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ENVIRONMENTAL DETERMINANTS



Family, neighborhood and psychosocial environmental factors and their associations with asthma in Australia: a systematic review and Meta-analysis

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ABSTRACT

Objective: Various associations between different environmental exposures and asthma have been reported in different countries and populations. We aimed to investigate the associations between family, neighborhood and psychosocial environmental factors and asthma-symptoms in Australia by conducting a systematic review and meta-analysis.

Data sources: We analyzed the primary research studies conducted in Australia across multiple databases, including PubMed, EMBASE and Scopus, published between 2000 and 2020.

Study selections: The reviews and analyses focused on the overall association of different environmental exposures with the exacerbation of asthma-symptoms or asthma-related hospital visits. Quality-effect meta-analysis was done to estimate the pooled odds ratio for different environmental exposures for asthma-symptoms.

Results: Among the 4799 unique published articles found, 46 were included here for systematic review and 28 for meta-analysis. Our review found that psychosocial factors, including low socioeconomic condition, maternal depression, mental stress, ethnicity, and discrimination, are associated with asthma-symptoms. Pooled analysis was conducted on family and neighborhood environmental factors and revealed that environmental tobacco smoking (ETS) (OR 1.69, 95% CI 1.19–2.38), synthetic bedding (OR 1.91, 95% CI 1.48–2.47) and gas heaters (OR 1.40, 95% CI 1.12–1.76) had significant overall associations with asthma-symptoms in Australia.

Conclusion: Although the studies were heterogeneous, both systematic review and meta-analysis found several psychosocial and family environmental exposures significantly associated with asthma-symptoms. Further study to identify their causal relationship and modification may reduce asthma-symptoms in the Australian population.

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1. Introduction

Asthma is a diverse syndrome and a major noncommunicable disease (NCD), affecting both children and adults. It is the most prevalent chronic medical condition among children worldwide (1). More than 339 million people are currently suffering from asthma-symptoms worldwide (1). The prevalence varies, with Australia having among the highest rates in the world (2). Based on self-reported data from the 2017–2018 National Health Survey (NHS), 2.7 million people (11% of the total population) had asthma in

Australia. The prevalence is significantly higher in socially disadvantaged and Indigenous people compared to the socially advantaged and non-Indigenous population in Australia (3). Although the prevalence rate for the overall population declined significantly in the 1980s and 1990s, it has been static over the last two decades (3,4), perhaps due to the failure of further identification and optimal control of the factors associated with this condition. Although asthma-related mortality is very low in Australia, asthma incurred \$1.2 billion in direct healthcare costs (including medication, hospital and out-of-hospital

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expenses) in 2015 (5). It also reduces the quality of life and increases psychological distress at the individual level. Therefore, emphasis should be given to controlling asthma-symptoms to reduce the healthcare burden and improve the quality of life (5).

Although prolonged and total control of symptoms can be achieved in some cases with appropriate treatment, there is no available therapeutic regimen to cure asthma permanently. Prevention is the best strategy to manage this disease. Many epidemiological studies in both children and adults have shown a comprehensive list of factors contributing to exacerbation of asthma-symptoms. The most frequently cited triggers are allergens (particularly pollens, molds, dust and pet dander), tobacco smoke, exercise, air pollutants/particulate matter, weather patterns/changes, psychological factors, stress and respiratory infections (6–8). Most of these triggering factors are found within the family or home, neighborhood and psychosocial environment, which can dramatically influence the asthma phenotype and exacerbate the condition (8–10). Knowledge about specific environmental exposures and their attributable association with asthma-symptoms is essential to understand, modify or eliminate those exposures for better control.

Reported associations between different environmental exposures and asthma-symptoms are highly divergent across different countries and populations (11,12). Reviews and meta-analyses have been conducted to identify specific environmental exposures and their associations with asthma-symptoms (13,14). However, many such reviews have failed to provide consistent evidence due to inconsistent methods, population, or geographic location across the studies (15,16). Prior reviews were more exposure-specific rather than population- or country-specific. The review and meta-analysis of local evidence, especially in a country with high prevalence, such as Australia, may help to identify specific environmental factors and the extent of their association with asthma-symptoms that may lead a better prevention and management strategy of this chronic health condition.

2. Methods

We followed the ‘Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA)’ protocols for systematic reviews and meta-analyses (17), and we registered the protocol under registration ID: CRD42020170863 at the beginning of the study in PROSPERO (<http://www.crd.york.ac.uk/PROSPERO/>). A PRISMA flowchart of the study is shown in Figure 1.

2.1. Inclusion and exclusion criteria

We followed PECO (Population, Exposure, Comparator, and Outcomes) criteria (18) for inclusion and exclusion of the studies (Table 1). We used this standard framework for formulating appropriate questions to assess the association between exposures and outcomes.

2.2. Data sources and search strategy

To identify the articles, we used different search engines: PubMed, EMBASE and Scopus. We conducted the search in August 2020. We searched for articles based on Australian studies published between January 2000 and July 2020 as we wanted to include recent articles published within the last 20 years. We used a combination of different keywords with appropriate ‘Boolean Operators’ to search for the articles as described in supplementary Table S1.

2.3. Study selection and data extraction

The screening was done by two independent reviewers (KMS and TB-1). Disagreements were discussed and resolved by group meetings. These reviewers also completed a standard data-extraction form, summarizing each article’s study design and other relevant data, including author, publication year, sample size, population, study type, exposure, and outcome (Table 2). We only included Australian studies that were original, full-text English language articles. We did not include review articles, editorials, or conference abstracts.

2.4. Working definition of outcome variable

We have considered ‘asthma-symptoms’ or ‘wheeze’ as our outcome variable because, asthma is a heterogeneous disease and has several clinical phenotypes. Wheeze is the most common symptom among patients with asthma, independently of their phenotype (19). A recent Lancet Commission has discouraged using ‘asthma’ as a single disease and proposed a more targeted approach to think about its mechanisms and treatment (20). In our reviewed studies, asthma was diagnosed by doctors at hospital [according to International classification of diseases, 10th revision (ICD-10): J45, J46], or from self-reporting questionnaire based on symptoms (such as wheeze). None of the studies mentioned the phenotypic diagnosis of asthma. So, we considered our outcome of interest as ‘asthma-symptoms’ rather than ‘asthma’.

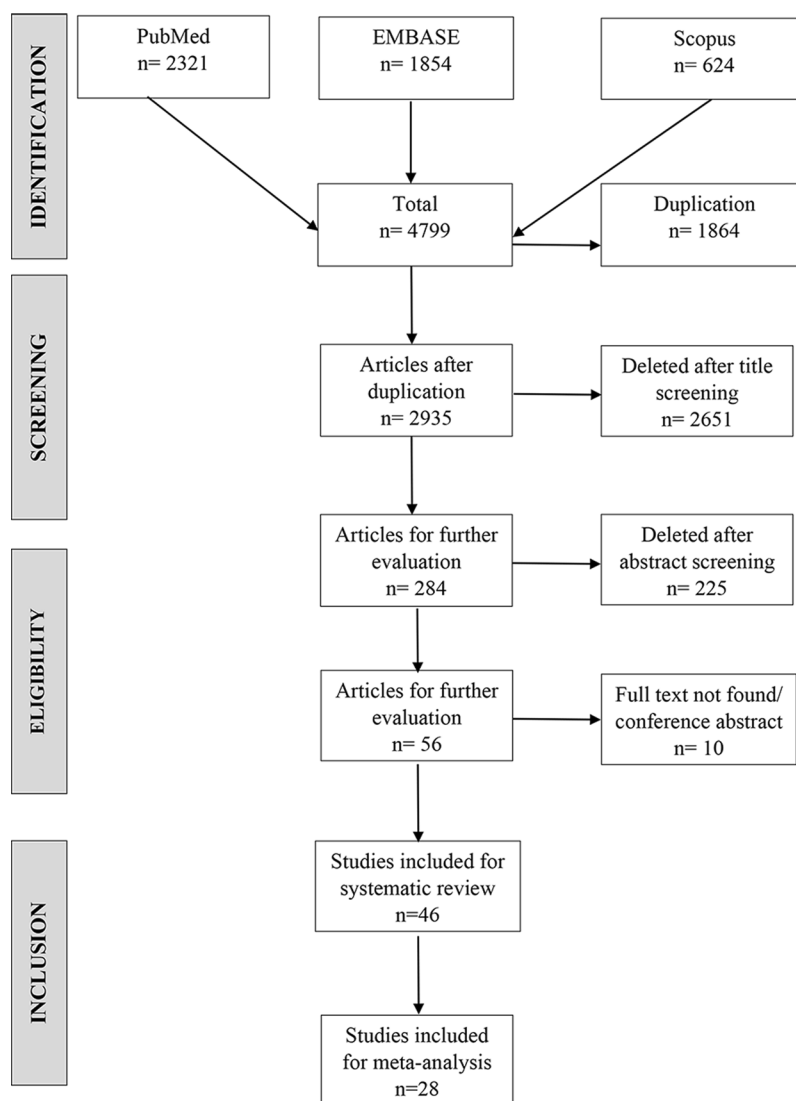


Figure 1. PRISMA flow chart of the study.

