

RESEARCH ARTICLE

Association between Occupational Exposure to Wood Dust and Cancer: A Systematic Review and Meta-Analysis

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Abstract

Objective

To perform a systematic review to analyze the association between occupational exposure to wood dust and cancer.

Methods

A systematic literature search of entries made in the MEDLINE-PubMed database between 1957 and 2013 was conducted to identify studies that had assessed the relationship between occupational exposure to wood dust and different types of cancer. A meta-analysis of selected case-control and cohort studies was subsequently performed.

Results

A total of 114 studies were identified and 70 were selected for review. Of these, 42 studies focused on the relationship between wood dust and nasal cancer (n = 22), lung cancer (n = 11), and other types of cancer (n = 9). Low-to-moderate quality evidence that wood dust acts as a carcinogen was obtained, and a stronger association between wood dust and nasal adenocarcinoma was observed. A lesser association between wood dust exposure and lung cancer was also observed. Several studies suggested that there is a relationship between wood dust and the onset of other cancers, although there was no evidence to establish an association. A meta-analysis that included four case-controls studies showed that workers exposed to wood dust exhibited higher rates of nasal adenocarcinoma than other workers (odds ratio = 10.28; 95% confidence interval: 5.92 and 17.85; $P < 0.0001$), although a large degree of heterogeneity was found.

Conclusions

Low-to-moderate quality evidence supports a causal association between cancer and occupational exposure to wood dust, and this association was stronger for nasal adenocarcinoma than for lung cancer. There was no evidence of an association between wood dust exposure and the other cancers examined.

Introduction

Dust generated in wood processing is one of the most common occupational and carcinogenic agents identified to date. The manipulation of wood can create fine and abundant dust with sanding, and thicker dust with milling or cutting [1,2,3]. The location and accumulation of particles has been found to depend on the size, shape, and density of the air flow available. Dust accumulates in the nose or the respiratory tract when the particles are larger or smaller than 5 microns, respectively [4,5].

Exposure to wood dust has been associated with several health problems, including pulmonary pathologies and other conditions [6,7]. In particular, cancer is a pathology that has been associated with wood dust [8–13]. Consequently, in 1995, the International Agency for Research of Cancer defined wood dust as a group I human carcinogenic substance [14].

Exposure to wood dust can vary considerably among populations, and it has not been found to be specific for a single sector or professional group, or for a single cancer. However, exposure to wood dust has been specifically linked to adenocarcinoma (ADCN). Currently, exposure to wood dust has a large impact on occupational health, and its occupational prevalence ranges from 10% to 15%. While occupational exposure to wood dust potentially contributes to an increased mortality rate for certain workers, it can also affect the mortality rate of the general population. Therefore, based on the health and social impacts of wood exposure, it is important to recognize this risk and to provide adequate professional and occupational protection.

Systematic reviews and/or meta-analyses represent useful methodological tools for assessing published data, and they also provide valid and reliable evidence for hypotheses [15,16]. Over the last few years, a consensus has been established to facilitate an assessment of the different primary studies that have been conducted, and to improve the quality and homogeneity of the systematic reviews that are conducted. With this in mind, it is appropriate and necessary to perform a systematic review that offers evidence on the relationship between different kinds of cancer and occupational exposure to wood dust.

Therefore, the aim of this systematic review was to analyze the data of previously published studies in relation to work exposure to wood dust and the onset of cancer.

Materials and Methods

Study design and selection criteria

A systematic review of the literature was conducted in order to identify studies that assessed the relationship and association between occupational exposure to wood dust and cancer. Selected articles (published in English or Spanish) that were available on Medline and included primary data collected between 1975 and September 2013 were selected. The exclusion criteria for this study ruled out works which consisted of opinions and/or recommendations from experts, as well as observational and experimental research studies.

Search strategy

To perform the initial bibliographic search of the MEDLINE database, the following MeSH descriptors and keywords were used to ensure a comprehensive recovery of entries: ((Cancer* [tw] OR tumour* [tw] OR neoplas* [tw] OR malignan* [tw] OR carcinoma* [tw] OR metasta* [tw]) OR ("Neoplasms" [Majr] OR "neoplasms/etiology" [Mesh])) AND (("wood dust" [tw] OR "Wood dust exposure" [tw]) OR ("Wood"[Majr] AND "Dust"[Majr:NoExp])) AND "humans"[MeSH Terms]. The Etiology/Broad filter was applied through the Clinical Queries tool. Related articles were also identified following a review of the references listed for most of the relevant works identified.

Information selection and extraction

After the relevant studies were identified and selected, a standardized set of information was collected from each article including: the name of the authors, the year of publication, the journal of publication, the characteristics of the sample, the study design, and the result variables and their measures of association and/or impact. This procedure was carried out according to the recommendations of the PRISMA Statement [17,18].

The literature search was performed by an experienced documentalist and data extraction was performed independently by two of the authors. All discrepancies were solved by consensus.

