Assessing Risk Factors Associated with Incidental Findings in Low-Dose CT Lung Cancer Screenings

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Abstract of "Assessing Risk Factors Associated with Incidental Findings in Low-Dose CT Lung Cancer Screenings", by Kevin Xi, MPH , Brown University, May 2025

Background & Aims

Significant Incidental Findings (SIFs) are widely reported in patients undergoing Low-dose CT (LDCT) lung screenings. Using data from the National Lung Screening Trial (NLST), we aim to identify occupational and medical conditions that may be associated with the detection of a SIF either with or without lung cancer at screening.

Methods

We analyzed data from the National Lung Screening Trial (NLST) which screened 53,452 participants accrued at 33 U.S. health centers. Participants were aged 55-74 at study entry, all current or former smokers who quit within the past 15 years. Participants were categorized based on whether they ever had a Significant Incidental Finding (SIF) and/or findings suspicious for Lung Cancer (POS) detected at screening during the National Lung Screening Trial, leading to 4 distinct outcome categories of ever POS only, ever SIF only, ever both POS/SIF, and always NEG.

We used multinomial logistic regression to determine the covariate-adjusted association of occupational, medical condition, and smoking-related risk factors on NLST screening results for POS, POS/SIF, SIF, and NEG. Exposures of interest included pack years, years since quitting, cohabitation with smokers, coworking with smokers, comorbidity history, history of high-risk employment, and disease history. Confounding variables adjusted for included age, gender, race/ethnicity, education, and BMI.

Results

No evidence was found of an increased association between occupational exposures and POS/SIF or SIF screening outcome. The exception was occupational history of cotton jute processing (OR 0.497, p=0.03) which was found to be inversely associated with POS/SIF screening outcome. The odds of POS/SIF screening outcome increased by 0.3% (OR 1.003,

p=0.006) for each additional pack year smoked, and increased by 2.2% (OR 1.02, p<0.001) for each year older a participant was when they stopped smoking.

Conclusion

Amongst the NLST screening population, occupational exposures did not appear to increase the likelihood of SIF detection during lung screening.

Introduction

The National Lung Cancer Screening Trial (NLST) reported a 20% reduction in lung-cancer mortality with annual low-dose computed tomography (LDCT) screening, and NELSON reported a reduction as high as 24% in lung-cancer specific mortality.[1,2] One feature of LDCT scanning is the frequent detection of significant incidental findings (SIFs), including emphysema, cardiovascular abnormalities, liver masses, and other findings.[3,4] At least one SIF has been noted in as many as 33.8%[5] of patients undergoing LDCT lung screening in the NLST during the three-year screening period.

Systematized reporting of SIF detection may lead to early diagnosis and treatment of various underlying conditions such metastatic masses [6-10] which would not have been detected without screening, potentially leading to reduced future healthcare costs and increased quality of life. Conversely, reporting of SIF detection may also lead to unnecessary health-care costs, patient burden, and increased iatrogenic mortality with little patient benefit if the risk of working up the SIF is greater than the risk of the SIF itself.[11,12]

While work has been done to characterize the types of SIFs detected in the NLST[5], the risk factors associated with such SIFs have not been well characterized. Gaining further insight into the risk factors associated with SIF detection would allow us to better anticipate the rate of specific SIFs in populations that will be screened in future. Additionally, SIF detection and treatment can have implications for lung screening cost-effectiveness, as incremental cost-effectiveness ratio can increase dramatically in populations with certain risk profiles.[13] The aim of the current study was to analyze risk factors for SIF detection for patients with and without

findings suspicious for lung cancer using the LDCT arm of the National Lung Cancer Screening Trial.

Methods

Data Collection

We conducted analyses using data collected for the NLST, a multi-institutional trial conducted from 2002-2009, comprising 53,452 participants at 33 US sites, designed to examine the relationship between screening with LDCT compared to chest radiography (CXR) on lung cancer mortality[1]. Participants were current and former smokers having quit within the previous 15 years, with a minimum of 30 pack-years of cigarette smoking and between 55-74 years of age at study entry. Participants were followed for five to seven years and detailed information on demographics, comorbidities, risk factors, history of cancer diagnosis, and potential cause of death was collected at baseline[1]. Participants were randomly assigned to the LDCT or CXR arms at study entry, and our study cohort focuses on participants recruited into the LDCT arm of the trial as LDCT is the current recommendation for cancer screening.

