Original Article

Annual Number of Lung Cancer Deaths Potentially Avertable by Screening in the United States

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BACKGROUND: The National Lung Screening Trial (NLST), which was conducted between 2002 and 2009, demonstrated that screening with low-dose computed tomography (LDCT) reduced lung cancer mortality by 20% among screening-eligible populations compared with chest x-ray. In this article, the authors provide an estimate of the annual number of lung cancer deaths that can be averted by screening, assuming the screening regimens adopted in the NLST are fully implemented in the United States. **METHODS:** The annual number of lung cancer deaths that can be averted by screening was estimated as a product of the screening effect, the US population size (obtained from the 2010 US Census data), the prevalence of screening eligibility (estimated using the 2010 National Health Interview Survey [NHIS] data), and the lung cancer mortality rates among screening-eligible populations (estimated using the NHIS data from 2000-2004 and the third National Health and Nutrition Examination Survey linked mortality files). Analyses were performed separately by sex, age, and smoking status, with Poisson regression analysis used for mortality rate estimation. Uncertainty of the estimates of the number of avertable lung cancer deaths was quantified by simulation. **RESULTS:** Approximately 8.6 million Americans (95% confidence interval [95% CI], 8.0 million-9.2 million), including 5.2 million men (95% CI, 4.8 million-5.7 million) and 3.4 million women (95% CI, 3.0 million -3.8 million), were eligible for lung cancer screening in 2010. If the screening regimen adopted in the NLST was fully implemented among these screening-eligible US populations, a total of 12,250 (95% CI, 10,170-15,671) lung cancer deaths (8990 deaths in men and 3260 deaths in women) would be averted each year. **CONCLUSIONS:** The data from the current study indicate that LDCT screening could potentially avert approximately 12,000 lung cancer deaths per year in the United States. Further studies are needed to estimate the number of avertable lung cancer deaths and the cost-effectiveness of LDCT screening under different scenarios of risk, various screening frequencies, and various screening uptake rates. ***Cancer* 2013;119:1381-5.** © *2013 American Cancer Society.*

KEYWORDS: lung cancer, screening, mortality, low-dose computed tomography, avertable death.

INTRODUCTION

Recently published results from the National Lung Screening Trial (NLST)[1] demonstrated that, compared with chest radiography (CXR), screening using low-dose computed tomography (LDCT) reduced lung cancer mortality by 20% among current and former smokers (those who quit $\leq$ 15 years previously) who were aged 55 years to 74 years and had smoked at least 30 pack-years. However, the annual number of lung cancer deaths that could potentially be averted nationally through the wide implementation of such an intervention is unknown. In this article, we estimated this number assuming the screening regimen adopted in the NLST is fully implemented among the entire screening-eligible population in the United States. In addition, we performed a brief literature review on the cost-effectiveness of LDCT screening.

MATERIALS AND METHODS

The number of lung cancer deaths avertable by screening was estimated using the following equation (Eq.1):

$$N = \sum_{i=1}^{2}\sum_{j=1}^{4}\sum_{k=1}^{2} E \times Pop_{ij} \times P_{ijk} \times R_{ijk} \tag{1}$$

in which N denotes the number of lung cancer deaths avertable by screening, i denotes sex, j denotes age group (55-59 years, 60-64 years, 65-69 years, and 70-74 years), k denotes smoking status (current and former smoker), E denotes the effect of screening on lung cancer mortality reduction (assuming a uniform effect of 20% for each group), Pop_{ij} denotes the population size for the group of sex i and age j, P_{ijk} denotes the prevalence of screening eligibility of smoking status k for the group of sex i and age j, and R_{ijk} denotes the lung cancer mortality rate for the smoking group k of sex i and age j. The values of each estimation parameter included in Eq.1 are listed in Table 1.

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See editorial on pages 1294-7, this issue.

