

Is exposure to pollen a risk factor for moderate and severe asthma exacerbations?

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# Introduction

Asthma is one of the most prevalent chronic diseases and represents a global public health problem affecting people of all age groups, mainly children and adolescents [(Erbas et al., 2018; Shrestha et al., 2021](https://paperpile.com/c/CtPClc/SZbjp+mBHhF).. According to the World Health Organisation (WHO) and the World Allergy Organisation (WAO) asthma prevalence is nearly 300 million people, being higher in males 0 to 14 years old and in females > 15 years [(Erbas et al., 2018)](https://paperpile.com/c/CtPClc/mBHhF). In 2019, 455,000 asthma related deaths occurred, most of them in low and middle income countries because of the challenge that represents the under-diagnosis and under-treatment [(*Asthma*, n.d.; Ishak et al., 2020; Vos et al., 2020)](https://paperpile.com/c/CtPClc/Vyog+y1ig+iGu0).

Persistent asthma is usually controlled with long-term medication, although severe exacerbations may occur requiring emergency department (ED) attendance and in some cases hospitalisation [(Erbas et al., 2018; Idrose et al., 2020)](https://paperpile.com/c/CtPClc/mBHhF+sArO). There are important triggers involved in asthma exacerbations, such as adherence to treatment, exercise, viral infections (Human rhinoviruses), tobacco smoke, chemicals exposure, high temperatures, air pollutants (PM2.5, ozone, nitrogen dioxide) and aeroallergens [(Erbas et al., 2018; Ishak et al., 2020; Shrestha et al., 2021)](https://paperpile.com/c/CtPClc/SZbjp+iGu0+mBHhF)..

Outdoor environment has become the spotlight as a primary trigger for asthma exacerbations in many studies, mostly fungal spores and airborne pollen. However, the wide variety of pollen types and reported results among different geographic regions create a great inconsistency on the evidence that leads to a knowledge gap that difficults the improvement of prevention strategies [(Erbas et al., 2018; Idrose et al., 2020; Ishak et al., 2020; Shrestha et al., 2021)](https://paperpile.com/c/CtPClc/mBHhF+SZbjp+iGu0+sArO).

The aim of this systematic review and meta-analysis is to synthesise and update the current scientific evidence of airborne pollen as a trigger for asthma exacerbations.

# Methods

## Design

We developed a systematic review, following, as guidance, the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2011), and adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement (Page 2021).

## Eligibility Criteria

Study Design

We included studies that measured pollen as the primary exposure variable and reported moderate and severe asthma exacerbation as the outcome of interest. We included observational studies (e.g. cohort studies, time-series studies).

Population

Patients, children or adults, with asthma. We stratified the population in the following subgroups:

* Age
  + Children (<18 years)
  + Adults (≥18 years)
  + General population

Exposure

The exposure of interest was seasonal pollen, expressed as the amount of pollen grains per cubic metre of air sampled (grains/m3). The eligible definition included exposure to mean daily total airborne pollen or exposure to mean daily airborne pollen of distinct types, including; birch, grass, ragweed, mugwort, olive, elm and/or hazel/alder pollen.

We also included studies that assessed the associations between pollen concentrations and symptoms during the same day (i.e. short-term exposure of 1 day) for which we performed a separate analysis.

Comparison

No exposure to seasonal pollen

Outcomes

* Critical
  + Asthma exacerbations, classified in two groups:
    - Moderate = temporary change in treatment (rescue or controller)
    - Severe = Emergency Department (ED)/hospitalisation with systemic steroid use OR systemic steroid for at least 3 days)
  + Asthma control
  + Quality of life
* Important
  + Lung function (FEV1, PEF)
  + Asthma symptoms/well days
  + Asthma medication

## Search Strategy

Sources

We used electronic algorithms with a combination of controlled vocabulary and search terms in the following databases: i) MEDLINE; ii) EMBASE, and; iii) Web of Science Core. The search algorithms were adapted to the requirements of each database, and we used validated filters to retrieve appropriate designs as needed. We also reviewed references of included studies, previous systematic reviews, and consulted experts in the field. See appendix 4.2 for the search strategy.

Abstracts or conference communications not published as full articles in peer review journals were excluded. We excluded publications in a language other than English. We report in the appendices, the complete search algorithms designed for each database, the hits retrieved, and the reasons for the exclusion of studies at the full text review stage.

Reference Manager

We used EndNote software to create a database for the management of the search results.

## Study Selection

Two reviewers screened the search results based on the title and abstract to identify potentially eligible studies after initial calibration. Two reviewers confirmed eligibility based on the full text assessment of the potentially relevant articles. Disagreements were consulted with a third reviewer.

## Data Collection

After calibration, one reviewer extracted relevant data from eligible studies including their main characteristics and results using pre-designed extraction forms. A second reviewer performed a quality control of this process (cross-check). Disagreements were consulted with a third reviewer.

We extracted from each study data regarding study design, method of analysis, study location, time period of the study, method of pollen collection, age range and number of children, exposure definition (pollen species such as grasses, weeds, trees), pollen count, outcome definition, effect estimates together with 95% confidence intervals.

## Risk of Bias

We used the Quality In Prognosis Studies (QUIPS) tool that has been developed by building upon tools for risk of bias assessment of randomised trials, diagnostic test accuracy studies and observational studies of interventions.

## Synthesis of the Results

For any outcomes where data was available from more than one study, we conducted a formal quantitative synthesis (meta-analysis) according to pollen concentration and day lag, using RevMan 5 by the generic inverse variance method with the random‐effects model. We used standard techniques for calculating SEs from 95% CIs.

We judged the magnitude of heterogeneity using the Higgings’ I2 statistic (0% to 40%: low, 30% to 60%: moderate, 50% to 90%: substantial, 75% to 100%: considerable). Additionally, we visually inspected the meta-analysis’ forest plots for consistency; given that I2 statistics might be artificially inflated when effect estimates from primary studies are very precise (Rücker 2008).

For any outcomes where it was not possible to calculate an effect estimate, a narrative synthesis is presented, describing the studies in terms of the direction and the size of effects, and any available measure of precision.

## Certainty of the Evidence

We rated the certainty of evidence for each outcome with the GRADE approach (Schünemann 2013). We rated the certainty of evidence across each outcome as high, moderate, low or very low, taking into consideration risk of bias, imprecision, inconsistency, indirectness, and publication bias.

# Results

## Search Results

We identified (3,244) individual records through our search after removing duplicates. We assessed (270) full texts and finally included (73) studies. The PRISMA flow chart summarising the screening process is available in the appendix 4.3. The reasons for exclusion of individual studies are available in the appendix 4.5.

