



## Original Article

## Incidence trends and spatial distribution of thyroid cancer in the Chinese female population from 1990 to 2019



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## ARTICLE INFO

## Keywords:

Thyroid cancer  
Trend analysis  
Spatial distribution  
Female

## ABSTRACT

**Objective:** This study aimed to analyze the incidence trends and spatial distribution characteristics of thyroid cancer among Chinese females from 1990 to 2019, thereby providing a scientific foundation and data support for the development of prevention and control policies.

**Methods:** Thyroid cancer incidence data from the Global Burden of Disease (GBD) research and the annual report from the Chinese Tumor Registration were utilized. The standardized thyroid cancer incidence rate among Chinese females 1990 to 2019 was described to understand the changes in developmental trends. The JoinPoint Regression Model was employed using Excel 2019, GraphPad Prism 8, JoinPoint Regression Program 4.8.0.1, and ArcGIS 10.2.

**Results:** Thyroid cancer's standardized incidence among female Chinese continued to increase at 1.7% per year (annual average percentage change [AAPC] = 1.7,  $P < 0.001$ ), and the spatial distribution was clustered. The main high-incidence areas were North, East, and Northwest China.

**Conclusions:** Thyroid cancer incidence in Chinese women is rapidly increasing, and its spatial distribution is concentrated. Strengthening monitoring, prevention, and control efforts in the relevant areas is warranted.

## Introduction

Thyroid cancer is a frequent and common disease of the endocrine system and the global malignant tumor statistics of the International Agency for Research on Cancer (GLOBOCAN 2018) show that thyroid cancer is the ninth most common malignant tumor in the world. The global standardized incidence rate of thyroid cancer among males and females is 3.1/100,000 and 10.2/100,000, respectively, and is showing a rapid growth trend. China has been facing the same situation, and the China Tumor Registry in 2015 shows that the incidence rate of thyroid cancer in China is 14.6/100,000, ranking seventh in incidence rate among all malignant tumors. Among females in China, the incidence rate is 22.56/100,000, ranking fourth in incidence rate, making thyroid cancer a serious threat to the health of females in China.<sup>1-4</sup>

## Methods

## Source material

This study used data from the Global Burden of Disease (GBD) database of standardized incidence rates of female thyroid cancer in China from 1990 to 2019 in the Chinese region and data from the Chinese Tumor Surveillance Sites of the 2018 Annual Report of the Chinese Tumor Registry.

The GBD study began in 1988, with support from the World Health Organization (WHO) and the World Bank, and was pioneered by the Harvard School of Public Health in the United States with the financial support of the Bill and Melinda Gates Foundation. The Center for Health Measurement and Evaluation Research at the University of Washington in the United States took the lead in setting up the GBD research group

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<https://doi.org/10.1016/j.apjon.2024.100529>

Received 1 April 2024; Accepted 28 May 2024

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and establishing The Global Health Data Exchange (GHDx) database, which is currently the most important database for global burden of disease research, containing data on seven measures of incidence, mortality, and prevalence for 364 diseases in 675 countries and territories worldwide since 1990. As the database is publicly available, any nonprofit organization or individual researcher can apply for access to and download the corresponding research data through the official website of the GHDx database.

The Annual Report of China's Tumor Registry is an indispensable and invaluable source of authority, authenticity, accuracy, and great influence on cancer prevention and control in China. By the end of 2018, 574 registries were conducting population-based tumor registration in China, covering a population of 438 million and providing a more comprehensive picture of the incidence of cancer, death, survival status, and development trends in China. The Annual Report of China's Tumor Registry (2018) summarizes cancer surveillance data from China's tumor registration areas in 2015, including a review and quality control of the data from 388 tumor registries across the country, covering 142 urban areas and 246 rural areas, with a population of 320,915,849 (162,763,047 females and 158,152,802 males), accounting for 23.55% of the country's 2015 year-end population.

*Data analysis*

Descriptive statistics were used to describe the overall trend of the standardized incidence rate of female thyroid cancer in China. The Joinpoint regression model was used to analyze the annual percentage change (APC), and annual average percentage change (AAPC) of the standardized incidence rate, and spatial autocorrelation analysis was performed using ArcGIS 10.2 to explore the characteristics of spatial distribution of the standardized incidence rate of female thyroid cancer in China.

