Cost effectiveness of the implantable cardioverter defibrillator

Introduction

The development of the implantable cardioverter defibrillator (ICD) has had a major impact on the practice of cardiac electrophysiology because of its established efficacy in rescuing patients from ‘malignant’ ventricular arrhythmia. But the high initial costs of implanting such a device attracts attention. The published results of a number of large prospective randomized studies (AVID\textsuperscript{[1]}, MADIT\textsuperscript{[2]}) presented at the North American Society for Pacing and Electrophysiology, Seattle, WA, U.S.A., 1996) and MUSTT (Multicenter Unsustained Tachycardia Trial (MUSTT), presented at the North American Society for Pacing and Electrophysiology, Toronto, Canada, U.S.A., 1999) support increased clinical application of ICD therapy in the future. However, current uptake is variable in the western world with the U.S.A. implanting at a rate of 200 per million population per year compared to the U.K. where the rate is 8 million population per year. This discrepancy probably reflects both differing health finance structure and referral patterns due to differing levels of physician awareness. In this review we will examine the principals behind cost-efficacy analysis in health care and identify current methods applied to the analysis of ICD cost efficacy. We will review results from published studies on ICD cost-effectiveness and identify future therapy cost trends.

Basic concepts of cost-efficacy

It is a fundamental feature of health care practice that resources available to meet the demands of the population are limited. Therefore, there needs to be a process of rationing. In order for patients to receive new therapy there has to be a means of evaluation of new and existing health care interventions. The first stage is usually an assessment of the scientific innovation based on observations in the pre-clinical, laboratory setting. The second stage is the assessment of the therapy in optimized clinical circumstances. This has to be based on careful study design limited by ethical constraints. The third stage is an examination of clinical practice. Is the intervention effective based upon an assessment of the clinical studies, clinical skills and expertise? In the fourth stage a cost assessment has to be made which is usually based upon a number of assumptions. Endpoints are selected (for example mortality and morbidity) and the cost to achieve them are calculated based either on locally available data or that previously published. The fifth stage identifies the issue of availability matching the location of supplies to patients who need them. The final stage evaluates the distribution. This entails an assessment of who benefits most from the health care intervention and who loses as a result of not receiving funding to their health care programme. As innovations cascade down this decision tree, so the quality and sophistication of the data used to support their clinical application rapidly degrades. Thus their introduction and dissemination to clinical practice may be determined by shallow characterizations and assumptions of the type used in cost efficacy analyses, rather than peer-reviewed pre-clinical and clinical science. Clinicians are frequently unconcerned with overall health care finances and perceive their patient population need to justify therapies regardless of resources available. Unawareness of the constraints of limited resources and the effect of competing costs on therapy availability compounds this. Thus cost-efficacy analyses do have an important role in allowing comparison of therapy costs in diverse health care areas.

Cost-efficacy models

The simplest forms of cost-efficacy assessment are average cost-effectiveness ratios. These are derived by dividing the average cost of treating patients with a therapy by the overall cost of the therapy. Whilst the calculation of average cost-effectiveness ratios is relatively easy its practical application is limited. The usual reason for analysis of cost-efficacy is to assess the financial implications of a new therapy compared to existing therapies. Average cost-effectiveness ratios
do not allow for this. It is therefore important that a comparative cost-effectiveness analysis is performed. The simplest result of a comparative cost efficacy is that the new intervention results in improved clinical outcome with lower cost. In this scenario there is no need to evaluate the therapy further before its implementation. However, in the majority of cases new therapy is associated with increased resource implications.

There are, broadly speaking, three forms of comparative (incremental) cost-effectiveness assessment, each with a different cost end-point. A cost-effectiveness ratio examines the cost in clinical terms of life years extended or prevention of premature deaths. If an examination of morbidity or quality of life is made then the analysis estimates cost-utility ratios. When the outcome is translated into a direct cost i.e. the cost to receive a given therapy it is known as a cost-benefit ratio. The cost is usually determined as the willingness of a patient to pay for the therapy or a reflection of a proportion of the patients’ income. All cost analyses are illustrated in Fig. 1.

