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 health intervention examined in the study was oral capecitabine (CAP) used for adjuvant or palliative treatment of patients with advanced colorectal cancer. CAP was administered at a dose of 1,250 mg/m^2 PO BID as an intermittent regimen of 3-week cycles, with 2 weeks of treatment followed by a 1-week rest period.

Type of intervention
Treatment and palliative care.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients with advanced colorectal cancer. Some inclusion criteria were reported such as no prior chemotherapy for metastatic disease and completion of adjuvant chemotherapy.

Setting
The setting was hospital and home. The economic study was carried out in The Netherlands.

Dates to which data relate
Effectiveness data were derived from studies published in 2001. Resource use data were gathered from 1999 to 2002. The price year was 2002.

Source of effectiveness data
The effectiveness data came from a synthesis of published studies.

Outcomes assessed in the review
The outcomes assessed from the literature were the efficacy of the two regimens and associated side-effects. In particular, the following probabilities were estimated for CAP and 5FL: probability of no toxicity, probability of neutropenia, probability of stomatitis, probability of nausea/emesis and probability of diarrhoea.

Study designs and other criteria for inclusion in the review
The clinical data were derived from 2 phase III clinical trials that were identified selectively. Details on the two studies were not reported, but it was stated that the sample size of the two studies was large.
Sources searched to identify primary studies
Not relevant.

Criteria used to ensure the validity of primary studies
The use of randomised, clinical trials ensures the internal validity of the primary data.

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

Number of primary studies included
Two primary studies were used as the source of clinical evidence.

Methods of combining primary studies
The method used to pool primary estimates was not described.

Investigation of differences between primary studies
Not stated.

Results of the review
The effectiveness of the two treatments, namely time to disease progression, time to treatment failure, and overall survival, was equivalent.

The side-effects of the two treatments were considered in order to calculate the resources associated with each regimen.

The incidence of neutropenia was 2% with CAP and 23% with 5FL (89.9% reduction with CAP).

The incidence of stomatitis was 2% with CAP and 15% with 5FL (85.5% reduction with CAP).

The incidence of hand-foot syndrome was 17% with CAP and 1% with 5FL (97.1% increase with CAP).

The frequency of other side-effects was not significantly different between the two treatment arms.

This led to the following probabilities of events for 5FL and CAP respectively: probability of no toxicity 0.61 versus 0.89, probability of neutropenia 0.18 versus 0.02, probability of stomatitis 0.15 versus 0.03, probability of diarrhoea 0.03 for both regimens, and probability of nausea/emesis 0.03 for both regimens.

Measure of benefits used in the economic analysis
No summary benefit measure was used in the economic analysis since the two interventions were equivalent. In effect a cost-minimisation analysis (CMA) was carried out.

Direct costs
The perspective adopted in the analysis was not clearly stated, but it appears to have been that of society. The following items were included in the study: inpatient day, day-care treatment, outpatient visits, drugs used for the chemotherapy regimen and the management of adverse events, and travel expenses from and to the hospital. Costs associated with the treatment of hand-foot syndrome were not taken into account since products used for the management of this adverse event usually do not contain pharmacologic agents. The estimation of resource use for 5FL was based on the medical records of 65 patients treated at a single institution from 1999 to 2002. Thirty-three patients were treated palliatively.
for metastatic disease with 5FL and 32 patients received 5FL as adjuvant treatment. Resource use and associated costs with CAP were estimated from a simulation, assuming that patients whose data were investigated were treated with CAP instead of 5FL. Unit costs were presented separately from quantities of resources used for most items. Prices came from the Dutch Guide to Investigation of Costs. The costs for chemotherapy and for medications for adverse effects were derived from the 2002 edition of the Formulary of the Dutch Foundation for Health Care Insurance. Discounting was not relevant as costs were incurred over a short time period. The price year was 2002.

**Statistical analysis of costs**
Costs appear to have been treated deterministically.

**Indirect Costs**
Indirect costs were not taken into account. The authors stated that patients are unlikely to incur any loss of productivity; given the severity of the disease, most patients cannot work when suffering from advanced metastatic colorectal cancer. In addition, many patients in the trial used for effectiveness data were older than 65 years.

