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Value of information analysis for a new technology: Computer-assisted total knee replacement

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Objectives: The aim of this study was to demonstrate how value of information analysis can measure the upper limit on returns to future research and identify the research priorities for computer-assisted total knee replacement (CAS-TKR).
Methods: Using a previous economic analysis of CAS-TKR compared with conventional TKR, the population expected value of perfect information (EVPI) was calculated using Monte Carlo simulation to provide an estimate of the upper limit on returns to future research. The population expected value of partial perfect information (EVPPI) for both individual parameters and groups of parameters was estimated to inform specific future research priorities.
Results: The UK individual EVPI would be £21.4 if the willingness to pay for one QALY (quality-adjusted life-year) were £30,000. The population EVPPI would be £8.3 million, assuming a 10-year time horizon for CAS-TKR. In this instance, the expected value of information is positively related to willingness to pay for one QALY for the range of £0 to £50,000. Although each individual parameter had an EVPPI of £0, groups of utility parameters had positive EVPPI. Population EVPPI was £5.6 million for utility parameters, £20,000 for transition probabilities relating to CAS-TKR, and £5,000 for transition probabilities related to conventional TKR.
Conclusions: The study provides evidence on which parameters further information may be of most value. Focusing research on the utility values associated with health states relating to TKR would be of greatest value.

Keywords: Total knee replacement, Computer-assisted surgery, Value of information analysis

Cost-effectiveness analysis (CEA) compares the costs and health outcomes of interventions to determine which intervention or policy is optimal given society's willingness to pay (WTP) for health outcomes. It is one of several criteria that should be used in decision making to inform the decision to adopt a technology, or not, given current knowledge. However, in the case of new technologies analyzed at an early stage in their cycle, considerable uncertainty about parameter values is likely when estimating cost-effectiveness. Decision makers need both to consider the uncertainties while making an immediate decision about adoption and

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to decide whether further research should be undertaken to reduce uncertainty in that decision. The expected value of information (EVI) theory in medical decision making is one such analytical technique that can identity the priorities for further research. The expected cost of making decisions under uncertainty can be referred to as the expected value of perfect information (EVPI) as it is the maximum a decision maker should be willing to pay to remove uncertainty concerning a decision (1). It is determined jointly by the probability that a decision based on existing information will be wrong and the consequences of the wrong decision. Within decision analysis, all parameters contribute to decision uncertainty. Estimating the expected value of partial perfect information (EVPPI) provides information on which parameters contribute most to this uncertainty and can provide the basis from which to determine future research priorities.

Total knee replacement (TKR) itself is a well-proven procedure. The demand for TKR is increasing mainly because of longer life expectancies and rising public expectations for quality of life and mobility in later years. TKR usually produces excellent results, although serious complications occur in around 5 percent of cases because of loosening, instability, dislocation, infection, or fracture (13). In 20–60 percent of patients, less serious complications such as anterior knee pain or limited movement are reported at approximately 3 years after operation (9–11). The surgeon's experience in patient selection, soft-tissue balancing, the alignment of the leg, the restoration of the joint line, and also the prosthetic design are all possible factors influencing the success of TKR (7).

Computer-assisted surgery (CAS) systems have been developed to improve limb and component alignment in TKR. However, as yet there is limited evidence of its contribution to the cost-effectiveness of TKR, although some studies of effectiveness have been undertaken (2–4;16). A Markov model had previously been used to make a preliminary assessment of the cost-effectiveness of computer-assisted TKR with that of conventional TKR (8). That study found, based on evidence from short-term radiographic studies demonstrating an improvement in the accuracy and precision of component and mechanical axis alignment with CAS and studies linking implant survival outcomes to these same alignments, that compared with conventional TKR, computer-assisted TKR is highly likely to be cost-saving and to offer a small quality-adjusted life-year (QALY) advantage.

However, there are multiple sources of uncertainty (e.g., utility values, costs, transition probabilities, and the effect of CAS) in the model. This finding is accentuated by the lack of long-term evidence from randomized clinical trials, which would provide a more definitive assessment of cost-effectiveness. Thus, in this study, value of information analysis is applied to measure the upper limit on returns to future research and to identify parameters for which future research may be warranted.

