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Original Article

Association Between Organic Dust Exposure and Adult-Asthma: A Systematic Review and Meta-Analysis of Case-Control Studies

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Disclosure
There are no financial or other issues that might lead to conflict of interest.

ABSTRACT

Background: Exposure to organic dust has been widely investigated as a potential risk factor for asthma with different results. To clarify a potential relationship, we performed the present meta-analysis to integrate the results of studies examining the association of organic dust exposure with asthma.
Methods: A comprehensive literature search in the electronic databases including EMBASE, PubMed and Cochrane Library databases (up to August 2018) was conducted. The adjusted odds ratios (ORs) with corresponding 95% confidence interval (CI) for organic dust exposure and asthma were retrieved and pooled to generate summary effect estimates in Revman 5.2.
Results: Database searches retrieved 1,016 records. A total of 17 studies containing 3,619 cases and 6,585 controls were finally included in our meta-analysis. The summary estimates suggested that organic dust exposure was positively associated with asthma (OR, 1.48; 95% CI, 1.26–1.75; $P < 0.00001$), whether among population-based case-control studies (OR, 1.24; 95% CI, 1.13–1.35; $P < 0.00001$) or hospital-based case-control studies (OR, 2.79; 95% CI, 1.27–6.12; $P = 0.01$). Subgroup analysis showed that paper/wood (OR, 1.62; 95% CI, 1.38–1.90; $P < 0.00001$), flour/grain (OR, 1.48; 95% CI, 1.11–1.97; $P = 0.008$), and textile dust (OR, 1.50; 95% CI, 1.08–2.09; $P = 0.02$) exposure were significantly associated with asthma.
Conclusions: Based on the studies evaluated, our meta-analysis results prompt that organic dust exposure is a risk factor inducing asthma, although precise analysis focus on specific organic dust materials is still warranted.

Keywords: Asthma; dust; meta-analysis; case-control studies

INTRODUCTION

Organic dust is an aggregate of viable and non-viable particulate matter from microbial (bacteria, fungi, viruses and protozoa), their metabolites (mycotoxins, peptidoglycans, endotoxins, glucans, enzymes, etc.), plant or animal origin (allergens including pollens, vegetal fibers, and epidermis).[1] It is a well-established major air pollutant within different workplaces due to its containing of bacteria, moulds and pollens. Inhaled organic dust leads to respiratory inflammatory responses,[2] with the potential mechanism of serving as a favorable medium for the numerous bacteria and microscopic fungi.[3]

However, epidemiological results are inconclusive. Several studies confirmed the asthma-inducing effect of organic dust exposure, while other articles reported the ambiguous results. A late recent meta-analysis similar to our topic also showed limited evidence of a causal association existing between long-term excess decline in pulmonary function and general exposure to organic dust.[4]

Given the inconsistencies of existing epidemiological studies, we performed the present meta-analysis to examine the association between organic dust and asthma among case-control studies. This is the first meta-analysis on this topic to our knowledge, using a unique manner to the existing literature by quantitatively synthesizing observational studies on asthma and organic dust.

MATERIALS AND METHODS

Data sources and searches

To estimate the odds of asthma associated with organic dust exposure, we searched EMBASE, PubMed and Cochrane Library databases, using the keywords "asthma" and "case-referent" or "case-control" and "organic dust" or "wood/paper/flour/grain/baker/agriculture/farm/soybean/textile dust" up to August 2018. We screened the list of references in previous reviews and selected papers to identify additional relevant studies besides databases searched above. The decision whether an identified article would be eligible for the review was made prior to initiating the search.

Study selection

Studies meeting the following criteria were included in the meta-analysis: case-control studies published in English that contained or reported the odds of asthma related to organic dust exposure with corresponding 95% confidence interval (CI). The control group of individual studies was from either healthy community members (population-based) or inpatients without asthma (hospital-based). The first 2 authors screened the titles and abstracts to identify relevant investigations independently according to the selection criteria, and resolved discrepancies on whether to include a study by consensus. We excluded the studies focused on childhood.

Quality assessment

The Newcastle-Ottawa Scale (NOS) was used to assess the quality of the studies enrolled. This tool comprises 3 parameters: selection, comparability and outcome.[5] Each parameter consists of subcategorized questions: selection (a maximum of 4 stars), comparability (a maximum of 2 stars), and exposure or outcome (a maximum of 3 stars). A study can be awarded a maximum of 9 stars, indicating the highest quality. The authors independently evaluated the quality of all the studies.

Data extraction

The authors retrieved data from each article independently on the first author's name, the year of publication, source of controls, age, sex, country, organic dust type, case/controls, NOS score, asthma diagnosis, exposure duration and covariates/confounders. The adjusted odds ratio (OR) for asthma reported was used for this meta-analysis. Data from the more recent one was selected in the analysis if different studies share the same population.