DOI: 10.1002/cncr.27813, **Received:** April 11, 2012; **Revised:** May 22, 2012; **Accepted:** May 24, 2012, **Published online** February 25, 2013 in Wiley Online Library (wileyonlinelibrary.com)

TABLE 1. Information Used for Estimating Annual Number of Lung Cancer Deaths Avertable by Screening in the United States

		Prevalence, %[b]		Lung Cancer Death Rate (per 100,000 Person-Years)	
Age, Years	Population[a]	Eligible Current Smokers (95% CI)	Eligible Former Smokers (95% CI)	Eligible Current Smokers (95% CI)[c]	Eligible Former Smokers (95% CI)[d]
Men					
55-59	9,523,648	9.91 (7.75-12.07)	7.83 (5.82-9.85)	381.0 (216.4-670.9)	282.2 (156.5-505.0)
60-64	8,077,500	11.35 (9.00-13.69)	7.98 (5.96-10.00)	872.6 (549.8-1385.0)	646.4 (391.8-1078.5)
65-69	5,852,547	8.97 (6.64-11.30)	11.17 (8.58-13.76)	1564.8 (1020.3-2400.0)	1159.1 (708.5-1906.3)
70-74	4,243,972	6.10 (3.73-8.47)	12.15 (8.27-16.03)	1760.2 (1042.5-2972.0)	1303.8 (750.4-2265.9)
Women					
55-59	10,141,157	6.69 (5.04-8.35)	4.51 (3.09-5.93)	259.9 (116.8-578.6)	192.5 (91.1-413.8)
60-64	8,740,424	6.53 (4.91-8.16)	4.13 (2.79-5.47)	259.4 (108.0-623.2)	192.2 (86.4-430.3)
65-69	6,582,716	5.07 (3.38-6.75)	7.99 (5.74-10.24)	816.0 (424.6-1568.4)	604.5 (318.8-1148.3)
70-74	5,034,194	4.85 (2.85-6.85)	4.61 (2.98-6.24)	1341.1 (778.7-2309.6)	993.4 (564.4-1771.2)

Abbreviation: 95% CI, 95% confidence interval.
[a] Based on 2010 US Census data.
[b] Based on data from the 2010 National Health Interview Survey (NHIS).
[c] Based on NHIS 2000 through 2004 linked mortality files. Follow-up ended on December 31, 2006.
[d] Derived according to the relative risk (RR) (eligible current smokers vs eligible former smokers) of lung cancer mortality rates. The RR adjusted for age and gender was 1.35 (95% CI, 0.89-2.02), which was estimated using National Health and Nutrition Examination Survey III llinked mortality files.

We used the 2010 US Census data for age-specific and sex-specific population estimates.[2] The prevalence of screening eligibility was estimated among 7138 participants (aged 55-74 years) in the 2010 National Health Interview Survey (NHIS). Lung cancer mortality rates for screening-eligible current smokers were estimated using the NHIS linked mortality files for surveys from 2000 through 2004, in which 3383 screening-eligible current smokers were followed for vital status through December 31, 2006. For screening-eligible former smokers, lung cancer mortality rates were derived using the rates for screening-eligible current smokers and the relative risks (RRs) between screening-eligible current and former smokers. The RRs were estimated using the third National Health and Nutrition Examination Survey (NHANES-III) linked mortality files, which included 1010 participants aged 55 years to 74 years who were interviewed between 1988 and 1994 and followed through December 31, 2006. We used this indirect method to estimate the death rates for former smokers because NHIS surveys for 2000 through 2004 lacked information regarding smoking quantity for former smokers. The NHIS and NHANES are 2 ongoing nationally representative surveys of the US general population. Detailed descriptions of the NHIS, NHANES-III, and their linked mortality files can be found elsewhere.[3-6]

Statistical Analysis

The CROSSTAB procedure of SUDAAN software (release 10.0; RTI International, Research Triangle Park, NC) was used to estimate eligibility prevalence, accounting for unequal probabilities of selection, nonresponse, and the complex sample design of the NHIS. Poisson regression models were fitted to estimate mortality rates and RRs using SAS statistical software (release 9.2; SAS Institute Inc, Cary, NC). The 95% confidence intervals (95% CI) for the estimates of the number of avertable deaths were determined using a simulation method, in which random numbers were generated for all the parameters included in Eq.1, assuming that prevalence rate, log death rate, and log RR followed a normal distribution. Because the NLST report[1] did not provide a standard error estimate for the screening effect, we calculated it based on the NLST-reported morality rates for the groups undergoing LDCT and CXR. The simulation process was replicated 10,000 times to obtain a relatively precise 95% CI. Sensitivity analyses were performed using various values of the parameters included in Eq.1.

RESULTS

Table 2 shows the number of individuals within the US population who were eligible for lung cancer screening. In 2010, 14.3% of the US population aged 55years to 74 years or approximately 8.6 million Americans (95% CI, 8.0 million -9.2 million) met the NLST criteria for lung cancer screening, including 5.2 million men (95% CI, 4.8 million -5.7 million) and 3.4 million women (95% CI, 3.0 million -3.8 million).

