LUNG CANCER IN URBAN CHINA



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As the result of an ageing population, high smoking prevalence and serious air pollution, lung cancer in China has increased significantly during the past decades. Notably, the incidence and mortality of lung cancer are higher in urban China than in rural areas, however, these differences between urban and rural areas have been decreasing. A great deal of effort has been made by the government of China to address this, including tobacco and air pollution control. Although lung cancer survival is better in urban areas than in rural China, the five-year survival rate of lung cancer patients in urban China is still as low as 19.5%, whilst most lung cancer cases are diagnosed at an advanced stage and accordingly lose the opportunity of surgery. Consequently, two government-sponsored screening programmes including lung cancer have been initiated in recent years, and Chinese guidelines on the diagnosis and treatment of primary lung cancer have been issued to standardize the diagnosis and treatment of lung cancer.

Lung cancer has become the leading cause of cancer death in China with a rapidly increasing trend over the past three decades, especially in urban areas. Smoking is the predominant risk factor for lung cancer. Also, rapid modernization and development has resulted in a large migration from rural areas to cities and a concomitant increase in urban air pollution *(1)*. Due to the high smoking prevalence, severe air pollution and ageing population, lung cancer incidence and mortality in urban China will increase in future decades. Lung cancer screening plays a key role in decreasing lung cancer morality and improving the prognosis of patients, and randomized controlled trials have confirmed the effect of low dose spiral CT screening (LDCT) *(2)*. Accordingly, LDCT screening was approved for Medcare in the United States recently. In urban China, two government-sponsored screening programmes, including lung cancer, were initiated in recent years. This article will give a brief introduction to the lung cancer epidemic, lung cancer prevention and its control in urban China.

Lung cancer epidemiology in urban China

Incidence and mortality

Lung cancer is the most common cancer and leading cause of cancer death in both urban and rural areas in China. According to recent data from a 2010 cancer registry report, there were 605,946 new cases (19.59% of the total) and 486,555 deaths (24.87% of the total) from lung cancer.

The incidence of lung cancer was 46.08/10^5, and the age-standardized rate by Chinese standard population (ASR China) was 35.23/10^5, while the mortality was 37.00/10^5, as well as ASR China was 27.93/10^5. Both the incidence and mortality rates in males were approximately twice those in females.

In urban areas, the incidence of lung cancer was 52.52/10^5 (70.39/10^5 in males and 33.78/10^5 in females) and mortality was 42.23/10^5 (56.72/10^5 in males and 27.04/10^5 in females), while incidence and mortality in rural areas were 39.54/10^5 and 31.69/10^5 respectively. Correspondingly, the ASR China for incidence and mortality in urban areas (36.62/10^5 and 28.88/10^5) were both higher than in rural areas (33.39/10^5 and 26.61/10^5) *(3)*.

Temporal trends

Lung cancer deaths have increased dramatically in the past three decades. There were three national cause of death retrospective surveys conducted by National Health and Family Planning Commission of the PRC (former MoH) from 1973–1975, 1990–1992 and 2004–2005 respectively. The data showed the mortality of lung cancer rose from 5.46 to 17.54, up to 30.83 (per 100,000), with the greatest increase among all cancers of 465% with the ranking for cancer death moving up from fifth to third, and up to first place (Fig. 1) *(4)*.

