<div align="center">Original Article</div>

Equity Chasm in Megacities: Five Leading Causes of Death in Tehran

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Abstract

Background: Inequity in megacities is a real concern in public health perspective. Tehran is a megacity with more than 8 million population that is divided into 22 regions (counties) with considerable diversity in socioeconomic status. On the other hand, spatial cluster detection is an important tool in disease surveillance for identifying areas of elevated risk and generating hypotheses about disease or mortality etiology. The present research aims to identify high or low-risk clusters for five non-communicable leading causes of death in 22 regions of Tehran province.

Methods: Cause-specific mortality rates were extracted from Behesht-e-Zahra registry system for Tehran province in 2011. Spatial scan statistic was chosen as the most common method in spatial cluster detection to detect clusters with elevated risk of death. Given the observed and expected number death in each region, a log likelihood ratio (LLR) criterion was used to test whether a cluster is significant.

Result: Two high-risk and two low-risk clusters were detected for each cause of death. All these clusters were statistically significant with P values less than 0.05. Mapping these clusters shows substantial differences between regions in Tehran. For mortality due to ischemic heart diseases, cerebrovascular diseases, hypertensive diseases, respiratory diseases, and stomach cancer, the high-risk clusters concentrated in the southern half of Tehran and low-risk clusters were in the northern half of Tehran. In the most situations, regions 2, 3, and 5 seemed to have lower rates of death compared with other regions. On the other hand, regions, 16, 19, and 20 were in the high rate clusters.

Conclusion: There was substantial disparity between regions of Tehran for five non-communicable causes of death studied in this article. Identifying factors affecting the observed differences is useful to set effective preventive interventions and can be investigated in future researches.

Keywords: Cause of death [http://www.ncbi.nlm.nih.gov/mesh/D002423]; non-communicable disease, spatial cluster detection, spatial scan statistic, Tehran

Introduction

Tehran, the largest metropolitan area of the country, comprises about 16% of the total population of Iran. There are 22 regions in Tehran, some of which are economically more developed than others. Furthermore, there are substantial differences in many lifestyle characteristics between these regions that suggest possible disparities among leading causes of death in this diverse area.

In recent years, the amount of attention given to spatial nature of many causes of death and diseases leads to strong motivation to develop models for geographic spatial analysis techniques to detect regions with elevated risk of mortality. These techniques aim to explore pattern and spatial distribution of death in the study regions.[1–3]

Mortality mapping permits the exploration of spatial patterns[4,5] and testing for statistical significance of spatial clusters of mortality.[6,7] Nowadays, important research effort has focused on the different clustering techniques to analyze spatial patterns,[7,8] and to provide reliable mortality maps in spatial epidemiology.[9] Spatial scan statistic introduced in 1997 by Kulldorff is the most common method for spatial cluster detection and used in this paper.

Complete and reliable death registration system provides valuable information about level and trend of mortality rates and distribution of cause of death.[10] This information enables policy makers to lead health care system more effectively.[11,12]

The Institute for Health Metrics and Evaluation (IHME) has assessed the causes of death globally for all countries including Iran. According to these results, the most important non-communicable causes of death are ischemic heart disease, stroke, hypertensive heart disease, stomach cancer and respiratory diseases in Iran.[13–15]

Despite these findings, there is no comprehensive study conducted at smaller area units of Iran such as provinces, districts or regions of some megacities like Tehran. In a study conducted

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by Rohani, *et al.* for investigating disparity in cancer incidence, the authors noticed substantial differences across various regions of Tehran.[16] However, the spatial pattern of cause-specific mortalities is less understood and studied. This issue prompted us to investigate the spatial distribution and detect potential clusters of age-standardized mortality rates by sex and causes of death in 22 regions of Tehran.

Materials and Methods

Study setting

Data of Tehran cemetery death registration system called Behesht-e-Zahra has been used in this study, which is the most comprehensive source of causes of death by regions in Tehran. Essential variables consisting of age, sex, cause of death and residence region have been extracted from the registration system.

We conducted a secondary analysis in order to explore the spatial pattern of some leading causes of death. These five leading non-communicable causes of death are ischemic heart disease (I20-I25), cerebrovascular diseases (I60-I69), hypertensive diseases (I10-I15), malignant neoplasm of stomach (C16), and diseases of the respiratory system (J00-J99). According to this category, we are going to cluster age-standardized mortality rates in 22 regions in Tehran via a spatial clustering model by sex and causes of death.

