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Air pollution and lung cancer risks in China—a meta-analysis

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Abstract

Lung cancer is a serious health problem in China, as in the rest of the world. Many studies have already proved that air pollution as well as other environmental factors can increase the risk of lung cancer. Based on epidemiological studies carried out in China, this paper proposes odds ratios (OR) to evaluate the risk of lung cancer from indoor air pollution for the Chinese population by applying the method of meta-analysis. For domestic coal use for heating and cooking, the pooled OR values are 1.83 (95% CI: 0.62–5.41) and 2.66 (1.39–5.07) for women and both sexes, respectively. For indoor exposure to coal dust, the OR values are 2.52 (95% CI: 1.94–3.28) and 2.42 (1.62–3.63) for women and both sexes, respectively. Cooking oil vapor is another factor increasing lung cancer risk. The OR values are 2.12 (95%CI: 1.81–2.47), 1.78 (1.50–2.12) and 6.20 (2.88–13.32) for nonsmoking women, women, and both sexes, respectively. Regarding environmental tobacco smoke, the pooled OR values are 1.70 (95% CI: 1.32–2.18) and 1.64 (1.29–2.07) for nonsmoking women and both sexes, respectively. Funnel plots with statistical test have been applied to examine the publication bias, and the results implied that the analysis of coal consumption and cooking oil pollution might be affected by publication bias. The meta-analysis results confirm the association between lung cancer and indoor air pollution for the Chinese population.

Keywords: Lung cancer; Indoor air pollution; Meta-analysis; Odds ratio; China

1. Introduction

Lung cancer is a serious health problem. According to the World Health Organization (WHO), each year more than 1 million people throughout the world die from lung cancer (WHO, 2002). In China, lung cancer takes the highest death toll of all cancer types in the cities, and the mortality and morbidity have increased significantly in both cities and rural areas. In the early 1970s, lung cancer mortality was 7 per 100,000 people (12.61 for urban areas), and it increased to 20.7 per 100,000 in 1998 (Li et al., 1997; Zhou et al., 2002). In 2000, it reached 40 per 100 000 (Yang, 2004), almost 5 times higher than three decades ago, and it is estimated that lung cancer morbidity in China increased by 26.9% from 2000 to 2005. In Xuanwei County, Yunnan Province, which has the highest prevalence of lung cancer in China, lung cancer mortality was reported to be 151.8 per 100,000 in some townships (Peng et al., 1998). Many studies have already proved that smoking has a significant association with lung cancer (Ezzati and Lopez, 2003; Alberg and Samet, 2003), but smoking cannot explain the relatively high rates of lung cancer observed among Chinese nonsmoking women (Lam et al., 2004). Environmental factors–including outdoor

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and indoor air pollution, exposure to asbestos and residential radon, arsenic and chlorination by-products in drinking water–as well as other factors such as diet, physical exercise and family history of cancer might also play a significant role in lung cancer mortality and morbidity (Boffetta and Nyberg, 2003; Lei et al., 1996; Gao, 1996).

Air pollution has become one of the most serious environmental problems in China, and the major source of atmospheric pollution in Chinese cities comes from coal burning for electricity generation and industrial production as well as residential heating and cooking. Sixty-one percent of 342 monitored cities, with 67% of total urban population, were out of compliance with at least one of the Chinese government's air quality standards for residential areas in 2004 (SEPA, 2004). Given the importance of coal combustion in energy supply, the main pollutants affecting air quality were particulate matters (PM) and sulfur dioxide (SO_2), which have been the focus of monitoring. In general, total suspended particulates (TSP) concentration levels in cities in northern China are higher than those in southern China, partly due to sand storms in the north, while SO_2 concentration levels do not differ much, and air pollution in winter is generally more serious than that in summer (Chen et al., 2004). In large cities where pollution conditions are complicated by both coal smoke and exhaust from the sharply increasing vehicle population, pollutants such as NOx and O_3 are becoming more and more significant.

Indoor air pollution affects a large share of the population in China, especially in rural areas, small cities, and in less developed peri-urban areas of large cities. Despite the increasing importance of natural gas in urban areas of China, coal, wood and other biomass fuels such as crop residues and dung remain the primary heating and cooking fuels for the great majority of the Chinese population (Alford et al., 2002). Solid fuels are typically burned in simple stoves, and a number of studies have implied that the resulting levels of indoor air pollution are very serious compared with outdoors. Since most people, especially women, spend a large percentage of time indoors, indoor air pollution has a disproportionate impact on human health. Qian et al. (2001) showed that across eight urban and suburban districts in four Chinese cities–Chongqing, Guangzhou, Lanzhou, and Wuhan–approximately 51% to 71% of households use coal for heating or cooking. Qin et al. (1991) carried out a study in four cities–Chengde, Shenyang, Shanghai and Wuhan–and found that the concentrations of PM_{10} in the kitchens that rely on coal (respectively 665, 651, 384 and 291 $\mu g/m^3$ in the four cities) were much higher than those using gaseous fuel (respectively 209, 355, 140 and 204 $\mu g/m^3$ in the four cities) during winter. Cai et al. (2000) investigated the indoor air condition of 47 families using coal or coal gas in Guangzhou and found that indoor concentrations of SO_2, NO_2 and PM_{10} for families using coal were 487, 62 and 706 $\mu g/m^3$, respectively, significantly higher than outdoor concentrations (11, 10 and 69 $\mu g/m^3$, respectively). Similarly, results given by Li et al. (2001) showed that indoor concentrations of SO_2, NOx and PM_{10} for coal-fueled houses were respectively 394, 157 and 853 $\mu g/m^3$, while outdoor concentrations were respectively 54, 48 and 789 $\mu g/m^3$ in Yinchuan city, Ningxia province. Pan et al. (2001) monitored indoor and outdoor air quality in rural Anqing and found PM_{10} levels were respectively 518 $\mu g/m^3$ (kitchen), 340 $\mu g/m^3$ (bedroom), 287 $\mu g/m^3$ (yard), and 270 $\mu g/m^3$ (cropland). These high levels of indoor air pollution are now widely believed to cause enormous damage to human health (e.g. World Bank, 1997; WHO, 2002; Schmidt, 2002).

