Original Article

# Sociodemographic and clinical characteristics associated with never-smoking status in patients with lung cancer: findings from a large integrated health system

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**Background:** Evidence is limited characterizing sociodemographically diverse patient populations with lung cancer in relation to smoking status.

**Methods:** In a cross-sectional analysis of adults diagnosed with lung cancer at ages ≥30 years from 2007–2018 within an integrated healthcare system, overall and sex-specific prevalence of never smoking were estimated according to sociodemographic and clinical characteristics. Adjusted prevalence ratio (aPR) and 95% confidence interval (CI) were also estimated using modified Poisson regression to identify patient characteristics associated with never smoking, overall and by sex. Similar analyses were conducted to explore whether prevalence and association patterns differed between non-Hispanic White and Asian/Pacific Islander patients.

**Results:** Among 17,939 patients with lung cancer, 2,780 (15.5%) never smoked and 8,698 (48.5%) had adenocarcinoma. Overall prevalence of never smoking was higher among females than males (21.2% *vs.* 9.2%, aPR 2.13, 95% CI: 1.98–2.29); Asian/Pacific Islander (aPR 2.85, 95% CI: 2.65–3.07) and Hispanic (aPR 1.72, 95% CI: 1.51–1.95) than non-Hispanic White patients; patients who primarily spoke Spanish (aPR 1.60, 95% CI: 1.32–1.94), any Asian language (aPR 1.20, 95% CI: 1.10–1.30), or other languages (aPR 1.84, 95% CI: 1.27–2.65) than English; patients living in the least vs. most deprived neighborhoods (aPR 1.36, 95% CI: 1.24–1.50); and patients with adenocarcinoma (aPR 2.57, 95% CI: 2.18–3.03), other non-small cell lung cancer (NSCLC) (aPR 2.00, 95% CI: 1.63–2.45), or carcinoid (aPR 3.60, 95% CI: 2.96–4.37) than squamous cell carcinoma tumors. Patterns of never smoking associated with sociodemographic, but not clinical factors, differed by sex. The higher prevalence of never smoking associated with Asian/Pacific Islander race/ethnicity was more evident among females (aPR 3.30, 95% CI: 2.95–3.47) than males (aPR 2.25, 95% CI: 1.92–2.63), whereas the higher prevalence of never smoking associated with living in the least deprived neighborhoods was more evident among males (aPR 1.93, 95% CI: 1.56–2.38) than females (aPR 1.18, 95% CI: 1.06–1.31). Associations between primary language and never-smoking status were found only among females. Overall and sex-specific prevalence and association patterns differed between Asian/Pacific Islander and non-Hispanic white patients.

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**Conclusions:** Our findings suggest that patterns of never-smoking status associated with sociodemographic and clinical characteristics are different across sex and race/ethnicity among patients with lung cancer. Such data are critical to increasing awareness and expediting diagnosis of this disease.

**Keywords:** Lung cancer; smoking status; characteristics; prevalence

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## Introduction

Lung cancer is the leading cause of cancer-related death, and it affects individuals who have never smoked tobacco in addition to those who have (1). On its own, lung cancer unrelated to smoking would be the seventh leading cause of cancer-related death (2). While the mortality of smoking-related lung cancer is declining in those who have smoked, lung cancer mortality among those who have never smoked may actually be on the rise (2,3).

About 10–15% of lung cancers in the United States arise among individuals with no history of smoking (3-5). It is becoming clear, however, that among patients with lung cancer, those who have never smoked have distinct characteristics when compared to those who have smoked in their lifetime. Among patients who have never smoked, females have been found to have higher rates of lung cancer than their male counterparts, and this is especially pronounced among Asian patients (6-14). Patients who have never smoked have also been found to have higher likelihood of adenocarcinoma than those who have ever smoked (7-9,11,15,16).

Importantly, some reports suggest that individuals with no smoking history are more likely to have delayed diagnoses of lung cancer and present with advanced stage tumors at diagnosis (8,12). It is therefore critical to characterize a sociodemographically diverse patient population with lung cancer more fully to increase physician awareness and knowledge about patient characteristics associated with never smoking, which may thereby reduce delays in diagnosis of lung cancer in those who have never smoked.

Using linked cancer registry and electronic health record data on a large, diverse population of patients diagnosed with primary lung cancer, we estimated prevalence of never-smoking status according to selected sociodemographic and clinical characteristics. We also estimated prevalence ratios to specifically determine which characteristics were independently associated with never-smoking status at lung cancer diagnosis. We postulated that the prevalence of never smoking and associated characteristics are influenced and differ by sex. We present the following article in accordance with the STROBE reporting checklist (available at https://tcr.amegroups.com/article/view/10.21037/tcr-22-1438/rc).

## Methods

### *Study population and setting*

Our study population was drawn from adults enrolled at Kaiser Permanente Northern California (KPNC), an integrated healthcare system that currently serves a socioeconomically and ethnically diverse membership of over 4.5 million individuals that is representative of the general population in Northern California (17,18). The KPNC healthcare system serves nearly one-third of the population in its service area. In this study, we included all patients newly diagnosed with lung cancer at ages 30 years and older from January 1, 2007 to December 31, 2018. Patients were excluded if smoking status or race/ethnicity were unknown. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the KPNC Institutional Review Board (No. 1667026-2) and individual consent for this retrospective analysis was waived.

### *Data sources and patient characteristics*

Eligible patients were identified using data from our institution's cancer registry, which follows the national Surveillance, Epidemiology, and End Results Program standards. Patient characteristics ascertained from the cancer registry included age at lung cancer diagnosis, histology, and stage. Additional patient characteristics were collected by linking individual-level cancer registry and electronic health record data by medical record number. Characteristics included smoking status, sex, self-reported

 

race/ethnicity, primary language, neighborhood deprivation index (NDI), and history of selected comorbidities that may affect lung cancer risk [chronic obstructive pulmonary disease (COPD), interstitial lung disease, and autoimmune lung disease], as determined at the date of lung cancer diagnosis. Regarding smoking status, those without any recorded history of tobacco use were considered to have never smoked. Otherwise, they were considered to have ever smoked. Based on residential address, NDI was calculated from eight census variables in the domains of income/poverty, education, employment, housing, and occupation using the method of Messer *et al.*, with patients classified into quintiles (with quintile 1 being the least deprived and quintile 5 being the most deprived) (19).

### *Statistical analysis*

Frequency distributions for individual patient characteristics were calculated, overall and by smoking status. Overall and sex-specific crude prevalence and 95% confidence interval (CI) of never smoking according to sociodemographic and clinical characteristics were estimated. Adjusted prevalence ratio (aPR) and 95% CI were also estimated using modified Poisson regression with robust variance estimation to determine patient characteristics independently associated with never smoking, overall and stratified by sex. In cross-sectional studies, modified Poisson regression is a preferred approach to generate prevalence ratio estimates for binary outcomes (e.g., never *vs.* ever smoking) that are more easily interpretable than odds ratio estimates from logistic regression. Models included all patient characteristics as described above, except for history of autoimmune disease (due to its rarity), for their potential association with smoking status. All measured variables were selected a priori for model inclusion, given our objective to identify all patient characteristics associated with never-smoking status at diagnosis of lung cancer. Since patterns of tobacco use are known to differ by sex, overall and sex-specific analyses were conducted to examine the extent to which the prevalence of never smoking and associated patient characteristics are influenced and differ by sex. These analyses were further conducted among Asian/Pacific Islander patients and non-Hispanic White patients separately to explore whether overall and sex-specific prevalence and association patterns differed between these two major racial/ethnic groups in our study population. Similar analyses could not be conducted for Black and Hispanic patients because of their limited numbers. All statistical analyses were performed using Statistical Analysis Software (SAS) version 9.4.

