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Histologic Lung Cancer Incidence Rates and Trends vary by Race/Ethnicity and Residential County

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Abstract

Introduction—Lung cancer incidence is higher among NH blacks compared with NH white and Hispanic populations in the U.S. However, national cancer estimates may not always reflect the cancer burden in terms of disparities and incidence in small geographic areas, especially urban-rural disparities. Moreover, there is a gap in the literature regarding rural-urban disparities in terms of cancer histology.

Methods—Using population-based cancer registry data—Surveillance, Epidemiology and End Results (SEER) and National Program of Cancer Registries (NPCR)—we present age-adjusted histologic rates and trends by race/ethnicity, and residential county location at the time of first cancer diagnosis. Rate ratios were calculated to examine racial/ethnic differences in rates. Annual percent change (APC) was calculated to measure changes in rates over time.

Results—We find that declines in squamous cell carcinoma (SCC) are occurring fastest in metropolitan counties, while rates of adenocarcinoma increased fastest in counties nonadjacent to metropolitan areas. Further, while NH black men have increased lung cancer incidence compared with NH white and Hispanic men in all geographic locations, we find that the degree of the disparity increases with increasing rurality of residence. Finally, we report that among women diagnosed at less than 55 years of age, the incidence of SCC and adenocarcinoma was higher for NH blacks compared with NH whites.

Conclusions—Our results highlight disparities among NH blacks in non-adjacent rural areas. These findings may have significant impact for the implementation of smoking cessation and lung cancer screening programs.

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Keywords

Lung cancer; Histology; Incidence; Surveillance; Health disparities; Registry

Introduction

Although cigarette smoking has significantly decreased over the past few decades, disparities in tobacco use and lung cancer incidence remain across race, ethnicity, education, and socioeconomic status (SES) in the United States (US)^{1–4}. The main types of lung cancer include small cell and non-small cell (adenocarcinoma, squamous cell carcinoma, and large cell carcinoma). Approximately 80–85% of lung cancers are non-small cell, compared with 10–15% of small cell cases. Most lung cancers are due to smoking; however, the strength of association varies by histological subtype⁵. Evidence suggests cigarette smoking is more strongly associated with small cell and squamous cell carcinomas and less associated with adenocarcinoma and large cell carcinoma^{6–8}. Public health campaigns around the negative health consequences of smoking initiated a decline in smoking prevalence and a decrease in lung cancer incidence towards the end of the last century. Squamous cell and small cell lung cancers declined, but the adenocarcinoma subtype increased. While some of these histological changes are attributed to the global decline in smoking prevalence,⁴ changes in the design and composition of cigarettes—both of which modified inhalation and patterns of use—are also attributable causes^{4,9–11}. Racial and ethnic differences in smoking behaviors and lung carcinogenesis¹² suggest that some racial/ethnic groups are more susceptible to lung cancer². For instance, despite lower smoking prevalence rates², later age of smoking initiation^{13–15}, and lower number of cigarettes smoked per day¹³, non-Hispanic (NH) blacks are disproportionately affected by lung cancer compared with NH whites^{13,16–19}. Furthermore, among Hispanic populations, the incidence of lung cancer is lower than NH whites²⁰—a trend that is also observed among first generation U.S. Hispanics²¹—while the prevalence of smoking in aggregate is approximately 40–50% lower compared with NH whites, though it is worth noting that there are marked differences in smoking patterns according to country of origin^{13,20}. Collectively, cigarette smoking patterns appear to contribute to, but not fully explain racial/ethnic disparities in lung cancer incidence^{22–26}. Thus, some aspects of racial/ethnic disparities in lung cancer incidence may be associated with modifiable exposures or other unmeasured facets of tobacco use²⁷.

Geographical residence—and associated environmental exposures such as smoking, radon, pollution and other unknown factors—is one potential co-factor that mediates racial/ethnic disparities in lung cancer incidence²⁸. Smoking rates and unhealthy behaviors, for example, are higher in rural areas^{29–31}. A recent comprehensive description of histologic lung cancer incidence rates and trends in the United States demonstrated that lung cancer rates overall are highest in the South, while lung adenocarcinoma rates are highest in the Northeast region^{3,19}. Moreover, recent work has suggested that higher altitude is associated with reduced incidence of lung cancer^{32–34}. Few studies have examined differences in lung cancer incidence using small or well-defined geographic regions. These studies are important, as they may help to identify regions with patients at high risk for lung cancer that can be targeted for outreach and implementation of low dose CT (LDCT) screening. Efforts

are also needed to reduce disparities in rural and urban lung cancer rates, however, to do so, one first needs to identify and characterize these disparities. In this study, we examined county-level lung cancer incidence rates by histology with an emphasis on racial/ethnic and geographical differences.

Materials and Methods

Data sources

Incident lung and bronchus cancer cases diagnosed between 2004 and 2013 were obtained from the Centers for Disease Control and Prevention National Programs of Cancer Registries (NPCR), and the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) registries. Together these two registries provide cancer incidence data for 100% of the U.S population without duplication of individual registries. NPCR and SEER are required to have <2 unresolved duplicates per 1000 cases in order to meet USCS publication. The Registry Plus™ Link Plus system is used to detect duplicate records. All registries that met the United States Cancer Statistics data quality standards were included. Minnesota and Kansas were excluded from the study due to missing county-level data, and Nevada was excluded because state-wide data did not meet high-quality standards for all study years, resulting in 96.5% coverage of the U.S. population.

Since the influence of cigarette smoke on the risk of lung cancer histological subtypes is not equal⁸, we examined incidence rates and trends for all major histologic lung cancer subtypes. Lung cancer histology groups were defined using International Classification of Diseases for Oncology version 3 (ICD-0-3): Small cell (8002–8005, 8041–8045); Non-small cell (8046); Squamous (8052, 8070–8076, 8078, 8083–8084, 8094, 8120, 8123); Adenocarcinoma (8050, 8140–8141, 8144, 8201, 8250–8255, 8260, 8290, 8310, 8320, 8323, 8333, 8470, 8480, 8481, 8490, 8507, 8550, 8570, 8572, 8574, 8576); Large cell (8012–8014, 8021, 8082); Carcinoma, NOS (8000, 8001, 8010, 8020, 8230); Other specified types (8022, 8030, 8031–8033, 8200, 8240, 8241, 8244–8246, 8249, 8430, 8560, 8562, 8575); Sarcoma (8800–8805, 8810, 8811, 8815, 8830, 8890, 8900, 8940, 9040, 9041, 9043, 9120, 9133, 9220, 9231, 9473, 9540) (Supplementary Table 1). Cases were restricted to non-Hispanic (NH) white, NH black and Hispanic adults (18 years and older), with Hispanic ethnicity being mutually exclusive from race categories. Cases verified by autopsy only or death certificate only and not microscopically confirmed were excluded from the study.

