;**19**:1103-09.
23. Claxton K. The irrelevance of inference: a decision-making approach to the stochastic evaluation of healthcare technologies. *J Health Econ* 1999;**18**:342-64.