LUNG CANCER IN RURAL CHINA



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Nearly half of the population live in rural China. Lung cancer is leading cause of cancer death in rural China, and its survival was significantly poorer in rural areas than in urban areas. However, lung cancer control and prevention are markedly weak mainly due to the urban-rural health disparities such as health awareness, accessibility and quality of health care. A tailored lung cancer prevention and control strategy should be developed for rural China.

In China, lung cancer has become the leading cancer-related cause of death since the beginning of the twenty-first century, mainly due to the severe tobacco epidemic, increasing air pollution and population ageing *(1)*. Over the past 30 years since its economic reform, China has experienced a rapid urbanization trend with an increase in the proportion of the urban population from 19.39% in 1980 to 53.73% in 2013. However, nearly half of the total population live in the rural areas *(2)*. Though the mortality and incidence of lung cancer in rural areas are lower than those in urban areas, the gaps between urban and rural areas is getting gradually smaller, and the lung cancer burden in rural areas is increasing *(3)*. Additionally, lung cancer survival in rural areas was significantly poorer than in urban areas (5-year survival, 11.2% vs. 19.5%) *(4)*. Due to the differences in etiological pattern and disparities in lung cancer treatment, a tailored lung cancer prevention and control strategy should be established for rural China. This article will give a brief introduction to the lung cancer epidemic, lung cancer prevention and control in rural China.

Lung cancer epidemiology in rural 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. It was estimated that there were 733,300 new lung cancer cases and 610,200 lung cancer deaths in China in 2015, and among them, 39.3% of new cases and 38.8% of deaths were from rural areas *(5)*. In 2011, the crude incidence rate in rural areas was 47.14/10^5, lower than that in urban areas (49.44/10^5). After age standardization, the incidence rate in rural areas was still slightly lower than that in urban areas.

It was estimated that 248,152 lung cancer deaths in rural areas in 2011, with crude and age standardized lung cancer mortalities of 37.80/10^5 (50.98/10^5 in males and 23.80/10^5 in females) and 27.58/10^5 (39.47/10^5 in males and 16.30/10^5 in females), respectively, both of them were lower than those in urban areas.

Age-specific rates of both lung cancer incidence and death were low in the groups under 40 years of age in rural areas, and with a rapid increase from 40–44 years of age and to reach a peak for groups aged 75–79 years for incidence and 80–84 age group for mortality, then followed a marked decrease in groups with older ages. Compared with urban areas, whether for incidence or mortality, the age-specific incidence in rural areas was higher in patients under 65 years of age and lower in patients aged 65 or over *(6)* (Fig. 1).

Temporal trend

According to three national death surveys, lung cancer mortality in urban and rural areas consistently increased from the 1970s to 2000s. The age-standardized lung cancer mortality in rural areas increased from 5.73/10^5 in 1973–1975, 16.90/10^5 in 1990–1992 to 24.33/10^5 in 2004–2005,

Figure 1: Age-specific lung cancer incidence and mortality in rural and urban China, 2011

