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Contribution of industrial density and socioeconomic status to the spatial distribution of thyroid cancer risk in Hangzhou, China

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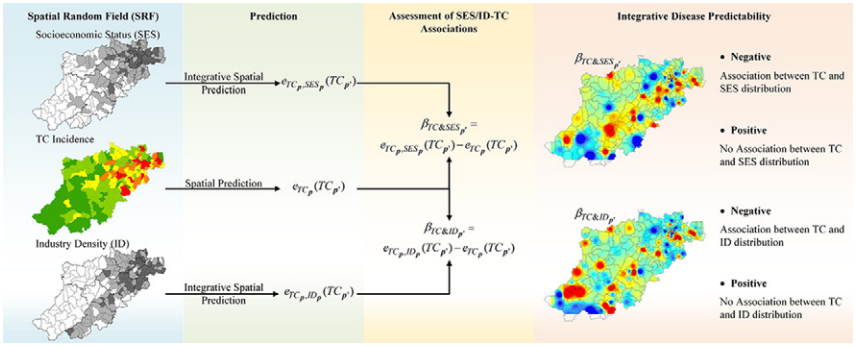
HIGHLIGHTS

- More accurate incidence maps produced by Bayesian maximum entropy
- Assess the spatially distributed strength of the "exposure-disease" association
- Socioeconomic status is a risk factor for thyroid cancer, overall and locally.

GRAPHICAL ABSTRACT



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ABSTRACT

Background: The thyroid cancer (TC) incidence in China has increased dramatically during the last three decades. Typical in this respect is the case of Hangzhou city (China), where 7147 new TC cases were diagnosed during the period 2008–2012. Hence, the assessment of the TC incidence risk increase due to environmental exposure is an important public health matter.

Methods: Correlation analysis, Analysis of Variance (ANOVA) and Poisson regression were first used to evaluate the statistical association between TC and key risk factors (industrial density and socioeconomic status). Then, the Bayesian maximum entropy (BME) theory and the integrative disease predictability (IDP) criterion were combined to quantitatively assess both the overall and the spatially distributed strength of the "exposure-disease" association.

Results: Overall, higher socioeconomic status was positively correlated with higher TC risk (Pearson correlation coefficient = 0.687, $P < 0.01$). Compared to people of low socioeconomic status, people of median and high socioeconomic status showed higher TC risk: the Relative Risk (RR) and associated 95% confidence interval (CI) were found to be, respectively, RR = 2.29 with 95% CI = 1.99 to 2.63, and RR = 3.67 with 95% CI = 3.22 to 4.19. The "industrial density-TC incidence" correlation, however, was non-significant. Spatially, the "socioeconomic status-TC" association measured by the corresponding IDP coefficient was significant throughout the study area: the mean IDP value was −0.12 and the spatial IDP values were consistently negative at the township level. It was found that stronger associations were distributed among residents mainly on a stripe of land from northeast to southwest (consisting mainly of sub-district areas). The "industrial density-TC" association measured by its IDP coefficient was spatially non-consistent.

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Conclusions: Socioeconomic status is an important indicator of TC risk factor in Hangzhou (China) whose effect varies across space. Hence, socioeconomic status shows the highest TC risk effect in sub-district areas.

1. Introduction

Thyroid cancer (TC) accounting for approximately 2% of all cancers diagnosed worldwide is the most common endocrine malignant tumor (Ferlay et al., 2015). During the last three decades, TC incidence, especially papillary sub-type TC, has increased dramatically in many countries (Zamora-Ros et al., 2015). Predominantly, this increase could be attributed to the increasing incidence of small (<2 cm) well-differentiated papillary TC. Therefore, previous studies have suggested that it is an over-diagnosis phenomenon, i.e. thyroid tumors that are indolent and would never cause symptoms were actually diagnosed due to the enhanced diagnostic ability to detect very small thyroid tumors (Davies and Welch, 2006, 2014). However, not all studies have supported this explanation. Instead, certain studies have suggested that the increasing number of all-size TC is due to actual incidence increase, particularly, part of the rising incidence may be attributed to demographic variables, changing lifestyle and environmental exposures (Chen et al., 2009; Vigneri et al., 2015).