*Joinpoint regression model*

The JPR Model computes annual % changes in the standardized incidence rate as well as the average annual % change in thyroid cancer among Chinese females in segmented regions by identifying turning points from 1990 to 2017. The model equation for the linkage point regression model is

$$E[y|x] = \beta_0 + \beta_1 x + \delta_1(x - \tau_1)^+ + \dots + \delta_k(x - \tau_k)^+$$

where,  $y$  is the dependent variable of the Joinpoint regression model, that is, the standardized thyroid cancer incidence rate among Chinese females;  $x$  is the independent variable of the Joinpoint regression model, that is, the year (1990, 1991, 1992, ..., 2017, 2018, 2019);  $\beta$  is the constant of the Joinpoint regression model;  $\delta_i$  is the regression coefficient of each segmented function in the Joinpoint regression model;  $\tau_i$  is the unknown turning point; and  $k$  is the number of turning points in the regression model.<sup>5,6</sup>

*Disease mapping*

Disease distribution maps depict geographical patterns of disease occurrence and reflect their spatial distributions. Disease mapping, crucial in spatial epidemiology, involves the use of spatial interpolation methods to estimate disease occurrence in unknown areas based on known observations, generating continuous disease maps. It is an essential tool for epidemiological research, disease prevention, and disease heterogeneity recognition.

Previous studies revealed spatial variations in thyroid cancer incidence rates. With economic, social, and demographic shifts, this study focuses on whether the geospatial distribution has changed and what changes have occurred. Using the annual standardized thyroid cancer incidence rates (1/100,000) among females in China and ArcGIS thematic mapping, we aimed to visually assess regional distribution variations, offering insights for further research.

*Spatial autoregressive analysis*

In the real geographic world, spatial objects do not exist independently but have a strong spatial dependence on each other owing to the interaction and spatial diffusion between neighboring features. Based on this, spatial autocorrelation analysis quantifies whether the attribute value of an element is associated with the attribute values of its neighboring spatial points by analyzing the potential dependence between the observed data of the attribute variables in the distribution area. Generally speaking, a positive correlation indicates that the attribute value features have the same trend as their spatial neighboring units, representing the existence of a spatial agglomeration phenomenon, whereas a negative correlation indicates that the attribute value features have the opposite trend with their spatial neighboring units, representing the existence of a spatial dispersion tendency, which is an important component of spatial statistics and has often been used in recent years for the study of the geographic distribution characteristics of epidemiology autocorrelation analysis.

Using ArcGIS spatial analysis tools to analyze the spatial autocorrelation of the regional distribution of the standardized thyroid cancer incidence rate among females in China, we can determine whether there is a spatial autocorrelation, providing clues for further analysis of the spatial aggregation.

In this study, global spatial autocorrelation and local spatial autocorrelation analyses were performed using Moran's I statistic, and the basic principles are as follows:

*Global Moran's I statistic.* Moran's index (Moran's I) is the most commonly used statistic to describe global spatial autocorrelation, and its expression is defined as

$$I = \frac{n}{\sum_i \sum_j w_{ij}} \cdot \frac{\sum_i \sum_j w_{ij}(z_i - \bar{z})(z_j - \bar{z})}{\sum_j z_i - \bar{z}}$$

where,  $w_{ij}$  is the weight between the objects  $i$  and  $j$ , calculated based on the spatial neighborhood, and is the attribute mean. After variance normalization, the value of Moran's I is normalized to the value of [-1,1].

- ① Positive correlation (> 0): represents the emergence of a clustering trend of similar values in neighboring areas, such as high - high, low - low;
- ② Negative correlation (< 0): represents the emergence of clustering characteristics of similar attribute values, such as high - low, low - high;
- ③ Random distribution (= 0): represents random distribution of attribute values without spatial autocorrelation feature.

*Local spatial autocorrelation.* Global spatial autocorrelation analysis reflects the overall spatial autocorrelation pattern of attribute data. However, it is difficult to find varying spatial autocorrelation features existing in different locations or regions. The local analysis index of spatial autocorrelation was calculated at different locations to reflect the clustering characteristics of their spatial neighbors.

