A cost-effectiveness and cost-utility study of lung transplantation

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 compared lung transplantation with no lung transplantation (i.e. patients who were still on the waiting list for a lung transplant).

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis and cost-utility analysis.

Study population
The study population comprised adult patients enlisted on the Quebec lung transplant waiting list. To enter the study, cohort members had to be listed, for the first time, as active candidates for lung transplantation as of 1 January 1997.

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

Dates to which data relate
The effectiveness evidence and resource use data were collected over 5 years. The closing date for entry into the cohort study was 31 May 2001, and patients were subsequently followed until 28 October 2001. The price year was 2001.

Source of effectiveness data
The effectiveness data were derived from a single study.

Link between effectiveness and cost data
The costing was undertaken on the same patient sample as that used in the effectiveness study. The cost data were ascertained in part retrospectively and in part prospectively.

Study sample
No sample size appears to have been determined in the planning phase of the study. In addition, no power calculations were performed retrospectively. A total of 124 patients (44.4% males) entered the Quebec lung transplant waiting list during the study period. Of these, 91 patients (44% males) became lung transplant recipients and 33 remained on the waiting list. The mean age at entry onto the lung transplant waiting list was 46.46 (standard deviation, SD=13.11) years. The mean age at transplantation was 47.55 (SD=13.37) years. No patients refused to participate.
Study design
The study was a historical and concurrent cohort study that was based on data from the Quebec lung transplant waiting list. The mean time spent on the waiting list was 8.79 (SD=5.79) months. Patients receiving transplantation were then followed up for a period of 15.62 (SD=12.65) months. Blinding of the assessment was not reported. No loss to follow-up was reported.

Analysis of effectiveness
All of the patients included in the study were accounted for in the analysis. The primary health outcomes assessed were the number of deaths and survival, both while on the waiting list and after lung transplantation. Survival after lung transplantation was compared with survival observed while waiting for a transplant, which was estimated from observations while on the waiting list. Waiting list survival was modelled on estimates observed, through a Kaplan-Meier life test, in the first year of the study cohort. Candidates that were still alive on the waiting list at the end of the study were attributed the half-life survival observed for the full cohort (2.5 years). It was unclear if the patient groups were comparable at analysis.

Effectiveness results
The number of patient months during the waiting list period was 1,090. During this period a total of 16 (12.9%) people died.

The number of patient months during the post-transplant period was 1,421.5. During this period a total of 24 (19.4%) people died.

Survival in each group was not reported. The authors only reported the number of life-years gained (LYG; see Measure of Benefits Used in the Economic Analysis- below).

Clinical conclusions
No clinical conclusion could be drawn.

Measure of benefits used in the economic analysis
The measures of benefits used were the LYG and the quality-adjusted life-years (QALYs) gained. Utility was assessed cross-sectionally by standard gamble on a sub-group of patients (34 candidates and 71 lung transplant recipients). The patients had to trade between choice 1 (current health state) and choice 2, which was described as "There is a pill that may restore you to perfect health ...; however, the intervention is associated with an immediate risk of death". The indifference search was started with a risk of death of 50% and preceded increments or decrements of 10% (depending whether or not risk of death was rejected) until the patient switched his or her choice on two adjacent questions, or was indifferent at that point. Both the LYG and QALYs gained were extrapolated for a period of 10 years using Kaplan-Meier survival curves. The health benefits were discounted at an annual rate of 5%.

Direct costs
The direct costs included in the economic analysis were those to the health care system. These covered the costs related to screening, the transplant programme, lung transplantation, postoperative care and those incurred while on the waiting list. The resources analysed in the study to determine the direct health care costs were one-day surgery, emergency room visit, ambulatory care visit, outpatient visit, home care visit, Quebec transplant organ-related resource use (retrieval and harvesting), outpatient medications, home oxygen therapy, therapeutic devices and physician fees. The health care resources were derived from medical files and through patient interview. The resource values were based on national and provincial cost data obtained from the University Health Network in Ontario and the Ministry of Health in Quebec. A correction factor of 58.2%, based on provincial differences of total operating teaching hospital costs per total patient-day, was applied to Ontario costs when they were used to estimate the costs. Physician fees for consultations and diagnostic acts, as well as medication costs, were derived from the Regie de l’Assurance Maladie du Quebec. The direct costs were extrapolated over a 10-year period, based on estimates observed in the third year of lung
transplantation.

