International Journal of Technology Assessment in Health Care, **23:2** (2007), 269–277.

DOI: 10.1017.S0266462307070365

Modeling payback from research into the efficacy of left-ventricular assist devices as destination therapy

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Objectives: Ongoing developments in design have improved the outlook for left-ventricular assist device (LVAD) implantation as a therapy in end-stage heart failure. Nevertheless, early cost-effectiveness assessments, based on first-generation devices, have not been encouraging. Against this background, we set out (i) to examine the survival benefit that LVADs would need to generate before they could be deemed cost-effective; (ii) to provide insight into the likelihood that this benefit will be achieved; and (iii) from the perspective of a healthcare provider, to assess the value of discovering the actual size of this benefit by means of a Bayesian value of information analysis.
Methods: Cost-effectiveness assessments are made from the perspective of the healthcare provider, using current UK norms for the value of a quality-adjusted life-year (QALY). The treatment model is grounded in published analyses of the Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure (REMATCH) trial of first-generation LVADs, translated into a UK cost setting. The prospects for patient survival with second-generation devices is assessed using Bayesian prior distributions, elicited from a group of leading clinicians in the field.
Results: Using established thresholds, cost-effectiveness probabilities under these priors are found to be low ($\sim$.2 percent) for devices costing as much as £60,000. Sensitivity of the conclusions to both device cost and QALY valuation is examined.

The authors are indebted to Reynolds Delgado III, MD, William Holman, MD, William Pierce MD, Evgenij Potapov MD, and Branislav Radovancevic MD for their individual and collective contributions to the prior assessments in section 4. A.J.G., J.G., and R.J.L. acknowledge support of this work through the MATCH Programme (EPSRC Grant GR/S29874/01), although the views expressed are entirely theirs.

Conclusions: In the event that the price of the device in use would reduce to £40,000, the value of the survival information can readily justify investment in further trials.

Keywords: Heart assist devices, Cost-effectiveness, Value of information, Bayesian analysis, Prior elicitation

Heart failure (HF) is a serious disease with prevalence rates in Europe and the United States ranging from .3 percent to 2 percent (15). A recent estimate has 5 million cases in the United States alone (2). Patients in end-stage heart failure (ESHF) have a poor prognosis, with 1-year mortality of 50 percent or more (12;37;50). Approximately 100,000 new cases of ESHF each year in the United States could benefit from advanced therapeutic intervention (30). In England and Wales, there are 10,000–15,000 new ESHF cases annually (11). Heart transplant (HT) offers the best outlook in terms of length and quality of life (20;25;34) but is unavailable in many cases (16;26;40). Long-term treatment with a left ventricular assist device (LVAD) was sanctioned by the US Food and Drug Administration (FDA) in 2002 (17) and is widely regarded as the most promising alternative for patients not eligible for HT (28;44;46).

There are several types of implantable LVADs. The so-called first-generation devices generate pulsatile flow using a displacement pump. Second-generation pumps provide continuous (nonpulsatile) blood flow and address some of the shortcomings of the first-generation devices (11;14;34;44;48). The only completed randomized controlled trial (RCT) of LVADs as destination therapy (the Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure [REMATCH] trial) (42) reported convincing evidence of efficacy and effectiveness for a first-generation device, but has led to unfavorable assessments of the cost-effectiveness of the treatment compared with optimal medical management (OMM). Based on REMATCH data, one study (4) estimated that LVADs are cost-effective at valuations of more than US$800,000 per quality-adjusted life-year (QALY), a figure well in excess of UK norms (39) and probably too expensive even for the richest healthcare provider.

Advances in pump technology (27), and improvements in the clinical management of LVAD patients (30) can be expected to improve the survival prospects for LVAD patients, perhaps to the extent where these improvements would outweigh the high cost of treatment. Second-generation nonpulsatile pumps offer particularly good prospects and are the subject of several ongoing surgical trials (27). Further randomized trials are contemplated, which might throw further light on the benefits of the therapy. At the same time, innovation in pump technology continues unabated (47), although doubts remain whether the so-called third-generation pumps can generate significant additional health benefit (24).

