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Review

Household air pollution and lung cancer in China: a review of studies in Xuanwei

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Abstract

Over half of the world's population is exposed to household air pollution from the burning of solid fuels at home. Household air pollution from solid fuel use is a leading risk factor for global disease and remains a major public health problem, especially in low- and mid-income countries. This is a particularly serious problem in China, where many people in rural areas still use coal for household heating and cooking. This review focuses on several decades of research carried out in Xuanwei County, Yunnan Province, where household coal use is a major source of household air pollution and where studies have linked household air pollution exposure to high rates of lung cancer. We conducted a series of case-control and cohort studies in Xuanwei to characterize the lung cancer risk in this population and the factors associated with it. We found lung cancer risk to vary substantially between different coal types, with a higher risk associated with smoky (i.e., bituminous) coal use compared to smokeless (i.e., anthracite) coal use. The installation of a chimney in homes resulted in a substantial reduction in lung cancer incidence and mortality. Overall, our research underscores the need among existing coal users to improve ventilation, use the least toxic fuel, and eventually move toward the use of cleaner fuels, such as gas and electricity.

Key words Coal, household air pollution, lung cancer

Household air pollution from the household burning of solid fuels, including biomass and coal, affects more than half of the world's population. The majority of these 3 billion people live in developing countries such as China and India. Household air pollution from solid fuel use has become a major public health problem and has been estimated to be one of the top five major risk factors for global disease in 2010 {4.3% [95% confidence interval (CI)= 3.4%–5.3%] of global disability-adjusted life-years (DALYs)}, after tobacco smoking[1], accounting for 3.9 million premature deaths[2]. Approximately 4.3 million deaths and 17% of premature lung cancer deaths in adults were attributed to household air pollution in 2012[3, 4].

According to the Ministry of Health of China, most pollutant exposure occurs indoors, where people spend the majority of their time, especially women and children[5]. The common sources of indoor pollutants include tobacco smoke, second-hand smoke, cooking fumes, formaldehyde and benzene from decorative and building materials, and household products such as pesticides[6]. Over 500,000 deaths from acute lower respiratory infections related to indoor air pollution in 2012 occurred in children under the age of 5 years[3]. The age-standardized rates (ASRs) of mortality of lung cancer in rural China have increased by almost 2 folds in the last two decades, from 22.5/100,000 in 1987–1991 to 42.4/100,000 in 2007–2009 in men and from 8.2/100,000 in 1987–1991 to 14.9/100,000 in 2007–2009 in women, reflecting a growing burden of tobacco smoking and air pollution[7]. Indeed, the lung cancer mortality in Xuanwei County, a rural area located in the northeast of Yunnan Province, is among the highest in China and is similar for both men and women (27.7/100,000 in men and 25.3/100,000 in women), despite that almost all women are non-smokers[8].

China is the largest producer and consumer of coal in the world[9]. Coal is used extensively in China for heating and cooking in homes,

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especially in rural areas. The Atlas of Lung Cancer Mortality in mainland China in the late 1970s first drew attention to the unusually high lung cancer mortality in Xuanwei, showing large variation among Xuanwei's communes and coal types used[8]. Most Xuanwei residents burn smoky (bituminous) coal for cooking and heating in poorly ventilated homes and are exposed to extremely high levels of polycyclic aromatic hydrocarbons (PAHs) throughout their lives. Previous studies have also identified household solid fuel use to be a major source of household air pollution in Xuanwei[10], attributing the high lung cancer mortality of this region to smoky coal use[8]. As such, Xuanwei provides a unique scientific opportunity to study the disease risks of household air pollution, and international research has been ongoing since the China-US Protocol for Scientific and Technical Cooperation in the Field of Environmental Protection was signed in 1980.

To clarify the etiology and underlying mechanisms of exposure to household air pollution in this rural region in China, we conducted a series of case-control and cohort studies in Xuanwei to further characterize the cancer risk in this population and the factors associated with it. In this review, we summarize important findings from epidemiologic studies conducted in China, specifically focus on Xuanwei. First, we characterize the trend of household air pollution and its health impacts in China. Second, we compare lung cancer risks across different fuel and stove types in Xuanwei and provide evidence linking smoky coal use and lung cancer in humans. Third, we review the current evidence regarding stove ventilation and lung cancer risk as well as lung cancer mortality in Xuanwei. Lastly, we discuss the role of genetic susceptibility in Xuanwei population and in Asian populations, as part of the Genome Wide Association Studies (GWAS) in the Female Lung Cancer Consortium in Asia (FLCCA).

