RESEARCH COMMUNICATION

Trends in Nasopharyngeal Carcinoma Mortality in China, 1973-2005

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Abstract

Nasopharyngeal carcinoma (NPC) is a disease with distinct ethnic and geographic distribution. The incidence of NPC in Chinese residing in Asia has declined over the last few decades, but NPC mortality trends in the entire Chinese population over time have not been systematically evaluated. In this study, we examined NPC mortality at the national level in China between 1973-2005. Mortality rates were derived from the databases of national retrospective surveys on cancer mortality conducted in the periods of 1973-1975, 1990-1992, and 2004-2005, respectively. NPC was classified according to the International classification of diseases. Age-adjusted mortality rates were calculated by direct standardization according to the world standard population. Trends in rates were evaluated by age, gender, geographic areas, and socioeconomic status. From 1973 to 2005, there was a general trend of decrease in NPC mortality in China, with higher rates in the south on a downward trend in the north. The age-standardized NPC mortality rates were 2.60 per 100,000 in 1973-1975, 1.94 per 100,000 in 1990-1992, and 1.30 per 100,000 in 2004-2005, respectively. The trend was similar in both men and women, in both urban and rural areas, but the declining rates in females were more remarkable than in males. The mortality rates were higher for the age groups above 50 years than those less than 50 years of age, both showing downward trend over 30-year period. In summary, the overall NPC mortality has consistently decreased in China over the past three decades, particularly in women and in old adults.

Keywords: Nasopharyngeal carcinoma (NPC) - mortality trends - China - 1973-2005

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Introduction

Nasopharyngeal carcinoma (NPC) is a tumor arising from the epithelial cells that cover the surface and line the nasopharynx. Although it is rare in most parts of the world with an incidence rate less than 1 case per 100,000 population (Parkin et al., 1997). NPC occurs particularly frequent in China and Southeast Asia, with an annual incidence rate of about >20 per 100,000 in endemic areas (Yu et al., 2002; Bray et al., 2005; Chang et al., 2006). Descendants of Chinese who emigrated to Western countries have lower NPC incident rates than do Chinese in Asia, but their rates remain higher than those of White populations in Western countries (Buell et al., 1974; Yu et al., 2009). Globally, NPC accounts for about 80,000 new cases and 50,000 deaths annually (Bray et al., 2005). In the past three decades, declining incidence of NPC has been observed in Chinese residing in Southeast Asia, including Hong Kong, Taiwan, and Singapore (Chang et al., 2006). However, NPC mortality trend in the entire Chinese population over time has not been evaluated.

Over the past three decades, The National Office for Cancer Prevention and Control (NOCPC), the Ministry of Health (MOH) of China, has organized three nationwide retrospective mortality surveys of the causes of cancer death in 1973-1975, 1990-1992, and 2004-2005, respectively (The Editorial Committee, 1979; Li et al., 1996; Jin et al., 1999; Cheng et al., 2008). These surveys provided sex- and age-specific mortality rates for major cancers affecting a fifth of the world's population. Studies of NPC mortality based on data derived from these national surveys have provided information on NPC incidence and mortality in China for limited population and time periods (Dai et al., 1999; Shugart et al., 2006; Yu et al., 2010). However, to date there is no attempt to systematically evaluate trends of NPC mortality on the national scale. In the present report, trends in NPC mortality has been updated to the year 2005. Since long-term trends provide useful information to understand recent patterns and to project most likely future trends (Boyle et al., 1998), the major aim of the present work is to provide a comprehensive documentation of the patterns of NPC mortality trends in Chinese population over a period of 32 years, and has therefore relevant implications for further primary and secondary prevention and public health intervention.

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Materials and Methods

All data used in this study was derived from the database of the National Retrospective Death-Causes Surveys (Ji et al., 1999), which had been carried out by the NOCPC of China for three times in 1973-1975, 1990-1992, and 2004-2005, respectively (NOCPC, 1979; Li et al., 1996; Jin et al., 1999; Cheng et al., 2008). The nation-wide survey of 1973-75 was conducted in 2392 counties and cities in 29 provinces (municipalities/autonomous regions), covering a population of about 850 million people, or 96.7% of the population of the country. This survey, for the first time, documented 18.4 million deaths over 3 years and provided the national profiles of cancer mortality in China (NOCPC, 1979; Hill K et al., 2004).

In the national retrospective survey of cancer mortality in selected areas from 1990-1992, an approximately 10% (335,213,493 person-years) sample of the whole population of China was investigated, using a two-stage randomized stratified cluster sampling method, based on the distribution of mortality rates in the survey of 1973-1975 (Li et al., 1997; Cheng et al., 2008; NOCPC, 2008). To select surveillance sites within each stratum, sampling was carried out with probability proportional to the number of counties/cities, ensuring that the sites selected were as much as uniformly distributed across 31 provinces. The cities of Beijing, Shanghai, and Tianjin were intentionally sampled as a single unit, respectively. A total of 263 sampling areas (189 counties & 74 cities) were selected from 2400 cities/counties in 27 provinces (municipalities/autonomous regions).