Using state-county American National Standards Institute codes, also referred to as Federal Information Processing Standards (FIPS) codes, incidence data were assigned 2003 county-level Rural-Urban Continuum Codes (RUCC) based on the county of residence at the time of first diagnosis. RUCC is a county-level assessment of rurality and urbanization where codes range from 1–9—the system was developed by the United States Department of Agriculture³⁵. For metropolitan/non-metropolitan variation analysis, counties were categorized into metropolitan (RUCC-M; 1–3), adjacent to metropolitan (RUCC-A; 4, 6, 8), and non-adjacent to metropolitan (RUCC-R; 5, 7, 9)²⁸. RUCC 1–3 correspond to counties in metropolitan areas of 250,000 or more; codes 4, 6 and 8 correspond to counties in urban and rural counties adjacent to metropolitan areas; codes 5, 7, and 9 correspond to urban and rural counties not adjacent to a metropolitan area.

Statistical analysis

Age-adjusted incidence rates were calculated for each year and by histologic subtype, sex, race/ethnicity, and county residence (rural-urban status). Racial/ethnic incidence rate ratios were calculated using NH white age-adjusted rate as the referent group compared with rates for NH black and Hispanic adults. Rates are calculated per 100,000 persons and 95% confidence intervals (CIs) were calculated for rates and rate ratios (4). Rate ratios were calculated to examine differences in rates between race/ethnic groups. Annual percent change (APC) was calculated to measure rate trends over time. Differences between racial/ethnic groups within each region were considered significant at $P < 0.05$. All data analyses were performed using SEER*Stat software version 8.2.1. The Tiwari method was used to calculate confidence intervals for rate ratios and rates³⁶.

Results

A total of 1,491,055 NH whites, 190,060 NH blacks, and 70,613 Hispanics were diagnosed with lung cancer between 2004 and 2013. The majority of cases resided in metropolitan counties at the time of first cancer diagnosis (Table 1). Rates for NH black and NH white men living in metropolitan counties are similar (61.1 & 60.2 per 100,000, respectively), whereas rates for NH white living in counties adjacent to metropolitan counties are higher than NH blacks (63.3 and 60.5 per 100,000, respectively) and rates for NH black living in counties not adjacent to metropolitan counties are higher than NH white (61.2 and 60.9 per 100,000, respectively). The overall rates of lung cancer among adults age 45–54 and 55–64 years were higher for NH blacks (54.4 and 154.0 per 100,000, respectively) and lower for Hispanics (15.5 and 55.3 per 100,000, respectively), compared with NH whites (43.4 and 131.3 per 100,000, respectively) (Table 1). Adenocarcinoma had the highest incidence followed by squamous cell carcinomas among all racial/ethnic groups. Incidence of late stage disease was higher among NH blacks (33.4 per 100,000), compared with NH white (30.8 per 100,000) and Hispanic adults (15.9 per 100,000).

As shown in Table 2, among U.S. adult males, <55 years of age, NH blacks have the highest incidence rates for squamous cell (2.3 per 100,000), adenocarcinoma (5.3 per 100,000), and large cell (0.5 per 100,000) lung cancers. Historically, NH black women have a lower incidence of lung cancer, compared with NH white women^{10,37,38}. However, our analysis demonstrates that among women <55 years of age, squamous cell (rate ratio: 1.19), adenocarcinoma (rate ratio: 1.10) and large cell carcinoma (rate ratio: 1.15) incidence rates are significantly higher, compared with NH white women (Table 2). The incidence for small cell cancers is significantly lower for Hispanic (rate ratio: 0.45) and NH black (rate ratio: 0.80) men compared with NH white men (Table 2). We further analyzed these data by looking at APCs during the period 2004 to 2013. Interestingly, our study finds that for most age groups (55+) the APC of lung adenocarcinoma is higher among NH black women than NH white women. Similar observations were made among men (Table 2).

Table 3 shows sex-specific histologic lung cancer incidence rates and trends by regional location and race. Rates of squamous cell among men were significantly higher in adjacent metropolitan (rate ratio: 1.25) and non-adjacent (rate ratio: 1.19) counties compared with rates for men living in metropolitan counties. Similar observations were observed for women

(Table 3). We noted that the incidence racial disparity persisted among men regardless of residential location. However, we observed that degree of disparity in incidence of lung squamous cell carcinoma between NH black men, and NH white men, increased linearly with decreasing proximity to metropolitan counties, rising from 24% to 29% to 45% in metropolitan, adjacent metropolitan and non-adjacent metropolitan locations, respectively.

We observed declining rate trends for small cell and squamous cell lung cancer in both men and women, with greater significant rate declines occurring in men and women living in metropolitan counties (Table 3). For small cell lung cancers, there is evidence that greater declines occur among NH Black men and women living in metropolitan counties (APC for men -3.6% , APC for women -2.3%).

The incidence of lung adenocarcinoma in metropolitan counties and counties not adjacent to metropolitan counties were significantly higher among NH black men compared with NH white men (Table 3). The degree of disparity between NH white and NH black men with lung adenocarcinoma was greater with increasing rurality of county, with rates increasing more rapidly among NH black men living in metropolitan counties (APC = 2.0%) and counties not adjacent to metropolitan counties (APC = 4.6%) (Table 3). Although lung adenocarcinoma rates for NH black women are significantly lower than NH white women for all geographic locations, rates increases are greater among NH black women (Table 3).

The incidence of large cell lung cancer was significantly higher in non-metropolitan counties compared to metropolitan counties, for both men and women. Compared to NH white men rates for NH black men in metropolitan counties and counties adjacent to metropolitan counties were significantly higher (rate ratio: 1.22 and 1.33 per 100,000, respectively) and significantly lower among Hispanics in all regional locations (rate ratio: 0.47, 0.53, and 0.47 per 100,000, respectively). Compared to NH white women, large cell lung cancer incidence was slightly lower among NH black (rate ratio: 0.93) and Hispanic women (rate ratio: 0.35), in metropolitan counties. The data also support a declining incidence of large cell lung cancer overall (Table 3).

