This article was originally published in Colorectal Disease 2008;10(9): 859-68 DOI: 10.1111/j.1463-1318.2008.01701.x and is available from URL: http://www3.interscience.wiley.com/journal/121494305/issue

Systematic review of economic evaluations of laparoscopic surgery for colorectal cancer

Authors: Rodolfo A. Hernández[1], MSc.; Robyn M. de Verteuil[1], MSc.; Cynthia M. Fraser[2], MA.; Luke D. Vale[1,2], PhD; On behalf of the Aberdeen Health Technology Assessment Group.

1. Health Economics Research Unit. Institute of Applied Health Sciences, College of Life Sciences and Medicine, University of Aberdeen. Aberdeen, Scotland, UK.
2. Health Services Research Unit. Institute of Applied Health Sciences, College of Life Sciences and Medicine, University of Aberdeen. Aberdeen, Scotland, UK.

Acknowledgements: The paper was developed from a Technology Assessment Review conducted on behalf of the National Institute for Health and Clinical Excellence (NICE) and was funded by the Department of Health on a grant administered by the National Coordinating Centre for Health Technology

Assessment. The authors are grateful for the comments from independent reviewers of the Technology Assessment Review on which this paper is based. The Health Economics Research Unit and the Health Services Research Unit are core funded by the Chief Scientist Office of the Scottish Government Health Directorates. The views expressed here are those of the authors and not necessarily those of the funding bodies.

Correspondence to: Rodolfo Hernández, Research Fellow, Health Economics Research Unit, University of Aberdeen, Polwarth Building, Foresterhill, Aberdeen, AB25 2ZD.

e-mail: r.a.hernandez@abdn.ac.uk

Tel.: +44-1224-558992

Fax: +44-1224-550926

Word count abstract: 248

Word count main text: 4287

ABSTRACT

Background

Colorectal cancer is common and the standard surgical treatment is open resection (OS) but laparoscopic surgery (LS) maybe an alternative. In 2000, a Health Technology Assessment (HTA) review found little evidence on costs and cost-effectiveness comparing the two methods. The evidence base has since expanded and this study systematically reviews the economic evaluations on the subject published since 2000.

Methods

Systematic review of studies reporting costs and outcomes of LS vs. OS for colorectal cancer. National Health Service Economic Evaluation Database (NHS EED) methods for abstract writing were followed. Studies were summarised and incremental cost-effectiveness ratios (ICER) for common outcomes calculated.

Results

Five studies met the inclusion criteria. LS generally had higher health care costs. Most studies reported longer operational time and shorter length of stay and similar long-term outcomes with LS vs. OS. Only one outcome, complications, was common across all studies but results lacked consistency (e.g. in two studies open surgery was less costly but more effective, in another laparoscopic surgery was less costly but more effective, and in the further two laparoscopic surgery could potentially be cost effective depending on the decision-makers willingness to pay for the health gain).

Conclusion

The evidence on cost-effectiveness is not consistent. LS was generally more costly than OS. However, the effectiveness data used in individual economic evaluation was imprecise and unreliable compared with data from systematic reviews of effectiveness. Nevertheless, short-term benefits of LS (e.g. shorter recovery) may make LS appear less costly when productivity gains are considered.

KEYWORDS

Economic evaluation, cost effectiveness, systematic review, laparoscopic surgery, colorectal cancer

1 Introduction

Colorectal cancer is one of the most common cancers in the Western world and is the second most common malignancy in England and Wales in terms both of incidence and mortality. Approximately 36,000 new cases were diagnosed in 2002 and 17,000 people died from colorectal cancer in the same year. About 80% of all patients diagnosed with colorectal cancer (including some with advanced disease) undergo surgery.[1]

Open resection is currently the standard method for surgical removal of primary colorectal tumours. Minimally invasive approaches to treat colorectal diseases were developed to take advantage of the benefits observed in laparoscopic procedures elsewhere in the gastrointestinal tract.[2] Laparoscopic surgery, includes total laparoscopic, laparoscopic assisted and hand assisted procedures. In practical terms a totally laparoscopic and laparoscopically-assisted procedure are considered comparable because of the size of incisions involved. In the remainder of this paper laparoscopic and laparoscopically-assisted surgery are referred to as laparoscopic surgery. In hand assisted laparoscopic surgery (HALS), the surgeon inserts a hand into the abdomen while pneumoperitoneum is maintained. Some surgeons find this easier than laparoscopic surgery particularly in the transitional phase between conventional and laparoscopic surgery. Advantages claimed for placing the hand in the abdomen include tactile feedback, the ability to palpate, blunt dissection, organ retraction, control of bleeding, and rapid organ removal.[3-5]

Laparoscopic surgery is less invasive and hence may lead to more rapid recovery from the operation but the potential impact on cure rates is unclear. The major concerns are that tumour recurrence might occur at port sites and that clearance of the tumour may be less complete than during open surgery. It has also been suggested that the reduced trauma to tissues may lower disruption to the immune system and hence reduce the risk of recurrence.[6] Additionally, it has been argued that there are disadvantages of laparoscopic surgery relating to the longer length of the operation, the cost of materials, and the effect of surgeon experience on patient outcomes.