## Characteristics of the included studies

Most studies were conducted in Europe (n=31, 43.05%) and 13 of these were from the United Kingdom. 22 (30.55%) studies were conducted in North America, with most from the United States (n=18). 13 (18.05%) studies are from Oceania, 12 of them from Australia. The 6 (8.33%) remaining studies were from Asia, Africa and South America.

Of the 72 included studies, 43 (59.72%) were longitudinal studies (including cohorts, case-control, prospective and retrospective studies), 21 (29.16%) were time-series studies, 5 (6.94%) were case-crossover studies, and 3 (4.16%) were cross-sectional. The number of included participants ranged from 10 to 400,819 in 53 studies, while 19 did not specify the sample size. 34 (47.22%) studies included participants of all ages, 28 (38.88%) included only participants under 18 years of age, and 5 (6.94%) only participants over 18 years of age. Five (6.94%) studies did not specify whether the participants were adults, children or general population.

29 (40.27%) of the studies did not specify whether they received funds for conducting the study (not reported), while 43 (59.77%) did, and of these 10 reported no funding.

See appendix 4.4 for the summary of the included studies.

## Results

Although many studies reported estimated effects, conducting meta-analysis for all outcomes was not possible due to substantial heterogeneity related to the pollen species, participant's age, method of analysis used to estimate the effect size, and the differences in lagged day effects considered for the analysis. Effect estimates were not standardised because a dose-response relationship in which increasing levels of exposure are associated with either an increasing or a decreasing risk of the outcome was not observed. However, we conducted a meta-analysis for severe asthma exacerbations associated with an increase of grass pollen, tree pollen, cypress and ragweed exposure.

## Total Pollen (not specified)

26 studies assessed the impact of total pollen counts on asthma. The study designs were longitudinal (n=18), time series (n=5), case-crossover (n=1), case-control (n=1), and cross-sectional (n=1). Among these, 8 assessed participants of all ages, of which 1 presented results stratified by age; 13 studies only assessed participants under 18 years of age, 4 only assessed participants over 18 years of age, and 1 did not specify the ages of the participants.

Severe Asthma Exacerbation

### *Under 18 years of age*

Two studies reported the association between asthma-related hospitalisations and total pollen concentrations on the same day (lag 0). A case-crossover study (Shrestha 2017) reported a positive though imprecise association with non-specified pollen concentrations, while a cohort study (Lowe 2012) reported a negative association with an interquartile range increase of 146 grains/m3, for infants (0-1 years old)(Table 1).

One longitudinal study reported a positive association between asthma-related Emergency Department (ED) visits and a non-specified pollen concentration lagged 3 days (Lierl 2003)(Table 1).

Two studies reported the association between asthma-related ED admissions or hospitalisations and total pollen counts when accounting for a cumulative, distributed or moving average lag. A case-crossover study (Shrestha 2017) reported a positive though imprecise association with a non-specified pollen concentration, while a time-series analysis (Chen 2016) reported a positive association with a 10 unit increase in total pollen (Table 1).

One longitudinal study reported no association between asthma-related ED visits with a 1 unit increase without specifying lag (Bouazza 2017)(Table 1).

Four studies did not account for potential confounders in their results (Marques-Mejias 2019, Gowrie 2012, Potter 1984,Garty 1998). See appendix 4.7 for results.

*Table 1: Severe Asthma Exacerbation in patients under 18 years of age exposed to total pollen counts (adjusted results)*

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study ID** | **Age** | **Outcome Definition** | **Exposure** | | **Effect Estimate** | | | |
| **Total pollen concentration** | **Lag** |  | **EE** | **95%CI** | |
| **Bouazza 2017** | median(IQR): 3.08 (1.58-6.25) | Asthma-Related ED Visits | 1 unit increase | Not specified | Percentage change (SE) | 0.00 | 0.00011 | p= 0.97 |
| **Lowe 2012** | 0-1 years | Asthma Hospitalisation | 146 grains/day/m3 (IQRI) | 0 | OR | 0.80 | 0.65 | 0.97 |
| **Shrestha 2017** | 2-18 years | Asthma Hospitalisation | 75th to 90th percentile increase\* | 0 | OR | 1.026 | 0.992 | 1.060 |
| Cumulative lag | 1.002 | 0.992 | 1.013 |
| **Chen 2016** | 0-17 years | Asthma-Related ED Admissions | 10 unit increase | distributed lag | RaR | 1.016 | 1.004 | 1.028 |
| moving average | 1.021 | 1.009 | 1.033 |
| **Lierl 2003** | Paediatrics | Asthma-Related ED Visits | Not specified | 3 | RR | 1.089 | 1.027 | 1.155 |

### *ED: Emergency Department, IQR: interquartile range, IQRI: interquartile range increase, SE: standard error, OR: odds ratio, RaR: incidence risk ratio, RR: risk ratio, 95%CI: 95% confidence interval*

### *\* geometric mean (SD) grains/m3 of total pollen: 4.8 (3.2)*

### *Over 18 years of age*

One time series analysis (Chen 2016) reported a positive though imprecise association between asthma-related ED admissions and an increase in 10 grains/m3 in distributed or moving average lags (Table 2).

One longitudinal study (Makra 2012) reported the association between asthma attacks and non-specified pollen concentrations lagged 5 days, and found that total pollen counts are in relevant inverse association with males, while positively associated with females (no estimator was presented by the study authors).

Two studies did not account for potential confounders in their results (Caminati 2019, Krmpotic 2011). See appendix 4.7 for results.

*Table 2: Severe Asthma Exacerbation in patients over 18 years of age exposed to total pollen counts (adjusted results)*

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study ID** | **Age** | **Outcome Definition** | **Exposure** | | **Effect Estimate** | | | |
| **Total pollen concentration** | **Lag** |  | **EE** | **95%CI** | |
| **Chen 2016** | 18+ years | Asthma-Related ED Admissions | 10 unit increase | distributed lag | RaR | 1.001 | 0.988 | 1.015 |
| moving average | 1.002 | 0.989 | 1.015 |

### *ED: Emergency Department, RaR: incidence risk ratio, 95%CI: 95% confidence interval*

### 

### *General Population*

Two studies, one case-control (Mazenq 2017b) and one time series analysis (Hanigan 2007), reported the association between asthma-related ED visits or admissions and total pollen concentrations on the same day (lag 0). Both reported a negative though imprecise association, Mazenq 2017 did so for pollen concentrations above 0 grains/m3 and Hanigan 2007 for pollen concentrations between the 50th and 75th percentiles. However, Hanigan 2007 also reported a positive though imprecise association for higher concentrations of pollen (above the 75th percentile) (Table 3).

