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### Coal mining is associated with lung cancer risk in Xuanwei, China

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#### Abstract

**Background**—Xuanwei, China, experiences some of the highest rates of lung cancer in China. While lung cancer risk has been linked to the household use of bituminous coal, no study has comprehensively evaluated the risk of lung cancer associated with the mining of this coal in Xuanwei. In Xuanwei, coal is typically extracted from underground mines, without ventilation, and transported to the surface using carts powered by manpower or electricity.

**Methods**—We evaluated the risk of lung cancer and working as a coal miner, in the absence of diesel exhaust exposure, in a population-based case-control study of 260 male lung cancer cases and 260 age-matched male controls with information on occupational histories. Odds ratios (ORs) and 95% confidence intervals (CIs) for working as a coal miner and years of working as a coal miner were calculated by conditional logistic regression, adjusting for potential confounders, such as smoking and household coal use.

**Results**—We observed an increased risk of lung cancer among coal miners (OR=2.7; 95% CI =1.3–5.6) compared to non-coal miners. Further, a dose-response relationship was observed for the risk of lung cancer and the number of years working as a coal miner ( $p_{trend}$ =0.02), with those working as miners for more than 10 years experiencing an almost 4-fold increased risk (OR=3.8; 95% CI=1.4–10.3) compared to non-coal miners.

**Conclusions**—These findings suggest that coal mining in Xuanwei may be a risk factor for lung cancer.

#### Keywords

Coal mining; lung cancer; occupation; Xuanwei; China

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#### Introduction

Numerous health effects associated with underground coal mining have been studied, including pneumoconiosis, tuberculosis, chronic obstructive pulmonary disease (COPD), and other non-malignant diseases of the lung (Merchant et al. 1986;Kuempel et al. 1995;Isidro, I et al. 2004). Studies evaluating the risk of lung cancer among underground coal miners have reported conflicting results (IARC Monographs on the Evaluation of the Carcinogenic Risks to Human 1997;Miller and MacCalman 2010;Attfield and Kuempel 2008;IARC Monographs on the Evaluation of the Carcinogenic Risks to Human 1997;Hoffmann and Jockel 2006;Jockel et al. 1998;Meijers et al. 1988;Ames et al. 1983;Skowronek and Zemla 2003;Swanson et al. 1993;Morabia et al. 1992).

In cohort and proportional mortality studies, either an increased, decreased, or no risk has been observed between lung cancer and coal mining (Miller and MacCalman 2010;Attfield and Kuempel 2008;IARC Monographs on the Evaluation of the Carcinogenic Risks to Human 1997). These inconsistencies have been partially attributed to the shortcomings of the study design, such as lack of individual data on risk factors, and potential influences associated with the healthy worker effect (Hoffmann and Jockel 2006). Similarly, case-control studies have reported inconsistencies for the risk of lung cancer among coal miners, with few studies having access to the workers' complete occupational histories (Hoffmann and Jockel 2006;Jockel et al. 1998;Meijers et al. 1988;Ames et al. 1983;Skowronek and Zemla 2003;Swanson et al. 1993;Morabia et al. 1992).

A retrospective cohort study of Xuanwei, China residents, who used either bituminous ("smoky coal") or anthracite ("smokeless coal") coal for their household cooking and heating needs, provided some of the strongest epidemiological evidence linking lung cancer and household coal burning, among both women and men (Lan et al. 2002;Hosgood, III et al. 2008). Interestingly, this study also observed an increased risk of lung cancer among men ever working as a coal miner (Lan et al. 2002;Hosgood, III et al. 2008); however, comprehensive occupational histories for these miners were not available. While surface mines are present in Xuanwei, coal is typically extracted from underground mines, without ventilation, and transported to the surface using carts powered by manpower or electricity. To follow-up our findings of the retrospective cohort study, and to further explore the lung cancer risk among coal miners, we evaluated a population-based case-control study conducted in Xuanwei with extensive occupational history information.

#### Methods

This population-based case-control study of lung cancer in Xuanwei, China has been previously described (Lan et al. 2008). Briefly, cases were comprised of all newly diagnosed lung cancer cases from November 1985 through February 1990 in four hospitals: Xuanwei County, Yun Dan, Laibin Coal Mine, and Xuanwei Traditional Medicine. Eligible participants included farmers 18–85 years of age, who resided in Xuanwei for more than one year prior to diagnosis. Eligible participants were restricted to farmers, as more than 90% of the total population in Xuanwei is farmers (Mumford et al. 1987). A total of 500 eligible lung cancer cases were enrolled. After exclusion of 2 cases with incorrect addresses, 498 cases were eligible for analysis. Cases were diagnosed based on sputum cytology, or pathological findings from needle biopsy, bronchofiberoscopy, or surgery (39%), or based on chest X-ray and clinical history (61%).