## Results

Of the 18,627 patients diagnosed with lung cancer at ages ≥30 years, 688 were further excluded for missing data on stage at diagnosis. The remaining 17,939 patients were included in our final analysis (*Figure 1*). Overall, the median age at diagnosis was 71 years; 52.7% were female. The racial/ethnic composition of our cohort was 68.5% non-Hispanic White, 12.3% Asian/Pacific Islander, 7.6% Black, 6.6% Hispanic, and 5.0% other/unknown. The most common histologic diagnosis was non-small cell lung cancer (NSCLC; 78.8%), including adenocarcinoma (48.5%), squamous cell carcinoma (16.0%), and other NSCLC subtypes (14.3%). Other histologic diagnoses included small cell carcinoma (8.8%), carcinoid (3.7%), and other/unknown (8.7%). The majority of patients were diagnosed with stage IV disease (51.2%), followed by stage I (22.9%), stage III (19.1%), and stage II (6.8%). Other patient characteristics are reported in *Table 1*.

With regard to smoking status, 2,780 (15.5%) of all patients with lung cancer had never smoked (*Table 1*). Never-smoking status was associated with all characteristics examined, except history of interstitial lung disease (*Table 2*). Specifically, patients aged 30–49 years (aPR 1.66, 95% CI: 1.49–1.85), 50–59 years (aPR 1.20, 95% CI: 1.10–1.32), and ≥80 years (aPR 1.35, 95% CI: 1.23–1.47) at diagnosis of lung cancer were slightly more likely to have never smoked than those aged 60–69 years. Female patients were twice as likely to have never smoked than male patients (aPR 2.13, 95% CI: 1.98–2.29). Compared to non-Hispanic White patients, Asian/Pacific Islander (aPR 2.85, 95% CI: 2.65–3.07) and Hispanic (aPR 1.72, 95% CI: 1.51–1.95) patients were more likely to have never smoked, whereas Black (aPR 0.82, 95% CI: 0.69–0.98) patients were less likely to have never smoked. Likewise, patients who primarily spoke Asian languages (aPR 1.20, 95% CI: 1.10–1.30), Spanish (aPR 1.60, 95% CI: 1.32–1.94), or other/unknown languages (aPR 1.84, 95% CI: 1.27–2.65) were more likely to have never smoked than patients who primarily spoke English. Patients who lived in the least (*vs.* most) deprived neighborhoods were also more likely to have never smoked (NDI quintile 1 *vs.* 5: aPR 1.36, 95% CI: 1.24–1.50). Patients with COPD were substantially less likely to have never smoked than those without COPD (aPR 0.13, 95% CI: 0.11–0.15). Compared to patients with squamous cell carcinoma tumors, patients who had adenocarcinoma (aPR

 

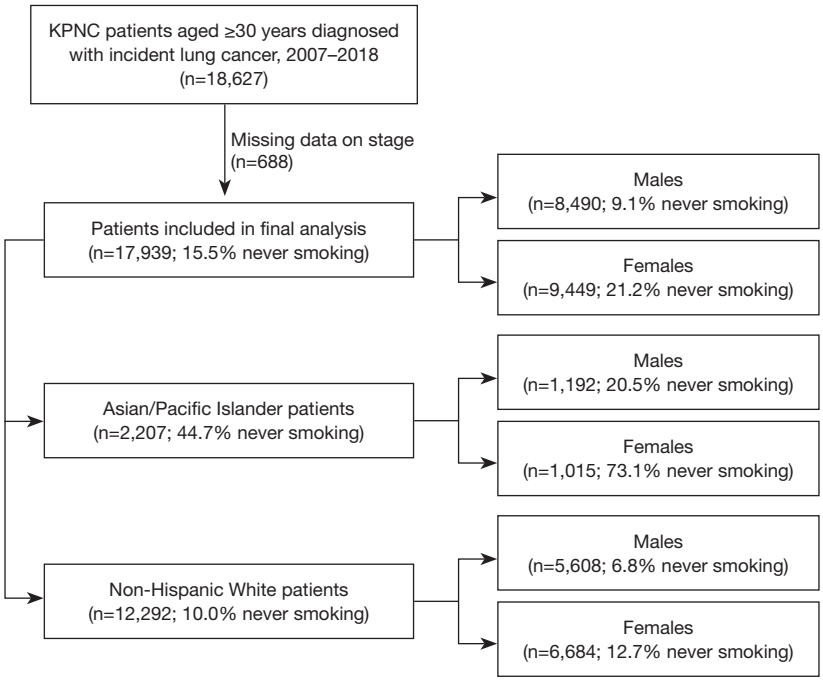


**Figure 1** Study design flowchart. KPNC, Kaiser Permanente Northern California.

**Table 1** Patient characteristics by smoking status

| Characteristics | Smoking status | | Overall (n=17,939) |
|---|---|---|---|
| | Never (n=2,780, 15.5%) | Ever (n=15,159, 84.5%) | |
| Age at diagnosis (years), n (%) | | | |
| <50 | 243 (8.7) | 329 (2.2) | 572 (3.2) |
| 50–59 | 481 (17.3) | 1,730 (11.4) | 2,211 (12.3) |
| 60–69 | 730 (26.3) | 4,464 (29.4) | 5,194 (29.0) |
| 70–79 | 720 (25.9) | 5,559 (36.7) | 6,279 (35.0) |
| ≥80 | 606 (21.8) | 3,077 (20.3) | 3,683 (20.5) |
| Median [IQR] | 69 [59, 79] | 71 [64, 78] | 71 [63, 78] |
| Sex, n (%) | | | |
| Male | 777 (27.9) | 7,713 (50.9) | 8,490 (47.3) |
| Female | 2,003 (72.1) | 7,446 (49.1) | 9,449 (52.7) |
| Race/ethnicity, n (%) | | | |
| Non-Hispanic White | 1,234 (44.4) | 11,058 (72.9) | 12,292 (68.5) |
| Asian/Pacific Islander | 987 (35.5) | 1,220 (8.0) | 2,207 (12.3) |
| Hispanic | 278 (10.0) | 912 (6.0) | 1,190 (6.6) |
| Black | 118 (4.2) | 1,243 (8.2) | 1,361 (7.6) |
| Other/unknown | 163 (5.9) | 726 (4.8) | 889 (5.0) |

**Table 1** *(continued)*

 