Coherent associations between ambient air pollution (mainly PM and sulfate) and lung cancer mortality have already been observed in a number of large USA studies, e.g. the Adventist Health Study on Smog (AHSMOG) (Abbey et al., 1999), the Harvard Six Cities study (Dockery et al., 1993; HEI, 2000), and the American Cancer Society (ACS) study (Pope et al., 1995; HEI, 2000; Pope et al., 2002). In Europe, more attention has been paid to gaseous pollutants such as SO_2 and NOx (Nafstad et al., 2003; Nyberg et al., 2000), as well as black smoke (Hoek et al., 2002). For indoor air pollution, Mzileni et al. (1999) evaluated the risks of lung cancer among women using wood or coal as main fuel in South Africa. Most of these studies provide relative risk (RR) values or odds ratio (OR) values to represent the association between air pollution and lung cancer. However, since the air quality and characteristics of air pollution differ significantly between China and most Western countries, the results found in these studies cannot simply be transferred to a Chinese context. The aim of this paper is therefore to perform a meta-analysis of Chinese epidemiological studies to derive a set of odds ratios for lung cancer from indoor air pollution that can be used in evaluating air pollution measures in China, and transferred to other developing countries with similar air pollution conditions. In the Chinese studies included in our meta-analyses, odds ratios related to different indicators of indoor air pollution were given or could be estimated. Similar studies have been conducted by Yao et al. (2002) and Yao and Shi (2003). They analyzed the environmental risk factors of lung cancer in China based on 41 epidemiological studies from 1990 to 2001, however, no comparison has been made between the results of different population groups (e.g. groups stratified by sex or smoking habits). In this paper, we aim at taking into account this aspect, in addition to adding results from the most recent literature, including 3 publications in 2002, with a more stringent analysis arrangement. Moreover, as opposed to many other Chinese meta-analyses, we explicitly address the issue of publication bias, by applying funnel plots and regression methods providing tests of a possible bias.

2. Materials and methods

2.1. Literature search

Epidemiological studies on air pollution and lung cancer in China published in English and Chinese during the period 1995–2004 have been collected through a systematic literature search. Web of Science, Chinese Journal Full-text Database (CJFD), and Chinese Science and Technology Journal Database were searched using the topic words “lung cancer” and “air pollution” and “China”/“Chinese”. Papers in languages other than Chinese and English were omitted. To be included the study had to meet the following criteria:

1) The study is a case-control or cohort study, with explicit population size and a clear study period and location in China.
2) The study provides sufficient information for calculating a standard effect estimate in the meta-analysis, i.e. the OR associated with indoor air pollution indicators with 95% CI (confidence intervals). This implies that the study reports prevalence or incidence rates of lung cancer associated with exposure to the given risk factor (the indoor air pollution indicator) as compared to non-exposure. (A study that reported only correlation coefficients between lung cancer prevalence and air pollution would not meet this criterion.) Indoor exposure here includes use of coal for cooking/heating, coal use above a certain amount, presence of coal dust above a certain level, use of certain cooking oils, or environmental tobacco smoke (ETS). “Non-exposure” here is use of cleaner fuels such as natural gas, liquefied petroleum gas (LPG), or kerosene, access to electricity, access to district heating, use of coal below a certain amount, coal dust levels being lower than a certain level, use of cleaner oils or no cooking oils, or absence of ETS.
3) The study includes efforts to control and discuss important confounding factors (e.g. active smoking, diet, and occupational exposure).

2.2. Meta-analysis methods

As a tool for extracting more information from a series of individual studies by pooling their results using certain statistical methods, meta-analysis was applied in this paper to establish quantitative estimates of the air pollution impacts on lung cancer in China.

Pooled OR values were first calculated by the fixed-effects model (inverse variance method), in which the estimated OR is a weighted average of the individual study values (e.g. Schlesselman and Collins, 2003; Yao and Shi, 2003). The weights used in the calculation are the inverse of the study variance. The standard error (SE) of the pooled result is the inverse of the square root of the sum of weights. Including the 95% confidence limits we get:

$$\mathrm{OR} = \exp\left[\frac{\sum W_i \ln(\mathrm{OR}_i)}{\sum W_i} \pm \frac{1.96}{\sqrt{\sum W_i}}\right] \tag{1}$$

where OR_i is the odds ratio of study i, and W_i is the weight of study i, which is set as the reciprocal of the variance of study i, V_i. The upper 95% confidence interval is applied to calculate the V_i in case it was not given explicitly:

$$V_i = [\ln(\mathrm{OR}_{\mathrm{ui}}/\mathrm{OR}_i)/1.96]^2 \tag{2}$$

where $\mathrm{OR}_{\mathrm{ui}}$ is the upper limit of the 95% confidence interval.

Heterogeneity was assessed by the Q statistic, which is the sum over all studies of the study weight multiplied with the square of the difference between the natural logarithms of OR_i and that of weighted average OR (see formula (3)). The Q statistic is referred to a chi-square distribution with $n-1$ degrees of freedom, where n is the number of studies that are pooled.

$$Q = \sum [W_i(\ln(\mathrm{OR}_i) - \ln(\mathrm{OR}))^2] \tag{3}$$

If the test shows heterogeneity to be statistically significant, i.e. $P<0.05$, there are considerable differences between the results of the pooled studies. Fixed-effects estimate should then be replaced with random-effects estimate. The additional variance is calculated as follows:

$$s^2 = \frac{Q - n + 1}{\sum W_i - \sum W_i^2 / \sum W_i} \tag{4}$$

and the W_i in formula (1) is replaced with

$$W_i^* = (W_i^{-1} + s^2)^{-1} \quad (5)$$

The weights thus become more similar and the standard error in Eq. (1) larger.

2.3. Test of possible publication bias

The meta-analysis is based on results published in peer-reviewed journals. These may not represent all available information because some relevant reports may be published in other formats or not published at all. Publication bias refers to the tendency for findings that support a particular hypothesis (in this case, that air pollution has an adverse effect on lung cancer) to be published preferentially in peer-reviewed journals (Dickersin, 1997; HEI, 2004). It might lead to an inaccurate estimate or conclusion regarding the degree of support in the literature for the hypothesis.

Funnel plots in which OR values are plotted in logarithmic scale against their standard error are applied in this study to assess the validity of the meta-analysis results. The assumption is that precision will improve as the sample size of a component study increases. Results from small studies will scatter widely at the bottom of the graph, with the spread narrowing among larger studies. If the data lack publication bias, the resulting scatter should be symmetric like an inverted funnel (Light and Pillemer, 1984).