Patient-borne costs were presented separately and were included in a sensitivity analysis for a societal perspective. These included direct non-medical costs such as transportation to and from medical care services, ambulance use and sleeping accommodations.

Discounting was relevant, as some costs were incurred in the future, and was appropriately performed at an annual rate of 5%. The study reported the mean costs. All costs were adjusted to 2001 prices using the Consumer Price Index for health care.

Statistical analysis of costs
The costs were reported alongside their 95% confidence intervals (CIs).

Indirect Costs
In a separate analysis, together with direct non-medical costs, the authors included the indirect costs. Such costs included the time spent by patients and family members seeking medical services. Discounting was relevant, as some costs were incurred in the future, and was appropriately performed at an annual rate of 5%. The study reported the mean costs. All costs were adjusted to 2001 prices using the Consumer Price Index for health care.

Currency
US dollars ($). The exchange rate used was $1 = Canadian dollar 1.55.

Sensitivity analysis
A sensitivity analysis was undertaken to study the influence of various parameters on the cost-effectiveness and cost-utility estimates. The parameters varied were survival time (no transplantation: 1 to 3 years; post transplantation: 2 to 8 years), utility values, and economic and clinical factors. A post hoc analysis restricted to the cystic fibrosis and bronchiectasis group was also presented.

Estimated benefits used in the economic analysis
The observed mean difference in LYG between the lung transplant phase and the waiting list phase was 0.57 (95% CI: 0.36 to 0.78; p<0.05).

The observed mean difference in QALYs gained between the lung transplant phase and the waiting list phase was 0.62 (95% CI: 0.50 to 0.73; p<0.05).

The extrapolated estimates of the mean LYG and QALYs gained between the lung transplant phase and the waiting list phase were 2.55 and 2.19, respectively.

Cost results
During the waiting time period, the mean discounted cost per patient was $9,687 (95% CI: 7,526 to 11,851). Costs due to the evaluation process ($5,879) and lung transplant programme fixed costs ($328) were also incurred during this period.

The mean discounted cost per patient for transplantation was $31,815 (95% CI: 25,301 to 44,816).

After transplantation, the mean discounted cost per patient was $21,706 (95% CI: 14,246 to 29,355) in year 1, $12,723 (95% CI: 7,810 to 17,734) in year 2, $13,541 (95% CI: 6,225 to 20,855) in year 3, $7,519 (95% CI: 5,944 to 9,095) in year 4, and $65,455 in years 5 to 10.

The authors also assessed, as part of the sensitivity analysis, the mean direct non-medical and indirect costs per month.
During the waiting time, the direct non-medical and indirect costs were $18 (95% CI: 13 to 24) and $93 (95% CI: 81 to 105). After transplantation, the mean direct non-medical costs ranged from $68 (95% CI: 47 to 89) per month in year 2 to $25 (95% CI: 21 to 29) per month in year 4. The mean indirect costs ranged from $208 (95% CI: 170 to 286) per month in year 1 to $45 (95% CI: 37 to 61) per month in year 4.

**Synthesis of costs and benefits**

The costs and benefits were combined using an incremental cost-effectiveness ratio (i.e. the additional cost per LYG) and an incremental cost-utility ratio (i.e. the additional cost per QALY gained). The cost-effectiveness and cost-utility estimates when lung transplant was compared with no transplant (i.e. waiting list) were $40,048 per LYG and $46,631 per QALY gained, respectively.

The sub-group analysis showed that for patients with cystic fibrosis and bronchiectasis, the cost-effectiveness and cost-utility estimates when lung transplant was compared with no transplant (i.e. waiting list) were $25,217 per LYG and $25,643 per QALY gained, respectively.

