Computed tomography screening for lung cancer in Hodgkin's lymphoma survivors: decision analysis and cost-effectiveness analysis
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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
Annual, low radiation dose, computed tomography (CT) screening for lung cancer in Hodgkin's lymphoma survivors was under investigation. This was compared with no screening.

Type of intervention
Screening.

Economic study type
Cost-utility analysis.

Study population
The study population comprised a hypothetical cohort of patients diagnosed with Stage IA-IIB Hodgkin's lymphoma at age 25, with screening starting 5 years after initial diagnosis and continuing until either death or the diagnosis of lung cancer.

Setting
The setting was not clear. The economic study was carried out in the USA.

Dates to which data relate
The effectiveness evidence was gathered from studies published between 1984 and 2003 and the Surveillance, Epidemiology and End Results (SEER) database for the period 1973 to 1999. The resource use and cost data were gathered from studies published between 1997 and 2002. The price year was 2002.

Source of effectiveness data
The effectiveness data were based on an ad hoc/non-systematic review of published studies, the SEER database and authors' assumptions.

Modelling
A Markov decision analytic model was used to compare annual, low-dose CT screening versus no screening in a hypothetical cohort of patients diagnosed with Stage IA-IIB Hodgkin's lymphoma at age 25, with screening starting 5 years after initial diagnosis. The model was used to predict the lifetime prognosis of the patients. The model consisted of several health states for Hodgkin's lymphoma survivors. These included no lung cancer, non-small-cell lung carcinoma (NSCLC) at localised, regional and distant stages, small-cell lung carcinoma and death. One-year cycles were running until the entire cohort of patients died.

The critical model structure assumptions included:
patients with a positive low-dose screening CT underwent a follow-up standard-dose diagnostic chest CT;

if the diagnostic chest CT showed benign disease, the patient underwent no further testing that year and continued with annual low-dose screening CT scans;

if the diagnostic chest CT showed suspicious findings, the patient underwent either a CT-guided biopsy or a thoracoscopic biopsy;

if the biopsy pathology was benign, the patient received no additional treatments that year and continued with annual low-dose screening CT scans; and

if the biopsy pathology was positive, the patient was diagnosed with and treated for lung cancer.

Outcomes assessed in the review
The following parameters were obtained from an ad hoc review:

l lung cancer incidence and stage;

m mortality from lung cancer;

s screening CT characteristics; and

q quality of life.

Study designs and other criteria for inclusion in the review
The study designs included in the review were retrospective studies, case-controlled studies and prospective studies. For data collected from the SEER registries, the study included only cases with invasive cancers that were actively followed. Cases identified by death certificate or autopsy data were excluded.

Sources searched to identify primary studies
The model parameters were based on journal references and the SEER public-use database.

Criteria used to ensure the validity of primary studies
Not reported.

Methods used to judge relevance and validity, and for extracting data
Not reported.

Number of primary studies included
Twenty-nine studies were included in the review as sources of effectiveness evidence.

Methods of combining primary studies
A narrative explanation was given of how the study results were combined. The range of results amongst the included studies was used for a sensitivity analysis of the parameters.

Investigation of differences between primary studies
The authors investigated differences between some of the primary studies, but they provided no explanation of these differences.
Results of the review

The probability of developing lung cancer in smokers per 10,000 person-years was 26.3% in 5 - 9 years after Hodgkin's lymphoma diagnosis, 44.5% in 10 - 14 years after the diagnosis, 69.6% in 15 - 19 years the diagnosis, and 90.1% in 20 or more years after the diagnosis.

The probability of developing lung cancer in non-smokers per 10,000 person years was 5.8% in 5 - 9 years after Hodgkin's lymphoma diagnosis, 9.8% in 10 - 14 years after the diagnosis, 15.4% in 15 - 19 years after the diagnosis, and 20.0% in 20 or more years after the diagnosis.

The prevalence of smoking was 25%. The proportion of lung cancers that were small-cell was 15%.

In unscreened patients, the percentages of patients at each NSCLC stage were 21.1% localised, 30.2% regional and 48.7% distant. In screened patients, the percentages were 82.8% localised, 16.2% regional and 1.0% distant.

