Cost-effectiveness of screening for lung cancer with low-dose computed tomography: a systematic literature review

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Background: On 31 December 2013, the US Preventive Services Task Force rated low-dose computed tomography (LDCT) for lung cancer screening as level ‘B’ recommendation. Yet, lung cancer screening implementation remains controversial, particularly when considering its cost-effectiveness. The aim of this work is to investigate the cost-effectiveness of LDCT screening program for lung cancer by performing a systematic literature review. Methods: We reviewed the published economic evaluations of LDCT in lung cancer screening. MEDLINE, ISI Web of Science and Cochrane databases were searched for literature retrieval up to 31 March 2015. Inclusion criteria included: studies reporting an original full economic evaluation; reports presenting the outcomes as Quality-Adjusted Life Years (QALYs) gained or as Life Years Gained. Results: Nine economic evaluations met the inclusion criteria. All the cost-effectiveness analyses included high risk populations for lung cancer and compared the use of annual LDCT screening with no screening. Seven studies reported an incremental cost-effectiveness ratio below the threshold of US$ 100 000 per QALY gained. Conclusions: Cost-effectiveness of LDCT screening for lung cancer is an highly debatable issue. Currently available economic evaluations suggest the cost-effectiveness of LDCT for lung cancer screening compared with no screening and indicate that the implementation of LDCT should be considered when planning a national lung cancer screening program. Additional economic evaluations, especially from a societal perspective and in an EU-setting, are needed.
Introduction

Lung cancer is the most common cause of death from cancer worldwide, accounting for 1.8 million new cases (12.9% of total cancer cases) and 1.59 million deaths (19.4% of total cancer deaths) in 2012. Lung cancer has a 5-year survival rate of 15%. Survival rates are directly linked to the stage at the diagnosis, with 5-year survival of 52% for localized disease, 24% for regional disease and 4% for distant metastases. The high mortality rates are partly due to late diagnosis. At advanced stages, the cancer is rarely curable and patients incur significant treatment-related pain and costs with little or no survival benefit. Thus, timely detection in individuals at risk could prevent, interrupt or delay lung cancer progression.

The aim of lung cancer screening is to reduce lung cancer-related mortality by detecting more patients in earlier and potentially curable stages. Historical results of randomized controlled trials (RCTs) on the use of periodical chest X-ray (CXR) and/or sputum cytology for the secondary intervention of lung cancer were negative, and screening based on these techniques is therefore not recommended.

Low-dose computed tomography (LDCT) is a rapidly evolving, commonly available, advanced imaging technology in which X-ray detectors rotate around the body to produce a three-dimensional image of internal structures. Several studies tried to investigate whether screening for lung cancer by LDCT in high-risk subjects would lead to a decrease in lung cancer mortality: the Early Lung Cancer Action Project (ELCAP), the International Early Lung Cancer Action Program (I-ELCAP), the Mayo Clinic Experience, the results reported by Pastorino et al., the Lung Screening Study Feasibility Phase and the Pittsburgh Lung Screening Study (PLuSS). In 2004, the US Preventive Services Task Force (USPSTF) found inadequate evidence to recommend for or against screening for lung cancer with LDCT, chest radiography, sputum cytologic evaluation or a combination of these tests. Since then, many RCTs have been done and published, resulting in more data on the benefits and harms of screening.

Most recently, the National Lung Screening Trial (NLST), a large RCT was conducted over a total of 53,439 asymptomatic participants, 55–74 years of age, with a history of at least 30 pack-years of smoking history. The results showed that screening high-risk patients for lung cancer with LDCT reduces lung cancer mortality by 20% compared with CXR, providing demonstration of lung cancer mortality reduction with LDCT screening. Further, on 31 December 2013, the USPSTF updated the previous statement and recommended the annual screening for lung cancer with LDCT in adults aged 55–80 years who have a 30 pack-year smoking history and currently smoke, or have quit within the past 15 years. The USPSTF rated LDCT for lung cancer screening as level ‘B’ recommendation, which means that there is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial. However, the USPSTF did not consider in its assessment the costs of providing a screening program or the potential savings from a reduction in treatment of advanced lung cancer treatment.

