Kidney transplantation in the elderly: a decision analysis

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 two treatment strategies studied were cadaveric kidney transplantation and continued dialysis, defined as thrice weekly in-centre hemodialysis.

Type of intervention
Treatment.

Economic study type
Cost-utility analysis.

Study population
The study population comprised a theoretical cohort of non-diabetic patients aged 65 years or more who were stable at dialysis at the time of the decision. It was assumed that patients were medically fit for transplantation and were excluded if they had ongoing malignancy, active cardiovascular disease, or a chronic infective condition. It was also assumed that there was a 2 year delay period between the decision to proceed with transplant and harvesting a suitable organ. Additional models were constructed for patients who were known to be diabetic at the time of being placed on the waiting list for transplantation, and for those with known cardiovascular disease.

Setting
The study setting was secondary care. The economic study was carried out in Canada.

Dates to which data relate
The date range of the studies used to derive effectiveness was from 1975 to 2000. 1999 prices were used.

Source of effectiveness data
Effectiveness data were obtained from a review and synthesis of previously completed studies.

Link between effectiveness and cost data
Not relevant.

Modelling
The major clinical events associated with transplantation and with dialysis were summarised using a Markov model programmed in Decision Maker, version 7.0(6). This technique involves identifying clinically important events and defining them as "health states". A theoretical cohort of patients moved cyclically from one health state to another, in cycles set at 3 months, until the time of death.
Outcomes assessed in the review
The following outcomes were assessed in the review: probability of surgical mortality; probability of acute rejection three, six and twenty four months after transplantation; overall probability of acute rejection in the first year of transplantation; probability of complication per three month period after transplantation; probability of complication in first year after transplantation; estimated annual mortality rate on dialysis; relative risk (RR) of death if acute rejection of transplanted organ occurs; RR of death if a complication occurs after transplantation; RR of a complication happening if acute rejection of transplanted organ occurs and probability of post-transplantation diabetes and the utility associated with dialysis and with transplantation.

In the model that included patients suffering from diabetes the following outcomes were assessed: RR of death and the RR of a complication after transplantation.

In the model that included patients with a known cardiovascular disease the following outcomes were assessed: RR of death in a patient continuing dialysis and RR of death in a transplanted patient.

Study designs and other criteria for inclusion in the review
The study designs and other criteria used by the authors for inclusion in the review were not stated.

Sources searched to identify primary studies
The authors searched the MEDLINE database to identify primary studies.

Criteria used to ensure the validity of primary studies
The criteria used to ensure the validity of primary studies were not stated.

Methods used to judge relevance and validity, and for extracting data
Those studies that most closely represented the population of interest were judged as relevant, for example those that focused on an over 65 year old population with first cadaveric graft.

Number of primary studies included
Approximately 32 primary studies were included in the analysis.

Methods of combining primary studies
If multiple studies were relevant, a mean value was calculated and used as the baseline estimate. Data from multiple studies were then used to estimate a clinically plausible range (PR) for each variable.

Investigation of differences between primary studies
The investigation of differences between primary studies was not reported.

Results of the review
The probability of surgical mortality was 0.02 (PR=0.00 - 0.02).

The probability of acute rejection three, six and twenty four months after transplantation was 0.24, 0.17 and 0.002 respectively.

The overall probability of acute rejection in first year after transplantation was 0.38.

