Special report: cost-effectiveness of implantable cardioverter defibrillators in a MADIT-II population

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Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
The use of implantable cardioverter-defibrillators (ICDs) to prevent death in patients who had experienced a myocardial infarction (MI) and had a low ejection fraction.

Type of intervention
Secondary prevention.

Economic study type
Cost-effectiveness analysis and cost-utility analysis.

Study population
The study population reflected an average patient from the MADIT-II. Patients of either sex who were older than 21 years of age were eligible if they had had a documented MI at least one month before entry and a documented ejection fraction of 30% or less within 3 months before entry. Patients were not eligible if they had an indication approved by the US Food and Drug Administration for an implantable defibrillator, were in New York Heart Association functional Class IV, had undergone coronary revascularisation within the proceeding 3 months, or had experienced an MI within the past month. They were also not eligible if they had advanced cerebrovascular disease, were of childbearing age and were not using prescribed contraceptive measures, or had any condition other than cardiac disease that was associated with a high likelihood of death during the trial.

Setting
The setting was secondary care and a hospital. The economic study was carried out in the USA.

Dates to which data relate

Source of effectiveness data
The effectiveness data were derived from a synthesis of completed studies and authors' opinions.

Modelling
A published decision model (including a Markov process) was used to estimate the costs and survival of a cohort of patients who could receive either prophylactic ICD (implanted without a thoracotomy) or conventional therapy. The time horizon of the model was lifetime and the cycle length was one month. Patients who received an ICD were at risk of dying from the implant procedure. Those patients who did not die from the ICD implantation and those patients on conventional treatment entered a Markov tree, which included the clinical events that could occur during each 1-month
period as a patient was followed until death. During each 1-month period, the patient could die from arrhythmic or
nonarrhythmic cardiac causes, or from non-cardiac causes. If none of these events occurred, the patient remained well
for the 1-month period. Patients who had an ICD could have a lead infection or failure that caused them to withdraw
from treatment (and to switch to conventional therapy). The model was validated using the follow-up of the MEDIT-II
study (20 months).

Outcomes assessed in the review
The outcomes estimated from the literature were:

- the starting age of the population with an ejection fraction equal to or less than 30;
- the total mortality and the arrhythmic mortality with conventional therapy;
- the total mortality, the arrhythmic mortality, the probability of ICD procedural death, the efficacy of ICD in reducing
  arrhythmic mortality, the frequency of ICD generator replacement, and the probability of lead problems requiring
  surgical intervention with ICD; and
- the utility value associated with post-MI.

Study designs and other criteria for inclusion in the review
It appears that a systematic review of the literature was not undertaken to identify relevant primary studies. Most of the
evidence came from the MADIT-II study, the design of which and study characteristics were described in detail.
Limited information on the other sources of evidence was provided. Non-cardiac mortality data were derived from US
life tables.

Sources searched to identify primary studies
Not stated.

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

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

Number of primary studies included
Seven primary studies provided the clinical evidence.

Methods of combining primary studies
Not stated.

Investigation of differences between primary studies
Not stated.

Results of the review
The starting age of the population with an ejection fraction equal to or less than 30 was 64.4 years (range: 30 - 80).
With conventional therapy, the total mortality (over a 20-month period) was 19.8%, while the arrhythmic mortality (over 20 months) was 10%.

With the ICD:
the total mortality (over 20 months) was 14.2%,
the arrhythmic mortality (over 20 months) was 3.8%,
the probability of ICD procedural death was 0% (range: 0 - 3),
the efficacy of ICD in reducing arrhythmic mortality was 67% (range: 30 - 100),
the frequency of ICD generator replacement was 7 years (range: 2 - 9), and
the probability of lead problems requiring surgical intervention (over 20 months) was 2.4% (range: 0 - 5).

The utility value associated with post-MI was 0.88 (range: 0.6 - 1).

Methods used to derive estimates of effectiveness
The authors made some assumptions that were used in the decision model.

Estimates of effectiveness and key assumptions
The utility value associated with the ICD was assumed to have been 0.88 (range: 0.6 - 1). Non-cardiac mortality was assumed to be equal to the age- and gender-specific non-cardiac mortality in the US general population. ICD treatment did not affect the frequency of arrhythmic events, but it did increase the chance of surviving an arrhythmic event if one occurred. ICD affected only the sudden cardiac death mortality. Patients who were hospitalised for lead infections received a utility toll of one day.

Measure of benefits used in the economic analysis
The summary benefit measures used were the expected life-years (LYs) and quality-adjusted life-years (QALYs). These were estimated using a modelling approach. An annual discount rate of 3% was applied, owing to the long time horizon of the analysis. No detailed information on the source of utility values used to derive the QALYs was provided.

Direct costs
Discounting was relevant since the lifetime costs were estimated, and an annual rate of 3% was applied. The unit costs were not presented separately from the quantities of resources used. The economic evaluation included the costs of the initial hospitalisation, ongoing therapy (including physician visits, laboratory tests and re-hospitalisation for ICD-related complications) and the ICD generator or lead replacement. The costs of follow-up (outpatient visits), patients’ travel and inconvenience were also considered.

The cost/resource boundary of the study was unclear. Inpatient costs came from the Myocardial Infarction Triage and Intervention (MITI) patient registry for patients on conventional therapy and from diagnostic-related group sources. Since charges were used, a cost-to-charge ratio was applied to estimate the true costs of the inpatient services. Hospitalisation costs for patients in the ICD arm were similar to those estimated for patients on conventional therapy, but for the cost of the ICD (implantation and replacement). Other categories of costs were derived from studies published between 1992 and 2002. All the costs were presented in 2003 values using the Gross Domestic Product Deflator.

