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Lung Cancer Mortality Among Women in Xuan Wei, China: A Comparison of Spatial Clustering Detection Methods

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Abstract

The identification of spatial clusters of lung cancer mortality can be a useful instrument in detecting locations with high risk of this disease. This study compared 2 methods for identifying spatial clusters of village-level women lung cancer mortality rates in Xuan Wei. One used a local indicator of spatial association to detect which groups of neighboring villages had lung cancer mortality rates that were significantly related to each other. The other was a spatial scan technique that calculated a maximum likelihood ratio of lung cancer deaths relative to the underlying population in order to identify the group of villages with relatively higher risk. As each technique based its cluster detection process on its own criteria, different clusters of villages were identified. However, the overlapping indicated that the 2 methods illustrated different components of the same clusters. These spatial analytic techniques were complementary to each other and can be used jointly rather than separately.

Keywords

lung cancer, mortality, women, geographic distribution, spatial scan analysis

Introduction

Lung cancer is the most common cause of cancer-related death in men and women in the world.[1] In 2008, the most recent year for which data were available, there were about 1.6 million new lung cancer cases and 1.4 million lung cancer deaths.[2] Lung cancer accounted for 12.7% of the total cases of cancer and 18.2% of the cancer deaths.[3] Lung cancer is a highly lethal disease, with similar incidence and mortality rates. Most patients who develop lung cancer die of it; and

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the 5-year survival rate remains less than 10% in most parts of the world.[4] Worldwide, the incidence and mortality of lung cancer is markedly higher among men than women, but the difference between the genders is less pronounced in developed nations.[5]

Lung cancer among women (usually nonsmokers) has progressed from being a rare disease in the early 1900s to become one of the most common cancers worldwide today.[6] Since China's first mortality survey in 1973-1975, which, for the first time, found that Xuan Wei County in Yunnan Province had the highest female lung cancer mortality, Xuan Wei County has been a lung cancer epidemiology study focus during the past 3 decades,[7-10] and a large-scale primary intervention, stove improvement, has been implemented in this area to reduce the indoor air pollution, which has been linked to the high lung cancer risk.[11] According to the most recent mortality survey in 2004-2005, however, lung cancer mortality rate was still very high in Xuan Wei (91 per 100 000, compared with China's average of 31 per 100 000),[12] and large geographical variation has been observed. However, there have been very few studies that assessed the geographical distribution pattern of lung cancer mortality among women in this area.[9] This is despite the fact that information on geographical distribution patterns is critical in identifying areas with unusually high rates, generating disease etiology hypothesis, and evaluating the effectiveness of intervention measurements.[13] Identification of spatial distribution patterns of the female lung cancer mortality rate is also important in guiding decisions on allocation of health resources for the disease control purpose.[14]

The increasing availability of geographically indexed health and population data and advances in computing, geographical information systems, and statistical methodology have enabled the realistic investigation of spatial variation in disease risk in recent decades. Spatial analysis is concerned both with describing and understanding such variations. In general, spatial analysis has been found to be useful in many areas of epidemiology.[15] Spatial patterns provide important insights into the role of environmental, social, and economic influences on morbidity and mortality. These exploratory spatial analyses can assist in identifying the etiological factors of specific diseases.[16]

The current study used 2 methods to detect statistically significant spatial clusters of female lung cancer mortality in Xuan Wei County at a village level: local indicators of spatial association (LISA), proposed by Luc Anselin,[17] and Martin Kulldorff's[18] spatial scan statistic, which uses a moving window with varying location and radius and a likelihood ratio calculation. Local measures of spatial association provide a measure of association for each unit and help identify the type of spatial correlation. Anselin's[17] Local Moran's Index was used as an indicator of local spatial association, which has been widely used in the epidemiological setting, such as infectious diseases, social behaviors, health service, and cancer mortality, and so on.[19] For example, Jacquez and Greiling[20] have conducted an analysis on the usefulness of LISA when exploring lung cancer mortality patterns in Long Island, New York. Kulldorff's[18] spatial scan statistic, gaining increasing attention in recent years, has been widely used to identify localized hot/cool spots of excess events, especially on study of cancers.[21] However, the differences between the 2 methods and the spatial distribution patterns for a particular study detected by these 2 methods have not been explored and need to be fully understood. This study compared these methods using the village-level female lung cancer mortality rate in Xuan Wei County. We examined and compared the clusters identified as significant by the 2 methods, and we explore the reasons for similarities and differences.

