Economic implications of hepatic arterial infusion versus intravenous chemotherapy or symptom palliation in the 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
The use of hepatic arterial infusion of 5-fluoro-2’-deoxyuridine.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients with nonresectable liver metastases from colorectal cancer.

Setting
The setting was secondary care. The economic analysis took place in Paris, France, and Palo Alto, USA.

Dates to which data relate
The effectiveness data were collected from studies published between 1986 and 1990. Resource use data were from 1995. The price year was 1995.

Source of effectiveness data
Effectiveness data were obtained from a meta-analysis of published randomised controlled trials (RCTs), the details of which were published elsewhere (see Other Publications of Related Interest).

Link between effectiveness and cost data
The effectiveness study was undertaken on a different group of patients to that used for the costing.

Outcomes assessed in the review
The outcome measure assessed was mean survival.

Study designs and other criteria for inclusion in the review
Only RCTs were included in the review. Inclusion and exclusion criteria were not given, although all trials were based on the intention to treat principle.
Sources searched to identify primary studies
The sources searched were reported in detail in the clinical publication of the meta-analysis. See "Other Publications of Related Interest" below.

Criteria used to ensure the validity of primary studies
The criteria were reported in detail in the clinical publication of the meta-analysis. See "Other Publications of Related Interest" below.

Methods used to judge relevance and validity, and for extracting data
The methods used were reported in detail in the clinical publication of the meta-analysis. See "Other Publications of Related Interest" below.

Number of primary studies included
Seven studies were included in the review.

Methods of combining primary studies
Original individual patient data were taken from the primary studies and, the Kaplan-Meier method, with a 5% annual discount rate, was used to calculate the mean survival and thus to estimate the gain in life expectancy. The meta-analysis amounted to individual data on 654 patients taken from 5 studies comparing with intravenous chemotherapy and 2 studies comparing with palliation.

Investigation of differences between primary studies
Five of the studies compared hepatic arterial infusion and intravenous chemotherapy, and 2 compared hepatic arterial infusion and an ad libitum control group in which some patients could be left untreated.

Results of the review
The hepatic arterial infusion group had a mean survival time of 16.3 (SE = 0.7) months versus 13.1 (SE = 0.7) months for control patients.

The mean gain in life expectancy was 3.2 (SE = 0.7) months, (p=0.0009).

Measure of benefits used in the economic analysis
Gain in life expectancy was used as a summary measure; the authors stated that the issue of quality of life was not addressed. Years gained were discounted at a rate of 5%.

Direct costs
Discounting took place at a 5% yearly rate. Costs were computed for two groups of patients, one in a Paris hospital and the other in a Palo Alto hospital, and not from patients in the effectiveness studies. Resource quantities were not reported separately to unit costs.

Direct medical costs included cost of purchasing the devices and cost of the procedures and hospitalisations, the cost of ambulatory treatment facilities (Paris) or outpatient clinic without hospitalisation (Palo Alto) for administering chemotherapy. Cost of chemotherapy drugs, computed from data on the number of chemotherapy cycles per patient in the trials, and average doses of drugs used. The cost of follow-up tests and the cost of treatment of severe toxicities, the frequency of which were estimated from the trials, were included in the meta-analysis.

Overhead costs included administrative and support services and capital costs. No costs were attached to patients.
allocated to the ad libitum groups, on the assumption that the costs of symptom palliation was the same for all patients regardless of their randomised treatment group. Values of hospital resources were drawn from the two cost accounting systems, one in Paris the other in Palo Alto, each being analysed separately. Actual costs (not charges) were used. The cost analysis was performed from the perspective of the decision maker.

**Statistical analysis of costs**
No statistical analysis was conducted and costs were treated deterministically.

**Indirect Costs**
Not applicable given the perspective adopted.

**Currency**
US dollars ($), no conversion factor was given although conversion took place.

**Sensitivity analysis**
A sensitivity analysis was conducted. The cost-effectiveness ratios were analysed assuming that the only comparator for hepatic arterial infusion was intravenous chemotherapy, only 5 of the 7 trials were included, 391 patients. A discount rate of zero percent was tested for both survival and costs.

**Estimated benefits used in the economic analysis**
The mean gain in life expectancy for the hepatic arterial infusion group was 3.2 (SE 0.7) months. A discount rate of 5% was used.

**Cost results**
The total cost of hepatic arterial infusion treatment in Paris was $29,562; the cost being given only in dollars.

The total cost of hepatic arterial infusion treatment in Palo Alto was $25,208.

The cost for the control group in Paris was $9,926 and in Palo Alto $5,928.

No currency conversion method was stated. The costs of complications were given per episode; they were then multiplied by the probability of occurrence and added to the cost of the corresponding strategy. All probabilities were given. The discount rate was 5%.

**Synthesis of costs and benefits**
Incremental analysis was performed. The cost-effectiveness ratio in Paris was $73,635 per life year gained and in Palo Alto $72,300 per life year gained. Figures were derived using 1995 prices and a discount rate of 5% for both costs and benefits. Sensitivity analysis revealed cost-effectiveness ratios for Paris of $73,680 and for Palo Alto of $87,012 when using the subset of 391 patients. No discounting produced values of $63,717 for Paris and $65,867 for Palo Alto. Cost-effectiveness ratios within the 95% confidence interval of survival gain were given in graphical format.

**Authors' conclusions**
The authors concluded that the cost-effectiveness of hepatic arterial infusion was "within the range of accepted treatments for other severe medical conditions, although it might be considered borderline by policy makers in some countries."
CRD COMMENTARY - Selection of comparators
The choice of comparators was clearly identified; they represented the standard practice for colorectal cancer treatment at the time of the study. The authors however mentioned that they might no longer be standard practice due to the advent of new technologies, although the difference is likely to be small.

Validity of estimate of measure of effectiveness
The authors did not state how the literature review was conducted, although the source, which was a meta-analysis previously conducted by the authors, was published (please refer to “Other Publications of Related Interest” below). All of the trials included in the meta-analysis were randomised control trials, with individual data on 654 patients, although it is questionable whether the gain in survival compared to different comparators can be combined. Sensitivity analysis was conducted on this, although it would, perhaps, have been more valid not to have combined at all or to have reported the results in the paper's summary.

Validity of estimate of measure of benefit
Life years gained were obtained directly from the effectiveness evidence. As the authors mentioned, the implications for quality of life will need further study.

Validity of estimate of costs
A clear description of cost categories and their sources was provided within the paper. However resource quantities were not presented separately from unit costs. Indirect costs were not included, although this would be consistent with the economic perspective.

Other issues
The authors’ conclusions were in keeping with the study population and sensitivity analysis partially addresses the issue of generalisability. The authors highlighted and justified their reasons for both methodological decisions and for the perspective taken throughout the study, and made comparisons with other studies.

Implications of the study
The author's recommend that prospective trials should ensure that cost information, both on medical costs and overall financial costs to society be collected. Other outcomes of interest that should be properly collected prospectively include possible return to work of patients treated and their quality of life. These recommendations seem reasonable in the light of the evidence from the study and its limitations, as discussed above.

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None stated.

Bibliographic details

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Other publications of related interest
Indexing Status
Subject indexing assigned by NLM

MeSH
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