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ARTICLE

Impact of Lung Cancer Screening Results on Smoking Cessation

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Background Lung cancer screening programs may provide opportunities to reduce smoking rates among participants. This study evaluates the impact of lung cancer screening results on smoking cessation.

Methods Data from Lung Screening Study participants in the National Lung Screening Trial (NLST; 2002–2009) were used to prepare multivariable longitudinal regression models predicting annual smoking cessation in those who were current smokers at study entry (n = 15 489, excluding those developing lung cancer in follow-up). The associations of lung cancer screening results on smoking cessation over the trial period were analyzed. All hypothesis testing used two sided *P* values.

Results In adjusted analyses, smoking cessation was strongly associated with the amount of abnormality observed in the previous year's screening ($P < .0001$). Compared with those with a normal screen, individuals were less likely to be smokers if their previous year's screen had a major abnormality that was not suspicious for lung cancer (odds ratio [OR] = 0.811; 95% confidence interval [CI] = 0.722 to 0.912; $P < .001$), was suspicious for lung cancer but stable from previous screens (OR = 0.785; 95% CI = 0.706 to 0.872; $P < .001$), or was suspicious for lung cancer and was new or changed from the previous screen (OR = 0.663; 95% CI = 0.607 to 0.724; $P < .001$). Differences in smoking prevalence were present up to 5 years after the last screen.

Conclusions Smoking cessation is statistically significantly associated with screen-detected abnormality. Integration of effective smoking cessation programs within screening programs should lead to further reduction in smoking-related morbidity and mortality.

Abbreviations ACRIN, American College of Radiology Imagining Network; CI, confidence interval; CXR, chest x-ray; BMI, body mass index; LDCT, low-dose computed tomography; LSS, Lung Screening Study; NCI, National Cancer Institute; NLST, National Lung Screening Trial; OR, odds ratio; PLCO, Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial.

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The US National Lung Screening Trial (NLST) demonstrated that annual low-dose computed tomography (LDCT) lung cancer screening reduces lung cancer mortality by 20% compared with chest x-ray (CXR) screening (1). Consequently, several organizations, as well as the United States Preventive Services Task Force (2), have recommended lung cancer screening of high-risk individuals (3–7). Although lung cancer screening itself confers benefit through early detection and treatment, screening and screening results (whether related to lung cancer or other non–lung cancer diagnoses), may provide a "teachable moment" that encourages smoking cessation (8–16). If this is the case, then lung cancer screening may have the potential to reduce morbidity and mortality through multiple mechanisms. The four major causes of mortality in developed countries—cancer, cardiovascular disease, stroke, and respiratory disease—are linked to smoking, and risks for these diseases decline after smoking cessation (17,18). Advancing smoking cessation is a public health priority.

Past studies have investigated smoking behavior in lung cancer screening trials (14–16,19) and in one screening program (13). Most of them have investigated the impact of screening vs no screening on smoking behavior (14,15,19) or, in screened individuals, the impact of an abnormal vs a normal screen (13–16,19), with all abnormalities pooled. Several other studies have been relatively small, have only looked at short-term effects, or have only included a single screen on the next smoking evaluation (9,10,12), with two exceptions (11,13). The long-term impacts of specific graded screening results on smoking cessation have not been assessed.

Our study aim was to evaluate the impact of lung cancer screening results on smoking cessation over time, with screening results measured in several refined categories. We evaluated the associations between screening results and subsequent smoking behavior in baseline current smokers, adjusted for important factors.

Methods

Study Design

Our study used data collected in the NLST, which was a randomized, controlled, screening trial that studied the effect on lung cancer mortality of three annual lung cancer screens with LDCT vs CXR. Recruitment took place between August 2002 and April 2004. Three annual screenings were carried out starting with baseline (T0) and at one (T1) and two (T2) years later. T3 through T7 refer to the annual summary updates for the NLST cohort occurring at 3, 4, 5, 6 and 7 years, which were completed by self-reported questionnaire. NLST design, methods, and results have been reported (1,20,21). Participants were current and former smokers with a 30 or more pack-year smoking history, had smoked within the past 15 years, and were aged 55 to 74 years. Epidemiological data were collected by structured questionnaire at baseline, and selected follow-up data were collected each year after baseline in an annual summary update and included a question on current smoking behavior. The NLST received institutional review board approval at each participating center and at the National Cancer Institute (NCI).

The NLST was a collaborative effort, including the Lung Screening Study (LSS) component (10 sites that were administered by a contract from the NCI Division of Cancer Prevention) and the American College of Radiology Imaging Network (ACRIN) component (23 sites that were administered through an NCI Division of Cancer Treatment and Diagnosis grant). Of the 53 452 individuals enrolled in NLST, LSS sites enrolled 34 612 (65%). Investigators from the LSS and ACRIN groups developed their own epidemiologic questionnaires, resulting in differences in smoking behavior questions. This substudy includes participants from the LSS sites, and the ACRIN group will present their smoking analyses separately.