Scientific evidence

All selected studies were classified according to their design type, based on the classification proposed by the US Task Force and the Centre for Evidence Based Medicine (CEBM) of Oxford [19,20]. The categories included: I) Evidence obtained from a single randomized controlled trial or a meta-analysis of randomized controlled trials; IIa) Evidence obtained from at least one well-designed controlled study without randomization; IIb) Evidence obtained from at least one well-designed quasi-experimental study; III) Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies, and case-control studies; and IV) Evidence obtained from expert committee reports or opinions and/or clinical experience of respected authorities. The levels according to CEBM include: level 1 (systematic review of randomized control trials), level 2 (observational study with dramatic effect), level 3 (cohort study), level 4 (case-series or case-control studies), and level 5 (mechanism-based reasoning). To improve the scientific rigor of the present systematic review, all of the published articles that were classified by each of the two reviewers as level 5 were excluded.

Meta-analysis

Case-control studies that analyzed the relationship between wood dust exposure and sinonasal ADCN were included in our meta-analysis. The following inclusion criteria were used: a) case-control studies published in peer-reviewed journals, b) description of occupational exposure to wood dust among cases and controls; and c) diagnosis of sinonasal ADCN by biopsy. The main purpose of the meta-analysis was to compare the presence of sinonasal ADCN among workers exposed to wood dust with non-exposed workers used as controls in case-control studies.

Data were extracted from the selected studies by three authors (A.-J.C, I.H.-G., and C.H.) and differences were solved by consensus. The odds ratio (OR), 95% confidence interval (CI), and *P* values are reported for the pooled results based on the use of a random effects model (DerSimonian and Laird method) [21]. A random effects model was chosen due to the low number of studies available and their observational nature. A *P*-value less than 0.05 was

considered statistically significant. Cochran’s Q-statistic was used to assess heterogeneity. A significant Q-statistic value ($P < 0.10$) indicated heterogeneity across the studies examined. The I^2 statistic was used to estimate inconsistency in the meta-analysis, thereby representing the percentage of the observed between-study variability due to heterogeneity rather than chance. The following suggested cut-off points were used: $I^2 = 0-25\%$, no heterogeneity; $I^2 = 25-50\%$, moderate heterogeneity; $I^2 = 50-75\%$, large heterogeneity; $I^2 = 75-100\%$, extreme heterogeneity [22].

A sensitivity analysis was performed to assess the effect of excluding individual studies in the results. The meta-analysis was performed by using the computer software package RevMan 5.0 [23].

Results

Systematic review

Among the articles that investigated the relationship between exposure to wood dust and cancer and were published between 1975 and September 2013, 70 studies were selected for this review. Reports which only included opinions and/or recommendations from experts were excluded. Of the 70 selected studies, 42 had investigated the relationship between wood dust exposure and cancer according to the incidence of nasal ADCN ($n = 22$), lung cancer ($n = 11$), and other cancers ($n = 9$) (see Fig 1).

The historical evolution of the publications indexed in Medline is shown in Fig 2. A total of 114 articles were collected, and their chronological evolution is demonstrated in the vertical cylinders graph. As shown in Fig 2 scientific publications have progressively increased until they reached a peak between 2000 and 2013.

As shown in Table 1 most of the selected studies addressed the causal relationship of wood dust with ADCN, and case-control studies [24–45] and case series studies were predominant.

