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PII: S1556-0864(22)01553-2

DOI: https://doi.org/10.1016/j.jtho.2022.08.011

Reference: JTHO 2513

To appear in: *Journal of Thoracic Oncology*

Received Date: 10 April 2022

Revised Date: 17 August 2022

Accepted Date: 19 August 2022

Please cite this article as: Vachani A, Carroll NM, Simoff MJ, Neslund-Dudas C, Honda S, Greenlee RT, Rendle KA, Burnett-Hartman A, Ritzwoller DP, Stage Migration and Lung Cancer Incidence After Initiation of Low-Dose CT Screening, *Journal of Thoracic Oncology* (2022), doi: https://doi.org/10.1016/j.jtho.2022.08.011.

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Funding: This work was supported by the National Cancer Institute of the National Institutes of Health under Award Number UM1CA221939. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Author Disclosures*:* AV reports grants from the Moore Foundation, PCORI, Lungevity, the National Comprehensive Cancer Network, Precyte Inc., and MagArray Inc. outside of the submitted work, and personal fees as scientific advisor for the Lung Cancer Initiative at Johnson and Johnson. MJS reports personal fees from Intuitive Surgical, Gongwin Biopharm, SpinQ, and Pulmonx. MJS reports personal fees from Intuitive Surgical, Gongwin Biopharm, and PulmonX. As of February 2022, MJS is 50% employed at Intuitive Surgical. CND reports grants from PCORI through a subcontract from the University of Pennsylvania, the Moore Foundation through a subcontract from the University of Pennsylvania, NCI Connect Study, Michigan Department of Health and Human Services, and Genentech outside of the submitted work. DPR, ABH, SH, RTG report grants from the Moore Foundation through a subcontract through the University of Pennsylvania. KR reports grants from the Moore Foundation, the Lung Cancer Research Foundation of Pfizer, Lungevity, and the National Comprehensive Cancer Network outside of the submitted work.

ABSTRACT

Introduction: Despite evidence from clinical trials of favorable shifts in cancer stage and improvements in lung cancer specific mortality, the effectiveness of lung cancer screening (LCS) in clinical practice has not been clearly demonstrated.

Methods: We performed a multicenter cohort study of patients diagnosed with a primary lung cancer between January 1, 2014, and September 30, 2019, at one of four US healthcare systems. The primary outcome variables were cancer stage distribution and annual age-adjusted lung cancer incidence. The primary exposure variable was receipt of at least one low-dose CT for LCS prior to cancer diagnosis.

Results: 3,678 individuals were diagnosed with an incident lung cancer during the study period; 404 (11%) of these patients were diagnosed after initiation of LCS. As screening volume increased, the proportion of patients diagnosed with lung cancer after LCS initiation also rose from 0% in Q1 of 2014 to 20% in Q3 of 2019. LCS did not result in a significant change in the overall incidence of lung cancer (AAPC, -0.8 [95% CI -4.7, 3.2]) between 2014 and 2018. Stage specific incidence rates increased for Stage I cancer (AAPC, 8.0 [95% CI 0.8, 15.7]) and declined for Stage IV disease (AAPC, -6.0 [95% CI -11.2, -0.5]).

Conclusions: Implementation of LCS at four diverse healthcare systems has resulted in a favorable shift to a higher incidence of Stage I cancer with an associated decline in Stage IV disease. Overall lung cancer incidence did not increase, suggesting a limited impact of over-diagnosis.

Key words: lung cancer, screening, stage migration

Abbreviations: National Lung Screening Trial (NLST); Nederlands–Leuvens Longkanker Screenings Onderzoek [NELSON); low dose CT (LDCT); lung cancer screening (LCS); Population-based Research to Optimize the Screening Process (PROSPR); Institutional Review Board (IRB); American Joint Commission on Cancer (AJCC); chronic obstructive pulmonary disease (COPD); body mass index (BMI); average annual percentage change (AAPC); multiple imputation by chained equations (MICE)

INTRODUCTION

Lung cancer represents a substantial portion of the overall burden of cancer worldwide and accounted for approximately 235,000 deaths in United States in 2021.[1] Survival is strongly associated with stage of disease at time of diagnosis, but historically, the majority of lung cancers are diagnosed at late stage when curative treatment options are expensive and survival probabilities are limited.[2] Five-year stage-specific survival rates range from greater than 53-69% for patients diagnosed with Stage I disease to less than 10% for patients with distant organ metastasis.[3,4]

In 2011, the National Lung Screening Trial (NLST) demonstrated a 20% relative reduction in lung cancer mortality with annual low dose CT (LDCT) among high-risk individuals.[5] The Dutch–Belgian lung-cancer screening trial (Nederlands–Leuvens Longkanker Screenings Onderzoek [NELSON]) recently confirmed the mortality benefit of annual LDCT screening.[6] Efforts in many countries are underway to either initiate or accelerate implementation of LCS given these recent findings. Both the NLST and NELSON trials demonstrated a significant shift in the distribution of cancer stage between LDCT and control arms, with more early stage and fewer advanced stage cancers identified with screening. The presence of this 'stage shift' coupled with timely evaluation, diagnosis and treatment likely represents the primary mechanism through which annual screening results in improved lung cancer specific mortality. The trial results also support our understanding of the natural history of lung cancer that suggest a progression of disease from undetectable lesions to localized tumors, followed by loco-regional involvement and later development of distant metastases. However, concerns persist regarding the detection of a large proportion of indolent cancers resulting in unnecessary diagnosis and over-treatment.[7]

