Cost-effectiveness of ventricular assist device use in the United Kingdom: results from the Evaluation of Ventricular Assist Device Programme in the UK (EVAD-UK)

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 ventricular assist device (VAD) implantation as a bridge to transplantation (BTT) for patients requiring a heart transplant. The four types of devices considered were Heart-Mate VE, Thoratec, Jarvik 2000 and HeartMate II.

Type of intervention
Treatment.

Economic study type
Cost-utility analysis.

Study population
The study population comprised patients requiring a heart transplant. Patients only receiving VAD designed for short-term support (<30 days) were excluded. Indications for VAD implantation were patients who were appropriate candidates for cardiac transplantation, those who would become appropriate after a period of VAD support, and those who had rapidly deteriorating heart function and clearly would not survive to transplant despite the provision of an "urgent" category nationally.

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

Dates to which data relate
The effectiveness and resource use data were gathered between April 2002 and December 2004. The costs were measured in 2004/05 prices.

Source of effectiveness data
The effectiveness evidence was derived from a single study and authors’ opinions.

Link between effectiveness and cost data
The costing was carried out prospectively on the same sample of patients as that used in the effectiveness study.

Study sample
Power calculations, if performed, were not reported. All 70 patients who had a VAD implanted at the three UK hospitals over the study period were included in the current analysis. The mean age of the sample was 41.9 (+/- 13.0) years and 84% were men. The principal diagnoses were dilated cardiomyopathy (59%) and ischaemic heart disease...
(29%). During the same period, a sample of 71 consecutive inotrope-dependent transplant candidates was considered in the prospective control group.

**Study design**
This was a prospective cohort study in which two groups were compared. The patients were followed up until the end of the study period (31 March 2005) or until death. No patient was lost to the follow-up assessment. Blinding was not performed.

**Analysis of effectiveness**
All of the patients included in the initial study sample were taken into account in the analysis of effectiveness. The primary clinical end points were survival and other outcomes associated with VAD implantation or heart transplantation, and quality of life. Quality of life was measured using the self-reported EuroQol EQ-5D within one month of VAD implant or listing, then every 3 months until transplant, and then at 3, 6, 12 and 24 months after transplant. The utilities associated with quality of life were estimated on the basis of UK population values. The clinical results of the study were used to populate the Markov model in terms of transition probabilities and utilities associated with the health states. The baseline comparability of the study groups was not discussed.

**Effectiveness results**
In the group of VAD-implanted patients (70 patients), 44% survived to heart transplant, 6% recovered myocardial function sufficiently to have the VAD explanted, and 7% had a VAD in place until the end of the study. The remaining 43% of patients died with a VAD in situ. Of the 31 patients transplanted, 16% died and 84% were alive at the end of the study. The median time on VAD support was 82 days, although patients implanted with a second-generation device were supported for a median of 292 days. The overall proportion alive at one year after VAD implant was 52% (95% confidence interval, CI: 41 to 65).

In the group of inotrope-dependent transplant candidates (71 patients), 86% underwent heart transplant, 3% were removed from the list, and 10% died while waiting for a donor heart. The median time on the waiting list for these patients was 16 days (in comparison with 87 days for non inotrope-dependent transplant candidates). The percentage of inotrope-dependent transplant candidates alive at one year after transplant listing was 79% (95% CI: 70 to 89). Survival after transplantation was 84% for VAD patients and 85% for inotrope-dependent patients, (p=0.983).

Quality of life improved in both groups. The improvement in the EQ-5D was 0.20 (95% CI: 0.11 to 0.29; p<0.001) in the VAD group and 0.16 (95% CI: 0.11 to 0.22; p<0.001) in the inotrope-dependent group.

Clinical data were translated into transition probability values. The probability of heart transplant for VAD-implanted patients was 4% (95% CI: 1 to 15) in the first month and 11% (95% CI: 8 to 15) in the following months. The probability of death was 26% (95% CI: 16 to 38) in the first month and 4% (95% CI: 2 to 8) in the following months.

The probability of heart transplant for inotrope-dependent transplant candidates was 58% (95% CI: 46 to 70) in the first month and 15% (95% CI: 9 to 23) in the following months. The probability of death was 1% (95% CI: 0 to 7) in the first month and 4% (95% CI: 1 to 10) in the following months.