Statistical analysis of costs
The costs were treated deterministically in the base-case.
Indirect Costs
The indirect costs were not considered in the economic evaluation.

Currency
US dollars ($).

Sensitivity analysis
Sensitivity analyses were performed to account for important model uncertainties. A univariate sensitivity analysis was carried out on all model inputs within ranges derived by the authors on the basis of literature estimates and experts' opinions. Multivariate sensitivity analyses were performed on key model inputs. The impact of considering populations with varying rates of sudden and non-sudden cardiac death was also considered.

Estimated benefits used in the economic analysis
The discounted LYs were 7.75 with the ICD and 5.90 with conventional therapy.

The discounted QALYs were 5.63 with the ICD and 4.30 with conventional therapy.

The analysis of intermediate outcomes showed that patients in the ICD arm experienced a greater probability of non-sudden cardiac death, owing to prolonged survival.

Cost results
The discounted costs were $144,000 with the ICD and $76,100 with conventional therapy.

Synthesis of costs and benefits
Incremental cost-effectiveness and cost-utility ratios were calculated to combine the costs and benefits of the strategies under examination.

The discounted incremental cost per LY saved with an ICD over conventional therapy was $36,700.

The discounted incremental cost per QALY saved with an ICD over conventional therapy was $50,900.

The univariate sensitivity analysis showed that the incremental cost per QALY saved ranged from $32,300 to $372,500. Utility, efficacy and the cost of the ICD represented the variables with the greatest influence on the base-case results. Starting age and frequency of battery replacement also had some effect.

If the efficacy of the ICD stopped after 3 years, then the cost per QALY was above the value of $100,000.

The cost-effectiveness of the ICD was influenced strongly by the total annual cardiac mortality and by the proportion of deaths that were sudden. There was a U-shaped relationship between the cost-effectiveness of the ICD and the total annual cardiac mortality, with the cost-effectiveness becoming less favourable at both low and high rates of total cardiac mortality. In addition, at any given annual cardiac mortality rate, the cost-effectiveness of the ICD improved significantly as the ratio of sudden cardiac death to non-sudden cardiac death increased.

Similar cost-effectiveness and cost-utility ratios were observed in populations of patients post-MI, those suffering from congestive heart failure, and in survivors of sudden cardiac death.

Authors' conclusions
The implantable cardioverter-defibrillator (ICD) was a cost-effective alternative to conventional care (with an incremental cost of $51,000 per QALY) in patients who had experienced a myocardial infarction (MI) and had a low
ejection fraction. Efficacy and cost of the ICD, impact of the intervention on quality of life, age of the patients, and frequency of generator replacement, were the most important determinant of the analysis. The ICD was more cost-effective in populations of patients with high rates of cardiac mortality and of sudden cardiac death, especially in the setting of low rates of death from other causes.

CRD COMMENTARY - Selection of comparators
The selection of the comparator was appropriate as it reflected usual care. However, no details of the interventions included in "conventional care" were provided. Further, the authors noted that no comparison with the anti-arrhythmic amiodarone was performed, which would have been interesting. You should decide whether this is a valid comparator in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness data came from published evidence. However, it was unclear whether a systematic review of the literature had been undertaken to identify relevant studies. Most of the evidence came from a clinical trial, which was described in detail. Characteristics of the patient sample and follow-up were provided. However, there was limited information on the design of the other sources. The methods used to extract and then combine the primary estimates were not reported. Some assumptions were also made. Extensive sensitivity analyses were performed to address the issue of uncertainty in the model estimates.

Validity of estimate of measure of benefit
The use of QALYs and L Ys as the summary benefit measures was appropriate as the interventions affected both dimensions of life expectancy and quality of life. Details of the source of the utility values were not reported. Discounting was applied, as recommended in US guidelines. Undiscounted results were also given. Both measures of benefits are comparable with the benefits of other health care interventions.

Validity of estimate of costs
The authors stated that a societal perspective was adopted. However, the indirect costs were not included in the economic evaluation. In addition, it was unclear whether such categories of costs could have been relevant bearing in mind the age of the typical patient considered in the model. The unit costs were not presented separately from the quantities of resources used, and a detailed breakdown of the cost items was not provided. In fact, the costs were presented as macro-categories, which reduces the possibility of replicating the analysis. The source of the data was reported. The costs were treated deterministically but were varied in the sensitivity analysis. The price year was given, thus aiding reflation exercises in other settings.

Other issues
The authors did not carry out extensive comparisons of their findings with those from other studies. The impact of the intervention on different populations of patients was investigated, and alternative values for model inputs were used in the sensitivity analysis, which enhances the external validity of the study. The authors noted that their analysis had some limitations, mainly related to the need for assumptions (because the trial data were often aggregate).

Implications of the study
The study results supported the use of ICDs in the prevention of death after MI. Future studies could identify large sub-groups of patients in whom the cost-effectiveness of prophylactic ICD implantation was different from the average of the population considered in the current study. The authors pointed out that the availability of more recent data would improve the robustness of the decision model.

Source of funding
None stated.
Bibliographic details

Other publications of related interest


Indexing Status
Subject indexing assigned by NLM

MeSH
Blue Cross Blue Shield Insurance Plans; Cardiac Pacing, Artificial /economics; Cost-Benefit Analysis; Defibrillators, Implantable /adverse effects /economics /utilization; Evidence-Based Medicine; Humans; Multicenter Studies as Topic; Myocardial Infarction /mortality; Randomized Controlled Trials as Topic; Treatment Outcome; United States; Ventricular Dysfunction, Left /etiology /mortality /therapy

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