Despite the evidence from NLST and NELSON on stage shift and lung cancer specific mortality, the effectiveness of LDCT screening in clinical practice has not been clearly demonstrated. Both trials were well-conducted, achieving high rates of adherence (>95%) and were performed largely in centers of excellence that may have resulted in optimal outcomes from diagnostic evaluation and subsequent cancer treatment. Enrolled participants were also younger, more educated, and had fewer comorbidities than the population of individuals that are potentially eligible for screening in real world settings.[8,9] Concerns have also been raised that harms from screening may be greater in clinical practice have persisted and may be contributing to the slow uptake of lung cancer screening that has been observed in the United States.[10,11] Emerging evidence also suggests that adherence to annual screening is considerably lower than the rates observed in the NLST and NELSON trials, which may diminish the mortality benefit observed in trial settings.[12–14]

Although the assessment of screening benefits, such as lung cancer mortality, are difficult to measure and may only be observed a decade after implementation of LCS in clinical practice, the distribution of cancer stage among screened individuals may allow for an early indication of the impact of screening on lung cancer outcomes. Cancer registry based analyses and individual lung cancer screening programs have started to report initial outcomes and many, though not all, have reported favorable distributions of cancer stage among their population of patients diagnosed after screening initiation.[15–18] Although promising, these studies have been limited by their inability to identify the source population and meaningfully compare stage outcomes among individuals with lung cancer diagnosed among screened and unscreened groups. The aim of the present study was to evaluate the impact of LDCT-based screening on shifting the stage distribution towards earlier stage disease across a well-characterized source population, assess the effect of screening on stage-specific

incidence over time, and identify factors, in addition to screening, which increase the likelihood of an early-stage diagnosis.

METHODS

Study Setting and Data Sources

The Population-based Research to Optimize the Screening Process (PROSPR) Lung Consortium is a collaboration of five diverse healthcare systems, including Henry Ford Health System (HFHS), Kaiser Permanente Colorado (KPCO), Kaiser Permanente Hawaii (KPHI), Marshfield Clinic Health System (MCHS), and the University of Pennsylvania Health System (UPHS). The current retrospective cohort analysis excluded MCHS due to incomplete cancer stage information for the full study period. PROSPR-Lung developed a standardized Common Data Model containing data on patients aged 35 to 89 who were affiliated with any of these five healthcare systems from January 1, 2010, through September 31, 2019. This Common Data Model includes harmonized data derived from administrative, electronic health record (EHR), and claims systems that is supplemented with limited chart review. Two of the healthcare systems (KPCO and KPHI) operate under an integrated care delivery model and the other two (HFHS and UPHS) limited the cohort to individuals that received primary care within their systems. Variables include patient demographics, details of lung cancer screening, procedures, diagnoses, census-based measures of socioeconomic status, and cancer registry variables collected in a manner consistent with the North American Association of Central Cancer Registries standards. Cancer registry data are obtained from manual review by certified tumor registrars and includes date of diagnosis, cancer stage, tumor characteristics, and first-course therapy. The study was reviewed and approved by the Institutional Review Board (IRB) at KPCO, the

IRB of record for PROSPR-Lung, which waived the informed consent requirement because this observational study presented minimal risks to the participants whose data were analyzed.

Study Population and Variables

We restricted the cohort to adults diagnosed with primary in situ or invasive lung cancer between January 1, 2014, and September 30, 2019. Participants were excluded if they had a previous diagnosis of lung cancer, were younger than age 55 or older than age 80 or had a tobacco use history documented as "Never" or was missing. The primary outcome variable was cancer stage based on the American Joint Commission on Cancer (AJCC) system in place in the year of diagnosis and was extracted by the local cancer registry at each of institution. The primary exposure variable was the performance of at least one LDCT for lung cancer screening prior to lung cancer diagnosis. LCS-LDCT scans were identified by resulted radiology scans under one of the following CPT or HCPC codes: G0297, S8032, or 71250. We collected sociodemographic and clinical variables including age, sex, prior malignancy, comorbid conditions, chronic obstructive pulmonary disease (COPD) in the year preceding lung cancer diagnosis, and self-reported race/ethnicity, and smoking behavior. We ascertained tobacco use and body mass index (BMI) at the last date with available data in the EHR prior to lung cancer diagnosis. We used the patient's home address mapped to census tract level information to determine the Yost Index as a measure of socioeconomic status.[19]