One longitudinal study reported the association between asthma-related ED admissions and total pollen concentrations lagged 2 and 3 days and stratified by sex and concentration quartiles (Gonzalez-Barcala 2013). For females, a trend was observed for an increased risk of admissions associated with higher concentrations of total pollen. However, for males this trend is only observed with the pollen concentrations lagged 3 days (Table 3).

One time series analysis (Chen 2016) reported the association between asthma-related ED admissions and total pollen concentrations with moving average lags and found a positive association with a 10 unit increase (Table 3).

Four studies did not account for potential confounders in their results (Brzezinska-Pawlowska 2016, Epton 1997, Jariwala 2011, Jariwala 2014). See appendix 4.7 for results.

*Table 3: Severe Asthma Exacerbation in the general population exposed to total pollen counts (adjusted results)*

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study ID** | **Age** | **Outcome Definition** | **Exposure** | | **Effect Estimate** | | | |
| **Total pollen concentration** | **Lag** |  | **EE** | **95%CI** | |
| **Mazenq 2017b** | 3-99 years | Asthma-Related ED Visits | >0 grains/m3 | 0 | OR | 0.95 | 0.79 | 1.16 |
| **Hanigan 2007** | all ages | Asthma-Related ED Admissions | 50-75% (ref 0-50%)\* | 0 | Percentage change | -28.12 | -54.99 | 14.78 |
| 75-90% (ref 0-50%)\* | 9.35 | -32.21 | 76.37 |
| 90-100% (ref 0-50%)\* | 41.42 | -20.94 | 153 |
| **Gonzalez-Barcala 2013** | all ages. Mean (SD): 52.1 (24.8) | Asthma-Related ED Admissions | 2nd quartile vs 1st quartile | 2 | RR male | 0.99 | 0.82 | 1.20 |
| RR female | 1.02 | 0.88 | 1.18 |
| 3 | RR male | 1.01 | 0.83 | 1.22 |
| RR female | 0.98 | 0.84 | 1.13 |
| 3rd quartile vs 1st quartile | 2 | RR male | 0.88 | 0.68 | 1.14 |
| RR female | 1.16 | 0.95 | 1.41 |
| 3 | RR male | 0.99 | 0.77 | 1.26 |
| RR female | 1.08 | 0.89 | 1.31 |
| 4th quartile vs 1st quartile | 2 | RR male | 0.98 | 0.71 | 1.35 |
| RR female | 1.11 | 0.87 | 1.41 |
| 3 | RR male | 1.06 | 0.78 | 1.43 |
| RR female | 1.17 | 0.93 | 1.48 |
| **Chen 2016** | all ages | Asthma-Related ED Admissions | 10 unit increase | distributed lag | RaR | 1.010 | 1.001 | 1.019 |
| moving average | 1.013 | 1.004 | 1.022 |

### *ED: Emergency Department, SD: standard deviation, OR: odds ratio, RR: risk ratio, RaR: incidence risk ratio, 95%CI: 95% confidence interval*

### *\*mean (50th centile, 90th centile) grains/m3 of total pollen: 15.4 (13.3, 31.1), ✝mean (IQR) grains/m3 of total pollen: 52 (13-142)*

### 

### *Age Not Specified*

One study did not account for potential confounders in their results (Jamason 1997). See appendix 4.7 for results.

Moderate Asthma Exacerbation

### *Under 18 years of age*

One longitudinal study examined the use of extra medication (i.e. medication above each person’s defined baseline) due to asthma exacerbation on the same day (lag 0) and lagged 3 days. Using multivariate regression analysis, they found no association with non-specified total pollen count (Ostro 2001).

### 

### *Over 18 years of age*

One longitudinal study examined the association between the use of extra medication (defined as at least two times more often than the individual’s usual use) and total pollen concentration on the same day (lag 0)(Epton 1997). They found no association with concentrations between 10-100 grains/m3 when compared to less than 10 grains/m3, although inconclusive (RR 95%CI: 1.00 (0.88, 1.13)).

This outcome was not reported for the other selected age groups.

Asthma Control

### *Under 18 years of age*

One longitudinal study examined the association of asthma control status with the preceding week’s pollen severity index and found that pollen severity was significantly associated with poorer asthma control after adjusting for the season effect and participant’s socio-demographics (Beta 95%CI: 0.44 (0.06, 0.83))(Li 2019).

This outcome was not reported for the other selected age groups.

Quality of Life

This outcome was not reported for any age group.

Lung Function

### *Under 18 years of age*

Two longitudinal studies assessed the association between lung function and total pollen counts. Klabuschnigg 1981 examined the changes in Forced Expiratory Volume (FEV) and Forced Vital Capacity (FVC) and total pollen counts accounting for weather conditions over a period of 6 weeks and found no association between them (no estimator was presented by the study authors). Ginis 2015 compared the Forced Expiratory Volume in 1 second (FEV1) and Forced Expiratory Flow at the 25% and 75% of pulmonary volume (FEF25-75) of participants between the “pollen season” and “out of pollen season” and found that the median of both parameters were significantly lower during the pollen season (p=0.004 and 0.05, respectively)(Table 4).

### *Over 18 years of age*

A longitudinal study examined whether total pollen counts had an influence in the Peak Expiratory Flow Rate (PEFR), and found that PEFR increased following days of moderate pollen counts compared with days of low pollen counts. However, there was no relationship between PEFR and 7 day rolling means of total pollen counts (Epton 1997)(Table 4).

This outcome was not reported for the other selected age groups.

*Table 4: Lung function in participants under and over 18 years of age exposed to total pollen counts (Adjusted results)*

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Study ID** | **Age** | **Outcome Definition** | **Exposure** | **Effect Estimate** | | | |
| **Total pollen concentration** |  | **EE** | **95%CI** | |
| **Ginis 2015** | 9-14 years | FEV1 | In season (march to october) | Median (IQR) | 91 | 82 | 100 |
| Out of season | 98 | 91 | 102 |
| FEF25-75 | In season (march to october) | 92 | 84 | 107 |
| Out of season | 103 | 90 | 113 |
| **Epton 1997** | 17-80 years | mean change in PEFR | Moderate (10-100 grains) vs low (<10 grains) | The mean change in PEFR between a low and a moderate pollen count day was 0.18% or 0.8L/min. | | | |

IQR: interquartile range, 95%CI: *95% confidence interval,* FEV-1= Forced expiratory volume in 1 second; FEF25-75: Forced Expiratory Flow at the 25% and 75% of pulmonary volume. PEFR= Peak Expiratory Flow Rate.

Asthma Symptoms/Well Days

### *Under 18 years of age*

One longitudinal study (Ostro 2001) examined the association of exposure to 13 grains/m3 of total pollen lagged 3 days with one day of symptoms (shortness of breath, cough and wheeze) and found a positive though imprecise association with shortness of breath and a negative but also imprecise association with the other two symptoms. They also explored the association with the onset of those symptoms (defined as the first day of symptoms after at least one day without) and found a positive though imprecise association with the onset of shortness of breath and cough (Table 5).