The third national retrospective stratified sampling survey of cancer mortality for the period of 2004-2005 was carried out in 2006. This survey selected 158 sampling areas (counties/cities) from 31 provinces (municipalities/autonomous regions, but not including Hong Kong, Taiwan, and Macau) in China. This two-year survey covered 142,660,482 person years in which 47,899,806 person years were observed in 61 urban areas, and 94,760,676 person years in 97 rural areas (Zhang et al., 2010). All information of deaths and causes of deaths was collected from police stations, hospitals, and family planning offices by trained investigators, using the standardized protocols and questionnaire provided by NOCPC. For each death, the age and gender of the person and the cause of death were recorded. All data are centralized at NOCPC through reporting system. Trained surveillance officers at each level verified data collection, data accuracy, and cause of death according to the surveillance manual to ensure high quality of data. In addition, surveillance professionals at provincial and national levels organized independent retrospective surveys to assess and verify completeness of original reporting cards, and accuracies of data collection and report (National Office for Cancer prevention and Control, 1979).

NPC was classified according to the definition of the International Classification of Diseases, 8th revision (ICD-8) and 9th revision (ICD-9) in the surveys before 2000, and the 10th revision (ICD-10) was used in 2004-2005 investigation. Counties and cities were stratified into urban and rural regions, using a classification system developed by the information and Statistics Center of the Ministry of Health of China (NOCPC, 1979, 2008; National Center of Health Information and Statistics, 1999). To adjust for the confounding of difference in age composition for different periods of surveys, age-standardized mortality rates of NPC were adjusted by direct standardization according to the national census population of China in 1980 (Population Census Office, 1982) and the world standard population in 1960 (Powell et al., 1976) by gender, age group (0-, 1-, 5-, 10-, 15-, 20-, 20-, 25-, 30-, 35-, 40-, 45-, 50-, 55-, 60-, 65-, 70-, 75-, 80-, 85-), respectively. Mortality rates are expressed as per 100,000 person.

Results

Overall trends in NPC mortality 1973-2005

Table 1 gives the overall age-standardized mortality

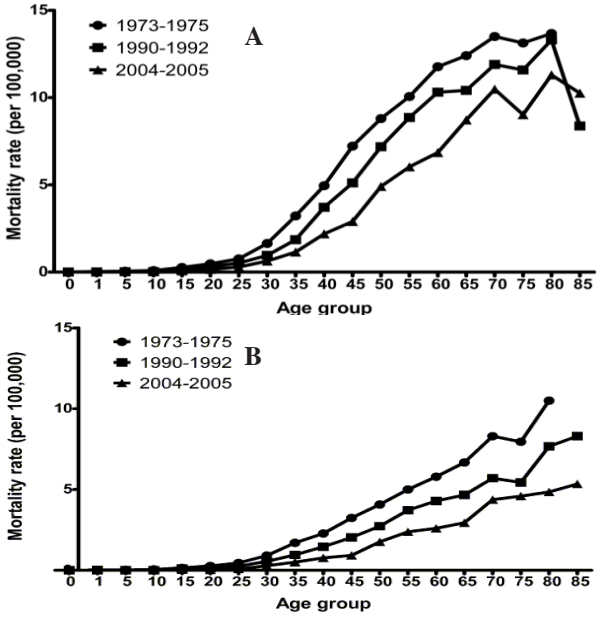

Figure 1. Age-specific NPC Mortality Rates (per 100,000) for Males (A) and Femals (B) in China, 1973-2005

Table 1. Overall Age-adjusted Mortality Rates (per 100,000) from NPC in China, 1973-2005

	1973-1975 (1)			1990-1992 (2)			2004-2005 (3)			Change (2)/(1)	Change (3)/(2)
	Overall	Men	Women	Overall	Men	Women	Overall	Men	Women	rate (%)	rate (%)
Unadjusted Rate	1.99	2.54	1.41	1.74	2.34	1.10	1.46	2.05	0.84	-12.56	-16.09
Adjusted rate[a]	2.00	2.70	1.40	1.53	2.11	0.93	1.01	1.46	0.55	-23.50	-33.99
Adjusted rate[b]	2.60	3.40	1.80	1.94	2.68	1.19	1.30	1.89	0.72	-25.38	-32.99
Constituent ratio (%)	2.68	3.01	2.22	1.61	1.73	1.37	1.07	1.21	0.84		
Rank	9	8	11	8	7	9	13	10	16		

[a]Adjusted to 1982 census population of China; [b]Adjusted to World's population in 1960

Table 2. Adjusted Mortality Rates (per 100,000) from NPC for Urban and Rural Areas in China, 1973-2005

	1973-1975 (1)			1990-1992 (2)			2004-2005 (3)			Change (2)/(1)	Change (3)/(2)
	Overall	Men	Women	Overall	Men	Women	Overall	Men	Women	rate (%)	rate (%)
Urban area											
Unadjusted rate	1.98	2.55	1.37	1.93	2.61	1.20	1.59	2.29	0.88	-2.53	-17.62
Adjusted ratea	2.00	2.60	1.30	1.52	2.11	0.92	1.00	1.48	0.53	-24.00	-34.21
Constituent ratio (%)	2.40	2.69	1.98	1.71	1.87	1.44	1.06	1.22	0.78		
Rank in cancer mortality	9	8	11	8	7	9	15	12	17		
Rural area											
Unadjusted rate	1.98	2.53	1.41	1.67	2.25	1.06	1.39	1.94	0.81	-15.66	-16.77
Adjusted rate*	2.00	2.70	1.40	1.53	2.11	0.93	1.01	1.45	0.56	-23.50	-33.99
Constituent ratio (%)	2.78	3.13	2.31	1.56	1.69	1.34	1.08	1.20	0.87		
Rank in cancer mortality	9	7	11	8	7	9	13	9	16		