Statistical Analysis

Descriptive statistics were computed using frequencies and proportions to describe the distribution of baseline patient and tumor characteristics among individuals with and without at least one LCS-LDCT prior to diagnosis and by year of diagnosis. Age-adjusted incidence rates, including both invasive and in-situ cancers, were calculated by year between 2014 and 2018 using the age

distribution of the US 2000 population as the standard. Patients of each healthcare system with a recorded encounter within the year of interest were included in the person-years-at-risk denominator calculation. Trends in incidence rates over time were analyzed using joinpoint regression analysis and summarized with average annual percentage change (AAPC) and 95% CI.[20] Differences in the distribution of categorical variables between screened and unscreened groups and by year of diagnosis were compared using chi-squared tests. Risk differences (and corresponding 95% confidence intervals) were calculated as the difference in the proportion of cancer stage and histological subgroups by screening history.

For multivariable analyses, we assessed factors associated with a greater likelihood of an early-stage diagnosis. For this analysis, cancer stage was categorized as early-stage, defined as an AJCC stage 0, I, or II, and late-stage, defined as AJCC stage III or IV. For this component of the analysis, we excluded lung cancer cases with unknown stage, carcinoid histology, or a diagnosis in 2014. (**Figure 1**) The proportion of early and late-stage lung cancer and corresponding 95% CI intervals were calculated overall and across subgroups of a priori identified variables. Generalized estimating equations (GEE) with a generalized logit distribution and unstructured covariance structure with robust standard errors were used to estimate adjusted odds ratios (OR) and 95% confidence intervals (CIs).[21] Models were clustered on healthcare system and included the following factors: age at time of lung cancer diagnosis, gender, race/ethnicity, year of diagnosis, histology (small vs non-small cell, excluding carcinoid), smoking history, receipt of prior lung cancer screening, COPD, a previous non-lung cancer malignancy, body mass index (BMI), and socio-economic status as measured by the Yost Index. Customary residual and effect statistics were examined to assess model fit and evaluate for outliers.

To address missing data for BMI (6%) and Yost Index (3%), we used multiple imputation by chained equations (MICE).[22] All variables (outcome, exposure, and covariates) in the outcome model were included as independent variables in the imputation models. We performed 20 iterations of imputation and combined them.[22,23] To assess the quality of our imputed data we compared distributional characteristics pre- and post-imputation. Analyses were performed using SAS® version 9.4M6 (SAS Institute Inc., Cary, North Carolina) and Joinpoint Regression Program version 4.8.0.1

RESULTS

Study Population

A total of 6012 individuals between the ages of 35 and 89 were diagnosed with a primary lung cancer during the study period. For the primary analysis, we excluded patients with a prior diagnosis of lung cancer (N=155), age < 55 or > 80 years (n=1,383), unknown/missing tobacco history (n=322), and individuals that never smoked (n=474), resulting in a cohort of 3678 individuals with an incident lung cancer; 404 (11%) individuals were diagnosed with lung cancer after screening. **(Supplemental Figure 1)** The median age of the cohort was 69 years (interquartile range [IQR], 64 to 74 years) and was composed of 1,922 female (52%) and 1,756 male (48%) patients. There were more previous (2,299 [63%]) than current smokers (1,379 [37%]). Most patients were non-Hispanic White (2,442 [66%]; Non-Hispanic Black (713 [19%]); or Asian, Native Hawaiian, or Pacific Islander (276 [8%]). (**Table 1)** Compared to patients diagnosed with lung cancer in the absence of screening, patients diagnosed after screening were more likely Non-Hispanic White, individuals who currently smoke, have greater comorbid illness, and more likely to have a diagnosis of COPD.

Lung Cancer Screening Activity and Lung Cancer Incidence

Lung cancer screening activity, measured by the combined volume of baseline and annual scans, increased steadily over the study period, increasing from a total of 1,238 screenings in first quarter (Q1) of 2014 to 3,059 screenings in the third quarter (Q3) of 2019. As screening volume increased, the proportion of patients diagnosed with lung cancer after screening also rose from 0% in Q1 of 2014 to 20% in Q3 of 2019. (**Figure 1**) Initiation of LCS did not result in a significant change in the overall incidence of lung cancer (AAPC, - 0.8 [95% CI -4.7, 3.]) between 2014 and 2018. (**Table 2**) Stage specific incidence rates increased for Stage I (AAPC, 8.0 [95% CI 0.8, 15.7]), declined for Stage IV (AAPC, -6.0 [95% CI -11.2, -0.5]), and were not significantly altered for Stage II (AAPC, -7.5 [95% CI -28.7, 20.1]) or Stage III (AAPC, -3.3 [95% CI -14.2, 9.0]) lung cancer. (**Table 2 and Figure 2**) Very few Stage 0 cancers (n=11) were diagnosed during this timeframe, limiting the assessment of incidence rate for in-situ cancers.

