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 investigated the long-term cost-effectiveness of five alternative chemotherapy strategies for the treatment of patients with advanced colorectal cancer. The authors concluded that, at conventional levels of cost-effectiveness in the UK, first-line combination therapy with the 5-fluorouracil plus irinotecan regimen was the most cost-effective strategy. The study methods seemed appropriate and were clearly and transparently reported. The authors' conclusions appear appropriate.

Type of economic evaluation
Cost-effectiveness analysis, cost-utility analysis

Study objective
The objective was to investigate the long-term cost-effectiveness of five alternative chemotherapy strategies for the treatment of patients with poor prognosis advanced colorectal cancer.

Interventions
The interventions considered in the economic analysis were five alternative treatments considered in a recent randomised controlled trial (RCT). The treatment strategies were: the standard approach of sequential single-agent modified de Gramont regimen (MdG) using fluorouracil until treatment failure, followed by single agent irinotecan (strategy A); first-line MdG regimen using fluorouracil until treatment failure, followed by doublet therapy with MdG plus irinotecan (strategy B-ir); first-line MdG regimen until treatment failure, followed by doublet therapy with MdG regimen plus oxaliplatin (strategy B-ox); first-line doublet therapy with MdG regimen plus irinotecan (strategy C-ir); and first-line doublet therapy with MdG regimen plus oxaliplatin (strategy C-ox). Salvage therapy (any chemotherapy initiated after failure of one of the five strategies) options were also offered.

Location/setting
UK/Secondary care.

Methods
Analytical approach:
A decision-tree model was used to extrapolate the results of a single clinical trial (FOCUS trial; Seymour, Maughan, et al. 2007, see 'Other Publications of Related Interest' below for bibliographic details) over an extended time period. The time horizon of the analysis was 10 years, which covered a time period over which most of the patients in the study population were expected to have died. The authors stated the study perspective to be that of the UK NHS.

Effectiveness data:
The effectiveness data were taken from the FOCUS trial. This was a randomised controlled trial, conducted in the UK, with a sample size of 2,135 patients. Median follow-up of patients was 26.5 months. The main clinical effectiveness estimate of patient survival was derived from the FOCUS trial.

Monetary benefit and utility valuations:
The source of utility values were the responses of patients to the European Quality of life (EQ-5D) questionnaire during the FOCUS trial, which were converted with utility estimates representing the UK population, using a scaled gamma model.
Measure of benefit:
The measure of benefit was quality-adjusted life-year (QALY), which was discounted at an annual rate of 3.5%.

Cost data:
The cost categories included the acquisition and administration of chemotherapy drugs, the use of primary and secondary healthcare services, and the cost of palliative care. The fixed costs of equipment and monitoring were based on the RCT protocol and published data. Healthcare resource use was based on data collected throughout the RCT and estimated using primary data from an NHS Trust (by personal communication), the British National Formulary for drug prices, and the Department of Health reference costs for primary and secondary care contacts. Some cost data were only reported in an online appendix (not available without subscription). Costs were presented in UK £ (2009 prices).

Analysis of uncertainty:
A probabilistic sensitivity analysis was performed to represent the impact of uncertainty around all parameter inputs on the results. The results of these analyses were presented in cost-effectiveness acceptability curves.

Results
The estimated costs of the alternative treatments ranged from an average of £15,965 per patient with strategy A (standard treatment) up to £18,034 per patient for strategy C-ir.

The mean QALYs associated with treatment ranged from 0.93 with strategy A to 1.07 with strategy C-ir.

Compared with strategy A, the incremental cost-effectiveness ratio of strategy C-ir was £14,877 per QALY gained. The probability that this strategy was cost-effective at a threshold of £20,000 per QALY was 59% and 68% at a threshold of £30,000 per QALY.

Using British National Formulary drug prices, strategy B-ir was the most cost-effective treatment, with an incremental cost per QALY gained of £19,753. The probability that this strategy was cost-effective at a threshold of £20,000 per QALY was 50% and 65% at a threshold of £30,000 per QALY.

Authors’ conclusions
The authors concluded that, at conventional levels of cost-effectiveness in the UK, first-line doublet therapy with a 5-fluorouracil plus irinotecan regimen was the most cost-effective strategy for advanced colorectal cancer.

CRD commentary
Interventions:
The level of reporting of the interventions was good. The interventions included appeared to be highly relevant to the study setting and may be applicable elsewhere. The study appeared to include the standard care for this population in the UK (palliative chemotherapy) for the setting (UK secondary care).

Effectiveness/benefits:
The source of effectiveness data was a single randomised controlled trial (FOCUS trial), which set out to specifically explore the optimum combination and sequencing of chemotherapy in the setting of UK secondary care. This source of data was of high methodological quality and well described. The source of utilities was well described and was appropriate for the study setting. The methods that supported the calculation of QALYs appeared to be appropriate.

Costs:
The costs included were consistent with the stated perspective of the UK NHS and were relevant to this setting. The base-case analysis used cost data which were not publicly available, which may limit the interpretation and replication of the results. However, the cost data were supplemented by a sensitivity analysis using published British National Formulary drug prices. The measurement of resource data was based on estimates from a high quality trial (FOCUS trial). The level of reporting of cost data was good, with cost estimates presented in a table. Adjustments to cost data were fully described.

Analysis and results:
It was appropriate to use an incremental analysis to explore the relative cost-effectiveness of the range of different
treatment options. A probabilistic sensitivity analysis was conducted, which was a thorough method to assess the impact on results of uncertainty for the key parameters. The results of the base-case and sensitivity analyses were presented in full. The authors discussed the limitations of their study in detail.

Concluding remarks:
The study methods seemed appropriate and were clearly and transparently reported. The authors' conclusions appear appropriate.

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