Statistical analysis

ORs were combined by means of a weighted average to generate summary estimates by RevMan (version 5.2; The Cochrane Collaboration, Oxford, UK). The I^2 was determined to quantify the percentage of variation across studies attributable to heterogeneity.[6] We chose the fixed-effects model when $I^2 < 50\%$. In contrast, a random-effects model was applied. Studies were identified as outliers if the 95% CI of their effect size did not overlap with the estimate line of the summary estimate on the forest plot.[7] Potential publication bias was evaluated using funnel plots.

Ethics approval

Human subjects' institutional review and approval was got from Institutional Review Board of Qilu Children's Hospital of Shandong University (approval No. 2016026).

RESULTS

The steps of our literature search are shown in **Fig. 1**. Briefly, the search yielded a total of 1,016 articles from EMBASE, PubMed, and Cochrane Library databases. No additional article was identified from articles' references screening. After full text screening, 17 studies[8-24] containing 3,619 cases and 6,585 controls met our inclusion criteria. The studies included in this review were of the same case-control design and applied different types of organic dust exposure (**Table**, **Supplementary Table S1**).

The studies that were included in our meta-analysis were published between 1994 and 2015. They were conducted mainly in Europe,[10,14,17-24] but also in North America,[15,16] China,[9,12] Thailand[11,13] and Singapore.[8] The risk of asthma increased by 48% among those exposed to organic dust (OR, 1.48; 95% CI, 1.26–1.75; $P < 0.00001$) (**Fig. 2**). Subgroup analysis showed

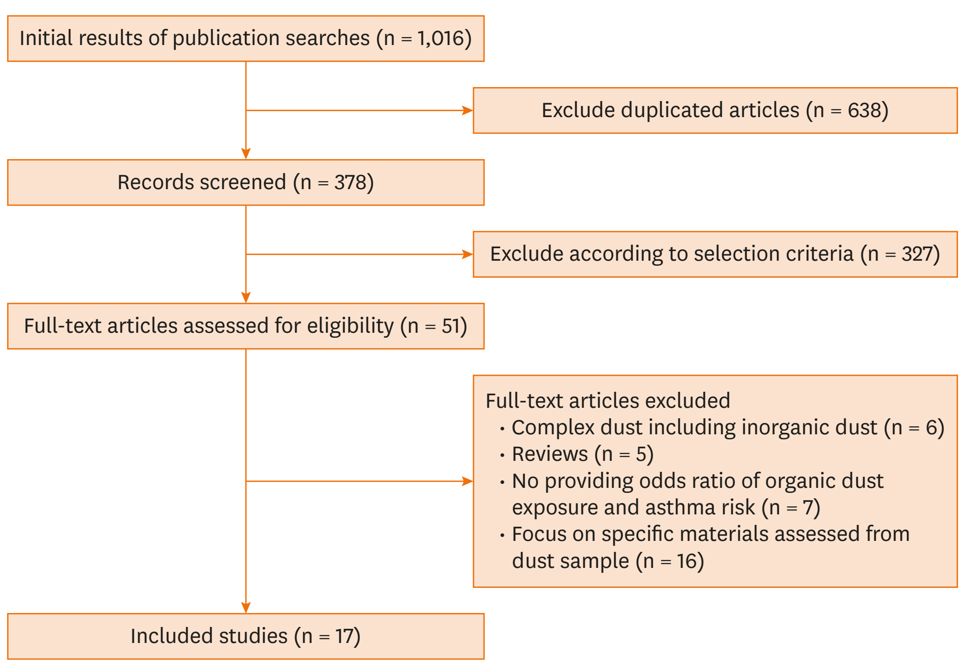

Fig. 1. Flow diagram of the literature search and study selection process.

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Table. Characteristics of included individual studies