**Table 1** *(continued)*

| Characteristics | Smoking status | | Overall (n=17,939) |
|---|---|---|---|
| | Never (n=2,780, 15.5%) | Ever (n=15,159, 84.5%) | |
| Primary language, n (%) | | | |
| English | 2,264 (81.4) | 13,638 (90.0) | 15,902 (88.6) |
| Any Asian* | 310 (11.2) | 331 (2.2) | 641 (3.6) |
| Spanish | 87 (3.1) | 155 (1.0) | 242 (1.4) |
| Other | 18 (0.7) | 55 (0.4) | 73 (0.4) |
| Unknown | 101 (3.6) | 980 (6.4) | 1,081 (6.0) |
| NDI†, n (%) | | | |
| Quintile 1 (least deprived) | 758 (27.4) | 2,820 (18.7) | 3,578 (20.0) |
| Quintile 2 | 575 (20.8) | 2,992 (19.8) | 3,567 (20.0) |
| Quintile 3 | 508 (18.3) | 3,075 (20.4) | 3,583 (20.0) |
| Quintile 4 | 489 (17.7) | 3,096 (20.5) | 3,585 (20.1) |
| Quintile 5 (most deprived) | 440 (15.9) | 3,124 (20.7) | 3,564 (19.9) |
| Comorbidity history, n (%) | | | |
| COPD | 121 (4.4) | 6,303 (41.6) | 6,424 (35.8) |
| Interstitial lung disease | 120 (4.3) | 789 (5.2) | 909 (5.1) |
| Autoimmune lung disorder | 8 (0.3) | 52 (0.3) | 60 (0.3) |
| Histology, n (%) | | | |
| Adenocarcinoma | 1,926 (69.3) | 6,772 (44.7) | 8,698 (48.5) |
| Squamous cell carcinoma | 131 (4.7) | 2,743 (18.1) | 2,874 (16.0) |
| Other NSCLC | 320 (11.5) | 2,253 (14.9) | 2,573 (14.3) |
| Small cell carcinoma | 33 (1.2) | 1,547 (10.2) | 1,580 (8.8) |
| Carcinoid | 189 (6.8) | 467 (3.1) | 656 (3.7) |
| Other/unknown | 181 (6.5) | 1,377 (9.1) | 1,558 (8.7) |
| Stage, n (%) | | | |
| I | 739 (26.6) | 3,369 (22.2) | 4,108 (22.9) |
| II | 168 (6.0) | 1,047 (6.9) | 1,215 (6.8) |
| III | 377 (13.6) | 3,051 (20.1) | 3,428 (19.1) |
| IV | 1,496 (53.8) | 7,692 (50.7) | 9,188 (51.2) |

*, Asian languages inclusive of Chinese (Mandarin, Cantonese, Mien, or other dialects), Hmong, Japanese, Korean, Laotian, Tagalog, Thai, Vietnamese, Burmese, Gujarati, Hindi, Iloko, Khmer, and Punjabi; †, excludes missing values. IQR, interquartile range; NDI, neighborhood deprivation index; COPD, chronic obstructive pulmonary disease; NSCLC, non-small cell lung cancer.

2.57, 95% CI: 2.18–3.03), other NSCLC (aPR 2.00, 95% CI: 1.63–2.45), or carcinoid (aPR 3.60, 95% CI: 2.96–4.37) tumors were at least twice as likely to have never smoked, while patients who had small cell tumors were much less likely to have never smoked (aPR 0.45, 95% CI: 0.31–0.64). Patients with stage I tumors were equally likely to have never smoked than patients with stage IV tumors, although more likely to have never smoked than patients with stage II

 

**Table 2** Prevalence ratio and aPR of never-smoking status associated with sociodemographic and clinical characteristics among patients with lung cancer, overall and by sex

| Characteristics | Overall (n=17,939) | | | Male (n=8,490) | | | Female (n=9,449) | | |
|---|---|---|---|---|---|---|---|---|---|
| | Prevalence (95% CI) | aPR | (95% CI) | Prevalence (95% CI) | aPR | (95% CI) | Prevalence (95% CI) | aPR | (95% CI) |
| Age at diagnosis (years) | | | | | | | | | |
| <50 | 42.5 (38.4, 26.6) | 1.66 | (1.49, 1.85) | 32.9 (15.5, 17.0) | 2.31 | (1.86, 2.86) | 49.5 (44.0, 55.1) | 1.44 | (1.28, 1.62) |
| 50–59 | 21.8 (21.0, 24.6) | 1.20 | (1.10, 1.32) | 12.5 (10.5, 14.7) | 1.17 | (0.96, 1.43) | 29.6 (27.1, 32.3) | 1.22 | (1.11, 1.35) |
| 60–69 | 14.1 (13.1, 15.0) | 1.00 | Reference | 8.5 (7.5, 9.7) | 1.00 | Reference | 19.1 (17.6, 20.6) | 1.00 | Reference |
| 70–79 | 11.5 (10.7, 12.3) | 0.96 | (0.88, 1.04) | 7.0 (6.1, 8.0) | 0.90 | (0.75, 1.07) | 15.7 (14.5, 17.0) | 0.98 | (0.89, 1.07) |
| ≥80 | 16.5 (15.3, 17.7) | 1.35 | (1.23, 1.47) | 8.8 (7.6, 10.2) | 1.14 | (0.94, 1.39) | 23.6 (21.7, 25.5) | 1.43 | (1.29, 1.57) |
| Sex | | | | | | | | | |
| Male | 9.2 (8.5, 9.8) | 1.00 | Reference | | | | | | |
| Female | 21.2 (20.4, 22.0) | 2.13 | (1.98, 2.29) | | | | | | |
| Race/ethnicity | | | | | | | | | |
| Non-Hispanic White | 10.0 (9.5, 10.6) | 1.00 | Reference | 6.8 (6.2, 7.5) | 1.00 | Reference | 12.7 (11.9, 13.5) | 1.00 | Reference |
| Asian/Pacific Islander | 44.7 (42.6, 46.8) | 2.85 | (2.65, 3.07) | 20.6 (18.3, 23.0) | 2.25 | (1.92, 2.63) | 73.1 (70.3, 75.8) | 3.20 | (2.95, 3.47) |
| Black | 8.7 (7.2, 10.3) | 0.82 | (0.69, 0.98) | 3.2 (2.0, 4.8) | 0.46 | (0.30, 0.70) | 13.8 (11.3, 16.5) | 0.99 | (0.82, 1.20) |
| Hispanic | 23.4 (21.0, 25.9) | 1.72 | (1.51, 1.95) | 14.6 (11.9, 17.7) | 1.62 | (1.28, 2.06) | 32.9 (29.1, 37.0) | 1.74 | (1.50, 2.01) |
| Other (including unknown) | 18.3 (15.8, 21.0) | 1.65 | (1.45, 1.89) | 9.0 (6.4, 12.2) | 1.47 | (1.09, 1.99) | 26.4 (22.5, 30.5) | 1.73 | (1.49, 2.01) |
| Primary language | | | | | | | | | |
| English | 14.2 (13.7, 14.8) | 1.00 | Reference | 8.9 (8.3, 9.6) | 1.00 | Reference | 18.9 (18.0, 19.7) | 1.00 | Reference |
| Any Asian* | 48.4 (44.4, 52.3) | 1.20 | (1.10, 1.30) | 16.6 (12.9, 20.8) | 0.81 | (0.62, 1.05) | 88.1 (83.7, 91.6) | 1.37 | (1.27, 1.48) |
| Spanish | 36.0 (29.9, 42.3) | 1.60 | (1.32, 1.94) | 20.1 (13.8, 27.8) | 1.36 | (0.91, 2.04) | 57.3 (47.1, 67.0) | 1.71 | (1.39, 2.11) |
| Other | 24.7 (15.5, 36.6) | 1.84 | (1.27, 2.65) | 12.8 (4.8, 25.7) | 1.63 | (0.83, 3.19) | 46.2 (26.6, 66.6) | 1.97 | (1.24, 3.13) |
| Unknown | 9.3 (7.7, 11.2) | 0.85 | (0.71, 1.02) | 4.7 (3.1, 6.8) | 0.70 | (0.48, 1.02) | 14.2 (11.4, 17.5) | 0.92 | (0.75, 1.12) |
| NDI | | | | | | | | | |
| Quintile 1 (least deprived) | 21.2 (19.9, 22.6) | 1.36 | (1.24, 1.50) | 14.6 (12.9, 16.4) | 1.93 | (1.56, 2.38) | 26.6 (24.7, 28.7) | 1.18 | (1.06, 1.31) |
| Quintile 2 | 16.1 (14.9, 17.4) | 1.13 | (1.02, 1.25) | 9.8 (8.4, 11.3) | 1.31 | (1.05, 1.64) | 21.8 (19.9, 23.7) | 1.06 | (0.95, 1.18) |
| Quintile 3 | 14.2 (13.0, 15.4) | 1.06 | (0.96, 1.18) | 7.7 (6.5, 9.0) | 1.15 | (0.91, 1.45) | 20.3 (18.5, 22.2) | 1.04 | (0.93, 1.17) |
| Quintile 4 | 13.6 (12.5, 14.8) | 1.03 | (0.93, 1.14) | 7.8 (6.6, 9.2) | 1.24 | (0.99, 1.57) | 18.9 (17.2, 20.7) | 0.96 | (0.85, 1.07) |
| Quintile 5 (most deprived) | 12.3 (11.3, 13.5) | 1.00 | Reference | 6.2 (5.1, 7.5) | 1.00 | Reference | 18.0 (16.3, 19.9) | 1.00 | Reference |
| Comorbidity history | | | | | | | | | |
| COPD | 1.9 (1.6, 2.2) | 0.13 | (0.11, 0.15) | 1.0 (0.6, 1.4) | 0.10 | (0.07, 0.14) | 2.7 (2.2, 3.4) | 0.14 | (0.12, 0.18) |
| Interstitial lung disease | 13.2 (11.1, 15.6) | 1.07 | (0.93, 1.23) | 7.3 (5.1, 10.0) | 1.07 | (0.79, 1.45) | 20.2 (19.4, 24.4) | 1.07 | (0.91, 1.25) |
| Histology | | | | | | | | | |
| Adenocarcinoma | 22.1 (21.3, 23.0) | 2.57 | (2.18, 3.03) | 13.8 (12.7, 14.9) | 2.81 | (2.12, 3.73) | 28.5 (27.2, 29.8) | 2.41 | (1.97, 2.93) |
| Squamous cell carcinoma | 4.6 (3.8, 5.4) | 1.00 | Reference | 3.1 (2.3, 4.0) | 1.00 | Reference | 6.5 (5.2, 8.1) | 1.00 | Reference |
| Other NSCLC | 12.4 (11.2, 13.8) | 2.00 | (1.63, 2.45) | 6.9 (5.6, 8.3) | 1.78 | (1.28, 2.47) | 18.6 (16.4, 20.9) | 2.05 | (1.65, 2.55) |
| Small cell carcinoma | 2.1 (1.4, 2.9) | 0.45 | (0.31, 0.64) | 1.9 (1.1, 3.2) | 0.57 | (0.33, 1.00) | 2.2 (1.3, 3.5) | 0.37 | (0.23, 0.60) |

