RESEARCH COMMUNICATION

Major Cancer Mortality and Changes in Yanting, 2004-2009: Introduction to Cancer Challenges in a High Risk Area

Jun Li[1&], Qingkun Song[2&], Xiaoqiao Zhou[3], Cuiping Jiang[1], Dong Wang[1*], Xiaorong Wang[2], Chengyu Huang[3]

Abstract

Yanting County is one of high risk areas of esophageal cancer in China. Recently, the economic level has improved to a new standard, but cancer issues have not been updated. This study aimed to describe the main cancer mortalities and change from 2004 to 2009 and provide an evidence base for future active strategies. Yanting Cancer Research Institute provided all cancer mortality data and age-standardized rates were calculated based on the world standard population 2000. Annual percentage change was used to estimate the time trend for each cancer. Mortality from upper gastrointestinal cancers, but not other cancers, was much higher than worldwide average figures. Rates for esophageal cancer declined over the 6 years, but lung cancer mortality showed an upward trend. For gastric and liver cancer, no obvious change was observed. Considering the high mortality from upper gastrointestinal cancers, it is necessary to take actions investigating the risk factors and addressing the issues of prevalent cancer challenges.

Keywords: High risk area - cancer mortality - esophageal cancer - gastric cancer - liver cancer - lung cancer - China

Asian Pacific J Cancer Prev, **12**, 409-413

Introduction

Cancer is now a leading cause of death and disability in poor countries and the burden of cancer becomes a major challenge to low-income and middle-income countries (Farmer et al., 2010). China, a deleloping country, there are many areas with high risk of cancers. Yanting, a rural and one the most indigent counties in Sichuan Province, locates in northeast of Chengdu city, at 105°latitude N and 31°longitude E. In 2007, the population was about 606,400 including 518,800 agricultural ones and 87,600 non-agricultural ones. Besides of poverty, Yanting was also well known for its serious challenge of esophageal cancer (EC) (Zhang et al., 2006). From 1998 to 2002, age-standardized incidence of EC in Yanting was $137.4/10^5$ for males and $80.0/10^5$ for females (Zhang et al., 2006), compared with the corresponding figures of $11.5/10^5$ and $4.7/10^5$ worldwide and $27.4/10^5$ and $12.0/10^5$ in China (Ferlay et al., 2004).

In 1970s, the Yanting Cancer Research Panel" had been established to investigate, analyze and prevent the cancer challenges locally. Though some studies on EC had been conducted (Yang et al., 2005; Yang et al., 2007), there was not any reports introducing the status of the cancers in Yanting, especially in recent years. And in 2010, WHO provided Global Cancer Statistics 2008 about the contemporary estimates of the incidence of, and mortality from major type of cancers, at national level, for all countries of the world. Therefore, we aimed to introduce the mortality and its temporal change of the main type of cancers in Yanting of recent years and make a complete comparison with the average figures of China and world.

Materials and Methods

Data about the cancer deaths was provided by Yanting Cancer Research Institute, which took the charge of all death causes registry in the whole county. Since 1971, a 3-level cancer reporting system has been founded in Yanting. The system includes 3 registry levels: village, township and county level. Each reporter in every village was responsible for the report of deaths and death causes occurring in the village by a standard card, then the cards were sent to the township health clinics. After verification, the cards were submitted to Yanting Cancer Research Institute, and there, they were checked, analyzed, coded and stored.

The study intended to describe the temporal changing trend of mortalities in total cancer, EC, gastric cancer, liver cancer and lung cancer, which accounted for more than 90% cancer deaths. The classification of cancers was accorded to ICD-10. The data collection was under the guidelines of Cancer Incidence in Five Continents Vol. IX from IARC (Curado et al., 2007), with more than 80% cases having pathological, cytological or hematological evidence. The number of population was the average of

*[1]Yanting Cancer Research Institute, Mianyang, China, [2]School of Public Health and Primary Care, The Chinese University of Hong Kong, [3]Sichuan University West China Center of Medical Sciences, Chengdu, China [&]Contributed equally *For correspondence : ytzlyy@gmail.com*

populations at the beginning and the end of each year. The world standard population of 2000 proposed by WHO (Curado et al., 2007) was chosen to standardize each cancer mortality.

The mortalities of each cancer was obtained from Global Cancer Statistics 2008 (International Agency for Research on Cancer, 2010).

