

# The effectiveness and cost-effectiveness of dual-chamber pacemakers compared with single-chamber pacemakers for bradycardia due to atrioventricular block or sick sinus syndrome: systematic review and economic evaluation

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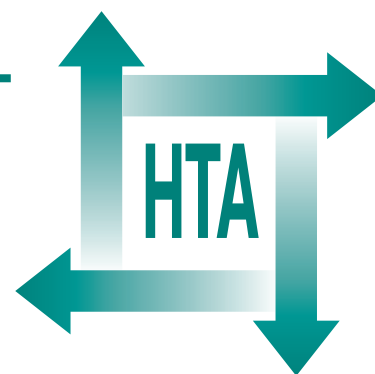
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## *Executive summary*

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## Executive summary

### Objective

The objective of the assessment was to estimate the effectiveness and cost-effectiveness of dual-chamber pacemakers versus single-chamber atrial or single-chamber ventricular pacemakers in the treatment of bradycardia due to sick sinus syndrome (SSS) or atrioventricular block (AVB).

### Description

A pacemaker consists of a small, battery-powered generator and one or more leads. In a single-chamber system, one lead is used, most commonly pacing the right ventricle. Dual-chamber pacemakers have two leads, placed in the right atrium and right ventricle. They act synchronously when a slow natural heart rate is detected to mimic the sequential physiological contraction of the atria and ventricles.

Single-chamber pacemakers may be atrial or ventricular. Atrial pacemakers are used where slow heart rate is due only to sinoatrial disease, i.e. where conduction between the atria and ventricles is intact. Single-chamber ventricular pacemakers, which are much more commonly used in practice, are appropriate where conduction between the atria and ventricles is impaired.

### Epidemiology and background

Bradycardia is abnormally slow heart rate. SSS is present when the heart's natural pacemaker, the sinoatrial node, fails to initiate cardiac contraction. It is mainly the result of chronic fibrodegenerative processes or local calcification in the atrial wall. Prevalence is around 0.03% and rises with age. AVB denotes defective conduction of the atrioventricular conduction system. It may be progressive, with higher grades carrying worse prognosis. Prevalence is around 0.04% and is higher in the elderly and in men.

### Methods

A systematic review was carried out of randomised controlled trials (RCTs) of the effectiveness of dual-

chamber pacemakers in the relevant populations compared with either ventricular or atrial devices. Studies were identified by searching electronic databases and relevant Internet sites, contact with device manufacturers and experts in the field, and searching bibliographies of studies retrieved. Inclusion criteria were applied by two researchers and related to the populations of interest, study types (systematic reviews or RCTs), language (English only), interventions (minimum 48 hours) and outcomes (restricted to patient-based measures). Data were extracted by one researcher and checked by another. Tabulation and narrative synthesis were carried out. Quality was appraised using standard frameworks, but not summary scores. Meta-analyses, using random effects models, were carried out where appropriate. Limited exploration of heterogeneity through stratification was possible.

A literature search was carried out for published economic evaluations or systematic reviews of such studies. Economic evaluations submitted to the NHS National Institute for Health and Clinical Excellence were obtained. Critical appraisal was carried out using two frameworks, for generic and decision-analytic economic evaluations.

A decision-analytic model was developed in a spreadsheet program, using a Markov approach, to estimate the cost-effectiveness of dual-chamber versus ventricular or atrial pacing over 5 and 10 years from the perspective of the UK NHS as cost per quality-adjusted life-year (QALY). Uncertainty was explored using one-way and probabilistic sensitivity analyses.

### Results

#### Number and quality of studies, and direction of evidence

The searches retrieved a systematic review of effectiveness and cost-effectiveness published in 2002, four parallel group RCTs and 28 cross-over trials.

The quality of the systematic review was good. It was used as the basis for reporting the existing published economic literature as no additional published studies of this type were identified. ►

The quality of the parallel group studies was reasonable. They included over 7000 participants and ran over 3–5 years, measuring clinically relevant outcomes [e.g. death, pacemaker syndrome, atrial fibrillation (AF), stroke, functional capacity and heart failure]. Two were trials of mode (in which a dual-chamber pacemaker is inserted and randomised to act in dual- or single-chamber mode) and two were trials of device, in which patients were randomised before implantation. One was in people with SSS only (MOST), two were in mixed populations (PASE and CTOPP) and one was in people with AVB only (UKPACE).