Symmetry or asymmetry of funnel plot has generally been defined informally through visual examination, and the conclusions will necessarily be subjective. A method for quantitatively evaluating funnel plot asymmetry of meta-analyses, and thus a possible publication bias, has been suggested by Egger et al. (1997). Here the standard normal deviate (SND), defined as the logarithm of odds ratio divided by its standard error, is regressed against the estimate's precision, the latter being defined as the inverse of the standard error (i.e. the regression equation is: $\text{SND} = a + b \times \text{precision}$). The points from a homogeneous set of trials, not distorted by selection bias, will thus scatter about a line that runs through the origin at standard normal deviate zero ($a = 0$), with the slope b indicating the size and direction of the effect. The intercept a provides a measure of asymmetry (Egger et al., 1997).

3. Results

Eighty-six papers (33 in English and 53 in Chinese) have been obtained through the search strategy described above. According to the criteria of literature inclusion, 27 papers (19 in English and 8 in Chinese) have been selected for the meta-analysis. These case-control studies mainly focused on the relation between lung cancer and indoor air pollution for Chinese people, accumulating totally 5563 cases and 8484 controls. As for the rest of the papers, 14 were rejected because they were not case-control or cohort studies, 17 because there was no description of relevant indoor air pollution indicators, 10 due to lack of necessary information for meta-analysis (e.g. OR with 95% CI, study period, etc.), and 5 due to repeated publication. Another 13 papers discussed lung cancer and outdoor air pollution in China, but no OR values were provided.

3.1. Lung cancer risk due to indoor air pollution from coal combustion

Coal combustion for heating and cooking is still very frequent in Chinese families, especially those in poor rural areas due to lack of electric power, and this leads to heavy indoor air pollution. Seven studies were selected for the meta-analysis on the association between coal use and lung cancer risk (see Table 1). They were carried out in Harbin (Dai et al., 1996), Gansu (Kleinerman et al., 2002), and Taiwan (Ko et al., 1997) for women, and Nanjing (Shen et al., 1996), Fuzhou (Luo et al., 1996), Harbin (Sun et al., 2002), Xuanwei (Lan et al., 2000), and Gansu (Kleinerman et al., 2002) for both sexes.

Dai et al. (1996) showed that using coal for heating was a statistically significant risk factor for female adenocarcinoma (OR = 5.81, 95%CI: 1.67–20.22) through a case-control study in Harbin involving interviews with 120 cases of nonsmoking women, matched 1:1 with controls. Kleinerman et al. (2002) interviewed 846 patients with lung cancer (626 men and 220 women aged 30 to 75 years) diagnosed between 1994 and 1998 with 1740 population-based controls in rural area of Pingliang and Qingyang, Gansu province. They found that the lung cancer risk for coal use compared with biomass in the homes of longest residence was increased (OR = 1.29 for both sexes and 1.03 for women). Ko et al. (1997) conducted a case-control study involving interviews with 117 female lung cancer patients (including 106 nonsmoking ones) and the same number of individually matched hospital controls in Kaohsiung, Taiwan between 1992 and 1993. Adjusted OR of coal or anthracite consumption for cooking compared with gas was 1.3 (95% CI: 0.3–5.8). Shen et al. (1996) found that RR was 3.72 (95% CI: 0.88–15.71) for those who used coal stoves for heating in winter

Table 1
Results selected for the meta-analysis from epidemiological studies in China

Air pollution issues	OR (95% CI)	Period	Study area	Sample size		Reference
				Case	Control	
Coal consumption (e.g. heating and cooking)						
Women	5.81 (1.67–20.22)	1992–1993	Harbin	120	120	Dai et al., 1996
	1.3 (0.3–5.8)	1992–1993	Taiwan	117	117	Ko et al., 1997
	1.03 (0.66–1.63)	1994–1998	Gansu	220	459	Kleinerman et al., 2002
Both sexes	3.72 (0.88–15.71)[a]	1986–1993	Nanjing	263	263	Shen et al., 1996
	7.6 (3.7–15.7)	1990–1991	Fuzhou	102	306	Luo et al., 1996
	2.22 (1.28–3.86)	1996–1999	Harbin	206	618	Sun et al., 2002
	2.4 (1.3–4.4)	1995–1996	Xuanwei	122	122	Lan et al., 2000
	1.29 (1.03–1.61)	1994–1998	Gansu	846	1740	Kleinerman et al., 2002
Exposure to coal dust						
Women	2.66 (1.09–6.52)	1992–1993	Harbin	120	120	Dai et al., 1996
	2.87 (1.83–4.55)	1991–1994	Shenyang	166	166	Wang et al., 1996b
	2.21 (1.16–4.21)[a]	1985	Guangzhou	283	283	Du et al., 1996
	2.38 (1.58–3.57)	1992–1994	Shanghai	504	601	Zhong et al., 1999b
Both sexes	1.8 (1.1–3.1)	1990–1991	Fuzhou	102	306	Luo et al., 1996
	3.5 (2.0–6.4)	1987–1993	Anshan	610	959	Xu et al., 1996
Indoor cooking oil						
Nonsmoking women	3.79 (2.29–6.27)	1992–1994	Shenyang	135	135	Wang et al., 1996a
	1.86 (1.39–2.47)	1992–1995	Tianjin	264	250	Wang et al., 2001
	1.56 (1.0–2.5)	1994–1998	Gansu	230	459	Kleinerman et al., 2000
	2.32 (1.59–3.41)	1992–1993	Shanghai	498	595	Liu et al., 2001
	2.15 (1.20–3.21)	1992–1993	Shanghai	504	601	Zhong et al., 1995
	1.84 (1.12–3.02)	1992–1994	Shanghai	504	601	Zhong et al., 1999b
	2.5 (1.4–4.3)	1993–1996	Taiwan	131	262	Ko et al., 2000
Women	1.71 (1.41–2.08)	1992–1995	Tianjin	264	250	Wang et al., 2001
	1.67 (1.0–2.5)	1994–1998	Gansu	233	459	Metayer et al., 2002
	4.53 (2.09–9.94)	1991–1995	Shenyang	72	72	Zhou et al., 2000
Both sexes	8.11 (3.13–21.05)	1996–1999	Harbin	206	618	Sun et al., 2002
	3.81 (1.06–13.73)	1986–1993	Nanjing	263	263	Shen et al., 1996
Environmental tobacco smoking exposure						
Nonsmoking women	1.15 (0.64–2.06)	1991–1994	Shenyang	166	166	Wang et al., 1996b
	2.52 (1.03–6.44)	1990–1993	Beijing	116	464	Zheng et al., 1997
	1.65 (1.10–2.47)	1992–1993	Shanghai	498	595	Liu et al., 2001
	2.70 (1.49–4.88)	1985–1987	Harbin	114	114	Wang et al., 1996c
	1.19 (0.66–2.16)	1986	Guangzhou	229	229	Lei et al., 1996
	1.7 (1.3–2.3)	1992–1994	Shanghai	504	601	Zhong et al., 1999a
	1.3 (0.7–2.5)	1992–1993	Taiwan	117	117	Ko et al., 1997
	3.14 (1.97–5.01)	1990–1994	Guangdong	200	200	Dai et al., 1997
	0.94 (0.45–1.97)	1991–1995	Shenyang	72	72	Zhou et al., 2000
Both sexes	2.3 (1.5–3.6)	1993–1994	Heilongjiang	128	128	Yu et al., 1996
	1.06 (0.63–1.80)	1996	Beijing	350	350	Li et al., 2000
	1.19 (0.7–2.0)	1994–1998	Gansu	886	1765	Kleinerman et al., 2000
	2.4 (1.1–5.1)	1990–1991	Fuzhou	102	306	Luo et al., 1996
	1.79 (1.08–2.97)	1990–1993	Guangdong	390	390	Wang et al., 1996d

OR: odds ratio. CI: confidence interval.