Of LSS participants, 16 265 (47.0%) were baseline current smokers. Of these, 776 (4.8%) developed lung cancer during follow-up and were excluded from analysis because their disease may have influenced their smoking behavior. Of the remaining 15 489 individuals, complete epidemiologic data for multivariable modeling were available for 14 621 (94.4%). We evaluated whether annual self-reported smoking behavior was associated with preceding screening results, adjusted for important factors. The LSS annual summary update questionnaire initially asked the question, "Did you smoke 20 cigarettes in the last 30 days?" On July 1, 2004, to attempt to better harmonize with ACRIN, the question was changed to "Have you smoked any cigarettes, even a puff, in the last seven days?" In the current analysis, we consider an individual to be a current smoker if they answered yes to either question. The transition from the first to second question was almost complete by T3 and is presented by study year in Supplementary Table 1 (available online).

Our primary predictor of interest was screening result, which was classified by study radiologists as one of the following: 1) normal, no abnormalities; 2) negative for lung cancer, minor other abnormality observed: LDCT, morphologically benign nodules or noncalcified nodules less than 4 mm; CXR, nodules containing benign patterns of calcification; 3) negative for lung cancer, clinically significant other abnormality observed: any finding requiring clinical follow-up (eg, chronic obstructive pulmonary disease); 4) positive (suspicious) for lung cancer: LDCT, noncalcified nodule measuring 4 mm or greater in any diameter; CXR, any noncalcified nodule or mass and adenopathy or effusion.

Screening results data collection forms were consistent between CXR and LDCT study arms. The study protocol did not advocate specific smoking cessation programs except to offer literature (Clear Horizons) to current smokers. Each site could elect to provide additional information, such as phone hotlines. No LSS sites provided active organized smoking cessation programs or involvement in randomized controlled trials of cessation.

Statistical Methods

Descriptive statistics overall and stratified by smoking status at study year 3 (T3) were carried out with contingency table analyses and χ^2 tests for categorical variables and t tests with unequal variances for continuous variables. T3 was selected as a relevant outcome point because it is the first time point when smoking behavior was reported after completion of the final screening at T2, given that we lagged the association of screening on smoking cessation by 1 year.

Generalized estimating equations with unstructured correlation and robust standard errors were used to prepare logistic regression models for longitudinal data. This method takes into account clustering of data within individuals due to repeated measures. In addition, we prepared longitudinal logistic regression random effects models. Both approaches led to identical conclusions. The generalized estimating equations results are more conservative and are presented here.

Covariables considered in models were those thought to be associated with smoking behavior a priori based on our previous research (19), expert opinion, and prior literature. Such covariables included sociodemographic factors (age, sex, race/ethnicity, education as an estimator of socioeconomic circumstance, and marital status), exposures (alcohol consumption, cigarette, cigar and pipe smoking histories, and secondhand smoke exposures), and medical history (body mass index [BMI], family history of lung cancer, personal history of cancer, history of comorbidities). We did not have data on biologic markers of smoking behavior and nicotine dependence. All models were adjusted for study year, randomization arm, and study center.

Nonlinear associations between continuous variables and the study outcome were assessed in models using restricted cubic splines (22). Four knots were used to describe three splines. Knot locations were based on percentile distribution of the data as described by Harrell (22) to ensure adequate coverage. Selected interactions of variables in the final model were evaluated. None were statistically significant, and they are not discussed further. We evaluated whether our final model and study conclusions differed by how the smoking status question was asked in the annual summary update by including these variables in the model and by stratifying on levels of these variables.

Statistics were produced using Stata MP 12.1 (StataCorp, College Station, TX). Hypothesis testing used two-sided tests with alpha error at less than .05.

Results

Study Population

The study population stratified by smoking status at T3 and overall is described in Table 1. Study participants were an average age of 60.6 years and were 58.7% male and 89.5% white. Table 2 presents

Table 1. Distribution of study variables in National Lung Screening Trial Lung Screening Study current smokers who were not diagnosed with lung cancer in study follow-up, overall and stratified by smoking status at study year 3 (T3)*

