EXAMINING LUNG CANCER DISPARITIES AND RISK FACTORS IN WISCONSIN, USA (2016-2020)

by

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ABSTRACT

EXAMINING LUNG CANCER DISPARITIES AND RISK FACTORS IN WISCONSIN, USA (2016-2020)

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The University of Wisconsin-Milwaukee, 2024

Under the Supervision of Professor Changshan Wu

Studies over the United States has shown that disparity still exists in lung cancer mortality. Such disparity has been attributed to several risk factors such as genetics, socio-economic status, comorbidities. This study investigates the spatial variations in lung cancer mortality rates in Wisconsin, USA, through analyzing county-level data from the Center for Disease Control (CDC) and National Cancer Institute's Surveillance, Epidemiology and End Results (SEER). Emphasis is placed on exploring the relationship between access to lung cancer services, socio-economic factors, and lung cancer mortality rate, utilizing American Community Survey and County ranking data. Scan Statistics (SaTScan) was used to identify mortality clusters, while regression analysis was employed to assess relationships between socio-economic factors and lung cancer mortality rate. The results reveal potential spatial patterns, indicating disparities and risks, with high relative risk cluster predominant in the Northern counties. In addition, poverty and smoking remain the major socio-economic factors contributing to lung cancer disparities in the state. Lastly, the result of the study also suggests that there is disparity in access to lung cancer screening sites in counties across Wisconsin, with southeastern part of Wisconsin having more access than other regions.

DEDICATION

To

God Almighty

My Family,

Friends,

and especially my advisor, Prof. Wu

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ACKNOWLEDGEMENTS

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1. Introduction

1.1 Background

Cancer is one of many diseases threatening the health of the United States (U.S) population. Cancer is the second most common cause of deaths in the U.S., with 1.9 million new cases and 609,360 deaths associated with cancer in 2022 (Siegel et al., 2022). In addition to claiming lives, cancer has caused enormous economic burdens to the U.S. population. With time expenses of $4.87 billion and out-of-pocket costs of $16.22 billion, the total national patients' economic burden related to cancer care in 2019 amounted to $21.09 billion (NCI, 2021).

Lung cancer, as a major type of cancer, has a remarkably high incidence rate globally, with an estimated 965,446 new cases in males and 386,875 cases in females annually (Kamanger et al., 2006). With cumulative deaths of 1,179,074, lung cancer is undoubtedly the leading cause of cancer deaths worldwide (Kamanger et al., 2006). In Wisconsin, 2,896 lung cancer related deaths and 4,190 new lung cancer cases were reported annually between the years of 2012 to 2016 (ACS, 2020).

Cancer disparity is the difference in cancer occurrence, treatments and mortality among different population groups, race, and ethnicity (Kamanger et al., 2006). Disparities in lung cancer exist across different racial and ethnic groups, socio-economic status, and environments. Understanding the spatial patterns of lung cancer mortality will help in decision making to reduce or eliminate these disparities.

Disparity in cancer persists across different socio-economic levels, races and ethnicity or group as illustrated by Minas et al (2020), due to lifestyle, occurrence of other diseases, and healthcare disparities. Certain types of cancer are prevalent in rural communities which may be due to poverty, poor health behavior, and fewer screening centers when compared to urban areas (Henley et al., 2018), as well as limited education and literacy (Robertson et al., 2023; Jemal et al., 2008). Here, we seek to understand: Does the risk of lung cancer mortality exhibit a uniform pattern across all counties in Wisconsin? Are there significant variations in risk levels among different counties within the State of Wisconsin?

The following questions will guide this thesis research:

1. What are the spatial clusters of lung cancer mortality in Wisconsin counties from 2016 to 2020?
2. To what extent do socioeconomic variables interact to influence lung cancer mortality rates across different counties in Wisconsin?
3. What are the variations in access to lung cancer screening facilities among different counties in Wisconsin?

2. Literature review

2.1 Health Disparity

Health disparity, also known as health inequalities, is the avoidable and often unjust difference in overall health outcome among different race and ethnicity, socio-economic status, and geographic location (Wan et al., 2012). Health disparity encompasses differences in access to healthcare facilities, leading to differences in incidence, survival, post-survival trauma and mortality. To explain the principles of equity and health, health disparity was defined as an unnecessary, avoidable, and believed to be unfair differences, based primarily on the notion that ideally and more pragmatically, no one should be prevented from realizing their full health potential (Wan et al., 2012; Whitehead, 1992). With this definition as a basis, various U.S departments and agencies have incorporated factors such as socio-economic status, race and ethnicity, and geographic location to estimate health disparity.

In this study, health disparity is defined according to Braveman (2006) as the differences that occur when affluent individuals consistently have better health and more access to healthcare than disadvantaged people. We also examine disadvantaged people according to socioeconomic status (poverty, income or median house income, level of education attainment), age, geographic location (rural, urban, and segregated areas), race and ethnicity.

2.2 Cancer Disparity

Cancer disparity can be defined as the difference in cancer incidence, survival, survival trauma and mortality with respect to race and ethnicity, socioeconomic, and geographic factors. Cancer is often described as a complex disease which is associated with uncontrolled growth and spreading of abnormal cells in the body. Cancer incidence is the number of new cases occurring in a particular place within a specific period (Last J.M, 1995). Cancer incidence can be due to a number several factors such as social stress, comorbidities, genetics, and socio-economic factors (Minas et al., 2020).

Similarly, cancer mortality is influenced by the incidence of cancer, tumor types, which can be malignant or benign, and stage at diagnosis response to treatment (Kamanger et al., 2006) and comorbidities, which is the presence of other diseases occurring at the same time as cancer in a person. Disparity in lung cancer also exists, with smoking primarily a major risk factor in lung cancer. Such disparity cuts across socioeconomic and geographic factors, as illustrated in a study at Kentucky which reveals lack of basic literacy as a contributing factor to disparity among Appalachian and Non-Appalachian residents (Robertson et al., 2023).

