
MINI-REVIEW

Review of the Cervical Cancer Disease Burden in Mainland China

Jing Li, Le-Ni Kang, You-Lin Qiao^{1*}

Abstract

Human papillomavirus (HPV) infection is a common sexually transmitted infection (STI) worldwide. HPV may cause several reproductive tract diseases and cervical cancer is the most serious health problem due to persistent high risk HPV infection. Although cervical cancer showed a declining trend over the past three decades in China, it remains a major health problem in Chinese women especially women living in rural China. The disease burden is believed to be underestimated given the relatively high HPV prevalence shown in recent studies. To date, prophylactic vaccination as a primary prevention of cervical cancer are available in many countries and regions of the world; yet, they are not yet accessible in mainland China. Before introduction of HPV vaccines, screening remains the predominant method of prevention. Selected population based screening sites are available in every province of China, yet, an organized screening program operating nationwide still does not exist. A better understanding of the disease burden is likely to help develop a comprehensive intervention policy for future management of cervical cancer in China. It is important to review the disease burden of cervical cancer and the current status of cervical cancer screening in mainland China.

Keywords: Cervical cancer - HPV infection - disease burden - mainland China

Asian Pacific J Cancer Prev, 12, 1149-1153

Introduction

Worldwide, approximately 500,000 new cases of cervical cancer (~1 case per minute) are diagnosed and 275,000 deaths from cervical cancer occur annually, making it the second most common female cancer. More than 80% of all cervical cancers occur in women in developing countries (Parkin et al., 2005). Due to the lack of a nationwide organized cervical cancer screening program, cervical cancer remains an important public health problem in mainland China. In 2005, there were approximately 58,000 new cervical cancer cases (National Office for Cancer Prevention and Control et al., 2009) and about 20,000 deaths (Zhao et al., 2010).

Although prophylactic HPV vaccines are available and have been approved in many countries, they are currently not accessible in mainland China. Screening remains the predominant method of prevention from cervical cancer before the introduction of HPV vaccines. There is a need to better understand the disease burden, to explore a potential strategy for smooth introduction of HPV vaccination into mainland China and to develop a comprehensive cervical cancer prevention strategy. In response to this need, this article reviews the cervical cancer disease burden in different populations, different geographic areas and different time periods.

Epidemiology of Cervical Cancer in China

Cervical Cancer in Different Populations

Incidence: In China, there is no well established systematic nationwide cancer registry. Existing cancer registries are geographically limited and currently the only source for cancer incidence, which is not representative of the whole country. The China cancer registry started with two sites in the 1960's (Shanghai and Linxian County) and has since expanded to 95 sites covering 31 provinces/autonomous regions/municipalities by the year 2009 under the leadership of the National Office for Cancer Prevention and Control.

According to Cancer in Five Continents Vol. IX (IARC), which includes qualified data from five registries in mainland China (1998~2002), a very low cervical cancer incidence was observed in women under 25 years of age. Two peaks were seen based on the age-specific incidence rate. The first one was in women aged 35-54 years and the rate ranged between $6.7/10^5$ and $7.3/10^5$, while the second peak was in women over 65 years, which ranged between $8.8/10^5$ and $21.3/10^5$ (Figure 1) (Curado et al., 2007; Shi et al., 2008).

According to the China Cancer Registration Annual Report 2004, cervical cancer was ranking the 8th most common malignancy among women, with a crude

Cancer Institute/Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing, China *For correspondence: qiaoy@cicams.ac.cn

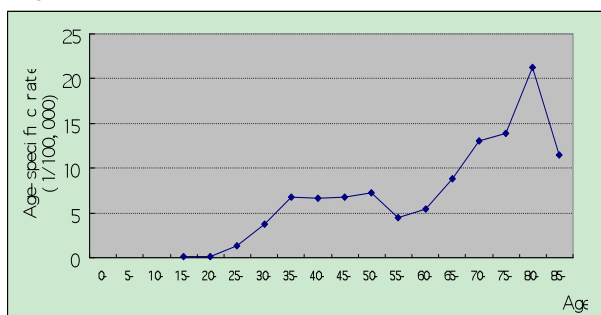


Figure 1. Age-specific Incidence Rate of Cervical Cancer in Five Cancer Registries (1998~2002) in Mainland China (Shi et al., 2008)

incidence rate of 8.55 per 100,000 women and a China Age-Standardized Rate (CASR) of 5.15 per 100,000 women. The age-specific incidence rate also had two peaks, with the first in women aged 40~44 years (18.7/10⁵) and the second in women aged 80~84 years (13.9/10⁵) (National Office for Cancer Prevention and Control, 2008). Data from year 2005 suggested that the crude incidence rate was 9.1/10⁵, and the CASR was 5.4/10⁵, making cervical cancer the 7th most common malignancy in Chinese women (National Office for Cancer Prevention and Control, 2009).