The probability of dying from Hodgkin's lymphoma or causes associated with Hodgkin's lymphoma in the 6th year after diagnosis was 0.022. The probability of dying from small-cell lung cancer in the first year after diagnosis was 0.663. The probabilities of dying from localised, regional and distant NSCLC in the first year after diagnosis were 0.252, 0.477 and 0.824, respectively. The probability of a 30-year-old dying in a year from causes other than Hodgkin's lymphoma or lung cancer was 0.001.

The false positives per 1,000 screening CT scans were 85 in the first year of screening and 51 in subsequent years. The number of biopsies due to false positives per 1,000 screening CT scans was 3 in the first year of screening and 1.7 in subsequent years.

The quality of life weights for localised, regional and distant stages of NSCLC were 0.88, 0.80 and 0.69, respectively. The quality of life weights were 0.82 for small-cell lung cancer, 1 for Hodgkin's lymphoma in remission and 0.88 for false-positive screening CT.

Methods used to derive estimates of effectiveness

The authors made assumptions to derive estimates of model parameters.

Estimates of effectiveness and key assumptions

Some key assumptions used in the model were as follows.

The histology and stage distribution of lung cancer in unscreened Hodgkin's lymphoma patients was similar to the histology and stage distribution of lung cancer in the general population.

CT screening did not affect the incidence of lung cancer but changed the stage distribution at diagnosis for NSCLC and annual CT screening, thereby caused a stage shift towards earlier, more localised stages.

CT screening did not affect the stage distribution for small-cell lung cancer.

Capital equipment and resources were in place for conducting a programme of CT screening for lung cancer, and all patients adhered completely to the annual screening programme.

Measure of benefits used in the economic analysis

The outcome measures were life-years gained and quality-adjusted life-years (QALYs). Health-related quality of life adjustments or utilities for Hodgkin's lymphoma, small-cell lung cancer and localised, regional and distant stages of NSCLC were obtained from the medical literature (Earle et al. 2000 and Ng et al. 1999, see 'Other Publications of Related Interest' below for bibliographic details). Patients who had false-positive screening CT scans were assigned short-term losses in utility with values derived from the literature (Earle et al. 2000).
Direct costs
The direct costs included the costs of medical care for lung cancer, the long-term costs of care for Hodgkin's lymphoma, and the costs for diagnostic tests and office visits. The direct costs of medical care for lung cancer were obtained from a published study (Fireman et al. 1997, see 'Other Publications of Related Interest' below for bibliographic details). The long-term costs of care for Hodgkin's lymphoma were assumed on the basis of long-term costs of care for breast cancer, prostate cancer, colon cancer and non-Hodgkin's lymphoma reported in Fireman et al. 1997. The costs for diagnostic tests and office visits were obtained from 2002 National Physician Fee Schedules Relative Value Scale (American Medical Association 2002, see 'Other Publications of Related Interest' below for bibliographic details).

The resource quantities and the unit costs were not reported separately. The costs were discounted at an annual rate of 3% in the baseline analysis, in accordance with the recommendations of the Panel on Cost-effectiveness in Health and Medicine. All costs were converted to 2002 US dollars using the medical care component of the Consumer Price Index to adjust for inflation. The price year was 2002.

Statistical analysis of costs
The costs were treated deterministically.

Indirect Costs
Although the authors reported that a modified societal perspective was adopted, the indirect costs were not included in the analysis.

Currency
US dollars ($).

Sensitivity analysis
One-way sensitivity analyses were carried out to evaluate the effects of uncertainty in the probabilities, utilities and costs on the results. Threshold analyses were performed to evaluate how much lead-time, length-time or overdiagnosis bias would be necessary to make the incremental cost-effectiveness ratio exceed $100,000/QALY. The selection of ranges was derived from published studies and based on authors' assumptions.

Estimated benefits used in the economic analysis
Smokers undergoing annual CT screening had a life expectancy of 29.60 years, while those not undergoing screening had a life expectancy of 28.96 years. Non-smokers undergoing CT screening had a life expectancy of 32.31 years, whereas those not undergoing screening had a life expectancy of 32.15 years.

The expected benefit with CT screening was 0.64 years (7.7 months) for smokers and 0.16 years (2.0 months) for non-smokers. The expected benefit in quality-adjusted life expectancy was 0.58 QALYs (7.0 quality-adjusted months) for smokers and 0.14 QALYs (1.6 quality-adjusted months) for non-smokers.