Major concerns exist about the financial burden that a national LDCT screening program would impose on the national health care systems in an era in which the majority of them struggle to contain escalating expenditure. In 2006, Black et al. conducted a systematic review of the clinical and cost-effectiveness of LDCT screening for lung cancer from the UK’s National Health Service perspective, but was unable to draw any definitive conclusion, neither regarding the clinical effectiveness nor the cost-effectiveness. Hence, lung cancer screening implementation is still a matter of controversy.

Given the potential of early lung cancer detection in improving diagnosis, treatment and survival, the aim of the present study is to perform an updated systematic review of the cost-effectiveness of LDCT in lung cancer screening. This information may be useful to policy makers and could provide a base for future recommendations as new information becomes available.

Methods

Bibliographic search and inclusion criteria

We searched electronic databases for economic evaluations that assessed LDCT screening cost-effectiveness for lung cancer in cohorts of high-risk individuals in terms of smoking history. Identification of full economic evaluation studies was carried out through a search of MEDLINE, ISI Web of Science and Cochrane databases up to 31 March 2015. The following key words were used and combined to search the databases: (i) ['screening for lung cancer' OR 'lung cancer screening' OR 'lung cancer CT screening' OR 'lung cancer low-dose CT'] AND [LDCT OR low-dose computed tomography OR computed tomography]; and (ii) ['economic evaluation*' OR health technology assessment*] OR ('cost AND (effectiveness OR benefit OR utility OR consequence)). Finally, (i), (ii) and (iii) were combined with AND.

Inclusion criteria were: English language publication; full cost-effectiveness or cost-utility analyses; evaluations assessing the cost-effectiveness of screening high-risk patient for lung cancer with LDCT vs. usual care (i.e. the care provided once a diagnosis following symptoms has been made); outcomes presented as Quality Adjusted Life Years (QALYs) gained or as Life Years Gained (LYGs); and studies performed from the third party payer or societal perspective. Studies using non-US cost were also included. When multiple publications were retrieved from the same cost-effectiveness model, only the latest publication was taken into consideration.

Relevant articles were reviewed and assessed by A.P., who screened the titles, the abstracts, and the full texts. A.B. was later consulted before the final inclusion or exclusion decision was reached for each study.

The systematic literature review was reported according to the PRISMA statement.

Data extraction

For each included study, data relating to economic study design and cost-effectiveness ratios for each strategy evaluated were extracted by A.P. and checked by A.B. Details were extracted on pretested data extraction forms. Adjustment was made for results reported in non-US costs. The cost estimates were not updated to current rates, but instead they were kept in the base year as reported in the original publications. None of the authors was contacted for further clarifications.

Economic evaluation studies’ characteristics are summarized as type of economic analyses, country and the period of the study, perspective, study population, and smoking history of the included individuals; type of intervention and competitors; cost items, cost data in terms of sources, date, currency and discount rates; characteristics of economic evaluation models, including the type of evaluation model and the related sensitivity analysis.

Results

Study characteristics

Our search identified 196 articles that were potentially relevant for inclusion in the systematic review. After adjusting for duplicates, 117 studies remained for screening. After title and abstract reading, 101 studies were excluded because they did not meet inclusion criteria. Thus, the full text was analyzed in the 16 remaining articles. It appeared that one study was the updated version of a previous one, so the older was excluded. Six more studies were excluded because they did not meet the inclusion criteria as described in Figure 1. The manual checking of the references of located relevant papers and of studies that have cited those papers did not
bring additional studies. The final number of studies relevant for our review was 9.

The nine included studies vary in terms of study settings, data retrieval and analysis. Characteristics of the nine included studies are reported in Table 1. Information on data sources, data costs and description of economic evaluation models are all summarized in Table 2. The heterogeneity of the studies gives different cost-effectiveness results. Cost-effectiveness results, including the incremental cost-effectiveness ratios of establishing the LDCT as a screening method for lung cancer and the relative sensitivity analysis results, are all summarized in Table 3.

