Decision tree sensitivity analysis for cost-effectiveness of FDG-PET in the staging and management of non-small-cell lung carcinoma

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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
Positron emission tomography (PET) using [18F] 2-fluoro-2-deoxy-D-glucose (FDG-PET) in combination with chest computed tomography (CT) forstaging non-small-cell lung cancer.

Type of intervention
Diagnosis.

Economic study type
Cost-effectiveness study.

Study population
A hypothetical cohort of white 64 year-old patients with NSCLC.

Setting
Secondary care and hospital. The economic study was carried out in the United States.

Dates to which data relate
The effectiveness data were obtained from studies published between 1988-1995. The resource use data and price year were not associated with any specific date.

Source of effectiveness data
The estimates for final outcomes were based on a review of previously completed studies and on opinion.

Modelling
The analysis for cost-effectiveness and patient life expectancy was performed using decision analysis. Two decision strategies for the selection of potential surgical candidates were compared: thoracic CT alone or thoracic CT + thoracic PET. Results for two models were reported. One model depicted a conservative scenario in which all PET-positive (for metastases) cases (regardless of the results of CT) for contralateral mediastinal lymph node involvement undergo biopsy to confirm that the patient is not a surgical candidate. The other, 'less conservative model', illustrated the decision rule that the biopsy was performed only when discordant findings between CT and PET test were obtained. Cases with positive findings for both diagnostic tests were ruled out from surgery. Otherwise, the patient was referred for surgery. The model covered the morbidity and mortality outcomes associated with each strategy.

Outcomes assessed in the review
The outcomes assessed were the sensitivity and specificity of CT and PET, and morbidity and mortality for all of the
studies in each of the decision trees, as well as the life expectancy for an otherwise healthy 64-year old man.

**Study designs and other criteria for inclusion in the review**
For the sensitivity and specificity of thoracic CT for staging of NSCLC the English literature for the period 1988-1995 was surveyed. Studies that used total or near total sampling of mediastinal lymph nodes by mediastinoscopy/thoracotomy, and that reported results in sufficient detail to allow averaging of sensitivities and specificities between primary studies were included. The criteria for the other outcomes assessed in the review were not described.

**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**
For the sensitivity and specificity of thoracic CT for staging of NSCLC eight papers were selected (five for diagnostic value based on patient analysis and three for that based on nodal station analysis). The corresponding figures for PET were derived from three studies.

**Methods of combining primary studies**
Results were pooled (i.e. individual results were weighted by sample size).

**Investigation of differences between primary studies**
Not stated.

**Results of the review**
For the sensitivity and specificity of thoracic CT for staging of NSCLC the authors adopted sensitivity and specificity of 67% (range: 61 - 73) and 73% (range: 62 - 86) respectively. Based on preliminary literature results in 121 patients the PET sensitivity and specificity values used were 90% (range: 82 - 100) and 91% (range: 81 - 100) respectively. The reported mortality associated with surgical resection of lung cancer ranged from 2.4% to 20%; the authors chose a baseline surgical mortality of 3% (range: 0 - 20). The authors subtracted 1 month (range: 0 - 1 year) for the morbidity associated with the recovery from thoracotomy. A baseline mortality of 0.3% (range: 0 - 5) was used for the biopsy procedure. The risk associated with CT was chosen as 0.0025% (range: 0 - 5). A baseline of 7 years was used as the life expectancy of a healthy 64 year old white man. The life expectancy for non-resectable lung cancer for patients with highly advanced disease was taken to be 1 year (range: 0.1 - 2 years). For patients with false positive CT and PET scans who were not operated on, a mean life expectancy of 2 years was chosen.

**Methods used to derive estimates of effectiveness**
The authors’ assumptions were also used to derive estimates of effectiveness.

**Estimates of effectiveness and key assumptions**
The average morbidity for anterior mediastinotomy was assumed to be about 10 days, the morbidity associated with the biopsy procedure was assumed to be 2.5 days. The accuracy of the biopsy was assumed to be 100%. The risk associated with PET was assumed to be negligible.

**Measure of benefits used in the economic analysis**

The measure of benefits in the economic analysis was life years gained (undiscounted), including the morbidity consequences of diagnosis and treatment, as estimated by a decision model. The authors assumed the extent of reduction in life expectancy due to the morbidity of the strategies.

**Direct costs**

Quantities of resource use were not analysed separately from the costs. Although costs were not discounted it seems that they were incurred within a period of one year after the hypothetical start of the interventions. The mean and range costs (technical and professional charges) of thoracic CT, thoracic PET, biopsy and curative surgery were included. The mean estimates were based on the approximate billed costs at the authors' institution. The ranges were based on approximate costs across various types of medical practices in the United States. The price year was not reported.

**Currency**

US dollars ($).

**Sensitivity analysis**

One- and two-way sensitivity analyses were performed over the ranges of uncertainty for the most relevant parameters of the model. Results were also presented in the form of a threshold analysis.

**Estimated benefits used in the economic analysis**

Under the conservative model, life expectancy was increased by 2.96 days with the CT + PET strategy compared to the CT alone strategy. Although the marginal effectiveness of using PET for staging was small, it was positive over a wide range of conditions. Results were not clearly reported for the 'less conservative' model.

**Cost results**

Under the 'conservative model', the mean cost of the CT + PET strategy was $24,480 compared to a mean cost of $25,634 for CT alone; a saving of $1,154 per patient. The 'less conservative' model would result in savings of $2,267 ($23,367 vs. $25,634). The former figures translate to approximately $98 million in health care cost savings per year, assuming approximately 85,000 patients per year undergo the diagnostic algorithm in the United States.

**Synthesis of costs and benefits**

Combination of costs and benefits was not necessary because analysis showed positive incremental benefits and negative incremental costs for the CT + PET strategy. To be more cost-effective than CT alone, the thresholds for PET sensitivity and specificity were determined to be 48% and 12% respectively. These relatively low values result from the added power of two tests in the CT + PET strategy reducing the mean costs significantly. Prevalence is a key variable in understanding the cost-effectiveness of each strategy. For a prevalence less than 16.9%, the CT + PET strategy will not save money over the CT alone strategy. Similarly, for a prevalence less than 5.6%, the CT + PET strategy cannot increase life expectancy over the CT alone strategy.

**Authors' conclusions**

The present study has quantitatively shown the cost-effectiveness of using a PET based strategy in the management of NSCLC. It has shown that a CT + PET strategy is more economical and has a marginal increase in patient life expectancy as compared to the conventional strategy of staging patients with CT alone. Even with the uncertainty in
various variables, the effectiveness of the CT + PET strategy has been shown over a large range. The present study supports the wider use of PET in managing NSCLC as a significant cost-effective tool that can save millions of dollars nationwide.

CRD COMMENTARY - Selection of comparators
The reason for the choice of the comparator is clear

Validity of estimate of measure of benefit
The authors did not report enough detail about the methodology used in the literature review and synthesis. The evidence for some of the variables used in the decision trees was based, necessarily, on the authors’ assumptions. However, sensitivity analyses were used to allow for possible inaccuracies in these assumptions. Given the lack of published data for some of the variables (in particular PET), the estimate of measure of benefit must be considered with caution. The health-related benefits were not discounted.

Validity of estimate of costs
Resource quantities were not reported separately from the prices. Moreover, no adequate details of cost estimation were given.

Other issues
The authors’ conclusions were justified in terms of the uncertainty in the most relevant parameters (ranges explored in sensitivity analyses) but the issue of generalisability to other countries was not addressed and may not be easy to assess, given the lack of methodological information in the paper.

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Other publications of related interest

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