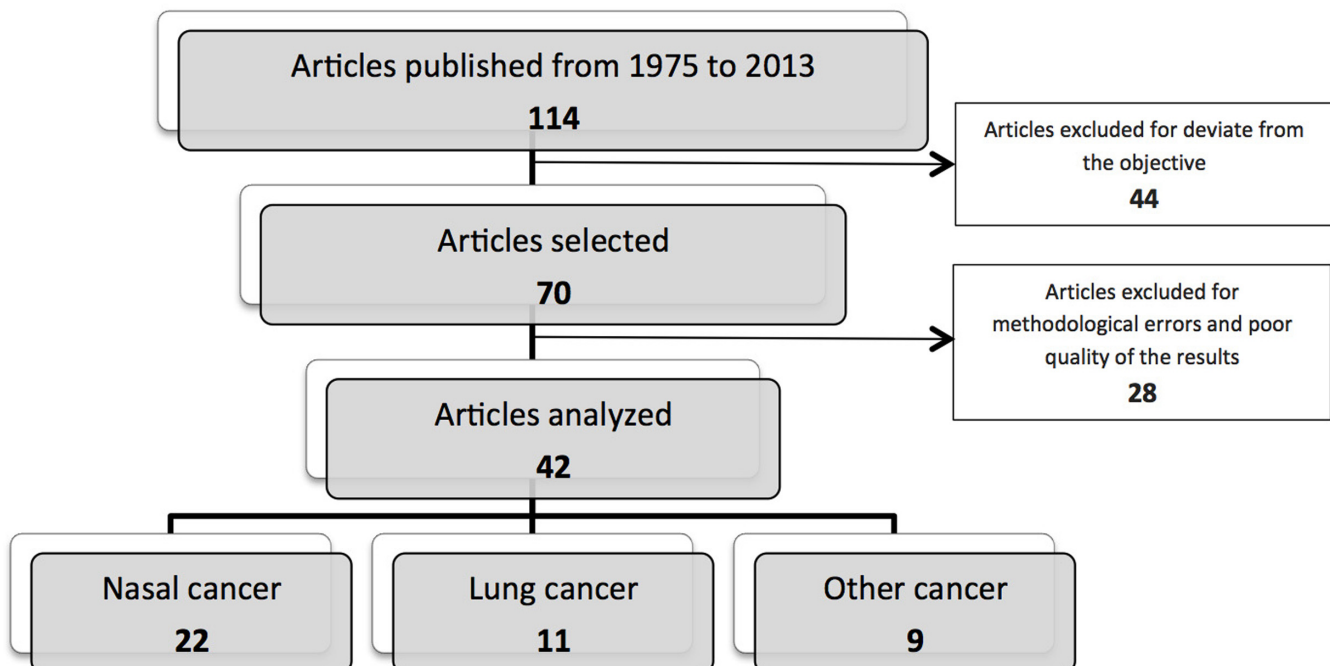


Fig 1. A PRISMA flowchart that illustrates the search strategy used to identify articles included in this systematic review.

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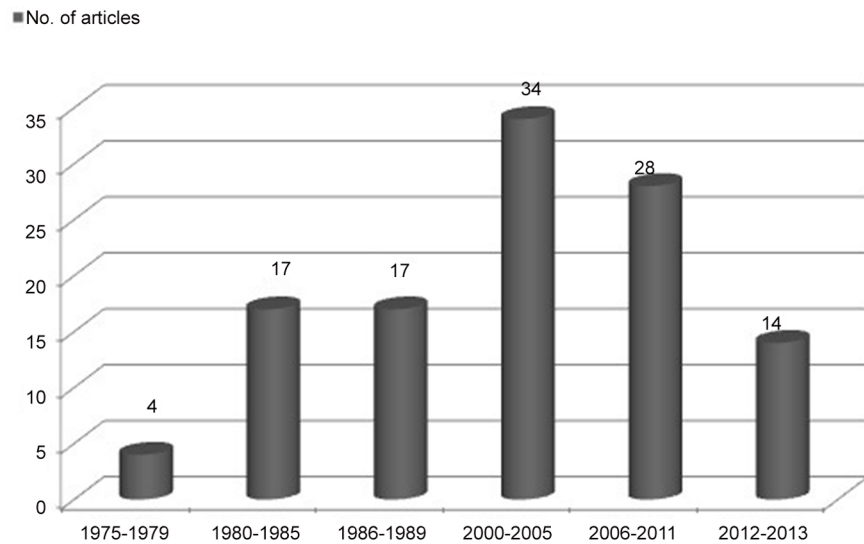


Fig 2. Temporal evolution of the publications related to wood dust exposure and cancer incidence that are indexed in Medline.

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However, there were other, less common study designs [27] and descriptive or population-based studies [35,38,41] as well. Furthermore, most of the studies assessed the epidemiological association by obtaining a clinical history and/or occupational history for each of the patients examined. The most widely analyzed profession was that of carpenters, followed by sawmill workers and other workers who manipulate wood in their work. OR values were the main measure of impact used in the studies. Bias control and control of confounding variables were reported in eleven studies [26,27,29–33,36,37,39–41], and these generally included research performed over the last decade. The most common risk factor that was adjusted for was tobacco consumption [26,29,30,33,41], and it was analyzed through logistic regression.

Table 2 lists eleven articles that analyzed the association between exposure to wood dust and lung cancer. Of these, seven were case-control studies [29–55] and three were population and retrospective studies [48,49,53]. OR was the main measure of impact used in these articles, and bias control and control of confounding variables were only present in four studies which were conducted over the last decade [46–48,50,55]. In nine of the studies, an association between lung cancer and wood dust exposure was observed. In the other two studies, a statistically significant association was not observed, potentially due to the low quality of these studies [52,53].

The nine studies that investigated the association between exposure to wood dust and other types of cancer are listed in Table 3. Two of these articles focused on the relationship between exposure to wood dust and lymphomas [56–58,60], while the other studies involved the following types of cancer: thyroid [61–62], mesothelioma [56], multiple myeloma [61], gastric cardia [59], glottic [63], and sarcoma [57]. Case-control studies were the most common ($n = 6$), followed by records and case reports ($n = 2$) and population-based cohort studies ($n = 1$). Except for a study of multiple myeloma, all of the other studies identified a statistically significant association between exposure to wood dust and cancer.

Table 4 lists the reviews that have been published regarding exposure to wood dust and cancer. The list includes a meta-analysis [64–65] of larynx cancer, two systematic reviews [66–69], and five narrative reviews [33,67,68,70,71]. In the former, it was concluded that there was no association between larynx cancer and wood dust exposure.

Table 1. Summary of published results on the relation between exposure to wood dust and nasal cancer—adenocarcinoma (ADCN).