Control subjects were randomly selected from the general population of Xuanwei (Lan et al. 2008). Controls were only eligible if there were farmers. Briefly, a three-stage, randomized recruitment strategy for control selection was used that first randomly selected a commune,

then a large farming group, and then a small farming group within that commune. Within the small farming groups, a control subject was matched to each case by randomly selecting an individual matched with the case based on age at interview (±2 years) and sex. The participation rate was 100% for cases and 97% for controls. This study was approved by the Institutional Review Board of the Chinese Academy of Preventive Medicine, and was conducted according to the recommendations of the World Medical Association Declaration of Helsinki for human study subject protection. Informed consent was obtained from all study subjects.

A questionnaire-based interview was administered to assess lifetime history of fuel use, residential history, cooking history, time spent indoors and outdoors, smoking history, environmental tobacco smoke exposure history, medical history, family history of cancer, socioeconomic status, and occupational history. The occupational history component of the questionnaire queried the type of job, the job location, the age started, and the age stopped for all jobs held throughout the subject's life. Subsequent questions asked if the subject had exposure to known or suspected lung carcinogens, such as asbestos, radiation, and arsenic, for each of their reported jobs.

While the total sample size of this case-control study was 498 cases and 498 controls, no women ever worked as coal miners. Thus, our analysis was restricted to male cases (n=260) and male controls (n=260). The risk of lung cancer associated with coal mining was estimated by odds ratios (ORs) and 95% confidence intervals (95%CIs) using conditional logistic regression. The risk of coal mining and lung cancer was first analyzed as ever having worked as a coal miner. Further analyses of the association were conducted by the number of years having worked as a coal miner, the age having started working as a coal miner, and the age having stopped working as a coal miner. Cut-points for years of coal mining and ages of starting and stopping work were based on the distributions among controls. All analyses were adjusted for subtype of fuel used for household heating and cooking (coal: Laibin, Longtan, Baoshan, Longchang, Yangchang, Wenxin, Tangtang, Shuanghe, Tianba, Yangliu, Xize; wood; none), educational status (literate, illiterate), lung cancer in first-degree relatives (yes, no), cumulative lifetime hours spent indoors at home (≤300,000, >300,000 hours), tobacco use (never users, sole users of other forms of tobacco (e.g. tobacco leaves) or cigarettes smoked with a water pipe,  $\leq 20$  pack-years of cigarettes smoked without a water pipe, >20 pack-years of cigarettes smoked without a water pipe), and passive smoke exposure history (yes, no). Interactions of coal mining with smoking and type of coal mined were assessed by including the respective product terms in the conditional logistic regression model. To assess the robustness of our findings, sensitivity analyses were performed by evaluating the risk of lung cancer associated with mining among subjects without a history of lung disease, and also among subjects without a history of a job with a potential exposure to asbestos, radiation, or arsenic. Associations between years mining, age started mining and age stopped mining were evaluated with Pearson correlation coefficients. Finally, to assess potential residual confounding by household coal burning, factors related to coal use in the home (ever cooking, having a chimney, amount of coal used, type of stove used, time spent indoors) were compared between coal mining cases and coal mining controls. Models were also further adjusted by these additional factors to assess potential residual confounding.

#### Results

Male cases were similar to controls in cooking history and passive smoking history (Table I). Cases tended to more often Han Chinese, literate, and smokers than controls. Further, cases had a greater frequency of history of lung cancer among first degree relatives and history of non-malignant lung diseases than controls. The mean (±standard deviation) years

In this population, male coal miners experienced an increased lung cancer risk compared to non-coal miners (Table II). A dose-response relationship was also observed for the risk of lung cancer and the number of years working as a coal miner ( $p_{trend}=0.02$ ), with those working as miners for more than 10 years experiencing an almost 4-fold increased risk compared to non-coal miners (Table II). Of note, when restricting our analysis to subjects who lived and worked in communes with bituminous coal mines, an elevated risk of lung cancer was also observed (OR=2.0; 95% CI=1.1–3.7). Years of coal mining did not interact with smoking status (p=0.41) or type of coal mine (i.e. bituminous versus anthracite) (p=0.87). Stratification of the analyses by passive smoking exposure and ever smoking found the risk of lung cancer associated with ever working as a coal miner to be present among subjects with passive smoking exposure (OR=2.6; 95% CI=1.1–6.1) and those who smoked (OR=2.3; 95% CI=1.0–5.0). The cell counts were sparse for subjects without passive smoking exposure (i.e. only 3 cases and 2 controls were ever miners) and for those who never smoked (i.e. 4 cases and 1 control were ever miners).

