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Wood dust exposure and lung cancer risk: a meta-analysis

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ABSTRACT

Occupational lung cancers represent a major health burden due to their increasing prevalence and poor long-term outcomes. While wood dust is a confirmed human carcinogen, its association with lung cancer remains unclear due to inconsistent findings in the literature. We aimed to clarify this association using meta-analysis. We performed a search of 10 databases to identify studies published until June 2014. We assessed the lung cancer risk associated with wood dust exposure as the primary outcome and with wood dustrelated occupations as a secondary outcome. Randomeffects models were used to pool summary risk estimates. 85 publications were included in the metaanalysis. A significantly increased risk for developing lung cancer was observed among studies that directly assessed wood dust exposure (RR 1.21, 95% CI 1.05 to 1.39, n=33) and that assessed wood dust-related occupations (RR 1.15, 95% CI 1.07 to 1.23, n=59). In contrast, a reduced risk for lung cancer was observed among wood dust (RR 0.63, 95% CI 0.39 to 0.99, n=5) and occupation (RR 0.96, 95% CI 0.95 to 0.98, n=1) studies originating in Nordic countries, where softwood dust is the primary exposure. These results were independent of the presence of adjustment for smoking and exposure classification methods. Only minor differences in risk between the histological subtypes were identified. This meta-analysis provides strong evidence for an association between wood dust and lung cancer, which is critically influenced by the geographic region of the study. The reasons for this region-specific effect estimates remain to be clarified, but may suggest a differential effect for hardwood and softwood dusts.

INTRODUCTION

Occupational lung cancers represent approximately 75% of all occupational cancers^{1–4} and are a major health burden with relatively poor 5-year survival rates compared with the majority of other cancers.⁵ ⁶ Up to 10–20% of lung cancers have been attributed to occupational exposures^{1–4} and a synergistic effect has been observed between smoking and many of the occupational exposures.^{1–4}

Occupational exposure to wood dust remains extremely common in a wide range of jobs, despite advances in occupational health and safety policies.^{7–10} Wood dust was confirmed as a group 1 human carcinogen in 1995 by the International Agency for Research on Cancer (IARC).⁷ However, wood dust has only been conclusively linked to sinonasal cancers, despite individual studies suggesting an association with a range of respiratory

and digestive tract cancers.^{7 8 11} Although the nasal cavity/sinuses appear to be the predominate locations for wood dust deposition, wood processing generally produces a wide variety of particle sizes, at least some of which have been shown to be able to deposit in the lungs.¹²⁻¹⁶ Wood dust has also been confirmed as a respiratory irritant and has been shown to be directly carcinogenic in lung cancer cell lines and to induce lung inflammation in animal models following nasal instillation.¹⁷⁻²⁰ While the evidence for lung deposition and direct cellular toxicity provide a plausible biological mechanism for wood dust-induced lung cancer, the relative frequency of deposition in each location may explain the stronger evidence for sinonasal versus lung cancer.^{7 8 14 16}

While wood dust exposure has been frequently associated with lung cancer, a confirmed association has not been established by the IARC due to heterogeneous results in the literature.^{7 8} A number of factors have been suggested to contribute to this heterogeneity, including the type of wood dust assessed (hardwood vs softwood),^{7 8} confounding by smoking¹⁻⁴ and misclassification bias related to the method used for determining dust exposure.²¹⁻²³ While, hardwood dust has been conclusively defined as a human carcinogen, limited evidence exists for softwood dust.^{7 8} However, very few occupational cancer studies have clarified the type of wood dust to which their cohort is exposed making assessment of this variable difficult. Interestingly, the primary wood type varies between countries, and so geographic region may serve as a proxy variable for the type of wood dust assessed in each study.⁷ ²⁴ In particular, wood exposure in Nordic countries is primarily to softwood dust, while hardwood dust exposure is relatively more prevalent in many other countries.^{7 24}

We performed a systematic review and meta-analysis of the available literature in order to clarify the association between wood dust and lung cancer. We also aimed to assess the influences of geographic region (as a measure of softwood dust exposure), adjustment for smoking and exposure classification methods using subgroup analyses.

METHODS

Search strategy

We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to conduct our review and analysis. A systematic search of the databases CINAHL (from 1982), EMBASE (from 1974), Google Scholar (from ~1980), JSTOR (from ~1909), MEDLINE (from 1946), PubMed (from 1946), ScienceDirect (from ~1856), Web of Science (from 1990) and Wiley Online Library (from ~1989) through to June 2014 was completed. The search terms used to search all databases were combinations of Wood Dust ('wood dust', 'sawdust', 'saw dust', 'hardwood dust', 'softwood dust') AND Lung Cancer ('lung cancer', 'lung adenocarcinoma', 'lung carcinoma', 'lung malignancy'). No additional restrictions were used in the search. A systematic search of the Chinese literature in the database CNKI (from 1915) through to June 2014 was also completed. The English search terms were translated into Chinese as: Wood Dust ('木屑', '鋸木 屑','軟木屑','硬木屑','木塵','木粉','木粉塵','軟木粉塵','硬 木粉塵', '木材性粉塵') and Lung Cancer ('肺癌', '肺腺癌', '肺'). The Google Scholar, JSTOR, ScienceDirect and CNKI databases perform full-text searches, and thus allow for the identification of studies without 'Lung Cancer' and/or 'Wood Dust' in the abstract.

To identify additional articles that assessed wood dust-related occupations and lung cancer risk, we performed an additional PubMed (from 1946) database search using terms for Wood-Related Occupations (occupation, hardwood, softwood, wood, woodworker, carpenter, furniture, cabinet, joiner, mill, sawmill) AND Cancer (cancer, carcinoma, adenocarcinoma). Cancer was used in the search string in order to identify articles where 'Lung Cancer' was not specifically listed in the abstract.

References in all identified publications, and in the IARC monographs on wood dust,^{7 8} were also reviewed for additional studies.

Eligibility criteria

This review included cohort and case–control studies looking at the relationship between wood dust and lung cancer. Papers assessing wood dust directly were chosen as the primary outcome, while studies that assessed wood dust-related occupations were included as a secondary outcome. We included all studies into the meta-analysis that met the following criteria:

- 1. Contained an estimate of relative risk for lung cancer or data allowing such estimates to be calculated.
- 2. Contained a risk estimate related to a dichotomous index of exposure (ever vs never) or data allowing such estimates to be calculated.
- Contained an explicit analysis of wood dust as an exposure category at an individual not occupational level OR
- 3b. Contained an analysis of a wood dust-related occupation (ie, woodworkers, carpenters and furniture/cabinet makers).
- 4. Were published in English or Chinese.

Study selection

All articles identified in the database searches were initially screened for eligibility based on their titles and abstracts, followed by a full-text review of eligible articles. All English language articles were independently screened by two authors (DGH and MEL). Chinese language articles were initially screened for eligibility based on their titles and abstracts by a single author (KLC), while all full-text reviews were discussed by two authors (DGH and KLC). Disagreements between reviewers were resolved by consensus among all authors (DGH, MEL and KLC).

Data extraction

Data was extracted manually by one author for both the English (DGH) and Chinese (KLC) literature, and was subsequently reviewed by another author (MEL/DGH). Risk estimates for

total lung cancer were extracted for the primary analysis, but risk estimates for histological subtypes were also extracted for subanalysis. When multiple methods for defining wood dust exposure were used in a single paper (ie, job-exposure matrix and self-reported), the risk estimate using the exposure classification method presented as the 'gold standard' by the authors of the paper was used. When males and females were analysed separately, the risk estimates for males were included as males represent the majority of those exposed to wood dust.

Publications presenting data on the same cohort of patients were identified by comparing the author lists and study locations. The most recent paper from each cohort was chosen unless a previous paper had a larger cohort size or presented a risk estimate adjusted for more confounding variables. In addition, when a study analysed a subset of the larger population in a cohort, we included the study that used the entire population, even if this was not the most recent study (eg, the full cohort vs the non-smoking subset of the full cohort). The choice of study publication was confirmed by consensus.

Information from each paper was extracted on (1) study design, (2) country of study, (3) sample size, (4) wood dust exposure measure/occupation (5) and measures of effect including 95% CIs and adjusting/matching variables. Byar's approximation was used to recalculate missing 95% CIs for cohort studies, while crude ORs were computed for case–control studies without summary effect measures. For data sets in which no events were observed in one of the groups, 0.5 was added to all observations.²⁵

Risk of bias in individual studies

The risk of bias in each study was determined using the Newcastle-Ottawa Scale, which assesses participant selection, comparability and outcome/exposure assessment to a maximum of nine stars.²⁶ We rated studies as having low bias (7–9 stars), medium bias (5–6 stars) and high bias (0–4 stars). The risk of bias was determined by two independent authors for English (MEL/DGH) and Chinese (KLC/DGH) publications. Discrepancies in score (generally no more than 1 point) were resolved via consensus.