One study did not account for potential confounders in their results (Klabuschnigg 1981). See Appendix 4.7 for results.

### *Over 18 years of age*

One longitudinal study (Epton 1997) assessed the effect of same day **(lag 0)** moderate total pollen counts (10-100 grains/m3) compared to low counts (<10 grains/m3) on the risk of occurrence of high-symptoms-scores day and waking up at night. They found a negative though imprecise association for both (Table 5).

This outcome was not reported for the other selected age groups.

*Table 5: Asthma symptoms in participants under and over 18 years of age exposed to total pollen counts (Adjusted results)*

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study ID** | **Age** | **Outcome Definition** | **Exposure** | **Lag** | **Effect Estimate** | | | |
| **Total pollen concentration** |  | **EE** | **95%CI** | |
| **Ostro 2001** | <18 years | Probability of a Day with Shortness of breath | IQR 13 grains/m3 | 3 | OR | 1.26 | 0.55 | 2.93 |
| Probability of a Day with Wheeze | 0.97 | 0.93 | 1.03 |
| Probability of a Day with Cough | 0.94 | 0.90 | 0.99 |
| Onset of Shortness of breath | 1.11 | 0.90 | 1.38 |
| Onset of Wheeze | 0.94 | 0.77 | 1.14 |
| Onset of Cough | 01.01 | 0.82 | 1.24 |
| **Epton 1997** | 17-80 years | High symptom score day: one on which the symptom score was at least one greater than the individual's modal score. | Moderate (10-100 grains) vs low (<10 grains) | 0 | RR | 0.93 | 0.83 | 01.04 |
| Symptom: Waking at night | 0.92 | 0.80 | 01.05 |

*IQR: interquartile range, OR: odds ratio; RR: risk ratio, 95%CI: 95% confidence interval*

*Onset: the 1st day, after at least 1 day without any symptoms, on which this symptom was reported.*

Mortality

### *General Population*

One longitudinal (retrospective) study assessed the relation between asthma-related mortality and total pollen concentrations (Mackay 1992). Mackay 1992 reported that no association between mortality and the total pollen counts was found, since the peak of the former happened in August, six to eight weeks after the peak of the latter.

This outcome was not reported for the other selected age groups.

## Grass Pollen

30 studies assessed the impact of grass pollen counts on asthma. The study designs were longitudinal (n=12), time series (n=9), case-crossover (n=5), case-control (n=2), and cross-sectional (n=2). Among these, 16 assessed participants of all ages, of which 5 presented results stratified by age; 12 studies only assessed participants under 18 years of age, and 2 did not specify the ages of the participants.

Severe Asthma Exacerbation

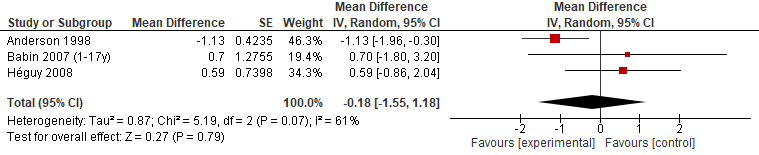
### 

### *Under 18 years of age*

Seven studies reported the association between asthma attacks or asthma-related ED admissions, visits or hospitalizations and the concentrations of grass pollen on the same day (lag 0). Four of these reported a positive, and three a negative association.

One time series analysis reported a positive though imprecise association with a 1 grain/m3 grass pollen increase (Lee 2019). Two longitudinal studies (Anderson 1998, Babin 2007) and one time series analysis (Heguy 2008) reported the association with a 10 grain/m3 increase (Figure 1). Anderson 1998 reported a negative association, while Babin 2007 and Heguy 2008 showed a positive although imprecise, association (Figure 1)(Table 6).   
  
We performed a quantitative synthesis (meta-analysis) for studies that measured this outcome on the same day (lag 0) (Figure 1). An increase in grass pollen concentrations from >0 to 50 grains/m3 showed a negative association to severe asthma exacerbation in patients younger than 18 years (MD = -0.18, 95% CI: -1.55, 1.18).

*Figure 1. Severe asthma exacerbations associated with an increase of 0 to 50 grains/m3 of grass pollen (lag 0) in patients under 18 years of age.*



Additionally, one case crossover study reported a positive association with a concentration of 34 grains/m3 (Batra 2021). On the other hand, one case-crossover study (Batra 2021) and one case-control study (Mazenq 2017) reported a negative though imprecise association, without specifying the grass pollen concentrations (Table 6).

Seven studies, including 4 case-crossover, 1 time series analysis and 2 longitudinal studies reported the association between asthma exacerbations or asthma-related ED visits or hospitalizations with concentrations of pollen lagged up to three days.

Of the case-crossover and time series analysis, Lee 2019 showed a positive, though imprecise association with a 1 grain/m3 increase in grass pollen. Gleason 2014 reported no association with a 10 grains/m3 increase of grass pollen. De Roos 2020 found a negative though imprecise association for grass pollen concentrations ranging from 8.5 to 33.8 grains/m3, a positive though imprecise association for concentrations ranging from 33.8 to 51.8 grains/m3, and a positive association for concentrations over 51.8 grains/m3. Batra 2021 and Shrestha 2017 found a positive though imprecise association, with concentrations of grass pollen of 112-133 grains/m3 and non-specified, respectively (Table 6).