2.3 Spatial cluster and geographic disparity in lung cancer mortality

According to Camiña et al (2022), in a study of spatial analysis of lung cancer incidence in Pennsylvania, scan statistics were used to identify five statistically significant clusters from 2010 to 2017. Areas of high clusters are associated with lowest per capita, highest percent poverty, poorest physical and mental health (Camiña et al., 2022), with African Americans as the highest percentage population in these areas of significant clusters. Most economic activity predominant in those areas of high clusters in the past includes steel manufacturing, machinery, and textile (Singh et al., 2016). Also, a report by Christian et al (2019), argued that there is a significantly higher risk for most types of lung cancer in areas of prevalent poverty, which are easily related with higher smoking rates. Hosgood et al (2013), in a similar spatial analysis of lung cancer histopathology in Maine, argued that there is a relationship between rurality and large cell lung cancer. On a global scale, cancer disparity exists in terms of cancer mortality rates, which is due to economic factors (Bray et al., 2018). Notably, lung cancer is the leading cause of cancer death worldwide, but it is under-represented in Sub-Saharan Africa, this is due to lower smoking prevalence in the region (Minas et al., 2020).

In the U.S., disparity in cancer mortality exists among different race, ethnicity, and groups (Siegel et al., 2020; Zeng et al., 2015). This is explained by issues such as access to healthcare, exposure to pathogens and carcinogens, unhealthy food diet and the kind of lifestyle one chooses to live (Nguyen et al., 2020) and genetic makeup (Flenaugh et al., 2006). There has been a considerable pattern in lung cancer mortality variation across the U.S., with north and west region having high mortality rates, while the rocky mountain states and the southern region have a much lower rate (Kerry et al., 2019).

In the State of Wisconsin, there is still a predominant disparity in cancer among different racial groups, as cancer is a leading cause of death in the state (Olson et al., 2020). Also, The American Cancer Society (ACS, 2020) data indicated that Wisconsin has an average of 32,000 residents diagnosed with cancer from 2012 to 2016 and over 11,000 deaths annually. It is important to know that Wisconsin has the second highest Black-White disparity in lung cancer mortality, with Milwaukee having the highest lung cancer disparity in Black and White racial group among all metropolitan in the U.S. (Olsen et al., 2020).

According to Singh et al (2011), rural counties have much lower cancer incidence and higher mortality rate when compared to counties that are in the metropolitan or urban counties, with an increasing death rate between the rural and urban counties (Henley et al., 2017). Studies have also argued that some types of cancer are more common in rural areas than urban areas (Henley et al., 2017; Zahnd et al., 2018). The Surveillance, Epidemiology, and End Results (SEER) database also suggests that rural patients have a higher incidence and mortality of small cell lung cancer (SCLC) cases, which is explained or associated with higher prevalence of smoking in rural areas (Atkins et al., 2017). Also, a review of the National Cancer Database (NCDB), reveals that rurality was associated with non- standard treatment or no treatment for patients with stage I Non-Small Cell Lung Cancer (NSCLC) (Ebner et al., 2020). Furthermore, an analysis of the NCDB found that rural patients within all stages of NSCLC have lower overall survival rates, when compared to patients in urban areas (Elliot et al., 2022). According to the SEER database, survival difference may be further explained by disparity in surgical care assess, as rural patients with stage I NSCLC has shorter survival compared to patients in urban areas (Atkins et al., 2017).

It is also important to draw to light another dimension of geographic disparity, which are racially segregated areas at population level (Elliot et al., 2022). In a study by SEER, it was demonstrated that lung cancer mortality was high for African Americans living in most segregated counties in the U.S., notwithstanding their socio-economic status (Hayanga et al., 2013). Nonetheless, areas with prevalent poverty rates can also be easily associated with factors like healthcare access, pattern of detrimental lifestyle behavior (Moss et al., 2020) of which according to (Matthews et al., 2017), rural areas, have a higher risk of cancer due to factors such as risky health behavior and tobacco use. In addition, residential segregation may prevent access to economic mobility and access to quality health, which may influence cancer mortality outcome (O'Keefe et al., 2015). The African American population is more adversely impacted due to high concentration within poorer and less economic viable neighborhoods than European Americans (Sharkey, 2014). Hayanga et al., (2013) posits that although there is higher lung cancer mortality among African American than European American, lung cancer mortality rates are higher in African American residing in segregated areas or neighborhoods. With 10 percent higher lung cancer mortality rate in African Americans residing in segregated areas when compared to those living in least segregated areas (O'Keefe et al 2015). Notably, Wisconsin has the second highest Black-White disparity in lung cancer mortality (Olsen et al., 2020), with a higher lung cancer mortality rate shown to be more prevalent in rural areas than urban areas.

2.4 Social-Economic Disparity in Lung Cancer Mortality

Lung cancer has a high incidence worldwide, with new cases annually estimated at 965,446 in male and 386,875 in females (Kamanger et al., 2006). Lung cancer is the leading cause of cancer death in the world with a total mortality of 1,179,074 (Kamanger et al., 2006). In the U.S., 80 to 90 percent of lung cancer is associated with smoking (CDC, 2014), with high mortality rates in lung cancer usually associated with cultural, economic, environmental and health lifestyle (Kerry et al., 2019).

In addition, ACS (2020) also illustrated that 80 percent of lung cancer as well as 80 percent of lung cancer deaths are due to smoking. In other words, it is necessary to know that people usually mimic habits and are likely to take part in unhealthy behavior, just because they assume everyone does it. (Olson et al., 2020). This was noted in an interview session with the participants in Wisconsin rural areas, as they stated that "everybody smokes, and everybody drinks" (Olson et al., 2020).