The local Moran's I can reveal the spatial heterogeneity characteristics embodied by the spatial autocorrelation features of the attribute data, used to identify the different correlation features existing in different regions, and is a commonly used LISA metric, defined as

$$I_i = \frac{n}{\sum_j w_{ij}} \cdot \frac{\sum_j w_{ij}(z_i - \bar{z})(z_j - \bar{z})}{\sum_i (z_i - \bar{z})}$$

Using the local spatial autocorrelation method, we analyzed the spatial aggregation characteristics of thyroid cancer incidence/mortality among females in China and clarified its aggregated geographic areas to provide a scientific basis for the next step of the government and the National Health Administrative Department to target the deployment

and allocation of medical manpower and material resources for the prevention and control of thyroid cancer.

*Statistical software*

This study employed Excel 2019 for data organization and statistics, GraphPad Prism8 for plotting, the Joinpoint Regression Program for trend analysis of thyroid cancer incidence/mortality among Chinese females, and ArcGIS 10.2 for mapping and spatial autocorrelation.

**Results**

*Trends in the standardized incidence rate of female thyroid cancer in China, 1990–2019*

From 1990 to 2019, there were 409,408 cases of female thyroid cancer in China, from 6931 cases in 1990 to 21,762 cases in 2019, an increase of 213.98%. In 1990, the standardized incidence rate of female thyroid cancer in China was 1.52 per 100,000, and in 2019, the standardized incidence rate reached 2.41 per 100,000, an increase of 58.55% (Figs. 1 and 2).

*Analysis of Joinpoint regression models*

The results of the descriptive statistical analysis of the trend in the standardized incidence rate of thyroid cancer among Chinese females showed that the incidence generally exhibited an increasing trend from 1990 to 2019. To clarify the yearly changes in long-term trends further, this study used a linkage point regression model to segment the data on the standardized incidence rates of female thyroid cancer over the past three decades to explore the long-term trends in the standardized incidence rates of female thyroid cancer further. Temporal trend analysis of female thyroid cancer incidence rate in China was expressed in terms of annual percentage change and annual average percentage change.

Overall, the APC values of the standardized incidence rate of thyroid cancer in females in China showed an increasing trend from 1990 to 2019. The Joinpoint regression model divided the observation period into five intervals (1990–2000, 2000–2003, 2003–2010, 2010–2016, and 2016–2019), in which the standardized incidence rates of thyroid cancer among Chinese females increased at an annual rate of 2.42%, 2.56%, and 3.29% in 1990–2000, 2003–2010, and 2016–2019, respectively.

The AAPC value for the standardized incidence rate of thyroid cancer in females in China from 1990 to 2019 was 1.7, indicating an annual rate increase of 1.7% over the past 30 years (Fig. 3).

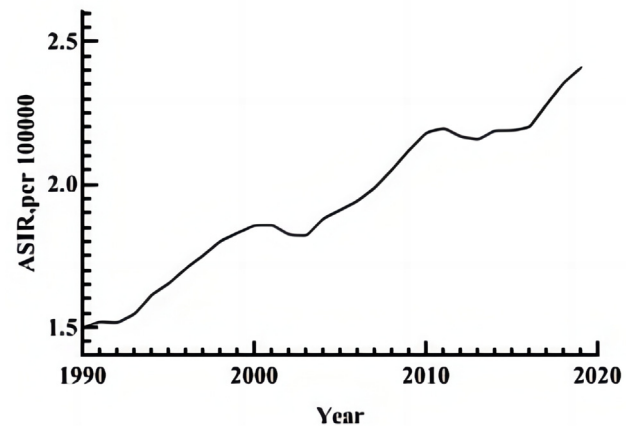


Fig. 2. ASIR of thyroid cancer in the Chinese female population. ASIR, age-standardized incidence rate.

*Spatial analysis*

*Map of standardized incidence rates of thyroid cancer in Chinese women*

The regional distribution map of the standardized incidence rate of thyroid cancer in females in China shows differences in the spatial distribution, with the standardized incidence rate for females in Northern, Eastern, and Northwestern China being significantly higher than that in other parts of the country (Fig. 4).

