Cost-effectiveness of semi-annual surveillance for hepatocellular carcinoma in cirrhotic patients of the Italian Liver Cancer population


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 examined the cost-effectiveness of annual versus semi-annual screening for liver cancer (hepatocellular carcinoma) in patients with cirrhosis. The authors concluded that both screening strategies could be recommended in cirrhotic patients, with semi-annual screening being more cost-effective in patients with compensated (mild to moderate) cirrhosis or as the annual liver cancer incidence increased. This analysis was based on a robust and transparent methodology that considered key areas of uncertainty. The authors’ conclusions appear valid.

Type of economic evaluation
Cost-utility analysis

Study objective
The study examined the cost-effectiveness of annual versus semi-annual surveillance for hepatocellular carcinoma in cirrhotic patients in Italy.

Interventions
Semi-annual screening was compared with conventional annual screening for hepatocellular carcinoma in patients with either compensated (mild to moderate) or decompensated (severe) cirrhosis. Screening was based on liver function tests, serum alpha-fetoprotein measurement, and liver ultrasonography.

Location/setting
Italy/secondary care.

Methods
Analytical approach:
The analysis was based on a Markov model with a ten-year time horizon. The authors stated that the analysis took the perspective of the payer.

Effectiveness data:
Two approaches were used to identify inputs for the model. Key evidence on screening strategies and survival was taken from a prospective database (ITA.LI.CA) involving 11 medical centres in Italy for 918 patients from 1987 to 2008 that met the inclusion criteria for the current model. Other inputs related to liver cancer incidence and natural history liver disease were identified through a literature review in the MEDLINE and EMBASE databases. Little information of studies selected was provided. Survival after a hepatocellular carcinoma diagnosis was a primary endpoint of the clinical analysis.

Monetary benefit and utility valuations:
Utility valuations were associated with the degree of liver dysfunction, presence of hepatocellular carcinoma, and treatment of tumours. These values were taken from the published literature.

Measure of benefit:
Quality-adjusted life-months (QALMs) were used as the summary benefit measure.

Cost data:
The cost categories included screening (abdominal ultrasound, complete blood exams, and computed tomography scan), compensated and decompensated cirrhosis (per year), hepatic resection, liver transplantation, percutaneous ablation, transarterial chemoembolisation, and palliative care. Costs related to these categories included inpatient and outpatient visits, diagnostic and laboratory testing, medications, and procedures. All economic data were extracted from current payments within the Italian National Health Service. Costs were in Euros (EUR). A 3% annual discount rate was applied. The price year was 2010.

Analysis of uncertainty:
A deterministic sensitivity analysis was carried out on all inputs of the model using published and assumed ranges of values. One-way and two-way sensitivity analyses were used.

Results
Over 10 years, among patients with compensated cirrhosis, the expected quality-adjusted life-months (QALMs) were 62.43 and the costs were EUR 19,070 with semi-annual surveillance; with annual surveillance the expected QALMs were 61.09 and the costs were EUR 16,384. The incremental cost per QALM with semi-annual versus annual surveillance was EUR 1,997, which was below the threshold of EUR 3,000 per QALM gained, that (the authors stated) corresponded to about EUR 50,000 per quality-adjusted life-year (QALY) gained.

The sensitivity analysis showed that the two most influential inputs were the expected annual incidence of liver cancer and the relative risk for the survival gain achievable with the semi-annual programme. At an incidence greater than 3.2%, semi-annual screening remained cost-effective at a threshold of EUR 3,000 per QALM. A two-way sensitivity analysis of these two variables showed that semi-annual surveillance was the optimal strategy at a threshold of EUR 1,000/QALM only for patients at very high risk, but it became cost-effective for most patients at a threshold of EUR 3,000. At a threshold of EUR 5,000, annual surveillance was preferred only in the case of very low liver cancer incidence and very low survival benefit expected from semi-annual surveillance.

In patients with decompensated cirrhosis, the incremental cost per QALY gained with semi-annual surveillance was EUR 3,814, which was above the cost-effectiveness threshold. Overall, the sensitivity analyses suggested that annual surveillance was more cost-effective in the decompensated cirrhosis patient population as long as incidence of liver cancer was lower than 10%.

Authors’ conclusions
The authors concluded that both screening strategies could be recommended in cirrhotic patients, with semi-annual surveillance being more cost-effective in patients with compensated cirrhosis or as the annual liver cancer incidence increased.

CRD commentary
Interventions:
The rationale for the selection of the comparators was clear. The authors evaluated the two screening frequencies documented in the literature.

Effectiveness/benefits:
Most clinical data on screening impact of survival came from a large Italian database that was representative of the real-world clinical practice in the authors’ setting. This represented a strength of the analysis, but the study design had also some drawbacks due to its retrospective nature and the potential selection bias. Other data were retrieved from a review of the literature that should have selected relevant studies, but these were not described. Some key inputs were varied in the sensitivity analysis. The use of QALMs as main benefit measure was appropriate given the impact of hepatocellular carcinoma both on survival and quality of life. Utility weights came from published studies not described. It was unclear whether future benefits were discounted.

Costs:
The authors stated that a societal perspective was adopted in the study but the types of costs included in the model and the sources used to derive them appear to suggest the viewpoint of the Italian National Health System. Most costs were reported as totals, so individual items could not be separated from the quantities of resources used. This might reduce the transparency of the economic side of the study and the possibility of replicating costs in other settings.
and clinical patterns were taken from a large Italian database that included 11 medical centres and was representative of the authors' setting. Discounting was appropriately performed. The price year was explicitly reported, which would allow reflation exercises in other time periods. Some costs were varied in the sensitivity analysis.

Analysis and results:
Average and incremental cost-utility ratios were appropriately used to synthesise costs and benefits of the alternative strategies. The study results were clearly reported and were presented separately for the compensated and decompensated cirrhotic populations. Uncertainty was satisfactorily investigated using a deterministic approach, which considered variations in key inputs; these results were reported clearly. The authors stated that the objective of the study was to use real-world data to populate the model, different to other published economic evaluations. The study results appeared specific to the Italian setting, but could be valid in other countries with similar epidemiological data and costs.

Concluding remarks:
This analysis was based on a robust and transparent methodology that considered key areas of uncertainty. The authors’ conclusions appear valid.

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