[a]Adjusted to 1982 census population of China

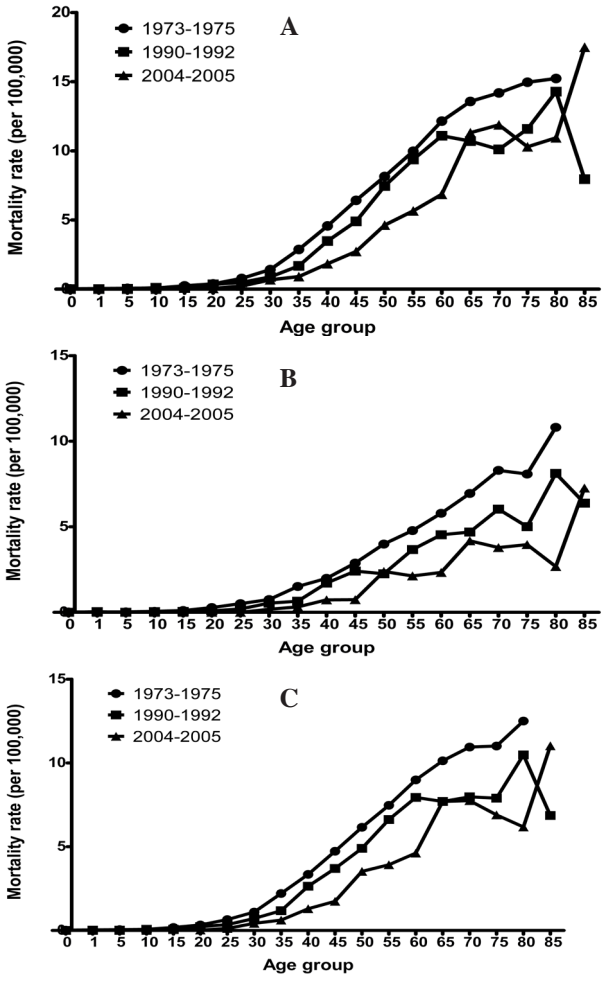

Figure 2. Age-specific NPC Mortality Rates (per 100,000) for Males (A), Females (B) and Totel (C) in Urban Areas in China, 1973-2005

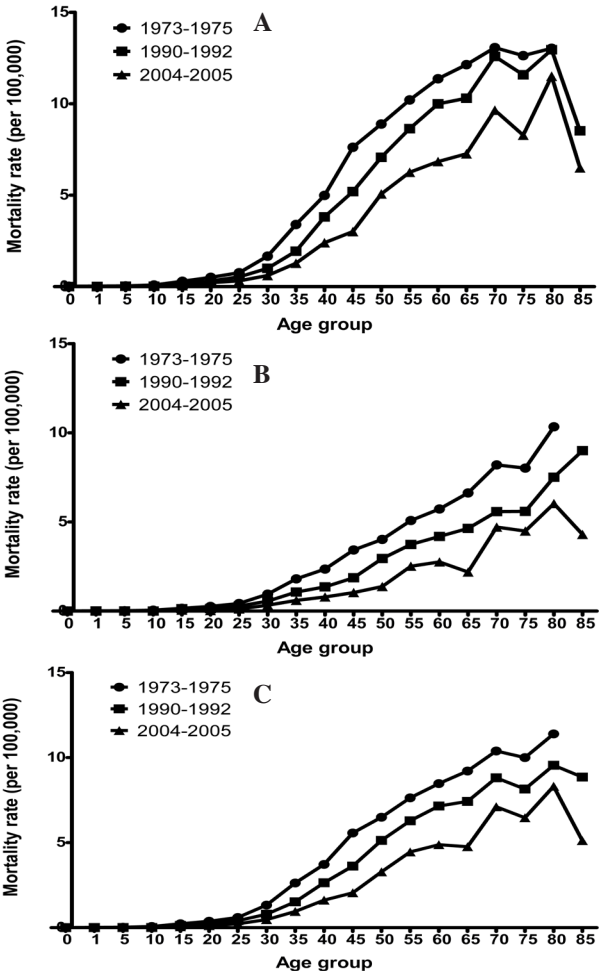

Figure 3. Age-specific NPC Mortality Rates (per 100,000) for Males (A), Females (B) and Totel (C) in Rural Areas in China, 1973-2005

rates for NPC per 1000,000 person in the 1973-1975, 1990-1992, 2004-2005, respectively; and the corresponding percent changes. During the survey period from 1973 to 2005, there has been a general trend of decrease in the NPC mortality rates in China. In 1970s, the world population-adjusted mortality rate for NPC in China was 2.60 per 100,000, which decreased to 1.94 per 100,000 in 1990s and further dropped to 1.30 per 100, 000 in 2000s. Compared with NPC mortality rate in 1970s and 1990s, the world population-adjusted mortality NPC mortality rates in 2000s has decreased by 25.38% and 32.99%, respectively. The decrease rates in females were more obvious (33.90%, 65.30%) than in males (21.12%, 29.48%). In addition, the lowest age at which NPC mortality was observed tended to increase over time. Figure 1A. shows the trends of mortality rate for each survey during the study period.

