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# Geographic Patterns in U.S. Lung Cancer Mortality and Cigarette Smoking

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## Abstract

**Background:** Despite the success of smoking cessation campaigns, lung cancer remains the leading cause of cancer death in the United States. Variations in smoking behavior and lung cancer mortality are evident by sex and region.

**Methods:** Applying geospatial methods to lung cancer mortality data from the National Vital Statistics System and county-level estimates of smoking prevalences from the National Cancer Institute's Small Area Estimates of Cancer-Related Measures, we evaluated patterns in lung cancer mortality rates (2005–2018) in relation to patterns in ever cigarette smoking prevalences (1997–2003).

**Results:** Overall, ever smoking spatial patterns were generally associated with lung cancer mortality rates, which were elevated in the Appalachian region and lower in the West for both sexes. However, we also observed geographic variation in mortality rates that is not explained by smoking. Using Lee's L statistic for assessing bivariate spatial association, we identified counties

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where the ever smoking prevalence was low and lung cancer rates were high. We observed a significant cluster of counties (n=25; p-values ranging from 0.001 to 0.04) with low ever smoking prevalence and high mortality rates among females around the Mississippi River region south of St. Louis, Missouri and a similar and smaller cluster among males in Western Mississippi (n=12; p-values ranging from 0.002 to 0.03) that has not been previously described.

**Conclusions:** Our analyses identified U.S. counties where factors other than smoking may be driving lung cancer mortality

**Impact:** These novel findings highlight areas where investigation of environmental and other risk factors for lung cancer is needed.

### Keywords

Lung cancer; smoking; sex differences; mortality; epidemiology

## INTRODUCTION

Lung cancer is the leading cause of cancer death among both males and females in the United States (U.S.) (1). Nearly a quarter of all cancer deaths are due to lung cancer, an estimated 82% of which are caused by cigarette smoking (2). Historical trends in cigarette consumption, with per capita consumption rising between the 1930s and the 1950s, largely influence today's mortality trends. In the U.S., cigarette smoking was primarily a male behavior until the 1930s, when tobacco advertisements began to specifically target females (3, 4). The prevalence of current smoking had reached more than 50% among males and about 34% among females in 1965 (5) but has been declining steadily since the 1964 Surgeon General's Report that clearly linked cigarette smoking with lung cancer risk (6). Some smokers have been able to quit; the proportion of the general population that are former smokers has varied around 30% among men and 20% among women (5). The resulting estimates of ever smokers, the sum of the current and former smokers, have declined from more than 70% and 40% among males and females, respectively, in 1965 to less than 50% and 35% in 2007 (5).

Lung cancer mortality rates have also changed over time, following trends in smoking prevalence but lagging by 20–30 years (2, 7, 8). Mortality rates rose exponentially among males from about 4 per 100,000 in 1930 to 24 in 1950 to 68 in 1970 before peaking at around 92 in 1990 (9, 10). The rates among females were lower but also rose rapidly from about 3 in 1930 to 6 in 1950, 13 in 1970, and 37 in 1990 before peaking around 42 during the early 2000s. In addition to the substantial variation in lung cancer rates by sex, the geographic patterns have changed over time (7). Lung cancer rates in the U.S. reflect historical differences in the prevalence of smoking as well as more recent differences in state and county/city smoking laws and societal influences that have helped to modify smoking prevalence (11, 12). The prevalence of cigarette smoking has remained high in Southern states and states in the Appalachian region, while decreasing over the last few decades in most other states, particularly those in the West (13). Smoking prevalence also varies both between and within states on the county level (14).

As national smoking prevalence has declined, lung cancer among non-smokers is of increasing public health interest, with secondhand smoke, hormones, and genetic predisposition as noted risk factors (15–17). To investigate other risk factors, cancer mapping and hot spot analyses have been used for decades to inform epidemiologic studies of associations between lung cancer and putative exposures (18–20), including environmental and occupational hazards that vary geographically. Early cancer mortality atlases (21) and subsequent case-control studies (22–24) revealed that shipyard work was associated with increased risk of lung cancer along southern coastal regions in the 1970s and early 1980s. This excess risk was later primarily attributed to asbestos exposure, and shipyards began phasing out asbestos-containing materials, leading to decreases in the relative rate of lung cancer across many coastal areas (25). As another example, long-term exposure to radon, a gas released from decaying radioactive materials, is associated with an increased risk of lung cancer, especially among non-smokers (16, 26). Similarly, exposures to diesel exhaust fumes and ambient particulate matter less than 2.5 μm in diameter are also associated with increased risk (16, 27). Exposures to these hazards vary across the U.S., including between nonmetropolitan and metropolitan areas.