Several research findings have demonstrated a relationship between low social economic status and advanced stage of lung cancer diagnosis (Elliot et al., 2022). This may be due to factors such as low education attainment and poverty, which for this study, is what will be used as socio-economic factor. According to a study on Metropolitan Detroit Cancer Surveillance System (MDCSS) of lung cancer patients, the socio-economic status was a major independent variable predicting the stage of diagnosis for lung cancer, with high socio-economic status predicting early stage of the disease. Early detection of cancer is important as it improves the patient's chances of survival. In a study by the National Cancer Database (NCDB) to determine factors influencing treatment refusal, shows that uninsured patient, patients with comorbidities, low household income and low education attainments were likely to refuse chemotherapy (Duma et al., 2020), which is easily associated with high mortality. Also, from the SEER registry, a study argued that lack of insurance was an independent risk factor in lung cancer mortality (Cole et al., 2019). Mortality rates for lung cancer are higher in people residing in counties with persistent poverty (i.e., ≥20% of residents below the federal poverty level) compared to people living in non-persistent poverty counties (60.9 deaths/100,000 people per year vs 52.3 deaths/100,000 people per year, respectively) (Moss et al., 2020). In addition, areas that have shown prevalent poverty rates are usually identified by social, structural, and behavioral challenges, and may increase the risk of cancer for the resident (Charlton et al., 2015).

Disparity in lung cancer is particularly significant between African American and European American men with 113.9 per 100,00 and 76.7 per 100,000 respectively, displaying a 48 percent higher lung cancer incidence rate in African American men (Flenaugh et al., 2006). Similarly, European American women showed lower lung cancer incidence when compared to African American women (Flenaugh et al., 2006). This has been associated with historical intense concentration of mentholated cigarettes, which is associated with more severe levels of smoking addiction (Elliot et al., 2022). Notably, African American bears a disproportionately high burden of cancer incidence and soaring death rate from breast, gastrointestinal tract, prostate, and lung cancer compared to all other U.S. population groups (DeSantis et al., 2019). Hispanic and Asian Americans, when compared to with non-Hispanic whites, have lower lung cancer mortality (Klugman et al., 2019). Also, Hispanic patients when compared with black and white patients have an improved survival rate (Klugman et al., 2020). American Indians and Alaskan natives experience a lower survival rate when compared to European American patients (Fesinmeyer et al., 2010).

Age is one of the risk factors of cancer mortality, however, patients of younger age still get diagnosed with cancer. Patients between the age range of 66 to 69 years were 2.6 times more likely to receive treatment compared to patients that are 80 years old and above, which is usually associated with improved 3 years survival (Nadpara et al., 2015). In addition, according to SEER Medicare review of patients with small cell lung cancer (SCLC), older patients of 85 and above when compared to patients aged 65 to 69 years are less likely to receive chemotherapy (Wickham et al., 2020). This can be due to factors such as frailty, comorbidities, personal and little or no legitimate reasons to pursue cancer therapy (Elliot et al., 2022).

Gender based disparities in lung cancer has been researched and surprisingly, there are high lung cancer incidence in young female patients who are light smokers or never smoked (Elliot et al., 2022). With smoking as a major risk factor of lung cancer, 80 percent of female lung cancer is associated with smoking and 90 percent for male patient (Elliot et al., 2022). It is important to note that high lung cancer mortality has been associated with several factors like socio-economic, illiteracy, poverty, lifestyle (Minas et al., 2020) and lead poisoning (Steenland et al., 2000). Furthermore, a review of the National Inpatient Sample argued a low postoperative morbidity and mortality in female lung cancer resection than male patients (LaPar et al., 2011). Death caused by lung cancer is a big issue in Wisconsin with an average death of 1,570 for male and 1,325 for female between 2012 to 2016 according to American Cancer Society (ACS, 2020).

Several studies have elaborated and documented on the negative impact of comorbidities on several dimensions of health, including psychological, physical outcome to mortality (Lankarani and Assari 2015; Assari et al., 2013). With Islam et al (2015) demonstrating that comorbidities are associated with low lung cancer survival in lung cancer patients after sex, age, gender, race, and histologic types has been adjusted. In addition, report based on SEER Medicare argued a higher prevalence of comorbidities in lung cancer patients when compared to other cancer patients, with chronic obstructive pulmonary disease, diabetes, congestive heart failure as some of the most prevalent comorbidities with 33.6%, 14.7%and 12.4% respectively (Edwards et al., 2014). Disparity in lung cancer also exist across geographic units with rural and segregated neighborhood more likely to have high rates of lung cancer mortality rates when compared to urban areas, this may be due to accessibility to healthcare facilities.

2.5 Access to healthcare services

According to the U.S. Department of Health (2000), access to healthcare services is the ability of people to get easy and readily available healthcare services that can bring them general and preeminent health outcomes. Access to health has been classified into potential and realized access (Joseph and Phillips, 1984). Potential access to health services entails easily accessible healthcare facilities, but does not necessarily assure utilization, while realized access incorporates potential access as well as actual utilization of these services (Wan et al., 2012). Correspondingly, based on some factors that influence accessibility, access to healthcare can be subdivided in spatial access which includes (travel time, distance, and spatial location) and non-spatial access (socio-economic factors) (Aday and Andersen, 1974).

Access to lung cancer screening services has the potential to influence lung cancer outcomes in several ways. This can be done through prevention of late diagnosis, as early diagnosis is a key factor to improve survival rates, and late diagnosis has shown little or no chances of survival. Similarly, access to these treatment services has a high propensity to guarantee a high likelihood of survival if socio-economic factors are at check. Sahar et al., (2020) acknowledged the existence of low utilization of lung cancer services within a U.S. population. The study found lack of access within 40 miles to lung cancer services for people aged 55 to 79, which may be stressful for this population age group.

3. Materials and methods

3.1 Study area

This study focuses on the state of Wisconsin, located in the Midwest region of the U.S. of America. Wisconsin is 54,153.1 square miles on land and 11,326.9 square miles on water, with Madison as the capital. By area, it is the twenty-fifth largest state in the U.S., with 72 counties and bordered by Illinois, Michigan, Iowa, and Minnesota.