Variables	Overall No. (column %) or mean (SD, range) (n = 14661>	Not smoking at T3 No. (row %)† or mean (SD) (n = 3448; 23.5%)	Smoking at T3 No. (row %)† or mean (SD) (n = 11213; 76.5%)	*P*‡
Sociodemographic				
Age, y	60.6 (4.7; 55–74)	61.0 (SD = 4.9)	60.4 (SD = 4.7)	<.001
Sex				
Female	6053 (41.3%)	1309 (21.6%)	4744 (78.4%)	
Male	8608 (58.7%)	2139 (24.9%)	6469 (75.2%)	<.001
Race/ethnicity				
White	13082 (89.5%)	3092 (23.6%)	9990 (76.4%)	.005
Black	668 (4.6%)	149 (22.3%)	519 (77.7%)	
Asian	420 (2.9%)	94 (22.4%)	326 (77.6%)	
American/Alaskan Native	59 (0.4%)	17 (28.8%)	42 (71.2%)	
Hawaiian native/Pacific Islander	81 (0.6%)	14 (17.3%)	67 (82.7%)	
Mixed race	257 (1.8%)	48 (18.7%)	209 (81.3%)	
Refused/unknown	44 (0.3%)	20 (45.5%)	24 (54.6%)	
Education				
Less than HS complete	969 (6.6%)	213 (22.0%)	756 (78.0%)	
HS complete	3704 (25.4%)	834 (22.5%)	2870 (77.5%)	
Some post-HS training, no college	2286 (15.7%)	479 (21.0%)	1807 (79.1%)	
Associate degree/some college	3449 (23.6%)	796 (23.1%)	2653 (76.9%)	
Bachelor's degree	2275 (15.6%)	596 (26.2%)	1679 (73.8%)	<.001
Graduate or professional degree	1926 (13.2%)	517 (26.8%)	1409 (73.2%)	
Marital status				
With spouse	9477 (65.0%)	2394 (25.3%)	7083 (74.7%)	<.001
Without spouse	5113 (35.0%)	1039 (20.3%)	4074 (79.7%)	
Medical				
Body mass index, kg/m^2	27.0 (4.7; 13.5–60.0)	27.2 (SD = 4.9)	26.9 (SD = 4.7)	.0008
Family history of lung cancer				
No	11514 (80.0%)	2720 (23.6%)	8794 (76.4%)	1.00
Yes	2887 (20.1%)	682 (23.6%)	2205 (76.4%)	
Personal history of cancer				
No	13973 (95.3%)	3295 (23.6%)	10678 (76.4%)	.42
Yes	688 (4.7%)	153 (22.2%)	535 (77.8%)	
Comorbidity				
0	6661 (45.4%)	1549 (23.3%)	5112 (76.8%)	.30
1	5014 (34.2%)	1189 (23.7%)	3825 (76.3%)	
2	2098 (14.3%)	480 (22.9%)	1618 (77.1%)	
≥3	888 (6.1%)	230 (25.9%)	658 (74.1%)	
Exposures				
Pack-years smoked	54.9 (22.6; 29–412)	53.5 (SD = 21.7)	55.3 (SD = 22.8)	<.0001
Smoking intensity, cigarettes/d	25.9 (9.6; 10–201)	25.2 (SD = 9.2)	26.1 (SD = 9.8)	<.0001
Smoking duration, y	42.5 (6.3; 10–66)	42.4 (SD = 6.6)	42.5 (SD = 6.2)	.54
Pipe: regular use				
No	11822 (81.6%)	2656 (22.5%)	9166 (77.5%)	<.001
Yes	2674 (18.5%)	754 (28.2%)	1920 (71.8%)	
Cigar: regular use				
No	12444 (85.4%)	2812 (22.6%)	9632 (77.4%)	<.001
Yes	2120 (14.6%)	613 (28.9%)	1507 (71.1%)	
Secondhand smoke at home				
No	1598 (11.0%)	434 (27.2%)	1164 (72.8%)	<.001
Yes	12977 (89.0%)	2995 (23.1%)	9982 (76.9%)	
Alcohol score§	4.70 (5.3; 0–25)	4.60 (SD = 5.1)	4.73 (SD = 5.4)	.19
Trial related				
Randomization arm				
Spiral computed tomography	7375 (50.3%)	1757 (23.8%)	5618 (76.2%)	.38
Chest x-ray	7286 (49.7%)	1691 (23.2%)	5595 (76.8%)	

* HS = high school; SD = standard deviation.

† Row percentages are presented to allow easy calculation of smoking prevalence ratios comparing different levels of exposure.

‡ The *P* value comparing smokers to nonsmokers at T3 for categorical data is by χ^2 test and for continuous variables is by *t* test with unequal variances. All tests were two-sided.

§ Alcohol score is the average number of drinks consumed when drinking times the average number of times per month that alcohol was consumed.

Table 2. Frequencies and proportions of National Lung Screening Trial Lung Screening Study baseline current smokers who remained smokers stratified by their preceding screening results

