



Review article

Grass pollen as a trigger of emergency department presentations and hospital admissions for respiratory conditions in the subtropics: A systematic review

Marko Simunovic^{a,*}, Divya Dwarakanath^a, Beth Addison-Smith^a, Nugroho H. Susanto^b,
Bircan Erbas^b, Philip Baker^c, Janet M. Davies^{a,d}

^a School of Biomedical Sciences, Institute for Health and Biomedical Innovation, Queensland University of Technology, Brisbane, Queensland, Australia

^b School of Public Health and Epidemiology, LaTrobe University, Bundoora, Victoria, Australia

^c School of Public Health and Social Work, Institute for Health and Biomedical Innovation, Queensland University of Technology, Brisbane, Queensland, Australia

^d Office of Research, Metro North Hospital and Health Services, Herston, Queensland, Australia

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ABSTRACT

Introduction: It is unknown if high concentration of airborne grass pollen, where subtropical grasses (*Chloridoideae* and *Panicoideae*) dominate, is a risk factor for respiratory health. Here we systematically reviewed the association between airborne grass pollen exposure and asthma emergency department (ED) presentations and hospital admissions in subtropical climates.

Objectives: A systematic review was performed to identify and summarise studies that reported on respiratory health (asthma ED presentations and hospital admissions) and airborne grass pollen exposure in subtropical climates.

Methods: Searches were conducted in: MEDLINE, Web of Science, Scopus, CINAHL (EBSCO), Embase and Google Scholar databases (1966–2019). Risk of bias was assessed using a validated quality assessment tool. A meta-analysis was planned, however due to the heterogeneity in study design it was determined inappropriate and instead a narrative synthesis was undertaken.

Results: Nineteen studies were identified for inclusion, with a total of 598,931 asthma ED presentation participants and 36,504 asthma hospital admission participants in six countries (Australia, India, Israel, Italy, Spain, USA). The narrative synthesis found airborne grass pollen appears to have a small and inconsistent increase on asthma ED presentations (judged as: probably little effect $n = 5$, may have little effect $n = 4$, no effect $n = 2$ and uncertain if there is an effect $n = 4$) and hospital admissions (judged as: probably increase slightly $n = 2$, probably little effect $n = 1$, may have a little effect $n = 1$, no effect $n = 3$ and we are uncertain if there is an effect $n = 4$) in the subtropics. Furthermore, the reported effect sizes were small and its clinical relevance may be difficult to discern.

Conclusion: Exposure to airborne grass pollen appears to have a small and inconsistent increase on asthma ED presentations and hospital admissions in the subtropics. These findings are comparable to reported observations from studies undertaken in temperate regions.

1. Introduction

The prevalence of asthma and allergic disease appears to be increasing globally, with an estimated 300 and 400 million people suffering from asthma and rhinitis respectively (Lai et al., 2009; To et al., 2012). The common coexistence of allergic disease in people with asthma, further complicates the burden of disease. Both asthma and

allergic rhinitis appear more prevalent in developed countries (Lai et al., 2009; To et al., 2012). The United Kingdom (UK) shares among the highest burden of asthma in Europe, with an estimated 10–13% of the population affected (Lai et al., 2009; To et al., 2012). While the UK is wholly located in a temperate region, other developed countries span temperate as well as subtropical climatic zones; United States of America (USA) and Australia suffer high asthma morbidity of 8 and

* Corresponding author. Simunovic School of Biomedical Sciences, Queensland University of Technology. Postal address: QIMR Berghofer Bancroft Building, 300 Herston Road, Herston, QLD, 4006, Australia.

E-mail address: m.simunovic@qut.edu.au (M. Simunovic).

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10% respectively (Australian Bureau of Statistics, 2018; Lai et al., 2009; To et al., 2012). A systematic review of observational studies reported high concentration of airborne grass pollen is a risk factor for child and adolescent asthma emergency department (ED) hospital presentations in numerous countries: USA, Canada, Australia, Spain and Israel (Erbas et al., 2018). The Melbourne thunderstorm asthma event of 21 November 2016, further showed an association between high concentration of airborne grass pollen and respiratory health (Lee et al., 2017; Rangamuwa et al., 2017; Sutherland et al., 2017; Thien et al., 2018). During the event, thunderstorm asthma was associated with an estimated 42% (95%CI: 40%, 44%) increase in the number of cases requiring emergency medical service and a 432% increase in emergency medical attendances for acute respiratory distress symptoms (Andrew et al., 2017). Research on risk of airborne grass pollen and asthma exacerbation, has primarily emanated from cooler climates where temperate grasses (*Pooideae*) dominate. The risk of airborne grass pollen on asthma ED presentations and hospital admissions may differ in regions where subtropical grasses (*Chloridoideae* and *Panicoideae*) dominate, such as parts of Americas, Africa, Australia, Asia and Europe (Osborne et al., 2014; Still et al., 2003). A knowledge gap exists in our understanding of the risk of airborne grass pollen on asthma ED presentations and hospital admissions, in populations from subtropical climates. To address this gap in knowledge, this review examined the effect of airborne grass pollen exposure on asthma ED presentations and hospital admissions in subtropical climates.

2. Methods

We conducted the review according to the published protocol: PROSPERO 2018 CRD42018109833 Available from: http://www.crd.york.ac.uk/PROSPERO/display_record.php?ID=CRD42018109833

2.1. Eligibility criteria

Studies undertaken in the subtropics were defined by the following Koppen climatic classifications: Hot semi-arid climate (BSh), Humid subtropical climate (Cfa), Hot-summer Mediterranean climate (Csa), Warm-summer Mediterranean climate (Csb), Monsoon-influenced humid subtropical climate (Cwa) and Tropical savanna climate (Aw) (Kottek et al., 2006). The population studied was people (all ages) visiting an emergency department (presentation) or being admitted into a hospital (admission), with a diagnosis of asthma or asthma like symptoms. Only studies reporting airborne grass pollen concentrations were considered.

2.2. Search strategy

The focus of this search was to identify literature that reported respiratory health burden and severity (asthma hospital presentations or admissions) in relation to airborne grass pollen exposure in subtropical climate zones. A systematic search was performed in the following databases: MEDLINE, Web of Science, Scopus, CINAHL, Embase and Google Scholar, with a date restriction 1966 to 2019. We reviewed the reference lists of included studies for additional studies. The search strategy for each database can be found in [Supplementary Table 1](#).

2.3. Study selection

Two independent reviewers assessed study eligibility. Screening by title and abstract included time series and case control studies, with asthma ED presentations or hospital admissions related to airborne grass pollen. Full text selection excluded abstracts, studies that did not analyse grass pollen separately, studies that did not analyse asthma separately and studies located outside subtropical climate zones. Any disagreement was resolved by a third party.

2.4. Data items

For each included study, a data extraction form was used to obtain the following information: study location, methods, controlling for confounders, aeroallergen measures, population and health measures and effect estimates.

2.5. Risk of bias in individual studies

Two independent reviewers assessed the quality of evidence and risk of bias for each study using the Zaza quality assessment tool (Zaza et al., 2000). Any disagreement was resolved by a third party. The Zaza quality assessment tool was modified to fit the time series study design. The quality assessment graded each study as having either high, moderate, low or very low quality of evidence and risk of bias. The modified Zaza quality assessment tool can be found in [Supplementary Table 2](#).

2.6. Synthesis of results

A meta-analysis was planned as described in the protocol, however due to the heterogeneity in study design it was determined to be inappropriate. Results were reported by stratifying different age groups of pediatric patients, adults, both pediatric and adults. Estimate of effect size was difficult to homogenise as it was determined using odds ratio, relative risk, mean change in risk, scaled beta coefficient (linear regression) and correlation coefficient. The estimated effect size was reported for different lag periods between exposure and outcome. This produced heterogeneity in reported outcomes, further complicating direct comparison between study results.

3. Results

3.1. Search results

The search identified 1077 studies after duplicates were removed ([Fig. 1](#)). Through screening by title and abstract 1033 studies were excluded. Full text eligibility screening was performed on the remaining 44 studies along with an additional 2 studies identified by citation tracking. Thirty of these studies were identified as ineligible and excluded (8 abstracts only, 6 grass pollen analysed together with other pollen, 15 were undertaken outside subtropical regions, 1 asthma analysed together with other respiratory conditions). An updated search was undertaken to identify any new literature which might have been published in 2019, which our original search didn't cover. The updated search identified three articles eligible for inclusion ([Supplementary Fig. 1](#)). Nineteen studies from 6 countries (Australia, India, Israel, Italy, Spain, USA) were included for review.

