RESEARCH COMMUNICATION

Esophageal Cancer Mortality Trends in Rural and Urban China Between 1987 and 2009

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Abstract

Esophageal cancer is one of the most commonly diagnosed malignant tumors in China. This study aimed to examine the temporal trend of esophageal cancer mortality rates during the period 1987-2009 in both rural and urban settings and to detect the effects of year of death and year of birth on the trends using joinpoint regression analysis and an age-period-cohort model. Age-standardized mortality rates were calculated by the direct method using the world population of 1960, and joinpoint regression was performed to obtain the annual percentage change (APC) in mortality rate. Poisson regression models were fitted to evaluate the period and cohort effects after adjusting for age. During the period 1987-2009, age-standardized mortality rates showed an overall significant decrease for rural females (APC=-2.3, 95% confidence interval [CI]: -3.3%, -1.2%), urban males (APC=-1.8, 95% CI: -2.6%, -1.0%) and urban females (APC=-3.7, 95% CI: -4.9%, -2.4%), but the decrease was not statistically significant for rural males (APC=-0.9, 95% CI: -2.0%, 0.3%). After adjusting for age and with the birth cohort of 1900-1904 or period 1987-1991 as reference, the relative risk of successive cohorts decreased steadily and that of more recent periods kept relatively stable. The decreasing birth cohort effect in the recent generations could correspond to increased adoption of healthy dietary habits and life-styles in the population.

Keywords: China - esophageal cancer - mortality - Poisson regression - trends

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Introduction

In China, esophageal cancer is one frequently observed malignant tumors that ranking the fourth among the top ten cancers according to a national death cause survey conducted in 2004-2005, with age-standardized mortality rates around 10.97 and 17.34 per 100,000 for urban and rural areas, respectively (Zhao et al., 2010). According to the GLOBOCAN project in 2008, there there were 481,000 new esophageal cancer cases and 406,000 deaths globally, and China was estimated to account for 53.6% of the new cases and 51.7% of the deaths worldwide respectively (Ferlay et al., 2010). However, the level of esophageal cancer mortality rates tended to differ markedly between the sexes, as well as the areas in China. As esophageal cancer becomes a serious public health challenge, understanding the current stage of esophageal cancer epidemics and access its temporal trends in China serves to provide comprehensive information for the primary prevention.

Many studies were conducted to understand the association between the prevalence of esophageal cancer and possible risk factors, mainly suggesting elevated risk was linked to lifestyle and environmental exposures, including cigarette smoking and alcohol consumption (Wang et al., 1992; Tran et al., 2005; Wu et al., 2006), eating of pickled vegetables (Wang et al., 1992; Yang et al., 2005; Yu et al., 2010), and intake of nitrosamine (Yokokawa et al., 1999; Lin et al., 2003). In contrast to the relatively intensive studies of pathogens, the national prevalence and long-term trends of esophageal cancer have not been reported, although there are several studies reported about the trends for limited Chinese populations and time periods in high-risk areas, such as the areas of Linxian, Cixian and Nanao (He et al., 2001; 2008; Su et al., 2007).

With respect to esophageal cancer incidence, it is presently impossible to obtain the national population incidence due to the absence of a nationwide cancer registry of new cases in China, however mortality is used in this study. The aim of this study is to provide a comprehensive and up-to-date overview of the temporal trends of esophageal cancer mortality in China with an emphasis on the region- and sex-specific differences observed by analyzing data extracted from public databases.

In general, modern statistical method such as joinpoint regression is used to describe secular trends in cancer rates by estimating the annual percent change of significant points in cancer trends (Pou, 2009). To evaluate the

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effects of age, period and birth cohort on time trends, age-period-cohort models have been widely used, which interpreting the temporal variations as the inner effects of age, period and birth cohort (Clayton et al., 1987; Tse et al., 2007; Trivers et al., 2008). In brief, period effect reflects the influence of related factors on all age groups simultaneously, and it may be caused by the changes in disease classification, the advancements in treatment, or the screening plan introduction. Cohort effects reflect exposure of environmental or life style-related factors in early life, and these factors will manifest their influence in one's whole life.

