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RESEARCH ARTICLE

The lag effect of water pollution on the mortality rate for esophageal cancer in a rapidly industrialized region in China

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Abstract

The Huai River basin (located in eastern China) has a population of 180 million and has the highest risk of esophageal cancer (EC) mortality in China. Some studies found that contaminants in drinking water are a major risk factor for cancers of the digestive system. However, the effect of water pollution in the historical period on the current EC mortality remains unclear. Data were collected on the EC mortality rate in 2004 in the Huai River basin in 11 counties, and data on the surface water quality in the region from 1987 to 2004 were used. The Pearson correlation and the GeoDetector q-statistic were employed to explore the association between water pollution and the EC mortality rate in different lag periods, from linear and nonlinear perspectives, respectively. The study showed apparently spatial heterogeneity of the EC mortality rate in the region. The EC mortality rate downstream is significantly higher than that in other regions; in the midstream, the region north of the mainstream has a lower average mortality rate than that south of the area. Upstream, the region north of the mainstream has a higher mortality rate than that in the southern area. The spatial pattern was formed under the influence of water pollution in the historical period. 1996, 1997, and 1998 have the strongest linear or nonlinear effect on the EC mortality rate in 2004, in which the Pearson correlation coefficient and the q-statistic were the highest, 0.79 and 0.89, respectively. Rapid industrialization in the past 20 years has caused environmental problems and poses related health risks. The study indicated that the current EC mortality rate was mainly caused by water pollution from the previous 8 years. The findings provide knowledge about the lag time for pollution effects on the EC mortality rate, and can contribute to the controlling and preventing esophageal cancer.

Keywords Esophageal cancer · Lag effect · Water pollution · Spatial analysis · Rapid industrialization

Introduction

Esophageal cancer (EC) is a type of digestive tract cancer, ranked the eighth most common cancer worldwide and the sixth deadliest cancer. The 5-year survival rate ranges from 15 to 25% globally (Ferlay et al. 2010).

According to GLOBOCAN statistics, it is estimated that about 400,200 people die of this disease annually worldwide, and the mortality rate for EC is increasing rapidly (Torre et al. 2015). Although great efforts have been made to control the risk of EC, no prevention or early detection strategy has been proven conclusively to reduce the risk (Reid et al. 2010; Pennathur et al. 2013). Understanding risk factors affecting EC and reducing the incidence and mortality of the disease remains a challenge.

EC is caused by various factors (Ribeiro et al. 1996). The association between the EC mortality rate and environmental pollution factors has been analyzed in a large number of studies. Researchers have investigated water pollution (van Maanen et al. 1996; Beaumont et al. 2008); coal cooking pollution in

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indoor environments (Pan et al. 1999); concentrations of harmful gases, such as PM10, PM2.5, and NO_2, in outdoor air (Huang et al. 2017; Weinmayr et al. 2018); and concentrations of heavy metals, for example, selenium (Se) and zinc (Zn), in soil (Semnani et al. 2010; Keshavarzi et al. 2012).

China has one of the highest incidence rates of EC in the so-called Asian belt, accounting for 51.9% of the people who die from EC globally (Di et al. 2016). In China, the Huai River basin has the highest risk of EC mortality. According to the Chinese Third National Causes of Death Sampling Survey (2004–2005), the national mortality rate for EC is 15.21 per 100,000, but the rate in the Huai River basin is five times higher than the average national rate (Wei et al. 2010).

