A cost-outcome analysis of long-term adjuvant goserelin in addition to radiotherapy for locally advanced prostate cancer
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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
The use of adjuvant goserelin (AG) in addition to radiotherapy (RAD) for locally advanced prostate cancer (LAPC). RAD consisted of treating the pelvis with a dose of 50 Gy/25 fractions over 5 weeks, followed by a boost to the prostate and seminal vesicles for a further 20 Gy/10 fractions over 2 weeks. AG (3.6 mg) was administered via subcutaneous injection every 4 weeks (starting at the beginning of RAD) for 3 years, along with one month of cyproterone acetate (150 mg/day orally) starting one week prior to the first dose of goserelin.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The inclusion criteria for the study population specified:

- patients under 80 years of age, with histologically proven prostatic adenocarcinoma that was intracapsular (T1) or confined to the gland (T2), without detectable involvement of regional lymph nodes (N0-X), and of World Health Organization histologic grade 3; or
- patients who had had prostate cancer of any histologic grade that extended beyond the capsule (T3) or infiltrated neighbouring structures (T4) without involving regional lymph nodes.

Patients with a prior malignant disease other than treated basal-cell carcinoma of the skin, and those with evidence of distant metastases (including metastases to common iliac or para-aortic lymph nodes) were excluded.

Setting
The setting was a hospital and primary care. The economic study was conducted in Canada.

Dates to which data relate
The effectiveness evidence was gathered from May 1987 to September 1995. The dates during which the resource use data were collected were not reported. The price year was 2000.

Source of effectiveness data
The effectiveness evidence was derived from a single study, which was published elsewhere (see Other Publications of Related Interest).
Link between effectiveness and cost data
The costing was not conducted on the sample of patients used in the effectiveness study.

Study sample
Power calculations were conducted in the preliminary phase of the study. These suggested that 75 patients in each group had to be followed up until relapse to detect a minimal increase from 40 to 55% in the 5-year disease-free rate. Of an initial group of 415 patients who entered the study, 14 patients were not evaluable. The final sample comprised 198 patients in the RAD group and 203 in the AG+RAD group. The median age was 70 years (age range: 51 - 80) in the RAD group and 71 years (age range: 54 - 80) in the AG+RAD group. The method of sample selection was not reported. Three patients in the RAD group and 8 in the AG+RAD group refused treatment.

Study design
This was a prospective, multicentre, randomised clinical trial. The centres where the study was conducted were not described. Randomisation was conducted by stratifying according to the institution, clinical stage of disease, results of extraperitoneal lymph-node biopsy, and irradiation technique. A minimisation technique was used at the central institution to allocate the patients to the study groups. The median duration of follow-up was 45 months. Fourteen patients were not available for evaluation. The outcome assessment was not blinded.

Analysis of effectiveness
The analysis of the clinical study was conducted on an intention to treat basis. The main outcome measures were:

- overall survival at 5 years,
- the disease-free rate in patients who survived after 5 years,
- the number of patients with disease progression,
- the 5-year local-control rate,
- the time until first treatment failure after a biologic response, and
- the 5-year failure-free rate after a biologic response.

Survival curves were estimated using the Kaplan-Meier approach. The two groups were shown to be comparable at baseline in terms of their demographic and clinical characteristics.

Effectiveness results
The overall survival rate at 5 years was 79% (95% confidence interval, CI: 72 - 86) in the AG+RAD group and 62% (95% CI: 52 - 72) in the RAD group, (p=0.001).

The disease-free rate in patients who survived after 5 years was 85% (95% CI: 78 - 92) in the AG+RAD group and 48% (95% CI: 38 - 58) in the RAD group, (p<0.001).

There were 20 patients with disease progression in the AG+RAD group versus 78 in the RAD group. The 5-year local-control rate was 97% in the AG+RAD group and 77% in the RAD group, (p<0.001).

The time until first treatment failure after a biologic response was 6.6 years in the AG+RAD group and 4.4 years in the RAD group.

The 5-year failure-free rate after a biologic response was 81% in the AG+RAD group and 43% in the RAD group.
Clinical conclusions
The effectiveness study showed that AG in addition to RAD led to significantly longer (disease-free) survival.

Measure of benefits used in the economic analysis
The summary benefit measure used in the economic analysis was the life-years gained (LYG) with each study intervention. It was calculated from the effectiveness analysis by extending the time horizon considered (from 5 to 10 years). This projected survival benefit was calculated from the graphs reported in the primary study. The benefits were discounted at a rate of 3%.

Direct costs
It appears that no discount rate has been applied, although discounting was relevant because the costs were incurred during 3 years. The unit costs were not reported separately from the quantities of resources used. A breakdown of the costs was provided, but the cost categories were not reported in detail. The health services included in the economic evaluation were AG, RAD, physician fees, pharmacy services and laboratory tests. Primary care physicians administered the hormone therapy (AG), while RAD was delivered at cancer centres. An institutional cost/resource boundary was adopted in the study. The costs and resource use data were estimated from local practices using an activity-costing model developed for the study at the Northeastern Ontario Regional Cancer Centre. The drug costs comprised pharmacy, dispensing and stocking fees. The authors assumed that subsequent medical expenses were similar for both groups of patients. The price year was 2000.

