Cost-effectiveness analysis of the treatment for intermediate risk endometrial cancer:
postoperative brachytherapy vs. observation


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 use of postoperative vaginal cuff brachytherapy versus observation followed by treatment for vaginal recurrence, as part of the treatment for intermediate risk endometrial cancer, was evaluated.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised women with intermediate risk endometrial cancer, that is, Stage 1C,1G3,2 (tumours limited to the uterus with greater than 50% myometrial invasion or with poor differentiation or with cervical metastasis).

Setting
The setting was secondary care. The economic study was conducted in the USA.

Dates to which data relate
The effectiveness evidence was derived from studies published between 1991 and 2001. The costs were based on 2001-2002 data. The price year was 2001.

Source of effectiveness data
The effectiveness data were derived from a review or synthesis of completed studies.

Modelling
An ad hoc model was used to compare, in terms of the costs and benefits, the two treatment algorithms. Cases with endometrial cancer either received postoperative brachytherapy (strategy 1), or did not receive brachytherapy and were treated only in the case of vaginal recurrence (strategy 2). The time horizon for the estimation of benefits was 5 years.

Outcomes assessed in the review
The outcomes assessed were:

the proportion of endometrial cancers that were intermediate risk;
the vaginal cuff recurrence rate for patients treated with postoperative vaginal cuff brachytherapy (strategy 1);
the vaginal cuff recurrence rate for intermediate risk endometrial cancer treated with observation alone (strategy 2);
the survival rate for patients with intermediate risk endometrial cancer originally treated with observation alone and
who developed vaginal cuff recurrence; and
the complication rates for teletherapy and brachytherapy.

Study designs and other criteria for inclusion in the review
The study designs for inclusion in the review were not explicitly stated. The effectiveness data were derived mainly
from prospective clinical trials, but retrospective data were also used. No further criteria for inclusion in the review
were reported.

Sources searched to identify primary studies
Not stated.

Criteria used to ensure the validity of primary studies
Not stated.

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

Number of primary studies included
Seven primary studies were included in the review.

Methods of combining primary studies
The results of the primary studies were not combined.

Investigation of differences between primary studies
No reference was made to differences between the primary studies.

Results of the review
The proportion of endometrial cancers that were of intermediate risk was 33%.

The vaginal cuff recurrence rate for patients treated with postoperative vaginal cuff brachytherapy (strategy 1) was 0%.

The vaginal cuff recurrence rate for intermediate risk endometrial cancer treated with observation alone (strategy 2)
was 8%.

The survival rate for patients with intermediate risk endometrial cancer originally treated with observation alone and
who developed vaginal cuff recurrence was 60%.

The complication rate was 38% for teletherapy and 4% for brachytherapy.

Measure of benefits used in the economic analysis
The measures of benefit used were survival and morbidity. Survival was limited to 5-year disease specific survival and
was expressed as the number of lives saved. Morbidity involved radiation complications, including gastrointestinal tract, genitourinary system and others. The health benefits were not discounted.

Direct costs
The costs included in the analysis were those associated with all operative procedures performed as part of the two strategies evaluated. More specifically, hysterectomy, oophorectomy and lymphadenectomy, brachytherapy (either at a low- or high-dose rate), examination under anaesthesia with biopsy, cystoscopy and proctoscopy, and teletherapy. The costs associated with morbidity following treatment were not considered. The quantities and the costs were not analysed separately. The costs were based on CPT (physician's current procedural terminology) and DRG (disease-related groups) reimbursement. Actual payer reimbursements were obtained during a 6-month collection period between 2001 and 2002. The median reimbursement for 10 consecutive patients for each CPT and DRG code was used in the analysis. Year 2001 prices were used. The total costs were derived using modelling. Discounting was not necessary since the costs referred to a time period shorter than one year.

Statistical analysis of costs
The costs were treated deterministically. No statistical analysis of the costs was undertaken.

Indirect Costs
The indirect costs were not included in the analysis.

Currency
US dollars ($).

Sensitivity analysis
A one-way sensitivity analysis was carried out to test the robustness of the results under the uncertainty of input parameters. The parameters examined were the survival rate for patients with intermediate risk endometrial cancer originally treated with observation alone and who developed vaginal cuff recurrence (45% and 75%), and the vaginal cuff recurrence rate (3%). In addition, a sensitivity analysis explored the impact of not performing examination under anaesthesia with biopsy, cystoscopy and proctoscopy for patients in strategy 2 who developed a vaginal cuff recurrence. A sensitivity analysis was not undertaken on the effectiveness data derived from large prospective studies. The ranges used were based on authors' assumptions.

Estimated benefits used in the economic analysis
Survival was decreased by 3% in strategy 2 where patients received no postoperative brachytherapy. This percentage varied from 2 to 4% in the sensitivity analysis. Based on the proportion of endometrial cancers of intermediate risk (33%), it was reported that survival would be reduced to 1% in strategy 2 compared with strategy 1. The projected radiation complication rates for the two strategies were similar (4% for strategy 1 and 3% for strategy 2). The total benefits associated with each strategy were not reported.

Cost results
The average cost per patient was $13,180 for strategy 2A (observation and treatment of vaginal recurrence with teletherapy and low-dose rate brachytherapy) and $18,985 for strategy 1A (postoperative low-dose rate brachytherapy to all cases). The cost of strategy 2A was 31% lower than that of strategy 1A.