Each incremental cost-effectivity ratio is meaningless on its own. It has to be compared with ratios relating to other practices so that its relative cost-efficacy can be compared and hence pertinent decisions made. Goldman et al. attempted to identify costs that would be considered acceptable or cost-effective (Fig. 2)\(^3\). However, with finite resources it is the direct comparison of one therapy with another that determines its acceptability.

### Limitations of cost-effectiveness models

The ratios are calculated by the investigators on the basis of many different methodologies all of which may have flaws. The initial assessment of the cost of a therapy is open to many errors. In the U.S.A. the simplest way to calculate the cost is to add up all of the charges made by the relevant medical insurance agency (e.g. Medicare). However, this does not represent the true cost but a charge for the therapy. Similarly, innovative procedures may not be covered by a finance code and so the cost may be omitted or calculated incorrectly. In the National Health Service in the U.K. there can be regional variations in the charges for the same procedure. Ensuring all of the costs are counted has to be rigorous. Cost-effectiveness calculations are invariably inaccurate at the time of publication as the costs of different therapies change. The cost of innovative therapies frequently becomes discounted with its acceptance and more widespread utilization. A number of assumptions inherently have to be made in projecting events of the future that cannot be known e.g. life expectancy. This can be estimated using the medical literature or individual clinical practices. However, identical population characteristics can never be assumed. In the majority of models it is presumed that the first appropriate discharge of the device associated with pre-syncope or syncope is life saving. This cannot be assumed to be always correct as some
patients’ arrhythmias may be self-terminating or the patient may have been resuscitated. No models make adequate allowance for more distant cost benefits, for example the economic consequence for the return of a family breadwinner to the work place by one therapy as opposed to welfare support by another.

In an attempt to correct for uncertainties, sensitivity analyses are made, although by scientific standards these appear to be little more than ‘fudge factors’. Figures are given for the relevant cost ratios for factors above and below the expected value i.e. if generator longevity is predicted to be 4 years the cost efficacy is quoted for 3 and 5 years in addition. This also provides a means of prioritizing the relative merits of each factor. If there is little change in the cost-efficacy with different sensitivities then it is likely that that factor has minimal overall effect on cost.

Overall quality of life assessment is wrought with pitfalls. Many factors influence the value of saving lives in different populations. The public opinion of paediatric care (oncology, intensive care etc) is viewed very differently from the value of a screening programme (e.g. hypercholesterolaemia). Comparing such programmes is therefore fraught with complications and may lead to inappropriate support being proffered or denied for various clinical practices.

Thus whilst cost-efficacy has no value in the care of the individual, it may be a political tool used in the rationing process.

**Cost-efficacy and implantable cardioverter defibrillators**

The initial cost of an ICD is perceived to be expensive. The cost of the device is typically in the range of £25 000 with an additional cost of up to £4000 with a dual chamber lead system. In addition are the costs of the hospital stay, investigations (including electrophysiology study), anaesthesia and laboratory/theatre time. ICDs are not the only therapeutic option for patients with ventricular arrhythmias.

Electrophysiology testing to guide drug therapy is an alternative or more frequently, the empirical use of amiodarone. The initial cost of these therapies is a fraction of that of an ICD. However, more important are the assessments of quality of life and life expectancy. With the publication of the data from the AVID, MADIT and other studies we can identify populations that benefit in terms of mortality from ICD vs drug therapy (Fig. 3).

There have been a number of models of cost-efficacy published in the literature over the past 10 years. All differ in methodology with none being the perfect analysis. Because of the speed with which ICD technology is advancing all of the studies are outdated. The initial studies investigated a population with epicardial systems which is clearly different from the current transvenous devices. Currently available devices have advanced arrhythmia detection algorithms (single and dual chamber) to prevent inappropriate shocks. Electrogram storage capability has improved enabling identification of appropriate/inappropriate therapy. These features have an impact on both mortality and quality of life. Despite this the message from all of the published ICD cost-efficacy literature is that this therapy is comparative to other accepted forms of medical intervention.