The main areas with high thyroid cancer standardized incidence rates among females (> 40/100,000) were Hangzhou, Daishan, Jiashan, Fuqing, Shangyu, Yinzhou, Jiaying, Wuhan, Dalian, Shanghai, Kelamayi, and Lucheng districts. The highest standardized incidence of thyroid cancer was observed in Hangzhou City, Zhejiang Province (62.08/100,000 individuals), (Fig. 5).

*Global spatial autocorrelation*

In this study, we used the ArcGIS spatial analysis tool to analyze the global spatial autocorrelation of the standardized incidence rate of thyroid cancer in Chinese females, and the results showed that the value of Moran's I of the standardized incidence rate of thyroid cancer in Chinese females in 2015 was 0.113736 ( $P < 0.001$ ), which indicated that the standardized incidence rate of thyroid cancer in Chinese women was not randomly distributed, but rather, there was a significant positive spatial autocorrelation. The distribution of the incidence rate of thyroid cancer in Chinese females was not randomly distributed. With a Z score of 17.63, the probability of randomly generating this clustering pattern is < 1% (Fig. 6).

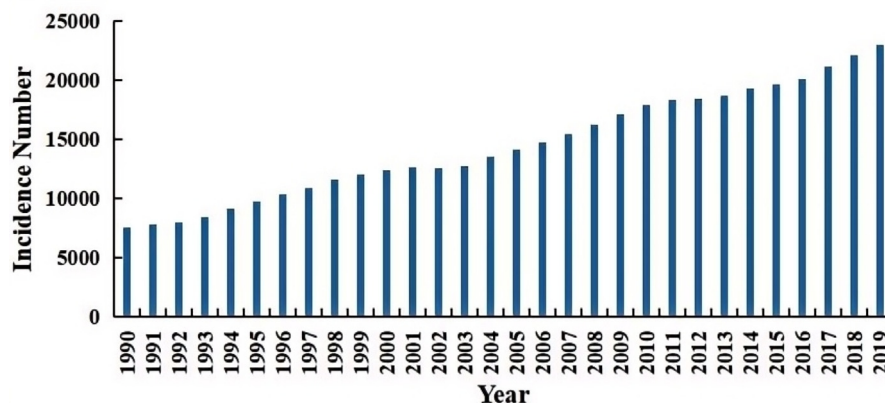


Fig. 1. Number of thyroid cancer in Chinese female population.

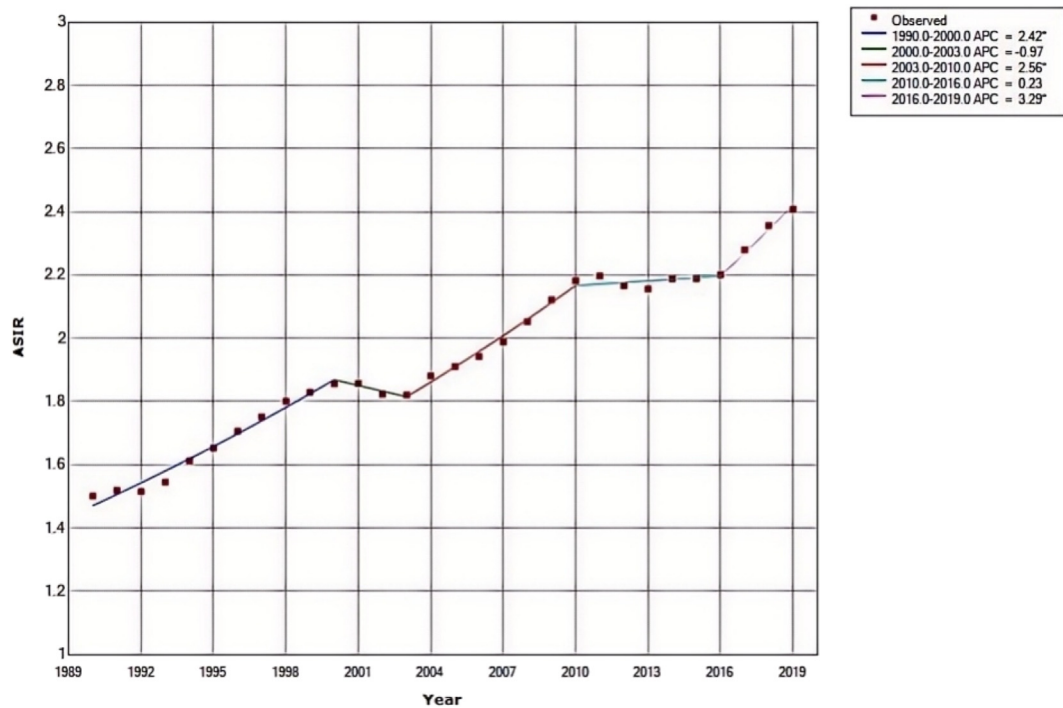


Fig. 3. Annual percent change of thyroid cancer in Chinese female population.