Household Air Pollution and Coal Use in China

Approximately 1.2 million premature deaths and 25 million DALYs were estimated to be attributable to overall air pollution in China[11]. According to the World Bank Report in 2007, 16 of the world's 20 most polluted cities are in China[12]. Coal consumption is highly correlated with nitrogen oxide (NO_x), sulfur dioxide (SO_2), and dust emission[13]. The first National Pollution Census in China in 2010 reported that 8.60% of total SO_2 emissions and 3.24% of total NO_x emissions were from domestic sources[14]. Although the percentage of homes burning coal is declining in major cities, the domestic burning of coal remains pervasive in rural China[15]. Indeed, solid fuels such as coal are widely used domestically for cooking and heating, exposing the residents to high levels of particulates and other air pollutants. Household air pollution due to solid fuel burning has been estimated to shorten the lives of 420,000 rural Chinese each year[16]. Nonetheless, the effect of household air pollution is often under-reported due to the lack of detailed surveillance and exposure assessments, especially in the rural areas of China, where the indoor levels of pollutants are often many times higher than the outdoor levels and might have far more significant hazardous effects on public health[17].

Coal Types, Smoky Coal Sources, and Lung Cancer Risk in Xuanwei

In Xuanwei, the combustion products from smoky coal were found to be more carcinogenic and mutagenic than the combustion products from smokeless coal and wood products[8]. There is a striking variation in risk estimates for lung cancer due to smoky coal sources (based on the coal type locations in different communes) in Xuanwei, with odds ratios (OR) ranging from 1.1 to 27.0, compared to smokeless coal and wood use (**Figure 1**), with a higher risk among smoky coal users compared to smokeless coal users[18]. These differences in risk estimates persisted after adjustment for the amount of coal used, time spent indoors, type of ventilation, active and passive tobacco exposure, and other potential risk factors in this population.

Lung cancer risk has been shown to vary with different smoky coal sources according to geographic region. A meta-analysis of 25 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 = 2.15, 95% CI = 1.61–2.89) in all regions of the world where the studies had been carried out, particularly in mainland China and Taiwan (OR = 2.27, 95% CI = 1.62–3.12). Furthermore, an analysis of the effects in mainland China and Taiwan by region found substantial variation (*P* for heterogeneity = 10^{-31}), with South/Southeast (OR = 3.27, 95% CI = 1.27–8.42) and Southwest China (OR = 2.98, 95% CI = 1.18–7.53) having the strongest associations with lung cancer (**Table 1**). Although heterogeneity exists for coal use and lung cancer risk by geographic location, the lung cancer risk was elevated for coal use in all locations[19].

These findings suggest that there is a wide variation in the exposure to carcinogenic compounds by coal type and source, requiring the collection of detailed exposure data on coal sources, coal use, and personal habits at home, including cooking practices and other activities that could influence exposure intensity or duration, to fully evaluate risk in this population.

Effect of Improved Stove Ventilation on Lung Cancer Risk and Mortality in Xuanwei

Stove improvement through chimney installation has been associated with a significantly reduced lung cancer risk in Xuanwei. Fuel burning for cooking and heating generates very high indoor concentrations of airborne particulate matter (PM), benzo[a]pyrene (BaP), and other organic compounds. Compared to unventilated burning, respirable particulate matter (PM_{10}) and BaP levels during ventilated burning were found to be 2–6 times lower (PM_{10}: 2.08 mg/m^3 for unvented stoves vs. 0.71 mg/m^3 for vented stoves; BaP: 1.66 μg/m^3 for unvented stoves vs. 0.25 μg/m^3 for vented stoves)[20]. Between the 1970s and 1980s, many residents changed from using unventilated fire pits to burn coal to using stoves with chimneys. Improved stove ventilation substantially decreased lung cancer rates