Table 1. PECOS criteria for inclusion and exclusion of studies.

Parameter	Inclusion criteria	Exclusion criteria
Population	All ages in both sexes	none
Exposure	Exposed with different family, neighborhood, and psychosocial environmental factors	none
Comparator	Not exposed with, or degree of exposure with family, neighborhood, and psychosocial environmental factors	none
Outcome	Asthma or wheeze	none
Study design	Observational study, Cross-sectional study, Cohort study, Case-control study, Case-crossover study, Time series analysis	Editorial, Review article, Methodological article, Conference abstract

2.5. Quality assessment

We adapted the modified Newcastle Ottawa Scale (21) for observational studies to assess the quality of the studies (Table S2). Two reviewers (KMS and TB-1) independently evaluated each of the included studies using the same tool and scored the studies accordingly (Table S3).

2.6. Data synthesis and analysis

Analyses were focused on the overall association for individual exposures to asthma-symptoms. Quantitative data synthesis was performed only when three or more studies were available with the estimates for a similar type of exposure; a descriptive analysis was done in other cases. Although most studies reported

Table 2. Characteristics of the studies.

SL	Author, publication year	Design, study site	Sample size and population	Exposures	Outcome
1	Gavin Pereira et al, 2010	Case-crossover, western Australia	$n=603$, 0–19 years	NO ₂ and CO	Asthma
2	Bircan Erbas et al, 2005	Cross-sectional, Melbourne	$n=8955$, 1–15 years	PM ₁₀ , NO ₂ , O ₃	Asthma
3	Bin Jalaludin et al, 2008	Case-crossover, Sydney	9130, 1–14 years	PM ₁₀ , PM _{2.5} , NO ₂ , O ₃ , CO, SO ₂	Asthma
4	K Rumchev et al, 2004	Case-control, Perth	$n=192$, 0.5–3 years	VOCs	Asthma
5	Anna Petroseshevsky et al, 2001	Time series analysis, Brisbane	$n=13246$, all ages	bsp, O ₃ , SO ₂ , NO ₂	Asthma
6	Don Vicendese et al, 2015	Case-control, Melbourne	$n=44$, 2–17 years	Airborne fungus, bedding, and other household allergens	Asthma
7	M C Matheson et al, 2005	Cohort, Melbourne	$n=360$, 20–45 years	Indoor allergens and fungus	Asthma
8	B Erbas et al, 2007	Cross-sectional, Melbourne	$n=147$, all ages	Grass pollen	Asthma
9	Desiree Meszaros et al, 2014	Cross-sectional, Tasmania	$n=5729$, adults	Mould, Smoking	Asthma
10	Jolanta Ciuk et al, 2001	Cross-sectional, Adelaide	$n=1341$, 4 years	NO ₂	Asthma
11	Rachel Tham et al, 2016	case-crossover, Melbourne	$n=644$, 2–17 years	Outdoor fungal spore,	Asthma
12	Fay H. Johnston et al, 2006	Cross-sectional, Darwin	$n=251$, all ages	PM ₁₀ , PM _{2.5}	Asthma
13	Fay H. Johnston et al, 2002	Cross-sectional, Darwin	$n=265$, all ages	PM ₁₀	Asthma
14	M Nitschke et al, 2006	Cohort, Adelaide	$n=174$, 5–12 years	NO ₂ , House dust mite (Der p I)	Asthma
15	Bin B Jalaluddin et al, 2004	Cross-sectional, Sydney	$n=125$, 8–10 years	Ozone, PM ₁₀ , NO ₂	Wheeze
16	P J Franklin et al, 2012	Cross-sectional, WA	$n=71$, adults	Gas heater	Wheeze
17	Gayan Bowatte et al, 2016	Cross-sectional, Tasmania	$n=1405$, adult	NO ₂ , distance from major road,	Wheeze and asthma
18	Diana J Bass et al, 2000	Cross-sectional, New South Wales	$n=206$, 5–80 years	Grass and Ragweed pollen	Asthma
19	C Rodriguez et al, 2007	Cohort, Perth	$n=263$, children	O ₃ , CO, NO ₂ , PM _{2.5} , bsp	Wheeze
20	M Wakefield et al, 2003	Cross-sectional, Victoria	$n=382$, adult	Secondhand smoking	Wheeze
21	I C Hanigan et al, 2007	Cross-sectional, Darwin	$n=1278$, 0–14 years	Pollen	Asthma
22	B Erbas et al, 2012	Cross-sectional, Victoria	$n=2559$, 0–15 years	Grass pollen	Asthma
23	Gea de Meer et al, 2004	Cohort, New South Wales	$n=224$, 8–10 years	Having a cat before age 18 only	Asthma
24	C M Bennett et al, 2007	Cross sectional, Melbourne	$n=1446$, adults	PM _{2.5}	Wheeze, asthma
25	A L Ponsonby et al, 2000	Cross-sectional, Tasmania	$n=863$, 7 years	Parental smoking, Gas heater, carpet, pet	Asthma
26	A L Ponsonby et al, 2003	Cross-sectional, Tasmania	$n=863$, 7 years	Synthetic pillow and quilt	Wheeze
27	A L Ponsonby et al, 2002	Cross-sectional, ACT	$n=758$, 8–10 years	Synthetic pillow or quilt	Asthma
28	Xiaoqi Feng et al, 2017	Cross-sectional, Australia (nationwide)	$n=4447$, 6–7 years	Green space, heavy traffic, safe area	Asthma
29	L F Trevillian et al, 2005	Cohort, Tasmania	$n=863$, infant	Synthetic bedding	Wheeze
30	S Dharmage et al, 2001	Cross-sectional, Melbourne	$n=485$, adults (24–48 yrs)	Allergy to fungi, cat, house dust mite	Asthma
31	Rachel Tham et al, 2017	case-crossover, NSW	$n=2098$, 2–18 years	Outdoor fungal spore,	Asthma
32	K.B. Rumchev et al, 2002	Cross-sectional, Perth	$n=192$, Children	Formaldehyde	Asthma
33	L L Phoa et al, 2004	Cross-sectional, Belmont	$n=627$, 8–11 years	fume emitting heaters	Asthma
34	P D Sly et al, 2007	Cohort, Perth	$n=1427$, 14 years	ETS	Wheeze
35	A L Ponsonby et al, 2002	Cross-sectional, Tasmania	$n=498$, children	House dust mite, Feather bedding	Wheeze
36	A L Ponsonby et al, 2004	Cross-sectional, Tasmania	$n=414$, children	Child bedding	Wheeze
37	B J Smith et al, 2000	Cross-sectional, Adelaide	$n=125$, all ages	Indoor NO ₂	Asthma
38	G Zhang et al, 2005	Cross-sectional, Perth	$n=996$, 4–12 years	Household cleanliness	Asthma
39	Som K. Shrestha et al, 2018	Cross-sectional, Sydney	$n=2098$, 2–18 years	Pollen	Asthma
40	K Chen et al, 2016	Time-series analysis and case-crossover, Adelaide	$n=36024$, all ages	PM _{2.5} , NO ₂ , PM ₁₀ , O ₃ , and pollen	Asthma
41	L. F. Trevillian, 2004	Cross-sectional, Tasmania	$n=863$, 7 years	Cocoon bedding	Wheeze
42	Anita L. Kozyrskyj, 2010	Cohort, WA	$n=2151$, 14 years	Parental SES	Asthma
43	Rebecca Giallo, 2015	Cohort, National	$n=4164$, 6–7 years	Maternal depression	Asthma
44	R J Adams, 2004	Cross-sectional, WA, NT, SA	$n=7619$, adult	Psychological distress	Asthma
45	Joan Cunningham, 2010	Cross-sectional, National	$n=20849$, adult	SES, ethnicity	Asthma
46	Carrington CJS, 2017	Cohort, National	$n=1239$, 5–10 years	Racial discrimination	Asthma

NO₂ = Nitrogen dioxide; CO = Carbon monoxide; PM₁₀ = particulate matter 10 micrometers or less in diameter; PM_{2.5} = particulate matter 2.5 micrometers or less in diameter; O₃ = Ozone; SO₂ = Sulfur dioxide; VOCs = Volatile organic compounds; bsp = measurement of light scattering of dry particles; ETS = Environmental tobacco smoking, SES = Socioeconomic status, WA = Western Australia, ACT = Australian Capital Territory, NSW = New South Wales, NT = Northern Territory.

the odds ratio (OR) as the measurement of association between exposures and outcome, some studies reported relative risk (RR). We consider both ORs and RRs together for meta-analysis as we assumed that the RRs (in six articles only) would be close to ORs due

to the low prevalence rate of the outcome (22). Where studies showed multiple estimates stratified analysis (e.g. stratified by age groups, locations), all of them were included in meta-analysis under the same author name. For a specific exposure group, different studies

used different 'unit of change' (e.g. per IQR change; per unit change; per 10 units change etc.) to calculate the association with the outcome. So, we standardized the 'unit of change' and re-calculated (23) the risk with their 95% CIs based on the standardized 'unit of change' to keep consistency among the estimates across the studies before doing pooled analysis. We elaborated Forest-Plot and estimated weighted overall association and their 95% CI following quality effects (QE) model (24), although random effects (RE) model (25) estimates were also generated (for comparison, see Figures S13-14). However, we considered the pooled estimates of QE model instead of the traditional RE model for a specific environmental exposure for asthma-symptoms in our study given the overwhelming evidence in support of the performance of this method over the RE method in meta-analysis (26,27). The heterogeneity of the articles was reported by the I^2 that measures the proportion of total variance between studies (28). We checked for publication bias through visualization by funnel plot and Doi plot (29). The asymmetric plot signifies the publication bias, which was measured through the LFK index of the Doi plot (29). All the analyses were conducted using the MetaXL software version 5.3 (30).