Vardulaki and colleagues[7] conducted a review of studies comparing the costs of the laparoscopic surgery and open surgery in 2000, (there were no economic evaluations available at this time), as part of the health technology assessment review (TAR) carried out by the National Institute for Clinical Excellence. Eight studies met their inclusion criteria and they reported that there was no significant difference in costs between the two procedures in most studies. Differences in cost were driven mainly by the estimates of cost of hospitalisation and time in theatre which varied between studies. Moreover, Vardulaki and colleagues[7] conducted a costing exercise but did not combine data on costs with data on effectiveness in an economic evaluation to assess cost-effectiveness. In addition to this, the evidence base (for effectiveness and cost) was very limited as no studies reported long-term outcomes and economic evidence was of limited quality. Therefore, in terms of efficiency no robust conclusions could be drawn from the HTA 2000 report.[7]

Since 2000 the evidence base has expanded and experience with laparoscopic technique has increased.[1] The present study is a systematic review of the economic evaluations conducted as part of a health technology assessment on laparoscopic surgery for colorectal cancer conducted on behalf of the UK's National Institute for Health and Clinical Excellence (NICE). Amongst other reasons, systematic reviews are important as they can establish whether scientific findings are consistent and can be generalisable to other populations and/or settings. Furthermore, explicit methods used in systematic reviews limit bias and improve reliability and accuracy of conclusions.

The paper reports a systematic review of the economic evaluations of laparoscopic and/or hand assisted laparoscopic techniques compared to open surgery for the treatment of colorectal cancer.

2 Methods

2.1 Search Strategies

Studies that reported both costs and outcomes of laparoscopic and/or HALS techniques compared to open surgery for the treatment of colorectal cancer were sought from a systematic review of the literature. No language restrictions were imposed but as this review is an update of an earlier review conducted in 2000, the searching was limited to studies available between 2000-2005.

Databases searched were Medline (2000 – May Week 2 2005), Embase (2000 - Week 21 2005), Medline Extra (23rd May 2005), Science Citation Index (2000 – 27th May 2005), National Health Service Economic Evaluations Database -NHS EED- (May 2005), Health Technology Assessment (HTA) Database (May 2005), Health Management Information Consortium (2000 – May 2005) and Journals @ Ovid Full Text (2000 – July 2005 for selected surgical journals). In addition, recent conference proceedings and reference lists of all included studies were scanned to identify additional potentially relevant studies. Other sources of information consulted included: references in relevant articles; selected experts in the field; references of consultees' submissions to NICE. Full details of the search strategies used are available from the authors.

2.2 *Inclusion and exclusion criteria*

To be included, studies had to compare, in terms of costs and outcomes, strategies involving laparoscopic and/or HALS compared to open surgery for treatment of colorectal cancer. Studies were included even if they made no formal attempt to relate cost to outcome data in a cost-effectiveness or cost-utility analysis. One reviewer assessed all abstracts for relevance and full papers were obtained for those that appeared potentially relevant.

2.3 *Data extraction strategy*

The following data were extracted for each included primary study using the framework provided for abstracts prepared for the NHS Economic Evaluation Database.[8]

a) Study identification information: author and year, interventions studied, type of economic evaluation, country of origin and currency reported; *b) the intervention, study design and main outcomes:* fuller description of treatment, numbers receiving or randomised to each intervention, outcomes studied; *c) Sources of data:* effectiveness data, mortality and comorbidity (if measured), cost data, quality of life (if measured); *d) methods and study perspective; e) results:* costs, benefits, incremental cost-effectiveness/utility ratio (ICER), sensitivity analyses; *f) additional comments relating to the design and reporting of the economic evaluation.*

No primary outcome was specified although all outcomes were prespecified in a protocol developed before the study started. Ideally all these measures might be synthesised into a single unitary measure such as quality adjusted life years (QALYs). In absence of such outcomes, data were abstracted on the following outcomes: mortality, survival; disease free survival; recurrences and complications (this latter outcome was the only one common across all studies).

2.4 Data synthesis

In economic evaluations, as well as in other research areas, is very important to know which methods the authors used to develop their calculations and analyses, as the results could eventually vary widely according to different methodologies used.[9] For instance, cost categories should be reported and it is desirable that health care resource used as well. Moreover, no matter what methodology is used, any economic evaluation is subject to uncertainty. The uncertainty (e.g. the type and sequence of relevant events considered, variability in data, etc.), can be addressed by conducting different types of sensitivity analyses.[10] Sensitivity analyses will tell the reader how reliable the results are.