The objective of this study was to describe recent patterns of lung cancer mortality and prior smoking behavior by sex using publicly available data and geospatial methods. By identifying counties where cigarette smoking prevalence has been low, but lung cancer mortality rates are high, we sought to identify regions where future studies of potential lung carcinogens may be fruitful.

## MATERIALS AND METHODS

Data for the county-level and state-level smoking prevalence estimates (ever smoking and current smoking) were obtained using the NCI's Model-based Small Area Estimates of Cancer-Related Measures. These estimates are based on self-reported data from the Behavioral Risk Factor Surveillance System (BRFSS) and National Health Interview Surveys (NHIS). Established in 1984, the BRFSS is an annual nationally representative telephone survey collecting data on health risk behaviors among adults from the 50 U.S. states, the District of Columbia, Puerto Rico, the U.S. Virgin Islands, and Guam (28). Similarly, the NHIS was established in 1957 and is an annual cross-sectional household survey that collects health information via interviews of adults (29). For ever smoking, a person must have reported smoking at least 100 cigarettes in their lifetime by the interview date. For current smoking, a person must have reported smoking at least 100 cigarettes in their lifetime and smoked cigarettes some days or every day by the interview date. Separate county-level and state-level models were used to produce the respective county- and state-level estimates of prevalence with adjustments to make aggregated county-level estimates agree with state-level estimates. Historical smoking data prior to the mid-1990s was only available at the state level. We used the small-area estimates for 1997–1999 and 2000–2003, available for persons aged 18 years and older, to calculate the combined prevalence percent for persons aged 18+ years during 1997–2003 by sex and county, and by sex and state, where the state-level prevalences were further combined to obtain prevalence percent by sex and the nine statistical divisions specified by the U.S. Census Bureau: New England, Middle

Atlantic, East North Central, West North Central, South Atlantic, East South Central, West South Central, Mountain, and Pacific.

National (conterminous U.S.), county-level, and census division-level lung and bronchus cancer (ICD-10 code C34: malignant neoplasm of lung and bronchus, hereafter referred to as lung cancer) mortality rates from 2005 to 2018 (the most recent year available) were calculated using National Vital Statistics System data from the National Center for Health Statistics (NCHS) (30). Deaths were available by 5-year age groups and we selected deaths among adults ages 20 years and older. Sex-specific rates were expressed per 100,000 person-years and age-adjusted with the 2000 U.S. standard population using SEER*Stat version 8.3.9 (31). Due to NCHS reporting guidelines, mortality count data were suppressed for counties with fewer than 10 deaths, which excluded 89 counties for males and 161 counties for females (32).

We calculated spatial autocorrelation among counties using Lee's L statistic for bivariate spatial association, identifying clusters with significant correlation between the two variables (i.e., smoking prevalence [X] and lung cancer mortality rate [Y]) in all four combinations (high-high, low-high, high-low, and low-low) (33, 34). Lee's L statistic integrates Pearson's $r$ and Moran's $I$ to reflect the association between two spatially defined variables by accounting for 1) their correlation within the same county and 2) the correlation of their spatially lagged values, allowing us to prepare maps with county-specific bivariate clustering results for each sex. Spatial neighbors were identified using a Queen's case adjacency matrix, which defines neighbors (and assigns a corresponding spatial weight) as counties that share a border. We calculated empirical p-values from 100,000 random permutations of the bivariate values for the given spatial weighting. We used the False Discovery Rate procedure to correct each bivariate analysis for multiple comparisons (35). All statistical analyses were calculated using SEER*Stat version 8.3.9 and the "spdep" package in R version 4.1.0 (36). R code used to calculate the Lee's L statistic and generate maps is available on GitHub (https://github.com/idblr/geo_US_lung_cancer_and_smoking). All spatial analyses excluded Alaska and Hawaii because of their spatial non-adjacency to the conterminous U.S.

### Data Availability

The data analyzed in this study included all counties in the conterminous U.S. and were obtained from the NCI's Model-based Small Area Estimates of Cancer-Related Measures and the National Vital Statistics System data from the NCHS (30, 37). Subject consent was not required for this aggregate-level analysis.

## RESULTS

### Lung Cancer Mortality

During 2005–2018, 1,188,445 males ages 20 years and older died of lung cancer in the U.S. (Table 1). The overall age-adjusted mortality rate was 78.1 per 100,000 person-years (95% CI: 77.9–78.2), and the rates ranged from a low of 56.8 (95% CI: 56.4–57.3) in the Mountain Division to a high of 113.2 (95% CI: 112.5–133.9) in the East South Central

Division. Across males, lung cancer mortality rates varied substantially by county with rates in the highest decile exceeding 126.9 per 100,000 person-years, more than twice those in the lowest decile with rates of 58.8 or lower (Figure 1A). The mortality rates were notably elevated across many areas of the southeast (e.g., East South Central and South Atlantic Divisions) and parts of the mid-west while relatively low in the upper plains, mountain, and western states.