Data preparation

The death registration systems suffer from many issues such as missing values, incompleteness of death registration system and misclassification of causes of death. These problems also exist in Tehran cemetery death registration. Therefore, we had to deal with them before conducting any analysis. Understanding the fact, we decided to assume that the distribution of incompleteness and misclassification were the same for all regions. Missing values in age, sex and region variables were imputed by multiple imputation approach using Amelia package in R statistical software.[17] For missing values of causes of death, with about 218 categories, Amelia package is not suitable and we used multiple imputation with mi command in STATA 12.0.[18] Because of the nature of characteristics of causes of death, a multinomial logistic link function was applied in this imputation model.

Cause of death is the key component in this study. Unfortunately, this variable was registered based on physician diagnosis. Therefore, an expert physician familiar with International Classification of Diseases (ICD) explored all registered causes of death and recoded them into 10th revision of the ICD. Non-valid underlying causes of death were recoded to missing values and then redistributed proportional to number of observed causes in the data set.[19]

To calculate mortality rates, we extracted the number of death by sex, age, region and causes of death. The at risk population for each region was extracted from the last Iranian population and housing census in 2011.[20] The direct method of age-standardization was used to adjust the effect of different age distribution in regions. Finally, the expected number of death for each cause in all regions was derived from age standardized death rate for males and females.

Spatial scan statistics clustering

Kulldorff spatial scan statistics is a statistical method to detect spatial, temporal and space-time clusters. The method constructs zones by consecutively aggregating nearest-neighboring areas and uses a moving circle of varying size to find a set of regions or points that maximize the likelihood ratio test. The test statistic λ of the likelihood ratio test can be written as[21]:

$$\lambda = sup_z \frac{\left(\frac{n_z}{\mu(z)}\right)^{n_z} \left(\frac{n_G - n_z}{\mu(G) - \mu(z)}\right)^{n_G - n_z}}{\left(\frac{n_G}{\mu(G)}\right)^{n_G}} I\left(\frac{n_z}{\mu(Z)} > \frac{n_G - n_z}{(\mu(G) - \mu(z))}\right)$$

where sup_z is the least upper bound of log likelihood ratio test in zone z, n_G and μ_G are the number of points and average rate in the study area, and n_z and μ_z are the number of points and average rate in each zone z. $L(z)$ is the likelihood function for rage in whole study area.. I(.) is the indicator function.

Given the observed number of causes of death, the likelihood of each zone is computed using distribution of outcome. This procedure reports the zone, which has the most likely cluster to have the highest or lowest value. The significance of clusters is tested via Monte Carlo sampling.

In this study, we used spatial scan statistics to locate clusters of regions where the number of deaths due to specific causes of death was significantly higher or lower than the expected value in comparison with other regions. Therefore, we examined the assumption of equality of cause-specific mortality rates inside and outside each cluster.

For spatial clustering, we used SaTScan software version 9.3.1.[22] We considered Poisson distribution for number of death in each region. In addition, we set 50% of the whole population at risk as the maximum size of scan window. Finally, when the high or low risk clusters were diagnosed, the test of cluster significance was run using Monte Carlo method. All significant clusters were illustrated by R statistical software version 3.1.2.

Result

A total of 13,328 persons died due to five top non-communicable causes of death in Tehran during 2011. Theses causes of death were responsible for more than one in four deaths in Tehran in this year. Among studied causes, respiratory disease had the highest percentage (11.32) and malignant neoplasm of stomach had the lowest percent (1.38%) among all causes of deaths. Table 1 displays mortality rates of these underlying causes of death.

Table 2 summarizes the result of the detected clusters and regions belonging to them using spatial scan statistics. In this table, log likelihood ratio (LLR) is the statistical criterion for testing whether a cluster is significant. Relative risk (RR) was defined as the chance of death due to each of these causes inside the cluster compared to the outside the cluster.