Author/year	Source of control	Country	Type of OD	Age (yr)	Male (%)	Case/controls	NOS score
Beach *et al.* (2012)[15]	P	Canada	Wood		48.3	74/48	9
			Flour	18–65	93.4	30/28	
			Agriculture		40.4	25/22	
			Textile		21.7	27/19	
Flodin *et al.* (1996)[20]	P	Sweden	-	20–65	N/A	79/304	9
Flodin and Jönsson (2004)[19]	P	Sweden	Wood	20–65	57.7	53/156	7
Jaakkola and Jaakkola (2007)[21]	P	Finland	Paper	21–63	45.4	133/316	7
Jaakkola *et al.* (2003)[22]	P	Finland	Paper wood	20–64	42.2	9/14	8
			Textile			9/13	
			Flour			7/7	
			Agriculture			15/35	
Kogevinas *et al.* (1996)[23]	P	Spain	Wood	20–44	48.2	136/1,799	8
			Agriculture				
			Flour				
Krstev *et al.* (2007)[9]	P	China	Wood	37	N/A	6/24	8
			Textile			183/732	
			Agriculture			143/572	
Lipscomb and Dement (1998)[16]	P	USA	Wood	40	97.1	109/225	8
			Grain flour			12/19	
Mastrangelo *et al.* (1997)[18]	H	Italy	Wood	15–64	N/A	387/387	8
						325/325	
Ng *et al.* (1994)[8]	H	Singapore	Wood textile agriculture	20–54	42.4	787/1,591	8
Sigsgaard and Schlunssen (2004)[25]	P	Denmark	Wood	37	76.0	222/129	7
Smit *et al.* (2014)[24]	P	Netherland	Agriculture	50	35.7	269/546	9
Sripaiboonkij *et al.* (2009)[13]	P	Thailand	Wood	18–60	55.3	103/76	9
Torén *et al.* (1999)[14]	P	Sweden	Wood paper grain flour textile	38	47.5	111/2,044	8
Vermeulen *et al.* (2002)[10]	P	Netherland	Paper wood agriculture textile	48	47.0	274/274	8
			Wood	50	45.6	8/4	
Wang *et al.* (2010)[12]	P	China	Agriculture			40/7	8
			Textile			9/4	
Wortong *et al.* (2015)[11]	H	Thailand	Textile	55	34.9	11/8	9
			Agricultural			23/124	

N/A, not available; OD, organic dust; H, hospital controls; P, population controls; NOS, Newcastle-Ottawa Scale.

that the risk of asthma increased by 24% among population-based case-control studies (OR, 1.24; 95% CI, 1.13–1.35; $P < 0.00001$) (**Fig. 3**) and by 179% among hospital-based case-control studies (OR, 2.79; 95% CI, 1.27–6.12; $P = 0.01$) (**Fig. 4**). Agriculture dust exposure was not significantly associated with an increased/reduced risk of asthma (OR, 1.06; 95% CI, 0.72–1.56; $P = 0.76$; **Fig. 5**), while strong relationship was found between asthma and paper/wood (OR, 1.62; 95% CI, 1.38–1.90; $P < 0.00001$) (**Fig. 6**), flour/grain (OR, 1.48; 95% CI,1.11–1.97; $P = 0.008$) (**Fig. 7**), and textile dust exposure (OR, 1.50; 95% CI, 1.08–2.09; $P = 0.02$) (**Fig. 8**).

Other subgroup analysis according to asthma diagnosis revealed that organic dust exposure was closely associated with asthma diagnosed with classic symptoms and objective outcomes from pulmonary function (OR, 1.77; 95% CI, 1.19–2.62; $P = 0.005$). When we focused on the cases whose exposure duration was not less than 3 years, no positive relationship could be found between organic dust exposure and asthma (OR, 0.95; 95% CI, 0.62–1.46; $P = 0.81$), which may be due to different exposure extents and incomplete data.