We will now review the key published studies in an attempt to identify the beneficial and detrimental aspects of each model so as to define theoretically the ideal cost-efficacy model.
Kupperman et al.\textsuperscript{[4]} performed an incremental cost-effectiveness study comparing ICD therapy with drug therapy using decision-analytical modelling in a U.S. population. They retrospectively studied a patient population of 203 (138 initial implants and 65 undergoing generator replacement) who had at least one episode of cardiac arrest not associated with a myocardial infarction. Efficacy data were obtained from the literature and estimates of resource use and associated costs were taken from the national Medicare carriers and an expert panel of cardiologists. The devices were epicardial systems with the assumption from the literature that the operative mortality would be 3\% with an arrhythmic mortality during the first year of implantation of 2\% and a total year-1 mortality of 14\%. They noted that in the literature the 1-year mortality for drug treatment varied from 4.3\% to 43.6\%. Arbitrarily they selected the mid-point for their base case. Their estimate of the incremental cost-effectiveness of the ICD, as it was used in 1986, was $17,400 per year of life saved. They performed sensitivity analyses to account for different year-1 arrhythmic mortalities, initial hospitalization costs, rehospitalization rates and likelihood that a patient with an ICD is also prescribed antiarrhythmic medication. They tried to project to a 1991 case scenario with an anticipated generator longevity of 5 years and a non-thoracotomy approach and calculated $7400 per life year saved. They made comparisons with other therapies and concluded that ICD therapy was more cost-effective than the treatment of mild hypertension in men aged 40, heart transplantation and dialysis for renal replacement therapy. There were no adjustments made within the model to adjust for quality of life.

Larsen et al.\textsuperscript{[5]} compared ICD therapy with both conventional antiarrhythmic drug therapy and amiodarone therapy in patients with recurrent sustained ventricular tachycardia or fibrillation refractory to conventional drug therapy. They constructed a Markov (state transition) model to make the comparisons and assumed that each of the three groups were identical apart from the therapy. They also assumed that no patient would cross from one group to another. Therapy and outcomes in the three groups were taken from the literature in order to calculate probabilities of both non-sudden and sudden cardiac death (Table 1 and Fig. 4). They assessed the costs for 64 patients (21 with ICDs and 43 receiving amiodarone therapy). Inpatient costs for the conventional therapy group were assumed to be the same as for the amiodarone group. The baseline case was assumed to have a device longevity of 2 years, but sensitivity analysis adjusted for 19–96 months. Cost per life year saved was calculated to be $6600 for amiodarone vs conventional therapy and $29,200 for ICD therapy vs amiodarone therapy. Adjusting for a 5-year device longevity reduced the cost per life year saved to $16,500. They felt that their data had shown that ICD therapy was comparative to coronary artery surgery.

\begin{table}[h]
\centering
\caption{Mortality results from the published literature comparing ICD therapy with amiodarone and conventional therapy}
\begin{tabular}{lcccc}
\hline
Patient receives: & Reported weighted & No. of & Reported weighted & No. of \\
& average yearly & studies & average yearly & total \\
& mortality rate, & & mortality rate, & patients & \\
& non-sudden & & sudden cardiac & \\
& cardiac death & & death & \\
& & & & \\
Conventional antiarrhythmic therapy & 9.3\% & 1 & 21.1\% & 5 & 223 \\
Amiodarone therapy & 9\% & 8 & 6.6\% & 8 & 955 \\
ICD therapy & 5.5\% & 5 & 1.8\% & 3 & 1296 \\
\hline
\end{tabular}
\end{table}

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{mortality_results}
\caption{ICD (■) vs drugs (●): reported mortality results (prospective randomized studies) for AVID, MADIT and Wever.}
\end{figure}
Figure 4  Reported yearly mortality rates for non-sudden (■) and sudden (□) cardiac death in ICD, amiodarone and conventional drug therapy groups.

bypass grafting for stable angina and less than hospital based haemodialysis. The study performed no formal documentation of quality of life but calculated that if the quality of life on amiodarone therapy was 40% lower than that with ICD, the marginal cost-effectiveness ratio for the ICD ($14 000/QALY) fell below that of amiodarone therapy ($17 000/QALY) making the use of the defibrillator the preferred strategy.