Statistical analysis

All statistical analyses were performed using the Metafor package in R.²⁷ For each meta-analysis, a random-effects model was specified using the restricted maximum-likelihood estimator method.²⁷ Random-effects models were chosen due to the significant heterogeneity in most analyses. For the purposes of pooling risk estimates, ORs were assumed to approximate the true risk ratio, since the baseline risks for lung cancer are generally low.²⁸ The primary meta-analysis was performed on all case-control and cohort studies assessing wood dust exposure and lung cancer (not separated into histological subtypes). A priori subgroup analyses were performed based on the geographic region of the study (studies originating outside and inside the Nordic countries (Denmark, Finland, Iceland, Norway, Sweden) as a measure of softwood dust exposure, the method for determining wood dust exposure (job-exposure matrix, self-reported or combination methods) and the use of adjustment for smoking. The Nordic countries were specifically chosen as a proxy variable of softwood dust exposure due to the predominant softwood dust exposure in these countries.⁷ ²⁴ ²⁹⁻³¹ Subanalyses were also performed on all studies that assessed histological subtypes of lung cancer (adenocarcinoma, squamous cell carcinoma, small-cell lung carcinoma or other) and on studies that assessed lung cancer risk among

wood dust-related occupations (ie, woodworkers, furniture makers, carpenters). Studies directly assessing wood dust exposure and those assessing wood dust-related occupations were analysed separately due to the inherent differences/limitations unique to each study design (ie, different misclassification errors, heterogeneity between occupation definitions and occupation-specific confounders).

The potential for publication bias was determined by assessing funnel plot asymmetry using the Egger regression test.²⁷ Asymmetry in a funnel plot (the effect estimates vs their SEs) tests for small study effects (with large SEs), which may suggest publication bias. However, asymmetry can also be due to true biological heterogeneity.³² Heterogeneity between studies was assessed using the I² statistic. Following the Cochrane handbook (http://www.cochrane-handbook.org), I² values were interpreted as showing moderate (30–60%), substantial (50–90%) and considerable (75–100%) heterogeneity.²⁵

RESULTS

Study characteristics

Figure 1 details our study selection process. A total of 85 articles were included in the final meta-analysis.⁵ ³⁰ ^{33–115} The included studies are detailed in online supplementary table S1. An additional 56 articles that met the inclusion criteria were identified (see online supplementary table S2), but not used in the meta-analysis as they represented publications on an overlapping cohort of patients, duplicate publications or publications missing information necessary for the meta-analysis. Five additional studies were excluded for presenting data that could not be dichotomised into ever versus never exposure.^{116–120} Forty studies⁵ ³⁰ ^{34–36} ³⁸ ⁴⁰ ^{42–44} ^{50–54} ⁶⁰ ⁶² ⁶⁴ ⁶⁵ ⁶⁷ ⁶⁹ ⁷⁰ ^{73–76} ⁸⁶ ⁶⁹ ⁹¹ ⁹³ ⁹⁶ ⁹⁷ ⁹⁹ 100 102 105 106 110 113 115</sup> were rated as having

a low risk of bias using the Newcastle-Ottawa Scale (see online supplementary table S1).

Primary meta-analysis on lung cancer and wood dust exposure

Twenty-four case-control, five nested case-control and nine cohort studies assessing the association between wood dust and lung cancer were included in the primary meta-analysis (figure 2). The studies originated from Belgium,⁵⁵ Canada,⁴² ⁶⁹ ⁹⁹ ¹⁰⁹ Chile,⁵⁹ China,⁴⁸ ⁶⁷ ⁷⁹ ¹⁰⁶ ¹¹¹ ¹¹³ ¹¹⁴ England,⁸⁴ Finland,³⁰ ⁷⁴ Holland,⁷⁶ India,⁶³ Iran,⁶⁸ Norway,⁷⁵ Pakistan,⁸¹ Poland,¹⁰⁵ Russia,³⁴ Sweden,⁷² ⁸⁶ Uruguay⁵² and the USA.³⁵ ³⁶ ^{38–40} ⁷³ ⁷⁸ ⁸⁸ ¹⁰² ¹¹⁰ Overall, a significantly increased risk for developing lung cancer following wood dust exposure was observed (RR 1.25, 95% CI 1.11 to 1.41, n=38), with 'considerable' heterogeneity between studies (I²=82.1%, p<0.01; figure 2).

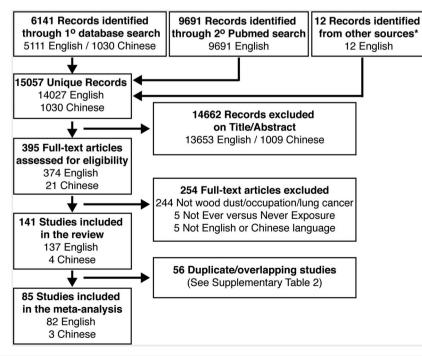
Subgroup analysis by geographic region of study

Owing to the well-described predominant softwood exposure in the Nordic countries,^{7 24} the geographic region of each study was used as a measure of the type of wood dust to which that cohort was exposed. In the subgroup analysis of studies originating outside of the Nordic countries (mixed hardwood and softwood dust), there was a significantly increased risk for developing lung cancer associated with wood dust exposure (RR 1.34, 95% CI 1.19 to 1.50, n=33), with 'moderate' heterogeneity (I^2 =39.4%, p=0.07; figure 3). In contrast, among studies originating in the Nordic countries (predominantly softwood dust exposure), there was a significantly reduced risk for developing lung cancer (RR 0.63, 95% CI 0.39 to 0.99, n=5), with 'moderate-substantial' heterogeneity (I^2 =55.6%, p=0.05; figure 3).

Subgroup analysis of smoking-adjusted studies

Twenty-three of the wood dust studies controlled for smoking (see online supplementary table S1). The overall association between wood dust and lung cancer incidence was maintained among all studies that controlled for smoking (RR 1.31, 95% CI 1.10 to 1.56, n=23). The significantly increased risk for lung cancer was also maintained among studies originating outside the Nordic countries (mixed hardwood and softwood dust) that controlled for smoking (RR 1.48, 95% CI 1.29 to 1.69, n=19, $I^2=0.0\%$). However, the reduced risk for lung cancer was no longer significant among studies originating within the Nordic countries (predominantly softwood dust exposure) that controlled for smoking (RR 0.64, 95% CI 0.40 to 1.01, n=4, $I^2=62.2\%$).

Figure 1 Flow chart of study selection strategy. *Other sources include the International Agency for Research on Cancer (IARC) monographs and the reference lists of relevant publications. Potentially relevant studies were not counted if they were identified using the database search.



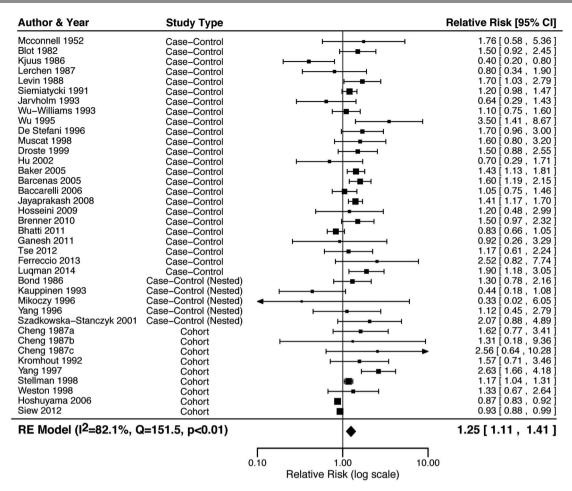


Figure 2 Forest plot of all studies assessing wood dust and lung cancer incidence.

Subgroup analysis on method for classifying wood dust exposure

Nineteen of the studies used self-reported exposure, 15 studies used a job-exposure matrix, and four studies used a combination of methods to determine wood dust exposure (see online supplementary table S1). Across all studies, a significantly increased risk for lung cancer incidence following wood dust exposure was identified in studies using self-reported exposure (RR 1.29, 95% CI 1.15 to 1.45, n=19, $I^2=23.5\%$) or combination methods (RR 1.47, 95% CI 1.11 to 1.96, n=4, $I^2=50.5$), but this association failed to reach significance among those studies using a job-exposure matrix (RR 1.18, 95% CI 0.93 to 1.48, n=15, $I^2=92.1\%$). However, a greater proportion of the studies that used a job-exposure matrix did not control for smoking and/or originated in the Nordic countries (where softwood dust is the predominate exposure). When this subgroup analysis was repeated in a post hoc analysis restricted to studies originating outside of the Nordic countries (mixed hardwood and softwood dust exposure) that also controlled for smoking, a significantly increased risk was observed among studies using the selfreported (RR 1.33, 95% CI 1.16 to 1.51, n=12, $I^2=20.0\%$), job-exposure matrix (RR 1.76, 95% CI 1.29 to 2.42, n=5, I^2 =28.9%) and/or combination (RR 2.09, 95% CI 1.01 to 4.34, $n=2, I^2=61.3\%$) methods.