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Study or subgroup	Log[OR]	SE	Weight	OR IV, random, 95% CI
Beach et al. (2012)[15] (agriculture)	0.1310	0.2946	3.2%	1.14 (0.64–2.03)
Beach et al. (2012)[15] (flour)	0.0677	0.2622	3.5%	1.07 (0.64–1.79)
Beach et al. (2012)[15] (textile)	0.3507	0.2992	3.2%	1.42 (0.79–2.55)
Beach et al. (2012)[15] (wood)	0.4389	0.1870	4.2%	1.55 (1.08–2.24)
Flodin et al. (1996)[20]	0.9163	0.3332	2.9%	2.50 (1.30–4.80)
Flodin and Jönsson (2004)[19] (wood)	0.3853	0.2153	4.0%	1.47 (0.96–2.24)
Jaakkola et al. (2003)[22] (agriculture)	0.1133	0.3270	2.9%	1.12 (0.59–2.13)
Jaakkola et al. (2003)[22] (flour)	0.5365	0.5517	1.6%	1.71 (0.58–5.04)
Jaakkola et al. (2003)[22] (textile)	0.1740	0.4527	2.1%	1.19 (0.49–2.89)
Jaakkola et al. (2003)[22] (wood paper)	0.5423	0.4514	2.1%	1.72 (0.71–4.17)
Jaakkola and Jaakkola (2007)[21] (paper)	0.6780	0.2321	3.8%	1.97 (1.25–3.10)
Kogevinas et al. (1996)[23] (agriculture)	1.2528	0.8359	0.8%	3.50 (0.68–18.01)
Kogevinas et al. (1996)[23] (flour)	0.4762	0.6979	1.1%	1.61 (0.41–6.32)
Kogevinas et al. (1996)[23] (wood)	−0.0619	0.5660	1.6%	0.94 (0.31–2.85)
Krstev et al. (2007)[9] (agriculture)	−0.0834	0.1111	4.9%	0.92 (0.74–1.14)
Krstev et al. (2007)[9] (textile)	0.1484	0.0966	5.0%	1.16 (0.96–1.40)
Krstev et al. (2007)[9] (wood)	0.6060	0.5329	1.7%	1.83 (0.65–5.21)
Lipscomb and Dement (1998)[16] (grain or flour)	0.5878	0.4137	2.3%	1.80 (0.80–4.05)
Lipscomb and Dement (1998)[16] (wood)	0.4055	0.4267	2.2%	1.50 (0.65–3.46)
Mastrangelo et al. (1997)[18] (wood)	1.9138	0.5427	1.6%	6.78 (2.34–19.64)
Mastrangelo et al. (1997)[18] (wood)	2.1163	0.5730	1.5%	8.30 (2.70–25.52)
Ng et al. (1994)[8] (agriculture)	0.6419	0.4811	1.9%	1.90 (0.74–4.88)
Ng et al. (1994)[8] (textile)	1.7630	0.5640	1.6%	5.83 (1.93–17.61)
Ng et al. (1994)[8] (wood paper)	0.5822	0.3341	2.9%	1.79 (0.93–3.45)
Sigsgaard and Schlunssen (2004)[25] (wood)	0.2927	0.4100	2.3%	1.34 (0.60–2.99)
Smit et al. (2014)[24] (agriculture)	−0.3567	0.1820	4.3%	0.70 (0.49–1.00)
Sripaiboonkij et al. (2009)[13] (wood)	1.8083	1.1097	0.5%	6.10 (0.69–53.69)
Torén et al. (1999)[14] (flour)	0.7885	0.3093	3.1%	2.20 (1.20–4.03)
Torén et al. (1999)[14] (grain)	0.2624	0.3158	3.0%	1.30 (0.70–2.41)
Torén et al. (1999)[14] (paper)	0.4055	0.2069	4.0%	1.50 (1.00–2.25)
Torén et al. (1999)[14] (textile)	0.4055	0.2069	4.0%	1.50 (1.00–2.25)
Torén et al. (1999)[14] (wood)	0.0000	0.2606	3.5%	1.00 (0.60–1.67)
Vermeulen et al. (2002)[10] (agriculture)	−1.4271	0.6287	1.3%	0.24 (0.07–0.82)
Vermeulen et al. (2002)[10] (textile)	−0.6733	0.6596	1.2%	0.51 (0.14–1.86)
Vermeulen et al. (2002)[10] (wood paper)	0.0100	0.6582	1.2%	1.01 (0.28–3.67)
Wang et al. (2010)[12] (agriculture)	1.8405	0.5031	1.8%	6.30 (2.35–16.89)
Wang et al. (2010)[12] (textile)	0.7419	0.6698	1.2%	2.10 (0.57–7.80)
Wang et al. (2010)[12] (wood)	0.8755	0.7425	1.0%	2.40 (0.56–10.29)
Wortong et al. (2015)[11] (agriculture)	−0.5798	0.3168	3.0%	0.56 (0.30–1.04)
Wortong et al. (2015)[11] (textile)	1.2060	0.5832	1.5%	3.34 (1.06–10.48)
Total (95% CI)			**100.0%**	**1.48 (1.26–1.75)**

Heterogeneity: $Tau^2 = 0.13$; $\chi^2 = 100.68$, df = 39 ($P < 0.00001$); $I^2 = 61\%$
Test for overall effect: $Z = 4.70$ ($P < 0.00001$)