3. Results

3.1. Search outcome

Out of 4799 references, 46 articles were included for final review and 28 for meta-analysis (Figure 1) as only these studies reported OR ($n=22$) or RR ($n=06$) with their 95% CI, and at least three studies had similar environmental exposures for asthma-symptoms.

3.2. Study characteristics

The 46 articles presented data of 137840 individuals of different ages. Four studies used nationally representative samples while the others collected data from different cities or states (Figure S1), with Western Australia and Victoria represented in a higher number of studies (9/46 each) followed by Tasmania (8/46) and New South Wales (7/46). Most studies (65%) reported on children, 20% on adults, and 15% on all ages (Figure S2). Most of the studies ($n=30$) were cross-sectional in design; however, 10 of them were cohort/time series, and six of them were case-control/case-crossover studies (Table 2). Based on the quality assessment (Table S2), 17 studies were high quality, scoring 8–9 out of 9, and the rest scored 6–7 out of nine (Table S3).

3.3. Systematic review

We found 23 individual studies that reported 12 different family environmental exposures; 18 individual studies reported ten different neighborhood environmental exposures and their association with asthma-symptoms. We found five individual studies that described five different psychosocial environmental factors and their association with asthma-symptoms.

Studies reported different indoor or household environmental exposures such as ETS, indoor fungi, dust mites, synthetic bedding, gas heaters (flued/unflued), volatile organic compounds (VOCs), formaldehyde, pets, carpet, building materials and the number of people living in the house. All such exposures were associated with asthma-symptoms, and showed differing levels of association.

Four individual studies showed the association of ETS with asthma-symptoms among the population of different ages. These studies showed a variable degree of risk for asthma-symptoms due to ETS exposure where the adjusted risk or odds ratio ranged from 1.46 to 4.26 (31–34) (Table S4). Most of the studies conducted in children reported the association of parental smoking with asthma-symptoms of their children. One cross-sectional study reported maternal smoking at home increased the risk of asthma-symptoms among their children (aRR 1.52, 95% CI 1.01–2.29) (34). Sly et al. reported that ETS exposure in the parents' car also increased the risk of current wheeze (aOR 1.55, 95% CI 1.02–2.35) for children (32). Two studies in adults showed ETS to be associated with current asthma-symptoms in nonsmokers (aOR 2.09; 95% CI 1.30–3.35) in the domestic environment (33), and in the workplace (aOR 4.26, 95% CI 1.78–10.21) (31).

Use of synthetic pillows and/or quilts was also found to be a potential indoor environmental exposure related to asthma-symptoms. One cross-sectional survey reported that using a synthetic quilt was associated with asthma-symptoms (aOR 1.67, 95% CI 1.05–2.65) compared to using a cotton-made quilt (35). The risk of asthma-symptoms was even higher when two or more synthetic items were used in an infant's bed (aOR 2.10, 95% CI 1.15–3.82) (36). However, Ponsonby et al. reported that synthetic quilts were associated with wheeze only when the children slept in a supine position; for non-supine sleepers, overlying synthetic-quilt use was not associated with wheeze (37).

Two studies on children reported that using fume-emitting heaters or gas heaters inside the bedroom was associated with the exacerbation of

asthma-symptoms (aRR 1.92; 95% CI 1.33–2.76) or recent wheeze (aRR 1.44, 95% CI 1.11–1.86) (34,38). Unflued gas heaters were also found to develop wheeze in older individuals (>55 years) (aOR 1.25, 95% CI 1.05–1.50) (39).

Although some studies showed that there was no significant association of asthma-symptoms with the exposure to total fungal spores, some specific fungal spores [such as *Cladosporium* (aOR 1.68, 95% CI 1.04–2.72), *Alternaria* (aOR 1.07, 95% CI 1.03–1.11), *Coprinus* (aOR 1.04, 95% CI 1.01–1.07)] had a greater association with hospitalization for childhood asthma (40–42).

House dust mites (HDM) were also reported as a potential risk for asthma. Ponsonby et al. reported that although HDM sensitization was strongly associated with frequent wheezing (aRR 19.61; 95% CI 6.94–55.56), it had a modest association with ever developed asthma-symptoms (aRR, 1.65; 95% CI 1.30–2.09) (43). Some studies showed the overall risk of asthma-symptoms varied with the sensitization of different concentrations of HDM in the household (42,44–46) (Table S4). The odds for asthma were different for HDM in different locations (bed, floor, etc.) (45), or for different types of HDM such as Der p 1 and Der f 1 (42). However, HDM allergen *Dermatophagoides pteronyssinus* (Der p) was most measured and had various degree of associations (43–45). There were some other indoor environmental exposures for asthma that were revealed in this review, including volatile organic compounds (VOCs) (46), formaldehyde (47), having a pet (34,42,48), and the presence of carpet (34).

Several neighborhood environmental exposures showed an association with asthma-symptoms. Most of these exposures were the indicators of air quality assessed by the amount of nitrogen dioxide (NO₂), carbon monoxide (CO), particulate matter 10 micrometers or less in diameter (PM₁₀), particulate matter 2.5 micrometers or less in diameter (PM_{2.5}), ozone (O₃), sulfur dioxide (SO₂) and pollen. One study investigated the association between the amount of neighborhood greenspace and a decrease in asthma-symptoms (49).

Our search found 12 studies that assessed NO₂ levels in the air and its association with asthma-symptoms. Four studies evaluated the level of NO₂ in the air primarily due to traffic-related air pollution and found a positive association with asthma-symptoms (44,50–52). However, eight studies found no statistically significant associations (52–59). Levels of CO in the air were assessed in three studies, with two reported positive association (50,60) and other study reported no association (55). The amount

of ozone (O₃) in the air showed no statistically significant association for asthma-symptoms in most studies (50,53–57). PM₁₀ was positively associated with asthma-symptoms per IQR increase of PM₁₀ (53,59,61,62). However, two studies reported no association (50,54). Particulate matter 2.5 micrometers (PM_{2.5} or less in diameter) was assessed in four studies (50,55,59,63), none of which reported association with asthma-symptoms.

Other outdoor exposures, such as living less than 200 m from a major road was associated with current wheeze (aOR, 1.38; 95% CI, 1.06–1.80) (52). Six studies examined the level of pollen in the air and its association with asthma-symptoms. Although we could not perform pooled analysis due to the lack of odds or risk ratio (most of the studies did linear regression), out of six studies, five studies reported statistically significant association with asthma-symptoms due to the increase of pollen count in the air (57,59,64–66). In our search, we also found one article regarding the relation between green space and asthma-symptoms. In this paper, Xiaoqi Feng et al. found the association between heavy traffic and asthma to be significantly lower for participants living in areas with over 40% greenspace coverage (aOR 0.32, 95% CI 0.12–0.84). However, when children were exposed to high-traffic volumes and areas with zero to 20% green space quantity, the risk of asthma was significantly high (aOR 1.87, 95% CI 1.37–2.55) (49).

We have found five studies that showed the association of different psychosocial-environmental exposures and asthma symptoms. Kozyrskyj et al. found a two-fold increased risk of asthma symptoms in children who had lived in a low-income family since birth (67). Another study from a nationally representative sample showed higher odds for asthma symptoms in non-indigenous people with the lowest household income than the highest household income (68). Asthma-symptoms in childhood were significantly associated (aOR 2.36, 95% CI 1.61–3.45) with the depressive illnesses of their mothers (69). Psychological distress in adults was also found more frequently in those with asthma-symptoms (17.9% v 12.2%, $p=0.01$) than those who did not suffer such symptoms (70). Racial discrimination, one of the causes of psychological distress, was found to be associated (aOR 2.04, 95% CI 1.19–3.48) with asthma-symptoms in Indigenous children (71).

3.4. Meta-analysis

Twenty-seven articles included in meta-analysis were divided into two groups: family-environmental factors and neighborhood-environmental factors.