Since the 1980s, water pollution has become a significant problem in China, due to rapid industry and agriculture growth (Fu et al. 2007). A national survey carried out in 2004 revealed that 28% of 412 sections monitored for water quality were over grade V, the worst grade in the national standard for water quality (Shao et al. 2006). The Huai River basin, located in eastern China, is a typical region representing industrialization in a densely populated area. Since the 1980s, the water quality in the Huai River basin has been deteriorating every year. By the end of 1995, more than 80% of the rivers and other water bodies in the areas examined were contaminated (Tan et al. 2005). Chemical contaminants from unprotected and untreated industrial and domestic wastewater put residents' health at risk (Zhang et al. 2010). Several previous epidemiological studies suggested that contaminants in drinking water, for example, nitrate and nitrite, are a major risk factor for cancers of the digestive system (Murphy 1991; Yang et al. 2007). Numerous studies have found associations between water pollution and the incidence or mortality rate for EC (Tao et al. 2000; Cai et al. 2002; Zhang et al. 2003; Zhang et al. 2014). However, to our knowledge, no studies have analyzed the lag effect of water pollution on the mortality rate for EC, and how long the effect of water pollution on EC in the Huai River basin of China lasts remains unclear.

This paper is organized as follows. The next section describes data and methods. The "Results" section presents the results from linear and nonlinear methods. Discussions and conclusions are in the "Discussion" section. In this study, the lag effect of water pollution on the mortality rate of EC was analyzed using mortality data for EC in 11 counties in the Huai River basin in 2004, as well as water pollution data from 1987 to 2004.

Data and methods

Study area

The Huai River basin, located in eastern China (30° 55′–36° 36′ N, 111° 55′–121° 25′ E), spans four provinces (Henan, Anhui, Jiangsu, and Shandong). The total area is about 270,000 km^2 (Fig. 1). The population density in the region is 615 people/km^2, which is four times the average population density of the entire country. Since the 1980s, the Huai River basin has been suffering serious water pollution.

Data

Data on the EC mortality rates in the Huai River basin were obtained from the Chinese Center for Disease Control and Prevention and were age-standardized based on the census data in 2000. The study area included 11 counties in four provinces: Xiping County, Shenqiu County, and Luoshan County in Henan Province; Lingbi County, Yongqiao County, Yingdong County, Shou County, and Mengcheng County in Anhui Province; Jinhu County and Xuyi County in Jiangsu Province; and Wenshang County in Shandong Province (Fig. 1).

Data on the quality of the surface water in the Huai River basin were obtained from the China Environmental Quality Report (1987–2004) released by the State Environmental Protection Administration (Fig. 2). The water quality monitoring indicators included biochemical oxygen demand (BOD), chemical oxygen demand (COD), NH_4^+, NH_3, and volatile phenol.

Overall, the water quality grade increased from 1987 to 1995 (higher grade represent more pollution), and by 1995, the water pollution level of the Huai River peaked. Between 1987 and 2003, the water quality deteriorated from upstream to downstream, ranging from Grade III to Grade VI (Water Quality Standards: GB3838-1988, GB3838-2002), which means that the water was not suitable for drinking directly (Fig. 3). The severe water pollution in the Huai River basin has attracted the attention of the Chinese government. In 1996, the State Council approved the Five-Year Plan for Water Pollution Prevention and Control in the Huai River basin policy. The policy stated that the Huai River had to be clean before the end of the twentieth century; thus, the pollution of the Huai River was alleviated during the following 5 years. This plan ended in 2000, and the pollution in the Huai River rebounded during the following 3 years due to the short-term decline in local government supervision.

Methods

The association between long-term exposure to water pollution and EC mortality rates was quantified with linear and nonlinear models. In a linear model, the parameters are clear, and the calculation is easy to implement and is repeatable. However, the relationship between disease and environment in reality is fundamentally nonlinear. A linear method is a first-order approximation for reality, and a