Statistical Analysis

Data was analyzed by SAS 9.1 software. Age-standardized rates of each cancer mortalities were calculated, with the reference of the world standard population in 2000. The temporal change of mortality was estimated by APC, which was calculated by fitting a regression line to the natural logarithm of the rates using calendar year as a regressor variable, i.e. y = mx + b where y = ln (rate) and x = calendar year. Then the APC = 100* (em -1) (Siesling et al., 2003). Testing the hypothesis that the APC is equal to zero is equivalent to testing the hypothesis that the slope of the regression line is zero, using the t-distribution of m/SEm. The number of degrees of freedom equals the number of calendar years minus 2. The standard error of m, i.e. SEm, is obtained from the fit of the regression line (Siesling et al., 2003). In the above formula, the "rate" denoted age-standardized rate of cancer.

Results

Total cancers

In 2008, the mortality of all cancers in China was 158.6/10^5 in males and 91.6/10^5 in females and worldwide it was 128.8/10^5 in males and 87.6/10^5 in females (Table 1). In Yanting, from 2004 to 2009, the average age-standardized rate of mortality was 172.39/10^5 in males and 91.05/105 in females, the cancer mortality in males higher than average figures of China and world (Table 1). During this period, age-standardized rate of total cancer mortality changed from 202.71/105 to 169.47/105 in males and from 116.22/105 to 90.63/105 in females (Table 2, Figure 1) However, the annual percentage change of total cancer mortality did not get the statistical significance (p>0.05) (Table 2).

In Yanting, the 6-year average age-standardized rate of EC mortality was 54.7/10^5 in males and 31.6/10^5 in females, but the corresponding figures were 18.7/10^5 and 8.2/10^5 in China and 8.6/10^5 and 3.4/10^5 worldwide (Table 1). In 2004, age-standardized rate of EC mortality was 65.1/10^5 in males and 45.1/10^5 in females; 6 years later the corresponding figures changed to 47.88/105 and 26.4/10^5 (Table 2). A significantly reducing trend was observed for EC mortality (Figure 2, 3). In females the annual reduce rate of EC mortality was 8.7% (p<0.05), however in males, the changing trend did not reach significance level (p>0.05) (Table 2).

Gastric cancer

The 6-year average age-standardized rate of gastric cancer mortality was 43.6/10^5 in males and 22.4/10^5 in females (Table 1). But in China gastric cancer mortality was 30.1/10^5 in males 14.6/10^5 in females; worldwide male

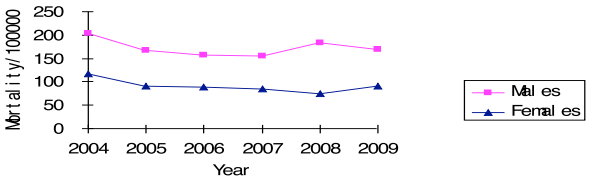

Figure 1. Age-standardized rate of Total Cancer Modality in Yanting 2004-2009#. # standardized by world standard population 2000; EC

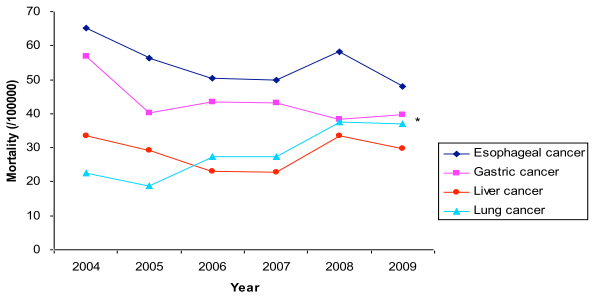

Figure 2. Age-standardized rate of Cancer Modalities of Males in Yanting 2004-2009. * p<0.05

