Economic implications of hepatic arterial infusion chemotherapy in treatment of nonresectable colorectal liver metastases


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
Using hepatic arterial infusion (HAI) of 5-fluoro-2'-deoxyuridine versus supportive care or intravenous chemotherapy in the treatment of nonresectable liver metastases from colorectal cancer.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
Patients with nonresectable liver metastases resulting from colorectal cancer.

Setting
Hospital. The economic study was carried out in Paris, France, and Palo Alto, California, USA.

Dates to which data relate
The effectiveness data were derived from seven studies published in 1986, 1987, 1989, 1990, 1992, and a meta-analysis published in 1994. Resource utilisation data were collected in 1995. 1995 prices were used.

Source of effectiveness data
The evidence for the final outcomes was derived from a synthesis of previously completed studies.

Link between effectiveness and cost data
The costing was not undertaken on the same patient sample as that used in the effectiveness study.

Outcomes assessed in the review
The outcome assessed in the meta-analysis was mean survival.

Study designs and other criteria for inclusion in the review
Randomized controlled trials based on the intention to treat principle.

Sources searched to identify primary studies

NHS Economic Evaluation Database (NHS EED)
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Not stated.

Criteria used to ensure the validity of primary studies
Not stated although the study containing the meta analysis stipulated its own inclusion criteria.

Methods used to judge relevance and validity, and for extracting data
The original data were extracted from the primary studies and the life expectancy outcome was estimated by the mean survival obtained from applying Kaplan-Meier methods to that data.

Number of primary studies included
Seven studies were included.

Methods of combining primary studies
Meta-analysis.

Investigation of differences between primary studies
Five studies used the intravenous chemotherapy option whereas the other two studies used the option of symptom palliation or ad libitum intravenous chemotherapy with, in most cases, fluorouracil alone.

Results of the review
The HAI group had a mean survival time of 16.3 (SE 0.7) months versus 13.1 (SE 0.7) months for the control (no HAI) group (logrank P= 0.0009).

Measure of benefits used in the economic analysis
Gain in life expectancy was used as the benefit measure. A 5% discount rate was applied to the life years gained.

Direct costs
Quantities were not reported separately from costs. The cost items were reported separately and the costs were discounted. The cost analysis was based on costs associated with the initial procedure, chemotherapy cycles, and main complications for the duration of the patient follow-up. Overhead and capital costs were included, whereas protocol-driven costs were excluded. The cost analysis was performed from the perspective of a health care system. The source of resource utilisation data was data from the two study sites in Paris and Palo Alto. The source of unit cost data was actual data from two centres (Paris and Palo Alto), each analysed separately. The price date was 1995. The costs of symptom palliation were omitted since they were believed to be common to the study groups.

Indirect Costs
Not considered.

Currency
US dollars ($).

Sensitivity analysis
A sensitivity analysis was conducted by excluding the data for those patients receiving the symptomatic palliation option only. This was equivalent to omission of two of the studies with such a comparator, so that only five studies were
included in the meta-analysis used to derive the estimates of effectiveness.

**Estimated benefits used in the economic analysis**
The mean gain in life expectancy by the hepatic arterial infusion group (relative to the control and using a 5% discount rate) was 3.2 months.

**Cost results**
Using a 5% discount rate, the mean total cost in France was $29,562, for the intervention, and $9,926 for the control. For Palo Alto, USA, the corresponding figures were $25,208 and $5,928.

**Synthesis of costs and benefits**
An incremental analysis was performed. The cost-effectiveness ratios, incremental (discounted) cost per (discounted) life year gained by the intervention relative to the control, in Paris were $73,635 and in Palo Alto were $72,300. These figures were derived using the price base of 1995 and a 5% discount rate for both costs and benefits. The sensitivity analysis yielded cost-effectiveness ratios of $73,680 for Paris and $87,012 for Palo Alto.

**Authors' conclusions**
The cost-effectiveness of localized chemotherapy for colorectal liver metastases is within the range of accepted treatments for serious medical conditions, although it may be considered borderline by policy-makers in some countries.

**CRD COMMENTARY - Selection of comparators**
The reason for the choice of comparators is clear. They represented the standard practice in the treatment of colorectal cancer. You should consider whether they are widely used health technologies in your own setting.

**Validity of estimate of measure of benefit**
The estimate of the benefit measure is likely to be internally valid even though the differences between studies (for example, in terms of the patient population and the way in which the outcomes were measured) and their potential effects on the results were not analysed.

**Validity of estimate of costs**
Quantities of resource use were not analysed separately from the costs. Adequate details of methods of cost estimation were provided in the paper. The indirect costs were not included in the economic study.

**Other issues**
The conclusions were justified given the uncertainties in effectiveness and unit cost data. The issue of generalisability was addressed by the sensitivity analysis, with the results showing small relative variations between the health systems of France and California, USA.

**Implications of the study**
As the authors recognized, further prospective studies are warranted, which consider additional aspects such as quality of life and costs (savings) associated with early return to work due to the administration of hepatic arterial infusion. Nevertheless, the present study yields some evidence of the potential benefits associated with such an intervention strategy.
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