3.2. Included studies

The 19 included studies used a time series ($n = 18$) and case control ($n = 1$) study design. Eight studies assessed hospital ED presentations for asthma (Carreno et al., 2019; Cirera et al., 2012; Darrow et al., 2012; Garty et al., 1998; Gleason et al., 2014; Singh et al., 2017; Sun et al., 2016; Wang and Yousef, 2007), eight studies assessed hospital asthma admissions (Caminati et al., 2019; Chakraborty et al., 2016; Ghosh et al., 2012; Hanigan and Johnston, 2007; Marques Mejias et al., 2019; Shrestha et al., 2018; Tobias et al., 2004; Tobias et al., 2003) and three studies assessed both (Babin et al., 2007; Jariwala et al., 2011; Witonsky et al., 2018). Among asthma ED presentation studies (598,931 participants combined), five assessed outcomes for children (Babin et al., 2007; Darrow et al., 2012; Garty et al., 1998; Gleason et al., 2014; Witonsky et al., 2018), two assessed outcomes for adults (Darrow et al., 2012; Witonsky et al., 2018) and eight studies assessed outcomes for adults and children together (Carreno et al., 2019; Cirera et al., 2012; Darrow et al., 2012; Jariwala et al., 2011; Singh et al.,

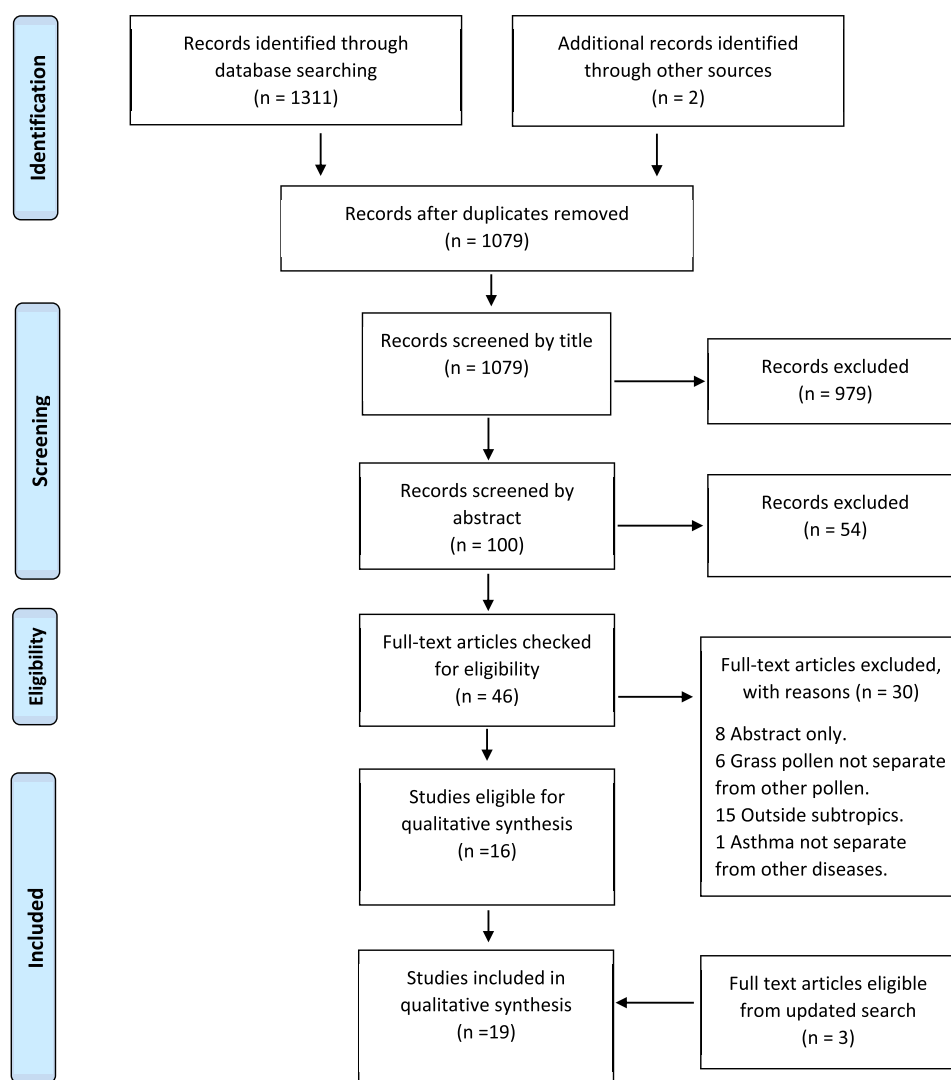


Fig. 1. PRISMA flow diagram, depicting how studies were identified, screened and included. After duplicates were removed 1077 studies were identified through our search. After screening by title, 100 studies remained. After screening by abstract, 46 studies remained. Sixteen studies were determined eligible based on full text. A further three studies were included from an updated search. Nineteen studies were included in the qualitative synthesis.

2017; Sun et al., 2016; Wang and Yousef, 2007; Witonsky et al., 2018). Among hospital admission studies (36,504 participants combined), three assessed outcomes for children (Babin et al., 2007; Marques Mejias et al., 2019; Shrestha et al., 2018), one assessed outcomes for adults (Chakraborty et al., 2016) and seven studies assessed outcomes for adults and children together (Caminati et al., 2019; Ghosh et al., 2012; Hanigan and Johnston, 2007; Jariwala et al., 2011; Tobias et al., 2004; Tobías et al., 2003; Witonsky et al., 2018). Statistical modelling using a general linear model (multiple regression) was undertaken in one study (Witonsky et al., 2018). Eight studies used generalized (Poisson, logistic, general additive model) linear models (Babin et al., 2007; Cirera et al., 2012; Darrow et al., 2012; Gleason et al., 2014; Hanigan and Johnston, 2007; Shrestha et al., 2018; Tobias et al., 2004; Tobías et al., 2003) and one study used a distributed lag nonlinear model (Sun et al., 2016). The remaining nine studies only reported correlations or statistical significance between airborne grass pollen and asthma: Pearson's correlation coefficient, Spearman rank correlation coefficient, Pearson's chi-square and T-test (Caminati et al., 2019; Carreno et al., 2019; Chakraborty et al., 2016; Garty et al., 1998; Ghosh et al., 2012; Jariwala et al., 2011; Marques Mejias et al., 2019; Singh et al., 2017; Wang and Yousef, 2007). The effect size of airborne grass pollens concentration on asthma ED presentation was estimated by

mean change ($n = 1$), relative risk ($n = 3$), odds ratio ($n = 1$), t -test ($n = 1$), scaled coefficient ($n = 1$) and correlation coefficient ($n = 4$). The effect size of airborne grass pollens concentration on asthma hospital admissions was estimated by mean change ($n = 3$), odds ratio ($n = 1$), relative risk ($n = 1$), correlation coefficient ($n = 2$), chi-square test ($n = 3$) and scaled coefficient ($n = 1$). Smoothing for airborne grass pollen concentration, was performed in assessing the outcomes of four asthma ED presentation and one asthma hospital admission study (3 day and 7 day moving average). The lag effect of airborne grass pollen concentration was examined in four asthma presentation and two asthma admission studies. Lags of 1, 2, 3 and 4 days, as well as a cumulative lag of 2–4 days, were used and reported in addition to same day effect (Table 2).

3.3. Risk of bias assessment

All included studies were assessed for risk of bias using the Zaza quality assessment tool (Zaza et al., 2000). Details of the risk of bias assessment are shown in Table 3. Whilst the average QA score was 76% for the 19 studies, the overall quality was found moderate for six studies, low for five studies and very low for eight studies (Table 3). Among the six moderate quality studies, they all reported a small

Table 1

Characteristics of included studies.

