Cost-effectiveness of dual-chamber pacing compared with ventricular pacing for sinus node dysfunction

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 study examined a rate-modulated, dual-chamber pacemaker (DDDR) and a single-chamber right ventricular pacemaker (VVIR).

Type of intervention
Treatment.

Economic study type
Cost-utility analysis.

Study population
The study population comprised a cohort of patients with sinus node dysfunction and in sinus rhythm. Patients were excluded if they had serious concurrent illnesses, scored less than 17 on the Mini-Mental State Examination, or were in heart failure at the time of implantation.

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

Dates to which data relate
The effectiveness data and most resource use data came from a study published in 2002. The price year was 2001.

Source of effectiveness data
The effectiveness evidence was derived from a single study.

Link between effectiveness and cost data
Most of the costing was performed prospectively on the same sample of patients as that used in the clinical study.

Study sample
There was limited information on the method used to select the sample since the primary study had already been published. Overall, a sample of 2,010 patients was enrolled. The median age was 74 years and 48% of the participants were women. There were 1,014 patients in the DDDR group and 996 patients in the VVIR group.

Study design
This was a prospective, randomised clinical trial. After lead placement, but before generator implantation, the devices
were randomly programmed to DDDR or VVIR. The length of follow-up was 4 years. Blinding was performed but it was unclear whether it was single or double.

**Analysis of effectiveness**
The analysis of the clinical study was conducted on an intention to treat basis. The outcomes measures estimated in the clinical trial and then used in the current economic evaluation were utility values and some event probabilities. Utility values were assessed using a standard time trade-off instrument. The baseline comparability of the study groups was not stated.

**Effectiveness results**
The authors stated that the clinical outcomes of patients randomised to DDDR pacing were consistently better than those of patients randomised to VVIR pacing. However, the differences were statistically significant only for the development of atrial fibrillation (adjusted hazard ratio, HR=0.77, p<0.01) and for hospitalisation for heart failure (adjusted HR 0.73, p<0.02). The utility values were:

0.833 with DDDR and 0.834 with VVIR during the first year and in subsequent years;

-0.046 for crossover to DDDR (only for VVIR patients);

-0.021 in both groups for first nonfatal event;

-0.040 in both groups for second nonfatal event;

-0.046 in both groups for death during the year;

-0.019 with VVIR for history of crossover to DDDR;

-0.030 in both groups for history of one prior nonfatal event; and

-0.059 in both groups for history of two or more nonfatal events.

Annual event probabilities (which were derived from the trial but calibrated in order to be used in the model) for DDDR and VVIR were, respectively:

0.1975 and 0.2469 for first nonfatal event in year 1;

0.1068 and 0.0956 for first nonfatal event in year 2;

0.0799 and 0.0933 for first nonfatal event annually after year 2;

0.0721 and 0.0902 for second nonfatal event;

0.0510 and 0.0470 for death as first event;

0.1112 and 0.1233 for death after 1 event;

0.1485 and 0.1306 for death after 2 events; and

0.1600 in year 1 and 0.0140 after year 1 for crossover from VVIR to DDDR.

**Clinical conclusions**
The effectiveness analysis provided clinical data for the within-trial analysis and also the inputs used in the model to extend the time horizon of the analysis.
Modelling
A Markov model was constructed to project the costs and quality-adjusted survival that were estimated within the trial timeframe (4 years) over the patient's lifetime. The cycle length was one year. US life tables were used to derive age-specific mortality rates. For total mortality and other outcomes, an incidence density analysis was applied to trial data to estimate rates of events, mortality and crossover. For patients with missing data on costs or quality of life before completion of the trial, predicted values from regression models were used to estimate cumulative costs and quality of life. The Markov model classified all individuals according to their actual mode of pacing and their history of nonfatal cardiac events (atrial fibrillation, new heart failure, stroke). The model was validated using real data derived from the clinical trial.

Measure of benefits used in the economic analysis
The summary benefit measure used was the quality-adjusted life-years (QALYs). These were estimated by combining survival data and quality of life estimates in the modelling approach. The utility weights came from the sample of patients included in the clinical trial. An annual discount rate of 3% was applied to expected survival.

Direct costs
Discounting was relevant since the costs were incurred during a long timeframe. An annual discount rate of 3% was applied. The unit costs were not presented separately from the quantities of resources used. The health services included in the economic evaluation were pacemaker implantation, follow-up outpatient costs, medication costs, and costs due to re-hospitalisation for cardiovascular events (e.g. atrial fibrillation, heart failure, stroke). Pacemaker implantation covered hardware, hospitalisation costs and professional fees. Outpatient costs were for emergency department visits, unscheduled outpatient visits, and 50% of scheduled visits during the trial. Other costs such as time costs and out-of-pocket costs were not included because their impact on the total costs was negligible.