The results of spatial scan statistics clustering showed that the distribution of each cause of death was different among regions of Tehran (Figure 1). Two high-risk and two low-risk clusters were detected for each cause of death. The results showed all these clusters were significantly different from expected at 0.05 *P* value level. Mapping these clusters showed substantial differences in cause-specific mortalities between regions of Tehran province. For most causes of death, the high-risk clusters concentrated in the southern half of Tehran and low-risk clusters were in the northern half of Tehran.
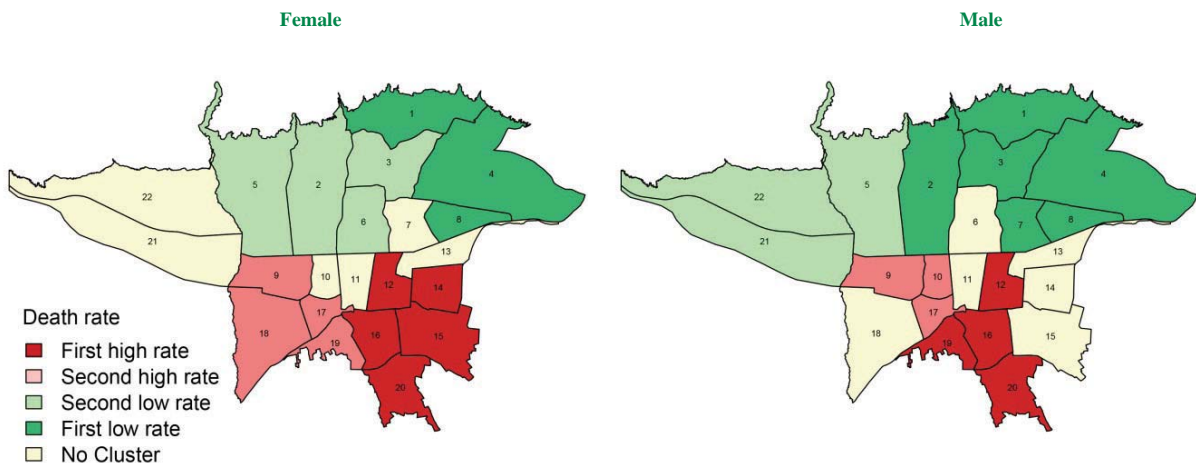
Table 1. Mortality rates per 100,000 of five non-communicable leading cause of death in Tehran 2011.

Cause of death	Mortality rates per 100,000	
	Female	Male
Ischemic heart disease	14.53	30.75
Cerebrovascular diseases	47.24	54.12
Hypertensive diseases	11.32	12.75
Malignant neoplasm of stomach	5.65	11.46
Respiratory Disease	56.71	83.32

Table 2. High and low-risk clusters of five non-communicable leading cause of death in Tehran 2011.

Sex		Female				Male			
Diseases	Death rate	Clusters (Regions of Tehran)	RR	LLR*	P-Value	Clusters (Regions of Tehran)	RR	LLR	P-Value
Ischemic heart disease	Highest	12, 14, 15, 16, 20	1.70	6.71	0.014	12, 16, 19, 20	1.91	60.59	<0.01
	High	9, 17, 18, 19	1.52	3.70	0.019	9, 10, 17	1.48	9.23	<0.01
	Low	2, 3, 5, 6	0.64	6.16	0.029	5, 21, 22	0.63	6.11	0.016
	Lowest	1, 4, 8	0.73	10.36	<0.01	1, 2, 3, 4, 7, 8	0.76	35.06	<0.01
Cerebrovascular diseases	Highest	9, 16, 17, 18, 19, 20	1.43	9.47	<0.01	9, 16, 17, 18, 19, 20	1.72	79.33	<0.01
	High	14, 15	1.21	5.26	0.02	15	1.15	25.33	<0.01
	Low	5, 21, 22	0.65	7.72	<0.01	5, 21, 22	0.78	7.46	<0.01
	Lowest	1, 2, 3, 4, 6, 7, 8, 13	0.79	27.15	<0.01	1, 2, 3, 4, 6, 7, 8, 13	0.82	69.73	<0.01
Hypertensive diseases	Highest	10, 11, 12, 13, 14, 15, 16, 17, 19, 20	1.62	8.93	<0.01	9, 10, 11, 12, 15, 16, 17, 19, 20	1.67	56.26	<0.01
	High	22	1.23	5.24	0.043	13, 14	1.36	32.66	<0.01
	Low	2, 5	0.58	5.48	0.042	2, 5	0.47	9.28	<0.01
	Lowest	1, 3, 4, 6, 7, 8	0.62	8.19	<0.01	1, 3, 4, 7, 8	0.61	15.30	<0.01
Malignant neoplasm of stomach	Highest	15, 16, 19, 20	3.85	19.30	<0.01	12, 16, 17, 19, 20	1.85	17.20	<0.01
	High	9	2.30	8.85	<0.01	9, 18	1.21	11.26	<0.01
	Low	2, 5	0.46	6.76	<0.01	2, 5, 6, 7, 10, 11	0.72	4.26	<0.01
	Lowest	1, 3, 4, 6, 7, 8, 13, 14	0.69	10.35	<0.01	1, 3	0.83	8.65	<0.01
Respiratory Disease	Highest	12, 16, 19, 20	1.71	46.75	<0.01	12, 14, 15, 16, 17, 19, 20	1.5	72.61	<0.01
	High	9	1.61	7.153	<0.01	9	1.12	2.36	<0.01
	Low	4, 8	0.75	8.15	<0.01	10, 11	0.8	5.16	<0.01
	Lowest	2, 3, 5, 6	0.78	15.265	<0.01	1, 2, 3, 4, 5, 7, 8	0.73	40.13	<0.01

*LLR stands for Log Likelihood Ratio

Female   **Male**

Death rate
- First high rate
- Second high rate
- Second low rate
- First low rate
- No Cluster

Figure 1. Spatial clusters for ischemic heart disease.