Compared to other causes of cancer deaths, the ranking of NPC as a cause of cancer death among other cancers has also declined over the past three decades. In 1973-1975, NPC was the number nine cause of cancer death in China. During the survey period of 1990-1992, NPC ranked as the 8th leading cause of cancer death. By the survey period of 2004-2005, however, NPC sharply fell to the 13th leading

Table 3. Age-specific Mortality Rates (per 100,000) of NPC in Urban and Rural Areas in China, 1973-2005

Age group	1973-1975				1990-1992				2004-2005			
	Total	Male	Female	Male/female	Total	Male	Female	Male/female	Total	Male	Female	male/female
Urban Areas												
0-	0.02	0.02	0.02	0.80	0.00	0.00	0.00	-	0.00	0.00	0.00	-
1-	-	-	-	-	0.02	0.00	0.04	0.00	0.00	0.00	0.00	-
5-	0.05	0.06	0.03	2.01	0.02	0.03	0.00	-	0.00	0.00	0.00	-
10-	0.07	0.08	0.06	1.50	0.07	0.10	0.04	2.50	0.00	0.00	0.00	-
15-	0.18	0.24	0.11	2.08	0.07	0.08	0.05	1.60	0.05	0.11	0.00	-
20-	0.33	0.38	0.28	1.38	0.23	0.35	0.09	3.89	0.03	0.05	0.00	-
25-	0.65	0.78	0.51	1.54	0.35	0.49	0.20	2.45	0.12	0.23	0.00	-
30-	1.10	1.42	0.75	1.88	0.72	0.88	0.54	1.63	0.43	0.68	0.18	3.86
35-	2.21	2.87	1.51	1.90	1.18	1.68	0.65	2.58	0.62	0.91	0.32	2.88
40-	3.35	4.57	1.99	2.29	2.64	3.48	1.71	2.04	1.30	1.84	0.73	2.53
45-	4.73	6.42	2.88	2.23	3.70	4.90	2.41	2.03	1.74	2.72	0.74	3.67
50-	6.16	8.15	3.99	2.04	4.90	7.46	2.25	3.32	3.53	4.63	2.39	1.94
55-	7.47	9.97	4.78	2.09	6.62	9.37	3.67	2.55	3.92	5.66	2.13	2.65
60-	8.99	12.2	5.79	2.10	7.94	11.1	4.53	2.45	4.62	6.86	2.33	2.94
65-	10.1	13.6	6.95	1.95	7.70	10.7	4.69	2.28	7.70	11.3	4.18	2.70
70-	11.0	14.2	8.30	1.71	7.98	10.1	6.03	1.67	7.75	11.9	3.79	3.13
75-	11.0	15.0	8.08	1.85	7.90	11.6	5.01	2.31	6.90	10.3	3.96	2.60
80-	12.5	15.2	10.8	1.41	10.5	14.3	8.12	1.76	6.18	10.9	2.68	4.08
85-	-	-	-	-	6.86	7.95	6.38	1.25	11.0	17.5	7.26	2.41
Overall	1.98	2.55	1.37	1.86	1.93	2.61	1.20	2.18	1.59	2.29	0.88	2.61
Rural Areas												
0-	0.01	0.02	0.01	1.31	0.00	0.00	0.00	-	0.00	0.00	0.00	-
1-	-	-	-	-	0.01	0.01	0.01	1.00	0.00	0.00	0.00	-
5-	0.03	0.04	0.02	1.89	0.01	0.02	0.01	2.00	0.02	0.03	0.00	-
10-	0.07	0.09	0.05	1.76	0.01	0.02	0.00	-	0.01	0.02	0.00	-
15-	0.23	0.29	0.16	1.79	0.13	0.13	0.13	1.00	0.05	0.05	0.05	0.94
20-	0.38	0.51	0.26	1.99	0.22	0.31	0.14	2.21	0.12	0.22	0.03	7.71
25-	0.60	0.76	0.43	1.79	0.41	0.53	0.28	1.89	0.23	0.32	0.12	2.66
30-	1.33	1.67	0.95	1.75	0.79	1.00	0.56	1.79	0.47	0.61	0.33	1.84
35-	2.63	3.40	1.81	1.88	1.52	1.94	1.07	1.81	0.95	1.28	0.60	2.14
40-	3.72	4.99	2.36	2.11	2.64	3.81	1.36	2.80	1.62	2.40	0.79	3.03
45-	5.57	7.62	3.43	2.22	3.62	5.20	1.87	2.78	2.05	3.01	1.04	2.90
50-	6.49	8.89	4.02	2.21	5.13	7.07	2.95	2.40	3.28	5.07	1.38	3.68
55-	7.63	10.2	5.08	2.01	6.28	8.64	3.74	2.31	4.45	6.25	2.52	2.48
60-	8.47	11.4	5.73	1.98	7.15	9.99	4.19	2.38	4.88	6.84	2.76	2.48
65-	9.21	12.1	6.63	1.83	7.42	10.3	4.64	2.22	4.76	7.26	2.19	3.31
70-	10.4	13.1	8.20	1.59	8.81	12.6	5.58	2.26	7.11	9.65	4.71	2.05
75-	10.0	12.6	8.02	1.58	8.15	11.6	5.59	2.07	6.46	8.28	4.49	1.68
80-	11.4	13.0	10.3	1.26	9.55	13.0	7.51	1.72	8.31	11.5	6.03	1.91
85-	-	-	-	-	8.85	8.52	9.00	0.95	5.12	6.49	4.30	1.51
Overall	1.98	2.53	1.41	1.79	1.67	2.25	1.06	2.12	1.39	1.94	0.81	2.38

cause of cancer death in China.

