Cost-effectiveness analysis of screening for lung cancer with low dose spiral CT (computed tomography) in the Australian setting

Manser R, Dalton A, Carter R, Byrnes G, Elwood M, Campbell D A

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 annual spiral computed tomography (CT) for the screening of lung cancer (LC) over a 5-year interval. Individuals were referred for screening by local medical officers. Suspicious lesions were referred to an appropriate specialist for evaluation, further diagnostic work up and treatment.

Type of intervention
Screening.

Economic study type
Cost-effectiveness analysis and cost-utility analysis.

Study population
The study population comprised a hypothetical cohort of individuals aged 60 years and older who were current smokers. Specific sub-groups of patients were considered in the analysis.

Setting
The setting was primary care. The economic study was carried out in Australia.

Dates to which data relate
The clinical data came from studies published from 1974 to 2003. The costs and some resource use data were estimated from sources published between 1995 and 2002. The price year was 2002.

Source of effectiveness data
The effectiveness evidence was derived from a synthesis of completed studies, supplemented with authors' opinions.

Modelling
A Markov model was constructed to assess the costs and benefits of spiral CT screening versus no screening in a hypothetical cohort of 10,000 individuals. The time horizon of the model was 15 years after the onset of screening. The cycle length was 3 months. The health states considered were:

healthy,
postoperative after surgery for false positive,
postoperative following surgery for lung cancer,
localised non-small-cell LC (NSCLC) (disease free after treatment),
regional NSCLC (disease free after treatment),
LC "overdiagnosed" by screening,
metastatic NSCLC,
terminal phase LC,
false positive (anxiety associated with expectant management), and
dead.

The decision trees considered for usual care or CT screening were depicted graphically.

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

the annual incidence of NSCLC;
the sensitivity and specificity of CT;
the proportion of cancers in the screened group that are Stage I;
the proportion of cancers detected that are "overdiagnosed”;
the probability of false-positive examinations being further investigated with fine needle aspiration or bronchoscopy;
the probability of false-positive results being referred for surgical biopsy;
the surgical mortality rate;
adherence with screening; and
the utility values.

All-cause mortality was also estimated from Australian life tables.

Study designs and other criteria for inclusion in the review
It was unclear whether a systematic review of the literature was undertaken to identify the primary studies. The primary studies appear to have been identified selectively. No details of the primary studies were reported.

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**
Approximately 17 primary studies provided evidence.

**Methods of combining primary studies**
Most of the primary estimates were combined by calculating weighted averages.

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

**Results of the review**
The annual incidence of NSCLC was 552 per 100,000 in the non-screened cohort.

The sensitivity of CT was 0.81 (best case 1; worst case 0.65) and the specificity was 0.76 (best case 0.95; worst case 0.49).

The sensitivity of an annual CT screen was 0.86 (best case 1; worst case 0.65) and the specificity was 0.97 (best case 0.99; worst case 0.87).

The proportion of cancers in the screened group that are Stage I was 0.69 (best case 0.85; worst case 0.4).

The proportion of cancers detected that are "overdiagnosed" was 0.12% (best case 0; worst case: 0.2).

The probability of false-positive examinations being further investigated with fine needle aspiration or bronchoscopy was 0.033 (best case 0.003; worst case 0.086).

The probability of false-positive results being referred for surgical biopsy was 0.019 (best case 0.006; worst case 0.067).

The surgical mortality rate was 0.02 (best case 0.016; worst case 0.04).

The utility in individuals with nodules being followed on CT was 0.98 (best case 1; worst case 0.96).

The utility in individuals with screen-detected localised cancer was 0.88 (best case 0.93; worst case 0.88).

The adherence with baseline screening was 100% (best case 100; worst case 86).

The adherence with annual screening was 86% (best case 98; worst case 74).

The utility values were:
0.88 for postoperative after surgery for false positive;
0.88 for localised NSCLC (disease free after treatment);
0.80 for regional NSCLC (disease free after treatment);
0.69 for both metastatic NSCLC and terminal phase LC; and
0.98 for false positive (anxiety associated with expectant management).