Female **Male**

Death rate
- First high rate
- Second high rate
- Second low rate
- First low rate
- No Cluster
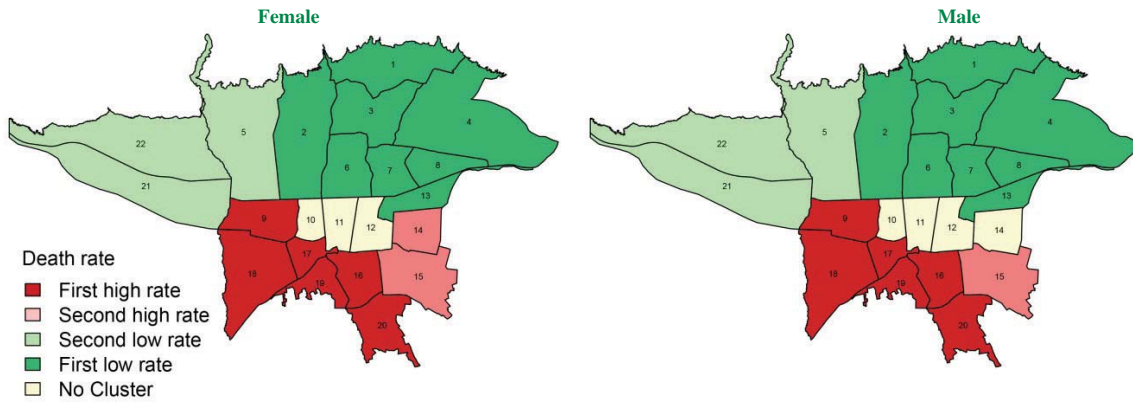
Figure 2. Spatial clusters for cerebrovascular diseases.

Female **Male**

Death rate
- First high rate
- Second high rate
- Second low rate
- First low rate
- No Cluster
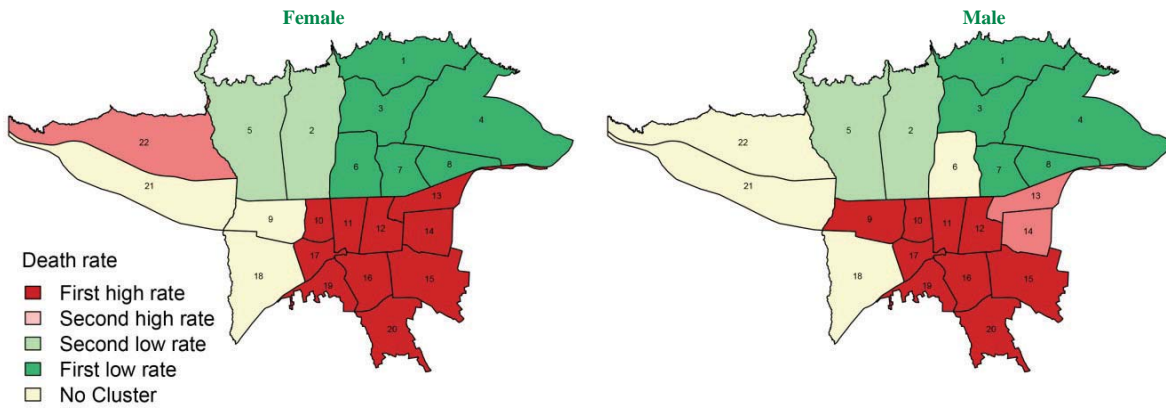
Figure 3. Spatial clusters for hypertensive diseases.

