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Geographic disparities in the decline of lung cancer mortality among women in the United States

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2015

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An abstract of
A thesis submitted to the Faculty of the
Rollins School of Public Health of Emory University
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Abstract

Geographic disparities in the decline of lung cancer mortality among women in the United States

By Katherine Ross

Lung cancer death rates began declining among women in the United States in 2002; little is known about spatial distribution of this decline among counties, which may have unique trends that are masked when only considering state or national rates. We examined spatiotemporal trends in county-level change in mortality among women in the U.S. from the national peak in 2002 to 2014, and quantified trends in spatial structure and geographic disparity in mortality over time. We obtained county-level mortality rates from the National Vital Statistics System from 1978 to 2014, and used a random effects Poisson model to produce smoothed estimates of change from 2002 to 2014. Local autocorrelation analysis was used to identify spatial clustering in the rates of decline, and mean log deviation (MLD) and between group variance (BGV) were used to measure relative and absolute disparity at the county-, state- and regional level. Demographic and socioeconomic characteristics of clusters were described using data from the 2010 U.S. Census. We identified substantial geographic heterogeneity in the decline of lung cancer death rates among women, including a cluster of 806 counties in the Midwest and central Appalachia with slow declines in lung cancer death rates. Absolute disparity in lung cancer death rates among women has been increasing at each geographic level since 1978, and relative disparity began increasing after the national decline in lung cancer mortality in 2002. Coordinated, targeted public health intervention could reduce the excess burden of lung cancer among women living in the Midwest and Central Appalachia and prevent widening geographic inequity.

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BACKGROUND

Introduction

Lung cancer is the leading cause of cancer death in women in the United States, and the second most commonly diagnosed cancer. In 2016, there are anticipated to be 106,470 new cases of lung cancer in women, and 72,160 deaths (1). One in four cancer deaths among women are attributable to lung cancer, more than from the next two leading causes of cancer death (colon and breast cancer) combined.

Definition of lung cancer

Lung cancer occurs in cells of the respiratory epithelium, which lines the respiratory tract. There are two broad categories of lung cancer: small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC) (2). SCLC is a less common but highly malignant tumor that represents 15% of lung cancer cases. SCLC is frequently diagnosed in late stages, and has a poor prognosis. NSCLC makes up the remaining 85% of lung cancer cases, and can be further divided into three histologic sub-types: adenocarcinoma, squamous cell carcinoma, and large cell carcinoma. Adenocarcinoma alone represents 38.5% of all lung cancer cases, and is the most common type of lung cancer in both smokers and never-smokers (3). Symptoms of lung cancer include persistent cough, blood in the sputum, chest pain, voice changes, worsening shortness of breath, and recurrent pneumonia or bronchitis (1).

Trends in lung cancer incidence, mortality, and survival in the United States

Lung cancer incidence and death rates are on the decline in the United States. The decline in mortality began in the mid-1990s for men, and the mid-2000s for women (1). Death rates have declined by 38% since 1990 among men, and by 12% since 2002 among women. From 2008 to 2012, death rates decreased by 2.9% annually among men, and 1.9% annually among women. Declines in death rates can be driven by two factors: improved survival, or decreased incidence of disease. Survival from lung cancer is much lower than other common cancers. Five-year relative survival for localized cancer is 57%, however, only 13% of lung cancers are diagnosed at a localized stage (4). Overall, five-year relative survival for lung cancer is 17.8%. In 1975, 5-year survival from lung cancer was 12.2% (5). Although this increase in survival is statistically significant, it cannot explain the substantial observed declines in mortality. Declines in lung cancer mortality can be primarily attributed to declines in lung cancer incidence. This decline in incidence began in the early 1990s for men (6), while women did not experience a decline until the early 2000s (7).

Cigarette smoking and lung cancer

The seminal risk factor for lung cancer is tobacco use, particularly cigarette smoking. Approximately 80% of deaths due to lung cancer are attributable to cigarette smoking (8). Cigarette smoke is highly carcinogenic, resulting in twenty- to thirty-fold increased risks for lung cancer among lifelong smokers when compared to nonsmokers (2). Risk increases with duration of exposure (years spent smoking), intensity of smoking (cigarettes per day), and intensity of inhalation. There are other risk factors for lung cancer, including air pollution, radon exposure, and occupational exposures; however, tobacco use is by far the most prevalent attributable cause of lung cancer.

History of tobacco use and cigarette smoking

Cigarette consumption was rare prior to the early 1900s. However, by the end of World War II, annual per capita cigarette consumption for adults rose from approximately 1000 cigarettes to 3500 cigarettes (9). Cigarette consumption continued to rise until 1964, when *Smoking and Health: Report of the Advisory Committee to the Surgeon General* was published. The report documented a clear link between cigarette smoking and lung cancer, estimating a nearly ten-fold increase in risk for average smokers and at least a twenty-fold increase in risk for heavy smokers (10). In addition, the report named smoking as a cause of bronchitis, emphysema, coronary heart disease, low birth weight for infants born to smoking mothers, and for the overall observed increase in mortality for smokers compared to non-smokers (RR = 1.7) (10). After the report, the number of Americans that believed smoking caused cancer doubled from 44% in 1958 to 78% in 1968 (9).

After the 1964 Surgeon General's Report, antismoking campaigns and changing social norms around smoking resulted in changes in public policy around cigarette smoking. Cigarette packages were required to display health warnings in 1965, and in 1969, cigarette advertisement was banned from television and radio (2). In addition, state- and federal excise taxes were placed on cigarettes, increasing their overall cost. The prevalence of cigarette smoking has sharply declined since 1965, from 42.4% of adults to 15.1% of adults in 2015 (11).

Gender-specific trends in cigarette smoking

Overall smoking prevalence statistics mask the sex-specific trends in smoking that have resulted in differing temporal patterns of lung cancer incidence and mortality between men and women in the United States. Women began smoking later than did men. Cigarette smoking was not seen as acceptable among women until the mid-1920s and 1930s, when female smoking became a symbol of the changing roles of women in society. Tobacco companies seized this opportunity to create marketing campaigns aimed at women that portrayed the cigarette as a "torch for freedom", or a symbol of women's emancipation (12).

The prevalence of cigarette smoking in women has consistently been lower than the prevalence of smoking in men. In 1955, the prevalence of smoking among adult men was 55%, more than twice that of women (25%) (9). However, rates among men plateaued from 1955 to 1965, while rates among women increased, reducing the gap to 20%. After the Surgeon General Report in 1964, smoking among men declined sharply – from 55% in 1965 to 40% in 1978. However, in this same interval, rates among women plateaued at 30% (9). In 1980, the Surgeon General published another report on smoking and health, dedicated to smoking among women. The preface of the report was titled "The Fallacy of Women's Immunity", due to the misconception at the time that women were less susceptible to the health effects of smoking than men. Much of the research in the 1964 report was based on the experience of male smokers, as smoking in women was less common and began later. However, by the time of the 1980 report, it was clear that women were beginning to show “the first signs of an epidemic of smoking-related disease” (13).

After 1980, smoking prevalence among women did begin to decline. However, this decline was much slower than the early decline observed among men (9). In 2002, a second report on women and smoking was published by the Surgeon General, which noted that despite clear evidence of the harmful health effects of smoking among women, smoking prevalence among women declined very little during the 1990s and increased dramatically among adolescent girls and young women (14). Although in 2015 men still had a higher prevalence of smoking than women (16.7% vs. 13.6%), women had a lower percent decline in smoking from 2005 to 2015, especially in 45 – 64 year olds (28.9% decline for men vs. 14.6% decline for women) (11). Women also have a lower smoking cessation rate than men. In 2005, the “quit rate”, or proportion of ever smokers that were not current smokers, was 50% higher in men than in women (7).

Geographic heterogeneity in smoking and tobacco control

There is substantial regional and state-level variation in tobacco control measures and the prevalence of tobacco use. Among women, prevalence of current tobacco use ranged from 8.3% in Utah to 28.4% in Kentucky in 2012 (15). The very low prevalence of smoking in Utah reflects the religious prohibition against smoking among members of the church of the Latter Day Saints (16). Current cigarette smoking is most prevalent in the Midwest (25.4% overall) and least prevalent in the West (18.0% overall). There are also state-level differences in the burden of disease attributable to smoking. In 2014, the top 5 ranked states for smoking-attributable cancer among women were Kentucky, Arkansas, Tennessee, Alaska, and Nevada (17). Six of the top ten ranked states for women were in the South.

Effective tobacco control measures include excise taxes, smoke-free policies, and youth access laws (18). Increases in state per capita spending on tobacco control programs are independently associated with declines in prevalence of cigarette smoking, indicating that tobacco control is effective in achieving reductions in tobacco use (19). Most Southern and Midwestern states have low excise taxes (7); taxes are especially low in tobacco-growing states (North Carolina, Kentucky, Tennessee, South Carolina, Virginia, Georgia, and Alabama), where tobacco products contribute to the state economy. California was the first state to implement a comprehensive tobacco control program, and has made the greatest progress in reducing tobacco use (20).

Geographic heterogeneity in lung cancer incidence and mortality in women

Geographic patterns in lung cancer incidence and mortality among women depend strongly on geographic patterns of smoking prevalence and tobacco control. From 1973 to 1996, lung cancer incidence among women increased significantly in every state except for California, Arizona, and Hawaii, where the increases were not statistically significant (21). From 1995 to 2005, incidence rates increased among women in eight states, predominantly in the Midwest, and decreased significantly only in California (7). From 1988 to 2008, rates of lung cancer incidence among women decreased in the West and stabilized in the Midwest (22).

From 1996 to 2005, lung cancer mortality significantly increased among women in thirteen states; all of these states were located in the South or the Midwest (Indiana, Iowa, Kansas, Michigan, South Dakota, Alabama, Arkansas, Kentucky, Louisiana, Mississippi, North Carolina, South Carolina, and Tennessee) (7). In a study using age-period-cohort modeling, lung cancer mortality rates declined continuously from 1973 to 2007 in California among women of all age groups, but in Southern and Midwestern states, rates among young women declined less quickly or increased (23), indicating that disparities between states may continue to increase as these women age.