There was no significant effect on mortality in single trials or meta-analysis. Dual-chamber pacing had a favourable and statistically significant effect on AF (pooled odds ratio = 0.76), but not on stroke or heart failure, although non-significant trends in favour of dual-chamber pacing were shown in some trials. The effect on AF was time dependent and more marked in trials including people with SSS. Functional capacity was not significantly improved. Effects on quality of life varied according to measurement method, were not large, may be subject to bias in one trial (MOST) and were likely to reflect differences in the incidence of pacemaker syndrome.

Pacemaker syndrome was reported only in trials of mode and occurred in more than a quarter of participants on ventricular pacing. It was associated with reduction in quality of life. In trials of mode, reprogramming to dual-chamber pacing was straightforward and achieved in most cases with improvement of symptoms. In trials of device, upgrading required an invasive procedure and this was carried out in less than 5% of cases.

The cross-over trials were much smaller and of shorter duration, with less complete reporting of methods and a wider range of outcomes studied. The shorter duration precluded the measurement of outcomes such as mortality, although positive effects were shown for some individual symptoms and exercise capacity (although this outcome is confounded by the use of rate-responsive pacemakers). The cross-over trials were carried out, in general, earlier than the larger parallel studies.

### Summary of benefits

Dual-chamber pacing was associated with lower rates of atrial fibrillation, particularly in SSS, than ventricular pacing, and prevents pacemaker syndrome. Higher rates of atrial fibrillation were seen with dual-chamber pacing than with atrial

pacing. Complications occurred more frequently in dual-chamber pacemaker insertion.

### Costs

The cost of pacemaker systems was highly variable. Dual-chamber devices are more expensive owing to the additional lead, more time involved in implantation and higher risk of complications. The need to upgrade single-chamber to dual-chamber devices offsets the additional acquisition costs over time. The cost of a dual-chamber system, over 5 years, including cost of complications and subsequent clinical events in the population, was estimated to be around £7400. Because of the additional clinical consequences of pacemaker syndrome and atrial fibrillation (and its sequelae) the overall cost difference between single and dual systems was not large over this period: around £700 more for dual-chamber devices.

### Cost-effectiveness

Published economic analyses were not informative. Sponsor evaluations were of variable quality and suggested that dual-chamber pacing was likely to yield benefits at low cost (or with savings to the NHS).


In the PenTAG model, the cost-effectiveness of dual-chamber compared with ventricular pacing was estimated to be around £8500 per QALY in AVB and £9500 in SSS over 5 years, and around £5500 per QALY in both populations over 10 years.

Atrial pacing dominated dual-chamber pacing at 5 and 10 years (i.e. was more effective at lower cost).

### Sensitivity analyses

There was considerable uncertainty in the models of cost-effectiveness, much arising because the differences in costs and benefits are small and so the incremental cost-effectiveness ratio is potentially subject to large variation.

In the comparison of dual and ventricular pacing, the differential cost of devices is clearly important. The incidence, duration and severity of pacemaker syndrome was a critical determinant of cost-effectiveness. Under more conservative assumptions regarding the persistence of mild pacemaker syndrome, the cost-effectiveness of dual-chamber pacing was around £30,000 per QALY. AF rates were a further source of uncertainty, in terms of overall relative risk and the relationship between risk and time.

The probabilistic sensitivity analysis showed that, under the base-case assumptions, 

dual-chamber pacing was likely to be considered cost-effective at levels of willingness to pay that are generally considered acceptable by policy makers.

Atrial pacing dominated dual-chamber pacing under all assumptions.

### **Limitations of the calculations (assumptions made)**

There were significant uncertainties and limitations in the underlying data. Pacemaker syndrome is the subject of clinical debate and its impact on quality of life is not clear. The utility values used in the model were inferred rather than measured directly in people with pacemaker syndrome.

The data underlying the analysis of dual versus atrial pacing were limited, being derived from a single small trial.