**Table 2** *(continued)*

**Table 2** *(continued)*

| Characteristics | Overall (n=17,939) | | | Male (n=8,490) | | | Female (n=9,449) | | |
|---|---|---|---|---|---|---|---|---|---|
| | Prevalence (95% CI) | aPR | (95% CI) | Prevalence (95% CI) | aPR | (95% CI) | Prevalence (95% CI) | aPR | (95% CI) |
| Carcinoid | 28.8 (25.4, 32.4) | 3.60 | (2.96, 4.37) | 18.0 (13.4, 23.4) | 3.31 | (2.28, 4.82) | 35.2 (30.6, 40.0) | 3.62 | (2.88, 4.55) |
| Other/unknown | 11.6 (10.1, 13.3) | 2.00 | (1.63, 2.45) | 8.1 (6.2, 10.3) | 2.35 | (1.63, 3.38) | 14.8 (12.4, 17.4) | 1.79 | (1.40, 2.28) |
| Stage | | | | | | | | | |
| I | 18.0 (16.8, 19.2) | 1.00 | Reference | 10.2 (8.8, 11.7) | 1.00 | Reference | 23.5 (21.8, 25.3) | 1.00 | Reference |
| II | 13.8 (11.9, 15.9) | 0.86 | (0.75, 0.99) | 8.8 (6.6, 11.5) | 1.01 | (0.76, 1.34) | 17.9 (15.0, 21.0) | 0.82 | (0.70, 0.95) |
| III | 11.0 (10.0, 12.1) | 0.80 | (0.73, 0.89) | 6.0 (4.9, 7.3) | 0.71 | (0.56, 0.88) | 15.8 (14.1, 17.6) | 0.86 | (0.77, 0.96) |
| IV | 16.3 (15.5, 17.0) | 0.98 | (0.91, 1.05) | 10.0 (9.1, 10.9) | 0.97 | (0.83, 1.14) | 22.5 (21.3, 23.7) | 0.99 | (0.91, 1.07) |

*, Asian languages inclusive of Chinese (Mandarin, Cantonese, Mien, or other dialects), Hmong, Japanese, Korean, Laotian, Tagalog, Thai, Vietnamese, Burmese, Gujarati, Hindi, Iloko, Khmer, and Punjabi. Statistical models included all other patient characteristics listed in the table. CI, confidence interval; aPR, adjusted prevalence ratio; NDI, neighborhood deprivation index; COPD, chronic obstructive pulmonary disease; NSCLC, non-small cell lung cancer.

(aPR 0.86, 95% CI: 0.75–0.99) or stage III (aPR 0.80, 95% CI: 0.73–0.89) tumors.

Patterns of never smoking associated with sociodemographic, but not clinical factors, appeared to differ by sex (*Table 2*). Only men aged 30–49 (*vs.* 60–69 years, aPR 2.31, 95% CI: 1.86–2.86) at diagnosis were more likely to have never smoked, whereas women who were both the youngest (aged 30–49 *vs.* 60–69 years: aPR 1.44, 95% CI: 1.28–1.62 and aged 50–59 *vs.* 60–69 years: aPR 1.22, 95% CI: 1.11–1.35) and oldest (aged ≥80 *vs.* 60–69: aPR 1.43, 95% CI: 1.29–1.57) at diagnosis were more likely to have never smoked. The higher prevalence of never smoking associated with Asian/Pacific Islander (*vs.* non-Hispanic White) race/ethnicity was more pronounced among women (aPR 3.30, 95% CI: 2.95–3.47) than men (aPR 2.25, 95% CI: 1.92–2.63). However, the lower prevalence of never smoking associated with Black (*vs.* non-Hispanic White) race/ethnicity was limited to men. Associations between primary language and never smoking status were noted only among women. The higher prevalence of never smoking associated with living in the least (*vs.* most) deprived was more evident in men (aPR 1.93, 95% CI: 1.56–2.38) than women (aPR 1.18, 95% CI: 1.06–1.31).

Overall and sex-specific association patterns further differed between Asian/Pacific Islander and non-Hispanic white patients (*Tables 3,4*). Among Asian/Pacific Islander patients, female sex was the characteristic most positively associated with never smoking (aPR 2.86, 95% CI: 2.54–3.21; *Table 3*); other characteristics positively associated with never smoking were being younger at diagnosis (ages 30–49 *vs.* 60–69), primarily speaking an Asian language, living in a lesser deprived neighborhood, and having tumors of adenocarcinoma, other NSCLC, or carcinoid histology. In analyses of Asian/Pacific Islander patients stratified by sex, however, younger age at diagnosis and living in a lesser deprived neighborhood were only associated with never smoking among men, and primarily speaking an Asian language was only associated with never smoking among women (*Table 3*). In contrast, among non-Hispanic White patients, all characteristics examined, except for primary language and interstitial lung disease, were either positively or negatively associated with never smoking as observed in all patients, and association patterns were generally similar between men and women, except on age at diagnosis (*Table 4*).