Area-level factors associated with lung cancer

Most studies of geographic heterogeneity in lung cancer use state-level data. Although many factors influencing lung cancer mortality are exerted at the state-level – for example, tobacco taxation – there are other area-level factors that influence lung cancer operating at lower levels of geography. One of these is population composition. Demographic risk factors for lung cancer – age, education, and socioeconomic status – may be inequitably distributed throughout states, resulting in within-state differences in lung cancer mortality rates. Another factor is differences between urban and rural communities. Persons living in rural communities are more likely to smoke, start smoking at a younger age, and are less likely to quit using tobacco than their urban counterparts (24).

Smoking behavior is also influenced by contextual factors, including neighborhood socioeconomic status. Neighborhood socioeconomic status has been associated with individual likelihood of smoking, even after controlling for individual socioeconomic status (25). In addition, a multilevel longitudinal study in Australia found that neighborhood deprivation is associated with reduced probability of smoking cessation, and that this association explained a large part of the widening inequality in smoking rates between high- and low-SES neighborhoods (26). Neighborhood psychosocial factors have also been associated with individual smoking, although studies of this association are mixed. The Dutch GLOBE study found that physical stressors, such as urban decay, police presence, air pollution, and population density, were associated with individual smoking behavior even after adjustment for SES; adjustment for physical stressors substantially reduced the association between SES and smoking (27). However, a recent study from Australia found that psychosocial characteristics such as crime, perceived safety, and social cohesion were not associated with smoking after adjustment for neighborhood deprivation (28). Studies of the association between access to tobacco vendors and individual smoking behavior found that their results were attenuated after adjustment for neighborhood deprivation (29, 30).

Other studies have suggested that neighborhood socioeconomic status plays a role in lung cancer incidence and mortality beyond its influence on individual-level smoking. A case-control study in Canada found that neighborhood socioeconomic deprivation increases the odds of lung cancer incidence, and that the association remained significant after adjustment for both individual socioeconomic status and smoking behavior (31). A retrospective cohort of patients with NSCLC in North Carolina found that lower area-level socioeconomic status was associated with decreased survival among lung cancer patients (32), a finding also observed in a similar study done in Georgia in 2014 (33). The relationship between area-level socioeconomic status and lung cancer has changed over time, as the socioeconomic determinants of smoking have changed. From 1950 to 1980, areas of high socioeconomic status had higher lung cancer mortality rates, a pattern that began to reverse for men in the mid-1980s (34). Cigarette smoking was initially more prevalent in high socioeconomic status populations; however, as unfavorable associations between cigarette smoking and health were discovered, high socioeconomic status populations had higher rates of smoking cessation and lower rates of smoking initiation than low socioeconomic status persons, resulting in a reversal of the socioeconomic gradient. As of 1998, this gradient had not yet reversed among women.

Previous studies on county-level lung cancer mortality trends

In 2017, Mokdad, Dwyer-Lindgren & Fitzmaurice published a report documenting trends in cancer mortality at the county level from 1980 – 2014, which found that lung cancer mortality among women displayed geographic clustering in 2014 and change in mortality from 1980 to 2014, although they ignored the rise, plateau, and decline of lung cancer mortality in women (35). Devesa, et al, (1999) published a report in 1999 documenting clusters of U.S. counties with slow declines in lung cancer mortality in men, concentrated in Appalachia and the Deep South (36). Other recent analyses of county-level trends only considered counties within one state or region (37, 38, 39).

Public health implications and study purpose

In this paper we will estimate and describe spatiotemporal trends in county-level lung cancer mortality in women in the United States, identify spatial clustering in patterns of change in mortality, and quantify trends in geographic structure and disparity in lung cancer mortality among women. There are notable gender differences in temporal patterns of lung cancer incidence and mortality. Focusing on women will allow us to identify geographic heterogeneity in more recent declines of lung cancer mortality, which could inform targeted intervention to prevent further disparity. Declines in smoking prevalence have begun to ameliorate the “full-blown epidemic” of smoking-related diseases identified among women in the 2002 Surgeon General’s report. However, this reduction has not occurred equally across the United States. Stagnating declines in incidence in areas with high smoking prevalence and low smoking cessation could widen pre-existing geographic disparities in lung cancer. Identifying areas that are lagging behind in developing favorable trends of decline could inform targeted intervention to reduce or prevent inequities in lung cancer mortality in women.

INTRODUCTION

Lung cancer is the leading cause of cancer death among women in the United States. In 2016, lung cancer is expected to cause more than 72,160 deaths among women, representing approximately 25% of female cancer mortality in the U.S. Lung cancer mortality rates have steadily declined among men since the mid-1990s, and began declining among women in the late 2000s (1). This trend is not due to an improvement in survival, which has not substantially changed since 1970 (4). Instead, declines in lung cancer mortality can be attributed to declines in lung cancer incidence, which began in the mid-1980s for men and early 2000s for women (7). These declines can further be attributed to changes in the prevalence of tobacco use, particularly cigarette smoking.

Cigarette smoking is the primary risk factor for lung cancer; heavy smokers have a 20-fold increase in risk of the disease compared to non-smokers (2). Smoking prevalence is higher in men than in women; in 2015, 16.7% of men were current smokers compared to 13.1%. This gap has narrowed significantly since 1960, when men were 50% more likely to smoke than women (9), primarily due to more rapid declines of smoking prevalence among men than women. From 2005 to 2015, women had a lower percent decline in smoking than men, especially among 45 – 64 year olds (28.9% decline for men vs. 14.6% for women) (11). Gender differences in smoking initiation and cessation explain observed differences in mortality– women began smoking approximately 25 years after men and have not quit at the same rate (9) resulting in the later appearance of disease and a plateau in mortality. Tobacco control measures implemented in recent decades, including tobacco taxes and clean air laws, have been successful in reducing tobacco use and its associated burden of disease (19).

There is substantial regional and state-level variation in tobacco control measures and the prevalence of tobacco use (7, 15). In parallel, there are geographic differences in the burden of lung cancer. Lung cancer incidence and mortality among women is highest in the South and the Midwest (7). Lung cancer mortality has declined more rapidly in West than in the rest of the U.S., a trend driven primarily by California, the first state to implement statewide comprehensive tobacco control (20). For women, mortality has significantly declined only in the West; other regions have exhibited rates that were stable or rising (7). At the state level, geographic variation can be observed in both the absolute burden of lung cancer mortality and in patterns of decline. While mortality rates among men declined in all fifty states from 1995 to 2005, for women, lung cancer mortality only declined in three states during that period (California, New Jersey, and Texas), and significantly rose in thirteen states, concentrated in the South and Midwest (7).

Little is known about the geographic distribution of decline in lung cancer mortality among women at the county level. In 2017, Mokdad, Dwyer-Lindgren & Fitzmaurice published a report documenting trends in cancer mortality at the county level from 1980 – 2014, which found that lung cancer mortality displayed geographic clustering at the county level in 2014 and in the overall change from 1980 to 2014 (35). However, changes in mortality were pooled across a period in which mortality was increasing, plateauing, and then declining; the geographic patterns observed may not represent recent patterns of decline. Devesa, et al, published a report in 1999 documenting clusters of U.S. counties with slow declines in lung cancer mortality among men, concentrated in Appalachia and the Deep South (36). Contextual factors, such as rurality and area-level socioeconomic status, have been shown to affect both individual smoking behaviors (5, 26, 27) and lung cancer incidence (31); these factors act on smaller areas such as counties. Counties may have unique trends in decline that are masked when only considering state or national rates.

Stagnating declines in incidence in areas with high smoking prevalence and low smoking cessation could widen pre-existing geographic disparities in lung cancer mortality. Identifying areas that are lagging behind in developing favorable trends could inform targeted intervention to reduce or prevent inequities in lung cancer mortality among women. Nationally, lung cancer mortality peaked for women in 2002, with subsequent declines. In order to identify spatial patterns in the rate of recent declines in mortality and to quantify change in the magnitude of geographic disparities, we examined spatiotemporal trends in county-level change in mortality among women from peak incidence in 2002 to 2014. We also quantified trends in spatial structure and geographic disparity in lung cancer mortality among women over time.

METHODS

Data for this study were obtained from the National Vital Statistics System (NVSS), a national surveillance system that captures all births and deaths that occur in the United States. NVSS is maintained by the National Center for Health Statistics (NCHS). County-level mortality data from 1969 to 2013 is accessible through SEER*Stat, an analytical software package created by the National Cancer Institute (NCI). Our study included all counties in the contiguous United States (excluding Hawaii and Alaska). Eight-year intervals beginning in 1978 were chosen to be long enough to provide rate stability but short enough to allow for analysis of recent trends. Rates from counties with fewer than ten deaths each eight-year interval are suppressed. Prior to 1978, lung cancer was rare among women, resulting in high rates of suppression among counties. Lung cancer deaths were identified based on the underlying cause of death using the International Classification of Disease (ICD) codes from C340 through C349. ICD codes were found to be highly accurate for identifying deaths from lung cancer (40). Rates were age-adjusted to the 2000 U.S. standard population.

Age-adjusted lung cancer mortality rates were calculated for women in each county. The geographic distribution of lung cancer mortality over four eight-year intervals (1978 - 1986, 1987 - 1995, 1996 - 2004, and 2005 – 2013) was mapped using ArcGIS 10.3.2. In order to quantify change in spatial autocorrelation over time, we calculated a global Moran’s I for each interval. Moran’s I is a measure of clustering that tests whether the degree to which like values (high rates or low rates) are located in neighboring counties; a value of 0 suggests a spatially random distribution with no spatial autocorrelation, while values close to -1 or 1 indicate nearly perfect autocorrelation, indicating that neighboring counties are very similar to one another. The Getis-Ord statistic was used to identify statistically significant clusters of counties with high or low mortality rates in each interval at an alpha level of 0.05.