Meta-analysis was conducted for ETS, synthetic bedding, gas heaters, and total fungal spore with the estimates derived from individual studies. Among them, ETS showed an association with asthma-symptoms. Exposure to passive smoking significantly increased the odds of exacerbating asthma-symptoms (OR 1.69, 95% CI 1.19–2.38). The use of synthetic bedding (OR 1.91, 95% CI 1.48–2.47) and gas heaters (OR 1.40, 95% CI 1.12–1.76) was also associated with exacerbating asthma-symptoms (Figure 2). Pooled analysis of three studies for total fungal spore (per 100 spores/ m^3 increase) showed no statistically significant association (OR 1.01, 95% CI 0.94–1.07) (Figure 2).

Estimates of ten studies were included in the meta-analysis; the overall association of NO_2 [for per 10 parts per billion (ppb) increase] with asthma-symptoms was not statistically significant (OR 1.04, 95% CI 0.98–1.10). Neither did exposure to an increased amount of other pollutant gases such as carbon monoxide [per parts per million (ppm) increase] (OR 1.22, 95% CI 0.88–1.70) and ozone (per ppb increase) (OR 1.00, 95% CI 0.99–1.02) show statistically significant association with asthma-symptoms. The presence of an increased amount of particulate matters such as PM_{10} (per $10 \mu\text{g}/\text{m}^3$ increase) (OR 1.05, 95% CI 0.96–1.15); $\text{PM}_{2.5}$ (per $\mu\text{g}/\text{m}^3$ increase)

(OR 1.01, 95% CI 0.98–1.05); and total pollen (per 10 grains/ m^3 increase) also showed no association (Figure 3).

4. Discussion

This is the first systematic review and meta-analysis to identify the potential family, neighborhood and psychosocial environmental exposures and their association with exacerbating asthma-symptoms among Australian children and adults. We found that family environmental exposures such as ETS using synthetic bedding and gas heaters were positively associated with asthma-symptoms in the pooled analysis. Individual studies in Australia also reported that some psychosocial factors such as parental socioeconomic condition, ethnicity, racial discrimination, maternal depression, and psychological distress were associated with asthma-symptoms in different populations. Although this review found several neighborhood environmental exposures, especially various air pollutants like NO_2 , CO, PM_{10} , $\text{PM}_{2.5}$, and O_3 , to be associated with asthma-symptoms, meta-analysis failed to prove any statistical significance. However, the studies had heterogeneity in measurements, study

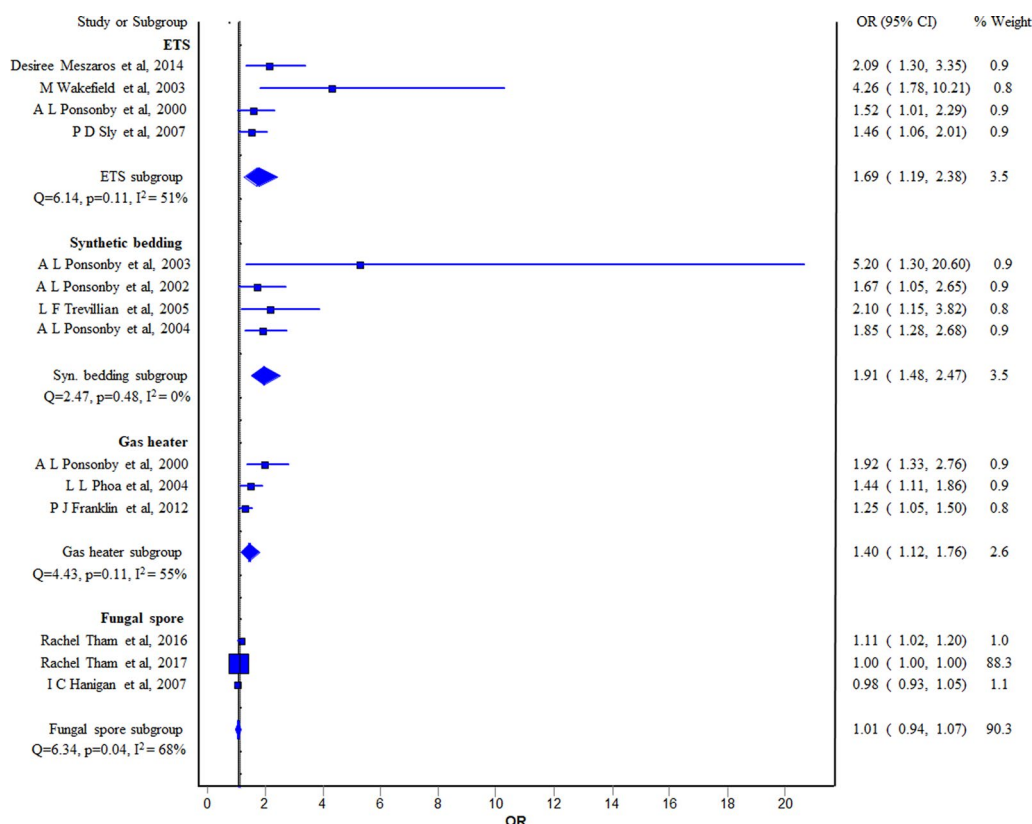


Figure 2. Forest plot showing the overall association of different family environmental factors with asthma-symptoms.

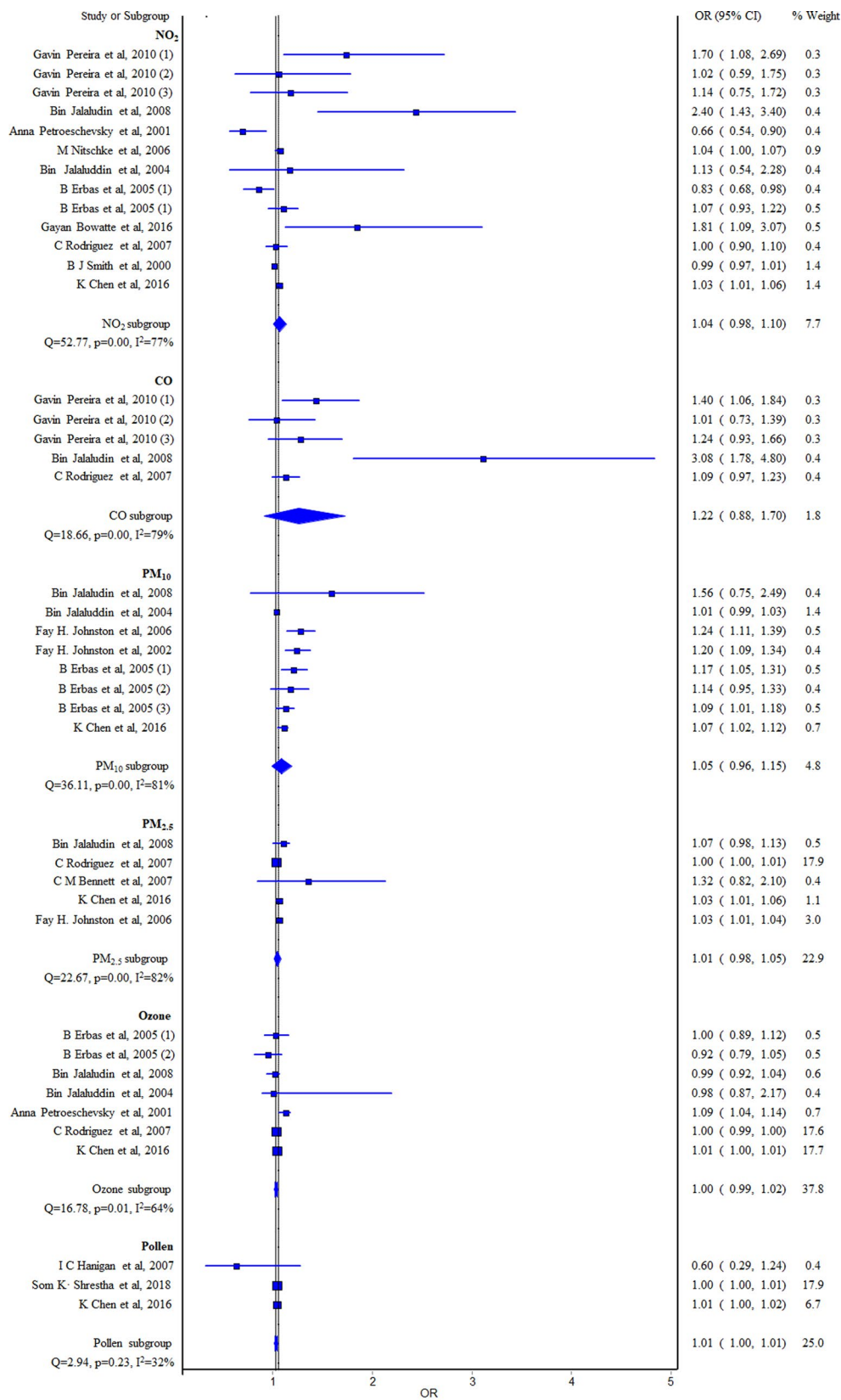


Figure 3. Forest plot showing the overall association of different neighborhood environmental factors with asthma-symptoms.

population and locations, which require further consideration.

