Using decision analysis to determine the cost-effectiveness of intensity-modulated radiation therapy in the treatment of intermediate risk prostate cancer


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 examined two treatments for a patient with intermediate risk of prostate cancer. One was intensity-modulated radiation therapy (IMRT) and the other was three-dimensional conformal radiation therapy (3D-CRT). IMRT consisted of a total dose of 81 Gy, delivered in 1.8 Gy fractions/day. 3D-CRT consisted of a total dose of 78 Gy, delivered in 2 Gy fractions/day.

Type of intervention
Treatment.

Economic study type
Cost-utility analysis.

Study population
The study population comprised a hypothetical cohort of 70-year-old patients with intermediate risk of prostate cancer.

Setting
The setting was a hospital. The economic study was carried out in the USA.

Dates to which data relate
The clinical data were derived from studies published between 2002 and 2004. No dates for resource use were reported. The price year was 2004.

Source of effectiveness data
The clinical data used in the model were:

the rate of biochemical disease-free survival (BDFS) with IMRT or 3D-CRT,
the rate of failure with IMRT or 3D-CRT,
the toxicity of the treatments,
the transition probabilities from the hormone responsive state to the hormone unresponsive rate, and
survival.

Modelling
A Markov model was constructed to simulate the clinical and economic outputs associated with the two treatment
strategies. The structure of the decision tree, the health states, cycle length and transition patterns were clearly described. Constant (not time dependent) transition rates over time were assumed. The time horizon of the analysis was not reported clearly, but it might have been the patient’s lifetime.

Sources searched to identify primary studies
Survival was based on US life tables. Other data were derived from the literature, but details of the primary studies were generally not given. The exception was rates of BDFS, which were derived from patients with intermediate-risk prostate cancer treated with IMRT at the Memorial Sloan-Kettering Cancer Center and 3D-CRT at the Fox Chase Cancer Center in Philadelphia, USA.

Methods used to judge relevance and validity, and for extracting data
The approach used to derive the clinical data was not reported, but no systematic search for primary studies was performed. Data representative of the US study population have generally been chosen.

Measure of benefits used in the economic analysis
The summary benefit measure used was the expected number of quality-adjusted life-years (QALYs). These were estimated using the modelling approach, in which survival was combined with changes in QoL. These values were obtained from a sample of 17 patients with intermediate-risk prostate cancer undergoing IMRT (without hormone therapy) using the EQ-5D instruments in an RCT. The corresponding values of QoL for patients treated with 3D-CRT came from a separate study enrolling 34 men and using the time trade-off technique. The benefits were discounted at an annual rate of 3%.

Direct costs
The perspective of the payer was adopted. The categories of costs included in the analysis were radiation treatment (IMRT or 3D-CRT), chemotherapy and hormone therapy. A breakdown of the cost items for radiation treatments was given. The unit costs were not presented separately from the quantities of resources used, but macro-categories of costs were given. The costs of radiation treatment were estimated from national Medicare reimbursement rates (thus, incorporating global costs), including both hospital and professional fees. The drug costs were based on average wholesale prices. The cost of chemotherapy came from a published study. Discounting was relevant, as the costs were incurred during more than 2 years, and an annual discount rate of 3% was applied. The price year was 2004.

Statistical analysis of costs
The costs were treated deterministically in the base-case but were assigned probabilistic distributions in the sensitivity analysis.

Indirect Costs
Productivity costs were not considered.

Currency
US dollars ($).

Sensitivity analysis
A probabilistic sensitivity analysis was performed to address the issue of uncertainty surrounding all model inputs, in order to generate cost-effectiveness acceptability curves. The probabilistic distributions given to the costs, utilities and probabilities were reported. One- and two-way sensitivity analyses were also carried out on cost and utility values. Alternative ranges of values were either derived from the literature or defined by the authors. Specifically:
the costs were assigned a log normal rather than a normal distribution (as in the base-case);

a lower reimbursement for IMRT was assumed as a result of potential negotiated discounts;

the cost of chemotherapy was increased;

a similar effectiveness was assumed for the two treatments, with only utility differing;

similar utilities were assumed;

different time horizons and patient ages were considered.