Trends of NPC mortality rates by gender and age

The NPC mortality rates in both males and females were declined between 1970s and 2000s in China. Compared with mortality rates in 1973-1975 and in 1990-1992, NPC mortality rate in males in 2004-2005 had declined by 19.29%, and 12.39%, respectively. Similar trends were also observed in females, but the declining rates in females were more remarkable than that observed in males. Compared with the standardized mortality rate in 1973-1975 and in 1990-1992, the NPC mortality rates of 2004-2005 in females have decreased by 40.42% and by 23.64%, respectively. Figure 1 shows the trends of age-specific standardized mortality for each considered age group by gender over the past three decades, In general, the mortality rates of NPC were relatively low in age groups < 25 years, but tended to increase with age. The highest mortality rates were observed in the age groups of ≥ 50 years. However, more obvious declining mortality rates were also seen for groups of age ≥ 50 years.

NPC mortality trends in urban and rural areas

In consistent with the overall trends of NPC mortality in the past three decades, there was a trend of decrease of NPC mortality rates in both urban and rural areas over the same period of time (Table 2). Figure 2 shows the steadily and substantially decreasing trend in NPC mortality in urban areas, Compared with standardized NPC mortality rates in 1973-1975, NPC morality rate decreased 24.00% by 1990-1992 and further declined 34.21% 2004-2005 in urban areas. The decreasing rates in female (29.23 % by 1990-1993 and further 42.39% by 2004-2005, respectively) were more remarkable than that in male (18.85%, 29.85%, respectively). Similarly, adjusted NPC mortality rates were also decreasing in rural

Table 4. Age-adjusted NPC Mortality Rates (per 100,000)[a] by Provinces/Municipalities/Autonomous Regions

Provinces/ municipalities	Mortality rates			Change rate	Change rate
	1973-1975 (1)	1990-1992 (2)	2004-2005 (3)	(2)/(1)	(3)/(2)
South					
Shanghai	1.48	2.51	2.51	69.6	0.00
Jiangsu	1.66	0.99	1.20	-40.4	21.2
Zhejiang	2.52	1.87	1.80	-25.8	-3.74
Anhui	1.55	1.14	1.08	-26.5	-5.26
Fujian	3.39	2.77	2.69	-18.3	-2.89
Jiangxi	2.33	1.78	2.55	-23.6	43.3
Hubei	2.22	1.83	1.72	-17.4	-6.01
Hunan	3.58	2.11	2.24	-41.1	6.16
Sichuan	2.00	1.57	1.33	-21.5	-15.3
Guizhou	1.75	1.99	1.17	13.7	-41.2
Yunnan	1.44	0.98	0.81	-31.9	-17.3
Guangdong	8.15	7.05	6.14	-13.5	-12.9
Guangxi	4.15	4.03	6.27	-2.89	55.6
Hainan	4.64	3.76	3.10	-18.6	-17.6
North					
Heilongjiang	1.41	0.69	0.82	-51.1	18.8
Liaoning	1.63	0.75	0.44	-33.7	-41.3
Jilin	1.52	0.51	0.48	-66.5	-5.88
Inner Mongolia	1.26	0.40	0.51	-68.3	27.5
Beijing	1.30	0.66	0.92	-49.3	28.3
Tianjin	0.91	0.92	0.79	1.10	-14.1
Hebei	1.14	0.45	0.42	-60.5	-6.67
Sanxi	1.04	0.33	0.26	-68.3	-21.2
Sandong	1.21	0.81	0.84	-33.1	3.70
Hernan	0.21	0.45	0.39	-62.8	-13.3
Shanxi	0.99	0.72	0.63	-27.3	-12.5
Ganshu	0.18	0.61	0.27	238.9	-55.7
Ningxia	0.76	0.61	0.28	-19.7	-54.1

[a]Adjusted to 1982 census population of China

areas. The overall adjusted NPC mortality rates in rural areas fell from 2.0 per 100,000 in 1973-1975 to 1.53 per 100,000 in 1990-1992, and 1.01 per 100,000 in 2004-2005. The overall decreasing rates were 23.50% (by 1990-1992) and 33.99% (by 2004-2005), respectively. In rural areas, the fall rate in NPC mortality rates in female (35.75% by 1990-1992, 39.78% by 2004-2005) were larger than those observed in males (22.2% by 1990-1992, 31.27% by 2004-2005) (Table 2, Figure 3).

Table 3 shows the results of the corresponding mortality rates for stratified age groups in urban and rural areas over the three decades period. The trends of NPC mortality in both urban and rural areas were consistent with those for overall population: as the age increased the mortality rates also rose, with the exception of a decreased mortality with age increase between 1990-1992 in group of age 80-. The lowest mortality was seen in the -20 age groups (<1 per 100,000 person) and the highest (>8 per 100,000 person) in the 70+ age groups.

NPC mortality trends by geographic regions

Analyses by region suggest a clear geographic variations in NPC mortality distribution, particularly a north-south pattern. Compared to population in the north (provinces/municipalities), where mortality rates are generally below 1 per 100,000, overall age- adjusted mortality rates in the south are generally higher than 1 per 100,000. The highest mortality rates were observed in Guangdong, Guangxi, and Hainan provinces. Regarding trends, age-adjusted mortality rates showed a substantial decline in the north and moderate decrease in the south. The north-south patterns were similar over the survey period between 1973 and 2005, yet some greater differences were observed across regions (Table 4).