As expected, the most commonly reported indoor exposure was ETS (31–34). The main sources of ETS in Australia were identified as smoking by a parent or other family member at home and secondhand smoking in the workplace. Children were the main victims of ETS, exposed to their parents' smoking, especially mothers, at home (33,34), or even in the car (32). Several studies across the world have demonstrated the association between ETS and childhood asthma-symptoms (72). A review article showed that up to 70% of children are exposed to ETS globally; maternal smoking and ETS exposure, influence infant lung development and are associated with childhood upper and lower respiratory tract infections, including asthma-symptoms (72). Maternal smoking, both antenatal and postnatal, is detrimental to several respiratory outcomes in children, including asthma-symptoms. Evidence also suggests that secondhand smoke exposure is a risk factor for new-onset asthma among adults and exacerbates preexisting adult asthma (73). ETS affects the immune function with a strong emphasis on the airway. Cigarette smoke alters a myriad of signaling pathways and immune responses, some of which are implicated in the development of allergic diseases like asthma (74). There are also other mechanisms how ETS causes asthma-symptoms, including a direct irritant effect of ETS.

Our review has also identified other family environmental factors that were significantly associated with asthma-symptoms in Australia, specifically the use of synthetic bedding and gas heaters. The synthetic bedding items have higher house dust mite allergen levels than feather-bedding items. It increases exposure to VOCs and is more prone to capture cat and dog allergens than feather pillows. Furthermore, the firmer weave of feather pillows makes them more protective in providing barriers to different allergens, leading to respiratory-wall irritation (37). Thus, household bedding should get extra attention where an atopic or asthma-prone child lives.

Although flued gas heaters have a flue to carry the exhaust gases away from the fireplace, using a flued gas heater inside was significantly associated with the exacerbation of childhood asthma-symptoms or recent wheeze (34,38). The pathophysiology of asthma-symptoms in this instance stems from respiratory mucosal irritation caused by NO₂ release from gas heaters (38). The randomized controlled trial on

heater replacement showed a significant reduction of NO₂ exposure and hence the prevalence of asthma (75). Unflued gas heaters can emit more NO₂ as they do not have any flue. One of our reviewed studies showed children exposed to either unflued or flued gas heaters in infancy had a similar risk for asthma-symptoms (34). The detrimental effect of unflued gas heaters in developing wheeze was also found in older people (>55 years) as they usually exposed greater time to this type of heaters due to increased need for heating, and more time spent indoors (39).

Although house dust mite and fungi exposures were associated with asthma-symptoms in some studies in Australia, the pooled estimate was not statistically significant. Some studies showed that the overall association with asthma-symptoms varied with the sensitization of different concentrations of HDM in the household (42,44–46). The odds for asthma-symptoms were different for HDM in different locations (bed, floor, etc.) (45), and for different allergens such as Der p 1, Der f 1, or in different concentrations (42–45). Dog dander is the principal source of Can f 1, and cat dander for Fel d 1 allergens (76). In places where pets live, the concentrations of HDM and these allergens are found to be higher. Therefore, the generalization of the association of all HDM and having furry pets with asthma-symptoms would be difficult. Similar findings occur in the case of fungi exposure. In meta-analysis, we did not find any overall significant association between increased amount (100 spores/m³) of total fungal spores' exposure and asthma-symptoms. However, some studies showed that specific fungal spores such as *Cladosporium*, *Alternaria*, and *Coprinus* had significantly higher associations with asthma-symptoms (40–42).

In this review, several neighborhood environmental exposures were identified as being associated with asthma-symptoms in individual studies. However, none of the exposures showed a significant association for asthma-symptoms in the pooled analysis. Our pooled analysis only included the association of outcome with same day lag of different exposures to make the exposures' time consistent for all studies. Most of the neighborhood environmental exposures were indicators of air quality. These are the various gases and particles in the air such as NO₂, CO, PM₁₀, PM_{2.5} and SO₂; the presence of these gases and particles in increased amounts indicates air pollution, especially traffic-related air pollution (TRAP) (77). TRAP is a type of air pollution that comes from

emissions due to the fossil-fuel combustion of motor vehicles. Most of the mentioned gases result from the burning of fossil fuels. TRAP was identified as the largest anthropogenic contributor to ambient air pollution in many cities (77). Many studies have reported the association between asthma-symptoms and local variation in traffic patterns within communities or neighborhoods (78). Although this evidence indicates that living near heavy traffic is associated with increased rates of asthma symptoms, some well-designed studies have found weak or no association (79). There is still controversy regarding the overall association of TRAP with exacerbating asthma-symptoms. Our review has also identified this inconsistency in different studies in Australia. Only four studies on increased NO₂ in air found a significant association with asthma-symptoms; eight studies did not. Similar patterns were found in other air pollutants (CO, SO₂, PM₁₀, PM_{2.5}, Ozone, etc.). Most of them had no association or weak association with asthma-symptoms. The reasons for these variable results are perhaps the heterogeneity of the methodologies, study populations, locations, and the measurements of outcome variables. Variabilities of results were found even in the same study for different locations, times (same day, different log days) (50,53) or diurnal variations (44). Another probable reason for this heterogeneity of results across the different studies would be that the measurements of these different air pollutants were taken from the monitoring stations of the respective study areas. The monitoring stations in every area do not monitor the same pollutants, limiting the exposure measurement's confidence. Furthermore, this indirect measurement may not accurately determine personal exposure to ambient pollutants (55). A prior study reported that air pollution levels recorded at network-monitoring stations are often poorly related to personal exposure (80). Based on the air quality analysis from 1999–2008 in Australia's major urban and regional monitoring regions, the national report on air quality in Australia reported significant decreases in the levels of several air pollutants in the last decade. These improvements are largely due to better standards for fuel quality and motor-vehicle emissions, which may explain the overall low association of air pollutants for asthma-symptoms in Australia. Although this review revealed that the outdoor air pollutants were not significantly associated with asthma-symptoms, individuals may expose to these pollutants at indoors in a higher concentrations and longer periods, which needs further investigation.

Besides TRAP, pollen was also identified as a potential air pollutant associated with asthma-symptoms in Australian studies. Most of the studies showed a significant association between pollen count in the air and the exacerbation of asthma-symptoms. Many types of flowering plants depend on the wind to distribute their pollen. These small, light, dry pollen grains can be easily breathed in by humans. When inhaled, proteins and glycoproteins associated with these pollens can interact with the immune systems of sensitive individuals to produce an allergic response in the form of hay fever or allergic asthma (81). In Australia, the pollen count varies with seasons, geographic locations, and wind direction (82). Thus, variabilities of the association of pollen with asthma were found in our reviewed studies.

It is evident that psychological stress has a deleterious effect on atopic disorders and asthma-symptoms (7). Precursors of stress are variable: what is stressful for one person may not be for another. Several studies outside of Australia reported that various psychological factors like maternal stress/depression, neighborhood safety, housing condition, discrimination, parents' socioeconomic status, family support and peer support etc. may ultimately develop stress and were associated with asthma-symptoms in both children and adults (83). However, in our review, we have found a scarcity of studies in Australia to evaluate the association between different psychological factors or stressors and asthma-symptoms. Although SES in the Indigenous people in Australia has had no independent association with asthma, Indigenous children exposed to direct and persistent vicarious racial discrimination were more likely to have asthma as well as mental health problems (71). Several studies worldwide have reported that maternal depressive symptoms are detrimental to several health outcomes in children. It has been also found that maternal depressive symptoms have been associated with increased asthma morbidity of their children, perhaps due to impairment of the mother's ability to manage her children with asthma (84) effectively. An Australian study from a nationally representative sample also reported findings consistent with this psychosocial factor (69).

5. Strength and limitations

The main strength of this review is its robust methodology, including quality scoring and use of QE model for meta-analysis (24). As we considered various types of environmental exposures in a single review, we expected variability in the study methodologies and outcomes among the studies. To address these

limitations, we did quality scoring (used different standardize tools for different types of studies) and followed the QE model to conduct the meta-analysis (24). This approach incorporates the methodological heterogeneity across the studies and reduces the risk-of-bias assessment (24,85). Thus, our study has produced relatively unbiased results. The main limitation of our study was having a small number of individual studies for a specific exposure to conduct a meta-analysis. We could not perform meta-analysis for some environmental exposures due to the small number (<3) of studies for a particular exposure group. We could not separately assess the association of different environmental exposures stratified by age groups, seasons, time of exposure, and time of outcome occurred due to the same reason. We thus considered the association of a generic exposure rather than the association of every sub-class for meta-analysis. However, we have included every study in the systematic review.

6. Conclusion

This review has identified several family, neighborhood and psychosocial environmental exposures that have a significant association with developing or exacerbating asthma-symptoms or asthma-related morbidity. Review and pooled analysis identified that ETS, synthetic bedding, gas heaters and pollen in the air were the most common factors that showed significant association with asthma-symptoms in Australia. This review also identified some important psychosocial environmental factors, such as parental socioeconomic condition, ethnicity, racial discrimination, maternal depression, and psychological distress, as being significantly associated with asthma-symptoms. Conducting intervention studies to reduce these detrimental factors would be of potential public health importance to prevent asthma-symptoms. However, our reviewed studies were heterogeneous in terms of population, measurements of exposures and outcome where stratified analyses were not possible due to small number of studies. The relatively small number of studies for a specific exposure may also undermine the result of our pooled analyses. Further longitudinal studies with common exposures for a defined population may strengthen the results of our review.