In this study, the author examined the time-dependent trends in mortality for esophageal cancer to provide a comprehensive overview of mortality trends for Chinese populations during the period 1987-2009.

Materials and Methods

National mortality rates from esophageal cancer for the period 1987-2009 by year of death, sex and 5-year age groups according to rural and urban areas were extracted from the WHO mortality database. The International Classification of Disease 10 revision was used for esophageal cancer cases coding. Mortality in 2001 was missing and interpolated by the average of that in the nearest two calendar years to ensure a sequential study period without gaps. Age-specific rates for each 5-year age group were calculated based on the certified deaths and population. Annual standardized mortality rates for esophageal cancer were calculated by the direct method using the world standard population of 1960 and expressed as rate per 100,000 person-years.

Joinpoint regression is a statistical procedure to identify changes in cancer mortality and incidence rates. Joinpoint regression model can be used to describe cancer trends as a link of several different segments connected together at the "joinpoint". To detect the significant joinpoints in data trends, grid-search method is used and permutation tests are performed to obtain the 95% confidence interval (95% CI) (Kim et al., 2000). In this paper, joinpoint regression models were fitted to estimate the annual percentage change (APC) in mortality rate as well as age-specific rate of different age groups under the assumption of same rate of change throughout the period for both genders according to rural and urban areas. Joinpoint analyses were performed using 'Joinpoint' Software from the Surveillance Research Program of the US National Cancer Institute (NCI, 2011).

To study the age, period, and birth cohort effects on the trends of cancer, classical age-period-cohort models can be used (Clayton et al., 1987). For this analysis, esophageal cancer deaths were regrouped into 14 five-year age groups, ranging from 20-24 to 85 or above, as there were very few esophageal cancer deaths documented at ages below 20. The studied period of 1987-2009 was divided into five intervals from 1987-1991 to 2007-2009. Based on the period and age groups, the author calculated 18 five-year birth cohorts from 1900-1904 to 1985-1987. Multiple Poisson regression models were performed for each gender by area to examine the effects of age, period and birth cohort on esophageal mortality trend using the SAS procedure GENMOD. A full age-period-cohort model including all 3 time variables was not fitted because it may involve serious methodological limitations, particularly the difficulties of estimating the individual effects of age, period or cohort due to a linear dependency between these three components (Clayton et al., 1987). Three models, age alone, age-period and age-cohort, were established. The effects were interpreted as the relative risks (RR) based on the reference categories of the 20-24 years age group, the 1987-1991 period and 1900-1904 birth cohort. To correct for the possible underestimation of the true standard error, which may be caused by the over-dispersion in Poisson distribution data, the 'pscale' option was selected in the procedure (Tse et al., 2007). The goodness of fit of the models was evaluated by the deviance. The closer the deviance to the degree of freedom, the better the model fit (Clayton et al., 1987).

Results

Age-standardized mortality rates of esophageal cancer for both genders among rural and urban areas were plotted in Figure 1. Steadily downward trends were seen among rural females and both genders from urban areas, but rural males did not experienced a decline during the same period. The visual declines in the trends of the age-standardized mortality rates were confirmed by the calculation of APC (Table 1). Age-standardized mortality rates during 1987-2009 exhibited an overall significant decrease for rural females (APC=-2.3, 95% CI: -3.3, -1.2), urban males (APC=-1.8, 95% CI: -2.6, -1.0) and urban females (APC=-3.7, 95% CI: -4.9, -2.4), respectively, but a small decrease was not statistically significant for rural males (APC=-0.9, 95% CI: -2.0, 0.3). In particular, a most noticeable decline (APC=-19.3, 95% CI: -27.2, -10.5) in the recent period of 2005-2009 emerged in urban females.