Discussion

This updated analysis describes NPC mortality trends in China over the last three decades. Although there were differences in age-standardized NPC mortality among different geographic regions, an overall decrease in NPC mortality trend has been observed during the survey periods from 1973 to 2005. The declining rate of NPC mortality was more pronounced in female than in male and in older age groups versus younger ones. The fall in NPC mortality has consistently occurred for both sexes in all age groups, and in both rural and urban areas.

This is essentially a descriptive report, because it provides an extensive picture of NPC mortality trend in China, and no inference is made on the statistical significance of rates and trends. Given that NPC mortality information was derived from nation-wide surveys in one fifth of the world's population over three decades, special cautions should be taken when interpreting the results from the present study. First, unlike the first national survey (1973-1975) in which death data were collected from almost all of China's counties and city districts that included more than 850 million people, the second (1990-1992) and the third (2004-2005) surveys were carried out in selected counties and cities (sampling sites) covering approximately 10% of the entire Chinese population (more than 1000 millions). However, the two-stage randomized stratified cluster sampling sites were mainly chosen based on the distribution of mortality rates in the survey of 1973-1975. Using the data of the first national morality survey in 1973-1975, it has been showed that the mortality rates for all causes was 6.7 for the sampling sites, 6.9 for the whole population; cancer mortality rate was 83.7 per 100,000 for sampling sites and 74.6 per 100,000 for whole country (Cheng et al., 2008). Therefore, cancer mortality data from the second and the third sampling surveys were considered to closely reflect the mortality rates of the entire population (Chen et al., 2003; Yang et al., 2004; Parkin et al., 2004). Second, the geographic area covered by the sampling surveys consists essentially of easily accessible counties/cities on the eastern seaboard, the most densely populated and urbanized area of China. In many cases, sites are included on the basis of their voluntary participation in the data collection exercise, and are not representative of the country as a whole (National Center of Health Information and Statistics, 1999). As a result, there is a nonrepresentative potential of the sampling data. However, since the eastern area of China accounts for more than 70% of the entire Chinese population, the effect of sampling on the overall mortality is likely to be limited. Third, the classification of rural counties was defined based on GDP per capita, due to rapid economic

development over the past three decades in China, some counties would be reclassified if assessed against more recent data.

Our results are broadly consistent with other studies describing the epidemiological characteristics of NPC. In Scotland, survival for NPC patients has increased between 1975-1979 and 1995-2001 (Anandan et al., 2008). Study in Hong Kong showed that the age-standardized mortality rate steadily decreased from 13.7 in 1980-84 to 7.8 in 1995-99 per 100,000 males, and from 4.5-2.2 per 100,000 females (Lee et al., 2003). A considerable improvement in NPC survival rate has also been observed in Asians in the United States in the last three decades (35.7% 5-year survival in the 1970s vs. 44.1% in the 1980s and 51% in the 1990s) (Lee et al., 2005).

The geographic north-south gradient of NPC mortality is generally compatible with the NPC incidence patterns with the highest NPC incidence in the south and a downward incidence rate toward the north (Dai et al., 1999; Chang et al., 2006). In addition, the degree of trends differed in urban and rural areas, reflecting the big differences in population structure, environment, socio-economic status, lifestyle and health care services between north and south, and between urban and rural areas (Cheng et al., 2008). The relationship between NPC and socioeconomic status, lifestyle, geographic locations have been recognized (Yu et al., 2003). During the study period, China's society underwent major transformations. Vigorous economic development was accompanied by important changes in social structure, with the increasing urban middle classes becoming predominant, and increases in per capita income and the percentage allocated to public health expenditure. All these changes, taken together with a notable improvement in lifestyles, may be generally responsible for the overall declines in NPC incidence, resulting in decreased overall mortality. During the last two decades of the 20th century, NPC incidence fell in Chinese men and women residing in Asia. In Hong Kong, NPC incidence rates have been declined since the end of the Pacific War, due to the improvements in socioeconomic and sanitary conditions following economic development (Yu et al., 1986). Singapore's economic boom followed 20 years behind Hong Kang's, following independence in 1965, and a declining NPC incidence trend is clearly seen (Dai et al., 1999).

The consistent falling trend in NPC mortality may partially be due to improvements in survival, as treatment becomes more available and effective in the last three decades. Overall NPC survival has improved during the past decades in several countries (Ou et al., 2007; Wong et al., 2007; Anandan et al., 2008). Prior to 1980s, NPC was primarily treated with once-daily radiotherapy with an additional brachytherapy boost. Since 1980s, patients receive twice-daily radiotherapy of 6000 to 7000 cGy through opposed lateral fields to the primary site and upper and lower necks. In recent years, chemotherapeutic regimens comprised of methotrexate, ciplatin, bleomycin, and 5-fluorouracil have also added to treatment protocols either as concurrent or neoadjuvant therapy (Kong et al., 2008; Lu et al., 2009). The addition of chemotherapy to radiation has shown to reduce the risk of distant metastases, and increase disease-free survival (Chan et al., 1998). It was found that patients treated with chemo-radiation had higher chance of survival than those treated with radiation alone. Similarly, the Head and Neck Intergroup study demonstrated superior 2-year survival rates for patients receiving concomitant chemoradiation versus radiotherapy alone (Baujat et al., 2006). Platinum-based combination chemoradiotherapy and aggressive management of metastatic disease has become more common during the past two decades and are associated with good-long term survival (Spano et al., 2003).