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Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article.

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8. References

1. Organization WH. Asthma 2019. Available from: <https://www.who.int/news-room/q-a-detail/chronic-respiratory-diseases-asthma>.
2. To T, Stanojevic S, Moores G, Gershon AS, Bateman ED, Cruz AA, Boulet L-P. Global asthma prevalence in adults: findings from the cross-sectional world health survey. *BMC Public Health*. 2012;12(1):204. doi:10.1186/1471-2458-12-204.
3. Australian Institute of Health Welfare. Asthma. Canberra: Australian Institute of Health Welfare; 2020.
4. Australian Bureau of Statistics. 4364.0 - National Health Survey: Summary of Results, 2001.
5. Asthma Australia. Asthma Statistics and Facts. Available from: <https://asthma.org.au/about-asthma/understanding-asthma/statistics/> [accessed 2 April 2020].
6. Vernon MK, Wiklund I, Bell JA, Dale P, Chapman KR. What do we know about asthma triggers? A review of the literature. *J Asthma*. 2012;49(10):991-998. doi:10.3109/02770903.2012.738268.
7. Plourde AP, Lavoie KLP, Raddatz CB, Bacon SLP. Effects of acute psychological stress induced in laboratory on physiological responses in asthma populations: a systematic review. *Respir Med*. 2017;127:21-32. doi:10.1016/j.rmed.2017.03.024.
8. Chida Y, Hamer M, Steptoe A. A bidirectional relationship between psychosocial factors and atopic disorders: a systematic review and meta-analysis. *Psychosom Med*. 2008;70(1):102-116. doi:10.1097/PSY.0b013e31815c1b71.
9. Burbank AJ, Sood AK, Kesic MJ, Peden DB, Hernandez ML. Environmental determinants of allergy and asthma in early life. *J Allergy Clin Immunol*. 2017;140(1):1-12. doi:10.1016/j.jaci.2017.05.010.
10. Kanchongkittiphon W, Mendell MJ, Gaffin JM, Wang G, Phipatanakul W. Indoor environmental exposures and exacerbation of asthma: an update to the 2000 review by the Institute of Medicine. *Environ Health*

- Perspect. 2015;123(1):6–20. doi:[10.1289/ehp.1307922](https://doi.org/10.1289/ehp.1307922).
11. Vork KL, Broadwin RL, Blaisdell RJ. Developing asthma in childhood from exposure to secondhand tobacco smoke: insights from a meta-regression. *Environ Health Perspect.* 2007;115(10):1394–1400. doi:[10.1289/ehp.10155](https://doi.org/10.1289/ehp.10155).
 12. McLeish AC, Zvolensky MJ. Asthma and cigarette smoking: a review of the empirical literature. *J Asthma.* 2010;47(4):345–361. doi:[10.3109/02770900903556413](https://doi.org/10.3109/02770900903556413).
 13. Apelberg BJ, Aoki Y, Jaakkola JJ. Systematic review: exposure to pets and risk of asthma and asthma-like symptoms. *J Allergy Clin Immunol.* 2001;107(3):455–460. doi:[10.1067/mai.2001.113240](https://doi.org/10.1067/mai.2001.113240).
 14. Burke H, Leonardi-Bee J, Hashim A, Pine-Abata H, Chen Y, Cook DG, Britton JR, McKeever TM. Prenatal and passive smoke exposure and incidence of asthma and wheeze: systematic review and meta-analysis. *Pediatrics.* 2012;129(4):735–744. doi:[10.1542/peds.2011-2196](https://doi.org/10.1542/peds.2011-2196).
 15. Hartley K, Ryan P, Brokamp C, Gillespie GL. Effect of greenness on asthma in children: A systematic review. *Public Health Nurs.* 2020;37(3):453–460. doi:[10.1111/phn.12701](https://doi.org/10.1111/phn.12701).
 16. Apfelbacher C, Frew E, Xiang A, Apfel A, Smith H. Assessment of pet exposure by self-report in epidemiological studies of allergy and asthma: a systematic review. *J Asthma.* 2016;53(4):363–373. doi:[10.3109/02770903.2015.1099161](https://doi.org/10.3109/02770903.2015.1099161).
 17. Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart LA, PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Syst Rev.* 2015;4:1–1. (doi:[10.1186/2046-4053-4-1](https://doi.org/10.1186/2046-4053-4-1)).
 18. Morgan RL, Whaley P, Thayer KA, Schünemann HJ. Identifying the PECO: a framework for formulating good questions to explore the association of environmental and other exposures with health outcomes. *Environ Int.* 2018;121(Pt 1):1027–1031. doi:[10.1016/j.envint.2018.07.015](https://doi.org/10.1016/j.envint.2018.07.015).
 19. Giff A. Global strategy for asthma management and prevention; 2020.
 20. Pavord ID, Beasley R, Agusti A, Anderson GP, Bel E, Brusselle G, Cullinan P, Custovic A, Ducharme FM, Fahy JV, et al. After asthma: redefining airways diseases. *Lancet.* 2018;391(10118):350–400. doi:[10.1016/S0140-6736\(17\)30879-6](https://doi.org/10.1016/S0140-6736(17)30879-6).
 21. Peterson J, Welch V, Losos M, Tugwell P. The Newcastle-Ottawa scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. Ottawa: Ottawa Hospital Research Institute; 2011.
 22. Egger M, Smith GD, Phillips AN. Meta-analysis: principles and procedures. *BMJ.* 1997;315(7121):1533–1537. doi:[10.1136/bmj.315.7121.1533](https://doi.org/10.1136/bmj.315.7121.1533).
 23. Katz MH. Multivariable analysis a practical guide for clinicians and public health researchers. 3rd ed. Cambridge: Cambridge University Press; 2011.
 24. Doi SAR, Thalib L. A quality-effects model for meta-analysis. *Epidemiology.* 2008;19(1):94–100. doi:[10.1097/EDE.0b013e31815c24e7](https://doi.org/10.1097/EDE.0b013e31815c24e7).
 25. DerSimonian R, Laird N. Meta-analysis in clinical trials. *Controlled Clin Trials.* 1986;7(3):177–188. doi:[10.1016/0197-2456\(86\)90046-2](https://doi.org/10.1016/0197-2456(86)90046-2).
 26. Doi SAR, Barendregt JJ, Khan S, Thalib L, Williams GM. Advances in the meta-analysis of heterogeneous clinical trials I: the inverse variance heterogeneity model. *Contemp Clin Trials.* 2015;45(Pt A):130–138. doi:[10.1016/j.cct.2015.05.009](https://doi.org/10.1016/j.cct.2015.05.009).
 27. Doi SAR, Furuya-Kanamori L. Selecting the best meta-analytic estimator for evidence-based practice: a simulation study. *Int J Evid-Based Healthc.* 2020;18(1):86–94. doi:[10.1097/XEB.0000000000000207](https://doi.org/10.1097/XEB.0000000000000207).
 28. Borenstein M, Higgins JP, Hedges LV, Rothstein HR. Basics of meta-analysis: I2 is not an absolute measure of heterogeneity. *Res Synth Methods.* 2017;8(1):5–18. doi:[10.1002/jrsm.1230](https://doi.org/10.1002/jrsm.1230).
 29. Furuya-Kanamori L, Barendregt JJ, Doi SAR. A new improved graphical and quantitative method for detecting bias in meta-analysis. *Int J Evid Based Healthc.* 2018;16(4):195–203. doi:[10.1097/XEB.0000000000000141](https://doi.org/10.1097/XEB.0000000000000141).
 30. Barendregt JJ, Doi SA. MetaXL user guide version 5.3. Queensland, Australia: EpiGear International Pty Ltd. 2016.
 31. Wakefield M, Trotter L, Cameron M, Woodward A, Inglis G, Hill D. Association between exposure to workplace secondhand smoke and reported respiratory and sensory symptoms: cross-sectional study. *J Occup Environ Med.* 2003;45(6):622–627. doi:[10.1097/01.jom.0000069242.06498.86](https://doi.org/10.1097/01.jom.0000069242.06498.86).
 32. Sly PD, Devereux M, Kusel MM, Holt PG. Exposure to environmental tobacco smoke in cars increases the risk of persistent wheeze in adolescents. *Med J Aust.* 2007;186(6):322. doi:[10.5694/j.1326-5377.2007.tb00915.x](https://doi.org/10.5694/j.1326-5377.2007.tb00915.x).
 33. Mészáros D, Burgess J, Walters EH, Johns D, Markos J, Giles G, Hopper J, Abramson M, Dharmage SC, Matheson M. Domestic airborne pollutants and asthma and respiratory symptoms in middle age. *Respirology.* 2014;19(3):411–418. doi:[10.1111/resp.12245](https://doi.org/10.1111/resp.12245).
 34. Ponsonby AL, Couper D, Dwyer T, Carmichael A, Kemp A, Cochrane J. The relation between infant indoor environment and subsequent asthma. *Epidemiology.* 2000;11(2):128–135. doi:[10.1097/00001648-200003000-00008](https://doi.org/10.1097/00001648-200003000-00008).
 35. Ponsonby AL, Gatenby P, Glasgow N, Mullins R, Hurwitz M, McDonald T. The association between synthetic bedding and adverse respiratory outcomes among skin-prick test positive and skin-prick test negative children. *Allergy.* 2002;57(3):247–253. doi:[10.1034/j.1398-9995.2002.1s3234.x](https://doi.org/10.1034/j.1398-9995.2002.1s3234.x).
 36. Trevillian LF, Ponsonby A-L, Dwyer T, Kemp A, Cochrane J, Lim LL-Y, Carmichael A. Infant sleeping environment and asthma at 7 years: a prospective cohort study. *Am J Public Health.* 2005;95(12):2238–2245. doi:[10.2105/AJPH.2004.047191](https://doi.org/10.2105/AJPH.2004.047191).
 37. Ponsonby A-L, Dwyer T, Trevillian L, Kemp A, Cochrane J, Couper D, Carmichael A. The bedding environment, sleep position, and frequent wheeze in childhood. *Pediatrics.* 2004;113(5):1216–1222. doi:[10.1542/peds.113.5.1216](https://doi.org/10.1542/peds.113.5.1216).
 38. Phoa LL, Toelle BG, Ng K, Marks GB. Effects of gas and other fume emitting heaters on the development of asthma during childhood. *Thorax.* 2004;59(9):741–745. doi:[10.1136/thx.2003.014241](https://doi.org/10.1136/thx.2003.014241).