One economist assessed included studies using the NHS-EED guidelines for reviewers.[8] This guidelines address all the important issues that should be reported when conducting an economic evaluation in health care. No attempt was made to synthesize quantitatively the primary studies that were identified. Data from all included studies were instead summarised and appraised in order to identify common results, variations and weaknesses between studies. If a study did not report incremental cost effectiveness ratios (ICERs) but provided sufficient data then, where possible, the data were reanalysed to provide estimates of ICERs. These ICERs are presented for the following clinical outcomes: mortality, survival; disease free survival; recurrences and complications.

3 Results

3.1 Number of studies identified

As a result of the literature searches, 392 study hits after deduplication were screened (Figure 1). From these, a total of 41 studies were selected for full assessment. Of these 41 studies, three studies[11-13] met the inclusion criteria. Two additional unpublished papers (that have since been published) also meeting the inclusion criteria were obtained from experts in the field.[14,15] A further study that compared laparoscopic surgery against HALS and, as a consequence did not meet the inclusion criteria, was also identified.[16]

3.2 Study identification and key elements

Two studies compared laparoscopic colon resection with open colon resection in the treatment of colon cancer,[11,13] one of which focused on right hemicolectomy.[13] A further study compared laparoscopic-assisted with conventional open resection for rectosigmoid carcinoma,[12] and two compared laparoscopic versus open resection for colorectal cancer.[14,15] One of these was in the context of an enhanced recovery program.[15]

Five studies were classified as cost-consequence analyses. That is, costs were compared with various different measures of effectiveness. Two were based on single centre RCTs[12,15], and two were based on multicentre RCTs.[11,14] The fifth study was based on a single centre cohort-matched study conducted in China (Table 1).[13] Two studies considered costs from a societal perspective[11,15] while the others adopted a hospital perspective (Table 1).[12,13] Franks and colleagues described their study as a cost analysis but included data on outcomes sufficient to calculate ICERs.[14]

The study by Franks and colleagues represented a preliminary analysis conducted on a subset of patients from the CLASICC trial[17] who had agreed to be included in the economic analysis. The dates for data collection were not reported. The Swedish study collected data from January 1999 to May 2002;[11] the study by King and colleagues from January 2002 to March 2004,[15] the study by Leung and colleagues, conducted in Hong Kong, collected data from September 1993 to October 2002,[12] and the Chinese study from September 2002 to February 2003.[13] In all five studies costs were estimated prospectively from the same sample as that used for collecting the effectiveness data.[11-15]

3.3 Patient group, study sample and study design

The sample sizes in four of the five studies were modest (Table 1). In the cohort matched study, 30 patients with colon cancer underwent laparoscopic right hemicolectomy surgery and were matched with 34 patients who received open right hemicolectomy surgery.[13] Patients for the open surgery group in this study were matched for gender, age, Dukes' staging, tumour site, previous abdominal operation and extent of resection. 34 patients were randomly selected from 87 patients who underwent open surgery during the same period.

The analysis in all studies was conducted on an intention to treat basis, however, the follow-up period as well as the outcome measures varied considerably between studies (Table 1).

3.4 Methods of economic analysis

The four trial based papers[11,12,14,15] presented details on which items were included in the cost calculations, but no details were reported in the non-randomised study.[13] Such information is useful as data on resource use can help readers judge the applicability of the study to their setting. Relatively good details of unit costs were presented in the Swedish and UK studies[11,14,15] while no unit costs were reported in the other two studies.[12,13] In economics, costs occurring into the future are given less weight than costs occurring now, i.e. they are discounted. Discounting was performed only in the Swedish study while it was actually relevant in all studies with a follow-up greater than 12 months. Indirect costs were calculated in three of the studies using the human capital approach (time off paid work)[11,14,15] Three papers did not use any summary measure of health benefits[12,13,15] and left the results disaggregated. One study focused primarily on costs.[14] In the Janson and colleagues study, the mean cost per re-operated patient for each arm of the trial was presented (although it is not reported in this paper).[11]

As previously stated, uncertainty is pervasive in every economic evaluation. Therefore, authors should allow for this by conducting different types of sensitivity analyses. One-way sensitivity analysis was performed in three studies.[11,14,15] Changes in perioperative, equipment, recovery, ICU and hospital costs were considered in the study by Franks and colleagues. They also considered a subgroup analysis by location of cancer (colon or rectum).[14] Cost per minute for the operating room, anaesthesia and recovery room time were explored in the Swedish study[11] while duration of in-patient stay and the consumption of community resources after discharge were explored in the Study by King and colleagues.[15]