Citation, Location	Study design, Duration	Analysis method	Method of collection	Asthma Outcome measure (Visit type; presentation or admission)	Age group	Sample size
Babin et al. (2007)	Time Series	Poisson regression	NR	ICD-9: 493: asthma (Both)	1 to 17	Not reported
Washington DC (USA)	Oct 2001 to Sep 2004			Asthma exacerbation (Admission)	NR	1745
Caminati et al. (2019)	Time Series	Chi-square test	Hirst	Asthma exacerbation (Admission)	NR	111
Verona & Padua (Italy)	Jan 2013 to Dec 2015			Asthma exacerbation (Presentation)	NR	9492
Carreno et al. (2019)	Time Series	Pearson's correlation coefficient	Burkard	ICD-10: asthma (Admission)	18 +	1617
Caceres (Spain)	Apr to Jun 2011			Two nurses identified asthma from ER registers (Presentation)	NR	400,819
Chakraborty et al. (2016)	Time series	Spearman rank correlation coefficient	Burkard	ICD-9: asthma (493.0–493.9) & wheeze (786.09/786.07) (Presentation)	All	
Habra (India)	Jan 2007 to Dec 2013					
Girera et al. (2012)	Time Series	Poisson regression (GAM)	Hirst			
Cartagena (Spain)	Jan 1995 to Dec 1998					
Darrow et al. (2012)	Time series Case cross over	Poisson regression	Rotorod			
Atlanta (USA)	Jan 1993 to Dec 2004					
Garty et al. (1998)	Time series	Pearson's correlation coefficient	Rotorod	Acute asthma attack (with wheezing) (Presentation)	1 to 18	1076
Petah Tikva (Israel)	Jan to Dec 1993			"Asthma related hospital cases" (Admission)	NR	1353
Ghosh et al. (2012)	Time series	Pearson chi-square	Burkard	ICD-9, 493: asthma (Presentation)	3 to 17	21,854
Kolkata (India)	2004 to 2009					
Gleason et al. (2014)	Time series Case cross over	Logistic regression	Rotorod			
New Jersey (USA)	Apr 2004 to Sep 2007					
Hanigan and Johnston (2007)	Time series	General linear model (GAM)	Burkard	ICD 10: asthma (J45–J46), COPD (J40 to J44, J47 and J67), Respiratory infection (J00 to J22) (Admission)	NR	184
Darwin (Australia)	Apr 2004 to Nov 2005					
Jariwala et al. (2011)	Time series	Spearman rank correlation coefficient	Burkard	ICD-9, 493: asthma (Both)	All	Presentation: 42,065 Admission: 10,132
New York (USA)	Jan 2001 to Dec 2008			Asthma exacerbation/bronchospasm (Admission)	0 to 15	2609
Marques-Mejias et al. (2019)	Time series	Pearson chi-square	NR			
Madrid (Spain)	Jan to Dec 2015					
Shrestha et al. (2018)	Time series Case cross over	Logistic regression	Burkard	ICD10-AM: J45, J46; SNOMED CT-AU: 195967001, 266365004; ICD9: 493.0; 493.1; 493.9; 493.2; 493.8 and 493.82. (Admission)	2 to 18	2098
Sydney (Australia)	May 2008 to May 2013			"Asthma and allergic rhinitis" (Presentation)	NR	3385
Singh et al. (2017)	Time series	Pearson's correlation coefficient	Burkard	ICD 9: 493.xx (asthma) (Presentation)	All	82,825
Jaipur (India)	Jan 2011 to Dec 2012					
Sun et al. (2016)	Time series	Distributed lag nonlinear model	Rotorod	Asthma, asthmatic bronchitis, spastic bronchitis, and bronchospasm (Admission)	All	4827
North Carolina (USA)	Mar 2006 to Oct 2012					
Tobias et al., 2003	Time Series	Poisson regression (GAM)	NR	ICD: 493, asthma (Admission)	All	2400
Madrid (Spain)	1995 to 1998					
Tobias et al. (2004)	Time Series	Poisson regression (GAM)	Burkard	ICD-9: 493, asthma (Presentation)	"Children"	106 cases 103 controls
Madrid (Spain)	1995 to 1998					
Wang and Yousef (2007)	Time series	Independent sample t-test	NR			
Wilmington (USA)	Case control					
Jan 2000 to Dec 2003						
Witonsky et al. (2018)	Time series	Multiple linear regression	Burkard	ICD-9 code 493 (Both)	All	Presentation: 43,729 Admission: 1664
New York (USA)	Jan 2001 to Dec 2008					

Note: GAM: generalized additive model, ICD: International Classification of Disease, NR: Not reported.

Table 2
Summary of findings: split into asthma emergency department presentation outcomes and asthma hospital admission outcomes.

Citation	Measure of effect Outcome	Summary of findings							Estimated effect (95% CI)
		Age	Daily average asthma	Sample size	Pollen concentration range grains m ³	Unit increase m ³	Lag	Multiple pollen adjusted	
Asthma emergency department presentations									
Babin et al. (2007)	Mean percent change	1 to 17	NR	NR	NR	10 grains	0	Yes	0.7 (−1.8, 3.1)
	Asthma ED	1 to 17	NR	NR	NR	10 grains	1	Yes	1.9 (−0.4, 4.3)
	Presentation	1 to 17	NR	NR	NR	10 grains	2	Yes	2.3 (−0.1, 4.7)
		1 to 17	NR	NR	NR	10 grains	3	Yes	2.6 (0.3, 5)
		1 to 17	NR	NR	NR	NR	4	Yes	−0.4 (12.9, 2.3)
Carreno et al. (2019)		5 to 12	NR	NR	NR	10 grains	0	Yes	1.6 (−2, 5.4)
		5 to 12	NR	NR	NR	10 grains	1	Yes	3.5 (0.1, 7.1)
		5 to 12	NR	NR	NR	10 grains	2	Yes	4.3 (0.9, 7.9)
		5 to 12	NR	NR	NR	NR	3	Yes	5.5 (2.2, 9)
		5 to 12	NR	NR	NR	NR	4	Yes	3.1 (−0.5, 6.8)
	Pearson's correlation coefficient	NR	1.2	111	NR	NA	0	No	0.313
	Asthma ED	NR	1.2	111	NR	NA	1	No	0.488
	Presentation	NR	1.2	111	NR	NA	3	No	0.575
	Relative Risk	NR	1	1617	0 to 10	1 grain	0	Yes	−3.7 (−7.7, 0.6)
	Asthma ED Presentation	NR	1	1617	10 to 28	1 grain	0	Yes	7.2 (3.1, 11.4)
Darrow et al. (2012)		NR	1	1617	28 to 53	1 grain	0	Yes	−4.2 (−10.7, 2.7)
	Relative Risk	0 to 18+	91.5	400,819	2.9 to 73.8	10 grains	0	No	1.022 (1.012, 1.033)
	Asthma ED	0 to 18+	91.5	400,819	2.9 to 73.9	10 grains	0	Yes	1.019 (1.008, 1.029)
	Presentation	0 to 4	24.7	108,147	2.9 to 73.8	9.1 grains	0	Unclear	1.007 (0.988, 1.026)
		5 to 17	20.9	91,386	2.9 to 73.8	9.1 grains	0	Unclear	1.02 (1.01, 1.04)
Garty et al. (1998)		18+	46	201,286	2.9 to 73.8	9.1 grains	0	Unclear	1.03 (1.017, 1.043)
	Pearson's correlation coefficient	1 to 18	3	1076	NR	NA	0	Unclear	NR (result not statistically significant)
	Asthma ED Presentation								
	Odds Ratio								
	Asthma ED Presentation								
Gleason et al. (2014)		3 to 17	30	21,854	NR	10 grains	0	No	0.99 (0.98, 1.00)
		3 to 17	30	21,854	NR	10 grains	1	No	0.99 (0.98, 1.00)
		3 to 17	30	21,854	NR	10 grains	2	No	1.01 (1.00, 1.01)
		3 to 17	30	21,854	NR	10 grains	3 x̄	No	0.99 (0.98, 1.00)
		3 to 17	30	21,854	NR	10 grains	5 x̄	No	1.02 (1.01, 1.03)
Jariwala et al. (2011)		3 to 17	30	21,854	NR	10 grains	3 x̄	yes	1.00 (0.99–1.01)
	Spearman rank correlation coefficient	All	15	42,065	NR	NA	0	No	NR (result not statistically significant)
	Asthma ED Presentation								
	Pearson's correlation coefficient	NR	4.6	3385	NA	NA	Monthx̄	No	0.59
	Asthma ED Presentation								
Singh et al. (2017)									
Sun et al. (2016)		All	48	82,825	NA	8	2 to 4	Yes	1.03 (0.97, 1.09)
	Relative Risk	All	48	82,825	NA	10	2 to 4	Yes	1.03 (0.98, 1.09)
	Asthma ED	All	48	82,825	NA	11	2 to 4	Yes	1.05 (1.00, 1.11)
	Presentation	NR	NA	106 cases	NR	NR	Monthx̄	No	NR (result not statistically significant)
	T test								
Wang and Yousef (2007)									
	Asthma ED Presentation								

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Table 2 (continued)