Small cell lung cancer is the one histological subtype where the incidence is lower in NH blacks and Hispanic adults compared with NH whites (Table 3). Lower rates among NH black and Hispanic adults remain consistent across regional locations. Incidence rates significantly decreased among adults living in metropolitan counties, and among women living in counties not adjacent to metropolitan areas (Table 3).

Discussion

Recent comprehensive studies of histologic lung cancer incidence rates and trends in the U.S. demonstrated that rates vary by both race/ethnicity and geographic location^{3,1939,40}. However, these studies addressed geographic variance using topographical analyses at the census¹⁹ or state-wide⁴⁰ level. This study uses national data to provide up-to-date racial/ethnic rates and trends of histologic type of lung cancers by U.S. residential county.

In this study, our main research question was whether there was geographic variance in racial disparities at the county level. Our results show that the higher incidence of lung

cancer in NH black men compared with NH white men is observed in metropolitan and non-adjacent counties, but that the degree of disparity increases the further counties are situated from metropolitan areas. We also observed significantly higher rates of large cell lung cancer incidence in NH black women living in counties adjacent to metropolitan counties compared to NH white counterparts. To our knowledge, this is the first time that these trends have been reported.

Studies show rural-urban differences in smoking behaviors³¹, where the smoking prevalence is higher in rural counties. Thus, it is possible that smoking contributes to the increased disparity in non-adjacent counties among NH black men. Studies that directly compare racial differences in smoking in rural areas are rare to our knowledge. One study, in adolescents, shows that cigarette smoking is higher among NH whites compared with NH blacks⁴¹. However, given the later age at which NH blacks initiate smoking, this is not necessarily surprising¹⁵. We are not aware of studies among adults that break down these observations by race/ethnicity and gender. In addition, smoking is a very complex exposure to capture. In addition to status (i.e., current, former and never), dose (cigarettes per day, CPD), duration, age at initiation, time to first cigarette and daily versus non-daily use are key aspects of smoking relevant to its relationship with cancer. Moreover, depth of inhalation, smoking efficiency, type of tobacco (filtered, menthol, smokeless, etc), are all factors that likely contribute to the complex relationship between smoking, lung cancer and racial disparities.

While several exposures have been linked with lung cancer, the effect size for smoking ranks the highest by far. Other environmental and lifestyle exposures could contribute to this disparity, including radon exposure, ambient air quality, and exposure to asbestos, pesticides, diesel, and additional pollutants. Indeed, NH blacks are disproportionately employed in jobs where they are exposed to these factors^{42,43} and often live in areas with higher sources of pollution⁴⁴⁻⁵¹. Data are sparse regarding the relationship between household radon levels with race and geographic location, thus it is difficult to evaluate radon's potential contribution to lung cancer disparities in this context^{52,53}. Interestingly, studies where the association between exposure to carcinogens and lung cancer risk have been examined in different racial/ethnic groups show that the effect of the relationship was stronger in NH blacks, compared with NH whites and stronger in rural counties⁵⁴.

We also examined how trends in lung cancer incidence are changing in the context of residential location. In accordance with the general literature and the most recent annual report⁵⁵, we observe a decrease in squamous cell carcinoma, large cell carcinoma and small cell carcinoma in both men and women. However, our analysis looked at these trends in greater detail and found that the greatest declines are generally observed in metropolitan counties, something that has not been described previously to the best of our knowledge. Interestingly, the one exception to this declining trend is adenocarcinoma, which continues to rise⁴. Our data show that the increases, at least in recent years, appear to be occurring more so in non-adjacent counties in both men and women, with some of the largest increases also observed among NH black men. This observation is consistent with recent work using SEER 18 showing that cancer incidence is highest in rural counties⁵⁶. Our work extends this by showing how rural and urban differences, defined by metropolitan county residence and

non-adjacent to metropolitan country residence, are affected by sex, histological and racial/ethnic factors.

Increases in adenocarcinoma have been documented for several decades^{4,10,38,55}, though whether there is an absolute increase in lung adenocarcinoma among never smokers remains controversial^{57–59}. Many factors contributed to these changes, including changes in smoking prevalence, and changes in cigarette design and composition^{4,60–62}. For example, cigarette ventilation, which modifies the delivery of carcinogenic constituents⁶³, gained market share due to the perception that it made smoking safer. It didn't. Rather, the ventilation of cigarettes changed the histological profiles of lung cancer. Possible explanations for the recent increases in lung adenocarcinoma include air pollution in the form of nitric oxides^{64,65} and industrialization^{66,67}.

One other key racial difference in smoking habits is the type of cigarette used; NH blacks preferentially use mentholated cigarettes. Due to its “cooling” properties, menthol counters the irritant effect of toxicants found in tobacco^{68,69}. Mentholation can affect smoking behavior^{68,70–75}. Indeed some studies have linked mentholated tobacco with reduced odds of quitting^{73–75}, which could contribute to the lower quit rates among AAs overall⁶⁸. However, studies do not support the hypothesis that menthol cigarettes are associated with a greater risk of lung cancer compared with other tobacco types^{24–26,76}.

In our study we tried to address whether changes in the histological classification of lung cancer could drive the increases in adenocarcinoma that we observed (Supplementary Table 2). Recent years have seen a trend whereby nonspecific classification of lung cancer is avoided and more cases are designated as either adenocarcinoma and squamous cell carcinoma or other specific subtypes⁶¹. As mentioned, we observed that increases in adenocarcinoma were occurring mostly in adjacent and non-adjacent counties. If this was driven primarily by differences in classification of other histological subtypes—such as non-small cell lung cancer (NSCLC), carcinoma not otherwise specified (NOS) and sarcoma—one might expect to see greater decreases in the same geographic areas for those subtypes. However, for both carcinoma, NOS and NSCLC, while decreases are observed for both, the greatest decreases are observed in metropolitan counties (Supplementary Table 2). Similarly, the slight increases in adenocarcinoma in non-adjacent counties in men do not seem to be driven by better classification of carcinoma NOS or NSCLC (Supplementary Table 2). Interestingly, a recent paper by Patel and colleagues that analyzed lung cancer incidence trends in California over a 28 year period found that increases in lung adenocarcinoma among women were more pronounced in areas of low neighborhood socioeconomic status. These data would appear to be congruent with our data regarding lung adenocarcinoma increases non-adjacent counties⁷⁷.