In this study, our purpose is threefold: (i) to examine the survival benefit that LVADs would need to generate to be cost-effective compared with OMM; (ii) to provide insight into the likelihood that this benefit will be achieved; and (iii) from the perspective of a healthcare provider, to assess the value of discovering the actual size of this benefit using a Bayesian value of information analysis (9;10). Our aims are addressed through a health–economic model for LVAD therapy based on the REMATCH experience translated into a UK cost setting. In the cost analysis, the price of the device itself is the most significant uncertainty, especially as it may well fall in response to future market growth (13;22). Expectations surrounding future patient survival are captured probabilistically using Bayesian prior distributions elicited from a group of leading experts.

A MODEL FOR LVADS AS DESTINATION THERAPY

The patient population is defined by the entry criteria to the REMATCH trial (41;42). It comprises adults with chronic ESHF not eligible for HT, and with ongoing symptoms of New York Heart Association class IV. This population is modeled as a homogeneous group, disregarding the possible impact of prior risk factors, such as patient age. The operation itself is taken as the starting point for both costs and patient survival, and the modeled pathway terminates with death. Waiting time for the operation to implant an LVAD is not considered here. The operation is followed by a period of "initial hospitalization," which terminates when the patient is discharged. Subsequently, patients receive ongoing medical care based on regular outpatient visits, and that care may include periods of readmission to the hospital. The treatment cost is taken to include the cost of the device, the cost of initial hospitalization (including all costs associated with the operation), and the ongoing costs of care until the death of the patient. The first two components are treated as fixed costs (i.e., independent of survival time) and the ongoing care cost as proportional to the patient's survival time after discharge. In the REMATCH trial, the initial hospitalization costs for patients successfully discharged from the hospital were substantially less than for those who were never discharged, both in aggregate and also when converted to a daily rate (35), a finding confirmed by subsequent experience (31). In the model, LVAD patients are divided into two groups: "Successes," those who are successfully discharged; and "Failures," who never leave the hospital. The ratio of average hospitalization costs for Successes and Failures is taken from the REMATCH experience as 1:2.3 per patient (35). The overall average hospitalization costs derive from UK estimates.

Improvements in LVAD therapy will increase both the patients' overall life expectancy and the proportion of treatment Successes. An increase in the latter is automatically associated with reduced hospitalization costs per patient.

Similarly, improvements in patient survival will affect the costs of ongoing medical care. The obvious effect is to increase them. Nevertheless, it is likely that recognized improvements in long-term survival will impact on follow-up protocols and also lead to a reduction in the *proportion* of survival time spent in hospital readmissions. These effects are modeled by allowing both the frequency of outpatient visits and the fraction of time in readmission to be inversely proportional to the average life expectancy among the treatment Successes. As a result, the outpatient interval ranges from 7 weeks (44) to 3 months under an optimistic life expectancy of 80 months postimplantation in the Success group. The time spent in readmission ranges from 10 percent (42) to an optimistic 5 percent of the time after initial discharge.

Table 1 summarizes the model parameters. Cost estimates rely heavily on the recent study by Clegg and others (11). The cost of the device is treated as an exceptional case. It was around US$60,000 for a first-generation device in the REMATCH trial (42), whereas Siegenthaler and colleagues (44) paid GB£60,000 for a second-generation device. In the future, the price may be affected by technological developments and changes in uptake. This uncertainty is treated here by presenting results over a range of device costs.

The incremental cost-effectiveness of LVAD therapy is defined relative to OMM, which entails regular outpatient visits and may include periods of admission to the hospital.