Female **Male**

Death rate
- First high rate
- Second high rate
- Second low rate
- First low rate
- No Cluster
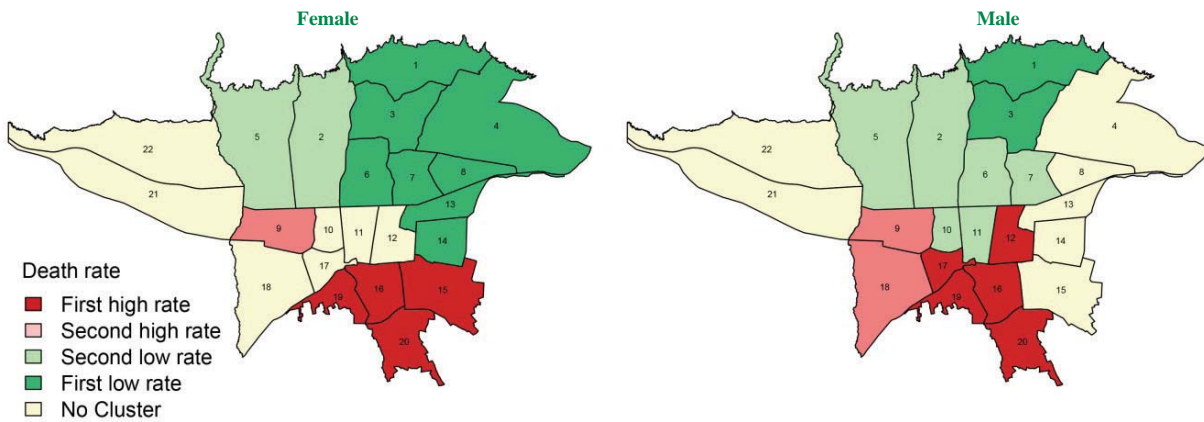
Figure 4. Spatial clusters for malignant neoplasm of stomach.

Female **Male**

Death rate
- First high rate
- Second high rate
- Second low rate
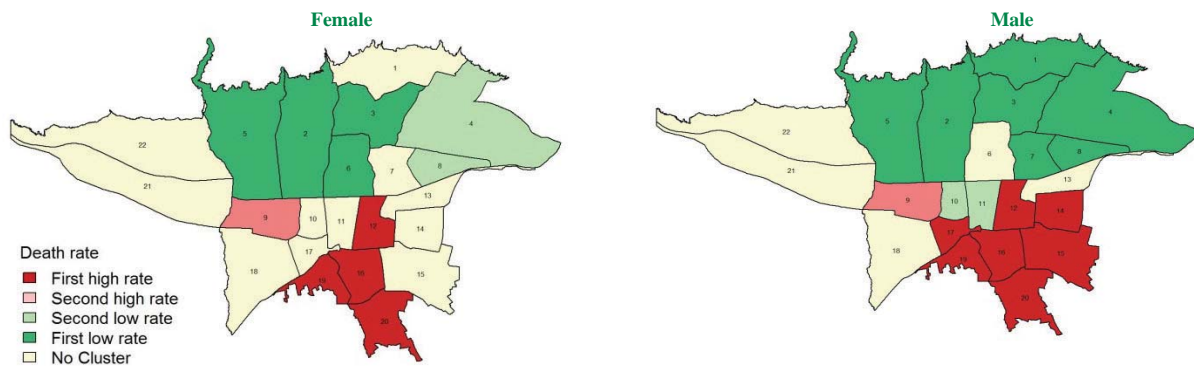- First low rate
- No Cluster

Figure 5. Spatial clusters for Respiratory disease.

Although the distribution of causes of death studied was different in regions, in the most situations regions 2, 3 and 5 seemed to have lower rates of death compared with other regions. On the other hand, region 16, 19 and 20 were in the high rate clusters.

In this study, we made a comparison of age standardized mortality rates between detected clusters for both genders. At first, we calculated the weighted average of age-adjusted death rates (per 100,000 population) for all clusters and then the differences between the highest and the lowest values were considered as a measure of disparity. The results showed that the variations of rates for male were higher than females in stroke, IHD, and respiratory diseases. The difference between males and females was 13.97, 31.57, and 34.57 per 100,000, respectively. Variation of hypertensive disease was almost equal: 12.75 in males and 13.79 in females. Finally, age-standardized rates in females were 17.68 higher than males for stomach cancer.

Discussion

To our knowledge, this is the first citywide population based study completed in Tehran. The study has assessed geographic clustering of causes of death and has described the relative risk of each cause by geographic clusters. Actually, this is the first study demonstrating the disparity of deaths regarding the five leading non-communicable causes of death in Iran.

The geographic cluster analysis has identified regions where the relative risks of the above-mentioned causes were significantly high or low. Diverse methods have been suggested to test for disease clusters. The most popular method for detecting spatial clusters is circular spatial scan statistic developed by Kulldorff.[23–25] In this study, we offer this frequentist approach, which uses maximum likelihood method to identify potential high or low risk clusters.

The Global Burden of Disease (the GBD) study conducted by IHME has obtained death rates by causes of death in 2010. Based on their findings, the leading causes of death ranged from ischemic heart disease to respiratory disease for both sexes in Iran.[26] Although the respiratory diseases had the first mortality rank in our study, it consist of several diseases such as acute upper respiratory infection, chronic lower respiratory disease, lung diseases due to external agents and etc. Therefore, we should not compare this cause with cause of death defined in GBD. Considering this issue, the result of Tehran death registration showed that ranking of causes of death in Tehran is almost similar with national level.

