Trends in cancer mortality in China: an update

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Background: Cancer deaths of China with the world population nearly a quarter will have a severe impact on global cancer trend and burden. The study aims to provide a comprehensive overview of long-term trends in cancer mortality in China.

Materials and methods: We used joinpoint analysis to detect changes in trends and generalized additive models to study birth cohort effect of risk factors between 1987 and 2009.

Results: Mortality of all cancers declined steadily in urban areas, but not in rural areas. Decreasing mortality from cancers of the stomach, esophagus, nasopharynx, and cervix uteri was observed, while lung and female breast cancer mortality increased. Mortality from leukemia remained relatively stable, and cancer of liver, colorectal, and bladder had different trends between the rural and urban areas. Generational risks peaked in the cohorts born around 1925–1930 and tended to decline in successive cohorts for most cancers except for leukemia, whose relative risks were rising in the very recent cohorts.

Conclusion: The observed trends primarily reflect dramatic changes in socioeconomic development and lifestyle in China over the past two decades, and mortality from cancers of lung and female breast still represents a major public health priority for the government.

Key words: birth cohort, cancer, China, mortality, trend

Introduction

Cancer is a major burden globally that continues to increase largely due to aging, population growth, and an increasing adoption of cancer-causing behavior [1]. Official data from China indicated that cancer had become the second most common cause of death in China during 2004–2005 [2]. The age-standardized mortality rate of cancer was 135.88 per million, accounting for 22.3% of the total deaths [2]. However, the level of cancer mortality rates differed markedly between the sexes, as well as the areas in China [3–5].

Previous studies reported the incidence and mortality trends of selected cancers for limited Chinese populations and time periods [6–9] and also for some specific cancers in high-risk areas [10–12]. Although Chinese data of cancer mortality on a national scale over the period of 1987–1999 had been reviewed recently [13], China has undergone many changes over the past decade. Therefore, an up-to-date evaluation of cancer trends is warranted. It is presently impossible to obtain the national population incidence; however, mortality is used in this study. Previous studies predominantly analyzed the temporal trends in cancer...
incidence or mortality by calculating an estimated annual percent change over time, using age–period–cohort models to evaluate the effects of age, period, and birth cohort on the trends [14–17]. In this paper, we examined the trends in cancer mortality in China in urban and rural areas during the period of 1987–2009.

**materials and methods**

National cancer mortality from 10 selected cancers for the period 1987–2009, coded and tabulated in the *International Classification of Disease (ICD-10)*, year of death, sex, and 5-year age groups by area (rural and urban), were extracted from the World Health Organization mortality databank and the China statistical yearbook database. Data for liver cancer have been available only since 2002. Mortality in 2001 was not available from the databases and was estimated by interpolation to ensure a sequential study period without gaps. Based on the certified deaths and resident population, age-specific rates for each 5-year age group (form 0 to 4 to 80 years or above) were computed. Age-standardized mortality rates per 100,000 males and females by area were calculated using the direct method based on the 1996 world standard population.

The estimated annual percent change along with its 95% confidence interval (CI) of the mortality trend is obtained using the Joinpoint regression model. Joinpoint analyses were carried out using 'Joinpoint' Software from the Surveillance Research Program of the US National Cancer Institute [18].

Cohort effects reflect the long-established generational influence of risk factors in early life, such as environmental carcinogens or specific lifestyles, which manifest them as a progressive increase or decline in cancer risk within the population and commonly show up as a birth cohort phenomenon.

Assuming the number of cancer deaths to follow a Poisson distribution, generalized additive models (GAMs) were fitted for each gender to examine the cohort effect on mortality trends. A full age–period–cohort model, including all three time variables was not established because this model may involve serious methodological limitations [14]. Cohorts can be obtained by subtracting the midpoints of 5-year age groups from the corresponding calendar year. To study the cohort effect, let model $A + C$ represent a GAM with smoothed age and cohort as the form: $\log(h) = \gamma + S(a) + S(c)$, where $h$ is the mortality rate for each age-specific group, $\gamma$ is the intercept, $S$ is a smoothing spline function, and $a$ and $c$ represent the age and birth cohort, respectively. Smoothing spline function can be automatically estimated by minimizing the generalized cross-validation score [19]. The relative risk (RR) for cohort $t$ with respect to a reference cohort is defined as:

$$RR = \frac{\text{total predicted morality cohort } c_t}{\text{total predicted mortality cohort } c_i} \times \frac{\exp(S(c_t))}{\exp(S(c_i))}$$

where $S(c_t)$ represents the estimated smooth function of cohort $c_t$ from the model $A + C$ where the cohort effect is adjusted for the age effect, and the initially observed cohort of 1900 was chosen as cohort $c_i$. The bootstrapped 95% CI for RR was estimated. The statistical software R was used for performing this analysis.