In the NLST, screening results were originally categorized as positive (suspicious for lung cancer) or negative (no findings suggestive of lung cancer) after each NLST screening visit, and any abnormalities suggesting clinically significant conditions other than lung cancer also were noted by NLST radiologists[14]. For the purposes of this paper, participants were reclassified in one of four categories based on whether they ever had a SIF detected and whether they ever had a positive LDCT screen: suspicious for lung cancer in the original data. If a SIF and findings suspicious for lung cancer were both detected, we refer to them as POS/SIF; if only findings

suspicious for lung cancer, we refer to them as POS; if only a SIF, we refer to them as SIF. Participants with no findings suspicious of lung cancer and no SIF reported at any of the three screening examinations were labelled as NEG.

Demographic risk factors include-age, gender, BMI, education, race, and ethnicity; smoking risk factors included pack years, years since quitting smoking, age at smoking cessation, age at smoking onset, cohabitation with smokers, and working with smokers; occupational exposure risk factors collected at baseline were determined by whether the participant currently or previously had employment in a "high-risk occupation" (Appendix A) with respect to lung cancer risk, which is defined by the NLST as "jobs and industries either previously demonstrated or thought to be associated with increased risk of lung disease or lung cancer."[14,41] Comorbidity, history of extrapulmonary cancer, and other diseases were also considered as risk factors in the analysis. These included, history of asbestosis, adult and childhood asthma, bronchiectasis, chronic bronchitis, COPD, diabetes, emphysema, lung fibrosis, heart attack, pneumonia, sarcoidosis, tuberculosis, hypertension, stroke, bladder cancer, breast cancer, cervical cancer, colorectal cancer, kidney cancer, oral cancer, and thyroid cancer.

Statistical Analysis

Differences in characteristics between groups were compared using the Student's t-test for continuous data, and the Chi-squared tests for categorical data.

Multinomial logistic regression was used to assess the association of risk factors and the screen findings (POS, POS/SIF, SIF) relative to neither lung cancer nor SIF detection (NEG), adjusted for covariates. Variance Inflation Factor (VIF) was calculated during regression variable selection to assess for collinearity.

Any risk factor with fewer than five NLST participants in any screening outcome group (POS, POS/SIF, SIF, or NEG) was excluded in the final multinomial logistic regression analysis due to sample size constraints. Risk factors excluded included history of silicosis, esophageal cancer, transitional cell cancer, stomach cancer, larynx cancer, pancreatic cancer, nasal cancer, and pharyngeal cancer comorbidities.

Statistical analysis was performed using R version 4.01, and differences were determined to be significant at $p < .05$.

Results

Table 1 reports on the demographic characteristics and risk factor distribution of LDCT participants in the NLST by screen results for POS/SIF, POS, SIF, and always NEG. Of the 26,445 participants over three screenings, 5,758 (21.8%) had screening examinations positive for Lung Cancer screen with SIF(s) detected, 3,196 (12.1%) were negative for lung cancer and had SIF(s) detected, 4,402 (16.6%) had a screen positive for Lung Cancer, and 13,099 (49.5%) screened negative for lung cancer and had no SIFs detected.

Those who ever had a SIF detected, regardless of lung cancer findings, were more likely to be male (SIF 62.2%, POS/SIF 60.0% vs POS 56.2%, NEG 58.8%, $p<0.001$) compared to female. Asian participants were less likely to have SIF(s) detected (SIF 1.7%, POS/SIF 1.4% vs POS 2.3%, NEG 2.4%, $p<0.001$). Those with POS/SIF screening outcomes were more likely to be underweight (POS/SIF 1.4% vs SIF 1.0%, POS 0.4%, NEG 0.7%, $p<0.001$) or normal weight (POS/SIF 33.1% vs SIF 26.9%, POS 25.1%, NEG 26.8%, $p<0.001$), and less likely to be obese (POS/SIF 24.2% vs SIF 30.2%, POS 31.9%, NEG 29.6%, $p<0.001$) compare to the other three outcomes. All screening outcomes had similar prevalences of overweight individuals (POS/SIF 41.3% vs SIF 42.0%, POS 42.5%, NEG 42.9%).

