Cost effectiveness of cardiac resynchronization therapy in Greece: an analysis based on the CArdiac REsynchronization in Heart Failure trial
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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.

CRD summary
The study evaluated the cost-effectiveness of cardiac resynchronisation therapy (CRT) in addition to pharmacological management compared to pharmacological management alone in patients with severe heart failure and poor response to pharmacological therapy. The authors concluded that CRT was cost-effective. Extensive methodological flaws and assumptions tended to favour CRT. Inadequate reporting made it difficult to assess the appropriateness of the authors’ conclusions.

Type of economic evaluation
Cost-utility analysis

Study objective
The study evaluated the cost-effectiveness of adding cardiac resynchronisation therapy (CRT or pacemaker) to usual care (pharmacological therapy) in patients with moderate to severe heart failure with markers of cardiac dyssynchrony.

Interventions
Patients were randomised to either pharmacological therapy alone or CRT in addition to pharmacological therapy. The interventions were not described in this study.

Location/setting
Greece/Hospital

Methods
Analytical approach:
The economic evaluation was based on the results of the CArdiac REsynchronization in Heart Failure (CARE-HF) trial (see Other Publications of Related Interest). Within-trial data were used up to the 29.4 month mean follow-up time and extrapolated beyond the follow-up using regression and data assumptions to generate lifetime cost-effectiveness results. The authors integrated data from other studies and governmental sources in order to adapt the CARE-HF trial to a Greek setting.

The analysis adopted a third party payer perspective, which corresponded to social insurance funds in Greece.

Effectiveness data:
The CARE-HF trial was a randomised controlled trial with 813 participants stratified by New York Heart Association (NYHA) function class. CARE-HF had been used in several national evaluations of CRT use in severe heart failure. The primary clinical effectiveness measure in the trial was survival without a cardiovascular event. The authors indicated that survival in the trial was regressed separately for each arm using an exponential distribution to predict long-term survival. The exponential distribution was used because it had the best Akaike information criterion rating, indicating that the exponential distribution best fit the data. The combination of trial data and extrapolated survival curves provided the basis for the analysis of cost-effectiveness.

Monetary benefit and utility valuations:
The trial measured EQ-5D utilities at baseline and at three months for both trial arms. Additional utility data was calculated by mapping Minnesota Living with Heart Failure (MWLHF) quality of life data taken at 18 months and at
the end of the study (29.4 months) to EQ-5D using a mixed model of the relationship between the two instruments derived from a published study (see Other Publications of Related Interest). A last available information carried forward approach was adopted for the extrapolation to lifetime.

Measure of benefit:
Quality-adjusted life-years (QALYs) was the summary measure of benefit. Benefits were discounted at 3% annually.

Cost data:
Costs included primary care, hospital care and procedures. The authors excluded pharmaceutical costs from the analysis as they were not statistically significantly different during the follow-up of the CARE-HF trial. The authors assumed that in the absence of data on failed operations or re-operations that their cost would equal the cost of a successful operation.

Health care resource use was taken from the CARE-HF clinical trial database. Resource costs were derived from Greek private and publicly funded health care. Reimbursement data was used from the main Greek social insurance fund, the Hellenic Social Insurance Fund (IKA). The IKA database contained data from 2004 to 2008 but only claims data from patients who had CRT in 2007 and 2008 were used for the study. Cost data were updated to 2011 figures using data from the National Procurement Committee in Greece. Costs were weighted by the type of CRT device used and proportions of private and public health expenditure. Costs were reported in Euros (€).

Analysis of uncertainty:
The authors analysed uncertainty by bootstrapping from the exponential distribution used to extrapolate survival. This bootstrapping was used to produce a cost-effectiveness acceptability curve (CEAC) to represent the probability that CRT was cost-effective at different thresholds of willingness to pay for a QALY.

Additional analyses included an analysis conducted using only the trial follow-up of 29.4 months and one-way sensitivity analyses that varied discount rates and survival assumptions.

Results
The base case results indicated that the incremental cost-effectiveness was €6,045 (95% CI 4,292 to 9,411) per QALY. CEAC showed that at an assumed threshold of €25,000 per QALY, CRT would be cost-effective nearly 100% of the time.

The analysis using only trial results had an ICER of €16,780 per QALY (95% CI 10,399 to 31,602). Other sensitivity analyses generally reduced the ICER.

Authors' conclusions
The authors concluded that CRT in addition to standard pharmacological therapy was a cost-effective treatment in Greece compared to pharmacological therapy alone and could be recommended for routine use in heart failure patients with dyssynchrony markers.

CRD commentary
Interventions:
The interventions were not described in this study but the original CARE-HF studies were referenced and should provide this information.

Effectiveness/benefits:
The authors did not report the parameter estimates or the model fit results for the survival analysis. The graph presenting the extrapolation did not appear to be the actual parametric curves. It was not possible to be sure that the extrapolation was appropriate. The authors stated that they did sensitivity analyses around the survival analysis that were conservative for CRT but the incremental cost-effectiveness ratios improved and the authors did not explain this result.

The authors acknowledged that carrying the last utility score forward was a weakness of the trial. This method did not account for patient aging and decreasing quality of life over time. As currently formulated, patients in the general population may eventually have worse quality of life than those living with heart failure.
The authors appropriately derived QALYs from the CARE-HF trial data and by applying a published mapping algorithm to trial data but the results of this mapping exercise were not presented. QALY data were only presented in aggregate at the end of the model. Utility value parameters were not reported.

Costs:
Costs were reported at an adequate level of detail using appropriate Greek sources.

Two assumptions in costing may have been problematic. Firstly, the authors eliminated drug costs from total cost estimates because there was a non-statistically significant difference. That was not a good reason to exclude costs if those costs might have a significant impact on the results. The uncertainty could have been incorporated in the analysis. Secondly, the authors assumed that failed operations and reoperations had the same cost as a successful operation. This assumed that failed operations and reoperations were identical to successful operations in complication risk and these assumptions may have favoured CRT. The study used an annuity to distribute the cost of the implanted pacemaker over the battery life of the device but the methods for calculating the annuity and annual cost were not reported.

Analysis and results:
Bootstrapping was an appropriate technique to capture uncertainty around ICERs; uncertainty around the extrapolation issues was noted in Effectiveness/benefits.

Sensitivity analyses conducted by the authors on survival benefit were opaque. No mortality rates were reported for alternative survival assumptions so assessing their validity was not possible.

The authors compared their study results to those of other studies based on the CARE-HF trial. Why these studies produced different results was not reported and this hindered evaluation of generalisability and external validity.

Concluding remarks:
Inadequate reporting made it difficult to assess the appropriateness of the authors' conclusions.

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