Materials and Methods

Materials

Xuan Wei County is located in northeastern Yunnan Province. It is 102 km from east to west and 91 km from north to south; its total area is 6257 km^2. Its population was about 1.2 million according to the fourth national population census. There are 342 administrative villages in Xuan Wei County, on which both the mortality data and geography data are based. Geographic map delineating the location and boundary of each village were extracted from the standard Xuan Wei Tourism and Transportation Map from Yunnan Provincial Cartographic Institute in a scale of 1:220 000.

The lung cancer mortality data used in the current study were extracted from China's second mortality survey during 1990-1992, where Xuan Wei County was selected as a site. The protocol of the survey has been described in detail previously.[22] In brief, the survey was organized by the National Office for Cancer Prevention and Control in Beijing. A standardized death certificate card and instructions were issued; all the 342 villages under the Xuan Wei County were asked to collect the information as to the deaths occurring in each village in the corresponding years. The death certificate card included information on name, sex, date of birth, residential address, occupation, cause of death, date and basis of death cause diagnosis, and so on. Based on this information, the health department staff could determine whether a case had already been reported and thus avoid duplication and reporting errors. Households were also visited and information on cause of death collected by interviews with relatives; local village doctors and neighborhood representatives were also interviewed to further verify each deceased person for possible misreporting and discover deaths not captured at death registration offices. When clinical records were missing or not available, possible diagnoses were solicited from the medical professionals who had once treated the patient. All identified information was also checked with the records from the local civil administration bureau. The village data were reported to the health department of the corresponding township, which was responsible to check the data quality of the village data; if any question was found, the village report would be sent back and get corrected and then resent to the township; finally the township data were reported to the county.

The age-specific population for each village of Xuan Wei County was obtained from the fourth census data in 1990.

The data were age-adjusted mortality rates averaged over 3 years and presented as a single rate per village. To calculate age-adjusted lung cancer mortality rates, the sex-specific lung cancer deaths in each village were standardized using the Chinese population profile in 2000 as a reference age distribution to better illustrate the influence of factors other than age.

Throughout the mortality survey periods, lung cancer was defined as code 162 using the International Classification of Diseases, 9th revision.

Methods

Local indicators of spatial association. The LISA was calculated using GeoDa 0.9.5-i in combination with an ArcGIS 9.0 (Environmental Systems Research Institute, Inc., Redlands, California) polygon shape file of Xuan Wei County. The Local Moran's I is a correlation-type index based on continuous data values; the index's scale does not have an interpretation corresponding to conventional correlation coefficients that take values in the range (−1, 1). The numeric scale of Moran's I is related to its expected value, $E(I)$, under a random spatial distribution assumption. Values less than $E(I)$ are typically associated with a uniform/dispersed pattern, and values greater than $E(I)$ typically indicate a clustered pattern. The criterion of contiguity used for calculating the spatial weights matrix was centroid distance. To create the weight matrix, a contiguity weights file using the queens convention was created from the shape file. The queens convention dictates that villages sharing a common node, and not necessarily a boundary line, are assigned as neighbors.

Spatial scan statistic. The spatial scan statistic was calculated using the SaTScan, version 9.1, software package developed by Kulldorff et al[18] specifically for calculating this statistic. This test has been shown to have good power for detecting localized hot spots of excess events.[23] The statistic is defined by imposing circular windows with variable radii ranging from zero up to a user-defined upper limit (usually a maximum radius that never includes more than 50% of the total population of the study area) on the map.

The windows include different sets of adjacent neighborhoods. If the window contains the center of a neighborhood, then the whole neighborhood is included in the window. The method creates a large number of distinct circular windows, each containing a distinct set of adjacent neighborhoods, and each is a possible candidate for containing a cluster of female lung cancer mortality. For each window, the method uses a Monte Carlo simulation to test the null hypothesis that there is not an elevated risk of female lung cancer mortality. Details of how the likelihood function is maximized over all windows under the Poisson distribution assumption have been described elsewhere.[24,25] In this study, retrospective spatial cluster analysis for higher and lower female lung cancer mortality rates was used, in which the maximum window radius was set to be smaller than 30% of the total population to find possible clusters. For each window of movable position and size change, the software tested the female lung cancer mortality rates within and outside the window using the null hypothesis of the same risk.

The coordinates for cases and population were needed in the spatial scan statistic. The present study used centroid locations of each village as surrogate locations for case and population, which has been successfully demonstrated in the literature.[24] When using aggregated data for the analysis, the statistic requires that the number of deaths and the underlying population at risk, in this case the population, were input separately rather than in the form of mortality rates. The age-adjusted number of deaths for each village was calculated by multiplying each age-adjusted mortality rate by the population.