A hospital-based retrospective study conducted in Xinjiang Cancer Hospital to explore the cancer distribution among inpatients during a 10 year period (1993~2002) found that in 3,412 cervical cancer inpatients, most cases occurred in women aged 31~60 years, with a peak in the age-group 41~50 years. This study also indicated that Uygur women accounted for 71.57% of all cervical cancer cases, followed by Han women (23.8%) and other ethnic minorities (4.63%). In Uygur women, cervical cancer was the most common malignancy (Zhu et al., 2004).

Mortality: In China, three national retrospective cause-of-death surveys were conducted in the 1970's, 1990's and 2000's, respectively. Very low cervical cancer mortality was seen in women under 35 years of age (2.65/10⁵ in the 1970's, 0.94/10⁵ in the surveys conducted in the 1990's and 2000's (Zhao et al., 2010)). In the first survey, however, the mortality almost doubled every five-years among women aged 20~44yrs, yet, it remained at very low level. Among women older than 44 years, the mortality increased moderately (Zhao et al., 2010; National Office for Cancer Prevention and Control, 1980; National Office for Cancer Prevention and Control, 2008; Ministry of Health of the People's Republic of China, 2008). It peaked at 72.2/10⁵ in women aged 70~74yrs. The same trend was observed in the 1990's, with the highest rate of 29.4/10⁵ in the same age group (Zhao et al., 2010). However, the third national retrospective cause-of-death survey showed differences compared to previous surveys. The first peak was 8.4/10⁵ in women aged 55~59yrs and the second peak was 20.8/10⁵ in women over 85 years (Zhao et al., 2010). In the 1970's, about 69% of deaths caused by cervical cancer happened between 50 and 70 years of age (National Office for Cancer Prevention and Control, 1980) while in the 1990's, this percentage was 65% (National Office for Cancer Prevention and Control, 2008). Statistics from

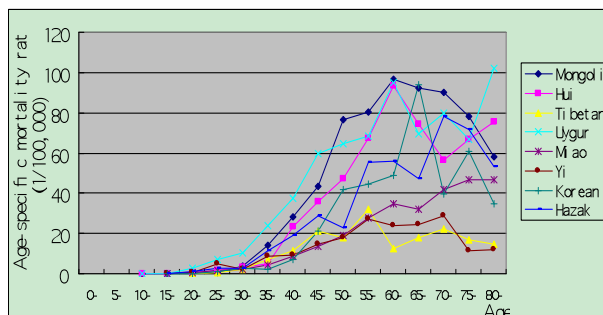


Figure 2. Age-specific Mortality Rate of Cervical Cancer in Eight Ethnic Minorities in Mainland China (Shi et al., 2008)

the China's Health Statistics Yearbook (2003~2008) also reported that the overall mortality was higher among women aged over 50 years (Ministry of Health of the People's Republic of China, 2003-2008).

The first survey also investigated cervical cancer mortality in eight ethnic minorities (Mongolian, Hui, Tibetan, Uygur, Miao, Yi, Korean, Hazak) in China. The age-specific mortality rates varied according to the minority under study. As shown in Figure 2, the highest mortality was observed in Uygur (17.3/10⁵), followed by Mongolian (15.7/10⁵) and Hui (12.3/10⁵). Mortality rates in the above three populations were higher than the national average rate (9.98/10⁵). Uygur also experienced the highest cumulative mortality rate (1.85% in 0~64yrs; 2.59% in 0~74 yrs). In Uygur, the age-specific mortality curve started at a higher level and increased sharply, while in Miao and Yi, the curve had a lower starting point with a slight upward slope. The mortality rate was much higher in Uygur women in every age group than that of Miao and Yi (National Office for Cancer Prevention and Control, 1980).