Table 1. Sources for Model Parameters

Mean survival			
	LVAD Successes	μ_S	Assessed from expert priors; REMATCH data consistent with $\mu_S = 30$ to 40 months (see Figure 1)
	LVAD Failures	2 months	(35)
	OMM	7.8 months	(4)
Proportion of LVAD treatment Failures		π	Assessed from expert priors. REMATCH data has $\pi = .33$ (35)
Utilities			
	LVAD	.81	(33)
	OMM	.55	(33)
Initial hospitalization cost (including theater costs, excluding device cost)			
	LVAD Successes	£27,821	Average cost £39,877 (11), apportioned between Successes and Failures in ratio observed in the REMATCH trial (35)
	LVAD Failures	£63,989	
Length of Initial hospitalization (LVAD Successes)		35 days	(35)
LVAD/OMM Hospital readmission cost, per month in the hospital		£16,170	(11)
Fraction of time in the hospital post–initial discharge (LVAD)		$4 \div \mu_S$	Assumed proportional to death rate from HF (see text), calibrated to REMATCH value (35) (.10) at $\mu_S = 40$ months
Fraction of time in the hospital (OMM)		.15	(42)
Outpatient cost per visit (LVAD and OMM)		£99	(11)
LVAD Outpatient visits (per month out of the hospital)		$25 \div \mu_S$	Assumed proportional to death rate from HF (see text), calibrated to value in (44) (every 6–8 weeks) at $\mu_S =$ 40 months
OMM Outpatient visits (per month out of the hospital)		.619	Same rate as for LVAD in (44), equivalence supported by (11)
Discount rate		3.5% p.a.	(23)

LVAD, left ventricular assist device; REMATCH, Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure (REMATCH); OMM, optimal medical management; HF, heart failure; p.a., per annum.

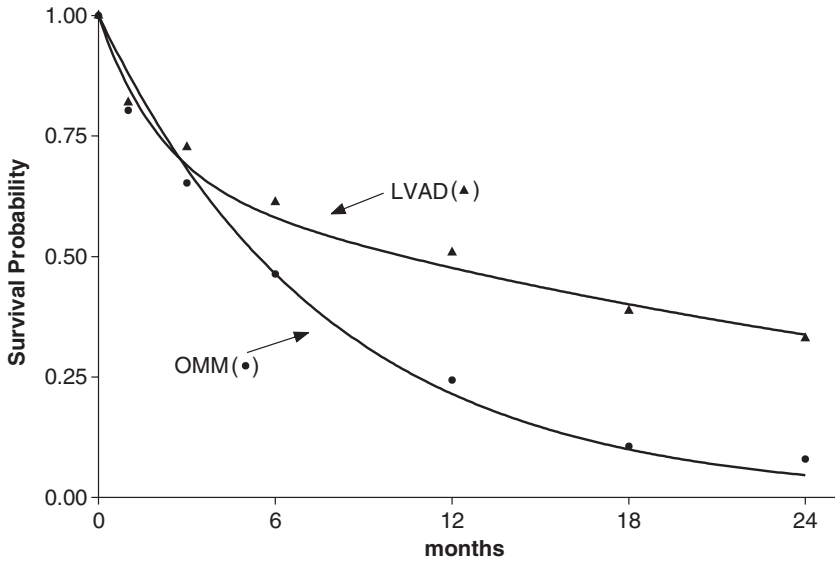

Figure 1. Actual and modelled survival of patients in the REMATCH trial. OMM, optical medical management. (Data from ref. 4 with revised 24 month LVAD estimate from Park et al. [36]).

The outpatient interval is taken as 7 weeks (44), and the hospitalization fraction as 15 percent (4). Daily hospitalization costs are assumed the same as those under LVAD.

Patient Survival

Patient survival under OMM is described by the exponential (constant hazard) distribution (4) in Figure 1, with mean survival suggested by the REMATCH trial (4). For LVAD patients, death can occur either during initial hospitalization (treatment Failure) or following discharge (treatment Success). Separate exponential survival distributions are used for Successes and Failures. The mean survival time for a Failure was taken as 2 months (35). This timing is the average length of stay in the hospital for a patient who does not survive the initial hospitalization, and is regarded as fixed. The key parameters for determining the life expectancy of patients under LVAD are as follows: π, the proportion of Failures; and μ_S, the mean survival time for Successes.