Table 2 reports on the smoking risk factor distribution of LDCT participants in the NLST stratified by ever POS and/or SIF screen results (POS/SIF, POS, SIF, NEG). Those who ever had SIF(s) detected with or without findings suspicious for lung cancer had a greater number of pack years smoked on average (SIF 57.5±25.2, POS/SIF 59.4±25.2 vs POS 54.5±23.3, NEG 54.7±23.2, $p<0.001$). Additionally, those with SIF(s) detected with or without findings suspicious for lung cancer had a higher average age at smoking cessation (SIF 55.1±6.5, POS/SIF 56.3±6.5 vs POS 54.5±6.3, NEG 54.1±6.3, $p<0.001$) as well as a lower average age of smoking onset (SIF 16.6±3.9, POS/SIF 16.5±3.6 vs POS 16.9±3.7, NEG 16.7±3.7, $p<0.001$). A history of living with smokers did not significantly influence the likelihood of a SIF detection or a detection of findings suspicious for lung cancer (POS/SIF 87.9%, POS 87.5%, SIF 87.5%, NEG 87.6%, $p=0.97$) relative to other outcomes, neither did a history of working with smokers (POS/SIF 86.1%, POS 85.5%, SIF 86.0%, NEG 85.9%, $p=0.064$). Average cigarettes per day and years since quitting risk factors were excluded as potential explanatory variables during multinomial logistic regression due to collinearity (VIF > 6).

Table 3 reports on the occupational exposure of LDCT participants in the NLST stratified by SIF/lung cancer screening outcome. Those exposed to Asbestos during employment had higher prevalence of the SIFs (SIF 5.6% vs POS/SIF 4.9%, POS 4.5%, NEG 4.4%, $p=0.035$). Those that worked in Farming (NEG 9.6% vs POS/SIF 11.6%, POS 11.1%, SIF 12.6%, $p<0.001$) or Welding (NEG 5.2% vs POS/SIF 6.0%, POS 5.9%, SIF 6.6%, $p=0.004$) had higher prevalence of all three positive outcomes relative to negative screening results over all NLST screenings.

Table 4 reports on the disease history reported at baseline by SIF/lung cancer screening outcome. Participants reporting a history of heart attack (SIF 16.2% vs POS/SIF 13.9%, POS 11.7%, NEG 12.1%, $p<0.001$) or hypertension (SIF 39.3% vs POS/SIF 33.7%, POS 35.5%, NEG 34.7%,

p<0.001) had higher prevalence of SIFs with or without positive lung cancer screening. Participants with a history of COPD had a higher prevalence of SIFs, but especially higher prevalence of POS/SIF (POS/SIF 7.6%, SIF 5.7% vs POS 3.7%, NEG 4.3%, p<0.001).

Table 5 presents the results of the multivariable logistic regression assessing the association between specific risk factors: smoking, disease history, occupational exposure, and demographic and ever POS and/or SIF screen results (POS/SIF, POS, SIF, NEG). Each additional pack-year smoked increased the odds of POS/SIF screening outcome by 0.3% (OR 1.003, p=0.006). Those who were older at smoking cessation were at higher odds of POS/SIF screening outcome, as each additional year increased the odds of that outcome by 2.2% (OR 1.02, p<0.001). Those with previous or current high-risk employment in cotton jute processing were at lower risk of POS/SIF screening outcome with 51.3% lower odds (OR 0.497, p=0.031), while participants who with previous or current high-risk employment involving farming had 23.7% higher odds of POS screening outcome (OR 1.24, p=0.009).

Participants with a history of asbestosis had 62.4% higher odds of POS/SIF screening outcome (OR 1.62, p=0.016), but 49.8% lower odds of SIF screening outcome (OR=0.502, p=0.036). Participants with self-reported history of COPD had 28.6% higher odds of POS/SIF screening outcome (OR 1.29, p=0.016), but 24.9% lower odds of positive lung cancer screening alone (OR=0.75, p=0.038). Participants with a self reported history of emphysema had higher odds of SIF detection both with a positive lung cancer screening (POS/SIF: OR 2.02, p<0.001) and without (SIF: OR 1.509, p<0.001). Participants with a self-reported history of fibrosis of the lung (OR 2.61, p<0.001) and heart disease/heart attack (OR 1.19, p=0.028) had higher odds of SIF screening outcome.

Participants with a history of colorectal cancer (OR 0.272, p=0.031) had 73.8% lower odds of SIF screening outcome, while participants with a self-reported history of thyroid cancer (OR 4.55, p=0.021) had 355.4% higher odds of POS screening outcome.