Citation	Measure of effect Outcome	Summary of findings								
		Age	Daily average asthma	Sample size	Pollen concentration range grains m ³	Unit increase m ³	Lag	Multiple pollen adjusted	Estimated effect (95% CI)	
Witonsky et al. (2018)	Scaled coefficient (B)	All ^a	14.4	42,065	NR	1 grain	0	Yes	0.129	
		All ^b	16.2	11,821	NR	1 grain	0	Yes	-0.002	
	Asthma ED Presentation	All ^c	8.5	6205	NR	1 grain	0	Yes	0.314	
		18+ ^a	7.8	22,717	NR	1 grain	0	Yes	0.163	
		18+ ^b	8.8	6375	NR	1 grain	0	Yes	0.043	
		18+ ^c	3.6	2608	NR	1 grain	0	Yes	0.277	
		0 to 18 ^a	6.6	19,348	NR	1 grain	0	Yes	0.064	
		0 to 18 ^b	7.5	5446	NR	1 grain	0	Yes	-0.042	
		0 to 18 ^c	4.9	3597	NR	1 grain	0	Yes	0.214	
	Asthma hospital admissions	Mean percent change	1 to 17	NR	NR	NR	10 grains	0	Yes	0.7 (-7.4, 9.5)
		Asthma hospital admission	5 to 12	NR	NR	NR	10 grains	0	Yes	1.8 (-9.4, 14.5)
		Chi-square test	NR	1.6	1745	NR	NA	0	No	P value < 0.05
Asthma hospital admission		18 to 75	NR	9492	NR	NR	Month $\bar{x}$	No	0.834	
Spearman rank correlation coefficient										
Ghosh et al. (2012)	Asthma hospital admission	NR	NR	1353	NR	NR	10 day $\bar{x}$	Yes	X ² = 3.25, P value 0.072	
	Pearson chi square								0.77 (-16.75, 21.97)	
	Asthma hospital admission	NR	0.3	184	0.5 to 24.3	unclear	0	Yes		
	Relative Risk									
	Asthma hospital admission	All	3.5	10132	NR	NA	0	No	NR (result not statistically significant)	
Marques-Mejias et al. (2019)	Asthma hospital admission	0 to 15	7.2	2609	NR	NA	0	No	P value < 0.01 (correlation measure not shown)	
	Pearson chi-square									
	Asthma hospital admission	2 to 18	1.2	2098	0 to 142	9 grains	0	Yes	1.037 (1.005, 1.070)	
	Odds Ratio	2 to 18	1.2	2098	1 to 142	10 grains	1 to 3	Yes	1.005 (0.995, 1.015)	
	Asthma hospital admission	All	3.3	4827	0 to 237.5	98.4 grains	3	No	27.5 (17, 38.9)	
Tobias et al., 2003	Asthma hospital admission	All	3.3	4827	0 to 237.5	98.4 grains	3	Yes	17.1 (3.2, 32.8)	
	Mean percent change	All	3.3	2400	0 to 237.5	4.7		No	13.6 (3.6, 23.2)	
Tobias et al. (2004)	Asthma hospital admission	All	3.3	2400	0 to 237.5	21.8		No	22.1 (10.9, 34.5)	
		All	3.3	2400	0 to 237.5	30.9		No	52.2 (32.0, 75.4)	
Witonsky et al. (2018)	Scaled coefficient (B)	All	3.3	2400	0 to 237.5	98.9		No	50.0 (30.6, 72.1)	
		All	3.3	2400	0 to 237.5	79.2		No	96.6 (58.9, 143.2)	
		All	3.3	2400	0 to 237.5	4.7		Yes	10.6 (0.0, 22.4)	
		All	3.3	2400	0 to 237.5	21.8		Yes	19.4 (5.6, 35.1)	
		All	3.3	2400	0 to 237.5	30.9		Yes	38.1 (14.3, 66.9)	
		All	3.3	2400	0 to 237.5	98.9		Yes	32.2 (6.9, 63.6)	
		All	3.3	2400	0 to 237.5	79.2		Yes	78.7 (34.6, 137.2)	
		All ^a	0.6	1664	NR	1 grain		Yes	0.061	
		All ^b	0.6	428	NR	1 grain		Yes	0.03	
		All ^c	0.5	338	NR	1 grain		Yes	0.054	

Table 3
Quality assessment and possible biases or limitations of included studies.

Study name	Agreed QA score rating (score/total) ^a	Identified biases and limitations
Babin et al. (2007)	Low (14/17)	SB Likely as children younger than 3 included. MB Likely as pollen collection (sampler type) not stated and count methods unexplained. AB Likely as no adjustment for gender.
Caminati et al. (2019)	Very Low (10/16)	SB Likely as study population poorly described. MB Possible as pollen count methods unexplained. AB Likely as no adjustment for meteorological, air pollution, Fungi or demographic variables. OL Only assessed correlation.
Carreno et al. (2019)	Very Low (9/16)	SB Likely as study population not described. MB Possible as pollen count methods unexplained. AB Likely as no adjustment for meteorological, air pollution, Fungi or demographic variables. Bias to single season; study contains 3 months of data. OL Only assessed correlation.
Chakraborty et al. (2016)	Very Low (8/16)	MB Possible as pollen count methods unexplained. AB Likely as no adjustment for demographics, Fungi or air pollutants. OL Only assessed correlation and analysed average monthly pollen.
Cirera et al. (2012)	Very Low (12/17)	SB Likely as study population not described. Possible as selection of asthma outcome done by two nurses. MB Possible as pollen count methods unexplained. AB Likely as no adjustment for demographics or Fungi.
Darrow et al. (2012)	Moderate (16/17)	SB Likely as children younger than 3 included. MB Possible as pollen count methods unexplained. AB Likely as no adjustment for demographics or Fungi.
Garty et al. (1998)	Low (13/17)	SB Likely as children younger than 3 included. MB Possible as pollen count methods unexplained. AB Likely as no adjustment for demographics. Bias to single season; study contains 1 year of data. OL Only assessed correlation.
Ghosh et al. (2012)	Very Low (12/16)	SB Likely as study population not described. MB Possible as pollen count methods unexplained. AB Likely as no meteorological or demographic adjustment. OL Only assessed correlation.
Gleason et al. (2014)	Moderate (16/17)	MB Possible as pollen count methods unexplained. AB Likely as no adjustment for Fungi.
Hanigan and Johnston (2007)	Low (14/17)	SB Likely as study population not described. MB Likely as pollen collection (sampler type) not stated and count methods unexplained. AB Likely as no adjustment for demographics. OL Study contains less than two years of data.
Jariwala et al. (2011)	Low (13/16)	SB Likely as children younger than 3 included. MB Possible as pollen count methods poorly explained. AB Likely as no adjustment for meteorological, air pollution or demographic variables. OL Only assessed correlation.
Marques-Mejias et al. (2019)	Very Low (10/16)	SB Likely as children younger than 3 included. MB Possible as pollen count methods unexplained. AB Likely as no adjustment for demographics or Fungi. Bias to single season; study contains 1 year of data OL Only assessed correlation.
Singh et al. (2017)	Very Low (10/16)	SB Likely as study population not described. MB Possible as pollen count methods unexplained. AB Likely as no adjustment for air pollution, meteorological variables, demographics or Fungi OL Only assessed correlation.
Shrestha et al. (2018)	Moderate (15/17)	MB Possible as pollen count methods unexplained. AB Likely as no adjustment for Fungi
Sun et al. (2016)	Moderate (16/17)	SB Likely as children younger than 3 included. MB Possible as pollen collection (sampler type) not stated and count methods poorly explained. AB Likely as no adjustment for demographics or Fungi.
Tobías et al., 2003	Moderate (15/17)	SB Likely as study population not described. MB Possible as pollen count methods unexplained. AB Likely as no adjustment for demographics or Fungi.
Tobias et al. (2004)	Moderate (15/17)	SB Likely as study population not described. MB Possible as pollen count methods unexplained. AB Likely as no adjustment for demographics or Fungi.
Witonsky et al. (2018)	Low (13/17)	MB Possible as pollen count methods poorly explained. AB Likely as no adjustment for Fungi.
Wang and Yousef (2007)	Very Low (11/16)	SB Likely as study population poorly described. MB Likely as pollen collection (sampler type) not stated and count methods unexplained. AB Likely as no adjustment for demographics. OL Only assessed correlation.

Note: QA: quality assessment. SB: Selection bias, MB: Measurement bias, AB: Analytical bias, OL: Other limitations.

^a Scores are based on the total sum of outcomes for each of the relevant QA questions assessed for a study out of the possible score for that study (up to a value of 17), and graded on a scale from very low to high (Supplementary Table 2).

positive association between airborne grass pollen and asthma. In the remaining 13 low and very low-quality studies, inconsistency in the reported association between airborne grass pollen and asthma was observed. Three aspects of concern were identified in the quality and risk of bias assessment. The study population was not adequately described in seven studies (Caminati et al., 2019; Carreno et al., 2019; Cirera et al., 2012; Ghosh et al., 2012; Hanigan and Johnston, 2007; Singh et al., 2017; Wang and Yousef, 2007), with a further 15 studies including paediatric cases under the age of 3 in their analysis (Caminati et al., 2019; Carreno et al., 2019; Garty et al., 1998; Ghosh et al., 2012; Hanigan and Johnston, 2007; Jariwala et al., 2011; Marques Mejias et al., 2019; Shrestha et al., 2018; Singh et al., 2017; Sun et al., 2016; Tobias et al., 2004; Tobías et al., 2003; Wang and Yousef, 2007; Witonsky et al., 2018), an age when diagnosis of asthma was prone to misclassification (Sly et al., 2011). The second concern was that 12 identified studies (Babin et al., 2007; Caminati et al., 2019; Carreno et al., 2019; Chakraborty et al., 2016; Cirera et al., 2012; Garty et al., 1998; Ghosh et al., 2012; Hanigan and Johnston, 2007; Jariwala et al., 2011; Marques Mejias et al., 2019; Shrestha et al., 2018; Wang and Yousef, 2007) did not provide adequate description of how airborne grass pollen was quantified (microscope magnification, transacts counted and estimating missing grass pollen data). There were differences in pollen and spore trap samplers used, nine studies used a Burkard continuous flow volumetric trap for pollen collection. Four studies used a Rotorod, two used Hirst and four studies did not state which spore trap they used (Table 1). Lastly the assumption of linear models, liner relationship between dependent and independent variable, independence between the dependent variables, normal distribution of dependent variable, multi-collinearity were not presented adequately and there was poor description of any controlling/transformation of the data to meet the assumptions. Both airborne grass pollen and asthma can display a high daily variability. There can also be an issue of frequent observations with a zero value.

