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Socioeconomic, environmental, and geographic factors and US lung cancer mortality, 1999–2009

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Abstract

Background: The American Cancer Society estimates that about 25% of all US cancer deaths will be due to lung cancer – more than from cancers of the colon, breast, and prostate combined.

Methods: We ascertained county-level age-adjusted and age-specific death rates and 95% confidence intervals from the Centers for Disease Control and Prevention Compressed Mortality File. Multiple regression analyses were used to estimate the strength and direction of relationships between county poverty, smoking, fine particulate matter (PM_{2.5}) air pollution, and US Census divisions and race- and sex-specific lung cancer deaths.

Results: Poverty, smoking, and particulate matter air pollution were positively and significantly related to lung cancer deaths among white men, but of these, only poverty and smoking were significantly associated with lung cancer deaths among white women. Residence in the South Atlantic, East South Central, and West South Central US Census divisions at the time of death was significantly associated with lung cancer deaths for both white men and white women. As with white men, poverty and smoking were associated with lung cancer deaths among black men, but of these, only adult smoking had a statistically significant association among black women.

Conclusions: The results support the need for further research, particularly in high-risk areas, to better differentiate factors specific to race and sex and to understand the impact of local risk factors.

Keywords: Lung cancer; mortality; geographic; risk factors; environmental; hot spot

Introduction

Lung cancer is one of the most common cancers worldwide, accounting for about 20% of all cancer deaths [1]. In the United States, the American Cancer Society estimates that there will be about 222,500 new cases of lung cancer (116,990 among men and 105,510 among women) in 2017; it also notes that about 25% of all US cancer deaths will be due to lung cancer – more than from cancers of the colon, breast, and prostate combined [2].

Among men, lung cancer incidence in the United States is highest among blacks, with white men ranking second; among US women, whites rank first and blacks second [3]. The risk factors for lung cancer include personal and second-hand smoking, outdoor air pollution, radon exposure, and workplace exposures such as exposure to asbestos, arsenic, beryllium, cadmium, diesel engine exhaust, nickel, some forms of silica, and chromium [4–7].

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Geographic variations may provide useful insights into high-risk areas and may generate hypotheses about possible risk factors [8]. Within the state of Kentucky, geospatial analysis suggested that coal mining might be a risk factor associated with increased risk, particularly in the eastern part of the state [9]. High rates of lung cancer have also been noted in northern Florida, possibly due to occupational exposures from paper and pulp manufacturing, shipbuilding, and/or petroleum distillation [10]. Regionally, a study of lung cancer in United States identified clusters in the southeastern near Oak Ridge National Laboratory, in eastern Tennessee, for both sexes, and in counties with high concentrations of pig farms and paper mill industries for men (occupational exposure) and in the vicinity of Atlanta, Georgia for women [11]. National US studies are scarce, although changes in regional variation were noted between 1950 to 1994 [12]. Clusters began appearing among white women in the 1950s, with higher rates on the Atlantic and Pacific coasts. At that time, the rates among blacks were found to be higher in northern areas than in the south [12]. In this article, we update information on national variations in the geographic distribution of US lung cancer deaths from 1999 to 2009. We aim to explore correlations between lung cancer mortality and socioeconomic, environmental, and geographic factors at the county level in the United States.

Methods

We ascertained county-level age-adjusted and age-specific death rates and 95% confidence intervals from the US Centers for Disease Control and Prevention Compressed Mortality File as provided on the WONDER public Internet site [13, 14]. This website also provides county averages for the concentration of fine particulate matter ($PM_{2.5}$) air pollution for 2003 to 2008 [15]. Measures of county socioeconomic characteristics were collected from the 2000 and 2010 United States Census of Population as compiled by GeoLytics (East Brunswick, New Jersey). GeoLytics bases its estimates on US Census Bureau reports and limited population estimates, then expands on those to provide multiple population-based variables [16]. Additionally, county-level estimates of black residential isolation were obtained from the publicly available website of the Arizona State University GeoDa Center [17]. Estimates of the percentage of smokers among persons aged 18 years or older

were obtained from the Behavioral Risk Factors Surveillance Survey [18].

