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Lung cancer risk and solid fuel smoke exposure: a systematic review and meta-analysis

Om Prakash Kurmi*, Pallavi Huma Arya#,¶, Kin-Bong Hubert Lam*,¶, Tom Sorahan* and Jon G. Ayres*

ABSTRACT: **The aim of this systematic review was to quantify the impact of biomass fuel and coal use on lung cancer and to explore reasons for heterogeneity in the reported effect sizes.**

A systematic review of primary studies reporting the relationship between solid fuel use and lung cancer was carried out, based on pre-defined criteria. Studies that dealt with confounding factors were used in the meta-analysis. Fuel types, smoking, country, cancer cell type and sex were considered in sub-group analyses. Publication bias and heterogeneity were estimated.

The pooled effect estimate for coal smoke as a lung carcinogen (OR 1.82, 95% CI 1.60–2.06) was greater than that from biomass smoke (OR 1.50, 95% CI 1.17–1.94). The risk of lung cancer from solid fuel use was greater in females (OR 1.81, 95% CI 1.54–2.12) compared to males (OR 1.16, 95% CI 0.79–1.69). The pooled effect estimates were 2.33 (95% CI 1.72–3.17) for adenocarcinoma, 3.58 (1.58–8.12) for squamous cell carcinoma and 1.57 (1.38–1.80) for tumours of unspecified cell type.

These findings suggest that in-home burning of both coal and biomass is consistently associated with an increased risk of lung cancer.

KEYWORDS: **Adenocarcinoma, biomass fuel, coal, indoor air pollution, squamous cell carcinoma**

AFFILIATIONS
*Institute of Occupational and Environmental Medicine, School of Population and Health Sciences, University of Birmingham, Birmingham, and
#Faculty of Medicine and Health Sciences, Medical School, Queen's Medical Centre, University of Nottingham, Nottingham, UK.
¶These authors contributed equally.

CORRESPONDENCE
O.P. Kurmi
Institute of Occupational and Environmental Medicine, School of Population and Health Sciences
University of Birmingham
Birmingham
B15 2TT
UK
E-mail: o.kurmi@bham.ac.uk

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Lung cancer is one of the leading causes of mortality accounting for 1.3 million deaths annually worldwide [1]. While smoking is the major risk factor, 25% of cases are not attributable to tobacco use [2]. Epidemiological studies have shown that globally while lung cancer in never-smokers is consistently more common in females than in males, geographical variations are substantial [2]. In eastern and southern Asia, up to 83% of female lung cancer cases are never-smokers, compared to 15% in the USA [2]. In developing countries an estimated 2.4 billion people (70%) use biomass (wood, charcoal, crop residues or dung) or coal, collectively known as solid fuels, for cooking and heating [3]. Emissions from combustion of solid fuels have been shown to have high concentrations of polycyclic aromatic hydrocarbons (PAHs), benzo[a]pyrene and particulate matter with a diameter of 2.5 μm or less, which in turn have been associated with high rates of lung cancer [2].

Recently, indoor emissions from household combustion of coal and biomass (mostly wood) have been classified as carcinogenic (Group 1) and probably carcinogenic (Group 2A) to humans [4]. However, data on the magnitude of lung cancer risk and the histological sub-type of lung cancer associated with solid fuel use are limited. In the literature, four meta-analyses were identified, but three [5–7] were limited to studies conducted in China and one [8] focused only on coal use. A recent paper included a pooled estimate from several countries, but data were restricted to studies from an international consortium [9].

In this meta-analysis we reviewed papers from all countries and calculated pooled estimates of the association of the use of solid fuels and lung cancer. We investigated whether these effects were influenced differently by other factors, notably the types of fuel used, smoking (including environmental tobacco smoke (ETS)) and study location. We also looked at whether there was a pattern of association between smoke exposure and lung cancer histological sub-type.

METHODS

Papers published from January 1980 to October 2010 were identified through a systematic literature search in Ovid Medline, EMBASE and Google Scholar.

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Search terms used for the initial search on exposure were ''biomass'', ''biofuel'', ''organic fuel'', ''black smoke'', ''wood'', ''indoor air pollution'', ''carbon monoxide'', ''respirable dust'', ''solid fuel'', ''dung'', ''charcoal'', ''crop residue'', and outcomes were ''carcinogen'', ''lung tumour'', ''adenoma'', ''adenocarcinoma'', ''squamous carcinoma'', ''carcinoma'', ''lung cancer'' and ''cancer''. The articles obtained by using different exposure search terms were combined using ''OR'' and the same was done for outcomes. The combining term ''AND'' was used to combine the article obtained for exposure and outcome. References in each of the identified papers were screened for any articles that were not identified in the original search. There was no restriction on language in the original search but articles in English and Chinese were retained for inclusion in the meta-analysis. The search was carried out by two authors (P.H. Arya and O.P. Kurmi).

Study selection

All potentially relevant articles were reviewed. Selection criteria were identified and defined by all co-authors. For studies to be part of the review and meta-analysis they had to meet the criteria listed in table 1. Most studies considered were those in which cases had cytological/histological findings alongside radiological confirmation. However, a minority of the studies where the assessment technique was not stated were still included in the review. No limitations were set for the age of participants in the studies or for the definition of exposure to solid fuels.

Data extraction

Selection of studies was undertaken at each stage by two authors (P.H. Arya and O.P. Kurmi) for studies written in English and one author for studies written in Chinese (K-B.H. Lam). Disagreements were settled by consensus. All data were extracted by two authors (P.H. Arya and K-B.H. Lam) independently and uncertainties were discussed with all authors. We used the Newcastle-Ottawa Quality Assessment Scale to assess the quality of the studies [10]. A pre-defined form was then used to extract information from selected studies under the following headings: author; journal; year; country of study; organisation/funding body; type of fuel considered; study design; smoking (type, measure and assessment technique); sample size; indoor air pollution exposure assessment; primary outcome (type and assessment of outcome); effect size (relative risk or odds ratio (OR) and the associated 95% confidence intervals (CI) and p-values); and possible confounding factors considered.