Table 1. Annual Percentage Changes (APC) of Age-standardized Mortality Rates Using Joinpoint Analysis, by Area for Both Genders

	APC (95%CI)	Trend 1		Trend 2		Trend 3	
	1987-2009	Years	APC (95%CI)	Years	APC (95%CI)	Years	APC (95%CI)
Rural							
Males	-0.9 (-2.0, 0.3)	1987-2002	-2.6* (-4.2, -0.8)	2002-2007	6.4 (-6.5, 21.1)	2007-2009	-8.3 (-39.1, 38.2)
Females	-2.3* (-3.3, -1.2)	1987-1999	-3.5* (-6.3, -0.6)	1999-2002	7.0 (-35.0, 76.1)	2002-2009	-5.9 (-12.0, 0.6)
Urban							
Males	-1.8* (-2.6, -1.0)	1987-1998	-3.5* (-4.7, -2.2)	1998-2005	3.2 (-0.1, 6.6)	2005-2009	-12.4* (-17.6, -6.8)
Females	-3.7* (-4.9, -2.4)	1987-1996	-7.0* (-9.8, -4.2)	1996-2005	2.1 (-1.5, 5.8)	2005-2009	-19.3*(-27.2, -10.5)

*Significantly different from 0 (P<0.05)

Table 2. Annual Percentage Changes (APC) in Age-Specific Mortality Rates of Esophageal Cancer, by Area for Both Genders

Age group	Rural males		Rural females		Urban males		Urban females	
	APC	95% CI	APC	95% CI	APC	95% CI	APC	95% CI
20-24	-7.6	(-20.2,6.9)	2.8	(-6.6,13.1)	-10.0	(-22.5,4.7)	6.1	(-7.4,21.6)
25-29	-13.5*	(-21.7,-4.5)	9.3	(-6.3,27.5)	6.0	(-3.2,16.0)	-8.5	(-21.8,7.0)
30-34	-9.7*	(-17.7,-1.0)	-27.2*	(-37.5,-15.4)	-2.7	(-6.1,0.7)	-9.7	(-21.2,3.4)
35-39	-6.0*	(-8.0,-4.0)	-19.4*	(-30.2,-6.8)	-1.0	(-3.1,1.2)	-4.3	(-12.4,4.6)
40-44	-3.6*	(-5.2,-2.0)	-7.1*	(-9.1,-5.1)	0.3	(-1.2,1.8)	-4.1*	(-6.7,-1.5)
45-49	-3.3*	(-4.7,-2.0)	-6.5*	(-8.3,-4.6)	2.1*	(0.9,3.4)	-6.1*	(-9.3,-2.7)
50-54	-0.8	(-2.2,0.5)	-3.5*	(-5.0,-1.9)	2.3*	(0.9,3.7)	-4.5*	(-6.8,-2.3)
55-59	-1.1	(-2.6,0.4)	-3.3*	(-4.4,-2.2)	-0.0	(-1.4,1.4)	-4.5*	(-6.4,-2.6)
60-64	-1.4*	(-2.6,-0.2)	-2.8*	(-3.9,-1.6)	-1.7*	(-2.8,-0.6)	-4.6*	(-6.2,-3.0)
65-69	-1.1	(-2.3,0.1)	-2.3*	(-3.5,-1.1)	-2.7	(-3.5,-1.9)	-4.9*	(-6.1,-3.6)
70-74	-0.9	(-2.0,0.2)	-1.7*	(-2.7,-0.7)	-3.2*	(-4.1,-2.3)	-3.8*	(-5.0,-2.6)
75-79	0.5	(-0.5,1.4)	-0.1	(-1.0,0.8)	-2.7*	(-3.4,-1.9)	-2.7*	(-3.8,-1.7)
80-84	1.4*	(0.0,2.8)	0.2	(-1.1,1.6)	-2.0*	(-2.7,-1.2)	-1.9*	(-2.9,-0.9)
85 or above	1.5	(-0.5,3.6)	-0.5	(-2.4,1.3)	-2.4*	(-3.4,-1.3)	-0.8	(-2.3,0.6)