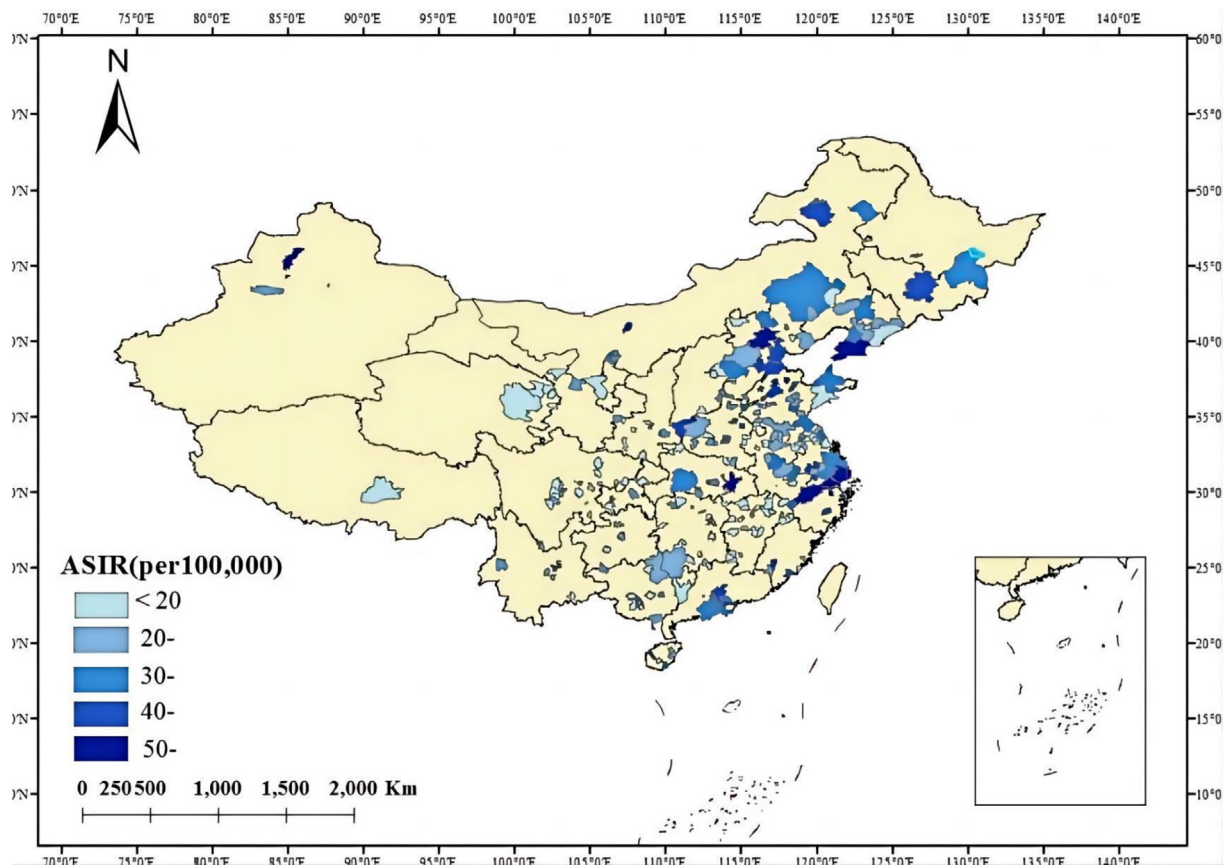


Fig. 4. ASIR of thyroid cancer map in China. ASIR, age-standardized incidence rate.