3.4. Management of confounders

Among the included studies for review, authors controlled for five main variables in their statistical analysis: airborne pollen (other than grass), meteorology, air pollution, airborne fungal spores and demographics (age and sex). Within ten studies, authors appropriately control for airborne pollen (other than grass) in their statistical analysis (Babin et al., 2007; Cirera et al., 2012; Darrow et al., 2012; Gleason et al., 2014; Hanigan and Johnston, 2007; Shrestha et al., 2018; Sun et al., 2016; Tobias et al., 2004; Tobías et al., 2003; Witonsky et al., 2018). Controlling for meteorological variables was performed in 13 studies (Babin et al., 2007; Chakraborty et al., 2016; Cirera et al., 2012; Darrow et al., 2012; Garty et al., 1998; Gleason et al., 2014; Hanigan and Johnston, 2007; Shrestha et al., 2018; Sun et al., 2016; Tobias et al., 2004; Tobías et al., 2003; Wang and Yousef, 2007; Witonsky et al., 2018). Air pollution variables were controlled for in 15 studies (Babin et al., 2007; Caminati et al., 2019; Cirera et al., 2012; Darrow et al., 2012; Garty et al., 1998; Ghosh et al., 2012; Gleason et al., 2014; Hanigan and Johnston, 2007; Marques Mejias et al., 2019; Shrestha et al., 2018; Sun et al., 2016; Tobias et al., 2004; Tobías et al., 2003; Wang and Yousef, 2007; Witonsky et al., 2018). Airborne fungal spore concentrations, potentially key in confounding the effect of airborne grass pollen exposure, was controlled for in six studies (Babin et al., 2007; Caminati et al., 2019; Garty et al., 1998; Ghosh et al., 2012; Hanigan and Johnston, 2007; Jariwala et al., 2011; Marques Mejias et al., 2019; Wang and Yousef, 2007). Demographic information was adequately provided in five studies (Darrow et al., 2012; Garty et al., 1998; Gleason et al., 2014; Shrestha et al., 2018; Witonsky et al., 2018). The effect of age and gender are known to significantly influence asthma and require controlling. Only one study controlled for all five identified sources of confounding variation (Babin et al., 2007).

3.5. Synthesis of results

3.5.1. Hospital emergency department asthma presentations

Seven studies examined the association of increasing airborne grass pollen concentration on asthma ED presentations, for populations that included both adults and children (Table 2). Carreno et al. (2019) reported a positive correlation between airborne grass pollen counts and asthma ED presentations. Based on Pearson correlation coefficient the same day effect had a correlation of 0.313 ($p < 0.01$), 1 day lag a correlation coefficient of 0.488 ($p < 0.01$) and at 3 days lag a correlation coefficient of 0.575 ($p < 0.01$). The sample size was 111 people, the study was conducted in Caceres (Spain). Cirera et al. (2012) reported airborne grass pollen on its own (range 10–28 grains/m³, at 0 days lag) with an increase of 1 grain/m³, showed an increase reported as relative risk increase of 7.2% (95% CI: 3.1, 11.4) for daily asthma ED presentations (daily asthma ED presentations median = 1, mean = 1, sample size 1617). The study was conducted in Cartagena (Spain). No statistical significance was reported for airborne grass pollen concentrations outside the 10 to 28 grains/m³ range. Darrow et al. (2012) reported airborne grass pollen adjusted for other pollen (range 2.9–73.9 grains/m³, at 0 days lag) with an increase of 10 grains/m³, showed an increase reported as relative risk increase of 1.019 (95% CI: 1.008, 1.029) for daily asthma ED presentations (daily median asthma ED presentations = 91.5, sample size 400,819). The study was conducted in Atlanta (USA). Sun et al. (2016) reported an airborne grass pollen concentration of 11 grains/m³, compared to 0 (at lag two to four days), showed an increase reported as relative risk of 1.05 (95% CI: 1.00, 1.11) for daily asthma ED presentations (daily median asthma ED presentations = 48, sample size 82,825). The study was conducted in Wake County, North Carolina (USA). Witonsky et al. (2018) reported airborne grass pollen (adjusted for other pollen), showed an increase of 1 grains/m³ was associated with: a beta coefficient of 0.314 for summer (sample size = 6,205, median asthma ED presentations = 8, mean = 8.5), a beta coefficient −0.002 for spring (sample size 11,821 daily median asthma ED presentations = 15, mean = 16.2), and a beta coefficient 0.129 for full year (sample size 42,065, daily median asthma ED presentations = 13, mean = 14.4). The study was conducted in Bronx (USA). Jariwala et al. (2011) reported no positive correlation, based on a spearman rank test (data not provided), between asthma ED presentations on high grass pollen days compared to low grass pollen days (daily mean asthma ED presentation = 15, sample size 42,065), in the Bronx (USA). Singh et al. (2017) reported that average monthly airborne grass pollen was significantly correlated with new asthma ED presentations ($r = 0.59$). Daily asthma ED presentations mean = 4.6, sample size 3,385, conducted in Jaipur (India).

Six studies examined the association of increasing airborne grass pollen concentration on asthma ED presentations, for populations of children only (Table 2). Babin et al. (2007) reported on 1–17 year old children, airborne grass pollen adjusted for other pollen with an increase of 10 grains/m³ (at 3 days lag) showed a 2.6% (95% CI: 0.3, 5) mean increase in the number of asthma ED presentations (sample size NR). The 5–12 years age group showed a 10 grains/m³ increase in airborne grass pollen was associated with a 3.5% increase (95% CI: 0.1 to 7.1) after 1 day, a 4.3% increase (95% CI: 0.9 to 7.9) after 2 days, and a 5.5% increase (95% CI: 2.2 to 9) after 3 days, for asthma related ED presentations (sample size NR). The study was conducted in Washington DC (USA). Darrow et al. (2012) reported on 0–4 year old children. An increase of 9.1 grains/m³ in airborne grass pollen (concentration range 2.9–73.8 grains/m³, at 0 days lag), reported a relative risk for asthma ED presentations of 1.007 (95% CI: 0.988, 1.026). The sample size was 108,147, and daily mean asthma presentation was 24.7. For 5–17 year olds, an increase of 9.1 grains/m³ in airborne grass pollen (concentration range 2.9–73.8 grains/m³, at 0 days lag) was associated with increased asthma ED presentations, reported as a relative risk of 1.02 (95% CI: 1.01, 1.04). The sample size was 91,386 and daily mean asthma presentation was 20.9. The study was conducted in

Atlanta (USA). Garty et al. (1998) reported on 1–18 year old children. Based on a Pearson correlation test, the study found that there was no positive correlation (data not provided) between airborne grass pollen concentration and asthma ED presentations. The sample size was 1,076, and a daily mean of 3 asthma ED presentations. The study was conducted in Petah Tikva (Israel). Gleason et al. (2014) reported on 3–17 year old children (unadjusted for other pollen), finding an increase of 10 grains/m³ of airborne grass pollen was not associated with increased asthma presentations: at 0 days lag, an odds ratio of 0.99 (95% CI: 0.98, 1.00), at 1 day lag 0.99 (95% CI: 0.98, 1.00), at 2 days lag 1.01 (95% CI: 1.00, 1.01), using a 3 day average 0.99 (95% CI: 0.98, 1.00) and using a 5 day average 1.02 (95% CI: 1.01, 1.03). An additional model, which was adjusted for other pollen, using a 3 day average, found no association reporting an odds ratio of 1.00 (95% CI: 0.99 to 1.01). The sample size was 21,854, and daily mean asthma ED presentations was 30. The study was conducted in New Jersey (USA). Wang and Yousef (2007) reported on children (age range not reported). Their case control study reported no significant differences (using an independent T test) between airborne grass pollen concentrations on high versus low asthma ED presentation days (data not provided). For low asthma days (0 asthma presentations), the sample size was 106. For high asthma days (> 7 asthma presentations), the sample size was 103. The study was conducted in Wilmington (USA). Witonsky et al. (2018) reported on children aged under 18 (unadjusted for other pollen), found an increase of 1 grain/m³ of airborne grass pollen showed a beta coefficient of 0.064 (full year, sample size 22,717, median daily asthma ED presentations = 7, mean = 7.8), –0.042 (in Spring, sample size 6,375, median daily asthma ED presentation = 8, mean = 8.8) and 0.214 (in Summer, sample size 2,608, median daily asthma ED presentation = 3, mean = 3.6). The study was conducted in Bronx (USA). Two studies examined the association of increasing airborne grass pollen concentration on asthma ED presentations, for populations of adults only (Table 2). Darrow et al. (2012) reported on adults (> 18 years), for every 9.1 grain/m³ increase in airborne grass pollen (airborne grass pollen concentration range of 2.9–73.8 grains/m³, at 0 days lag), an increase reported as a relative risk of 1.03 (95% CI: 1.017, 1.043) for daily asthma ED presentations. The sample size 201,286, and the daily mean asthma ED presentation was 46. The study was conducted in Atlanta (USA). Witonsky et al. (2018) reported on adults (> 18 years), an increase of 1 grain/m³ of airborne grass pollen (unadjusted for other pollen), had a beta coefficient of 0.163 (for full year, sample size 19,348, daily median asthma ED presentation = 6, mean = 6.6), 0.043 (for Spring, sample size 5,446, daily median asthma ED presentation = 7, mean = 7.5) and 0.277 (for Summer, sample size 3,597, daily median asthma ED presentation = 4, mean = 4.9), in the Bronx (USA).

