Decision analysis for the cost-effective management of recurrent colorectal cancer

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
A strategy of computed axial tomography (CT) with (18F)2-fluoro-2-deoxyglucose positron emission tomography (FDG-PET), for the diagnosis of recurrences in postsurgical patients with colorectal cancer (CRC), was examined.

Type of intervention
Screening.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised hypothetical patients with an increase in carcinoembryonic antigen (CEA) of greater than 5 ng/mL during follow-up testing after the resection of their primary CRC.

Setting
The setting was secondary care. The model used data from the USA.

Dates to which data relate
The effectiveness data were derived from studies published from 1993 to 1997. Neither the price year nor the dates for resource use were reported.

Source of effectiveness data
The effectiveness evidence came from published studies and the authors’ assumptions.

Modelling
A decision tree model was used to estimate the costs and benefits of the two diagnostic strategies for recurrent CRC. In both strategies, the patients were evaluated by CT of the thorax, abdomen and pelvis. The patients were grouped in three categories. There were those with recurrent CRC involving the liver (hepatic involvement), those with recurrent CRC in locations throughout the body other than the liver (extrahepatic involvement), and those with no recurrences. The model focused on the identification of patients with isolated liver recurrence eligible for curative hepatic resection. The subsequent management of the patients depended on the sub-group in which they were included.

Outcomes assessed in the review
The outcomes estimated in the review were, in the preliminary decision tree, the sensitivity and specificity of CEA and the prevalence of recurrent CRC.
The outcomes estimated in the review were, in the main decision tree:

- the sensitivity and specificity of CT, FDG-PET and biopsy in the liver and whole body;
- years of morbidity after biopsy or surgery;
- the death rate after biopsy or surgery;
- the discounted life expectancy (based on 60-year-old patient of any race or gender) for a normal postsurgical patient and for a recurrent patient (with no treatment, after surgical cure); and
- the probabilities of frequency of hepatic involvement, frequency of hepatic plus extrahepatic in hepatic involvement patients, prevalence of recurrence in follow-up, and liver-only recurrence.

**Study designs and other criteria for inclusion in the review**
Not stated.

**Sources searched to identify primary studies**
MEDLINE was searched from 1980 to 1999.

**Criteria used to ensure the validity of primary studies**
Not stated.

**Methods used to judge relevance and validity, and for extracting data**
Not stated.

**Number of primary studies included**
Three primary studies were included in the review.

**Methods of combining primary studies**
The authors did not state how they derived the parameters from the primary studies.

**Investigation of differences between primary studies**
Not stated.

**Results of the review**
In the preliminary tree, the sensitivity of CEA was 0.604 (range: 0.582 - 0.667) and the specificity was 0.875 (range: 0.84 - 0.93). The prevalence of recurrent CRC was 0.327 (range: 0.309 - 0.334).

The sensitivity and specificity results in the main decision tree were as follows:
- the sensitivity of CT in the liver was 0.79 (range: 0.75 - 0.842) and the specificity was 0.883 (range: 0.778 - 0.948);
- the sensitivity of CT in the whole body was 0.757 (range: 0.467 - 0.821) and the specificity was 0.557 (range: 0.5 - 1);
- the sensitivity of FDG-PET in the liver was 0.963 (range: 0.940 - 1) and the specificity was 0.986 (range: 0.670 - 1);
- the sensitivity of FDG-PET in the whole body was 0.97 (range: 0.950 - 1) and the specificity was 0.756 (range: 0.690 -
The years of morbidity were 0.001 (range: 0 - 0.001) after biopsy and 0.024 (range: 0.019 - 0.038) after surgery.

The death rate was 0.2 (range: 0 - 0.5) after biopsy and 3.4 (range: 2 - 3.70) after surgery.

The discounted life expectancy was 5.681 years for a normal postsurgical patient, 2 years for a recurrent patient with no treatment, and 3.804 years for a recurrent patient after surgical cure. The discount rate was not specified.

The frequency of hepatic involvement was 0.285 (range: 0.163 - 0.377).

The frequency of hepatic plus extrahepatic in hepatic involvement patients was 0.81 (range: 0.5 - 1).

The prevalence of recurrence in follow-up was 0.702.

The probability of liver-only recurrence (resectable) was 1.

**Methods used to derive estimates of effectiveness**
The authors made some assumptions to derive model inputs that were not available in the published literature.

**Estimates of effectiveness and key assumptions**
The discounted life expectancy was 2.663 years for recurrent patient after chemotherapy and 4.545 years for normal postsurgical patients with chemotherapy. The authors set both the sensitivity and specificity of biopsy as 1. They assumed that performing a biopsy on FDG-PET information alone was possible, although this may not have not been true in practice.

**Measure of benefits used in the economic analysis**
Life expectancy (LE) was used as the benefit measure in the economic analysis. It was obtained using the decision model and was discounted, although the discount rate was not reported.

**Direct costs**
Discounting was not reported, although it could have been relevant. The unit costs were reported, but the quantities of resources were not given. The health services included in the analysis were CT, FDG-PET, biopsy, surgery and chemotherapy. The cost/resource boundary adopted in the study was not reported. However, it is likely to have been that of the third-party payer, as the costs were based on Medicare reimbursement rates. The source of the cost data was not reported. The total costs were calculated using the decision model. No price year was reported.