The results of the sensitivity analysis showed that the cost-effectiveness and cost-utility estimates were sensitive to variations in cost increases for the lung transplantation procedure and additional hospitalisation. In addition, the cost-utility estimates were found to be sensitive to utility weights during the non transplantation period. The authors also found that prolonging survival without lung transplantation increased the incremental cost-effectiveness ratio, but decreased the cost-utility ratio.

**Authors’ conclusions**

Although lung transplantation is expensive, the cost-effectiveness and cost-utility ratios for some patient groups proved to be an acceptable cost for the benefits observed.

**CRD COMMENTARY - Selection of comparators**

The choice of the comparator (i.e. waiting list) was justified as it represented the option with no lung transplantation. However, the authors should have provided more details on the health care services delivered to patients on the waiting list, so that the reader could determine if they represented current practice in their own setting.

**Validity of estimate of measure of effectiveness**

The analysis was based on a historical and concurrent cohort study whereby patients were assessed in part retrospectively and in part prospectively. In this study, the comparison group comprised all patients on the waiting list, including those who later received lung transplantation and those who were still waiting at the end of the study. However, it was unclear which patients or during what period the patients were followed retrospectively. Although the results would have been more internally valid by the use of an experimental study design (e.g. randomised controlled trial, whereby patients are randomised to lung transplantation or no lung transplantation), it is unclear as to whether this would have been ethical. The study sample was representative of the study population. It was unclear whether the patient groups were comparable at analysis. The authors reported that their analysis underestimated the survival experience without lung transplantation, because patients were censored from the waiting list due to the transplant procedure. Consequently, the authors expanded the pre-transplantation phase and presented case scenarios that simulated different person-time experiences.

**Validity of estimate of measure of benefit**

The estimation of benefits (LYG and QALYs gained) was obtained directly from the effectiveness analysis, and then extrapolated into the future using Kaplan-Meier survival curves. The authors reported in detail how utility values were elicited in order to create QALYs. They acknowledged that the method used to derive utilities might have prompted some discussion, as utility was elicited from patients rather than from the general population and the use of standard gamble might have overestimated the true utility for people who are risk averse whilst underestimating it for people who are not risk averse. The authors did not report in great detail how the benefits were extrapolated into the future.
Validity of estimate of costs
All the categories relevant to the perspective adopted in the base-case scenario (i.e. health care system) were included in the analysis. No relevant major costs appear to have been omitted from the analysis. The authors also adopted a societal perspective in the sensitivity analysis. This included direct non-medical costs (e.g. transport costs and accommodation) and indirect costs (e.g. time spent by patients and family members seeking medical services). However, this societal perspective did not include relevant costs such as productivity losses due to mortality and morbidity.

The costs and the quantities were not reported separately, which will limit the generalisability of the authors' results. The costs were derived from published sources, with a limited one-way sensitivity analysis of the costs being performed. The authors reported disaggregated mean costs (i.e. mean costs for each period in the study), but did not report the total mean costs for each group. Therefore, it is not possible to replicate the incremental cost-effectiveness and cost-utility ratios reported in the paper. The authors converted costs from Canadian dollars to US dollars and reported the exchange rate used. Since the costs were incurred over a long timeframe, all future costs were appropriately discounted. The price year was reported, which will aid any possible future inflation exercises.

Other issues
The authors made appropriate comparisons of their findings with those from other studies undertaken in Canada, USA, the Netherlands, and the UK, all of which found similar cost-effectiveness estimates. The issue of generalisability to other settings was partly addressed in the sensitivity analysis. The authors do not appear to have presented their results selectively. However, they should have reported more detail on the extrapolation of the study's results into the future and the mean total costs used to derive cost-effectiveness estimates. The authors reported no further limitations to their study.

Implications of the study
The authors would appear to recommend the use of lung transplantation in Canada, especially for some groups of patients (i.e. patients with cystic fibrosis and bronchiectasis).

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