Our analysis also highlighted a disparity among young NH black women, compared with NH white women for squamous cell, adenocarcinoma and large cell lung cancers. Overall, NH black women had lower rates of adenocarcinoma, compared with NH white women. However, as noted earlier, this trend was reversed among women diagnosed with lung cancer <55 years of age. While this observation is not often discussed, previous studies have also highlighted a similar trend^{78–80}. Moreover, a meta-analysis of never smokers (without age

stratification) also described increased incidence of lung cancer in NH black women compared with NH white women. One possible explanation for this relates to the recent apparent rise of lung cancer in never smokers⁸¹. Adenocarcinoma mostly occurs in never smokers and never smokers tend to be diagnosed at an early age^{58,82}. However, this is just speculative and will need to be addressed in future studies. We also noted that the recent increases in adenocarcinoma among women are primarily occurring among NH blacks.

Similar to previous work, we observed lower lung cancer incidence, of every histological subtype, in Hispanics compared with NH black and white adults. These decreases in incidence did not appear to correlate with any specific geographic location. There is perhaps one exception in that the incidence of carcinoma NOS seemed to be higher in Hispanics, compared with NH whites. However, as the trend was not statistically significant, it is not possible to draw conclusions on what it might mean. Moreover, our data confirmed decreasing incidence of SCC in Hispanic men. While rates of squamous cell lung cancer appeared to be rising in women, the increases were not statistically significant. Reasons for this observation are not clear, but deserve further follow up. Of note, the greatest changes in the incidence of carcinoma NOS, NSCLC and other histological types of lung cancer occurred among Hispanics (Supplementary Table 2).

In 2015, LDCT screening was approved for CMS reimbursement. However, studies show that the screening uptake remains low, is currently lower among NH blacks and that targeted intervention strategies may be needed, both to maximize the potential to reduce lung cancer mortality overall and to possibly reduce racial disparities and rural-urban disparities in lung cancer outcome⁸³. Importantly, our data confirm the previously observed trend that lung cancer is diagnosed at a later stage in NH blacks, something that contributes to disparities in outcomes. To ensure that disparities in stage at presentation do not widen in the era of LDCT⁸⁴, dedicated efforts should be made to ensure that the most vulnerable populations have access to screening. Our data show that disparities are highest in non-adjacent counties and that some of the main increases in lung adenocarcinoma are also occurring in these areas. As such, these counties could be targets for more intensive interventions. However, to plan for both smoking cessation and LDCT intervention programs, more extensive analyses are needed on smoking prevalence by race, gender and urban–rural residence.

Our study has several strengths and limitations. We are the first to assess lung cancer disparities at a small geographic county level across the main histological subtypes. Secondly, our study covers over 96% of the U.S. population. This was possible as using NPCR-SEER data meant that we had greater population coverage than SEER alone. However, limitations include the possibility that the classification of rural populations into a single category is not optimal. By pooling counties together, we did not have the ability to define discrete pockets of disparity—if any indeed exist. As noted²⁸, the classification of ‘rural’ or ‘non-adjacent’ counties is not in itself, a homogenous classification. Also, county-level associations do not reflect individual exposures. In addition, we cannot rule out the potential misclassification of Hispanic ethnicity (60), which could bias some of our findings. It is also possible that a delay in cancer reporting may result in underestimation of incidence (61), but since we used data from multiple years, our estimated cases are likely to be only a slight underestimation. Moreover, important risk factor data, such as smoking behaviors, are

not available within our cancer registry data set and therefore we were unable to directly examine the influence of these risk factors on our findings.

Using nationwide county-level data, our study demonstrates significant county-level differences in lung cancer rates and trends in NH white, NH black and Hispanic U.S. adults. We observed significant and increasing disparities in adenocarcinoma in non-adjacent counties and among NH black men and women, suggesting the need for further study of this population. It is possible that factors that confound the increase of adenocarcinoma in the general population could also be responsible for the rural trends we observe^{4,10,38,55,60–62}. The variations observed by race and geography, along with the continuing rise of adenocarcinoma, point to potential knowledge gaps in our understanding of all the risk factors—behavioral, social and environmental—that drive lung cancer incidence in addition to, or in cooperation with, smoking in the United States. It will be important to implement primary prevention (smoking prevention and cessation and reduced exposure to other lung carcinogens) and lung cancer screening strategies that target specific population groups. Evidence already suggests both racial and urban-rural disparities in the uptake of screening programs for other cancer types^{85–87}. Therefore, as the practice of low dose computed tomography screening becomes more widespread across the United States, it will also be important to continue monitoring such trends in lung cancer incidence across racial and geographic groups⁸⁴ by age so that appropriate resources can be put in place to reduce disparities in lung cancer incidence and death.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention

Acronyms

SEER	Surveillance, Epidemiology and End Results
NPCR	National Program of Cancer Registries
SCC	squamous cell carcinoma
NH	non-Hispanic
APC	annual percentage change
LDCT	low dose computed tomography
CMS	Center for Medicare and Medicaid Services

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Table 1

Racial/ethnic invasive lung cancer incidence rates ^a, by select demographic characteristics, histology type ^b, and diagnosis stage: United States, 2004–2013^c