The probability of death post-heart transplant was 11% (95% CI: 7 to 16) in the first month, 3% (95% CI: 1 to 6) in the second month, and 0.3% (95% CI: 0 to 0.5) in the following months.

The utility weights for VAD-implanted patients were 0.50 (95% CI: 0.40 to 0.62) in the first month and 0.66 (95% CI: 0.63 to 0.69) in the following months. The utility weights for inotrope-dependent transplant candidates were 0.50 (95% CI: 0.32 to 0.68) in the first month and 0.51 (95% CI: 0.40 to 0.62) in the following months. The utility weight was 0.76 (95% CI: 0.73 to 0.79) for all patients after heart transplant.

**Clinical conclusions**
The effectiveness analysis showed that the two groups improved similarly in terms of survival and quality of life.
Modelling
A Markov model with time-dependent transition probabilities was used to extrapolate (quality-adjusted) survival and costs over the total lifetime of the patients. Monthly cycles were considered. The health states of the model were VAD (or transplant listing for patients in the inotrope-dependent group), heart transplant and death. A schematic representation of the model was reported.

Methods used to derive estimates of effectiveness
The authors made some assumptions about the worst-case scenario.

Estimates of effectiveness and key assumptions
VAD-eligible patients died within 30 days in the absence of a VAD. The probability of death in the first month was set at 100%. The utility of patients in the worst-case scenario was similar to that of VAD patients in the first month (0.51).

Measure of benefits used in the economic analysis
The summary benefit measure used was the expected number of quality-adjusted life-years (QALYs). This was estimated by combining utility values and survival derived from the patient cohorts included in the effectiveness analysis by means of the Markov model. Future benefits were discounted at a rate of 3.5%. Unadjusted survival was also reported although it was not combined with the costs.

Direct costs
The viewpoint of the NHS was adopted in the analysis. The categories of costs included were procedure and subsequent stay in the intensive care unit (ICU) or cardiac ward, devices, heart transplant procedure and associated ICU and ward stay, transplant assessment (inotrope-dependent patients only), follow-up readmissions to the ICU or ward, outpatient visits, investigations, blood tests and drugs. Resources associated with adverse events were also considered. The unit costs and the quantities of resources used were not presented separately, but the total costs associated with each health state and for different time periods were reported. Resource use was derived from the sample of patients included in the effectiveness analysis. The sources of the costs were not reported but they might have reflected the viewpoint of the NHS. The cost calculations were described. Discounting was relevant, as the long-term costs were assessed, and an annual rate of 3.5% was used. The costs were measured using 2004/05 prices.

Statistical analysis of costs
The costs were presented as mean values with CIs.

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

Currency
UK pounds sterling (£). The costs were also converted to US dollars ($). The conversion rate was 1 = $1.8182.

Sensitivity analysis
A univariate sensitivity analysis was carried out to assess the robustness of the cost-utility ratios to variations in some model inputs. Specifically:
explanted patients were assumed to live for 30 years and had zero costs after explant;
the costs of devices were reduced to 50% of their current levels;
ICU and ward stay were reduced;
second-generation devices were excluded;
mortality on VAD support was reduced;
monthly transplant rates were reduced, while monthly death rates were increased for inotrope-dependent transplant candidates; and
health utilities were estimated using an alternative instrument (i.e. the SF-36).

Alternative values were mainly based on authors’ opinions.

**Estimated benefits used in the economic analysis**
The expected number of QALYs was 3.27 (95% CI: 2.56 to 4.01) in the VAD group, 4.99 (95% CI: 4.41 to 5.58) in the inotrope-dependent group, and 0.02 in the worst-case scenario.

The expected mean survival was 5.63 years (95% CI: 4.35 to 7.05) in the VAD group, 8.62 years (95% CI: 7.49 to 10.29) in the inotrope-dependent group, and 0.04 years in the worst-case scenario.

**Cost results**
The mean total costs per patient were 173,841 (+/- 9,269) ($316,078) in the VAD group, 130,905 (+/- 6,488) ($238,011) in the inotrope-dependent group, and 14,400 ($26,182) in the worst-case scenario.

**Synthesis of costs and benefits**
Incremental cost-utility ratios were calculated in order to combine the costs and benefits of the alternative strategies.