During 2005–2018, 984,645 females aged 20 years and older died of lung cancer in the U.S. (Table 1). The lung cancer mortality rates for females were lower than males overall and for all Divisions, but the relative ranking across Divisions was similar. The overall age-standardized mortality rate was 50.3 per 100,000 person-years (95% CI: 50.2–50.4), and rates ranged from a low of 41.7 (95% CI: 41.3–42.0) in the Mountain Division to a high of 61.6 (95% CI: 61.1–62.0) in the East South Central Division. The county-level mortality rates ranged from 38.7 or less in the lowest decile to 72.6 or more in the highest decile (Figure 2A). Counties with elevated rates stretched from West Virginia through Kentucky and across to northeastern Texas but not across the deep south. There were also several counties with high (top decile) mortality rates in the west, including in Oregon (n=2 counties), Nevada (n=3), and Arizona (n=1).

## Ever Smoking Prevalence

The national prevalence of ever smoking from 1997 to 2003 was 52.6% (95% CI: 52.0–53.2) among males, ranging from 48.4% (95% CI: 47.0–49.9) in the Pacific Division to 57.4% (95% CI: 56.0–58.8) in the East South Central Division (Table 1). The prevalence of ever smoking among males also varied across counties, from 65.3% or more in the highest decile to 50.7% or less in the lowest decile (Figure 1B). Elevated ever smoking prevalence stretched across many areas in the Appalachian region and several areas in the north central states. Ever smoking was lowest across the states in the middle of the country, namely parts of Texas, Oklahoma, and Kansas, and throughout most of the Southwest.

Among females, the 1997–2003 national ever smoking prevalence was 40.2% (95% CI: 39.6–40.8), ranging from 34.0% (95% CI: 32.7–35.3) in the Pacific Division to 46.6% (95% CI: 44.8–48.3) in the New England Division (Table 1). As shown in Figure 2B, the prevalence of ever smoking ranged from 49.1% or more in the highest decile to 33.4% or less in the lowest decile. Counties in the highest decile of ever-smoking prevalence were concentrated in the northeast and stretched through the Appalachian region (New England, Middle Atlantic, and parts of the East North Central Division). There were also several counties with high prevalence around the Great Lakes and in the Pacific Northwest. The lowest rates were in the mid- and south- Atlantic states and across the south-central and western areas of the U.S. (West South-Central Division and the southern-most part of the Pacific Division).

## Bivariate Analysis for Ever Smoking Prevalence and Lung Cancer Mortality

Among males, results from the Lee’s L statistic of bivariate spatial association revealed that although most counties did not have significant associations, there were several counties with statistically significant high ever smoking prevalence and high mortality rates stretching across mid-Appalachia from West Virginia to Arkansas (Figure 1C). A few counties with low ever smoking prevalence and high mortality rates were scattered throughout the southeast, with a cluster on the western border of Mississippi (n=12 counties; p-values from 0.002 to 0.03). Several counties with high ever smoking prevalence and low mortality rates were in the South Atlantic, the upper Midwest, and across the Pacific and Mountain West divisions. Counties with low ever smoking prevalence and low mortality rates appeared throughout the West and clustered in eastern coastal cities.

Among females, counties with high ever smoking prevalence and high mortality rates stretched across the mid-Appalachia region and from Wisconsin to Michigan and parts of Maine (Figure 2C). A few counties with low ever smoking prevalence and high mortality rates were scattered throughout Kentucky, with a line of counties running down the Mississippi River (n=25 counties; p-values from 0.01 to 0.04). There were a few counties with high ever smoking prevalence and low mortality rates, including in the Middle Atlantic and the West, spread mostly throughout the Mountain Division. Counties with low ever smoking prevalence and low mortality rates were located across the southeast, with some clusters on the Mississippi and Alabama border, in Georgia, around the District of Columbia, and across the southwest.

### Current Smoking Prevalence and Lung Cancer Mortality

Among males, the 1997–2003 national current smoking prevalence was 25.6% (95% CI: 25.4–26.5), less than half the 52.6% prevalence of ever smoking, and ranged from 20.4% in the Pacific Division to 29.8% in the East South Central Division (Supplementary Table S1). Similar patterns were apparent for the prevalence of current smoking as for ever smoking, although not as prominent in the north central states, and they were more widely spread across the southeast (Supplementary Figure S1B). For females, the national prevalence of current smoking was 21.3% (95% CI: 20.7–21.6), ranging from 14.6% in the Pacific Division to 25.6% in the East South Central Division. It was highest in the Appalachian region and central portions of the country (Supplementary Figure S2B). The Lee’s L analysis yielded fewer statistically significant clusters of counties with both high current smoking prevalence and high mortality rates compared to ever smoking analyses, but patterns of association were similar (Supplementary Figures S1A, S2A, S1C and S2C).