Figure 1: Temporal trends of cancer mortality rate for the top 10 cancers

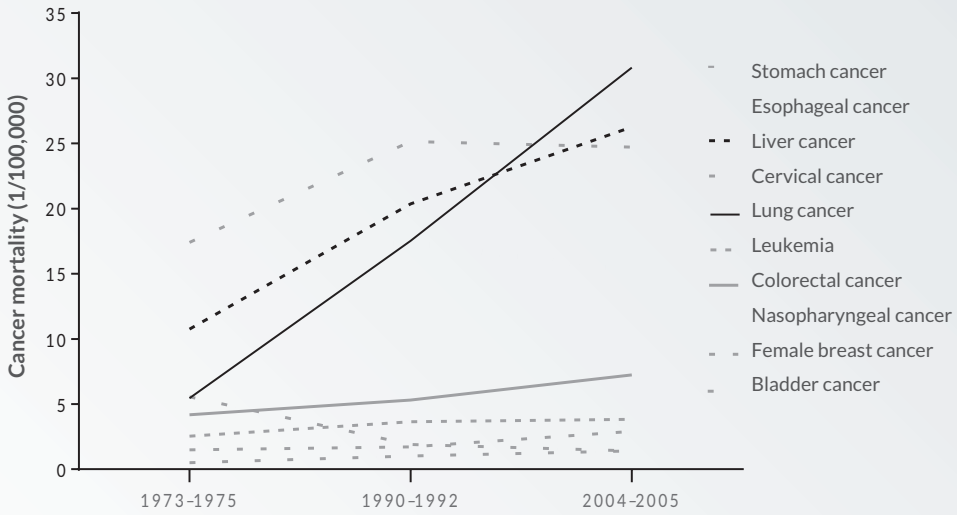
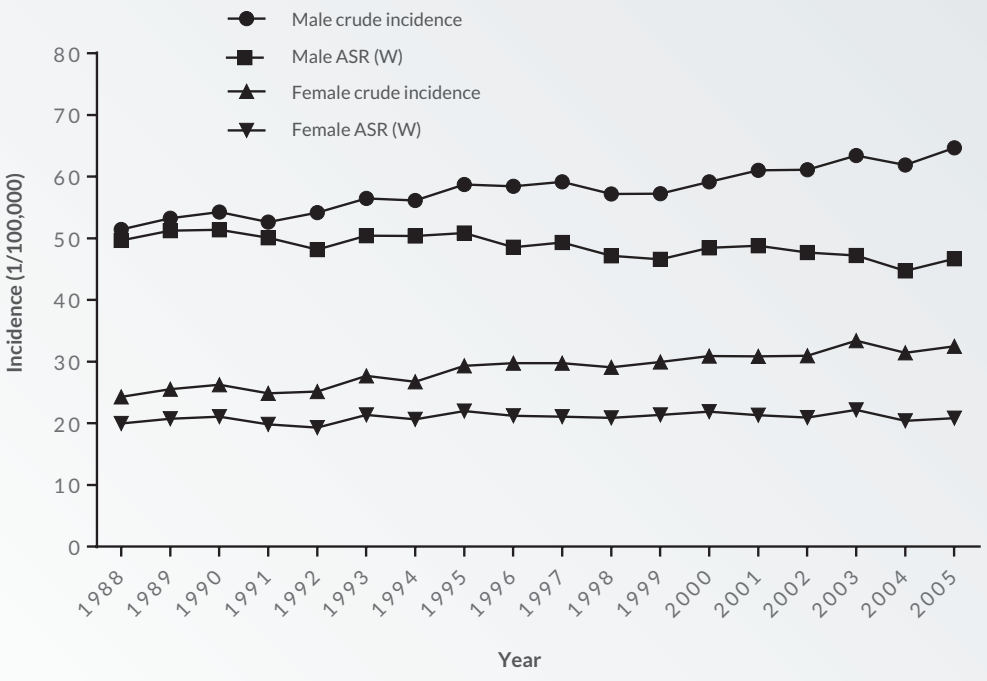


Figure 2: Tendency of lung cancer incidence in 10 registries from 1988–2008 in China (ASR(W): Age-standardized incidence (world))



From 1988 to 2005, lung cancer incidence had a annual increase of 1.63%, partly due to the ageing population (Fig. 2) *(5)*.

Although the mortality and incidence of lung cancer in urban areas or males is higher than in rural areas or females, the differences between urban and rural areas, males and females have been gradually getting smaller year-by-year. The incidence rate ratio (IRR) between urban and rural areas remarkably decreased from 2.07 to 1.14 while IRR for male and female changed from 2.45 to 2.21 during 1989–2008 *(6)*.

Etiology

Ranked as the most common cancer, and leading cause of cancer death, lung cancer constitutes a more and more serious health burden in China, following rapid economic development that brought cultural and behavioural changes, increasing high prevalence of smoking, ageing population

Table 1: Baseline screening in some cities in China (supported by a public health special subsidy from central government)

Province (City)	Time	Partici-pants	Cases	Detection rate (%)	No of early lung cancers	Early detection rate (%)	No of treatments	Treatment rate (%)
Tianjin	2010	1000	4	0.40	3	75.00	3	75.00
	2010.7–2011.6	1000	9	0.90	4	44.40	8	88.90
	2011.7–2012.6							
	2012.7–2013.6	1082	6	0.57	2	33.30	3	100.00
	2013.7–2014.6	245	0	0	0	0	0	0
	Total	**3227**	**19**	**0.57**	**9**	**47.23**	**17**	**89.47**
Beijing	2012.7–2013.6	682	2	0.29	2	100	2	100
	2013.7–2014.6	1254	1	0.08	0	0	1	100
Yunnan (Gejiu)	2013.7–2014.6	1018	7	0.69	4	57.14	6	57.14
Sichuan (Nanchong)	2013.7–2014.6	1050	2	0.19	2	100	2	100
(Chengdu)	2013.7–2014.6	1031	5		0	0	4	80
Total		**8262**	**36**	**0.44**	**17**	**47.22**	**32**	**88.89**

and air pollution.