TABLE 1 Inclusion criteria for meta-analysis

1. Papers of primary studies written in English or Chinese
2. Case–control, cross sectional or cohort study design that controlled for smoking
3. Solid fuel used primarily for household cooking and/or heating in the study population
4. Provided adjusted odds ratios or relative risks to measure the association between lung cancer and exposure to solid fuels with corresponding 95% confidence intervals or p-values
5. Specify the technique by which exposure and lung cancer were assessed and ascertained (although we specified no definitive criteria)

Statistical analysis

Initially all studies were pooled and a sensitivity analysis was carried out to assess the impact of methodological concern by grouping them into different sub-groups, which include fuel types (biomass/mixed fuel/coal), sex (female only/male only/male and female), cancer histological sub-type (unspecified/adenocarcinoma/squamous carcinoma), adjustment for smoking (yes/non-smokers), adjustment for ETS exposure (yes/no), study design (population/hospital based), sample size (median >368/$\leqslant 368$), study location (China/Taiwan/India/other), year when study was conducted (2000 onwards/prior to 2000), year of publication (2000 onwards/prior to 2000), language of publication (Chinese/English), Newcastle-Ottawa score (median >6/$\leqslant 6$), and the quality of exposure assessment based on the Newcastle-Ottawa criteria (1/2/3 stars). The natural logarithm of odds ratio and the associated standard error were used to estimate the effect size of all studies and the sub-groups. Within-group heterogeneity was evaluated using Q tests and/or I^2 statistics. Heterogeneity between different studies was visually explored using Galbraith plots, and sources of heterogeneity were systematically examined by meta-regression. We used random effects models as there was significant heterogeneity on Q tests ($p<0.05$) and/or I^2 statistic value $>50\%$. Begg's funnel plot and Egger's test were used to assess publication bias [11]. All analyses were performed in STATA (version 11; STATA, College Station, TX, USA).

RESULTS

The initial search revealed 11,398 articles of which 2,012 duplicates and 7,908 irrelevant papers were removed by screening the titles. The abstracts of the remaining 1,478 papers were reviewed and 203 were selected for full paper review, of which 51 papers were related to lung cancer and solid fuel use (fig. 1). 28 studies (table 2) were included in the meta-analysis, the other 23 papers were excluded either because of failure to meet the inclusion criteria or because data were unusable, or both (table S1). The results presented are from 12,419 cases and 34,609 controls.

Effect estimates

The pooled effect estimate size was obtained using the random effect model because of heterogeneity across studies (Q=statistic 107.30, degrees of freedom=40, $p<0.001$; $I^2=62.7\%$; $\tau^2=0.081$, $Z=7.99$, $p<0.001$). The pooled OR was 1.70 (95% CI 1.50–1.94) for all studies.

Sub-group analyses were performed using random effect models. The values related to biomass, mixed fuel and coal were OR 1.50 (95% CI 1.17–1.94), OR 1.13 (0.52–2.46) and OR 1.82 (1.60–2.06), respectively (fig. 2). Forest plots are presented in figures S1–S8. Coal contributed 68.8% to the pooled effect sizes of lung cancer followed by biomass (19.8%) and mixed fuel (11.5%). The associated risk for females was greater compared to that for males ($p=0.034$) (table 3). The greater risk observed in the Chinese publications compared to those in English ($p=0.006$) remained after adjusting for potential confounders including types of fuel used, sex, smoking and quality of the study assessed by the Newcastle-Ottawa score. The same trend was found in both smoking and nonsmoking participants.

Studies were then stratified according to the type of fuel used and then by various sub-groups (table 4). No significant heterogeneity was observed in the different strata for studies related to the exposure to biomass smoke but heterogeneity