[a] OR was approximated with RR from original study.

compared with those who did not have any house heating in Nanjing through a case-control study with 263 lung cancer cases. The case-control study on risk factors for lung cancer in Fuzhou by Luo et al. (1996) matched 102 newly diagnosed primary lung cancer cases (78 male and 24 female cases) with 306 population-based controls. Results showed that indoor burning of coal for cooking was associated with an increased risk of lung cancer (OR = 7.6, 95% CI: 3.7–15.7). Sun et al. (2002) conducted a 1:3 matched case-control study in Harbin, indicating that, after correcting for some confounding factors, ORs increased 122% for those using 46 kg/(m^2·a) or more of coal compared to those using less than 46 kg/(m^2·a). Lan et al. (2000) found that the OR of lung cancer risk for those using large amounts of smoky coal (>130 tons during their lifetime) was 2.4 (95% CI, 1.3–4.4) compared to subjects who used less than 130 tons in Xuanwei, Yunnan province.

The pooled OR values with 95% CI obtained using the fixed-effect model are 1.27 (0.84–1.92) and 1.67 (1.38–2.01) for women and both sexes respectively. The *Q*-statistic test showed high heterogeneity (see Table 2). Therefore, the random-effect model was applied and the pooled OR values were then adjusted to 1.83 (95% CI: 0.62–5.41) and 2.66 (1.39–5.07), respectively. The meta-analysis results indicate that there is an association between coal consumption and lung cancer risk, although not significant for women. People who live in homes using coal as fuel have twice the lung cancer risk of other people. Since the definition and measurement of coal use and "non-exposure" in these studies differs a lot, it is difficult to set a strict criterion for selection of studies for meta-analysis. This might partly explain the high heterogeneity.

The studies by Dai et al. (1996) and Luo et al. (1996) mentioned above, and four other studies carried out in Shenyang (Wang et al., 1996b), Guangzhou (Du et al., 1996), Shanghai (Zhong et al., 1999b) and Anshan (Xu et al., 1996b) also report the association between lung cancer risk and another indicator of indoor air pollution: indoor coal dust exposure. Dai et al. (1996) found that exposure to coal dust for more than 10 years was a significant lung cancer risk factor for women in Harbin (OR = 2.66, 95% CI: 1.09–6.52). Luo et al. (1996) indicated that persons who had a history of contact with dust or coal dust or other industrial dust in the workplace had an elevated risk of lung cancer (OR = 1.8, 95% CI: 1.1–3.1). Wang et al. (1996b) carried out a case-control study on nonsmoking women in the urban area of Shenyang between 1991 and 1994 involving 166 newly diagnosed lung cancer cases and an equal number of controls matched for age and sex, and found that coal dust exposure in bedroom and kitchen was significantly associated with lung cancer (OR = 2.87, 95% CI: 1.83–4.55). Du et al. (1996) analyzed more than 6000 cases of lung cancer death in Guangzhou, accumulated over 9 years. The 849 (566 men and 283 women) lung cancer deaths in 1985 were analyzed for evaluating the risks associated with exposure to burning coal, showing that it was a highly significant risk factor for lung cancer in women (RR = 2.21, 95% CI: 1.16–4.21). Zhong et al. (1999b) conducted a population-based, case-control study of lung cancer among nonsmoking women living in Shanghai involving 504 lung cancer cases diagnosed from February 1992 through January 1994 with a control group of 601 nonsmoking women, finding that lung cancer was related to smokiness of the kitchen during cooking (OR = 2.38, 95% CI: 1.58–3.57). Xu et al. (1996) interviewed 610 cases of lung cancer diagnosed during 1987–1993 and 959 randomly selected controls in Anshan, and found high lung

Table 2
Odds ratios resulting from meta-analyses

Air pollution issues	Fixed-effect model OR (95% CI)	Heterogeneity *Q*-stat (*P* value)	*df*	Random-effect model OR (95% CI)
Coal consumption (e.g. heating and cooking)				
Women	1.27 (0.84–1.92)	6.51 (0.04)	2	1.83 (0.62–5.41)
Both sexes	1.67 (1.38–2.01)	25.55 (<0.0001)	4	2.66 (1.39–5.07)
Exposure to coal dust				
Women	2.52 (1.94–3.28)	0.56 (0.91)	3	–
Both sexes	2.42 (1.62–3.63)	2.57 (0.11)	1	–
Indoor cooking oil				
Nonsmoking women	2.12 (1.81–2.47)	8.45 (0.21)	6	–
Women	1.78 (1.50–2.12)	5.69 (0.06)	2	–
Both sexes	6.20 (2.88–13.32)	0.86 (0.35)	1	–
Environmental tobacco smoke exposure				
Nonsmoking women	1.73 (1.46–2.04)	15.85 (0.04)	8	1.70 (1.32–2.18)
Both sexes	1.64 (1.29–2.07)	7.36 (0.12)	4	–

OR: odds ratio. CI: confidence interval. *df*: degrees of freedom. *Q* values indicate degree of heterogeneity; for cases where the corresponding *P* value < 0.05, the estimate using the random-effect model instead of the fixed-effect model is suggested.

cancer risks of exposure to coal dust (OR = 3.5, 95% CI: 2.0–6.4).

The pooled OR values with 95% CI obtained using the fixed-effect model are 2.52 (1.94–3.28) and 2.42 (1.62–3.63) for women and both sexes, respectively (see Table 2). Since no significant heterogeneity was found, this estimate was accepted as final results for lung cancer risks of indoor coal dust exposure.

