



## Original Article

# Spatial and temporal patterns of nasopharyngeal carcinoma mortality in China, 1973–2005



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## ABSTRACT

We fitted generalized linear models using data from three national retrospective surveys on cause of death in China to explore the spatial and temporal patterns of nasopharyngeal carcinoma (NPC) mortality over the period 1973 to 2005. The results suggest that there was a significant decrease in NPC mortality in China over time ( $p < 0.0001$ ), the mortality rate ratio (RR) for the two later time periods were 0.59 (95% CI: 0.55–0.64) for 1990–1992 and 0.42 (95% CI: 0.39–0.45) for 2004–2005 compared to that of 1973–1975. Residents living in the South China areas have an elevated risk of mortality from NPC compared to those living in North China across all three time periods, with the RR being 4.96 (95% CI: 4.31–5.70) in 1973–1975, 12.83 (95% CI: 10.73–15.34) in 1990–1992 and 15.20 (95% CI: 12.34–18.72) in 2004–2005. Although NPC mortality in most areas of China has reduced to very low levels, the widening geographical disparities in NPC mortality are still noteworthy. It may be necessary to target public health policies to address the widening geographical disparities in NPC mortality.

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## Introduction

Nasopharyngeal carcinoma (NPC) is a rare malignancy in most parts of the world, with the age-standardized incidence rate (ASIR) in most countries being well below 1 per 100,000 for both genders. There are, however, some remarkable geographic and racial differences in NPC incidence, and in particular it occurs much more frequently in Southeast Asia and China (>20 per 100,000 among southern Chinese) [1,2]. Rates of NPC also continue to be elevated in people who migrate to Western countries from these areas [3–5].

Epidemiological trends during the past decade suggest that mortality from NPC has fallen considerably around the world [6]. In China the age-standardized mortality rate (ASMR) decreased

substantially over the same period, with annual percentage changes of –2.5% in males and –2.2% in females between 2000 and 2011 [7]. Although the declining trends observed, there were an estimated 20,404 deaths in 2012 caused by NPC in China, accounting for 40% of the worldwide number of deaths from NPC [1].

Previous studies have shown that there is a marked geographic variation in NPC mortality rates across China [8–10]. The highest rates were seen in Guangdong province and the rates for the surrounding provinces (Guangxi, Hainan, Fujian and Hunan) were also somewhat elevated, with the general pattern being that rates were lower in the northern areas of China than in the south [8,11]. Based on the data from the national retrospective surveys on cancer mortality carried out in the periods of 1973–1975, 1990–1992, and 2004–2005, several studies have also shown that there was a downward trend in NPC mortality across all of mainland China [8,11]. Although one previous study [8] described the NPC mortality trends over time by province in China, they did not statistically examine whether the temporal trends for geographical variation

Abbreviations: NPC, nasopharyngeal carcinoma; ASIR, age-standardized rates; ASMR, age-standardized mortality rates; CMR, crude mortality rates; RR, rate ratio.

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observed were significant or not. In addition, they only compared the north-south patterns in NPC mortality. For this reason, this study aimed to use the data from three nationally representative death surveys to provide a spatial-temporal analysis of NPC mortality in China from 1973 to 2005 by seven geographical regions in China (much more homogeneous in each region than the north-south division) and used a statistical model to test whether the temporal trends for geographical variation were significant.

## Materials and methods

### Data sources

NPC mortality data were extracted from three national retrospective surveys on cause of death, conducted by the Chinese Ministry of Health in 1973–1975, 1990–1992 and 2004–2005. The data included the number and age of people dying from NPC, and the population of each geographical area. The three surveys of cause of death in China have been described in detail in previous publications [12–14]. Briefly, the First National Survey of Death Causes for the period 1973–1975 covered nearly all regions of mainland China (excluding Taiwan, Hong Kong, Macao, and 35 sparsely populated counties), with a total of 2514 million person-years [12]. The Second National Retrospective Sampling Survey of Death Causes for the period 1990–1992 included 263 sample points so that a total of 335 million person-years were investigated, accounting for 9.8% of the total national population [13]. The Third National Retrospective Sampling Survey of Death Causes for the period 2004–2005 covered 213 counties/cities/districts, accounting for 212 million person-years between 2004 and 2005 [14].

### Geographic unit of analysis

The basic geographic unit of analysis (building block) used in this study is province, or autonomous region or municipality of Beijing, Tianjin, Shanghai and Chongqing.

We divided mainland China into seven geographical regions (Fig. 1) in order to fit a space-time model. The list of provinces included in these regions can be found in Appendix A.

### Data analysis

We first calculated age-standardized mortality rates (ASMR), using the direct standardization method (to the Segi standard population), for each province and geographic region and each of the three death surveys.

The provincial level data were then aggregated into seven geographical regions. We used generalized linear models with a negative binomial error structure (to overcome over-dispersion [15]) to calculate rate ratio (RR) of death from NPC for the aggregated data for geographical region (with North China as a reference) after controlling for the other factors included in the model. A detailed description of the

models can be found in our previous publications [16–18]. Briefly, these analyses consisted of three models. First, we fitted a model with the main-effect variables of age group at death, sex and region, stratified by the period of death causes surveys (1973–1975, 1990–1992 and 2004–2005) to test whether the effect of region was significant in each survey period. Then we fitted the second model with the variables of age group and region included, stratified by sex and survey period to see if the effect of region for males and females was significant in each survey period. In the third model, we included the variables of age group, sex, region and survey period to test whether the effect of survey period was significant and also to validate whether the effect of region was still significant after further adjustment for survey period. Lastly, we added an interaction term between geographical region and survey period to the third model, and then a likelihood ratio test was conducted to determine if this interaction was significant to see whether the geographical variation over survey period is significant.

All significance tests with  $p$ -value  $< 0.05$  were taken to indicate statistical significance. Statistical analyses were performed in R software (version 3.2.5; R Foundation for Statistical Computing). All maps were created using ESRI (Environmental Systems Research Institute, Inc. Redlands, CA) ArcGIS 10.2 software.

## Results

### Mortality rate

From the mid-1970s to the mid-2000s there was a decrease in NPC mortality in China, as shown in Table 1. Average crude mortality rates (CMR) decreased from 1.99 per 100,000 in 1973–1975, to 1.74 per 100,000 in 1990–1992 and 1.57 per 100,000 in 2004–2005, and ASMR decreased from 2.56 per 100,000 in 1973–1975, to 1.94 per 100,000 in 1990–1992 and 1.38 per 100,000 in 2004–2005.

Values for the provincial ASMR estimates are presented in Appendix B. The overall NPC ASMR by province for the three mortality surveys are shown in Fig. 2. The provincial distribution map for male and female NPC ASMR can be found in Appendix C. In the period 1973–1975 Guangdong, Hainan and Guangxi had the highest ASMR (8.48 per 100,000 to 5.98 per 100,000), while the provinces in North China had lower rates (from 1.02 per 100,000 for Beijing to 1.66 for Shanxi). In the period 1990–1992 Guangdong still had the highest NPC ASMR (7.88 per 100,000), followed by two other provinces in South China (4.88 and 4.69 per 100,000 for Guangxi and Hainan respectively), while the ASMR for provinces in



Fig. 1. Schematic diagram of the division of China into seven geographical regions.

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