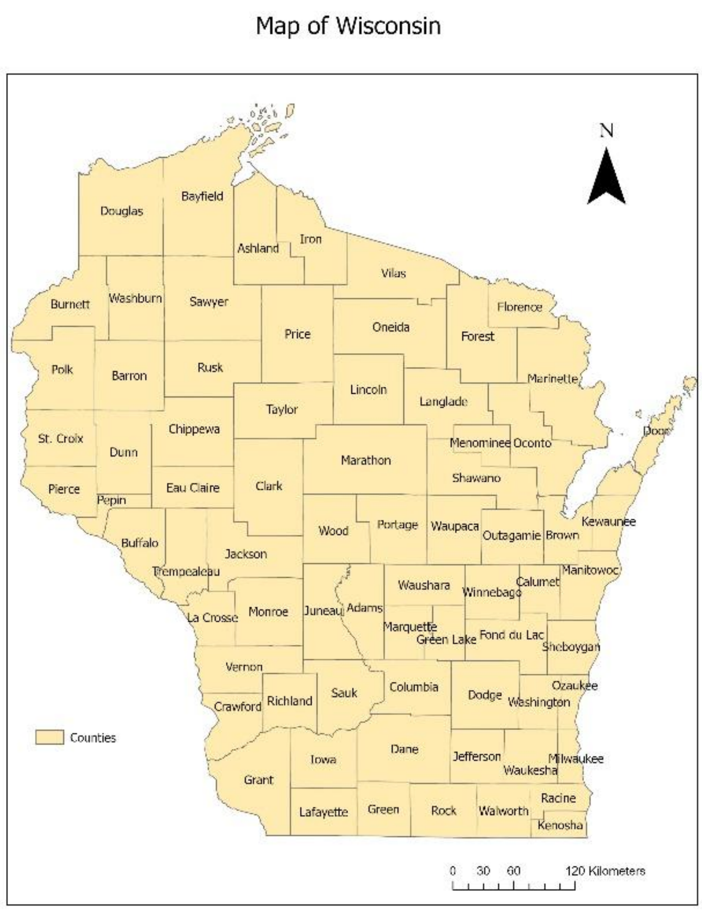


Fig 1. Study area (Wisconsin, U.S.A. with 72 counties).

The total population of Wisconsin is 5,893,718, were White Americans accounts for 4,737,545, also 376,256 were Black or African Americans, Asian Americans accounts for 175,702, while 60,426 are American Indian and Alaska Native, Native Hawaiian and Other Pacific Islander accounts for 2,199 persons (ACS, 2020).

3.2 Data Source

For this study, lung cancer mortality county level data from the U.S. Center for Disease Control (CDC) and, the National Cancer Institute's (NCI) Surveillance, Epidemiology and End Results (SEER), which is age-adjusted according to the 2000 U.S standard million population were used. Also, county level social economic data of Wisconsin counties were gathered from the American Community Survey, and County Data Ranking. For lung cancer screening services, the dataset was from testing sites enlisted by the American College of Radiology (ACR).

3.3 Methods

3.3.1 Cluster Analysis

Scan statistics were used to explore and analyze the spatial cluster of lung cancer mortality. The scan statistics (SaTScan) software was developed jointly by Martin Kulldorff, the National Cancer Institute, and Farzad Mostashari of the New York City Department of Health and Mental Hygiene (Christian et al., 2019). The scan statistics have been used to study the spatiotemporal pattern of different types of cancer (Kulldorff et al., 1997; Amin and Burns, 2014), dengue disease (Abd Naeeim et al., 2021), disease outbreak (Neill, 2009) and clustering for Covid-19 (Zhao et al., 2022). Hence, in this research, scan statistics were used to investigate significant clusters in lung cancer mortality across Wisconsin counties. Scan statistics provides a better cluster compared to other process like Local Moran's I, as Local Moran's I has multiple testing issues. Scan statistics account for correction for differences in population density and possible confounding factors (Kulldorff et al., 1997). Also, by not determining the size or placement of the window size before analysis, thereby preventing preselection bias; In addition to that is that it also considers numerous tests and provides a single p-value indicating whether the null hypothesis should be accepted or rejected (Kulldorff et al., 1997).

Scan statistics (SaTScan) version 10.1 were used to analyze the existence of spatial clusters of significant high and low lung cancer mortality risk across counties in Wisconsin. Spatially, scan statistics compare the rate of an event within many candidate clusters, this is determined by drawing concentric ring of circles around a specified set of event locations (aggregating events) or regular grid points, to the corresponding rate outside each candidate cluster (Kulldorff et al., 1997). This expands continually until it reaches the maximum spatial cluster size specified. Here, the default 10% maximum spatial cluster size threshold was used for the study time frame (2016 to 2020), this represents the maximum cluster size of the population at risk.

The alternative hypothesis is that there is a higher risk inside the scanning window than there is outside, for any location and size of the window (Kulldorf et al., 1997). According to Poisson assumption, the likelihood ratio for a given window is illustrated using the formular:

$$\text{LR} = \left(\frac{c}{E[c]}\right)^{c}\left(\frac{C-c}{C-E[c]}\right)^{C-c} I()$$ (1)

where C is the total number of cases, c is the number of cases that were observed to be inside the window, and E[c] is the number of cases that were predicted to be within the window under the null hypothesis after covariate adjustment (Kulldorff et al., 1997). Nonetheless, C-E[c] represents the anticipated number of cases beyond the window because the analysis is dependent on the overall number of cases observed (Kulldorff et al., 1997). The function *I ()* is an indicator. If SaTScan is configured to search just for high-rate clusters, then *I ()* equal 1 if the window contains more cases than expected under the null hypothesis, and 0 in all other situations (Kulldorff et al., 1997). If SaTScan is configured to look solely for low-rate clusters, the opposite situation occurs. When the program scans for clusters with either high or low rates, then *I ()* = 1 for all windows. The most likely cluster is the cylinder with the highest logarithm of LR (LLR) (Kulldorff et al., 1997).

The Monte Carlo stimulation was used to generate statistically significant clusters at 0.05 level, this was done through 999 replications. For the relative risk (RR) which is the estimated risk within the cluster divided by the estimated risk outside the cluster (Kulldorff et al., 1997). It is calculated as the observed divided by the expected within the cluster divided by the observed divided by the expected outside the cluster. In mathematical notation, it is:

$$RR = \frac{c / E[c]}{(C-c)/(E[C]-E[c])} = \frac{c / E[c]}{(C-c)/(C-E[c])}$$ (2)

where c is the number of observed cases within the cluster and C is the total number of cases in the data set. Note that since the analysis is conditioned on the total number of cases observed, E[C] = C (Kulldorff et al., 1997). Once the output is generated as a dbase file, using the ArcGIS Pro 3.1.2, it was spatially joined with the Wisconsin county shapefile, which was then used to visualize the map of the detected clusters.