Of the nine included studies, seven studies were set in USA,
16–22 one in Australia, 23 and one in Israel. 24 Furthermore, three studies were published between 2001 and 2003, 20–22 four studies between 2005 and 2013 18,19,23,24 and two studies in 2014. 16,17 All the studies compared the use of LDCT for lung cancer screening with no screening in a high risk population in regards to smoking history, defined in terms of pack-years. An hypothetical cohort was modeled for a 15-year time horizon in three studies 18,19,23 and for a 40-year time horizon in one study, 20 whereas five studies constructed a decision tree. 16,17,21,22,24

**Base case incremental cost-effectiveness ratios**

Among the five studies that constructed a decision tree, two studies constructed a decision analytic model and evaluated the cost-effectiveness of annual LDCT screening in a US high-risk population defined following the USPSTF recommendation criteria; 16,17 in one study, the annual helical CT scan was compared with no screening using the published results from the ELCAP; 23 and two studies evaluated the cost-effectiveness of a single LDCT scan compared with usual care also incorporating data from the ELCAP 23 or using data from the Hadassah-Hebrew University Medical Center and from the Israel National cancer Registry. 24 Using a societal perspective, Black et al. 16 estimated the cost-effectiveness of screening with LDCT in the NLST. When no screening was compared with radiography, the latter was dominated, because it was more expensive than no screening but provided no health benefit; when LDCT screening was compared with no screening, the calculated incremental cost-effectiveness ratios (ICERs) were US$ 52 000 per life-year gained and US$ 81 000 per QALY gained. Pyenson et al. 17 evaluated the cost-effectiveness of LDCT lung cancer screening of the Medicare population at high risk for lung cancer that, following USPSTF recommendation criteria, accounted for approximately 4.9 million beneficiaries. From the Medicare perspective, the analysis estimated that one life-year is saved at a cost of US$ 18 452. ELCAP data were used by Marshall et al. 22 to develop a decision analytic model to compare the annual screening strategy with no screening in a high-risk cohort of patients between 60 and 74 years of age and with at least 10 pack-years of smoking history. Over a period of 5 years, they generated an incremental cost-effectiveness ratio of US$ 19 533 per QALY saved. Also Wisnivesky et al. 21 evaluated the cost-effectiveness of a single baseline LDCT scan for lung cancer screening individuals by incorporating data from the ELCAP into a decision analysis model and found an incremental cost-effectiveness ratio of US$ 2500 per year of life saved. Shmueli et al. 24 used a decision analytic framework to evaluate the decision to screen or not to screen from the health system perspective, and found a base-incremental cost per QALY gained of US$ 1464.

In four studies, hypothetical high-risk populations were used to build simulation models to estimate the cost-effectiveness of annual LDCT screening. 18–20,23 Villanti et al. 18 used a hypothetical

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**Figure 1** Flowchart of the study selection process

Records identified through MEDLINE database searching (n = 63)
 Records identified through ISI Web of Science database searching (n = 102)
 Records identified through Cochrane database searching (n = 31)

Records after duplicates removed (n = 117)

Records screened (n = 117)

Full-text articles assessed for eligibility (n = 16)

Studies included in qualitative synthesis (n = 9)

Records excluded because title and abstract were not relevant (n = 101)

Full-text articles excluded because analyses were not original, results were not in cost/QALY or cost/LYGs, studies were published before 2005, the study was on older version of a more recent article (n = 7)
Table 1 Characteristics of the nine studies included