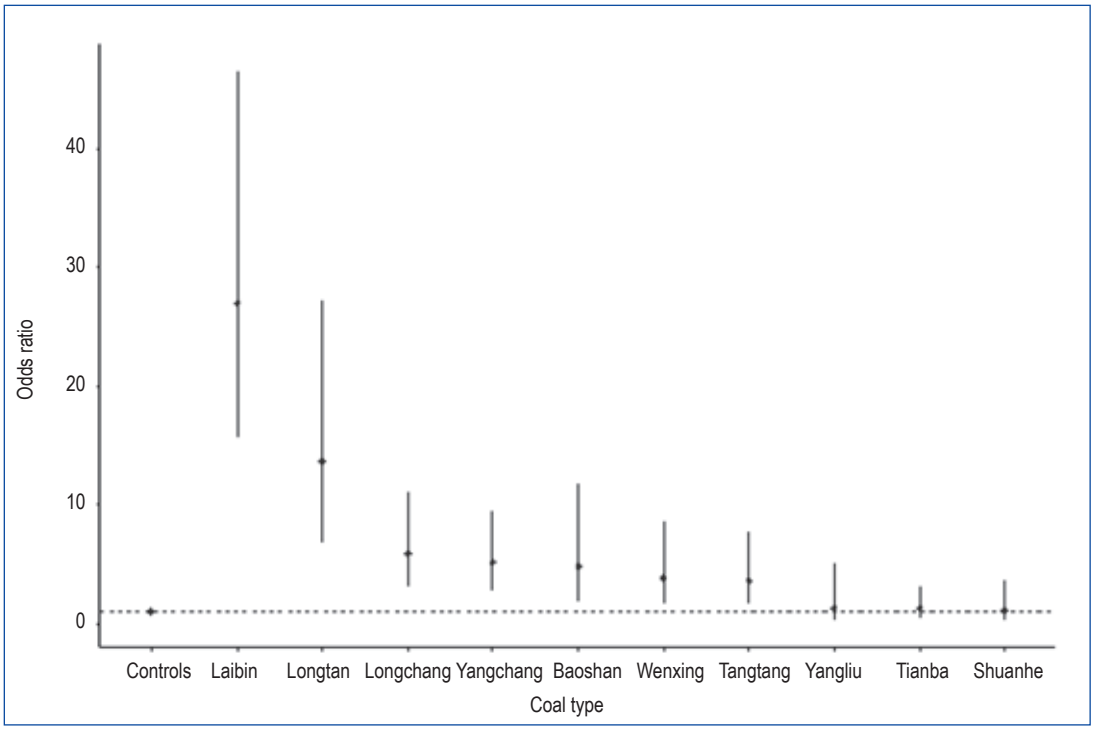

Figure 1. **Adjusted odds ratios (ORs) and 95% confidence intervals (CIs) of lung cancer in relation to smoky coal sources compared with controls (smokeless coal and wood combined). All models were adjusted for age, sex, literacy, lung cancer in first-degree relatives, hours spent at home per day, lung disease history, coal-mining work history, smoking, and passive smoke exposure history. Coal types are named after the districts at Xuanwei where they are mined.**

Table 1. Summary association estimates of lung cancer risk with household coal use for heating and cooking throughout mainland China and Taiwan

Region	Number of studies	OR (95% CI)[a]
North China	1	1.99 (1.16–3.43)
Northwest China	1	1.29 (1.03–1.61)
Northeast China	6	2.04 (1.45–2.87)
South/Southeast China	3	3.27 (1.27–8.42)
Southwest China	3	2.98 (1.18–7.53)
East China	3	1.85 (1.42–2.40)
Taiwan	3	1.88 (1.16–3.04)

Adapted from Hosgood HD *et al.*[19], Int J Epidemiol, 2011, 40:719–728. OR, odds ratio; CI, confidence interval. [a]The random effects summary ORs and 95% CIs were calculated using each study's published adjusted OR and 95% CI.

in Xuanwei. Indeed, changing from a fire pit to a stove with a chimney was associated with a significant reduction in the lung cancer incidence for both men [risk ratio (RR) = 0.59, 95% CI = 0.49–0.71] and women (RR = 0.54, 95% CI = 0.44–0.65)[20]. Changing to a stove with a chimney was also significantly associated with reduced lung cancer mortality [hazard ratio (HR) = 0.70, 95% CI = 0.62–0.80][21].

Stove changes have also been associated with reductions in respiratory diseases other than lung cancer in Xuanwei. Installing a chimney was associated with a 50% reduction in pneumonia deaths in both men (HR = 0.49, 95% CI = 0.31–0.78) and women (HR = 0.53, 95% CI = 0.32–0.88) and also in both smoky (HR = 0.52, 95% CI = 0.34–0.80) and smokeless coal users (HR = 0.45, 95% CI = 0.22–0.94)[22]. The incidence of chronic obstructive pulmonary disease also significantly decreased with improved stove ventilation[23].

Portable stoves, which allow people to light the stove outdoors in the morning and only bring it indoors after most of the visible smoke has dissipated, was also found to reduce lung cancer mortality. In fact, changing from a fire pit to a portable stove was associated with a significant reduction in lung cancer mortality for both men (HR = 0.62, 95% CI = 0.46–0.82) and women (HR = 0.41, 95% CI = 0.29–0.57) who were lifelong smoky coal users[24].