Subanalysis of lung cancer histological subtypes

Ten studies assessed the effect of wood dust exposure on various histological subtypes of lung cancer (see online supplementary table S1). A significantly elevated risk for developing all of the histological subtypes of lung cancer was observed following wood dust exposure (figure 4). The elevated risk ratios were highest for squamous cell carcinomas (RR 1.54, 95% CI 1.24 to 1.92, n=4), followed by those for adenocarcinomas (RR 1.32, 95% CI 1.08 to 1.60, n=7) and small-cell lung carcinomas (RR 1.32, 95% CI 1.05 to 1.66, n=7). Similar trends were observed when the analysis was restricted to studies that controlled for smoking.

Subanalysis on lung cancer and wood dust-related occupations

Fifty-nine studies assessed the association between wood dust-related occupations and lung cancer risk (see online supplementary table S1). Consistent with the wood dust meta-analysis, a significantly increased risk for lung cancer was observed across all studies (RR 1.15, 95% CI 1.07 to 1.23, n=59), with 'considerable' heterogeneity between studies (I²=88.8%, p<0.01; figure 5). This association remained significant when the multiple subcohorts from a single paper were removed (RR=1.15).^{33 58 115} This association was also not dependent on a single occupational group and remained significant when studies assessing 'furniture makers' (RR=1.16, n=55) or 'carpenters' (RR=1.09, n=40) were removed in a post hoc analysis. Finally, this association was also not dependent on the study type, as the association remained significant when case-control (RR 1.17, n=34) and cohort (RR 1.12, n=26) studies were analysed separately.

A significantly increased risk for lung cancer (RR 1.15, 95% CI 1.07 to 1.24, n=58) was observed among the studies

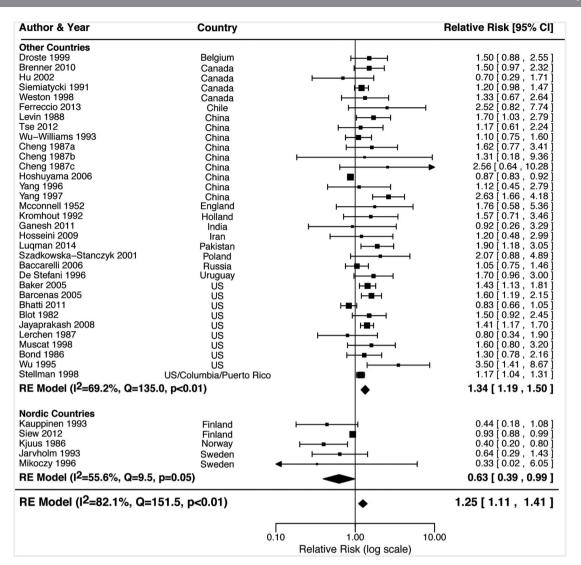


Figure 3 Forest plot all studies assessing wood dust and lung cancer incidence, subdivided based on the geographic region of study origin.

originating outside the Nordic countries, while a significantly reduced risk for lung cancer (RR 0.96, 95% CI 0.95 to 0.98) was observed in the one included study⁵ that originated in the Nordic countries (predominantly softwood dust exposure; figure 5).

Publication bias

No evidence for publication bias was observed on visual inspection of funnel plot asymmetry across all wood dust studies (see online supplementary figure S1A) and there was no evidence using Egger's test for small study bias (p=0.456). There was some suggestion of funnel plot asymmetry across the wood dust-related occupational studies (see online supplementary figure S1B), although this failed to reach significance using Egger's test for small study bias (p=0.080).

DISCUSSION

Occupational exposure to wood dust was confirmed to be carcinogenic to humans (group 1) by the IARC in 1994, but the evidence as a risk factor for lung cancer has been inconsistent.⁷ The recent IARC monograph Volume 100C also failed to confirm an association between lung cancer and wood dust due to the heterogeneous findings in the literature.⁸ ¹¹ Our robust literature search and meta-analysis showed a significantly elevated risk for developing lung cancer following wood dust exposure when pooling all studies (figure 2). We also observed this significantly elevated risk in studies that assessed lung cancer risk among wood dust-related occupations, and not wood dust exposure per se (figure 5). Importantly, evidence for wood dust deposition in the lungs and its in vitro carcinogenicity provide a biological mechanism to support the observed elevated risk for lung cancer.^{7 8} ¹⁴ ¹⁶ The results of this meta-analysis were maintained when studies that had not controlled for smoking were excluded. Smoking is the strongest risk factor for lung cancer, and confounding due to cigarette smoking often limits the accurate assessment of the effects of other lung carcinogens.^{1 4}

We had initially hypothesised that studies originating from the Nordic countries would show a proportionally lower risk for lung cancer due to the predominant softwood dust exposure in these countries⁷ ²⁴ ^{29–31} and the limited evidence supporting the carcinogenicity of softwood dust.⁷ ⁸ In support of this hypothesis, we observed a significantly elevated risk for developing lung cancer among studies originating outside of the Nordic countries and a significantly decreased risk among studies originating from the Nordic countries (figures 3 and 5). Furthermore, the only two wood dust studies in this meta-analysis that specified the type of dust to which their

Author & Year	Subtype	Country	Relative Risk [95	% CI]
Adenocarcinoma Blot 1982 Schraub 1989 Barcenas 2005 De Stefani 2005 Jayaprakash 2008 Tse 2012 De Stefani 1996 RE Model for Subgroup	Adenocarcinoma Adenocarcinoma Adenocarcinoma Adenocarcinoma Adenocarcinoma Adenocarcinoma Adenocarcinoma (l ² =0.0%, Q=5.3, p=0.51)	US France US Uruguay US China Uruguay	1.00 [0.39 , 1.06 [0.44 , 1.47 [1.01 , 0.80 [0.41 , 1.38 [1.03 , 1.38 [1.03 , 1.30 [0.51 , 1.32 [1.08 ,	2.54] 2.13] 1.55] 1.85] 3.65] 3.29]
Small–Cell Lung Carcin Blot 1982 Osann 2000 Barcenas 2005 De Stefani 1996 Siemiatycki 1991 Jayaprakash 2008 Wu 1995 RE Model for Subgroup	oma SCLC SCLC SCLC SCLC SCLC SCLC SCLC SCL	US US US Uruguay Canada US US	→ → → → → → → → → → → → → → → → → → →	2.26] 2.32] 5.81] 1.84] 1.84] 4.87]
Squamous Cell Carcino Blot 1982 Jayaprakash 2008 Siemiatycki 1991 De Stefani 1996 RE Model for Subgroup	ma Squamous Squamous Squamous Squamous (I ² =7.0%, Q=2.7, p=0.44)	US US Canada Uruguay	Image: 1.20 [0.54 , 1.93 [1.18 , 1.93 [1.18 , 1.93 [1.18 , 1.40 [1.09 , 1.40 [1.09 , 1.40 [1.13 , 1.40 [1.13 , 1.40 [1.13 , 1.40 [1.24 , 1.40 [1.24 , 1.40 [1.24 , 1.40 [1.24 , 1.40 [1.24 , 1.40 [1.24 , 1.40 [1.24 , 1.40 [1.24 , 1.40 [1.24 , 1.40 [1.24 , 1.40 [1.24 , 1.40 [1.24 , 1.40 [1.24] 1.40	3.16] 1.79] 3.90]
Other Barcenas 2005 Jayaprakash 2008 Tse 2012 Wu 1995	Other non–SCLC LCLC Squamous/SCLC Non–SCLC	US US China US	Image: 1.88 1.88 1.32 Image: 1.40 0.90 , Image: 1.64 0.68 , Image: 1.29 2.39 1.29	2.18] 3.97]
RE Model (I ² =0.0%, Q	e=20.1, p=0.51)		♦ 1.46 [1.31 , 1	1.62]
			0.10 1.00 10.00 Relative Risk (log scale)	

Figure 4 Forest plot of all studies assessing wood dust and histological subtypes of lung cancer, subdivided based on histological subtype. SCLC, small-cell lung carcinoma; LCLC, large-cell lung carcinoma.

cohort was exposed independently concluded that their identification of a decreased risk was due to the predominant softwood dust exposure in their cohorts.^{30 38} However, one of these studies originated in the USA³⁸ indicating that wood dust type rather than region is the likely cause of the differential risk effects of hardwood and softwood dusts on lung cancer. Consistent with these findings, all studies assessing wood dust-related occupations that described predominant exposure to softwood dust also showed a decreased or non-significant risk for lung cancer, independent of their origin in the Nordic countries.^{5 38 96 101}

While we used the geographic region of the study population as a measure for the type of wood dust exposure, there are a number of other potential explanations that may contribute to the region-specific trends observed in this meta-analysis. This includes unidentified confounders,² ³ ³¹ genetics⁷ ⁸ ¹²¹ ¹²² and/ or differences in occupational health and safety standards between countries.^{2 5} ^{123–126} A potential confounder for the decreased risk for lung cancer with wood dust exposure is bacterial endotoxins, arising from bacterial colonisation of either stored wood or loose wood dust.^{31 38 127} Bacterial endotoxin is thought to protect against lung cancer,¹²⁷ and thus increased exposure to this bacterial contamination among wood workers compared with the general population may help explain the reduced risk estimates for lung cancer in the Nordic countries.^{31 38} The contrasting risk estimates may also be due to region-specific differences in genetics, environment or health

policies, which might reduce the size of any increased risk. Nordic countries are generally thought to be world leaders in occupational health and safety practice, especially at the time when majority of these studies were conducted.⁵ ¹²³ ¹²⁴ The lack of any increased risk among the Nordic countries may therefore be due to differences in the wood dust-exposed workers, such as exposure to relatively lower levels of wood dust or other harmful exposures as a result of better occupational health and safety practice.² ¹²⁵ ¹²⁶