In the REMATCH trial of first-generation devices, π is estimated as .33 (=17/51) (35), and a good fit to the survival distribution reported to the FDA (3) is obtained by taking $\mu_S = 35$ months, as in Figure 1. Subsequent improvements in survival under LVAD (30;36) can be modeled by increasing μ_S and/or by reducing π.

The mean survival time is modeled as $2\pi + \mu_S(1 - \pi)$. Provided that Successes account for more than half the patients, the median survival time is (approximately) $m = \mu_S \log_e\{2(1 - \pi)\}$.

In this model, the probability of death in the hospital within 30 days of the LVAD implantation is given by $0.39 \times \pi$. Hence, π is proportional to a clinical "perioperative mortality rate," whereas the value of μ_S is just the life expectancy of successfully treated patients.

THE FUTURE COST-EFFECTIVENESS OF LVAD THERAPY

LVAD therapy can be considered cost-effective compared with OMM if the (discounted) value of the additional QALYs it generates exceeds the additional (discounted) treatment costs incurred. The analysis is conducted under valuations of a QALY derived from current UK norms (39). The model can then be used to identify threshold values of the survival parameters under which the therapy is *just* cost-effective. The results are shown in Figure 2 for devices at several different prices, including (for reference purposes) a hypothetical device that would cost nothing at all.

For ease of clinical interpretation, the parameter plotted on the vertical axis is the overall median survival under LVAD therapy rather than μ_S, the mean survival time among treatment Successes. For a given device price, a point on the curve corresponds to a combination of survival parameters at which the incremental cost-effectiveness ratio (ICER) for LVAD compared with OMM is exactly equal to the hypothesized value of a QALY. Points above or to the right of the curve have ICERs lower than the QALY valuation and correspond to an LVAD therapy that is cost-effective. Points below or to the left do not give a cost-effective result.

The survival experience of LVAD patients in the REMATCH trial corresponds to a median survival of 408 days (42)—or 13.4 months—combined with a Failure proportion π of .33 (35). From Figure 2, it is clear that this could not represent a cost-effective therapy at current UK QALY valuations at any positive value of the device cost. This conclusion concurs with that suggested by the model in one study (4), despite using more favorable UK treatment costs in the current work. It is clear that the cost-effectiveness of the