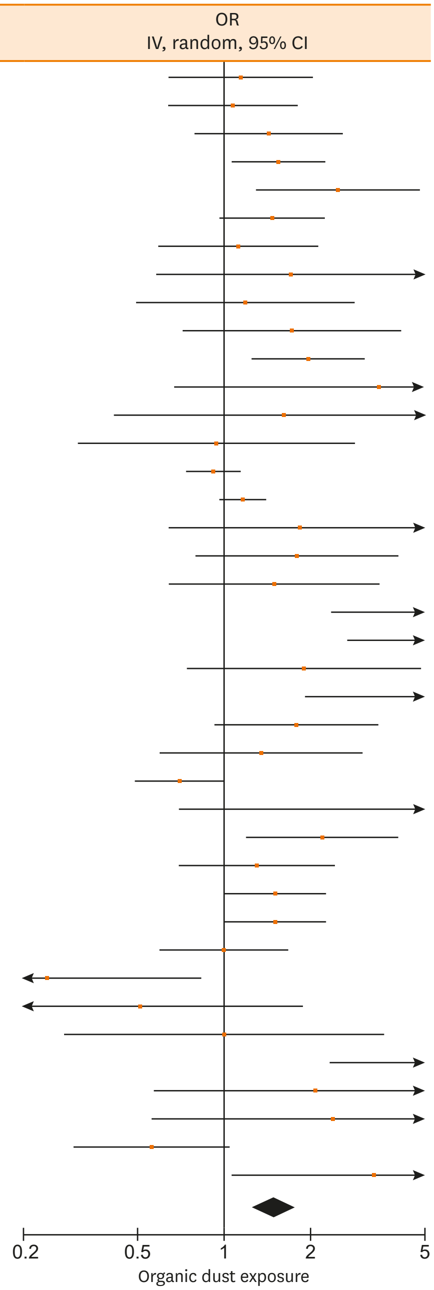

Fig. 2. Summary of the OR of the association between the risk of asthma and organic dust exposure.
SE, standard error; OR, odds ratio; CI, confidence interval.

Study or subgroup	Log[OR]	SE	Weight	OR IV, fixed, 95% CI
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Jaakkola et al. (2003)[22] (flour)	0.5365	0.5517	0.7%	1.71 (0.58–5.04)
Jaakkola et al. (2003)[22] (textile)	0.1740	0.4527	1.0%	1.19 (0.49–2.89)
Jaakkola et al. (2003)[22] (wood paper)	0.5423	0.4514	1.0%	1.72 (0.71–4.17)
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Wang et al. (2010)[12] (textile)	0.7419	0.6698	0.5%	2.10 (0.57–7.80)
Wang et al. (2010)[12] (wood)	0.8755	0.7425	0.4%	2.40 (0.56–10.29)
Total (95% CI)			**100.0%**	**1.24 (1.13–1.35)**

Heterogeneity: χ^2 = 61.58, df = 32 (P = 0.001); I^2 = 48%
Test for overall effect: Z = 4.63 (P < 0.00001)

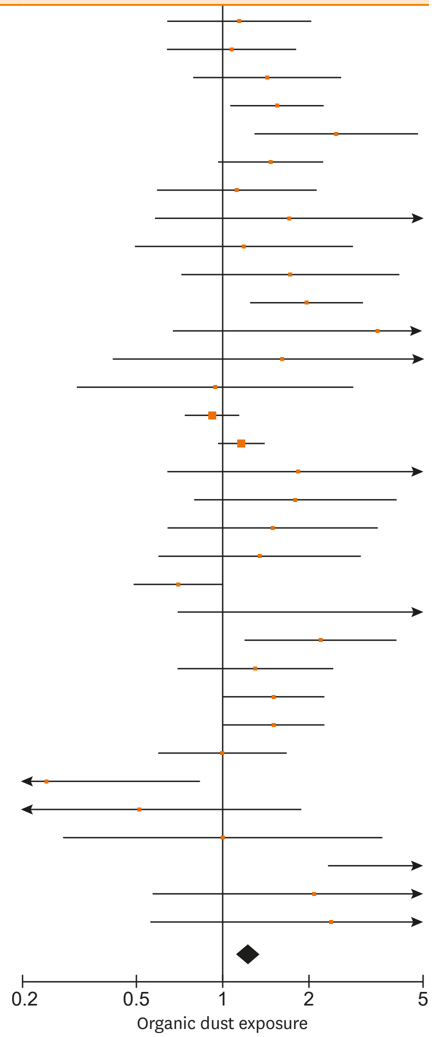

Fig. 3. Summary of the OR of the association between the risk of asthma and organic dust exposure among population-based case-control studies. SE, standard error; OR, odds ratio; CI, confidence interval.

Study or subgroup	Log[OR]	SE	Weight	OR IV, random, 95% CI
Mastrangelo et al. (1997)[18] (wood)	1.9138	0.5427	13.6%	6.78 (2.34–19.64)
Mastrangelo et al. (1997)[18] (wood)	2.1163	0.5730	13.2%	8.30 (2.70–25.52)
Ng et al. (1994)[8] (agriculture)	0.6419	0.4811	14.4%	1.90 (0.74–4.88)
Ng et al. (1994)[8] (textile)	1.7630	0.5640	13.3%	5.83 (1.93–17.61)
Ng et al. (1994)[8] (wood paper)	0.5822	0.3341	16.1%	1.79 (0.93–3.45)
Wortong et al. (2015)[11] (agriculture)	−0.5798	0.3168	16.3%	0.56 (0.30–1.04)
Wortong et al. (2015)[11] (textile)	1.2060	0.5832	13.1%	3.34 (1.06–10.48)
Total (95% CI)			**100.0%**	**2.79 (1.27–6.12)**

Heterogeneity: Tau^2 = 0.89; χ^2 = 31.86, df = 6 (P < 0.0001); I^2 = 81%
Test for overall effect: Z = 2.56 (P = 0.01)

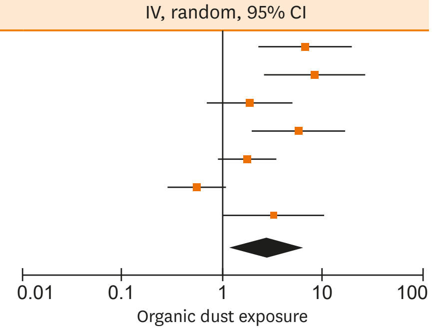

Fig. 4. Summary of the OR of the association between the risk of asthma and organic dust exposure among hospital-based case-control studies. SE, standard error; OR, odds ratio; CI, confidence interval.

