## TRANSPLANT QUESTION

| L. Longworth, T. Young, M. J. Buxton, J. Ratcliffe, J. Neuberger, A. Burroughs, and S. Bryan. Midterm cost-effectiveness of the liver transplantation program of England and Wales for three disease groups. Liver Transplantation 9:1295-1307, 2003. Ref ID 914. | | | | |
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| **Study details** | **Population & interventions** | **Health outcomes** | **Costs** | **Cost effectiveness** |
| **Economic analysis:**<br>Cost-effectiveness analysis (reporting cost per QALY gained)<br><br>**Study design:**<br>Patient-level data were prospectively collected for the transplant cohort. For the non-transplant cohort, data were obtained from patient-specific pre-transplantation data and from prognostic models. These models are based on historical cohorts of patients treated for PBC, ALD, or PSC.<br><br>**Perspective:**<br>England and Wales (NHS transplant Centres).<br><br>**Time horizon:**<br>27 months (the analysis commences at the time patients were assessed for their suitability for a liver transplantation. 27 months was chosen because this represents | **Population:**<br>Adult patients (ages 16 years and older) with PBC, ALD, or PSC, placed on the waiting list for liver transplant<br><br>**Intervention 1:**<br>Patients attending a liver transplantation.<br><br>**Intervention 2:**<br>Patients experiencing the absence of liver transplantation. | **Health outcomes incorporated:**<br>• Mean patient survival, with and without transplantation (table 2 on the paper);<br>• EQ-5D scores.<br><br>**Primary outcome measure:**<br>QALYs (mean)<br><br>Transplant:<br>• PBC: 1.30 (1.18-1.43);<br>• ALD: 1.12 (0.97-1.24);<br>• PSC: 1.41 (1.20-1.57).<br><br>No transplant:<br>• PBC: 0.76 (0.65-0.91);<br>• ALD: 0.57 (0.48-0.69);<br>• PSC: 0.83 (0.68-0.98). | **Cost components incorporated:**<br>Initial assessment for transplantation, inpatient stay, outpatient visits, drugs, blood products, nutrition, physiotherapy sessions, dietician sessions, tests, treatments, and the transplant operation.<br><br>**Total costs (mean):**<br>Transplant:<br>• PBC: £52,525 (£46K-£61K);<br>• ALD: £66,049 (£57K-£81K);<br>• PSC: £60,612 (£49K-£77K).<br><br>No transplant:<br>• PBC: £37,301 (£27K-£54K);<br>• ALD: £40,336 (£29K-£60K);<br>• PSC: £48,430 (£28K-£74K).<br><br>**Currency & cost year:**<br>1999 UK GBP | **Base case ICERs:**<br>• PBC patients : £29,000 per QALY gained (£1,000 to £59,000);<br>• ALD patients: £48,000 per QALY gained (£12,000 to £83,000);<br>• PSC patients: £21,000 per QALY gained (£23,000 to £60,000).<br><br>**Analysis of uncertainty**<br>Extensive sensitivity analyses were undertaken. Data varied during this analysis were:<br>• Predictions of survival in the absence of transplantation;<br>• Deterioration of HRQL without transplantation;<br>• Adding a cost for organ retrieval;<br>• Unit costs for key items of resource use (inpatient stay, outpatient visits, and transplantation operation);<br>• Daily cost for treating patients in the absence of transplantation.<br><br>The ICER for PSC and ALD was sensitive to the use of an alternative prognostic model (especially for ALD patients).<br><br>The addition of a cost for organ retrieval increased the ICER substantially and uniformly |

