Life expectancy gains and cost-effectiveness of implantable cardioverter/defibrillators for the primary prevention of sudden cardiac death in patients with hypertrophic cardiomyopathy

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.

CRD summary
The study examined the cost-effectiveness of using implantable cardioverter/defibrillator (ICD) insertion or amiodarone therapy for the prevention of sudden cardiac death (SCD) in patients with hypertrophic cardiomyopathy (HCM), with no history of cardiac arrest but a significant risk of SCD. The study results support the cost-effectiveness of ICD insertion from the perspective of the US third-party payer, especially for patients with HCM aged 25 years with one or more risk factor for SCD, and for patients aged 45 or 65 years with 2 or more risk factors for SCD. The authors' conclusions are likely to be valid and robust despite limited reporting of the sources used to derive clinical and economic estimates.

Type of economic evaluation
Cost-effectiveness analysis, cost-utility analysis

Study objective
The objective of the study was to examine the cost-effectiveness of using implantable cardioverter/defibrillator (ICD) insertion or amiodarone therapy for the prevention of sudden cardiac death (SCD) in patients with hypertrophic cardiomyopathy (HCM), with no history of cardiac arrest but a significant risk of SCD.

Interventions
The three strategies considered were ICD insertion, amiodarone therapy and no therapy.

Location/setting
Canada/secondary care.

Methods
Analytical approach:
A Markov model was developed in order to simulate the management of eligible patients under the three scenarios considered. The analysis focused on benefits in terms of increased survival, and risks in terms of adverse events. A patient's lifetime horizon was considered. The authors stated that the perspective of a third-party payer was adopted.

Effectiveness data:
The clinical estimates were derived from published sources. The methods and conduct of a review of the literature were not reported and the approach used to identify the sources was not described. The mortality rates were taken from cohort studies, while data on effectiveness and the side-effects of ICD were obtained both from ICD registries and cohort studies. There was little information on the published studies used to estimate the other model parameters, although the base-case values and ranges were reported. Further details can be found in the online appendix. Key clinical estimates were the rates of mortality and risk of atrial fibrillation for patients with HCM, and different risk of SCD with the three different options.

Monetary benefit and utility valuations:
Utility valuations were derived from published studies, details of which were not provided. However, as no evidence was available for patients with HCM, it was assumed that the utility of uncomplicated HCM would be equivalent to that of New York Heart Association functional Class II angina. The authors also pointed out that some assumptions about
Measure of benefit:
The summary benefit measures were the life-years (LYs) and quality-adjusted life-years (QALYs). These were estimated using the decision model. An annual discount rate of 3% was applied.

Cost data:
The health service costs included in the analysis were related to hospitalisation, treatment of severe neurologic disability, ICD insertion and the treatment of ICD-related complications, amiodarone therapy and its complications, cardioversion, warfarin therapy, the treatment of stroke with or without sequelae, and the treatment of minor and major bleeding. The costs and resources were presented as macro-categories and were derived from published studies (details not given). The costs were expressed in US dollars ($). The price year was 2005. Future costs were discounted at an annual rate of 3%.

Analysis of uncertainty:
A deterministic univariate sensitivity analysis was undertaken in order to identify the most influential inputs. The authors stated that plausible ranges were used and most of these extreme values appear to have been derived from the literature. Furthermore, the analysis was replicated in different scenarios based on alternative combinations of age and number of risk factors for SCD, using published data. A first-order Monte Carlo simulation based on 10,000 trials was also carried out to estimate the lifetime occurrence of adverse events associated with each strategy.

Results
Under the base-case assumptions, the expected LYs and QALYs were 13.2 and 11.8, respectively, with no therapy, 16.5 and 14.6 with amiodarone, and 18.5 and 16.5 with ICD insertion.

The expected lifetime costs were $18,500 with no therapy, $123,400 with amiodarone and $161,300 with ICD insertion.

The incremental costs per LY and QALY gained versus no therapy were, $31,500 and $37,300, respectively, with amiodarone and $26,500 and $30,000 with ICD insertion.

The incremental cost per QALY for ICD insertion versus amiodarone was $19,400. Thus, amiodarone was dominated by ICD insertion through extended dominance (more effective and with lower incremental cost per QALY or LY with respect to the next more effective strategy).

Cost-effectiveness and cost-utility ratios were lower in high-risk populations and higher in low-risk patients.

The sensitivity analysis corroborated the base-case findings, in that prophylactic ICD insertion yielded the greatest QALYs and remained cost-effective (cost per QALY below the threshold of $50,000) in most scenarios. In particular, ICD insertion was highly cost-effective relative to no therapy in two specific scenarios: for patients with HCM aged 25 years with one or more risk factor for SCD, and for patients aged 45 or 65 years with 2 or more risk factors for SCD.

In general, the most influential model inputs were the annual risk of SCD, starting age of the cohort and the utility of ICD therapy.

Authors' conclusions
The authors concluded that ICD insertion for the primary prevention of SCD in patients with HCM was a cost-effective strategy from the perspective of the US third-party payer in comparison with either amiodarone therapy or no therapy. The authors noted that the selection of the most appropriate patients eligible for prophylactic ICD insertion remains the most controversial step in the prevention of SCD. However, the current study identified the sub-groups of patients who might achieve the greatest benefits at an affordable cost from ICD insertion. Individual patient preferences might play a key role in the selection of the most appropriate strategy.

CRD commentary
Interventions:
The choice of the comparators was appropriate in that they are likely to reflect the available options for the prevention of SCD. They should also be considered as valid options in other settings.

Effectiveness/benefits:
Little information on the characteristics of the sources used to derive clinical estimates and on the approach used to identify these sources was provided. Given the large number of variables required, it is likely that more details will be found in the online appendix. However, from the information provided in this paper, it is not possible to judge the validity of the primary data. The authors pointed out the lack of randomised clinical trials providing efficacy data on ICD therapy. Nevertheless, the fact that the ranges of values tested in the sensitivity analysis were derived from published sources suggests that plausible estimates were considered in the base-case analysis, leaving less likely estimates to the alternative scenarios. This represents a strength of the analysis. The use of QALYs is another advantage of the study given the importance of patient preferences for a prophylactic therapy in potentially asymptomatic patients, especially in the case of younger individuals.

Costs:
The analysis of the costs was consistent with the authors' stated perspective. A breakdown of the cost items was not given, and the costs were presented as macro-categories since they were derived from published sources in which aggregated costs were reported. This is a common approach although it has the disadvantage of being less transferable to other settings. Statistical analyses of the costs were not performed as they were treated deterministically. However, the costs were varied in the (deterministic) sensitivity analyses.

Analysis and results:
The costs and benefits of the alternative strategies were appropriately combined using an incremental analysis, which eliminated the dominated strategy (i.e. amiodarone). The results of the analysis were presented clearly, with tables and graphical representations. The impact of the most influential model inputs was described. The issue of uncertainty was extensively addressed in the sensitivity analysis. The authors did not discuss the generalisability of their results to other settings.

Concluding remarks:
The quality of the study methodology was good, but sources used to derive the clinical and economic data were not described in detail (more information was provided in the online appendix). Nevertheless, the extensive use of sensitivity analysis and the consequent robustness of the study results make the authors' conclusions valid.

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