*Local spatial autocorrelation*

The spatial clustering and distribution of outliers of the standardized incidence rate of thyroid cancer in females in China were analyzed by

local autocorrelation using the LISA statistic to identify the hotspots, coldspots, and spatial outliers with statistical significance. In 2015, the standardized incidence rate of thyroid cancer in China showed a “high”

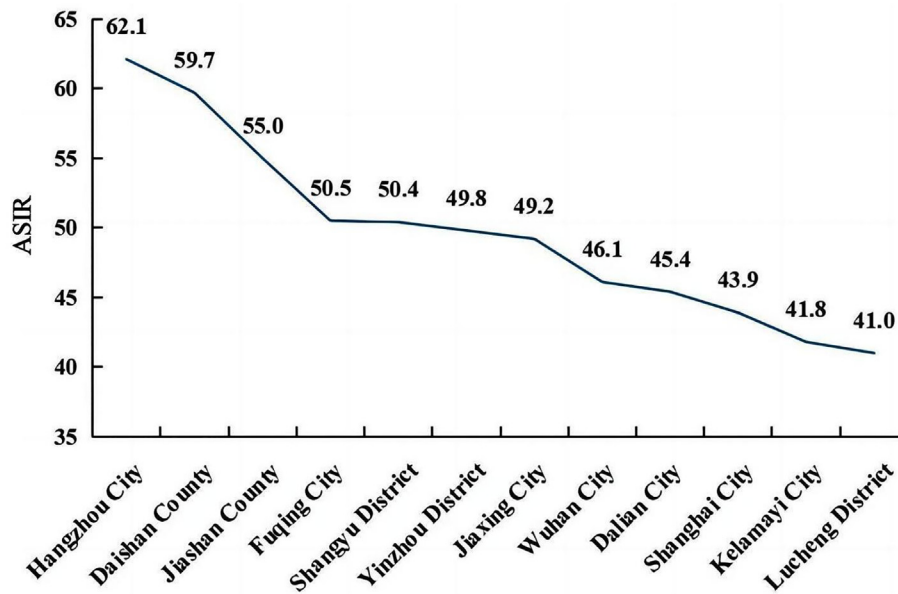


Fig. 5. ASIR of district in China (> 40, per 100,000). ASIR, age-standardized incidence rate.

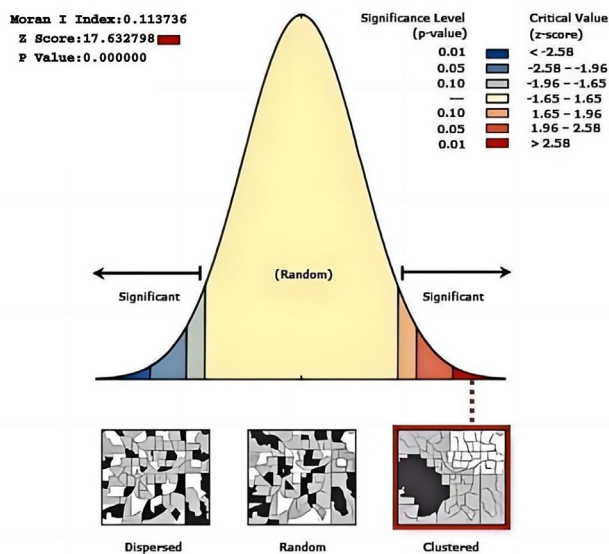


Fig. 6. Global Moran's I of ASIR in China. ASIR, age-standardized incidence rate.

density. In 2015, the standardized incidence rate of thyroid cancer showed a “high” aggregation of areas, mainly in North, East, and Northwest China, which should be focused on as high incidence density aggregation areas (Fig. 7).

**Discussion**

Thyroid cancer is a malignant tumor that is predisposed to sex. According to global cancer statistics, the global incidence of thyroid cancer among females is three times higher than that in males, accounting for 5.1% of the total cancer burden in females. In Korea, the incidence of thyroid cancer is the highest in both males and females, and in Canada, Australia, New Zealand, and East Asia, the incidence is much higher in females than in males.<sup>7-12</sup>

China has a large female population, an important part of the force of social production and an indispensable core member of every family.

Women’s health is related to all aspects of the country’s future development.