First author, ref. no., year (in chronological order)	Quality of evidence ^{a/b}	No. of cases ^c	Those exposed/ type of exposure	Quality indexes	Assessment of exposure	Results	Measure of association/results
Bonzini M ²⁴ , 2013	III/4	65	Workers	No	Working exposure	Retrospective association with exposure	Higher risk with occupational exposure
Gómez ME ²⁵ , 2010	III/4	117	Wood workers	No	Carpenter's workshop	Association with exposure	Higher risk
D'Errico A ²⁶ , 2009	II-b/3b	113 cases of clinical incidents and 336 hospital controls	Exposure to wood, leather dust, and solvents	Yes. Adjusted for age, gender, tobacco, and other exposures	Occupational history	ADCN associated with exposure	Dose-response relationship (OR = 58)
Pukkala E ²⁷ , 2009	II-b/2b	Cases of cancer until 2005	Occupational exposure, to wood dust	Yes. Standardized incidence ratio	Occupational history	ADCN associated with wood dust exposure	Mortality (SIR = 5.5) (IC 95%, 4.6–6.56)
Fontana L ²⁸ , 2008	III/4	46, retrospective	Carpenters and cabinetmakers	No	Occupational history	92% ADCN after 20 years of exposure (11–27 y)	Exposure time is important
JayapraKash V ²⁹ , 2008	II-b/3b	1522 cases of oropharyngeal cancer and 1522 controls	General population	Yes. Adjusted for other risks and tobacco	Regular exposure to wood dust for more than 20 years	Exposure increases the risk of tumors (OR = 1.32; 95% CI: 1.01–1.8)	Mildly higher risk. No OR.
Pesch B ³⁰ , 2008	II-b/3b	86 cases, 204 controls	Wood workers, carpenters, or cabinetmakers	Yes. Adjusted for age, tobacco, and other risks	Exposure	Assessment of exposure levels, mg/m ³	Increased risk with exposure >3.5 mg/m ³
Arias Bahia SH ³¹ , 2005	III/4	138	Exposure of workers to fine wood dust	No	Occupational history	High mortality rate for tumors OR (CMOR)	Increased risk of oropharyngeal tumors
Helmet M ³² , 2004	III/4	Population study, 91 (78%) cases and 195 (75%) controls from municipal records	Wood workers	Yes. Adjusted for age and socioeconomic level	Wood sector (hard and soft)	Higher incidence in exposed workers	SIR = 1.9 (95% CI: 1.5–2.4) Soft wood SIR = 7.3 (95% CI: 1.4–22) Both SIR = 10 (95% CI: 4.7–18)
Jansing PJ ³³ , 2003	III/4	28 cases of ADCN, retrospective analysis	Wood workers with exposure to hard and soft wood dust	Yes. Adjusted for other risks, tobacco, and histological type	Occupational history	No significant differences between exposure to wood types and histological types	No association between wood type and histological type of nasal cancer (epidermoid and ADCN)
Bussi M ³⁴ , 2002	II-b/3b	68 cases and 81 volunteers	Carpenters with 10 years of exposure	No	Occupational history	Clinical protocol for early diagnosis	Increased metaplasia in nasal epithelium of exposed patients
Luce D ³⁵ , 2002	III/4	12 studies in 7 countries	Workers without exposure	No	Occupational history	Exposure to wood dust and increased chances of developing ADCN	No available evidence
Hildesheim A ³⁶ , 2001	II-b/3b	375 patients with ADCN and 325 controls	General population	Yes. Adjusted with LR for other risks and exposures. Blinded experiment.	Occupational history	ADCN is associated with wood dust exposure	Significant and consistent association if exposed before age 25 for more than 10 years

(Continued)

Table 1. (Continued)

First author, ref. no., year (in chronological order)	Quality of evidence ^{a/b}	No. of cases ^c	Those exposed/ type of exposure	Quality indexes	Assessment of exposure	Results	Measure of association/results
t'Mannetje A³⁷, 1999	II-b/3b	Population study, cases: 104 W/451 M; controls: 241 W/1464 M	Population study	Yes	Occupational history	ADCN associated with wood dust (39%) in men, with excess risk	OR = 2.36 (95% CI: 1.7–3.2)
Stellman SD³⁸, 1998	II-b/2b	Population study, Cancer Prevention Program	Wood-related workers	No	Occupational history	Small but significant excess risk	RR = 1.17 (95% CI: 1.11–1.24); RR of death = 1.17 (95% CI: 1.05–1.3)
Leclerc A³⁹, 1994	II-b/3b	207 cases and 409 controls	General population	Yes. Individual assessment of each case.	Exposure to wood dust	Assessment of duration and average exposure level	Doubled risk with exposure to fine wood dust, but not with other kinds of dust
Vaughan TL⁴⁰, 1991	II-b/3b	Studies in USA from 1979 to 1987	Population study, exposure to soft wood dust	Yes. Control of risk factors	Occupational history	Wood dust associated with increased risk	OR = 7 (95% CI: 1.4–34) for sinonasal and squamous nasopharyngeal cancer
Hayes RB⁴¹, 1986	II-b/3b	Population study	Wood workers	Yes. Adjusted for age and tobacco.	Several wood-related exposures	Association between ADCN and occupational activity	Wood industry (OR = 11.9) Furniture workers and cabinetmakers (OR = 39) and carpenters (OR = 16.3)
Battista G⁴², 1983	III/4	36 cases and 164 controls	Exposure to wood	No	Occupational history	ADCN associated with wood dust exposure	OR = 5.4 (95% CI: 1.7–17 for all ADCN and 87 for mucinous ADCN)
Roush GC⁴³, 1980	III/4	Cases and controls	Occupational exposure	No	Occupational history	ADCN associated with wood dust exposure	OR = 4 (95% CI: 1.5–10.8)
Cecchi FA⁴⁴, 1980	III/4	69, 13 diagnosed cases	Exposure to wood and leather	No	Occupational history	ADCN associated with wood dust exposure	Significant association with occupation
Ironside P⁴⁵, 1975	III/4	19 ADCN cases, retrospective analysis	General population	No	Clinical history and occupational exposure	More ADCN in wood workers than in general population	Significant association and different from general population