3.3.2 Regression Analysis

Robertson et al (2023) in their study of lung cancer used regression analysis to evaluate the relation between lung cancer mortality and education attainment using aggregated data from 2014 to 2018. This forms a basis for my study, as I built on it using up to date CDC data, and addition of other variables.

Table 1: Explanation of multiple regression variables.

Variables	Meaning
Lung cancer mortality rate (Dependent variable)	Rate of death per 100,000 people, age-adjusted to the 2000 U.S. standard population.
Poverty	Percentage of population for whom poverty status is determined: Income in the past 12 months below poverty level.
Smokers	Percentage of adults aged 18 years or older, who reported they ever smoked 100 cigarettes.

Less than High School	Percentage of population aged 25 years and above with less than high school education.
White American	Percentage of White population alone.
Black or African American	Percentage of Black or African American population alone.
American Indian or Alaska Native	Percentage of American Indian or Alaska Native population alone.
Asian American	Percentage of Asian population alone.
Hispanic or Latinos	Percentage of Hispanic or Latinos population alone.
Diabetes	Percentage of adults aged 20+ Years diagnosed with diabetes.

For regression analysis, multiple linear regression was employed using R programming to estimate the relationship between the dependent variable which is the aggregated lung cancer death rate for the study period and independent variables. For the independent variables, we considered socio-economic, race and ethnicity, comorbidities, and behavioral factors. Also, for the socio-economic variables, poverty, and percentage of the population with less than high school education was used as the variable. In addition to that, for behavioral factor, resident adults aged 18 years or older, who reported they ever smoked 100 cigarettes. In addition, for comorbidities, diabetes was used as a variable for the study. For race and ethnicity, White Americans, Black Americans, Asian American, American Indians and Hispanic or Latino ethnic groups were utilized for this study.

3.3.3 Access to healthcare services

With early diagnosis as a major factor in higher rate of cancer survival in most cancer types across different population groups and geographic regions, equal access to medical services becomes very crucial for lung cancer prevention, treatment, and survival (Wan et al., 2012). This is because low access to medical services will lead to poor treatment quality, lower chances, and high death rate. In other words, ensuring access to equal and high-quality health among all races and ethnicities, socio-economic and geographic areas will adversely reduce disparity. Wan et al (2012) argued that medical services accessibility is impacted by spatial and nonspatial factors. Also, potential spatial accessibility to medical services is crucial for improving health and eliminating health disparities as it forms the basis for the use of these medical services (Wan et al 2012).

Lung cancer screening sites addresses from the American College of Radiology was geocoded using ArcGIS Pro 3.3 and was overlayed on the state county map. To calculate travel time in minutes, the Service Area Network in ArcGIS Pro was employed.

4. Results

4.1 Spatial Cluster of Lung Cancer Mortality in Wisconsin from 2016 to 2020.

Using the scan statistics in the analysis of lung cancer mortality, all statistically significant spatial clusters of lung cancer mortality rate were identified. The top five (5) clusters were detected and shown in Table 2 and the cluster map depicted in fig 2. Map of the cluster relative risk was also visualized fig 3. Here, the most likely cluster was a low-risk cluster located in Dane county. Dane county when compared to other county in the state had a 41% lower risk of mortality from lung cancer (RR 0.59, LLR 95.3) with statistical significance ($p<0.001$). The remaining clusters ranked by their LLR were in Northern counties of Wisconsin with a higher risk cluster. The counties here include Douglas, Bayfield, Burnette, Washburn, Sawyer, Polk, Barron, Chippewa, Rusk, Taylor, Price, Lincoln, Oneida, Villas, Iron, and Forest. Similarly, clusters of higher risk were observed in central Wisconsin, which consists of counties like Jackson, Wood, Monroe, Vernon, Richland, Sauk, Juneau, Adam, Waushara, and Marquette. Lower risk clusters were also identified in some counties like Outagamie, Brown, and some parts of Calumet. Lastly, higher risk cluster was also identified in counties like Marinette, Menominee, and Oconto.

Map of lung cancer mortality cluster

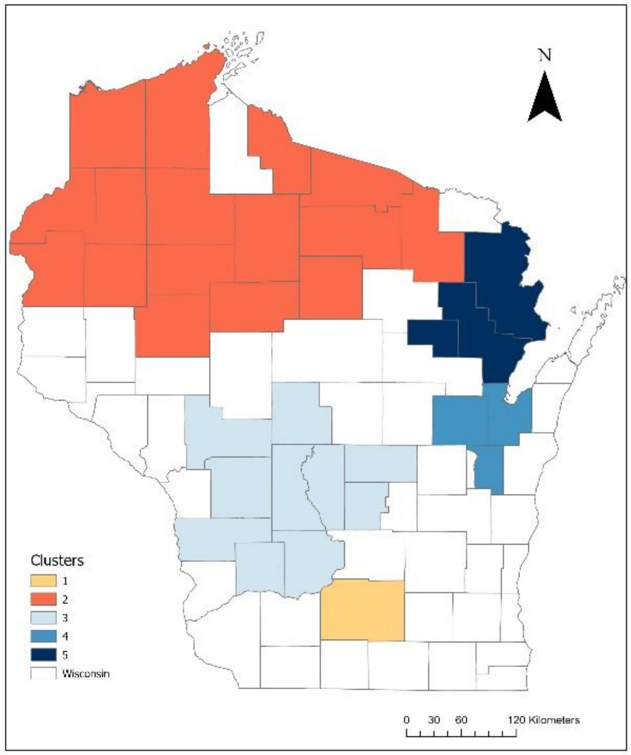


Fig. 2. Map of Wisconsin showing lung cancer mortality clusters, 2016 to 2020.

Table 2. Spatial cluster of lung cancer mortality.