Demographic and clinical characteristics	Total (N = 1,751,728)		NH White (N = 1,491,055)		NH Black (N = 190,060)		Hispanic (N = 70,613)	
	N (%) [*]	Rate (CI)	N (%) [*]	Rate (CI)	N (%) [*]	Rate (CI)	N (%) [*]	Rate (CI)
County Residence^d								
Metropolitan	1,419,987 (81.1%)	57.5 (57.4,57.6)	1,185,705 (79.5%)	60.2 (60.1,60.3)	168,651 (88.7%)	61.1 (60.8,61.4)	65,631 (92.9%)	29.4 (29.2,29.6)
Adjacent to Metropolitan	223,295 (12.7%)	62.4 (62.1,62.7)	204,531 (13.7%)	63.6 (63.3,63.8)	15,564 (8.2%)	60.5 (59.6,61.5)	3,200 (4.5%)	31.4 (30.3,32.6)
Non-adjacent to Metropolitan	107,444 (6.1%)	59.7 (59.3,60.1)	99,936 (6.7%)	60.9 (60.5,61.3)	5,753 (3.0%)	61.2 (59.6,62.9)	1,755 (2.5%)	27.6 (26.3,29)
Region^e								
Northeast	359,607 (20.5%)	59.5 (59.3,59.7)	314,246 (21.1%)	61.6 (61.4,61.8)	31,871 (16.8%)	57.4 (56.7,58)	13,490 (19.1%)	34.8 (34.2,35.4)
Midwest	396,877 (22.7%)	62.8 (62.6,63)	352,539 (23.6%)	62.7 (62.5,62.9)	39,750 (20.9%)	73.3 (72.6,74)	4,588 (6.5%)	30.9 (29.9,31.9)
South	724,236 (41.3%)	61.4 (61.3,61.6)	591,838 (39.7%)	65.2 (65,65.3)	103,504 (54.5%)	59 (58.6,59.3)	28,894 (40.9%)	30.5 (30.2,30.9)
West	271,008 (15.5%)	45.7 (45.6,45.9)	232,432 (15.6%)	49 (48.8,49.2)	149,35 (7.9%)	57 (56.1,58)	23,641 (33.5%)	26 (25.7,26.4)
Sex								
Men	942,116 (53.8%)	70.2 (70,70.3)	795,011 (53.3%)	71.7 (71.5,71.8)	107,635 (56.6%)	83.4 (82.9,83.9)	39,470 (55.9%)	38.6 (38.2,39)
Women	809,612 (46.2%)	49.1 (49,49.3)	696,044 (46.7%)	52.4 (52.2,52.5)	82,425 (43.4%)	45.9 (45.5,46.2)	31,143 (44.1%)	22.9 (22.6,23.2)
Age (years)								
< 45	30,496 (1.7%)	2.0 (1.9,2.0)	23,101 (1.5%)	2.2 (2.2,2.2)	4,794 (2.4%)	2.2 (2.1,2.3)	2,601 (3.7%)	0.9 (0.9,0.9)
45–54	167,974 (9.6%)	41.3 (41.1,41.5)	131,642 (8.8%)	43.3 (43.1,43.5)	28,689 (15.1%)	54.4 (53.7,55)	7,643 (10.8%)	15.5 (15.2,15.8)
55–64	404,644 (23.1%)	126.8 (126.4,127.2)	333,449 (22.4%)	131.1 (130.7,131.6)	55,133 (29.0%)	154 (152.7,155.3)	16,062 (22.7%)	55.3 (54.4,56.1)
65–74	592,230 (33.8%)	307.2 (306.4,308)	509,985 (34.2%)	322.1 (321.2,323)	59,222 (31.2%)	308.2 (305.7,310.7)	23,023 (32.6%)	151.1 (149.1,153.1)
75+	556,384 (31.8%)	330.8 (329.9,331.7)	492,878 (33.1%)	343.5 (342.5,344.4)	42,222 (22.2%)	305.9 (303,308.8)	21,284 (30.1%)	198.6 (195.9,201.3)
Histology								
Small cell	256,549 (14.6%)	8.4 (8.4,8.5)	228,054 (15.3%)	9.2 (9.2,9.3)	20,053 (10.6%)	6.5 (6.4,6.5)	8442 (12.0%)	3.5 (3.4,3.5)
Non-small cell	233,268 (13.3%)	7.8 (7.7,7.8)	195,226 (13.1%)	8 (7.9,8)	28,935 (15.2%)	9.2 (9.1,9.3)	9,107 (12.9%)	3.8 (3.7,3.9)
Squamous Cell	402,483 (23.0%)	13.5 (13.4,13.5)	343,312 (23.0%)	14 (13.9,14)	45,623 (24.0%)	15.3 (15.2,15.4)	13,548 (19.2%)	6 (5.9,6.1)
Adenocarcinoma	673,810 (38.5%)	22.3 (22.3,22.4)	568,326 (38.1%)	23.1 (23.1,23.2)	75,480 (39.7%)	23.7 (23.6,23.9)	30,004 (42.5%)	12.4 (12.2,12.5)

Demographic and clinical characteristics	Total (N = 1,751,728)		NH White (N = 1,491,055)		NH Black (N = 190,060)		Hispanic (N = 70,613)	
	N (%) [*]	Rate (CI)	N (%) [*]	Rate (CI)	N (%) [*]	Rate (CI)	N (%) [*]	Rate (CI)
Large cell	46,876 (2.7%)	1.6 (1.5,1.6)	39,775 (2.7%)	1.6 (1.6,1.6)	5,520 (2.9%)	1.7 (1.7,1.8)	1,581 (2.2%)	0.7 (0.6,0.7)
Carcinoma, NOS	56,596 (3.2%)	1.9 (1.9,1.9)	46,256 (3.1%)	1.9 (1.9,1.9)	6,848 (3.6%)	2.3 (2.2,2.3)	3,492 (4.9%)	1.5 (1.5,1.6)
Sarcoma	2,631 (0.2%)	0.1 (0.1,0.1)	2,140 (0.1%)	0.1 (0.1,0.1)	288 (0.2%)	0.1 (0.1,0.1)	203 (0.3%)	0.1 (0.1,0.1)
Other specified types	77,797 (4.4%)	2.6 (2.6,2.6)	66,553 (4.5%)	2.8 (2.7,2.8)	7,134 (3.8%)	2.2 (2.2,2.3)	4,110 (5.8%)	1.6 (1.5,1.6)
Stage at Diagnosis								
Localized	340,956 (19.5%)	11.4 (11.4,11.5)	298,219 (20.0%)	12.2 (12.2,12.3)	30,759 (16.2%)	10.2 (10.1,10.3)	11,978 (17.0%)	5.1 (5.5,5.2)
Regional	430,528 (24.6%)	14.3 (14.3,14.3)	369,030 (24.7%)	15 (15,15.1)	45,913 (24.2%)	14.7 (14.5,14.8)	15,585 (22.1%)	6.5 (6.4,6.6)
Distant	902,941 (51.5%)	29.8 (29.8,29.9)	758,755 (50.9%)	30.8 (30.7,30.9)	105,337 (55.4%)	33.4 (33.2,33.6)	38,849 (55.0%)	15.9 (15.8,16.1)
Unknown	77,303 (4.4%)	2.6 (2.6,2.6)	65,051 (4.4%)	2.6 (2.6,2.7)	8,051 (4.2%)	2.7 (2.7,2.8)	4,201 (5.9%)	1.9 (1.8,1.9)

Abbreviation: NH = non-Hispanic; CI = confidence interval

Cases diagnosed by death certificate only or autopsy-only are excluded from all analyses.

^aRates are per 100,000 and age-adjusted to the 2000 US Std Population (19 age groups - Census P25-1130) standard; Confidence intervals (Tiwarei mod) are 95% for rates and ratios.

^bLung cancer histology groups were defined using International Classification of Diseases for Oncology version 3 (ICD-0-3); see supplementary table 1.