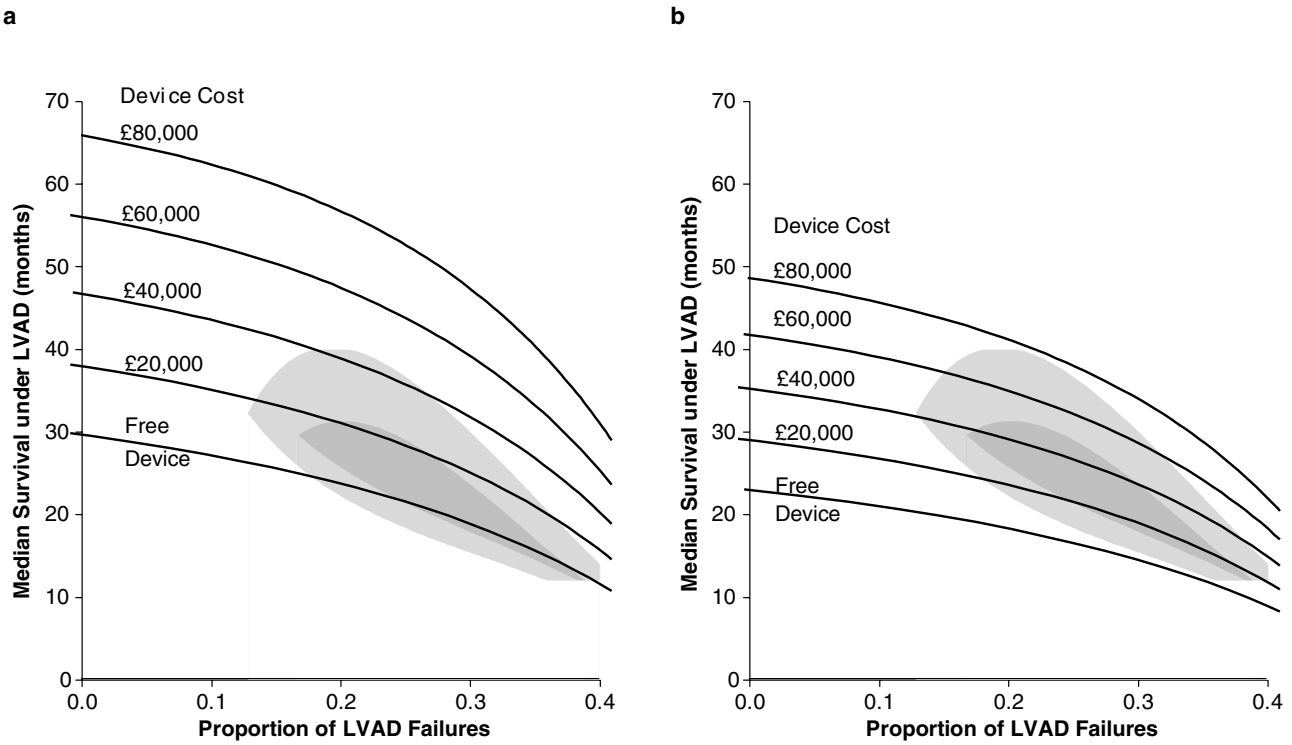

Figure 2. Cost-effectiveness thresholds under different assumptions about device cost and quality-adjusted life-year (QALY) valuations, with contours of the joint prior distribution superimposed. Under the model assumptions, the curves show combinations of survival parameters under which left vertical assist device (LVAD) therapy would be just cost-effective compared to optical medical management (OMM) at £30,000 per QALY (**a**) and £40,000 per QALY (**b**). The inner shaded region represents 50 percent and the entire shaded region 90 percent of the prior probability.

therapy will depend on substantial improvements in survival being achieved by later generations of devices.

PRIOR ASSESSMENTS OF LVAD SURVIVAL PARAMETERS

It is difficult to give precise estimates of the survival benefits of the latest generations of LVADs. The REMATCH trial is the only RCT to report results for LVADs as destination therapy, and these results were for first-generation pulsatile devices. While further results are awaited, a way forward can be found by exploring the expert opinions of those cardiac specialists best able to assess the likely effectiveness of the current generation of devices. This assessment was done by eliciting Bayesian prior distributions for the survival parameters. The priors were used in two ways: first to estimate the probability that LVADs will turn out to be cost-effective when their full benefits are known; and second in a Bayesian value-of-information analysis (32) to arrive at a prospective monetary valuation of the information that a future trial might uncover.

A group of five leading clinicians was assembled at the 51st annual conference of the American Society for Artificial Internal Organs (ASAIO) in Washington (2005). All had substantial experience with the use of current generation LVADs for the treatment of ESHF. The elicitation procedure was that described in Garthwaite et al. (21). It was applied to obtain priors for the perioperative (30-day) mortality and the overall median survival for LVAD in patients fulfilling the entry criteria to the REMATCH trial: New York Heart Association (NYHA) class IV/American College of Cardiology and the American Heart Association (ACC-AHA) class D, with contraindications rendering them ineligible for cardiac transplant. For each parameter, the procedure entails a discussion of a small number of quantiles of the prior distribution among the group, feeding back a computer-generated density function in real time, which is then amended as necessary until a shape satisfactory to the whole group is obtained. Consensus was achieved for both parameters. For median survival, the consensus density occupied the range 12–40 months, was centered on 25 months, and attached a prior probability of .22 to the range 12–20 months and a prior probability of .23 to the range 30–40 months. The density for 30-day mortality occupied the range 3–16 percent, was centered on 10 percent, and attached prior probabilities of .22 and .25, respectively, to the ranges 3–8 percent and 12–16 percent. These results are similar to those obtained during 2005 in separate

elicitations from six individual clinicians in the United Kingdom as described by one of the authors (J.G.) in a forthcoming study (unpublished, 2007). The individual elicitations furnish a useful check on those from the Washington group but have not been formally incorporated into the current analysis.