3.5.2. Hospital asthma admissions

Seven studies examined the association of increasing airborne grass pollen concentration on asthma hospital admissions, for populations that included both adults and children (Table 2).

Caminati et al. (2019) reported statistical significance using a chi-square test between monthly asthma hospital admissions and the monthly peak of airborne grass pollen count. Statistical significance was attained ($p < 0.05$) between asthma hospital admissions peaks in April and May and airborne grass pollen counts for the same months. The sample size was 1,745, the study was conducted in Verona and Padua (Italy).

Ghosh et al. (2012) reported a ten day average of airborne grass pollen had a statistically insignificant ($\chi^2 = 3.25$, $p = 0.072$) association with asthma hospital admissions. The sample size was 1353. The study was conducted in Kolkata (India).

Hanigan and Johnston (2007) reported for an airborne grass pollen concentration range of 0.5–24.3 grains/m³ at 0 days lag (unadjusted for other pollen), there was no significant association between airborne grass pollen and asthma hospital admissions. The relative risk percent change was 0.77 (95% CI: –16.75, 21.97). The daily mean asthma

hospital admissions was 0.3 and the sample size 184. The study was conducted in Darwin (Australia).

Jariwala et al. (2011) reported no positive correlation (data not shown, based on a spearman rank test) between asthma hospital admissions on high grass pollen days compared to low grass pollen days. The daily mean asthma ED admissions was 3.5 admissions, and the sample size 10,132. The study was conducted in Bronx (USA).

Tobias et al. (2003) reported an increase of 98.4 grains/m³ (airborne grass pollen concentration range of 0–237.5 grains/m³, at 3 days lag), was significantly associated with asthma hospital admissions (unadjusted for other pollen), reported as a mean percentage change of 17.1 (95% CI: 3.2, 32.8). The sample size was 4,827, and daily mean asthma hospital admissions was 3.3. The study was conducted in Madrid (Spain).

Tobias et al. (2004) reported an increase of 4.7 grains/m³ (airborne grass pollen concentration range of 0–237.5 grains/m³, at 3 days lag), was significantly associated with asthma hospital admissions (unadjusted for other pollen), increase reported as a mean percentage change of 10.6 (95% CI: 0.0, 22.4). Furthermore a 21.8 grains/m³ increase, reported an MPC of 19.4 (95% CI: 5.6, 35.1). A 30.9 grains/m³ increase reported an MPC of 38.1 (95% CI: 14.3, 66.9). A 98.9 grains/m³ increase reported an MPC of 32.2 (95% CI: 6.9, 63.6), and a 79.2 grains/m³ increase reported an MPC of 78.7 (95% CI: 34.6, 137.2). The sample size was 2,400, and the daily mean asthma hospital admissions was 3.3. The study was conducted in Madrid (Spain).

Witonsky et al. (2018) reported an increase of 1 grains/m³ (adjusted for other pollen) showed: a beta coefficient of 0.054 for summer (sample size = 338, mean asthma hospital admissions = 0.5), a beta coefficient 0.03 for spring (sample size 428 daily mean asthma hospital admissions = 0.6), and a beta coefficient 0.061 for full year (sample size 1,664, daily mean asthma hospital admissions = 0.6). The study was conducted in Bronx (USA).

Three studies examined the association of increasing airborne grass pollen concentration on asthma hospital admissions, for populations including children only (Table 2).

Babin et al. (2007) reported no statistical significance between increasing airborne grass pollen concentration and asthma hospital admissions. For 1–17 year old children, an increase of 10 grains/m³ (adjusted for other pollen, at 0 days lag) was reported as a mean change of 0.7% (95% CI: –7.4, 9.5) in the number of asthma hospital admissions (sample size NR). For 5–12 year old children an increase of 10 grains/m³ (adjusted for other pollen, at 0 days lag), was reported as a mean change of 1.8% (95% CI: –9.4 to 14.5), in the number of asthma hospital admissions (sample size NR). The study was conducted in Washington DC (USA).

Marques Mejias et al. (2019) reported a positive correlation ($P < 0.0001$) between airborne grass pollen counts and asthma hospital admissions for 0–15 year old children (correlation measure not reported). The sample size was 2,609, the study was conducted in Madrid (Spain). Shrestha et al. (2018) reported an increase of 9 grains/m³ (airborne grass pollen concentration range of 0–142 grains/m³, at 0 days lag) to have a significant increase reported as an odds ratio of 1.037 (95% CI: 1.005, 1.070) for asthma hospital admissions (unadjusted for other pollen). An increase of 10 grains/m³ (airborne grass pollen concentration range of 1–142 grains/m³, at 1–3 days lag) showed an insignificant increase reported an odds ratio of 1.005 (95% CI: 0.995, 1.015) for asthma hospital admissions. The sample size was 2,098, and the daily mean asthma hospital admissions 1.2. The study was conducted in Sydney (Australia).

One study examined the association of increasing airborne grass pollen concentration on asthma hospital admissions, for a study population including adults only (Table 2).

Chakraborty et al. (2016) reported the monthly averaged airborne grass pollen count to have a correlation coefficient $r = 0.834$, $P < 0.01$ (adjusted R-squared = 0.848) with asthma hospital admissions. The sample size was 9,492, and the daily mean asthma hospital

admissions was 3.7. The study was conducted in Habra (India).

4. Discussion

4.1. Summary of main results

The synthesis of findings from this systematic review, demonstrate evidence that airborne grass pollen appears to have a small effect on increasing asthma ED presentations and hospital admissions in sub-tropical climates. Whilst statistical significance was reported in 12 of 15 asthma ED presentation study outcomes, the effect size was small, and its clinical relevance may be difficult to discern. The authors of this review weighted the reported outcomes by Cochrane's matrix of quality assessment and effect estimate (Glenton et al., 2010). Based on this matrix (Supplementary Table 3) standardised language was used to make a judgement in airborne grass pollens effect on asthma ED presentations and hospital admissions. In asthma ED presentation studies for populations that included both adults and children, findings from Darrow et al. (2012) and Sun et al. (2016) showed there is probably little effect on asthma ED presentations related to airborne grass pollen. Outcomes from Witonsky et al. (2018) likewise showed a positive association, but to a lesser extent, in that airborne grass pollen may have little effect on increase in asthma ED presentations. Outcomes from another three studies also showed a positive association, however based on a low quality assessment score (and possible risks of bias) we are uncertain whether airborne grass pollen increased asthma ED presentations in this instance (Carreno et al., 2019; Cirera et al., 2012; Singh et al., 2017). A single study showed airborne grass pollen may have no effect on increase in asthma ED presentations (Jariwala et al., 2011).

In studies examining asthma ED presentations for populations of children only, Darrow et al. (2012) and Gleason et al. (2014) showed there is probably little effect on increased asthma ED presentations related to airborne grass pollen. Based on the outcomes from another two studies, a positive association was also observed, in that airborne grass pollen may have little effect on increase in asthma ED presentations (Babin et al., 2007; Witonsky et al., 2018). An outcome from a single study, showed airborne grass pollen may have no effect of asthma ED presentations (Garty et al., 1998). Wang and Yousef (2007) also reported no association between airborne grass pollen and asthma ED presentations, however based on a low quality assessment score we were uncertain whether airborne grass pollen increased asthma ED presentations from their study.

Based on the outcomes from Darrow et al. (2012), looking at asthma ED presentations for a population of adults only, they showed there is probably little effect on increase in asthma ED presentations related to airborne grass pollen. Another positive association was found in Witonsky et al. (2018), in that airborne grass pollen may have little effect on increased asthma ED presentations.