METHODOLOGY

Markov Model and Monte Carlo Simulation

In our previous study (8), we designed a nine-state Markov model (Figure 1). A 10-year cohort simulation with a starting number of 1,000 TKRs was carried out. We selected a time horizon of 10 years given the average age of patients at operation was 70. Effectiveness was expressed by QALYs. Both costs and QALYs were discounted at 3.5 percent in line with 2003 Treasury guidelines (12). The differences between CAS and the conventional technique were expressed by the incremental cost-effectiveness ratio (ICER).

The model was made probabilistic using Monte Carlo simulation (MCS). We refined the model not only by keeping the hierarchical relationship between the utilities of states "Normal health after primary TKR," "TKR with serious complications," and "TKR with minor complications" in our previous study (8), but also by retaining the hierarchical relationship between the costs of states "Complex revision," "Simple revision," and "TKR operation for knee problem" in the simulation. We ran 10,000 120-cycle (a cycle length is 1 month) cohort simulations trials, randomly sampling from the distributions of transition probabilities, costs, and utilities. The assumed parameter distribution was showed in Table 1. In each of the 10,000 simulated trials, we calculated the net benefits of both CAS and conventional techniques at the level of £30,000 per QALY, the upper value suggested by the National Institute for Health and Clinical Excellence (15).

EVPI

EVPI is the difference between "the average of the maximized net-benefits" and "the maximum of the averages." It refers to the expected value of information per individual presenting at the decision point. This value can be calculated as follows: (i) Conduct an MCS by sampling from the probability density functions for all parameters. (ii) Calculate the mean net benefits for each treatment option, and identify the optimal option as that with the maximum net benefits. (iii) For each replication within the MCS, calculate the difference between the net benefits of the optimal treatment and the maximum net benefits across all treatments. (iv) EVPI is the expected value from step iii.

Population EVPI

Population EVPI reflects the effective EVI that is relevant to a decision about further research. Population EVPI equals individual EVPI multiplied by the discounted effective population over a time horizon of the technology. The effective "population" of TKR operations per year was assumed as 44,898 in England and Wales (14). The time horizon over which the information on CAS-TKR would be relevant to decision makers was assumed as 5, 10, 15, and 20 years, so that we could see the change of population EVPI in

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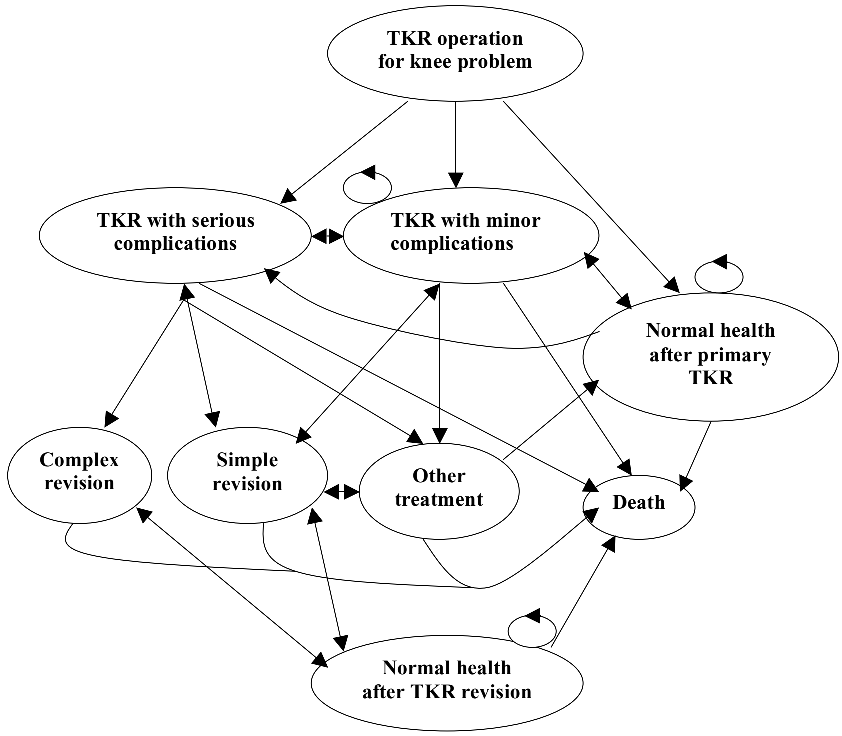

Figure 1. Markov state transition model for total knee replacement (TKR).

quantity as the increase of the time horizon of a technology. The discount rate is 3.5 percent.