A downturn in NPC mortality trend may also be attributable to the improvement in the management of NPC, through increased surveillance of subjects at high risk for NPC and early diagnosis, with consequent improved survival in carefully selected patients. It has been established that Epstein-Barr virus (EBV) infection is a major risk factor in the pathogenesis of NPC in both endemic and non-endemic areas (Pathmanathan et al., 1995; Rischin et al., 2002). For example, in population-based large scale serological surveys in southern China, it has been found that about 3% of the population were EBV/IgA/VCA) positive and were at the highest risk for NPC (Deng et al., 1995; Huang et al., 1997; Chien et al., 2001; Guo et al., 2009). Cohort studies in NPC high risk areas in Zhongshan, Sihui, and Guangzhou covering more than 100,000 subjects for 10 years have in fact showed that EB antibody screening could increase early diagnosis rate and decrease mortality rate (Zhang et al., 2004). However, the impact on mortality at the population levels is still unclear, because EB antibody screening has not been a routine screening approach due to sensitivity/ specificity, and cost-effective issues.

There are several limitations in this study. First, all data were collected from the causes of cancer death surveillance system, and there is a lack of survey data to provide tobacco exposure, body mass index, and concurrent comorbidities that could affect the survival of NPC. Second, NPC stage information was not available in these national-wide population-based registries. Therefore, it is impossible to determine whether the stage distribution of cases has become more favorable over time. Third, trends in cancer mortality have been known to be different by ethnicity and socio-economic status and may change over time (Zhang et al., 2004). Nevertheless, the original objectives of the national surveys focused on causes of cancer death only. Information on socio-economic status have not been included in data collection. Thus, the influences of socio-economic status on NPC mortality rates remains to be characterized in more details.

In summary, although distinct geographic variations and different patterns of changes in the mortality of NPC remained, a consistent generally decrease in NPC mortality has been observed in China during the survey periods of 1970s and 2000s. In general, there was a geographic gradient with lowest mortality in the North and highest mortality in the South. It remains unclear to what extent the decreasing trend in mortality reflect true changes in NPC incidence, or represent the improvements in treatment, diagnosis, and screening strategies. Further research, including more thorough epidemiologic studies,

should seek to identify and quantify the particular factors, such as socio-economic, environment, lifestyles, genetic factors, and clinical factors, and their interactions that contribute to the pathogenesis and prognosis of NPC. There is also a great need to understand and explore prognostic and predictive markers in NPC patients, so that patients at risk for inferior outcome could be offered more effective and adjunct treatment.

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References

Anandan C, Elton R, Hitchings A, Brewster DH (2008). Nasopharyngeal cancer incidence and survival in Scotland, 1975-2001. *Clin Otolaryngol*, **33**, 12-27.

Banister J, Hill K (2004). Mortality in China 1964-2000. *Popul Stud*, **58**, 55-75.

Baujat B, Audry H, Bourhis J, et al (2006). MAC-NPC Collaborative Group. MAC-NPC Collaborative Group. Chemotherapy as an adjunct to radiotherapy in locally advanced nasopharyngeal carcinoma. *Cochrane Database Syst Rev*, **6**, CD004329.

Buell P (1974). The effect of migration on the risk of nasopharyngeal cancer among Chinese. *Cancer Res*, **34**, 1189-91.

Chan AT, Teo PM, Leung TW, Johnson PJ (1998). The role of chemotherapy in the management of nasopharyngeal carcinoma. *Cancer*, **82**, 1003-12.

Chang ET, Adami HO (2006). The enigmatic epidemiology of nasopharyngeal carcinoma. *Cancer Epidemiol Biomarkers Prev,* **15**, 1765-77.

Cheng Z (2008). Report on the third national retrospective death-causes sampling survey in China. Peking Union Medical College Press, Beijing, 1-214.

Chien YC, Chen JY, Liu MY, Yang HI, et al (2001). Serologic markers of Epstein-Barr virus infection and nasopharyngeal carcinoma in Taiwanese men. *N Engl J Med*, **345**, 1877-82.

Dai XD, Li LD, Lu FZ (1999). Trend of China nasopharyngeal carcinoma in 20 years and its prediction in the near future. *J Prac Oncol*, **13**, 1-5.

Deng H, Zeng Y, Lei Y, et al (1995). Serological survey of nasopharyngeal carcinoma in 21 cities of south China. *Chin Med J,* **108**, 300-3.

Faggiano F, Partanen T, Kogevinas M, Boffetta P,et al (1997). Socioeconomic differences in cancer incidence and mortality. *IARC Sci Publ*, **138**, 65-176.

Guo X, Johnson RC, Deng H, Liao J, Guan L, et al (2009). Evaluation of nonviral risk factors for nasopharyngeal carcinoma in a high-risk population of Southern China. *Int J Cancer*, **124**, 2942-7.

Huang TB, Wang HM, Li JL, et al (1997). Identification of high risk populations for nasopharyngeal carcinoma. *Chin J Cancer,* **16**, 81-4.

Jia WH, Huang QH, Liao J, et al (2006). Trends in incidence and mortality of nasopharyngeal carcinoma over a 20-25 year period (1978/1983-2002) in Sihui and Cangwu counties in southern China. *BMC Cancer*, **6**, 178.

Jin F, Devesa SS, Chow WH, Zheng W, Ji BT,et al (1999). Gao YT. Cancer incidence trends in urban shanghai, 1972-1994: an update. *Int J Cancer*, **83**,435-40.