Discussion

Our study found little association between occupational exposures and increased odds of SIF detection, with the exceptions of occupational cotton jute processing which lowered odds of POS/SIF screening outcome and farming which increased odds of POS screening outcome. The odds of POS/SIF screening outcome increased with pack-years smoked, and for former smokers additionally increased with later age at quit.

The high overall prevalence of SIFs such as COPD and emphysema in the POS/SIF is consistent with the well-established link between smoking, these diseases, and lung cancer. Namely, smoking is the leading cause for lung cancer, introducing multiple carcinogens to the body and simultaneously causing mutations in key oncogenes and tumor suppressor genes.[17,18] Similarly, smoking is a primary risk factor for chronic respiratory conditions, contributing to both COPD and emphysema by causing inflammation, oxidative stress, and alveolar destruction.[19,20] These SIFs independently increase the risk of lung cancer through non-smoking-related mechanisms, thereby compounding overall risk.[21,22] Multiple cohort studies, including other lung cancer screening trials, have demonstrated that individuals with COPD face a two- to fourfold increased risk of developing lung cancer compared to those without.[23,24] This dual pathway can explain the higher risk of POS/SIF outcome with increased pack years and higher age of cessation. These findings suggest that targeted lung cancer screening strategies may be particularly warranted for individuals with SIFs associated with the COPD spectrum of diseases."

Numerous studies have shown the pathogenic and/or carcinogenic potential of various occupational hazards, including exposure to asbestos, airborne silicates, and other chemicals prevalent in industrial settings.[25-28] These exposures have been linked to an elevated risk of cancer, particularly lung cancer, mesothelioma, and bladder cancer, among others.[29-31] Moreover, occupational exposures have been implicated in the development of non-cancerous conditions such as chronic obstructive pulmonary disease (COPD), interstitial lung diseases, and cardiovascular disorders,[32,33] all of which may manifest in the form of significant incidental findings during routine medical imaging. Contrary to findings in the general literature, our study revealed that individuals in these professions (with the exception of farming) were not associated with an increased risk of lung cancer or SIF detection, despite the prior associations with lung related pathogens/carcinogens. These findings may be attributed to several factors, including the healthy worker effect, the adjustment for pre-existing conditions, the crude manner in which occupational exposures were measured, or it may have been attributable to the large number of statistical tests without correction for multiple comparisons.

The healthy worker effect refers to the tendency for employed populations to exhibit better health outcomes compared to the general population, due to the self-removing nature of individuals with severe health conditions from the workforce. It is possible that in our population of smokers, those with especially debilitating health conditions were never able to find consistent work in the fields surveyed or left work in those fields early, leading to those smokers less affected by SIFs/lung cancer to be overrepresented in the employment surveys. An additional portion of the lack of increased lung cancer or significant incidental findings (SIF) risk among the occupational workers in our cohort may be attributed to the smoking history among the participants. Our cohort consisted entirely of former or current smokers with a substantial

number of pack-years, the average being 56.0. Thus, lung damage from smoking may obscure or modify the effect of concurrent lung damage due to exposure to fumes, chemicals, and dust encountered in their respective professions. Lastly, it is important to acknowledge that the NLST was not a dedicated study on the effects of occupational history, and thus did not employ highly rigorous standards of employment verification such as personnel files[21] or computerized work records[22] as usually seen in studies of this kind. In addition, it did not gather granular data such as work-years or site conditions, only binary data on employment history at specific high-risk occupations. These limitations may have introduced misclassification and reduced precision, potentially attenuating the association between high-risk occupations and SIF detection in the NLST.

Certain professions are known to be prone to occupational significant incidental findings (SIFs) and lung cancer.[25-34] Baking has been linked to wheat-triggered asthma, emphysema, and COPD hypothesized to be induced by chronic particulate exposure to flour.[34] Many industrial occupations such as construction, steel working, and mining operate in environments with high levels of fibrous silicates in air that lead to pathologies such as silicosis and lung cancer.[25-27,30] Farmers are exposed to a host of potential SIF inducing hazards such as exhaust toxicity, inhalation of organic spores and fertilizing chemicals, and grain dust.[35-37] Despite this, Farming was the only occupation in our study in which occupational exposure was associated with increased odds of any findings in screening examinations (POS/SIF, SIF, POS), with greater odds of positive lung cancer screening alone (POS). This finding may be due to the unique mechanism of pesticide-induced lung cancer pathways which act independently of smoking related pathways. Chemical exposure to pesticide has been shown to be a major determinant of lung cancer, either by skin or respiration.[35,36] This is supported by the absence of significant finding in the POS/SIF category, suggesting that lung cancer development, typically mediated

through intermediate pathways associated with SIFs such as COPD and emphysema, was not observed.