Results

The distribution of female lung cancer mortality rates by village in Xuan Wei County is shown in Figure 1. Moran's *I* was calculated as 0.465, with a *P* value of .001. The positive and significant *I* value indicated strong clustering of the female lung cancer mortality rates in the villages of Xuan Wei County. Figure 2 depicts the clusters whose Local Moran's index have a significance level of up to .05, along with the type of association between the villages and its neighbors as identified by the Moran scatterplot. A total of 30 villages had Local Moran's index more than 1 and significant at the .05 level as high-risk villages surrounded by high-risk neighbors; 7 villages were identified as high-risk areas surrounded by neighboring villages that had lower risk; there were other 7 villages were identified as low-risk villages surrounded by the high risk-neighbors; and 28 villages were identified as low-risk areas surrounded by low-risk villages.

Figure 3 illustrates the significant clusters identified by the spatial scan technique. Table 1 lists the detailed results of the analysis. Three secondary clusters were detected in addition to the primary cluster. The primary cluster is a high rate cluster made up of 55 villages in the central region of Xuan Wei County. The first of the 3 secondary clusters was located in the south section of Xuan Wei County, including 84 villages, being identified as a low rate cluster with a relative risk of 0.19. The other 2 secondary clusters were also belonging to the low rate cluster, and located in the north part of this county.

Comparison of results by the 2 methods showed that although similar results could be found by these 2 methods, the pattern of similarity was complex. Examination of Figures 2 and 3, compared with the mortality rates in Figure 1, showed that both methods detected the high rates located in the central villages. The LISA detected those villages as the core of the high-rate cluster. It also excluded several villages in the central areas from the high-rate category; whereas

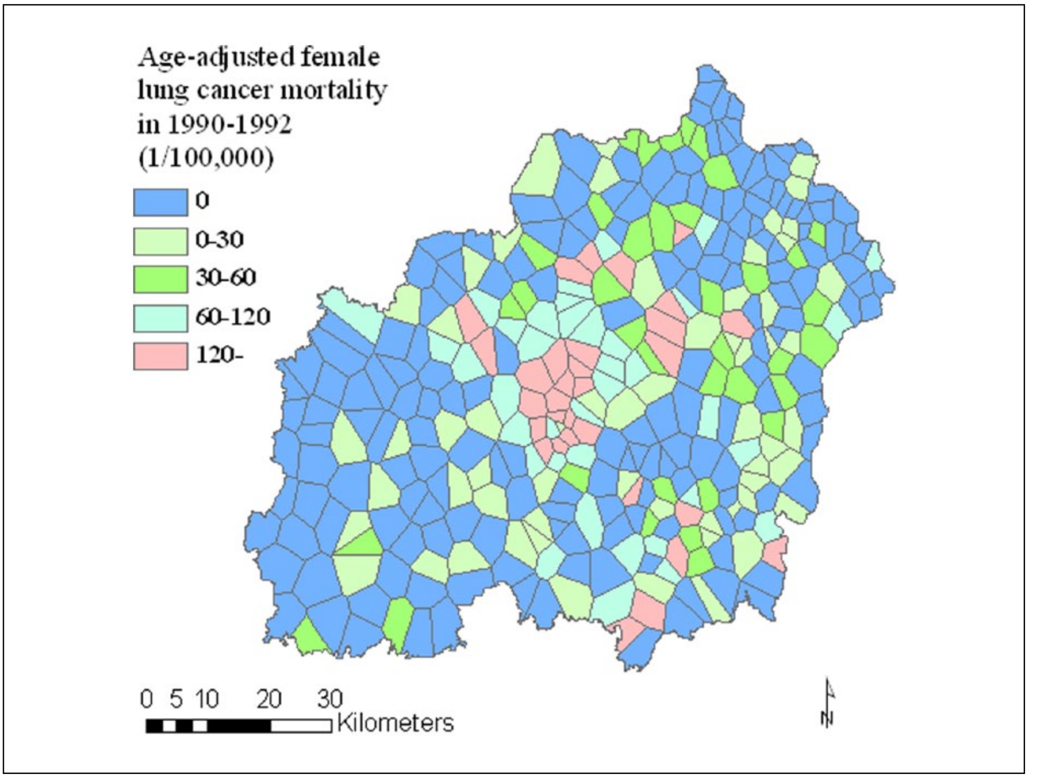

Figure 1. Age-adjusted female lung cancer mortality rate in Xuan Wei County in 1990-1992.