Impact of Screening on Histology and Stage Migration

The distribution of tumor histology between screened and unscreened patients did not differ significantly between groups. (**Table 3**) In particular, there were no differences in the proportion of two most common histological subtypes, adenocarcinoma (47.0 vs. 42.8%; risk difference [RD], - 4.2 [95% CI, -9.3, 1.0]) and squamous cell carcinoma (23.1% vs. 26.5%, RD 3.4 [95% CI -1.1, 8.0]) between the unscreened and screened groups. Screening was, however, associated with an increase in the proportion of Stage I cancer (54.7% vs. 27.9%, RD 26.8 [95% CI 21.7, 31.9]) with a concomitant decrease in Stage IV cancer (17.6% vs. 41.7%, RD -24.1 [95% CI -28.2, -20.0]) compared to the population diagnosed with lung cancer detected without prior screening. In contrast to the observed

rates with Stage I and IV, the proportion of Stage II and III lung cancer were similar between screened and unscreened groups. (**Table 2**)

Factors Associated with a Diagnosis of Early-Stage Lung Cancer

Among those with lung cancer, we used multivariable regression to identify factors associated with a diagnosis of early-stage disease (Stage 0, I, and II) independent of lung cancer screening. Compared to patients diagnosed without prior lung cancer screening, a diagnosis of lung cancer after any screening had an increased odds of early-stage diagnosis in both unadjusted and multivariable models (aOR: 3.61, 95% CI: 2.81-4.65). (**Figure 3; Supplemental Table 1**) Additional factors associated with the an increased likelihood of an early-stage diagnosis included: older age (aOR1.36, 95% CI 1.08-1.70, for ages 75-80 years compared to ages 55-64 years), female sex (aOR 1.49, 95% CI 1.27-1.75), former tobacco use (aOR1.29, 95% CI 1.08-1.54), a diagnosis of COPD (aOR 1.61, 95% CI 1.37-1.90) or prior malignancy other than lung cancer (aOR 1.82, 95% CI 1.43-2.33), and an elevated BMI (aOR 1.27, CI 1.04-1.55 for BMI >30 kg/m^2 compared to BMI < 25 kg/m^2). (**Table 3**) Patients with small cell lung cancer had a decreased odds of early-stage disease compared to those with non-small cell histology (aOR 0.12, CI 0.09-0.18). There was no association of socioeconomic status or race and ethnicity with early-stage diagnosis.

DISCUSSION

Although trials have shown that lung cancer screening with LDCT reduces lung cancer specific mortality, the effectiveness of LDCT in clinical practice has not been clearly demonstrated. In this multicenter cohort analysis, we examined the impact of screening on the distribution of cancer stage and lung cancer incidence and demonstrate several important findings during this relatively early

phase of lung cancer screening implementation. First, among individuals who were diagnosed with lung cancer after being screened during this time period, most (64%) were identified at an early-stage, and this was accompanied by a concomitant decrease in patients with metastatic lung cancer. Second, at the population level across the four healthcare systems evaluated in this analysis, the overall annual incidence of lung cancer was relatively stable; however, there were notable changes in the incidence of stage-specific disease as the rate of screening increased over time. The annual rate of Stage I lung cancer increased by an average of 8.4% and was accompanied by an average decline of 6.6.% in Stage IV disease. By 2018, these changes in incidence resulted in a higher rate of Stage I compared to Stage IV cancers. This migration to early-stage disease with no change in the overall incidence of lung cancer suggests that implementation of screening was achieving the desired effect of identifying early-stage lung cancers that were destined to progress to more advanced stages of disease, and without resulting in a significant rate of overdiagnosis. While over-diagnosis is difficult to explicitly define, our findings stand in contrast to the evidence of overdiagnosis from LDCT screening in a largely nonsmoking population of women in Taiwan noted by Gao et.al[24] who reported a 6-fold increase in the incidence of early-stage lung cancer without change in the incidence of late-stage lung cancer.

Differences between efficacy and effectiveness with respect to the benefit of lung cancer screening may exist if implementation varies in important aspects from how it was administered in the randomized trials. The NLST and NELSON trials were conducted primarily in urban academic centers and had resources and processes in place to optimize study procedures, evaluation of positive findings, including timely evaluation and minimizing harms from invasive evaluation. Whether the results observed in these trials will result in similar outcomes with screening in

community-based settings as a part of standard clinical care remains unclear. For example, study procedures utilized in the NLST and NELSON trials resulted in very high adherence to annual screening, but observed rates in community settings have been considerably lower, including at the health systems included in this analysis.[12,14,25]

Despite lower adherence across the four systems, the distribution of cancer stage was nearly as favorable as the distribution observed in the NLST and NELSON trials. For example, when compared to NLST we observed a slightly lower rate of stage I disease (55% vs. 61%) diagnosed after screening, but this was considerably higher than the rate of stage I disease in the non-screened population (28%). Our findings build on the results of prior analyses from community and academic settings which have shown a favorable shift in stage distribution among screened populations, including a prior report from one healthcare system within our multicenter cohort.[26] In the first year of screening (2013-2014) in a veterans affairs (VA) medical system, Okerke et al. reported an early-stage disease rate of 67% compared to 35% in the prescreening period.[27] An 8-site VA demonstration project and a multisite program within a large integrated health system both reported a 71% rate of early-stage disease.[15,28]