One of the most commonly cited limitations of the observational studies on wood dust exposure is the potential for measurement bias in the exposure assessment.²² ⁷⁶ Self-reported exposure strategies are generally susceptible to recall bias, while job-exposure matrix strategies can be susceptible to variations in true exposure under a given job title.²² ⁷⁶ However, an increased risk for lung cancer was observed across all methods of determining wood dust exposure, especially after controlling for geographic region and smoking. This finding was supported by three studies that directly compared the exposure methods and showed no significant differences between methods.^{36 55 76}

We also assessed the association between wood dust exposure and the different histological subtypes of lung cancer (figure 4). We observed significantly increased risk estimates for all histological subtypes of lung cancer, with the highest risk for squamous cell carcinomas (although CIs largely overlapped). This appears to contradict data on sinonasal cancers, where adenocarcinomas have been most frequently observed among

Author & Year	Occupation	Country		Relative Risk [95% CI]
Other Countries				
Pezzotto 1999	Carpenter	Argentina		0.90 [0.30 , 2.70]
Matos 2000 Wunsch-Filho 1998	Woodworker	Argentina		0.70 0.31 , 1.57 1.41 0.71 , 2.81
Arias Bahia 2005a	Woodworker Woodworker	Brazil Brazil		101 0 74 1071
Arias Bahia 2005a	Woodworker	Brazil		1 70 1 1 00 0 01 1
Arias Bahia 2005b Arias Bahia 2005c	Woodworker	Brazil		0.69 0.42 , 1.13
Sallagher 1985 Finkelstein 1995 MacArthur 2009 Levin 1988 Wu–Williams 1993	Woodworker	Canada		1.06 0.94 1.20
Finkelstein 1995	Carpenter	Canada	⊢ ∎−1	1.68 [1.00 , 2.82]
MacArthur 2009	Woodworker	Canada	H=H	0.82 0.69 , 0.98
-evin 1988	Woodworker	China		1.20 0.68 2.13 0.90 0.49 1.66
Nana 1995	Woodworker Woodworker	China		1.24 [0.95 , 1.62]
Vang 1995 Pronk 2009	Carpenter	China China		1.24 0.95 , 1.62 H 2.30 [1.11 , 4.75]
nnos 2000 Guida 2011	Furniture	Estonia	H	1.07 [0.88 , 1.30]
Guida 2011	Furniture Carpenter	France	} −∎−1	1.45 1.01 2.08
Barthel 1989	Furniture	Germany		0.68 0.35 , 1.31
lahn 1999 Bruske-Hohlfeld 2000	Woodworker	Germany		1.60 0.66 , 3.90] 1.36 1.11 , 1.66]
Chatzis 1999	Woodworker Carpenter	Germany Greece	LH■H	- 5 30 0 76 37 02
Chatzis 1999 Notani 1993 Buiatti 1985	Woodworker	India	'H	
Buiatti 1985	Woodworker	Italy	⊢ • ∔I	0.60 0.31 , 1.15
KONCO 1988	Woodworker	Italy	. ⊢	2.79 0.93 8.39
Richiardi 2004 Smailyte 2012	Carpenter	Italy		0.90 0.57 , 1.42
Peters 2012	Woodworker Woodworker	Lithuania Multiple*		0.85 0.61 , 1.19 1.19 1.07 , 1.32
lersluvs 1949	Carpenter	Netherlands		0.94 [0.67 , 1.31
/ersluys 1949 Firth 1996	Woodworker	New Zealand	· 7 🛥	1.51 1.34 1.70
Corbin 2011	Woodworker	New Zealand New Zealand	⊢⊸	1 44 [0 84 2 46
accarelli 2005	Woodworker	Russia	F∔∎1	1.20 0.82 1.75
Bouchardy 2002	Woodworker	Switzerland		0.80 0.71 , 0.91
Elci 2003 Coggon 1986	Carpenter Woodworker	Turkey		0.80 0.40 1.60 1.70 0.98 2.94
Simpson 1999	Carpenter	UK UK		104 146 050
De Stefani 1996	Carpenter	Uruguay		1.10 0.47 , 2.56
Enterline 1963 Enterline 1963 Menck 1976	Carpenter	ŬŠ		1.12 1.00 , 1.25
Enterline 1963	Furniture	US	⊢∎∔4	0.79 0.52 . 1.19
Vienck 19/6	Woodworker Woodworker Woodworker Woodworker	US	<u>}</u>	1.14 0.83 , 1.56 1.15 0.83 , 1.59
Harrington 1978 Gottlieb 1979	Woodworker			1.00 0.87 1.14
Blot 1982	Woodworker	US		1.34 0.82 2.19
Swanson 1982	Woodworker	ŭš	<u>i i</u>	1.56 0.86 2.82
Ailne 1983	Woodworker	ŬŜ	F → = − 1	1.33 0.67 2.64
Dubrow 1984	Carpenter	US	₩	1.24 0.94 , 1.64
zehm 1989a	Woodworker Carpenter	US		1.13 0.96 , 1.34 1.30 1.00 , 1.69
ahm 1989b	Furniture	115		1:301051 3:34
Burns 1991	Woodworker	üs	·	1.30 0.51 , 3.34 1.12 0.70 , 1.80
Stellman 1984 Stellman 1984 Zahm 1989a Zahm 1989b Burns 1991 Vu 1995	Woodworker	ŬŠ	- <u></u>	2.50 0.39 15.86
Koninson 1995	Carpenter	US		1.16 [1.11 , 1.21 1.45 [1.22 , 1.72
Dement 1996 Leigh 1996	Carpenter Carpenter Woodworker	US		1.45 1.22, 1.72 0.88 0.55, 1.41
Robinson 1996	Carpenter			0.88 0.55 , 1.41 1.06 0.93 , 1.20
ipscomb 1998	Carpenter	115		1.30 0.77 2.19
Barcenas 2005	Woodworker	ŬŠ	` `⊢ ••	2 15 1 15 6 95
3hatti 2011	Carpenter	Uruguay US US US US US US US US US US US US US	⊢∎⊣	0.70 0.49, 0.99
Calvert 2012	Carpenter	US	=	1.58 1.50 1.67
Stellman 1998 Demers 1995	Woodworker	US/Columbia/Puerto Rico		1.14 0.94 , 1.38 0.80 0.71 , 0.91
RE Model (I ² =81.1%, G	Woodworker	US/UK		1.15 [1.07 , 1.24
Vordic Countries	x=014.1, p<0.01)		•	1.13[1.07,1.24]
Pukkala 2009	Mandus alian	Neudia Osuntuisa		0.96 [0.95 , 0.98]
	Woodworker	Nordic Countries		
RE Model (I ² =88.8%	, Q=548.3, p<0.0	1)	•	1.15 [1.07 ,1.23]
		0.10	1.00 Dick (log co	10.00
		Re	elative Risk (log sc	ale)

Figure 5 Forest plot all studies assessing wood dust-related occupations and lung cancer incidence, subdivided based on the geographic region of study origin.

woodworkers,^{7 8} although some studies have identified squamous cell carcinomas more commonly.^{30 128} Overall, these data suggest that wood dust increases the risk for all subtypes of lung cancer, and not only a specific subtype.

To the best of our knowledge, this is the first systematic review or meta-analysis assessing wood dust and lung cancer risk, outside of the IARC publications.^{7 8} We performed a robust search of the English and Chinese literature and identified a large number of studies not included in the IARC publications. Our analysis also included a large number of studies where wood dust and lung cancer was not the primary outcome of the paper, thereby reducing the likelihood of publication bias of positive results, which was supported by our assessment of funnel plot asymmetry. However, it is also possible that studies assessing a large number of exposures would provide a less accurate assessment of true wood dust exposure, although we found no evidence to support this hypothesis.

In the current meta-analysis, we chose to primarily focus on studies that specifically assessed wood dust exposure in order to provide the most direct assessment of the relationship between wood dust exposure and lung cancer risk. We also aimed to avoid some of the inherent challenges/limitations of assessing purely occupation-based studies, including the heterogeneity in occupational classifications and the greater risk for individual occupation-specific factors obscuring any wood dust-specific effects.²⁵ ¹⁰³ ¹²⁹ ¹³⁰ Consistent with this, some of the studies showed a large degree of variation in the individual risk estimates when multiple different wood dust-related occupations analysed within the same paper (not shown).45 103 However, the observation of a significantly elevated risk for lung cancer (of similar magnitude) among these occupation-based studies (figure 5) adds further weight to the association between wood dust and lung cancer, and also suggests that our focus on wood dust-specific studies did not bias the results of this meta-analysis.