It was found that the incidence of thyroid cancer in the Chinese female population continued to increase from 1990 to 2019, with a fast growth rate, which is one of the major diseases affecting women’s health; therefore, the prevention and control of thyroid cancer needs to be further strengthened.<sup>6,13-15</sup>

According to previous studies, the incidence of thyroid cancer is related to the level of regional economic development,<sup>16</sup> industrial lifestyle and environmental factors have an impact on the occurrence of thyroid cancer. In the past 30 years, with the rapid development of industrialization in China, processed foods are rich in food additives, as well as environmental pollutants such as construction materials, may change thyroid function and induce thyroid cancer.<sup>17</sup> In addition, lack of exercise and diet preference also have adverse effects on the occurrence of thyroid cancer.<sup>18,19</sup>

We analyzed the spatial autocorrelation of the incidence rate of thyroid cancer among females in different regions of China and explored in depth the characteristics of spatial aggregation of thyroid cancer incidence rate in different regions, and found that spatially, there is a large risk of thyroid cancer incidence among females in different regions. The results showed that the incidence of carcinoma of thyroid in Chinese women was not uniform and showed spatial aggregation. The regions with high incidence of thyroid cancer in Chinese women were mostly located in the eastern and northern coastal regions, where the population was dense and the economy was developed, which was consistent with the previous studies.<sup>20-24</sup>

To effectively reduce the incidence rate of thyroid cancer and address the challenges posed by its spatial clustering, comprehensive prevention and control efforts must be implemented at multiple levels.

Firstly, the policy level should strengthen its emphasis on thyroid cancer prevention and control, formulate and improve relevant policies, increase investment in thyroid cancer research, and promote the development of early screening and diagnostic technologies for thyroid cancer. At the same time, medical assistance for thyroid cancer patients should be enhanced to reduce their financial burden, improve treatment outcomes, and enhance their quality of life.

Secondly, public education and promotion are also crucial. Wide-spread campaigns should be conducted to disseminate knowledge about thyroid cancer prevention and control, raising public awareness and