Statistical significance was reported in eight of 11 study outcomes looking at associations between asthma hospital admissions and airborne grass pollen. In populations of both adults and children, Tobías et al. (2003) and Tobias et al. (2004) showed that airborne grass pollen probably slightly increases asthma hospital admissions, based on outcomes from two studies. Outcomes from another study of adults and children also found a positive association, in that airborne grass pollen may have little effect on increased asthma hospital admissions (Witonsky et al., 2018). Hanigan and Johnston (2007) and Jariwala et al. (2011) didn't find a positive association, and showed airborne grass pollen may have no effect on increased asthma hospital admissions. The outcome from (Caminati et al., 2019) and Ghosh et al. (2012) reported a positive association, however the quality assessment score (and possible risks of bias) from the studies made us uncertain whether airborne grass pollen increased asthma hospital admissions in a population of children and adults in this instance.

Three studies reported on airborne grass pollens effect on asthma

hospital admissions in a population of children only. Shrestha et al. (2018) found there is probably little effect on increased asthma hospital admissions related to airborne grass pollen. In contrast Babin et al. (2007) didn't find a significant association and showed airborne grass pollen may have no effect on increased asthma hospital admissions in children. Whilst Marques Mejias et al. (2019) reported a positive association, the quality assessment score (and possible risks of bias) from this study made us uncertain whether airborne grass pollen increased asthma hospital admissions in this instance. A single study looking at an adult population only, found a positive association. However based on the quality assessment score (and possible risks of bias) from this study we are uncertain whether airborne grass pollen increased asthma hospital admissions in adults (Chakraborty et al., 2016).

4.2. Timing of grass pollen flowering

Temporal variation of airborne grass pollen flowering is observed between the subtropics and temperate climates (Medek et al., 2016). In the reviewed studies from subtropical regions, airborne grass pollen flowering spans numerous seasons including spring, summer and autumn, with multiple peaks previously observed in the subtropics throughout the year (Beggs et al., 2015). In contrast a much shorter flowering season is observed through temperate climates, with a single peak (Beggs et al., 2015). This long lasting duration or multiple flowering in the subtropics, can be problematic for detection of a strong association between airborne grass pollen and respiratory health. The observed difference in timing and duration of flowering, highlights the probable difference in presence of dominant grass species. Temperate grass species such as ryegrass or timothy grass, were regarded as the primary allergenic source in early studies of airborne grass pollen exposure and respiratory health (Davies and Smith, 1973). These studies were performed in temperate regions of Europe and America. While a significant allergen in temperate regions, there is evidence to suggest disparity in warmer regions where subtropical grasses dominate. Frequency sensitization to both subtropical (*Chloridoideae* and *Panicoideae*) and temperate (*Pooideae*) grass subfamilies was observed among Melbourne Epidemic Thunderstorm Asthma (ETSA) patients (Lee et al., 2017). With concentration specific IgE to Ryegrass pollen (a dominant temperate grass in the area) being higher than Bermuda grass (common subtropical grass found in Australia) in the same cohort. However, in the subtropics of Queensland (Australian) patients with allergic rhinitis showed higher levels of allergic sensitivity by skin prick test and by serum IgE reactivity with subtropical species of grass pollen, Bahia (*Paspalum notatum*) and Bermuda grass (*Cynodon dactylon*) pollen (Davies et al., 2012; Nony et al., 2015). Furthermore, in nearby Northern New South Wales, Bass et al. (2000) observed a correlation between allergic rhinitis and asthma in children with sensitization and exposure to subtropical Bahia and Bermuda grass pollen in late summer. With evidence suggesting difference between different sensitization profiles and grass sources, individual sensitization adjustment to grass pollen, would have further increased confidence in evaluating association between airborne grass pollen exposure and respiratory health outcomes. Studies performed on a population level over a period of time, can be problematic when trying to explain individual level outcomes. For example, in the reviewed studies it is assumed grass pollen collection sites and patient asthma presentations are the relevant location of exposure that triggered symptoms. However, there is limited evidence which suggests microheterogeneity of pollen exposure within urban areas. Individual exposure may have some level of representation for a broader region (Katelaris et al., 2000).

4.3. Limitations of reviewed studies

4.3.1. Study design

All nineteen reviewed studies used an observational study design, where the unit of analysis was on a group level. When determining

association between airborne grass pollen and asthma ED presentations and hospital admissions using an ecological study design, true meaning may be difficult to attain (Gueyffier and Cucherat, 2019; Sedgwick, 2014). Group level results are assumed to apply to individual level (ecological fallacy). The studies assume a direct effect of airborne grass pollen exposure on asthma but there may be multiple pathways of influence (confounding), such as depression of antiviral immunity by allergen exposure, adjuvant effects of pollen and other pollutants. Population dynamics; tourist destinations can have a seasonal spike in population size, annual events can attract large masses, and school holidays can exhibit large migration from a particular region to another. All these are examples of how an estimated outcome may be affected by confounding. Furthermore, a major limitation of most population level asthma and pollen studies, is that levels of sensitization to grass pollen were not routinely measured in ED settings. As a result, there is no way of knowing the proportion of people presenting with asthma that are allergic to grass pollen. It is possible that whilst the effect size at population level may be small, the effect of grass pollen exposure on grass pollen sensitised individuals may not be evident in these observational studies.

Measurement bias; Measurement (collection: spore sampler, air-flow, position height and quantification: microscope magnification, pollen transacts counted and estimating missing data) of airborne grass pollen exposure varied considerably in methodology, introducing a possible measurement bias when determining association of airborne grass pollen exposure and asthma ED presentations and hospital admissions. Furthermore, airborne pollen concentration data was obtained from an external source, without adequate description (poorly described collection and quantification methods in reviewed articles), potentially compromising the reliability of estimated airborne grass pollen concentrations.

Observer bias and selective reporting: the majority of studies focused on effect size estimates which produced statistical significance, arguing for an association. A common trend observed was for authors not to report results if statistical significance was not attained. Even when statistical significance was attained, effect size should be interpreted along with population size, expected daily asthma ED presentations or hospital admissions, and possible risks of bias. In doing so it gives us a clearer idea to what the findings actually represent; is there real clinical meaning in the variation in daily asthma ED presentations and hospital admission rates.

Selection bias: A number of studies with child patients had an inclusion of children under the age of 3, this is considered an age when correct diagnosis of asthma can be difficult and prone to misclassification (Sly et al., 2011).

Analytical bias: Confounding due to lack of controlling for demographics, meteorology, air pollution, fungal spores or other pollen, possibly distorted the estimated association between airborne grass pollen and respiratory health outcomes. Furthermore, when assessing a short-term relationship between airborne grass pollen and asthma ED presentations and hospital admissions, caution should be applied since the results could have been influenced by large seasonal events, not representative of usual conditions.

Among the six studies determined to be of moderate quality, a high consistency of effect estimates were reported for airborne grass pollens effect on asthma. The effect of airborne grass pollen on asthma ED presentations and hospital admissions showed a consistently small but positive association among the six moderate quality studies. In the remaining 13 low and very low-quality studies, there was inconsistency and large variation in the reported effect estimates for airborne grass pollens effect on asthma ED presentations and hospital admissions. It would be difficult to draw a conclusion about the effect of airborne grass pollen on asthma ED presentations and hospital admissions, from the 13 low and very low-quality studies.

4.3.2. Review-level limitations

There was a limitation to this study since we were unable to homogenise effect estimates across the studies to perform a meta-analysis. Homogenising the results would have given more confidence in the review findings. Due to the heterogeneity of the effect estimates a narrative synthesis was performed. As previously stated, effect estimates were reported for a number of different lag periods, airborne grass pollen concentrations and unit increases. If statistical significance was not attained, then the authors did not report the result, choosing to focus on statistically significant outcomes. As a consequence, we were unable to retrieve all the data which was not statistically significant. We did not have enough data to make an interpretation about the effect of lag.

5. Conclusion

Airborne grass pollen appears to have a small and inconsistent increase on asthma ED presentations and hospital admissions in the subtropics. Policy makers should consider to what extent airborne grass pollen can impact on health service provision. This may mean there could be increase in asthma hospital ED presentations and hospital admissions, which could differ among metropolitan and regional hospitals. Similar to temperate regions, these findings underpin the importance of further research considering population characteristics and grass species, in determining how airborne grass pollen exposure may impact respiratory health. Future research should consider population sensitization profiling and local grass species DNA metabarcode analysis (Bell et al., 2016) to give certainty as to which grass species are present in the study region. This review identified several risks of bias that result in uncertainty when determining association between airborne grass pollen and respiratory disease. The following factors were identified as risks of bias which could have been accounted for, improving transparency in collection and quantification of ambient airborne grass pollen concentrations, performing multi-year studies, adjustment for known demographic confounders, co-existing air pollution, meteorology and the presence of other types of pollen and fungal spores.

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CRediT authorship contribution statement

Marko Simunovic: Conceptualization, Methodology, Formal analysis, Validation, Data curation, Investigation, Writing - original draft, Writing - review & editing. **Divya Dwarakanath:** Validation, Writing - review & editing. **Beth Addison-Smith:** Data curation, Writing - review & editing. **Nugroho H. Susanto:** Investigation, Writing - review & editing. **Bircan Erbas:** Conceptualization, Methodology, Writing - review & editing. **Philip Baker:** Formal analysis, Writing - review & editing. **Janet M. Davies:** Conceptualization, Methodology, Writing - review & editing, Supervision.