*Significantly different from 0 (P<0.05)

Table 3. Comparision of Different Poisson Regression Models for Esophageal Cancer in China, 1987-2009

Area	Variables in the model	DF	Deviance		Deviance/DF		P-value for Chi-square	
			Males	Females	Males	Females	Males	Females
Rural	Age	308	1513.0	793.0	4.91	2.57	<0.0001	<0.0001
	Age + period	52	94.9	58.8	1.82	1.13	<0.0001	<0.0001
	Age + cohort	39	114.0	32.5	2.92	0.83	<0.0001	<0.0001
Urban	Age	308	862.5	532.7	2.80	1.73	<0.0001	<0.0001
	Age + period	52	27.9	21.6	0.54	0.42	<0.0001	<0.0001
	Age + cohort	39	22.9	25.9	0.59	0.66	<0.0001	<0.0001

DF, degree of freedom

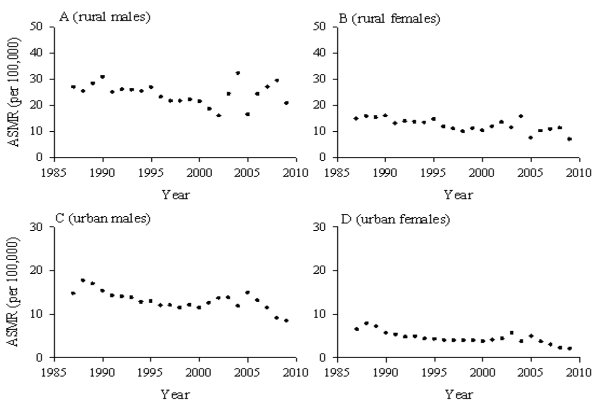

Figure 1. Age-standardized Mortality Rate (ASMR) of Esophageal Cancer in China During the Period of 1987-2009, Using Who World Standard Population as Reference

Table 2 presented the joinpoint analysis of the trends of age-specific mortality rates. Significant declines in esophageal cancer mortality rates occured mainly in the middle age group of 30-49 for both genders in rural areas, but the declines in the age group of 60-84 for urban populations. Declines in the age-specific mortality rates were observed more frequently in females than in males.

Figure 2 demonstrated graphically the relation between age-specific mortality rate of esophageal cancer and successive birth cohorts for both genders in the two types of areas. The parallelism in the cohorts curves confirmed the strong cohort effects on the mortality rates of esophageal cancer. For all birth cohorts, the rates for the same age group were consistently higher in males than

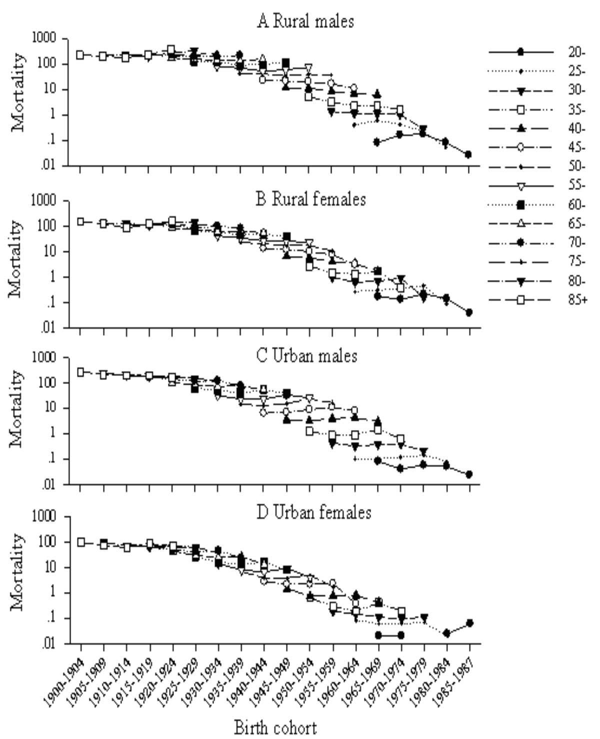

Figure 2. Age-specific Mortality Rates of Esophageal Cancer (Log Scale) by 5-year Age Groups and Birth Cohorts for Both Genders in Rural and Urban China, 1987-2009

in females, irrespectively of area.