Study or subgroup	Log[OR]	SE	Weight	OR IV, random, 95% CI
Beach et al. (2012)[15] (agriculture)	0.1310	0.2946	13.2%	1.14 (0.64–2.03)
Jaakkola et al. (2003)[22] (agriculture)	0.1133	0.3270	12.4%	1.12 (0.59–2.13)
Kogevinas et al. (1996)[23] (agriculture)	1.2528	0.8359	4.3%	3.50 (0.68–18.01)
Krstev et al. (2007)[9] (agriculture)	−0.0834	0.1111	17.6%	0.92 (0.74–1.14)
Ng et al. (1994)[8] (agriculture)	0.6419	0.4811	8.9%	1.90 (0.74–4.88)
Smit et al. (2014)[24] (agriculture)	−0.3567	0.1820	16.1%	0.70 (0.49–1.00)
Vermeulen et al. (2002)[10] (agriculture)	−1.4271	0.6287	6.5%	0.24 (0.07–0.82)
Wang et al. (2010)[12] (agriculture)	1.8405	0.5031	8.4%	6.30 (2.35–16.89)
Wortong et al. (2015)[11] (agriculture)	−0.5798	0.3168	12.6%	0.56 (0.30–1.04)
Total (95% CI)			**100.0%**	**1.06 (0.72–1.56)**

Heterogeneity: $Tau^2 = 0.21$; $\chi^2 = 29.62$, df = 8 ($P = 0.0002$); $I^2 = 73\%$

Test for overall effect: Z = 0.30 ($P = 0.76$)

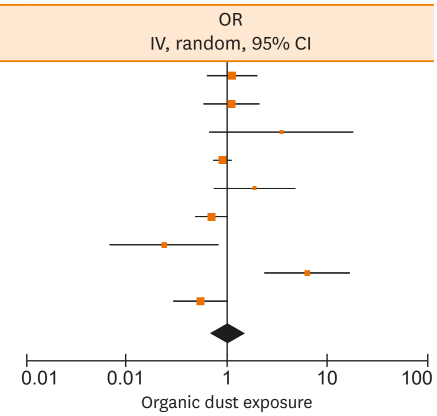

Fig. 5. Summary of the OR of the association between the risk of asthma and agriculture dust exposure.
SE, standard error; OR, odds ratio; CI, confidence interval.

Study or subgroup	Log[OR]	SE	Weight	OR IV, fixed, 95% CI
Beach et al. (2012)[15] (wood)	0.4389	0.1870	19.0%	1.55 (1.08–2.24)
Flodin and Jönsson (2004)[19] (wood)	0.3853	0.2153	14.4%	1.47 (0.96–2.24)
Jaakkola et al. (2003)[22] (wood paper)	0.5423	0.4514	3.3%	1.72 (0.71–4.17)
Jaakkola and Jaakkola (2007)[21] (paper)	0.6780	0.2321	12.4%	1.97 (1.25–3.10)
Kogevinas et al. (1996)[23] (wood)	−0.0619	0.5660	2.1%	0.94 (0.31–2.85)
Krstev et al. (2007)[9] (wood)	0.6060	0.5329	2.3%	1.83 (0.65–5.21)
Lipscomb and Dement (1998)[16] (wood)	0.4055	0.4267	3.7%	1.50 (0.65–3.46)
Mastrangelo et al. (1997)[18] (wood)	1.9138	0.5427	2.3%	6.78 (2.34–19.64)
Mastrangelo et al. (1997)[18] (wood)	2.1163	0.5730	2.0%	8.30 (2.70–25.52)
Ng et al. (1994)[8] (wood paper)	0.5822	0.3341	6.0%	1.79 (0.93–3.45)
Sigsgaard and Schlunssen (2004)[25] (wood)	0.2927	0.4100	4.0%	1.34 (0.60–2.99)
Sripaiboonkij et al. (2009)[13] (wood)	1.8083	1.1097	0.5%	6.10 (0.69–53.69)
Torén et al. (1999)[14] (paper)	0.4055	0.2069	15.6%	1.50 (1.00–2.25)
Torén et al. (1999)[14] (wood)	0.0000	0.2606	9.8%	1.00 (0.60–1.67)
Vermeulen et al. (2002)[10] (wood paper)	0.0100	0.6582	1.5%	1.01 (0.28–3.67)
Wang et al. (2010)[12] (wood)	0.8755	0.7425	1.2%	2.40 (0.56–10.29)
Total (95% CI)			**100.0%**	**1.62 (1.38–1.90)**