<table>
<thead>
<tr>
<th>Study</th>
<th>Type of evaluation/synthesis</th>
<th>Country/time horizon/perspective</th>
<th>Study population</th>
<th>Smoking history of study population</th>
<th>Interventions</th>
<th>Competitors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Black et al. (2014)</td>
<td>CEA; total cost per LYG; CUA; total cost per QALY gained</td>
<td>USA; within-NLST trial and lifetime horizons; Societal</td>
<td>NLST population: 53,452 persons of age between 55 and 74 years</td>
<td>≥30 pack-years of smoking history</td>
<td>Three annual LDCT screening</td>
<td>No screening</td>
</tr>
<tr>
<td>Pyenson et al. (2014)</td>
<td>CEA; total cost per LYG</td>
<td>USA; Lifetime; US Commercial payers</td>
<td>High-risk US population covered by Medicare (smokers and former smokers aged 55–80 years counting for approximately 4.9 million beneficiaries</td>
<td>≥30 pack-years of smoking history and had smoked within the previous 15 years</td>
<td>Initial baseline protocol (first time an individual is screened) and annual repeat protocol (subsequent screenings)</td>
<td>No screening</td>
</tr>
<tr>
<td>Shmueli et al. (2013)</td>
<td>CUA; total cost per QALY gained</td>
<td>Israel; Lifetime; Healthcare system</td>
<td>842 asymptomatic moderate-to-heavy smokers (≥45 years old) for the screening program; 2906 patients diagnosed with NSCLC for the usual care arm</td>
<td>571 participants aged ≥50 years, with a smoking history of ≥10 pack-years. 271 participants aged ≥40 years, with any smoking history</td>
<td>Single CT scan</td>
<td>No screening</td>
</tr>
<tr>
<td>Villanti et al. (2013)</td>
<td>CUA; total cost per QALY gained</td>
<td>USA; 15-year follow up; US commercial payers</td>
<td>High-risk hypothetical cohort of 18 million adults (adults aged 50–64 years)</td>
<td>≥30 pack-years of smoking history</td>
<td>Annual LDCT screening over 15 years</td>
<td>No screening</td>
</tr>
<tr>
<td>McMahon et al. (2011)</td>
<td>CUA; total cost per QALY gained</td>
<td>USA; Up to 15 years of follow-up; Societal</td>
<td>Six hypothetical US high-risk cohorts of 500,000 individuals (males and females aged 50, 60 or 70 in 1990)</td>
<td>≥20 pack-years of smoking history</td>
<td>Annual CT screening</td>
<td>No screening</td>
</tr>
<tr>
<td>Manser et al. (2005)</td>
<td>CUA; total cost per QALY gained</td>
<td>Australia; 15-year follow up; Government as a third-party funder</td>
<td>High-risk hypothetical cohort of 10,000 Australian current male smokers (60–69 years)</td>
<td>Current smokers with a smoking history of 40 cigarettes per day for 40 years</td>
<td>Annual scan with spiral CT for 5 years starting at the age of 60 years</td>
<td>No screening</td>
</tr>
<tr>
<td>Mahedevia et al. (2003)</td>
<td>CUA; total cost per QALY gained</td>
<td>USA; 40-year time horizon; Societal</td>
<td>High-risk population of 100,000 hypothetical 60-year-old heavy smokers</td>
<td>&gt;20 pack-years of smoking history</td>
<td>Annual helical CT screening</td>
<td>No screening</td>
</tr>
<tr>
<td>Wisnivesky et al. (2003)</td>
<td>CEA; total cost per LYG</td>
<td>USA; Lifetime; Healthcare system</td>
<td>Persons aged ≥60 years, smokers, fit to undergo thoracic surgery, and no prior history of cancer</td>
<td>≥10 pack-years of smoking history</td>
<td>Single baseline LDCT scan</td>
<td>No screening</td>
</tr>
<tr>
<td>Marshall et al. (2001)</td>
<td>CEA; total cost per LYG; CUA; total cost per QALY gained</td>
<td>USA; 5-year time horizon; Healthcare system</td>
<td>Hypothetical cohort of 100,000 high-risk individuals between the ages of 60 and 74 years</td>
<td>≥10 pack-years of smoking history</td>
<td>Annual helical CT screening</td>
<td>No screening</td>
</tr>
</tbody>
</table>