## DISCUSSION

In this analysis of U.S. cancer surveillance data, we observed that lung cancer mortality rates and smoking prevalence, both ever and current, vary substantially across the nine statistical divisions and the counties within states. Generally, patterns of cigarette smoking were positively associated with lung cancer mortality. Furthermore, we identified areas where smoking prevalence was low and lung cancer mortality rates were high, findings that reveal the potential value of further exploration of possible environmental, occupational, behavioral, and sociodemographic risk factors for lung cancer.

Findings from our lung cancer mortality analyses at the county level are consistent with results from a previous study that reported patterns on the county level for 2014 (38). For both sexes, the lowest mortality rates were in the Mountain Division and throughout the West, and the highest rates were in the East South Central Division and across the Appalachian region. There were substantial geographic variations in the trends in lung cancer mortality rates between 1980–2014, with declines in the northeast and west and increases in the mid-Appalachian and Midwest regions (38). These trends reflected the dramatic changes in the geographic patterns of lung cancer mortality by decade over the 1950–1994 period (7).

We also observed patterns in both ever and current cigarette smoking similar to those from other studies that have reported county-level differences and variation in smoking prevalence between sexes. Both sexes had high ever smoking prevalence across the Appalachian region, but patterns of elevation among females were more diffuse than those for males. Like previous studies, we found a higher prevalence of smoking in rural areas, including counties in and around Appalachia and the Southwest. One investigation found that this rural-urban divide persisted through an additional 10 years of current smoking data beyond those included in our analysis (14). We found that the lowest ever and current smoking prevalences occurred for both sexes within the Pacific division, but the pattern of elevated rates differed between sexes by division, which is consistent with maps for current smoking for 1992–2007 using data from another source, the Tobacco Use Supplement to the Current Population Survey (39).

Our Lee's L analysis identified counties with significantly high ever smoking prevalence and high lung cancer mortality rates primarily through Appalachia, and clusters of counties with low ever smoking and low mortality rates mostly in the West and around cities along the Atlantic coast for both males and females. These patterns were expected given the well-established link between smoking and lung cancer mortality risk. Counties with high ever smoking and low mortality rates were dispersed throughout the West for both sexes. These counties may experience an increase in lung cancer mortality rates in the future after the latency period for lung cancer following smoking has elapsed, estimated to be 20–30 years (2, 8, 16). Our Lee's L evaluation of ever-smoking patterns also allowed for the detection of areas with high mortality in the absence of current smoking (i.e., arguably the strongest lung cancer risk factor), thus potentially revealing the role of other risk factors. For instance, counties with concordant high mortality rates and low smoking prevalence across sexes may suggest community-specific environmental exposures. We observed several counties with this pattern, which has not been previously reported. Among males, the analysis yielded several significant clusters throughout the Southeast and on the western border of Mississippi. Additional groupings of counties with low smoking prevalence but high mortality rates were observed among both sexes throughout Kentucky and a prominent line of counties running down the Mississippi River south of St. Louis, Missouri, the latter of which had clearer clustering among females than males. Just south of this cluster is the lower Mississippi River region, a 100-mile industrial corridor in southeastern Louisiana colloquially referred to as "Cancer Alley" after multiple studies related the high number of petrochemical plants and other industrial sources in this region with elevated rates of lung, stomach, and kidney cancers (40). The cluster of counties we identified is north of Cancer Alley, on the border between Mississippi and Arkansas.

We postulate several potential explanations for this cluster along the Mississippi River and the difference between sexes. These differences could be driven by occupational exposures; most occupational studies of lung cancer have focused on males since females entered these occupations later than men (41–43), whereas the risks associated with common female-centric jobs or industries are less well-understood. These findings may also suggest some important drivers of risk among women, such as exposure to second-hand smoke (44). Given the historical differences in smoking patterns by sex, i.e., with higher smoking prevalence among males, second-hand hand smoke exposure may contribute to the elevated lung cancer mortality rates among females with low levels of active smoking. Like the industrial exposures connected to Cancer Alley, the general pattern of high lung cancer rates with low smoking prevalence could reflect localized environmental hazards (45, 46). While such hazards would theoretically exist for both sexes, the lower smoking prevalence among females versus males in the region could make the risk pattern more discernable in females. The federally designated Mississippi Delta Region is a poor and largely rural region with documented elevated rates of all-cancer and lung cancer mortality (47). Several of the counties where smoking prevalence was low but mortality rates among women were high were in eastern Kentucky, an area known for intense coal production and where clusters of lung cancer cases have been previously observed (48). Like some of the spatial patterns we observed, a prior analysis identified significant clustering of lung cancer cases in eastern areas of the state with high levels of coal production as well as in western areas where coal mining was less common. These findings were robust to analyses among women only, indicating they may not just reflect risk from occupational coal exposures (48, 49). Arsenic is another candidate environmental exposure of interest, given its known association with lung cancer (16). A map of the probability that arsenic levels in private well drinking water is greater than 5ppb (1/2 the regulatory limit) across the U.S. included several of the 9 states with significant findings in our Lee's L analysis among women (50). However, the proportion of the population on domestic wells in these states ranges from about 10 to 22% (51), and arsenic levels tend to be lower in public drinking water supplies, so it seems unlikely that arsenic would exclusively drive the patterns observed in our data. Radon is also an environmental risk factor for lung cancer and naturally exhibits clear geographic patterns (52). Local policies and mitigation practices greatly influence indoor radon levels, so evaluating this exposure on an individual level will be important for future studies.