## Discussion

We found distinct differences in the prevalence and association of never smoking with sociodemographic and clinical characteristics among lung cancer patients. Many of these solidify previous reports regarding characteristics among patients with lung cancer who have never smoked, while others provide new insights that help further characterize such patients.

As in our study, a multitude of reports have found that females comprise a larger proportion of lung cancer patients who have never smoked than males (4,6-9). Our findings are also consistent with previous studies in South Korean and Japanese populations, as well as in the United States population, showing that Asian female patients with lung cancer are especially more likely to have never smoked (11-14,20). Interestingly, we found an increased

 

**Table 3** Prevalence ratio and aPR of never-smoking status associated with sociodemographic and clinical characteristics among Asian/Pacific Islander patients with lung cancer, overall and by sex

| Characteristics | Overall (n=2,207) | | | Male (n=1,192) | | | Female (n=1,015) | | |
|---|---|---|---|---|---|---|---|---|---|
| | Prevalence (95% CI) | aPR | (95% CI) | Prevalence (95% CI) | aPR | (95% CI) | Prevalence (95% CI) | aPR | (95% CI) |
| Age at diagnosis (years) | | | | | | | | | |
| <50 | 71.3 (63.6, 78.3) | 1.28 | (1.13, 1.45) | 50.0 (37.0, 63.0) | 2.30 | (1.64, 3.22) | 85.3 (76.5, 91.7) | 1.08 | (0.97, 1.21) |
| 50–59 | 49.3 (44.3, 54.3) | 1.08 | (0.97, 1.20) | 22.2 (16.9, 28.4) | 1.25 | (0.91, 1.72) | 80.6 (74.2, 86.1) | 1.05 | (0.96, 1.16) |
| 60–69 | 42.4 (38.5, 46.2) | 1.00 | Reference | 16.8 (13.1, 20.9) | 1.00 | Reference | 77.0 (71.6, 81.8) | 1.00 | Reference |
| 70–79 | 39.5 (35.7, 43.5) | 0.98 | (0.88, 1.08) | 18.5 (14.5, 22.9) | 1.18 | (0.87, 1.59) | 66.2 (60.3, 71.7) | 0.90 | (0.82, 0.99) |
| ≥80 | 41.5 (36.4, 46.7) | 1.00 | (0.88, 1.14) | 20.4 (14.9, 26.9) | 1.37 | (0.96, 1.96) | 63.5 (55.9, 70.6) | 0.91 | (0.81, 1.03) |
| Sex | | | | | | | | | |
| Male | 20.6 (83.0, 87.1) | 1.00 | Reference | | | | | | |
| Female | 73.1 (70.3, 75.8) | 2.86 | (2.54, 3.21) | | | | | | |
| Primary language | | | | | | | | | |
| English | 44.4 (41.9, 47.0) | 1.00 | Reference | 22.8 (19.9, 25.8) | 1.00 | Reference | 68.6 (65.0, 71.9) | 1.00 | Reference |
| Any Asian* | 47.6 (43.6, 51.7) | 1.11 | (1.03, 1.21) | 16.7 (12.8, 21.1) | 0.77 | (0.59, 1.01) | 88.0 (83.4, 91.7) | 1.26 | (1.17, 1.35) |
| Other/unknown | 29.9 (20.5, 40.6) | 0.92 | (0.69, 1.22) | 11.5 (4.3, 23.4) | 0.78 | (0.37, 1.65) | 57.1 (39.3, 73.7) | 0.94 | (0.70, 1.24) |
| NDI | | | | | | | | | |
| Quintile 1 (least deprived) | 53.8 (49.2, 58.3) | 1.22 | (1.07, 1.39) | 31.8 (25.6, 38.5) | 2.20 | (1.50, 3.22) | 71.4 (65.5, 76.8) | 1.00 | (0.89, 1.12) |
| Quintile 2 | 49.8 (45.0, 54.6) | 1.19 | (1.05, 1.36) | 24.2 (18.8, 30.1) | 1.58 | (1.07, 2.33) | 80.0 (73.8, 85.3) | 1.06 | (0.95, 1.19) |
| Quintile 3 | 39.6 (35.1, 44.2) | 1.07 | (0.93, 1.23) | 17.2 (12.9, 22.1) | 1.32 | (0.88, 1.99) | 70.9 (64.0, 77.2) | 1.01 | (0.89, 1.14) |
| Quintile 4 | 43.1 (38.4, 47.8) | 1.10 | (0.96, 1.25) | 17.5 (12.9, 22.9) | 1.43 | (0.95, 2.17) | 73.9 (67.2, 79.8) | 1.01 | (0.90, 1.13) |
| Quintile 5 (most deprived) | 34.9 (30.1, 40.0) | 1.00 | Reference | 13.0 (8.9, 18.1) | 1.00 | Reference | 67.8 (59.6, 75.2) | 1.00 | Reference |
| Comorbidity history | | | | | | | | | |
| COPD | 8.4 (5.7, 11.7) | 0.25 | (0.18, 0.36) | 3.7 (1.8, 6.7) | 0.18 | (0.10, 0.33) | 22.7 (14.5, 32.9) | 0.34 | (0.23, 0.50) |
| Interstitial lung disease | 44.3 (34.2, 54.8) | 1.13 | (0.95, 1.33) | 19.6 (10.2, 32.4) | 1.24 | (0.75, 2.05) | 78.0 (62.4, 89.4) | 1.08 | (0.94, 1.25) |
| Histology | | | | | | | | | |
| Adenocarcinoma | 53.4 (50.8, 55.9) | 1.58 | (1.25, 1.98) | 27.0 (23.7, 30.5) | 2.27 | (1.36, 3.78) | 76.8 (73.7, 79.8) | 1.24 | (1.01, 1.53) |
| Squamous cell carcinoma | 20.7 (15.4, 26.8) | 1.00 | Reference | 8.9 (5.0, 14.5) | 1.00 | Reference | 56.9 (42.2, 70.6) | 1.00 | Reference |
| Other NSCLC | 37.0 (31.1, 43.2) | 1.35 | (1.05, 1.74) | 15.2 (10.1, 21.7) | 1.47 | (0.81, 2.67) | 73.5 (63.6, 81.9) | 1.23 | (0.97, 1.55) |
| Small cell carcinoma | 5.9 (2.2, 12.4) | 0.35 | (0.16, 0.76) | 4.6 (1.3, 11.4) | 0.51 | (0.18, 1.44) | 13.3 (1.6, 40.5) | 0.26 | (0.08, 0.85) |
| Carcinoid | 48.8 (32.9, 64.9) | 1.46 | (1.06, 2.03) | 18.2 (5.2, 40.3) | 1.32 | (0.48, 3.66) | 84.2 (60.4, 96.6) | 1.32 | (0.99, 1.75) |
| Other/unknown | 31.1 (23.3, 39.7) | 1.24 | (0.91, 1.69) | 16.4 (8.8, 26.9) | 1.65 | (0.83, 3.29) | 49.2 (35.9, 62.5) | 0.99 | (0.72, 1.35) |
| Stage | | | | | | | | | |
| I | 50.6 (46.1, 55.1) | 1.00 | Reference | 21.9 (16.6, 28.0) | 1.00 | Reference | 73.5 (67.8, 78.6) | 1.00 | Reference |
| II | 43.1 (34.8, 51.6) | 0.90 | (0.75, 1.07) | 19.1 (10.6, 30.5) | 0.88 | (0.52, 1.48) | 64.5 (52.7, 75.1) | 0.89 | (0.76, 1.04) |
| III | 36.3 (31.3, 41.4) | 0.93 | (0.82, 1.06) | 14.5 (10.2, 19.6) | 0.70 | (0.47, 1.03) | 73.7 (65.5, 80.9) | 1.03 | (0.93, 1.15) |
| IV | 45.1 (42.3, 48.0) | 1.01 | (0.93, 1.11) | 22.4 (19.3, 25.7) | 1.02 | (0.77, 1.34) | 74.0 (70.0, 77.7) | 1.02 | (0.94, 1.11) |

*, Asian Languages inclusive of Chinese (Mandarin, Cantonese, Mien, or other dialects), Hmong, Japanese, Korean, Laotian, Tagalog, Thai, Vietnamese, Burmese, Gujarati, Hindi, Iloko, Khmer, and Punjabi. Statistical models included all other patient characteristics listed in the table. CI, confidence interval; aPR, adjusted prevalence ratio; NDI, neighborhood deprivation index; COPD, chronic obstructive pulmonary disease; NSCLC, non-small cell lung cancer.