Zero-order correlations (Pearson) were used to assess the bivariate strength of the relationship between each independent variable and lung cancer deaths since relatively high correlations among many of the independent variables could mask the impact of any single variable in a multivariate regression. Analyses were performed to estimate the strength and direction of linear relationships between pairs of continuous variables, including the percentage of the county population with an annual income below the poverty level, the percentage of persons aged 18 years or older who are current smokers, the average concentration of $PM_{2.5}$ air pollution for 2003 to 2008, and US Census divisions, and race (black/white)- and sex-specific percentages of the county population [19]. To estimate the magnitude of the association between the aforementioned factors and race- and sex-specific, age-adjusted (25–85 years of age), and county-lung cancer deaths, we used ordinary least squares multiple regression analysis [20] after ensuring that assumptions for ordinary least squares were met. Values were transformed to natural log values for these analyses. Geis-Ord G^* analysis [21] was used to identify hot spots for lung cancer on the basis of county age-adjusted (25–85 years of age), race, sex, and ethnicity (non-Hispanic) lung cancer death rates.

Results

Table 1 presents the results for zero-order correlations between poverty, smoking, $PM_{2.5}$ air pollution, and US Census division and race- and sex-specific lung cancer deaths. Weak to moderate ($r=0.1$ to 0.6) positive correlations were found for poverty and smoking regardless of race or sex. For $PM_{2.5}$ air pollution, however, statistically significant positive correlations were found among whites but not blacks. Geographic correlations were similar for white men and women, being generally negative or not significant in the northern and eastern United States and positive and statistically significant in the South Atlantic, East South Central, and West South Central US Census divisions. Dissimilarities were found between black men and black women. Correlations for the East North Central and West North Central US Census divisions were positive and statistically significant for women but not men, while correlations



Table 1. Zero-order correlations between lung cancer deaths (non-Hispanic, 25–85 and older years) and county characteristics, United States, 1999–2009

Characteristic	White men	White women	Black men	Black women
Percentage of population with annual income below poverty level	0.470 <i>P</i> <0.001	0.293 <i>P</i> <0.001	0.335 <i>P</i> <0.001	0.101 <i>P</i> =0.005
Percentage of smokers aged 18 years or older	0.599 <i>P</i> <0.001	0.449 <i>P</i> <0.001	0.286 <i>P</i> <0.001	0.215 <i>P</i> <0.001
Average concentration of fine particulate matter (2.5 µm)	0.472 <i>P</i> <0.001	0.200 <i>P</i> <0.001	0.050 <i>P</i> =0.115	0.033 <i>P</i> =0.362
New England US Census division	-0.079 <i>P</i> <0.001	0.002 <i>P</i> =0.915	-0.106 <i>P</i> <0.001	-0.027 <i>P</i> =0.449
Middle Atlantic US Census division	-0.104 <i>P</i> <0.001	-0.043 <i>P</i> =0.002	-0.131 <i>P</i> <0.001	0.029 <i>P</i> <0.001
East North Central US Census division	-0.027 <i>P</i> =0.143	-0.034 <i>P</i> =0.067	0.017 <i>P</i> =0.590	0.241 <i>P</i> <0.001
West North Central US Census division	-0.224 <i>P</i> <0.001	-0.279 <i>P</i> <0.001	-0.131 <i>P</i> =0.148	0.224 <i>P</i> <0.001
South Atlantic US Census division (DE, DC, FL, GA, MD, NC, SC, WV, VA)	0.177 <i>P</i> <0.001	0.119 <i>P</i> <0.001	-0.138 <i>P</i> <0.001	-0.289 <i>P</i> <0.001
East South Central US Census division (AL, MS, KY, TN)	0.420 <i>P</i> <0.001	0.186 <i>P</i> <0.001	0.185 <i>P</i> <0.001	-0.138 <i>P</i> =0.701
West South Central US Census division (AR, LA, OK, TX)	0.137 <i>P</i> <0.001	0.133 <i>P</i> <0.001	0.168 <i>P</i> <0.001	0.104 <i>P</i> =0.004
Mountain US Census division	-0.342 <i>P</i> <0.001	-0.152 <i>P</i> <0.001	-0.131 <i>P</i> <0.001	-0.035 <i>P</i> =0.330
Pacific US Census Division	-0.156 <i>P</i> <0.001	0.060 <i>P</i> =0.001	-0.125 <i>P</i> <0.001	0.007 <i>P</i> =0.830

