Effectiveness and cost-effectiveness of implantable cardioverter defibrillators in the treatment of ventricular arrhythmias among Medicare beneficiaries

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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 in the treatment of ventricular arrhythmias was investigated.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised Medicare patients who were discharged from a US hospital, and who had a primary discharge diagnosis of ventricular fibrillation or ventricular tachycardia (International Classification of Diseases, ICD-9-CM codes 427.1, 427.4, 427.5). Recipients were defined as patients who received a device within 90 days of hospital admission (ICD-9-CM procedure codes 37.94 to 37.96). Patients who underwent generator replacements or lead revisions were excluded. Also excluded were patients who:

- were younger than 65 years;
- did not reside in the USA;
- were enrolled in a health maintenance organisation;
- had non-continuous enrolment in Medicare Part A or Part B during the year following initial admission;
- were admitted to a non-acute care hospital, federal hospital, or hospital outside the USA;
- had invalid mortality data; or
- who had missing Write-off file data (the Medicare Beneficiary Health Insurance Skeletonized Eligibility write off file was used to exclude patients).

The authors also excluded patients with possible miscoding of ventricular arrhythmia as the primary diagnosis:

- discharge with a total stay of less than 2 days,
- admission on the same day as, or the day after discharge from an admission unrelated to ventricular arrhythmia, acute myocardial infarction during index admission, or elective admission.
Elective defibrillator implantations that were thought to be unrelated to the index ventricular arrhythmia event were eliminated by excluding patients who received an implant on the day of index admission or the day after admission. Further, to avoid bias arising from the selection of therapy in moribund patients, only those discharged alive from the index admission were included in the study.

**Setting**
The setting was secondary care. The economic study was carried out in the USA.

**Dates to which data relate**
The effectiveness and resource use data were collected from 1 January 1987 to 30 September 1995. The price year was 1999.

**Source of effectiveness data**
The effectiveness data were derived from a single study.

**Link between effectiveness and cost data**
The costing was undertaken retrospectively on the same patient sample as that used in the effectiveness study.

**Study sample**
No power calculations to determine the sample size were reported and no specific sample size was planned. Patients were identified using the Health Care Financing Administration Medicare Provider Analysis and Review inpatient hospitalisation file. A single longitudinal record for each patient was created by linking the index admission to all prior and subsequent admissions. The authors began inclusion in 1987 because it was the first year in which at least 1% of the patients in the cohort received an implantable defibrillator.

A total of 125,892 patients met all the entry criteria and were therefore included in the study. Of these, 7,789 (6.2%) received an implantable defibrillator within 90 days of hospital admission and the remaining 118,103 patients received only medical treatment. The mean age of the patients who received an implantable defibrillator was 71 (+/- 5) years and 17% of the patients were females. For those not receiving an implantable defibrillator, the mean age was 76 (+/- 7) years and 40% of the patients were females.

**Study design**
This was a retrospective cohort study. The patients were followed for up to 8 years. As this was a retrospective study, there was no loss to follow-up.

**Analysis of effectiveness**
All the patients included in the study were accounted for in the analysis. The outcome was all-cause mortality at 1, 2 and 3 years.

The authors found that recipients of a defibrillator were more likely to be younger, white, male and urban dwelling. They were also more likely to have ischaemic heart disease or heart failure, and to be admitted with a diagnosis of ventricular fibrillation to hospitals that were capable of coronary bypass surgery and defibrillator implantation procedures. These patients were also more likely to receive other interventional procedures such as angiography, coronary angioplasty and coronary bypass surgery, within 90 days of initial admission.

To address the possibility that the primary outcome might be biased by the selection of patients for treatment with an implantable defibrillator, the authors performed a propensity score adjustment. Demographic and clinical data thought to be predictive of treatment selection were entered as independent variables in a multivariable logistic regression that
had receipt of an implantable defibrillator as the dependent variable. A propensity score was then calculated for each patient that yielded the probability, from 0 to 1, of receipt of an implantable defibrillator. Patients who received a defibrillator were then matched one to one with patients who did not receive a defibrillator but who had an equivalent propensity score, defined as an absolute value (propensity score for defibrillator patient minus propensity score for non-defibrillator patient) of less than or equal to 0.01. Those who did not receive a defibrillator were accepted as matches only if their survival time was equal to or greater than the time to device implantation for the corresponding defibrillator patient.

The matching procedure resulted in 7,612 pairs with equal overall probability of receiving a defibrillator, based on all of the variables included in the propensity score model. The baseline characteristics between matched pairs were similar, although patients who received a defibrillator were more likely to have undergone subsequent coronary angiography and coronary bypass surgery within 90 days of hospitalisation.

Mortality for the matched cohort at 1, 2 and 3 years was estimated using logistic regression. The 8-year Kaplan-Meier cumulative survival was also estimated. One-, 2- and 3-year mortality for a sub-set of matched pairs within the middle tertile of propensity score was also examined, using logistic regression to assess the outcomes of patients with an intermediate likelihood of receiving either course of therapy.

**Effectiveness results**
In the unmatched analysis, mortality was found to be lower in patients who received a defibrillator:

- 11% versus 23% at 1 year (odds ratio, OR=0.43, 95% confidence interval, CI: 0.39 - 0.46),
- 21% versus 34% at 2 years (OR 0.50, 95% CI: 0.47 - 0.54), and
- 29% versus 43% at 3 years (OR 0.55, 95% CI: 0.51 - 0.59).

Survival of the entire patient cohort improved significantly for patients enrolled more recently. The trend toward improved survival over time was statistically significant for the defibrillator recipients, but not for those who did not receive a defibrillator (results not shown).