**Table 4** Prevalence ratio and aPR of never-smoking status associated with sociodemographic and clinical characteristics among non-Hispanic White patients with lung cancer, overall and by sex

| Characteristics | Overall (n=12,292) | | | Male (n=5,608) | | | Female (n=6,684) | | |
|---|---|---|---|---|---|---|---|---|---|
| | Prevalence (95% CI) | aPR | 95% CI | Prevalence (95% CI) | aPR | (95% CI) | Prevalence (95% CI) | aPR | (95% CI) |
| Age at diagnosis (years) | | | | | | | | | |
| <50 | 27.1 (21.7, 32.9) | 2.07 | (1.67, 2.56) | 19.6 (12.6, 28.4) | 2.13 | (1.43, 3.17) | 32.4 (24.9, 40.6) | 2.04 | (1.58, 2.63) |
| 50–59 | 14.2 (12.4, 16.2) | 1.41 | (1.20, 1.66) | 9.7 (7.5, 12.4) | 1.33 | (0.99, 1.78) | 17.9 (15.2, 20.8) | 1.46 | (1.20, 1.76) |
| 60–69 | 8.5 (7.6, 9.4) | 1.00 | Reference | 6.4 (5.3, 7.7) | 1.00 | Reference | 10.2 (8.9, 11.7) | 1.00 | Reference |
| 70–79 | 7.4 (6.7, 8.2) | 0.98 | (0.85, 1.14) | 5.1 (4.2, 6.1) | 0.89 | (0.69, 1.15) | 9.3 (8.2, 10.5) | 1.04 | (0.87, 1.23) |
| ≥80 | 12.9 (11.6, 14.2) | 1.63 | (1.41, 1.87) | 7.7 (6.3, 9.3) | 1.21 | (0.93, 1.58) | 17.4 (15.4, 19.4) | 1.86 | (1.57, 2.19) |
| Sex | | | | | | | | | |
| Male | 6.8 (6.2, 7.5) | 1.00 | Reference | | | | | | |
| Female | 12.7 (11.9, 13.5) | 1.71 | (1.53, 1.91) | | | | | | |
| Primary language | | | | | | | | | |
| English | 10.1 (9.6, 10.7) | 1.00 | Reference | 7.0 (6.3, 7.7) | 1.00 | Reference | 12.8 (11.9, 13.6) | 1.00 | Reference |
| Other (including unknown) | 8.8 (7.0, 10.9) | 0.99 | (0.80, 1.22) | 5.3 (3.4, 7.9) | 0.90 | (0.60, 1.34) | 12.3 (9.4, 15.8) | 1.05 | (0.82, 1.34) |
| NDI | | | | | | | | | |
| Quintile 1 (least deprived) | 15.3 (14.0, 16.8) | 1.42 | (1.19, 1.69) | 11.6 (9.8, 13.5) | 1.87 | (1.33, 2.62) | 18.4 (16.4, 20.4) | 1.27 | (1.04, 1.55) |
| Quintile 2 | 10.2 (9.1, 11.4) | 1.07 | (0.89, 1.28) | 7.4 (5.9, 9.0) | 1.30 | (0.90, 1.86) | 12.6 (10.9, 14.4) | 0.99 | (0.80, 1.22) |
| Quintile 3 | 8.8 (7.7, 10.0) | 1.01 | (0.84, 1.22) | 5.2 (4.0, 6.6) | 1.08 | (0.73, 1.57) | 12.0 (10.3, 13.8) | 0.99 | (0.80, 1.23) |
| Quintile 4 | 7.5 (6.5, 8.7) | 0.92 | (0.76, 1.13) | 5.1 (3.9, 6.6) | 1.12 | (0.75, 1.65) | 9.6 (8.0, 11.3) | 0.86 | (0.68, 1.08) |
| Quintile 5 (most deprived) | 7.4 (6.2, 8.6) | 1.00 | Reference | 4.2 (3.0, 5.7) | 1.00 | Reference | 10.1 (8.3, 12.1) | 1.00 | Reference |
| Comorbidity history | | | | | | | | | |
| COPD | 1.4 (1.1, 1.7) | 0.11 | (0.09, 0.14) | 0.7 (0.3, 1.1) | 0.07 | (0.04, 0.13) | 2.0 (1.5, 2.6) | 0.13 | (0.10, 0.16) |
| Interstitial lung disease | 7.8 (5.8, 10.2) | 0.96 | (0.74, 1.25) | 5.6 (3.4, 8.6) | 0.97 | (0.63, 1.50) | 10.5 (7.2, 14.6) | 0.95 | (0.68, 1.30) |
| Histology | | | | | | | | | |
| Adenocarcinoma | 14.2 (13.2, 15.1) | 3.17 | (2.47, 4.07) | 10.2 (9.0, 11.5) | 2.85 | (1.95, 4.16) | 17.0 (15.7, 18.3) | 3.44 | (2.46, 4.79) |
| Squamous cell carcinoma | 3.0 (2.3, 3.8) | 1.00 | Reference | 2.5 (1.7, 3.6) | 1.00 | Reference | 3.5 (2.4, 4.9) | 1.00 | Reference |
| Other NSCLC | 8.5 (7.3, 9.9) | 2.36 | (1.47, 3.19) | 5.4 (4.0, 7.0) | 1.77 | (1.14, 2.77) | 11.8 (9.7, 14.0) | 2.57 | (1.78, 3.71) |
| Small cell carcinoma | 1.4 (0.8, 2.2) | 0.45 | (0.27, 0.77) | 1.4 (0.6, 2.8) | 0.58 | (0.27, 1.25) | 1.4 (0.6, 2.6) | 0.39 | (0.19, 0.79) |
| Carcinoid | 25.1 (21.3, 29.3) | 4.78 | (3.60, 6.35) | 16.8 (11.4, 23.3) | 3.84 | (2.38, 6.19) | 29.6 (24.6, 35.1) | 5.47 | (3.78, 7.91) |
| Other | 8.9 (7.3, 10.7) | 2.36 | (1.74, 3.19) | 6.9 (4.9, 9.5) | 2.51 | (1.55, 4.06) | 10.5 (8.2, 13.2) | 2.32 | (1.57, 3.43) |
| Stage | | | | | | | | | |
| I | 12.2 (11.0, 13.5) | 1.00 | Reference | 8.8 (7.2, 10.5) | 1.00 | Reference | 14.5 (12.9, 16.3) | 1.00 | Reference |
| II | 8.7 (6.8, 10.8) | 0.82 | (0.66, 1.03) | 6.9 (4.5, 10.0) | 0.94 | (0.63, 1.39) | 10.0 (7.5, 13.1) | 0.78 | (0.59, 1.03) |
| III | 7.0 (6.0, 8.1) | 0.76 | (0.64, 0.90) | 4.6 (3.4, 6.0) | 0.64 | (0.47, 0.89) | 9.1 (7.6, 10.8) | 0.81 | (0.66, 0.99) |
| IV | 10.4 (9.6, 11.2) | 0.93 | (0.82, 1.04) | 6.9 (6.0, 7.9) | 0.80 | (0.64, 1.01) | 13.6 (12.4, 14.8) | 0.99 | (0.86, 1.13) |

Statistical models included all other patient characteristics listed in the table. CI, confidence interval; aPR, adjusted prevalence ratio; NDI, neighborhood deprivation index; COPD, chronic obstructive pulmonary disease; NSCLC, non-small cell lung cancer.