for the East South Central and West South Central US Census divisions were positive and statistically significant for men, and the correlation for the West South Central US Census division was less strong for women and not statistically significant for the East South Central US Census division.

Table 2 shows the results for multiple regression analyses. Poverty, smoking, and PM_{2.5} air pollution were positively and significantly related to lung cancer deaths among white men, but of these, only poverty and smoking were significantly associated with lung cancer deaths among white women. Additionally, residence in the South Atlantic, East South Central, and West South Central US Census divisions at the

time of death was significantly associated with lung cancer deaths for both white men and women. As with white men, poverty and smoking were associated with lung cancer deaths among black men, but of these, only adult smoking had a statistically significant association among black women. Finally, while residence in the East South Central and West South Central US Census divisions was positively associated with lung cancer deaths among black men, residence in these areas was significantly and negatively associated with lung cancer deaths among black women.

Figures 1 to 4 present hot spot analyses of county-level lung cancer deaths for white men (Fig. 1), white women (Fig. 2),



Table 2. Lung cancer deaths (natural log transformations): metric coefficients, 95% confidence limits, standardized regression coefficients, and P-values

Characteristic	White men	White women	Black men	Black women
Percentage with annual income below poverty level	0.991 (0.807–1.174) 0.156 <i>P</i> <0.001	0.358 (0.151–0.565) 0.067 <i>P</i> <0.001	0.787 (0.605–0.969) 0.265 <i>P</i> <0.001	–0.253 (–0.19 to 0.012) –0.072 <i>P</i> =0.063
Percentage of smokers aged 18 years or older	0.019 (0.017–0.020) 0.351 <i>P</i> <0.001	0.017 (0.015–0.019) 0.367 <i>P</i> <0.001	0.009 (0.005–0.013) 0.152 <i>P</i> <0.001	0.015 (0.010–0.020) 0.221 <i>P</i> <0.001
Average concentration of fine particulate matter (2.5 µm)	0.026 (0.020–0.032) 0.032 <i>P</i> <0.001	0.0002 (–0.004 to 0.009) 0.018 <i>P</i> =0.507	0.009 (–0.003 to 0.021) 0.053 <i>P</i> =0.200	0.022 (0.005–0.385) 0.107 <i>P</i> =0.107
South Atlantic US Census division (DE, DC, FL, GA, MD, NC, SC, WV, VA)	0.0124 (12.4% > reference) (0.097, 0.151) 0.164 <i>P</i> <0.001	0.080 (0.050–0.110) 0.126 <i>P</i> <0.001	No statistically significant association	No statistically significant association
East South Central US Census division (AL, MS, KY, TN)	0.187 (0.154–0.219) 0.200 <i>P</i> <0.001	0.042 (0.006–0.078) 0.055 <i>P</i> =0.021	0.067 (0.001–0.133) 0.090 <i>P</i> =0.046	–0.298 (–0.384 to –0.211) –0.334 <i>P</i> <0.001
West South Central US Census division (AR, LA, OK, TX)	0.198 (0.166–0.238) 0.211 <i>P</i> <0.001	0.096 (0.060–0.132) 0.123 <i>P</i> <0.001	0.097 (0.025–0.169) 0.129 <i>P</i> =0.009	–0.148 (–0.243 to –0.053) –0.169 <i>P</i> =0.002