There are a number of potential limitations to our meta-analysis. First, we were unable to perform any analyses to assess the dose-response relationship between wood dust and lung cancer or to determine any effects related to duration of exposure. These factors were generally not assessed or assessed using a variety of approaches making a quantitative synthesis unfeasible. Second, the included studies varied greatly in their study design/population characteristics and accounting for all these factors in our meta-analysis was not feasible. Finally, unknown confounding exposures might still explain our findings. Asbestos, silica, formaldehyde, solvents and exhausts are all associated with wood dust-related professions and have been independently linked with lung cancer.3 7 8 However, the studies included in this meta-analysis analysed wood dust exposure from a diverse range of occupational contexts, thereby limiting the possibility that a single confounding exposure accounted for the observed associations.

In conclusion, this meta-analysis has demonstrated significant associations between lung cancer and wood dust exposure or employment in wood dust-related occupations, with an increased risk among studies that originated outside of the Nordic countries (mixed hardwood and softwood dust exposure). The reduced risk for lung cancer observed following wood dust exposure in Nordic countries may be due to the predominant softwood dust exposure in these countries. Larger studies designed to explore the causes of these differing associations are needed.

Contributors DGH was involved in study design and supervision, analysis and interpretation of data, statistical analysis, and drafting of the manuscript. MEL and KLC were involved in analysis and interpretation of data, and critical revision of the manuscript. RJW was involved in statistical analysis and critical revision of the manuscript. EMS was involved in drafting of the manuscript and critical revision of the manuscript.

Competing interests None declared.

Provenance and peer review Not commissioned; externally peer reviewed.

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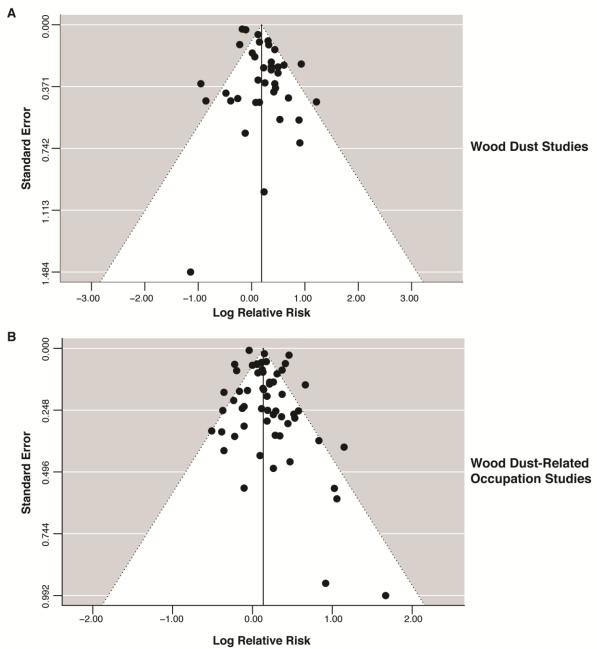
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Supplementary Figure 1. Funnel plot of all a) studies assessing wood dust and lung cancer risk and b) studies assessing wood dust-related occupations and lung cancer risk.

Author Date [Ref]	Туре	Outcome	Control	Measure	Smoking Control	Country	Years	Cancer	Point Estimate	Cases/Ctrls OR Obs/Total Cohort	NOS
Arias Bahia 2005a [1]	Cohort	Incidence	-	Occup (W)	N	Brazil	1988- 1991	Lung	SIR 1.2(0.7-1.9)	18/138	4
Arias Bahia 2005b [1]	Cohort	Incidence	-	Occup (W)	N	Brazil	1988- 1991	Lung	SIR 1.8(1.1-2.8)	18/138	4
Arias Bahia 2005c [1]	Cohort	Incidence	-	Occup (W)	N	Brazil	1988- 1991	Lung	SIR 0.7(0.4-1.1)	18/138	4
Baccarelli 2006 [2]	Case- Control	Mortality	Н	JEM	Y	Russia	1993- 1998	Lung	OR 1.1(0.8-1.5)	210/717	9
				Occup (W)				Lung	OR 1.2(0.8-1.7)	540/582	
Baker 2005 [3]	Case- Control	Incidence	Н	SR	Y	US	1982- 1998	Lung	OR 1.4(1.1-1.8)	993/986	7
Barcenas 2005 [4]	Case- Control	Incidence	Н	0	Y	US	1995- 2002	Lung	OR 1.6(1.2-2.1)	1368/1192	7
								Adenocarcinoma	OR 1.5(1-2.1)	573/1192	
								SCLC	OR 1.1(0.5-2.3)	96/1192	
								Squamous/LCLC	OR 1.9(1.3-2.7)	544/1192	
				Occup (W)				Lung	OR 3.2(1.5-6.9)	1368/1192	
Barthel 1989 [5]	Cohort	Incidence	-	Occup (F)	N	Germany	1973- 1984	Lung	SIR 0.7(0.3-1.2)	162/759	6
Bhatti 2011 [6]	Case- Control	Incidence	Р	JEM	N	US	1993- 1996	Lung	OR 0.8(0.7-1.0)	258/456	7
				Occup (C)				Lung	OR 0.7(0.5-1)	440/845	
Blot 1982 [7]	Case- Control	Incidence	Н	SR	N	US	1978- 1979	Lung	OR 1.5(0.9-2.4)	83/342	6
								Adenocarcinoma	OR 1.0(0.4-2.6)	53/254	
								SCLC	OR 3.2(1.4-7.6)	57/241	
								Squamous	OR 1.2(0.5-2.5)	57/267	
				Occup (W)				Lung	OR 1.3(0.8-2.2)	181/342	
Bond 1986 [8]	Nested Case-	Mortality	Р	JEM	N	US	1940- 1980	Lung	OR 1.3(0.8-2.2)	308/588	7

Supplementary Table 1. Summary of case-control and cohort studies included in the meta-analysis

	Control										
Bouchardy 2002 [9]	Cohort	Incidence	-	Occup (W)	N	Switzerland	1980- 1993	Lung	OR 0.8(0.7-0.9)	236/58134	6
Brenner 2010 [10]	Case- Control	Incidence	Р	SR	Y	Canada	1997- 2002	Lung	OR 1.5(1-2.4)	308/771	8
Bruske- Hohlfeld 2000 [11]	Case- Control	Incidence	Р	Occup (W)	Y	Germany	1988- 1996	Lung	OR 1.4(1.1-1.7)	3541/3498	7
Buiatti 1985 [12]	Case- Control	Incidence	Н	Occup (W)	Y	Italy	1981- 1983	Lung	OR 0.6(0.3-1.1)	376/892	7
Burns 1991 [13]	Case- Control	Incidence	Н	Occup (W)	Y	US	1980	Lung	OR 1.1(0.7-1.8)	5935/3956	6
Calvert 2012 [14]	Case- Control	Incidence	Н	Occup (C)	Ν	US	1988- 2007	Lung	OR 1.6(1.5-1.7)	13268/97669	5
Chatzis 1999 [15]	Case- Control	Incidence	Н	Occup (C)	Y	Greece	1987- 1988	Lung	OR 5.3(0.7- 32.2)	256/458	5
Cheng 1987a [16]	Cohort	Mortality	-	JEM	Ν	China	1964- 1983	Lung	SMR 1.6(0.7- 3.2)	7/649	6
Cheng 1987b [16]	Cohort	Mortality	-	JEM	Ν	China	1968- 1983	Lung	SMR 1.3(0.1- 6.1)	1/162	6
Cheng 1987c [16]	Cohort	Mortality	-	JEM	Ν	China	1964- 1983	Lung	SMR 2.6(0.5- 8.2)	2/105	6
Coggon 1986 [17]	Case- Control	Incidence	Н	Occup (W)	Ν	UK	1975- 1980	Lung	OR 1.7(1-3)	738/2214	6
Corbin 2011 [18]	Case- Control	Incidence	Р	Occup (W)	Y	New Zealand	2007- 2008	Lung	OR 1.4(0.8-2.5)	458/796	7
De Stefani 1996 [19]	Case- Control	Incidence	Н	SR	Y	Uruguay	1993- 1994	Lung	OR 1.7(0.9-2.8)	270/383	7
								Adenocarcinoma	OR 1.3(0.5-3.2)	NS/383	
								SCLC	OR 2.0(0.7-5.9)	NS/383	
								Squamous	OR 2.1(1.1-3.8)	NS/383	
				Occup (C)				Lung	OR 1.1(0.5-2.7)	270/383	
De Stefani 2005 [20]	Case- Control	Incidence	Н	SR	Y	Uruguay	1994- 2000	Adenocarcinoma	OR 0.8(0.4-1.5)	338/1014	7
Dement 2003 [21]	Cohort	Incidence	-	Occup (C)	N	US	1979- 2000	Lung	SIR 1.5(1.2-1.7)	137/13354	7
Demers	Pooled	Mortality	-	Occup	Ν	US/UK	1940-	Lung	SMR 0.8(0.7-	575/28704	7