3.2. Lung cancer risk due to indoor air pollution from cooking oil

Indoor cooking oil pollution is another important risk factor for lung cancer in China due to Chinese cooking traditions (e.g. frequent deep frying) and poor ventilation in the kitchens. Eleven studies were selected for the meta-analysis, carried out in Shenyang (Wang et al., 1996a; Zhou et al., 2000), Tianjin (Wang et al., 2001), Gansu (Kleinerman et al., 2000; Metayer et al., 2002), Shanghai (Liu et al., 2001; Zhong et al., 1999b; Zhong et al., 1995), and Taiwan (Ko et al., 2000) for women, and Harbin (Sun et al., 2002) and Nanjing (Shen et al., 1996) for both sexes.

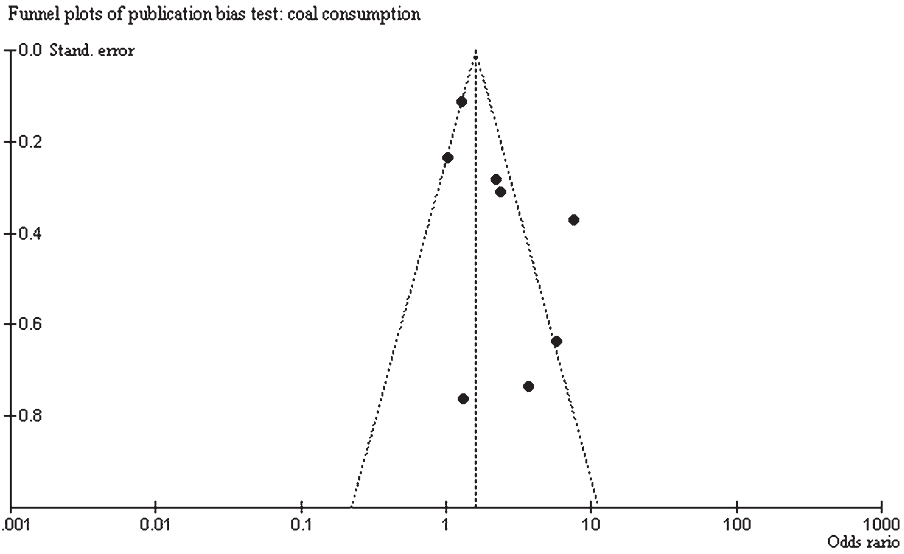
Wang et al. (1996a) evaluated the risk factors for lung cancer in lifetime nonsmoking women through a hospital-based case-control study in the urban area of Shenyang, between April 1992 and May 1994 involving 135 newly diagnosed lung cancer cases and an equal number of controls, matched for age and sex, and found a relatively high OR value of 3.79 (95% CI: 2.29–6.27). Zhou et al. (2000) also indicated in Shenyang that exposure to cooking fumes increased the OR of lung adenocarcinoma by 4.53 (2.09–9.94) according to the analysis on 72 new female lung cancer cases with same number of controls from 1991 to 1995. Wang et al. (2001) analyzed the risk of heavy cooking oil for women and nonsmoking women after adjusting for age, through a case-control study involving 264 female lung cancer cases and 250 controls during March 1992 and February 1995 in Tianjin, indicating that the OR values of heavy cooking oil pollution were 1.86 (95% CI: 1.39–2.47) and 1.71 (95% CI: 1.41–2.08) for non-smoking women and women, respectively. Kleinerman et al. (2000) and Metayer et al. (2002) conducted case-control studies in rural Gansu between 1994 and 1998 to analyze the increased risk of cooking with rapeseed oil to linseed oil, which is considered to be relatively clean cooking oil, for nonsmoking women (OR = 1.56, 95% CI: 1.0–2.5) and women (OR = 1.67, 95% CI: 1.0–2.5). Liu et al. (2001) conducted a population-based case-control study involving with 498 new cases and 595 controls aged 35–69 years for 1992 and 1993 to explore the risk factors of lung cancer among nonsmoking women in Shanghai. It was shown that exposure to cooking oil fumes was associated with elevated risk of lung cancer (OR = 2.32, 95% CI: 1.59–3.41). Zhong et al. (1999b) (mentioned above) also implied that lung cancer risk would increase for nonsmoking women due to frequent using of rapeseed oil. Zhong et al. (1995) implied that there is a significant association between lung cancer and frequent exposure to cooking oil based on the same study samples as Zhong et al. (1999b). The OR values were 1.84 (95% CI: 1.12–3.02) and 2.15 (95% CI: 1.20–3.21), respectively. Ko et al. (2000) conducted a study on food cooking and lung cancer in nonsmoking women in Taiwan based on 131cases and 262 controls form 1993 to 1996, and found that the OR of cooking oil pollution was 2.5 (1.4–4.3). For both sexes, the OR values from Sun et al. (2002) and Shen et al. (1996) were 8.11 (3.13–21.05) and 3.81 (1.06–13.73), respectively.

The pooled OR values with 95% CI obtained using the fixed-effect model are 2.12 (1.81–2.47), 1.78 (1.50–2.12) and 6.20 (2.88–13.32) for nonsmoking women, women and both sexes, respectively (see Table 2), and no significant heterogeneity was found. Similar to coal use, indoor cooking oil pollution varies considerably in different areas due to differences in economic level and energy supply.

3.3. Lung cancer risk due to environmental tobacco smoke

A range of studies have shown that environmental tobacco smoke (ETS) might increase the lung cancer risk for the Chinese population, especially nonsmoking women, although the uncertainties in the studies are high. Fourteen studies were selected for the meta-analysis, carried out in Beijing (Zheng et al., 1997), Guangdong (Lei et al., 1996; Dai et al., 1997), Shenyang (Wang et al., 1996b; Zhou et al., 2000), Shanghai (Liu et al., 2001; Zhong et al., 1999a), Harbin (Wang et al., 1996c), and Taiwan (Ko et al., 1997) for nonsmoking women, and Heilongjiang (Yu et al., 1996), Beijing (Li et al., 2000), Gansu (Kleinerman et al., 2000), Fuzhou (Luo et al., 1996) and Guangdong (Wang et al., 1996d) for both sexes.