black men (Fig. 3), and black women (Fig. 4). As reflected in the multiple regression analyses, the geographic hot spots are similar for both white men and white women, with both showing the highest occurrence in the South Atlantic, East South Central, and West South Central US Census divisions – especially Kentucky, Tennessee, West Virginia, and Virginia. An additional hot spot for men is centered in Georgia, with lesser extension to northern Florida and southern Alabama. White women also show moderate clustering in this area, but the hottest areas are located in northern Florida. Black men and black women present contrasting geographic patterns. For black men, the hottest spots are found along the Mississippi River basin, from the junction of Missouri, Kentucky, Tennessee, and Mississippi in the north parts of Louisiana and Arkansas (with extension to parts of Oklahoma and Texas) in the south. In contrast, these are relatively cool areas for black women, whose hottest spots are scattered throughout Ohio, Indiana, Illinois, Kentucky, and Missouri.

Discussion

This study confirms the importance of such factors as poverty, smoking, and outdoor air pollution as important independent risk factors for lung cancer, although the patterns were not identical for each race or sex group. The data also show marked geographic variations in lung cancer death within the United States, some of which are detectable even after poverty, smoking, and outdoor air pollution have been accounted for. The geographic patterns were similar for white men and women, but different for black men and women. The high frequency of lung cancer death among black men along the Mississippi River and westward coupled with relatively low mortality among black women in the same area is consistent with the hypothesis that occupational exposures affecting men but not women may be key; an analytic epidemiologic study would be required to test this hypothesis.

The association between socioeconomic vulnerability and lung cancer has been documented in previous studies