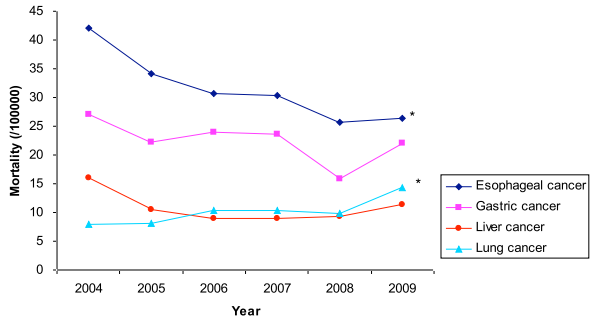

Figure 3. Age-standardized rate of Cancer Modalities of Females in Yanting 2004-2009· * p<0.05

mortality was 14.3/10^5 and female mortality was 6.9/10^5 (Table 1). Mortality of gastric cancer in yanting was higher than China and world. Age-standardized rate of gastric mortality in 2004 was 56.95/10^5 in males and 27.01/10^5 in females and in 2009 it was 39.75/10^5 in males and 22.06/10^5 in females (Table 2). But from 2004 to 2009, the mortality did not change significantly (Figure 2, 3). And the annual percentage change of gastric cancer mortality during the 6-year period did not have a significant change in both genders (Table 2).

Liver cancer

For liver cancer, the average age-standardized rate of mortality in Yanting was 28.7/10^5 in males 10.9/10^5 in females, and from IARC documents, the corresponding figures were 34.1/10^5 and 13.1/10^5 in China and 14.6/10^5 and 5.7/10^5 globally (Table 1). Yanting's figures were similar as China, but much higher than World (Table 1). It did not observe any significant change of liver cancer mortality from 2004 to 2009 in both genders (Figure 2,3). In the 6-year period liver mortality was from 33.4/10^5 to 29.8/10^5 in males and from 16.0/10^5 to 11.4/10^5 in females (Table 2). The APC of liver mortality was not significant in either gender (Table 2).

Lung cancer

During the 6 years, the average age-standardized rate of lung cancer mortality was 28.43/10^5 in males and

Table 1. The Comparison of Main Cancer Mortalities (/10^5) in Yanting 2004-2009 and Average Figures (/10^5) in China and Worldwide in 2008*

Cancer Sites	Average Mortality in Yanting 2004-2009	China 2008	World 2008
Total cancer			
male	172.39	158.6	128.8
female	91.05	91.6	87.6
EC			
male	54.68	18.7	8.6
female	31.60	8.2	3.4
Gastric cancer			
male	43.62	30.1	14.3
female	22.43	14.6	6.9
Liver cancer			
male	28.66	34.1	14.6
female	10.85	13.1	5.7
Lung cancer			
male	28.43	39.6	29.4
female	10.15	18.3	11.0

* The cancer mortalities of China and World were obtained from International Agency for Research on Cancer (International Agency for Research on Cancer, 2010)

Table 2. Age-standardized rate of cancer mortality (/10^5) and annual percentage changes in Yanting County, 2004-2009#

Cancer sites	2004	2005	2006	2007	2008	2009	APC(%)
Total cancer	156.30	127.02	122.44	121.37	129.79	129.73	-2.47
Male	202.71	166.83	156.29	155.25	183.77	169.47	-1.69
Female	116.22	91.13	88.42	84.95	74.95	90.63	-5.16
EC	51.97	44.47	40.39	39.97	42.11	37.17	-5.16*
male	65.14	56.31	50.42	49.97	58.33	47.88	-4.02
female	42.12	34.17	30.75	30.40	25.74	26.42	-8.70*
Gastric cancer	40.99	31.10	33.77	33.42	27.20	30.40	-5.26
male	56.95	40.14	43.53	43.11	38.22	39.75	-5.45
female	27.01	22.16	23.89	23.62	15.88	22.06	-5.64
Liver cancer	25.23	19.96	16.23	16.08	21.57	20.76	-2.18
male	33.44	29.32	23.00	22.85	33.58	29.75	-0.50
female	15.99	10.57	8.99	8.89	9.26	11.38	-5.82
Lung cancer	15.64	13.74	19.25	19.13	24.20	26.06	12.86*
male	22.66	18.77	27.39	27.35	37.47	36.97	13.77*
female	7.88	8.14	10.40	10.28	9.91	14.30	10.74*

standardized by world standard population 2000; * $p<0.05$

$10.15/10^5$ in females. Though the mortality in Yanting was similar to worldwide level, it was a little lower than the figure in China (Table 1). Lung cancer mortality had a significant increase in both genders during the 6-year observation (Figure 2, 3). From 2004 to 2009, the mortalities increased to $36.97/10^5$ from $14.30/10^5$ in males and to $22.66/10^5$ from $7.88/10^5$ in females (Table 2). And the increasing speed per year was 13.77% in males and 10.74% in females, both with statistical significance (Table 2).