Heterogeneity: $\chi^2 = 23.17$, df = 15 ($P = 0.08$); $I^2 = 35\%$

Test for overall effect: Z = 5.94 ($P < 0.00001$)

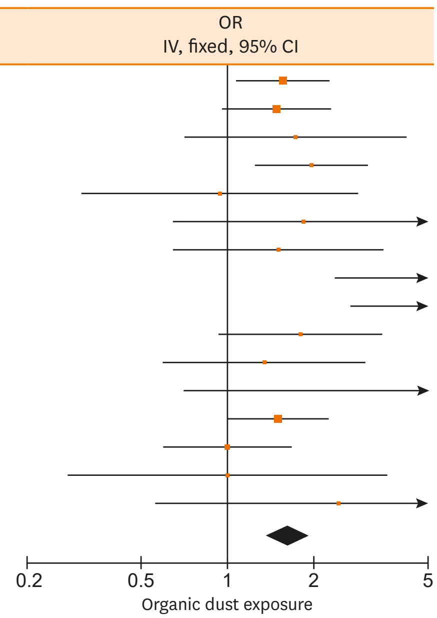

Fig. 6. Summary of the OR of the association between the risk of asthma and paper/wood dust exposure.
SE, standard error; OR, odds ratio; CI, confidence interval.

Study or subgroup	Log[OR]	SE	Weight	OR IV, fixed, 95% CI
Beach et al. (2012)[15] (flour)	0.0677	0.2622	31.5%	1.07 (0.64–1.79)
Jaakkola et al. (2003)[22] (flour)	0.5365	0.5517	7.1%	1.71 (0.58–5.04)
Kogevinas et al. (1996)[23] (flour)	0.4762	0.6979	4.4%	1.61 (0.41–6.32)
Lipscomb and Dement (1998)[16] (grain or flour)	0.5878	0.4137	12.6%	1.80 (0.80–4.05)
Torén et al. (1999)[14] (flour)	0.7885	0.3093	22.6%	2.20 (1.20–4.03)
Torén et al. (1999)[14] (grain)	0.2624	0.3158	21.7%	1.30 (0.70–2.41)
Total (95% CI)			**100.0%**	**1.48 (1.11–1.97)**

Heterogeneity: $\chi^2 = 3.65$, df = 5 ($P = 0.60$); $I^2 = 0\%$

Test for overall effect: Z = 2.65 ($P = 0.008$)

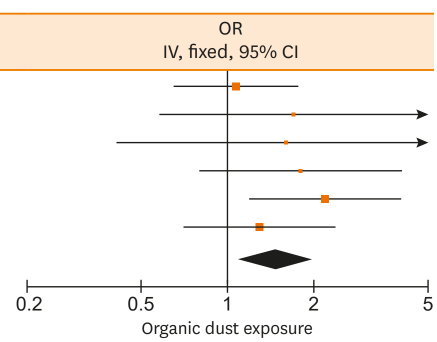

Fig. 7. Summary of the OR of the association between the risk of asthma and grain/flour dust exposure.
SE, standard error; OR, odds ratio; CI, confidence interval.

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Study or subgroup	Log[OR]	SE	Weight	OR IV, random, 95% CI
Beach et al. (2012)[15] (textile)	0.3507	0.2992	15.9%	1.42 (0.79–2.55)
Jaakkola et al. (2003)[22] (textile)	0.1740	0.4527	9.7%	1.19 (0.49–2.89)
Krstev et al. (2007)[9] (textile)	0.1484	0.0966	28.6%	1.16 (0.96–1.40)
Ng et al. (1994)[8] (textile)	1.7630	0.5640	7.0%	5.83 (1.93–17.61)
Torén et al. (1999)[14] (textile)	0.4055	0.2069	21.4%	1.50 (1.00–2.25)
Vermeulen et al. (2002)[10] (textile)	−0.6733	0.6596	5.4%	0.51 (0.14–1.86)
Wang et al. (2010)[12] (textile)	0.7419	0.6698	5.3%	2.10 (0.57–7.80)
Wortong et al. (2015)[11] (textile)	1.2060	0.5832	6.6%	3.34 (1.06–10.48)
Total (95% CI)			**100.0%**	**1.50 (1.08–2.09)**

Heterogeneity: Tau^2 = 0.09; χ^2 = 14.19, df = 7 (P = 0.05); I^2 = 51%

Test for overall effect: Z = 2.41 (P = 0.02)

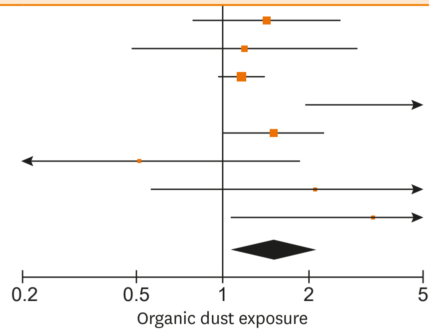

Fig. 8. Summary of the OR of the association between the risk of asthma and textile dust exposure.
SE, standard error; OR, odds ratio; CI, confidence interval.