Cervical Cancer in Different Geographic Areas of China

Incidence: Incidence of cervical cancer varies by region according to a recent analysis of cancer incidence and mortality from 30 cancer registries in China (1998~2002) (National Office for Cancer Prevention and Control et al., 2007). Results of this analysis suggest that the World Age-Standardized Rate (WASR) ranged from 0.0 per 100,000 women (Feicheng City, Shandong Province) to 81.0 per 100,000 women (Yangcheng County, Shanxi Province) (National Office for Cancer Prevention and Control et al., 2007).

According to the China Cancer Registration Annual Report 2004, in which, 43 cancer registries were included, the incidence was similar between urban (CASR 5.29/10⁵) and rural areas (CASR 4.88/10⁵) (National Office for Cancer Prevention and Control, 2008). In urban areas, cervical cancer mainly occurred in women aged 30~59yrs, while in rural areas, women aged over 40 were at higher risk of suffering from cervical cancer (National Office for Cancer Prevention and Control, 2008). The Chinese Cancer Registration Annual Report 2008 suggested a similar trend, with CASR of 5.47/10⁵ in urban areas and 5.54/10⁵ in rural areas (National Office for Cancer

Prevention and Control, 2009).

Mortality: According to Yang et al (2003), Gansu ($11.88/10^5$), Shanxi ($11.23/10^5$) and Shaanxi ($7.28/10^5$) were the three provinces with the highest cervical cancer mortality. These three provinces are located in central and western China and are among the least developed. The third national retrospective cause-of-death survey also showed that cervical cancer mortality was more severe in central (CARS $2.35/10^5$) and western (CARS $2.38/10^5$) China compared to eastern China (CASR $1.19/10^5$)(Zhao et al., 2010; Ministry of Health of the People’s Republic of China, 2008).

Mortality caused by cervical cancer was unbalanced between rural and urban areas. In the 1970’s, the CASR in large cities was the lowest ($8.76/10^5$), followed by medium-size cities ($10.06/10^5$) and small cities ($10.59/10^5$), while it was $10.29/10^5$ in rural areas. The age-specific mortality rate suggested that mortality among women younger than 40 years in large cities was one third of that in rural women in the same age group. This difference became less obvious in women aged 40 and disappeared among women aged 60–64 years. In women aged 65 years or above, the mortality rate in large cities was higher than that in rural areas(National Office for Cancer Prevention and Control, 1980). In the 1990’s, it was reported that the median age at death from cervical cancer in China was 63.2 years old, while it was 66.5 years in urban areas and 62.2 years in rural areas(National Office for Cancer Prevention and Control, 2008). Data from the China Health Statistics Yearbook (2003~2008)(Ministry of Health of the People’s Republic of China, 2003-2008) also suggested that rural areas were characterized by a higher mortality compared to urban areas. When urban areas were classified as large, medium and small cities, the highest mortality was observed in medium and small cities, followed by rural areas, while the lowest was seen in large cities.

From Zhao et al, mortality rate was lower in urban areas than in rural areas in mainland China, but it varied among different regions. In urban areas, the highest rate was observed in western China (CASR $2.45/10^5$), followed by central China (CASR $2.06/10^5$) and eastern China (CASR $1.08/10^5$). In rural areas, the highest rate was seen in central China (CASR $2.50/10^5$), with western China (CASR $2.35/10^5$) ranking the second and eastern China (CASR $1.27/10^5$) ranking the last (Zhao et al., 2010).

These results show that although the cervical cancer mortality rate has decreased during the past 30 years, it still remains a major health problem for women especially women living in rural areas of central and western China, where health care resources as well as access to care is limited.

Cervical Cancer in Different Time Periods

Incidence: An analysis of the incidence of cervical cancer in Qidong city, Jiangsu Province, showed a descending trend of cervical cancer incidence among women of all age-groups from 1973 to 2000 (Fig. 3)(Chen et al., 2004). This study also reported that the incidence among women aged over 55 years during a recent 14-year

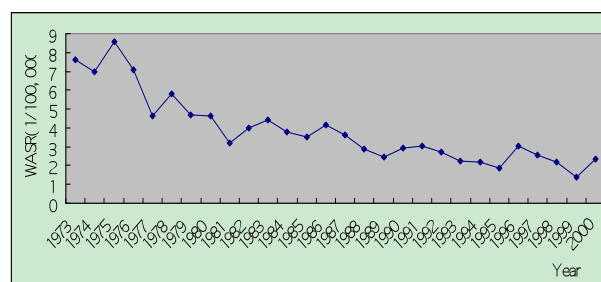


Figure 3. Time Trend of Cervical Cancer Incidence during 1973-2000 in Qidong, Jiangsu Province (Chen et al., 2004)

period (1987~2000) was significantly lower compared to that in a previous 14-year period (1973~1986) ($P < 0.01$).