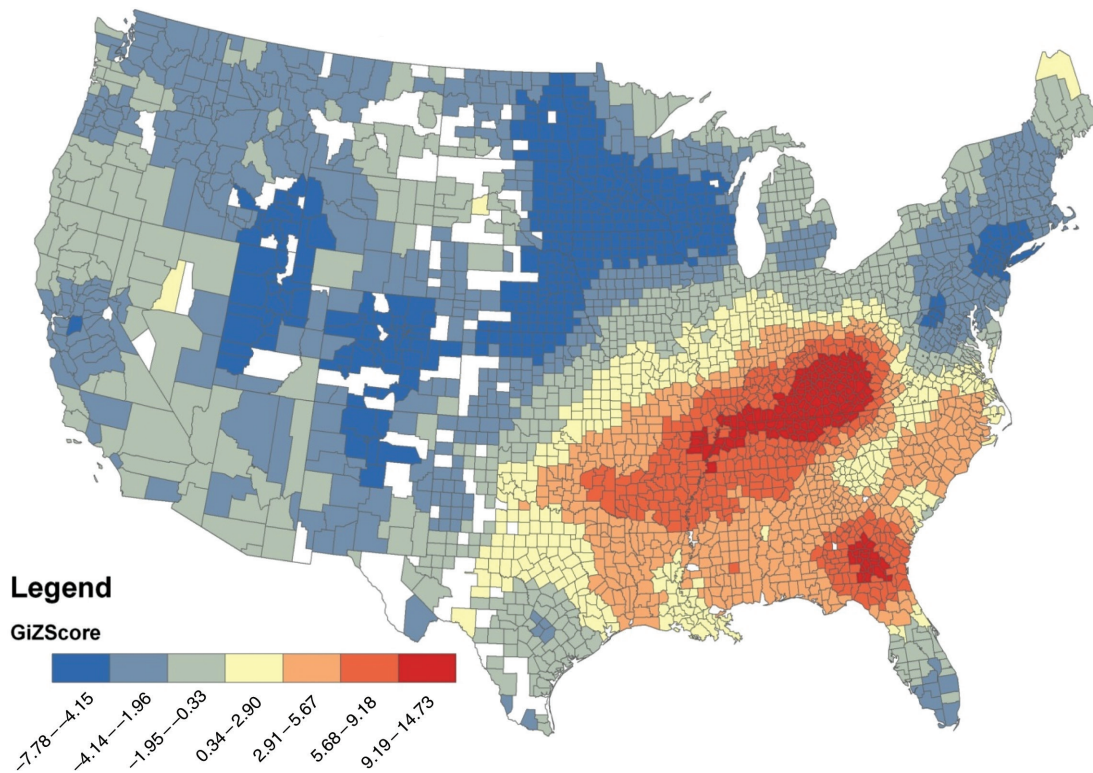


Fig. 1. Hot spot analysis of age-adjusted deaths form malignant neoplasm of the trachea, bronchus and lung among non-Hispanic white men ages 25 to 85+ years. USA. 1999–2009

encompassing both the United States and other nations [8, 22–30]. As in the present study, which shows positive correlations with the percentage of people living in poverty, those with lower socioeconomic status have been repeatedly found to be at high risk of lung cancer. In the United States, black patients have been found to constitute a significant portion of low-income patients with lung cancer, to have received a diagnosis at an earlier age, and to present with more advanced disease. Blacks are more susceptible to smoking-induced lung cancer and have less access to health care services compared with whites, both of which might contribute to the higher lung cancer incidence in the black population [31]. In addition, data show that even when lung cancer is diagnosed early, blacks are less likely than whites to have the option of surgical resection, the gold standard treatment, even after socioeconomic factors have been accounted for [32, 33]. However, in an equal-access health care system (the US military health system), where routine access to cancer care is comparable

for blacks and whites, both groups were found to have similar risks of survival [34].

Smoking has long been identified as a cause of lung cancer and many other illnesses [35]. Smoking may explain some of the observed geographic variation in these data; at least 28.6% of cancer deaths in the United States (in 2014) are attributable to cigarette smoking [35]. Specifically, the incidence of lung cancer has been found to be higher in tobacco-producing states such as Kentucky, where smoking is more common, and lower in states such as Utah, a non-tobacco-producing state, where smoking is not permitted for observant Mormons, the predominant religious group [36]. In the present data, associations with smoking prevalence are also stronger among whites and men. In men, approximately 40% of cancer deaths in the top-ranked states (Arkansas, Louisiana, Tennessee, West Virginia, and Kentucky, which are all southern tobacco-producing states) were explained by smoking. Conversely, smoking explains a quarter (>26%)

