Cost-effectiveness of modern radiotherapy techniques in locally advanced pancreatic 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.

CRD summary
The objective was to evaluate the cost-effectiveness of gemcitabine alone, compared with gemcitabine with other therapies, for the management of locally advanced pancreatic cancer. The addition of tissue-sparing radiotherapy was not cost-effective, but the addition of stereotactic radiotherapy was effective and could be cost-effective. The methods were appropriate and the results were adequately presented, but there were a few limitations to the reporting of the effectiveness data, so the authors’ conclusions should be considered carefully.

Type of economic evaluation
Cost-effectiveness analysis, cost-utility analysis

Study objective
The objective was to evaluate the cost-effectiveness of gemcitabine alone, compared with gemcitabine combined with other therapies, for the management of locally advanced pancreatic cancer.

Interventions
Four interventions were considered: gemcitabine alone, gemcitabine with radiotherapy, gemcitabine with radiotherapy and tissue sparing, and gemcitabine with stereotactic radiotherapy. Gemcitabine was given in cycles of 1g per m² weekly for three out of four weeks for a maximum of five cycles. Radiotherapy was given at 50.4 grays (Gy) in 28 fractions, with weekly gemcitabine at 600mg per m², followed by gemcitabine cycles. Tissue sparing was a technique to spare the surrounding normal tissue. Stereotactic body radiotherapy was given at 25 Gy in a single fraction, after one cycle of gemcitabine, and followed by cycles of gemcitabine.

Location/setting
USA/secondary care.

Methods
Analytical approach:
A health-state transition model was developed, using data mostly from one trial (Loehrer, et al. 2008, see ‘Other Publications of Related Interest’ below for bibliographic details). The time horizon was five years. The authors stated that the perspective was that of the payer.

Effectiveness data:
The effectiveness estimates were from the published randomised phase III clinical trial (Loehrer, et al. 2008) for the first three treatment options, and were based on data from the authors’ institution (Stanford Cancer Centre, USA) for gemcitabine with stereotactic radiotherapy. The key effectiveness estimates were the probabilities of disease progression, death, or toxicity.

Monetary benefit and utility valuations:
The utility estimates for stable disease were based on expert opinion and for the other model health states (local progression, local and distant failure, and death) they were from published literature.

Measure of benefit:
Quality-adjusted life-years (QALYs) were the summary benefit measure. Future benefits were discounted at a rate of 3% per year.
Cost data:
The direct cost categories were the costs of treatment (radiotherapy and chemotherapy), toxicity events, and additional medical care unrelated to treatment (office visits, medications, and laboratory and radiology costs). The costs were from Medicare Physician Fee schedules and the Medicare Part B reimbursement schedule, or estimates in the published literature. They were presented in US $ and adjusted to 2009 prices, using the medical component of the consumer price index. Future costs were discounted at a rate of 3% per year.

Analysis of uncertainty:
One-way and probabilistic sensitivity analyses were conducted to assess the impact of uncertainty in the clinical and economic estimates on the results. The results were presented in tables and cost-effectiveness acceptability curves. An additional analysis excluding gemcitabine with stereotactic radiotherapy was considered.

Results
The estimated cost per patient was $42,900 for gemcitabine alone, $56,700 for gemcitabine with stereotactic radiotherapy, $59,900 for gemcitabine with radiotherapy, and $69,500 for gemcitabine with tissue-sparing radiotherapy.

The estimated mean QALYs per patient were 0.581 for gemcitabine alone, 0.778 with stereotactic radiotherapy, 0.714 with radiotherapy, and 0.721 with tissue-sparing radiotherapy.

Compared with gemcitabine alone, the addition of stereotactic radiotherapy had an incremental cost per QALY gained of £69,500. The addition of stereotactic radiotherapy dominated radiotherapy and tissue-sparing radiotherapy, as it was less costly and more effective.

Excluding stereotactic radiotherapy, the addition of radiotherapy had an incremental cost-effectiveness ratio of $126,800, compared with gemcitabine alone, and tissue-sparing radiotherapy had an incremental cost-effectiveness ratio of $1,584,100, compared with conventional radiotherapy.

One-way sensitivity analyses showed that the results were most sensitive to the assumptions for mean survival. The survival with tissue-sparing would have to increase by 4.8 months over conventional radiotherapy before it became cost-effective at a $50,000 per QALY gained threshold.

Authors' conclusions
The authors concluded that the addition of tissue-sparing radiotherapy was not cost-effective, but the addition of stereotactic radiotherapy to gemcitabine was effective and could be cost-effective.

CRD commentary
Interventions:
The reporting of the interventions was sufficient, but it was not clear whether all the relevant treatment options were included. The interventions might be relevant and available in other settings.

Effectiveness/benefits:
The authors did not fully describe the design of the main source for the effectiveness data, and they did not report the inclusion and exclusion criteria and number of participants. This makes it difficult to assess the quality of the effectiveness data. The authors did not describe the methods used to search for relevant studies so it is not clear whether the best available evidence was used. Similarly, the utility estimates for the QALYs, their sources and the methods used to identify them were not described, but the references and the values used were reported.

Costs:
On the whole, the reporting of the cost data was good. The costs appear to have been relevant to the stated perspective and the study setting. The resource use was from published treatment schedules and the adjustments to the cost data were reported. The methods used to identify the cost estimates in the published literature were not described, so it is unclear if better sources were available. The price year, currency and discount rate were reported.

Analysis and results:
The analytical approach was reported and a diagram of the model structure was provided. The incremental analysis was appropriate for assessing the relative cost-effectiveness of the treatment options. The time horizon was sufficient to capture the differences in costs and effects between strategies. The methods used to assess the impact of uncertainty were appropriate and more details were available in an online appendix. The reporting was sufficient for the results, and will allow an assessment of their generalisability to other settings. There were a number of limitations to the study, some of which were identified and discussed by the authors.

Concluding remarks:
The methods were appropriate and the results were adequately presented, but there were a few limitations to the reporting of the effectiveness data, so the authors’ conclusions should be considered carefully.

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