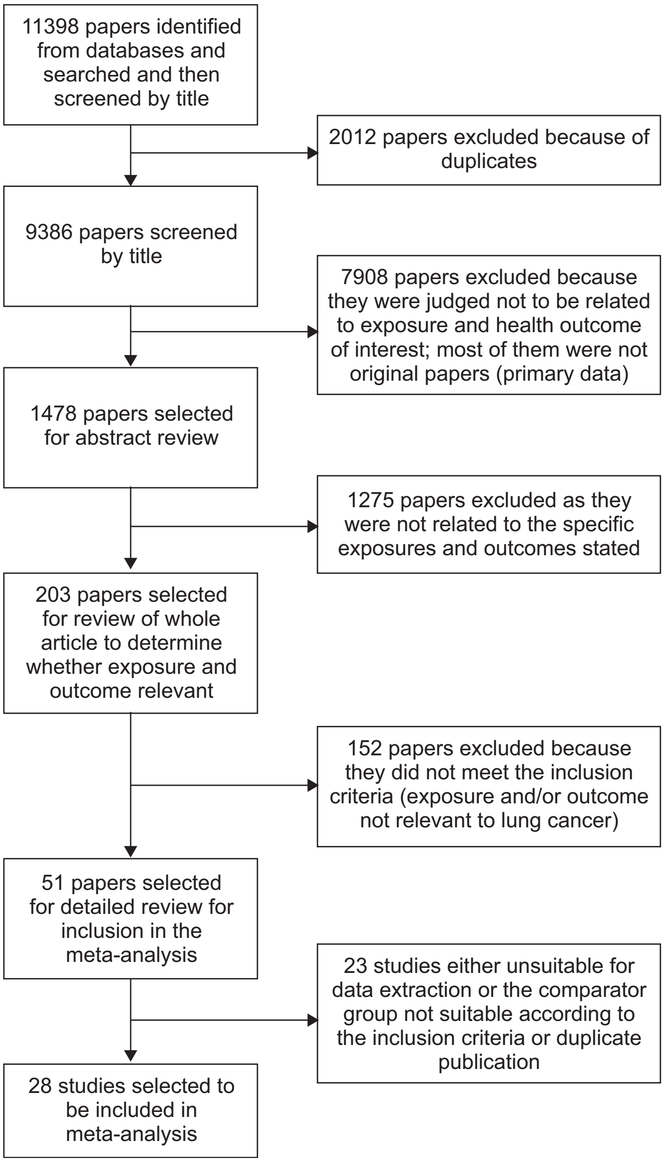


FIGURE 1. Flow chart showing studies related to lung cancer and exposure to solid fuel.

among hospital-based studies approached significance (I^2=54.3%, p=0.053). However, there was significant heterogeneity among studies with coal smoke exposure in relation to squamous cell carcinoma (I^2=61.2%, p=0.035), unspecified types of lung cancer (I^2=38.1%, p=0.047), females only (I^2=45.5%, p=0.043), population-based (I^2=60.4%, p=0.001) and hospital-based studies (I^2=43.4%, p=0.008), and those with sample size $\leqslant$368 (I^2=49.3%, p=0.019).

Of the 28 studies included in the meta-analysis, 14 collected data on ETS exposure and only seven made adjustments for ETS. Even more surprising was the fact that only three out of seven of the female only studies that measured ETS actually adjusted for ETS. Pooled effect estimates from studies that adjusted for ETS (OR 1.28, 95% CI 0.91–1.80) were significantly lower (p=0.034) compared to those that did not (OR 1.91, 95% CI 1.65–2.22).

The studies with poor quality, particularly in the exposure assessment, as measured by the Newcastle-Ottawa score, tend to report greater effect size (tables 3, 4 and S7).

Publication bias

Funnel plots suggested potential publication bias for the biomass (fig. S7) and coal smoke (fig. S8) studies. However, Egger's test showed substantial publication bias only in coal smoke studies (bias=1.04, p=0.016) (fig. S10), which disappeared when two outlying studies were removed (bias=0.76, p=0.093) [26, 29]. The pooled effect estimate (OR 1.64, 95% CI 1.45–1.86) was slightly attenuated after excluding the two outliers.

Heterogeneity by meta-regression

Heterogeneity was initially explored by graphical display (Galbraith plot) (fig. S11 for biomass and fig. S12 for coal), then by meta-regression to assess contributions by sex, histological sub-type, smoking, adjustment for ETS exposure, sample size, study location, year in which the study was carried out, year of publication, and language of publication. In studies of biomass smoke exposure, significant but small heterogeneity was observed in sex (coefficient= -0.253, p=0.025), although there was a nonsignificant heterogeneity in lung cancer histology (coefficient=0.636, p=0.057). However, in studies of coal smoke exposure, language of publication (coefficient=0.308, p=0.032) and histology (coefficient=0.273, p=0.058) had similar magnitude of heterogeneity, although the latter was not statistically significant. We did not find evidence of heterogeneity (p=0.116) between the studies of better quality (Newcastle-Ottawa score $>$6) and poorer quality ($\leqslant$6).

DISCUSSION

This meta-analysis included studies conducted in China, Taiwan, Japan, India, Mexico, Morocco, USA and Canada, as well as a study carried out jointly in seven European countries (Czech Republic, Hungary, Poland, Romania, Russia, Slovakia and the UK). The pooled effect estimates that the risk of lung cancer among users of solid fuels is 70% (95% CI 50–94%) higher than non-users.

The magnitude of association between coal use and lung cancer (OR 1.82, 95% CI 1.60–2.06) was greatest followed by biomass (predominantly wood, OR 1.50, 95% CI 1.17–1.94) and mixed fuel (OR 1.13, 95% CI 0.52–2.46), although the differences were not statistically significant. The higher risk of lung cancer in coal users was not surprising as combustion products obtained from in-home coal burning contain a range of Group 1 carcinogenic PAHs [4]. While there is sufficient evidence to suggest exposure to biomass smoke is a risk factor for chronic obstructive pulmonary disease (COPD) in adults [40] and acute respiratory infection in children [41], the International Agency for Research on Cancer (IARC) has classified combustion products from biomass (primarily wood) as probable human lung carcinogens (Group 2A), citing there was ''limited evidence'' in humans and experimental animals [4]. The pooled effect size obtained from studies using population-based controls (carrying 56% weight; OR 1.83, 95% CI 1.51–2.21) was similar to that using hospital-based controls (39% weight; OR 1.63, 95% CI 1.34–1.97). Among the 28 studies included, two population-based studies [16, 38] and two hospital-based studies [33, 36] did not find an increased risk of lung cancer. Of these, three were related to biomass use [16, 33, 38] and the other to coal use [36] supporting the IARC