Anderson and Camm[6] recognised limitations of the previous studies. They identified that they did not allow for different survival data or costs and therefore tried to establish a more flexible model. However, their model is not a true cost-comparative study as ICD therapy was not compared incrementally to an alternative strategy. They simplified the cost efficacy calculation to:

\[
\text{Cost-efficacy} = \frac{\text{total cost of use of ICD in a group}}{\text{gain in years of life in the group}}
\]

The costs were based on 1991 U.K. purchasing prices for investigations, devices, hospital stay and follow-up. Costs were calculated on the basis of 40 implants in their practice and a database of more than 500 survivors of myocardial infarction. They determined their figures over a fixed period of 3 years dividing the total ICD costs in that 3 years by the difference in mortality of the ICD group over medical therapy. A noteworthy omission from their calculations was the cost of replacement generators when battery life had been reached. They determined that the cost of ICD therapy ranged from £22 400 for the high risk groups to £57 000 for the low risk groups with an electrophysiological study per life year saved. Interestingly they identified that in their high-risk population of post infarction patients if the ICD generator were free the cost of this strategy would still be £19 500 a life year. There was, however, no evaluation of quality of life in this study. Whilst this analysis succinctly illustrates the effects on cost-efficacy of different populations it is not possible to compare it to other studies of incremental cost-efficacy.

Kupersmith et al[7] examined the cost-effectiveness of the epicardial and endocardial ICD with electrophysiology guided drug therapy. They retrospectively examined 218 patients who had undergone ICD implantation from 1980 to 1987 and in whom the time of first ICD discharge was known (assumed to be time of death without ICD). All underwent electrophysiological studies. Kaplan–Meier curves were computed for electrophysiologically guided therapy and ICD. Costs were based on Medicare charges, and ICD longevity was assumed to be 4 years. The following specific circumstances were analysed: ejection fraction <0.25 (n=60), ICD without prior electrophysiological study and endocardial ICD (n=20). Base-case cost-effectiveness was $31 100/year life saved. Cost effectiveness if the ejection fraction was <0.25 was $44 000/YLS compared to $27 200/ YLS if the ejection fraction ≥0.25. Implanting an ICD without an electrophysiological study resulted in a significant reduction to $18 100/YLS. With an endocardial system and with no pre-implant electrophysiological study the cost was found to be reduced to $14 200/YLS. One assumption of most cost-effectiveness models is that the first shock represents death without an ICD (i.e. 100% mortality). In this study it was found that the cost-effectiveness was insensitive to alteration in this assumption and only changed significantly when it decreased to <38%.

Wever et al[8] studied 60 post myocardial infarction survivors of cardiac arrest caused by ventricular tachycardia or ventricular fibrillation. They were randomly assigned ICDs as first choice of therapy (n=29) or tiered therapy (n=31) starting with anti-arrhythmic drugs and guided by electrophysiological testing. They were followed for a median of 729 days. They calculated the cost per day alive to be $66 in the early ICD arm and $99 in the tiered therapy group (Table 2).