**Estimated benefits used in the economic analysis**
The expected QALYs were 5.62 with 3D-CRT and 6.27 with IMRT.

**Cost results**
The expected costs were $21,865 with 3D-CRT and $47,931 with IMRT.

**Synthesis of costs and benefits**
Incremental cost-utility ratios were calculated in order to combine the costs and benefits of the alternative treatments.

The incremental cost per QALY gained with IMRT in comparison with 3D-CRT was $40,101, which is generally considered cost-effective as it falls below the threshold of $50,000 per QALY.

The probabilistic sensitivity analysis revealed that the probability of IMRT being cost-effective at a threshold of $50,000 per QALY was 55.1%.

The deterministic sensitivity analysis showed that the cost-utility of IMRT improved when a lower Medicare reimbursement rate was used ($16,804 per QALY gained). The cost-effectiveness of IMRT also improved when the cost of chemotherapy was increased. Also, longer time horizons improved the value-for-money of IMRT. However, unfavourable results for the IMRT strategy were achieved when similar utilities were assumed. In general, the analysis showed a strong impact of the utility values on the results of the analysis, and the use of similar utilities raised the incremental cost per QALY to $126,644. Changes in other model inputs or in the probabilistic distribution assigned to costs did not substantially alter the base-case conclusions.

**Authors’ conclusions**
Intensity-modulated radiotherapy (IMRT) was a cost-effective alternative to three-dimensional conformal radiation therapy (3D-CRT) in the treatment of a 70-year-old man with intermediate-risk prostate cancer, although this conclusion was heavily affected by some assumptions of the analysis, such as those related to quality of life (QoL) improvements after treatment.

**CRD COMMENTARY - Selection of comparators**
The authors described clearly their rationale for the choice of the comparators and hypothesised the superior clinical profile (but also the higher cost) of IMRT over 3D-CRT. You should decide whether they are valid comparators in your own setting.

**Validity of estimate of measure of effectiveness**
It was unclear whether the clinical data were derived from a review of the literature. No details of the methods and conduct of a review were reported. Little information on the primary studies was provided, which makes any objective assessment of the validity of the clinical sources difficult. The authors tended to use US data that represented their study population. Both a probabilistic and a deterministic approach were used to deal with the issue of uncertainty in the
clinical estimates.

**Validity of estimate of measure of benefit**
The benefits of the treatments (QALYs) were modelled using a Markov model. The sources of QoL values were reported. The authors noted that a potential drawback of the analysis was the fact that utility values for the two treatments were elicited using different techniques. The impact of utility values on the final cost-effectiveness ratios was highlighted by the results of the sensitivity analyses. Appropriate discounting was performed, as recommended in US guidelines. QALYs can be compared with the benefits of other health care interventions.

**Validity of estimate of costs**
The perspective adopted in the analysis of the costs was explicitly reported. As such, all the relevant categories of costs appear to have been included. There was little information on the unit costs and quantities of resources used, most items being reported as macro-categories. This could limit the possibility of replicating the analysis in other settings. However, this is often the case in US studies when Medicare is used as the main source of the costs. The sources of the data were reported for all items. Statistical analyses of the costs were performed. The price year was reported, which has positive implications for the generalisability of the study results.

**Other issues**
The authors reported the findings from some published studies evaluating the cost-effectiveness of radiation treatments in patients with prostate cancer. The issue of the generalisability of the study results to other settings was not explicitly addressed. However, the extensive use of sensitivity analysis enhances the external validity of the model results. The authors pointed out that the results of the analysis cannot be extrapolated to the treatment of men with good-risk prostate cancer since epidemiological data referred to patients with intermediate-risk disease.

**Implications of the study**
The study results support the use of IMRT for the treatment of intermediate-risk prostate cancer, although this conclusion was highly dependent on the time horizon of the analysis and the improvements in QoL associated with treatment. The authors noted that further studies should investigate the potential of increased second malignancies with IMRT.

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None stated.

**Bibliographic details**


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