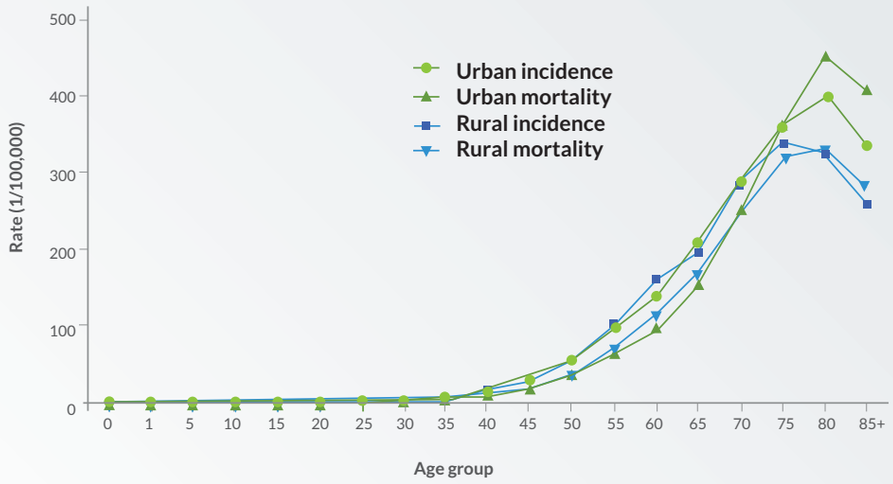
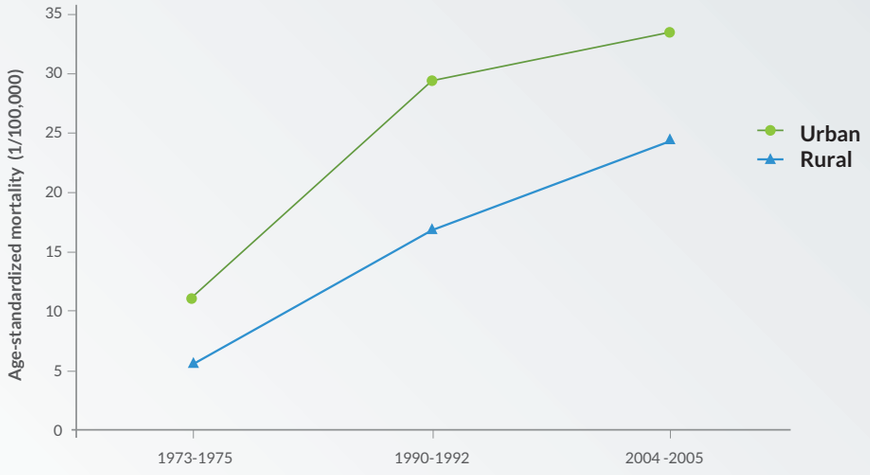


Figure 2: Temporal trend of lung cancer mortality rate from 1970s to 2000s



with an increment of 425%, which was higher than the increment in urban areas of 297% (11.24 /10^5 in 1973–1975, 29.47/10^5 in 1990–1992 to 33.39/10^5 in 2004–2005, respectively) *(7)* (Fig. 2). In another study, after age adjustment, lung cancer incidence in rural areas still shows a increasing trend from 1989 to 2010, which suggest that this increase can not be completely attributed to population ageing, while the corresponding increase in urban areas might largely due to the ageing process *(3, 8)* (Fig. 3).

Lung cancer survival

The 5-year survival of lung cancer in China was 16.1%, similar to that of Australia, Europe and the United States. However, it was only 11.2% in rural China, which was considerably lower than the survival of 19.5% in urban areas *(4)*. This difference directly reflects the disparity of health awareness, health-care accessibility and quality of health care between rural and urban areas. For example, patients in rural areas usually prefer Chinese medicine or to undergo chest X-ray examination only, which resulted in a delay in diagnosis, and subsequent loss of the chance of best treatment *(9)*. Also, qualified staff for cancer care are not evenly distributed across the country, and rural areas still experience shortages of health staff due to the movement of

qualified health professionals from grassroots, rural health facilities to larger, urban facilities *(10)*. These disparities point to the need for expanded access to lung cancer screening and treatment in rural areas.

Lung cancer etiology

Smoking is a well-known health issue globally and a leading cause of lung cancer. Recently, two nationwide prospective studies reported the tobacco-attributed mortality in China. The relative risks (RRs) of lung cancer for smokers compared with non-smokers in rural men in these two studies increased from 1.76 (95% CI: 1.62–1.91) in the first cohort study conducted between 1991–1999 to 2.30 (95% CI: 2.13–2.48) in the second study conducted in 2006–2014. However, the RRs of lung cancer risk for smoking in rural men were lower than those in urban men, which were 2.32 (95%CI:2.08–2.59) and 2.98 (95%CI:2.66–2.33), respectively *(11)*. The reason that the hazard associated with a given current smoking pattern in rural areas is lower than urban areas might be because cigarette consumption became widespread earlier in urban than in rural areas, mainly due to limited rural availability. However, this urban-rural difference is likely to diminish, or even be reversed, over the next few decades, because rural men born after the 1960s not only tended to start at the same age as urban men and to smoke only cigarettes, but also had a somewhat higher smoking prevalence. There were also significant dose-response effects of lung cancer risk in relation to age when smoking started and the daily amount smoked. In rural men, compared with non-smokers, the RRs for the age when smoking started in groups of <20, 20–24 and ≥25 were 2.91, 2.45 and 1.63 in the second cohort study (2006–2014) respectively, while the RRs for daily amount smoked in groups of <15, 15–24 and ≥25 were 1.81, 2.38 and 3.20 respectively *(11)*.