The mortality and incidence of lung cancer is higher in urban areas than in rural areas, but the gap between the two areas has significantly reduced in recently years. The reason may be due to the process of industrialization and urbanization in rural areas which leads to similar lifestyles and environments to urban areas, as well as a higher prevalence of smoking in rural areas.

Smoking is the predominant cause of lung cancer. As the world's largest producer and consumer of tobacco, the current smoking rate was 66% for males and 3.1% for females *(7)*. Tobacco use in China accounts for 75.04% of lung cancer deaths in men and 18.35% in women *(8)*. Tobacco control in China is imperative.

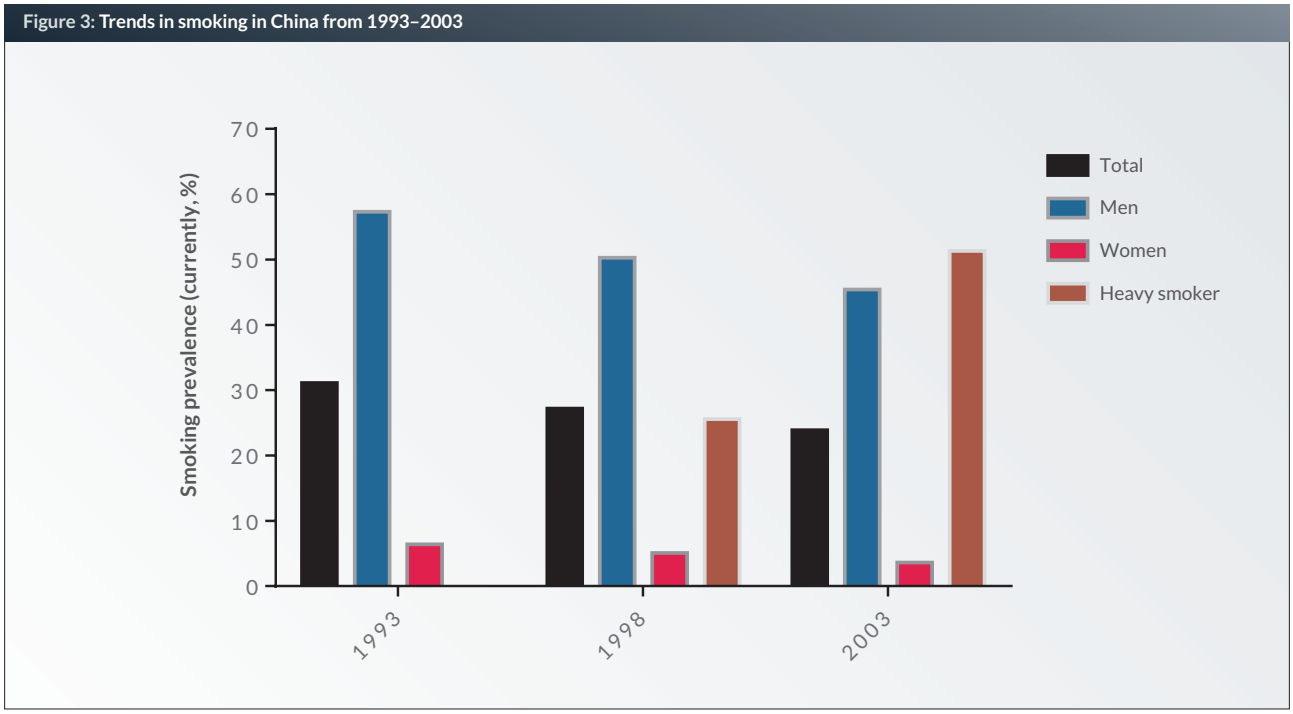
Outdoor and indoor air pollution is another important risk factor for lung cancer, and lung cancer attributable to air pollution in China has not yet been well quantified. With rapid economic development and urbanization, air quality in China is among the worst in the world, especially in cities, where it is mainly caused by coal, motor vehicles and industrial dust *(9)*. The average annual PM2.5 concentration in Beijing in 2011 has reached 100 μg/m^3, which is nearly 10 times higher than the World Health Organization guidelines of 10 μg/m^3 *(10)*.