3.5 Cost effectiveness results from the included studies

The results of the included studies are summarised in Table 2. In Franks and colleagues, total costs, including productivity costs, for both the base-case and both subgroups were not significantly different between the laparoscopic and open groups, although the confidence interval was very wide (mean additional cost of laparoscopic surgery was £268, 95% CI: –690 to 1460). Productivity costs were not a major determinant of this additional cost although hospitalisation costs (less for laparoscopic surgery) and costs for re-operations and other complications (greater for laparoscopic surgery) were. Although there was no evidence of a statistically significant difference in clinical outcomes, confidence intervals would be sufficiently wide for clinically and economically important differences to exist.[14]

In Janson and colleagues total costs, including productivity loss, were not significantly different between the laparoscopic surgery and open surgery. However, total costs, excluding productivity losses (that is cost to the healthcare system), were significantly higher for the laparoscopic surgery compared with open surgery (€9474 vs. €7235; $P=0.018$), as were the costs related to the first admission, and the costs of primary surgery.[11]

In King and colleagues the results reflected the increased duration of laparoscopic procedures and also the increased use of disposable equipment in theatre. However, in their analysis, King and colleagues found that these costs were more than offset by lower post-operative costs such as re-operations, and productivity cost savings resulting from the earlier return to usual activities.[15]

Similarly, the health service costs from Leung and colleagues were also higher for laparoscopic surgery than for open surgery and this difference, as with the other two RCT-based analyses, was statistically significant ($P<0.001$).[12]

However, no significant difference was observed in the total cost of operation and drugs between the two groups in the Chinese study (Table 2 - CNY1000 circa £65.8 - www.bloomberg.com 5/02/2007).[13]

Overall, the magnitude of the mean additional cost of laparoscopic compared with open surgery varied considerably between studies. For example the relative cost of laparoscopic surgery compared with open surgery varied between 95%(13) and 130%.[12]

Table 3 reports the estimated ICERs for the different clinical outcomes. Only one measure of effectiveness was common across all studies: major complications. In terms of mortality (2 studies[11,12]) 5 year survival (1 study[12]); 5 year disease free survival (1 study[12]) and recurrence (1 study[12]) it is unlikely that in terms of mean differences costs and outcomes that laparoscopic surgery would be considered cost-effective. However, confidence intervals would probably be wide enough to include clinically and economically important differences favouring either type of surgery. Table 3 also reports the number of complications (see Table 1 for types of complications) in each study. Only two studies reported P-values for the difference between the number of complications in the laparoscopic and open groups[13,15] and in this study the difference was not statistically significant. These results are in line with those of a recent systematic review of effectiveness conducted by Murray and colleagues.[1] Murray and colleagues considered data from 18 randomised controlled trials (RCTs) of general good quality. The authors considered amongst other outcomes, the occurrence of complications such as anastomotic leakage, abdominal wound breakdown, incisional hernia, and wound and urinary tract infections. They found no statistically significant differences between open and laparoscopic surgery within these outcome categories, although confidence intervals were wide enough for clinically important differences to exist.

Incremental costs per major complication avoided were calculated using the data from the original studies (Table 3). Based on mean data for costs and complications open surgery is dominant (i.e. less costly and more effective) in two studies[11] while in another, laparoscopic surgery was dominant.[15] A forth study laparoscopic surgery could avoid a major complication at a cost of CNY10,008,[13] (circa £659). Complications from surgery could be avoided at a cost of USD 76,872[12] (approximately £39,220) according to Leung and colleagues. Finally, using data from Franks and colleagues [13] on number of total complications, using laparoscopic surgery could avoid a complication at an extra cost of between £229,000 and £268,000.[14]

One study conducted a subgroup analysis by location of disease (colon or rectum).[14] Overall, surgery for colon cancer was on average approximately £3000 less costly than rectal cancer regardless of the method of surgery. For both subgroups the mean total costs including indirect costs were greater for laparoscopic surgery although they were not statistically significant. When indirect costs were excluded laparoscopic surgery was less costly for colon cancer but more costly for rectal cancer. For colon cancer the main drivers of this cost difference was that the higher theatre cost was more than compensated by the reduced hospitalisation and complications cost. For rectum cancer patients the higher operation cost for laparoscopic surgery was almost matched by the lower hospitalisation costs, but there was a statistically significant higher cost of complications following laparoscopic surgery (Table 4). The sample sizes for these subgroup analyses were modest (between 230 and 222 for laparoscopic surgery and 118 to 112 for open surgery for colon and rectum cancer respectively) and it is unclear whether the differences in total costs were mostly associated with different risks of complications between the surgeries or different types of complication occurring.

4 Discussion

In the previous review conducted for NICE on this subject, there was no economic evaluations identified and therefore, no evidence reported on cost-effectiveness. Full economic evaluations need to bring together costs and effects on order to provide information on efficiency; it is the interplay of costs and effects that is important. The HTA 2000[7] reported some evidence in costs (e.g. eight costing studies were identified), and provided an economic costing exercise but this in itself does not provide evidence on cost effectiveness. That review found no statistically significant differences in costs between open surgery and laparoscopic surgery in the reviewed studies. However, it was clear from their effectiveness review[7] that length of stay was consistently shorter (although not always statistically significantly shorter) for laparoscopic surgery.