Although tobacco smoking is an important risk factor for lung cancer incidence and mortality, previous studies conducted in Xuanwei observed only a weak association between tobacco smoking and the risk of lung cancer[25]. Furthermore, a differential effect of smoking was also apparent before and after stove improvement. The association between smoking duration and lung cancer mortality significantly increased after stove improvement with a chimney compared with that before stove improvement (P = 0.002 for interaction between smoking and stove improvement)[21]. A similar trend was observed with lung cancer risk. It has been suggested that the association between smoking and lung cancer risk becomes stronger after stove improvement and the subsequent reduction in indoor coal smoke exposure. Kim *et al*.[26] explored the differential association of tobacco smoke and lung cancer risk according to the intensity, duration, and type of coal used. They observed a decreased relative risk of lung cancer per cigarette per day as the annual use of coal increased (0–3 tons: OR = 1.09, 95% CI = 1.03–1.17; >3 tons: OR = 0.99, 95% CI = 0.95–1.03) among men in Xuanwei. A possible explanation for these findings is that some degree of metabolic saturation of carcinogens in tobacco smoke may be occurring in the presence of smoky coal exposure and that household air pollution may be a strong competing risk with smoking in lung cancer. It is also possible that the constituents of coal may induce the detoxification of tobacco smoke carcinogens and that smoky coal exposure may have increased tobacco smoke clearance[26,27]. Hence, the adverse effects of tobacco may become more apparent as China continues to switch to cleaner fuels for homes; thus, there should be a combined effort to reduce both household air pollution and smoking.

Genetic Susceptibility and Lung Cancer in Xuanwei

A pilot study was conducted in Xuanwei to evaluate genetic variation in high-priority candidate genes and lung cancer[28]. An interaction between smoky coal use and the glutathione S-transferase M1 (*GSTM1*)-null genotype was found, which resulted in a diminished capacity to detoxify PAHs. Individuals with the *GSTM1*-null genotype were more likely to have lung cancer than individuals with a *GSTM1*-positive genotype: the overall risk for lung cancer increased 1.7-fold per 100 tons of lifetime coal use (95% CI = 1.3–2.4). When stratified by *GSTM1* genotype, there was a 1.2-fold higher risk (95% CI = 0.8–1.9) per 100 tons for *GSTM1*-positive subjects and a 2.4-fold higher risk per 100 tons for those with the *GSTM1*-null genotype (95% CI = 1.6–3.9, P = 0.05 for interaction)[28]. A meta-analysis of 6 published studies (912 cases and 1,063 controls) in various Asian populations exposed to high levels of indoor combustion products containing PAHs and where indoor air pollution contributes substantially to lung cancer risk showed that carriers of the *GSTM1*-null genotype had increased lung cancer risk (OR = 1.31, 95% CI = 0.95–1.79, P = 0.10)[29]. Furthermore, this association was particularly evident in regions that use coal for heating and cooking (OR = 1.64, 95% CI = 1.25–2.14, P = 0.0003 from 4 studies), with no evidence of either heterogeneity in the risk estimate or publication bias. The glutathione S-transferase theta 1 (*GSTT1*)-null genotype was also found to be associated with an increased lung cancer risk (OR = 1.49, 95% CI = 1.17–1.89, P = 0.001)[29].

Genetic Susceptibility and Lung Cancer in Asia (FLCCA)

As part of our expanded efforts to study the etiology of lung cancer among Asian female never-smokers, we initiated the Female Lung Cancer Consortium in Asia (FLCCA), consisting of 18 studies in mainland China, Hong Kong, Taiwan, South Korea, Singapore, and Japan, with 6,609 cases and 7,457 controls. FLCCA is the largest survey of lung cancer among non-smokers to date. We conducted a GWAS of lung cancer among non-smoking women in the consortium and identified 5 susceptibility loci from chromosomes 3q28, 5p15.3, 6q22.2, 6p21.32, 10q25.2, and 17q24.3, with significant interaction of a single nucleotide polymorphism (SNP), rs2395185, in the human leukocyte antigen (*HLA*) class II region gene with environmental tobacco smoke[30,31]. These continuing efforts will contribute to the understanding of the role of genetic variation in lung cancer pathogenesis among never-smokers.

Summary and Recommendations

More than half of the world's population still burns solid fuels for daily use, and most people in underdeveloped and middle-income countries such as China use poorly ventilated stoves. Therefore, household air pollution from household solid fuel use remains an important global health problem.

Studies to date in Xuanwei, both case-control and cohort, have shown that smoky coal is associated with an increased risk of lung cancer in this region and that the effects vary markedly depending on the coal source. In addition, studies have demonstrated the effectiveness of inexpensive ways to improve indoor ventilation to reduce lung cancer risk and mortality in populations that burn coal, which might substantively lower the disease burden in other parts of the developing world. Genetic factors may also play a role in lung cancer pathogenesis in this area. Taken together, these data provide additional support for the need to improve ventilation and to switch to clean fuel sources, such as gas and electricity.

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