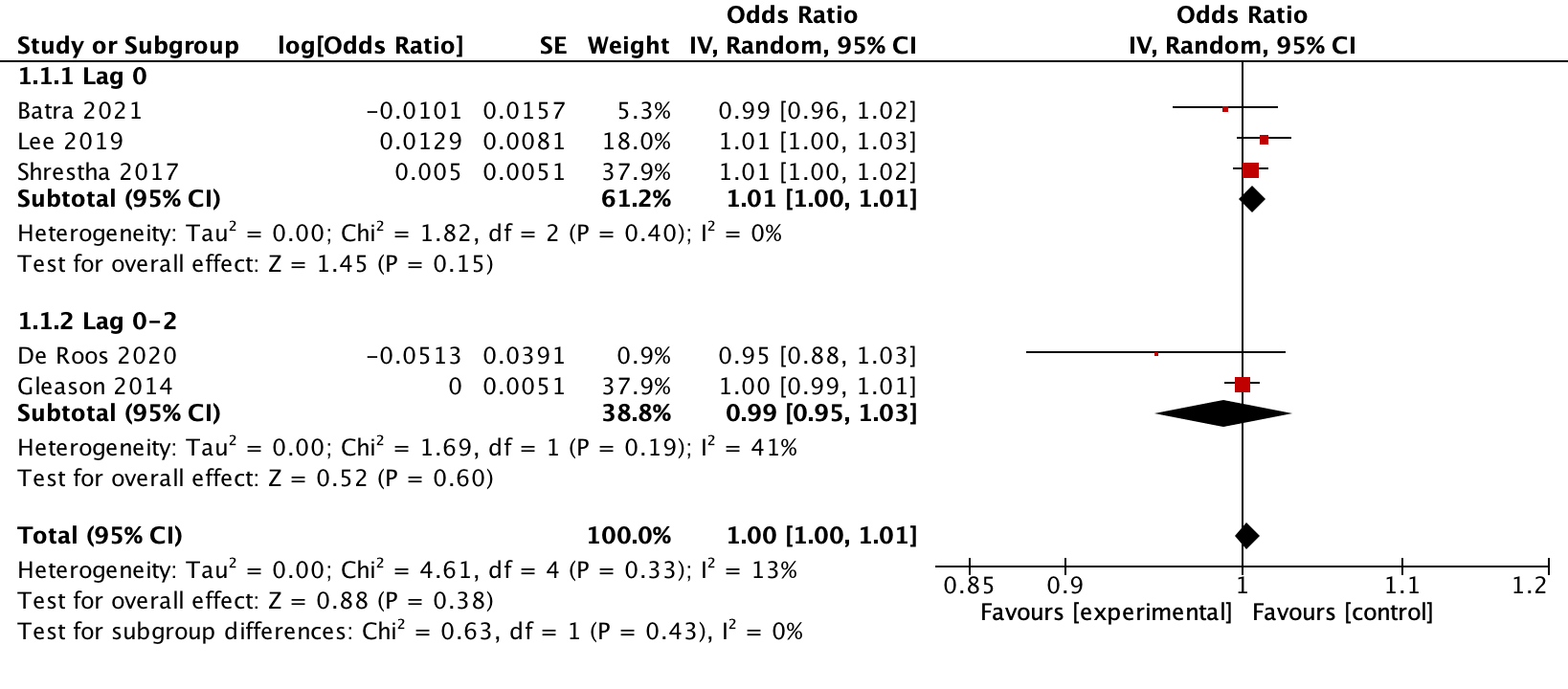
Both longitudinal studies did not specify the pollen concentrations, Khot 1998 found a positive but imprecise association, while Witonsky 2018 reported an increase in asthma-related admissions during summer and the full year, but a negative and imprecise association during spring (Table 6).

One time series analysis showed a positive though imprecise association between asthma-related ED visits for an increase in 12 grains/m3 with a cumulative lag 0-6 days (Guilbert 2018)(Table 6).

Four studies did not account for potential confounders in their results (Murray 2006, Klabuschnigg 1981, Marques-Mejias 2019, Wang 2007). See appendix 4.7 for results.

We performed a quantitative synthesis (meta-analysis) for studies that measured this outcome between lag 0 to 2 (figure 2). For lag 0 an increase in grass pollen concentrations from >0 to 50 grains/m3 showed positive association to severe asthma exacerbation in general population (OR = 1.01, 95% CI: 1.00, 1.01), but for lag 0 to 2 a negative association to severe asthma exacerbation in patients younger than 18 years was observed (OR = 0.99, 95% CI: 0.95, 1.03).

Figure 2. *Severe asthma exacerbations associated with an increase of >0 to 50 grains/m3 of grass pollen (lag 0-2) in patients under 18 years of age.*

****

### *Table 6: Severe Asthma Exacerbation in patients under 18 years of age exposed to grass pollen (adjusted results)*

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study ID** | **Age** | **Outcome Definition** | **Exposure** | **Lag** | **Effect Estimate** | | | |
| **Grass pollen concentration** |  | **EE** | **95%CI** | |
| **Anderson 1998** | 0-14 years | Asthma-Related ED Admissions | 10 unit increase | 0 | Percentage change | -1.13 | -1.96 | 0.0 |
| **Babin 2007** | 1-17 years | Asthma-Related ED Visits | 10 unit increase | 0 | Percentage change | 0.7 | -1.8 | 3.1 |
| **Heguy 2008** | 0-9 years | Asthma-Related ED Visits | 10 unit increase | 0 | Percentage change | 0.59 | -0.86 | 02.06 |
| **Mazenq 2017** | 3-18 years | Asthma-Related ED Visits | Not specified | 0 | OR | 0.99 | 0.99 | 01.01 |
| **Batra 2021** | 2-17 years | Asthma Attacks | 34 grains/m3 | 0 | OR | 0.999 | 0.96 | 1.011 |
| 112-133 grains/m3 | 2 | 1.017 | 0.999 | 1.035 |
| **Shrestha 2017** | 2-18 years | Asthma Hospitalisation | 75th to 90th percentile increase\* | 0 | OR | 1.037 | 1.005 | 1.070 |
| Cumulative lag | 1.005 | 0.995 | 1.015 |
| **Khot 1988** | 18months-16 years | Asthma-Related ED Admissions | Not specified | 1 | Contribution to the Regression Analysis | 5.4 | d.f 1 |  |
| **Lee 2019** | 0-2 years | Asthma-Related ED Visits | Increment 1 grain/m3 | 2 | RR | 1.004 | 0.999 | 1.009 |
| 2-5 years | 2 | 1.001 | 0.995 | 1.006 |
| 6-17 years | 0 | 1.013 | 0.997 | 1.030 |
| **De Roos 2020** | <18 years | Asthma Exacerbation | >0 to 8.5 grains/m3 | Cumulative 0-2 | OR | 1.04 | 0.99 | 1.10 |
| >8.5 to 23.2 grains/m3 | Cumulative 0-2 | 0.96 | 0.90 | 01.02 |
| >23.2 to 33.8 grains/m3 | Cumulative 0-2 | 0.95 | 0.88 | 01.03 |
| >33.8 to 51.8 grains/m3 | Cumulative 0-2 | 1.04 | 0.95 | 1.14 |
| >51.8 grains/m3 | Cumulative 0-2 | 1.38 | 1.19 | 1.60 |
| **Witonsky 2018** | Paediatric | Asthma-Related ED Admissions | Full year | 3 day moving average | Beta Linear regression model | 0.064 | p=0.008 | - |
| Spring | -0.042 | p=0.459 | - |
| Summer | 0.214 | p=0.000 | - |
| **Gleason 2014** | 3-17 years | Asthma-Related ED Visits | 10 unit increase | lag 0-2 average | OR | 1.00 | 0.99 | 01.01 |
| **Guilbert 2018** | 0-14 years | Asthma Hospitalisation | 12 grains/m3 (IQRI) | Cumulative 0-6 | Percentage change | 5.2 | −0.9 | 11.5 |

### *ED: Emergency Department, IQRI: interquartile range increase, OR: odds ratio, RR: risk ratio, 95%CI: 95% confidence interval*

### *\* geometric mean (SD) grains/m3 of total pollen: 4.8 (3.2)*

### 

### *Over 18 years of age*

Two studies reported the association between asthma-related ED visits or admissions and concentrations of pollen on the same day (lag 0). A time series analysis (Lee 2019) reported positive though imprecise association with an increment of 1 grain/m3 of grass pollen, while a longitudinal study (Anderson 1998) reported a negative though imprecise association with a 10 unit increase. The association observed by Lee 2019 was also present at lag 1 (Table 7).