At the national level, lung cancer mortality in women peaked in 2002, and has since declined. To determine whether this decline occurred in a spatially random fashion, or whether there was spatial structure (e.g. spatial autocorrelation or clustering) in this decline, we calculated the difference between the lung cancer mortality rate from 1996 - 2004 to 2005 – 2014 lung cancer mortality for each county. We then fitted a random effects Poisson model to the data in order to smooth responses and account for differences in population size. The model contained a fixed effect for year, and a random intercept and slope for year for each county. We used the Gedis-Ord statistic to identify clusters of "high" change (counties where mortality either increased or did not decline) and "low" change (counties where the magnitude of decline in lung cancer mortality was large). To identify an appropriate fixed distance band for analysis, we assessed incremental spatial autocorrelation of change in lung cancer mortality for 10 distance bands ranging from 50km to 500,000 km. We then used an optimized hotspot analysis that selected an appropriate distance band based on incremental spatial autocorrelation and mean distance to 30 nearest neighbors. Random slopes were also used to determine whether counties had changes that were statistically significantly different than the overall average. Slopes were considered to be significant at a p-value of 0.05.

Regions that were identified as local 'hot' or 'cold' spots with respect to rate of change in lung cancer mortality were further summarized in several ways. First, biennial mortality rates from 1978 through 2014 were calculated and contrasted to one another and to the U.S. as a whole. Second, demographic characteristics of clusters were described using county-level information obtained from the 2010 Census, including median age, percent of families living in poverty, percent women, percent White, percent Black, percent Hispanic of any race, unemployment race, percent finishing high school, percent finishing college, and percent of the county living in a rural area.

Change in geographic disparity over time was assessed by using mean log deviation (MLD) as a measure of relative disparity and the between group variance (BGV) as a measure of absolute disparity (41). MLD is a population-weighted measure that can be used to summarize the difference in shares of health and shares of population among unordered groups, such as states or counties. BGV is a population-weighted measure that represents variance among unordered groups that is sensitive to large departures from the national average. Change in disparity from 1978 to 2014 was assessed separately for regions, states, and counties to quantify trends at different geographic scales.

RESULTS

Lung cancer mortality rates rose rapidly among women during the study period, from 13.1 per 100,000 in 1970 to 41.3 per 100,000 in 2002 (Figure 1). After 2002, national lung cancer mortality rates began to decline, to 39.7 per 100,000 from 2005 – 2009. In the latest interval, 2010 – 2014, the national lung cancer mortality rate among women declined further, to 36.3 per 100,000.

In the late 1970s and early 1980s, the largest burden of lung cancer among women occurred on the West Coast (in California, Oregon, and Washington), in the Northeast, and in Southern Florida (Figure 2). Although lung cancer rates rose everywhere in the following three decades, rates did not rise as quickly in these regions, resulting in a shift in the highest burden of lung cancer to the Midwest and Central Appalachia (Figure 2). The global Moran’s I for lung cancer mortality among women increased over time, from 0.24 in 1978 – 1985 to 0.38 in 2005 – 2014, indicating an increase in the autocorrelation of county-level rates (Figure 3). Hotspot analysis identified significant lung cancer mortality clusters from 1978 – 1986 (Figure 4), covering the majority of the West Coast and the Northeast, in addition to Florida, Southern Louisiana, and the Midwest (Ohio, Indiana, Michigan, and parts of Illinois). From 1987 – 1995, the West Coast cluster of high rates had shrunk to no longer include Southern California, and a new significant cluster of high rates appeared that included parts of Texas, Arkansas, Missouri, Tennessee, and Kansas. From 1996 – 2004, the clusters of high rates in the Northeast and Florida began to recede. In the latest interval (2005 – 2014), there was a large cluster of high lung cancer mortality rates that included central Appalachia and the Midwest (Figure 4). Smaller clusters were still identified in northern Florida and New York; however, trends from the previous intervals indicate that those clusters are receding.

Figure 5 maps the geographic distribution of absolute change in county-level lung cancer mortality from the interval containing peak rates (1996 – 2004) to the present (2005 – 2014). Strong declines can be seen in the Western United States, parts of Texas, coastal New England, and parts of Florida; other places in the U.S. had little or no change, or even increased mortality rates. A random effects Poisson model was fitted to the data to smooth rates and determine whether county-level changes in lung cancer mortality were statistically significantly different from the national average. Random slopes and t-values were mapped to examine geographic patterns (Figure 6). A county-level random slope indicates the amount by which the county-level change deviated from the national average. Counties in the Midwest, Appalachia, and Southeast were more likely to have positive random slopes, which indicate either slower decline or increase in lung cancer mortality in comparison to the national average change. T-values measure the size of the difference in lung cancer mortality, relative to existing variation in the data; high t-values are more likely to be statistically significant. The sign of the t-value indicates the sign of the slope. High negative t-values were observed in southern California, western Washington, parts of Texas (Houston and Dallas), southern Florida, and coastal New England. Positive t-values were found in the Midwest and central Appalachia; however, these were not as large in magnitude as the negative t-values. Of the 84 counties with changes in mortality that were statistically significantly different than the national average ($p < 0.05$), only 3 were increases; the remaining 81 had stronger declines than average.

Incremental spatial autocorrelation analysis was performed to quantify local spatial autocorrelation; there were no distinct peaks of autocorrelation (Figure 7). Optimized hot spot analysis was used to identify clusters of the smoothed change in lung cancer mortality among women (Figure 8). Four-hundred and forty one counties were identified as part of six distinct clusters of fast decline along the West Coast (62 counties; 51 in California, 7 in Arizona, 3 in Nevada, and 1 in Utah), in Western Washington (35 counties; 25 in Washington and 10 in Oregon), in the Mountain West (51 counties; 23 in Colorado, 6 in New Mexico, 12 in Utah, and 2 in Wyoming), in Texas (113 counties, 112 in Texas and 1 in New Mexico), in Florida (32 counties), and in New England (148 counties; 7 in Connecticut, 3 in the Delaware, 1 in Washington, D.C., 22 in Maryland, 12 in Massachusetts, 2 in New Hampshire, 19 in New Jersey, 10 in New York, 22 in Pennsylvania, 5 in Rhode Island, 39 in Virginia, and 6 in West Virginia). One large cluster of 806 counties with slow changes in lung cancer mortality was identified; comprising 25 counties in Alabama, 39 in Arkansas, 7 in Georgia, 82 in Illinois, 68 in Indiana, 3 in Iowa, 13 in Kansas, 112 in Kentucky, 19 in Michigan, 79 in Missouri, 39 in North Carolina, 62 in Ohio, 32 in Oklahoma, 1 in Pennsylvania, 18 in South Carolina, 89 in Tennessee, 19 in Virginia, 25 in West Virginia, and 32 in Wisconsin.

Rates were calculated separately pooling all counties within each of the seven identified clusters. Compared to the national average, both types of clusters had unique trends in lung cancer mortality among women. In the California and Texas clusters, lung cancer mortality rates among women were significantly higher than the national average in the early 1970s and 1980s (Figure 9). However, mortality peaked early for these clusters, and was followed by a steady decline in mortality that brought rates below the national average. In the Seattle and Florida clusters, mortality was well above the national average during peak incidence periods, but had strong declines from 2005 – 2014, bringing rates to or below the national average. Mortality among women in the New England cluster peaked in the mid-1990s, and declined to below the national average in the most recent interval. Rates in the Mountain West have consistently been far below the national average, and were accompanied by a sharp decline from 2005 – 2014.

Rates in the cluster of slow decline were lower than the national average until 1990 (Figure 10). While national rates increased only slightly from 1990 – 2004 (37.3 per 100,000 to 41.3 per 100,000), rates in the Midwest/central Appalachia cluster of slow decline increased dramatically (37.3 per 100,000 to 45.2 per 100,000), and plateaued at 45.3 per 100,000 in 2005 – 2009, despite a decline in the national rate during this interval. In the latest interval, the cluster rate did decline to 42.7 per 100,000. However, strong national declines have resulted in an increasing absolute and relative difference between the cluster of slow decline and the national average since the mid-1990s, from 1.1 per 100,000 in 1993 – 1995 to 6.4 per 100,000 in 2010 – 2014, and from a rate ratio of 1.03 in 2002-2004 to 1.18 in 2010-2014.

Demographic and economic characteristics of cluster communities were described using data from the 2010 Census (Table 1). Counties in the cluster of slow decline had higher proportions of White and rural residents and fewer Black or Hispanic residents than the national average, in addition to higher poverty rates, higher unemployment, and lower educational attainment than the rest of the United States. Counties in clusters of fast decline had higher proportions of Black and Hispanic residents, were less rural, and were younger than the national average. The Seattle, California, Mountain West, and New England clusters had a higher proportion of residents with a college degree or higher than the national average. With the exception of Texas, clusters of fast decline had lower poverty rates than the national average.

Trends in summary measures of health disparity vary between relative and absolute measures and across scales of geography. Relative disparity, as measured by mean log deviation, is much higher at the county-level than at the state or regional level (Figure 10). At all three levels, MLD increased from 1996 – 2004 to 2005 - 2014 (4.8% at the county level, 68.6% at the state level, and 236.6% at the regional level). Absolute disparity has steadily increased since 1978 at all three geographic scales (67.4% increase since 1978 at the county level, 108.3% increase at the state level, and 81.3% increase at the region level) (Figure 12). County-level absolute disparity is higher than both regional absolute disparity and state-level absolute disparity. Regional absolute disparity is larger than state absolute disparity, while state relative disparity is larger than regional relative disparity.

DISCUSSION

There is substantial geographic heterogeneity in county-level lung cancer mortality among women, both in absolute rates, and in the geographic patterns of change. Absolute geographic disparity in lung cancer mortality has steadily increased since 1978, and relative disparity increased in the most recent interval. In contrast with the observed national decline in lung cancer mortality among women after 2002, we identified a distinct area in the Midwest and central Appalachia where progress has lagged. The excess burden of lung cancer mortality among women in the Midwest and central Appalachia compared to the national average has grown consistently since the mid-1990s.