CEA, Cost-Effectiveness Analysis; CUA, Cost-Utility Analysis; LDCT, Low-Dose Computed Tomography; LY, Life-Year; LYG, Life-Year Gained; NLST, National Lung Screening Trial; NRT, Nicotine Replacement Therapy; NSCLC, Non-Small Cell Lung Cancer; QALY, Quality-Adjusted Life-Year.
### Table 2 Characteristics of the nine papers reporting on economic evaluations of lung cancer screening

<table>
<thead>
<tr>
<th>Study</th>
<th>Cost items</th>
<th>Cost data sources</th>
<th>Date/Currency/Discount rate</th>
<th>Type of model</th>
<th>Sensitivity analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Black et al. (2014)</td>
<td>Directs medical costs (screening examination, diagnostic workup for positive screening results, lung cancer treatment) and indirect costs (time and travel for the subject and the caregiver)</td>
<td>Medicare reimbursement fees (2009); 2009 US pricing for hourly earning and automobile-mileage reimbursement</td>
<td>2009/US$/3%</td>
<td>Decision analysis model</td>
<td>One-way</td>
</tr>
<tr>
<td>Pyenson et al. (2014)</td>
<td>CT scanning, diagnostic evaluation, additional LDCT scan, biopsy, course of antibiotics, 30-min smoking-cessation program</td>
<td>Medicare reimbursement fees (2014)</td>
<td>2014/US$/None</td>
<td>Decision analysis model</td>
<td>One-way</td>
</tr>
<tr>
<td>Shmueli et al. (2013)</td>
<td>Stage-specific treatment costs and lifetime costs by stage at diagnosis (diagnostic and imaging procedures; inpatient and outpatient oncological care and treatments)</td>
<td>Medical records from the Hadassah Medical Center (2003–04)</td>
<td>2011/US$/Not stated</td>
<td>Decision analysis model</td>
<td>One-way and probabilistic</td>
</tr>
<tr>
<td>Villanti et al. (2013)</td>
<td>Annual lung cancer screening, all follow-up from suspicious nodules identified in the screening, lung cancer treatment for stages A, B and C in the first year of diagnosis, alternative types of smoking cessation programs</td>
<td>Medicare reimbursement fees (2012)</td>
<td>2012/US$/None</td>
<td>Actuarial model</td>
<td>One-way</td>
</tr>
<tr>
<td>McMahon et al. (2011)</td>
<td>CT screening; lung cancer diagnosis, staging, treatment; non-lung cancer medical costs; patient-time, caregiver-time; pharmaceuticals; smoking cessation intervention</td>
<td>Medicare reimbursement fees (2006); SEER-Medicare linked data; US Bureau of Labor Statistics (2006); Red Book, ThomsonReuters</td>
<td>2006/US$/None</td>
<td>Mathematic microsimulation model</td>
<td>One-way</td>
</tr>
<tr>
<td>Manser et al. (2005)</td>
<td>CT scan, follow up and treatment costs for positive screening tests (physician-based and hospital-based direct medical costs), out-of-pocket patient expenses</td>
<td>Medicare Benefits Schedule (2002)</td>
<td>2002/AUS$/3%</td>
<td>Markov Model</td>
<td>One-way</td>
</tr>
<tr>
<td>Mahedevia et al. (2003)</td>
<td>Screening (helical CT, follow-up diagnostic CT, antibiotic course, opportunity costs, travel time), cancer care, informal caregiving, diagnostic workup, specialty visit, chest radiograph, surgery, diagnostic complications, fine-needle aspiration biopsy</td>
<td>American Medical Association's 2001 National Physician Fee Schedules Relative Value Scale; literature</td>
<td>2001/US$/3%</td>
<td>Markov Model</td>
<td>One-way and multi-way</td>
</tr>
<tr>
<td>Wisnivesky et al. (2003)</td>
<td>LDCT scan, diagnostic CT scan, follow-up CT scan, physician-based and hospital-based direct medical costs incurred in the treatment of lung cancer, costs in the first year after the diagnosis, stage-specific costs for treatment</td>
<td>New York Presbyterian Hospital's financial system cost database</td>
<td>2000/US$/3%</td>
<td>Decision analysis model</td>
<td>One-way</td>
</tr>
</tbody>
</table>