^cData are from population-based registries that participate in the National Program of Cancer Registries and/or the Surveillance, Epidemiology, and End Results and meet high-quality data criteria. Nevada was excluded because it did not meet USCS publication criteria, and Minnesota and Kansas were excluded due to missing county data. These registries cover 96.5% of the US population 2004-2013.

^dCountries were categorized by Rural-Urban Continuum Codes (RUCC) into urban (RUCC 1-3), adjacent urban (RUCC 4, 6, 8), and non-adjacent rural (RUCC 5, 7, 9).

^eCategorized by US census region

* Column percentages.

Table 2

Invasive squamous, adenocarcinoma, small cell and large cell histologic^a lung cancer incidence rates^b for U.S. men and women by race/ethnicity and age at diagnosis, 2004–2013^c

	Squamous Cell						Adenocarcinoma					
	Men			Women			Men			Women		
	Rate (95% CI)	Rate Ratio	APC	Rate (95% CI)	Rate Ratio	APC	Rate (95% CI)	Rate Ratio	APC	Rate (95% CI)	Rate Ratio	APC
Total												
NH White	19.5 (19.5,19.6)	Ref	0.0	9.5 (9.5,9.6)	Ref	1.5**	24.9 (24.8,25)	Ref	1.2**	22.0 (22.0,22.1)	Ref	2.7**
NH Black	24.1 (23.8,24.4)	1.23*	-2.0**	9.4 (9.3,9.5)	0.99	0.4	29.6 (29.2,29.9)	1.19*	2.0**	19.8 (19.6,20)	0.90*	3.3**
Hispanic	9.2 (9.9,4)	0.47*	-1.7**	3.6 (3.5,3.7)	0.37*	0.9	14.5 (14.2,14.7)	0.58*	0.6	10.9 (10.7,11.1)	0.49*	2.0**
<55 years												
NH White	1.9 (1.9, 1.9)	Ref	-0.9**	0.9 (0.9, 1.0)	Ref	0.1	3.3 (3.3, 3.3)	Ref	0.7	4.3 (4.2, 4.3)	Ref	2.7**
NH Black	2.3 (2.2, 2.4)	1.22#	-5.1**	1.1 (1.1, 1.2)	1.19#	-5.1**	5.3 (5.2, 5.4)	1.61#	-1.3**	4.7 (4.6, 4.8)	1.10#	1.3
Hispanic	0.5 (0.5, 0.5)	0.26#	-6.0**	0.3 (0.3, 0.3)	0.33#	-4	1.5 (1.4, 1.5)	0.44#	-2.4**	1.8 (1.7, 1.8)	0.41#	0.3
55–64 years												
NH White	38.0 (37.6,38.3)	Ref	-1.4**	17.5 (17.2,17.7)	Ref	-1.1**	50 (49.6,50.4)	Ref	0.5**	49.7 (49.3,50.1)	Ref	0.9**
NH Black	49.4 (48.3,50.5)	1.30#	-3.7**	19.0 (18.4,19.6)	1.09#	-1.8**	80.3 (78.9,81.7)	1.06#	1.7**	52.7 (51.7,53.7)	1.06#	3.4**
Hispanic	13.5 (12.9,14.1)	0.36#	-4.7**	5.6 (5.2,6)	0.32#	-1.9	26.0 (25.1,26.9)	0.52#	0.1	22.5 (21.8,23.3)	0.45#	1.9**
65–74 years												
NH White	106.1 (105.3,106.8)	Ref	-0.8**	56.9 (56.4,57.4)	Ref	0.8	127.3 (126.5,128.1)	Ref	0.4	113.4 (112.7,114.1)	Ref	2.2**
NH Black	130.2 (127.7,132.7)	1.23#	-1.2	52.5 (51.1,53.8)	0.92#	1.3**	146.2 (143.5,148.8)	1.15#	2.4**	94.2 (92.4,96)	0.83#	3.5**
Hispanic	47.4 (45.7,49.1)	0.45#	-3.0**	19.7 (18.8,20.7)	0.35#	0.4	72.4 (70.4,74.5)	0.57#	0.2	53.2 (51.7,54.8)	0.47#	1.8**
75+ years												
NH White	128.2 (127.3,129.2)	Ref	1.4**	57.9 (57.3,58.4)	Ref	3.8**	157.8 (156.7,158.8)	Ref	2.4**	113.7 (113,114.5)	Ref	4.4**
NH Black	156.0 (152.5,159.6)	1.22#	-1.2	56.5 (54.9,58.1)	0.98	2.1**	144.4 (141.1,147.9)	0.92#	3.6**	87.3 (85.4,89.3)	0.77#	4.4**
Hispanic	75.4 (72.8,78.1)	0.59#	0.4	25.4 (24.2,26.7)	0.44#	3.1**	104.3 (101.2,107.5)	0.66#	1.6**	66.6 (64.6,68.6)	0.59#	2.7**
				Small Cell						Large Cell		