The current study indicated that there are statistically significant regional variations in all five leading causes of death in Iran. For most of these causes, all regions with low-risk were concentrated in the northern part of Tehran and regions with high-risk were in the southern part. In addition, significant region disparities have been observed in the mortality rate for all of these causes of death.

International studies in geographic variations provide background information in which a disease may have a reasonably different incidence and resulting mortality as a function of area of residency.[27–35]

A number of risk factors can be responsible for the variation on regional level. Based on previous studies, Socio-Economic Status (SES) is one of the most important risk factors of death for different diseases. These findings have been repeated across different geographical regions.[36–40] SES influences three major elements of health: health care, environmental exposure, and health behavior.[41]

Furthermore, growing evidence suggests that long-term exposure to air pollution contributes to risk of cardiovascular disease and other causes of mortality.[42–44] In addition, an inverse association is seen between healthy lifestyle factors including non-smoking and physical activity and the risk of all-cause mortality in a healthy Italian population during a 20-year follow-up study.[45–47] Previous studies suggested that these risk factors have a heterogeneous distribution in Tehran.[48–51] The above-mentioned factors could be considered as possible causes of observed regional differences in mortality in our study. Finding justification for these variations can be assessed in future researches.

Studies like this can provide information about health conditions in big cities like Tehran. According to our study, all five causes have different distribution in regions of Tehran. This disparity might be an alarm of inequality in available health cares in these regions. So the results of this study can be used for policymakers to set interventions and allocate resources more effectively by region.

Finally, there are some limitations in results of this study. Since there is no reliable estimate of the percentage of incompleteness for different regions of Tehran, we could not adjust these results according to accurate percentage of incompleteness for each region. However, incompleteness percentage of death registration system is not substantially different to confound the result of analysis. In addition, we have used an expert opinion to determine the correct causes of death based on ICD-10 codes for ill-defined and garbage causes of death and this can cause some type of bias in the presented results.

In conclusion, we have exhibited the main spatial clusters in Tehran based on five leading causes of death. The regions 2, 3, and 5 were low risk and 16, 19, and 20 were high risk in the final clustering model. Cluster detection is an important part of spatial epidemiology because it may help suggest potential factors associated with disease and mortality.[52–57] We only used data of year 2011 and spatial correlation in our analysis, so future studies can concentrate on temporal correlation in analysis and make a temporal or space time clusters for these data. In addition, in future studies, the most important covariates should be considered to model each cause to determine their level in different regions and use these results to identify possible preventive strategies for these regions.

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Competing interest

The authors declare that they have no competing interests.