**results**

**long-term trends by calendar period 1987–2009**

Table 1 gives the overall and truncated age-standardized mortality rates from selected cancers during the periods 1987–1991, 1997–2001, and 2007–2009 and the corresponding percent changes.

**rural areas.** Total cancer mortality in rural males was stable in the first decade, but increased from 146.0 in 1997–2001 to 172.9/100 000 in 2007–2009. For males, decreasing mortality trends were observed for cancers of the nasopharynx and stomach over the two decades except the colorectal and lung cancer. Mortality from bladder cancer and leukemia was stable during the period. For females, the mortality was steady over the two decades from 81.9 to 81.2/100 000. Similar patterns of mortality trends from stomach, esophageal, and nasopharyngeal were observed for females. Mortality from lung cancer increased, whereas rates from bladder cancer and leukemia were stable. Trends in mortality from female breast and cervical cancer were different, with an increase of 20.1% and a decline of 47.8% in the former and the latter during the last decade, respectively.

For the truncated age groups, favorable trends were observed for all cancer combined mortality among females over the last decade, whereas the total mortality among males increased by 7.3%. Mortality patterns in the age groups were roughly similar to the overall population.

**urban areas.** Favorable trends were observed for total cancer mortality in both sexes over the last two decades. For males, an unfavorable trend was observed for colorectal cancer, and mortality from bladder cancer and leukemia was relatively stable. For urban females, decreasing mortality was observed for most cancers except for breast. For the truncated age groups, the cancer mortality patterns were similar to that in the overall population.

**joinpoint analysis for mortality from selected cancers**

The findings from the joinpoint analysis are shown in Table S1 and S2 (available as supplementary data in *Annals of Oncology* online). The recent trends in mortality of selected cancers during 2003–2009 are illustrated in Figure 1.

For the rural population, age-standardized mortality rates of 1987 and 2009 were higher among males than females. Lung cancer was the first contributory cause of cancer death in both sexes in 2009. For cancers of the stomach, esophagus, nasopharynx and cervix uteri, mortality tended to decrease significantly over the 23-year period, with the major declines by $\sim6.5\%$ per year and 5.7% for cervix uteri cancer in females at all ages and at the ages of 35–64 years. However, unfavorable trends in mortality were observed for female breast cancer and lung cancer in both sexes.

For the urban population, lung cancer was also the primary contributory cause of cancer death in 2009, although the overall trends in mortality were decreasing for females. For most cancers, mortality was downward in both sexes, and the major decline was observed for liver cancer, by $\sim4.7\%$ per year and 6.0% among males and females at all ages. Other major reductions in recent years in both sexes were cancer sites of the nasopharynx, esophagus, and stomach.

**birth cohort patterns based on GAM analyses**

Figures 2 and 3 summarize the changing patterns in the trends of birth cohort by cancer site according to sex and area.

In rural areas, there are clearly similar stages of the temporal development for most cancers (colorectal and anus, lung, nasopharynx, esophagus, and stomach cancer) in relation to

<table>
<thead>
<tr>
<th>Area−sex</th>
<th>Cancer site</th>
<th>All ages</th>
<th>Truncated 35−64 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rural−male</td>
<td>All cancers</td>
<td>147.3</td>
<td>164.0</td>
</tr>
<tr>
<td></td>
<td>Bladder</td>
<td>1.7</td>
<td>1.7</td>
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<tr>
<td></td>
<td>Colorectal and anus</td>
<td>6.7</td>
<td>6.9</td>
</tr>
<tr>
<td></td>
<td>Leukemia</td>
<td>3.8</td>
<td>3.6</td>
</tr>
<tr>
<td></td>
<td>Liver (2001−2009)</td>
<td>22.5</td>
<td>29.4</td>
</tr>
<tr>
<td></td>
<td>Lung</td>
<td>2.4</td>
<td>2.4</td>
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<tr>
<td></td>
<td>Esophagus</td>
<td>27.3</td>
<td>21.1</td>
</tr>
<tr>
<td></td>
<td>Stomach</td>
<td>34.7</td>
<td>29.0</td>
</tr>
<tr>
<td>Rural−female</td>
<td>All cancers</td>
<td>81.9</td>
<td>80.5</td>
</tr>
<tr>
<td></td>
<td>Bladder</td>
<td>0.4</td>
<td>0.6</td>
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<tr>
<td></td>
<td>Breast</td>
<td>3.2</td>
<td>4.1</td>
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<tr>
<td></td>
<td>Cervix uteri</td>
<td>5.3</td>
<td>3.7</td>
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<tr>
<td></td>
<td>Colorectal and anus</td>
<td>5.2</td>
<td>5.6</td>
</tr>
<tr>
<td></td>
<td>Leukemia</td>
<td>3.2</td>
<td>2.6</td>
</tr>
<tr>
<td>Urban−male</td>
<td>All cancers</td>
<td>164.3</td>
<td>156.7</td>
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<tr>
<td></td>
<td>Bladder</td>
<td>3.0</td>
<td>3.1</td>
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<td>Colorectal and anus</td>
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<td>10.0</td>
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<tr>
<td></td>
<td>Leukemia</td>
<td>4.2</td>
<td>3.8</td>
</tr>
<tr>
<td>Urban−female</td>
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<td>93.5</td>
<td>88.0</td>
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<tr>
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<td>Bladder</td>
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<td>13.9</td>
<td>10.6</td>
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sex, with birth cohorts of both sexes (1925–1930) tending to reach their maximum risk. The similar pattern is repeated in the urban areas. For females, regardless of area, the maximum risks of cervix uteri and breast cancer, respectively, peak in the generations born around 1925 and 1950. For rural females, however, there is a rising risk of bladder cancer among recent birth cohorts after 1975. In particular, irrespective of sex and area, a rising risk of leukemia cancer is observed in very recent generations born after 1975, while the risks of other cancers have been decreasing steadily among the generations born after the year corresponding to the maximum risk value.