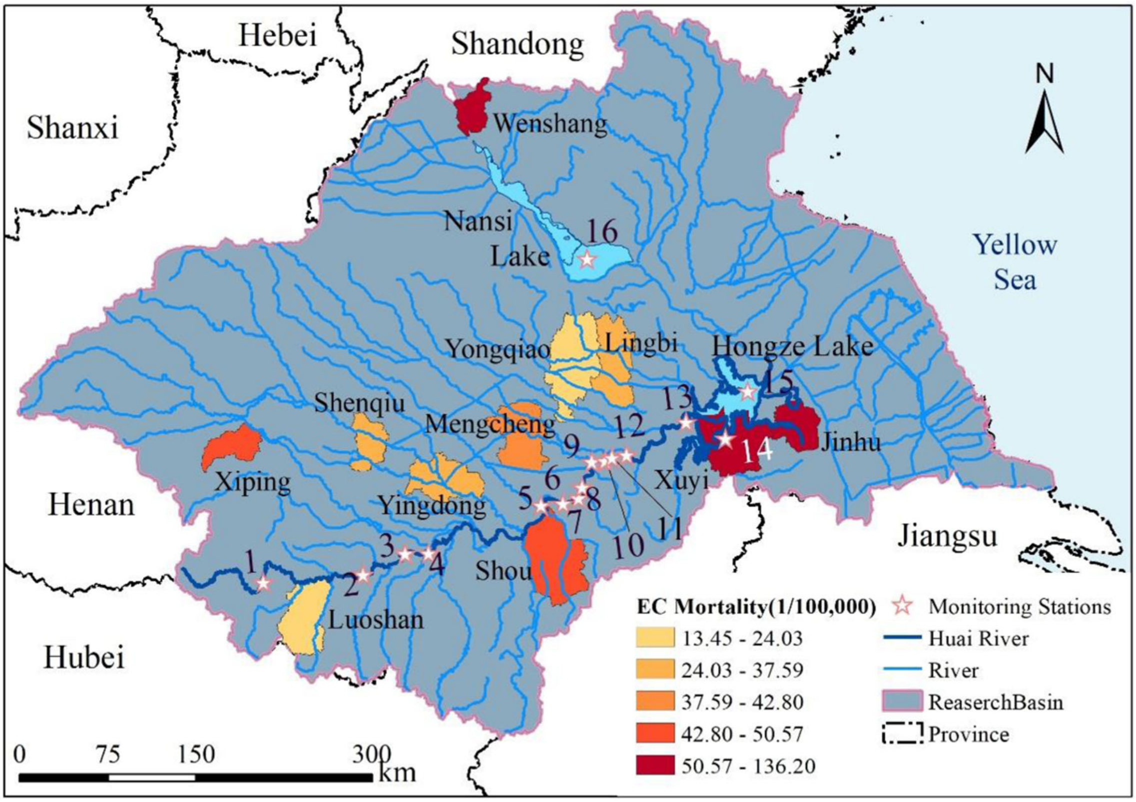


Fig. 1 EC mortality rate for 11 counties in the Huai River basin and 16 monitoring stations

linear model cannot fully account for the relationship compared with nonlinear methods. In this study, the Pearson correlation coefficient and the GeoDetector q-statistic were selected to reveal the association between long-term exposure to water pollution and EC mortality rates, in linear and nonlinear perspectives.

The GeoDetector q-statistic is a novel method for exploring the spatial heterogeneity of a natural phenomenon and the underlying explanatory factors (Wang et al. 2010). When there is a nonlinear relationship between an explained variable and explanatory variables, this method is more applicable than a linear model (Wang et al. 2016). The q-statistic can be expressed as follows:

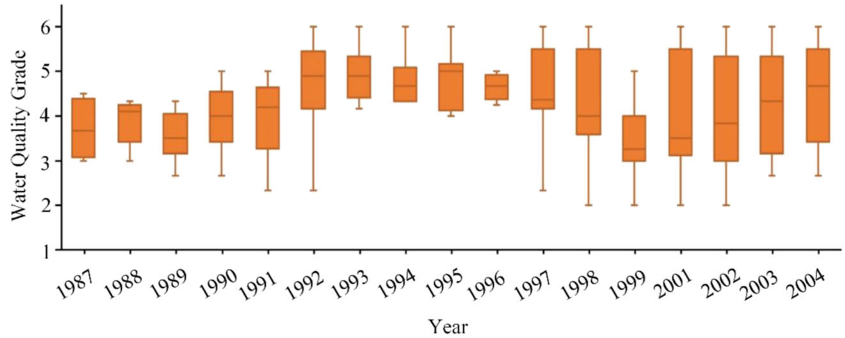
$$q = 1 - \frac{\sum_{h=1}^{L} N_h \sigma_h^2}{N\sigma^2} = 1 - \frac{SSW}{SST}$$

