Mass screening for early detection of hepatocellular carcinoma by setting a high-risk population with alpha-fetoprotein and its glycoforms

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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.

Health technology
Mass screening programme for detecting hepatocellular carcinoma (HCC).

Type of intervention
Screening.

Economic study type
Cost-effectiveness analysis.

Study population
Elderly Japanese people attending a periodic mass screening programme for the aged.

Setting
Hospital. The economic study was carried out in Japan.

Dates to which data relate
Effectiveness and resource use data were collected during the period April 1993 to March 1996. The price year was not stated.

Source of effectiveness data
The evidence for final outcomes was derived from a single study.

Link between effectiveness and cost data
The costing was undertaken retrospectively on the same patient sample as that used in the effectiveness analysis.

Study sample
A total of 24,839 inhabitants were entered into the study, 74% were female and overall 12% were aged below 50, 22% were aged 50-59, 49% were aged 60-69 and 17% were aged 70 or older. 808 individuals with AST and/or ZTT above pre-defined cut-off levels were considered a high-risk group for HCC and further evaluated by analysis of serum AFP level. Power calculations were not used to determine the sample size.

Study design
Prospective cohort study in a specific population.
Analysis of effectiveness
The basis of the analysis of the clinical study was not stated. The primary outcome used in the analysis was the number of cases of HCC detected.

Effectiveness results
Of the 808 high risk individuals, 33 (4.1%) had serum AFP levels above 20ng ml⁻¹ and their sera were subsequently assayed for AFP glycoforms. Seven out of these 33 people (21.2%) were found to have AFP L-3 and/or AFP P-4 percentages above the cut-off values of 15 and 12%, respectively, indicating the presence of various stages of HCC at a sensitivity of 88% and a specificity of 99.7% for the combined evaluation of the test results. Five individuals with AFP L-3 and/or AFP P-4 above the cut-off levels were diagnosed with HCC using further diagnostic imaging (three cases were reported to be treatable), while two patients were under follow-up in the referred hospital.

Clinical conclusions
The detection rate of AFP glycoforms (0.02%) was comparable to that of ultrasound-based mass screening of HCC.

Measure of benefits used in the economic analysis
The number of cases of HCC detected was used as the outcome measure in the economic analysis.

Direct costs
The cost per session of ultrasound, and cost per test utilised for AST, ZTT, AFP, AFP-L3 and AFP-P4, were considered. The estimation of quantities was based on actual data whilst the estimation of costs was based on the recommendations by the Ministry of Health and Welfare for health insurance purposes. Costs and resource quantities were reported separately.

Currency
US dollars ($). The exchange rate used was $1.00 = 100 Yen.

Estimated benefits used in the economic analysis
Five individuals with AFP L-3 and/or AFP P-4 above the cut-off levels were diagnosed with HCC.

Cost results
24,839 AST and ZTT tests were performed at a total cost of $79,485 and $44,710 respectively; 808 AFP tests were performed at a cost of $17,776; 33 AFP-L3 and 33 AFP-L4 tests were performed at a cost of $990 for both tests. The total costs were therefore $143,951.

Synthesis of costs and benefits
The cost of detecting one case of HCC using determination of AST, ZTT, serum AFP and its glycoforms without ultrasound examination before screening the super high-risk population in this study was calculated to be $28,790. The presumptive cost calculated for the ultrasound mass screening including the two diagnosed HCC cases (without referring to the results of AFP L-3 and AFP P-4) was $1,241,950; a cost per case of $620,975. The authors pointed out that, although the detection rate in this study was comparable to the gold standard by the ultrasound-based screening method, false negative cases of HCC were not accounted for and an additional (50%) cases of early HCC might have been present.

Authors’ conclusions
Measurements of both AFP L3 and AFP-P4 should be added to the mass screening methods used for the detection of
HCC in patients with abnormal results of AST and/or ZTT and who are also found to have elevated serum AFP levels. Other recently developed diagnostic imaging techniques should be performed for HCC diagnosis in those patients with positive results for either AFP-L3 or AFP-A4.

**CRD COMMENTARY - Selection of comparators**
The reason for the choice of comparators is clear.

**Validity of estimate of measure of benefit**
The estimate of the measure of benefit used in the economic analysis is likely to be internally valid.

**Validity of estimate of costs**
Resource quantities were reported separately from costs. Only a limited perspective of costs was adopted, covering simply the costs of the test themselves with no comment on additional resources that might be required to administer and evaluate the tests.

**Other issues**
The issue of generalisability to other countries was not addressed.

**Source of funding**
None stated.

**Bibliographic details**

**MeSH**
Adult; Aged; alpha-Fetoproteins /analysis; Carcinoma, Hepatocellular /ultrasonography /diagnosis /prevention & control; Clinical Enzyme Tests; Japan; Mass Screening; Biomarkers, Tumor /blood

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