Ionizing radiation exposure (especially during childhood), history of benign thyroid disease, family history of TC and change of thyroid stimulating hormone are known TC risk factors (Hemminki et al., 2005; Evangeliou et al., 2014; Fei et al., 2014; Zamora-Ros et al., 2015). Despite improved knowledge concerning TC risk factors, a large part of TC etiology still remains unknown (Harari and Singh, 2016). Over the past three decades, China in general, and Hangzhou city in particular, have experienced rapid socioeconomic and industrial growth which also caused serious environmental problems, such as (*a*) air pollution ($PM_{2.5}$, PM_{10}, O_3 NO_2, CO, SO_2) from local and regional industrial factories (Yu et al., 2014), (*b*) heavy metals pollution (Cd, Co, Cr, Cu, Fe, Mn, Ni, Pb and Zn) from industrial and commercial zones with heavy traffic (Zhang and Wang, 2009), and (*c*) environmental endocrine-disrupting chemical pollution related to the rapid development of paper, printing and textile industries (Lou et al., 2012). Industry density is linked to exposure to environmental hazard chemicals (such as heavy metals), environmental endocrine-disrupting chemicals (polychlorinated biphenyls, PCBs, polybrominated diphenyl ethers, PBDEs), toxins and pesticides that could change the thyroid hormone level associated with TC (Leux and Guenel, 2010; Fernández-Navarro et al., 2012; Christensen, 2013). On the other hand, TC risk due to socioeconomic status (usually linked to healthcare access, use of detection tools and lifestyle) has also been previously reported (Roche et al., 2011; Reitzel et al., 2014; Siu et al., 2014). However, few studies have assessed quantitatively the "industry density/socioeconomic status-TC risk" association across a study area.

In public health research, confirming a deterministic association between disease and environmental exposure is a very important yet complicated issue. Although very desirable, such a deterministic association is rarely materialized in health practice, since it requires that all relevant physical and biological factors concerning the "exposure-disease" association are completely known (Christakos et al., 2014). On the other hand, although a stochastic association does not usually imply a definite (necessary and sufficient) association, it is a realistic and practical notion that provides useful insights into "exposure-disease" matters under conditions of uncertainty (Rothman et al., 2008). In the stochastic association setting above, the present work proposes an approach that integrates the Bayesian maximum entropy (BME; Christakos, 2000) theory with the integrative disease predictability (IDP) criterion to study "exposure-disease" associations. Specifically, the BME theory combines hard and soft data (in this case, corresponding to TC and risk factors, respectively) into a quantitative approach seeking to generate disease spread maps; and the IDP criterion provides a quantitative assessment of the strength (overall as well as locally distributed) of the "exposure-disease" association based on successful disease predictions by the BME theory (Christakos and Kolovos, 1999; Christakos and Serre, 2000a, 2000b). Hence, herein the proposed "exposure-TC incidence" association approach will be termed the BME-IDP approach. Lastly, there are other important aspects of the increased TC burden and the corresponding "exposure-TC risk" associations that remain unknown, particularly, how these associations are spatially distributed. The BME-IDP approach of the present work, also, aims to assess quantitatively the spatial distribution of the strength of the "industrial density/socioeconomic status-TC risk" associations.

2. Methods

2.1. TC data

As an ecological epidemiology study, the cancer records used in the present study were anonymized by the Cancer Registry Center (CRC), prior to analysis and processing. Totally, there are 7147 newly diagnosed TC cases in Hangzhou during 8.70 million person-years (International Classification of Disease: ICD-10 code C73). These cases were confirmed by the Hangzhou Center for Disease Control and Prevention (CDC) during the period 2008–2012. Detailed information about the TC incidence in Hangzhou could be found in the relevant literature (Fei et al., 2016a, 2016b). Briefly, all the cases were allocated to 200 specific Hangzhou townships according to their detailed residential information. Based on township-level, age-specific population data and TC incidence for different age-categories throughout China (available by the Chinese National Cancer Center (Hao and Chen, 2012)), the age-standardized TC incidence was calculated at the township level. In order to reduce unstable incidence estimation at the township level (which could be caused by small populations), 5-year average TC incidence was calculated and plotted in Fig. 1 (the total population for each township during the five years was estimated by multiplying their 2010 population by 5). From Fig. 1, it is apparent that the highest TC incidence values occur in the northeast part of Hangzhou. These 5-year average TC incidence values will be used below to assess quantitatively the TC association with potential risk factors.

2.2. Assessment of potential risk factors

A total of 10,309 industrial factories with their geographical location information in 2010 (in longitude and latitude) were obtained from the Hangzhou Environmental Protection Bureau (EPB). Chemical industry (17.61%), machinery and equipment industry (16.14%), non-metallic mineral industry (15.51%), metallurgical industry (10.84%), paper industry (9.23%), textile industry (6.68%), agricultural production industry (6.58%), food industry (6.28%), electronic communications industry (6.10%) and printing industry (1.59%) were the top ten industrial types, accounting for >96% of all industrial factories. After allocating these factories into specific townships, the industrial density (ID) for each township was calculated as the number of factories in every square kilometer ($1/km^2$). The ID values at the township level ranged from 0 to 11.46. According to the tertile values of ID, the spatial distribution of industry density in Hangzhou is shown in Fig. 2A. The industrial suburbanization started in Hangzhou in the 1980s and its pace was accelerated at the end of the 20th century (Feng and Zhou, 2005), hence most areas with the highest IDs were located in the suburban region of Hangzhou.