The probability of complication per three-month period after transplantation was 0.20 (PR=0.1 - 0.5).
The probability of complication in first year of transplantation was 0.9.
The estimated annual mortality rate on dialysis was 9.82% (PR= 7.5 - 13.3%).
The RR of death if acute rejection of transplanted organ occurs was 1.22 (PR= 1.0 - 2.0).
The RR of death if a complication occurs after transplantation was 1.8 (PR=1.5 - 4.0).
The RR of a complication happening if acute rejection of transplanted organ occurs was 2.0 (PR= 1.5 - 6.7).
The probability of post-transplantation diabetes was 0.07 (PR=0.03 - 0.15).
The RR of death if a patient suffers from diabetes was 2.67 (PR=1.2 - 5.0).
The utility associated with dialysis was 0.49 (PR=0.34 - 0.55) and that associated with transplantation was 0.78 (PR=0.45 - 0.82).
The RR of a complication occurring in a diabetic patient after transplantation was 2.0 (PR=1.0 - 5.0).
The RR of death for a patient suffering from cardiovascular disease and continuing dialysis was 2.35 (PR=1.5 - 5.0).
The RR of death for a patient suffering from cardiovascular disease and who has been transplanted was 1.74 (PR=1.5 - 3.0).

These data formed the principal effectiveness parameters used in the model.

**Measure of benefits used in the economic analysis**
The health benefits used in the economic analysis were life years gained and quality-adjusted life years (QALYs). Utility estimates were derived from a literature search using MEDLINE, which identified seven studies reporting the utility of dialysis or transplantation using the time trade-off or the standard gamble methods. However, time trade-off values reported for patients aged 60 years or more were used as the baseline estimates.

**Direct costs**
Resource quantities and costs were not reported separately. The direct costs of the third party payer were included in the analysis. The direct costs included in the analysis were: hemodialysis (per year), transplant workup, transplant surgery and recovery, acute rejection, complications, transplant follow-up (per year) and restarting dialysis after a failed transplant. Costs were estimated from published data, and the annual costs of transplantation and dialysis were estimated from Medicare data. Both health outcomes and costs were discounted at 3% per year, as the time horizon used for the analysis was the lifetime of the patient. Because newer medications are more commonly used now than in the period from which the cost estimates were drawn, the cost of transplant follow-up was increased. 1999 prices were used.

**Statistical analysis of costs**
No statistical analysis of costs was reported.

**Indirect Costs**
No indirect costs were included in the analysis.

**Currency**
US dollars ($). Costs were converted to US dollars using the median 1999 exchange rate and the Bureau of Labour Statistics Consumer Price Index.
Sensitivity analysis
A series of one-way sensitivity analyses was carried out for all probability, costs, utility and mortality estimates. The clinically plausible range of each variable was used in the sensitivity analysis. Time to transplantation was also varied from 0 to 6 years to reflect the range of possible waiting times. The model was said to be sensitive to the variable if the value at which quality adjusted life expectancy was equal to either strategy (i.e. kidney transplantation or continued dialysis).

Estimated benefits used in the economic analysis
In the base case scenario an incremental life expectancy (LE) of 1.2 years and an incremental quality-adjusted life expectancy (QALE) of 1.1 QALYs were used. In the model for diabetic patients the estimated benefits were an incremental LE of 1.1 years and an incremental QALE of 0.7 QALYs, with the same estimated benefits for the model of patients with cardiovascular disease.

Cost results
The discounted costs for patients receiving dialysis were $277,000 versus $345,000 for patients receiving a cadaveric graft after a two-year waiting period.

Synthesis of costs and benefits
A synthesis of costs and benefits was carried out by calculating a cost-utility ratio (additional cost required per QALY). For patients aged 65 and 70 years the value of this ratio was $67,779 and $79,360 per QALY, respectively (assuming a two year wait period before transplantation). Transplantation remained economically favourable only in those aged less than 70 years. For patients aged 75, 80 and 85 years, the value of the cost-utility ratio was $99,553, $137,999 and $231,158 per QALY. For 65-year-old patients with diabetes the cost-utility ratio was $138,660 per QALY, and for 65-year-old patients suffering from CVD that ratio was $110,327 per QALY. The results were highly sensitive to the duration of time spent on the waiting list (threshold, 6.7 years), and moderately sensitive to the utility of transplantation. The threshold for the dialysis mortality rate was significantly lower than the clinically plausible range. The results were not sensitive to other variables.