Screening result Study year*	Normal (referent group for OR)	Minor abnormality, not suspicious for lung cancer†	Major abnormality, not suspicious for lung cancer†	Suspicious for lung cancer but stable from last screening image†	Suspicious for lung cancer (new or changed from last screen)†
Smokers at T1* by T0 screening result (n = 14 692)	4723/5403 (87.4%)	4749/5495 (86.4%) OR= 0.917 (0.819 to 1.026)	904/1064 (85.0%) OR= 0.813 (0.672 to 0.985)	Not applicable	2230/2730 (81.7%) OR= 0.642 (0.565 to 0.730)
Smokers at T2 by T1 screening result (n = 13 907)	3916/4713 (83.1%)	5051/6148 (82.2%) OR= 0.937 (0.847 to 1.037)	426/529 (80.5%) OR= 0.842 (0.668 to 1.068)	1412/1782 (79.2%) OR= 0.777 (0.675 to 0.893)	550/735 (74.8%) OR= 0.605 (0.502 to 0.730)
Smokers at T3 by T2 screening result (n = 13 525)	3406/4351 (78.3%)	5499/7210 (76.3%) OR= 0.892 (0.814 to 0.977)	365/498 (73.3%) OR= 0.761 (0.614 to 0.948)	555/751 (73.9%) OR= 0.786 (0.655 to 0.943)	514/715 (71.9%) OR= 0.710 (0.591 to 0.851)
Smokers at T4 by T2 screening result (n = 13 352)	3160/4291 (73.6%)	5114/7124 (71.8%) OR= 0.911 (0.835 to 0.993)	337/493 (68.4%) OR= 0.773 (0.630 to 0.952)	517/740 (69.9%) OR= 0.830 (0.697 to 0.988)	479/704 (68.0%) OR= 0.762 (0.639 to 0.909)
Smokers at T5 by T2 screening result (n = 13 129)	2881/4230 (68.1%)	4729/7017 (67.4%) OR= 0.968 (0.891 to 1.051)	310/481 (64.5%) OR= 0.849 (0.693 to 1.041)	469/717 (65.4%) OR= 0.886 (0.747 to 1.050)	435/684 (63.6%) OR= 0.818 (0.689 to 0.972)
Smokers at T6 by T2 screening result (n = 12 846)	2669/4140 (64.5%)	4372/6869 (63.7%) OR= 0.965 (0.890 to 1.047)	280/463 (60.3%) OR= 0.839 (0.686 to 1.027)	431/709 (60.8%) OR= 0.854 (0.723 to 1.010)	386/664 (58.1%) OR= 0.765 (0.645 to 0.907)
Smokers at T7 by T2 screening result (n = 10 777)	2190/3545 (61.8%)	3462/5703 (60.7%) OR= 0.956 (0.876 to 1.043)	235/386 (60.9%) OR= 0.963 (0.773 to 1.203)	354/609 (58.1%) OR= 0.859 (0.719 to 1.027)	303/534 (56.7%) OR= 0.812 (0.672 to 0.980)

* T0 to T7 refer to the study year after baseline. Three annual screenings were carried out starting with baseline (T0) and at one (T1) and two (T2) years later. T3 to T7 refer to the annual summary updates for the National Lung Screening Trial cohort occurring at 3, 4, 5, 6, and 7 years.

† Odds ratios (ORs) (95% confidence intervals) are for smoking for each follow-up period compared with normal screen as the referent group. Individuals who developed lung cancer in the follow-up period are excluded.

the cumulative cross-sectional proportions of participants who were smoking at follow-up stratified by screening results.

At T0, T1, and T2 screenings, 36.8 % (Table 2, example 5403/14 692), 33.9%, and 32.2% of screens were normal, respectively. Similarly, a positive (suspicious for lung cancer) result (new, unstable or stable) was received by 18.6%, 18.1%, and 10.8%, respectively, and 7.2%, 3.8%, and 3.7% were negative (not suspicious) for lung cancer but had another clinically significant abnormality found.

Screening Results and Subsequent Smoking

Table 2 and Figure 1 show the proportion of baseline current smokers who were smokers in subsequent years stratified by their preceding screening result. In almost all years for each screening result strata, smoking declined over time. Generally, for each study year, the relative relationship between screening result and smoking remained constant. The one exception occurred in individuals who had a T2 screen that had a major abnormality not suspicious for lung cancer. In this group, at T7, a slight increase occurred in smoking prevalence compared with at T6. This was the smallest subgroup and was vulnerable to response fluctuations. T7 occurred at the end of the trial, and a large decline in the cohort size occurred from T6 to T7 (16.1%).

The highest proportion of smoking occurred in those with a normal screen. The second highest proportion occurred in those who had a screen that had a minor abnormality not suspicious for lung cancer. An even lower fraction of smoking was observed in those whose screen had a major abnormality not suspicious for lung cancer. The smoking proportions in individuals who had screens that were suspicious for lung cancer but that were stable, unchanged from the previous screen, were similar to individuals with screens that had a major abnormality not suspicious for lung cancer. The lowest rate of smoking was observed in those who had a screen that was suspicious for lung cancer, which was a new or changing abnormality.

The cumulative impact of screening results on smoking prevalence appeared to be durable. Five years after the last screening (T7), a statistically significant difference was still observed between the different screening results (Figure 1; Table 2). For example, the proportion smoking at T7 in those who had T2 screens that were normal was 0.618 and in those who had screens that had an abnormality suspicious for lung cancer, stable or unstable, was 0.575 (odds ratio [OR] = 0.836; 95% confidence interval [CI] = 0.729 to 0.960).

Multivariable Longitudinal Logistic Regression Model Predicting Smoking

Our final multivariable logistic model of continued smoking in baseline current smokers (Table 3) found that increased risk of continued smoking was associated with younger age, lower education, being spouseless, lower BMI, history of heavier smoking intensity (cigarettes smoked per day), longer smoking duration, exposure to secondhand smoke at home, and no history of regular pipe or cigar smoking. BMI had a nonlinear relationship with subsequent smoking ($P_{\text{nonlinearity}} = .004$).