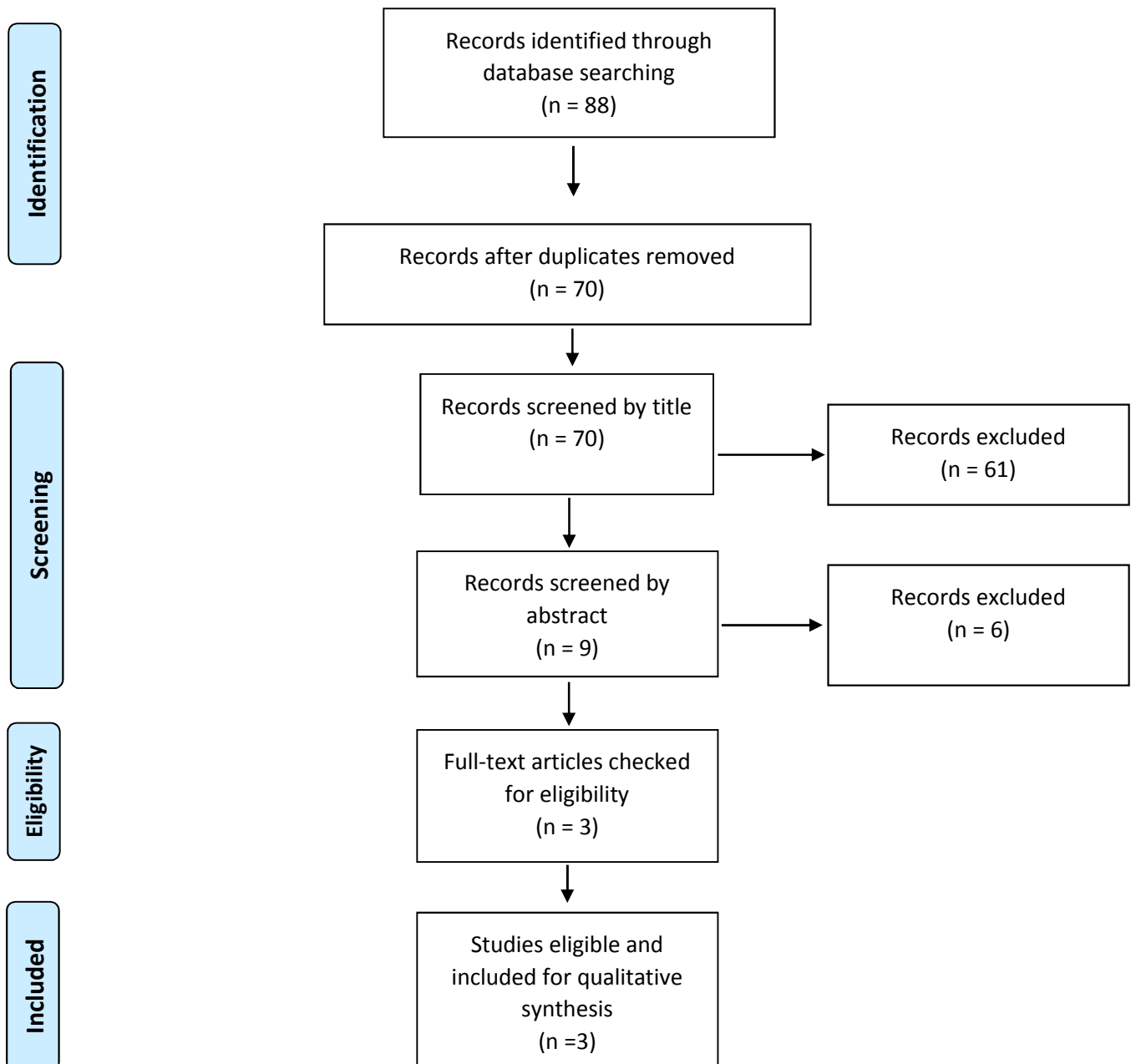
Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.envres.2020.109125>.

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Supplementary Figure 1. PRISMA flow diagram depicting how studies were identified, screened and included in our updated search. After duplicates were removed 70 studies were identified through our search. After screening by title nine studies remained. After screening by abstract three studies remained. All three studies were determined eligible based on full text and included for qualitative synthesis.



Supplementary Table 1. Database search strategy.

Search terms developed with librarian

	Concepts		Key words and subject headings
	Grass	OR Terms	Poaceae[MeSh], "Grass"
AND	Pollen	OR Terms	"Grass pollen*", Pollen[MeSH]
AND	Asthma/COPD	OR Terms	Asthma[Mesh], "asthma",
AND	ED presentations or Admissions	OR Terms	"Hospitalisation", "emerg*", "hospital emerg*", "emergency service", "emergency department", "hospital emergency service", "hospitali?ation", "presentation*", "admission*", Hospitalization[MeSH], hospital [MeSH], Emergency Service, Hospital[MeSH]
AND	Human	OR Terms	Explained below

Database Searches

An original search was conducted on the 14/09/2018 in all databases, (1966 to 14/09/18).

An updated search was conducted on the 5/12/2019 in all databases, (15/08/2018 to 05/12/19).

Database	PubMed (Medline)
Search Terms used	((((((("Poaceae"[Mesh]) OR (grass) AND ("Pollen"[Mesh]) OR (grass pollen*))) AND ("asthma"[Mesh] OR asthma))) AND (hospitalisation OR hospitalization OR emerg* OR hospital emerg* OR Emergency services OR hospital emergency service OR emergency department OR present* OR admission* OR admitted OR "emergency service, hospital"[Mesh] OR "hospitalization"[Mesh]))) NOT (("Animals"[Mesh] NOT ("Animals"[Mesh] AND "Humans"[Mesh])))
Original search results	269
Updated search results	14

Database	Web of Science
Search Terms used	TS=(Poaceae OR grass) AND TS=(Pollen OR grass pollen*) AND TS=(asthma) AND TS=(hospitalisation OR hospitalization OR emerg* OR hospital emerg* OR Emergency services OR hospital emergency service OR emergency department OR present* OR admission* OR admitted)
Original search results	492
Updated search results	32

Database	Scopus
Search Terms used	TITLE-ABS-KEY ((poaceae OR grass) AND (pollen OR grass AND pollen*) AND (asthma) AND (hospitalisation OR hospitalization OR emerg* OR hospital AND emerg* OR emergency AND services OR hospital AND emergency AND service OR emergency))
Original search results	45
Updated search results	4

Database	Embase (Excluding Medline)
Search Terms used	('poaceae'/exp OR grass) AND ('pollen'/exp OR pollen OR 'grass'/exp OR grass) AND ('asthma'/exp OR asthma) AND (hospitalisation OR hospitalization OR 'hospitalization'/exp OR 'hospital'/exp OR 'emergency ward'/exp OR 'hospital admission'/exp OR admitted OR admission OR presentation) AND (pollen* OR 'pollen'/exp) AND [embase]/lim NOT ([embase]/lim AND [medline]/lim)
Original search results	306
Updated search results	30

Database	CINAHL
Search Terms used	TX ((MH "Pollen") or grass pollen or pollen) AND TX (grass or poaceae) AND TX ((MH "Respiratory Tract Diseases+") OR asthma) AND TX ((MH "Emergency Service+") OR (MH "Hospitalization+") OR (MH "Patient Admission") or emergency department or presentation)
Original search results	110
Updated search results	1

Database	Google Scholar
Search Terms used	allintitle: (grass pollen OR poaceae) AND (asthma)
Original search results	92
Updated search results	7

Supplementary Table 3. Matrix of quality assessment and effect estimate used to determine vocabulary for reported effect size (Glenton et al, 2010).

Level (Quality) of evidence	Effect estimate			
		Important benefit or harm	Less important benefit or harm	No important benefit/harm or null effect
	High	Increases	Increases slightly	Little or no effect
	Moderate	Probably increases	Probably increase slightly	Probably little or no effect
	Low	May increase	May increase slightly	May have little or no effect
	Very low	We are uncertain whether airborne grass pollen increases asthma ED presentations (or hospital admissions)		

A vocabulary matrix was developed to standardize language used in the discussion section of the systematic literature review. The vocabulary is dependent on level (quality) of evidence, determined by the Quality assessment score (high, moderate, low or very low) and the reported estimate of the effect size (important harm, less important harm or no important harm of null effect). The vocabulary from the matrix is used to describe the effect of airborne grass pollen on asthma ED presentations or hospital admissions. Estimate of effect size was difficult to homogenize as it was determined using odds ratio, relative risk, mean change in risk, scaled beta coefficient and correlation coefficient. We therefore used Chen et al. (2010); Durlak (2009); Olivier et al. (2017) as a guide, along with the reported sample size and the average daily asthma ED presentations or hospital admissions to determine effect estimate for each study.

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