discussion

This study provides a comprehensive and up-to-date overview of temporal trends in cancer mortality in China over the past two decades, emphasizing the different trends between rural and urban areas and the different stages of cancer epidemics. The dataset used in this article is based on the death reporting system operated by the Center for Health Information and Statistics (CHIS), which is a main data source considered to provide the most representative information on national mortality patterns [20]. The CHIS indeed provides a proper estimation of cancer mortality on a national scale, although
problems in population estimates, validity of death certification and coding practice may in part affect the data accuracy.

Mortality from cancers of the lung, colon–rectum, bladder, and female breast has long been high among urban populations compared with rural populations, who have remarkably higher rates for cervical, esophageal, and stomach cancers. The rapid growth of China’s economy over the past decades has been greeted with increasing affluence in cities and countrysides. Due to the dramatically improving economy, there have been impressive changes in the health care conditions with respect to primary health care, health services, public hygiene, and medical diagnostic and treatment techniques. The wealth created, however, has not been evenly distributed and reflected in income gaps between the two areas. According to official statistics in 2010, rural residents had an annual average per capita disposable income of 5919 yuan ($900). That is less than a third of the average annual per capita disposable income of urban residents, which stood at 19 109 yuan ($2906) [21]. These disparities in socioeconomic circumstance, health care and lifestyle between urban and rural areas have probably influenced cancer mortality patterns in China.

As in most areas of the world [1], mortality from stomach cancer in China has decreased substantially over the last few decades, and it was lower than that observed in Korea and Japan, as well as Belarus, though still higher than in most countries of North America and Europe [22]. The encouraging trends in stomach cancer mortality, particularly among successive birth cohorts born in 1930, were observed among both sexes in urban and rural areas. Studies indicated that the increasing intake of fresh fruits and vegetables were the protective factors for stomach cancer, while salted and preserved food, and chronic \textit{H. pylori} infection might be risk factors [22, 23]. This favorable trend may be due to the changes in environmental exposure and lifestyle in the populations.

Esophageal cancer mortality decreased steadily over the last two decades for both sexes in the two areas, and this is also reflected in the generational trends and successive declines in risk among both sexes born approximately after 1925. In China, esophageal cancer mainly occurs in the form of esophageal squamous cell carcinoma (ESCC), which accounts for ~90% of the total esophageal cancer cases [23]. Risk factors for ESCC among the Chinese are mainly suggested to include
**Rural males**

**Urban males**

**Figure 2.** The relative risks curves (solid lines) of cohort effects with bootstrapped 95% confidence intervals (dashed lines) with respect to a base year from the generalized additive models for rural and urban males, respectively.
low intake of fruits and vegetables, nutritional deficiencies, ingestion of nitrosamines, and drinking beverages at high temperatures [24–26]. According to official statistics from the Food and Agriculture Organization of the United Nations, the average per capita supply of vegetables increased from 85.6 kg in 1987 to 245.6 kg in 2007 and fruit from 6.0 to 25.1 kg [27]. During 1987–2007, there was a remarkable increase in the consumption of eggs (from 5.1 to 17.4 kg), meat (from 21.8 to

Figure 3. The relative risks curves (solid lines) of cohort effects with bootstrapped 95% confidence intervals (dashed lines) with respect to a base year from the generalized additive models for rural and urban females, respectively.
Mortality from nasopharyngeal cancer had been favorable for both sexes and the decreasing risks were also observed among successive birth cohorts born in 1930. According to world area, incidence from nasopharyngeal cancer in the areas of South-Eastern Asia, including Malaysia, Indonesia, Singapore, and China, has long been high compared with North America, western Europe, and Africa [1, 28], but decreasing or stable trends in recent years were observed in high-risk areas of Southern China [28, 29]. Increased risks of this neoplasm were suggested to be linked to infection with Epstein–Barr virus, genetic factors, and lifestyles-related factors such as eating salted fish, preserved foods, and hot spices [30, 31].