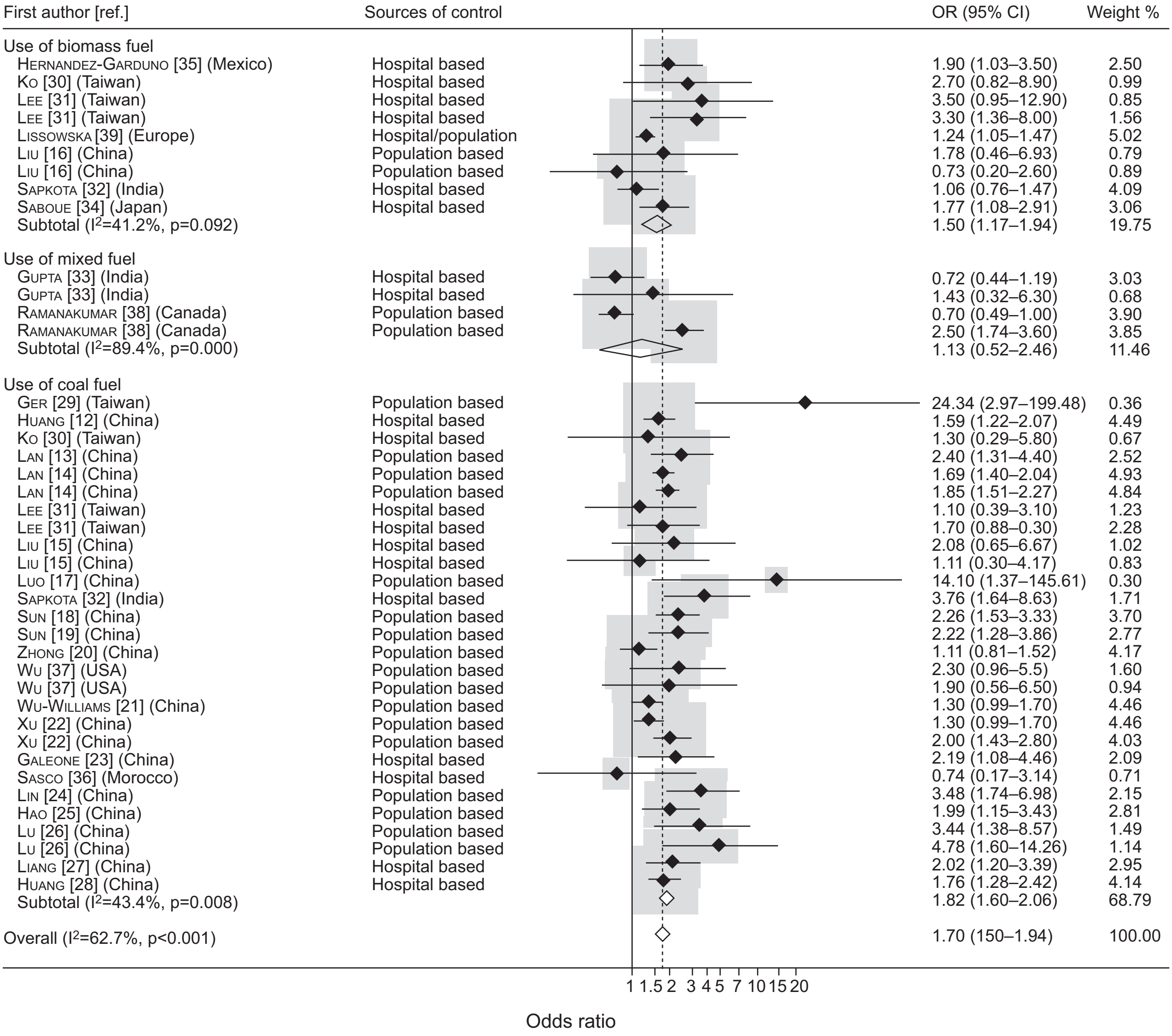
TABLE 2 Summary of studies included in the meta-analysis

First author [ref.]	Study location	Study period	Study design	Fuel type	Sex	Cancer type	Cases n	Controls n
Huang [12]	China	1990–1991	Hospital based, case–control	Coal	M and F	Unspecified	135	135
Lan [13]	China	1995–1996	Population based, case–control	Coal	M and F	Unspecified	122	122
Lan [14]	China	1976–1992	Population based, case–control	Coal	F	Unspecified	684	9380
				Coal	M	Unspecified	700	10648
Liu [15]	China	1983–1984	Hospital based, case–control	Coal	F	Unspecified	92	92
				Coal	M	Unspecified	224	224
Liu [16]	China	1985–1986	Population based, case–control	Biomass	F	Unspecified	54	202
				Biomass	M	Unspecified	56	224
Luo [17]	China	1990–1991	Population based, case–control	Coal	M and F	Squamous	39	306
Sun# [18]	China	1985–1987	Population based, case–control	Coal	F	Unspecified	418	398
Sun# [19]	China	1996–1999	Population based, case–control	Coal	M and F	Unspecified	206	618
Zhong¶ [20]	China	1992–1994	Population based, case–control	Coal	F	Unspecified	504	601
Wu-Williams [21]	China	1985–1987	Population based, case–control	Coal	F	Unspecified	956	953
Xu [22]	China	1985–1987	Population based, case–control	Coal	F	Unspecified	520	557
				Coal	M	Unspecified	729	788
Galeone [23]	China	1987–1990	Hospital based, case–control	Coal	M and F	Unspecified	216	435
Lin#,¶ [24]	China	1985–1990	Population based, case–control	Coal	F	Adenocarcinoma	122	122
Hao# [25]	China	1981–1986	Population based, case–control	Coal	M and F	Unspecified	220	440
Lu# [26]	China	1998–2001	Population based, case–control	Coal	M and F	Unspecified	445	445
				Coal	M and F	Squamous	185	185
Liang# [27]	China	2001–2002	Hospital based, case–control	Coal	M and F	Adenocarcinoma	89	89
Huang# [28]	China	1993–1996	Hospital based, case–control	Coal	M and F	Unspecified	122	244
Ger [29]	Taiwan	1990–1991	Population based, case–control	Coal	M and F	Squamous	59	118
Ko¶ [30]	Taiwan	1992–1993	Hospital based, case–control	Biomass	F	Unspecified	91	89
				Coal	F	Unspecified	52	66
Lee [31]	Taiwan	1993–1999	Hospital based, case–control	Biomass	F	Adenocarcinoma	162	273
				Coal	F	Adenocarcinoma	162	273
				Biomass	F	Squamous	84	134
				Coal	F	Squamous	84	134
Sapkota [32]	India	2001–2004	Hospital based, case–control	Biomass	M and F	Unspecified	381	237
				Coal	M and F	Unspecified	35	10
Gupta [33]	India	1995–1997	Hospital based, case–control	Mixed	F	Unspecified	30	90
				Mixed	M	Unspecified	232	431
Sobue¶ [34]	Japan	1985	Hospital based, case–control	Biomass	F	Unspecified	144	731
Hernandez-Garduno¶ [35]	Mexico	1986–1994	Hospital based, case–control	Biomass	F	Unspecified	113	273
Sasco [36]	Morocco	1996–1998	Hospital based, case–control	Coal	M and F	Unspecified	118	235
Wu [37]	USA	1981–1982	Population based, case–control	Coal	F	Adenocarcinoma	149	149
				Coal	F	Squamous	71	71
Ramanakumar [38]	Canada	1996–2001	Population based, case–control	Mixed	F	Unspecified	315	381
				Mixed	M	Unspecified	438	588
Lissowska [39]	Europe+	1998–2001	Hospital/population based, case–control	Biomass	M and F	Unspecified	2861	3118