These findings expand on previous studies that showed state- and region-level disparities in lung cancer mortality (7) and are consistent with a recent study that examined overall county-level change in cancer mortality from 1980 to 2014 (35). We also characterize geographic variation in the period since the national peak among women. Given the importance of tobacco smoking to lung cancer mortality, our findings are consistent with previous studies of high rates of tobacco use among women in the Midwest and central Appalachia (15).

Clusters were heterogeneous with regards to their demographic and socioeconomic profiles. The cluster of slow decline was more White and more rural than the nation as a whole, with lower educational attainment and higher poverty than the national average. Clusters of fast decline displayed more heterogeneity in socioeconomic characteristics, although each had a less White and less rural population than the national average. The lack of consistent pattern between education, poverty and cluster membership indicates that these factors may not be related to the spatial distribution of decline in lung cancer mortality at the county level. These findings are in contrast to previous research that found associations between area-level socioeconomic status and lung cancer incidence and mortality (31, 34) although these studies did not explicitly examine associations with the rate of change in incidence or mortality, which likely have different determinants.

The geographic cluster of slow rates of decline tend to be composed of predominantly White and rural counties. This is in agreement with previous studies that found that White women were more likely to smoke than any other racial or ethnic group of women aside from American Indian/Alaska Native women (11). From 2005 to 2013, the decline in smoking prevalence for White women was lower than among Black women or Hispanic women, indicating that declines in incidence and death rates may slow for this group in the future (11). Smoking prevalence is higher in rural areas than in urban areas (24), and the decline in tobacco-associated cancer incidence and mortality is lower than in urban or metropolitan areas (42). Our results are consistent with these previous studies.

Tobacco control measures, such as excise taxes, have been shown to be successful in reducing the prevalence of cigarette smoking (19). California was the first state to implement comprehensive tobacco control (20); our findings show that lung cancer mortality declines in California have been stronger than the national average. The Midwest/central Appalachia hotspot comprises states where both excise taxes on tobacco and spending on tobacco control measures at the state-level are very low (7). Sustained efforts to reduce smoking prevalence among women in hotspot regions, who are more likely to smoke (15) and less likely to quit smoking (11), may reduce lung cancer mortality.

Our findings that relative and absolute geographic disparity has increased since peak lung cancer death rates among women, as measured by mean log deviation and between group variance, agree with those of a study by Jemal et al in 2012, which used age-period-cohort modeling to show that lung cancer mortality among young women was increasing in the South and Midwest, and not in the rest of the nation (23). While a focus on tobacco cessation may reduce mortality among women in the Midwest and central Appalachia, the long latency period of lung cancer means that the effects of these efforts may not be felt for years, during which time the excess burden of lung cancer among women in the Midwest and central Appalachia may continue to rise. One potential tool for reducing mortality among current smokers is computed-tomography screening for lung cancer, which was recommended for by the U.S. Preventive Services Task Force in 2014 for asymptomatic adults aged 55 – 80 with a 30-year pack history. Increasing awareness and uptake of lung CT screening among providers and current smokers in the Midwest and central Appalachia may reduce mortality (43) and prevent growing inequities in lung cancer among women.

The strengths of our study include the use of spatial analysis to characterize spatial and temporal trends in lung cancer mortality among women. To our knowledge, this is the first study to examine the geographic distribution of change in lung cancer mortality among women from its peak in 2002 to the present interval (2010 – 2014).

This study has several limitations. First, the availability of the data in biennial intervals means that recombining data into decades or five-year intervals was not feasible. Second, county-level suppression of data occurred primarily in rural areas of the Western United States, limiting our ability to examine lung cancer mortality trends in these areas. Third, the ecological nature of the study means that it is not possible to draw inference about why certain areas experienced different patterns of decline in lung cancer mortality among women.

Although lung cancer mortality among women is declining in the United States, women living in the Midwest and central Appalachia may not be experiencing the benefits of this decline. Efforts to reduce smoking prevalence may reduce lung cancer mortality in these areas; however, the effects of these interventions may not be felt for many years. Coordinated, targeted public health intervention could reduce the excess burden of lung cancer among women living in these areas and prevent widening geographic inequity.

PUBLIC HEALTH IMPLICATIONS AND FUTURE DIRECTIONS

Our findings indicate that there is geographic inequity in the distribution of lung cancer mortality among women, and that this inequity has increased over time. Women in counties in the Midwest and Central Appalachia may experience slower declines in lung cancer mortality than the rest of the nation, which could lead to further disparity. The cluster identified in this study may benefit from targeted public health intervention to prevent smoking among women, encourage smoking cessation among current smokers, and promote lung cancer screening among those women that meet the current guidelines in order to reduce mortality.

Further research might include exploration of how both state and local tobacco control ordinances influence the rate of decline in lung cancer mortality. Identifying policies that accelerate decline in lung cancer mortality and the levels at which they act could be useful for public health professionals and policy makers across the country. In addition, further studies could identify other county-level predictors of decline, such as poverty, educational attainment, or employment status. Although we examined the distribution of these factors in our clusters, the purpose of the spatial analysis we performed is to identify correlation among counties near to each other, not to predict the rate of decline. It is possible that there are counties with slow declines in mortality that are not near to other counties with similar patterns; these counties would not be part of a cluster but may still benefit from targeted public health intervention.

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TABLES AND FIGURES

Figure 1. Trends in lung cancer mortality rates per 100,000 among women in the United States, 1969 – 2014.

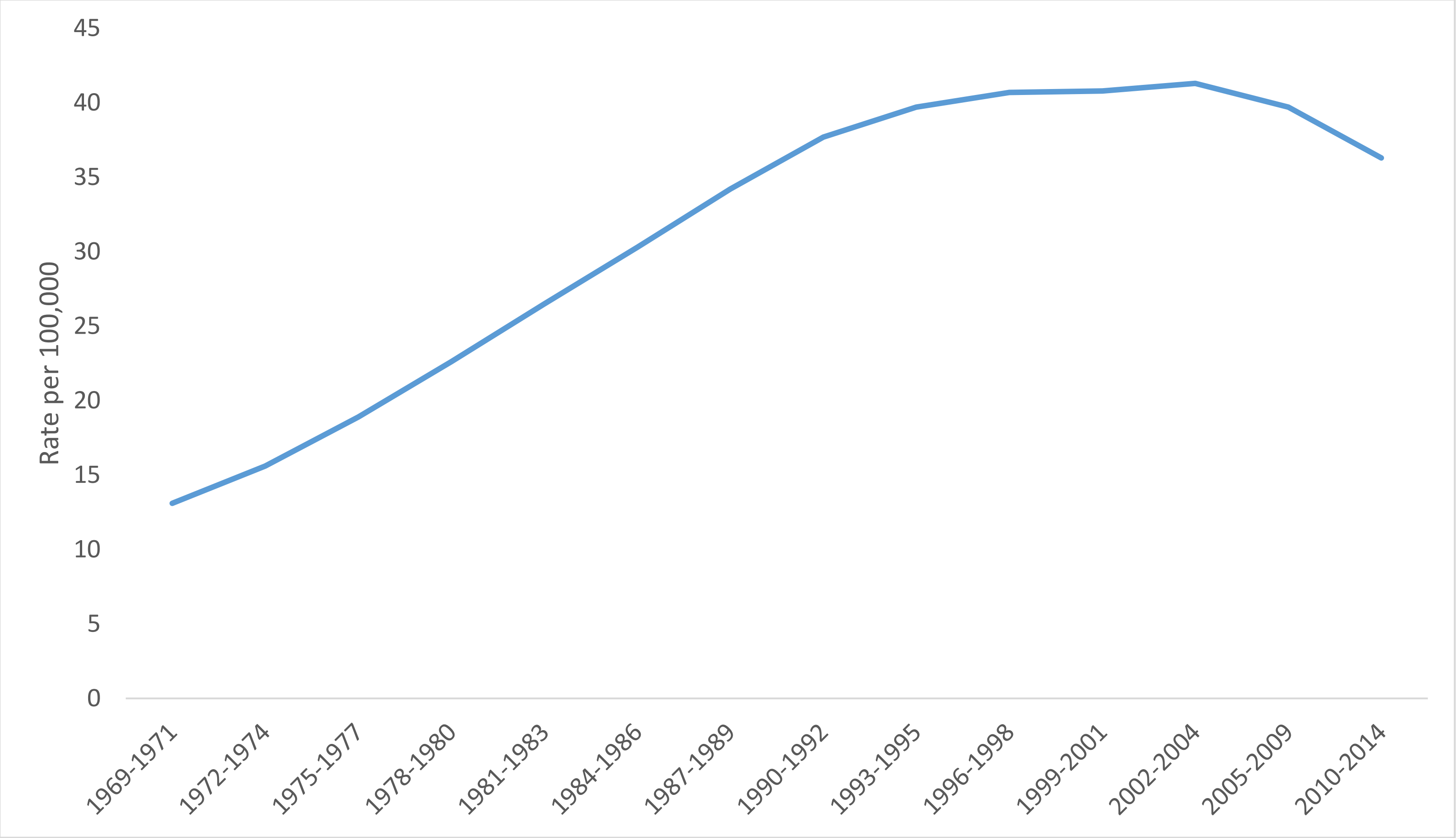


Figure 2. County-level lung cancer mortality rates per 100,000 women in the contiguous United States, in four intervals, from 1978 to 2014.