Our study reports evidence on cost-effectiveness and not only on costs and effects separately. The four RCT-based analyses identified by this updated review appear to have statistically significant longer operating times for laparoscopic surgery. This is consistent with the data in the recent review of effectiveness reported by Murray and colleagues,[1] even though, the study by Zheng and colleagues[13] reported no statistically significant difference. With respect to length of hospital stay this appeared to be longer in the open groups: again, a result consistent with the review of effectiveness reported in Murray and colleagues.[1] Overall in terms of these findings the results of the review presented in this paper are consistent with the earlier more limited findings of Vardulaki and colleagues.[7] Namely, Verdulaki and colleagues[7] reported a operating time mean difference of 62 minutes (e.g. open shorter) and length of hospital stay of -2.14 days (e.g. open longer) between laparoscopic and open surgery, while Murray and colleagues[1] a weighted mean difference of 40 minutes and -2.63 days, respectively. Therefore, the trend in resource use in favour of laparoscopic surgery (shorter operating time difference and longer length of stay difference compare with open surgery) seems to exist but not with the strength predicted by Verdulaki and colleagues[7] who concluded that the difference in cost is "expected to disappear in the next 5 years".

The mean total health care cost of laparoscopic appeared to be greater than open surgery in all studies except in King and colleagues.[15] However, there was no evidence of a statistically significant difference in total health care cost between laparoscopic surgery and open surgery, although confidence intervals were wide.

One concern with laparoscopic surgery is the conversion rate to open surgery. Conversions are likely to increase the total cost of laparoscopic surgery as a conversion increases operation time. Although as reported by Murray and colleagues,[1] the evidence for comparing converted, non-converted laparoscopic and open patients is limited. It is likely that as experience increases the rates of conversion would fall.

The incremental cost per complication avoided, shown in the previous section, should be interpreted extremely cautiously. All the studies had relatively small sample sizes and differences in the number of complications (used as the effectiveness measure in these calculations) between laparoscopic surgery and open surgery were not statistically significant. Furthermore, different types of complications might have different effects in morbidity and, therefore, quality of life. Using another measure of effectiveness within the economic evaluation (e.g. QALYs) might overcome this problem. With respect to the estimates of complications the estimates of the individual studies are likely to be less reliable than estimates derived from the review of effectiveness provided by Murray and colleagues.[1] Data from their review of effectiveness provides no evidence of a difference in complication rates, although confidence intervals were sufficiently wide enough for clinically important differences to exist.

The measure of total cost used differed substantially between studies. For example, Franks and colleagues,[14] Janson and colleagues[11] and King and colleagues[15] considered indirect costs while the other two studies considered only direct costs from surgery and hospital stay.[12,13] The costing methodology was also poorly described in these latter two studies. For example Zheng and colleagues reported only final cost figures and provided no details on the way calculations were performed.[13]

It is unclear the extent to which the costs from the three non-UK studies would be applicable to the UK. One UK study had a very small sample size, and it was based on a single centre.[15] The second UK study had a much larger sample size and more precise estimates of cost. However, both the rate of conversions from laparoscopic to open (30%) and the higher rates of complications following laparoscopic surgery would tend to increase the difference between laparoscopic and open surgery.

The relatively short follow-up in all studies indicates that a modelling exercise, using the best available effectiveness data with a longer time horizon (e.g. the time over which cost and effects may differ between the treatments), might add valuable information for decision-making. Such an exercise should follow the usual guidelines of good practice for conducting an economic evaluation.[9,15,18-20] Namely, incorporate the best available effectiveness evidence, include all relevant cost categories according to the perspective adopted, use a relevant measure of effectiveness (e.g. life years gained, quality adjusted life years), and incorporate discounting as the relevant time horizon for the analysis is likely to be longer than a year. This suggests that the best economic evidence should come from a well designed economic model which uses the best available data which has been systematically assembled.

Recently, two model based economic evaluations have been published[22,23] that seem to move forward the cost effectiveness. Hayes and colleagues[23] developed a simple model and found laparoscopic surgery to be potentially cost-effective (e.g. mean incremental cost per QALY $70,389 – circa £28,296). However, their results were sensitive to assumptions on the time needed to resume normal activities (e.g. between 12 and 33 days), and the cost of disposable equipment used within laparoscopic surgery. Moreover, the authors conducted only one way sensitivity analyses. The study by de Verteuil and colleagues[23] reports a more sophisticated analysis based on a Markov model populated with data retrieved from systematic reviews of the literature. The study managed to predict long term outcomes and concluded that laparoscopic surgery. The authors conducted several sensitivity analyses, including probabilistic sensitivity analysis. They concluded that laparoscopic surgery was more costly and has a likelihood of being considered cost effective of between 30 and 80 percent, depending on assumptions made about survival (e.g. relative risk of 1.03 or 1 –equal–), and disease free survival (e.g. relative risk of 1.03 or 1 –equal–).