39. Franklin PJ, Loveday J, Cook A. Unflued gas heaters and respiratory symptoms in older people with asthma. *Thorax*. 2012;67(4):315–320. doi:[10.1136/thoraxjnl-2011-200236](https://doi.org/10.1136/thoraxjnl-2011-200236).
40. Tham R, Vicendese D, Dharmage SC, Hyndman RJ, Newbiggin E, Lewis E, O'Sullivan M, Lowe AJ, Taylor P, Bardin P, et al. Associations between outdoor fungal spores and childhood and adolescent asthma hospitalizations. *J Allergy Clin Immunol*. 2017;139(4):1140–1147 e4. doi:[10.1016/j.jaci.2016.06.046](https://doi.org/10.1016/j.jaci.2016.06.046).
41. Tham R, Katelaris CH, Vicendese D, Dharmage SC, Lowe AJ, Bowatte G, Taylor P, Burton P, Abramson MJ, Erbas B. The role of outdoor fungi on asthma hospital admissions in children and adolescents: A 5-year time stratified case-crossover analysis. *Environ Res*. 2017;154:42–49. doi:[10.1016/j.envres.2016.12.016](https://doi.org/10.1016/j.envres.2016.12.016).
42. Vicendese D, Dharmage SC, Tang ML, Olenko A, Allen KJ, Abramson MJ. Bedroom air quality and vacuuming frequency are associated with repeat child asthma hospital admissions. *J Asthma* 2015;52(7):727–731. doi:[10.3109/02770903.2014.1001904](https://doi.org/10.3109/02770903.2014.1001904).
43. Ponsonby AL, Kemp A, Dwyer T, Carmichael A, Couper D, Cochrane J. Feather bedding and house dust mite sensitization and airway disease in childhood. *J Clin Epidemiol*. 2002;55(6):556–562. doi:[10.1016/s0895-4356\(01\)00519-4](https://doi.org/10.1016/s0895-4356(01)00519-4).
44. Nitschke M, Pilotto LS, Attewell RG, Smith BJ, Pisaniello D, Martin J, Ruffin RE, Hiller JE. A cohort study of indoor nitrogen dioxide and house dust mite exposure in asthmatic children. *J Occup Environ Med*. 2006;48(5):462–469.
45. Matheson MC, Abramson MJ, Dharmage SC, Forbes AB, Raven JM, Thien FCK, Walters EH. Changes in indoor allergen and fungal levels predict changes in asthma activity among young adults. *Clin Exp Allergy*. 2005;35(7):907–913. doi:[10.1111/j.1365-2222.2005.02272.x](https://doi.org/10.1111/j.1365-2222.2005.02272.x).
46. Rumchev K, Spickett J, Bulsara M, Phillips M, Stick S. Association of domestic exposure to volatile organic compounds with asthma in young children. *Thorax*. 2004;59(9):746–751. doi:[10.1136/thx.2003.013680](https://doi.org/10.1136/thx.2003.013680).
47. Rumchev K, Spickett J, Bulsara M, Phillips M, Stick SM. Domestic exposure to formaldehyde significantly increases the risk of asthma in young children. *Eur Respir J*. 2002; 20(2):403–408. doi:[10.1183/09031936.02.00245002](https://doi.org/10.1183/09031936.02.00245002).
48. de Meer G, Toelle BG, Ng K, Tovey E, Marks GB. Presence and timing of cat ownership by age 18 and the effect on atopy and asthma at age 28. *J Allergy Clin Immunol*. 2004;113(3):433–438. doi:[10.1016/j.jaci.2003.10.008](https://doi.org/10.1016/j.jaci.2003.10.008).
49. Feng X, Astell-B T. Is neighborhood green space protective against associations between child asthma, neighborhood traffic volume and perceived lack of area safety? Multilevel analysis of 4447 Australian children. *IJERPH*. 2017;14(5):543. doi:[10.3390/ijerph14050543](https://doi.org/10.3390/ijerph14050543).
50. Jalaludin B, Khalaj B, Sheppeard V, Morgan G. Air pollution and ED visits for asthma in Australian children: a case-crossover analysis. *Int Arch Occup Environ Health*. 2008;81(8):967–974. doi:[10.1007/s00420-007-0290-0](https://doi.org/10.1007/s00420-007-0290-0).
51. Ciuk J, Volkmer RE, Edwards JW. Domestic nitrogen oxide exposure, urinary nitrate, and asthma prevalence in preschool children. *Arch Environ Health*. 2001;56(5):433–438. doi:[10.1080/00039890109604478](https://doi.org/10.1080/00039890109604478).
52. Bowatte G, Lodge CJ, Knibbs LD, Lowe AJ, Erbas B, Dennekamp M, Marks GB, Giles G, Morrison S, Thompson B, et al. Traffic-related air pollution exposure is associated with allergic sensitization, asthma, and poor lung function in middle age. *J Allergy Clin Immunol*. 2017;139(1):122–129. doi:[10.1016/j.jaci.2016.05.008](https://doi.org/10.1016/j.jaci.2016.05.008).
53. Erbas B, Kelly A-M, Physick B, Code C, Edwards M. Air pollution and childhood asthma emergency hospital admissions: estimating intra-city regional variations. *Int J Environ Health Res*. 2005;15(1):11–20. doi:[10.1080/09603120400018717](https://doi.org/10.1080/09603120400018717).
54. Jalaludin BB, O'Toole BI, Leeder SR. Acute effects of urban ambient air pollution on respiratory symptoms, asthma medication use, and doctor visits for asthma in a cohort of Australian children. *Environ Res*. 2004;95(1):32–42. doi:[10.1016/S0013-9351\(03\)00038-0](https://doi.org/10.1016/S0013-9351(03)00038-0).
55. Rodriguez C, Tonkin R, Heyworth J, Kusel M, De Klerk N, Sly PD, Franklin P, Runnion T, Blockley A, Landau L, et al. The relationship between outdoor air quality and respiratory symptoms in young children. *Int J Environ Health Res*. 2007;17(5):351–360. doi:[10.1080/09603120701628669](https://doi.org/10.1080/09603120701628669).
56. Petroschevsky A, Simpson RW, Thalib L, Rutherford S. Associations between outdoor air pollution and hospital admissions in Brisbane, Australia. *Arch Environ Health*. 2001;56(1):37–52. doi:[10.1080/00039890109604053](https://doi.org/10.1080/00039890109604053).
57. Erbas B, Chang J-H, Dharmage S, Ong EK, Hyndman R, Newbiggin E, Abramson M. Do levels of airborne grass pollen influence asthma hospital admissions? *Clin Exp Allergy*. 2007;37(11):1641–1647. doi:[10.1111/j.1365-2222.2007.02818.x](https://doi.org/10.1111/j.1365-2222.2007.02818.x).
58. Smith BJ, Nitschke M, Pilotto LS, Ruffin RE, Pisaniello DL, Willson KJ. Health effects of daily indoor nitrogen dioxide exposure in people with asthma. *Eur Respir J*. 2000;16(5):879–885. doi:[10.1183/09031936.00.16587900](https://doi.org/10.1183/09031936.00.16587900).
59. Chen K, Glonek G, Hansen A, Williams S, Tuke J, Salter A, Bi P. The effects of air pollution on asthma hospital admissions in Adelaide, South Australia, 2003–2013: time-series and case-crossover analyses. *Clin Exp Allergy*. 2016;46(11):1416–1430. doi:[10.1111/cea.12795](https://doi.org/10.1111/cea.12795).
60. Pereira G, Cook A, Vos AJBM, Holman CDJ. A case-crossover analysis of traffic-related air pollution and emergency department presentations for asthma in Perth, Western Australia. *Med J Aust*. 2010;193(9):511–514. doi:[10.5694/j.1326-5377.2010.tb04034.x](https://doi.org/10.5694/j.1326-5377.2010.tb04034.x).
61. Johnston FH, Webby RJ, Pilotto LS, Bailie RS, Parry DL, Halpin SJ. Vegetation fires, particulate air pollution and asthma: a panel study in the Australian monsoon tropics. *Int J Environ Health Res*. 2006;16(6):391–404. doi:[10.1080/09603120601093642](https://doi.org/10.1080/09603120601093642).
62. Johnston FH, Kavanagh AM, Bowman DM, Scott RK. Exposure to bushfire smoke and asthma: an ecological study. *Med J Aust*. 2002;176(11):535–538. doi:[10.5694/j.1326-5377.2002.tb04551.x](https://doi.org/10.5694/j.1326-5377.2002.tb04551.x).
63. Bennett CM, Simpson P, Raven J, Skoric B, Powell J, Wolfe R, Walters EH, Abramson MJ. Associations between ambient PM2.5 concentrations and respiratory