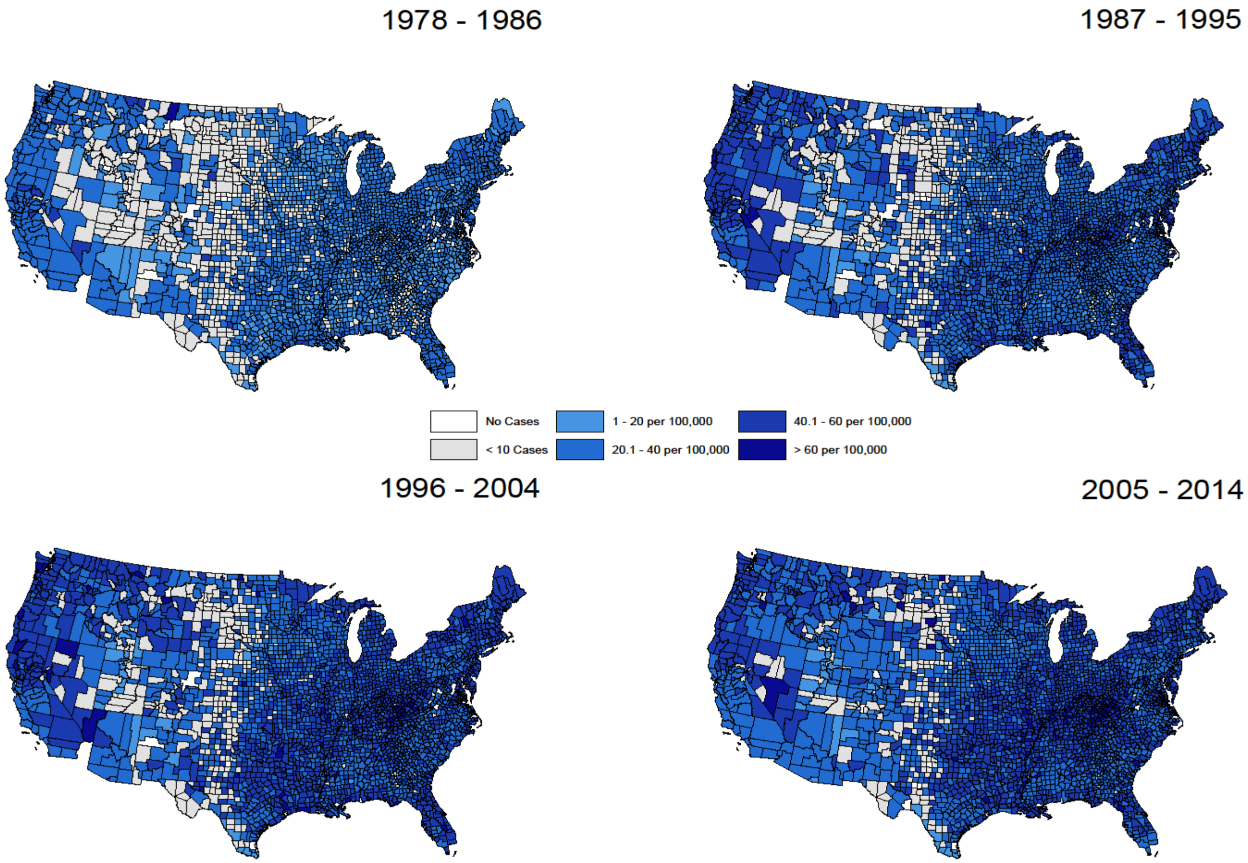


Figure 3. Spatial autocorrelation in lung cancer mortality rates among women from 1978 to 2014.

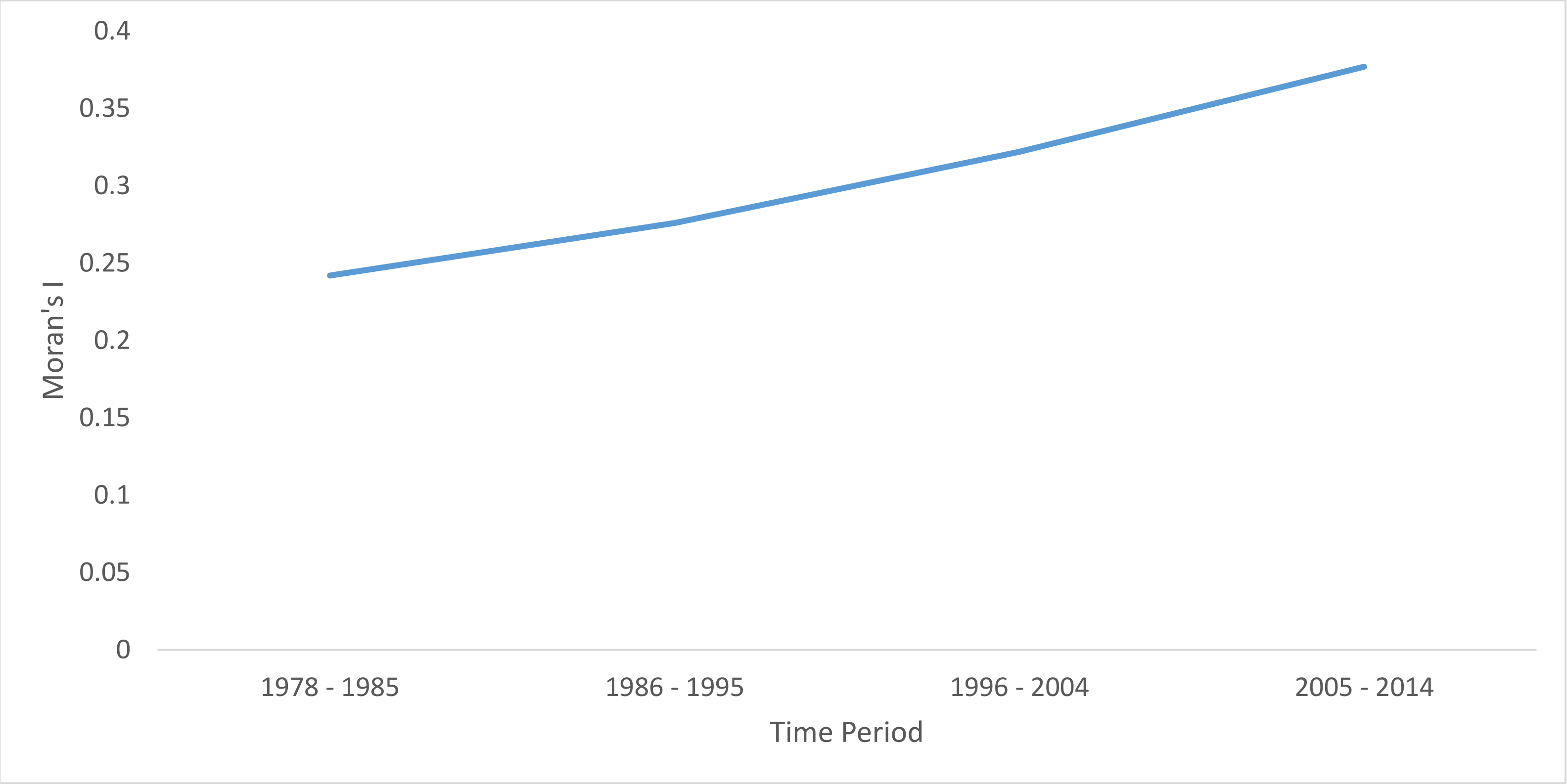


Figure 4. Hotspot analysis of lung cancer mortality rates among women in the contiguous United States, in four intervals, from 1978 to 2014.

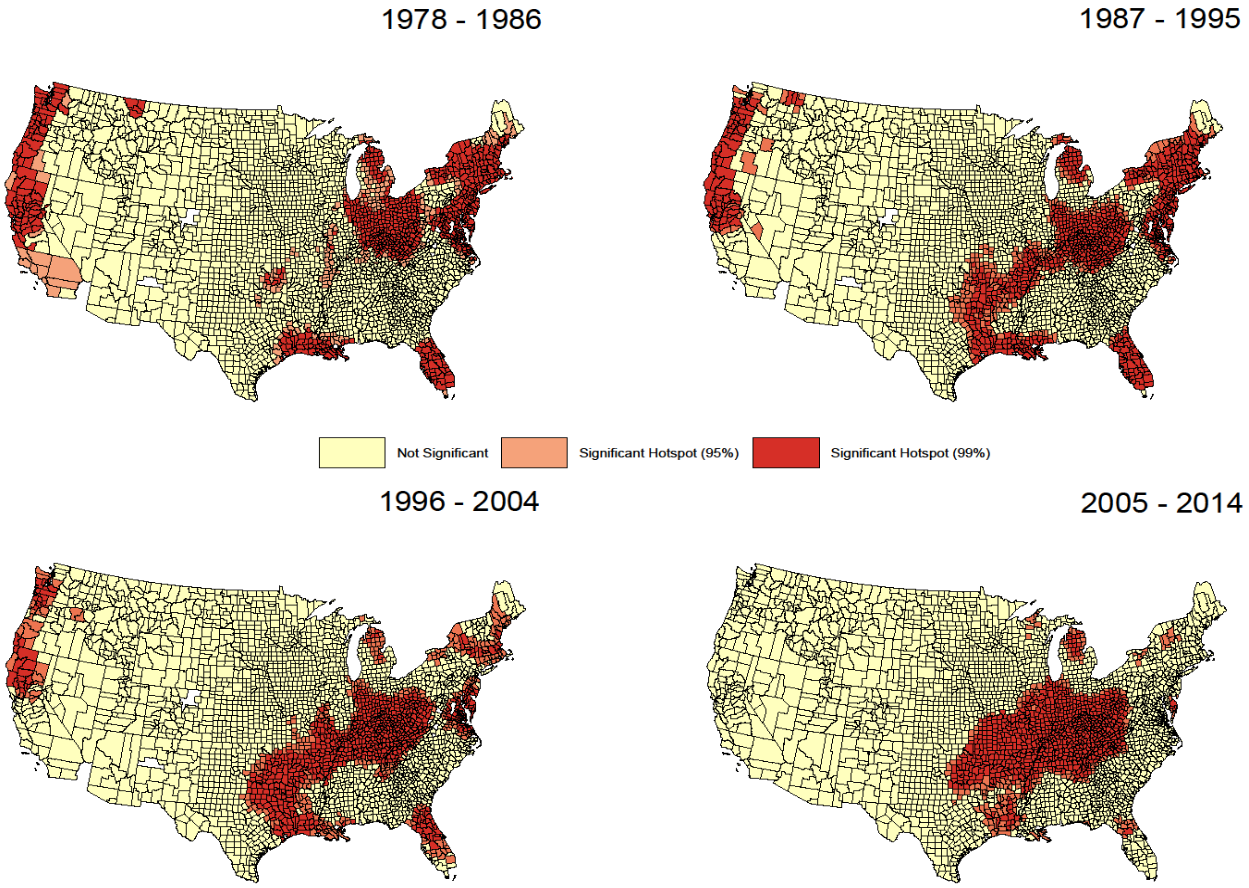


Figure 5. Change in county-level lung cancer mortality rates among women from 1996 – 2004 to 2005 – 2014.