	Squamous Cell						Adenocarcinoma					
	Men			Women			Men			Women		
	Rate (95% CI)	Rate Ratio	APC	Rate (95% CI)	Rate Ratio	APC	Rate (95% CI)	Rate Ratio	APC	Rate (95% CI)	Rate Ratio	APC
Total												
NH White	10.0 (9.9, 10.0)	Ref	-3.2**	8.7 (8.6, 8.7)	Ref	-1.8**	2.0 (2.0, 2.0)	Ref	-12.2**	1.3 (1.3, 1.3)	Ref	-11.1**
NH Black	8.0 (7.8, 8.2)	0.80*	-3.5**	5.4 (5.3, 5.5)	0.63*	-2.0**	2.4 (2.4, 2.5)	1.21*	-11.3**	1.2 (1.1, 1.3)	0.92*	-9.2**
Hispanic	4.5 (4.4, 4.6)	0.45*	-3.8**	2.7 (2.6, 2.8)	0.31*	-1.6**	0.9 (0.9, 1.0)	0.46*	-14.6**	0.4 (0.4, 0.5)	0.34*	-13.7**
<55 years												
NH White	1.5 (1.5, 1.5)	Ref	-3.8**	1.6 (1.5, 1.6)	Ref	-1.8**	0.3 (0.3, 0.3)	Ref	-11.4**	0.3 (0.3, 0.3)	Ref	-10.9**
NH Black	1.1 (1.1, 1.2)	0.76#	-5.3**	0.9 (0.9, 1.0)	0.60#	-3.5**	0.5 (0.5, 0.6)	1.67#	-11.3**	0.3 (0.3, 0.3)	1.15#	-11.0**
Hispanic	0.4 (0.3, 0.4)	0.24#	-8.1**	0.3 (0.3, 0.4)	0.21#	-3.1	0.1 (0.1, 0.1)	0.28#	~	0.1 (0.1, 0.1)	0.26#	~
55-64 years												
NH White	24.3 (24.0, 24.6)	Ref	-4.0**	23.1 (22.9, 23.4)	Ref	-29**	4.4 (4.3, 4.5)	Ref	-11.8**	3.1 (3.0, 3.2)	Ref	-12.6**
NH Black	19.7 (19.0, 20.4)	0.81#	-4.5**	14.3 (13.7, 14.8)	0.62#	-27**	6.6 (6.2, 7.0)	1.51#	-11.5**	3.1 (2.9, 3.4)	1.01	-10.7**
Hispanic	9.1 (8.6, 9.7)	0.38#	-6.8**	6.5 (6.1, 6.9)	0.28#	-1.6**	1.6 (1.4, 1.8)	0.36#	~	1.0 (0.8, 1.1)	0.31#	~
65-74 years												
NH White	53.2 (52.7, 53.7)	Ref	-3.0**	48.5 (48.0, 49.0)	Ref	-1.9**	10.3 (10.1, 10.6)	Ref	-12.3**	6.8 (6.6, 7.0)	Ref	-11.0**
NH Black	41.4 (40.0, 42.8)	0.78#	-3.1**	29.1 (28.1, 30.1)	0.60#	-1.9**	11.6 (10.8, 12.3)	1.12#	-11.5**	5.8 (5.4, 6.3)	0.86#	-7.8**
Hispanic	24.9 (23.7, 26.1)	0.47#	-2.5**	15.8 (14.9, 16.6)	0.32#	-2.5	5.2 (4.7, 5.8)	0.51#	-14.4**	2.1 (1.8, 2.5)	0.31#	~
75+ years												
NH White	52.4 (51.8, 53.0)	Ref	-2.7**	36.7 (36.2, 37.1)	Ref	-0.8**	11.6 (11.3, 11.9)	Ref	-12.6**	6.2 (6.0, 6.4)	Ref	-10.1**
NH Black	44.0 (42.1, 45.9)	0.84#	-2.4**	25.2 (24.2, 26.3)	0.69#	-0.6	11.2 (10.2, 12.1)	0.96	-10.9**	4.9 (4.5, 5.4)	0.80#	-8.3**
Hispanic	29.4 (27.8, 31.1)	0.56#	-3.0**	13.8 (12.9, 14.7)	0.38#	0.1	6.4 (5.6, 7.2)	0.55#	-14.1**	2.8 (2.4, 3.2)	0.45#	~

Abbreviation: NH = non-Hispanic, APC = annual percent change; CI = confidence interval, Ref = referent group

Cases diagnosed by death certificate only or autopsy-only are excluded from all analyses.

⁴Lung cancer histology groups were defined using International Classification of Diseases for Oncology version 3 (ICD-O-3); see supplementary table 1.

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^q Rates are per 100,000 and age-adjusted to the 2000 US Std Population (19 age groups - Census P25-1130) standard; Confidence intervals (Tiwari mod) are 95% for rates and ratios.

^c Data are from population-based registries that participate in the National Program of Cancer Registries and/or the Surveillance, Epidemiology, and End Results and meet high-quality data criteria. Nevada was excluded because it did not meet USCS publication criteria, and Minnesota and Kansas were excluded due to missing county data. These registries cover 96.5% of the US population 2004–2013.

* Rate for is significantly different than the rate for NH white (referent) (P < 0.05)

Rate is for age category is significantly different than the rate for NH white counterpart (referent) (P < 0.05)

** The APC is significantly different from zero (p<0.05).

~ Statistic could not be calculated due to case count in one or more years <16.

Age-adjusted invasive lung cancer incidence rates^a and annual percent change (APC) stratified by histology type^b, sex, race and county designation^c, 2004–2013^d

Table 3

	Male		Rate Ratio	Female		Rate Ratio
	Rate (95% CI)	APC		Rate (95% CI)	APC	
Squamous cell						
<i>Metropolitan</i>	18.3 (18.3,18.4)	-0.5	Ref	8.8 (8.8,8.9)	1.0*	Ref
NH White	18.8 (18.7,18.9)	-0.1	Ref	9.4 (9.3,9.4)	1.3*	Ref
NH Black	23.3 (23.0,23.6)	-2.2*	1.24 [^]	9.5 (9.4,9.7)	0.4	1.02
Hispanic	9.2 (9.0,9.4)	-1.7*	0.49 [^]	3.5 (3.4,3.6)	0.9	0.37 [^]
<i>Adjacent to metropolitan</i>	22.9 (22.7,23.2)	0.0	1.25 [^]	9.9 (9.7,10)	2.2*	1.11 [^]
NH White	22.9 (22.7,23.2)	0.1	Ref	10.1 (10.0,10.3)	2.3*	Ref
NH Black	29.5 (28.4,30.6)	-0.8	1.29 [^]	8.3 (7.9,8.8)	0.7	0.82 [^]
Hispanic	10.3 (9.4,11.3)	-3.1	0.45 [^]	4.5 (4.0,5.2)	~	0.45 [^]
<i>Non-adjacent to metropolitan</i>	21.8 (21.5,22.1)	0.1	1.19 [^]	9.7 (9.5,9.9)	2.7*	1.09 [^]
NH White	21.8 (21.5,22.2)	0.2	Ref	9.9 (9.7,10.1)	2.9*	Ref
NH Black	31.7 (29.9,33.6)	0.0	1.45 [^]	9.1 (8.3,10.0)	-0.2	0.91
Hispanic	8.1 (7.1,9.2)	~	0.37 [^]	4.2 (3.5,5.0)		0.42 [^]
Adenocarcinoma						
<i>Metropolitan</i>	24.7 (24.6,24.8)	1.0*	Ref	21.3 (21.2,21.4)	2.4*	Ref
NH White	25.1 (25.0,25.2)	1.0*	Ref	22.7 (22.6,22.8)	2.5*	Ref
NH Black	29.6 (29.3,29.9)	2.0*	1.18 [^]	20.4 (20.1,20.6)	3.1*	0.90 [^]
Hispanic	14.7 (14.4,14.9)	0.7*	0.58 [^]	11.0 (10.8,11.1)	1.9*	0.48 [^]
<i>Adjacent to metropolitan</i>	24.5 (24.3,24.8)	1.8*	0.99	19 (18.8,19.2)	3.5*	0.89 [^]
NH White	24.5 (24.3,24.8)	1.9*	Ref	19.6 (19.4,19.8)	3.5*	Ref
NH Black	29.1 (28.1,30.2)	1.6	1.19 [^]	15.0 (14.4,15.7)	4.4*	0.77 [^]