1995 [22]	Cohort			(W)			1984		0.9)		
Droste 1999 [23]	Case- Control	Incidence	Н	JEM	Y	Belgium	1995- 1997	Lung	OR 1.5(0.9-2.6)	199/257	6
Dubrow 1984 [24]	Nested Case- Control	Mortality	-	Occup (C)	Ν	US	1971- 1973	Lung	OR 1.2(0.9-1.6)	48/34879	5
Elci 2003 [25]	Case- Control	Incidence	Н	Occup (C)	Y	Turkey	1979- 1984	Lung	OR 0.8(0.4-1.6)	1354/1519	6
Enterline 1963a [26]	Cohort	Mortality	-	Occup (F)	N	US	1950	Lung	SMR 0.8(0.5- 1.2)	23/?	6
Enterline 1963b[26]	Cohort	Mortality	-	Occup (C)	N	US	1950	Lung	SMR 1.1(1-1.3)	316/?	6
Ferreccio 2013 [27]	Case- Control	Incidence	Р	SR	Y	Chile	2007- 2010	Lung	OR 2.5(0.8-7.7)	17/135	6
Finkelstein 1995 [28]	Case- Control	Mortality	Р	Occup (C)	Ν	Canada	1979- 1988	Lung	OR 1.7(1-2.8)	576/2219	7
Firth 1996 [29]	Cohort	Mortality	-	Occup (W)	Ν	New Zealand	1972- 1984	Lung	SIR 1.5(1.3-1.7)	278/26207	6
Gallagher 1985 [30]	Cohort	Mortality	-	Occup (W)	Ν	Canada	1950- 1979	Lung	SMR 1.1(0.9- 1.2)	283/457083	7
Ganesh 2011 [31]	Case- Control	Incidence	Н	SR	Ν	India	1997- 1999	Lung	OR 0.9(0.3-3.3)	408/1383	4
Gottlieb 1979 [32]	Cohort	Mortality	-	Occup (W)	Ν	US	1960- 1975	Lung	OR 1.0(0.9-1.2)	2805/2805	7
Guida 2011 [33]	Case- Control	Incidence	Р	Occup (C)	Y	France	2001- 2007	Lung	OR 1.5(1.0-2.1)	2241/2770	8
Harrington 1978 [34]	Case- Control	Mortality	Р	Occup (W)	Ν	US	1961- 1974	Lung	OR 1.2(0.8-1.6)	595/539	6
Hoshuyama 2006 [35]	Cohort	Mortality	-	JEM	Ν	China	1980- 1993	Lung	SRR 0.9(0.8- 0.9)	26/90182	7
Hosseini 2009 [36]	Case- Control	Incidence	М	SR	N	Iran	2002- 2005	Lung	OR 1.2(0.5-3.1)	242/484	6
Hu 2002 [37]	Case- Control	Incidence	Р	SR	N	Canada	1994- 1997	Lung	OR 0.7(0.3-1.8)	161/483	8
Innos 2000 [38]	Cohort	Incidence	-	Occup (F)	N	Estonia	1968- 1995	Lung	SIR 1.1(0.9-1.3)	105/6786	7
Jahn 1999 [39]	Case- Control	Incidence	Р	Occup (W)	Y	Germany	1988- 1993	Lung	OR 1.6(0.6-3.8)	686/712	5
Jarvholm	Case-	Incidence	Р	SR	Ν	Sweden	1983-	Lung	OR 0.6(0.3-1.5)	147/131	5

1993 [40]	Control						1984				
Jayaprakash 2008 [41]	Case- Control	Incidence	Н	SR	Ν	US	1982- 1998	Lung	OR 1.7(1.2-2.4)	651/1260	7
								Adenocarcinoma	OR 1.4(1.0-1.9)	205/1260	
								LCLC	OR 1.4(0.9-2.2)	77/1260	
								SCLC	OR 1.2(0.8-1.8)	97/1260	
								Squamous	OR 1.9(1.2-3.2)	209/1260	
Kauppinen 1993 [42]	Nested Case- Control	Incidence	Р	JEM	Y	Finland	1957- 1982	Lung	OR 0.4(0.2-1.1)	117/408	8
Kjuus 1986 [43]	Case- Control	Incidence	Н	SR	Y	Norway	1979- 1983	Lung	OR 0.4(0.2-0.8)	176/176	7
Kromhout 1992 [44]	Cohort	Incidence	-	JEM	Y	Holland	1960- 1985	Lung	HR 1.6(0.7-3.4)	69/856	8
Leigh 1996 [45]	Cohort	Mortality	-	Occup (W)	Ν	US	1979- 1984	Lung	SMR 0.9(0.5- 1.3)	?/173438	5
Lerchen 1987 [46]	Case- Control	Incidence	Р	SR	Y	US	1980- 1982	Lung	OR 0.8(0.3-1.7)	333/501	5
Levin 1988 [47]	Case- Control	Incidence	Р	SR	Y	China	1984- 1985	Lung	OR 1.7(1-2.7)	269/308	6
				Occup (W)				Lung	OR 1.2(0.7-2.2)	733/760	
Lipscomb 1998 [48]	Cohort	Incidence	-	Occup (C)	Ν	US	1989- 1992	Lung	SIR 1.3(0.7-1.9)	13/10938	6
Luqman 2014 [49]	Case- Control	Incidence	Н	SR	Ν	Pakistan	2010- 2013	Lung	OR 1.9(1.2-3.1)	400/800	4
MacArthur 2009 [50]	Case- Control	Incidence	Н	Occup (W)	Y	Canada	1983- 1990	Lung	OR 0.8(0.7-1.0)	2964/10223	5
Matos 2000 [51]	Case- control	Incidence	Р	Occup (W)	Y	Argentina	1994- 1996	Lung	OR 0.7(0.3-1.5)	200/397	6
Mcconnell 1952 [52]	Case- Control	Incidence	Н	SR	Ν	England	1946- 1950	Lung	OR 1.8(0.6-5.4)	100/200	4
Menck 1976 [53]	Cohort	Mortality	-	Occup (W)		US	1968- 1973	Lung	SMR 1.1(0.8- 1.5)	39/3938	5
Mikoczy 1996 [54]	Nested Case- Control	Incidence	Р	JEM	N	Sweden	1958- 1959	Lung	OR 0.3(0-6.7)	22/55	7
Milne 1983	Cohort	Mortality	-	Occup	Ν	US	1958-	Lung	SMR 1.3(0.7-	925/6420	5

[55]				(W)			1962		2.6)		
Muscat 1998 [56]	Case- Control	Incidence	Н	SR	Y	US	1978- 1992	Lung	OR 1.6(0.8-3.2)	365/251	6
Notani 1993 [57]	Case- Control	Incidence	Н	Occup (W)	Y	India	1986- 1990	Lung	OR 2.9(0.9-9.6)	246/212	6
Osann 2000 [58]	Case- Control	Incidence	Р	SR	Y	US	1990- 1993	SCLC	OR 0.8(0.3-2.4)	98/204	8
Peters 2012 [59]	Case- Control	Incidence	Н	Occup (W)	Y	Multiple	1985- 2005	Lung	OR 1.2(1.1-1.3)	13479/16510	7
Pezzotto 1999 [60]	Case- Control	Incidence	Н	Occup (C)	Y	Argentina	1992- 1997	Lung	OR 0.9(0.3-2.7)	367/586	5
Pronk 2009 [61]	Cohort	Incidence	-	Occup (C)	Y	China	1996- 200	Lung	RR 2.3(1.1-4.7)	8/71067	8
Pukkala 2009 [62]	Cohort	Incidence	-	Occup (W)	N	Nordic Countries	1961- 2005	Lung	SIR 1(0.9-1)	10941/15mil	7
Richiardi 2004 [63]	Case- Control	Incidence	Р	Occup (C)	Y	Italy	1990- 1992	Lung	OR 0.9(0.6-1.5)	956/1253	6
Robinson 1995 [64]	Cohort	Mortality	-	Occup (C)	N	US	1984- 1986	Lung	SMR 1.2(1.1- 1.2)	1489/876731	6
Robinson 1996 [65]	Cohort	Mortality	-	Occup (C)	N	US	1987- 1990	Lung	SMR 1.1(0.9- 1.2)	2648/27362	7
Ronco 1988 [66]	Case- Control	Mortality	Р	Occup (W)	Y	Italy	1976- 1980	Lung	OR 2.8(0.9-8.4)	164/492	8
Schraub 1989 [67]	Case- Control	Incidence	Р	SR	N	France	1978- 1985	Adenocarcinoma	OR 1.1(0.4-2.5)	53/160	5
Siemiatycki 1991 [68]	Case- Control	Incidence	Н	0	Y	Canada	1979- 1983	Lung	OR 1.2(1.0-1.5)	174/NS Exposed	7
Siew 2012 [69]	Cohort	Incidence	-	JEM	Y	Finland	1971- 1995	Lung	RR 0.9(0.9-1.0)	2750/1.2mil	8
Simpson 1999 [70]	Cohort	Incidence	-	Occup (C)	Ν	UK	1971- 1990	Lung	RR 1.9(1.4-2.6)	50/381915	7
Smailyte 2012 [71]	Cohort	Incidence	-	Occup (W)	Ν	Lithuania	1978- 2007	Lung	SIR 0.9(0.6-1.2)	36/1518	6
Stellman 1984 [72]	Cohort	Mortality	-	Occup (W)	Ν	US	1959- 1972	Lung	SMR 1.1(1-1.3)	135/417120	5
Stellman 1998 [73]	Cohort	Mortality	-	SR	Y	US, Columbia, Puerto Rico	1982- 1988	Lung	IDR 1.2(1.0-1.3)	317/315,266	7
				Occup				Lung	RR 1.1(0.9-1.4)	111/315266	