Author's contributions

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References

1. Lawson AB. Disease map reconstruction. *Stat Med*. 2001; 20(14): 2183-204.
2. Elliot P, Wakefield JC, Best NG, Briggs D. *Spatial Epidemiology: Methods and Applications*. UK: Oxford University Press; 2000.
3. Rushton G. Public health, GIS, and spatial analytic tools. *Annu Rev Public Health*. 2003; 24(1): 43-56.
4. Benach J, Yasui Y, Borrell C, Rosa E, Pasarín MI, Benach N, et al. Examining geographic patterns of mortality. *Eur J Public Health*. 2003; 13(2): 115-23.
5. James WL, Cossman RE, Cossman JS, Campbell C, Blanchard T. A brief visual primer for the mapping of mortality trend data. *Int J Health Geogr*. 2004; 3(1): 7
6. Jemal A, Kulldorff M, Devesa SS, Hayes RB, Fraumeni JF. A geographic analysis of prostate cancer mortality in the United States, 1970–89. *Int J Cancer*. 2002; 101(2): 168-74.
7. Munasinghe RL, Morris RD. Localization of disease clusters using regional measures of spatial autocorrelation. *Stat Med*. 1996; 15(7-9): 893-905.
8. Assuncao RM, Reis EA. A new proposal to adjust Moran's I for population density. *Stat Med*. 1999; 8(16): 2147-62.
9. Wakefield J, Elliott P. Issues in the statistical analysis of small area health data. *Stat Med*. 1999; 18(17-18): 2377-99.
10. Mohammadi Y, Parsaeian M, Farzadfar F, Kasaeian A, Mehdipour P, Sheidaei A, et al. Levels and trends of child and adult mortality rates in the Islamic Republic of Iran, 1990–2013; protocol of the NASBOD study. *Arch Iran Med*. 2014;17(3):176-81.
11. Mikkelsen L, Phillips DE, AbouZahr C, Setel PW, de Savigny D, Lozano R, et al. A global assessment of civil registration and vital statistics systems: monitoring data quality and progress. *Lancet*. 2015. pii: S0140-6736(15)60171-4.
12. Phillips DE, AbouZahr C, Lopez AD, Mikkelsen L, de Savigny D, Lozano R, et al. Are well functioning civil registration and vital statistics systems associated with better health outcomes? *Lancet*. 2015. pii: S0140-6736(15)60172-6.
13. Forouzanfar MH, Sepanlou SG, Shahraz S, Dicker D, Naghavi P, Pourmalek F, et al. Evaluating causes of death and morbidity in Iran, global burden of diseases, injuries, and risk factors study 2010. *Arch Iran Med*. 2014; 17(5): 304-20.
14. Metrics IfH, Evaluation. The Global Burden of Disease: Generating Evidence, Guiding Policy. IHME Seattle^ eWA WA; 2013.
15. Murray CJ, Lopez AD. Measuring the global burden of disease. *N Engl J Med*. 2013; 369(5): 448-57.
16. Rohani-Rasaf M, Abdollahi M, Jazayeri S, Kalantari N, Asadi-Lari M. Correlation of cancer incidence with diet, smoking and socio-economic position across 22 districts of Tehran in 2008. *Asian Pac J Cancer Prev*. 2013; 14(3): 1669-76.
17. Honaker J, King G, Blackwell M. Amelia II: A program for missing data. *J Stat Softw*. 2011; 45(7): 1-47.
18. Lawlor DA, Timpson NJ, Harbord RM, Leary S, Ness A, McCarthy MI, et al. Exploring the developmental overnutrition hypothesis using parental-offspring associations and FTO as an instrumental variable. *PLoS Med*. 2008; 5(3): e33.
19. Sheidaei A, Mansouri A, Kasaeian A, Khosravi A, Rezaei N, Parsaeian M, et al. National and subnational patterns of cause of death in Iran 1990-2014: Applied methods. *Arch Iran Med*. 2015. In press
20. Statistical Centre of Iran 2015. Available from: URL: http://www.amar.org.ir/.
21. Kulldorff M. Spatial scan statistics: models, calculations, and applications. In: Glaz J, eds. *Scan Statistics and Applications*. Netherland: Springer; 1999: 303-22.
22. Kulldorff M. *SaTScan-Software for the Spatial, Temporal, and Space-time Scan Statistics*. Boston: Harvard Medical School and Harvard Pilgrim Health Care; 2010.
23. Kulldorff M. A spatial scan statistic. *Communications in Statistics - Theory and Methods*. 1997; 26(6): 1481-96.
24. Zhang T. Spatial scan statistics; spatial and temporal modeling and analysis. *Encyclopedia of Environmetrics*. UK: John Wiley & Sons, Ltd; 2013.
25. Duczmal L, Buckeridge DL. A workflow spatial scan statistic. *Stat Med*. 2006; 25(5): 743-54.
26. GBD Arrow Diagram Seattle. WA: IHME, University of Washington: Institute for Health Metrics and Evaluation (IHME); 2013. Available from: URL: http://vizhub.healthdata.org/irank/arrow.php.
27. Kubo M, Kiyohara Y, Kato I, Tanizaki Y, Arima H, Tanaka K, et al. Trends in the incidence, mortality, and survival rate of cardiovascular disease in a Japanese community The Hisayama Study. *Stroke*. 2003; 34(10): 2349-54.
28. Braveman PA, Kumanyika S, Fielding J, LaVeist T, Borrell LN, Manderscheid R, et al. Health disparities and health equity: the issue is justice. *Am J Public Health*. 2011; 101(S1): S149-S55.
29. Pickle LW, Gillum RF. Geographic variation in cardiovascular disease mortality in US blacks and whites. *J Natl Med Assoc*. 1999; 91(10): 545.
30. Müller-Nordhorn J, Binting S, Roll S, Willich SN. An update on regional variation in cardiovascular mortality within Europe. *Eur Heart J*. 2008; 29(10): 1316-26.
31. Finegold JA, Asaria P, Francis DP. Mortality from ischaemic heart disease by country, region, and age: statistics from World Health Organisation and United Nations. *Int J Cardiol*. 2013; 168(2): 934-45.
32. Seppä K, Hakulinen T, Läärä E. Regional variation in relative survival—quantifying the effects of the competing risks of death by using a cure fraction model with random effects. *J R Stat Soc Ser C Appl Stat*. 2014; 63(1): 175-90.
33. Henau K, Van Eycken E, Silversmit G, Pukkala E. Regional variation in incidence for smoking and alcohol related cancers in Belgium. *Cancer Epidemiol*. 2015; 39(1): 55-65.
34. Innos K, Mägi M, Tekkel M, Aareleid T. Place of residence predicts breast cancer stage at diagnosis in Estonia. *Eur J Public Health*. 2010; 21(3): 376–80.
35. Jongsthapongpanth A. *Geographical Analysis of Disease Incidence, Mortality, and Deprivation: A Study of People Living with HIV/AIDS in Northern Thailand*. US: ProQuest. 2007.
36. Friedman E. Socioeconomic inequalities in cardiovascular disease mortality. *Eur Heart J*. 2001; 22(8): 715.
37. Mohammadzadeh Y, Ahmadi AM, Sadeghi H, Hasanzadeh A. Socioeconomic Inequalities in Iran Health Sector. *MEJSR*. 2013;15(4): 469-76.
38. Myint SW. An exploration of spatial dispersion, pattern, and association of socio-economic functional units in an urban system. *Applied Geography*. 2008; 28(3): 168-88.
39. Alkerwi Aa, Vernier C, Sauvageot N, Crichton GE, Elias MF. Demographic and socioeconomic disparity in nutrition: application of a novel Correlated Component Regression approach. *BMJ Open*. 2015; 5(5): e006814.
40. Britton JR. Effects of social class, sex, and region of residence on age at death from cystic fibrosis. *BMJ*. 1989; 298(6672): 483-7.
41. Adler NE, Newman K. Socioeconomic disparities in health: pathways and policies. *Health Aff*. 2002; 21(2): 60-76.
42. Brajer V, Hall J, Rahmatian M. Air pollution, its mortality risk, and economic impacts in tehran, iran. *Iran J Pub Health*. 2012; 41(5): 31.
43. Laurent O, Bard D, Filleul L, Segala C. Effect of socioeconomic status on the relationship between atmospheric pollution and mortality. *J Epidemiol Community Health*. 2007; 61(8): 665-75.
44. Dockery DW, Pope CA, Xu X, Spengler JD, Ware JH, Fay ME, et al. An association between air pollution and mortality in six US cities. *N Engl J Med*. 1993; 329(24): 1753-9.
45. Weisburger J. Lifestyle, health and disease prevention: the underlying mechanisms. *Eur J Cancer Prev*. 2002; 11(2): 1-7.
46. Blackmore HL, Ozanne SE. Programming of cardiovascular disease across the life-course. *J Mol Cell Cardiol*. 2015; 83: 122-30.
47. Glendinning A, Hendry L, Shucksmith J. Lifestyle, health and social class in adolescence. *Soc Sci Med*. 1995; 41(2): 235-48.
48. Atash F. The deterioration of urban environments in developing countries: Mitigating the air pollution crisis in Tehran, Iran. *Cities*. 2007; 24(6): 399-409.
49. Shamsipour M, Farzadfar F, Gohari K, Parsaeian M, Amini H, Rabiei K, et al. A framework for exploration and cleaning of environmental data-tehran air quality data experience. *Arch Iran Med*. 2014; 17(12):