In multivariable analysis (Table 3), continued smoking was statistically significantly associated with screening result from the previous year ($P < .0001$). Compared with having a normal screen, the odds ratio for continuing smoking between T1 and T3 for

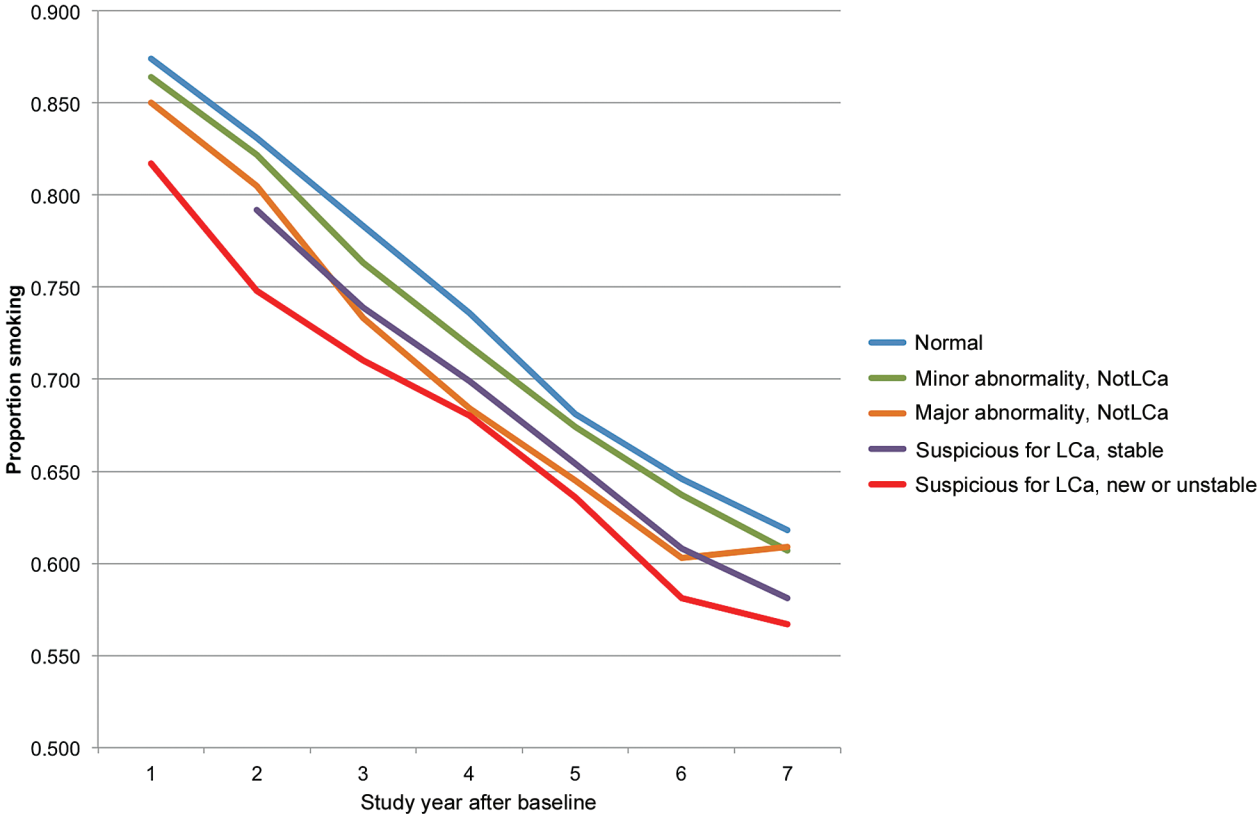

Figure 1. Proportion of National Lung Screening Trial (NLST) Lung Screening Study (LSS) baseline current smokers smoking at follow-up by screening result lagged to the preceding screen. The numbers and proportions corresponding to the line points in this figure are presented in Table 2. Proportion smoking at year 1 was classified by the baseline screening result, proportion smoking at year 2 was classified by year 1 screening result, proportion smoking at years 3 through 7 were classified by the last screen result, which occurred in study year 2. LCa, lung cancer; NotLCa, not suspicious for lung cancer.

individuals with screens that had a minor abnormality that was not suspicious for lung cancer was 0.914 (95% CI = 0.859 to 0.974; $P = .005$); for individuals with screens that had a major abnormality that was not suspicious for lung cancer, the odds ratio was 0.811 (95% CI = 0.722 to 0.912; $P < .001$); for individuals with screens that were suspicious for lung cancer but were stable from the previous screen, the odds ratio was 0.785 (95% CI = 0.706 to 0.872; $P < .001$); and for individuals with screens that were suspicious for lung cancer that were new or unstable, the odds ratio was 0.663 (95% CI = 0.607 to 0.724; $P < .001$). The likelihood of continued smoking was inversely associated with severity of screening results.