Qidong city has a more comprehensive cancer registry system. Another article reporting results from an analysis of cancer incidence from 2001 to 2005 suggested that the incidence of cervical cancer declined every five years and the WASR was $4.2/10^5$ in 1978~1982, $3.7/10^5$ in 1983~1987, $2.6/10^5$ in 1988~1992, $2.1/10^5$ in 1993~1997, and finally $2.8/10^5$ in 2001~2005. A more sustainable trend of incidence rate was seen in recent years (Zhu et al., 2006).

Mortality: An obvious decline was observed according to three national retrospective cause-of-death surveys in mainland China. The crude mortality rate for cervical cancer was 11.35 per 100,000 women in the 1970’s, 3.89 per 100,000 women in the 1990’s and 2.86 per 100,000 women in the 2000’s. The CASR declined by 41.85% from the 1990’s to the 2000’s. When data from the first and third national survey were compared, cervical cancer CASR decreased by 82.9%. The WASR changed from $14.50/10^5$ to $4.29/10^5$ and to $2.45/10^5$ in the latest survey (Zhao et al., 2010). Cervical cancer ranked from the 3rd most fatal malignancy to the 6th during the 1970’s to the 1990’s, and it became the 9th most fatal malignancy in the 2000’s (Table 1) (Zhao et al., 2010).

Yang et al analyzed the cervical cancer mortality trend from the 1970’s to the 1990’s in China. In both time periods, an increasing trend among women aged over 20 years was observed, and the mortality reached its peak at the age of 70 years. However, the rate in the 1990’s was

Table 1. Cervical Cancer Mortality and Proportions in 3 Retrospective National Cause-of-death Surveys (Zhao et al., 2010)

Time	CR(/10 ⁵)	CASR(/10 ⁵)	WASR(/10 ⁵)	(%)	Rank
1973-1975					
Urban	11.3	11.0	-	16.3	2
Rural	11.4	11.2	-	18.6	3
All	11.4	11.1	14.5	17.9	3
1990-1992					
Urban	3.27	2.45	-	3.93	7
Rural	4.11	3.60	-	5.21	6
All	3.89	3.25	4.29	4.86	6
2004-2005					
Urban	2.83	1.67	-	2.53	11
Rural	2.88	2.01	-	3.07	9
All	2.86	1.89	2.45	2.86	9

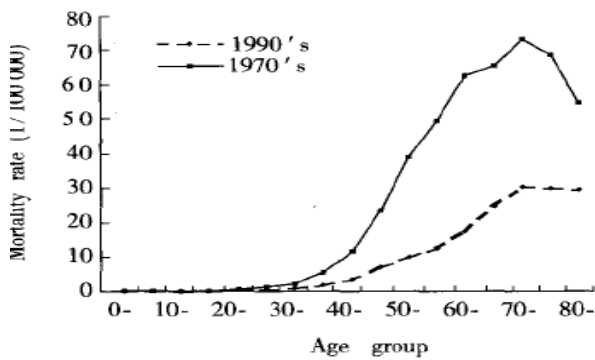


Figure 4. Age-specified Mortality Rate for Cervical Cancer in China, 1970's and 1990's (Yang et al., 2003)

