Cost-effectiveness of systemic and regional chemotherapy for the treatment of patients with unresectable colorectal liver metastases
Durand-Zaleski I, Earlam S, Fordy C, Davies M, Allen-Mersh T G

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
Systemic and regional chemotherapy for patients with unresectable colorectal liver metastases.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
Male and female survival patients with unresectable colorectal liver metastases. Inclusion criteria were a history of primary colorectal carcinoma excision, the presence of up to 60% liver replacement by unresectable metastases and no evidence of extrahepatic abdominal metastases on computed tomography (CT) scan or of lung metastases on chest X-ray.

Setting
Hospital. The economic study was carried out in London, UK.

Dates to which data relate
The main effectiveness data were obtained from a single trial conducted between April 1988 and December 1995. Resource and cost data were taken from 1988-95 sources. The price year was 1995.

Source of effectiveness data
The estimates of quality of life scores, survivals, median number of treatment courses administered, number of patient who developed more than 50% tumour shrinkage on CT scans at 4 months after treatment compared with prior to starting treatment and complications were obtained from a single study.

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

Study sample
The patients included in this study were drawn from two randomized studies carried out over different time periods. One hundred and thirty-four patients were randomly allocated to a systemic chemotherapy group (34), to a hepatic arterial infusion (HAI) group (51) and to a symptom control group (49). Fifty-one systemic chemotherapy patients were recruited as control patients for both the systemic and HAI chemotherapy groups. The mean age was 55, 63 and 59
years in the HAI, systemic chemotherapy and symptom control group, respectively. Power calculations to determine the sample size were not undertaken.

**Study design**
This was a randomised controlled study. The duration of the follow-up was between 2 and 7 years. The loss to follow-up was not clearly reported as the survival days were provided (patients survived for a maximum of 864 days).

**Analysis of effectiveness**
The analysis of effectiveness was based on intention to treat. The primary health outcomes were quality of life scores, survivals, median number of treatment courses administered, number of patient who developed more than 50% tumour shrinkage on CT scans at 4 months after treatment compared with prior to starting treatment, complications, days worked and days not worked. The patient groups were shown to be comparable with respect to variables which affect quality of life and the ability to work.

**Effectiveness results**
Survival was 486 days in the HAI group, 298 days in the systemic chemotherapy group and 254 days in the symptom control group. Survival with normal quality of life scores were 318, 127 and 62 days in the HAI, systemic chemotherapy and symptom control groups, respectively. Duration of survival was discounted at a 5% yearly rate. The median number of treatment courses administered was 9 for both HAI and systemic chemotherapy patient. Forty-one percent in the HAI group and 24% in the systemic chemotherapy group developed greater than 50% tumour shrinkage on CT scans at 4 months after treatment compared with prior to starting treatment. Device-related complications occurred at a rate of 8%, and hospital admission for pump or catheter infection in 6%, of HAI patients. Port blockage or leakage requiring port replacement occurred in 12% of systemic chemotherapy patients. Total days worked were 150 for the HAI group, 15 for the systemic chemotherapy group and 90 for the symptom control group. Total days not worked were 240, 180 and 150 for HAI, systemic chemotherapy and symptom control groups, respectively.

**Clinical conclusions**
Management of unresectable colorectal liver metastases with HAI was shown to increase the survival and survival with normal quality of life scores with respect to systemic chemotherapy. Both produced better outcomes when compared with the controls.

**Measure of benefits used in the economic analysis**
The benefit measures were survival and survival with normal quality of life scores. Quality of life was estimated by standard instruments for the assessment of physical symptoms and mood which were completed monthly.

**Direct costs**
Direct costs included total costs of each treatment both to the health care system and to society. Health care costs included: purchasing and implanting a pump in HAI patients, hospital admission, hospital outpatient clinic visits (including travel costs), nurse visits and chemotherapy or other drug treatments. The costs to the hospital were taken from the Chelsea and Westminster Healthcare Trust cost accounting system. Costs to society included prescription charges paid by patients and disability living allowance paid to the patient by the State. The quantities were reported separately from the costs. A 5% discount rate was applied. The price year was 1995.

**Statistical analysis of costs**
Not undertaken.

**Indirect Costs**
Costs to society included the wage costs of days lost from work as an estimate of the opportunity cost of the patient’s disability living allowance paid to the patient by the State. The quantities were reported separately from the costs. A 5% discount rate was applied. The price year was 1995.

Currency
UK pounds sterling (€).

