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 study assessed the treatment of colorectal cancer using laparoscopic surgery compared with open surgery.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis, cost-utility analysis

Study population
The study population included a cohort of typical patients for the alternative treatments. No further details of the study population were provided.

Setting
The setting was inpatient and outpatient care. The economic study was carried out in the UK.

Dates to which data relate
The majority of the effectiveness and epidemiological data used to populate the model came from studies included in a systematic review (2006). Other clinical data came from studies published between 2002 and 2005. The cost data were collected from studies published between 2005 and 2006. The costs were based on 2004 prices.

Modelling
A Markov model was developed. The cohort of patients was modelled for a maximum of 25 years. The cycle length was 6 months. The health states and transition probabilities were presented in full in the paper, along with a number of modelling assumptions which were fully justified.

Study designs and other criteria for inclusion in the review
The clinical and epidemiological data included the baseline transition probabilities and relative effect sizes for the following parameters: mortality, recurrence, mortality (non-operative cancer), emergency operation rate, risk of hernia and re-operation rate (after recurrence).

Sources searched to identify primary studies
The main source of clinical and epidemiological data was a systematic review (Murray et al. 2006, see 'Other Publications of Related Interest' below for bibliographic details). The risk of death and recurrence were taken from an individual patient data (IPD) meta-analysis (Bonjer et al. 2007, see 'Other Publications of Related Interest' below for bibliographic details). The risk of hernia was derived from two trials identified in the systematic review (Murray et al. 2006) and a focused search of non-randomised studies. The risk of an emergency re-operation was taken to be equal to the risk of anastomotic leakage, based on clinical advice. The baseline risk of anastomotic leakage was taken from the systematic review (Murray et al 2006). There was no published estimate available for the re-operation rate after recurrence, therefore, this value was based on expert opinion. Data on the relative effect sizes were derived from the systematic review and the IPD meta-analysis.

Methods used to derive estimates of effectiveness
The authors reported that the strongest source of data required for each clinical and epidemiological parameter was a
systematic review (Murray et al. 2006). The methods of the review were not fully reported in this paper. Where possible, the clinical data were derived from the papers included in the review, although some additional papers were required and there was no explicit justification for their selection. Some of the model parameters were estimated by two clinical experts and using authors' assumptions, for which justifications were provided.

**Measure of benefits used in the economic analysis**
The summary measure of benefit used in the cost-effectiveness analysis was the number of life-years gained with laparoscopic surgery. The measure of benefit used in the cost-utility analysis was the quality-adjusted life-years (QALYs) gained. The utility data were taken from one study (Norum et al. 1997, see ‘Other Publications of Related Interest’ below for bibliographic details) where the utility values were retrieved through the EQ-5D questionnaire. The benefits were discounted at a rate of 1.5%.

**Direct costs**
The direct costs included in the analysis were those of the health service. Resource data for operation costs were derived from a UK randomised controlled trial with short follow-up of costs combined with estimates of length of stay and postoperative complications from the systematic review. The costs of follow-up visits were added to the operation costs, based on consultation with clinical experts. A re-operation due to recurrence was costed as an open procedure.

The costs of emergency surgery and surgery for hernia were the product of the probability of those complications occurring, combined with standard UK unit costs (NHS reference costs). The cost for a recurrence, where re-operation was not indicated, was the cost of a typical drug regimen, as advised by a clinical expert. Resources and unit costs were not reported separately. The price year was 2004. The costs were discounted at an annual rate of 6%.

**Statistical analysis of costs**
Given the nature of the analysis undertaken, no statistical analysis of the costs was conducted.

**Indirect Costs**
In line with the perspective stated, no productivity losses were considered.

**Currency**
UK pounds sterling (£).

**Sensitivity analysis**
Parameter uncertainty was investigated using probabilistic analysis, one-way and multi-way sensitivity analyses, threshold analysis and sub-group analysis. Prior probability distributions were assigned to some of the transition probabilities and costs. The parameter distributions used in the probabilistic sensitivity analysis were all defined, and a rationale for the distributions used was provided for the clinical parameters. Two multi-way analyses were performed for survival and disease-free survival estimates for open and laparoscopic patients. One of these analyses was based on the meta-analysis of all trials in the systematic review (Murray et al. 2006); the other assumed equal survival between the two procedures. Other analyses considered various quality-of-life estimates, the baseline risk of hernia, mortality rates for patients with non-operative cancer, and rates of re-operation. It would appear that a sub-group analysis on the effect of stage of the disease was conducted. No other information on these other sensitivity analyses was provided.

**Estimated benefits used in the economic analysis**
For the base-case, the life-years gained with laparoscopic surgery were fewer than those gained with the open procedure (15.298 versus 15.351).

For the equal survival analysis, the life-years gained with laparoscopic surgery were the same as those gained with the open procedure (both 15.351).

When applying QALYs to the base-case model, the new procedure delivered fewer QALYs than the open procedure (14.630 versus 14.679).

When using the two pooled estimates derived for overall survival and disease-free survival from the meta-analysis, laparoscopic surgery delivered 15.541 life-years while the open procedure delivered 15.351 life-years.
Cost results
For the base-case, the costs of laparoscopic surgery were higher than those of the open procedure (£10,463 versus £10,174).

For the equal survival analysis, the costs of laparoscopic surgery were also higher than those of the open procedure (£10,490 versus £10,174).