Two studies reported the association between asthma-related ED visits or admissions with 3 day moving average concentrations of grass pollen. One case-crossover study reported a positive association (Darrow 2012), and one longitudinal study reported a positive association during summer and full year, but not for the spring (Witonsky 2018)(Table 7).

One time series analysis reported a positive but imprecise association between asthma hospitalizations and an increase in 12 grains/m3 in a 0-6 days cumulative lag (Guilbert 2018)(Table 7).

One study did not account for potential confounders in their results (Caminati 2019). See appendix 4.7 for results.

*Table 7: Severe Asthma Exacerbation in patients over 18 years of age exposed to grass pollen (adjusted results)*

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study ID** | **Age** | **Outcome Definition** | **Exposure** | | **Effect Estimate** | | | |
| **Grass pollen concentration** | **Lag** |  | **EE** | **95%CI** | |
| **Anderson 1998** | >65 years | Asthma-Related ED Admissions | 10 unit increase | 0 | Percentage Change | -0.63 | -2.69 | 1.48 |
| **Lee 2019** | 18-59 years | Asthma-Related ED Visits | Increment 1 grain/m3 | 0 | RR | 1.008 | 0.996 | 1.020 |
| 60+ years | 1 | 1.005 | 0.998 | 1.012 |
| **Darrow 2012** | >18 years | Asthma-Related ED Visits | NR | 3 day moving average | RR | 1.030 | 1.017 | 1.043 |
| **Witonsky 2018** | Adults | Asthma-Related ED Admissions | Full year | 3 day moving average | Beta Linear regression model | 0.163 | p= 0.000 | |
| Spring | 0.043 | p= 0.432 | |
| Summer | 0.277 | p= 0.000 | |
| **Guilbert 2018** | >60 years | Asthma Hospitalisation | 12 grains/m3 (IQRI) | Cumulative 0-6 | Percentage Change | 4.1 | −2.1 | 10.7 |

### *ED: Emergency Department, IQRI: interquartile range increase, RR: risk ratio, 95%CI: 95% confidence interval*

### *General Population*

Four studies reported the association between asthma-related ED visits, admissions or hospitalizations and grass pollen concentrations for the same day (lag 0).

One time series analysis reported a positive association to grass pollen with non-specified concentrations (Erbas 2007). In contrast, two time series analyses and one longitudinal study reported negative associations. The longitudinal analysis (Anderson 1998) did so with a 10 unit increase. Both time series analyses reported a negative though imprecise association with a non-specified concentration (Hanigan 2007), and between 30-149 grains/m3 (Osborne 2017). However, with concentrations over 150 grains/m3, Osborne 2017 reported a more precise negative association (Table 8).

Two studies (a time series analysis and a longitudinal study) assessed the association between asthma-related ED admissions and grass pollen concentrations lagged 1 day. Both found a negative but imprecise association with a non-specified concentration (Osborne 2017), and a 10 unit increase (Anderson 1998). However, when the time series analysis (Osborne 2017) examined this association lagged 2 days they reported a positive though imprecise association (Table 8)

Five studies assessed the association between asthma-related ED visits or admissions with pollen concentrations lagged 3 days and all found positive associations. A time series analysis (Lee 2019) reported an imprecise association with an increase in 1 grain/m3. The case-crossover study found this association with an increase in 10 units (Darrow 2012). The other three time series analyses also reported this association with concentrations between 50 and >150 grains/m3 (Osborne 2017), 98.4 grains/m3 (Tobias 2003), and an increment over the 50th percentile of grass pollen concentrations (Tobias 2004)(Table 8).

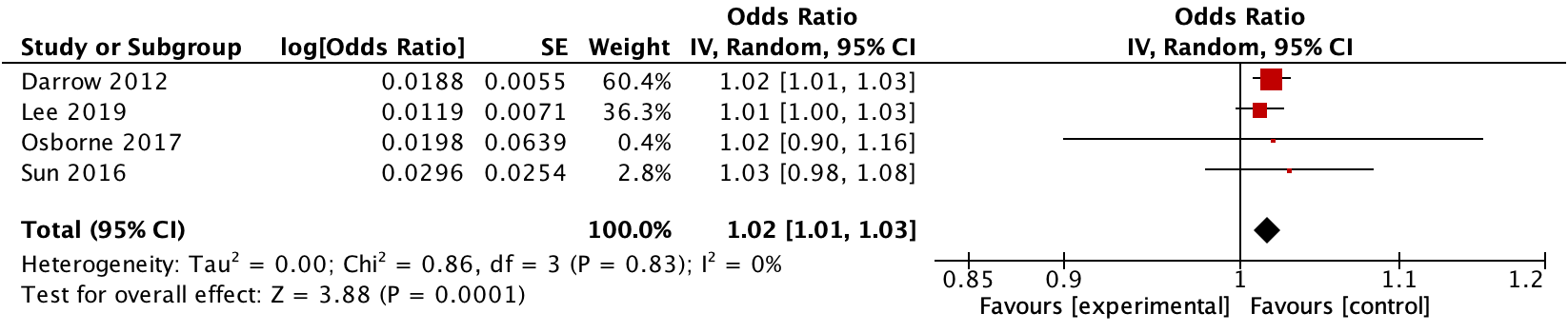
One longitudinal study reported the association between asthma-related ED visits or admissions with **3 day moving average** concentrations of grass pollen, and reported a positive association with ED visits during summer and the full year, and with ED admissions during the full year analysis (Witonsky 2018)(Table 8).

Three studies reported the association between asthma-related ED Visits or hospitalizations with pollen concentrations with cumulative lags up to 6 days. One longitudinal study reported a positive though imprecise association with 10 grains/m3 (Sun 2016). This association became more evident in the two time series analysis, with a 12 grains/m3 increase (Guilbert 2018) and with 14 grains/m3 increase in grass pollen concentrations (Dales 2004)(Table 8).

We performed a quantitative synthesis (meta-analysis) for studies that measured this outcome between lag 2 to 4 (figure 3). An increase in grass pollen concentrations from >0 to 50 grains/m3 showed a positive association to severe asthma exacerbation in general population (OR = 1.02, 95% CI: 1.01, 1.03).