In additional to LCS-LDCT, we identified additional factors that were associated with a diagnosis of early-stage lung cancer. A personal history of extrathoracic cancer and a history of COPD were associated with a diagnosis of early-stage lung cancer, likely reflecting higher utilization of thoracic imaging in these individuals. Patients with prior cancer generally undergo several years of surveillance which can identify lesions suspicious for lung cancer prior to clinical presentation. Patients with COPD also undergo more frequent chest imaging to establish the diagnosis or for ongoing assessment and management of symptoms and exacerbations which can similarly identify

suspicious lung lesions. Individuals with an increased BMI of >30 were also more likely to be diagnosed with early-stage disease, which may also reflect greater healthcare utilization, including higher rates of imaging.

Limitations

Our study has limitations. First, our results are derived from a retrospective study of four diverse health systems in the US but may not reflect the stage distribution and stage specific rates observed in other settings or more broadly across the US. Second, our study utilizes health system level EHR data allowing accurate identification of screening events, but we could not differentiate between screen detected or interval cancers. Third, although prior studies have shown that those who elect to receive screening are healthier in ways that are difficult to measure,[29] given that a 30 pack-year smoking history is an LCS eligibility requirement, we believe healthy-user bias is minimal in the PROSPR-Lung screened population. Lastly, while cancer case ascertainment relied on local cancer registry information, individuals may have sought care outside of one of the four health systems included in our analysis. We believe this was a relatively rare event given that two of the healthcare systems operate under an integrated care delivery model and the other two limited the cohort to individuals that received primary care within their systems and retain patients diagnosed with cancer given their role as comprehensive cancer centers. Furthermore, any out migration prior to lung cancer diagnosis would be anticipated to occur at similar rates for unscreened and screened individuals since there was no socioeconomic difference between the two groups.

Conclusions

To our knowledge, this is the first study to determine the impact of LCS on cancer stage migration using a population based multicenter cohort. Our results suggest that LCS results in a shift to early-

stage disease coupled with a decline in the proportion diagnosed with metastatic lung cancer when compared to the unscreened population. The distribution of stage was similar to rates observed in prior clinical trials despite limitations such as lower adherence to annual screening that have been observed outside of trial settings. By the end of the study, approximately 20% of those diagnosed with lung cancer had received at least one prior LCS LDCT. While over-diagnosis remains a concern, at this rate of screening we did not observe an increase in the overall rate of lung cancer. As screening implementation progresses, future population-based studies are needed to assess the impact of screening on other effectiveness outcomes, including rates of harms related to screening and the impact on lung cancer mortality.

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FIGURE LEGENDS

Figure 1. **Screening Volume and Lung Cancer Diagnoses, 2014-2019**

Bars demonstrates the proportion of incident lung cancer diagnoses after at least one prior LCS-LDCT by quarter between 2014 and 2019. The gray line demonstrates the total volume of LCS-LDCT scans performed in that quarter.

Figure 2. **Stage-Specific Trends in Lung Cancer Incidence, 2014-2018**

Figure 3. Factors Associated with a Diagnosis of Early-Stage Lung Cancer

TABLE 1. Baseline Characteristics of Patients Diagnosed with Lung Cancer, 2014-2019

Variable	Lung Cancer Diagnoses , No (%)			
	Overall (N=3678)	No Prior LCS (N=3274)	LCS (N=404)	p-value
Age at Diagnosis				0.0020
55 - 64	1025 (28)	908 (28)	117 (29)	
65 - 74	1741 (47)	1526 (47)	215 (53)	
75 - 80	912 (25)	840 (26)	72 (18)	
Sex				0.0889
Female	1922 (52)	1727 (53)	195 (48)	
Male	1756 (48)	1547 (47)	209 (52)	
Race and Ethnicity				0.0098
Non- Hispanic White	2442 (66)	2147 (66)	295 (73)	
Non-Hispanic Black	713 (19)	657 (20)	56 (14)	
Asian, Native Hawaiian, or Pacific Islander	276 (8)	254 (8)	22 (5)	
Hispanic	112 (93)	98 (3)	14 (3)	
American Indian, Other, or Unknown	135 (4)	118 (4)	17 (4)	
Smoking History				< .0001
Current	1379 (37)	1161 (35)	218 (54)	
Former	2299 (63)	2113 (65)	186 (46)	
Health System				< .0001
Site 1	1368 (37)	1227 (37)	141 (35)	
Site 2	1031 (28)	851 (26)	180 (45)	
Site 3	414 (11)	384 (12)	30 (7)	
Site 4	865 (24)	812 (25)	53 (13)	
Modified CCI[a]				0.0028
0	589 (16)	544 (17)	45 (11)	
1	514 (14)	450 (14)	64 (16)	
2	563 (15)	483 (15)	80 (20)	
3+	2012 (55)	1797 (55)	215 (53)	
COPD[b]	1683 (46)	1438 (44)	245 (61)	< .0001
Previous Cancer	445 (12)	403 (12)	42 (10)	0.2659
BMI				0.0983
< 25	1437 (39)	1267 (39)	170 (42)	
25 – 29	1197 (33)	1058 (32)	139 (34)	
30 +	991 (27)	903 (28)	88 (22)	
Missing	53 (1)	46 (1)	7 (2)	
Socioeconomic Status (Yost Index)				0.4173
Quintile 1 (lowest)	894 (24)	810 (25)	84 (21)	
Quintile 2	603 (16)	534 (16)	69 (17)	
Quintile 3	668 (18)	587 (18)	81 (20)	
Quintile 4	613 (17)	535 (16)	78 (19)	
Quintile 5 (highest)	769 (21)	690 (21)	79 (20)	
Missing	131 (4)	118 (4)	13 (3)	