Our Lee's L analysis also identified a smaller and more geographically dispersed set of counties with high prevalence of ever smoking and low lung cancer rates. More than 80% of lung cancer deaths in the U.S. are attributed to smoking (17), but smoking is also associated with risk of several other chronic health conditions, including chronic obstructive pulmonary disease, cardiovascular disease (17), and stroke (53), all of which are leading causes of death in the U.S. Therefore, it is possible that smoking-related deaths from other health conditions might mask the association between smoking and lung cancer mortality in these counties. Socio-economic status (SES) and related behaviors may also contribute to this pattern, as SES is inversely associated with lung cancer risk (54). Several counties where we observed this discordant pattern are in states like Colorado, where poverty rates are relatively low, compared to states where we observed many counties with both high smoking prevalence and high lung cancer mortality rates, like Kentucky, West Virginia, and Louisiana (55).

We also analyzed data for current smoking and found similarities with the ever smoking maps, including both sexes having the highest rates in the East South Central and South Atlantic Divisions and lowest rates in the West (Mountain and Pacific Divisions). Overall, the maps of current smoking during 1997–2003 resemble the mortality maps for 2005–2018 more closely than the maps of ever smoking across both sexes. This concordance between current smoking prevalence and lung cancer mortality patterns emphasizes the public health significance of smoking cessation programs that have been shown to be highly effective at reducing smoking prevalence (56–58). Further, while many modern anti-smoking policies have been enacted on the state-level, evidence from our analysis and prior studies suggest that smoking behaviors continue to differ within states on the county level. We note however that our analyses of ever-smokers captured data from both current and former smokers, increasing the statistical power of our investigation. Lung cancer mortality is lower in former smokers than current smokers, but former smokers continue to have elevated risk relative to never smokers (59, 60). The most widely used state-level anti-smoking policy is an excise tax on tobacco products, which decreases smoking initiation, particularly among vulnerable groups like young individuals and those of lower SES (61). On the other hand, evidence that taxing and other economic anti-smoking policies promote smoking cessation is lacking (62). On the neighborhood level, tobacco industry marketing is a major driver of smoking behavior (63). Individual-level factors also drive smoking behaviors, including family smoking history, social pressure, stress, and other environmental and genetic factors (61). As the prevalence of these influences varies within states and across communities, our study can offer insight into geographic regions where smoking cessation programs or policies have been implemented or have been most successful and highlight counties where further public health measures may be warranted.

The primary limitation of this study is the inability to control for confounding, particularly at the individual-level, by lung cancer risk factors such as occupational and environmental exposures, body mass index, and nonmalignant respiratory disease. However, since none of these have been identified as particularly strong risk factors for lung cancer mortality when compared to smoking, our analysis is still informative for describing spatial patterns that may direct next steps in this area of research (16, 27). Although it would have been preferable to have several decades between our smoking measures and the lung cancer rates, we used the earliest smoking data available at the level of detail necessary and the most recent subsequent mortality data. Additionally, it would have been advantageous to describe patterns by race and ethnicity since there are documented variations in both smoking and lung cancer rates across racial/ethnic groups (64, 65). Socioeconomic factors are also of interest, especially in areas where lung cancer rates and smoking prevalences were discordant and environmental exposures are postulated, as previous studies have demonstrated disproportionally high percentages of low-income residents living near petrochemical plants, refineries, landfills, and factories (66–68). However, the small-area race/ethnicity-specific smoking prevalence estimates were not available, the existing mortality data were sparse at the county level except for White non-Hispanics, and the Lee's L method can accommodate only one comparison at a time. Another limitation of Lee's L is that the results should not be directly compared between sexes because the significance tests are conducted within each sex rather than between groups (and sensitive to their respective mean values) (33). However, the Lee's L analysis allowed us to better describe and formally identify statistically significant spatial patterns in associations between two variables on the county level. We note that mortality data for a small proportion of counties were suppressed by NCHS and these counties were not included in the computations of the Lee's L statistic.