Sex, Hispanic ethnicity, comorbidities and intervention arm were evaluated in the multivariable model, and all had P values greater than .15 and had no important impact on estimates for the cessation outcome. Table 4 shows the adjusted odds ratios for screening result and continued smoking, stratified by intervention arm. Generally, the associations are present in both groups. The only exception occurs in those who were in the LDCT arm who had a minor abnormality not suspicious for lung cancer; they had no decline in smoking relative to those with a normal result.

During the course of the NLST, the annual LSS question that inquired about current smoking changed. In analysis we treated the two questions as if they equivalently measured current smoking status. We assessed whether the version of smoking question impacted the final model. In multivariable logistic modeling, the question version was not associated with the study outcome (OR = 1.046; 95% CI = 0.971 to 1.126; $P = .23$), and our study estimates for screen results did not change substantially. When the final model was stratified on smoking question version, the associations between screening results and smoking remained similar to those presented in Table 3. Version of study question did not impact findings.

Discussion

Our study found many factors to be associated with continued smoking in the lung cancer screening setting. Our current NLST LSS findings agree with our recent Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial findings that continued smoking is associated with younger age, lower socioeconomic circumstance, being spouseless, lower BMI, smoking intensity and duration, and secondhand smoke exposure (19). Our findings are consistent with those observed in other studies (11,13,14).

Our study demonstrates that in adjusted analysis, screening result is an important and statistically significant predictor of subsequent smoking and that smoking was inversely associated with severity of the screening result. These associations, for the most part, held whether the screening was by CXR or LDCT. These strong consistent associations have not been described previously. It has been speculated that individuals whose screens are normal

Table 3. Multivariable generalized estimating equation logistic regression model* for current smoking status (yes vs no) at study years 1, 2, and 3 after baseline for baseline current smokers (n = 14 621)

Predictor variables	Odds ratio (95% CI) *P*
Age, per 1 y	0.949 (0.941 to 0.959) <.001
Race/ethnicity†	
White	Referent group
Black	1.028 (0.867 to 1.218) .75
Asian	1.109 (0.845 to 1.455) .46
American/Alaskan Native	0.943 (0.555 to 1.602) .83
Hawaiian native/Pacific Islander	1.172 (0.679 to 2.021) .57
Mixed race	1.218 (0.922 to 1.611) .17
Refused/unknown	0.357 (0.219 to 0.582) <.001
Education, per 1 unit increase in 6 possible levels‡	0.976 (0.953 to 1.000) .051
Marital status, without partner vs with	1.261 (1.169 to 1.360) <.001
Body mass index,* kg/m^2, assessed with 3 RCSplines	NA§
Smoking intensity, cigarettes/d	1.010 (1.006 to 1.014) <.001
Smoking duration, y	1.028 (1.020 to 1.035) <.001
Secondhand smoke exposure at home, yes vs no	1.132 (1.018 to 1.259) .02
Pipe smoking, past or current regular user, yes vs no	0.830 (0.756 to 0.912) <.001
Cigar smoking, past or current regular user, yes vs no	0.740 (0.670 to 0.817) <.001
Screening result, lagged 1 year‖	
Normal	Referent group
Minor abnormality, not suspicious for lung cancer	0.914 (0.859 to 0.974) .005
Major abnormality, not suspicious for lung cancer	0.811 (0.722 to 0.912) <.001
Positive, suspicious for lung cancer but stable from previous screen	0.785 (0.706 to 0.872) <.001
Positive, suspicious for lung cancer, new or changed from previous screen	0.663 (0.607 to 0.724) <.001
Model constant, unexponentiated	4.794325

* This model is additionally adjusted for study year, study center, and randomization arm. CI = confidence interval; NA = not applicable; RCSplines = restricted cubic splines.

† The likelihood ratio test evaluating nested models with and without race/ethnicity had a *P* value of .04.

‡ Education levels are less than high school completed, high school completed, some post–high school, associate degree or some college, bachelor degree, and graduate or professional degree.

§ The exponentiated beta coefficients are not directly interpretable as odds ratios so are not presented here. The likelihood ratio tests *P* value for nested models including and excluding the three restricted cubic splines was .0003. The *P* value testing the nonlinearity of body mass index was .003. The knot locations for the body mass index splines were at 20.02, 25.74, 29.05, and 37.12. The beta coefficients for body mass index restricted cubic splines 1, 2, and 3 were −0.0472887, 0.1661889, and −0.5223123, respectively.

‖ To ensure a correct temporal sequence the previous years screening result was used to predict smoking behavior as reported in the annual summary update.

continue their unhealthy behaviors because they think they have a clean bill of health—the health-certificate effect. Although our findings do not present proof dispelling the health-certificate effect, our findings suggest that they were not a major problem, because those with normal screens had sharply declining prevalences of smoking over time that paralleled those observed in participants with abnormalities.

