Cost-effectiveness of preoperative radiotherapy in rectal cancer: results from the Swedish Rectal Cancer Trial

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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.

Health technology
A short-term regimen of high-dose, fractionated, preoperative radiotherapy (RT) (5 x 5 Gy), given over 5 to 7 days to patients with resectable rectal cancer, was examined.

Type of intervention
Secondary care.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients less than 80 years old with resectable cancer for whom abdominal surgery was planned. Patients were eligible if they had a histopathologically proven adenocarcinoma situated below the promontory, as shown on a lateral projection on barium enema. The exclusion criteria were locally nonresectable tumour, a plan to perform only local excision, known metastatic disease, prior RT to the pelvis, and other malignant disease.

Setting
The setting was a hospital. The economic study was carried out in the Uppsala-Orebro health care region in Sweden.

Dates to which data relate
The effectiveness and resource use data were gathered from March 1987 to February 1990. The price year was 1998.

Source of effectiveness data
The effectiveness data were derived from the Swedish Rectal Cancer Trial (SRCT), the results of which were published in 1997 (see Other Publications of Related Interest).

Link between effectiveness and cost data
The costing was performed retrospectively on a sub-sample of patients used in the effectiveness study.

Study sample
Preliminary power calculations were performed. A minimum sample of 1,100 patients was required to detect a statistically significant difference in different clinical outcome measures. An overall sample of 1,168 eligible patients was enrolled in the trial from 70 hospitals in Sweden.
Study design
This was a multicentre, randomised controlled trial. Randomisation was stratified according to hospital, but the actual method used to allocate the patients to the study groups was not reported. The trial was carried out in 70 Swedish hospitals. The patients were followed for an average of 75 months (range: 60 - 96). Fifty-eight patients (30 in the RT+ group and 28 in the RT- group) did not undergo the final evaluation. The main reasons were non-eligibility after allocation to the study groups, or no resection performed (for technical reasons or for patient refusal). No blinded assessment was performed.

Analysis of effectiveness
The analysis of the clinical study was conducted on an intention to treat basis. The primary health outcomes used in the analysis were the overall recurrence rate and 5-year survival rate (calculated using actuarial methods). The study groups were well balanced and were comparable at baseline in terms of their demographic and clinical characteristics. Regression analyses were conducted to evaluate potential biases and confounding factors.

Effectiveness results
The overall recurrence rate was 28% in the RT+ group and 38% in the RT- group, (p<0.001).

The 5-year survival rate was 58% (95% confidence interval, CI: 54- 62) in the RT+ group and 48% (95% CI: 44 - 52) in the RT- group.

Thus, RT+ was associated with an increase of 21% (95% CI: 8 - 34) in overall survival.

Clinical conclusions
The effectiveness analysis showed that RT+ was significantly more effective than RT- in terms of recurrence rates and overall survival.

Measure of benefits used in the economic analysis
Survival was used as the benefit measure in the economic analysis. It was derived from the effectiveness study.

Direct costs
A 3% discount rate was applied since the costs were incurred over more than two years. The unit costs were reported separately from the quantities of resources used. The health services included in the economic evaluation were preoperative RT, primary surgery, outpatient follow-up (routine follow-up or due to complication and cancer recurrence), and readmissions, surgical time excluding primary surgery and intensive care (all in relation to complications or to cancer recurrence). Preoperative RT covered beams, hotel nights, in-hospital admission, and distance to RT department, while primary surgery covered in-hospital admission, surgical time and intensive care). The travel costs were calculated for all patients who did not have an RT department in their own community. The costs of treating diseases unrelated to the treatment of rectal cancer or its complications were not included. The cost/resource boundary adopted in the study was not explicitly stated. Resource use was estimated from data collected alongside the effectiveness trial from March 1987 to February 1990, and was retrospectively analysed. A sample of 98 patients (50 in the RT- group and 48 in the RT+ group) was involved in the costing. The costs were estimated from average prices in the University Hospital in Uppsala. The price year was 1998.

Statistical analysis of costs
The costs were treated deterministically in the base-case.