EVPPI and Population EVPPI

The EVPPI is the difference between the expected value of a decision made with perfect information about a particular parameter and the current optimal decision. Several methods for estimating individual EVPPI have been suggested (5;6). For this analysis, we adopted a two-stage MCS approach, which is calculated as follows: (i) Single values are randomly selected from the probability density functions of the parameters for which we wish to estimate EVPPI. (ii) The parameters are fixed at the values selected in step i, and the net benefit for all treatment options is estimated by conducting MCS by sampling from the probability density functions of all other parameters. (iii) For each simulation conducted in step ii, the net benefit of the optimum therapy from the base analysis is subtracted from the maximum net benefit over all therapeutic options. (iv) Steps i–iii are repeated numerous times with different sets of values for the parameters of interest. (v) EVPPI is then the expectation of values obtained from repeating step iii.

Population EVPPI equals the individual EVPPI multiplied by the discounted effective population over a time horizon of the technology. Population EVPPI is a function of the chosen time horizon of a technology. However, the rank order of EVPPIs will be the same regardless of the different time horizon.

RESULTS

Markov Model and Distributions of Parameters

Figure 1 shows the nine-state Markov model and the transition relationship between the health states. Table 1 shows the distributions of the parameters in the Markov model. Uncertainties around the cost-related parameters were characterized by Gamma distribution function, making the distributions skewed with a lower bound of 0. Uncertainties around the utility values were characterized by a Beta distribution function, which has bounds of 0 and 1. Uncertainties around the transition probabilities were characterized by the Dirichlet distribution function—the multinomial equivalent to the Beta distribution (8).

Individual and Population EVPI

Figure 2 shows the EVPI for the UK population with TKR for different assumed time horizons of the technology, from 5 years to 20 years. In this instance, the population EVPI increase with the amount of WTP for one QALY is shown. If the WTP for one QALY were £30,000, the population EVPI assuming a 10-year time horizon for CAS-TKR would be £8.3 million, while the individual EVPI would be £21.4.

EVPPI

The overall EVPI for the model is a useful upper limit on returns to future research. However, of crucial importance

Table 1. Distributions of Assumed Parameters

Parameters	Mean	Range
Cost related (£)		
TKR operation for knee problem	5,197	121–10,090
Simple revision	6,234	1,337–11,032
Complex revision	7,326	4,161–11,741
Other treatments	2,844	1,467–5,625
Utility related		
TKR operation for knee problem	.72	.00026–1
Normal health after primary TKR	.78	.00026–1
TKR with minor complications	.66	.00000–1
TKR with serious complications	.35	.00000–.79542
Simple revision	.66	.00076–1
Complex revision	.51	.00000–.99997
Other treatments	.72	.00005–1
Normal health after TKR revision	.68	.00004–1
Transition related		
TKR operation for knee problem → Normal health after primary TKR	.94220	.91606–.96639
TKR operation for knee problem → TKR with minor complications	.04285	.02338–.07686
TKR operation for knee problem → TKR with serious complications	.01495	.00576–.03355
Serious complication → Minor complication	.01385	.00428–.03200
Serious complication → Complex revision	.02469	.01141–.04978
Serious complication → Simple revision	.00523	.00073–.01763
Serious complication → Other treatments	.95236	.93027–.97291
Minor complication → Serious complication	.00921	.00327–.02704
Minor complication → Normal health after primary TKR	.94236	.91959–.96569
Minor complication → Simple revision	.00250	.00011–.01224
Minor complication → Other treatments	.01701	.00780–.04165
Remain in the minor complication state	.02505	.01214–.04941
Normal health after primary TKR → Minor complication	.01385	.00372–.03206
Normal health after primary TKR → Serious complication	.00921	.00267–.02568
Remain in the normal health after primary TKR state	.97307	.95397–.98925
Complex revision → Serious complication	.02545	.01289–.05332
Complex revision → Normal health after TKR revision	.96963	.95063–.98668
Simple revision → Serious complication	.01590	.00696–.03382
Simple revision → Minor complication	.00816	.00235–.02361
Simple revision → Other treatments	.01701	.00621–.03753
Simple revision → Normal health after TKR revision	.95400	.93353–.97556
Other treatments → Serious complication	.00921	.00232–.02643
Other treatments → Minor complication	.01385	.00633–.03213
Other treatments → Simple revision	.00250	.00007–.01361
Other treatments → Normal health after primary TKR	.97057	.94070–.98605
Normal health after TKR revision → Complex revision	.02003	.00925–.03904
Normal health after TKR revision → Simple revision	.01038	.00308–.02717
Remain in the normal health after TKR revision state	.96468	.94502–.98283
Death probability related to TKR for patients after primary TKR	.00046	.00000–.00709
Death probability related to revision for patients after TKR revision	.00151	.00002–.00959
Death related to all reasons	.00341	.00021–.01598
CAS related		
Effect of CAS	.33910	.08261–.95753
Extra cost of CAS	235	110–498