Although studies have investigated lung cancer screening and smoking behavior, none have looked at smoking cessation and screening results in detail. Styn and colleagues (2009) found that computed tomography (CT) screening results that led to abnormal results and a physician referral were associated with increased likelihood of smoking cessation 1 year later (23). Their study did not have repeated measurements or long follow-ups and had a simple summary measure of screening result. Townsend et al. (2005) evaluated the impact of three annual lung cancer screenings using CT (11). They used longitudinal analysis and found that an abnormal screening result was associated with smoking cessation. In the Early Lung Cancer Action Program (ELCAP) (13), an abnormal screening result was associated with a higher rate of point abstinence compared with those with normal results. This difference occurred primarily during the early screens, when the positive screening results were most likely to occur, and suggests that the impact of a positive screening result might be short-lived. Our much larger study included a richer assortment of covariables in modeling and used a refined multilevel measure of screening results and was able to evaluate a dose–response relationship. Failure of some studies to find an association between screening results and smoking cessation is likely because of misclassification or poor classification of screen results, lack of lagging predictor in analysis, and limited study power. In summary, our study agrees with some past studies and extends the relationship between screening result and smoking cessation.

Our study does have limitations. Our analysis summarized overall smoking cessation behavior but did not evaluate changing patterns of cessation–relapse. Such an analysis was not practical because the number of permutations is large (ie, 128).

Current smoking status was determined by self-report and was not biologically validated. This is not expected to lead to great misclassification and has been the assessment method in most lung cancer screening studies (10,11,13,15,16). Studts and colleagues conducted a validation study of self-reported smoking status among participants in a lung screening trial using urine cotinine as the gold standard (24). Excluding nicotine patch users, the kappa statistic for agreement was 0.96 (95% CI = 0.88 to 1.00), indicating excellent agreement.

Table 4. Multivariable generalized estimating equation logistic regression model* odds ratios for current smoking status (yes vs. no) and screening result, stratified by randomization arm

Screening result	Chest x-ray arm (n = 7239) Odds ratio (95% CI) *P*	Computed tomography arm (n = 7382) Odds ratio (95% CI) *P*
Normal	Referent group	Referent group
Minor abnormality, not suspicious for lung cancer	0.860 (0.796 to 0.930) <.001	1.009 (0.906 to 1.123) .88
Major abnormality, not suspicious for lung cancer	0.809 (0.651 to 1.005) .06	0.865 (0.742 to 1.008) .06
Positive, suspicious for lung cancer, but stable from previous screen	0.719 (0.548 to 0.942) .02	0.836 (0.727 to 0.962) .01
Positive, suspicious for lung cancer	0.714 (0.642 to 0.817) <.001	0.685 (0.601 to 0.781) <.001

* The model covariables included age, race/ethnicity, education, marital status, body mass index (kg/m^2), family history of lung cancer, smoking intensity and duration, exposure to secondhand smoke in the home, regular pipe or cigar smoking, study year, and study center as described in Table 3. Smoking status data were for years 1, 2, and 3 after baseline. The screening results were lagged to 1 year before smoking status and came from baseline and years 1 and 2 after baseline, respectively. Individuals who developed lung cancer in the follow-up period were excluded from analysis. CI = confidence interval.

The LSS annual summary update question asking about current smoking status changed during the course of follow-up. However, the study findings were consistent and statistically significant when the analysis was limited to one or the other question. Furthermore, the Pan-Canadian Early Detection of Lung Cancer Study of 2537 smokers asked both of these questions and found 96.7% and 96.2% agreement between them at years 1 and 2, indicating consistency between measures (25).

The LSS did not measure some potential confounders, such as nicotine dependence. However, we did include smoking intensity, a strong correlate of nicotine dependence, in multivariable models. Furthermore, it is unlikely that nicotine dependence or other potential confounders would lead to such a highly statistically significant consistent dose–response association ($P < .0001$).

Our study has several strengths. The NLST is a large, prospective study with repeated measures of smoking behavior and careful systematic classification of screening outcomes. In addition, it had a high percentage of women (41%), more than 10% of individuals from minority groups, and retention of 73% over 7 years. Our longitudinal data analysis made efficient use of data and provided interpretable summary statistics.

Our findings suggest that in the lung cancer screening setting, abnormal screening results may present a "teachable moment." On average, those with abnormal results suspicious for lung cancer reported approximately 6% lower rate of smoking compared with those with normal results. This represents a clinically relevant difference. Proven smoking cessation programs applied to such receptive individuals might further increase smoking cessation. Our findings strongly indicate that smoking cessation programs be incorporated into lung cancer screening programs.

Our findings need to be validated in other high-quality prospective studies in different populations. Future cost-effectiveness analyses and microsimulation models evaluating various lung cancer screening scenarios should take into account that abnormal lung screens are common in high-risk individuals and they are associated with increased rates of smoking cessation, which generally reduce morbidity and mortality and extend life expectancy.

Our study found that lung cancer screening results statistically significantly impact subsequent smoking behavior and may present a "teachable moment" for smoking cessation interventions. Future lung cancer screening programs should take advantage of this opportunity to apply effective smoking cessation programs.