Zheng et al. (1997) conducted a population-based case-control study involving 309 lung cancer cases (of which 94 were nonsmokers) in Beijing during 1990 to 1993 to explore the etiology of lung cancer in nonsmoking women. The results showed that there was association between passive smoking and lung cancer in nonsmoking women (OR = 2.52, 95% CI: 1.03–6.44), and its strength also increased with cigarette-years of smoking. Dai et al. (1997) found the similar result in Guangdong with OR 3.14 (1.97–5.01) based on 200 cases and 200 controls from 1990 to 1994. In contrast, Lei et al. (1996) found no significant association between lung cancer and passive smoking in their investigation of the relationship between lifestyle factors and lung cancer based on all lung cancer deaths registered in 1986 in Guangzhou. In Shenyang, both Wang et al. (1996b) and Zhou et al. (2000) implied that there was no significant association between ETS exposure and lung cancer for women. Zhong et al. (1999a) indicated that OR for nonsmoking women exposed to ETS at work for more than 2 years was 1.7 (1.3–2.3) in Shanghai, based on the same samples as in Zhong et al. (1999b). In Harbin, Wang et al. (1996c) carried out a case-control study of childhood and adolescent exposure to ETS and the risk of lung cancer in women, finding that the OR was 2.70 (95% CI: 1.49–4.88) for exposure to maternal smoking under 14 years old and 1.40 (0.79–2.50) for exposure to paternal smoking. Ko et al. (1997) found no significant association between ETS exposure from spouses and lung cancer in Taiwan. For both sexes, Yu et al. (1996) conducted a 1:1 matched case-control study in Heilongjiang province from October 1993 to April 1994, involving 128 lung



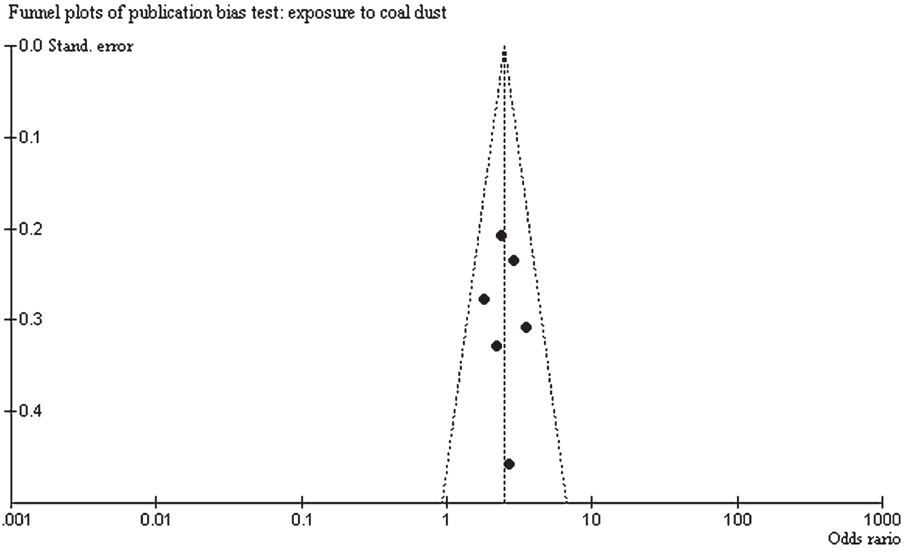


Fig. 1. Funnel plots for analysis of publication bias in OR estimates of lung cancer from indoor air pollution. Horizontal axis represents the ORs and vertical axis represents standard errors. Pooled OR values by the fixed-effect model are shown by vertical dashed lines and the 95% CI limits by the dashed lines bounding the funnel.

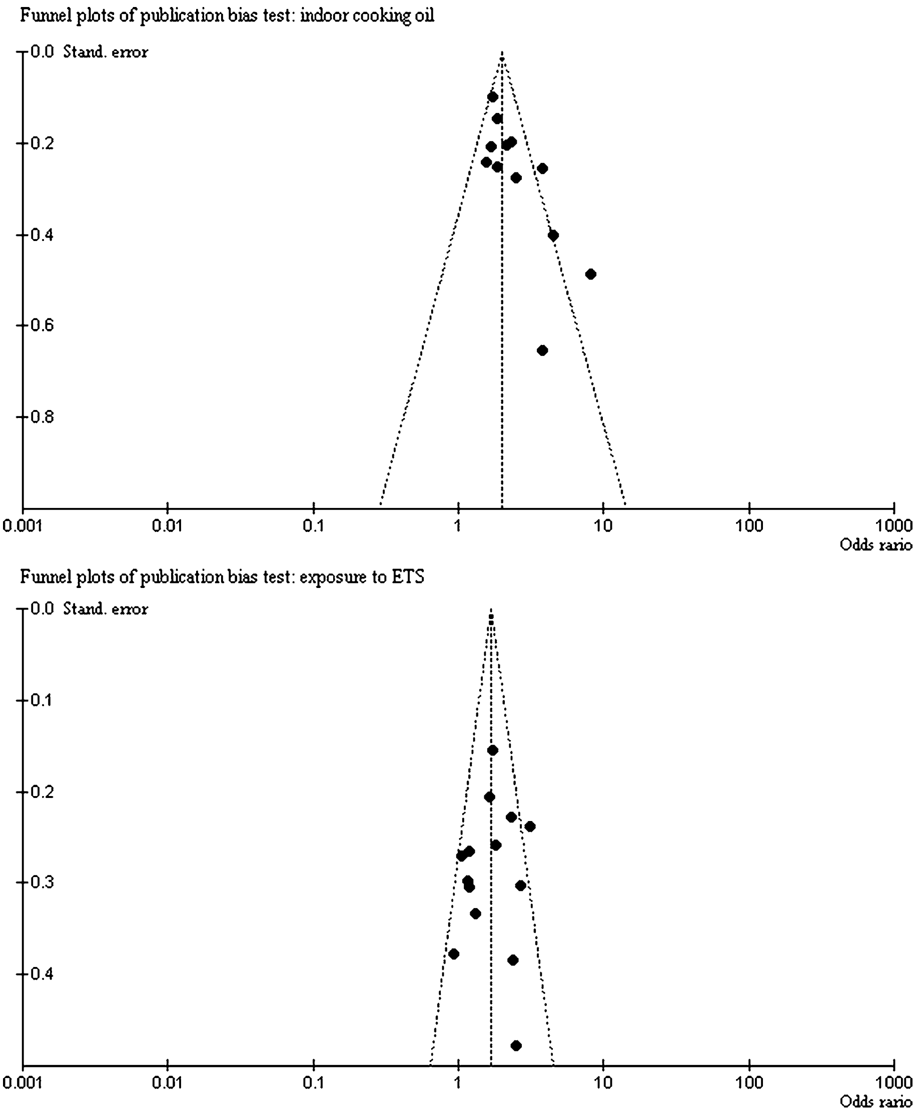


Fig. 1. (*continued*).

cancer cases, showing that ETS exposure during childhood was associated with an OR of 7.8 (95% CI: 3.1–19.8), and during adulthood with an OR of 2.3 (1.5–3.6). However, Li et al. (2000) found no significant association between ETS and lung cancer in Beijing through a study with 350 cases matched 1:1 with controls. The same conclusion was also drawn in Gansu by Kleinerman et al. (2000). In the study in Fuzhou, Luo et al. (1996) found that exposure before 20 years of age was associated with squamous cell carcinoma. Wang et al. (1996d) carried out a case-control study involving 390 lung cancer cases matched 1:1 with controls in Guangdong province. They concluded that exposure to ETS in the home and at workplace were independent risk factors for lung cancer.