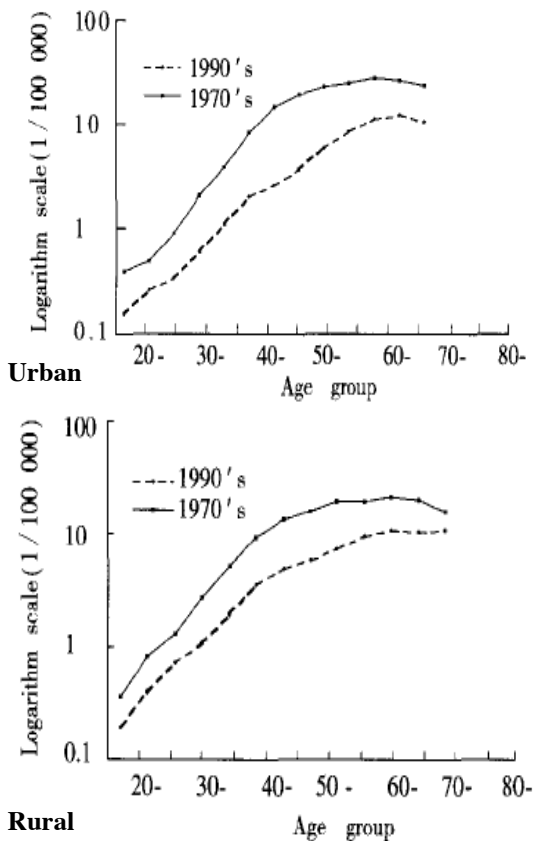


Figure 5. Age-specific Mortality Rates in Areas of China (1970's~1990's) (Yang et al., 2003)

lower than that in the 1970's in age (Figure 4) (Yang et al., 2003).

When the second and the third national surveys comparing, the mortality was also showing a descending trend over time, except for the age-groups 30~34, 35~39 and 40~44. It indicated that the risk of cervical cancer became more severe in younger women (Zhao et al., 2010). Although declining mortality trend was seen in most provinces/autonomous regions/municipalities in mainland China, the decline was not consistent across geographic areas. Mortality seemed to decline less significantly in rural areas compared to urban areas (Figure 5) (Yang et al., 2003).

The same pattern was observed from year 1987 to 1999. Although cervical cancer mortality declined in both rural and urban areas, the decline observed was more significant in urban females (from $3.5/10^5$ to $1.5/10^5$)

compared to rural females (from $5.8/10^5$ to $3.5/10^5$) (Yang et al., 2006).

Population-based Cervical Cancer Screening in China

The “Program of Cancer Prevention and Control in China (2004-2010)” was initiated in 2002 and launched in 2003, the process of this planning was taken by the World Health Organization (WHO) as an example of a “Top-Down” planning process for cancer control (World Health Organization, 2007). In this program, cervical cancer was one of the major cancers that take the priority in China’s cancer control program. According to the WHO, mass screening, early diagnosis and treatment are recommended for cervical cancer control in the developing countries as there are evidence-based, cost-effective and low-cost technologies available. China is a very large country with variable socio-economic status across the country. In order to appropriately explore potential models for cervical cancer screening in different settings of China before devising a nationwide strategy, the government has set up two demonstration sites for the early detection, diagnosis and treatment for cervical cancer in 2005: one was in Shenzhen, a prosperous neighborhood of Hong Kong and the other was in the poverty-stricken county of Xiangyuan in the mid-western coal mining province of Shanxi (Wen, 2005). The two sites are committed to “working out two different screening models, one catering to abundant urban areas and the other to underdeveloped regions burdened with high incidence, with simple, inexpensive, yet safe and cost-effective technologies to screen for pre-cancerous lesions in the cervix, which would otherwise develop into invasive cancer if not detected early”. Based on the experience from the demonstration sites, cervical cancer screening sites were increasingly expanded to a total of 43 sites by 2009, covering every province and autonomous region.

In year 2009, free cervical cancer screening was available for rural women between 35 and 59 years under a government-sponsored program proposed by the Ministry of Health (MOH) and the All-China Women’s Federation. During the following 3 years (2009-2011), 10 million rural women in less developed central and western regions will be able to have access to this free service (Editorial, 2009). This program was proposed by the All-China Women’s Federation, and was integrated into the existing women’s health care system. This new government-sponsored program is a step towards provision of cervical cancer screening nationwide, although with an estimated 500 million women in rural China the public health challenge is substantial. This is the first time that the Chinese Government has proposed to gradually widen access to cancer prevention services, so that women in rural China are included. If this program succeeds, it could provide a valuable experience on introducing a step-wise population-based cervical cancer screening for other developing countries.