For lung cancer, high mortality rates were observed among both sexes in the two areas over time, and the rates continued to increase in recent years with more unfavorable trends observed in rural populations. The RR of lung cancer peaked in the generations born between 1925 and 1930 and decreased among the successive cohorts. The decreasing risk according to the cohort patterns could not correspond to these unfavorable trends in lung cancer mortality. According to previous reports, lung cancer rates in China have been increasing over the past decades at relatively high rates on a worldwide scale, as compared with the decreasing death rates in most western countries [13, 22, 32]. The observed variations in lung cancer rates and trends largely reflected the different phases of the tobacco epidemic. In 2010, an estimated 28.1% of adults in China (52.9% of men and 2.4% of women) were current smokers, and the prevalence of smoking among men in rural area was significantly higher than that of urban men [33]. A recent report from China’s Tobacco Control Office suggested the impact of tobacco control was insufficient, and smoking prevalence in males remained at a high level [34]. The increasing epidemic of cigarette smoking is a major factor that contributes to the increasing trends in lung cancer mortality. However, the smoking situation among Chinese men is quite different from that among women. For men, the high mortality rates reflect high smoking prevalence, but the burden of lung cancer in women is thought to be linked to indoor air pollution from unventilated coal-fueled stoves and cooking fumes [32].

Liver cancer mortality had different trends among the two types of populations. An estimated 748 300 new liver cancer cases and 695 900 cancer deaths occurred worldwide in 2008, and China was thought to account for half of these figures [1]. Epidemiological studies suggest that chronic infection with hepatitis B virus and dietary aflatoxin exposure are the major etiological determinants of liver cancer in China [13]. The reduced infection of hepatitis B virus and changed diet possibly account for the decreasing trends in urban populations, but the influences of these factors were limited in rural populations.

Mortality from colorectal cancer was substantially higher in urban than rural areas and in males than in females. The trends were different between urban and rural populations, with significantly increasing rates in recent years observed in urban area irrespective of sex. Colorectal cancer mortality increased at 17.9% between 1973–1975 and 2004–2005 [5], and the increasing trends were also observed in some urban areas [35, 36]. Data from the 2002 national nutrition and health survey showed that 14.7% of Chinese were overweight and another 2.6% were obese, such that there were 184 million overweight people in 2002, and a further 31 million obese people, out of a total population of 1.3 billion [37]. The changes in the dietary patterns and physical activity may contribute to the increasing risk of colorectal cancer.

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Relatively stable mortality trend from leukemia was observed over the recent decade. The increasing rates among successive birth cohorts tended to give way to short-term stabilizations among more recently born cohorts. In China, as in other East Asian countries, leukemia mortality was lower than in most developed areas of the world, remaining a middle level in the worldwide context [38]. Although there has been an increase in childhood leukemias worldwide, the certain cause of this neoplasm is not well established except for ionizing radiation, a major recognized risk factor of childhood leukemias [39].

Declines in bladder cancer mortality have been observed in urban populations from 1987 through 2009, but the decreasing trends did not emerge in rural areas. As reported, occupational exposure to chemical substances like benzidine and changing dietary habits are the recognized risk factors of bladder cancer in Chinese populations [40, 41]. The different distributions of risk factors between areas may be in part responsible for the mortality patterns of bladder cancer.

With reference to breast cancer, mortality rates over the past two decades increased among rural females, whereas the rates had been increasing up to the late 1990s, but have leveled off in most recent years for urban females. This may partially be explained by reproductive patterns of successive cohorts of women [42, 43], whose birth rates dropped from 20.6 to 13.2 per 1000 people between 1990 and 2005 [44]. Changes in lifestyle and dietary habits may also have influenced the rising trends from breast cancer in Chinese [45, 46]. For cervix cancer, there are substantial declines observed in both areas. The large declines may be in part attributable to the introduction of screening programs based on Pap smear cytology as well as the improvements in medicines [13].

In conclusion, the article provides the overall information of mortality trends from the selected cancers in China over the past two decades. We should improve the access to health services to increase survival in case of cancer, especially for rural populations.

disclosure

The authors have declared no conflict of interest.

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references