**Currency**
Euros (EUR).

**Sensitivity analysis**
Univariate sensitivity analyses were carried out to assess the robustness of cost results to variations in costs and some rates of adverse events. For example, the same rates of stomatitis and neutropenia were assumed for CAP and 5FL; the number of inpatient days with CAP was increased; the number of inpatient days due to hand-foot syndrome was increased; no outpatient visits associated with CAP was assumed; different CAP dose reductions were taken into account; different purchase and preparation costs were used. Alternative ranges were based on published estimates or were set by the authors. A multivariate sensitivity analysis was also conducted and clinical/economic data were unfavourable for CAP treatment.

**Estimated benefits used in the economic analysis**
Please refer to the effectiveness results reported above.

**Cost results**
Mean total costs per patient for palliative treatment were EUR 5,614 with 5FL and EUR 4,004 with CAP.

The extra drug costs of CAP over 5FL were more than compensated for by lower travel expenses, lower costs for toxicity management, and less hospital care for the administration of chemotherapy.

The sensitivity analysis showed that, even in the scenarios favourable to 5FL, CAP remained the least expensive option, with cost-saving ranging from EUR 891 to EUR 2,010.

Mean total costs per patient for adjuvant treatment were EUR 4,704 with 5FL and EUR 3,770 with CAP.

Again, the sensitivity analysis showed that CAP remained the least expensive option, with cost-saving ranging from EUR 588 to EUR 1,348.

**Synthesis of costs and benefits**
A synthesis of costs and benefits was not relevant as a cost-minimisation analysis was carried out.
Authors' conclusions
The authors concluded that oral CAP is a very cost-effective intervention for the treatment of colorectal cancer in The Netherlands. CAP was as effective as conventional 5FL but it had a more favourable toxicity profile and was also cost-saving.

CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparator, namely 5FL, was clear since this is the most widely used chemotherapy regimen. Doses were clearly reported for both treatments. You should decide whether they are valid interventions in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness evidence came from two clinical trials, whose results were combined to assess the effectiveness and safety of the two regimens. The primary studies were identified selectively rather than through a systematic review of the literature. The size of the sample included in the two studies was reported, but details on patient characteristics and on the design of the study were not reported. The two populations were pooled but the method of combination was not reported. The issue of heterogeneity of the two trials was not addressed. The randomised design should have enhanced the validity of primary estimates.

Validity of estimate of measure of benefit
No summary benefit measure was used in the analysis because a cost-minimisation analysis was performed. Please refer to the commentary reported above under 'Validity of estimate of measure of effectiveness'.

Validity of estimate of costs
The perspective taken in the study was not stated, but it may have been societal. The exclusion of indirect costs, namely productivity losses, should not have affected the results of the analysis since patients in both groups were at the same stage of disease and were not of working age. Thus, only direct costs were included in the analysis and the rationale for the exclusion of some cost items was clearly stated. Information on unit costs and quantities of resources used was provided for almost all items, which enhances the possibility of replicating the analysis of costs in other settings. Statistical analyses of costs were not performed, but the impact of changing cost estimates and other variables affecting the cost results was investigated. The price year was reported, which means that reflation exercises in other time periods should be possible.

Other issues
The authors reported the results of other economic evaluations of oral CAP extensively, which supported the cost-effectiveness of CAP and were comparable with the results of the current study. The issue of the generalisability of the study results to other settings was not explicitly addressed, but the use of sensitivity analysis enhances the external validity of the analysis. The results of the study were clearly presented. The authors noted some limitations of their analysis. First, resource use data were analysed retrospectively and were derived from a single institution, which might limit the transferability of the cost results to other settings. Second, CAP toxicity data for palliative treatment were also used for adjuvant treatment, but toxicity profiles might differ. Third, clinical data were extrapolated from clinical trials, which may not reflect a real-world setting.

Implications of the study
The study results support the use of oral CAP not only for the palliative treatment of colorectal cancer, for which it is already indicated, but also for the adjuvant treatment of the disease.

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None stated.
Bibliographic details

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15189755

Other publications of related interest


Indexing Status
Subject indexing assigned by NLM

MeSH
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