LDCT, Low-Dose Computed Tomography.
population of adults aged 50–64 at high risk for lung cancer to assess the cost-effectiveness of LDCT screening for lung cancer over a 15-year time horizon. From a commercial payer perspective, the model revealed that the cost–utility ratio of repeated annual lung cancer screening compared with no screening was US$28 240 per QALY gained. McMahon et al. 19 applied a microsimulation model of lung cancer development to six US cohorts with smoking histories reflecting observed US patterns. Compared with no screening, annual screening per person with at least 20 pack-years of smoking history reduced lung cancer-specific mortality by 17.98–25.16% at 10 years at a cost of US$126 000–US$169 000 per QALY. Restricting screening to individuals with ≥40 pack-years, current smokers, or current smokers and recent quitters yielded a 25.16% at 10 years at a cost of US$126 000–US$169 000 per QALY. Restricting screening to individuals with a smoking history reduced lung cancer-specific mortality by 17.98–25.16% at 10 years at a cost of US$126 000–US$169 000 per QALY. Restricting screening to individuals with a smoking history reduced lung cancer-specific mortality by 17.98–25.16% at 10 years at a cost of US$126 000–US$169 000 per QALY.

The variation of the cost-effectiveness results with implementation of smoking cessation interventions was estimated by two studies. 18,19 Smoking cessation rates from 3% to 6%: US$ 75 300/QALY gained for quitting smokers; US$ 94 400/QALY gained for former smokers from US$ 300 to US$ 150, no anxiety from indeterminate nodules: US$ 42 500/QALY gained for current smokers; US$ 75 300/QALY gained for quitting smokers; US$ 94 400/QALY gained for former smokers from US$ 300 to US$ 150, no anxiety from indeterminate nodules: US$ 42 500/QALY gained for current smokers; US$ 75 300/QALY gained for quitting smokers; US$ 94 400/QALY gained for former smokers.

Sensitivity analyses
All the nine included studies performed a range of sensitivity analyses to the robustness of their findings. One-way sensitivity analysis was conducted by all the authors. Additionally, Mahedevia et al. 20 and Shmueli et al. 24 also performed a multi-way and a probabilistic sensitivity analyses, respectively. Results are summarized in Table 3.

All the studies evaluated changes in the cost of LDCT screening 16–24 overdiagnosis bias was addressed by six studies, 16,17,21–24 lead-time bias by three studies 21,22,24 and the stage shift probability by one. 20 The variation of the cost-effectiveness results with implementation of smoking cessation interventions was estimated by two studies. 18,19 In four studies, changes in the costs of lung cancer screening resulted in a slightly changed Incremental Cost Utility Ratio.

<table>
<thead>
<tr>
<th>Study</th>
<th>Base case results (expressed in terms of ICER)</th>
<th>Sensitivity analysis results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Black et al. (2014)</td>
<td>US$ 52 000/QALY and US$ 81 000/QALY gained</td>
<td>LDCT cost from US$ 285 to US$ 100; US$ 56 000/QALY gained</td>
</tr>
<tr>
<td>Pyenson et al. (2014)</td>
<td>US$ 18 452/QALY</td>
<td>LDCT cost from US$ 285 to US$ 500; US$ 110 000/QALY gained</td>
</tr>
<tr>
<td>Shmueli et al. (2013)</td>
<td>US$ 1464/QALY gained</td>
<td>50% decrease of overdiagnosis: US$ 55 000/QALY gained</td>
</tr>
<tr>
<td>Villanti et al. (2013)</td>
<td>US$ 28 240/QALY</td>
<td>LDCT cost from US$ 283 to US$ 188; US$ 120 000/QALY gained in men age 50</td>
</tr>
<tr>
<td>McMahon et al. (2011)</td>
<td>US$ 149 000/QALY gained</td>
<td>Smoking cessation rates from 3% to 1.5%: US$ 880 000/QALY gained in men age 50 and US$ 1 034 000/QALY gained in women age 50</td>
</tr>
<tr>
<td>Manser et al. (2005)</td>
<td>AUS 105 090/QALY gained</td>
<td>Smoking cessation rates from 3% to 6%: US$ 73 000/QALY gained in men age 50 and US$ 40 000/QALY gained in women age 50</td>
</tr>
<tr>
<td>Mahedevia et al. (2003)</td>
<td>116 300/QALY gained; US$ 558 600/QALY gained</td>
<td>LDCT cost from AUS 280 to AUS 140: AUS 60 651/QALY gained</td>
</tr>
</tbody>
</table>