The cost/resource boundary of the study was unclear, although the authors stated that a societal perspective was adopted. The resource use data came mainly from the sample of patients included in the clinical trial. Outpatient generator replacements were assumed to be necessary every 8 years for DDDR pacemakers and every 11 years for VVIR pacemakers. The costs came from national averages for the appropriate diagnosis-related group (DRG). To account for physician fees, inpatient costs were inflated by 16.6%. The price year was 2001.

Statistical analysis of costs
Some statistical analyses of the costs were carried out.

Indirect Costs
The indirect costs were not included in the economic evaluation.

Currency
US dollars ($).

Sensitivity analysis
A bootstrap approach, generating 1,000 different study simulations by resampling with replacement from the study population, was used to examine the stability of the results. Confidence intervals (CIs) were generated. One-way sensitivity analyses were also performed. These investigated the discount rate, implantation costs, generator replacement cost and delay, impact of a history of crossover on quality of life or costs, the effect of pacing mode on quality of life, mortality rates and age. The ranges of values used were mainly obtained from the primary sources used to derive clinical and economic data.

Estimated benefits used in the economic analysis
Over the 4-year timeframe of the trial, the cumulative (discounted) QALYs were 2.690 with DDDR and 2.677 with VVIR (difference 0.0129, 95% CI: -0.1074 - 0.1442).

Over a patient's lifetime, the cumulative (discounted) QALYs were 6.49 with DDDR and 6.35 with VVIR (difference 0.14).

Cost results
Over the 4-year timeframe of the trial, the cumulative (discounted) costs were $27,441 with DDDR and $26,760 with VVIR (difference $681, 95% CI: -1,426 - 2,964).

Over a patient's lifetime, the cumulative (discounted) costs were $59,104 with DDDR and $58,160 with VVIR (difference $944).

Synthesis of costs and benefits
An incremental cost-utility ratio was calculated to combine the costs and benefits of the two strategies under evaluation.

Using actual trial data (4 years), the incremental cost per QALY gained with DDDR over VVIR was $52,814.

Over a patient's lifetime, the incremental cost per QALY gained with DDDR over VVIR was $6,800.

The bootstrap analysis showed that DDDR pacing saved money and prolonged quality-adjusted life expectancy in 15.9% of simulations, and was more costly but associated with better quality-adjusted life expectancy in another 73.4% of simulations. DDDR pacing was cost-effective in 91.9% of simulations at a threshold of $50,000 per QALY, and in 93.2% of simulations at a threshold of $100,000.

Other interesting results were also found. For example, from the univariate sensitivity analysis, if the DDDR generator had to be replaced every 6 years on average rather than every 8 years, the cost-effectiveness ratio would rise to $39,000 per QALY. The cost per QALY was robust to variations in the cost of the device or other variables.

Authors' conclusions
For patients with sick sinus syndrome requiring pacing, the rate-modulated, dual-chamber pacemaker (DDDR) increases quality-adjusted life expectancy at a cost that is generally considered acceptable.

CRD COMMENTARY - Selection of comparators
The selection of the comparators was based on the interventions compared in the primary clinical trial that provided the data. You should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness evidence came from a clinical trial, which was appropriate for the study question. There was limited information on the design and patients' characteristics because the trial had already been published. Thus, it was difficult to examine the validity of the study. However, the robustness of the clinical evidence was ensured by the randomised design and the large group of patients recruited.

Validity of estimate of measure of benefit
The summary benefit measure (QALYs) was appropriate because it considers the impact of the interventions on both quality of life and survival. Discounting was applied, as recommended in US guidelines. The utility weights were derived from the same sample of patients as that used in the clinical analysis.

Validity of estimate of costs
The categories of costs considered in the economic study appear to have been consistent with the perspective of a third-party payer, although the authors stated that a societal perspective was adopted. The unit costs were presented, although a detailed breakdown of items was not. In fact, some costs were presented as macro-categories. The source of the data was reported. Some key economic items were varied in the sensitivity analysis. The price year was reported, which aids reflation exercises in other time periods. The authors noted that only health care costs were included in the analysis, but noncovered costs associated with events and pacemaker syndrome would have presumably reduced the incremental cost of the DDDR.

Other issues
The authors compared some of their clinical findings with those from other studies and, in general, comparable results were observed. The issue of the generalisability of the study to other settings was not explicitly addressed, although sensitivity analyses were performed on key model inputs. This enhances the external validity of the analysis. The study referred to patients with sinus node dysfunction and this was reflected in the authors' conclusions. The authors noted that the observed differences in costs and benefits between the groups were small.

Implications of the study
The study results suggested that the benefits of DDDR in comparison with VVIR might be worth its cost. The authors stated that future investigations should evaluate biventricular pacing for patients whose underlying conduction system disease may require frequent ventricular pacing.

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Other publications of related interest

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