Table 3 presents the annual number of lung cancer deaths that were avertable by screening. If LDCT screening is fully implemented among eligible populations, a

TABLE 2. US Population (in Thousands) Eligible for Lung Cancer Screening in 2010

Age, Years	Male		Female		Total	
	No.	95% CI	No.	95% CI	No.	95% CI
Current smokers						
55-59	944	738-1149	679	512-846	1621	1344-1899
60-64	916	727-1106	571	429-713	1486	1240-1732
65-69	525	389-661	334	223-445	859	678-1040
70-74	259	158-360	244	144-345	502	358-646
Former smokers						
55-59	746	554-938	457	313-602	1202	953-1450
60-64	645	482-808	361	244-478	1004	804-1205
65-69	654	502-805	526	378-674	1180	969-1391
70-74	516	351-680	232	150-314	741	557-924
Total	5211	4761-5661	3398	3043-3754	8596	8000-9193

Abbreviation: 95% CI, 95% confidence interval.

TABLE 3. Annual Number of Lung Cancer Deaths Avertable by Low-Dose CT Screening in the United States

Age, Years	Male		Female		Total	
	No.	95% CI	No.	95% CI	No.	95% CI
Current smokers						
55-59	719	304-1332	353	130-770	1072	583-1813
60-64	1599	707-2798	296	106-694	1895	966-3191
65-69	1643	732-2840	545	208-1097	2188	1209-3511
70-74	912	363-1716	654	257-1260	1566	(865-2575
Former smokers						
55-59	421	164-876	176	59-418	597	306-1113
60-64	834	350-1622	139	44-350	973	484-1795
65-69	1516	632-2886	636	228-1375	2152	1163-3735
70-74	1346	515-2723	461	179-951	1806	920-3286
Total	8990	6943-11,972	3260	2446-4720	12,250	10,170-15,671

Abbreviations: 95% CI, 95% confidence interval; CT, computed tomography.

total of 12,250 lung cancer deaths (95% CI, 10,170 deaths-15,671 deaths) could potentially be delayed or prevented annually in the United States through screening, including 8990 deaths (95% CI, 6943 deaths-11,972 deaths) in men and 3260 deaths (95% CI, 2446 deaths - 4720 deaths) in women.

Table 4 presents the results from sensitivity analyses with various screening eligibility rates, screening uptake rates, and screening effects. Under the optimal scenario (100% screening uptake rate and a 30% reduction in lung cancer death rates), the number of lung cancer deaths averted by LDCT screening is 18,375. If 70% of the 8.6 million eligible people are screened annually, there would be 8575 lung cancer deaths averted by LDCT screening.

DISCUSSION

We estimated that approximately 8.6 million Americans met the NLST criteria for lung cancer screening in 2010. Implementation of LDCT screening among NLST-defined screening-eligible populations has the potential to avert approximately 12,000 or 7.6% of the total lung

TABLE 4. Sensitivity Analysis of the Annual Number of Lung Cancer Deaths Avertable by Low-Dose CT Screening in the United States

	Annual No. of Lung Cancer Deaths Averted	
	7.0 Million Individuals Eligible for Screening as Reported in >the NLST[a]	8.6 Million Individuals Eligible for Screening as Estimated in the Current Study[a]
Base scenario[b]	9971	12,250
Screening effect		
15% reduction in lung cancer death rate	7478	9188
30% reduction in lung cancer death rate	14,956	18,375
Screening uptake rate		
50%	4985	6125
70%	6980	8575

Abbreviations: CT, computed tomography; NLST, National Lung Screening Trial.
[a] Assuming the age-gender distributions and ratios of former versus current smokers are the same between the 2 populations.
[b] Base scenario assumed that low-dose CT screening reduces lung cancer death rates by 20% and the screening uptake rate is 100%.

cancer deaths reported each year in the United States. Our estimate of the size of the screening-eligible population is larger than that estimated in the NLST report (7 million),[1] in which data sources and methods were not described. Our estimate was based on the most recently available NHIS survey (2010) and US census (2010) data.