The results of comparison of different Poisson regression models for esophageal cancer were showed

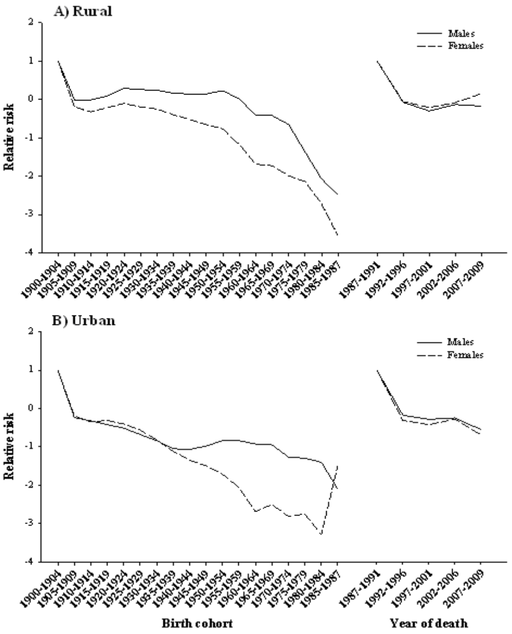

Figure 3. Period and Birth Cohort Effects from Age-Period and Age-cohort Analysis in Rural and Urban China Population During the Period 1987-2009

in Table 3. The age-period and age-cohort models were highly statistically significant for both genders in rural and urban areas. The deviance of age-period model was similar to that of the age-cohort for urban males and females, respectively. But the pattern of deviance statistics among rural males was different to that among females, suggesting a better model fit of the data in the age-period model for rural males and a better one in the age-cohort model for rural females.

The RR of esophageal cancer mortality rates by time period and birth cohort were estimated based on Poisson regression models with the adjustment of age and showed in Figure 3. From the period 1987-1991 to 2007-2009, the RRs dropped dramatically during the first two periods and then level off around the value of zero for both genders among the two areas. With respect to the birth cohort 1900-1904, the RRs of successive birth cohorts appeared to drop slowly earlier and then began to reduce remarkably for both genders among the two areas with a slightly greater cohort effect being observed among females. An increase of mortality occured in the latest birth cohort of urban females was seen, but it should be noted that there were less data available for these groups.

Discussion

This study showed the overall mortality trends of esophageal cancer in China during the period of 1987-2009, taking into consideration the differences between the genders and areas, and the changing patterns of age, period and birth cohort effects on mortality trend. Clear downward trends in age-standardized mortality rates of esophageal cancer were observed for rural females and both genders in urban areas respectively during the studied period. The mortality was decreasing significantly in adults and birth cohort with more rapid decline in females.

The data used in this study were integrated from public database to provide the comprehensive information about the burden of esophageal cancer on a national scale in China. The information of cancer death are derived from the death reporting system of Center for Health Information and Statistics. At present, this system is considered to provide the representative data on cancer mortality patterns in China. In general, cause of death is checked and obtained from medical sources, and the death certificates are collected and signed by the local vital statistics offices. A proper estimation of esophageal cancer mortality is given by this system, although problems in validity of death certification and coding practice may not be ignored.