### **Other important issues regarding implications**

Over 70% of the eligible population currently receive dual-chamber pacemakers, although overall UK pacing rates are lower than in the rest of Europe.

Around 10% of candidates for pacing are likely to have atrial fibrillation at the time of implant, and so a theoretical maximum for diffusion of dual-chamber pacing is around 90% of the eligible population.

## **Conclusions**

Dual-chamber pacing results in small but potentially important benefits in populations with SSS and/or AVB compared with ventricular pacemakers. There is no evidence of superiority in terms of mortality in the medium term (up to 5 years), which increases the importance of intermediate outcomes such as AF and of impacts on quality of life through, for example, pacemaker syndrome.

As well as the potential avoidance of a small number of important cardiovascular disease consequences, pacemaker syndrome is a crucial factor in determining cost-effectiveness. However, difficulties in standardising diagnosis and measurement of severity make it difficult to quantify precisely its impact.

At 5 years, dual-chamber pacing in SSS and AVB is likely to yield additional QALYs at a cost of less than £10,000, although there is some uncertainty around this estimate, particularly with regard to pacemaker syndrome. More conservative assumptions suggest that the cost-effectiveness ratio may be around £30,000 per QALY.

The evidence base comparing dual-chamber with single atrial pacing is much smaller and less robust. A single, small, parallel pilot RCT is available and informs the cost-effectiveness analysis. This suggests that atrial pacing is likely to be cost-effective compared with dual-chamber pacing.

Dual-chamber pacing is in common usage in the UK. Recipients are more likely to be younger. Insufficient evidence is currently available to inform policy on specific groups who may benefit most from pacing with dual-chamber devices, although overall the assessment is that the technology is likely to yield benefits at a level that is generally considered acceptable value for money compared with ventricular devices.

## **Need for further research**

The following areas are recommended for further research.

- An individual patient data meta-analysis of existing trials is required and underway.
- Further trials of dual versus atrial pacing are required and one is underway (DANPACE).
- Publication of the economic evaluation of UKPACE and reporting of utility by health state is needed urgently.
- Further research into the classification, diagnosis and utility associated with pacemaker syndrome is needed.
- There is currently no evidence for the effectiveness of pacemakers in children.

## **Publication**

Castelnuovo E, Stein K, Pitt M, Garside R, Payne E. The effectiveness and cost-effectiveness of dual-chamber pacemakers compared with single-chamber pacemakers for bradycardia due to atrioventricular block or sick sinus syndrome: systematic review and economic evaluation. *Health Technol Assess* 2005;**9**(43).

# NHS R&D HTA Programme

The research findings from the NHS R&D Health Technology Assessment (HTA) Programme directly influence key decision-making bodies such as the National Institute for Health and Clinical Excellence (NICE) and the National Screening Committee (NSC) who rely on HTA outputs to help raise standards of care. HTA findings also help to improve the quality of the service in the NHS indirectly in that they form a key component of the 'National Knowledge Service' that is being developed to improve the evidence of clinical practice throughout the NHS.

The HTA Programme was set up in 1993. Its role is to ensure that high-quality research information on the costs, effectiveness and broader impact of health technologies is produced in the most efficient way for those who use, manage and provide care in the NHS. 'Health technologies' are broadly defined to include all interventions used to promote health, prevent and treat disease, and improve rehabilitation and long-term care, rather than settings of care.

The HTA Programme commissions research only on topics where it has identified key gaps in the evidence needed by the NHS. Suggestions for topics are actively sought from people working in the NHS, the public, service-users groups and professional bodies such as Royal Colleges and NHS Trusts.

Research suggestions are carefully considered by panels of independent experts (including service users) whose advice results in a ranked list of recommended research priorities. The HTA Programme then commissions the research team best suited to undertake the work, in the manner most appropriate to find the relevant answers. Some projects may take only months, others need several years to answer the research questions adequately. They may involve synthesising existing evidence or conducting a trial to produce new evidence where none currently exists.

Additionally, through its Technology Assessment Report (TAR) call-off contract, the HTA Programme is able to commission bespoke reports, principally for NICE, but also for other policy customers, such as a National Clinical Director. TARs bring together evidence on key aspects of the use of specific technologies and usually have to be completed within a short time period.

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