References

1. Aberle DR, Adams AM, Berg CD, et al. Reduced lung-cancer mortality with low-dose computed tomographic screening. *New Engl J Med*. 2011;365(5):395–409.
2. Moyer VA. Screening for lung cancer: U.S. Preventive Services Task Force Recommendation Statement. *Ann Intern Med*. 2013. [published ahead of print December 31, 2013].
3. Bach PB, Mirkin JN, Oliver TK, et al. Benefits and harms of CT screening for lung cancer: a systematic review. *JAMA*. 2012;307(22):2418–2429.
4. Wood DE, Eapen GA, Ettinger DS, et al. Lung cancer screening. *J Natl Compr Canc Netw*. 2012;10(2):240–265.
5. Jacobson FL, Austin JH, Field JK, et al. Development of the American Association for Thoracic Surgery guidelines for low-dose computed tomography scans to screen for lung cancer in North America: recommendations of the American Association for Thoracic Surgery Task Force for Lung Cancer Screening and Surveillance. *J Thorac Cardiovasc Surg*. 2012;144(1):25–32.
6. Jaklitsch MT, Jacobson FL, Austin JH, et al. The American Association for Thoracic Surgery guidelines for lung cancer screening using low-dose computed tomography scans for lung cancer survivors and other high-risk groups. *J Thorac Cardiovasc Surg*. 2012;144(1):33–38.
7. Wender R, Fontham ET, Barrera E Jr, et al. American Cancer Society lung cancer screening guidelines. *CA Cancer J Clin*. 2013;63(2):106–117.
8. McBride CM, Emmons KM, Lipkus IM. Understanding the potential of teachable moments: the case of smoking cessation. *Health Educ Res*. 2003;18(2):156–170.
9. Ostroff JS, Buckshee N, Mancuso CA, et al. Smoking cessation following CT screening for early detection of lung cancer. *Prev Med*. 2001;33(6):613–621.
10. Cox LS, Clark MM, Jett JR, et al. Change in smoking status after spiral chest computed tomography scan screening. *Cancer*. 2003;98(11):2495–2501.
11. Townsend CO, Clark MM, Jett JR, et al. Relation between smoking cessation and receiving results from three annual spiral chest computed tomography scans for lung carcinoma screening. *Cancer*. 2005;103(10):2154–2162.
12. Taylor KL, Cox LS, Zincke N, et al. Lung cancer screening as a teachable moment for smoking cessation. *Lung Cancer*. 2007;56(1):125–134.
13. Anderson CM, Yip R, Henschke CI, et al. Smoking cessation and relapse during a lung cancer screening program. *Cancer Epidemiol Biomarkers Prev*. 2009;18(12):3476–3483.
14. Ashraf H, Tonnesen P, Holst Pedersen J, et al. Effect of CT screening on smoking habits at 1-year follow-up in the Danish Lung Cancer Screening Trial (DLCST). *Thorax*. 2009;64(5):388–392.
15. van der Aalst CM, van Klaveren RJ, van den Bergh KA, et al. The impact of a lung cancer computed tomography screening result on smoking abstinence. *Eur Respir J*. 2011;37(6):1466–1473.
16. Shi L, Iguchi MY. "Risk homeostasis"or "teachable moment"? the interaction between smoking behavior and lung cancer screening in the Mayo Lung Project. *Tob Induc Dis*. 2011;9(1):2.
17. Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health. *How Tobacco Smoke Causes Disease: The Biology and Behavioral Basis*

for Smoking-Attributable Disease: A Report of the Surgeon General. Atlanta: Centers for Disease Control and Prevention; 2010.
18. United States Public Health Service, Office of the Surgeon General, Office on Smoking and Health. *The Health Consequences of Smoking: A Report of the Surgeon General*. Rockville, MD: US Department of Health and Human Services, Public Health Service; 2004.
19. Barry SA, Tammemagi MC, Penek S, et al. Predictors of adverse smoking outcomes in the Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial. *J Natl Cancer Inst*. 2012;104(21):1647–1659.
20. Aberle DR, Berg CD, Black WC, et al. The National Lung Screening Trial: overview and study design. *Radiology*. 2011;258(1):243–253.
21. Aberle DR, Adams AM, Berg CD, et al. Baseline characteristics of participants in the randomized national lung screening trial. *J Natl Cancer Inst*. 2010;102(23):1771–1779.
22. Harrell FE. *Regression Modeling Strategies: With Applications to Linear Models, Logistic Regression, and Survival Analysis*. New York: Springer; 2001.
23. Styn MA, Land SR, Perkins KA, et al. Smoking behavior 1 year after computed tomography screening for lung cancer: effect of physician referral for abnormal CT findings. *Cancer Epidemiol Biomarkers Prev*. 2009;18(12):3484–3489.
24. Studts JL, Ghate SR, Gill JL, et al. Validity of self-reported smoking status among participants in a lung cancer screening trial. *Cancer Epidemiol Biomarkers Prev*. 2006;15(10):1825–1828.
25. McWilliams A, Tammemagi M, Mayo J, et al. Probability of cancer in pulmonary nodules detected on first screening computed tomography. *New Engl J Med*. 2013;369(10):910–919.

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