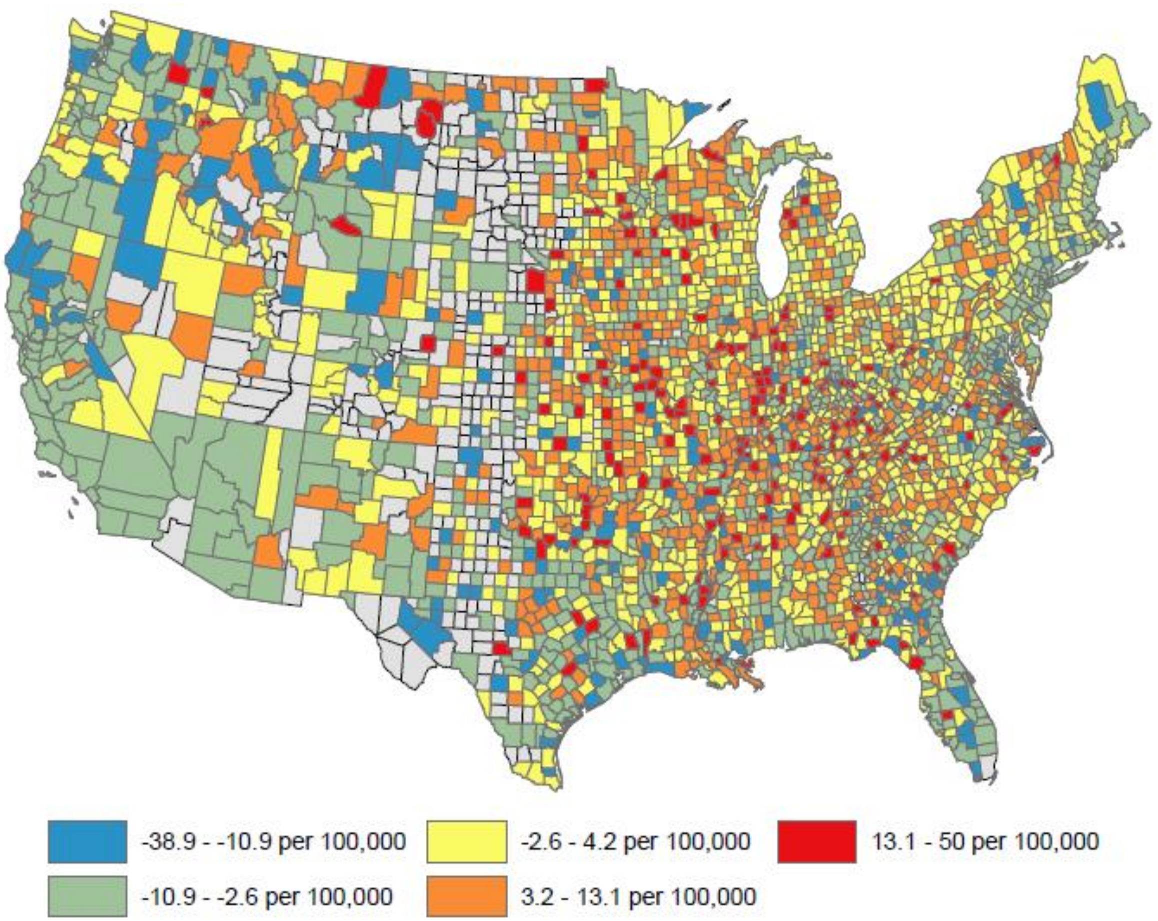
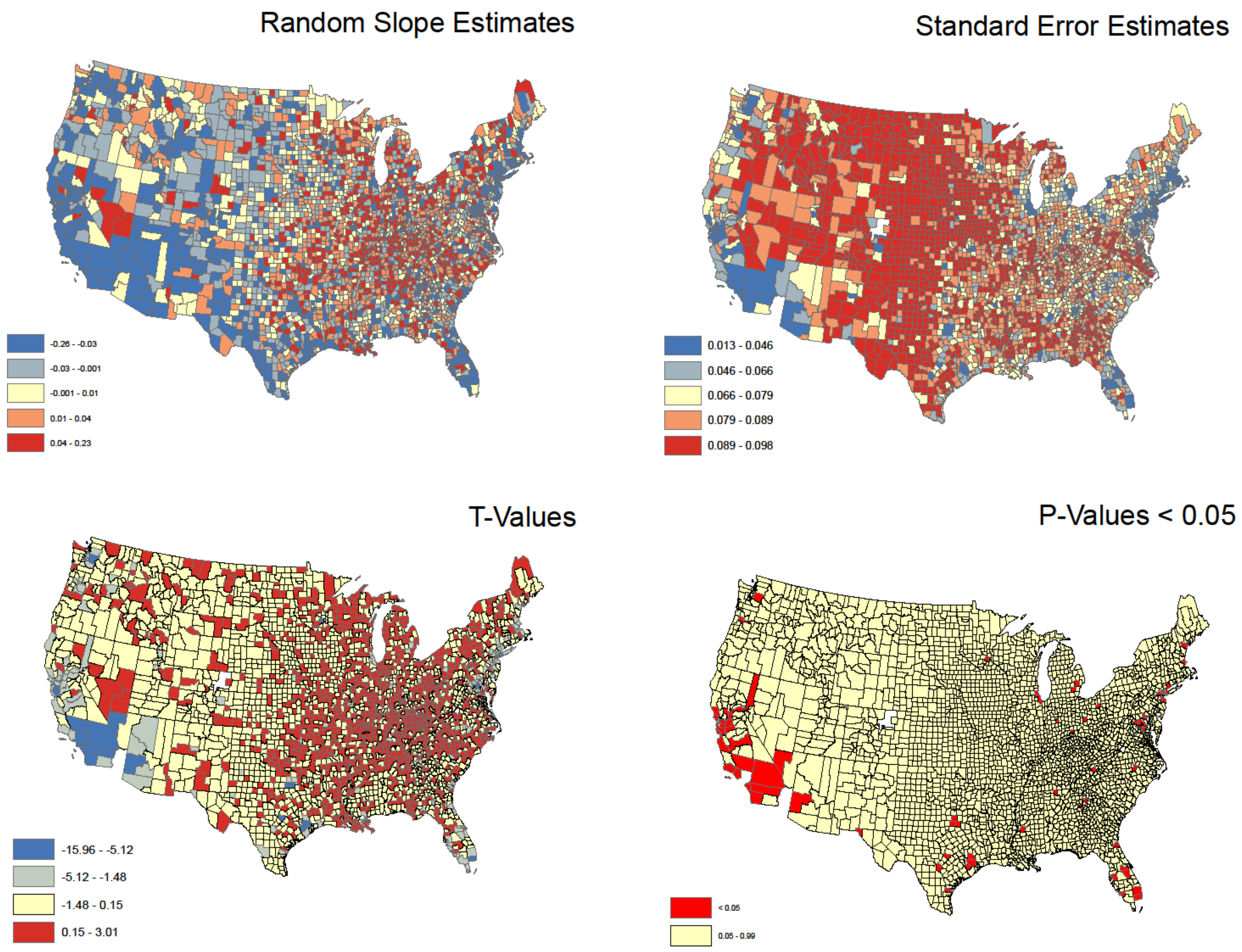


Figure 6. Random effects modeling of county-level change in lung cancer mortality among women from 1996 – 2004 to 2005 – 2014.



Random Slope Estimates

Standard Error Estimates

T-Values

P-Values < 0.05

Figure 7. Results of incremental spatial autocorrelation modeling of 15 fixed distance bands with a minimum of 50 km.