	Male		Rate Ratio	Female		Rate Ratio
	Rate (95% CI)	APC		Rate (95% CI)	APC	
Hispanic	13.1 (12.0,14.2)	0.3	0.55 [^]	9.9 (9.0,10.8)	3.1	0.50 [^]
<i>Non-adjacent to metropolitan</i>	23.2 (22.8,23.5)	1.9 [*]	0.94 [^]	18.2 (18,18.5)	3.7 [*]	0.86 [^]
NH White	23.3 (22.9,23.6)	1.9 [*]	Ref	18.8 (18.5,19.1)	3.6 [*]	Ref
NH Black	29.2 (27.5,30.9)	4.6 [*]	1.25 [^]	14.9 (13.9,16.0)	5.9 [*]	0.79 [^]
Hispanic	11.2 (10.0,12.5)	-3.3	0.48 [^]	9.6 (8.6,10.8)	0.6	0.51 [^]
Small cell						
<i>Metropolitan</i>	8.9 (8.9,9)	-3.6 [*]	Ref	7.5 (7.5,7.6)	-2.3 [*]	Ref
NH White	9.6 (9.5,9.6)	-3.3 [*]	Ref	8.4 (8.4,8.5)	-2.0 [*]	Ref
NH Black	7.9 (7.7,8.0)	-3.5 [*]	0.82 [^]	5.5 (5.4,5.6)	-2.2 [*]	0.65 [^]
Hispanic	4.5 (4.3,4.6)	-3.7 [*]	0.47 [^]	2.6 (2.5,2.7)	-1.7 [*]	0.31 [^]
<i>Adjacent to metropolitan</i>	11.4 (11.3,11.6)	-2.9 [*]	1.29 [^]	9.2 (9.1,9.3)	-1.0 [*]	1.22 [^]
NH White	11.9 (11.7,12.0)	-2.8 [*]	Ref	9.7 (9.6,9.9)	-1.0 [*]	Ref
NH Black	8.9 (8.3,9.5)	-3.7 [*]	0.75 [^]	4.9 (4.5,5.3)	-0.8	0.50 [^]
Hispanic	5.2 (4.6,5.9)	-6.5 [*]	0.44 [^]	4.1 (3.6,4.7)	-0.2	0.42 [^]
<i>Non-adjacent to metropolitan</i>	10.9 (10.6,11.1)	-2.9 [*]	1.22 [^]	9 (8.8,9.2)	-1.5 [*]	1.20 [^]
NH White	11.2 (11.0,11.5)	-2.9 [*]	Ref	9.5 (9.3,9.7)	-1.5 [*]	Ref
NH Black	9.5 (8.5,10.5)	-1.6	0.84 [^]	4.4 (3.8,5.0)	~	0.46 [^]
Hispanic	4.5 (3.7,5.3)	~	0.40 [^]	3.8 (3.2,4.6)	~	0.40 [^]
Large cell						
<i>Metropolitan</i>	1.9 (1.9,1.9)	-12.4 [*]	Ref	1.2 (1.2,1.2)	-11.2 [*]	Ref
NH White	1.9 (1.9,2.0)	-12.3 [*]	Ref	1.3 (1.3,1.3)	-11.1 [*]	Ref
NH Black	2.4 (2.3,2.5)	-11.9 [*]	1.22 [^]	1.2 (1.1,1.2)	-9.9 [*]	0.93 [^]
Hispanic	0.9 (0.9,1.0)	-14.6 [*]	0.47 [^]	0.4 (0.4,0.5)	-14.0 [*]	0.35 [^]
<i>Adjacent to metropolitan</i>	2.5 (2.4,2.5)	-11.2 [*]	1.29 [^]	1.4 (1.4,1.5)	-10.0 [*]	1.22 [^]

	Male		Rate Ratio	Female		Rate Ratio
	Rate (95% CI)	APC		Rate (95% CI)	APC	
NH White	2.4 (2.4,2.5)	-11.5*	Ref	1.5 (1.4,1.5)	-10.7*	Ref
NH Black	3.2 (2.9,3.6)	-6.9*	1.33 [^]	1.4 (1.2,1.6)	-0.7	0.92
Hispanic	1.3 (1.0,1.7)	~	0.53 [^]	0.4 (0.3,0.7)	~	0.30 [^]
<i>Non-adjacent to metropolitan</i>	2.1 (2.2,2)	-13.4*	1.11 [^]	1.3 (1.2,1.4)	-11.6*	1.10 [^]
NH White	2.2 (2.0,2.3)	-13.6*	Ref	1.3 (1.3,1.4)	-11.3*	Ref
NH Black	2.3 (1.8,2.8)	~	1.06	1.3 (1.0,1.6)	~	0.96
Hispanic	1.0 (0.7,1.5)	~	0.47 [^]	~	~	~

Abbreviation: NH = non-Hispanic, APC = annual percent change; CI = confidence interval, Ref = referent group

Cases diagnosed by death certificate only or autopsy-only are excluded from all analyses.

^aRates are per 100,000 and age-adjusted to the 2000 US Std Population (19 age groups - Census P25-1130) standard; Confidence intervals (Tiwari mod) are 95% for rates and ratios.

^bLung cancer histology groups were defined using International Classification of Diseases for Oncology version 3 (ICD-0-3); see supplementary table 1.

^cCountries were categorized by Rural-Urban Continuum Codes (RUCC) into urban (RUCC 1-3), adjacent urban (RUCC 4, 6, 8), and non-adjacent rural (RUCC 5, 7, 9).

^dData are from population-based registries that participate in the National Program of Cancer Registries and/or the Surveillance, Epidemiology, and End Results and meet high-quality data criteria. Nevada was excluded because it did not meet USCS publication criteria, and Minnesota and Kansas were excluded due to missing county data. These registries cover 96.5% of the US population 2004-2013.

* The APC is significantly different from zero (p<0.05).

[^] The rate ratio indicates that the rate is significantly different than the rate for NH White (p<0.05).

~ Statistic could not be calculated due to case count in one or more years <16.