Conclusion

In summary, the incidence and mortality of cervical cancer vary widely by population, geographic area and time period. Cervical cancer is among the ten most common malignancies in Chinese women. It is more incident in the middle-aged women while more fatal among women aged over 50 years. Uygur women seem to suffer a higher disease burden, in terms of both incidence and mortality, compared to other ethnic groups. Although a declining trend in mortality was seen in most areas of mainland China, it was less significant in rural compared to urban areas. Some central and western rural areas suffer a considerable mortality. One alarming trend observed was that the risk of cervical cancer is becoming more severe in younger women. Although a nation-wide screening program does not yet exist, the Chinese government has taken measures to control cervical cancer by conducting screening in selected sites located all over the country, demonstrating its plans to curb the disease.

Acknowledgement

We thank the Cancer Institute of the Chinese Academy of Medical Sciences (CICAMS) with providing their expertise in the development of the study. Scientific review and editorial support were provided by Dr. Johannes E Schmidt (MD MPH, Belgium, GSK Biologicals). The authors also thank GlaxoSmithKline Biologicals for supporting this literature review. GSK Bio was given the opportunity to revise the document. The relevance of the comments was evaluated on a case-by-case basis by the authors and modifications done accordingly in the manuscript.

References

- Chen J. G, Zhang Y. H, Zhu J, et al (2004). Analysis on incidence for cervical cancer in Qidong during 1972 - 2000]. *Zhonghua Fu Chan Ke Za Zhi*, **39**, 505-7.
- Curado M. P, Edwards B, Shin H. R, et al (2007). Cancer incidence in five continents, Vol. IX, Lyon: International Agency for Research on Cancer.
- Editorial (2009). Women's health in rural China. *Lancet*, **374**, 358.
- Ministry of Health of the People's Republic of China (2003-2008). China's Health Statistics Yearbook]. Peking Union Medical College Press, Beijing.
- Ministry of Health of the People's Republic of China (2008). Third national retrospect spot-check of death-causation. Peking Union Medical College Press, Beijing.
- National Office for Cancer Prevention and Control (1980) [Investigation of China cancer mortality (1973~1975)]. People's Medical Publishing House, Beijing.
- National Office for Cancer Prevention and Control (2008) [Investigation of China cancer mortality (1990~1992)]. People's Medical Publishing House, Beijing.
- National Office for Cancer Prevention and Control, National Center for Cancer Registries & Disease Prevention and Control Bureau (2007). Cancer incidence and mortality in selected cities and counties in China, 1998-2002 Volume III]. People's Medical Publishing House, Beijing.

- National Office for Cancer Prevention and Control, National Central Cancer Registries, Disease Prevention and Control Bureau & Ministry of Health (2008) China Cancer Registration Annual Report 2004. Peking Union Medical College Press, Beijing.
- National Office for Cancer Prevention and Control, National Central Cancer Registry, Disease Prevention and Control Bureau & Ministry of Health (2009) Chinese Cancer Registry Annual Report 2008. Military Medical Science Press, Beijing.
- Parkin DM, Bray F, Ferlay J, et al (2005). Global cancer statistics, 2002. *CA Cancer J Clin*, **55**, 74-108.
- Shi JF, Qiao YL, Smith JS, et al (2008). Epidemiology and prevention of human papillomavirus and cervical cancer in China and Mongolia. *Vaccine*, **26**, M53-9.
- Wen C (2005). China's plans to curb cervical cancer. *Lancet Oncol*, **6**, 139-41.
- World Health Organization (2007). WHO Guide for Effective Programmes: Cancer Control Planning. World Health Organization, Geneva.
- Yang L, Huangpu XM, Zhan SW, et al (2003). Changes of mortality rate for cervical cancer during 1970's and 1990's periods in China]. *Zhongguo Yi Xue Ke Xue Yuan Xue Bao*, **25**, 386-90.
- Yang L, Li LD, Chen YD, et al (2006). Time trends, estimates and projects for breast cancer incidence and mortality in China]. *Zhonghua Zhong Liu Za Zhi*, **28**, 438-40.
- Zhao FH, Hu SY, Zhang SW, et al (2010). Cervical cancer mortality in 2004 - 2005 and changes during last 30 years in China. *Zhonghua Yu Fang Yi Xue Za Zhi*, **44**, 408-12.
- Zhu J, Chen JG, Zhang YH (2006). An analysis of cancer incidence from 2001 to 2005 in Qidong, Jiangsu. *China Cancer*, **15**, 646-9.
- Zhu X Y, Qiu J, Lai XJ (2004). An analysis of in-patients cancer type distribution in a period of 10 years in Xinjiang cancer hospital. *China Cancer*, **13**, 712-4.