EQ-5D, standardised instrument for use as a measure of health outcome; ICER, Incremental Cost-Effectiveness Ratio; LDCT, Low-Dose Computed Tomography; LY, Life-Year; LYG, Life-Year Gained; QALY, Quality-Adjusted Life-Year.

*2002 AUD/USD average exchange rate was 0.543050.
The effects of overdiagnosis were assessed also by Shmueli et al., 24 effectiveness ratio exceeded the US$ 50,000 per year of life saved. The link between the cost-effectiveness of CT screening for lung cancer and smoking cessation was also discussed by McMahon et al. 19 The group showed that incrementing smoking cessation rates from 3% to 6% brought to a reduction of the ICUR to US$ 73,000 per QALY saved in men and to US$ 40,000 per QALY saved in women aged 50 years.

Incorporating smoking cessation interventions in the annual lung cancer screening programs, resulted in ICURs ranging from US$ 16,198 to US$ 23,185 per QALY saved for the intensive intervention using generic Nicotine Replacement Therapy (NRT) and for light intervention, respectively. 18 The link between the cost-effectiveness of LDCT for lung cancer screening and smoking cessation was also discussed by McMahon et al. 19 The group showed that incrementing smoking cessation rates from 3% to 6% brought to a reduction of the ICUR to US$ 73,000 per QALY saved in men and to US$ 40,000 per QALY saved in women aged 50 years.

**Discussion**

Our systematic literature review gives an overall picture of the cost-effectiveness analyses of LDCT in lung cancer screening performed up-to-date. Despite the variation of the magnitude of the results reported by the economic evaluations included in our study, there is a consistent pattern that suggests the cost-effectiveness of LDCT for lung cancer screening. In fact, seven of the nine cost-effectiveness analyses reported an incremental cost-effectiveness ratio below the threshold of US$ 100,000 per QALY gained, indicating that the implementation of LDCT should be considered when planning a national lung cancer screening program.

Although economic evaluations, particularly in the USA, commonly use a figure of US$ 50,000 per life-year or quality-adjusted life-year gained as a threshold for assessing the cost-effectiveness of an intervention, 25 a common consensus has not been reached yet. In fact, leading health economists have recently recommended the use of a threshold of either US$ 100,000 or US$ 150,000 per QALY gained. 26 Consequently, the use of LDCT for lung cancer screening compared with no screening was reported to be cost-effective by five studies when the threshold of US$ 50,000 per QALY was considered. 17,18,21,22,24 The cost-effectiveness was proved by two additional studies when the threshold was raised to US$ 100,000 per QALY 16,23 and by further two studies when raised to US$ 150,000 per QALY. 16,19,20,23

The nine included studies vary in terms of logistical approaches to screening and incorporated quite different assumptions about survival, mortality and quality of life, leading authors to significant different conclusions. Depending on the modelling used and on the results obtained, in fact, some authors provided enthusiastic conclusions, whereas others were more conservative.