 

likelihood of never smoking among Hispanic (*vs.* non-Hispanic White) male and female patients with lung cancer. Hispanic ethnicity represents another potentially important demographic characteristic among lung cancer patients who have never smoked. This finding aligns with a recent study by Siegel *et al.* showing a higher percentage of never smoking among Asian/Pacific Islander and Hispanic patients with lung cancer, relative to their non-Hispanic White and Black counterparts (4).

Like prior studies, we found that adenocarcinoma histology was associated with never smoking status (7-9,11). Additionally, we found other subtypes of NSCLC (aside from adenocarcinoma and squamous cell carcinoma), carcinoid, and other/unknown histology were more common than squamous cell and small cell carcinoma among those who have never smoked. As for other clinical characteristics, it is particularly noteworthy that a higher proportion of lung cancer patients diagnosed with stage I or IV disease had never smoked, relative to those with stage II or III disease. This is consistent with a prior study in South Korea that found that patients who have never smoked were more likely to be diagnosed with lung cancer either incidentally or in delayed fashion compared to patients who have smoked (12). It also emphasizes the need for increased awareness that lung cancer arises among persons who have never smoked to help prevent unnecessary delays in diagnosis. It also highlights the opportunity for more effective strategies to improve earlier identification of the disease among those who have never smoked.

Of the characteristics examined that have been less studied, having a primary language other than English was associated with a higher likelihood of never having smoked. In the sex-stratified analyses, however, this association was observed exclusively among female patients. This finding suggests that underlying etiologic factors of lung cancer in those who have never smoked differ between men and women. Although our study is not designed to identify risk factors for lung cancer, non-English speaking individuals are likely foreign-born immigrants, and potential factors include exposures to environmental carcinogens, such as from radon exposure, work conditions, household cooking methods, and air pollution, that may be more common among immigrants, as shown previously (21-23). Radon exposure, for example, has been associated with specific genetic mutations found among never-smoking patients with lung cancer (24). While we do not have nativity data, the patients in our study that primarily speak an Asian language may include many of those who were born in Asian countries and are likely to be the most similar to the patients studied in the previously cited papers from Asian countries in which high proportions of females were found among the never-smoking lung cancer population (12,13). Our study also found an overall higher prevalence of never smoking among lung cancer patients living in the least *vs.* most deprived neighborhoods. This association, however, was not found among female Asian/Pacific Islander patients, further supporting that characteristics of this patient subgroup are distinct from others.

Because Asian/Pacific Islander patients comprised 12% of our population, we had the unique opportunity to explore whether overall and sex-specific patterns of never smoking associated with sociodemographic and clinical characteristics vary between patients of Asian/Pacific Islander and non-Hispanic White race/ethnicity. Association patterns appeared to differ between these racial/ethnic groups, and among Asian/Pacific Islander patients only, association patterns also differed by sex. Prevalence of never smoking was highest among both Asian/Pacific Islander male and female patients diagnosed with lung cancer at the youngest ages (30–49 years). However, the positive association between never-smoking status and early age at diagnosis was observed only in Asian/Pacific Islander males, when accounting for other characteristics. In a retrospective analysis examining cancer registry data from three Southern California counties, earlier age of lung cancer diagnosis was more common in male never-smokers than female never-smokers; however, these data were not stratified by race/ethnicity (25). To our knowledge, our study is the first to show that only Asian/Pacific Islander male (but not female) patients with lung cancer who live in the least (*vs.* most) deprived neighborhoods are less likely to have smoked, while this association was noted among both non-Hispanic White male and female patients. Whether this finding reflects greater exposure to certain risk factors related to higher socioeconomic status, or only that a larger proportion of patients living in less deprived neighborhoods have never smoked, is unknown (26). Regardless, the finding is important because it suggests that higher socioeconomic status alone should not necessarily lower one's suspicion when evaluating never-smoking patients for potential lung cancer.

This in-depth characterization of a diverse patient population with lung cancer according to smoking status is important because, in the United States, there does not appear to be a widespread understanding among physicians regarding characteristics that are more common among

 

never-smoking patients with lung cancer. This is critical for thoracic surgeons, oncologists, pulmonologists, radiologists, and primary care physicians alike to understand because diagnosis in lung cancer is frequently performed by radiographic features of pulmonary nodules identified on imaging rather than tissue biopsy (27,28). Similarly, these radiographic features may determine if a patient simply undergoes surveillance rather than immediate biopsy or intervention (27,28). However, these decisions typically do not take patient sociodemographic factors into account (29). Without a pathologic diagnosis, increased understanding of the common characteristics of never-smoking patients with lung cancer may help physicians adjust the threshold for biopsy or surgical intervention for pulmonary nodules when first detected. The high percentage of stage IV diagnoses among never-smoking patients with lung cancer in our study emphasizes the importance of this understanding among physicians. As Ruano-Ravina *et al.* point out, a large percentage of patients are asymptomatic at the time of lung cancer diagnosis, including 25% of those diagnosed with stage IV disease (30). Thus, it is critical to consider both patient and radiologic characteristics in order to guide lung nodule management and avoid missing potential diagnoses.

Our data suggest that patient characteristics to consider depend on race/ethnicity and sex. Among non-Hispanic White patients, characteristics associated with never smoking included younger age (30–49 years), and among females only, older age (≥80 years); living in the least deprived neighborhoods; and having no history of COPD. Among Asian/Pacific Islander male patients, such characteristics are similar, including younger age (30–49 years), living in the least deprived neighborhoods; and having no history of COPD. Whereas among Asian/Pacific Islander female patients, characteristics associated with never smoking were speaking an Asian language primarily and having no history of COPD.

Our study does have some limitations. First, our study population was drawn from a single integrated healthcare system, potentially reducing the generalizability of our findings. However, our patient population is large, ethnically diverse, and sociodemographically similar to the population in Northern California (17,18), which provided the opportunity to estimate prevalence of never smoking among patient groups that are often underrepresented in other studies of lung cancer, including the Hispanic and Asian/Pacific Islander populations. Second, while studies to improve screening criteria are essential and can help reduce mortality due to lung cancer, our study population was limited to patients with lung cancer (31,32). Thus, we cannot comment on screening criteria for the overall population. Third, although our study included a sizable proportion of Asian/Pacific Islander patients, we did not have disaggregated data to conduct subgroup analyses. We plan to look at disaggregated data in future studies. Fourth, while self-reported race/ethnicity data, such as what was used in our study, may help avoid some of the misclassification and misidentification that occurs in many hospital systems, it is not possible to account for the potential subjectivity inherent to self-reporting (33,34). Lastly, we only had access to data routinely captured in our cancer registry and electronic health record databases from 2007 to 2018, precluding further characterization of patients by genetic mutations and by occupational, environmental, and other lifestyle exposures.