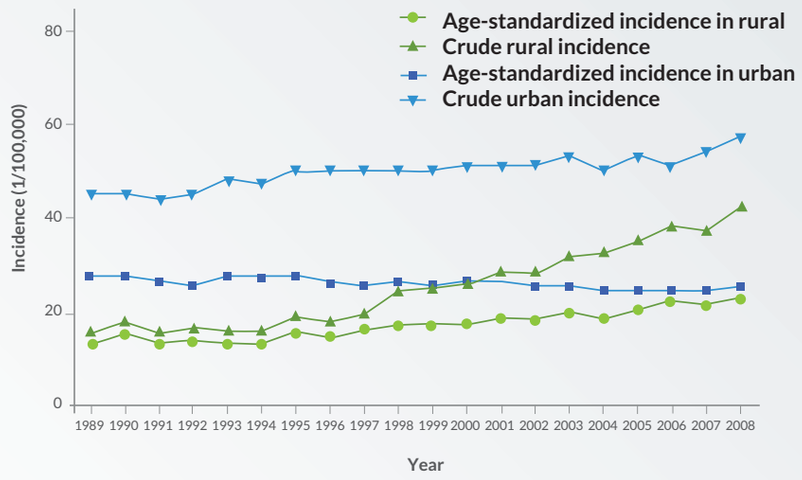
Second-hand smoking, also known as environmental tobacco smoke, has been classified as a known human (class A) carcinogen *(12)*. Nonsmokers who live with a smoker had a 20% to 30% increased risk of lung cancer than those without passive smoking exposure *(13)*. Second-hand smoking is estimated to cause 22,000 lung cancer deaths per year in China *(14)*. Exposure to second-hand smoking has not changed over the last ten years, and is estimated that some 740 million non-smokers suffered from exposure to second-hand smoking in 2010 in China, and SHS exposure in rural areas was higher than that in urban areas (74.2 vs. 70.5% in 2010) *(15)*.

Indoor emissions from household coal combustion has also been classified as carcinogenic to humans by the International Agency for Research on Cancer (IARC), and evidence was based largely on studies of lung cancer in China, especially in rural China *(16)*. While household coal use in urban areas is declining as it is being replaced with gas stoves and with space heating methods, indoor air pollution from unventilated coal-fueled stoves and cooking fumes have always been major risk factors for lung cancer in rural China over the past decades, and most households continue to burn biomass fuels, such as coal and wood, for cooking and heating in open stoves in poorly ventilated homes in rural China. These low efficiency practices result in higher emission factors than industrial coal and internal combustion engines. A meta-analysis of 20 case-control studies (10,142 cases and 13,416 controls) of lung cancer and household coal use found that household coal use was associated with an elevated lung cancer risk (OR = 2.27, 95% CI = 1.62–3.12) in Mainland China and Taiwan *(17)*. A classic example of indoor air pollution is Xuanwei County in Yunnan Province, which had an extremely high lung cancer incidence due to indoor air pollution from smoky coal burning. Since the 1970s, numerous epidemiological and intervention researches have been conducted in Xuanwei, and provided substantial scientific evidence of the carcinogenic effect of the indoor combustion of coal *(18, 19)*.

In recent years, new pollution problems have arisen from crop residues in rural areas. As a main renewable biomass resource, crop residue contributes about 30–45% of total energy consumption in rural China *(20)*. Due to the low combustion efficiency in cooking stoves, various incomplete products, including particulate matter (PM), organic carbon (OC) and parent polycyclic aromatic hydrocarbons (pPAHs) *(21)*, from residential stove burning or burning in the field are usually much higher than those from industrial combustions, leading to widespread ambient and indoor pollution.