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| 2 years post-transplantation plus the average length of time on the transplant waiting list [3 months]).<br><br>**Discounting:**<br>Costs were discounted at 6% and QALYs at 1.5%. | | | | across the three disease groups.<br><br>Results were also sensitive when varying cost estimates, particularly the daily cost for treating patients in the absence of transplantation.<br><br>See Table 5 on the paper for more details. |
| **Data sources** | | | | |
| **Health outcomes:**<br>Survival for transplant cohort:<br>• Patient-level data were prospectively collected for the transplant cohort (1995-1996 cohort study).<br>Survival for non-transplant cohort:<br>• Obtained from patient-specific pre-transplantation data and from prognostic models (based on historical cohorts of patients treated for PBC, ALD, or PSC);<br>• *Beclere* model for ALD patients [1].<br>• A mean of the *Royal Free* and *European* models was used for the PBC group [2].<br>• A single model (*international* model) was used for the PSC group [3].<br>• Other models were applied to the sensitivity analysis.<br><br>[1] - Poynard T, Barthelemy P, Fratte S, Boudjema K, Doffoel M, Vanlemmens C, et al. Evaluation of efficacy of liver transplantation in alcoholic cirrhosis by a case-control study and simulated controls. Lancet 1994;344:502-507.<br>- Poynard T, Naveau S, Doffoel M, Boudjema K, Vanlemmens C, Mantion G, et al. Evaluation of efficacy of liver transplantation in alcoholic cirrhosis using matched and simulated controls. J Hepatol 1999;30:1130-1137.<br>- Anand AC, Ferraz-Neto BH, Nightingale P, Mirza DF, White AC, McMaster P, Neuberger JM. Liver transplantation for alcoholic liver disease: Evaluation of a selection protocol. Hepatology 1997;25:1478-1484.<br><br>[2] - Hughes MD, Raskino CL, Pocock SJ, Biagini MR, Burroughs AK. Prediction of short-term survival with an application in primary biliary cirrhosis. Stat Med 1992;11:1731-1745.<br>- Christensen E, Altman DG, Neuberger J, De Stavola BL, Tygstrup N, Williams R. Updating prognosis in primary biliary cirrhosis using a time dependent Cox regression model. Gastroenterology 1993;105:1895-1876.<br>- Christensen E, Neuberger J, Crowe J, Altman DG, Popper H, Portmann B, Doniach D, et al. Beneficial effect of azathioprine and prediction of prognosis in primary biliary cirrhosis: Final results of an international trial. Gastroenterology 1985;89:1084-1091.<br><br>[3] - Dickson ER, Murtaugh PA, Wiesner RH, Grambsch PM, Fleming TR, Ludwig J, LaRusso NF, et al. Primary sclerosing cholangitis: Refinement and validation of survival models. Gastroenterology | | | | |

1992;103:1893-1901.

**Quality-of-life weights:**
Health-related quality-of-life (HRQL) was assessed using the EuroQol EQ-5D classification system, administered to patients by postal questionnaire at time of listing, at 3-month intervals until transplantation, and then at 3, 6, 12, and 24 months post-transplantation.

Missing EQ-5D scores were replaced by a mean of the scores from the adjacent time points, or the last value was carried forward. Multiple imputation using the software package NORM6 (Version 2. Schafer, PA; 1997) were undertaken (when EQ-5D scores were not available at any time point during the study).

**Cost sources:**
Unit costs for resource use, at 1998-1999 financial year prices, were sought from each of the six liver transplant centres in England*, and mean costs were calculated weighted by the number of transplantations performed at each centre. Overhead costs incurred by transplant centres were included in the unit-cost estimate. Drug costs were taken from the British National Formulary. Based on detailed information of the staff costs from one centre, the costs for surgery and for inpatient medical staffs were attributed over the transplant program activity.

*Addenbrooke's Hospital (Cambridge), Freeman Hospital (Newcastle), King's College Hospital (London), Queen Elizabeth Hospital (Birmingham), Royal Free Hospital (London), and St James's Hospital (Leeds).

**Comments**

**Source of funding:**
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**Limitations:**
The main driver for the poorer cost-effectiveness estimates for ALD was the cost associated with assessing a larger proportion of patients who were considered unsuitable for liver transplantation. The study included assessment and time on the waiting list because these are integral components of the liver transplantation program. If calculated from time of transplantation, the ICERs would all be lower; especially for PSC and ALD patients, which used more resources during the pre-transplantation period (ICER for these two indications would be over 50% lower).

This analysis rests heavily on the use of prognostic models to estimate survival in the absence of transplantation. The results for ALD and PSC patients were sensitive to the choice of prognostic model (the only prognostic model to show superiority over another was the *Beclere* model, used for predicting survival of ALD patients in the base case).

The cost of the maintenance and retrieval of the donor was not included because it was not possible to collect reliable data for these costs.

This analysis has measured cost-effectiveness of liver transplantation only up to 27 months from time of listing. Ideally, a longer time frame would be taken because the

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| incremental costs and benefits of liver transplantation are likely to change beyond this time point, and it is likely that the ICERs would improve over time. | | |
| **Overall quality*: *Potentially serious limitations*** | **Overall applicability**: *Partially applicable*** | |

Abbreviations: ICER = incremental cost-effectiveness ratio; PBC = primary biliary cirrhosis; ALD = alcoholic liver disease; PSC = primary sclerosing cholangitis; QALY = cost per quality-adjusted life-years; NHS = National Health Service; HRQL = Health-related quality-of-life; UK = United Kingdom; GBP - Great British Pound.

*Very serious limitations/Potentially serious limitations/Minor limitations; **Directly applicable/Partially applicable/Not applicable