Indirect Costs
The indirect costs were not included in the analysis.
Currency
US dollars ($). Swedish crowns (SEK) were converted into US$. The conversion rate in 1991 was SEK 10 = US$1.

Sensitivity analysis
Sensitivity analyses were conducted to evaluate the robustness of the estimated cost-effectiveness ratio to variations in the survival rate, local recurrence rate, incidences in early and late effects, and costs of complications. Local recurrence rates were derived from a series of patients evaluated in the study by Kapiteijn et al. (see Other Publications of Related Interest) in The Netherlands.

Estimated benefits used in the economic analysis
The estimated survival was 81 months in the RT+ group and 60 months in the RT- group.

Cost results
The estimated total costs per patient were $30,080 in the RT- group and $35,268 in the RT+ group. The difference of $5,188 favoured the RT+ group.

Synthesis of costs and benefits
An incremental cost-effectiveness ratio was calculated to combine the costs and benefits of the two interventions. The extra cost per life-year gained with RT+ in comparison with RT- was $3,654 when both the costs and benefits were discounted. The sensitivity analyses showed that, in the worst case, with a survival benefit of 10 months, the incremental cost per life-year was $15,228.

Authors’ conclusions
A short course of high-dose preoperative radiotherapy (RT) proved to be a cost-effectiveness treatment, compared with surgery alone, in patients with resectable rectal cancer.

CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparator was clear. Surgery alone was selected as the objective of the study was to evaluate the active value of RT in the treatment of patients with rectal cancer. Surgery alone was the comparator in the randomised trial, which was used as the primary source of effectiveness evidence. You should decide whether it represents a valid comparator in your own setting.

Validity of estimate of measure of effectiveness
The analysis of the effectiveness used a randomised controlled trial, which was appropriate for the study question. The actual method of randomisation was not reported. The internal validity of the analysis was enhanced by the performance of power calculations, the intention to treat basis of the clinical study, and the baseline comparability of the study groups. The length of follow-up was reported. The study was multicentred. The study sample appears to have been representative of the study population. The outcome assessment was not blinded. Statistical analyses were conducted to evaluate the impact of possible confounding factors.

Validity of estimate of measure of benefit
The benefit measure used in the economic analysis was survival, which was derived from the effectiveness study.

Validity of estimate of costs
The study was reported to have been conducted from a societal perspective, but the indirect costs were explicitly
excluded from the economic analysis. Thus, it was unclear whether all the relevant categories of costs were included in
the analysis. The source of cost data was reported, as well as the source of resource consumption data, which was
derived directly from the effectiveness study. The unit costs were reported separately from the quantities of resources
used and the price year was provided. These factors enhance the reproducibility of the study results in other settings.
The costs were treated deterministically in the base-case, but limited sensitivity analyses were conducted. The authors
acknowledged that the costing was performed only on a sub-sample of patients involved in the effectiveness study, and
that this approach was not optimal. The authors also noted that the costs used in the study may not reflect the true costs
of the services, but the expenses used in the analysis were those actually paid for the interventions and available in
Sweden. In addition, there were no protocol-driven costs.

Other issues
The authors compared their findings with those from published studies and reported the cost-effectiveness ratio of
other medical interventions. The issue of the generalisability of the study results to other settings was not addressed and
only limited sensitivity analyses were conducted. Thus, the external validity of the analysis was low. The study enrolled
patients with resectable rectal cancer and this was reflected in the conclusions of the analysis.

Implications of the study
The study suggests that the preoperative RT in resectable rectal cancer leads to a significantly greater survival, at an
acceptable cost, in comparison with surgery alone.

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Bibliographic details
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54(3): 654-660

Other publications of related interest
Swedish Rectal Cancer Trial. Improved survival with preoperative radiotherapy in resectable rectal cancer. New

Kapiteijn E, Marijnen CA, Nagtegaal ID, et al. Preoperative radiotherapy in combination with total mesorectal excision
improves local control in resectable rectal cancer: Report from a multicenter randomized trial. New England Journal of

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