**Statistical analysis of costs**
The costs were treated deterministically in the base-case.

**Indirect Costs**
The indirect costs were not included in the analysis.

**Currency**
US dollars ($).

**Sensitivity analysis**
One-way sensitivity analyses were performed on all model inputs in order to assess the uncertainty of the parameters.
estimated from the literature review. A worst-case scenario, in which all the variables favouring FDG-PET were reduced by 15%, was also considered. In addition, there was a further worst-case scenario in which all the variables favouring CT alone were inflated by 15%, while maintaining the 15% penalty on favourable FDG-PET variables.

Estimated benefits used in the economic analysis
The LE was 3.5634 years with CT alone and 3.5895 years with CT plus FDG-PET. The difference in LE was 0.0261 years and favoured the CT plus FDG-PET strategy.

Cost results
The total costs per patient were $8,354 with CT alone and $8,783 with CT plus FDG-PET. The difference in costs was $429 in favour of the CT alone strategy.

Synthesis of costs and benefits
An incremental cost-effectiveness analysis was conducted to combine the costs and benefits of the two screening strategies. The incremental cost per life-year gained with CT plus FDG-PET, relative to CT alone, was $16,437. In the scenario penalising PET, the incremental cost per life-year gained was $33,556. In the scenario penalising PET and favouring CT, the incremental cost per life-year gained was $111,000. The most influential model inputs were disease prevalence, sensitivity of CT, specificity of biopsy, cost of FDG-PET, and LE. Variations in such variables affected the cost-effectiveness of the FDG-PET strategy. Specifically, CT plus FDG-PET dominated CT alone at a prevalence rate higher than 90%, while at a CT sensitivity higher than 0.879 or at a biopsy specificity lower than 0.803. CT plus FDG-PET resulted in an incremental cost-effectiveness ratio higher than $50,000, considered to be the relevant threshold for the funding of new interventions.

Authors' conclusions
The screening strategy based on computed axial tomography (CT) with (18F)2-fluoro-2-deoxyglucose positron emission tomography (FDG-PET), although initially more expensive, was cost-effective under several scenarios. This was mainly due to the avoidance of unnecessary surgery in patients with suspected recurrences.

CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparator was clear. CT alone was selected since the aim of the study was to assess the active value of FDG-PET for the diagnosis of recurrences among patients who had been surgically treated for CRC. You should decide whether it represents a widely used diagnostic approach in your own setting.

Validity of estimate of measure of effectiveness
The analysis of effectiveness used a review of published studies. The authors reported the source searched and some details of the search. However, the inclusion criteria and the designs of the primary studies were not reported. Also, the authors did not state how the primary studies were combined, and it was unclear whether they considered the differences in the studies when estimating the effectiveness. Due to uncertainty in the effectiveness estimates, the authors performed sensitivity analyses on all model inputs, using ranges of values that were derived from the literature.

Validity of estimate of measure of benefit
LE was the benefit measure used. It was calculated using a decision model, which was reported in detail in the paper. Discounting was conducted, although the discount rate was not reported. The use of LE permits comparisons to be made with the benefits of other programmes.

Validity of estimate of costs
The perspective adopted in the study was not stated. However, it is likely to have been that of the third-party payer, as
reimbursement rates were used to estimate the costs. The health services included in the economic evaluation were all associated with the performance of the diagnostic tests and surgery. The unit costs were reported, but no details of resource consumption were given. The costs were treated deterministically, but extensive sensitivity analyses were carried out on the key cost items. No price year was reported, thus making reflation exercises in other settings difficult. There was no mention of discounting, which was relevant.

Other issues
The authors validated their model by comparing intermediate node results with those found in the literature. However, they did not compare the overall health benefit of life expectancy with other studies, perhaps because no cost-effectiveness studies such as this had been conducted. The authors did not discuss the issue of the generalisability of the study results to other settings, but sensitivity analyses were performed which may help. On the whole, the external validity of the analysis was low. The authors commented on some limitations of their study. First, the analysis focused only on hepatic recurrences and resectability. Second, the decision model was fairly complicated and neglected patient preferences for treatments. Third, several assumptions were made in the decision model.

Implications of the study
The study provides a policy guideline for the management of recurrent CRC and suggests that CT plus FDG-PET may represent a cost-effective diagnostic approach. The authors note that the study results could be useful for the design of future clinical trials.

Source of funding
Supported in part by the DOE (contract DE-FC03-87ER60615) and the Ahmanson Foundation.

Bibliographic details

PubMedID
11224617

Other publications of related interest

Indexing Status
Subject indexing assigned by NLM

MeSH
Colorectal Neoplasms /economics /mortality /pathology; Cost-Benefit Analysis; Decision Trees; Direct Service Costs; Fluorodeoxyglucose F18; Humans; Life Expectancy; Liver Neoplasms /economics /mortality /radiography /radionuclide imaging /secondary; Models, Theoretical; Neoplasm Staging /economics /methods; Radiopharmaceuticals; Sensitivity and Specificity; Survival Analysis; Tomography, Emission-Computed /economics /methods; Tomography, X-Ray Computed /economics

AccessionNumber
22001000628

Date bibliographic record published
30/09/2003

Date abstract record published