The pooled OR values with 95% CI obtained by the fixed-effect model are 1.63 (1.36–1.96) and 1.64 (1.29–2.07) for nonsmoking women and both sexes, respectively (see Table 2). Significant heterogeneity was found for nonsmoking women, and the random-effect estimate was 1.70 (1.32–2.18). The meta-analysis results show that the risk of ETS for nonsmoking women is a little higher than that for other people.

3.4. Publication bias

Fig. 1 shows the funnel plots of meta-analysis for association between lung cancer risk and indoor air pollution in China. It can be seen from the figures that the studies related to most risk factors distribute quite

Table 3
Statistical regression results of publication bias test

Air pollution issues	Estimated coefficient	S.E.	*t*-value	Significance
Coal consumption (e.g. heating and cooking)				
a	2.309	1.129	2.046	0.087
b	−0.002	0.277	−0.009	0.993
Exposure to coal dust				
a	0.232	1.541	0.151	0.888
b	0.851	0.425	2.006	0.115
Indoor cooking oil				
a	2.452	0.708	3.466	0.006
b	0.255	0.143	1.787	0.104
Environmental tobacco smoking exposure				
a	−0.560	1.341	−0.418	0.684
b	0.668	0.350	1.909	0.080

The regression equation is SND $=a+b\times$precision. The *t*-values are obtained by the *t*-test method.

symmetrically with the pooled estimate as midline. Almost all the results of studies for certain risk factors are within the 95% CI lines, with an exception of those for cooking oil pollution, which have three studies exceeding the limit.

The method suggested by Egger et al. (1997) was applied to quantitatively test publication bias. Results of the regressions are listed in Table 3. It is clear that at a confidence level of 0.05 there is no funnel plot asymmetry for all the indoor air pollution risk factors in the meta-analyses except that for cooking oil. With respect to coal consumption, however, the *t*-value for a is just above 2 and thus a is significantly different from zero.

In this paper we are not able to separate the impact of publication bias from other factors (e.g. possible exclusion of other valid resources) on the observed asymmetry in funnel plots. More studies on indoor pollution of coal consumption and cooking oil are needed.

4. Discussion

Indoor air pollution has been considered an important lung cancer risk for the Chinese population. According to the results of our meta-analysis, coal consumption and coal dust exposure were the factors that had the highest OR values, followed by cooking oil exposure and then ETS exposure. The extremely high OR of indoor cooking oil for both sexes is excluded from the comparison due to the paucity of studies that address men's exposures. It is thus reconfirmed that coal burning and cooking oil are the main lung cancer risk factors of indoor air pollution for the Chinese population. Special attention should be paid to the uncertainty which is introduced by the fact that the assumed "non-exposure" in some original studies may actually have fairly high pollution levels. For example, people using biomass (which would also cause indoor air pollution) were considered as a "non-exposure" group by Kleinerman et al. (2002). This might cause the pooled OR values to be underestimated to a greater or lesser degree. With respect to ETS, some studies implied significant association but others did not, and the pooled OR values are the lowest among all three risk factors. Therefore, regarding the effect of ETS on lung cancer ambiguity still prevails.

Lung cancer risk for women, especially nonsmoking women, was the main concern in most studies. Our meta-analysis results showed that the pooled OR values for women are lower than those for both sexes for coal consumption and indoor cooking oil pollution, and similar results could be obtained by combining the outcomes of some other meta-analysis given by Zhang et al. (2001), Yao et al. (2002), Yao and Shi (2003) and Smith et al. (2004). This does not necessarily imply that indoor air pollution has less impact on women than men, but may be related to the fact that there is a higher prevalence of lung cancer in men, attributed mainly to cigarette smoking. It is difficult to disentangle the synergistic effect of active smoking and other environmental factors thoroughly in single-factor analysis in epidemiological studies. It seems clear that indoor air pollution derived from cooking fuel and household coal consumption is a highly significant risk factor for lung cancer in Chinese females (Du et al., 1996).

As mentioned above, several other studies also conducted meta-analysis on indoor air pollution and lung cancer for Chinese, e.g. Zhang et al. (2001), Yao et al. (2002), and Yao and Shi (2003). Compared with the association between lung cancer risk and coal consumption given by Yao et al. (2002) and Yao and Shi (2003) (OR = 1.27 and 1.50 for women and both sexes respectively), our random-effect estimate is a bit higher, probably due to inclusion of studies with rather high effect estimates (e.g. Dai et al., 1996; Luo et al., 1996). For indoor coal dust exposure, our outcomes are higher than the pooled result of 1.84 (0.94–3.59) for women by Yao et al. (2002) but lower than 3.20 (1.79–5.71) for both sexes by Yao and Shi (2003). Another meta-analysis study covering the entire Chinese population (Smith et al., 2004; Smith and Tian, 2005) indicated that the relative risk (RR) for lung cancer from exposure to coal smoke was 1.94 (95% CI: 1.09–3.47) for Chinese women over 30 years of age and 2.55 (95% CI: 1.58–4.10) for both sexes. This result is also quite comparable with our estimate. With respect to indoor cooking oil, our outcomes are lower than the meta-analysis results of 2.52 (2.12–2.91) for nonsmoking women by Zhang et al. (2001) and 2.98 (1.91–4.66) for women by Yao et al. (2002). Based on very limited studies, our OR for both sexes is extremely high due to the findings in Harbin (Sun et al., 2002). For ETS exposure, our estimates are a little higher than the meta-analysis result of 1.37 (0.88–2.12) for women by Yao et al. (2002) and 1.42 (1.14–1.77) for both sexes by Yao and Shi (2003).