Note. Gamma distribution is used for cost-related parameters. Beta distribution is used for utility-related parameters. Lognormal distribution is used for "effect of CAS," and the Dirichlet distribution is used for transition-related parameters.
TKR, total knee replacement; CAS, computer-assisted surgery.

is which particular parameters (or groups of related parameters) are most important in terms of representing the greatest value of information. In the EVPPI analyses (10-year time horizon of the technology), all individual parameters had an EVPPI of 0. However, three groups of parameters had positive EVPPIs (Table 2). Population EVPPI was £5.6 million for utility parameters, £20,000 for transition probabilities relating to CAS-TKR, and £5,000 for transition probabilities related to conventional TKR.

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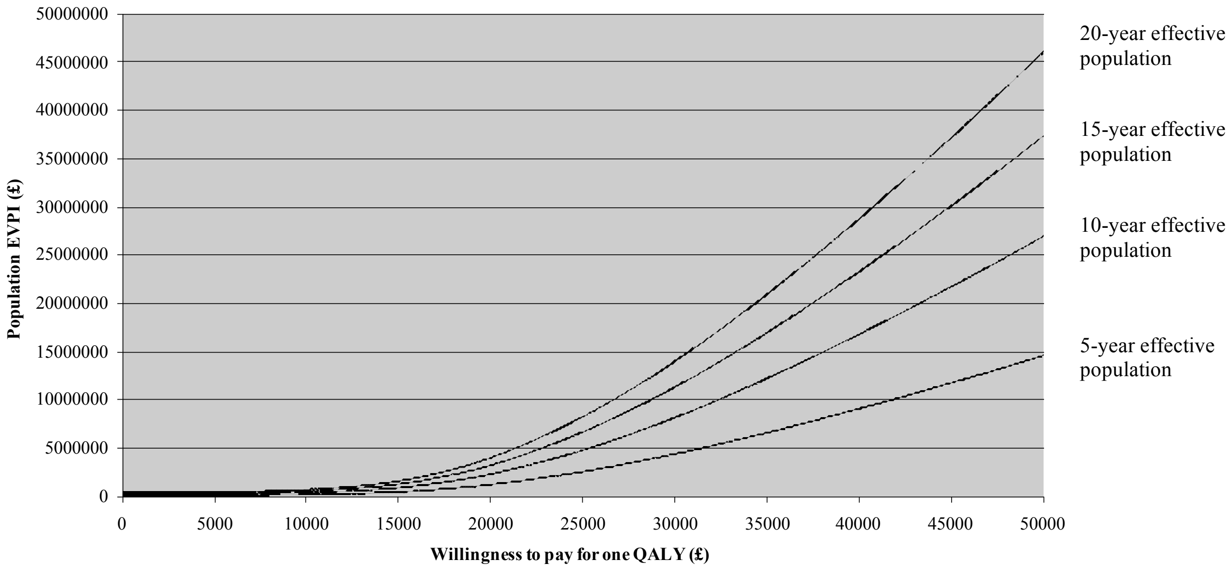

Figure 2. EVPI for UK population with TKR. EVPI, expected value of perfect information; TKR, total knee replacement; QALY, quality-adjusted life-year.