Using a discount rate of 3%, the discounted life expectancy and QALYs were also reported.

Cost results
At the discounting rate of 3%, the total lifetime cost for smokers was $82,500 with annual low-dose CT screening and $74,500 without CT screening. The total discounted lifetime cost for non-smokers was $81,700 with annual low-dose CT screening and $75,500 without CT screening.

The discounted incremental lifetime cost of annual CT screening was $8,000 for smokers and $6,200 for non-smokers.
**Synthesis of costs and benefits**
The estimated benefits and costs were combined by calculating the incremental cost-effectiveness ratio.

The discounted incremental cost-effectiveness ratio for annual CT screening versus no screening was $30,800 per life-year ($34,100/QALY) for smokers and $97,400 per life-year ($125,400/QALY) for non-smokers.

The results were sensitive to the rates of lung cancer in Hodgkin's lymphoma survivors, the proportion of NSCLC detected at a localised stage by CT screening, the mortality rates from lung cancer, Hodgkin's lymphoma and other causes associated with Hodgkin's lymphoma, the cost of the annual low-dose screening and lead-time bias.

The threshold analysis showed that the incremental cost-effectiveness ratio for smokers exceeded $100,000/QALY only for a lead-time of 2.4 years or greater. In addition, the incremental cost-effectiveness ratio for smokers exceeded $100,000/QALY only if overdiagnosis accounted for 90% of the lung cancers detected in the first year of screening.

**Authors' conclusions**
Under the assumptions and literature-based estimates in the model, computed tomography (CT) screening for lung cancer increased expected survival by 7.7 months for smokers and 2.0 months for non-smokers. If early promising results for lung cancer screening hold, CT screening for lung cancer may increase survival and quality-adjusted survival among long-term survivors of Hodgkin's lymphoma. Further, CT screening appears to have a favourable cost-effectiveness ratio compared with other widely accepted screening tests, especially for smokers.

**CRD COMMENTARY - Selection of comparators**
Although no explicit justification was provided for the comparator used, it would appear to represent current practice in the authors' setting. You should decide if the comparator represents current practice in your own setting.

**Validity of estimate of measure of effectiveness**
The model parameters were based on an ad hoc review of the literature and authors' assumptions. No systematic review was undertaken. Although this is common practice with models, it does not always ensure that the best data available are used in the model. The estimates of parameters were arrived at by narrative synthesis. The authors did not report the methods used to derive the estimates of parameters and did not consider the impact of differences between the studies identified when estimating them. The authors justified some of their assumptions about the model parameters.

**Validity of estimate of measure of benefit**
The authors had defined the study type as a cost-effectiveness analysis. However, the correct type of analysis should be cost-utility analysis since the benefit was measured in QALYs. The health-related quality of life weights or utilities were obtained from medical literature. Since the model predicted lifetime benefit, effectiveness was discounted and the choice of discount rate was justified.

**Validity of estimate of costs**
The authors reported that the study had been conducted from a modified societal perspective, but the indirect costs were not included. The direct costs only covered medical costs and incurred (downstream) costs. The quantities and the costs were not reported separately. Since the model predicted lifetime costs, all costs were discounted and the choice of the discount rate was justified. The costs were adjusted for inflation and the price year was reported, which will aid any future reflation exercises.

**Other issues**
The authors compared their findings with those from other studies, finding them generally to be in agreement. The authors clearly addressed the issue of the generalisability of the results to other settings. The authors do not appear to have presented their results selectively and their conclusions reflected the scope of the analysis.
The authors reported a number of limitations to their study. For example, the long-term risk of lung cancer was derived from three large retrospective studies on Hodgkin's lymphoma patients from earlier years, who may not be representative of patients treated in the current era. In addition, the stage distribution of NSCLC in screened patients was derived from non-randomised, uncontrolled studies with short follow-up, which might have limited validity, and the actual stage-shift from CT screening might have been smaller. Finally, the analysis assumed that all patients adhered completely to the annual screening programme, which might have been overoptimistic.

Implications of the study
The results from this study implied that annual low-dose CT screening for lung cancer should be considered for long-term survivors of Hodgkin's lymphoma who have a significant smoking history (such as 10 pack-years). However, these results may not necessarily be applicable to Hodgkin's lymphoma patients treated in the current era.

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Other publications of related interest


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