The elicited densities were combined to form a joint prior density for the proportion of Failures (π) and the median survival (m). Contours of the joint density are present in Figure 2a and 2b. They were derived assuming prior independence between the proportion of Failures and the survival prospects for treatment Successes—that is, treating π and μ_S as statistically independent parameters. Details of the calculations are available on request from the corresponding author.

COST-EFFECTIVENESS PROBABILITIES AND THE VALUE OF FURTHER INFORMATION

In Figure 2a and 2b, the probability assigned to the area above and to the right of a threshold curve can be interpreted as the chance, as perceived by leading clinical experts, that the device will turn out to be cost-effective at a specified QALY valuation. Results of this kind over a range of LVAD costs are included in Table 2.

The tabulated cost-effectiveness probabilities confirm that LVAD therapy is extremely unlikely to be cost-effective at current UK QALY valuations of around £30,000 if the device costs as much as the £60,000 incurred by Siegenthaler and colleagues (44). In fact the cost-effectiveness probability is no more than 84 percent even in the (implausible) case that the device costs nothing at all! Nevertheless, the figures are not inconsistent with an ultimately favorable assessment of LVAD therapy if the cost of the device were to fall in the future.

The subjective nature of the cost-effectiveness probabilities means that healthcare providers may view them with little more than academic interest – even in systems (such as the UK National Health Service) where economic evaluations form an explicit component of reimbursement decisions. It is generally recognized that the highest grade of evidence for such decisions is supplied by the results of RCTs, and it is therefore unlikely that an answer to the primary question of whether to reimburse LVAD treatment as destination therapy would be given on the basis of the prior probabilities reported here, however eminent the clinical source. Nevertheless, the absence of a definitive evidence base means that any decision to carry out an RCT will be taken in the light of an opinion about its possible benefits that must be, at least in part, speculative. It has been argued that Bayesian prior distributions are the natural vehicle for the quantification of such opinion (29;43;45). Here, the principal area of scientific uncertainty concerns the likely survival benefits of LVAD therapy. Thus, prior distributions for the survival parameters have a role to play when addressing the secondary question of whether further trials in this area should be conducted. In fact, they can be used to generate a formal value of information

Table 2. Cost-Effectiveness Results over a Range of LVAD Costs

Value of QALY		Free device	Device @ £20,000	Device @ £40,000	Device @ £60,000	Device @ £80,000
£20,000	ENB	−£10,952	−£30,952	−£50,952	−£70,952	−£90,952
	EVI	£946	£5	<£1	<£1	<£1
	C/E Prob.	.14	<.001	<.001	<.001	<.001
£25,000	ENB	+£1,141	−£18,859	−£38,859	−£58,859	−£78,859
	EVI	£4188	£577	£6	£0	<£1
	C/E Prob.	.48	.08	.002	<.001	<.001
£30,000	ENB	+£13,234	−£6,766	−£26,766	−£46,766	−£66,766
	EVI	£1,064	£3,303	£395	£6	<£1
	C/E Prob.	.84	.28	.05	.002	<.001
£35,000	ENB	+£25,327	+£5,327	−£14,673	−£34,673	−£54,673
	EVI	£325	£4,065	£2,255	£294	£6
	C/E Prob.	.96	.59	.19	.04	.002
£40,000	ENB	+£37,420	+£17,420	−£2,580	−£22,580	−£4,580
	EVI	£132	£1,438	£6,497	£1,645	£231
	C/E Prob.	.98	.83	.39	.13	.03
£45,000	ENB	+£49,514	+£29,514	+£9,514	−£10,486	−£30,486
	EVI	£64	£562	£4,177	£4,762	£1,260
	C/E Prob.	.99	.94	.65	.28	.10