The average cost per patient was $12,981 for strategy 2B (observation and treatment of vaginal recurrence with teletherapy and high-dose rate brachytherapy) and $16,505 for strategy 1B (postoperative high-dose rate brachytherapy to all cases). The cost of strategy 2B was 21% lower than that of strategy 1B.
From the sensitivity analysis, not performing an examination under anaesthesia with biopsy, cystoscopy and proctoscopy in strategy 2 following vaginal recurrence would result in the above differences in cost becoming 38% and 30%, respectively.

Based on the proportion of endometrial cancers of intermediate risk (33%), it was reported that, for intermediate risk endometrial cancer, strategy 2A would be less costly by 11% compared with strategy 1A, while strategy 2B would be less costly by 7% compared with strategy 1B.

**Synthesis of costs and benefits**
The costs and benefits were combined in the form of incremental cost-effectiveness ratios. It was not explicit how these ratios were calculated as the total costs and benefits for each strategy assessed were not reported.

The cost per life saved for all patients with endometrial cancer was $191,565 with postoperative low-dose brachytherapy (strategy 1A) and $116,292 with high-dose brachytherapy (strategy 1B), compared with strategies involving initial observation (2A and 2B respectively).

Based on the proportion of endometrial cancers of intermediate risk (33%), it was reported that, for patients with intermediate risk endometrial cancer, these ratios were $63,855 (strategy 1A, low-dose brachytherapy) and $38,764 (strategy 1B, high-dose brachytherapy). The impact of a sensitivity analysis on these results was not discussed.

**Authors’ conclusions**
Withholding postoperative brachytherapy for intermediate risk endometrial cancer was cost-effective as it resulted in a 31% decrease in cost, a 3% decrease in survival and similar radiation complication rate. However, postoperative high-dose rate brachytherapy would still be an acceptable intervention since it demonstrated a cost per life saved equal to $38,764, which is lower than the threshold of $50,000 per life saved.

**CRD COMMENTARY - Selection of comparators**
The selection of the comparator was not explicitly justified. However, it was reported that the treatment of intermediate risk endometrial cancer varied widely. The comparator represented an alternative treatment strategy suggested by some gynaecologic oncologists. You should consider whether this reflects widely used technology in your own setting.

**Validity of estimate of measure of effectiveness**
The input parameters were obtained from published studies. However, the authors did not report that a systematic review of the literature had been undertaken to identify all relevant research and minimise biases, nor did they report the sources searched to identify relevant research. The authors did not provide details of any criteria that they used to select the primary studies from which they obtained the input parameters for their model. The effectiveness rates from different studies were not combined. The impact of differences between the primary studies was not considered when estimating effectiveness. Uncertainty around two outcomes was evaluated in the model using a sensitivity analysis. Values for the vaginal cuff recurrence rate were derived from the literature, whereas no justification was provided for the values used for survival rate.

**Validity of estimate of measure of benefit**
The estimation of benefits was modelled. The ad hoc model used to derive a measure of health benefit was, in principle, appropriate, although the subsequent economic analysis was characterised by methodological errors (see the 'Other issues' field, below).

**Validity of estimate of costs**
The perspective of the analysis was stated to reflect the payer's actual cost. As such, it appears that all the categories of cost relevant to the perspective adopted have been included in the analysis. However, the costs associated with the
treatment of complications due to brachytherapy were not included in the analysis. Consequently, the cost-effectiveness of postoperative brachytherapy might have been overestimated. The costs and the quantities were not reported separately, which hinders the generalisability of the results. A sensitivity analysis of the costs was not conducted, and this limits the interpretation of the results. The use of payer's costs was consistent with the perspective adopted. Discounting was not necessary, as the costs referred to a time period of less than one year, and therefore was not undertaken. The date to which the prices referred was reported, and this improves the reproducibility of the results.

Other issues
The authors did not compare their findings with those of other studies, as they stated that this was the first cost-effectiveness analysis of the treatment of intermediate risk endometrial cancer comparing postoperative brachytherapy versus observation and treatment only in the case of recurrence. The issue of generalisability to other settings was not addressed. The results were not reported in full for areas such as total benefits and outcomes of the sensitivity analysis. The authors reported separate results (both cost and cost-effectiveness) for all patients with endometrial cancer in general, and for patients with intermediate risk endometrial cancer in particular. The results for the latter sub-group were derived from the results reported for the total population of patients with endometrial cancer, by taking the proportion of endometrial cancers that were intermediate risk into consideration. This approach constitutes a methodological error, as it implies that the proportion of intermediate risk endometrial cancers out of all endometrial cancers is equal to the proportion of the associated respective costs and benefits, which is obviously not the case. In addition, it was unclear whether the results were based on effectiveness data derived from trials of patients with intermediate risk endometrial cancer, or with endometrial cancer in general. Finally, the authors' conclusions about the cost-effectiveness of withholding postoperative therapy were based on cost considerations only, given that the benefit results were not favouring this strategy.

Implications of the study
It might be inferred, based on authors' conclusions, that both techniques evaluated were acceptable alternatives for the treatment of intermediate risk endometrial cancer in terms of cost-effectiveness. However, since the analysis was characterised by strong methodological errors, no safe recommendations can be made on the basis of the study's conclusions.

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Other publications of related interest

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