$$SSW = \sum_{h=1}^{L} N_h \sigma_h^2$$

$$SST = N\sigma^2$$

If $h = 1,2\ldots, L$ is the stratum of the explanatory variable; where N_h and N present the number of units in stratum h and in the whole area, respectively; σ_h^2 and σ^2 present the variances of the stratum h and the whole study area, respectively. SSW and SST are the Within Sum of Squares and the Total of Sum of Squares, respectively. The range of q is [0,1]; this means the

Fig. 2 Water pollution grades for 16 monitoring stations from 1987 to 2003



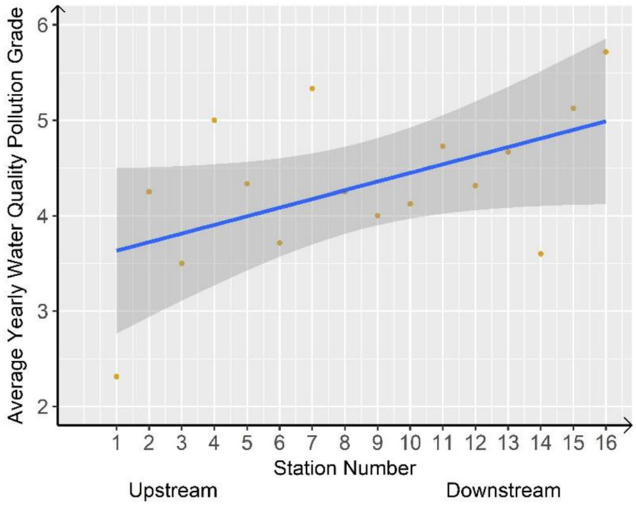


Fig. 3 Average yearly water pollution grade for 16 monitoring stations between 1987 and 2003

selected factor explains $q \times 100\%$ of the explained variable. The bigger the q value, the stronger the relationship between the explained variable and the explanatory variables, and the larger the nonlinear association within them.

If h is the stratum of the explained variable, then the q value calculated by this formula represents the spatial heterogeneity of the explained variable itself. The range of q is in [0,1], and the bigger the q value, the stronger the spatial heterogeneity of the explained variable.

In this study, the spatial heterogeneity of the EC mortality rate among counties was measured with the q-statistic, and the lag effect of water pollution on the EC mortality rate was assessed by calculating the association between them at different lag times, for example, the Pearson correlation coefficient or the q-statistic for the EC mortality rate in 2004 and water pollution in each year between 1987 and 2004.

Results

The study showed that there is statistically significant spatial heterogeneity of the EC mortality rate in the study region, with a q-statistic of 0.90 ($p < 0.05$). The EC mortality rate in the downstream region was apparently higher than in other regions. For example, Xuyi and Jinhu counties in the downstream region next to Hongze Lake, and Wenshang County close to Nansi Lake, had an average mortality rate of $108.43/10^5$, while the other regions presented an average mortality rate of $36.21/10^5$. In the midstream region, the region north of the mainstream region had a lower average mortality rate ($32.82/10^{5)}$, while the region south of the mainstream region showed an average mortality rate of $50.57/10^5$. In the upstream region, the region north of the mainstream region presented a higher mortality rate ($41.90/10^{5)}$, while the region south of the mainstream region had a lower mortality rate, $24.03/10^5$.

The study found that the EC mortality rate was not spatially consistent with the water quality in the same year. In 2004, the highest EC mortality rate was present in the downstream region, while the highest water pollution level was found in the midstream region, and during the historical period, higher water pollution levels were measured in the region. This result indicates that the current EC mortality rate is related to the water environment's historical period. The corresponding question is in which period does water pollution have the largest influence on the current EC mortality? Therefore, the association between the EC mortality rate and water pollution at different time lags was analyzed further.