Our study had several strengths, including an attempt to account for the latency between smoking and lung cancer mortality by incorporating smoking data for the decade preceding the mortality data. We used the earliest smoking data available by sex at the county level, combining the estimates for 1997–99 with those for 2000–03 to reduce the variance of the estimates. It would be interesting to compare the mortality patterns with earlier smoking data, but they do not exist at the geographic level needed to extend our analysis farther back in time. While other studies have used the same data sources to describe trends in smoking and mortality separately, we believe this is one of the first to integrate publicly available data sources for a county-level epidemiological analysis. As such, our study identified some geographic patterns that are not apparent in studies using national or state-level estimates. The results have several implications and can be used to generate hypotheses about determinants of lung cancer mortality and identify areas where analytic studies may clarify factors driving these patterns. These findings can also be used to identify regions where smoking cessation programs and policies could be particularly effective in reducing lung cancer mortality. Further, studies in counties where smoking prevalence was high but mortality rates are low could reveal factors that potentially mitigate or interfere with the mortality risk attributable to smoking. Trends in the rates of the three main histologic types of lung cancer (adenocarcinoma, squamous cell, and small cell carcinoma) have differed over time (69, 70) and the association with cigarette smoking is much stronger for the latter two types (17). Histology information was not available for the mortality dataset, as it is generally not recorded on death certificates. However, histologic type is collected and coded by cancer registries. In future analyses, it will be useful to explore the geographic patterns of lung cancer incidence across by histologic type to further our understanding of the roles of smoking and other exposures in their etiology.

## CONCLUSIONS

We described geographic variation in lung cancer mortality and smoking prevalence by county and sex across the U.S., accounting for some latency between smoking and mortality. We found that most areas with high smoking prevalence had elevated mortality rates in the following decade, which is consistent with the established risk due to cigarette smoking. We also identified several counties with discordant mortality and smoking patterns that have not been previously described. Among these, a stretch of counties with elevated mortality rates but low previous smoking prevalence among females and, to a lesser extent among males, along the Mississippi River warrants future investigation of the factors driving this observation.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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## ABBREVIATIONS:

| | |
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| **U.S.** | United States |
| **NCHS** | National Center for Health Statistics |
| **BRFSS** | Behavioral Risk Factor Surveillance System |
| **NHIS** | National Health Interview Survey |

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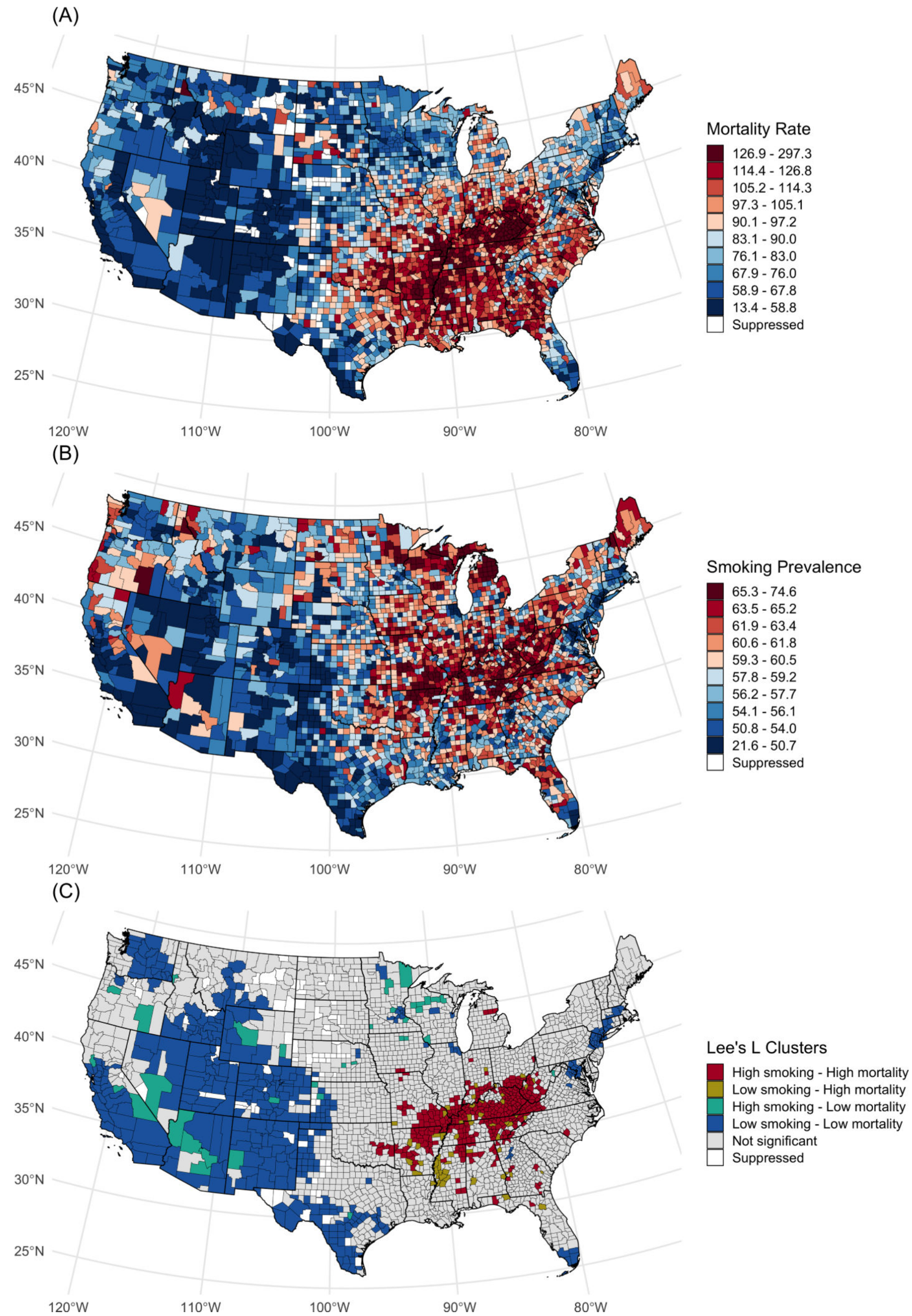


