Analysis models to assess cost effectiveness of the four strategies for the work-up of solitary pulmonary nodules

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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
Four strategies for the investigation of solitary pulmonary nodules (SPNs) discovered on screening chest radiographs were examined.

Computed tomography (CT) alone strategy: all patients in whom an SPN was diagnosed as lung cancer on the initial chest CT proceeded to surgical resection without pathological confirmation.

CT plus sodium iodide fluorine-18 fluorodeoxyglucose positron emission tomography (FDG-PET) strategy: all patients who were CT positive underwent chest FDG-PET. If the FDG-PET was also positive, the patients proceeded to surgical resection. If a chest FDG-PET examination was negative after a positive CT examination, the patients were followed up by an unenhanced chest CT.

CT plus PET plus CT-guided needle biopsy strategy: if both CT and FDG-PET were positive, patients proceeded to the mixed biopsy/surgery pathways, which allowed flexibility for the surgeons and/or patients who prefer to have a confirming biopsy before surgery. If the chest CT examination was positive but FDG-PET was negative, some patients underwent CT-guided needle biopsy while others were followed up by an unenhanced chest CT.

CT plus CT-guided needle biopsy strategy: if the initial CT was positive, it was followed directly by a CT-guided needle biopsy. If the biopsy was also positive, the patients underwent surgical resection. If a CT-guided needle biopsy was negative, the patients were followed up by an unenhanced chest CT.

Type of intervention
Diagnosis.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised a hypothetical cohort of patients with an SPN. An SPN was defined as a single, well-circumscribed, spherical radiographic opacity that measured 1 to 4 cm in diameter and was surrounded completely by aerated lung with no calcium visible on a standard chest radiograph. Patients with known malignancy were not included, nor were those with radiographs that had already established the stability of the rate of growth of the nodule.

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

Dates to which data relate
The effectiveness data came from studies published between 1986 and 2003. Some resource use data came from studies
published between 1996 and 2000. Some costs were estimated in 2002, but the price year was unclear.

**Source of effectiveness data**
The effectiveness evidence was derived from a synthesis of completed studies and some authors' opinions.

**Modelling**
A decision tree model was constructed to assess the diagnostic strategies for the management of SPNs. A graphical representation of the four arms of the model, was based on the pathways described for the four strategies, was presented. The tree structure reflected treatment patterns in Japan.

**Outcomes assessed in the review**
The outcomes estimated from the literature were:

- the prevalence of lung carcinoma; and
- the sensitivity and specificity of chest CT, FDG-PET, CT-guided needle biopsy, and serial CT used for follow-up.

**Study designs and other criteria for inclusion in the review**
The authors stated that a review of the literature was undertaken to identify the primary studies. It was unclear whether the review was systematic. Prevalence data came from the Japan Cancer Society, while the diagnostic performance of the tests was estimated from published studies (including a meta-analysis).

**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**
Five primary studies provided evidence.

**Methods of combining primary studies**
The primary studies do not appear to have been combined since each study provided a single estimate.

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

**Results of the review**
According to data from the Japan Cancer Society, lung carcinomas were suspected on screening chest radiographs in 2.48% of individuals; 97% of whom proved to have benign lesions. Thus, the prevalence of carcinoma among SPNs suspected on the screening radiographs was estimated at no higher than 10%.
The sensitivity and specificity were, respectively:

- 0.99 and 0.63 with chest CT,
- 0.968 and 0.778 with FDG-PET,
- 0.769 and 0.936 with CT-guided needle biopsy, and
- 0.56 and 0.95 with serial CT used for follow-up.

**Methods used to derive estimates of effectiveness**
The authors made some assumptions to derive estimates of effectiveness, based on their clinical experience.

**Estimates of effectiveness and key assumptions**
In the CT plus PET plus CT-guided needle biopsy strategy arm, if both CT and FDG-PET were positive, it was assumed that 20% of the patients underwent direct surgery and 80% underwent CT-guided needle biopsy. When the chest CT examination was positive but FDG-PET was negative, it was assumed that 20% of the patients underwent CT-guided needle biopsy, while 80% were followed up by an unenhanced chest CT.

**Measure of benefits used in the economic analysis**
The summary benefit measure was the accuracy associated with each diagnostic strategy. It was obtained using a modelling approach. The number of surgeries for benign SPN (false-positives) and the number of cancer misdiagnosed as a benign SPN (false-negatives) were also reported for each strategy.

**Direct costs**
The perspective adopted in the study appears to have been that of the National Health Insurance system in Japan. The health services considered in the economic evaluation were diagnostic tests (including the costs of diagnostic procedure and radiological or/and pathological interpretations) and thoracotomy. The treatment of complications associated with needle biopsy (such as pneumothorax) was also considered. The unit costs were not presented separately from the quantities of resources used. The cost of thoracotomy came from the authors’ institution, while the costs of diagnostic tests were estimated from data from the Japanese Ministry of Health, Labour and Welfare. The resource use data came mainly from the literature. The price year was not explicitly reported. Discounting was not relevant since the costs were incurred during a short timeframe.