Two studies did not account for potential confounders in their results (Porcel Carreño 2020, Jariwala 2014). See appendix 4.7 for results.

Figure 3. *Severe asthma exacerbations associated with an increase of 0 to 50 grains/m3 of grass pollen (lag >2) in patients in the general population*



*Table 8: Severe Asthma Exacerbation in the general population exposed to grass pollen (adjusted results)*

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study ID** | **Age** | **Outcome Definition** | **Exposure** | | **Effect Estimate** | | | |
| **Grass pollen concentration** | **Lag** |  | **EE** | **95%CI** | |
| **Erbas 2007** | all ages | Asthma Hospitalisation | Not specified | 0 | Smooth term df (Chi square) | 5.1 | 13.49 | p= 0.01 |
| **Hanigan 2007** | all ages | Asthma-Related ED Admissions | IQR change in pollen load for linear responses\* | 0 | Percentage change in relative risk | 0.77 | -16.75 | 21.97 |
| **Anderson 1998** | all ages/ mean 35.1 | Asthma-Related ED Admissions | 10 unit increase | 0 | Percentage change | -1.16 | -1.82 | -0.5 |
| 15-64 years | 1 | -0.073 | -1.71 | 0.26 |
| **Osborne 2017** | 16-64 years | Asthma-Related ED Admissions | Increase from 0 to 104 grains/m3 | 0 | Percentage change | −6.18 | -14,69 | 2.33 |
| 1 | −6.69 | -16.19 | 2.82 |
| 2 | 6.2 | -3.28 | 15.69 |
| 3 | 1.24 | -7.67 | 10.15 |
| 4 | 17.23 | 8.93 | 25.54 |
| 5 | 14.11 | 6.22 | 22.01 |
| 6 | 5.95 | −2.04 | 13.94 |
| 7 | 3.31 | −4.21 | 10.83 |
| Medium ≥30 grains/m3 & ≤49 grains/m3 | 0 | RaR | 0.95 | 0.85 | 1.06 |
| 3 | 1.02 | 0.90 | 1.14 |
| High ≥50 grains/m3 & ≤149 grains/m3 | 0 | 0.98 | 0.88 | 1.09 |
| 3 | 1.14 | 1.01 | 1.28 |
| Very High ≥150 grains/m3 | 0 | 0.72 | 0.59 | 0.87 |
| 3 | 1.46 | 1.20 | 1.78 |
| **Lee 2019** | all ages | Asthma-Related ED Visits | Increment 1 grain/m3 | 3 | RR | 1.012 | 0.998 | 1.006 |
| **Tobias 2003** | all ages | Asthma-Related ED Admissions | p95-p99 variation: 98.4 grains/m3 | 3 | Percentage change | 17.1 | 3.2 | 32.8 |
| **Tobias 2004** | all ages | Asthma-Related ED Admissions | p50-p75 | 3 | Percentage change in risk | 10.6 | 0.0 | 22.4 |
| p75-p90 | 19.4 | 5.6 | 35.1 |
| p90-p95 | 38.1 | 14.3 | 66.9 |
| p95-p99 | 32.2 | 6.9 | 63.6 |
| p99-max | 78.7 | 34.6 | 137.2 |
| **Darrow 2012** | all ages | Asthma-Related ED Visits | 10 grains/m3 | 3 | RR | 1.019 | 1.008 | 1.029 |
| **Witonsky 2018** | all ages | Asthma-Related ED Admissions | Full year | 3 day moving average | Beta Linear regression model | 0.061 | p= 0.026 | |
| Spring | 0.030 | p= 0.602 | |
| Summer | 0.054 | p= 0.255 | |
| Asthma-Related ED Visits | Full year | 0.129 | p= 0.000 | |
| Spring | –0.002 | p= 0.969 | |
| Summer | 0.314 | p= 0.000 | |
| **Sun 2016** | all ages mean (SD)= 32 (22) | Asthma-Related ED Visits | 10 grains/m3 | 2-4 | RR | 1.03 | 0.98 | 1.09 |
| **Dales 2004** | all ages | Asthma-Related ED Visits | Increase in 14 grains/m3 | Cumulative 0-5 | Percentage change | 1.95 | 1.08 | 2.83 |
| **Guilbert 2018** | all ages 0 to +60 | Asthma Hospitalisation | 12 grains/m3 (IQRI) | Cumulative 0-6 | Percentage change | 5.9 | 0.0 | 12.0 |

### *ED: Emergency Department, SD: standard deviation, IQR: interquartile range, IQRI: interquartile range increase, RaR: incidence risk ratio, RR: risk ratio, 95%CI: 95% confidence interval. \*daily mean (SD): 2.7 (4.4) grains/m3*

### *Age Not Specified*

Two studies reported the association between asthma-related ED visits or admissions and grass pollen counts on the same day (lag 0).

A longitudinal study (Ghosh 2012) reported that grass pollen counts (non-specified) were not associated with asthma-related hospital admissions. Through a retrospective chart review, Cirera 2012 reported an increased risk of asthma Emergency Department visits for a rise of 1 grain/m3 of grass pollen in the concentration range of 10 to 28 grains/m3. For the other two ranges (0-10 and 58-53 grains/m3) there was a negative but imprecise association (Table 9).

*Table 9: Severe Asthma Exacerbation in patients over 18 years of age exposed to grass pollen (adjusted results)*

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study ID** | **Age** | **Outcome Definition** | **Exposure** | | **Effect Estimate** | | | |
| **Grass pollen concentration** | **Lag** |  | **EE** | **95%CI** | |
| **Ghosh 2018** | NR | Asthma-Related ED Admissions | Not specified | 0 | Regression Analysis Estimate/Chi-square/pr>chi square | 1.001 | 3.25 | 0.072 |
| **Cirera 2012** | NR | Asthma-Related ED Visits | increase of 1 grain/m3 within the range 0-10 grains/m3 | 0 | RR | -3.7 | −7.7 | 0.6 |
| increase of 1 grain/m3 within the range 10-28grains/m3 | 7.2 | 3.1 | 11.4 |
| increase of 1 grain/m3 within the range 28-53 grains/m3 | -4.2 | −10.7 | 2.7 |

### *NR: not reported, ED: Emergency Department, RR: risk ratio, 95%CI: 95% confidence interval*

Moderate Asthma Exacerbation

This outcome was not reported for any age group.

Asthma Control

This outcome was not reported for any age group.

Quality of Life

This outcome was not reported for any age group.