**Methods used to derive estimates of effectiveness**
The authors made some assumptions to derive estimates of effectiveness.
Estimates of effectiveness and key assumptions
The utility values were 0.80 for postoperative following surgery for LC and 0.88 for LC "overdiagnosed" by screening. It was assumed that all individuals attended for follow-up and treatment of any abnormalities detected.

Measure of benefits used in the economic analysis
The summary benefit measures used were the life-years (LYs) and quality-adjusted life-years (QALYs). These were estimated using a modelling approach. QALYs were calculated as the sum of the LYs estimated to have been spent in each health state, after multiplying each year by the utility weight. The utility weight was either derived from the literature or based on authors' opinions. Expected survival was discounted at an annual rate of 3%.

Direct costs
The perspective adopted in the analysis was that of the health care sector, although some out-of-pocket patient expenses (the Medicare gap) were also included. The health services included were CT scan, physician consultation for those with positive CT but not requiring immediate invasive investigation, surgery, stage-related treatment (including radiotherapy and medical follow-up care), terminal care, chemotherapy, and recruitment (using a letter recommending screening).

The unit costs were not presented separately from the quantities of resources used for most items, as some costs were reported as macro-categories. Most of the costs were estimated from Medicare Benefits Schedule. The cost of recruitment came from an Australian coordinate breast cancer-screening programme. The costs of surgery were taken from Australian Refined Diagnosis Related Groups. Resource use was estimated from published sources and experts’ opinions. Discounting was relevant, owing to the long timeframe of the analysis, and a discount rate of 3% was applied. The price year was 2002 and those costs estimated in earlier times were updated to 2002 values using the health deflation from the Australian Institute of Health and Welfare Health Expenditure series.

Statistical analysis of costs
No statistical analyses of the costs were carried out.

Indirect Costs
The indirect costs were not taken into consideration.

Currency
Australian dollars (Aus$).

Sensitivity analysis
Extensive sensitivity analyses were performed to assess the robustness of the model results (cost-effectiveness and cost-utility ratios) to variations in the model inputs. Both clinical and economic parameters were varied in the sensitivity analysis. Alternative values were generally derived from the literature or, alternatively, set by the authors. The recruitment costs were not considered in the base-case but were added only in the sensitivity analysis. The discount rates were varied between 0 and 7%. Best and worst scenarios for screening were also considered. The relationship between efficacy of screening (in terms of the expected reduction in lung cancer mortality at 7 years) and expected cost-effectiveness was investigated.

Estimated benefits used in the economic analysis
In a hypothetical cohort of 10,000 males aged 60 - 64 years with an annual probability of LC of 0.0052, the number of LYs was 104,121 in the screened group and 103,834 in the no screening group. The QALYs estimated in the two groups were not reported.
Cost results
In a hypothetical cohort of 10,000 males aged 60 - 64 years with an annual probability of LC of 0.0052, the total discounted costs were Aus$20,130,658 (undiscounted Aus$21,133,955) in the screening group and Aus$3,644,419 (undiscounted Aus$4,002,828) in the no screening group.

Synthesis of costs and benefits
Incremental cost-effectiveness ratios and cost-utility ratios were calculated to combine the costs and benefits of the screening strategy over the no screening strategy.

In a hypothetical cohort of 10,000 males aged 60 - 64 years with an annual probability of LC of 0.0052, the incremental cost per LY saved was Aus$57,325 and the incremental cost per QALY saved was Aus$88,583.

The corresponding values were:
- Aus$68,079 and Aus$137,798 for males aged 65 - 69 years with the same annual probability of LC;
- Aus$51,001 and Aus$88,583 for females aged 60 - 64 years with the same annual probability of LC;
- Aus$114,056 and Aus$278,219 for males aged 60 - 64 years with an annual probability of LC of 0.00283 (the probability for a current smoker aged 60 years who has smoked 15 cigarettes per day for 40 years); and
- Aus$33,617 and Aus$53,968 for males aged 60 - 64 years with an annual probability of LC of 0.00984 (the probability for a current smoker aged 60 years with a history of asbestos exposure who has smoked 50 cigarettes per day for 45 years).

Using a threshold of Aus$50,000 per LY saved to define a cost-effective intervention, screening was cost-effective only in specific cases. For example, low cost of CT, no discount, high proportion of Stage I cancers detected by screening, high CT sensitivity, or high CT specificity.

