Cost-effectiveness of extending Medicare coverage of immunosuppressive medications to the life of a kidney transplant


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 investigated the extension of Medicare coverage of immunosuppressive medication to the life of a kidney transplant. This strategy was compared with the current Medicare policy, whereby those kidney transplant patients not maintaining Medicare status through disability or age lose their Medicare coverage of immunosuppression 3 years after transplantation.

Type of intervention
Treatment.

Economic study type
Cost-utility analysis.

Study population
The study population comprised recipients of kidney transplants from 1995 to 1999 in the USA. Patients were excluded from the economic analysis if no Medicare transplant hospitalisation payment was listed, or if the Medicare payment for transplant hospitalisation indicated that Medicare was the secondary payer.

Setting
The study setting was secondary care. The economic study was conducted in the USA.

Dates to which data relate
The effectiveness data were derived from studies published between 1997 and 2002. The resource use data were collected from the United States Renal Data System (USRDS), published in 2002. Year 2000 prices were used.

Source of effectiveness data
The effectiveness data were derived from a review of published studies, and from the USRDS database.

Modelling
A Markov model was used to estimate survival and the costs of the current system of 3-year coverage in comparison with lifetime immunosuppression coverage. The time horizon of the model was 20 years post-transplant.

Outcomes assessed in the review
The outcomes assessed in the review were:

the transplant survival rate at years 1, 2, 3 and 5;
the long-term transplant loss rate;
the proportion of transplant failure owing to death;
the death risk after transplant loss within 1 year;
the death risk after transplant loss in the second year;
the 4-year patient survival on the waiting-list given 2-year survival;
the long-term annual death rate on the waiting-list;
the relative reduction in transplant loss in patients without alternative immunosuppression coverage with lifetime Medicare immunosuppression coverage; and
the health state values associated with perfect health, successful transplant, dialysis and death.

Patient survival and transplant survival were calculated using multivariate Cox regression. All outcomes were adjusted to the mean patient characteristics.

Study designs and other criteria for inclusion in the review
Not reported.

Sources searched to identify primary studies
Not reported.

Criteria used to ensure the validity of primary studies
Not reported.

Methods used to judge relevance and validity, and for extracting data
Not reported.

Number of primary studies included
The authors included three primary studies in their review. Estimates from Woodward et al. (see Other Publications of Related Interest) were applied to predict the improved graft survival from extended coverage. Estimates from Wolfe et al. (see Other Publications of Related Interest) were applied to predict the wait-listed patient survival while on dialysis. Data from Hornberger et al. (see Other Publications of Related Interest) were used to derive health state values for different health states. In addition, the authors used data from the USRDS. The USRDS analyses and distributes data on the prevalence, treatment modality, survival and costs of care for end-stage renal disease (ESRD) in the USA.

Methods of combining primary studies
Not relevant.

Investigation of differences between primary studies
Not relevant.

Results of the review
The transplant survival rate was 90.5% at year 1, 86.9% at year 2, 83.2% at year 3, and 76.0% at year 5.
The long-term transplant loss rate (calculated as the rate from year 2 to year 4) was 4.4%.

The proportion of transplant failure due to death was 40.8%.

The death risk after transplant loss within 1 year was 16.6%.

The death risk after transplant loss in the second year was 6.1%.

The 4-year patient survival rate on the waiting-list given 2-year survival was 87.1%.

The long-term annual death rate on the waiting list (calculated as the rate from year 2 to year 4) was 6.7%.

The relative reduction in transplant loss in patients without alternative immunosuppression coverage with lifetime Medicare immunosuppression coverage was 27%.

The health state value associated with perfect health was 1.00, with successful transplant 0.84, with dialysis 0.68, and with death 0.0.

**Measure of benefits used in the economic analysis**

The measure of benefits used was the quality-adjusted life-years (QALYs). The authors estimated quality of life with health state values reported in a study by Hornberger et al. of 878 first-transplant recipients in the USRDS Case-Mix Severity Study (see Other Publications of Related Interest). The health benefits were discounted at an annual rate of 5%.

**Direct costs**

The costs and resource use and were not reported separately. The direct costs to Medicare were included in the analysis. These were the costs associated with transplant hospitalisation, organ procurement, care during the first year post-transplant, maintenance post transplantation during months 12 and 24, and the first year following transplant loss. The costs were calculated using actual Medicare payments for all medical services. However, Medicare payments for organ acquisition were unavailable, so the authors used an estimate from the Centres for Medicare and Medicaid Services. Since the costs could be incurred during a 20-year period, discounting was relevant and was appropriately performed at a rate of 5% per annum. The costs were reported in year 2000 prices, and were adjusted for inflation using the medical component of the Consumer Price Index. The average costs were reported.

**Statistical analysis of costs**

Medicare costs were calculated using linear regression analysis. They were adjusted to mean patient characteristics for recipient age, race, gender, degree of immunologic sensitisation (as assessed by panel reactive antibody), insulin dependence, donor age and gender, cause of ESRD, duration of pre-transplant dialysis, number of human leukocyte antigen mismatches, and year of transplant.

**Indirect Costs**

The indirect costs were not reported.

**Currency**

US dollars ($).