**Figure 1.**

Geographic patterns in the conterminous United States by county among males: a) lung and bronchus cancer mortality rates per 100,000 person-years during 2005–2018, ages 20+ years, b) ever-smoking prevalence percents during 1997–2003, ages 18+ years, c) Lee's L analysis findings with colors indicating statistically significant counties.

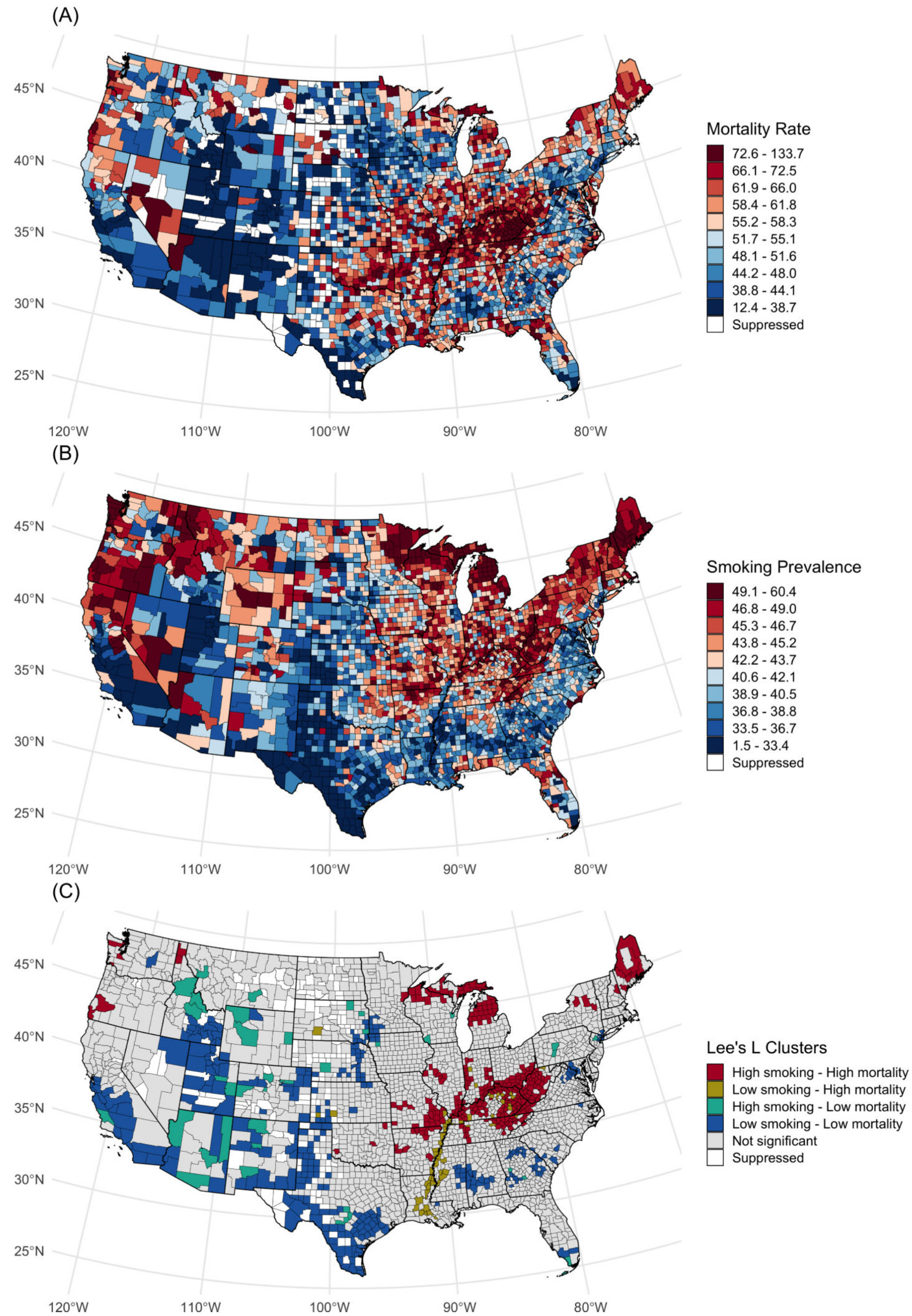


**Figure 2.**

Geographic patterns in the conterminous United States by county among females: a) lung and bronchus cancer mortality rates per 100,000 person-years during 2005–2018, ages 20+ years, b) ever-smoking prevalence percents during 1997–2003, ages 18+ years, c) Lee's L analysis findings with colors indicating statistically significant counties.

**Table 1.**

Lung and bronchus cancer mortality rates ages 20+ for 2005–2018 and ever smoking percent ages 18+ for 1997–2003 in the conterminous United States by sex and by United States Census Division.

| | Lung and Bronchus Mortality | | Ever Smoking |
|---|---|---|---|
| | **Deaths** | **Rate* (95%CI)** | **Prevalence* (95% CI)** |
| **Males** | | | |
| Conterminous U.S. | 1,188,445 | 78.1 (77.9–78.2) | 52.6 (52.0–53.2) |
| New England | 55,670 | 73.3 (72.7–73.9) | 54.3 (52.8–55.9) |
| Middle Atlantic | 151,656 | 72.5 (72.1–72.9) | 52.4 (51.0–53.8) |
| East North Central | 202,667 | 86.8 (86.4–87.2) | 55.1 (54.0–56.1) |
| West North Central | 85,753 | 80.9 (80.4–81.5) | 55.0 (53.7–56.2) |
| South Atlantic | 263,674 | 82.9 (82.6–83.2) | 54.2 (53.2–55.3) |
| East South Central | 104,958 | 113.2 (112.5–113.9) | 57.4 (56.0–58.8) |
| West South Central | 133,583 | 83.7 (83.2–84.2) | 52.3 (50.8–53.7) |
| Mountain | 60,940 | 56.8 (56.4–57.3) | 48.9 (47.5–50.3) |