When applying QALYs to the base-case model, the costs of the laparoscopic procedure (£10,463) and the open surgery (£10,174) were the same as the costs for the base-case analysis.

When using the two pooled estimates derived for overall survival and disease-free survival from the meta-analysis, the costs of laparoscopic surgery were £10,511 while those of the open procedure were £10,174.

Synthesis of costs and benefits
The costs and benefits were combined by estimating the cost per life-year gained and the cost per QALY gained from the perspective of the health system. These results were estimated incremental to open surgery.

For the base-case, equal survival and when applying QALYs to the base-case model, laparoscopic surgery was more costly and no more or less effective, and was therefore dominated by open resection.

When using the two pooled estimates derived for overall survival and disease-free survival from the meta-analysis, laparoscopic surgery was more costly (by approximately £350) but more effective, with an incremental cost-effectiveness ratio of £1,778 per life-year gained.

The authors commented that the results were very sensitive to the estimates of survival and disease-free survival.

Probabilistic sensitivity analysis was used to generate cost-effectiveness acceptability curves (CEACs). The authors presented CEACs for the base-case and for the equal survival analysis, comparing laparoscopic with open surgery in terms of life-years. For the base-case analysis, laparoscopic surgery had a 30% chance of being cost-effective if society were willing to pay £30,000 for a life-year. It was shown that open surgery had a higher chance of being considered cost-effective, for both cases, at the various threshold values of society's willingness to pay. However, assuming equal survival and disease-free survival, laparoscopic surgery had a greater chance of being considered cost-effective. When using pooled estimates of survival and disease-free survival from the systematic review, the CEAC showed that laparoscopic surgery had a higher probability of being cost-effective, for all thresholds.

The results of the threshold analysis showed that, for a £30,000/QALY threshold, and given the mean incremental cost of laparoscopic surgery of £289, the QALY gain would have to be at least 0.010 QALYs for laparoscopic surgery to be considered cost-effective.

It would appear that a sub-group analysis was conducted on the stage of the disease. However, the authors stated only that the results were broadly similar to the base-case analysis and provided no other information.

The authors noted that the results from most of the other sensitivity analyses were similar to the base-case results. However, these results were not presented.

Authors' conclusions
The authors concluded that laparoscopic surgery is likely to be associated with short-term quality-of-life benefits, similar long-term outcomes, and an additional cost of £300 per patient. A judgment is required as to whether the short-term benefits are worth this extra cost.

CRD COMMENTARY - Selection of comparators
A justification was given for the comparator used. The authors stated that open surgery represented current practice in the study setting as the treatment of colorectal cancer is almost always performed as open surgery. You should decide if the comparator represents current practice in your own setting.
Validity of estimate of measure of effectiveness
The parameters were mainly derived from published sources, augmented by expert opinion or authors' assumptions when necessary. The main source used was a systematic review. However, the reader was referred to the original study for details of the methods used. No explanation was given for the selection of other published studies. In general, the authors justified the choice of all their parameters estimates. The relative treatment effect parameters were obtained from published meta-analyses, which potentially have the greatest level of internal validity. The relative risks of two complications were based on authors' assumptions.

Validity of estimate of measure of benefit
Two measures of benefit were used, the life-years gained and QALYs gained. These were derived using a Markov model and were appropriately discounted. Both measures seem to have been appropriate, with QALYs enabling comparisons with other technologies and fully capturing relevant health outcomes. The utilities for the cost-utility analysis were taken from a published study of this disease and were based on authors' assumptions. However, as the authors acknowledged, the utility data were sparse and the QALYs did not capture gains associated with an earlier recovery following laparoscopic surgery.

Validity of estimate of costs
The analysis of the costs was performed from the perspective of the national health services paying for the surgical procedures. It appears that all the relevant categories of costs and the associated unit costs have been included in the analysis. The resource use data were taken from published sources and were determined by running the model. The unit costs were taken from national published sources. The costs were discounted, which was appropriate given the time horizon of the study. In addition, the costs were adjusted to the year 2004, although details of the method of adjustment were not reported. The costs were assigned prior distributions to characterise their uncertainty and its effect on the results. The cost data seem to have been adequately reported.

Other issues
The authors did not compare their findings with those from other studies, although they noted that their study was the first economic evaluation to use a Markov model to predict long-term outcomes in this area. The authors acknowledged variation in the patient population through a sub-group analysis on the stage of the disease. The impact of uncertainty in the model inputs on the results was analysed by probabilistic sensitivity analysis and this enhances the generalisability of the findings. The authors do not appear to have presented their results selectively, although they did not always report results from the sensitivity analysis that they performed. The study modelled a cohort of typical patients for the alternative surgical treatments, and this was reflected in the authors' conclusions. The authors acknowledged a number of limitations to their study, which they reported in full.

Implications of the study
The authors indicated that, given the similar long-term outcomes compared with open surgery and potential short-term benefits, there is a case for increasing the current level of laparoscopic surgery provision. However, they also noted the implications this would have for training given the increased number of laparoscopic resections.

The authors called for longer term randomised data. They also noted the need for further work to gather better utility data; gather better cost data from a larger sample; model the effect of conversion; explore whether management would differ between surgeries; conduct sub-group analyses for age, gender, cancer site and stage of disease; and obtain longer term data on survival and disease-free survival.

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Other publications of related interest
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