**Sensitivity analysis**

The sensitivity of the results to variations in the input values was assessed by several methods. First, the input values were varied to the 5th and 95th percentiles of their expected distributions based on standard errors estimated from the data. Second, a 10,000 iteration Monte Carlo simulation was run with input values drawn from their expected
distributions based on the estimated standard errors. Third, the utility values and discount rates were varied along plausible ranges.

**Estimated benefits used in the economic analysis**
An average 8.8 discounted QALYs per patient were gained with extended coverage, 8.5 discounted QALYs per patient were gained with existing coverage, and 5.4 discounted QALYs were gained with lifetime dialysis.

**Cost results**
The expected total discounted costs through 20 years post-transplant were $320,676 with existing immunosuppression coverage, $311,473 with lifetime coverage, and $530,746 with lifetime dialysis. The authors reported that, given current kidney transplant rates, the expected discounted societal saving from lifetime coverage would be $136 million annually.

In cases where extended coverage would be used by a patient, the expected discounted costs to Medicare, through 20 years post-transplant, were $234,894 with kidney transplant and existing coverage and $268,946 with transplant and extended coverage.

**Synthesis of costs and benefits**
From the societal perspective, the costs and benefits were not combined as lifetime coverage was found to be both more effective and less expensive than current immunosuppression coverage.

From the Medicare perspective, the authors reported that, using the costs and outcomes of dialysis as the boundary criteria for cost-effectiveness analysis, the incremental benefit of a lifetime coverage extension was as cost-effective to Medicare as the overall benefit of dialysis if the average annual cost of immunosuppression to Medicare was no more than $6,784 per patient. However, the average annualised Medicare payments for immunosuppression were $7,452 per patient transplanted between 1995 and 1997. Using these figures, an immunosuppression coverage extension would be cost-effective to Medicare if no more than 91% of patients not already covered used this coverage, and would break-even if 32% of patients not already covered used extended coverage.

The results of the sensitivity analysis showed that when the survival benefit of extended coverage was varied by 20%, Medicare's budget was expected to break-even, with 25 to 37% of patients using extended coverage, and the cost-effectiveness threshold ranged from 75 to 100% of patients. With a discount rate of 3%, Medicare's breakdown patient fraction rose from 32 to 38% and the cost-effective fraction from 91 to 96%. Varying the cost of maintenance dialysis by 20% generated ranges for the break-even and cost-effective fractions of patients who could use extended immunosuppression coverage of 27 to 35% (break-even) and 76 to 100% (cost-effectiveness), respectively.

**Authors' conclusions**
Extending Medicare immunosuppression coverage to the life of a kidney transplant recipient should result in better clinical and economic outcomes.

**CRD COMMENTARY - Selection of comparators**
A justification was given for the comparator used. Unless kidney transplant recipients maintained Medicare status through disability or age, recipients lost their Medicare coverage of immunosuppression 3 years after transplantation. You should decide if this represents current practice in your own setting.

**Validity of estimate of measure of effectiveness**
The authors did not report that a systematic review of the literature had been undertaken to identify all relevant research and minimise biases. The sources searched for relevant research were not described, and there were no details of any criteria the authors used to choose primary studies to obtain the input parameters for their model. It is therefore
unlikely that all relevant research was identified. The authors performed adequate sensitivity analyses, with what appear to have been appropriate ranges, to test for uncertainty in the model parameters.

Validity of estimate of measure of benefit
The estimation of benefits was modelled. The Markov model used for this purpose was appropriate, as it enabled the estimation of long-term benefits obtained by adopting each of the strategies examined. All future benefits were discounted at a rate of 5% per annum. The QALYs were derived using utilities from a published study. The method used in the later study to estimate utility values from transplanted patients was not reported in the present study.

Validity of estimate of costs
Although the authors reported that the costs were estimated from a societal perspective, the indirect costs were not included. Further, as the authors did not give much detail of the resource use categories, it is unclear whether all the relevant costs were considered. For example, it is unclear from how the authors reported the resource use categories whether the costs associated with extending Medicare coverage over the lifetime of the transplant were accounted for. The costs and the quantities were not reported separately, thus limiting the extrapolation of the results to other settings. The costs were calculated using actual Medicare payments for all medical services provided, with the exception of organ acquisition costs, where an estimate was derived from the Centres for Medicare and Medicaid Services. Appropriate sensitivity analyses of the costs were performed, which enhances the interpretation of the results. Discounting was necessary, as the costs were incurred during a 20-year period, and was appropriately performed. The price year was reported, which will aid any possible inflation exercises.

Other issues
The authors did not compare their findings with those from other studies. The issue of generalisability to other settings was partially addressed in the sensitivity analysis. The authors do not appear to have presented their results selectively and their conclusions reflected the scope of the analysis. The authors reported a number of further limitations to their study. First, Woodward's estimate of graft survival benefits of extended coverage could be conservative. Second, it was assumed that the inability to afford immunosuppression led to non-compliance and transplant failure, although the reasons for non-compliance appear to be multifactorial. Finally, reliance was put on future estimates on the basis of current observation.

Implications of the study
The authors reported that covering immunosuppressive medications to the life of a renal allograft would diminish the risks of transplant failure and death in those unable to otherwise afford therapy. They suggested that it would be wise to prospectively follow changes in outcomes following a change in policy to lifetime immunosuppression coverage.

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