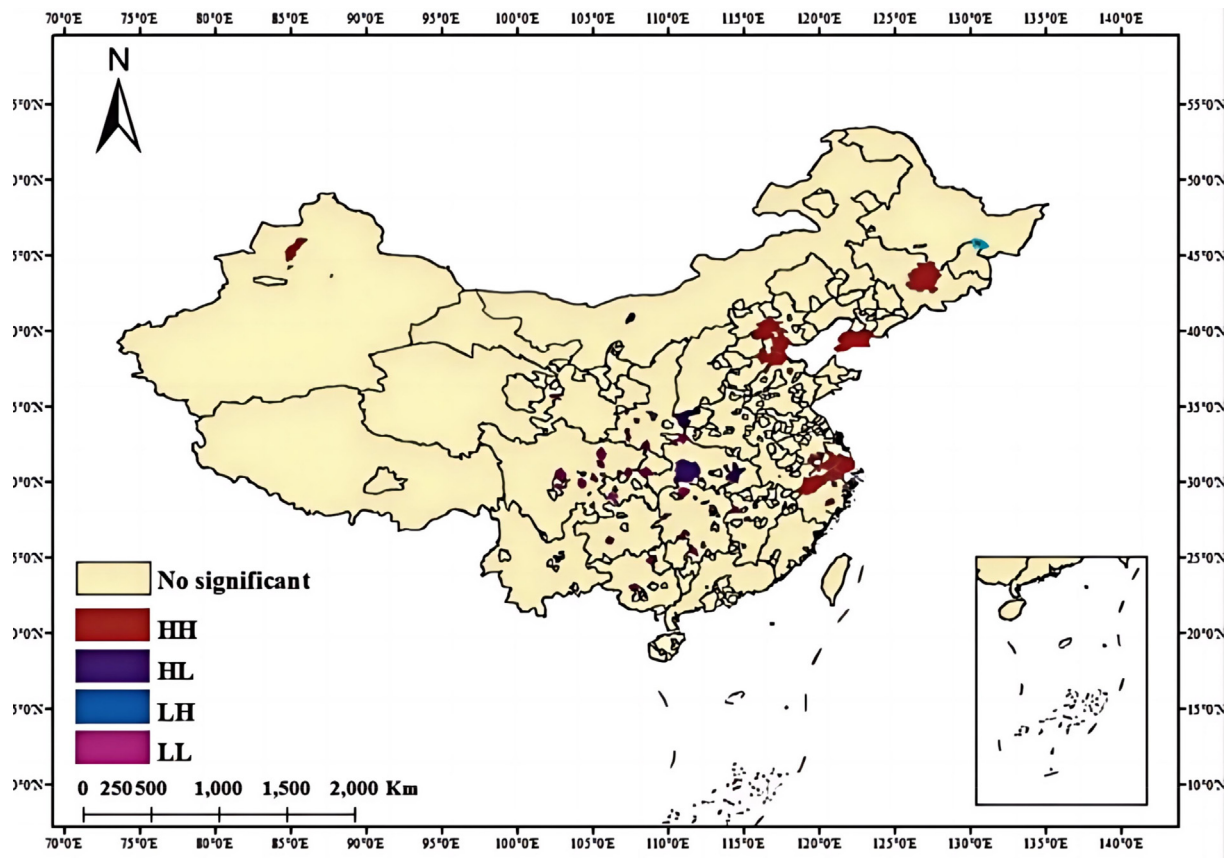


Fig. 7. LISA of ASIR of thyroid cancer in the Chinese female population. ASIR, age-standardized incidence rate.

attention to the disease. Advocating healthy lifestyles, including balanced diets, moderate exercise, and the reduction of unhealthy habits, can help reduce the risk of thyroid cancer.

Furthermore, medical institutions should strengthen their diagnostic and treatment capabilities for thyroid cancer. By training healthcare professionals and enhancing their expertise in thyroid cancer diagnosis, treatment, and nursing, they can provide better medical services to patients. Additionally, establishing sound diagnostic norms and quality control systems for thyroid cancer ensures that patients receive scientific and standardized treatment.

In addressing the spatial clustering of thyroid cancer, we need to strengthen cooperation and exchange among regions. Sharing medical resources, conducting joint research, and establishing regional thyroid cancer prevention and control networks can optimize resource allocation and share experiences, thereby improving the overall level of thyroid cancer prevention and control in the region.

Lastly, we should also pay attention to the mental health issues of thyroid cancer patients. Enhancing psychological counseling and support can help patients reduce psychological pressure and anxiety, improving their quality of life and sense of well-being.

#### Limitations

This study analyzed the incidence trend and spatial distribution of thyroid cancer in Chinese female population from 1990 to 2019, and provided theoretical basis for the development of thyroid cancer prevention and control measures in China. However, there are still limitations. First, the data sources of this study are Global Disease and Health Database and Chinese Cancer Registry annual report, which may have

data authenticity bias and underreporting. In addition, this study only analyzed the spatial distribution pattern of thyroid cancer incidence in women in China, and no further analysis was performed on the areas with strong spatial clustering.

#### Conclusions

In the past three decades, the incidence rate of thyroid cancer among women in China has continued to rise, with a continuously increasing number of cases and a significant spatial clustering characteristic. This is a complex social and health issue that requires comprehensive prevention and control efforts on multiple levels. We recommend taking measures such as policy guidance, public education, strengthening mutual cooperation among medical institutions, providing more precise nursing and psychological support for patients, in order to reduce the incidence of thyroid cancer in Chinese female population and improve their quality of life.

#### Ethics statement

We did not require ethical approval for our study specifically, as the GBD data were unidentified and aggregated by the University of Washington Institute for Health Metrics and Evaluation, which received informed consent waivers approval from the University of Washington Institutional Review Board.

#### Funding

This study did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

### CRedit authorship contribution statement

X.Q: Data curation, Writing – Original draft preparation; Y.C: Conceptualization, Methodology; C.M: Software, Methodology; Ch.Ma: Visualization, Investigation; B.B: Writing – Reviewing and Editing; C.W: Supervision, Validation. All authors had full access to all the data in the study, and the corresponding author had final responsibility for the decision to submit for publication. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

### Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

### Data availability statement

All data are openly available in the Global Health Data Exchange GBD Results Tool, <http://ghdx.healthdata.org/gbd-results-tool>.

### Declaration of generative AI and AI-assisted technologies in the writing process

No AI tools/services were used during the preparation of this work.

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