Valenti et al[9] retrospectively examined 35 patients for the year before and year after ICD implantation in their centre (1989–93). All devices had been implanted for documented and reproducible ventricular arrhythmias. On reviewing hospital records and interviewing general practitioners they examined the
number of hospitalizations, the primary reason for each hospitalization and the duration of each stay in the 12 months before and after device implantation. They found a significant reduction in the number of hospitalizations after device implantation (0.9 vs 3.3 hospitalizations/patients/year, P<0.05). The most frequent cause of admission before implantation was ventricular arrhythmia and afterwards was following a shock from the device. The duration of stay was reduced after ICD implantation with a mean of 9 days/patient/year compared to 33 days before the device. They also noticed a reduction in 90% from 1085 to 106 days patient time spent in hospital for cardiac reasons following device implantation. The study assessed the cost using 1991 estimates for hospitalization and devices. They estimated the cost per patient to be 46 982 SFr before and 10 463 SFr after with the average cost of implantation being 58 061 SFr. On this basis the calculated payback period for ICD investment was 19 months. While this study retrospectively analysed hospitalization there was no formal assessment of quality of life issues. Costs were calculated in a simplistic method for the group as a whole and did not take account of investigations and any other concomitant therapy. However, this study is unique in that the patient group acted as its own control.

Mushlin et al.[10] reported the first randomized prospective cost-efficacy study by careful cost evaluation of therapy in patients enrolled in the MADIT study. This was a particularly important group because of the unique ICD population studied. Patients were enrolled if, post myocardial infarction they were found to have a low ejection fraction along with non-sustained ventricular tachycardia. They followed 181 of the U.S. patients that were randomized with 1–61 months of follow-up data. The cost methodology used a combination of utilization data from each implanting site with national price and cost data sources. The exception to this was hospitalization costs that used the charges for the specific admission and the cost-to-charge ratios for that hospital. They calculated a cost of $22 800 per life year saved for a transvenous device that was projected to $16 900 for an 8-year device. The study has demonstrated the potential of cost-efficacy analyses alongside carefully designed prospective studies.

Owens et al.[11] used a Markov transition state model to estimate the quality-adjusted length of life and expenditures for a population of patients who received amiodarone or an ICD. They analysed three arms: (1) ICD implant only, (2) amiodarone switching to ICD if resuscitated from ventricular tachycardia/ventricular fibrillation, (3) amiodarone only. They used time trade-off techniques to calculate quality adjusted life years with the base-case current health taken as 0.75. It was assumed that quality of life did not change with amiodarone therapy or ICD implantation. Survival rates were based upon randomized trials and patient registries. In sensitivity analyses they compared survival rates of ICD vs amiodarone from 5% to 60%. Numerous co-morbidities were studied for both the ICD and amiodarone arms, taken from published data. Treatment with an ICD was the most expensive of the regimens but it resulted in the greatest quality adjusted life expectancy. In high-risk patients the marginal cost-effectiveness of treatment with an ICD relative to amiodarone ranged from $74 400 per quality adjusted life year gained (assuming ICD use reduces total mortality by 20%) to $37 300 (assuming 40% reduction in mortality). Sensitivity analyses indicated that estimates of the cost effectiveness of ICD therapy were particularly influenced by relative reduction in mortality, quality of life with therapy, frequency of generator replacement along with the initial cost of implantation. The amiodarone-to-ICD arm was expensive having a relatively high mortality but with the costs of amiodarone and ICD therapy being accrued. This would therefore suggest the benefit of early ICD implantation.

### Discussion

It is estimated that the use of ICDs in secondary prevention may account for up to 1% of the total U.S. health budget. It is therefore reasonable to analyse the cost-efficacy of such a therapy. However, historically it has been difficult to develop accurate models of ICD cost-efficacy. The overriding challenge has been the paucity of prospective randomized data on the efficacy of ICDs in comparison to conventional therapy. However, with the announcement of MADIT and AVID more rigorous data can be applied to the models. In spite of this the cost-efficacy of ICD therapy is still viewed with great scepticism. Percutaneous coronary angioplasty (PTCA) is universally accepted therapy in the management of