In the matched analysis, patients receiving a defibrillator also had significantly lower mortality than matched patients who did not receive a defibrillator:

- 11% versus 19% at 1 year (OR 0.57, 95% CI: 0.51 - 0.63),
- 20% versus 30% at 2 years (OR 0.66, 95% CI: 0.60 - 0.72), and
- 28% versus 39% at 3 years (OR 0.70, 95% CI: 0.63 - 0.77).

The higher survival among these recipients persisted during the 8 years of follow-up, (p=0.0001).

Median undiscounted survival was 5.7 years (95% CI: 5.5 - 6.0) in the defibrillator group and 4.6 years (95% CI: 4.3 - 4.8) in the non-defibrillator group.

The sub-group analysis of the 1,269 matched pairs representing the middle tertile of the propensity score confirmed a significantly lower mortality among patients who received a defibrillator than among those who did not.

**Clinical conclusions**
The authors concluded that the use of implantable cardioverter defibrillators was associated with significantly lower mortality in comparison with medical treatment.

**Measure of benefits used in the economic analysis**
The measure of benefit used was the life-years gained. The benefits were discounted at an annual rate of 3%.

**Direct costs**
The resource quantities and the costs were not reported separately. The direct costs included appear to have been those of the health service (i.e. Medicare). The authors did not report the direct costs included in the analysis, they only reported that expenditures were defined as the sum of diagnostic-related group payments plus outlier payments. Although not explicitly reported by the authors, it seems that prices have been derived from Medicare charges. The cost analysis was based on the match-pair analysis of effectiveness. Discounting was relevant as the costs could be incurred during an 8-year period. The costs were appropriately discounted at a rate of 3% per annum. The study reported the average costs. All prices were normalised to 1999 prices using the Gross Domestic Product Deflator inflation index.

**Statistical analysis of costs**
The mean costs were reported with their associated standard deviations.

**Indirect Costs**
The indirect costs were not included in the analysis.

**Currency**
US dollars ($).

**Sensitivity analysis**
No sensitivity analyses were performed.

**Estimated benefits used in the economic analysis**
The discounted mean survival was 4.6 years for the defibrillator group and 4.1 years for the non-defibrillator group.

**Cost results**
Expenditures during the first year of follow-up were $48,700 (+/- 20,500) for the defibrillator group versus $17,000 (+/- 18,500) for the non-defibrillator group.

Expenditures during the 8 years of follow-up were $78,700 for the defibrillator group versus $37,200 for the non-defibrillator group. This represented a difference of $41,500 in discounted cumulative expenditures.

**Synthesis of costs and benefits**
The costs and benefits were combined by calculating a cost-effectiveness ratio (additional cost required per life-year gained). The resulting marginal cost-effectiveness ratio of defibrillator versus non-defibrillator treatment was $78,400 per life-year gained during 8 years of follow-up. At 3 years, the marginal cost-effectiveness ratio was $133,500 per life-year gained.

**Authors’ conclusions**
The use of implantable cardioverter defibrillators in the treatment of ventricular arrhythmias was associated with significantly lower mortality and higher costs. The cost-effectiveness was higher than many, but not all, generally accepted therapies used in the USA.
Implantable cardioverter defibrillators were compared with treatment without defibrillators, because not all patients in the USA receive these defibrillators. You should decide if this represents current practice in your own setting.

Validity of estimate of measure of effectiveness
The study was based on a retrospective cohort design. This was appropriate for the study question as it allowed the identification of a very large number of patients, making the results of the study more generalisable. Even though the exclusion criteria were numerous, the study sample was very large (over 125,000 patients) and appears to have been representative of the study population. The effectiveness analysis was handled credibly. As the patient groups were shown not to be comparable at analysis on virtually all demographic and clinical characteristics, and to overcome the possibility that the primary outcomes might be biased by the selection of patients for treatment, the authors used a multivariable propensity score that included patient and hospital characteristics to match pairs of patients, with one patient in each pair receiving a defibrillator and the other not. This approach enhances the validity of the results.

Validity of estimate of measure of benefit
The estimation of benefits was obtained directly from the effectiveness analysis. The life-years gained were appropriately discounted at a rate of 3% per annum.

Validity of estimate of costs
The authors did not explicitly report the perspective used in the economic analysis. However, as the analysis was carried out using Medicare databases, it would appear that the perspective adopted was that of Medicare. However, it was unclear which costs were included in the analysis, and whether any relevant categories of costs and costs were omitted. The costs and the quantities were not reported separately, which will hamper the generalisability of the results of the economic analysis. Again, the source of the unit costs was not reported, but it would appear to have been based on Medicare charges. No statistical or sensitivity analyses of the costs were undertaken to evaluate the uncertainty or variability in the estimates. Discounting was necessary, as the costs could be incurred during an 8-year period, and was appropriately undertaken at a rate of 3% per annum. The price year was reported, which will aid any future inflation exercises.

Other issues
The authors made appropriate comparisons of their findings with those form other randomised trials that had found similar results. The authors pointed out that their results extended the findings from other trials since they were based on a less selected population in wider practice settings and had a longer follow-up. The issue of generalisability to other settings was addressed, as this study was based on settings across the USA and had a very large study sample. The authors do not appear to have presented their results selectively and their conclusions reflected the scope of the analysis. One interesting observation from the authors was the fact that the survival advantage of defibrillator recipients relative to non-recipients narrowed substantially with longer follow-up. However, the authors reported that this could have been due to the relatively small number of patients remaining at risk late in follow-up, which will limit the statistical power of these observations.

Implications of the study
The authors reported that, even though the cost of care for defibrillator-treated patients was consistently higher than for non-recipients, the higher costs could be acceptable in light of improved survival in patients with ventricular tachycardia or ventricular fibrillation.

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Other publications of related interest


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MeSH
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