Clusters	Approximate Locations	Observed deaths (Number of cases in each cluster)	Expected death	Relative risk (RR)	Likelihood Ratio (LLR)	P-value
(Most likely cluster) Cluster 1	Dane County	783	1271	0.59	95.3	<0.001
Cluster 2	Douglas, Bayfield, Burnette, Washburn, Sawyer, Polk, Barron, Chippewa, Rusk,	1457	1046	1.44	72.1	<0.001

	Taylor, Price, Lincoln, Oneida, Villas, Iron, and Forest					
Cluster 3	Jackson, Wood, Monroe, Vernon, Richland, Sauk, Juneau, Adam, Waushara, and Marquette	968	681	1.45	48.9	<0.001
Cluster 4	Outagamie, Brown, and Calumet.	835	1053	0.78	25.6	<0.001
Cluster 5	Marinette, Menominee, and Oconto.	269	183	1.48	25.6	<0.001

Cluster relative risk of lung cancer mortality

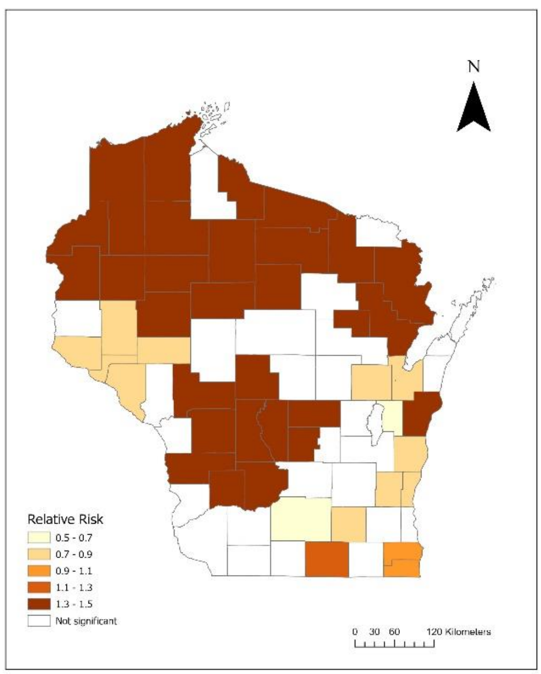


Fig 3. Map of cluster relative risk of lung cancer mortality in Wisconsin, 2016 to 2020.

4.2 Statistical Analysis of Socio-Economic Impact of Lung Cancer Mortality in Wisconsin.

During the study period, age-adjusted lung cancer mortality rates were high in Wisconsin when compared to most states and the U.S. national rate with 35.6 deaths per 100,000.

Table 3. Regression between lung cancer mortality and socio-economic factors.

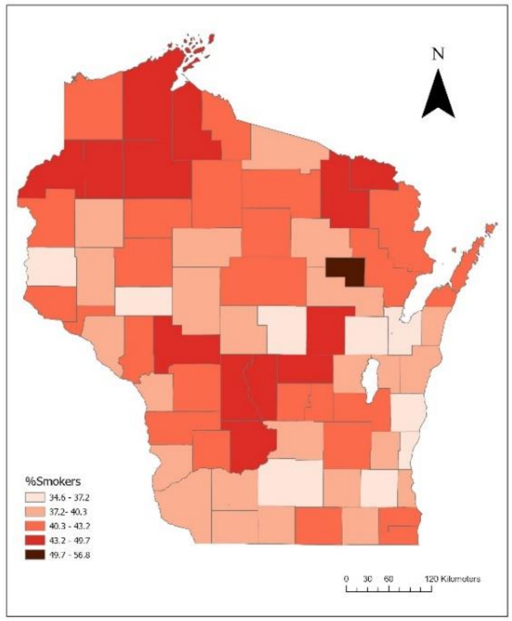
Coefficient	Estimate	Std. Error	t value	Pr(>|t|)
(Intercept)	87.0821	97.1486	0.896	0.3735
Poverty	0.8108	0.4079	1.988	0.0513*
Smokers	0.7737	0.3391	2.281	0.0260*
Less than High School	-0.4185	0.4364	-0.959	0.3413
White American	-0.9672	0.9314	-1.039	0.3031
Black or African American	-1.0595	1.0115	-1.047	0.2990
American Indian and Alaska Native	-1.8528	0.9140	-2.027	0.0470*
Asia	-2.3101	1.3269	-1.741	0.0866.
Hispanic or Latino	-0.1838	0.6190	-0.297	0.7676
Diabetes	1.3625	0.9955	1.369	0.1761

(Significant levels: '**' 0.01 '*' 0.05 '.' 0.1. Multiple R-squared: 0.5037, Adjusted R-squared: 0.43 17).

In addition to geographic disparity analysis, lung cancer mortality risk factors were identified through the multivariate regression analysis and the results are shown in Table 5.

Results suggest that several risk factors significantly contribute to the lung cancer mortality, including population with poverty, smoking, American Indian and Alaska Native, and Asian population. For poverty, significant correlation was observed for lung cancer mortality (*p =0.05.*). The coefficient suggests that a one percent point increase in the percentage of poverty is associated with an increase in lung cancer mortality, when other values are held constant. Similarly, the coefficient of smoking indicated that a one percent point increase in the percentage of smoking is associated with an increase in lung cancer mortality by 0.7737, when other values are held constant. For American Indian and Alaska Native, as well as Asian population, the result suggests a negative estimate. This may be influenced small sample representation of American Indian and Asian population-thus the result may not be generalizable. For Diabetes, the result illustrated that an increase in the percentage of diabetes is associated with an increase in lung cancer mortality rate by 1.3625, when other values are held constant, but it is not statistically significant. Less than high school education was also statistically not significant (*p= 0.34).* To give a visual perspective, a map of percentage smokers and poverty was also depicted in fig 4.