---

**Table 2 Mortality and cost for different therapy arms of Wever study (1996)**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>% deaths</th>
<th>Cost per day alive ($)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early ICD (29)</td>
<td>14</td>
<td>66</td>
</tr>
<tr>
<td>Tiered therapy total:</td>
<td>35</td>
<td>99</td>
</tr>
<tr>
<td>Antiarrhythmic drugs only</td>
<td>70</td>
<td>210</td>
</tr>
<tr>
<td>Late ICDs (16)</td>
<td>19</td>
<td>103</td>
</tr>
<tr>
<td>VT surgery (5)</td>
<td>20</td>
<td>91</td>
</tr>
</tbody>
</table>

---

Eur Heart J, Vol. 21, issue 9, May 2000
coronary artery disease. The individual cost of each procedure is less than that for ICD therapy but so is the overall survival benefit. It may be because of this that PTCA has not undergone the same scrutiny as ICD therapy in the analysis of its cost-efficacy. The overriding message from all of the above studies is that ICD therapy is comparable to other forms of accepted medical practice (Fig. 5).

Most of the above studies reviewed have been for ICDs reserved for life-threatening situations such as failed sudden cardiac death. However, with studies such as MADIT and MUSTT there is the likelihood of greater ICD therapy even in primary prevention. It is likely that the cost per life year saved will increase with these strategies and so the need for more accurate models of cost efficacy will increase. On the other hand advances in ICD technology will likely lead to increased device longevity, patient acceptability and increased efficacy.

In most of the above models analyses are based upon projected events such as mortality and generator longevity. Whilst this enables an overall picture to become more apparent it inherently has flaws. It is impossible to be certain that the same population characteristics apply to the group being studied as that from which the projections are being made. Equally in those studies that are based upon actual costing and events of a set population the true cost-efficacy is impossible to accurately gauge as it will only be with the course of time that the true cost of a therapy will become apparent. This is perhaps particularly applicable to ICD therapy with its initial large outlay cost. In the past 10 years there have been dramatic changes in device technology resulting in significant changes in projected longevity, which is up to 12 years in some circumstances. This makes previous cost efficacy calculations invalid. It may be that the ideal cost-efficacy model consists of a hybrid of projections from the latest literature and actual patient characteristics from one’s own practice allowing for the individual tailoring of the model. In the current climate of increasing financial constraints, the necessity to justify the cost-efficacy of a practice is increasing. Such a model therefore would be an appealing method of informing the purchasers and auditing one’s own practice.

While a number of the above studies make estimates of the cost of quality of life years gained none has a comprehensive assessment of quality of life in patients with ICDs or on conventional antiarrhythmic therapy. Vlay et al.[12] demonstrated high levels of anxiety and anger in patients receiving ICDs. However, they showed that there was no change in this level after implantation of the device. In this group patients became accustomed to the device after a mean of 3.6 months and were able to resume normal activities. In contrast, Luderitz et al.[13] demonstrated that 47 of 57 patients felt that their...
symptoms were improved with an ICD system. However a significant proportion had fear of ICD discharges and discomfort from the device. Forty-seven percent of patients were unable to resume normal active life after device implantation. Psychological and social costs or benefits of ICDs have only been briefly touched upon in cost–efficacy analysis but it is clearly an important aspect. It is most likely that with advances in technology inappropriate discharges and size reduction will lead to ICD therapy becoming more acceptable to the patient and hence reduce the relative cost contribution of this aspect of the treatment.

Conclusions

Whilst there have been a series of cost–efficacy analyses of ICD therapy they do have design flaws. ICD therapy is perceived to be expensive because of the initial costs of the device implantation. Other practices in medicine are well accepted and their cost–efficacy rarely questioned. However, ICD therapy has been repeatedly shown to exhibit comparative cost–efficacy to these practices.

Clinicians and health economists need to be aware that the cost efficacy analysis should be used to guide the development of sensible clinical practice but it can easily be corrupted to a tool for crude rationing. Purchasers of health care should remember that, historically, technological advance has been the solution, not the problem.

P. R. ROBERTS
T. R. BETTS
J. M. MORGAN
Wessex Cardiothoracic Centre,
Southampton General Hospital,
Southampton, U.K.

References