Lung cancer prevention and control in urban China

Tobacco control is the most important measure of primary prevention of lung cancer. In 2005, China joined the WHO Framework Convention on Tobacco Control (WHO FCTC). Since then, many measures have been implemented including enforcing smoke-free policies in public places and increasing taxes. In 2012, The China Tobacco Control Programme (2012–2015) was released. Since 2009, China has raised the tobacco tax for grade A and B cigarettes and cigars from 45% to 56%, 30% to 36% and 25% to 36%, respectively. However, the cigarette retail prices did not change after the 2009 tax adjustment, which suggests a further increase of tobacco tax in the future *(11)*. An online-based survey demonstrated that a smoking ban had a significant effect on Chinese internet users' smoking-related behaviours *(12)*, but the true effect of this measure needs to be further assessed. Also, recently the Beijing Government approved rules to ban smoking in all indoor public places, workplaces and public transport vehicles, which took effect in June 2015. However, according to the results of a national survey, though smoking prevalence has decreased in urban areas from 1993–2003, heavy smoking has increased substantially and only 6.9% of current smokers reported that they intended to quit in urban locations (Fig. 3) *(13)*. In addition, former smokers with long-term abstinence still have elevated lung cancer risk. Therefore, the effect of tobacco control on lung cancer prevention has not been seen in recent years.

Outdoor air in China is more polluted in cities than in rural areas. In 2013, the State Council released the Action Plan for Air Pollution Prevention and Control which would be the

Figure 3: **Trends in smoking in China from 1993–2003**



guide for national air pollution prevention and control over the next time period, and for the monitoring of PM2.5 which will be implemented in all cities in China by 2015. However, similar to tobacco control, it will take a long time to reduce outdoor air pollution and its negative health effects in urban China.

Lung cancer remains a highly lethal disease and most patients are not diagnosed early enough for surgery. Though impressive progress has been made in recent years with the national cancer registry system, including an increase in cancer registries numbers to cover pollution and enlargement data scope from single mortality to incidence and survival, however, detailed information including stage distribution of lung cancer are currently unavailable. In a recent population-based study, the overall five-year survival rate of lung cancer in China was 19.5% and 11.2% in urban and rural areas respectively *(14)*. However, its prognosis is more favourable when diagnosed at an earlier stage, and this provides a rationale for lung cancer screening as the secondary lung cancer prevention measure.

To be efficient, lung cancer screening is focused on high risk populations. Though tobacco smoking is the most important cause of lung cancer, and more interest is aroused because of the effect of air pollution on lung cancer in last decade in China *(9,15)*, however, before the early twenty-first century, mass lung cancer screening was only conducted among occupational miners of the Yunnan Tin Corporation (YTC) in Gejiu City, Yunnan Province, which was known as the "Tin metropolis" of the world. Gejiu was found to have the highest lung cancer mortality in men among 2392 counties or cities across China in the nationwide mortality survey conducted in 1973–1975 *(16)* which was mainly due to occupational radon and arsenic exposure, and smoking *(16,17)*. In the mid-1970s, Chinese Premier Zhou Enlai sent a team of medical professionals to the Yunnan Tin Corporation, directing them to reduce lung cancer deaths in the miners. Since 1973, an average of approximately 7000 active and retired miners have been screened for lung cancer annually by chest X-ray and cytologic examination of the sputum.

From 1992 to 1999, a collaborative project entitled "Early marker study of lung cancer among tin miners in Yunnnan, China" had been conducted by the National Cancer Institute (NCI), the Cancer Institute of Chinese Academy Medical Sciences (CICAMS) and YTC, and was followed up at the end of 2001 *(19,20)*. Based on this project, a screening cohort had been established which enrolled 9295 tin miners with at least 10 years of occupational radon and/or arsenic exposure. Over the period 1992–2001, a total of 468 lung cancer cases were histologically confirmed. Among the 468 lung cancer cases, 234 (50%) were screen-detected cases, 78 (16.7%) were interval cases, while 156 (33.3%) were post-screening cases. The proportion of early lung cancer and survival was highest in lung cancer cases when detected by sputum cytological examination, then followed by X-ray alone, dual detected and interval cases, and was lowest in post-screening lung cancer cases. However, as a working screening programme, the effectiveness of screening with X-ray and sputum cytology could not be evaluated.