Discussion

Yanting was one of high risk areas of esophageal cancer in China. But its challenge of all cancers was unclear. In this study we chose EC, gastric cancer, liver cancer and lung cancer, which accouned for more than 90% of total cancer deaths in Yanting to describe their mortality and temporal trend. The primary goal of this study was to show a whole picture of cancers in the high risk area in recent years. 6-year duration was not enough to observe a long term trend for mortalities. With the reference to the studies in other high risk areas, the 6-year observation could reflect the long term trend, to some extents. The data of cancer deaths was obtained from Yanting Cancer Research Institute, who had a more than 30-year history in cancer and death reporting.

Total cancer mortality of Yanting in the 6-year period was $172.4/10^5$ in males and $91.0/10^5$ in females. In contrast to the whole China and world in 2008, all cancer mortality in males in Yanting was much higher, especially with the comparison of world (International Agency for Research on Cancer, 2010). The higher mortality in males living in Yanting might be the results of the high challenges of cancers to male individuals. From 2004 to 2009 in Yanting, total cancer mortality was stable and did not change significantly, although the research about cancer risks had been conducted in Yanting for decades.

Although EC mortality reduced to lower level, it was still higher than average China: the average EC mortality in Yanting was $54.7/10^5$ in males and $31.6/10^5$ in females, corresponding to $18.7/10^5$ and $8.2/10^5$ in China and $8.6/10^5$ and $3.4/10^5$ worldwide of 2008 (International Agency for Research on Cancer, 2010). Yanting was still the high risk area for EC, possibly the outcomes of continuous exposing to risks of EC. It was necessary to take some actions to investigate the risks for EC and reduce the exposures. From 2004 to 2009, EC mortality had a significantly reducing trend. The similar decrease trend was also observed in another two high risk areas: Linxian and Nan'ao (Li, 2002). The decline mortality might relate with the socio-economic status locally. Low socio-economic status was regarded as a risk factor for EC from previous studies (Wu et al., 2006; Baastrup et al., 2008). In recent decades, Yanting's economic level has improved to a higher level: in 1985 the GDP per capita in Yanting was 385 RMB, in 1995 the figure increased to 2394 RMB and in 2007 it reached to 7138 RMB (Sichuan Bureau of Statistics, 2008). As indicated, in China the high occurrence of esophageal cancer mainly associated with the nutritional deficiency (Parkin et al., 2005). The improved socio-economic status might led local population to a more healthier diet, such as fresh vegetables, fruits, egg and fresh meat, the protective factors of EC and decrease intake of pickled vegetables, salted meat and foods with long-term preservation, the risk factors of EC. The overall decreased EC mortality might be explained by the improved economic status. But in males, it failed to get some significant change in the 6-year period. On the contrary, one study in Linxian observed the EC mortality decline in males from 1972-1997 (Li, 2002), and another study carried out in the whole Henan Province showed the similarly reducing trend in males from 1974-1998 (Lu et al., 2003). The 6-year observation period for males possibly was not adequate to observe a significant trend. It was possible to obtain a significant reducing in a longer observation period.

From 2004 to 2009, gastric cancer mortality was $43.6/10^5$ in males and $22.4/10^5$ in females in Yanting, which was not much higher than average of China in

2008: 30.1/10^5 in males and 14.6/10^5 in females, but much higher the worldwide figures (International Agency for Research on Cancer, 2010). Therefore, though Yanting was not a high risk area for gastric cancer in China, compared with worldwide average it was a high risk area of gastric cancer probably. Gastric cancer mortality in 2004 was 41.0/10^5 and in 2009 it changed to 30.4/10^5. But the annual percentage change of gastric cancer mortality did not reach a statistical significance: during the 6-year period, gastric cancer mortality was stable. This result was not consistent with the reports from China Ministry of Health, which indicated that from 1987 to 1999, gastric cancer mortality significantly but slight declined based on the survey among 10% of Chinese population (Yang, 2003; Yang et al., 2003). The reducing trend of gastric cancer incidence was also founded in Qidong from 1978-2002 (Chen et al., 2006). As indicated, improved socio-economic status and lifestyle might be responsible for the declining risk of gastric cancer (Yang et al., 2003). H. pylori infection, the sufficient carcinogen to gastric cancer by IARC, was related to the socioeconomic status too (Parkin et al., 2005). Since Yanting had a notable socio-economic status improvement, the non-significant change of gastric cancer mortality in Yanting was possibly resulted from short-term observation. It was necessary to explore the trend of gastric cancer mortality in a longer period.