In addition to the studies comparing laparoscopic surgery with open surgery a further study was identified comparing conventional laparoscopic surgery with HALS.[16] The authors concluded, "Although it is a more aggressive procedure, HALS preserves the feature of minimally invasive approach, maintains all the oncological features of conventional laparoscopic surgery, and does not increase the cost."

Other relevant issues that influence the decision about whether or not to adopt LS are speed of patient recovery and surgeon training. Murray and colleagues[1] reported that laparoscopic surgery seems to offer patients some short term quality of life advantages without compromising safety or long term outcomes (at least up to three years). However, relatively few surgeons are trained in this form of surgery and this therefore limits access to laparoscopic surgery. Furthermore, a low conversion rate seems to be key for laparoscopic surgery to be beneficial and this depends on experience.[1] Should a decision be taken to increase the use of laparoscopic surgery then training programmes need to be put in place,[1] and the cost implications of this need to be considered before making the final decision on which technology to adopt.

5 Conclusions

This study presents the overall evidence available on cost-effectiveness analyses of laparoscopic surgery for colorectal cancer compared to open surgery, based on a systematic review of the literature. Laparoscopic surgery generally had higher health care costs than open surgery as the former seems to involve longer operation times and higher equipment costs, although including productivity gains from earlier recovery make laparoscopic surgery appear less costly. However, the measurement and inclusion of such costs (indirect costs) in an economic evaluation is contentious.[18,19]

With respect to effectiveness, the data used by the individual studies is likely to be imprecise and unreliable when compared to the data available from a recent systematic review of effectiveness.[1] Thus, the evidence provided by the included economic evaluations using longer-term outcomes such as survival is likely to be imprecise and unreliable. Two more recently and better designed economic evaluations add to the cost-effectiveness evidence. However, their results seem to ratify the need for more data on long-term performance.

References

1 Murray A, Lourenco T, de Verteuil R *et al.* Clinical effectiveness and cost-effectiveness of laparoscopic surgery for colorectal cancer: systematic reviews and economic evaluation. *Health Technol Assess* 2006; **10:** 45.

2 Sgambati SA, Ballantyne GH. Minimally invasive surgery for diseases of the colon & rectum: the legacy of an ancient tradition. In: Jager RM, Wexner S, eds. *Laparoscopic colorectal surgery*. New York: Churchill Livingstone, 1996: 13-23.

3 Darzi A. Hand-assisted laparoscopic colorectal surgery. *Semin Laparosc Surg* 2001; **8**: 153-60.

4 Litwin DEM, Darzi A, Jakimowicz J *et al.* Hand-assisted laparoscopic surgery (HALS) with the handport system: Initial experience with 68 patients. *Ann Surg* 2000; **231** : 715-23.

5 Romanelli JR, Kelly JJ, Litwin DE. Hand-assisted laparoscopic surgery in the United States: an overview. *Semin Laparosc Surg* 2001; **8**: 96-103.

6 Lacy AM, Garcia-Valdecasas JC, Delgado S *et al.* Laparoscopy-assisted colectomy versus open colectomy for treatment of non-metastatic colon cancer: a randomised trial. *Lancet* 2002; **359**: 2224-9.

7 Vardulaki KA, Bennett-Lloyd BD, Parfitt J *et al.* *A systematic review of the effectiveness and cost-effectiveness of laparoscopic surgery for colorectal cancer [document on the Internet].* London: National Institute for Clincial Excellence: 2000 [accessed June 2005] .

8 I*mproving access to cost-effectiveness information for health care decision making: the NHS Economic Evaluation Database*. CRD Report No 6. 2nd edn. York: NHS Centre for Reviews & Dissemination, 2001.

9 National Institute for Clinical Excellence. *Guidance on the methods of technology appraisal (reference N0515)* [document on the Internet]. London: National Institute for Clinical Excellence; 2004 [accessed September 2006] .

10 Briggs A. Handling uncertainty in economic evaluation and presenting the results. In: Drummond M, McGuire A, eds. *Economic evaluation in health care: merging theory with practice*. Oxford: Oxford University Press, 2001: 172-214.

11 Janson M, Bjorholt I, Carlsson P *et al.* Randomized clinical trial of the costs of open and laparoscopic surgery for colonic cancer. *Br J Surg* 2004; **91:** 409-17.

12 Leung KL, Kwok SP, Lam SC *et al.* Laparoscopic resection of rectosigmoid carcinoma: prospective randomised trial. *Lancet* 2004; **363**: 1187-92.

