Cost-effectiveness of the surveillance program of hepatocellular carcinoma depends on the medical circumstances

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
The study assessed the cost-effectiveness of a surveillance programme with ultrasonography every 6 months for the detection of hepatocellular carcinoma (HCC) in comparison with no surveillance, considering different scenarios that resembled different medical environments. The study demonstrated that the cost-effectiveness of surveillance depended on specific conditions such as the proportion of small HCC detected incidentally, the annual incidence of HCC and the adoption of liver transplantation. The quality of the study methodology was difficult to judge given the limited reporting of the sources used. However, the appropriateness of the sensitivity analysis enhances the validity of the authors' conclusions.

Type of economic evaluation
Cost-utility analysis

Study objective
The objective of the study was to assess the cost-effectiveness of a surveillance programme with ultrasonography every 6 months for the detection of hepatocellular carcinoma (HCC) in a hypothetical cohort of 45-year-old patients with Child-Pugh class A cirrhosis. The analysis considered different scenarios that resembled different medical environments in order to identify the most cost-effective conditions for HCC surveillance.

Interventions
The two strategies under examination were no systematic surveillance of HCC versus surveillance with ultrasonography every 6 months. Small HCC could also be detected incidentally outside of the surveillance programme. Patients who were positive for the screening test received a confirmatory test consisting of α-foetoprotein, spiral computed tomography and fine-needle biopsy.

Location/setting
Japan/secondary care.

Methods
Analytical approach:
A Markov model was developed to simulate the natural history of disease and the management of patients (including liver transplantation) under the two scenarios. A lifetime horizon was considered. The authors stated that the perspective of the health care system was adopted.

Effectiveness data:
The clinical data used in the model and the assumptions made were based on published evidence. Details of the approach used to identify relevant published sources were not reported. Similarly, no information on the features of the primary studies was given. It was only stated that the probability of obtaining a liver transplantation was based on data from the United Network for Organ Sharing. Key clinical estimates were the incidence of HCC and the probability of detecting small HCC incidentally without surveillance.

Monetary benefit and utility valuations:
Utility valuations were derived from the literature. However, information on the primary sources was not given, although utility weights were reported.
Measure of benefit:
The summary benefit measure was the quality-adjusted life-years (QALYs). These were estimated using the decision model. QALYs were discounted at an annual rate of 3%.

Cost data:
The health services included in the analysis were ultrasonography, confirmatory test, angiography, transcatheter arterial embolisation, transplantation, terminal care, treatment of compensated and decompensated liver cirrhosis, and post-transplantation care. The authors stated that the costs and resources used for surveillance and medical care were estimated from the pertinent literature (details not given). The costs were in US dollars ($). An annual discount rate of 3% was applied to future costs. The price year was not reported.

Analysis of uncertainty:
A deterministic univariate sensitivity analysis was undertaken on all model inputs, using published evidence for ranges of values. A two-way sensitivity analysis was performed on the proportion of small HCC detected incidentally and the choice of liver transplantation. A three-way sensitivity analysis was carried out to examine the effect of annual incidence of HCC in combination with the proportion of small HCC detected incidentally and the choice of liver transplantation.

Results
Under the key assumptions that no small HCC were detected incidentally in the non-surveillance arm of the model, and transplantation was not selected for the therapy of HCC or decompensated liver cirrhosis (this scenario resembles the Japanese setting), surveillance led to a gain of 0.50 QALYs and an additional cost of $15,500 over no surveillance. This resulted in an incremental cost per QALY gained of $29,900. This figure increased, thus making surveillance less attractive, at higher rates of small HCC detected incidentally. However, even assuming that 40% of cases of small HCC were detected incidentally without surveillance, the incremental cost per QALY would be lower than $50,000.

In the scenario where transplantation was a treatment option, the incremental cost per QALY was higher ($59,900), even when no small HCC was detected incidentally. Thus, at a threshold value of $50,000 per QALY, surveillance was cost-effective only when transplantation was not a potential treatment option.

The sensitivity analysis showed that the most influential model inputs were the progression of small HCC to large HCC with no treatment, the availability of liver transplantation and the annual incidence of HCC. In general, the incremental cost-utility ratios decreased as the incidence of HCC increased. Moreover, the largest gain in QALYs was achieved when the screening programme started when patients were 40 years old.

Authors' conclusions
The authors concluded that a surveillance programme for the detection of HCC was cost-effective in Japan. However, the cost-effectiveness of such a programme depended on specific conditions, such as the proportion of small HCC detected incidentally, the annual incidence of HCC and the adoption of liver transplantation.

CRD commentary
Interventions:
The choice of the comparators (i.e. surveillance versus no surveillance) was appropriate for the authors' setting. The wide range of scenarios considered in the sensitivity analysis covers possible relevant strategies for other health care systems.

Effectiveness/benefits:
No information on the approach used to identify the clinical estimates and their sources was given. Thus, it is not possible to judge the validity of the clinical inputs used in the model. The use of sensitivity analysis gave some insight into the most influential model inputs but did not clarify the uncertain nature of some estimates. The authors noted that the mortality rates were derived from US studies and might not be appropriate for other populations. Similarly, the sources of utility valuations used for the calculation of QALYs were not described, and it was not clear whether these values were derived from the general population or from samples of patients or health care professionals. Nevertheless, the use of QALYs is appropriate since they capture the impact of the interventions on both quality of life and survival.
Furthermore, they allow comparisons to be made with the benefits of other health interventions.

**Costs:**
There was little information on the cost analysis. The authors reported most costs using macro-categories, which are quite common in these types of studies. The sources used to derive the cost estimates were not described. The authors stated that the pertinent literature was used but this does not permit a proper assessment of the quality of these estimates. Key cost estimates were varied in the sensitivity analysis but no statistical analysis of the costs was performed.

**Analysis and results:**
The synthesis of the costs and benefits was carried out appropriately and the results of the sensitivity analyses were presented clearly. The issue of uncertainty was satisfactorily addressed as different scenarios were considered; this enhances the external validity of the study. The authors noted some limitations to their analysis such as the fact, for example, that transplantation patterns change over time and are difficult to capture in a decision model. The strengths of the analysis were also pointed out and the authors stated that their study elucidated the future perspectives of HCC surveillance.

**Concluding remarks:**
Overall, the analysis was characterised by limited reporting of the sources used to derive the clinical estimates. However, the sensitivity analysis considered different scenarios and wide ranges of values, highlighting the most influential parameters. Thus, despite the lack of details of the sources used, the authors’ conclusions were well presented and appear valid.

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