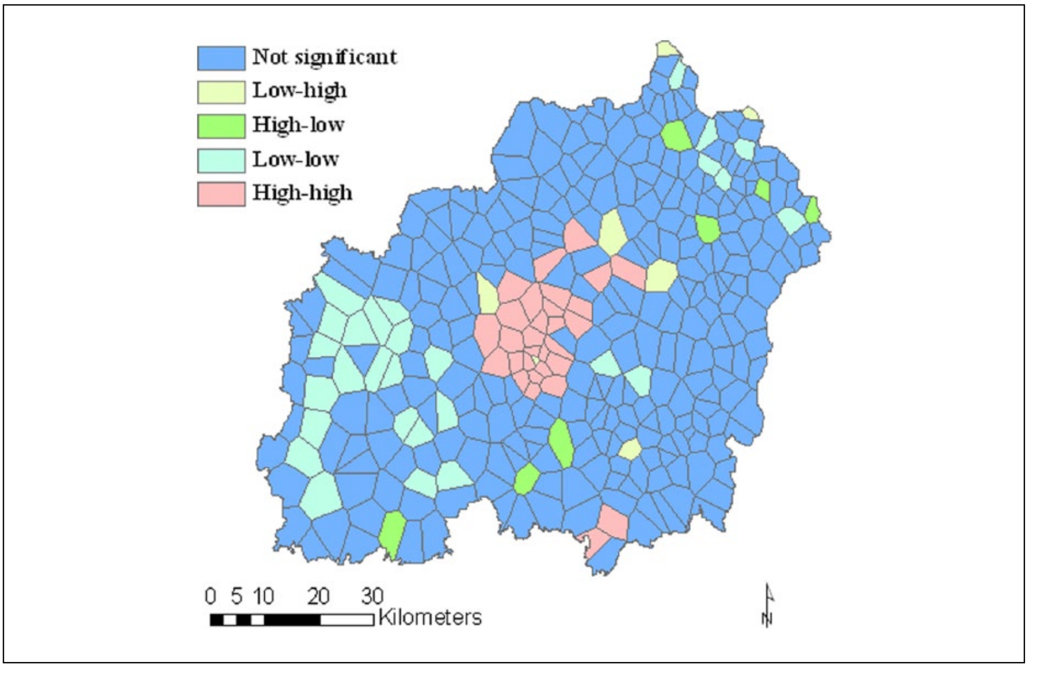

Figure 2. Spatial clusters by Local Moran's *I* methods for female lung cancer mortality in 1990-1992 in Xuan Wei County, China.