Note. Given are the following: (i) the expected value of the net benefit per patient under LVAD therapy (ENB), (ii) the expected value of acquiring perfect information about LVAD survival parameters (EVI), and (iii) the probability that LVAD therapy is cost-effective compared to OMM (C/E Prob.). Results are computed using expert priors for the survival parameters in the model described in section 2, with UK treatment costs from Table 1. Several plausible device costs and QALY valuations derived from UK practice are represented. LVAD, left ventricular assist device; QALY, quality-adjusted life-years.

analysis, following the methods advocated in several reports (6;7;18).

The value of information analysis proceeds by examining the likely change in the estimate of net benefit to be expected from LVAD therapy induced by the results of a very large (fully informative) trial. Here, net benefit is defined as the discounted value of the extra QALYs associated with the therapy compared with OMM, net of any additional (discounted) costs. The rows labeled ENB (i.e., expected net benefit) in Table 2 contain current estimates, that is, the net benefit per patient treated averaged over the elicited prior distribution for the survival parameters. A positive value of ENB indicates that LVAD therapy is estimated to be cost-effective under the best information currently available; a negative ENB, that it is estimated to be cost-ineffective.

Thus in theory, an ENB from Table 2 *could* be used to inform an interim reimbursement decision for a second-generation LVAD. Nevertheless, the possibility remains that the wrong decision will have been taken. For example, at the £30,000 threshold, a decision not to reimburse a device costing £20,000 will be taken knowing that there is a 28 percent chance that the therapy will be cost-effective, because of the uncertainties surrounding the survival parameters. For this reason, it may be sensible to sponsor an investigation—for example, an RCT—to refine the estimates of these parameters so that a better-informed reimbursement decision can be taken. Taking the perspective of an insurance provider, expenditure on such an investigation cannot be justified unless it is outweighed by the likely benefits that would be attached to updating the reimbursement decision. Under the precepts of value-of-information analysis, these benefits are identified with the opportunity loss associated with taking the wrong reimbursement decision in the first place. For example, suppose it becomes apparent after a trial that the device is associated with a cost-effective destination therapy. (This finding could happen if the true values of the survival parameters were at the optimistic end of the prior distribution.) Then the opportunity loss associated with the (incorrect) decision not to reimburse would be equal to the true net benefit of the therapy, which is now known to be positive. Expenditure on the trial would then have been justified provided its cost per patient affected had been no greater than the size of the revised net benefit. On the other hand, the trial might simply reveal that the original impression that the device is not cost-effective was correct. In this case, the trial will have no impact on the original decision and will have had no value in terms of avoided opportunity loss. In practice, such calculations cannot be made in advance, because it is not known what the results of a trial will reveal. Instead, the expected value of the opportunity loss can be computed using currently available prior distributions for the survival parameters. This quantity is known as the "expected value of perfect information" (denoted by EVI in Table 2) (38). As expected, it turns out that EVI is greatest when the current reimbursement decision is least clear-cut as reflected by cost-effectiveness probabilities close to .5.

IMPLICATIONS FOR FUTURE TRIALS

The EVI values in Table 2 are computed on a per patient basis. The expected value of the information to the healthcare provider is obtained by aggregation over an appropriate patient population during the anticipated lifetime of the technology, or over a time horizon chosen for political or accounting reasons. For England and Wales, it has been estimated that there are up to 15,000 new cases of ESHF annually. Taking these cases as the patient population, then, over a time horizon of N years, the total (discounted) EVI will be

$$\left(1+\frac{1}{1+r}+\frac{1}{(1+r)^2}+\cdots+\frac{1}{(1+r)^{N-1}}\right) \times (\text{EVI per patient}) \times 15{,}000,$$

where the discount rate is $100r$ percent per annum. At 3.5 percent over $N=5$ years, this value is $4.67 \times$ (EVI per patient) $\times$ 15,000.