M: male; F: female #: papers published in Chinese; ¶: studies with non-smoking participants only; +: Czech Republic, Hungary, Poland, Romania, Russia, Slovakia and the UK.

notion that the evidence of the carcinogenicity of biomass smoke is still not conclusive.

The association between lung cancer and solid fuel use persisted even after stratifying for sex, fuel types, smoking and study location. The duration of exposure in most of the studies was not clearly defined and there was marked variability in reported exposure intensity across studies but the number of studies were too small to determine any dose–response relationship. Of the 28 studies included in this meta-analysis, two studies scored the maximum of three stars on the Newcastle-Ottawa criteria for exposure whereas 18 studies scored two and eight studies scored only one star. The studies with the highest quality in exposure assessment have lower effect sizes suggesting that misclassification and residual confounding might be operating, thereby inflating the risk estimate. Users of biomass often switch from one type of biomass to another. A detailed history on the type, duration and intensity of fuel use (such as average number of hours exposed) must be gathered in future studies to better estimate the risks from particular biomass fuels as combustion products from different types of biomass burning have variable toxicity [42].



First author [ref.]	Sources of control	OR (95% CI)	Weight %
Use of biomass fuel			
Hernandez-Garduno [35] (Mexico)	Hospital based	1.90 (1.03–3.50)	2.50
Ko [30] (Taiwan)	Hospital based	2.70 (0.82–8.90)	0.99
Lee [31] (Taiwan)	Hospital based	3.50 (0.95–12.90)	0.85
Lee [31] (Taiwan)	Hospital based	3.30 (1.36–8.00)	1.56
Lissowska [39] (Europe)	Hospital/population	1.24 (1.05–1.47)	5.02
Liu [16] (China)	Population based	1.78 (0.46–6.93)	0.79
Liu [16] (China)	Population based	0.73 (0.20–2.60)	0.89
Sapkota [32] (India)	Hospital based	1.06 (0.76–1.47)	4.09
Saboue [34] (Japan)	Hospital based	1.77 (1.08–2.91)	3.06
Subtotal (I^2=41.2%, p=0.092)		1.50 (1.17–1.94)	19.75
Use of mixed fuel			
Gupta [33] (India)	Hospital based	0.72 (0.44–1.19)	3.03
Gupta [33] (India)	Hospital based	1.43 (0.32–6.30)	0.68
Ramanakumar [38] (Canada)	Population based	0.70 (0.49–1.00)	3.90
Ramanakumar [38] (Canada)	Population based	2.50 (1.74–3.60)	3.85
Subtotal (I^2=89.4%, p=0.000)		1.13 (0.52–2.46)	11.46
Use of coal fuel			
Ger [29] (Taiwan)	Population based	24.34 (2.97–199.48)	0.36
Huang [12] (China)	Hospital based	1.59 (1.22–2.07)	4.49
Ko [30] (Taiwan)	Hospital based	1.30 (0.29–5.80)	0.67
Lan [13] (China)	Population based	2.40 (1.31–4.40)	2.52
Lan [14] (China)	Population based	1.69 (1.40–2.04)	4.93
Lan [14] (China)	Population based	1.85 (1.51–2.27)	4.84
Lee [31] (Taiwan)	Hospital based	1.10 (0.39–3.10)	1.23
Lee [31] (Taiwan)	Hospital based	1.70 (0.88–0.30)	2.28
Liu [15] (China)	Hospital based	2.08 (0.65–6.67)	1.02
Liu [15] (China)	Hospital based	1.11 (0.30–4.17)	0.83
Luo [17] (China)	Population based	14.10 (1.37–145.61)	0.30
Sapkota [32] (India)	Hospital based	3.76 (1.64–8.63)	1.71
Sun [18] (China)	Population based	2.26 (1.53–3.33)	3.70
Sun [19] (China)	Population based	2.22 (1.28–3.86)	2.77
Zhong [20] (China)	Population based	1.11 (0.81–1.52)	4.17
Wu [37] (USA)	Population based	2.30 (0.96–5.5)	1.60
Wu [37] (USA)	Population based	1.90 (0.56–6.50)	0.94
Wu-Williams [21] (China)	Population based	1.30 (0.99–1.70)	4.46
Xu [22] (China)	Population based	1.30 (0.99–1.70)	4.46
Xu [22] (China)	Population based	2.00 (1.43–2.80)	4.03
Galeone [23] (China)	Hospital based	2.19 (1.08–4.46)	2.09
Sasco [36] (Morocco)	Hospital based	0.74 (0.17–3.14)	0.71
Lin [24] (China)	Population based	3.48 (1.74–6.98)	2.15
Hao [25] (China)	Population based	1.99 (1.15–3.43)	2.81
Lu [26] (China)	Population based	3.44 (1.38–8.57)	1.49
Lu [26] (China)	Population based	4.78 (1.60–14.26)	1.14
Liang [27] (China)	Hospital based	2.02 (1.20–3.39)	2.95
Huang [28] (China)	Hospital based	1.76 (1.28–2.42)	4.14
Subtotal (I^2=43.4%, p=0.008)		1.82 (1.60–2.06)	68.79
Overall (I^2=62.7%, p<0.001)		1.70 (150–1.94)	100.00