- symptoms in Melbourne, 1998–2005. *J Toxicol Environ Health*. 2007;70(19):1613–1618. doi:[10.1080/15287390701434695](https://doi.org/10.1080/15287390701434695).
64. Bass DJ, Delpech V, Beard J, Bass P, Walls RS. Late summer and fall (March–May) pollen allergy and respiratory disease in Northern New South Wales, Australia. *Ann Allergy Asthma Immunol*. 2000;85(5):374–381. doi:[10.1016/S1081-1206\(10\)62549-5](https://doi.org/10.1016/S1081-1206(10)62549-5).
 65. Erbas B, Akram M, Dharmage SC, Tham R, Dennekamp M, Newbiggin E, Taylor P, Tang MLK, Abramson MJ. The role of seasonal grass pollen on childhood asthma emergency department presentations. *Clin Exp Allergy*. 2012;42(5):799–805. doi:[10.1111/j.1365-2222.2012.03995.x](https://doi.org/10.1111/j.1365-2222.2012.03995.x).
 66. Shrestha SK, Katelaris C, Dharmage SC, Burton P, Vicendese D, Tham R, Abramson MJ, Erbas B. High ambient levels of grass, weed and other pollen are associated with asthma admissions in children and adolescents: a large 5-year case-crossover study. *Clin Exp Allergy*. 2018;48(11):1421–1428. doi:[10.1111/cea.13225](https://doi.org/10.1111/cea.13225).
 67. Kozyrskyj AL, Kendall GE, Jacoby P, Sly PD, Zubrick SR. Association between socioeconomic status and the development of asthma: analyses of income trajectories. *Am J Public Health*. 2010;100(3):540–546. doi:[10.2105/AJPH.2008.150771](https://doi.org/10.2105/AJPH.2008.150771).
 68. Cunningham J. Socioeconomic status and self-reported asthma in Indigenous and non-Indigenous Australian adults aged 18–64 years: analysis of national survey data. *Int J Equity Health*. 2010;9(1):18. doi:[10.1186/1475-9276-9-18](https://doi.org/10.1186/1475-9276-9-18).
 69. Giallo R, Bahreinian S, Brown S, Cooklin A, Kingston D, Kozyrskyj A. Maternal depressive symptoms across early childhood and asthma in school children: findings from a longitudinal Australian population based study. *PLoS One*. 2015;10(3):e0121459. doi:[10.1371/journal.pone.0121459](https://doi.org/10.1371/journal.pone.0121459).
 70. Adams RJ, Wilson DH, Taylor AW, Daly A, d’Espaignet ET, D, Grande E, Ruffin RE. Psychological factors and asthma quality of life: a population based study. *Thorax*. 2004;159(11):930–935. doi:[10.1136/thx.2003.010256](https://doi.org/10.1136/thx.2003.010256).
 71. Shepherd CC, Li J, Cooper MN, Hopkins KD, Farrant BM. The impact of racial discrimination on the health of Australian Indigenous children aged 5–10 years: analysis of national longitudinal data. *Int J Equity Health*. 2017;16(1):116. doi:[10.1186/s12939-017-0612-0](https://doi.org/10.1186/s12939-017-0612-0).
 72. Vanker A, Gie RP, Zar HJ. The association between environmental tobacco smoke exposure and childhood respiratory disease: a review. *Expert Rev Respir Med*. 2017;11(8):661–673. doi:[10.1080/17476348.2017.1338949](https://doi.org/10.1080/17476348.2017.1338949).
 73. Eisner MD. Passive smoking and adult asthma. *Immunol Allergy Clin North Am*. 2008;28(3):521–537. viii. doi:[10.1016/j.iac.2008.03.006](https://doi.org/10.1016/j.iac.2008.03.006).
 74. Strzelak A, Ratajczak A, Adamiec A, Feleszko W. Tobacco smoke induces and alters immune responses in the lung triggering inflammation, allergy, asthma and other lung diseases: a mechanistic review. *IJERPH*. 2018;15(5):1033. doi:[10.3390/ijerph15051033](https://doi.org/10.3390/ijerph15051033).
 75. Pilotto LS, Nitschke M, Smith BJ, Pisaniello D, Ruffin RE, McElroy HJ. Randomized controlled trial of unflued gas heater replacement on respiratory health of asthmatic schoolchildren. *Int J Epidemiol*. 2004;33(1):208–211. doi:[10.1093/ije/dyh018](https://doi.org/10.1093/ije/dyh018).
 76. Dávila I, Domínguez-Ortega J, Navarro-Pulido A, Alonso A, Antolín-Amerigo D, González-Mancebo E, Martín-García C, Núñez-Acevedo B, Prior N, Reche M, et al. Consensus document on dog and cat allergy. *Allergy*. 2018;73(6):1206–1222. doi:[10.1111/all.13391](https://doi.org/10.1111/all.13391).
 77. Hilpert M, Johnson M, Kioumourtoglou M-A, Domingo-Relloso A, Peters A, Adria-Mora B, Hernández D, Ross J, Chillrud SN. A new approach for inferring traffic-related air pollution: Use of radar-calibrated crowd-sourced traffic data. *Environ Int*. 2019;127:142–159. doi:[10.1016/j.envint.2019.03.026](https://doi.org/10.1016/j.envint.2019.03.026).
 78. Gauderman WJ, Avol E, Lurmann F, Kuenzli N, Gilliland F, Peters J, McConnell R. Childhood asthma and exposure to traffic and nitrogen dioxide. *Epidemiology*. 2005;16(6):737–743.
 79. Oftedal B, Nystad W, Brunekreef B, Nafstad P. Long-term traffic-related exposures and asthma onset in schoolchildren in oslo, norway. *Environ Health Perspect*. 2009;117(5):839–844. doi:[10.1289/ehp.11491](https://doi.org/10.1289/ehp.11491).
 80. Payne-Sturges DC, Burke TA, Breyse P, Diener-West M, Buckley TJ. Personal exposure meets risk assessment: a comparison of measured and modeled exposures and risks in an urban community. *Environ Health Perspect*. 2004;112(5):589–598. doi:[10.1289/ehp.6496](https://doi.org/10.1289/ehp.6496).
 81. Traidl-Hoffmann C, Kasche A, Menzel A, Jakob T, Thiel M, Ring J, Behrendt H. Impact of pollen on human health: more than allergen carriers? *Int Arch Allergy Immunol*. 2003;131(1):1–13. doi:[10.1159/000070428](https://doi.org/10.1159/000070428).
 82. Australian Society of Clinical Immunology and Allergy. Pollen Allergy. 2020. Available from: <https://www.allergy.org.au/patients/allergic-rhinitis-hay-fever-and-sinusitis/pollen-allergy>.
 83. Barnhouse M, Jones BL. The impact of environmental chronic and toxic stress on asthma. *Clin Rev Allergy Immunol*. 2019;57(3):427–438. doi:[10.1007/s12016-019-08736-x](https://doi.org/10.1007/s12016-019-08736-x).
 84. Pak L, Allen PJ. The impact of maternal depression on children with asthma. *Pediatr Nurs*. 2012;38(1):11–9, 30.
 85. Stone JC, Glass K, Munn Z, Tugwell P, Doi SAR. Comparison of bias adjustment methods in meta-analysis suggests that quality effects modeling may have less limitations than other approaches. *J Clin Epidemiol*. 2020;117:36–45. doi:[10.1016/j.jclinepi.2019.09.010](https://doi.org/10.1016/j.jclinepi.2019.09.010).