Table 2. EVPPI for Parameter Groups

Parameter group	EVPPI (£)
Conventional TKR cost-related parameters	0
CAS-TKR cost-related parameters	0
Utility-related parameters	14.4859
Conventional TKR transition-related parameters	.0128
CAS-TKR transition-related parameters	.0447
Both effect of CAS and extra cost of CAS	0

Note. EVPPI was calculated based on a WTP of £30,000/quality-adjusted life-year. All individual parameters had an EVPPI of 0.
EVPPI, expected value of partial perfect information; TKR, total knee replacement; CAS, computer-assisted surgery; WTP, willingness to pay.

DISCUSSION

In our earlier study (8), based on short-term evidence from the studies that have compared the clinical effectiveness of CAS with that of conventional TKR in terms of correct alignment of components, we found that compared with conventional TKR, computer-assisted TKR is a cost-saving technology in the long-term and may offer small additional QALYs.

Our analysis here of the value of additional information related to specific parameters or parameter groups confirms the results of parameter importance analysis from our early study (8). Using the analysis of covariance approach to explore the proportion of the total model sum of squares that is explained by each individual input parameter, it was found that utility-related parameters and transition probabilities were the most important.

However, population EVPI and EVPPI are more informative measures of parameter importance as they measure the maximum possible payoff to additional research. The population partial EVPI can help to focus research priorities as it allows identification of the parameters contributing most to decision uncertainty (5). In our earlier study (8), it was found that, at £30,000 per QALY, there was a 92 percent probability that CAS was the more cost-effective technology. Given this high degree of certainty, it is not surprising that individual EVPI is not high, although given the high use of the technology population EVPI is of more interest.

The key assumption in the earlier study was that CAS surgery, due to improving alignment of components, could reduce complication rate and revision rate. This assumption is associated with a high degree of uncertainty because of the lack of direct longer-term evidence in support. However, despite this degree of uncertainty, the partial value of perfect information showed that transition-related parameters have only limited information value, and to be justified, future research related to these parameters would have to have value for decision making relating to a large number of patients outside the UK setting.

In the value of information analysis, the annual size for the relevant patient population and the time horizon over which the evidence is relevant (and, hence, the size of the total patient population who might benefit from a reduction in uncertainty) are critical parameters and can only be a matter of judgment. Moreover, these two parameters may well differ for different items of information. For example, reducing the uncertainty around the effectiveness of CAS will only be relevant as long as the specific technology does not change or develop—which is likely to be a relatively short time period. However, during this short period, well-conducted studies of relative effectiveness would probably have relevance to patients in a range of countries where the

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technology might be adopted (our analysis only considers patients in England and Wales).

On the other hand, better estimates of patient utilities in different health states might have longer-term relevance (for the evaluation of future developments in TKR surgery) in the United Kingdom but might not necessarily be seen as generalizable to patients from all other countries interested in the technology. UK cost data are likely to be of interest only in the United Kingdom and to be relatively rapidly outdated. Thus, comparison of (UK) population EVPPI for different parameters judged under a single time horizon may be misleading in terms both of the value beyond the UK population and for different time horizons.

Furthermore, special attention should be paid to generalizing the results of the current study to other countries. We did the analysis from the UK National Health Service point of view in terms of the relevant costs. Other countries will have different cost structures for these procedures, which would influence the mean value and variance of the cost in each health state. Thus, our results can only provide information for UK decision makers and may not be applicable in other countries. It is encouraged that other countries repeat the analysis applying their own cost and size of relevant patient patients.

In addition, population EVPI and EVPPI are the upper limit for additional research in one country. If analysis were repeated in other countries, the EVPI for parameters that are common across countries would be greater, providing greater rationale for a coordinated program of future research.

CONCLUSION

Based on the value of information analysis, from a UK perspective, it is likely to be worthwhile to have additional research related to patient utilities at different health states. Further research related to transition probabilities may be of value, but only from a more global perspective.

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