Yanting was not an area with higher liver cancer mortality in China: liver cancer mortality in Yanting was 28.7/10^5 in males 10.8/10^5 in females in the 6-year period, and in China the corresponding figures were 34.1/10^5 and 13.1/10^5 in 2008 (International Agency for Research on Cancer, 2010). But in terms of the worldwide liver cancer mortality, the mortality of liver cancer was much higher (International Agency for Research on Cancer, 2010). Despite the change of liver cancer mortality from 25.2/10^5 to 20.6/10^5 during the 6-year period, the difference did not get statistical significance. And the 95% confidence interval for annual percentage change was too wide: from -15.2% to 12.9%.

Worldwide, because of the poor prognosis, the death number of liver cancer was almost the same during recent decades (Parkin et al., 2005). Italian Network of Cancer Registries reported that liver cancer mortality was stable during 1986-1997, though increased incidence of liver cancer had been documented (Ferretti et al., 2004). From the reports of China Ministry of Health, the trend of liver cancer mortality was opposite in rural and urban areas: in rural areas the annual increase rate of mortality was 1.0% in females, but not significant in males; in urban areas 1.0% of mortality reduced annually in males, but in females no significant change was observed (Yang et al., 2003). Both infection with hepatitis B virus and dietary aflatoxin exposure were the major etiological determinants of the high rates of liver cancer in China (Yang et al., 2003; Parkin et al., 2005). Vaccination for hepatitis B virus infection had been promoted since 2002, so the declines of incidence and mortality of liver cancer could not be observed in 2004-2009 (Parkin et al., 2005). The non-significant change of liver cancer mortality might result from the stable exposure to risk factors in Yanting region. Furthermore, it would be expected to take a longer time to see the beneficial effects of hepatitis B vaccination promotion in China.

In Yanting, male average lung cancer mortality was 28.4/10^5 and female average mortality was 10.2/10^5 and the average figures of China was 39.6/10^5 in males and 18.3/10^5 in females in 2008 (International Agency for Research on Cancer, 2010). The challenge of lung cancer to Yanting population is increasing in future. Some actions needed to be taken to cope with the upward challenge of lung cancer in Yanting. Lung cancer was the most common cancer and the most common death cause from cancer worldwide (Parkin et al., 2005). In Yanting area, from 2004 to 2009, lung cancer mortality increased to 26.1/10^5 from 15.6/10^5, with annual increase rate higher than 10% in both genders.

The lung cancer mortality had been significantly increased in US from 1975-1990 in both genders; since 1990 the corresponding figure had began to decline in males, but in females it still had been in an upward trend (Jemal et al., 2008). And across the whole China, lung cancer mortality increased significantly from 1987 to 1999 (Yang et al., 2003). Tobacco smoking was considered as major contributor to lung cancer, which influenced the geographic and temporal patterns of lung cancer incidence and mortality and accounted for more than 80% of lung cancer (Parkin et al., 2005; Boyle et al., 2008). From 1991 to 2001 the production of cigarettes in China increased by 2 million boxes (National Bureau of Statistics of China, 2002) and the sale rate was up to 99.3% (National Bureau of Statistics of China, 2002). In China 67% of males were smokers, but the proportion in females was only 4% (Peto et al., 2009). The increased mortality of lung cancer in Yanting was consistent with the upward consumption of tobacco in China. Despite the relatively low proportion of female smokers, lung cancer mortality in women living in Yanting still proved to be increased, which might be the consequence of elevated exposure to second hand tobacco smoking as well as other forms of environmental pollution.

Summarily, in China, Yanting was a high risk area for EC but not other cancers, but worldwide gastric and liver cancer mortalities were both much higher than average figures. And in the 6-year observation, it failed to get a significant decline trend for the mortalities of all cancers and liver cancer. But for Esophageal cancer, the mortality was processing a downward trend. And it was possible to see a significantly reducing tendency for gastric cancer mortality in a longer observation period. On the contrary, lung cancer mortality had a significantly increase tendency: the annual increase rate was higher than 10%. From the worldwide perspectives, Yanting was a high risk area for upper gastrointestinal cancers (esophagus, stomach and liver), and it called for an action to figure out their risk factors and some interventions to address their burdens.