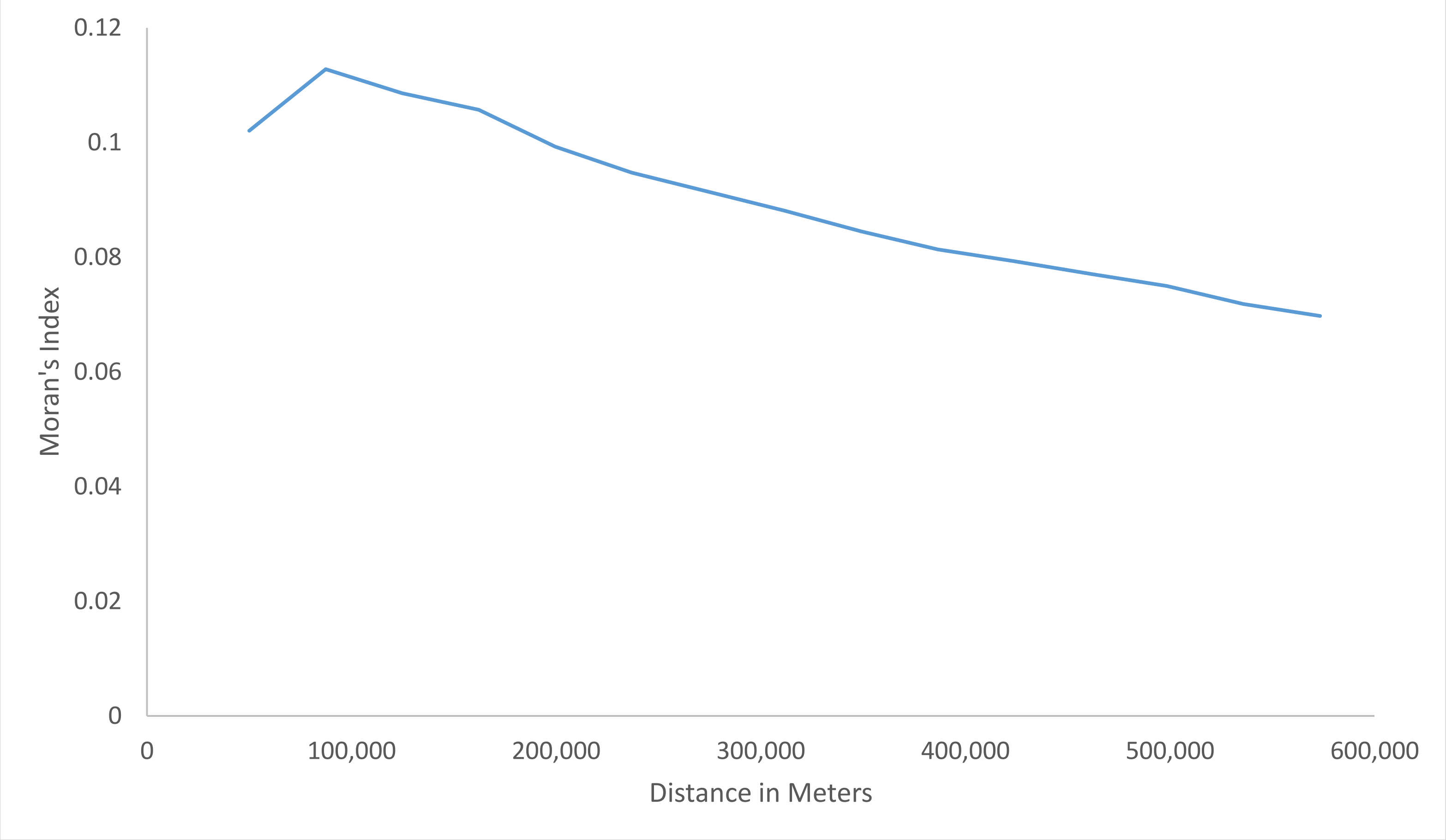


Figure 8. Clusters of fast and slow declines in county-level lung cancer mortality rates among women from 1996 – 2004 to 2005 – 2014.

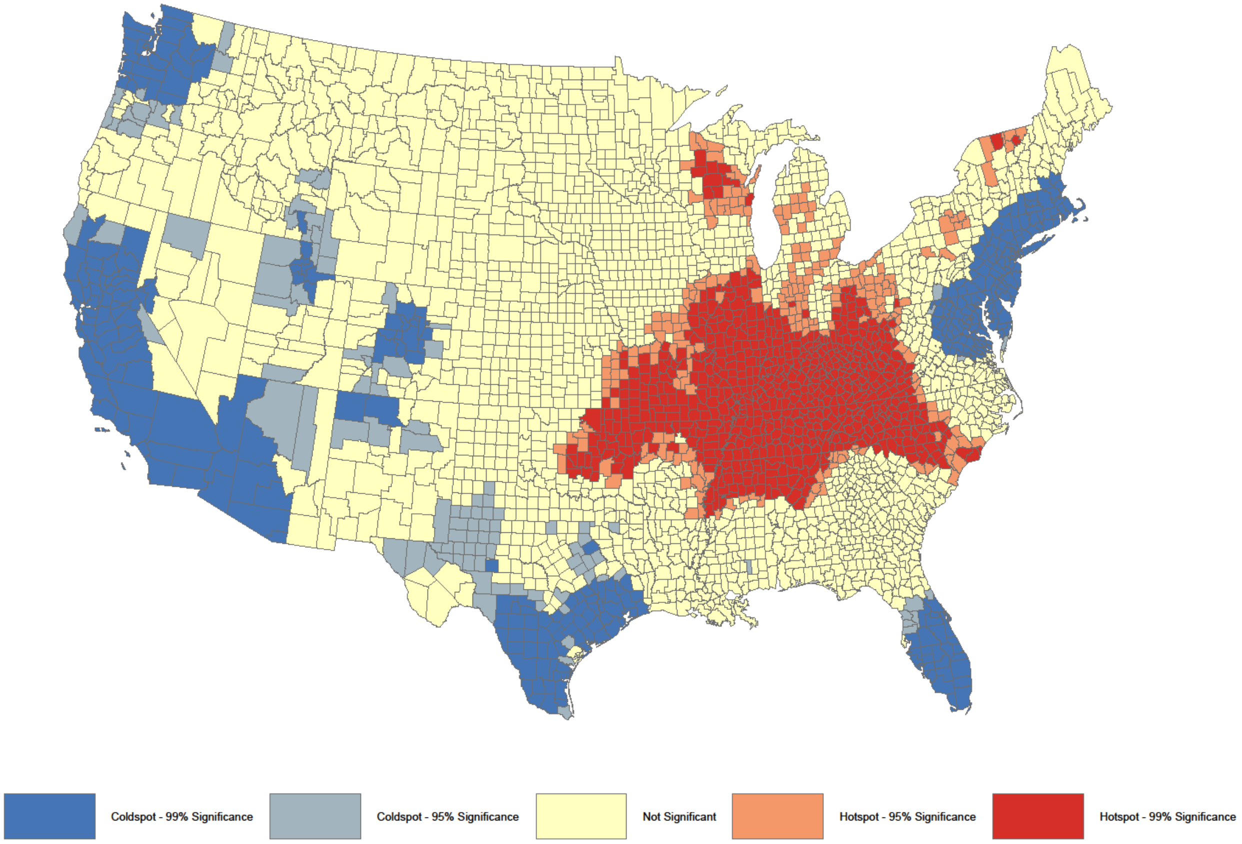


Figure 9. Trends in lung cancer mortality rates per 100,000 among women in clusters of fast decline, compared to the national average, 1969 – 2014.

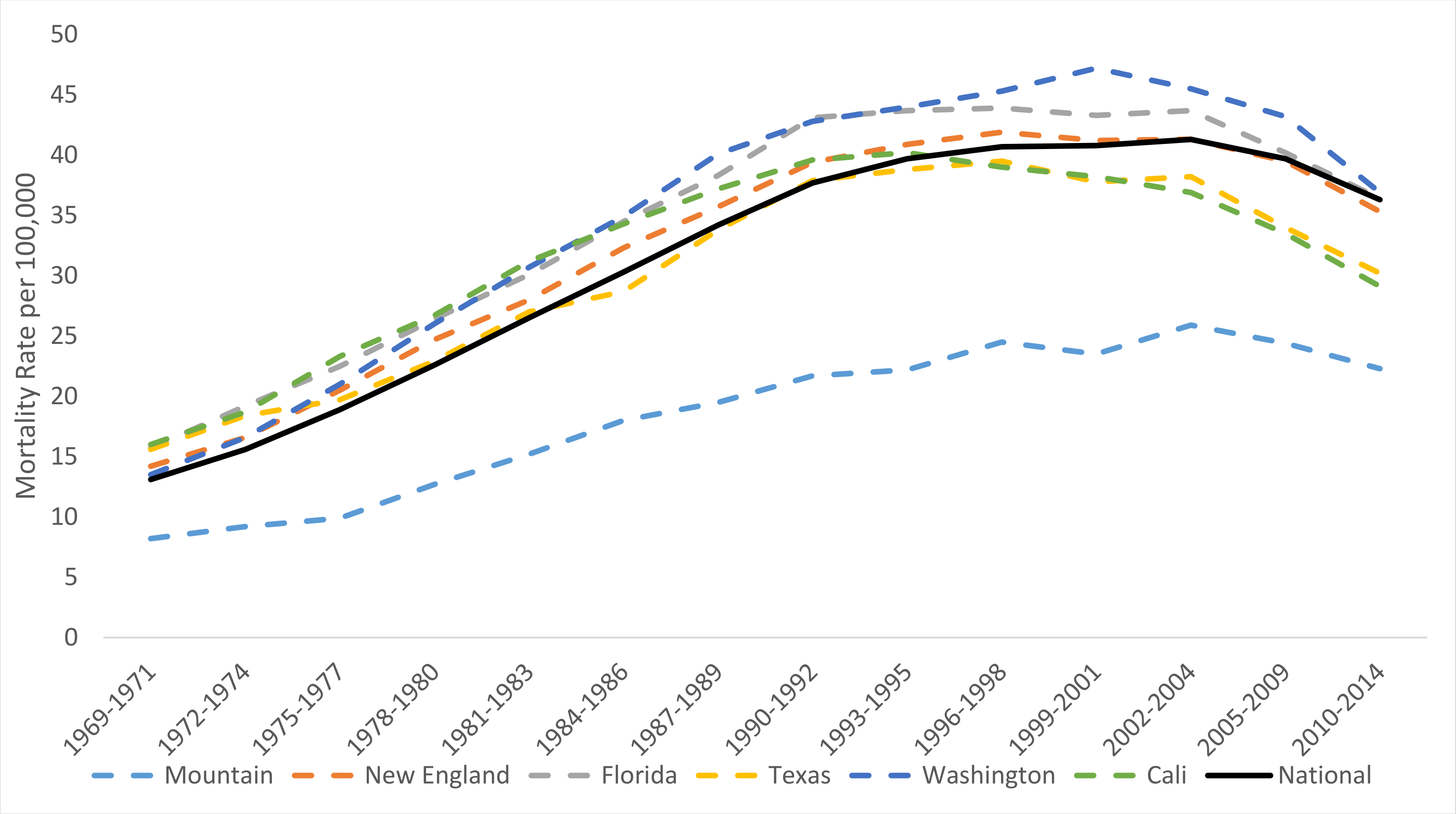


Figure 10. Trends in lung cancer mortality rates per 100,000 among women in clusters of slow decline, compared to the national average, 1969 – 2014.

