Which is more cost-effective under the MELD system: primary liver transplantation, or salvage transplantation after hepatic resection or after loco-regional therapy for hepatocellular carcinoma within Milan criteria?
Landman MP, Feurer ID, Pinson CW, Moore DE

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.

CRD summary
This study assessed the cost-effectiveness of hepatic resection or locoregional therapy (radiofrequency ablation), followed by salvage orthotopic liver transplantation (OLT) versus primary OLT, for hepatocellular carcinoma that was within the Milan criteria, in patients with Child-Pugh class A cirrhosis. The authors concluded that primary OLT improved survival and quality of life and reduced costs and was therefore cost-effective. The methods were conventional and the authors' conclusions appear to be robust, but the data sources were insufficiently described.

Type of economic evaluation
Cost-utility analysis

Study objective
This study assessed the cost-effectiveness of hepatic resection or locoregional therapy (radiofrequency ablation), followed by salvage orthotopic liver transplantation (OLT) versus primary OLT, for hepatocellular carcinoma that was within the Milan criteria, in patients with Child-Pugh class A cirrhosis.

Interventions
The three interventions were hepatic resection followed by salvage OLT, locoregional therapy followed by salvage OLT, and primary OLT.

Location/setting
USA/hospital.

Methods
Analytical approach:
The analysis was based on a Markov model, with a 10-year time horizon. The authors stated that it was carried out from a societal perspective.

Effectiveness data:
The clinical inputs were from a critical review of the literature on hepatocellular carcinoma in the PubMed database. Reviews or meta-analyses were selected, if available, otherwise randomised controlled trials or prospective studies were selected. Some assumptions were made. Five-year survival was a key input and was from the selected studies.

Monetary benefit and utility valuations:
The utility values for the health states were from the literature.

Measure of benefit:
Quality-adjusted life-years (QALYs) were the summary benefit measure and they were discounted at an annual rate of 3%.

Cost data:
The economic analysis included the costs of the treatments, long-term care, and compensated cirrhosis. These estimates were from published studies of institutional costs and studies in which Medicare or similar data were used. All costs
were in US dollars ($). The price year was 2008 and costs were discounted at an annual rate of 3%.

Analysis of uncertainty:
One- and two-way sensitivity analyses were carried out on the model inputs, using ranges of values from published literature. A multi-way probabilistic sensitivity analysis was performed, using a Monte Carlo simulation.

Results
The 10-year costs were $286,000 with primary OLT, $290,000 with locoregional therapy, and $296,000 with hepatic resection. The QALYs were 5.5 with primary OLT, 3.9 with locoregional therapy, and 3.1 with hepatic resection. Primary OLT was dominant as it was more effective and less expensive than the other two treatments.

The sensitivity analysis confirmed that these base case results were robust; primary OLT remained the preferred strategy in most simulations. Only when the cost of primary OLT exceeded $350,000 or the QALYs dropped to 0.5, did salvage OLT become the preferred strategy. Primary OLT was dominant when mortality after primary OLT was lower than 17% or the probability of primary OLT while on the waiting list was over 48%.

The probabilistic sensitivity analysis showed that primary OLT was dominant in most simulations.

Authors’ conclusions
The authors concluded that primary OLT improved survival and quality of life and reduced costs, compared with salvage OLT, and was therefore cost-effective.

CRD commentary
Interventions:
The rationale for the selection of the comparators was clear, as the available treatment options were considered. The authors stated that some patients might not be eligible for resection.

Effectiveness/benefits:
The clinical data were identified by a review of the literature, which should have ensured the inclusion and selection of valid sources. Most of the data were from clinical trials and prospective studies, which were appropriate for the model parameters, but the details of these studies were not provided. Extensive sensitivity analysis was conducted on all the clinical inputs. QALYs appear to have been a valid benefit measure as they capture the impact of cancer on the patients’ health and they allow cross-disease comparisons to be made. The derivation of the utility values was not described.

Costs:
The authors did not describe the costs in detail. They were not broken down into individual items and the resource quantities were not given. They stated that the analysis was carried out from a societal perspective, but they only included the direct medical costs. The data sources were not well described, but appear to have been standard for the USA. The impact of variations in the cost estimates was tested in the sensitivity analyses. The price year was reported, making reflation exercises possible.

Analysis and results:
The results were clearly reported. Average cost-utility ratios were calculated and an incremental approach was used to synthesise the costs and benefits of the three strategies. Valid approaches were used to assess uncertainty and the results were extensively presented and discussed. The authors compared their results with those of other published studies, highlighting the similarities and differences. The results appear to be specific to the USA and their transferability was not discussed.

Concluding remarks:
The methods were conventional and the authors’ conclusions appear to be robust, but the data sources were not sufficiently described.

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