FIGURE 2. Forest plot of studies reporting lung cancer associated with exposure to solid fuels stratified by types of fuel used. Weights are from the random effects analysis.

Cigarette smoking has been widely accepted as the main contributory factor to lung cancer worldwide [43, 44]. We excluded two papers on the basis that smoking had not been allowed for in the risk estimates [45, 46], and all studies included in this review have either adjusted for smoking or studied a population of nonsmokers. A recent meta-analysis included effect estimates from Chinese studies that did not adjust for smoking [8]. The extent of confounding is, however, difficult to predict. While it is accepted that self-reported smoking history is the best that can be achieved when considering life-long smoking details, objective measurement of smoking, such as salivary cotinine, is becoming more easily usable in field studies and provides information on current smoking, which may, to a certain extent, help reduce exposure misclassification. This is particularly the case for females from countries who hesitate to admit to smoking for the fear of marginalisation.

Although half of the studies included in the meta-analysis measured ETS, only 25% of them presented data with adjusted ETS exposure. In studies that did, the pooled effect size (OR 1.47, 95% CI 1.13–1.91) was smaller than (but not statistically significant, p=0.230) those that did not (OR 1.74, 95% CI 1.60–1.89). In females the pooled effect estimate with adjusted ETS was significantly lower compared to non-adjusted ETS suggesting the overall pooled effect estimate, particularly in females, might be lower than presented here. Only one study out of eight related to biomass smoke exposure adjusted for ETS and had an effect size higher than those that were not adjusted for ETS. Thus, ambiguity regarding the combined effect of smoking, combustion products of solid fuels and ETS exposure still prevails and future studies need to address this issue, particularly in females from Asian sub-continent as they are highly likely to be exposed to ETS. There is evidence from occupational studies that smoking and some occupational exposures (*e.g.* asbestos and PAHs) have a multiplicative rather than an additive effect on lung cancer risk [47, 48] and it is, therefore, possible that such a potentiating effect may be seen with respect to smoke from solid fuel burning, especially that from coal.

TABLE 3 Sub-group analyses of lung cancer risk associated with the use of solid fuels

Sub-groups	Studies n[#]	Heterogeneity		OR (95% CI)	p-value
		I^2 %	p-value		
Types of solid fuel used					
Biomass fuel	7	41.2	0.092	1.50 (1.17–1.94)	0.180[##]
Mixed fuel	2	89.4	<0.001	1.13 (0.52–2.46)	0.235[¶¶]
Coal	22	43.4	0.008	1.82 (1.60–2.06)	
Sex					
Female	12	36.8	0.051	1.81 (1.54–2.12)	0.034[++]
Male	6	80.1	<0.001	1.16 (0.79–1.69)	
Male and female[¶]	13	66.0	<0.001	1.93 (1.53–2.44)	
Cancer histological sub-type					
Unspecified	22	64.1	<0.001	1.57 (1.38–1.80)	
Adenocarcinoma	4	0.0	0.553	2.33 (1.72–3.17)	0.335[§§]
Squamous carcinoma	5	51.8	0.065	3.58 (1.58–8.12)	
Adjustment for smoking					
Yes	24	64.6	<0.001	1.70 (1.47–1.96)	0.710
Non-smokers only	7	69.2	0.001	1.85 (1.21–2.81)	
Adjustment for ETS					
Yes	9	65.6	0.003	2.27 (1.31–3.96)	1.709
No	32	63.1	<0.001	1.67 (1.46–1.91)	
Study design					
Population based	15	71.3	0.106	1.83 (1.51–2.21)	0.402
Hospital based	12	37.8	0.055	1.63 (1.34–1.97)	
Sample size					
>368[+]	17	72.7	<0.001	1.60 (1.36–1.87)	0.110
⩽368	15	24.4	0.161	1.99 (1.60–2.46)	
Study location					
China	17	43.5	0.016	1.77 (1.56–2.00)	
Taiwan	3	34.8	0.163	2.34 (1.39–3.94)	
India	2	73.5	0.010	1.30 (0.70–2.42)	
Other countries	6	76.4	<0.001	1.49 (1.05–2.13)	
Year study conducted					
2000 onwards	2	80.3	0.006	1.85 (0.93–3.67)	0.813
Prior to 2000	26	61.7	<0.001	1.70 (1.49–1.95)	
Year study published					
2000 onwards	13	72.7	<0.001	1.70 (1.39–2.08)	1.000
Prior to 2000	15	43.7	0.020	1.70 (1.45–2.01)	
Language of publication					
Chinese	8	0.0	0.468	2.16 (1.81–2.59)	0.006
English	33	62.7	<0.001	1.56 (1.35–1.81)	
Newcastle-Ottawa score					
>6[§]	28	64.3	<0.001	1.58 (1.36–1.85)	0.116
⩽6	13	48.6	0.025	1.97 (1.57–2.47)	
Quality of exposure assessment[ƒ]					
1 star	10	55.5	0.017	1.91 (1.45–2.53)	
2 stars	27	68.0	<0.001	1.64 (1.41–1.91)	
3 stars	4	0.0	0.754	1.78 (0.94–3.37)	

