# Long-term Oncologic and Financial Implications of Lung Cancer Screening

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**KEYWORDS**

- Lung cancer screening • Cost effectiveness • Oncologic implications
- Computed tomography screening future implementation

**KEY POINTS**

- Likely scenarios for implementation of computed tomography screening for lung cancer with focus on the screened populations and the screening method, the lung cancer detection rates, and the number of lives saved.
- Oncologic implications of computed tomography screening with focus on consequences of changes in disease stage, changes in pathology, and long-term scenarios and future research areas.
- Financial Implications of computed tomography screening with focus on costs of computed tomography screening, cost effectiveness, and long-term scenarios, including ways to increase cost effectiveness.

## INTRODUCTION

Low-dose computed tomography (LDCT) screening for lung cancer has not been implemented on a national scale anywhere in the world. In the United States, the recent recommendation by the US Preventive Services Task Force (USPSTF) to implement annual lung cancer screening[1] makes it probable that in the United States, national lung cancer screening in high-risk individuals will be a reality within a few years. Knowledge of effects and consequences of lung cancer screening is currently derived from randomized trials and selected cohort studies, and therefore predictions of possible general consequences must be interpreted with caution. Nevertheless, implementation of CT screening is expected to have substantial implications for lung cancer health care and treatment. Here the authors discuss the possible scenarios for CT lung cancer screening and give some suggestions for the long-term oncologic and financial implications of its implementation.

## BACKGROUND AND LIKELY SCENARIOS

### *The Screened Populations*

The National Lung Screening Trial (NLST) randomly assigned 53,454 current or former heavy smokers to either chest radiography (CXR) or LDCT for 3 annual screenings. The NLST study documented a statistically significant reduction in overall mortality by LDCT (relative risk [RR], 0.93; 95% confidence limits (cl), 0.86–0.99) and is the only trial showing statistically significant effect on lung cancer mortality (RR, 0.80; 95% cl, 0.73–0.93).[2] The NLST enrolled participants 55 to 74 years of age at the time of randomization who had a smoking history of at least 30 pack-years

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and were current smokers or had quit within the last 15 years.[2] The USPSTF recommends that the NLST criteria are followed, but the age limit should be extended to 80 years, and that screening should be discontinued once the individual has not smoked for 15 years.[1] The American Association for Thoracic Surgery has recommended similar selection criteria but additionally recommends screening in persons with a 20 pack-year smoking history and other conditions that produce a cumulative risk of lung cancer for at least 5% over the next 5 years in addition to lung cancer survivors 55 to 79 years of age.[3] The National Comprehensive Cancer Network recommends screening in persons ages 55 to 74 years who have at least a 30 pack-year smoking history and, if a former smoker, 15 years or less since quitting or persons ages 50 years or older who have at least a 20 pack-year smoking history and 1 additional risk factor. It does not recommend lung cancer screening in persons who are at moderate risk (age >50 years and >20 pack-year smoking history or secondhand smoke exposure but no additional lung cancer risk factors) or low risk (younger than 50 years or smoking history of <20 pack-years).[4] In our opinion, it is most likely that the USPSTF criteria will be adopted when screening is implemented in the United States. In Europe and Asia the scenario may well be much more differentiated. In the United Kingdom, the current CT screening trial, the UK Lung Screening Study (UK LS), has more restrictive selection criteria, targeting individuals with greater than 5% lung cancer risk to increase cost effectiveness.[5–7] The remaining European screening trials have adopted enrollment criteria close to the NLST criteria, although most included individuals with 20 pack-year smoking history and age down to 50 years.[8–13] Screening compliance will also have a great influence on the number of persons that will actually be screened when CT screening programs are initiated. In the UK Lung Screen,[5,14] compliance was only 30%, and in the NLST only between 10% and 15 % satisfied the criteria.[15]

### *Screening Method and Lung Cancer Detection*

In most trials including the NLST, screening has been performed annually,[2,10,11,13,16] but in the NELSON[17,18] and Multicentric Italian Lung Detection (MILD)[12] trials, both annual and biennial CT is evaluated. In the UK Lung Screen, a single CT screen approach has been adopted for the screening trial,[7] and biennial testing is evaluated before an eventual implementation of screening.[6] The USPSTF concluded that annual screening provides the greatest benefit in decreasing lung cancer mortality.[1,19] The NELSON trial has not yet reported their final results, but these are expected to have great influence on the policy in Europe. In the NLST, overall sensitivity of LDCT was 93.8% and was specificity 73.4%.[20]

The lung cancer detection rates depend on whether screening is a first (baseline) or subsequent incidence screening.[21] When discussing long-term effects of screening, it would seem most appropriate to use data from incidence screenings to simulate long-term implementation. One of the most critical issues raised by the NLST is the high false-positive rates of nearly 24%.[2] However, these rates may partly be explained by the lung nodule size cutoff criteria defining a positive screening result,[21] and only 2.5% of those with positive test results required further invasive diagnostic procedures.[2] In the European trials, false-positive and recall rates were much lower.[13,17,18] It is expected in the future that false-positive rates will be reduced by changes in definitions of a positive test result[22,23] and by extended use of radiologic volumetric software.[14,17,18,24]

In the NLST, a significant shift in lung cancer stages after screening was documented for the first time. This shift leads to an increase in frequency of lower lung cancer stages (stages I–II) and reduction in higher stages (stage III–IV).[2] Further analysis of the NLST data showed that the effect of screening on reducing in lung cancer mortality was dependent on the histology of the tumor. Patients with adenocarcinoma had the greatest reduction in mortality, and in squamous cell lung cancer, the effect was not significant.[25]

The number of lives saved by implementation of screening in the United States is estimated to be approximately 12.250 per year[15] and in the United Kingdom to be 956 lives saved per year.[6] The screening protocol suggested by USPSTF would result in a 14% reduction in lung cancer mortality or an estimated 521 lung cancer deaths prevented per 100,000 persons in the screened population. The harms associated with this screening protocol are an estimated overdiagnosis of 10% of screen-detected cases and radiation-induced lung cancer deaths of less than 1%.[1]

## ONCOLOGIC IMPLICATIONS

A recent systematic review of lung cancer screening studies using LDCT found 8 randomized trials and 13 cohort studies.[26] The largest study by far is NLST in the United States,[2] which has given us the compelling data leading to implications for all specialties involved in lung cancer diagnosis and treatment. Below are some implications concerning the oncologic specialty outlined.