[a] Modified CCI: Excludes AIDS diagnosis

[b] COPD diagnosis code (ICD 9/10: 491, 492, 496, J41, J42, J43, J44) in year prior to lung cancer diagnosis

TABLE 2. Age-Standardized Overall and Stage-Specific Lung Cancer Incidence Rates, 2014 to 2018[a]

Year[b]	Overall		Stage 0		Stage I		Stage II		Stage III		Stage IV		Unknown Stage	
	Lung Cancer Diagnoses	Lung Cancer Rate	Lung Cancer Diagnoses	Lung Cancer Rate	Lung Cancer Diagnoses	Lung Cancer Rate	Lung Cancer Diagnoses	Lung Cancer Rate	Lung Cancer Diagnoses	Lung Cancer Rate	Lung Cancer Diagnoses	Lung Cancer Rate	Lung Cancer Diagnoses	Lung Cancer Rate
2014	560	151.6	0	0.00	138	37.96	61	16.40	100	26.63	240	65.01	21	5.6
2015	650	164.4	4	1.07	178	44.91	59	15.38	126	31.40	271	68.54	12	3.1
2016	652	158.5	0	0.00	205	50.23	37	9.06	129	30.93	260	63.23	21	5.0
2017	690	153.7	2	0.48	211	47.17	68	15.30	132	28.35	259	58.06	18	4.3
2018	739	150.3	5	0.97	263	54.31	52	11.15	119	23.67	259	51.85	41	8.4
AAPC	-0.8 [95%CI, -4.7, 3.2]		N/A[c]		8.0 [95%CI, 0.8-15.7]		-7.5 [95%CI, -28.7, 20.1]		-3.3 [95%CI, -14.2, 9.0]		-6.0 [95%CI, -11.2, -0.5]		12.0 (95%CI, -22.1, 60.9)	

[a] 132 individuals that were age 80 were combined with the individuals aged 75-79 for the age adjustment calculations.
[b] Total person-years by year: 413,511.3 (2014); 440,530.4 (2015), 468,131.5 (2016), 490,317.4 (2017), 520,511.2 (2018).
[c] The AAPC is not reported for Stage 0 given the small number of cases which does not allow for an accurate calculation.
Abbreviations: AAPC (Average Annual Percent Change)

TABLE 3. Differences in Lung Cancer Stage by Prior LCS, 2014-2019

	No LCS (N=3274)	LCS (N=404)	Risk Difference (95% CI)
Tumor Histology, N (%)			
Adenocarcinoma	1538 (47.0)	173 (42.8)	-4.2 (-9.3, 1.0)
Squamous Cell	755 (23.1)	107 (26.5)	3.4 (-1.1, 8.0)
Large Cell	22 (0.7)	7 (1.7)	1.1 (-0.2, 2.4)
Non-Small Cell/Other	440 (13.4)	58 (14.4)	0.9 (-2.7, 4.5)
Small cell	456 (13.9)	47 (11.6)	-2.3 (-5.6, 1.1)
Carcinoid	63 (1.9)	12 (3.0)	1.1 (-0.7, 2.8)
AJCC Stage, N (%)			
0/I	915 (27.9)	221 (54.7)	26.8 (21.7, 31.9)
II	268 (8.2)	36 (8.9)	0.7 (-2.2, 3.7)
III	601 (18.4)	66 (16.3)	-2.0 (-5.9, 1.8)
IV	1365 (41.7)	71 (17.6)	-24.1 (-28.2, -20.0)
Unknown/Missing/Occult/NA	125 (3.8)	10 (0.5)	-1.3 (-3.0, 0.3)

