Cost implications of new treatments for advanced colorectal cancer
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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.

CRD summary
This study measured the costs and cost-effectiveness of sequential regimens of chemotherapy and/or monoclonal antibodies for the treatment of patients with metastatic colorectal cancer. The authors concluded that treatment of metastatic colorectal cancer with the most effective regimens came at very high additional costs. The methods were adequate and the results were sufficiently reported. The authors’ conclusions appear to be appropriate, but limited costs were analysed.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
The objective was to measure the costs and cost-effectiveness of sequential regimens of chemotherapy and/or monoclonal antibodies, for the treatment of patients with newly diagnosed metastatic colorectal cancer.

Interventions
The authors studied nine treatment strategies, but, for clarity, only four strategies were presented.

Strategy A was 5-fluorouracil with leucovorin as first-line therapy, followed by supportive care.
Strategy C was 5-fluorouracil with leucovorin and irinotecan (FOLFIRI) as first-line therapy, followed by 5-fluorouracil with leucovorin and oxaliplatin (FOLFOX) as second-line therapy, followed by supportive care.
Strategy G was FOLFIRI and bevacizumab as first-line therapy, followed by FOLFOX as second-line therapy, followed by cetuximab as third-line therapy, followed by supportive care.
Strategy I was FOLFOX and bevacizumab as first-line therapy, followed by irinotecan as second-line therapy, followed by cetuximab and irinotecan as third-line therapy, followed by supportive care.

Location/setting
USA/in-patient secondary care.

Methods
Analytical approach:
A Markov model was used to evaluate the interventions, for a hypothetical cohort of 1,000 patients, and the time horizon was the lifetime of the patient. The authors reported that the perspective adopted was that of the third-party payer.

Effectiveness data:
The effectiveness data were from multicentre phase-two, and randomised phase-three trials, as well as unpublished data from another trial. These results were extrapolated, to a lifetime, using US life tables. The main effectiveness estimates were the rates of progression and toxicity. The progression rates were trial results converted to weekly probabilities, while trial toxicities were converted to probabilities of fatal or nonfatal outcomes.

Monetary benefit and utility valuations:
Not relevant.

Measure of benefit:
The benefit measure was life-years gained and these were discounted at an annual rate of 3%.

Cost data:
Only the costs of the treatments, including supportive care, were analysed. These costs were based on average sale prices from Medicare and Medicaid. The price year was 2008 and future costs were discounted at an annual rate of 3%. The currency was US dollars ($).

Analysis of uncertainty:
A series of one-way sensitivity analyses was undertaken by varying the toxicity rates, progression, drug costs, time on supportive care, and cost of supportive care. A Monte Carlo simulation, of 1,000 patients, was undertaken by assigning probability distributions to each model parameter. The results of the sensitivity analyses were presented in cost-effectiveness frontiers and a scatter plot.

Results
The incremental cost was $57,689 for strategy C compared with strategy A, $67,313 for strategy G compared with C, and $44,388 for strategy I compared with G. The life-weeks gained were 36.28 for strategy C was compared with A, 21.54 for strategy G compared with C, and 8.56 for strategy I compared with G.

The additional cost per life-year gained was $102,347 for strategy C compared with A, $170,896 for strategy G compared with C, and $243,096 for strategy I compared with G.

These results were most sensitive to changes in the first-line therapy, while changes in efficacy and toxicity had no major impact on the incremental cost-effectiveness ratios.

Authors’ conclusions
The authors concluded that treatment of metastatic colorectal cancer with the most effective regimens came at very high additional costs.

CRD commentary
Interventions:
The interventions were reported clearly and appear to have been appropriate comparators. Only four of the nine interventions were presented, because they represented the increasingly effective treatments.

Effectiveness/benefits:
The effectiveness data were from published and unpublished trials, but the method used to identify these trials was not reported, which makes it unclear if all the best available evidence was used. The authors justified their choice of the benefit measure, which was appropriately discounted.

Costs:
Only the costs of the drugs and supportive care were included. This did not include the costs of the management of toxicity, radiographic studies, physician visits, and indirect costs, which might have been relevant for the third-party payer perspective. This omission could have biased the results; for example, those drugs with lower toxicity would have lower costs for the treatment of side-effects than those with higher toxicity. The sources for the costs were sufficiently reported. The price year, time horizon, discount rate, and currency details were all given.

Analysis and results:
The costs and outcomes were appropriately synthesised in a Markov model. The details of the model and a diagram were reported. A series of one-way and probabilistic sensitivity analyses assessed the uncertainty in the model. The results of the one-way analyses were presented in full, but those of the probabilistic analysis were only presented in a scatter plot and were not discussed. The main limitation to the study was highlighted by the authors and this was that the toxicity effectiveness estimates were from clinical trials that were not consistently reported.

Concluding remarks:
The methods were adequate and the results were sufficiently reported. The authors’ conclusions appear to be
appropriate, but the limited costs that were analysed should be considered.

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