Acknowledgments

We appreciate the support of Dr. Junze Chen during performance of this research work.

References

Baastrup R, Sørensen M, Hansen J, et al (2008). Social inequality and incidence of and survival from cancers of the oesophagus, stomach and pancreas in a population-based study in Denmark, 1994-2003. *Eur J Cancer*, **44**, 1962-77.

Boyle P, Levin B (2008). World Cancer report 2008. International Agency for Research on Cancer, Lyon pp 391-5.

Chen JG, Zhu J, Parkin DM, et al (2006). Trends in the incidence of cancer in Qidong, China, 1978-2002. *Int J Cancer*, **119**, 1447-54.

Curado MP, Edwards B, Shin HR, et al (2007). Cancer Incidence in Five Continents Vol. IX. IARC Scientific Publications No. 160. Lyon pp 961.

Farmer P, Frenk J, Knaul FM, et al (2010). Expansion of cancer care and control in countries of low and middle income: a call to action. *Lancet*, **376**, 1186-93.

Ferlay J, Bray F, Pisani P (2004). GLOBOCAN 2002: Cancer incidence, mortality and prevalence worldwide. IARC World Health Organization, available from http://www-dep.iarc.fr/.

Ferretti S, Gafà L (2004). "Upper gastrointestinal tract cancers: oesophagus, stomach, liver, gallbladder and biliary ducts, pancreas. *Epidemiol Prev*, **28**, 34-42.

International Agency for Research on Cancer (2010). Globocan 2008 Cancer Incidence and Mortality Worldwide in 2008, IARC Press, available from http://globocan.iarc.fr/.

Jemal A, Siegel R, Ward E, et al (2008). Cancer Statistics, 2008. *CA Cancer J Clin*, **58**, 71-96.

Li K (2002). Mortality and incidence trends from esophagus cancer in selected geographic areas of China circa 1970-90. *Int J Cancer*, **102**, 271-4.

Lu JB, Sun XB, Dai DX, et al (2003). Epidemiology of gastroenterologic cancer in Henan Province, China. *World J Gastroenterol*, **9**, 2400-3.

National Bureau of Statistics of China (2002). China Statistical Yearbook 2002. China Statistics Press, available from http://www.stats.gov.cn/yearbook2001/2002/m1322c.htm.

National Bureau of Statistics of China (2002). China Statistical Yearbook 2001, China Statistics Press, available from http://www.stats.gov.cn/yearbook2001/indexC.htm.

Parkin DM, Bray F, Ferlay J, et al (2005). Global Cancer Statistics, 2002. *CA Cancer J Clin*, **55**, 74-108.

Peto R, Chen ZM, Boreham J (2009). Tobacco: the growing epidemic in China. *CVD Prev Control*, **4**, 61-70.

Sichuan Bureau of Statistics (2008). Statistical Yearbook of Sichuan Province in 2008. Sichuan Bureau of Statistics, available from http://www.sc.stats.gov.cn/nj/NjWin.asp.

Siesling S, Dijck JAAMv, Visser O, et al (2003). Trends in incidence of and mortality from cancer in The Netherlands in the period 1989-1998. *Eur J Cancer*, **39**, 2521-30.

Wu M, Zhao JK, Hu XS, et al (2006). Association of smoking, alcohol drinking and dietary factors with esophageal cancer in high- and low-risk areas of Jiangsu Province, China. *World J Gastroenterol*, **12**, 1686-93.

Yang CX, Wang HY, Wang ZM, et al (2005). Risk factors for esophageal cancer: a case-control study in south-western China. *Asian Pac J Cancer Prev*, **6**, 48-53.

Yang L (2003). Incidence and mortality of gastric cancer in China. *World J Gastroenterol*, **12**, 17-20.

Yang L, Parkin DM, Li LD, et al (2003). Time Trends in Cancer Mortality in China: 1987-1999. *Int J Cancer*, **106**, 771-83.

Yang SJ, Wang HY, Li XQ, et al (2007). "Genetic polymorphisms of ADH2 and ALDH2 association with esophageal cancer risk in southwest China." *World J Gastroenterol*, **13**, 5760-4.

Zhang SW, Chen WQ, Kong LZ, et al (2006). " An analysis of cancer incidence and mortality from 30 cancer registries in China, 1998-2002." *Zhong Guo Zhong Liu*, **15**, 430-48.