| Pacific | 129,544 | 59.6 (59.3–59.9) | 48.4 (47.0–49.9) |
| **Females** | | | |
| Conterminous U.S. | 984,645 | 50.3 (50.2–50.4) | 40.2 (39.6–40.8) |
| New England | 52,737 | 53.2 (52.7–53.7) | 46.6 (44.8–48.3) |
| Middle Atlantic | 134,374 | 48.2 (48.0–48.5) | 41.9 (40.5–43.2) |
| East North Central | 166,990 | 56.3 (56.1–56.6) | 41.8 (40.7–43.0) |
| West North Central | 85,753 | 50.8 (50.1–51.6) | 42.5 (41.0–43.9) |
| South Atlantic | 203,306 | 50.9 (50.7–51.1) | 39.2 (38.2–40.2) |
| East South Central | 72,909 | 61.6 (61.1–62.0) | 42.6 (41.0–44.2) |
| West South Central | 98,700 | 49.4 (49.1–49.7) | 35.6 (34.3–36.8) |
| Mountain | 52,702 | 41.7 (41.3–42.0) | 38.2 (36.6–39.9) |
| Pacific | 117,174 | 42.8 (42.5–43.0) | 34.0 (32.7–35.3) |

*Mortality rates are per 100,000 person-years and are age-adjusted to the 2000 U.S. standard population. Ever smoking prevalence estimates are percents. CI= Confidence Interval. The nine U.S. Census Divisions include the following states: New England (Connecticut, Maine, Massachusetts, New Hampshire, Rhode Island, and Vermont), Mid-Atlantic (New Jersey, New York, and Pennsylvania), East North Central (Illinois, Indiana, Michigan, Ohio, and Wisconsin), West North Central (Iowa, Kansas, Minnesota, Missouri, Nebraska, North Dakota, and South Dakota), South Atlantic (Delaware, Florida, Georgia, Maryland, North Carolina, South Carolina, Virginia, District of Columbia, and West Virginia), East South Central (Alabama, Kentucky, Mississippi, and Tennessee), West South Central (Arkansas, Louisiana, Oklahoma, and Texas), Mountain (Arizona, Colorado, Idaho, Montana, Nevada, New Mexico, Utah, and Wyoming), and Pacific (California, Oregon, and Washington).