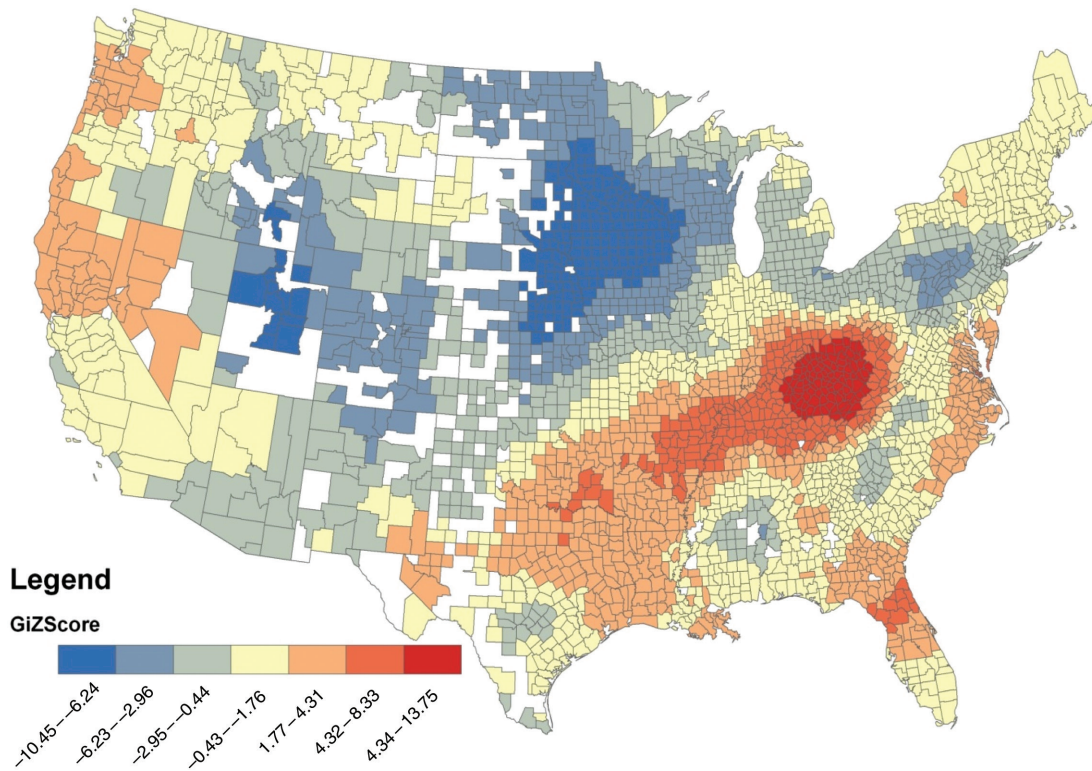


Fig. 2. Hot spot analysis of age-adjusted deaths form malignant neoplasm of the trachea, bronchus and lung among non-Hispanic white women ages 25 to 85+ years. USA. 1999–2009

of all cancer deaths in women (three southern states – Kentucky, Arkansas, and Tennessee – and two Western states – Alaska and Nevada) [37]. In part, this may reflect corresponding relationships between race, sex, and smoking in the US population [36].

After poverty, smoking, and geographic location have been accounted for, outdoor air pollution is associated with lung cancer death only among white men in the data. While outdoor air pollution has been associated with lung cancer death [38, 39], race- and sex-specific data are sparse among US populations. An extended follow-up of the Harvard Six Cities Study found a statistically significant 37% increase in lung cancer death for each 10- $\mu\text{g}/\text{m}^3$ increase in $\text{PM}_{2.5}$ concentration [38]. While these studies did not provide race- and sex-specific results, a descriptive study of nitrogen oxide emissions found that incidence rates of adenocarcinoma of the lung in black males was about 50% higher than that in white males and that this could be explained by differences in air quality related

to site and size [39]. On the other hand, a study of fine particulate air pollution in relation to carotid artery intima-media thickness found that fine particulate matter air pollution was not related to intima-media thickness differences in blacks and Hispanics compared with whites [40]. Further research is important, in part, because of biologic plausibility. The lungs are the organs subject to the most direct effects of particulate air pollution. Fine particles may carry potentially carcinogenic toxic chemicals and can reach the lung alveoli, where clearance is slow. There they can induce sustained pulmonary and systemic inflammation [34].

In addition to air pollution, the present data show statistically significant associations between lung cancer death and specific geographic areas, even after poverty, smoking, and $\text{PM}_{2.5}$ air pollution have been accounted for. The location of hot spots for black men but not black women extending along the Mississippi River and westward (Figs. 3 and 4) is similar to a pattern observed in Belgium for men living in subdistricts with