821-9.

50. Naddafi K, Hassanvand MS, Yunesian M, Momeniha F, Nabizadeh R, Faridi S, et al. Health impact assessment of air pollution in megacity of Tehran, Iran. *J Environ Health Sci Eng*. 2012; 9(1): 28.

51. Amini H, Taghavi-Shahri SM, Henderson SB, Naddafi K, Nabizadeh R, Yunesian M. Land use regression models to estimate the annual and seasonal spatial variability of sulfur dioxide and particulate matter in Tehran, Iran. *Sci Total Environ*. 2014; 488-489: 343-53.

52. Mahmoud T. Spatial Disease Cluster Detection: An Application to Childhood Asthma in Manitoba, Canada. *Journal of Biometrics & Biostatistics*. 2012; 7: 2.

53. Nkhoma ET, Hsu CE, Hunt VI, Harris AM. Detecting spatiotemporal clusters of accidental poisoning mortality among Texas counties, US,

1980–2001. *Int J Health Geogr*. 2004; 3(1): 25.

54. Namosha E, Sartorius B, Tanser F. Spatial clustering of all-cause and HIV-related mortality in a rural South African population (2000–2006). *PloS One*. 2013; 8(7): e69279.

55. Rogerson P, Yamada I. *Statistical Detection and Surveillance of Geographic Clusters*. Boca Raton, FL: CRC Press; 2008.

56. Nana Yakam A, Noeske J, Dambach P, Bowong S, Fono L, Ngatchou-Wandji J. Spatial analysis of tuberculosis in Douala, Cameroon: clustering and links with socio-economic status. *Int J Tuberc Lung Dis*. 2014; 18(3): 292-7.

57. Li X, Chen K. Scan statistic theory and its application in spatial epidemiology. *Zhonghua Liu Xing Bing Xue Za Zhi*. 2008; 29(8): 828-31.