Over the last three decades, rural China has also faced an overlap of traditional and modern risks mainly the outdoor air pollution accompanied with rapid economic development (Fig. 4). Outdoor air pollution and particulate matter from outdoor air pollution was classified as carcinogenic to humans by IARC in 2013, and only one epidemiological study in China was available for review by IARC *(22)*. In this prospective cohort study conducted in 31 Chinese cities, the adjusted RRs for lung cancer in relation to SO_2, NOx and PM2.5 were 1.04 (95% CI: 1.02–1.06), 1.03 (95% CI: 0.99–1.07) and 1.03 (95% CI:1.00–1.07) per 10 μg/m^3, respectively *(23)*. In a recent spatiotemporal analysis in China, the RR of lung cancer incidence related to a10μg/m^3 increase in 2-year average PM2.5 were 1.037 (95% CI:

Figure 3: Annual lung cancer incidence in rural and urban China from 1989 to 2008



0.998–1.078) for rural populations, slightly lower than that for urban communities (RR=1.060, 95% CI: 1.044–1.075) *(24)*. However, outdoor air pollution in both rural and urban areas also presents marked regional characteristics: the pollution is heavier in northern and central China, where it is more densely populated and in the more economically advanced parts of rural China (Fig. 5).

Lung cancer prevention and control in rural China

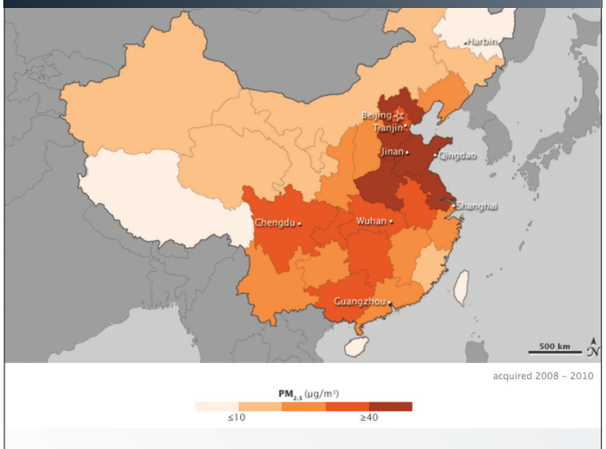
It is well known that smoking cessation can reduce lung cancer risk. Since the Framework Convention on Tobacco Control (FCTC) was ratified in China in 2006, there has been a strong push for national legislation, and progress is being made in China, including enforcing smoke-free policies in public places and increasing taxes. In December 2012, the Government of China issued the China National Tobacco Control Plan 2012–2015, which includes an ambitious target of reducing the adult smoking rate from the 2010 rate of 28.1%, to 25% in 2015 *(25)*. In the same year, the Ministry of Health published the first official report on the harms of smoking to strengthen the tobacco control efforts *(26)*. In addition, in recent years, many cities have approved rules to ban smoking in all indoor public places, workplaces and public transport vehicles. However, currently no smoke-free legislation and policies have been made for rural China.

The smoking prevalence in rural areas was higher than that in urban areas, and males in rural areas are more likely to be smokers than males in urban areas. However, there were more quitters in urban areas than in rural areas. More people in rural areas quit smoking for financial reasons than in urban areas (8% versus 13%, respectively), and less for prevention in rural areas (28% versus 26%, respectively) *(27)*. In rural areas, pressure from cigarette sharing and gifting customs was the major barrier to smoking cessation

Figure 4: Outdoor air pollution in rural China in the winter of 2015

Source: http://news.xinhuanet.com/english/china/2013-01/13/c_132099286.htm

Figure 5: Satellite-derived map of PM2.5 averaged over 2001–2010 in China



Source:http://earthobservatory.nasa.gov/IOTD/view.php?id=77495&eocn=image&eoci=related_image

(28). Besides, the rate of awareness that smoking and second-hand smoking could cause lung cancer was lower among rural residents than their urban counterparts *(29)*. The unique features of tobacco use in rural China, including sociocultural factors associated with smoking initiation and cessation, lack of awareness among the public about the hazards of smoking and weak support from the government, are major reasons for the lack of effectiveness of current tobacco control measures in rural areas, and specific effective intervention efforts should be developed for rural China.