^{a/b}Quality of evidence according to US Task Force on Preventive Health Care 1989 (first column)/Centre for Evidence-based Medicine, Oxford (second column).

^cNo. of ADCN cases, unless otherwise specified.

ADCN: adenocarcinoma; OR: odds ratio; RR: relative risk; SIR: standardized incidence ratio; CI: confidence interval.

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Meta-analysis

Among the studies included in our systematic review, and according to the predefined criteria for this study, five reports were selected for a meta-analysis [26,35,43,44]. The summary OR under the random-effects model showed that subjects with wood dust exposure exhibited higher rates of sinonasal ADCN compared with non-exposed workers (see Fig 3: OR = 10.28; 95% CI: 5.92 and 17.85, respectively; $P < 0.0001$). A large degree of heterogeneity was also

Table 2. Summary of published results on the relation between exposure to wood dust and lung cancer.

First author, ref. no., year (in chronological order)	Quality of evidence ^{a/b}	No. of cases/controls	Exposed workers	Quality indexes	Assessment of exposure	Results	Conclusion
Rake C ⁵⁶ , 2009	III/4	457/792	Population study	Yes, potential confounding factors	Occupational history	Low risk for mesothelioma	OR = 4.63 (95% CI: 1.05–20.29)
Bhatti P ⁴⁷ , 2011	III/4	440/845	Wood workers	No	Clinical history	Risk for sawmill workers, but not for any other workers	OR = 1.5 (95% CI: 1.1–2.1)
Fritschi L ⁵⁸ , 2005	III/4	1522 cases of lung and oropharyngeal cancer/1522	Workers exposed to wood dust	No	Exposure to wood dust	Higher risk for non-Hodgkin lymphoma	OR = 1.69 (95% CI: 1.2–2.4)
Jansson C ⁵⁹ , 2005	III/4	Population study	Population exposed to wood dust	No	Workers exposed to wood dust	Increased risk	SIR = 1.11 (95% CI: 1.2–11)
Briggs NC ⁶⁰ , 2003	IIb/3b	1368/1192	Population study, African Americans and Mexicans	Yes, adjustments	Occupational history	Higher risk of cancer in Afro-American men	OR = 3.15 (95% CI: 1.45–6.86)
Lee WJ ⁶¹ , 2003	III/4	69/237	Construction workers	No	Occupational history	Exposure to wood dust	OR = 3 (95% CI: 0.9–4.9)
Innos K ⁵³ , 2000	III/4	Population study, 3723 M/3063 W	Furniture factory workers	No	Occupational history	Higher risk	SIR = 1.43 (95% CI: 0.8–1.7)
Maier H ⁶³ , 1992	III/4	199/393	Exposed workers	No	Occupational exposure	Higher risk	OR = 4.8 (95% CI: 1.2–19.0)
Wu X ⁵⁵ , 1995	III/4	113 African Americans, 67 Mexican-Americans/270	Occupational exposure in ethnic groups	Yes, stratification	Occupational history	Wood dust is identified as a risk factor for African-Americans	OR = 5.5 (95% CI: 1.6–19)

^{a/b}Quality of evidence according to US Task Force on Preventive Health Care 1989 (first column)/Centre for Evidence-based Medicine, Oxford (second column).

ADCN: adenocarcinoma; OR: odds ratio; RR: relative risk; SIR: standardized incidence ratio; CI: confidence interval.

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observed between the studies ($I^2 = 85\%$). However, in the sensitivity analysis, the exclusion of individual studies did not change this significant result (see [Table 5](#)).

Discussion

The studies that were selected and reviewed show that: 1) wood dust may act as a carcinogen, and 2) there is an association between exposure to wood dust and nasal ADCN, and to a lesser extent, with lung cancer. The results of several studies also suggest that there is a relationship between exposure to wood dust and other types of cancer, although there is currently not sufficient data or evidence to clearly establish this association. Moreover, the design of the included studies (mostly case-control studies) potentially limits the strength of the latter association.