This paper showed more unfavorable trends for males than females, especially for rural males whose mortality remained unchanged throughout the time period. The comparably favorable trends of mortality in women than men have also been observed in Asian country like Japan over recent decades (Qiu et al., 2005). Actually, the different reductions in mortality between males and females may result in the variations in the trends. It was indicated that mortality from esophageal cancer in both genders among rural and urban areas decreased between the period of 2004-2005 and 1990-1992 (Wei et al., 2010), however a study from a rural area of Nanao in South China showed a rising incidence in males during 1995-2004 (Su et al., 2007).

During 1987-2009, the average mortality rates were 24.32 and 13.08 among rural males and urban males, respectively; corresponding rates among rural females and urban females were 12.32 and 4.54. The trends in esophageal cancer mortality were quite different between rural areas and urban areas. The late stage of diagnosis and limited access to treatment were considered to account for the poorer cancer survival in underdeveloped regions (Ahmedin et al., 2011). Variations in the socio-economic status of the populations between the two areas have certainly contributed to the trends observed in this study. The regional differences in the esophageal cancer trends may reflect different distribution of risk factors between regions (Bray et al., 2004; Schmassmann et al., 2009). Previous reports conducted in China showed that a specific dietary pattern with high consumptions of pickled vegetables and salt food was a risk factor in developing esophageal cancer (Yang et al., 1980).

Cohort effects reflect carcinogenic exposures in early life and would maintain their influence in cancer risk of the birth cohort throughout the whole life. If changes in these risk factors emerged in the population over time, successive generations will experience a progressively decreasing or increasing trend in cancers throughout their life time. The age-cohort model fitted the data quite well for esophageal cancer in both genders, indicating changes in the birth cohort-related risk factors were likely to be involved. Concerning the cohort effect, the decreasing birth-cohort curve is probably relevant to the reduced diet-related exposures. Potential changes in dietary habits of populations have been believed to play an important part in the prevalence of esophageal cancer. Dietary-related factors, such as the high consumption of fresh meat, eggs, fruits and vegetables, could also help to protect against esophageal cancer (Tran et al., 2005; Yang et al., 2005; Yu et al., 2010). A nationwide nutritional survey by the health ministry in China reported the residents' diet quality had improved between 1992 and 2002, with a higher consumption of eggs and meat from 210 to 248 g/person/day for city residents, and from 69 to 126 g/person/day for rural residents, respectively (The Ministry of Health of China et al., 2004). The improvements in diet quality may be partially attributable to the decreasing cohort effect. Although the decreasing risk of cohort effect on esophageal cancer was observed in both genders, it was more noticeable in females, suggesting a fact that females were much more motivated to accept the healthy behaviours than males.

Studies also showed the alcohol consumption and cigarette smoking were associated with esophageal cancer in Chinese population (Wang et al., 1992; Tran et al., 2005). According to the China's Tobacco Control Office, the impact of tobacco control in China is poor and the smoking prevalence remains at a high level in Chinese population at present (China CDC, 2011). So the decreasing cohort effects observed may not be due to the change in smoking habits.

In contrast to the obviously decreasing cohort effects, relatively stabilized period effects especially in latter time periods were seen in both genders among the two areas, although the RRs of period effects dropped noticeably from 1987-1991 to 1992-1996. If period effect-related factors exist, for example, changes in registration ability and diagnostic accuracy of cancer, mortality rates of esophageal cancer may be affected. With the improved death registration ability, death of esophageal cancer may be documented better than before thus resulting in the increasing mortality of esophageal cancer. On the other hand, the misclassification between gastric and esophageal cancer, especially in the gastroesophageal junction, may also affect mortality from esophageal cancer. From the result of analysis, these potential factors may tend to be able play.

In conclusion, we have estimated the annual percentage changes of esophageal cancer mortality rates in China during 1987-2009 and found that the mortality rates among rural females and residents in urban areas significantly decreased, whereas rural males did not experience such decreasing trends. The differences in mortality were reflected between areas as well as genders, and these variations could correspond to the changes in age-, period- and cohort-related factors in population. Further research is necessary to determine the causes.

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