The incremental analysis revealed that VAD patients incurred higher mean costs and gained lower mean QALYs than patients in the inotrope-dependent group. Therefore, VAD implantation was dominated in this comparison. However, in comparison with the worst-case scenario, the incremental cost per QALY gained with VAD implantation was 49,384 ($89,790).

The sensitivity analysis showed that base-case results were quite robust to changes in model assumptions. The only scenario in which the inotrope-dependent patients had poorer survival than VAD patients was in a situation reflecting an increase in transplant referrals and waiting time for transplantation. In this case, the incremental cost per QALY gained with VAD was 145,900 ($265,275). In the sensitivity analysis, the incremental cost per QALY gained with VAD in comparison with the worst-case scenario ranged from 39,552 ($71,913) to 58,186 ($105,794).

**Authors’ conclusions**
Ventricular assist device (VAD) implantation as a bridge to transplantation (BTT) was more expensive and less effective than care management for inotrope-dependent transplant candidates. Therefore, VAD implantation should not be extended to other transplant candidates unless it is likely that they would not survive to transplantation under the current urgent listing scheme in the UK, or that they could not undergo transplantation without a period of stabilisation using mechanical support.

**CRD COMMENTARY - Selection of comparators**
The authors pointed out that inotrope-dependent patients and worst-scenario patients represented two extreme situations, with many patients falling somewhere between these two extreme scenarios. It was stated that it was very difficult to find an adequate comparison for VAD patients, and that neither inotrope-dependent patients nor worst-scenario patients were entirely appropriate. You should decide whether they are valid comparators in your own setting.
Validity of estimate of measure of effectiveness
The effectiveness data were derived from prospective cohorts of patients that formed part of a UK study. The study was not randomised, which might have led to some selection bias. The authors pointed out the difficulties of performing randomised controlled trials of sufficient size for the treatments under analysis. This was the main reason for choosing this alternative design. However, the enrolment of consecutive patients represented a strong feature of the analysis. The authors did not discuss the baseline comparability of the study groups, although the demographics of VAD patients were reported. The evidence came from multiple centres, which means that the study sample should have been representative of the patient population. Effectiveness data for the hypothetical control group, which were based on authors' opinions, were used to populate the decision model. The issue of uncertainty surrounding clinical estimates and assumptions was investigated in the sensitivity analysis. More information on follow-up and clinical end points was reported in a separate study.

Validity of estimate of measure of benefit
The benefit measure used in the analysis was appropriate as QALYs reflect the impact of the interventions on the most relevant dimensions of health for patients requiring cardiac transplantation (i.e. quality of life and survival). Life expectancy was also reported. QALYs can be compared with the benefits of other health care interventions. The approach used to calculate the QALYs was reported and the use of an alternative approach was tested in the sensitivity analysis. Discounting was performed in accordance with international guidelines and UK discount rates.

Validity of estimate of costs
The analysis of the costs was consisted with the perspective of the analysis. Only the direct medical costs were included since they were relevant from the viewpoint of the health care payer. A detailed breakdown of cost items was not provided since most details of the analysis were reported in another study. Similarly, no information on the sources of the costs was given. Thus, the scarcity of information on the cost analysis will limit the possibility of replicating the analysis of in other settings. Resource consumption came from the sample of patients treated at the study hospital, and thus is likely to reflect actual treatment patterns in the UK. Changes in cost estimates were investigated in the sensitivity analysis. The price year was reported, which will facilitate reflation exercises in other time periods. The authors noted that the costs used in the analysis might be somewhat lower than other reported costs. Reasons for this included the setting (established transplant centres where set-up costs were not considered) and the use of US cost studies for comparison (US costs might be higher than those observed in the UK).

Other issues
The authors reported the results from other studies and compared them with the findings of the current analysis. Differences were partly justified on the grounds of model assumptions. The issue of the generalisability of the study results to other settings was not explicitly addressed, but the use of sensitivity analysis enhances the external validity of the study. The study referred to patients requiring cardiac transplantation and this was reflected in the authors' conclusions. The authors noted that the rates of successful BTT recovery were presumably due to the use of a range of devices and the impact of a learning curve.

Implications of the study
The study results do not support the use of BTT VAD implantation. The current study confirmed the findings of longer effectiveness for second-generation devices.

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Christopher F, Clegg A. Left ventricular assist devices (LVADs) for end stage heart failure. Southampton: Wessex Institute for Health Research and Development; 1999.


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