The historical evolution of studies in this field has grown in parallel with the interest and impact of wood dust as an occupational exposure. At first, epidemiological research was mainly observational, and was based on case studies that involved occupations where exposure to wood dust was a factor. Thus, the early studies were of carpenters and sawmill workers. However later on, the studies included other situations where wood is manipulated or processed as a secondary and/or complementary activity. Analytical case-control studies also started to be conducted, thereby adding scientific rigor to the hypothesis by establishing comparisons with

Table 3. Summary of published results on the relationship between exposure to wood dust and other types of cancer.

First author, ref. no., year (in chronological order)	Quality of evidence ^{a/ b}	No. of cases / controls	Exposed workers	Quality indexes	Assessment of exposure	Results	Conclusion
Rake C ⁵⁶ , 2009	III/4	622 / 1420	Population study	No	Occupational history in construction (carpenters)	Low risk for mesothelioma	OR = 50.0 (95% CI: 25.8–96.8)
Merletti F ⁵⁷ , 2006	III/4	Multicentric case-control study in 7 countries. 96/2632	Exposed workers	No	Clinical history, wood exposure, and exposure to other factors	Higher risk for bone sarcoma	OR = 2.68 (95% CI: 1.36–5.29)
Fritschi L ⁵⁸ , 2005	IIb/3b	70/45	Total cases from 2001 and 694 controls from electoral roll	Yes	Occupational history and interview for exposure over 15–30 years.	Higher risk for non-Hodgkin lymphoma	Wood dust slightly increases risk
Jansson C ⁵⁹ , 2005	IIb/2a	Population-based cohort study	Construction workers	Yes. Standardization	Workers exposed to wood dust	Higher incidence of cardia adenocarcinoma	RR = 4.8 (95% CI: 1.2–19.4)
Briggs NC ⁶⁰ , 2003	IIb/3b	2073 cases of lymphoma, 612 of sarcoma/1910	African American and Caucasian workers	Yes	Occupational history of wood dust exposure	Higher risk of cancer in African American men	OR = 4.6 (95% CI: 1.6–13) for Hodgkin lymphoma and OR = 3.7 (95% CI: 1.6–8.6) for sarcomas
Lee WJ ⁶¹ , 2003	III/4	446/0	Construction workers	Yes	Occupational history	No risk of multiple myeloma associated with wood dust	RR < 1
Fincham SM ⁶² , 2000	III/3b	1277/2666	Workers in wood processing for pulp and papermaking	Yes	Occupational history	Higher risk of	OR = 2.5 (95% CI: 1.1–5.8) for thyroid cancer
Maier H ⁶³ , 1992	III/4	164/656	Exposed workers	Yes	Clinical history and exposure	Higher risk of glottic cancer	RR = 3.18 (95% CI: 1.1–9.0)
Kawachi I ⁶⁴ , 1989	III/4	19,904 cancer patients	Sawmill workers (S), carpenters (C), Foresters (F), and loggers (L)	No	Occupational history	Higher risk of cancer for different occupational exposures	Lung adenocarcinoma (OR = 1.76), lip ca. (OR = 2.28) and lung ca. (OR = 1.27) F/L, Nasopharyngeal ca. (OR = 6.02)

^{a/b}Quality of evidence according to US Task Force on Preventive Health Care 1989 (first column)/Centre for Evidence-based Medicine, Oxford (second column).

ADCN: adenocarcinoma; OR: odds ratio; RR: relative risk; CI: confidence interval.

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healthy controls. The addition of multicentric studies provided further strength to the observed associations.

Most of the evidence presented in the present study was extracted from case-control analytical observational studies. This type of study design, as pointed out in two previous systematic reviews [66,69], is the most appropriate since it makes it possible to study diseases with a large latency period and to assess several types of exposure concomitantly. This study design is also economical and rapid. However, case-control studies do have limitations. For example, potential bias exists in the selection of controls, the temporal relationship between the presumed

Table 4. Summary of systematic reviews and meta-analyses of exposure to wood dust.