				(W)							
Swanson 1982 [74]	Cohort	Incidence		Occup (W)	Ν	US	1970- 1978	Lung	SMR 1.6(0.8- 2.7)	11/1070	6
Szadkowska -Stanczyk 2001 [75]	Nested Case- Control	Mortality	Р	JEM	Y	Poland	1968- 1995	Lung	OR 2.1(0.9-4.9)	79/237	7
Tse 2012 [76]	Case- Control	Incidence	Р	SR	Y	China	2004- 2006	Lung	OR 1.2(0.6-2.2)	1208/1069	7
								Adenocarcinoma	OR 1.7(0.8-3.6)	440/1069	
								Squamous/SCLC	OR 1.6(0.7-4)	490/1069	
Versluys 1949 [77]	Cohort	Mortality	-	Occup (C)	Ν	Netherland s	1931- 1935	Lung	SMR 0.9(0.7- 1.3)	35/51124	6
Wang 1995 [78]	Case- Control	Incidence	Н	Occup (W)	Ν	China	1981- 1987	Lung	OR 1.2(1.0-1.6)	4806/14685	6
Weston 1998 [79]	Cohort	Mortality	-	0	Ν	Canada	1971- 1991	Lung	RR 1.3(0.7-2.6)	9/52,390	6
Wu 1995 [80]	Case- Control	Incidence	Н	Ο	Y	US	?-1995	Lung	OR 3.5(1.4-8.6)	180/270	7
								Non-SCLC	OR 2.4(1.3-4.4)	180/270	
								SCLC	OR 0.2(0.0-4.1)	180/270	
				Occup (W)				Lung	OR 2.5(0.4-6.1)	180/270	
Wu- Williams 1993 [81]	Case- Control	Incidence	Р	SR	Y	China	1985- 1987	Lung	OR 1.1(0.8-1.7)	966/960	6
				Occup (W)				Lung	OR 0.9(0.5-1.7)	966/960	
Wunsch- Filho 1998 [82]	Case- Control	Incidence	Н	Occup (W)	Y	Brazil	1990- 1991	Lung	OR 1.4(0.7-2.8)	398/860	5
Yang 1996 [83]	Nested Case- Control	Mortality	Р	JEM	Y	China	1972- 1992	Lung	OR 1.1(0.5-2.8)	21/75 Exposed	8
Yang 1997 [84]	Cohort	Mortality	-	JEM	Y	China	1972- 1992	Lung	SMR 2.6(1.6- 4.1)	20/2362	6
Zahm 1989 [85]	Case- Control	Incidence	Н	Occup (C)	Y	US	1980- 1985	Lung	OR 1.3(1-1.7)	4431/11326	7
Zahm 1989	Case-	Incidence	Н	Occup	Y	US	1980-	Lung	OR 1.3(0.5-3.3)	4431/11326	7

	[85]	Control	(F)		1985				
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H=Hospital; P=Populations; SR=Self-Reported - Wood Dust Exposure; JEM=Job-Exposure Matrix - Wood Dust Exposure; Occup=Wood-Dust Related Occupation (W = Woodworker; F = Furniture; C = Carpenter); O=Other Wood Dust Exposure; SCLC= Small-cell lung carcinoma; LCLC=Large-cell lung carcinoma; OR=odds ratio; IDR=Incidence Density Ratio, HR=Hazard Ratio; RR=Risk Ratio; SMR=Standardised Mortality Ratio; SRR=Standardised Rate Ratio; SIR=Standardised Incidence Ratio; NOS=Newcastle-Ottawa Scale score. Recalculated odds-ratio not controlled for smoking.

Author Date [Ref]	Study	Reason for Exclusion	Summary of Findings
		Used in Pooled Cohort of	Significant association between wood dust-related occupation and a reduced risk of lung cancer
Acheson 1984 [86]	Cohort	Demers 1995 [22]	(SMR 0.8, 95% CI 0.7-0.9) - UK
			No significant association between wood dust-related occupation and lung cancer (Denmark = SIR
		Same Cohort as Pukkalla 2009	1.0, 95% CI 1.0-1.1); Significant increased risk (Finland = SIR 1.1, 95% CI 1.1-1.2); Significant
Andersson 1999 [87]	Cohort	[62]	reduced risk (Norway = SIR 0.8, 95% CI 0.8-0.9; Sweden = SIR 0.7, 95% CI 0.7-0.7) -
		Same Cohort as Pukkalla 2009	No significant association between wood dust-related occupation and lung cancer (SMR 1.3, 95%
Andersson 2001 [88]	Cohort	[62]	CI 0.6-3.1) - Sweden
		Same Cohort as Pukkalla 2009	Significant association between wood dust-related occupation and a reduced risk of lung cancer
Andersson 2010 [89]	Cohort	[62]	(SMR 0.7, 95% CI 0.4-1.0) - Sweden
		Same Cohort as Pukkalla 2009	Significant association between wood dust-related occupation and a reduced risk for lung cancer
Andersson 2013 [90]	Cohort	[62]	(SIR 0.6, 95% CI 0.3-0.9) - Sweden
	Case-	Same Cohort as Baccarelli 2006	Mixed association between wood dust-related occupation and an increased risk for lung cancer
Baccarelli 2005 [91]	Control	[91]	(Wood Industry = OR 9.3, 95% CI 2.0-42.8; Carpenters = OR 1.2, 95% CI 0.3-4.2) - Russia
Bardin-Mikolajczak	Case-		Significant association between wood dust-related occupation and an increased risk for lung cancer
2007 [92]	Control	Same Cohort as Peters 2012 [59]	(OR 7.5, 95% CI 1.5-39.9) - Czech Republic, Hungary, Poland, Romania, Russia, Slovakia
		Used in Pooled Cohort of	No significant association between wood dust-related occupation and lung cancer (SMR 1.0, 95%
Blair 1985 [93]	Cohort	Demers 1995 [22]	CI 0.7-1.3) - US
		Used in Pooled Cohort of	No significant association between wood dust-related occupation and lung cancer (SMR 1.5, 95%
Blair 1990 [94]	Cohort	Demers 1995 [22]	CI 0.8-2.4) - US
Carpenter 1999 [95]	Cohort	Same Cohort as Simpson 1999	Significant association between wood dust related occupation and an increased risk for lung cancer
	Conon	[70]	(PRR 1.71, 95% CI 1.05-2.66) - UK
		Same Cohort as Pukkalla 2009	No significant association between wood dust-related occupation and lung cancer (OR 1.0, 95% CI
Carstensen 1988 [96]	Cohort	[62]	0.9-1.1) - Sweden
	Case-		No significant association between wood dust-related occupation and lung cancer (OR 1.0, 95% CI
Consonni 2010 [97]	Control	Same Cohort as Peters 2012 [59]	0.6-1.5) - Italy
Correa 1984 [98]	Case-	No data for 95% Confidence	Significant association between wood dust and an increased risk for lung cancer (OR 1.4) in
Conea 1904 [90]	Control	Interval	Louisiana, US
Demers 1998 [99]	Cohort	Duplicate - see Demers 1995	
Deniers 1776 [77]	Conon	[22]	
	Case-	Same Cohort as Barcenas 2005	Significant association between wood dust and an increased risk for lung cancer (OR 1.5, 95% CI
Etzel 2008 [100]	Control	[4] - Less Specific for Wood	1.1-2.1)
	Control	Dust	
Gerhardsson 1985		Same Cohort as Pukkalla 2009	No significant association between wood dust-related occupation and lung cancer (SIR 0.9, 95%
[101]	Cohort	[62]	CI 0.7-1.2) - Sweden
Gorlova 2006 [102]	Case-	Same Cohort as Barcenas 2005	Significant association between wood dust and an increased risk for lung cancer in non-smokers
	Control	[4] - Less Specific to Wood Dust	(OR 2.6, 95% 1.1-6.4)
Haldorsen 2004	Cohort	Same Cohort as Pukkalla 2009	Significant association between wood dust-related occupation and an increased risk of lung cancer

Supplementary Table 2. Summary of studies that met the inclusion criteria but were not included in the meta-analysis with justifications for their exclusion