Cotton jute processing was negatively associated with SIF detection risk combined with positive lung cancer screening in LDCT NLST individuals, despite being originally included in the selection as an occupation thought to be associated with an increased risk of lung cancer. This finding is consistent with findings of current epidemiologic literature regarding the chemical endotoxin, which generally observes an inverse exposure-response relation between cumulative exposure to endotoxin (found in cotton dust) and lung cancer risk.[38,39]

There are potential factors limiting the validity of this study. An important limitation of this analysis is the issue of multiple comparisons, where examining rare occupations such as cotton jute processing in such a large sample size can destabilize estimates and increase the likelihood of spurious associations due to chance. Additionally, inconsistencies in the rate of radiologic reporting have been known to affect the diagnostic rate of SIFs, and underscore the need for standardized reporting of lung cancer screening incidental findings. One study found the odds of reported incidental findings were 5.4 times higher for patients being imaged exclusively in a university imaging center compared to a community imaging center[40], highlighting the inconsistencies in reporting rate when under trial level scrutiny compared to industry standard. These stark rates between hospital/community and university imaging centers, likely driven by a difference in radiologic expertise and confidence in abnormality reporting, could explain the large range of SIF detection rates in the literature.

Conclusion

This study represents one of the first efforts to investigate the effects of smoking, occupational, and comorbidity risk factors on significant incidental findings and lung cancer detection in a national dataset composed of current/former smokers. We found little association between occupational exposure or medical comorbidity and SIF findings, with the exception of smoking related pathways in COPD and emphysema. Multiple smoking risk factors increased the dual risk of POS/SIF outcome, emphasizing the need for lung cancer screening strategies targeted towards individuals with SIFs associated with the COPD/emphysema.

Table 1. Demographic Characteristics of NLST LDCT participants stratified by SIF and/or positive Lung Cancer screening outcome (n=26,455)

		POS		NEG		
Demographics & Risk Factors	Overall n = 26,445	SIF n = 5,758	No SIF n = 4,402	SIF n = 3,196	No SIF n = 13,099	p-val*
Age, Mean (sd)	61.4 (5.0)	62.4 (5.2)	61.4 (5.0)	61.9 (5.1)	60.9 (4.9)	<0.001
Gender, n (%)						<0.001
Male	15,622 (59.1)	3,455 (60.0)	2,476 (56.2)	1,988 (62.2)	7,703 (58.8)	
Female	10,833 (40.9)	2,303 (40.0)	1,926 (43.8)	1,208 (37.8)	5,396 (41.2)	
Race, n (%)						<0.001
White	24,123 (91.2)	5,370 (93.3)	4,041 (91.8)	4,041 (91.8)	11,785 (90.0)	
Asian	548 (2.1)	79 (1.4)	103 (2.3)	55 (1.7)	311 (2.4)	
Black or African American	1,179 (4.5)	221 (3.8)	153 (3.5)	147 (4.6)	658 (5.0)	
Other	605 (2.3)	88 (1.5)	105 (2.4)	67 (2.1)	345 (2.6)	
Ethnicity, n (%)						
Neither Hispanic or Latino	25,878 (98.2)	5,660 (98.8)	4,299 (98.2)	3,136 (98.6)	12,783 (97.9)	<0.001
Hispanic or Latino	470 (1.8)	69 (1.2)	78 (1.8)	44 (1.4)	279 (2.1)	
Education, n (%)						
Did not finish High School	1,626 (6.3)	404 (7.2)	237 (5.5)	231 (7.4)	754 (5.9)	
High School graduate / GED	16,067 (62.0)	3,613 (64.0)	2,681 (62.1)	1,981 (63.5)	7,792 (60.7)	
Bachelors Degree or Higher	8,227 (31.7)	1,630 (28.9)	1,401 (32.4)	909 (29.1)	4,287 (33.4)	
BMI, Mean (sd)	27.9 (5.0)	27.1 (4.8)	28.3 (5.1)	28.0 (5.0)	28.1 (5.1)	<0.001
BMI category, n (%)						<0.001
Underweight	227 (0.9)	82 (1.4)	19 (0.4)	31 (1.0)	95 (0.7)	
Normal	7,247 (27.9)	1,872 (33.1)	1,087 (25.1)	843 (26.9)	3,445 (26.8)	
Overweight	11,011 (42.4)	2,336 (41.3)	1,840 (42.5)	1,317 (42.0)	5,518 (42.9)	
Obese	7,496 (28.9)	1,368 (24.2)	1,380 (31.9)	946 (30.2)	3,802 (29.6)	