13 Zheng MH, Feng B, Lu AG *et al.* Laparoscopic versus open right hemicolectomy with curative intent for colon carcinoma. *World J Gastroenterol* 2005; **11**: 23-6.

14 Franks PJ, Bosanquet N, Thorpe H *et al.* Short-term costs of conventional vs laparoscopic assisted surgery in patients with colorectal cancer (MRC CLASICC trial). *Br J Cancer* 2006; **95**: 6-12.

15 King PM, Blazeby JM, Ewings P *et al.* Randomized clinical trial comparing laparoscopic and open surgery for colorectal cancer within an enhanced recovery programme. *Br J Surg* 2006; **93**: 300-8.

16 Targarona EM, Gracia E, Garriga J *et al.* Prospective randomized trial comparing conventional laparoscopic colectomy with hand-assisted laparoscopic colectomy:

applicability, immediate clinical outcome, inflammatory response, and cost. *Surg Endosc* 2002; **16:** 234-9.

17 Guillou P.J, Quirke P, Thorpe H *et al.* Short-term endpoints of conventional versus laparoscopic-assisted surgery in patients with colorectal cancer (MRC CLASICC trial): multicentre, randomised controlled trial. *Lancet* 2005; **365:** 1718-26.

18 Drummond M, Sculpher M. Common methodological flaws in economic evaluation. *Med Care* 2005; **43(7 Suppl):** 5-14.

19 Gold MR, Siegel JE, Russell LB, Weinstein MC. *Cost-effectiveness in health and medicine.* Oxford: Oxford University Press, 1996.

20 Philips Z, Ginnelly L, Sculpher M *et al.* Review of guidelines for good practice in decision-analytic modelling in health technology assessment. *Health Technol Assess* 2004; **8:** 1-158.

21 Weinstein MC, O'Brien B, Hornberger J *et al.* Principles of good practice for decision analytic modeling in health-care evaluation: report of the ISPOR Task Force on Good Research Practices--Modeling Studies. *Value Health* 2003; **6:** 9-17.

22 de Verteuil R, Hernandez R, Vale L. Economic evaluation of laparoscopic surgery for colorectal cancer. *Int J Tech Assess Health Care* 2007; **23:** 464-72.

23 Hayes JL, Hansen P. Is laparoscopic colectomy for cancer cost-effective relative to open colectomy? *Aust N Z J Surg* 2007; **77:** 782-6.

Table 1 Characteristics of the included studies

Study id	Design	Sample	Follow-up	Perspective	Endpoints
Franks 2005[14](UK)	Multicentre RCT (CLASICC)	Laparoscopic: 452 Open: 230	3 months	Stated as Hospital (NHS) but Societal	None specified although rates and types of complications and re-operations were assumed to be the same and were used to generate costs
Janson 2004[11](Sweden)	Multicentre RCT (COLOR Trial)	Laparoscopic: 98 Open: 112	36 months	Societal. (Unit costs retrieved from a single centre)	Complication rate (e.g. anastomotic leak, bowel perforation, wound rupture, ileus, post-operative bleeding, incarcerated abdominal hernia, endoscopic dilation, closure loop ileostomy); Re-operations; Mortality; 3-year survival
King 2005[15] (UK)	Single centre RCT	Laparoscopic: 43 Open: 19	3 months	Societal	Requirement of opioid analgesia; Anti-emetic administration; Major morbidity (e.g. haemorrhage, anastomatic leak, wound dehiscence and sepsis requiring at least high dependency support)-; Hospital stay; Length of stay for readmissions; Mortality
Leung 2004[12] (Hong Kong)	Single centre RCT	Laparoscopic: 203 Open: 200	52.7 months (mean) 49.2 months (mean)	Hospital	Duration of operation; Blood loss; Anastomotic leakage; Lymph node retrieval; Completeness of resection/ margins of tumour clearance; Conversion; Wound infection; Urinary tract infection; 30 day mortality; Post-operative pain; Survival; Disease-free survival; Recurrence
Zheng 2005[13](China)	Single centre cohort matched	Laparoscopic: 30 Open: 34	27 months (mean) 26 months (mean)	Hospital	Operation time; Blood loss; Specimen length; Lymph node yield; Pathological staging (Dukes' staging); Analgesic requirements; Time to flatus passage; Time to resume normal diet; Duration of hospitalisation; Morbidity; Local recurrence rate; Metachronous metastasis rate; Mortality; Cumulative survival probability