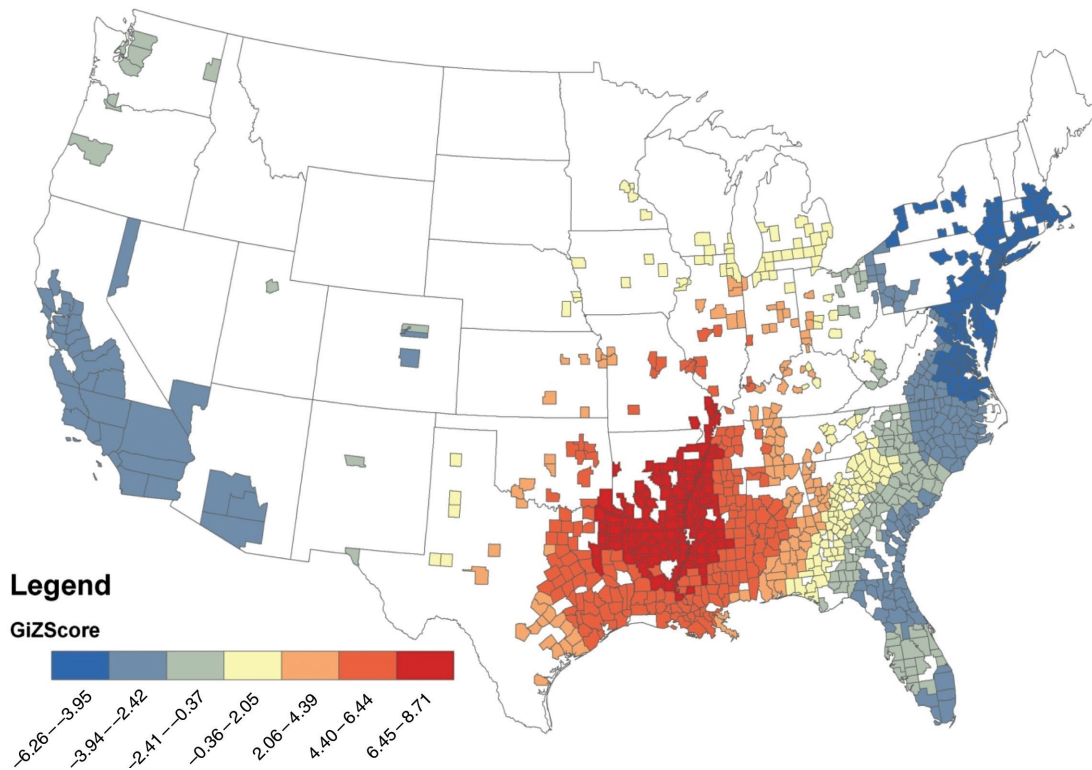


Fig. 3. Hot spot analysis of age-adjusted deaths form malignant neoplasm of the trachea, bronchus and lung among non-Hispanic black and African American men ages 25 to 85+ years. USA. 1999–2009

a particular occupational exposure (i.e., mining) [8]. In these subdistricts, the incidence of lung cancer was significantly higher among men but not women. Since the hot spots along the Mississippi River and westward are highly agricultural, it is tempting to speculate that airborne pesticides or other potentially toxic agents used in agriculture may be responsible. Clear links between agricultural chemical exposure and lung cancer are difficult to establish because of the low number of individuals with lung cancer cases exposed to some pesticides, the changing agricultural chemical landscape, and the potential lags of 10–15 years between exposure and cancer development [41]. An analytic epidemiologic study with individual exposure information on occupational exposures in areas of high mortality would be needed to test such hypotheses.

Other geographic hot spots in these data confirm previous observations of increased lung cancer deaths in the Appalachian region of the United States (which incorporates portions of the South Atlantic and East South Central US

Census divisions, both of which were significantly associated with lung cancer deaths in these data). Mining operations in Appalachia create an unhealthy and stressful environment because of all the associated industries that create increased noise, diesel fuel emissions and particulates, dust, odors and truck traffic, and road congestion, which has previously been associated with increased cancer risk [42]. The present data also confirm previous observations of lung cancer clustering in central Georgia [11] (although the present results are positive for men as well as women) and northern Florida [10]. By locating high-risk areas, both the present results and the results of previous studies help to locate places where an analytic epidemiologic investigation might be most effective for development of a better understanding of how factors such as race and sex may interact and what public health policies might be most effective in reducing risk.