In the best-case scenario, the cost per LY saved was Aus$10,569 and the cost per QALY saved was Aus$10,834. In the worst-case analysis, screening was harmful with 67 LYs lost and 319 QALYs lost in the screened group (relative to no screening).

In the base-case analysis, LC mortality (including deaths related to surgery, but excluding deaths from other causes in individuals with LC) was reduced by 27% and all-cause mortality by 2.1%.

Using a threshold value of Aus$50,000 per QALY, a 40% or greater reduction in lung cancer mortality by screening would be considered cost-effective. The authors pointed out that these values are dependent on model assumptions. Thus, for example, if the cost of CT was reduced to Aus$140 then a 30% or greater reduction in LC mortality was considered cost-effective. However, when model assumptions resembling actual epidemiological and clinical data were used, reductions in LC mortality of less than 20% were unlikely to be cost-effective.

The cost-utility ratios were sensitive to the utility values used in the model.

Authors' conclusions
Computed tomography (CT) for the screening of lung cancer (LC) would appear to be potentially cost-effective from the perspective of an Australian payer, but only if it is targeted at very high-risk individuals and screening is either highly effective or if CT screening costs fall substantially.

CRD COMMENTARY - Selection of comparators
The selection of the comparator (i.e. no screening) was appropriate because it represented usual care in Australia. You should decide whether this is a valid comparator in your own setting.
Validity of estimate of measure of effectiveness
The effectiveness evidence came from the literature. However, the methods and conduct of the review were not reported. In effect, it appears that the primary studies have been identified selectively. No information on the search and inclusion or exclusion criteria was provided. The number of studies included in the review was reported but the primary studies were not described. Thus, it was not possible to assess the validity of the primary studies. The methods used to calculate some clinical inputs were reported. Some assumptions were also made. The issue of uncertainty was extensively addressed in the sensitivity analysis.

Validity of estimate of measure of benefit
The benefit measures used in the analysis were appropriate as they captured the impact of the interventions on the most relevant dimensions of care, that is, survival and quality of life. Further, the use of QALYs and LYS enables comparisons with the benefits of other health care interventions. However, there was no information on the source use to derive the utility weights or the approach used to calculate the QALYs. The utility data appears to have come from a sample of experts. Discounting was applied, as Australian guidelines recommend.

Validity of estimate of costs
The perspective of the study was explicitly stated. It appears that all the relevant categories of costs have been included in the analysis. Details of the unit costs and quantities of resources used were not reported, as most of the costs were presented using macro-categories. This limits the possibility of replicating in detail the analysis in other settings. However, the presentation of macro-categories of cancer costs by stage is quite common. The source of the costs was reported and the assumptions made in the analysis were explicit. The cost estimates were treated deterministically but, as in the analysis of clinical data, extensive sensitivity analyses were performed to address the issue of uncertainty. The authors stated that learning curve issues or start-up costs were not considered in the model. The price year was reported, which aids reflation exercises in other time periods.

Other issues
The authors stated that their conclusions were consistent with those from a published study that found that CT screening is unlikely to be cost-effective without substantial reductions on mortality, high rates of adherence, or lower costs. However, the authors noted that more favourable estimates of CT screening cost-effectiveness had been published. The issue of the generalisability of the study results to other settings was not explicitly addressed, although several alternative scenarios were considered in the analysis. These enhance, in part, the external validity of the analysis. It was also pointed out that the screening evaluated in the current analysis was opportunistic and the cost-effectiveness of a more comprehensive screening programme was not investigated, although recruitment costs were investigated in the sensitivity analysis.

The authors noted that most of the variables used in the decision model were imprecise, owing to the high level of uncertainty. The model also had other limitations. For example, the use of assumptions favouring the screening option, imprecise estimates, and the fact that the potential impact of radiation exposure from CT examinations was not investigated (although current studies showed that such an impact was likely to be minimal).

Implications of the study
The study results showed the conditions under which opportunistic CT screening for LC could be cost-effective. The authors suggested that the availability of local epidemiological and economic data, as well as more robust quality of life estimates, could improve the validity and accuracy of the decision model.

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