Sensitivity analysis
A one-way sensitivity analysis was undertaken on nurses’ costs, 6-day hospital stay after HAI, productivity of treated patients in employment and discount rate.

Estimated benefits used in the economic analysis
Results for the HAI, systemic chemotherapy and symptom control groups were as follows:

Survival, 486, 298 and 254 days;
Survival with normal quality of life scores, 318, 127 and 62 days;
(duration of survival was discounted at a 5% yearly rate)
Total days worked, 150, 15 and 90;
Total days not worked, 240, 180 and 150.

Cost results
The total hospital costs were 14,019 (HAI), 4,518 (systemic chemotherapy) and 588 (symptom control). The total ambulatory costs were 18,243, 6,089 and 2,136, respectively.

Synthesis of costs and benefits
The extra cost per year of added survival was 24,604 (HAI versus systemic chemotherapy), 32,788 (systemic chemotherapy versus symptom control) and 26,157 (HAI versus symptom control). The extra cost per year of survival with normal quality of life scores was 24,218, 24,280 and 23,705 for the same comparisons. If the costs of nurse visits were estimated by an equivalent of the relative value scale, the health care cost per life-year gained would be 23,323 for HAI compared with systemic chemotherapy, and 32,916 for systemic chemotherapy compared with symptom control. Applying a 0% discount rate would increase the costs of HAI, systemic chemotherapy and symptom control by 53, 67 and 1 each, respectively. Reducing the total hospital stay for HAI patients to 6 days would decrease the total hospital costs to 11,754 and the total health care costs to 15,998. This would result in a health care cost per life-year gain of 19,328 for HAI compared with systemic chemotherapy.

Authors’ conclusions
This study shows that the least expensive management strategy for CLM was symptom control, whereas systemic and HAI chemotherapies were equally cost-effective in producing added normal quality survival for health care resources expended.

CRD COMMENTARY - Selection of comparators
The reason for the choice of the comparator is clear. The survival of patients with unresectable colorectal liver metastases can be prolonged by either systemic or HAI chemotherapy. However, although HAI produces more tumour response than systemic chemotherapy and sustains normal quality of life in addition to prolonging survival, its treatment
costs include the purchase of an implantable chemotherapy pump and the hospital cost of hepatic artery cannulation. You, as a user of this database, should consider whether these are widely health technologies in your own setting.

**Validity of estimate of measure of benefit**
The estimates of measure of benefit used in the economic analysis are likely to be internally valid. However, as the control group data were taken from a study reported in the literature, some elements of bias might have been introduced into the analysis. A sensitivity analysis was conducted to validate the robustness of the findings.

**Validity of estimate of costs**
Resource quantities were reported separately from the prices. The quantity/cost boundary adopted was both the health care system and society. Adequate details of methods of quantity/cost estimation were given and no important cost items appear to have been omitted. However, as no statistical analysis was conducted, the costs need to be treated with a degree of caution.

**Other issues**
The authors' conclusions are likely to be justified given the uncertainties in the data. However, as stated by the authors, the cost benefit was difficult to interpret because of uncertain attitudes regarding continued work during terminal illness. Bias between groups in unidentified factors controlling treatment cost-effectiveness cannot be excluded. Considering the alternative costing of nurses based on the relative value-based scale, the results of this study are applicable to treatment centres with a different nursing structure. As the authors noted, variations in treatment procedures between different hospitals and countries place limitations on the extension of this cost-effectiveness analysis to another setting. Appropriate comparisons were made with other studies in terms of survival rates. The results do not appear to have been presented selectively.

**Implications of the study**
The cost-effectiveness of both chemotherapies were within the same range as those of other treatments for cancer and chronic disorders, which the health care systems in developed countries currently support.

**Source of funding**
S Earlam and C Fordy were funded by MacMillan Cancer Relief, London, UK, M Davies was supported by Colon Cancer Concern, London, UK and I Durand-Zaleski was supported by the French Cancer Research Association, Paris, France.

**Bibliographic details**

**PubMedID**
9731890

**Other publications of related interest**

**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Antineoplastic Agents /administration & dosage; Colorectal Neoplasms /pathology; Cost-Benefit Analysis; Costs and Cost Analysis; Health Care Costs; Humans; Infusions, Intra-Arterial /economics; Liver Neoplasms /drug therapy /economics /secondary; Quality of Life; Survival Rate; Treatment Outcome

**AccessionNumber**
21998001343