Pyenson et al. 17 stated the low-cost and cost-effectiveness of LDCT screening, claiming that the strategy fits well with the standard Medicare benefits. Shmueli et al. 24 concluded that LDCT lung cancer screening presents a good value for money and should be considered for inclusion in the Israeli National List of Health Services. Wisnivesky et al. 21 affirmed that their preliminary findings suggested the cost-effectiveness of LDCT screening for lung cancer. The findings in the cost-utility analysis of Villanti et al. 18 indicated that repeat annual lung cancer screening in a high risk cohort of adults aged 50–64 is highly cost-effective. Moreover, offering smoking cessation interventions with the annual screening program improved the cost-effectiveness of lung cancer screening between 20% and 45%. Also McMahon et al. 19 stated that the cost-effectiveness of CT screening will likely be strongly linked to achievable smoking cessation rates.

On the other side, the 2005 Australian study reported that the LDCT is unlikely to be a cost-effective intervention assuming a society’s willingness to pay US$ 50,000 per life years saved unless it achieved >20% reduction in lung cancer mortality; 23 and in 2003, Mahadevia did not consider advisable the direct-to-consumer marketing of helical CT screening for lung cancer. 20

Finally, Black et al. 16 concluded that, as soon as their cost-effectiveness results are obtained within the NLST, the determination of whether screening outside the trial will be cost-effective will depend on how the screening is implemented. Most probably justified by the year of publication, also Marshall conclusions were cautious, stating that the assumptions embedded in their model allowed to conclude that annual screening of high-risk elderly patients for lung cancer might be cost-effective under optimal conditions, but that longer term data were needed to confirm their results. 22

Several factors may explain the heterogeneity of the results obtained by the authors. First, the included studies base theirs analyses on assumptions rather than on robust evidence over the clinical effectiveness of LDCT. In fact, most of the authors made assumptions regarding the levels of mortality reduction in patients undergoing CT screening for lung cancer. These assumptions were based either on national registries or on literature findings. Only McMahon et al. and Black et al. estimations of life expectancy were grounded in strong evidence as it adopted the results of the NLST, which is the only completed clinical trial in the field performed up to date. 16,19 Second, survival rates are often reported in screening studies and used in cost-effectiveness reports. However, survival rates are said to be subject to lead-time bias and overdiagnosis bias as defined in the risk of bias for individual studies. The methods used for tackling these biases were reported in some but not in all studies included. Finally, all of the studies tried to estimate the actual size of the population to be screened if such an intervention was covered by an insurance scheme. However, only five of them managed to adopt a societal perspective, 16–20 whereas the other had a limited informative power for policymakers.

**Limitations**

Our systematic review has few limitations. First, only English-language publications were included. Second, the included studies relied on different methodologies, incorporated varying types of cost and were conducted in different country settings, making the comparison difficult. Another issue that should be considered is that the studies were conducted in different time periods.

**Conclusions**

Lung cancer is a lethal disease associated with substantial medical and economic burden. Although the USPSTF recommended the annual screening for lung cancer with LDCT, the assessment did not consider the costs of providing the service and many issues remain unresolved in the debate over the true cost-effectiveness of this intervention.

Our results suggest that the implementation of LDCT should be considered when planning a national lung cancer screening.
program. Seven of the nine studies that were included in our systematic literature review, in fact, reported an incremental cost-effectiveness ratio below the threshold of US$ 100,000 per QALY gained.

However, several issues require further investigation. Additional cost-effectiveness studies will need to base their estimations on actual clinical evidence and manage to successfully adopt a societal perspective when conducting their analyses. Further economic analyses are also necessary when considering the country setting, with particular attention to Europe. In such a way, decision makers will be better informed about whether or not to adopt LDCT under public coverage, given the scarcity of resources available.

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Key points

- The vast majority of the economic analyses of low-dose computed tomography (LDCT) in lung cancer screening performed up-to-date does not exceed the threshold of US$ 100,000 per Quality-Adjusted Life Year gained.
- From an economic point of view, the implementation of LDCT should be considered when planning a national lung cancer screening program.
- Additional data from sufficiently powered clinical trials will potentially strengthen the evidence of LDCT’s value for money.
- Further cost-effectiveness evaluations from a societal perspective and in EU-setting will likely be useful to decision makers that need to evaluate its adoption under public coverage.

References