Map of Wisconsin showing percentage of smokers



Map of Wisconsin showing percentage of poverty

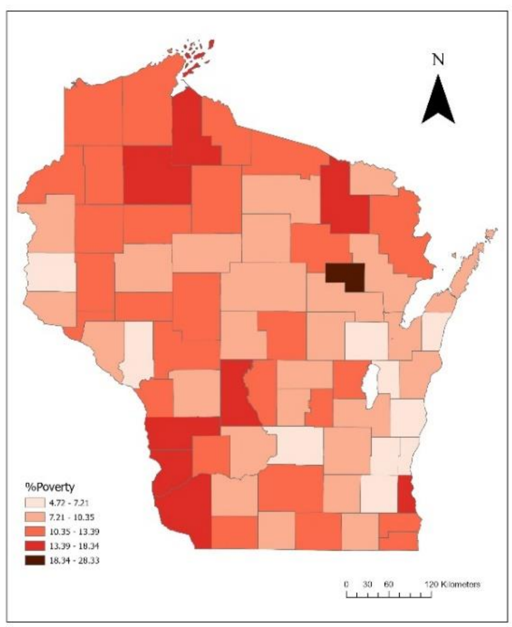


Fig 4. Maps showing percentages of smokers (a) and with poverty (b) for each county in Wisconsin, U.S.A.

4.3 Analysis of Spatial Access to Lung Cancer Services in Wisconsin.

The geographic patterns of spatial access to lung cancer screening services in Wisconsin are shown in Figure 5 and 6. In general, urban counties and areas has a high cluster of lung cancer screening services and high access to primary care physicians (PCPs) when compared to rural areas. Access to PCPs as observed, was low in most parts of the state except some counties which are mostly urban.

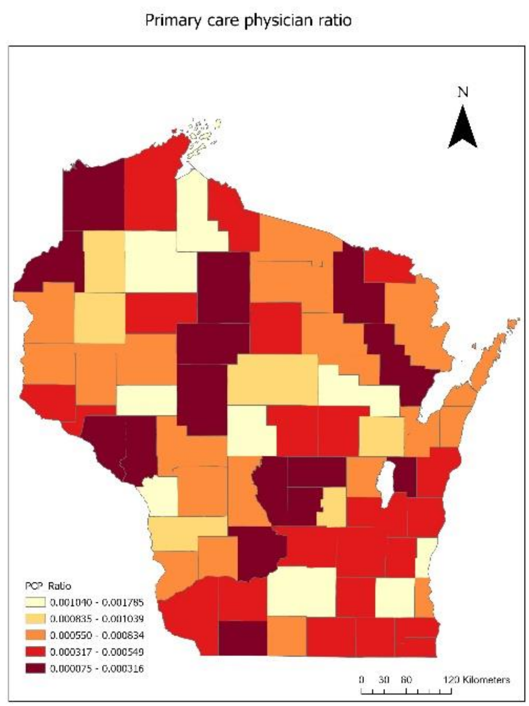
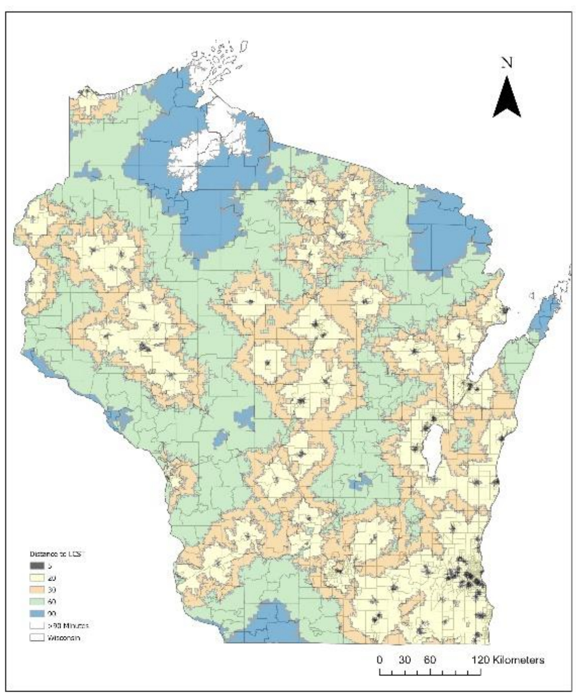


Fig. 5. A Map showing primary care physician access ratio in Wisconsin.

Similarly, spatial access to lung cancer screening services is also more readily available in the Southeastern part of the state. Distance to these services was more than 30 minutes in most regions of the state, with some parts of the Northern region, which a mostly rural areas having a travel time of over 60 minutes to these services. The Southeast region, which is predominantly an urban area, has the best access to lung cancer screening services with at most 30 minutes travel time to these services. This is evident as the region has a high cluster of these services, more than any other part of the State. The travel time of (5, 20, 30, 60, 90 and >90) minutes were arbitrary for the service area analysis.

In general, urban areas have a higher cluster of lung cancer screening services and greater access to PCPs than in rural areas. Access to PCPs as observed, was low in most parts of the state, except some counties which are mostly urban. The map below shows the geographic patterns of spatial access to lung cancer screening services in Wisconsin. In addition, Kernel density was used to show the concentration of these facilities with majority of the facilities situated in the Southeast region of the state.

Spatial access to lung cancer screening services



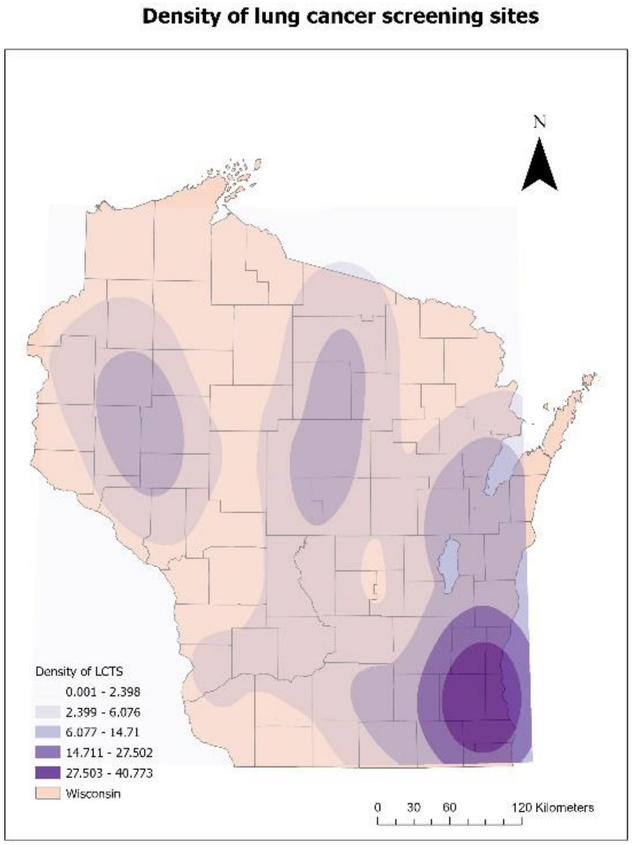


Fig. 6. Map of spatial access to lung cancer screening services (in minutes) and Kernel Density map of lung cancer screening sites.