We directly used the NLST-reported screening effect as an estimation parameter with which to estimate the number of avertable lung cancer deaths by screening. This approach is straightforward and easy to understand. However, the direct use of the NLST-reported screening effect confines our estimates to be interpreted within the context of the NLST study design and screening protocol. In the NLST,[1] there were 20% fewer lung cancer deaths reported over 6.5 years in the group invited to LDCT screening compared with the group invited to CXR screening among the randomized population of current and former smokers who were aged 55 years to 74 years and had smoked at least 30 pack-years. It is unclear whether screening also is effective among current or former smokers with a smoking history of < 30 pack-years and whether initiating screening at age < 55 years would result in additional lung cancer deaths being averted.[7] In addition, as noted in the NLST report, a 20% reduction in lung cancer mortality may be an underestimated effect of an ongoing screening program.[1] Ultimately, the magnitude of potential benefit from LDCT screening in the community remains to be determined. These are issues that need to be addressed with additional research, especially new findings from the NLST and other ongoing studies.[8-10]

In addition to the total number of avertable deaths, the cost-effectiveness of LDCT lung cancer screening is another area that deserves further research. The large variations noted among the existing estimates have prohibited researchers and policymakers from drawing a firm conclusion regarding the cost-effectiveness of LDCT screening.[11-16] Based on the number needed to screen to prevent 1 death from lung cancer in the NLST, Goulart et al estimated that the additional cost of LDCT screening to avoid 1 lung cancer death is $240,000.[11] Although this number is higher than conventional benchmarks for cost-effectiveness, it is based on an intention-to-treat analysis, includes cases diagnosed within the follow-up period after the screening rounds had ceased, and is a point-in-time estimate when not all study participants have equal follow-up. Via microsimulation modeling, McMahon et al found that the annual screening of current and former smokers aged 50 years to 74 years with at least 20 pack-years of cigarette exposure cost between $126,000 to $169,000 per quality-adjusted life-year gained.[14] In contrast, Pyenson et al reported that the annual screening of current and former smokers aged 50 years to 64 years with at least 30 pack-years of smoking saves a life-year at a cost of approximately $19,000.[15] Results from the Early Lung Cancer Action Program (ELCAP) indicated that the cost for a life-year saved by a single baseline CT scan was only $2500.[16]

Several factors might have affected our estimate of the annual number of lung cancer deaths avertable by screening. First, the control group in the NLST received screening with CXR, whereas the general population of the United States is unlikely to receive any screening. This could potentially lead to an underestimation of the number of avertable lung cancer deaths if CXR was of benefit in preventing lung cancer mortality. According to a review from the US Preventive Services Task Force in 2004, CXR screening is not beneficial compared with usual care.[17] However, recently published results from the Prostate, Lung, Colorectal, and Ovarian cancer screening trial indicated that CXR screening reduced lung cancer mortality by 11% (RR, 0.89; 95% CI, 0.80-1.00) when the analysis was restricted to cases diagnosed within 6 years of randomization and lead time was accounted for. Although no benefit was observed over long-term follow-up (approximately 12 years), the investigators were motivated to perform the restricted analysis because of concerns that a small effect had washed out because of the long enrollment period and cessation of screening after 4 rounds.[18] Second, the lung cancer mortality rates for screening-eligible populations were estimated based on deaths occurring between 2000 and 2006, possibly overestimating the current rates. However, the overestimation, if any, is expected to be small because age-specific, gender-specific, and smoking-specific death rates were used and survival for lung cancer has shown little improvement during the past decade.[19] Third, the use of self-reported smoking data may lead to an underestimation of the true number of screening-eligible individuals because smokers have been found to underreport their tobacco use. Finally, we assumed 100% screening of the target population, although this is unlikely to be achieved in practice. If the uptake rate is 70%, which is approximately the prevalence rate of mammography screening during the past 2 years among US women aged $\geq$ 50 years in 2010,[20] approximately 8600 lung cancer deaths would be averted annually by LDCT screening performed within the United States.

We estimated that approximately 12,000 lung cancer deaths could potentially be averted per year through the full implementation of LDCT screening among eligible heavy smokers in the United States, based on our current knowledge of screening. Further studies are needed to estimate the number of avertable lung cancer deaths and the cost-effectiveness of LDCT screening under different scenarios of risk, various screening frequencies, and various screening uptake rates.

FUNDING SUPPORT

Supported by the Intramural Research Department of the American Cancer Society.

CONFLICT OF INTEREST DISCLOSURES

The authors made no disclosures.

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