FIGURE 1. Screening Volume and Lung Cancer Diagnoses, 2014-2019

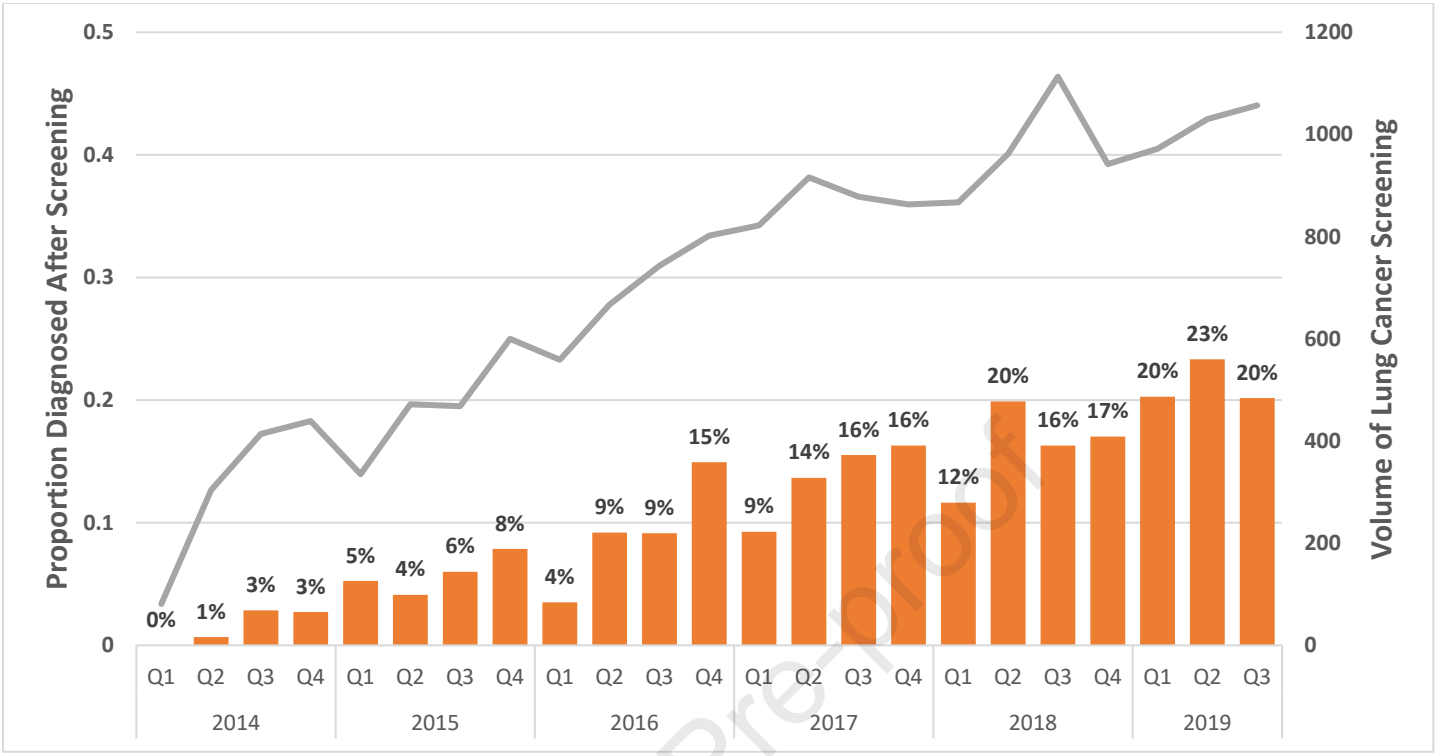
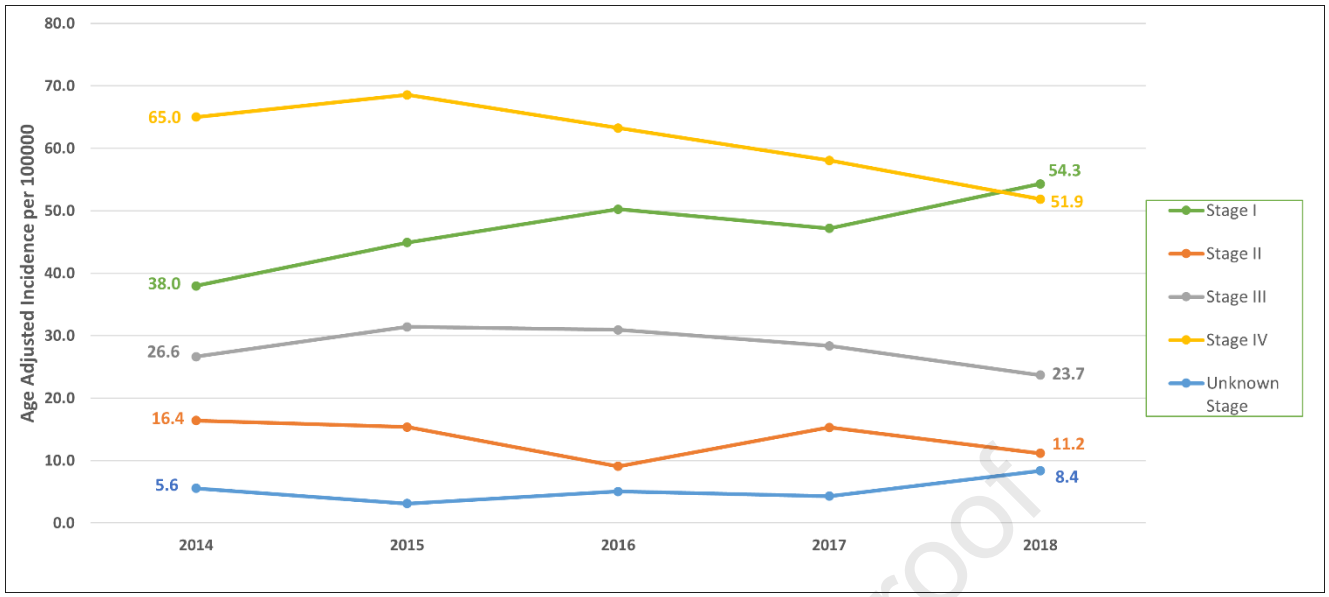
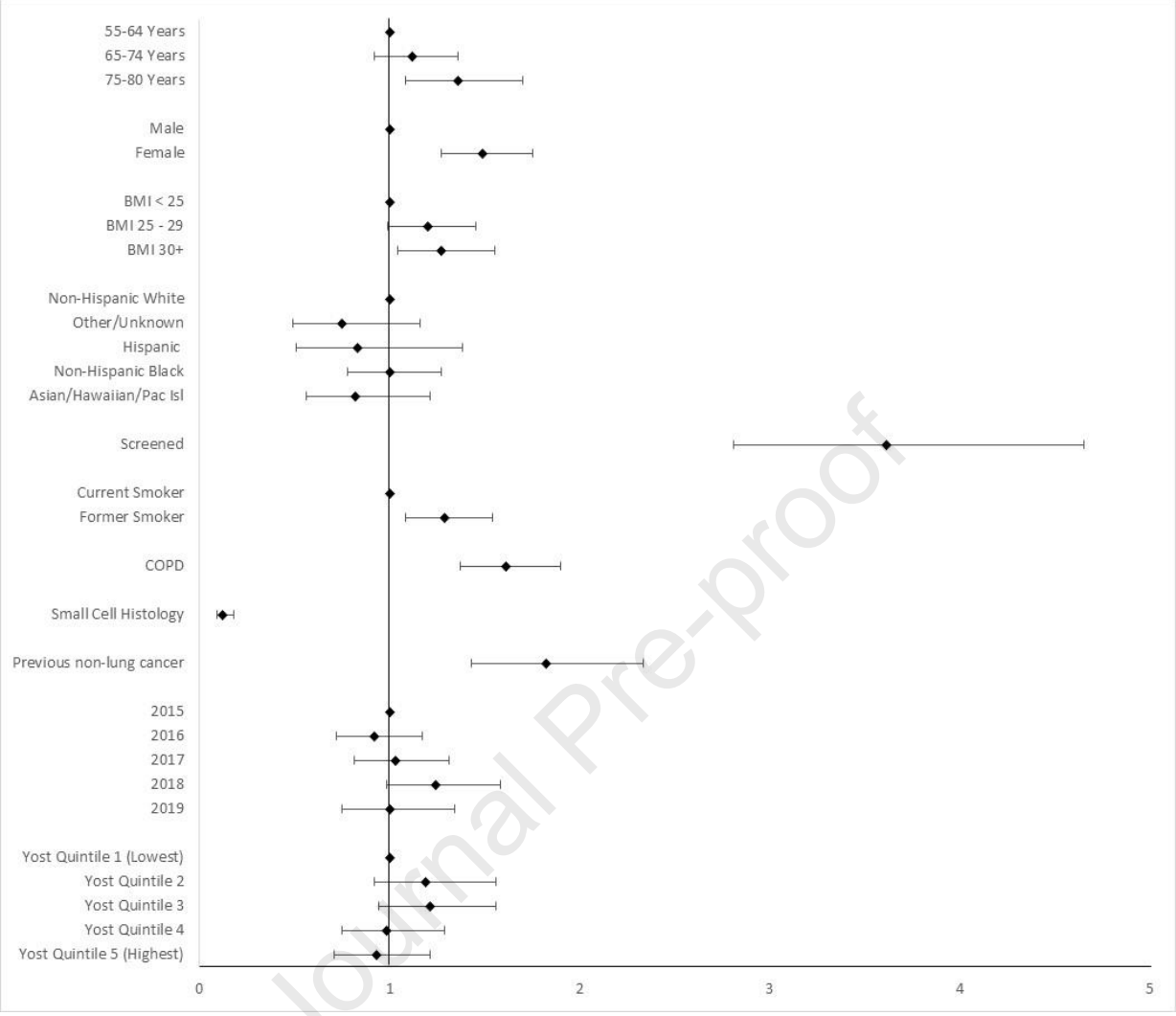


FIGURE 2. Stage-Specific Trends in Lung Cancer Incidence for Overall Cohort, 2014-2018[a]



[a] Stage 0 lung cancer excluded given the small number of in-situ lung cancer diagnoses (n=11)

FIGURE 3. Factors Associated with a Diagnosis of Early-Stage Lung Cancer[a]



[a] early stage defined as Stage 0, I, and II

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