## Conclusions

Overall, this study is the first to analyze contemporary real-world data from a large, sociodemographically diverse population of patients with lung cancer on the prevalence of never smoking associated with sociodemographic and clinical characteristics, providing greater insight about the unique characteristics of patients with lung cancer with respect to smoking status. We found that prevalence of never smoking differed according to sex, race/ethnicity, histology, and other demographic and clinical characteristics, including age at diagnosis, primary language, NDI, and history of COPD. Association patterns of never-smoking status with sociodemographic characteristics also differed across sex and race/ethnicity. These data may be informative in developing proactive strategies and models that consider patient characteristics to aid in the earlier diagnosis of lung cancer, particularly among those who have never smoked.

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## Footnote

*Reporting Checklist:* The authors have completed the STROBE reporting checklist. Available at https://tcr.amegroups.com/article/view/10.21037/tcr-22-1438/rc

*Data Sharing Statement:* Available at https://tcr.amegroups.

 

com/article/view/10.21037/tcr-22-1438/dss

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*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the KPNC Institutional Review Board (No. 1667026-2) and individual consent for this retrospective analysis was waived.



## References

1. Schabath MB, Cote ML. Cancer Progress and Priorities: Lung Cancer. Cancer Epidemiol Biomarkers Prev 2019;28:1563-79.
2. Rivera GA, Wakelee H. Lung Cancer in Never Smokers. In: Ahmad A, Gadgeel S. editors. Lung Cancer and Personalized Medicine: Current Knowledge and Therapies. Cham: Springer International Publishing, 2016:43-57.
3. Hosgood HD 3rd, Cosgrove C, Klugman M, et al. Lung Cancer Mortality Among Smokers and Never-Smokers in the United States. Epidemiology 2020;31:e24-5.
4. Siegel DA, Fedewa SA, Henley SJ, et al. Proportion of Never Smokers Among Men and Women With Lung Cancer in 7 US States. JAMA Oncol 2021;7:302-4.
5. Lariscy JT, Hummer RA, Rogers RG. Lung cancer mortality among never-smokers in the United States: estimating smoking-attributable mortality with nationally representative data. Ann Epidemiol 2020;45:5-11.
6. Mederos N, Friedlaender A, Peters S, et al. Gender-specific aspects of epidemiology, molecular genetics and outcome: lung cancer. ESMO Open 2020;5:e000796.
7. Tang A, Ahmad U, Toth AJ, et al. Non-small cell lung cancer in never- and ever-smokers: Is it the same disease? J Thorac Cardiovasc Surg 2021;161:1903-17.e9.
8. Casal-Mouriño A, Valdés L, Barros-Dios JM, et al. Lung cancer survival among never smokers. Cancer Lett 2019;451:142-9.
9. Pallis AG, Syrigos KN. Lung cancer in never smokers: disease characteristics and risk factors. Crit Rev Oncol Hematol 2013;88:494-503.
10. Samet JM, Avila-Tang E, Boffetta P, et al. Lung cancer in never smokers: clinical epidemiology and environmental risk factors. Clin Cancer Res 2009;15:5626-45.
11. DeRouen MC, Canchola AJ, Thompson CA, et al. Incidence of Lung Cancer Among Never-Smoking Asian American, Native Hawaiian, and Pacific Islander Females. J Natl Cancer Inst 2022;114:78-86.
12. Lee JY, Na II, Jang SH, et al. Differences in clinical presentation of non-small cell lung cancer in never-smokers versus smokers. J Thorac Dis 2013;5:758-63.
13. Toh CK, Ong WS, Lim WT, et al. A Decade of Never-smokers Among Lung Cancer Patients-Increasing Trend and Improved Survival. Clin Lung Cancer 2018;19:e539-50.
14. Lui NS, Benson J, He H, et al. Sub-solid lung adenocarcinoma in Asian versus Caucasian patients: different biology but similar outcomes. J Thorac Dis 2020;12:2161-71.
15. Govindan R, Ding L, Griffith M, et al. Genomic landscape of non-small cell lung cancer in smokers and never-smokers. Cell 2012;150:1121-34.
16. Mazières J, Rouquette I, Lepage B, et al. Specificities of lung adenocarcinoma in women who have never smoked. J Thorac Oncol 2013;8:923-9.
17. Gordon N, Lin T. The Kaiser Permanente Northern California Adult Member Health Survey. Perm J 2016;20:15-225.
18. Gordon N. Member Health Survey. Division of Research

 

Member Health Survey-Special Reports. 2006 [cited 2022 Jun 22]. Available online: https://divisionofresearch.kaiserpermanente.org/projects/memberhealthsurvey/specialreports
19. Messer LC, Laraia BA, Kaufman JS, et al. The development of a standardized neighborhood deprivation index. J Urban Health 2006;83:1041-62.
20. Kakinuma R, Muramatsu Y, Asamura H, et al. Low-dose CT lung cancer screening in never-smokers and smokers: results of an eight-year observational study. Transl Lung Cancer Res 2020;9:10-22.
21. Vermeulen R, Downward GS, Zhang J, et al. Constituents of Household Air Pollution and Risk of Lung Cancer among Never-Smoking Women in Xuanwei and Fuyuan, China. Environ Health Perspect 2019;127:97001.
22. Wong JYY, Downward GS, Hu W, et al. Lung cancer risk by geologic coal deposits: A case-control study of female never-smokers from Xuanwei and Fuyuan, China. Int J Cancer 2019;144:2918-27.
23. United States Environmental Protection Agency. Health Risk of Radon. 2014 [cited 2022 Jun 22]. Available online: https://www.epa.gov/radon/health-risk-radon
24. Ruano-Ravina A, Torres-Durán M, Kelsey KT, et al. Residential radon, EGFR mutations and ALK alterations in never-smoking lung cancer cases. Eur Respir J 2016;48:1462-70.
25. Ou SH, Ziogas A, Zell JA. Asian ethnicity is a favorable prognostic factor for overall survival in non-small cell lung cancer (NSCLC) and is independent of smoking status. J Thorac Oncol 2009;4:1083-93.
26. Garrett BE, Martell BN, Caraballo RS, et al. Socioeconomic Differences in Cigarette Smoking Among Sociodemographic Groups. Prev Chronic Dis 2019;16:E74.
27. Mazzone PJ, Lam L. Evaluating the Patient With a Pulmonary Nodule: A Review. JAMA 2022;327:264-73.
28. Chen W, Zhu D, Chen H, et al. Predictive model for the diagnosis of benign/malignant small pulmonary nodules. Medicine (Baltimore) 2020;99:e19452.
29. Senent-Valero M, Librero J, Pastor-Valero M. Solitary pulmonary nodule malignancy predictive models applicable to routine clinical practice: a systematic review. Syst Rev 2021;10:308.
30. Ruano-Ravina A, Provencio M, Calvo de Juan V, et al. Are there differences by sex in lung cancer characteristics at diagnosis? -a nationwide study. Transl Lung Cancer Res 2021;10:3902-11.
31. Wu FZ, Huang YL, Wu YJ, et al. Prognostic effect of implementation of the mass low-dose computed tomography lung cancer screening program: a hospital-based cohort study. Eur J Cancer Prev 2020;29:445-51.
32. Colson YL, Shepard JO, Lennes IT. New USPSTF Guidelines for Lung Cancer Screening: Better but Not Enough. JAMA Surg 2021;156:513-4.
33. Boehmer U, Kressin NR, Berlowitz DR, et al. Self-reported vs administrative race/ethnicity data and study results. Am J Public Health 2002;92:1471-2.
34. Kressin NR, Chang BH, Hendricks A, et al. Agreement between administrative data and patients' self-reports of race/ethnicity. Am J Public Health 2003;93:1734-9.

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