It is often believed that air pollution occurs mainly in cities where most power stations, industrial facilities and motor vehicles are concentrated, accordingly, more measurements for pollution control have been implemented in cities. Currently, atmospheric PM10 is extensively monitored in urban areas, and monitoring on PM2.5 has became a routine in many cities. However, routine environmental monitoring was not used in rural China.

It was reported that across northern China, the annual mean PM10 concentrations in urban, rural village and rural field sites were similar which suggested that strong localized emissions and severe contamination in rural residential areas are due to the solid fuel combustion in households *(30)*. In China, coal and biomass fuels are extensively used in rural areas for cooking and heating, resulting in severe air pollution both indoors and outdoors. To reduce indoor air pollution from solid fuels, China's National Improved Stoves Programme has introduced more than 180 million improved stoves since the early 1980s, however, the magnitude of pollutant concentration reduction varies substantially depending on the type of improved stove *(31)*. Unfortunately, this programme ended in the mid-1990s, and the situation appears to be getting worse as coal use in rural areas is rising. However, efforts to reduce indoor air pollution have never stopped and in 2012, China joined the Global Alliance for Clean Cook Stoves which aims to scale up access to clean cooking and heating stoves for poor, primarily rural households, who are likely to continue using solid fuels beyond 2030 *(32)*.

Though smoking control is the most effective measure of the primary prevention of lung cancer, an upward trend of lung cancer incidence and mortality is still expected in future decades in China because of the high prevalence of smoking and severe air pollution. In addition, lung cancer survival is closely related to the stage at diagnosis, that is, its prognosis is more favourable when diagnosed at an earlier stage. Accordingly, as a measure of secondary prevention, screening and early detection play an important role in lung cancer control.

With the increasing disease burden from lung cancer, the widespread availability of spiral CT scanners in China, and the excellent survival of early lung cancer cases detected by LDCT, in 2009, lung cancer screening with LDCT was included in a programme of early detection and treatment of cancer, funded by a public health special subsidy from the central government *(33)*. This programme was renamed as early detection and treatment of cancer in rural China. From 2009 to 2015, lung cancer screening in this programme has expanded from two centres to ten centres in six provinces/municipalities. Up until now, a total of 32,898 LDCT scans were conducted with a detection rate of 0.74% and an early detection rate of 58% in annual screening rounds. However, among the ten screening centres, nine of them were in urban areas or suburbs, except for Xuanwei County. The reason might be that the LDCT screening programme requires experienced experts with multidisciplinary academic backgrounds, including oncology, thoracic surgery, radiology, pathology and epidemiology, while most hospitals or health-care providers in rural counties could not fulfil that, and this is why technical training for local doctors and technical personnel was included in the lung cancer screening programme.

Lung cancer treatment in rural China

Though treatment guidelines are available, the heterogeneity in the quality of care between urban and rural areas has resulted in inconsistent care to patients with lung cancer *(34)*. In China, most health-care providers, such as clinics, hospitals and specialists, are located in urban areas. In 2014, the number of hospital beds per 1,000 people was 7.84 in urban areas and 3.54 in rural areas. The number of doctors and nurses per 1,000 people in urban areas is also much higher than in rural areas (3.54 vs. 1.51, 4.30 vs.1.31 respectively) *(35)*. As a result, rural residents frequently face difficulties in obtaining health-care services due to either limited availability of health-care providers or long travel distances to health-care providers. Though the new cooperative medical system covers most rural residents (98.9% in 2014), it does not provide even partial coverage for cancer treatments, especially for advanced NSCLC, for which the average mean cost of all care in the final three months of life is US$ 16,955, far exceeding the financial ability of most households *(36)*. Thus, rural patients have high out-of-pocket burdens.

In conclusion, similar to urban China, rural areas are also suffering from the hazard of tobacco smoking, indoor and outdoor air pollution. Also, due to the socioeconomic

differences, including education level, accessibility and quality of lung cancer care between rural and urban areas, true disparities in lung cancer control and treatments do exist and will last into the near future. Accordingly, definite strategy and comprehensive, tailored actions are needed for the effective prevention and control of lung cancer in rural China. ■

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