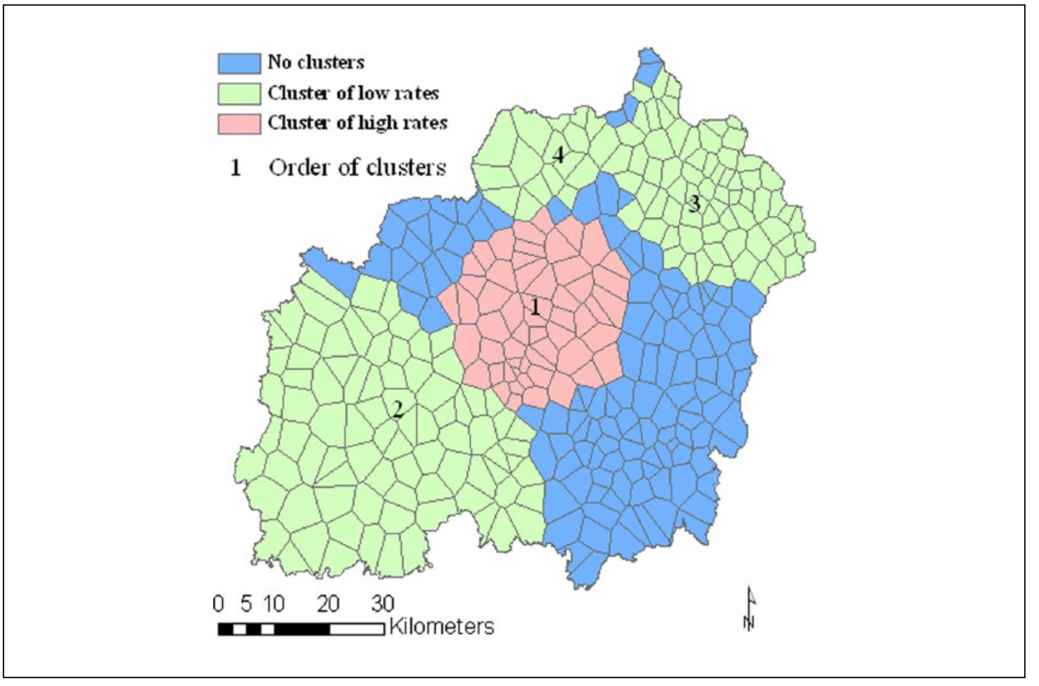

Figure 3. Spatial clusters by spatial scan statistics for female lung cancer mortality in 1990–1992 in Xuan Wei County, China.

Table 1. Results of the Spatial Scan Analysis.

Cluster Level	Order of Cluster	No. of Villages[a]	Relative Risk	Log Likelihood Ratio	*P*	Cluster Type
Primary	1	55	6.01	240.68	.001	High
Secondary	2	84	0.19	76.57	.001	Low
	3	68	0.26	40.18	.001	Low
	4	17	0.31	9.87	.03	Low

[a]Number of the villages included in each cluster.

the spatial scan statistic classified more villages in the central area as the high-rate cluster. Figure 1 showed that the female lung cancer mortality rate for several villages in the central area was not much higher, relatively, than some of the others in the central region, so the exclusion by the LISA method in this cluster was not surprising. However, their inclusion the high-rate category by the spatial scan analysis was also reasonable, as the mechanism of the approach was based on the circular window.[26] Tango[27] also found that the most likely cluster in the spatial scan analysis was usually very large and contained neighboring areas that did not have elevated risk.

The 3 secondary clusters detected by the spatial scan method were all classified as the low-rate clusters, most of which had no exact correspondence in the LISA analysis. Most of villages in the secondary spatial clusters were classified into the not significant cluster in the LISA analysis; 7 and 2 villages were grouped into high–low and low–high categories, respectively; and 26 villages had the same classification in the 2 methods.

Further comparison of the results by the 2 methods showed that villages in the first and third quadrants had very similar results in both methods, most of which were identified as the not significant clusters; whereas 2 villages in the third quadrant were identified as the high-rate cluster in the LISA analysis, which was supported by Figure 1. This is most likely attributable to the foundation underlying the conservative *P* values of the secondary clusters in the spatial scan analysis. Since secondary clusters were only reported if their likelihood is the highest of all of the simulated clusters based on that centroid, it was possible for clusters composed of only 1 or 2 villages with high rate to go undetected if they had a larger group of low-rate villages.[18,28]

Discussion

The manner in which both methods measure neighbors or adjacency made it possible that results by both methods had been influenced by the boundary or edge effect, a well-documented phenomenon where an observation's position on or near the boundary of the study area affected the statistical inference involving neighbor measurement.[29] The boundary effect might account for the absence of 2 villages in the third quadrant from a significant cluster in the spatial scan analyses. Future research should investigate its influence in this context.

The choice of a weight matrix was a key component of LISA analysis and depended directly on the assumptions of the spatial relationship among the geographic units. For instance, a matrix could be used that reflected the length of each shared boundary, if it was assumed that the interaction depended on the amount of physical contact between each village. An inverse distance weighting function could also be used, with the results subject to the same centroid problems described above. The spatial scan was not affected by spatial interaction considerations, being a point-pattern type of analysis method, but covariates may be used, and their selection depends heavily on the assumptions of demographic or environmental relationships in the study area.

The LISA, focusing on an observation's correlation with its neighbors, was more suitable for detecting where 2 or more villages were clustered together, such as the villages in the central Xuan Wei County. Another benefit of the LISA was the way it identified inverse associations, or ''hot spots'' of high rates within locally low rates or lows within highs. These can either point to neighboring clusters or stand out themselves as outliers or as at-risk locations (depending on whether the observations were high or low rates). Several villages stood out as examples of relatively high-rate villages in otherwise low-rate ones, and each may be examined as both an anomaly in an otherwise stable area and a potential threat to that stability through its geographic process. The identification of such hot spots can be just as important to lung cancer epidemiology and treatment as identifying high-and low-rate clusters.