First author, ref. no., year, type of study	Quality of evidence ^{a/b}	No. of studies included	Objective	Workers	Conclusions
Paget-Bailly S ⁶⁵ , 2012. Meta-analysis	II-b/3a	10 studies with homogeneous exposure	Incidence of laryngeal cancer	Different types of occupational exposure (wood dust)	Risk is not significantly associated with workers exposed to wood dust
Puñal-Riobóo J ⁶⁶ , 2010. Systematic review	II-b/3b	10 cases and controls selected by 2 researchers	Association between occupational exposure to substances and cancer	Occupational exposure. Statistical association between cancer and exposure	Exposure is associated with a higher risk of nasopharyngeal and hypopharyngeal cancers. There are non-concurrent data
De Gabory L ⁶⁷ , 2009. Narrative review	III/5	Classic review that assesses scientific evidence	Association between ADCN and wood dust	Risk is important from the first year. When the period of exposure is > 30 y, only 10% of patients are < 50-years-old	Exposure to wood dust plays an essential role in the development of nasal ADCN
Jansing PJ ³³ , 2003. Narrative review	III/4	Retrospective study of 28 patients with nasal cancer	Profiles of different risk factors, occupational and non-occupational	Risk is important from the first year, and the period is generally > 30 y, only 10% of patients are < 50-years-old	Preventive activities are recommended
Blot WJ ⁶⁸ , 1997. Narrative review	III/5	Population study, USA and EU	Assessment of occupational history	Wood workers	Threshold dose equivalent to 8 h at 5 mg/m ³
Demers PA ⁶⁹ , 1995. Systematic review	III/3b	Review of 12 studies in 7 countries	Risk of nasal cancer	OR = 45.5 (95% CI: 28.3–72.9). Risk increases according to the time of occupational exposure	Results increase consistency of individual studies between ADCN and wood dust
Nylander LA ⁷⁰ , 1993. Narrative review	III/5	Opinion from experts	Risk of nasal cancer	Higher risk of occupational cancer	No data or direct experimental evidence for the dangers of wood dust
Wills H ⁷¹ , 1982. Narrative review	III/4	Register data from 12 countries	Population study	Higher risk of occupational cancer	61% of neoplasms of the respiratory tract and 78% of ADCNs are associated with furniture manufacture or manipulation

EU: European Union; CI: confidence interval; ADCN: adenocarcinoma.

^{a/b}Type of epidemiological design determined according to US Task Force on Preventive Health Care 1989/Centre for Evidence-based Medicine, Oxford.

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cause and the studied effect cannot be determined, and there is a need for specific biases to be controlled through adjustment techniques. These considerations have been highlighted in most of the studies and works published over the last two decades. However, advances in statistical techniques or procedures have made it possible to control confounding factors and biases, thus improving the quality of the observations.

Overall, a positive evolution in the methodological quality of the studies and research on wood dust exposure has led to the publication of evidence that has greater validity and reliability. There was also a wide geographical distribution for the studies that were considered, with the majority conducted in Europe and the United States, followed by studies conducted in Brazil and Colombia. The first study was conducted in 1975 in Australia [45]. However, very few of these studies were included in our meta-analysis.

Apart from the relationship between wood dust and nasal ADCN, the association between exposure to wood dust and other neoplasms, such as lung cancer, has also been assessed. Based on the data of the studies published to date, this association has not been established. Primarily due to the low quality of the evidence collected, the association has been weakly demonstrated in most studies, and evidence was nonexistent in two other studies [52,53]. Consequently, while a potential association exists, it remains to be validated.

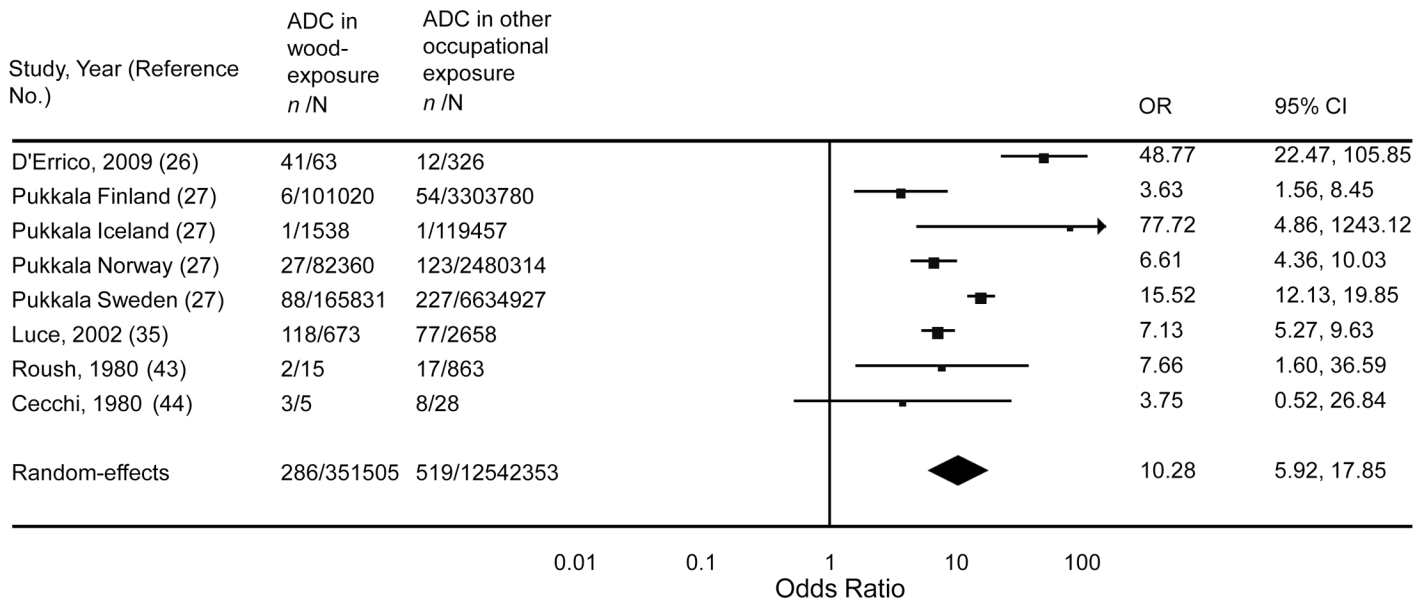


Fig 3. Meta-analysis of the association of sinonasal ADCN with wood exposure. Labor-based wood exposure was compared with other occupational exposures. Test for overall effect: $Z = 8.28$ ($P < 0.0001$). Test for heterogeneity: $\chi^2 = 46.17$ ($P < 0.0001$), $I^2 = 85\%$.