The Pearson correlation coefficients between the EC mortality rate in 2004 and water quality in 1987–2004 were calculated. The results show that the r value was highest in 1997 and 1998 (0.81 and 0.82, $p < 0.05$, respectively). This result indicates that these 2 years have high linear correlations with the EC mortality rate in 2004 (Table 1).

The GeoDetector q-statistic was also calculated between the EC mortality rate in 2004 and the water quality in 1987–2004. The results show that the strongest association was between the EC mortality rate in 2004 and the water quality in 1996, with a q of 0.92 ($p < 0.05$); see Table 1.

Based on the findings above, we identified that 1996, 1997, and 1998 had the strongest linear or nonlinear effect on the EC mortality rate in 2004. To get a stable relationship between the EC mortality rate in 2004 and water pollution on a larger time scale, the Pearson correlation and the q-statistic between the EC mortality rate in 2004 and water pollution in a 3-year average of 1987–1989, 1990–1992, 1993–1995, 1996–1998, 1999–2001, and 2002–2004 were calculated.

The results from linear and nonlinear methods both showed that water pollution in the 1996–1998 period presented the strongest association with the EC mortality rate in 2004, having the Pearson correlation coefficient of 0.79 and q-statistic of 0.89 ($p < 0.05$), respectively (Table 2). This implied that water pollution in the period had the greatest impact on the EC mortality rate in 2004 in the Huai River basin of China, and the lag period was about 8 years.

Discussion

In China, residents in the Huai River basin region have the highest risk of EC mortality. In this region, located in a densely populated area of China, the water quality has been deteriorating, due to the growing and unrestrained use of industrial chemical pesticides in agriculture since the 1980s (Zhang et al. 2010). Some studies suggested that contaminants in drinking water are a major risk factor of cancers of the digestive system. However, the effect of water pollution during the historical

Table 1 Association between water pollution and EC mortality rate in each year

Index	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2001	2002	2003	2004
r	− 0.26	− 0.37	− 0.12	0.48	0.49	0.32	0.46	0.48	0.55	0.60	0.81*	0.82*	0.34	0.51	0.44	0.39	0.51
p value	0.53	0.32	0.77	0.19	0.22	0.40	0.21	0.20	0.13	0.09	0.01	0.01	0.45	0.17	0.23	0.30	0.16
q	0.25	0.30	0.18	0.33	0.65	0.29	0.66	0.44	0.29	0.92*	0.65	0.55	0.57	0.57	0.57	0.56	0.30
p value	0.65	0.64	0.69	0.16	0.24	0.55	0.16	0.43	0.44	0.01	0.12	0.21	0.19	0.19	0.19	0.19	0.19

r indicates Pearson's correlation; *q* indicates the GeoDetector *q*-statistic. * indicates $p < 0.05$

period on the EC mortality rate was unclear. In this study, the lag effect of water pollution on the EC mortality rate in 2004 in the Huai River basin was analyzed. Linear and nonlinear models indicated that there was an 8-year lag period of water pollution on the EC mortality rate.

Studies have indicated human activities, such as the increased water consumption by industry or agriculture, as well as natural processes, such as storm-water runoff or drought (Sliva and Williams 2001, Simeonov et al. 2003). The industrial structure and geographic conditions in the Huai River basin have strong spatial heterogeneity. In general, the southern Huai River basin is a hilly region with a large proportion of paddy fields and woodlands while the northern Huai River basin is a plains region dominated by dryland. The annual average precipitation in the Huai River basin gradually decreases from south to north. In the upstream and midstream of the Huai River, the population engages in agriculture, and about 80% of the total population engages in industry. In the downstream of the river, in Xuyi and Jinhu counties, most of the population is engaged in industry. These socioeconomic and nature conditions play an important role leading to diversity in the water pollution and the EC mortality rate in the Huai River basin.