**Statistical analysis of costs**
The costs were treated deterministically.

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

**Currency**
Japanese yen (¥). The costs were also reported in US dollars ($).

**Sensitivity analysis**
A univariate sensitivity analysis was carried out to assess the impact of changing the prevalence rate (range: 0 - 100%) on the results of the decision model. The costs were not varied because they were considered fixed in Japan.
Estimated benefits used in the economic analysis
The estimated accuracy was 0.67 with CT alone, 0.92 with CT+PET, 0.96 with CT+PET+biopsy and 0.95 with CT+biopsy.

In a cohort of 1,000 patients with a 10% prevalence of lung cancer (100 patients):
the number of false-positives was 361.4 with CT alone, 115.2 with CT+PET, 65.8 with CT+PET+biopsy and 65.2 with CT+biopsy; and
the number of false-negatives was 1 with CT alone, 4.2 with CT+PET, 21.4 with CT+PET+biopsy and 23.9 with CT+biopsy.

Cost results
The estimated cost per patient was Y765,203 ($6,337) with CT alone, Y405,997 ($3,383) with CT+PET, Y328,733 ($2,739) with CT+PET+biopsy and Y308,724 ($2,573) with CT+biopsy.

Synthesis of costs and benefits
An incremental cost-effectiveness ratio (i.e. the cost per accurate case) was calculated to combine the costs and benefits of the alternative diagnostic strategies.

The incremental analysis showed that CT+PET, CT+PET+biopsy and CT+biopsy dominated the reference strategy of CT alone, which was less effective and more expensive. The most cost-effective strategy was CT+biopsy. However, the number of lung cancer cases that were incorrectly diagnosed as a benign SPN was larger in the strategies using CT-guided needle biopsy and/or FDG-PET than in the CT alone strategy.

The sensitivity analysis showed that the costs increased regardless of the strategy when prevalence increased. At a very high prevalence rate, the cost per patient with the four strategies was similar.

The use of FDG-PET and/or CT-guided needle biopsy had the higher accuracy between a prevalence of 0 and 60% in comparison with the CT alone strategy. Also, the CT plus PET strategy had the higher accuracy at a prevalence of cancer up to 80%.

At a prevalence of cancer up to 55%, all strategies using CT-guided needle biopsy or/and FDG-PET were cost-saving. CT plus CT-guided needle biopsy was the optimal strategy at a prevalence of up to 85%.

Authors’ conclusions
The use of computed tomography (CT)-guided needle biopsy and/or fluorodeoxyglucose positron emission tomography (FDG-PET) was a cost-effectiveness diagnostic option for the work-up of solitary pulmonary nodules (SPNs) in Japan. This conclusion held under a wide range of prevalence rates. The authors noted that the selection of CT-guided needle biopsy and FDG-PET should depend not only on the cost-effectiveness, but also on variable patient factors (patient preferences) and accessibility to the modalities.

CRD COMMENTARY - Selection of comparators
The selection of the comparators was appropriate as it reflected the diagnostic tools available for the investigation of SPNs. However, the authors pointed out that FDG-PET was not readily available in Japan. You should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness evidence came from a review of the literature. The methods and conduct of the review were not reported. In addition, the search methods and inclusion or exclusion criteria for the primary studies were not described. Some details on the design and characteristics of the patients enrolled in the primary studies were provided. The issue
of homogeneity of the primary studies was not addressed and the primary estimates were not combined. Some assumptions were made. Only one key clinical input (cancer prevalence) was varied in the sensitivity analysis.

Validity of estimate of measure of benefit
The summary benefit measure represents an intermediate clinical end point because the final impact of the interventions on the patients' health was not assessed. Further, the use of accuracy as a benefit measure limits the possibility of making comparisons with the benefits of other health care interventions.

Validity of estimate of costs
The cost analysis reflected the context of the Japanese health care system, thus it is hardly transferable to other settings. The source of the data was reported. The breakdown of the cost categories was reported in a narrative manner, but the unit costs were not presented separately from the quantities of resources used. The price year was not reported, although some costs were estimated in 2002. In general, it is difficult to replicate the analysis in other settings and to reflate the cost results in other time periods. The costs were treated deterministically, and no sensitivity analyses were carried out because the authors stated that costs were fixed within the Japanese health care system.

Other issues
The authors compared their findings with those from a published study carried out in Japan that had reached different conclusions. The authors explained that different model assumptions were made, which could justify the contrasting results. The issue of the generalisability of the study results to other settings was not addressed, and the analysis focused on the Japanese setting. A very limited sensitivity analysis was performed, thus the external validity of the analysis was low. The authors noted some limitations of their study. First, all SPNs were assumed to be operated on regardless of cancer staging, which might not reflect actual treatment patterns. Second, the amount of time required to obtain a diagnosis was an important factor in the choice of strategy, which is strictly related to the availability of the diagnostic tool.

Implications of the study
The study results suggested that the introduction of CT-guided needle biopsy and FDG-PET to chest CT for the assessment of SPNs has the potential to be cost-effective in Japan.

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None stated.

Bibliographic details

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Other publications of related interest

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