In 2003, with the increasing burden of cancer, the Ministry of Health of China issued a *Compendium of Cancer Prevention and Control in China for year 2004–2010 (21)*. The compendium stated clearly that early detection, early diagnosis and early treatment of cancer should be carried out according to local conditions. On the basis of the principle of this Compendium, in 2005, the Ministry of Finance and the Ministry of Health have included the cancer early detection and treatment programme into a special fund programme supported by the public health special subsidy from the central government, i.e. the central government would assign special funds to run the programme for early detection and treatment of cancer. By the end of 2009, six kinds of cancers (cervical cancer, esophageal cancer, liver cancer, colorectal cancer, nasopharyngeal cancer and gastric cancer) had been included into this programme. However, even though numerous studies have shown the benefit of stage shift and cancer survival from LDCT since the 1990s, due to the effectiveness of screening, these had not been confirmed and lung cancer screening was not included into this programme.

In 2010, in view of the burden of lung cancer in China and the excellent survival of early lung cancer cases detected by LDCT, lung cancer screening was included in this programme though its effectiveness had not been confirmed by the National Lung Cancer Screening Trial (NLST) at that time *(2,22)*. For the smooth implementation of the project, the administration of this programme includes three levels: Cancer Foundation of China which represents the Disease Prevention and Control Bureau of the Ministry of Health, the Provincial Department of Public Health, and county Department of Public Health. For its implementation, this project is conducted in local hospitals at county level, and academic support is provided by national and provincial experts *(22)*. This pilot project is an ongoing, prospective, multi-centre observational study of screening with LDCT initiated in 2010. Up to now, several cities have been involved in this project, including Beijing, Tianjin, Chengdu in Sichuan province, Gejiu in Yunnan province, Hangzhou in Zhejiang province and Shenyang in Liaoning province. Table 1 shows the preliminary results of baseline screening between 2010 and 2014.

In 2012, another government-backed cancer screening programme was launched in China. This five-year project is being jointly undertaken by the Disease Prevention and Control Bureau under the Ministry of Health, the National Cancer Centre and the Cancer Institute & Hospital (CIH) under the Chinese Academy of Medical Sciences. Its focus is on lung, breast, colorectal, upper digestive tract and liver cancer early diagnosis and treatment in urban China. The project will cover 14 provinces and 700,000 high-risk people will be screened with an estimated budget of 480 million Yuan. As regards lung cancer, 2000 high-risk people were scheduled to be screened in each city in nine provinces in 2012, and 3000 high-risk people were scheduled to be screened each city in 12 provinces in 2013, thus a total of 54,000 high-risk people would receive LDCT lung cancer screening by the end of 2013, according to the programme schedule. Through this programme, the National Cancer Centre expects to establish a long-term cancer prevention and control system and network including lung cancer in urban China *(23)*.

Besides LDCT screening, the above two screening programmes involved several other items including health promotion to increase screening acceptance, technical training for local doctors and technical personnel, delivery of smoking cessation intervention, biomarker discovery and validation to evaluate whether the early lung cancer biomarker can be refined for high-risk populations and augment LDCT accuracy through classifying nodules detected by LDCT. In addition, to keep a sustainable development of a national screening programme, the two programmes have been included in the special programme for medical insurance system reform in China to explore the possibility of incorporating lung cancer screening in the routine health insurance system in China.

Currently, it is not the right time to cover LDCT screening among high-risk populations nationwide due to the uncertainties regarding reducing the side-effects due to LDCT screening, how to translate the NLST result into clinical practice and the unknown cost-effectiveness of LDCT in China. For these reasons, the two screening programmes only cover a small fraction of high-risk pollution with the aim of exploring the feasibility of LDCT screening in China.

Lung cancer treatment in urban China

Up to now, no nationwide database for the clinical characteristics of lung cancer has been established. Thus, information about stage distribution of lung cancer in urban China is unavailable. However, there was no doubt that most lung cancer cases were diagnosed at an advanced stage and accordingly lost the chance of surgery. To standardize the diagnosis and the treatment of lung cancer, Chinese guidelines on the diagnosis and treatment of primary lung cancer were issued in 2011 *(24)*. In these guidelines, an individualized multidisciplinary treatment model combining surgery, chemotherapy, radiotherapy and targeted biological therapy was recommended. There is marked urban–rural disparity in lung cancer treatment. Compared to rural

patients, those who live in urban environments are more likely to access to health care with high quality. Most tertiary hospitals which can provide optimal level treatments are located in urban areas. However, the five-year survival of lung cancer in urban China was still as low as 19.5%.

In conclusion, in view of the high prevalence of tobacco smoking and serious air pollution, policy-makers for lung cancer health policy in the China government might focus on both smoking cessation, improving air quality and the early detection of lung cancer. •

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