[103]		[62]	(SIR 1.3, 95% CI 1.2-1.3) - Norway
		Same Cohort as Dement 2003	No significant association between wood dust-related occupation and lung cancer (SIR 2.5, 95%
Hall 1991 [104]	Cohort	[21]	CI 0.9-6) - US
Jappinnen 1989		Same Cohort as Pukkalla 2009	No significant association between wood dust-related occupation and lung cancer (SIR 1.0, 95%
[105]	Cohort	[62]	CI 0.6-1.4) - Finland
		Same Cohort as Pukkalla 2009	No significant association between wood dust-related occupation and lung cancer (SIR 0.8, 95%
Ji 2005 [106]	Cohort	[62]	CI 0.7-0.8) - Sweden
Lealed 1002 [107]	Case-	Same Cohort as Bruske-	No significant association between wood dust-related occupation and lung cancer (OR 0.7, 95% CI
Jockel 1992 [107]	Control	Hohlfeld 2000 [11]	0.3-1.9) - Germany
	Case-	Same Cohort as Bruske-	No significant association between wood dust-related occupation and lung cancer (OR 1.3, 95% CI
Jockel 1998 [108]	Control	Hohlfeld 2000 [11]	0.9-1.8) - Germany
Kauppinen 1986	Case-	Same Cohort as Kauppinen 1993	No similificant and intervention of the standard and the second (OD 1 (2))
[109]	Control	[42] - Earlier Study	No significant association between wood dust and lung cancer (OR 1.68)
	Case-		Significant association between wood dust-related occupation and an increased risk of lung cancer
Kawachi 1989 [110]	Control	Same Cohort as Firth 1996 [29]	(OR 1.3, 95% CI 1.2-1.6) - New Zealand
	Case-	Same Cohort as Bruske-	Significant association between wood dust-related occupation and an increased risk of lung cancer
Kreuzer 1999 [111]	Control	Hohlfeld 2000 [11]	(OR 1.3, 95% CI 1.1-1.6) - Germany
	Case-	Same Cohort as Bruske-	Significant association between wood dust-related occupation and an increased risk of lung cancer
Kreuzer 2002 [112]	Control	Hohlfeld 2000 [11]	(OR 13.4, 95% CI 1.6-112.2) - Germany
		Same Cohort as Pukkalla 2009	No significant association between wood dust-related occupation and lung cancer (SIR 1.6, 95%
Kvale 1986 [113]	Cohort	[62]	CI 0.9-2.8) - Norway
Lealdronen 2006		Sama Cabort of Sieve 2012 [60]	No significant association between wood dust and lung cancer in low (SIR 1.1, 95% CI 1.0-1.2)
Laakkonen 2006 [114]	Cohort	Same Cohort as Siew 2012 [69] - Earlier study	medium (SIR 1.0, 95% CI 1.0-1.0) and high (SIR 0.9, 95% CI 0.7-1.0) exposure categories in
[114]		- Earlier study	Finish males. Similar results for females
Laakkonen 2008	Cohort	Duplicate - See Laakkonen 2006	
[115]	Conort	[114]	
	Case-		
Matos 1998 [116]	control	Duplicate - see Matos 2000 [51]	-
	Case-	Same Cohort as Barcenas 2005	
Mchugh 2010 [117]	Case- Control	[4] - Subset of Mexican-	No significant association between wood dust and lung cancer (OR 1.3, 95% CI 0.9-2.1)
	Control	Americans	
		Used in Pooled Cohort of	No significant association between wood dust-related occupation and lung cancer (SMR 0.9, 95%
Miller 1989 [118]	Cohort	Demers 1995 [22]	CI 0.6-1.2) - US
		Used in Pooled Cohort of	No significant association between wood dust-related occupation and lung cancer (SMR 1.0, 95%
Miller 1994 [119]	Cohort	Demers 1995 [22]	CI 0.8-1.1) - US
Marchia 1002 [120]	Case-	No data for 95% Confidence	No significant association between wood accumulation and lying concer (OP 1.4)
Morabia 1992 [120] Case- Control Interval No significant association between wood occupation	No significant association between wood occupation and lung cancer (OR 1.4)		
		Same Cohort as Pukkalla 2009	No significant association between wood dust-related occupation and lung cancer (SMR 0.9, 95%
Olsen 1979 [121]	Cohort	[62]	CI 0.6-1.5) - Denmark

	~ .	Same Cohort as Pukkalla 2009	No significant association between wood dust-related occupation and lung cancer (SMR 1.1, 95%
Olsen 1979 [122]	Cohort	[62]	CI 0.9-1.3) - Denmark
		Same Cohort as Pukkalla 2009	No significant association between wood dust-related occupation and lung cancer (Woodworker =
Olsen 1987 [123]	Cohort	[62]	SIR 0.9, 95% CI 0.8-1.1; Carpenter = SIR 1.1, 95% CI 0.9-1.3) - Denmark
		Same Cohort as Pukkalla 2009	No significant association between wood dust-related occupation and lung cancer (Processing =
Olsen 1988 [124]	Cohort	[62]	SIR 0.9, 95% CI 0.7-1.1; Manufacture = SIR 1.0, 95% CI 0.9-1.1) - Denmark
Pohlabeln 2000	Case-		No significant association between wood dust-related occupation and lung cancer (OR 0.6, 95% CI
[125]	Control	Same Cohort as Peters 2012 [59]	0.3-1.0) - Germany/Italy/Portugal/UK/France/Spain/Sweden
		Same Cohort as Pukkalla 2009	Significant association between wood dust-related occupation and an increased risk of lung cancer
Pukkala 1983 [126]	Cohort	[62]	(SIR 1.3, 95% CI 1.2-1.4) - Finland
		Overlap with Pooled Cohort of	No significant association between wood dust-related occupation and lung cancer (SMR 0.8, 95%
Rang 1981 [127]	Cohort	Demers 1995 [22]	CI 0.6-1.1) - UK
		Used in Pooled Cohort of	No significant association between wood dust-related occupation and lung cancer (SMR 0.8, 95%
Robinson 1986 [65]	Cohort	Demers 1995 [22]	CI 0.6-1.1) - US
		Used in Pooled Cohort of	No significant association between wood dust-related occupation and lung cancer (SMR 1, 95% CI
Roscoe 1992 [128]	Cohort	Demers 1995 [22]	0.8-1.3) - US
			Significant association between wood dust-related occupation and an increased risk of lung cancer
		Same Cohort as Pukkalla 2009	(Carpenters = SIR 1.3, 95% CI 1.2-1.4); No significant association (Woodworkers = SIR 1.3, 95%
Sankila 1990 [129]	Cohort	[62]	CI 0.8-2) - Finland
	0	Same Cohort as Barcenas 2005	
Schabath 2005 [130]	Case-	[4] - Less Specific for Wood	Significant association between wood dust and an increased risk for lung cancer (OR 1.7, 95% CI
	Control	Dust	1.3-2.1)
Schoenberg 1987	Case-	No data for 95% Confidence	No Significant association between wood dust and lung cancer (Carpenters or Furniture = OR 0.9-
[131]	Control	Interval	1) - US
Siemiatycki 1986	Case-	Duplicate - see Siemiatycki	
[132]	Control	1991 [68]	-
Siemiatycki 1990	Case-	Duplicate - see Siemiatycki	
[133]	Control	1991 [68]	-
		Same Cohort as Barcenas 2005	
Spitz 2007 [134]	Case-	[4] - Less Specific for Wood	No significant association between wood dust and lung cancer for never smokers (OR 0.9, 95% CI
	Control	Dust	0.5-1.7), former smokers (OR 1.2, 95% CI 0.9-1.7), and current smokers (OR 1.2, 95% CI 0.9-1.6)
T 0011 [107]	Case-	Same Cohort as Tse 2012 [76]	No significant association between wood dust and lung cancer (OR 1.4, 95% CI 0.3-7.6) or lung
Tse 2011 [135]	Control	- Subset of non-smokers	adenocarcinomas (OR 2.2, 95% CI 0.4-12.0)
		No data for 95% Confidence	
Wang 1999 [136]	Cohort	Interval	Association between wood dust-related occupation and lung cancer (SMR 1.19)
Yang 1996 [137]	Cohort	Duplicate - see Yang 1997 [84]	
Yenugadhati 2009a	Case-	Same Cohort as MacArthur	No significant association between wood dust-related occupation and lung cancer (OR 1.3, 95% CI
[138]	Control	2009 [50]	1.0-1.8) - Canada
Yenugadhati 2009b	Case-	Same Cohort as MacArthur	No significant association between wood dust-related occupation and lung cancer (OR 0.9, 95% CI
i chuguanati 20070	Cube-	Sume Conort as Macrinian	The significant association between wood dust related becupation and rung cancel (OK 0.9, 95% CI

[139]	Control	2009 [50]	0.8-1.1) - Canada
	Case-		No significant association between wood dust-related occupation and lung cancer (OR 0.7, 95% CI
Zeka 2006 [140]	Control	Same Cohort as Peters 2012 [59]	0.3-2.2) - Czech Republic, Hungary, Poland, Romania, Russia, Slovakia, UK

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