We also explored the lung cancer association by the age the men started or stopped working as a coal miner. Men who started working as a coal miner at 20 years old or younger experienced a higher risk of lung cancer than those that started mining later in life (Table II). Similarly, men who stopped working as a coal miner at more than 30 years old experienced a higher risk of lung cancer than those that stopped mining at an earlier age (Table II). These results were anticipated given the high correlation between the number of years worked as a coal miner and the age of starting (all subjects: r=0.58, p<0.001; cases: r=0.64, p<0.001; controls r=0.53, p<0.001) and stopping this work (all subjects: r=0.86, p<0.001; cases r=0.91, p<0.001; controls: r=0.77, p<0.001).

To test the robustness of our findings, we restricted our analyses to matched pairs without a history of lung disease. The association between ever coal mining and risk of lung cancer remained in this subset (OR=2.0; 95% CI=1.0–3.9). Similarly, the association remained when excluding matched pairs that had a case or control with a history of a job with potential exposure to asbestos, radiation, or arsenic (OR=2.8; 95% CI=1.2–6.6). Further adjustment of our analyses for herbicide and fertilizer use yielded similar results (OR=2.7; 95% CI=1.3–6.0). To assess potential residual confounding by household coal burning, we compared factors related to coal use between cases and controls who were miners, and found that they were similar in cooking status (p=0.72), type of stove used in the home (p=0.45), using a chimney in the home (p=0.21), tons of coal used in the home (p=0.84) and time spent in the home, using a chimney in the home, and tons of coal used in the homes yielded similar results (data not shown).

#### Discussion

Our analysis found that men working as coal miners in Xuanwei experienced an elevated risk of lung cancer. Further, as the years of mining increased, so did the risk of lung cancer associated with coal mining. These findings are of public health importance given that China produces more bituminous and anthracite coal than any other country in the world (United States Bureau of Mines 1992). Further, our findings add to the international weight of evidence exploring lung cancer risk and coal mining.

Our findings in Xuanwei are consistent with a large case-control study (n=1,793 male cases) conducted in the United States, which reported an increased risk of lung cancer associated

with exposure to coal dust, particularly among men with 10 or more years of exposure (Morabia et al. 1992). Another study in the United States comparing 3,792 lung cancer cases to 1,966 colorectal cancer cases that were used as controls, found a suggested increased risk of lung cancer among coal miners (Swanson et al. 1993). Working as a coal miner was also reported to be associated with increased risk of lung cancer in Europe (Skowronek and Zemla 2003). Three smaller case-control studies in the United States and Europe, however, found no evidence of this association (Jockel et al. 1998;Meijers et al. 1988;Ames et al. 1983). Conflicting findings for lung cancer risk and coal mining have also been observed in cohort and proportional mortality studies, with some studies finding an increased risk, some a decreased, and others no risk (Miller and MacCalman 2010;Attfield and Kuempel 2008;IARC Monographs on the Evaluation of the Carcinogenic Risks to Human 1997). Of note, a cohort study of 8,899 working coal miners in the United States, including 331 lung cancer deaths, found a lack of association between lung cancer mortality and coal mining (Attfield and Kuempel 2008).

Inconsistencies among these studies may be attributed to differing factors related to workplace exposures, such as the use of personal protective equipment or hours spent underground, and factors related to potential confounders, such as tobacco smoke, diesel exhaust, silica, and radon levels (Tian et al. 2008;Fisne et al. 2005;Hoffmann and Jockel 2006). Therefore, caution should be used when evaluating results from studies of lung cancer and coal mining when information on these factors is missing. Further, a lack of information regarding the levels of the coal dust components, such as coal, silica, and metals, also hinders interpretation of the findings (IARC Monographs on the Evaluation of the Carcinogenic Risks to Human 1997).