5. Discussion

The evidence for spatial clusters in lung cancer mortality from the period of 2016 to 2020 has been depicted in this study. This has shown disparity in lung cancer mortality rate across different counties of Wisconsin spatially. The examination of geographical variation in lung cancer mortality rate is crucial as it facilitates the identification of significant high and low clusters. The result in this study suggests that socio-economic factors play a crucial role in the underlying patterns of cluster across the counties. High socio-economic deprivation in some parts of Northern Wisconsin might account for high mortality rates in this area. Research collaborations across several fields of studies, including genetics, epidemiology, public health, and social sciences, are needed to completely explain the reasons behind the clustering patterns.

Exposure to unhealthy behavior such as smoking has also led to lung cancer mortality across population groups in the state. In addition, persistent high-risk clusters of lung cancer mortality in the Northern region of Wisconsin suggests that there are other factors which may contribute to such consistency. With the understanding of lung cancer multifactorial etiology, clusters may be due to genetic, lifestyle, environment, or interplay of all (Wan et al., 2012). Also, local population unhealthy habits such as tobacco smoking can also explain a high-risk cluster pattern. This can influence incidence and survival in lung cancer which might impact mortality risk as well. It is crucial to distinguish lung cancer incident risk from mortality risk. Prevailing factors that over time consistently lead to high incident risk and short survival among the population may partially impact mortality risk (Xu et al., 2018).

Moreover, to understand the role of socio-economic, statistical analysis was used to evaluate for significance. From our study, socio-economic factors like poverty were significant as poverty level impact lung cancer incidence, survival, and mortality rates. Education attainment as a risk factor of lung cancer mortality was not significant, this is also in corroboration with Robertson et al (2023), which illustrated significant spatial autocorrelation between the population who did not complete high school and lung cancer incidence but not mortality in Kentucky.

Additionally, unhealthy behavior like tobacco smoking was also significant. Smoking is a major risk factor in lung cancer incidence and is also a risk factor in lung cancer mortality. Moreover, access to healthcare facility like lung cancer screening centers also illustrated that there is a difference in spatial access to lung cancer screening services for people living in urban and rural Wisconsin, as it suggests that rural Wisconsin population has low access to these services. This is also witnessed in previous studies that illustrate geographical disparities between urban and rural dwellers (Wan et al., 2012). It is obvious that although disparity exists among different socio-economic, racial, and ethnic backgrounds, this is minor compared to rural urban disparity in lung cancer screening services.

Moreover, when compared to other parts of the state, the Southeast region had the highest availability in terms of PCPs ratio. This suggests that compared to their counterparts in other locations, the people living in this region have better access to primary care services. Comparable differences were observed between different parts of the state, in the investigation of spatial availability to lung cancer screening services. Most regions reported considerable travel times longer than thirty minutes to obtain these services, with rural northern region having very lengthy trip times longer than sixty minutes. The Southeast region, on the other hand, was distinguished by its remarkable accessibility, with travel times to lung cancer screening services regularly falling within 30 minutes. This was reinforced by the region's large concentration of these services, which further highlighted its fortunate position in terms of access to healthcare.

When comparing to white and African Americans on access to lung cancer screening services, African Americans by the predisposition of choice of geographic living space, have more access to these services, as most African American population in the state of Wisconsin lives in urban areas, unlike white Americans who also lives in the urban areas but have a much higher population of rural dwellers when compared to African American. Nevertheless, access to screening services does not usually suggest utilization as African American has lower median household income when compared to white American. Similarly, Hispanic share similar urban dwelling tendency with African American and as well are likely to have access to these services. Also, accessibility of primary care physicians and distance to screening services may also influence utilization. Notably, since white American has the highest population concentration in most Northern Wisconsin counties, they may also suffer more from the impact of distance to lung cancer screening services and PCPs. This may suggest government and relevant agencies intervention to eliminate unequal access to lung cancer screening services in rural and urban areas across counties in the state of Wisconsin.

6. Conclusions

This study explored lung cancer mortality clusters across all the counties in the state of Wisconsin, and to my knowledge, it is the first study to use space-time statistics to identify such clusters in the state. High cluster relative risk was identified mostly in the Northern counties in Wisconsin with counties like Douglas, Burnett, Sawyer, Bayfield. Lower relative risk was also observed in Dane county which is in southern counties in the State. In addition, medical facilities should also be evaluated, and adequate allocation of resources ensured, especially in areas with high-risk clusters.

In addition, the impact of socio-economic status and smoking to lung cancer survival cannot be overemphasized, a robust health insurance policy is needed as that will help in lung cancer service utilization which will improve survival and certainly reduce mortality. Similarly, continual discouragement of unhealthy behavior such as smoking should be ensured.

As observed, there are differences in access to lung cancer screening sites and PCPs across Wisconsin. Additionally, there is still disparity in travel time to facility across counties of the state. Awareness and intervention programs should be employed in disparate areas and affected communities which are rural areas. Also, studies like this should be done on a regular basis to ensure consistent monitoring of communities by exposing and identifying changes in accessibility as they occur over time, thereby addressing gaps. Also, relevant agencies should engage in awareness campaigns to build trust and encourage utilization of screening facilities, while ensuring additional facilities are strategically located to minimize travel time and stress for disparate communities.

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