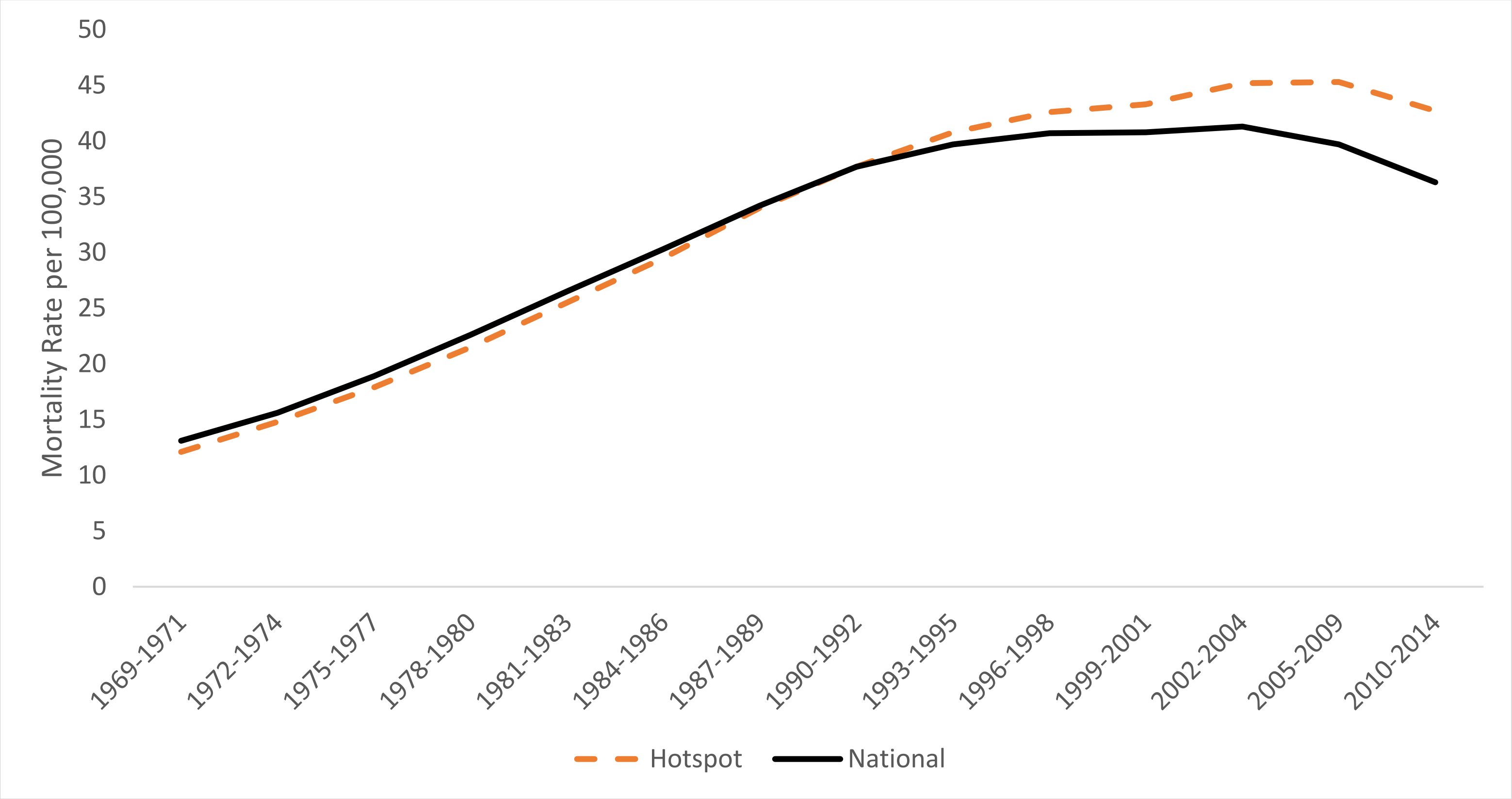


Table 1. Sociodemographic characteristics of clusters with fast and slow declines in lung cancer mortality among women from 1996 – 2004 to 2005 – 2014.

	Nation	***Hotspot***	***California***	***Seattle***	***Mountain West***	***Texas***	***Florida***	***New England***
Median age (IQR)	40.3 (37.4, 43.4)	40.2 (38.5, 42.2)	38.6 (33.6, 43.6)	40.2 (36.8, 47.3)	35.8 (31.8, 42.0)	37.0 (34.5, 40.7)	45.5 (38.6, 47.7)	40.3 (38.4, 42.6)
% women, mean (SD)	50.0 (2.2)	50.4 (1.6)	49.5 (2.2)	50.0 (0.79)	48.7 (1.8)	49.1 (3.1)	50.1 (2.7)	50.8 (1.3)
% White, mean (SD)	82.9 (16.9)	87.6 (14.3)	71.3 (14.4)	84.5 (7.1)	85.2 (14.6)	79.8 (9.0)	79.1 (8.9)	78.5 (14.7)
% Black, mean (SD)	8.9 (14.5)	7.4 (12.7)	3.2 (3.2)	1.2 (1.5)	0.9 (1.7)	6.2 (6.7)	10.7 (5.3)	12.0 (11.8)
% Hispanic, mean (SD)	8.3 (13.2)	3.1 (3.0)	27.4 (17.4)	11.8 (10.2)	16.9 (17.9)	43.3 (24.5)	18.6 (11.3)	8.2 (7.0)
% of families living in poverty, mean (SD)	11.4 (5.5)	12.8 (5.3)	10.0 (4.1)	9.7 (2.8)	8.2 (4.8)	14.5 (7.5)	10.1 (3.6)	6.7 (3.1)
% rural	21.0%	30.7%	7.4%	17.6%	16.4%	12.1%	6.9%	11.7%
% with a high school education or higher, mean (SD)	83.1 (7.4)	80.8 (7.0)	82.8 (7.6)	87.8 (5.3)	89.3 (6.6)	74.4 (9.3)	83.3 (8.1)	86.7 (4.8)
% with a college degree or higher, mean (SD)	19.0 (8.7)	16.1 (7.2)	24.0 (10.1)	24.4 (8.8)	29.1 (12.6)	16.5 (7.1)	21.5 (7.4)	29.7 (12.3)
Unemployment rate, mean (SD)	7.5 (3.4)	8.7 (2.8)	9.9 (2.5)	8.0 (2.0)	5.8 (2.0)	6.5 (3.0)	9.7 (1.8)	6.6 (1.9)

Figure 11. Relative geographic disparity in lung cancer mortality rates among women, at the county-, state-, and regional level, from 1978 – 2014.

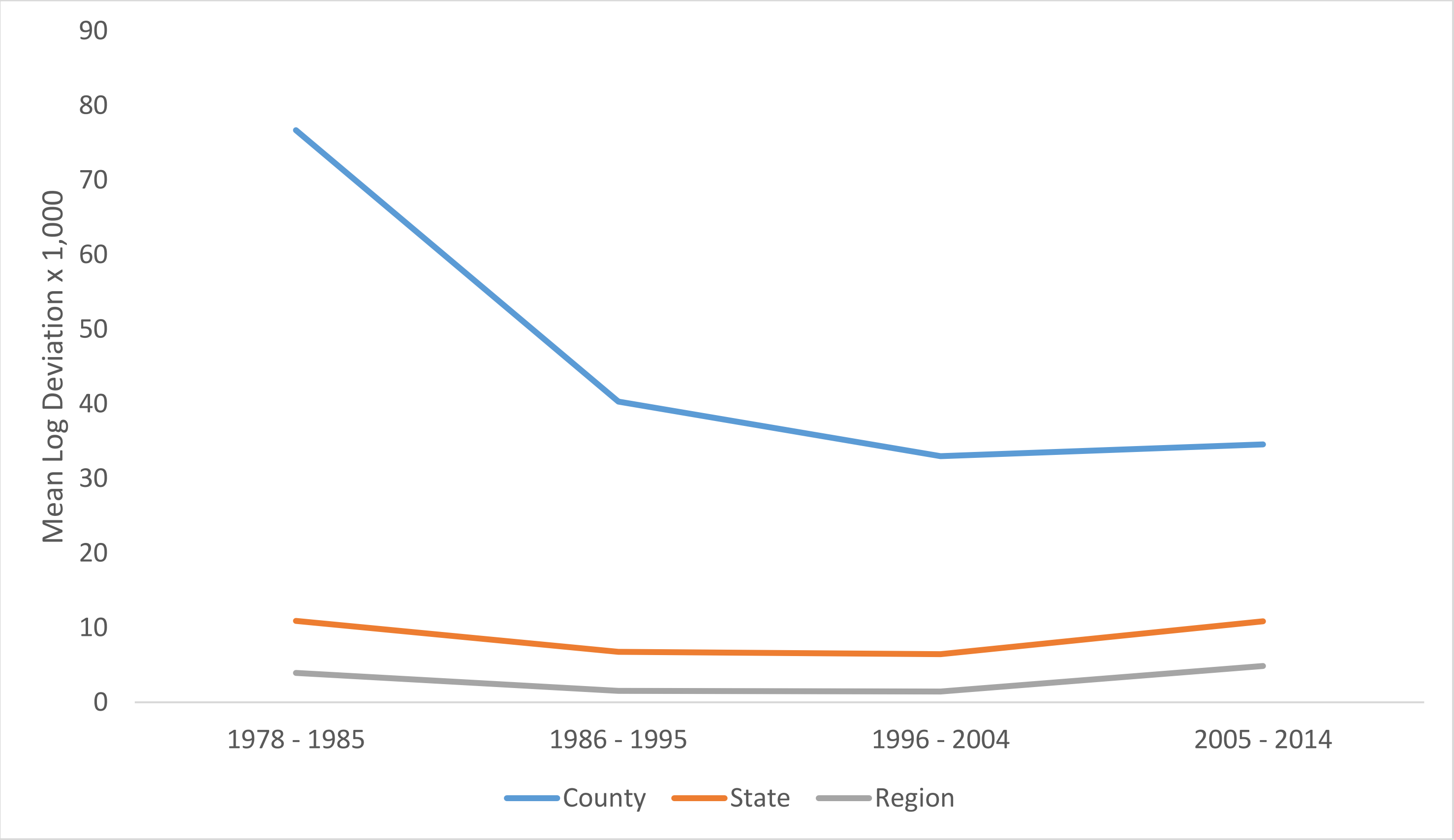


Figure 12. Absolute geographic disparity in lung cancer mortality rates among women, at the county-, state-, and regional level, from 1978 – 2014.