For example, suppose the price of the device is the £60,000 paid by Siegenthaler et al. (44). Then, at £30,000 per QALY, the expected value of gaining complete information about the survival parameters for patients over the next 5 years is $4.67 \times £6 \times 15{,}000 = £420{,}000$. Over 10 years, the expected value would be $8.61 \times £6 \times 15{,}000 = £775{,}000$. Both these values are substantially less than the anticipated costs associated with a meaningful RCT of second-generation LVADs. On the other hand, a trial of a device with a long-term price of £40,000 could yield information with an expected value of $4.67 \times £395 \times 15{,}000 = £28$ million over 5 years and $8.61 \times £395 \times 15{,}000 = £51$ million over 10 years—enough to justify a substantial outlay on an RCT.

The expected value of information calculation attempts to place an upper bound on the justifiable cost to the healthcare provider of a further trial when LVAD research is in competition with other uses to which limited resources can be put. Hence, it can help to prioritize a research agenda, and assist in the allocation of resources between research and direct medical care. Here, it suggests that the costs of a future LVAD trial could not be recouped over any reasonable period unless the cost of the device were substantially less than £60,000, a value that has actually been incurred in a UK context (44). On the other hand, the report by Clegg and colleagues (11) entertains a lower range of device prices (around £30,000–60,000) based on a submission from a device manufacturer. In any case, reductions in price are not implausible once the market expands and have been observed for other medical product (5).

DISCUSSION

Value of information is used here as a form of sensitivity analysis to explore the decision-value of parameter uncertainties in a cost-effectiveness model. The focus of our attention is the uncertainty surrounding the survival benefits of second-generation LVADs where these are used as destination therapy in ESHF. The other major source of uncertainty is the price at which the device can be made available, and this price is treated as an exogenous variable in our calculations. It must be emphasized that the relevant price is not the one that is obtained today, nor even over the next few months; it is the price at which the device will be sold in future, assuming a sizeable market. To a large degree, this price is under the control of the manufacturing companies and is difficult to predict without access to commercially sensitive information. Of course, a reimbursement decision—or even a decision to sponsor a trial—can be sensibly taken only when this price is specified, at least within plausible limits. Then the results presented here can be used to inform these decision-making processes.

Uncertainty surrounding other parameters in the model—in particular the treatment costs *excluding* the cost of the device—does not figure in our analysis. This strategy is both deliberate and rational. The motivation for the example in this study is to assess the potential impact on reimbursement decisions of future trials designed principally to uncover the survival benefits of LVADs. The underlying assumption is that such decisions are informed by a cost-effectiveness analysis using the best available estimates of all model parameters, with only informal attention paid to parameter uncertainties. Following a future trial, the reimbursement decision will likewise be taken in the light of the best available estimates, accompanied by an informal consideration of model sensitivities. Our concern has been to map the effect on this process of a change in the values of the best estimates of a small number of (survival) parameters. Uncertainties in cost parameters make no formal contribution to this process. This approach has been described as "partial" value of perfect information analysis, because it contemplates the effect of eliminating *all* uncertainty about only *some* of the parameters (8;19). In practice, this will not be achieved by a single trial, however large. Some statistical uncertainty in the results is unavoidable. Thus, an analysis based on valuing perfect information places an upper bound on the justifiable cost of any trial, but without confirming that any particular trial ought to go ahead. A formal analysis of the information value in a realistic finite trial can be made using previously described sample information methods (1;49).

Our aim has been to explore the case for a new trial of second-generation LVADs, given the best available current evidence and clinical opinion. In conclusion, it appears that such a trial would represent value for money in a UK setting, assuming a plausible device-cost of around £40,000.

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