**Study design:** 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.

**Perspective:** England and Wales (NHS transplant Centres).

**Time horizon:** 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

**Base case ICERs:**
- PBC patients: £29,000 per QALY gained (£1,000 to £59,000);
- ALD patients: £48,000 per QALY gained (£12,000 to £83,000);
- PSC patients: £21,000 per QALY gained (£23,000 to £60,000).

**Analysis of uncertainty** Extensive sensitivity analyses were undertaken. Data varied during this analysis were:
- Predictions of survival in the absence of transplantation;
- Deterioration of HRQL without transplantation;
- Adding a cost for organ retrieval;
- Unit costs for key items of resource use (inpatient stay, outpatient visits, and transplantation operation);
- Daily cost for treating patients in the absence of transplantation.

The ICER for PSC and ALD was sensitive to the use of an alternative prognostic model (especially for ALD patients).

The addition of a cost for organ retrieval increased the ICER substantially and uniformly.
2 years post-transplantation plus the average length of time on the transplant waiting list (3 months).

Discounting:
Costs were discounted at 6% and QALYs at 1.5%.

Results were also sensitive when varying cost estimates, particularly the daily cost for treating patients in the absence of transplantation.

See Table 5 on the paper for more details.

Data sources

Health outcomes:
Survival for transplant cohort:
- Patient-level data were prospectively collected for the transplant cohort (1995-1996 cohort study).

Survival for non-transplant cohort:
- Obtained from patient-specific pre-transplantation data and from prognostic models (based on historical cohorts of patients treated for PBC, ALD, or PSC);
- Beclere model for ALD patients
- A mean of the Royal Free and European models was used for the PBC group
- A single model (international model) was used for the PSC group
- Other models were applied to the sensitivity analysis.


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.

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Comments
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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).

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
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.

<table>
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<th>Overall quality*: Potentially serious limitations</th>
<th>Overall applicability**: Partially applicable</th>
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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