* Pearson's Chi-squared test; Kruskal-Wallis rank sum test

Table 2. Smoking risk factor distribution of NLST LDCT participants stratified by SIF/Lung Cancer screening outcome (n=26,455)

		POS		NEG		
Demographics & Risk Factors	Overall	SIF	No SIF	SIF	No SIF	p-val*
	n = 26,445	n = 5,758	n = 4,402	n = 3,196	n = 13,099	
Age at smoking cessation, Mean (sd)	54 (6.4)	56.3 (6.5)	54.5 (6.3)	55.1 (6.5)	54.1 (6.3)	<0.001
Pack years, Mean (sd)	56.0 (24.0)	59.4 (25.2)	54.5 (23.3)	57.5 (25.2)	54.7 (23.2)	<0.001
Age at smoking onset, Mean (sd)	16.7 (3.7)	16.5 (3.6)	16.9 (3.7)	16.6 (3.9)	16.7 (3.7)	<0.001
Lived with smokers, n (%)	23,107 (87.6)	5,045 (87.9)	3,833 (87.5)	2,790 (87.5)	11,439 (87.6)	0.9
Worked with smokers, n (%)	22,660 (86.1)	4,989 (87.2)	3,736 (85.5)	2,735 (86.0)	11,200 (85.9)	0.064

* Pearson's Chi-squared test; Kruskal-Wallis rank sum test

Table 3. Occupational exposure risk factor distribution of NLST LDCT participants stratified by SIF/Lung Cancer screening outcome (n=26,455)

		POS		NEG		
Occupational Risk Factors, n (%)	Overall	SIF	No SIF	SIF	No SIF	p-val*
	n = 26,445	n = 5,758	n = 4,402	n = 3,196	n = 13,099	
Asbestos	1,227 (4.6)	280 (4.9)	197 (4.5)	178 (5.6)	572 (4.4)	0.025
Baking	593 (2.2)	142 (2.5)	94 (2.1)	82 (2.6)	275 (2.1)	0.2
Butchering / Meat Packing	564 (2.1)	119 (2.1)	90 (2.0)	77 (2.4)	278 (2.1)	0.7
Chemicals / Plastics Manufacturing	1,633 (6.2)	376 (6.5)	266 (6.0)	218 (6.8)	773 (5.9)	00.15
Coal Mining	167 (0.6)	42 (0.7)	23 (0.5)	24 (0.8)	78 (0.6)	0.4
Cotton Jute Processing	192 (0.7)	40 (0.7)	27 (0.6)	27 (0.8)	98 (0.7)	0.7
Farming	2,815 (10.6)	668 (11.6)	490 (11.1)	404 (12.6)	1,253 (9.6)	<0.001
Fire Fighting	476 (1.8)	125 (2.2)	78 (1.8)	53 (1.7)	220 (1.7)	0.12
Flour Feed / Grain Milling	288 (1.1)	69 (1.2)	45 (1.0)	36 (1.1)	138 (1.1)	0.8
Foundry Steel Mining	1,151 (4.4)	267 (4.6)	167 (3.8)	157 (4.9)	560 (4.3)	0.072
Hard Rock Mining	202 (0.8)	50 (0.9)	42 (1.0)	20 (0.6)	90 (0.7)	0.2
Painting	1,363 (5.2)	317 (5.5)	224 (5.1)	178 (5.6)	644 (4.9)	0.3
Sandblasting	455 (1.7)	97 (1.7)	82 (1.9)	68 (2.1)	208 (1.6)	0.2
Welding	1,497 (5.7)	347 (6.0)	260 (5.9)	212 (6.6)	678 (5.2)	0.004