Authors’ conclusions
The authors concluded that transplantation offers substantial gains in both life expectancy and quality-adjusted life expectancy for older patients. The benefits were shown to be higher in those receiving a transplant immediately than in those who were transplanted after a prolonged waiting time. Cadaveric transplantation was also found to be economically attractive for otherwise healthy patients up to the age of 70 years and in the younger elderly with some comorbidity.

CRD COMMENTARY - Selection of comparators
A justification was given for the choice of comparator used, namely that clinicians view dialysis as a stable strategy with an acceptable survival and few short-term risks, and that it is common practice for those patients with renal failure. You, as a user of this database, should decide whether it represents a valid comparator in your setting.

Validity of estimate of measure of effectiveness
The authors stated that a systematic review of the literature using MEDLINE had been undertaken. However, it is unclear if the review was conducted in a systematic way to identify relevant studies and minimise biases. If multiple studies were found by the authors to be relevant (for example, those that focused on an over 65 year old population with first cadaveric graft) a mean value was calculated and used as the baseline estimate, with data from multiple studies being used to estimate a clinically plausible range that was used in the sensitivity analyses. An inherent problem with this method of combining primary studies is that it does not weight studies with regard to their sample sizes or the quality of the study. However, uncertainty in the data was appropriately explored in the sensitivity analyses, which tends
to minimise the above limitation.

**Validity of estimate of measure of benefit**
The measure of health benefit was obtained through modelling parameters. As patients with end-stage renal failure were expected to be dialysis-dependent for life, the outcome was measured as life expectancy, both with and without quality adjustment. The methods of derivation were clearly described and appeared to be valid for the patient domain studied.

**Validity of estimate of costs**
All categories of cost relevant to the perspective adopted (i.e. the third party payer) appear to have been included in the analysis. For each category of cost, all relevant costs were included in the analysis. However costs and quantities were not reported separately. Estimates of costs were taken from the published literature. A sensitivity analysis of costs was conducted. Appropriate conversions were performed to 1999 US dollars by using the median 1999 exchange rate and the Bureau of Labour Statistics Consumer Price index. However, the exchange rate was not given. Since costs were incurred over the lifetime of the patient, discounting was necessary and both health outcomes and costs were appropriately discounted at 3% per annum. For the annual costs of dialysis and transplantation, charges were used to proxy prices as Medicare data from 2000 were used to estimate these costs.

**Other issues**
The authors made appropriate comparisons of their finding with those from other studies. Dialysis vintage, gender and race were not adjusted for in this analysis. For example, the authors stated that in the case of black patients, especially women, one would expect higher gain from transplantation than for white patients of the same age and comorbidity profile. The authors do not appear to have presented their results selectively. The authors’ conclusions reflect the scope of the analysis as they examined hypothetical patients aged over 65 years and this was reflected in their conclusions. The authors recognised that the results might be somewhat conservative for several reasons, specifically:

Medicare charges tend to underestimate the actual costs of providing dialysis care. In addition, the costs of acute rejection or transplant-related complications reflect those cases requiring hospitalisation rather than those managed in an outpatient setting. These two factors result in an overestimation of the costs of transplantation, and an underestimation of the costs of dialysis.

The analysis used pessimistic utilities for the complications of transplantation as it assumed a utility of zero for the whole period of hospitalisation for transplant surgery, rejection episodes, complications and the initial surgery. Again, this could result in a bias that favours dialysis.

**Implications of the study**
The results confirm that many older patients will benefit from renal transplantation. However, as the authors acknowledged, renal transplantation for the elderly may introduce ethical problems with arguments against the allocation of scarce cadaveric organs to older patients, and waiting list problems where the number of potential recipients for each organ harvested would increase the waiting list. Thus the authors recommended that individual health care providers would need to develop their policies on the basis of local availability of organs. The authors also recommended financing transplantation, in particular living donor transplantation, in this population.

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None stated

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Other publications of related interest

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