Table 2 Cost data reported in the included studies

Study id		Laparoscopic	Open	Difference (%)	P value / 95% CI
Franks 2005[14] (UK)	Total cost	£6900	£6632	£268 (4.0)	95% CI: -689 to 1458
Perspective: Societal (£, price year not stated)	Total costs, excl. productivity losses	£5867	£5648	£229 (4.0)	Not available
	Total costs, excl. prod losses & complications	£5105	£5085	£20 (0.0)	Not available
Franks 2005[14] (UK) (colon))	Total cost	£5587	£5503	£84 (1.5)	95% CI: -642 to 792
(£, price year not stated)	Total costs, excl. productivity losses	£4640	£4728	-£88 (-1.9)	Not available
Franks 2005[14] (UK) (rectum)	Total cost	£8260	£7820	£439 (5.6)	95% CI: -1294 to 2857
(£, price year not stated)	Total costs, excl. productivity losses	£7148	£6595	£553 (8.4)	Not available
Janson 2004[11](Sweden)	Total cost*	€11,660	€9814	€1,846 (18.8)	P=0.104
Perspective: Societal (€, 2001 prices)	Total costs, excl. productivity losses*	€9474	€7235	€2,239 (30.9)	P=0.018
	First admission*	€6931	€5375	€1,556 (28.9)	P=0.015
	Primary surgery*	€3493	€2322	€1,171 (50.4)	P=0.001
King 2005[15] (UK)	Total Cost	£6433	£6790	-£357 (-5.3)	95%CI: -2167 to 2992
Perspective: Societal (£, 2002)	Total Costs – indirect costs	£5,985	£6,068	-83 (-1.4)	NA
	Theatre Costs	£2885	£1964	£921 (46.9)	95%CI: 586 to 1251
Leung 2004[12](Hong Kong) Perspective: Hospital (USS dollar, price year not stated)	Direct costs**	USD9297	USD7148	USD2,149 (30.1)	P<0.001
Zheng 2005[13](China) Perspective: Hospital (Chinese renminbi, yuan, price year not stated)	Total cost operation and drugs***	CNY11,499 (sd: 2619)	CNY10,228 (sd: 2373)	CNY1,271 (12.4)	P=0.131

* €1 circa £0.66 (16)
** USD1 circa £0.51 (16)
*** CNY=Chinese Yuan (Renminbi); CNY1 circa £0.0658 (16)

Table 3 Incremental cost per unit of effectiveness avoided

Outcome	Study	Incremental Cost	Effectiveness Laparoscopic (%)	Effectiveness Open (%)	P value	Incremental Effectiveness (%)	ICER
Mortality	Janson 2004[11](Sweden)						
	Societal Perspective	1,846 €	1 (1.0)	0 (0)	NA	1.0%	Open Dominates
	Health Service Perspective	2,239 €	1 (1.0)	0 (0)	NA	1.0%	Open Dominates
	Leung 2004[12] (Hong Kong)	USD 2,149	38 (22.8)	40 (23.5)	0.97	0.7%	USD 307,000
5-years Survival	Leung 2004[12] (Hong Kong)	USD 2,149	76.1%	72.9%	0.61	3.2%	USD 67,156
5-years Disease Free Survival	Leung 2004 [12] (Hong Kong)	USD 2,149	75.3%	78.3%	0.45	3.0%	Open Dominates
Recurrence	Leung 2004 [12](Hong Kong)	USD 2,149	37 (22.2)	30 (17.6)	0.37	4.6%	USD 46,717
Total Complications	Franks 2005[14] (UK)						
	Societal Perspective	£268	154 (35.7)	77 (35.8)	NA	0.1%	USD 268,000
	Health Service Perspective	£229	154 (35.7)	77 (35.8)	NA	0.1%	USD 229,000
Major Complications	Janson 2004[11] (Sweden)						
	Societal Perspective	1,846 €	33 (33)	26 (23.2)	NA	9.8%	Open Dominates
	Health Service Perspective	2,239 €	33 (33)	26 (23.2)	NA	9.8%	Open Dominates

Table 3 Incremental cost per unit of effectiveness avoided (cont.)

Outcome	Study	Incremental Cost	Effectiveness Laparoscopic (%)	Effectiveness Open (%)	P value	Incremental Effectiveness (%)	ICER
Major Complications	Franks 2006[14] (UK)						
	Societal Perspective	£268	62 (14.4)	23 (10.7)	NA	3.7%	Open Dominates
	Health Service Perspective	£229	62 (14.4)	23 (10.7)	NA	3.7%	Open Dominates
	King 2006[15] (UK)						
	Societal Perspective	-£357	6 (15)	5 (26)	0.208	11.0%	Laparoscopic dominates
	NHS Perspective	-£83	6 (15)	5 (26)	0.208	11.0%	Laparoscopic dominates
	Zheng 2005[13] (China)	CNY 1,271	5 (16.7)	10 (29.4)	0.23	12.7%	CNY 10,008
Complications of surgery	Leung 2004[12] (Hong Kong)	USD 2,149	40 (19.7)	45 (22.5)	NA	2.8%	USD 76,872

£=Pound Sterling; €=Euros; USD=US dollars; CNY=Chinese Yuan

Figure 1: Study selection flow diagram