An important influence of human activities is that water pollution greatly affects the health of residents, and this pollution has been identified as an important factor of EC in the Huai River basin in China. For example, Yang and Zhuang (2014) described water environment changes and cancer in the Huai River basin and showed that there was a strong association between water pollution and the EC mortality rate. Several studies revealed that a positive correlation exists between nitrate intake and the risk of cancer (Bruningfann and Kaneene 1993). Lu et al. (Lu et al. 1986) compared the urinary excretion of N-nitrosamino acids and nitrate by residents of high- and low-risk areas for EC in northern China, and found that populations with high rates of EC excrete high levels of nitrate. Similar effects of nitrate on stomach cancer were found by other researchers (Zatonski et al. 1989). The present study showed that water pollution has high determinant power, e.g., 92% for the *q*-statistic; this value is consistent with previous studies.

Although most of the domestic water used by residents in the study area is taken from underground, contaminants enter the groundwater due to the leaching and infiltration of surface water and the lateral seepage of the river, resulting in continuous accumulation of groundwater pollutants (Wang et al. 2019). Another method of exposure is intake of contaminated vegetables. Although the surface water has been polluted, local residents still use it for irrigation because clean water is usually expensive for farmers. Contaminants in surface water can accumulate in the soil and be absorbed by plants.

The lag effect is a common phenomenon in epidemiology, which usually is an important parameter in a model because it is critical to reveal the mechanism in disease, especially in cancer. The lag period calculated from data on past risk factors and cancer mortality rates can help assess the influence of the water environment in a historical period, adjust the policy, and estimate the trend of future mortality. For example, researchers speculated lag time could be used to analyze the relationship between the EC mortality rate and the levels of tobacco and alcohol consumption, and dietary patterns during different periods (Gao et al. 2017). However, the lag parameter was only an assumed value, and statistical analysis has not been conducted to verify the hypothesis. To our knowledge, few studies focusing on the EC mortality rate have considered the lag period.

This study has several limitations, which introduce some uncertainty in the results. The variation in the population in

Table 2 Association between water pollution and EC mortality rate in different periods

Index	1987–1989	1990–1992	1993–1995	1996–1998	1999–2001	2002–2004
r	− 0.26	0.47	0.57	0.79*	0.60	0.46
p value	0.49	0.20	0.17	0.01	0.09	0.22
q	0.15	0.65	0.44	0.89*	0.55	0.57
p value	0.74	0.13	0.42	0.02	0.21	0.19

r indicates Pearson's correlation; *q* indicates the GeoDetector *q*-statistic. * indicates $p < 0.05$

the study years affects the conclusions. In the study, the population was stable, and the total migration rate was no more than 4% in the 10 years among the four provinces (Ping 2004). Thus, the influence was limited. In addition, data on the water pollution grades, which is a comprehensive indicator of BOD, COD, NH_4^+, NH_3, and volatile phenol in water, were used in this study because there were no records of separate statistical data for each indicator from 1987 to 2004 in China. In the future, with improvements in water pollution monitoring systems and regulatory initiatives, detailed information on pollutants causing water pollution will be used in the assessment of the effects of water quality on the EC mortality rate. In conclusion, rapid industrialization has made China's economy develop rapidly in the past 20 years, but also has brought an opportunity to improve health care and the quality of life. However, the increase in industrial waste has caused environmental problems and posed a health impact to residents exposed to pollutants. The study results indicated that the current EC mortality rate was mainly caused by water pollution from about 8 years before. Although the study focused on the EC mortality rate in the Huai River basin, it also provides a valuable perspective on how the lag time for pollution affects human health for other diseases.

Authors' contribution CDX and DFX conceived and designed the study. DFX and CDX conducted the main analyses. JFW and GXX contributed to refining the ideas and carrying out additional analyses. All authors discussed the results and revised the manuscript.

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Compliance with ethical standards

Competing interests The authors declare that they have no competing interests.

Abbreviations EC, esophageal cancer

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