This study was based on death certificates and is both descriptive and, at least in part, ecological. Both the source

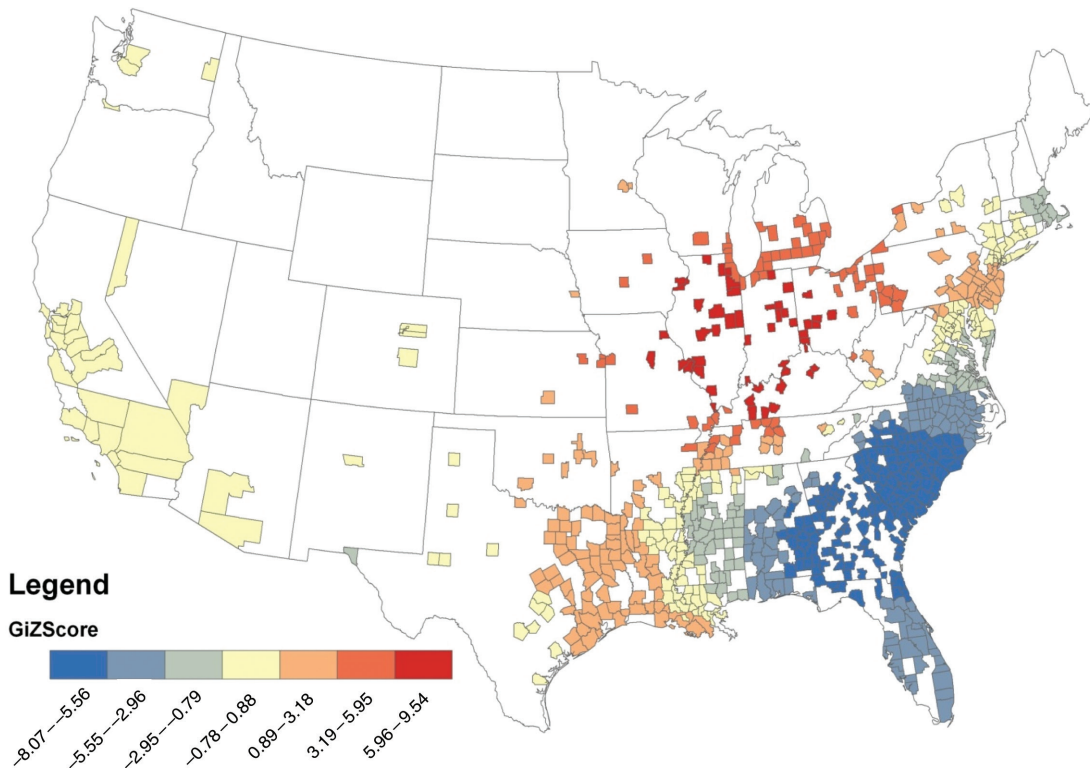


Fig. 4. Hot spot analysis of age-adjusted deaths form malignant neoplasm of the trachea, bronchus and lung among non-Hispanic black and African American women ages 25 to 85+ years. USA. 1999–2009

of the data and the study design place limitations on the way the results may be interpreted. The limitations of death certificates are well known [43]. Nonetheless, death certificates may be generally more valid for cases in which cancers are listed as the underlying cause of death, and death certificates have been specifically found to be valid for cases of lung cancer [44]. Descriptive data are suitable for the generation but not the testing of hypotheses, so any hypotheses generated by these descriptive data would require an analytic epidemiologic investigation designed a priori to do so. Contextual poverty and smoking information in these data are ecological and not specifically linked to cases of lung cancer death. The results suggest an independent effect for lung cancer in the county-level context; however, because of privacy rules; the analysis lacks individual level socioeconomic data, which could have had at the very least independent or confounded impacts on lung cancer death. Confidence in the validity of the present

observations, however, is supported by their corroboration by the aforementioned studies based on individual information. Finally, there are limitations as to the types of data that are available. We used a broad age range for mapping in these data so as to maximize the number of counties with sufficient numbers of lung cancer deaths that had reliable data. This, however, meant that we could not focus on older age groups even though lung cancer death rates are highest among the elderly. Additionally, we did not have race-specific data pertaining to smoking prevalence.

In summary, the present data show statistically significant relationships between death from lung cancer and exposure to poverty, smoking, fine particulate matter, and place of residence at the time of death. They support the need for further research, particularly in high-risk areas, to better differentiate factors specific to race and sex and understand the impact of local risk factors.



Conflict of interest

The authors declare no conflict of interest.

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