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Limitations

It is possible that certain factors in each research or review process can alter the final results. The main limitation of the results of the present review derives from the type of study design

Table 5. Patients with ADCN according to their occupational exposure from studies included in the meta-analysis.

First author, ref. no., year	Criteria selection	ADCN among those exposed to wood dust			ADCN with other		
		Events	Controls	Total	Events	Controls	Total
d'Errico et al ²⁶ , 2009	OE: Information was collected regarding lifetime occupational exposure	41	22	63	12	314	326
Pukkala et al ²⁷ , 2009		122	350627	350749	405	12538073	12538478
-Finland substudy	OE: Obtained from the national adaptations of the Nordic Occupational Classification	6	101014	101020	54	3303726	3303780
-Iceland substudy	OE: Obtained and converted from the International Standard Classification of Occupations from 1968 (ISCO-68)	1	1537	1538	1	119456	119457
-Norway substudy	OE: Obtained from the national adaptations of the Nordic Occupational Classification	27	82333	82360	123	2480191	2480314
-Sweden substudy	OE: Obtained from the national adaptations of the Nordic Occupational Classification	88	165743	165831	227	6634700	6634927
Luce et al ³⁵ , 2002	OE: Detailed information on occupational history was collected in all studies, including job description and years of employment for each job held	118	555	673	77	2581	2658
Roush et al ⁴³ , 1980	OE: Obtained from death certificates and directories from occupational information	2	13	15	17	846	863
Cecchi et al ⁴⁴ , 1980	OE: Occupational history data	3	2	5	8	20	28

ADCN: Adenocarcinoma.; OE: occupational exposure.

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that was employed in most of the studies conducted. For example, most of the evidence available is from observational studies, and specifically, from analytical case-control studies. Consequently, a temporal relationship between wood dust exposure and cancer cannot be determined. We also acknowledge that the use of other databases apart from PubMed could have yielded additional results, although we hypothesize that the final result of our work would be similar.

The most important limitation of the articles that were analyzed in this systematic review is that the characterization of occupational exposure in many of the articles published, particularly up until the 1990s, has been retrospective. In addition, the characterization was assessed through the working and occupational history of the patients examined. The latter aspect may be further biased by the quality of the documents examined, the maintenance of the working and occupational history files, and the memory of the workers. Other important limitations include the low number of studies with a cohort-type or prospective monitoring design, the sample size of individual studies, and the existence of few multicentric studies; although the latter is diminished by the wide geographic distribution of the studies that have been conducted. Another limitation of the earlier studies is the lack of adjustment for occupational or environmental risk factors that can act as confounders. These should be adjusted and/or neutralized since they can be linked to both the exposure (cause) and the effect; with a specific example being tobacco.

Regarding the meta-analysis performed, there were very few studies that met the inclusion criteria due to methodological differences. In addition, large heterogeneity was observed between the included studies. Therefore, although our meta-analysis confirms that a significant relationship between wood dust and nasal ADCN exists, this result should be approached with caution.

Conclusions

The conclusion of this systematic review is that there is low-to-moderate quality evidence that supports a causal association between the incidence of cancer and occupational exposure to wood dust. However, the association between exposure to wood dust and nasal ADCN is stronger, largely because most of the causal criteria established by Bradford Hill have been assessed [72]. In regard to lung cancer, caution is still advised in establishing an association with wood dust exposure given the low number of studies that have been conducted and their poor methodological quality.

Nevertheless, it is apparent that there is a need to implement preventive measures for workers exposed to wood dust. We propose that it is appropriate and adequate to establish a series of primary and secondary preventive measures in professional and working environments in order to improve the working health, hygiene, and safety of workers exposed to wood dust. It is critical that future studies overcome the limitations that have been observed in the present systematic review, particularly by identifying the characteristics of occupational exposure, adjusting for other exposures and confounding factors, increasing the sample size, and making comparisons with better control groups.

Supporting Information

S1 File. PRISMA checklist.
(DOC)

S2 File. Supplementary Methods.
(DOCX)

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Author Contributions

Conceived and designed the experiments: JAMC. Performed the experiments: JAMC MAS. Analyzed the data: IHG CH AJC. Contributed reagents/materials/analysis tools: JAMC MAS MM. Wrote the paper: JAMC MAS MM AJC. Searched for articles: HIdS HMR.

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