Simvastatin after orthotopic heart transplantation: costs and consequences
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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.

Health technology
Prevention protocols to reduce incidence of graft vessel disease (GVD) in heart transplant patients using either a dietary strategy alone or diet plus the HMG-CoA reductase inhibitor Simvastatin.

Type of intervention
Secondary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
Patients who have previously received heart transplants.

Setting
Hospital. The economic analysis was conducted in Haar, Germany.

Dates to which data relate
Effectiveness and resource data were collected from a 4 year study published in 1997. In addition estimates of longer term survival were extrapolated from a 1996 data source. 1997 prices were used.

Source of effectiveness data
Effectiveness data were derived from a single study and expert opinion.

Link between effectiveness and cost data
Cost data were collected retrospectively from the same patient sample used in the effectiveness analysis.

Study sample
72 patients were randomised between the diet plan plus Simvastatin (n=35) and diet plan only (n=37). It is not clear whether power calculations were used to determine sample size.

Study design
This was a single centre non-blinded randomised controlled trial. The duration of follow up was four years after commencing treatment. There was no loss to follow up or cross over between patients in the two groups.
Analysis of effectiveness
The analysis of effectiveness was based on intention to treat. The primary health outcomes used in the analysis were life years gained.

Effectiveness results
Patients in the diet plan plus Simvastatin group had an additional undiscounted 0.64 life years compared with the diet plan only cohort.

Clinical conclusions
Including Simvastatin in treatment protocols along with diet plans for patients who have received heart transplants significantly improves four year life expectancy compared with patients whose prevention strategy consists of diet plans only.

Measure of benefits used in the economic analysis
The benefit measure was life years gained. To determine life expectancy for patients in the Simvastatin plus diet and diet only groups from years 5 to 12 following transplantation, survival rates from a database of 32,579 subjects reported in the 1996 14th Annual Report of the International Society for Heart and Lung Transplantation (ISHLT) were used. Beyond year 12 the absolute mortality risk was determined based on regression calculations using the ISHLT data.

Direct costs
Direct costs associated with the two treatment protocols were estimated. These costs included acquisition costs for Simvastatin using 1997 German pharmacy retail prices, excluding 5% rebate under German insurance system. Clinical monitoring costs were determined using the 1997 German Physician Fee Ordinance. Costs of a first heart transplantation were taken from 1997 data published by the ISHLT, and an estimation of the costs of post-transplant care and cost per year for patients not receiving a heart transplant were also estimated from a 1994 German publication. 1997 price years were used and costs and benefits were both discounted at a rate of 3% per annum.

Indirect Costs
Not calculated.

Currency
US dollars ($). Converted from German Marks ($1 = DM1.747).

Sensitivity analysis
A series of one way sensitivity analyses was conducted. Parameters examined included cost of Simvastatin (using US retail prices), life expectancy estimates (recalculated using the Weibull failure time model), life years gained (adjusted to take account of quality using a previously derived utility factor of 0.74 under the time trade off method). Costs associated with heart transplantation and annual maintenance costs were also varied. The cost implications of the need for additional heart transplantations, rates of heart rejections and percutaneous transluminal coronary angioplasty were also considered. Incidence, mortality and costs associated with rhabdomyolysis were also evaluated.

Estimated benefits used in the economic analysis
In the base case scenario the mean number of discounted life years gained per patient during their lifetime was 1.84 using Simvastatin plus diet plan compared with the diet plan only. This represented a 27.4% increase compared with the use of the diet plan only. The maximum duration of benefits was assumed to be 30 years. Overall heart transplantation, standard care and four years of Simvastatin therapy yielded an additional 8.54 years of life compared
with no heart transplant.

Cost results
The incremental cost of 4 years treatment in the Simvastatin plus diet plan was estimated to be $1,920 per patient, 1.3% greater than in the control group. This difference was not statistically significant. A discount rate of 3% was used. The total costs for the comparator were not explicitly stated. However, the mean total lifetime costs of heart transplantation and care including the diet plan, excluding Simvastatin were estimated to be $151,830 per patient in both groups. Within the trial the 5, 10 or 15mg of Simvastatin were taken for 52%, 32.8% and 14.7% of the study period, with a mean daily dose of 8.11mg.

Synthesis of costs and benefits
The incremental cost per life year gained discounted at a rate of 3% using 4 years of Simvastatin therapy in addition to a diet plan was estimated to be $1,050 if a lifetime time frame were used (possible maximum 30 years, although average life expectancy less than 12 years). Within the 4 year time frame of the clinical trial the cost per life year gained was estimated to be $3,160 using Simvastatin. The average cost per life year gained for heart transplant patients who also received Simvastatin fell to $18,010 compared with an average cost effectiveness ratio per patient of $22,650 when compared with patients not receiving 4 years of Simvastatin therapy. In sensitivity analysis including additional post transplantation costs increased the incremental cost per life year saved to $15,400. All other parameters did not vary the baseline results greatly with incremental cost effectiveness ranging from $800 to $1,420 (when including adjustment for quality of life). The average cost effectiveness of heart transplant plus Simvastatin versus no intervention ranged from $17,130 to $21,090. If US transplantation costs were used rather than German costs then the average cost effectiveness would range from $25,750 - $30,140.

Authors' conclusions
The authors concluded that not only had Simvastatin been demonstrated to reduce the incidence of coronary heart disease, but had now also been demonstrated to be effective and safe and to improve the cost-effectiveness of heart transplantation. Post-transplantation care protocols should now consider the use of interventions which have been demonstrated to reduce the incidence of GVD and therefore reduce morbidity and improve long term life expectancy.

CRD COMMENTARY - Selection of comparators
Justification was provided by the authors for the choice of comparator. Counselling to use a diet plan only represents a well founded and accepted strategy for the prevention of post-heart transplant morbid events.

Validity of estimate of measure of benefit
Single centre randomised clinical trial, according to the authors, represents the only study examining the use of Simvastatin and diet plans conducted thus far. The authors noted the small sample size of the trial but pointed out that 72 patients represent one sixth of all heart transplant patients in Germany. Extrapolation of longer term survival rates for heart transplant patients were derived from an international database of more than 32,000 patients. Larger population samples are noted as desirable by the authors although they question whether, for ethical reasons, these should be randomised trials rather than observational studies.

Validity of estimate of costs
Sufficient information on the source of cost data was provided. It might have been useful, however, to have provided a specific estimate of the costs of diet counselling. In addition, although the authors did note that little absence from work was observed in the study sample, it may be useful also to consider in an economic analysis the costs to others in society such as patients and caregivers and costs arising from productivity losses.

Other issues
results of the study, particularly costs, may not be generalisable to other settings outside the German health care system. However, the authors believe that in the case of a highly specialised technical medical intervention such as heart transplantation, practices and patient populations are likely to be similar in other countries with transplantation programmes. Moreover, when using US costs the intervention remained cost-effective.

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