A major strength of our study is the extensive occupational histories available for analysis, along with detailed information on confounders, such as smoking, familial lung cancer, and household fuel use. Our ability to control for smoking and other confounders, the lack of diesel exhaust exposures in the mines, and this population-based case-control study's very high participation rates, adds confidence in our observations. A limitation of our study is the lack of quantitative exposure assessment measurements. While personal or area measurements of coal dust would allow for the evaluation of our results quantitatively, given that most workers perform similar tasks in the same mine throughout their careers, the duration of working as a miner is likely to be a reasonable proxy for duration of exposure. Measures of the levels of potential lung carcinogens, such as silica and radon, experienced underground would also aid in determining the influence of these potentially confounding factors on our findings (Tian et al. 2008;Fisne et al. 2005;Hoffmann and Jockel 2006). Although confounding from these factors cannot be completely ruled out, they are unlikely to fully explain our observed risks, given that silica is associated with only about a 50% increased risk of lung cancer (Steenland et al. 2001).

In summary, our population-based case-control study observed an increased risk of lung cancer among coal miners, and in a dose-dependent fashion with years of mining. Further research on co-exposures such silica and radon exposures is needed to refine the present estimates of mining-associated lung cancer risk in Xuanwei.

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# Table I

Characteristics of male lung cancer patients and population controls in Xuanwei, China.

Cases (n = 260) Controls (n = 260)

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	u	%	N	%	p-value <sup>*</sup>
Ethnicity					
Han	257	98.8	245	94.2	
Other	3	1.2	15	5.8	0.004
Education status					
Illiterate	123	47.3	149	57.3	
Literate	136	52.3	111	42.7	0.025
History of chronic bronchitis, emphysema, asthma, or tuberculosis					
No	197	75.8	249	95.8	
Yes	63	24.2	11	4.2	<0.0001
History of lung cancer in first-degree relatives					
No	238	91.5	259	9.66	
Yes	22	8.5	-	0.4	<0.0001
History of cooking					
No	164	63.1	170	65.4	
Yes	95	36.5	88	33.8	0.54
Passive smoke exposure **					
No	22	8.5	34	13.1	
Yes	238	91.5	110	42.3	0.09
Smoking status					
Never smoker	26	10.0	34	13.1	
Other tobacco ***	112	43.1	123	47.3	
≤20 pack-years cigarettes	64	24.6	81	31.2	
>20 pack-years cigarettes	55	21.2	21	8.1	<0.0001
* chi-squared test, or Fisher's exact test when cell counts <5, comparing cases and controls;	ses and co	ontrols;			
** Smoking by any family member who lived with subject;					

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\*\*\* Sole users of other forms of tobacco (e.g. tobacco leaves) or cigarettes smoked with a water pipe. Table II

Lung cancer risk associated with coal mining in Xuanwei, China

Cases (n = 260) Controls  $(n = 260)^*$ 

	ц	%	N	%	OR (95% CI) <sup>**</sup>	p-trend
Never worked as a coal miner	212	81.5	236	90.8	1.0 (reference)	
Worked as a coal miner	48	18.5	24	9.2	2.7 (1.3–5.6)	
Never worked as a coal miner	212	81.5	236	90.8	1.0 (reference)	
Worked less than 10 years as a coal miner	18	6.9	12	4.6	1.8 (0.6–5.6)	
Worked 10 or more years as a coal miner	30	11.5	10	3.8	3.8 (1.4–10.3)	0.020
Never worked as a coal miner	212	81.5	236	90.8	1.0 (reference)	
Started coal mining more than 20 years old	19	7.3	11	4.2	2.0 (0.8–5.5)	
Started coal mining 20 or less years old	29	11.2	13	5.0	3.5 (1.3–9.4)	0.025
Never worked as a coal miner	212	81.5	236	90.8	1.0 (reference)	
Stopped coal mining 30 or less years old	18	6.9	13	5.0	1.4 (0.5–4.4)	
Stopped coal mining more than 30 years old	30	11.5	11	4.2	4.1(1.6 - 11.0)	0.016

I we controls did not have information on the years they worked as a coal miner;

lifetime hours spent at home(<300,000, >300,000 hours), tobacco use (never users, sole users of other types of tobacco or cigarettes smoked with a water pipe, <20 pack-years of cigarettes smoked without Baoshan, Longchang, Yangchang, Wenxin, Tangtang, Shuanghe, Tianba, Yangliu, Xize; wood; none), educational status (literate, illiterate), lung cancer in first-degree relatives (yes, no), cumulative \*\* Odds ratios (ORs) and 95% confidence intervals (CIs) estimated by conditional logistic regression and adjusted for subtype of fuel used for household heating and cooking (coal: Laibin, Longtan, a water pipe, >20 pack-years of cigarettes smoked without a water pipe), and passive smoke exposure history (yes, no)