Statistical analysis of costs
No statistical tests of the costs or resources were conducted.

Indirect Costs
The indirect costs were not included in the economic evaluation.

Currency
Canadian dollars (Can$). The costs were also reported in US dollars ($) but the exchange rate was not given.

Sensitivity analysis
One-way sensitivity analyses were conducted to test the robustness of the estimated cost-effectiveness ratios to variations in the cost of the drugs (+20%) and benefit discount rate (5% rather than 3%).

Estimated benefits used in the economic analysis
The estimated (discounted) long-term benefit of AG+RAD in comparison with RAD was 1.2 years.

Cost results
The total costs of RAD were Can$9,000 ($6,000), while the costs of AG were Can$19,800 ($13,200). Thus, the costs of AG+RAD were Can$28,800 ($19,200).

Synthesis of costs and benefits
An incremental cost-effectiveness ratio (ICER) was calculated to combine the costs and benefits of AG+RAD relative to RAD.

The ICER was Can$16,500 ($11,000) per LYG.
When the drug costs were increased by 20%, the ICER was Can$19,800. When the discount rate for benefits rose to 5%, the ICER was Can$18,000. However, in the worst-case scenario (+20% drug costs and 5% discount rate for benefits), the ICER was Can$21,600 ($14,400) per LYG.

The ICER was never above the well-accepted threshold of $50,000 per LYG.

**Authors' conclusions**

Even under pessimistic scenarios, the combined treatment of adjuvant goserelin (AG) and radiotherapy (RAD) represented a cost-effective intervention for patients with prostate cancer in Canada. In addition, it compared favourably with other medical interventions.

**CRD COMMENTARY - Selection of comparators**

The rationale for the choice of the comparator was clear. RAD alone represented the standard approach for treating patients with LAPC. You should decide whether it represents a valid comparator in your own setting.

**Validity of estimate of measure of effectiveness**

The analysis of effectiveness used a randomised trial, which was appropriate for the study question. The study was multicentred and prospective. Power calculations were conducted and the study groups were comparable at baseline. Few patients were lost to follow-up and the basis of the clinical study was intention to treat. These issues tend to enhance the internal validity of the analysis. The study sample is likely to have been representative of the study population. The use of randomisation reduced the impact of potential confounding factors and bias. However, the method of sample selection was not reported.

**Validity of estimate of measure of benefit**

The benefit measure was overall survival, which was taken from the effectiveness study. The discounting applied was appropriate and different discount rates were tested in the sensitivity analysis. The use of survival represents a benefit measure comparable with the benefits of other health interventions. The authors stated that the use of quality-adjusted survival was not feasible due to the lack of quality of life data for the interventions considered in the study.

**Validity of estimate of costs**

The perspective adopted in the study was explicitly stated. It appears that all the relevant categories of costs have been included in the analysis. Some of the costs in the two group were considered similar and were not included in the economic analysis. The price year was reported, thus simplifying reflation exercises in other settings. The costs were estimated using local data and only the drug costs were varied in the sensitivity analysis. Thus, the cost estimates were specific to the study setting. No statistical tests of resource use or unit costs were conducted. The authors provided a breakdown of the costs, but details on the unit costs or quantities of resources used were not provided. The prices were reported in Canadian and US dollars. Discounting would have been appropriate because the drug costs were estimated for 3 years, but no discount rate was reported. The approach used to estimate resource use and costs was developed in Ontario.

**Other issues**

The authors compared their findings with those from other studies. They found that their costs compared favourably with those observed in the literature. The cost-effectiveness ratios of other accepted systemic cancer therapies and other commonly used medical interventions were reported to show that goserelin was cost-effective for patients with LAPC. However, the issue of the generalisability of the study results to other settings was not addressed. The authors noted some limitations of their analysis. First, the costs associated with the treatment of side effects were not considered, although the authors noted that the inclusion of such costs would not have changed their conclusions. Second, the 10-year benefit was projected and was not based on real data because the trial follow-up was about 5 years.
Implications of the study
The study results supported the use of long-term hormone therapy, in addition to RAD, for men with LAPC from the perspective of the health service provider. Future studies should evaluate the appropriate duration of hormone therapy in LAPC patients.

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Bibliographic details

Other publications of related interest

Indexing Status
Subject indexing assigned by NLM

MeSH
Adenocarcinoma /drug therapy /economics /pathology /radiotherapy; Antineoplastic Agents, Hormonal /economics /therapeutic use; Capital Expenditures; Chemotherapy, Adjuvant /economics; Combined Modality Therapy /economics; Cost-Benefit Analysis; Drug Costs; Fees, Medical; Fees, Pharmaceutical; Goserelin /economics /therapeutic use; Hospital Costs; Humans; Male; Ontario; Prostatic Neoplasms /drug therapy /economics /pathology /radiotherapy; Radioisotope Teletherapy /economics; Randomized Controlled Trials as Topic; Research Support, Non-U.S. Gov't; Survival Analysis; Treatment Outcome

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