Kong L, Zhang YW (2008). Historical evolution in the diagnosis and treatment of nasopharyngeal carcinoma. *China Oncol*, **18**, 641-7.

La Vecchia C, Negri E, Levi F, Decarli A, Boyle P (1998). Cancer mortality in Europe: effects of age, cohort of birth and period of death. *Eur J Cancer*, **34**, 118-41.

Lee AW, Foo W, Mang O, et al (2003). Changing epidemiology of nasopharyngeal carcinoma in Hong Kong over a 20-year period (1980-99): an encouraging reduction in both incidence and mortality. *Int J Cancer*, **103**, 680-5.

Lee JT, Ko CY (2005). Has survival improved for nasopharyngeal carcinoma in the United States? *Otolaryngol Head Neck Surg*, **132**, 303-8.

Li LD, Lu FZ, Zhang SW, et al (1996). Analysis of cancer mortality and distribution in China from year 1990 through 1992. An epidemiologic study. *Chin J Oncol*, **18**, 403-7.

Lu TX (2009). Diagnosis and treatment of nasopharyngeal carcinoma: 30 years of change and progress in China. Chinese J Clinicians;3 (Electronic Version).

National Office for Cancer prevention and Control (NOCPC) (1979). Investigation of Cancer Mortality in China. People's Health Publishing House, 1979.

National Center of Health Information and Statistics (NCHIS) (1999). Annual report for national health information and statistics. Beijing, P.R. China, 1999.

National Office for Cancer prevention and Control (NOCPC) (2008). Survey of Cancer Mortality in China (1990 ~ 1992). People's Health Publishing House. P.1-629.

Ou SH, Zell JA, Ziogas A (2007). Anton-Culver H. Epidemiology of nasopharyngeal carcinoma in the United States: improved survival of Chinese patients within the keratinizing squamous cell carcinoma histology. *Ann Oncol*, **18**, 29-35.

Parkin DM, Bray F, Ferlay J, Pisani P (2005). Global cancer statistics, 2002. *CA Cancer J Clin*, **55**, 74-108.

Parkin DM,Whelan SL,Ferlay J, et al (1997). Cancer incidence in five continents.Vol 7. Lyon, France: International Agency for Research on Cancer, 334-7.

Pathmanathan R, Prasad U, Sadler R, Flynn K, Raab-Traub N (1995). Clonal proliferations of cells infected with Epstein-Barr virus in preinvasive lesions related to nasopharyngeal carcinoma. *N Engl J Med*, **333**, 693-8.

Population Census Office (1982). National Bureau of Statistics. 1982 Population Census of China. China Statistics Press, Beijing.

Rischin D, Corry J, Smith J, et al (2002). Excellent disease control and survival in patients with advanced nasopharyngeal cancer treated with chemoradiation. *J Clin Oncol,* **20**, 1845-52.

Spano JP, Busson P, Atlan D, et al (2003). Nasopharyngeal carcinomas: an update. *Eur J Cancer*, **39**, 2121-35.

The Editorial Committee (1979). Atlas of cancer mortality in the people's Republic of China. Shanghai, China Map Press. P. 1-99.

Waterhouse J, Muir C, Correa P, Powell J (1976). Cancer incidence in five continents. Lyon, IARC Sci Publ: 456.

Wei KR, Yu YL, Yang YY, et al (2010). Epidemiological trends of nasopharyngeal carcinoma in China. *Asian Pac J Cancer Prev*, **11**, 29-32.

Wong CH, Kelly LE, Tripcony LB (2007). Nasopharygeal carcinoma in Queensland, Australia: a review of 10 years experience. *Australia Radiol*, **51**, 276-82.

Yang L, Parkin DM, Li L, Chen Y (2003). Sources of information

on the burden of cancer in China. *Asian Pac J Cancer Prev,* **4**, 23-30.

Yang L, Parkin DM, Li LD, Chen YD, Bray F (2004). Estimation and projection of the national profile of cancer mortality in China: 1991-2005. *Br J Cancer,* **90**, 2157-66.

Yang L, Parkin DM, Li L, Chen Y (2004). A comparison of the sources of cancer mortality in China. *Cancer Causes Control*, **15**, 681-7.

Yu MC, Ho JH, Lai SH, Henderson BE (1986). Cantonese-style salted fish as a cause of nasopharyngeal carcinoma: report of a case-control study in Hong Kong. *Cancer Res*, **46**, 956-61.

Yu MC, Yuan JM (2002). Epidemiology of nasopharyngeal carcinoma. *Semin Cancer Biol*, **12**, 421-9.

Yu WM, Hussain SS (2009). Incidence of nasopharyngeal carcinoma in Chinese immigrants, compared with Chinese in China and South East Asia: review. *J Laryngol Otol*, **123**, 1067-74.

Zhang CQ, Zhong YS, Sun Y, et al (2004). The application of serum EBNA1- IgA and EA- IgG markers in early diagnosis of nasopharyngeal carcinoma. *Chin J Oncol*, **26**, 482-4.

Zhang SW, Chen WQ, Wei WQ, Li GL, Li N (2010). Ovary cancer mortality in China 2004 - 2005: results from the Third National Retrospective Sampling Survey of Death Causes. *Chin J Prev Med*, **44**, 418-22

Zhou YS, Zhang SW, Li LD (1997). Analysis for death for all and malignant tumors for Chinese population. *Bull Chin Can*, **6**, 9-11.