Exposure to indoor air pollution from combustion sources used for heating and cooking as well as high levels of cooking oil vapors resulting from certain cooking methods have also been identified as risk factors for lung cancer in other countries. However, the results are inconclusive and difficult to interpret due to high variation in exposure measures. In a case control study from the Northern province of South Africa (Mzileni et al., 1999), the OR of lung cancer among women using wood or coal as the main fuel was 1.4 (95% CI: 0.6–3.2), showing a positive correlation with lung cancer, although not significant. This value is comparable with our meta-analysis results in China. In Europe and North America, however, use of electricity or natural gas for cooking is much more frequent, deep frying is less common, and kitchens are generally larger, better ventilated and separated from the living quarters. Central heating is increasingly common, and open combustion sources indoors are infrequent (Boffetta and Nyberg, 2003). Therefore, indoor air quality is usually better than in rural China and does not represent a large health risk.

Regarding exposure to ETS, the International Agency for Research on Cancer (IARC) has evaluated the evidence of a carcinogenic risk from exposure to environmental tobacco smoke, and has classified it as an established human carcinogen (IARC, 2002). A meta-analysis of epidemiological studies of lung cancer and adult exposure to environmental tobacco smoke was conducted, resulting in risk ratios (RRs) of 1.22 (95% CI 1.12–1.32) in women and 1.36 (95% CI 1.02–1.82) in men from spousal exposure, and of 1.15 (95% CI 1.05–1.26) in women and 1.28 (95% CI 0.88–1.84) in men from workplace exposure. These values are similar to, or a bit lower than, our meta-analysis results for Chinese population (OR = 1.63 for nonsmoking women and 1.64 for both sexes), implying that passive smoking and ETS exposure might be a more serious lung cancer risk factor in China compared with other regions of the world.

Compared to Europe and the USA, there are few epidemiological studies on the association between outdoor atmospheric pollution and lung cancer in China, especially studies focusing on specific pollutants (e.g. SO_2, NOx, PM, etc.). Several studies have simply indicated the correlation between lung cancer and levels of certain pollutants. A study in Fuzhou for the years 1984–1993 using a regression model showed that the mortality of lung cancer correlated significantly with TSP levels (correlation factor (r) equals to 0.603, $P<0.01$) and dust fall ($r=0.618$, $P<0.01$) (Zhuang and Zhou, 1996). Zhang and Lin (1994) found that there was a significant correlation between TSP level and mortality of lung cancer ($P<0.05$) in Chongqing from 1985 to 1990. The correlation coefficients between mortality of lung cancer and SO_2, NOx, and TSP pollution in Hefei, Anhui Province, were reported as 0.94 ($P<0.01$), 0.41 ($P>0.05$), and 0.94 ($P<0.01$), respectively by Wang et al. (1998). When they considered the three pollutants simultaneously, only SO_2 had significant association with lung cancer. A death retrospective survey of all causes from 1985 to 1989 was carried out in 13 districts of Shandong Province (Li et al., 1994). The results of correlation analysis showed that increasing mortality of lung cancer was related significantly to SO_2 ($P=0.004$). A study in Wulumuqi, Xinjiang Province for the years 1979–1992 found significant association between mortality of lung cancer and pollutant levels ($r=0.728$ for NOx, 0.658 for SO_2, and 0.558 for TSP) (Feng et al., 2001). Some studies have estimated the association between lung cancer and an air pollution index. Zhang et al. (1994) and He et al. (1995) found a significant association between the Babcock pollution index (Babcock, 1970) and lung cancer (latent period = 4 years) in Qingdao (Shandong Province), with $r=0.976$ and $r=0.970$ ($P<0.001$) for morbidity and mortality, respectively, after adjusting for smoking and cooking styles. Sun (1999) confirmed the association between the Babcock pollution index and lung cancer mortality (latent period = 5 years) in Qingdao, with $r=0.852$.

However, very few studies have provided OR values for lung cancer of outdoor air pollution, or exposure–response functions, and it is thus difficult to evaluate the impacts of outdoor air pollution quantitatively. RR values of Western studies, corresponding to a 10 $\mu g/m^3$ increment of specific pollutants, are summarized in Table 4. It can be seen that American studies tend to report the association between lung cancer and PM, while European studies focus more on gaseous pollutants. The RRs of these studies tend to show an increased risk of lung cancer with high pollutant exposure, which does not seem to be attributable to confounding factors. For want of better data we tentatively suggest using these functions for China at present,

Table 4
Summary of estimated relative risks of lung cancer with a 10 μg/m^3 increment of specific pollutants in USA and European countries

Reference	Location	Period	Pollutants	RR (95% CI)
Abbey et al., 1999	California, USA	1977–1992	PM_{10}	1.66 (1.21–2.27)
Dockery et al., 1993	6 cities, USA	1974–1989	$PM_{2.5}$	1.18 (0.89–1.57)
Pope et al., 1995	151 cities, USA	1982–1989	$PM_{2.5}$	1.01 (0.91–1.12)
			Sulfate	1.17 (1.05–1.29)
HEI, 2000	6 cities, USA	1974–1989	$PM_{2.5}$	1.15 (0.86–1.54)
	151 cities, USA	1982–1989	$PM_{2.5}$	1.00 (0.91–1.11)
			Sulfate	1.15 (1.05–1.27)
Pope et al., 2002	151 cities, USA	1982–1998	$PM_{2.5}$	1.14 (1.04–1.23)
Hoek et al., 2002	Netherlands	1986–1994	Black smoke	1.06 (0.43–2.63)
			NO_2	1.08 (0.75–1.55)
Nafstad et al., 2003	Oslo, Norway	1972–1998	NOx	1.08 (1.02–1.15)[a]
			SO_2	1.01 (0.94–1.08)[a]
Nyberg et al., 2000	Stockholm, Sweden	1985–1990	NO_2	1.10 (0.97–1.23)
			SO_2	1.01 (0.98–1.03)

RR: relative risk.
[a] Only for men.

although transferring results from Western countries to China leads to high uncertainties due to different ambient air quality and other effect-modifying factors. More careful studies on the lung cancer risk due to outdoor air pollution in China are thus needed.

5. Conclusions

It is generally believed that air pollution has a large effect on the prevalence of lung cancer in the Chinese population. This is especially true for people who live in rural areas and are exposed to high levels of indoor air pollution due to lack of clean fuels for heating and cooking. A meta-analysis was conducted based on case-control epidemiological studies in China, evaluating the association between lung cancer and indoor air pollution in China. The pooled estimate reconfirmed that coal combustion and cooking oil are the main lung cancer risk factors of indoor air pollution. With respect to the effect of ETS exposure the results are more ambiguous, but still indicate a clear association. The results of coal consumption and cooking oil pollution may be affected by publication bias according to statistical tests. Regarding outdoor air pollution, there are very few studies providing OR values or exposure–response functions for lung cancer in China, and more studies are needed.

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