* Pearson's Chi-squared test

Table 4. Disease history risk factor distribution of NLST LDCT participants stratified by SIF/Lung Cancer screening outcome (n=26,455)

		POS		NEG		
Disease History Risk Factors, n (%)	Overall n = 26,445	SIF n = 5,758	No SIF n = 4,402	SIF n = 3,196	No SIF n = 13,099	p-val*
Bladder Cancer	112 (0.4)	27 (0.5)	24 (0.5)	16 (0.5)	45 (0.3)	0.2
Breast Cancer	349 (1.3)	87 (1.5)	60 (1.4)	39 (1.2)	163 (1.2)	0.5
Cervical Cancer	360 (1.4)	72 (1.3)	66 (1.5)	38 (1.2)	184 (1.4)	0.6
Colorectal Cancer	108 (0.4)	31 (0.5)	12 (0.3)	6 (0.2)	59 (0.5)	0.032
Kidney Cancer	37 (0.1)	8 (0.1)	5 (0.1)	7 (0.2)	17 (0.1)	0.6
Oral Cancer	50 (0.2)	11 (0.2)	11 (0.3)	9 (0.3)	19 (0.1)	0.3
Thyroid Cancer	35 (0.1)	10 (0.2)	9 (0.2)	5 (0.2)	11 (0.1)	0.13
Asbestosis	275 (1.0)	85 (1.5)	30 (0.7)	37 (1.2)	123 (0.9)	<0.001
Asthma, adult	1,644 (6.2)	384 (6.7)	277 (6.3)	195 (6.1)	788 (6.0)	0.4
Asthma, childhood	925 (3.5)	198 (3.4)	154 (3.5)	100 (3.1)	473 (3.6)	0.6
Bronchiectasis	848 (3.2)	206 (3.6)	131 (3.0)	121 (3.8)	390 (3.0)	0.030
Chronic Bronchitis	2,567 (9.7)	652 (11.3)	400 (9.1)	318 (10.0)	1,197 (9.1)	<0.001
COPD	1,337 (5.1)	436 (7.6)	163 (3.7)	181 (5.7)	557 (4.3)	<0.001
Diabetes	2,566 (9.7)	485 (8.4)	453 (10.3)	356 (11.1)	1,272 (9.7)	<0.001
Emphysema	2,038 (7.7)	729 (12.7)	236 (5.4)	296 (9.3)	777 (5.9)	<0.001
Lung Fibrosis	69 (0.3)	19 (0.3)	11 (0.3)	12 (0.4)	27 (0.2)	0.2
Heart Disease	3,420 (12.9)	800 (13.9)	516 (11.7)	517 (16.2)	1,587 (12.1)	<0.001
Pneumonia	5,892 (22.3)	1,395 (24.2)	966 (22.0)	731 (22.9)	2,800 (21.4)	<0.001
Sarcoidosis	46 (0.2)	11 (0.2)	9 (0.2)	7 (0.2)	19 (0.1)	0.7
Tuberculosis	278 (1.1)	67 (1.2)	53 (1.2)	32 (1.0)	126 (1.0)	0.4
Hypertension	9,298 (35.2)	1,940 (33.7)	1,563 (35.5)	1,255 (39.3)	4,540 (34.7)	<0.001
Stroke	751 (2.8)	187 (3.2)	109 (2.5)	114 (3.6)	341 (2.6)	0.002

* Pearson's Chi-squared test

Table 5 Multinomial regression analysis of SIF/Lung Cancer screening outcomes in relation to smoking and work history, risk factors in participants of the LDCT screening arm of the NLST.