ETS: environmental tobacco smoke. [#]: the total number of studies was 28 but as some studies reported more than one sub-group type the number of studies does not add up to 28 in all sub-groups; [¶]: studies reporting risk estimates from males and females combined; [+]: the median sample size of all 28 studies; [§]: the median Newcastle-Ottawa score; [ƒ]: the Newcastle-Ottawa score assigns a maximum of stars on the exposure assessment; [##]: biomass fuel *versus* coal; [¶¶]: mixed fuel *versus* coal; [++]: females *versus* males; [§§]: adenocarcinoma *versus* squamous carcinoma.

TABLE 4 Sub-group analyses of lung cancer risk according to fuel type

Sub-group types	Studies n	Heterogeneity		OR (95% CI)	p-value
		I^2 %	p-value		
Exposure to biomass smoke[#]					
Sex					
Female	5	0.0	0.434	1.98 (1.44–2.73)	0.881[¶]
Male	1	NA	NA	1.78 (0.46–6.93)	
Male and female	2	0.0	0.404	1.20 (1.03–1.39)	
Cancer histological sub-type					
Unspecified	6	15.8	0.309	1.31 (1.09–1.58)	
Adenocarcinoma	1	NA	NA	3.30 (1.36–8.00)	0.942[+]
Squamous carcinoma	1	NA	NA	3.50 (0.95–12.90)	
Adjustment for smoking					
Yes	3	44.1	0.111	1.36 (0.99–1.86)	0.183
Non-smokers only	4	0.0	0.814	1.89 (1.31–2.73)	
Study design					
Population based	1	NA	NA	1.11 (0.44–2.80)	0.327
Hospital based	5	54.3	0.053	1.84 (1.23–2.76)	
Sample size					
>368	5	55.6	0.061	1.45 (1.10–1.91)	0.485
⩽368	3	10.8	0.339	1.88 (0.96–3.70)	
Language of publication					
Chinese	0	NA	NA	NA	
English	9	41.2	0.092	1.50 (1.17–1.94)	
Newcastle-Ottawa score					
>6	7	43.0	0.104	1.42 (1.04–1.94)	0.326
⩽6	2	0.0	0.860	1.82 (1.24–2.68)	
Quality of exposure assessment					
1 star	1	NA	NA	1.90 (1.03–3.50)	
2 stars	7	43.9	0.098	1.42 (1.07–1.87)	
3 stars	1	NA	NA	2.70 (0.82–8.90)	
Exposure to coal smoke[#]					
Sex					
Female	10	45.5	0.043	1.70 (1.40–2.06)	0.490[¶]
Male	3	26.0	0.259	1.54 (1.25–1.88)	
Male and female	12	39.9	0.068	2.19 (1.74–2.76)	
Cancer histological sub-type					
Unspecified	16	38.1	0.047	1.70 (1.51–1.92)	
Adenocarcinoma	4	0.0	0.501	2.22 (1.60–3.08)	0.324[+]
Squamous carcinoma	5	61.2	0.035	3.81 (1.37–10.58)	
Adjustment for smoking					
Yes	19	33.4	0.054	1.82 (1.62–2.06)	0.909
Non-smokers only	3	76.7	0.014	1.73 (0.73–4.10)	
Study design					
Population based	13	60.4	0.001	1.89 (1.59–2.25)	0.730
Hospital based	9	43.4	0.008	1.82 (1.60–2.06)	
Sample size					
>368	13	36.0	0.087	2.04 (1.59–2.61)	0.246
⩽368	11	49.3	0.019	1.72 (1.49–2.00)	
Language of publication					
Chinese	8	0.0	0.468	2.16 (1.81–2.59)	0.022
English	20	42.3	0.024	1.65 (1.43–1.91)	
Newcastle-Ottawa score					
>6	20	42.3	0.024	1.65 (1.43–1.91)	0.022
⩽6	8	0.0	0.468	2.16(1.81–2.59)	
Quality of exposure assessment					
1 star	7	0.0	0.584	2.11 (1.75–2.56)	
2 stars	18	53.8	0.004	1.72 (1.47–2.02)	
3 stars	3	0.0	0.765	1.50 (0.71–3.20)	

NA: not available. [#]: the total number of biomass studies is seven but as some studies reported more than one sub-group the number of studies do not add up to seven in all sub-group types; similarly, the total number of coal studies is 22; [¶]: females *versus* males; [+]: adenocarcinoma *versus* squamous carcinoma.

Females in developing countries do most of the cooking and, thus, are more likely to be exposed to indoor air pollution than males. The pooled effect size shows that the risk of lung cancer is greater in females (OR 1.81, 95% CI 1.54–2.12) compared to males (OR 1.16, 95% CI 0.79–1.69), similar to that reported in a limited earlier meta-analysis for females only (OR 1.83, 95% CI 0.62–5.41) [7]. Many published meta-analyses reported data for males and females combined. In this study, the pooled effect size for both sexes was 1.93 (95% CI 1.53–2.44), smaller than that reported by ZHAO *et al.* [7] (OR 2.66, 96% CI 1.39–5.07), probably because the latter was obtained from the coal using population in China. The pooled effect size in our study would have been reduced to 1.80 (95% CI 1.46–2.22) if the two studies with effect sizes of 24.34 (95% CI 2.97–199.48) [29] and 14.10 (95% CI 1.37–145.61) [17] were excluded.