A primary advantage of spatial scan statistics was that this method was specifically designed for cluster detection and testing the statistic significance. The cluster sizes and locations did not have to be specified in advance and thereby overcame preselection bias. The hypotheses were clearly defined, and the test statistic was based on a likelihood ratio and not on an ad hoc procedure. The capability of controlling for covariates in the analysis had made the spatial scan statistic widely used in the spatial epidemiology researches and hypothesis testing. Kulldorff[18] successfully controlled for race in his study of infant mortality in North Carolina, illustrating that the application of covariates depended on a priori assumptions about the process under investigation. Similarly, characteristics known to be related with lung cancer mortality, such as cigarette smoking and air pollution, could be applied to control for the differences due to these factors and achieve substantially different results. Future researches on lung cancer mortality should consider controlling for the covariates that were known to be associated with lung cancer and that would provide additional insights into the nature of the clusters; and there had been a successful example. However, for the purpose of comparison between the spatial scan statistic and LISA method in the current study, covariates were not used.

It seemed apparent that the 2 methods are more complementary than repulsive in the spatial analysis of female lung cancer mortality rate in this area. These 2 methods were also used and compared in a study investigating Burkitt's lymphoma in Kenya, and general agreement between them was found in identifying disease clusters.[30] In Long Island, New York, Jacquez and Greiling[20] used both the spatial scan statistic and Local Moran's I test to examine geographical patterns of 3 types of malignancy.[20] They also suggested that it was necessary to use more than one method in detecting spatial clusters of cancer mortality.

The detected high-risk areas were still distributed in those villages using bituminous coals as the main fuels, which indicated that bituminous coal was still the major risk factor for lung cancer in Xuan Wei, although indoor air pollution has been reduced after the stove improvement.[11] It was possible that bituminous coal burning indoors could also contribute to outdoor air pollution.[7] One study investigated the outdoor air pollution in this area and found that benzo[a]pyrene levels in 20 outdoor air samples were higher than the national criteria (10 ng/m^3) of China, and subsequent analysis suggested that indoor coal combustion was the predominant source for the outdoor air pollution. It was also possible that the bituminous coals have been used more widely in Xuan Wei areas, which might be one reason for the high risk in some villages that have not been reported to have high lung cancer rate.

The strength of this study was that it used lung cancer mortality data from a comprehensive survey in one county with extremely high lung cancer rate, and 2 commonly used spatial analysis methods were compared to find the similarity and differences. Although the issues of mortality data quality among the study areas arose that were relevant to the examination of regional variation in the lung cancer mortality, all data at the same survey period were collected using uniform criteria, thereby ensuring a reasonable degree of comparability; so the survey process should not have distorted the observed geographic distribution pattern to a great extent. In general, for any health event there is always the potential for diagnostic error or misclassification; however, lung cancer is such a common and serious disease that local clinic practitioners at different levels should have high confidence of the disease diagnosis, although misdiagnosis was sometimes inevitable.

An exploration of the spatial variations of lung cancer mortality could be an important tool in targeting the prevention and control of this illness. Spatial analysis may be especially appropriate for recognizing clusters because lung cancer was known to be associated with many environmental factors, such as cigarette smoking, air pollution, radon, and so on. The identification of clusters of lung cancer mortality had important substantive value for health services, planning, and policies. Clusters of high mortality rates could be used to identify locations for enhanced proper prevention programs and improved access to general health care and priority for etiological studies. Low-rate clusters were areas where specific factors, such as some protective factors and adequate prevention services, were likely to be responsible for the positive health outcome. A low-rate area adjacent to high-rate areas may have the tendency to develop more lung cancer cases in the future and thus require additional attention; whereas a high-rate area surrounded by low-rate areas may be useful for researchers to detect the special risk factors that the residents were exposed to, and thus valuable for etiologic studies. Health services planners can use these results as a guide to potential changes in their health service plan, and researchers can use the differences between the high- and low-rate places as hypotheses for future studies.

Conclusion

Each of the LISA and spatial scan methods had its own strength and can both be applied in a complementary manner. The LISA can be used to identify high- and low-rate clusters considering the geographical correlation among the neighbors and where there existed significant local outliers of either high or low rates. The spatial scan statistic can be applied to search for high and low rates and to examine potential risk factors related to the clusters, confirming the location of clusters identified by the LISA and delineating their extent. By combining the 2 methods, a more comprehensive measure of spatial clusters of lung cancer mortality and other illnesses can be achieved, ultimately increasing the effectiveness and efficiency of public health response and minimizing mortality and other adverse health outcomes.

Authors' Note

Hualiang Lin and Bofu Ning contributed equally to this article.

Declaration of Conflicting Interests

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