DISCUSSION

Our results showed that organic dust exposure was positively associated with asthma, whether among population-based case-control studies or hospital-based case-control studies. Subgroup analysis indicated that paper/wood, flour/grain, and textile dust exposure, namely, most varieties of organic dust are related with asthma significantly.

Workers who are recurrently exposed to organic dust are at increased risk for several respiratory symptoms, including asthma.[25] A recent research revealed that sensitization to dust extracellular vesicles was an independent risk factor for non-eosinophilic asthma (adjusted OR, 3.3; 95% CI, 1.1–10.0), and even chronic obstructive pulmonary disease and lung cancer.[26] Agricultural work and multiple types of livestock are independent risk factors for developing asthma in adults.[27] Self-reported exposure to any gas, smoke or dust, organic dust, dampness and mold, cold conditions and physically strenuous work, and jobs handling low molecular weight agents were associated with exacerbation of asthma. Reduction in such occupational exposures may help reduce exacerbation of asthma.[28] A study from Norway revealed that dust exposure was associated with an increased incidence of work-related asthma-like symptoms.[29] Garshick *et al.*[30] reported exposure to vehicular emissions by living near heavily trafficked roadways might contribute to symptoms of chronic respiratory disease including persistent wheeze.

A previous study confirmed that exposure to inhaled organic dusts would activate inflammatory responses of monocyte, macrophages and epithelial cells through rapidly stimulating secretion of tumor necrosis factor.[31] Neutrophil recruitment, pyrexia and airway epithelial cells activation could be induced by monocyte/macrophage-derived inflammatory mediators and lead to direct bronchial hyperreaction.[32] Toll-like receptor 2,[33] myeloid differentiation factor 88-dependent signaling[34] and pattern recognition scavenger receptor A/CD204 all participate in the regulation of organic dust-induced airway inflammation. Robbe *et al.*[35] demonstrated that exposure to agriculture dust would increase the proportion of interleukin-17 and interferon-γ positive T cells, with similar results presenting the increased frequency of activated lung macrophages (CD11c+/CD11b+) obtained from animal models exposure to organic dust extracts.[36,37] Poole *et al.*[38] found that a mixed T helper cell (Th)1 and Th17 immune response was induced by repeated intranasal organic dust exposure in a murine model.

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Guillam *et al.*[39] found that Hatchery workers in sorting rooms were at increased risk of compromised respiratory health such as asthma and rhinitis due to dust exposure. Hinson *et al.*[40] indicated that medical interventions and technical prevention should be encouraged in the place where textile industry upgrades the local economic status such as Benin. Christiani *et al.*[41] conducted a longitudinal study of 445 cotton workers over 11 years and found a decrease in forced expiratory volume 1 in individuals exposed to cotton dust. Moreover, respiratory functions decreased depending on the concentration and time of dust exposure in the workplace.[42] The higher risks for women compared to men for asthma onset were robust, regardless of work exposure categories.[43] Poultry farm workers are more prone to suffer from respiratory disorders due to higher concentrations of particulate matter in dust.[44]

Different from our results, a recent cohort study from Canada provided further evidence that living in a farming environment during childhood is protective of asthma incidence in adolescence and adulthood and supports the protective effect of the farm environment on asthma.[45] Furthermore, farm exposure may have immunomodulatory effects by decreasing mDC proportions and asthma incidence as well.[46] We think the difference in inclusion criteria may have been responsible for the discrepancy. We enrolled the studies aiming at adulthood and failed to get the positive results because exposure during childhood may be a protective factor, whereas prolonged exposure during adulthood did not influence the risk of asthma.

Considering the harm brought by organic dust, intervention programs aimed at reducing exposure to dust will ameliorate occupational working conditions and improve health conditions. The value of measuring organic dust content in occupational settings was emphasized to make differences in health effects for exposed workers.[47] Another recent study[48] proposed the extraction method using Tris/EDTA to more accurately assess the endotoxin content and pro-inflammatory potential.

In conclusion, our meta-analysis revealed an overall asthma susceptibility rate in excess of 48% among individuals exposed to organic dust compared with controls, especially for those exposed to paper/wood, flour/grain and textile dust.

SUPPLEMENTARY MATERIAL

Supplementary Table S1

Asthma diagnosis, exposure duration and covariates of included individual studies

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