The pooled effect estimate in studies published in the Chinese language (OR 2.16, 95% CI 1.81–2.59) was significantly greater ($p=0.006$) than studies published in English. When scrutinising the Chinese papers, we found a consistently large effect size. While the effect could be real, as Chinese papers focused on the coal using Chinese population and that coal has been recognised by the IARC as a carcinogen, this raises a concern on the overall quality of the research published in Chinese journals.

Table 5 presents the main findings from previously published meta-analyses (including our study). Over 60% of these (five out of eight) included studies either from China or the Chinese population only and examined only the effects of coal use. In contrast, the current meta-analysis presents the pooled results from various geographical regions, and has investigated the effects of biomass and coal exposure separately. In addition, we have specified in our inclusion criteria that only those studies that have adjusted for smoking or used a nonsmoking sample would be included, therefore, minimising potential confounding from smoking.

To our knowledge, this is the first assessment of whether solid fuel smoke is associated with specific histological sub-types. Cell type was reported in eight papers but the criteria for histological classification were not provided. The pooled effect size for squamous cell carcinoma (OR 3.58, 95% CI 1.58–8.12) was greatest followed by adenocarcinoma (OR 2.33, 95% CI 1.72–3.17) and unspecified type of lung cancer (OR 1.57, 95% CI 1.38–1.80). Squamous cell lung cancer is more commonly associated with cigarette smoking [52] although reported series of lung cancers have recently shown an increase in the proportion of adenocarcinoma which cannot simply be attributed to changes in classification/grading [53]. If cell type reflects different carcinogenic properties of different exposures then future studies studying the risk of lung cancer from solid fuel would benefit by classifying the types of lung cancer by fuel type.

Most of the studies included in this meta-analysis are from China where coal is the main fuel. The pooled effect size in Taiwan (three studies: OR 2.34, 95% CI 1.39–3.94) is greater than that in China (17 studies: OR 1.77, 95% CI 1.57–2.00). None of the studies included from China and Taiwan have looked at the association between coal type and lung cancer risk. Nevertheless, evidence from a community with high lung cancer mortality in China suggested that bituminous or "smoky" coal, with a high volatile content (23.1%), was more carcinogenic compared to smokeless

TABLE 5 Pooled effect estimates from previous meta-analyses on solid fuel use and lung cancer

First author [ref.]	Year	Papers n	Fuel type	Study location	Sex	Pooled effect estimate (95% CI)	Remarks
Current study		28	Biomass and coal	No limitation	F	1.81 (1.54–2.12)	All studies included were adjusted for smoking or were from non-smokers
					M	1.16 (0.79–1.69)	
					M and F	1.93 (1.53–2.44)	
HOSGOOD [8]	2011	25	Coal	No limitation	F	2.50 (1.56–4.00)	Covers all geographic areas; risk estimates of some studies were not adjusted for smoking
					M	2.76 (1.44–5.27)	
					Non-smoking F	2.93 (1.40–6.12)	
					M and F	2.15 (1.61–2.89)	
HOSGOOD [9]	2010	7	Wood and coal	Asia, Europe and North America	F	1.60 (1.41–1.82)	Large sample size; not systematic review
					M	1.42 (1.27–1.59)	
					M and F	1.56 (1.44–1.69)	
HOSGOOD [49]	2007						Results not reported here as the meta-analysis focused on genotypes
ZHAO [7]	2006	27	Coal	China	F	1.83 (0.62–5.41)	Studies based in China only
					M and F	2.66 (1.39–5.07)	
SMITH [50]	2004	12	Coal	China	F	1.94 (1.09–3.47)	Not systematic review
					M	1.51 (0.97–2.46)	
					M and F	2.55 (1.58–4.10)	
YAO [5]	2003	5	Coal	China	M and F	3.20 (1.79–5.71)	Chinese population only
YAO [51]	2002	NS	Coal	China	F	1.84 (0.94–3.59)	Chinese population only
ZHANG [6]	2001	4	Coal	China	Non-smoking F	1.42 (1.30–1.55)	Studies based in China only

M: male; F: female; NS: not specified.

coal which contains relatively high sulfur (1.9%) but low volatiles (13.8%) [54]. Further investigation [54, 55] concluded that compared to wood and smokeless coal, smoky coal contains more methylated PAH compounds, nitrogen heterocyclic compounds and dibenzo[a,l]pyrene, a potent carcinogen with the highest mutagenic activity in mice.

Most studies did not measure exposure quantitatively. Understanding the shape of the dose–response curve has been a challenge for a range of outcomes arising from biomass smoke exposure (*e.g.* COPD [40] and acute respiratory infections in children [41]), but is crucial in determining to what extent exposures would need to be reduced in order to confer a significant health benefit. However, measuring current exposures may only partially reflect historical exposures, even though in many areas where solid fuel is burnt, practice and, therefore, exposures have probably remained similar for decades. Nevertheless, if formal quantification of exposures can be undertaken in future studies this will provide relevant information to address this issue.

Our results suggested an element of publication bias which could be due to fewer positive studies being rejected and more positive studies, some with flawed methodology, being accepted. The meta-regression showed that there was significant heterogeneity among studies reporting different types of lung cancer.

Conclusion

Our meta-analysis suggested that coal is highly associated with lung cancer compared to other types of biomass. The risk was greater in females and in China which could be because Chinese females used coal. Future studies need to look at objective measurements of smoking and also the carcinogenic potential of different coal subtypes to explain some of the variability seen in the risk estimates.

STATEMENT OF INTEREST

None declared.

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