	POS		**NEG**	
	SIF	No SIF	SIF	No SIF
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Smoking Risk Factors				
Age at smoking cessation	**1.021 (1.01 - 1.03)**	0.999 (0.988 - 1.009)	1.001 (0.989 - 1.013)	1.000
Pack years	**1.003 (1 - 1.004)**	0.999 (0.996 - 1)	1 (0.997 - 1.002)	1.000
Age at smoking onset	0.99 (0.976 - 1.004)	1.008 (0.993 - 1.022)	0.999 (0.981 - 1.015)	1.000
Lived with smokers	0.962 (0.837 - 1.104)	0.96 (0.833 - 1.105)	1.023 (0.867 - 1.208)	1.000
Worked with smokers	1.021 (0.896 - 1.189)	1.006 (0.873 - 1.159)	1.02 (0.86 - 1.208)	1.000
Occupational Risk Factors				
Asbestos	1.083 (0.846 - 1.386)	0.999 (0.767 - 1.301)	1.125 (0.848 - 1.491)	1.000
Baking	1.113 (0.802 - 1.544)	1.162 (0.832 - 1.621)	1.315 (0.911 - 1.896)	1.000
Butchering / meat packing	0.914 (0.646 - 1.294)	1.142 (0.815 - 1.6)	1.066 (0.723 - 1.571)	1.000
Chemicals / plastics manufacturing	1.064 (0.867 - 1.304)	1.056 (0.853 - 1.307)	1.166 (0.923 - 1.471)	1.000
Coal mining	1.158 (0.65 - 2.061)	1.162 (0.633 - 2.131)	0.814 (0.371 - 1.783)	1.000
Cotton jute processing	**0.497 (0.263 - 0.939)**	0.62 (0.31 - 1.234)	0.575 (0.268 - 1.231)	1.000
Farming	1.113 (0.951 - 1.301)	**1.237 (1.055 - 1.45)**	1.116 (0.926 - 1.342)	1.000
Fire fighting	1.21 (0.87 - 1.681)	0.858 (0.587 - 1.253)	0.737 (0.465 - 1.165)	1.000
Flour feed / grain milling	1.144 (0.727 - 1.797)	0.986 (0.602 - 1.611)	0.863 (0.488 - 1.523)	1.000
Foundry steel milling	0.884 (0.691 - 1.129)	0.826 (0.63 - 1.081)	0.99 (0.745 - 1.314)	1.000
Hard rock mining	1.106 (0.652 - 1.873)	1.511 (0.914 - 2.496)	0.478 (0.201 - 1.133)	1.000
Painting	1.059 (0.832 - 1.346)	0.9 (0.691 - 1.171)	0.881 (0.655 - 1.184)	1.000
Sandblasting	0.785 (0.505 - 1.218)	1.302 (0.857 - 1.977)	1.488 (0.952 - 2.324)	1.000
Welding	1.2 (0.783 - 1.249)	1.136 (0.945 - 1.524)	0.99 (0.867 - 1.477)	1.000

*Adjusted for demographic risk factors

Table 5b Multinomial regression analysis of SIF/Lung Cancer screening outcomes in relation to comorbidity risk factors in participants of the LDCT screening arm of the NLST.

	POS		**NEG**	
	SIF	No SIF	SIF	No SIF
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Comorbidity Risk Factors				
Bladder Cancer	1.218	0.989	1.159	1.000
Breast Cancer	1.132	0.844	0.819	1.000
Cervical Cancer	0.911	1.022	0.991	1.000
Colorectal Cancer	0.820	0.533	**0.290**	1.000
Kidney Cancer	1.603	1.021	1.333	1.000
Oral Cancer	1.530	2.020	1.600	1.000
Thyroid Cancer	1.789	4.996	1.802	1.000
Asbestosis	1.044	1.268	0.309	1.000
Asthma, adult	1.071	1.017	0.916	1.000
Asthma, childhood	1.028	1.118	0.895	1.000
Bronchiectasis	1.023	0.994	1.123	1.000
Chronic Bronchitis	0.974	0.899	0.923	1.000
COPD	**1.349**	**0.759**	1.059	1.000
Diabetes	0.926	1.036	1.146	1.000
Emphysema	**2.061**	1.002	**1.514**	1.000
Lung Fibrosis	1.281	1.501	**2.440**	1.000
Heart Disease	1.107	0.978	**1.191**	1.000
Pneumonia	1.087	1.019	1.048	1.000
Sarcoidosis	2.051	1.999	1.742	1.000
Tuberculosis	1.148	1.012	0.904	1.000
Hypertension	0.994	0.968	1.126	1.000
Stroke	1.054	0.835	1.156	1.000

*Adjusted for demographic risk factors

Appendix A: List of occupations deemed to have occupational risk of lung cancer

1. Asbestos
2. Baking
3. Butchering / Meat Packing
4. Chemicals Plastics Manufacturing
5. Coal Mining
6. Cotton Jute Processing
7. Farming
8. Fire Fighting
9. Flour Feed / Grain Milling
10. Hard Rock Mining
11. Painting
12. Sandblasting

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