Lung Function

### *Under 18 years of age*

Two longitudinal studies reported the association between lung function and grass pollen concentrations. Lambert 2020 reported positive though imprecise association between an interquartile range increase of 7 grains/m3 for lags 0 to 3 and Forced Expiratory Volume during the first second (FEV1) and Forced vital capacity (FVC), although for this last parameter the association was negative and imprecise for the 8-years-old participants (Table 10). Klabuschnigg 1981 reported that no correlation was established between FEV and FVC and their changes according to non-specified grass pollen counts (Table 10).

### *18 years of age*

Idrose 2020 conducted a cross sectional study and reported that exposure to higher levels of grass pollen (increase in 29 grains/m3) at lag 0, 1, 2, and cumulative lag 3 were associated with an increase in absolute bronchodilator response (BDR) and Fractional exhaled Nitric Oxide (FeNO) in subjects with current asthma (Table 10).

### *General Population*

Kralimarkova 2014 conducted a randomised clinical trial and for the asthmatic group they reported the mean FEV1 before the pollen season and during the season, defined as when high atmospheric grass pollen counts triggered symptoms in the sensitised population. The difference between the means before and after the pollen season was not statistically significant (p=0.71)(Table 10).

*Table 10: Lung function in participants under 18 years of age and the general population exposed to grass pollen (Adjusted results)*

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study ID** | **Age** | **Outcome Definition** | **Exposure** | | **Effect Estimate** | | | |
| **Grass pollen concentration** | **Lag** |  | **EE** | **95%CI** | |
| **Lambert 2020** | 8 years | FEV1 (<80% predicted) | 7 grains/m3 IQRI | 0-3 | OR | 0.68 | 0.13 | 3.74 |
| FVC (<80% predicted) | 1.32 | 0.46 | 3.83 |
| FEV1 | % predicted value | 0.72 | -6.98 | 5.54 |
| FVC | -0.30 | -7.2 | 6.6 |
| 14 years | FEV1 | 0.73 | -1.4 | 2.9 |
| FVC | 0.32 | -1.6 | 2.2 |
| **Klabuschnigg 1981** | 7-14 years | "No correlations between FEV and FVC and their changes according to pollen and spore counts and general and local weather situation could be established over the 6 weeks investigated." | | | | | | |
| **Idrose 2020** | 18 years | FeNO (ppb) | increase in 29 grains/m3. | 0-3 | coefficient | 13 | 1.3 | 24 |
|  |  | Absolute BDR | 0-3 | 2.0 | -0.4 | 4.6 |
| **Kralimarkova 2014** | 7-55 years | FEV-1 (% predicted) | Before season | Not applicable | mean (SE) | 104.8 | 3.4 | Difference: p= 0.71. |
| FEV-1 (% predicted) | During season | 103.6 | 3.6 |

*IQRI: interquartile range increase, OR: odds ratio, SE: standard error, 95%CI: 95% confidence interval, FEV-1= Forced expiratory volume in 1 second, FVC= forced vital capacity, FeNO= fractional exhaled nitric oxidel BDR= bronchodilator response*

Asthma Symptoms/Well Days

### *General Population*

Kralimarkova 2014 conducted a randomised clinical trial and for the asthmatic group they reported the overall discomfort from symptoms with a 100 mm VAS scale ranging from worst symptoms ever (100) to no symptoms (0) relevant for the time of the visit and the 72hrs before. The mean (SD) VAS score was 93.2 (2.2) before the pollen season and 69.9 (4.8) during the pollen season (defined as when high atmospheric grass pollen counts triggered symptoms in the sensitised population) with a difference that was statistically significant (p=0.001).

This outcome was not reported for the other selected age groups.

Mortality

### *General Population*

Two longitudinal (retrospective) studies assessed the relation between asthma-related mortality and grass pollen concentrations. Targonsky 1995 reported that grass pollen concentrations were not significantly different between days on which asthma related deaths occurred and days on which such deaths did not occur, and Mackay 1992 reported no association between the peak in mortality and the peak in grass pollen counts (Table 11). This outcome was not reported for the other selected age groups.

*Table 11: Death caused by asthma in the general population exposed to grass pollen.*

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study ID** | **Age** | **Outcome Definition** | **Exposure** | | **Effect Estimate** | | | |
| **Grass pollen concentration** | **Lag** |  | **EE** | **95%CI** | |
| **Targonski 1995** | 5-34 years | Death caused by asthma | 100 grains per cubic metre increase | 0 | OR | 01.03 | 0.67 | 1.59 |
| **Mackay 1992** | 5-44 years | “The peak in mortality which was present in August occurred six to eight weeks after the peak in grass pollen counts” | | | | | | |

*OR: odds ratio, 95%CI: 95% confidence interval*

## Tree Pollen

19 studies assessed the impact of tree pollen counts on asthma. The study designs were time series (n=6), longitudinal (n=7) , case-crossover (n=5), and cross-sectional (n=1). Among these, 12 assessed participants of all ages, of which 3 presented results stratified by age; 5 studies only assessed participants under 18 years of age, 1 only assessed participants over 18 years of age and 1 did not specify the ages of the participants.

Severe Asthma Exacerbation

### *Under 18 years of age*

Four studies assessed the association between asthma exacerbations, ED visits or hospitalisations and tree pollen concentrations on the same day **(lag 0)**. Three reported a positive association, while one reported a negative one.

One time series analysis reported a positive though imprecise association with an increase in 100 grains/m3 of tree pollen counts (Lee 2019), and a longitudinal study found this association to be significant (Babin 2007). Additionally, a case-crossover study reported a positive though imprecise association with a non-specified concentration (Shrestha 2017). On the other hand, another case-crossover study reported a negative association with tree pollen concentrations between 60-216 grains/m3 (Batra 2021)(Table 12).

Two studies reported the association with asthma-related ED visits and tree pollen **lagged 1 day**. A time series analysis and a longitudinal study reported a positive though imprecise association with an increment of 100 grains/m3 (Lee 2019, Babin 2007)(Table 12).

When **lagged 2 days**, Babin 2007 reported a positive though imprecise association with a 100 grains/m3 increase, but a case-crossover study reported no association with higher concentrations (614-747 grains/m3)(Batra 2021)(Table 12).

At **lags 3 and 4** both Lee 2019 and Babin 2007 reported a positive but imprecise association (Table 12).

Three case-crossover studies examined the association of asthma exacerbations, hospitalisations or ED visits with tree pollen concentrations with either **cumulative** **lags (0-2) or the 3 day average**. Shrestha 2017 found a positive though imprecise association with a non-specified concentration, while De Roos 2020 and Gleason 2014 found positive associations with concentrations from >0 to 537 grains/m3, and with a 10 unit increase, respectively. A longitudinal study which also assessed the 3 day average found a positive association durgin the full year and spring, though not during the summer (Witonsky 2018)(Table 12).

We performed a quantitative synthesis (meta-analysis) for studies that measured this outcome between lag 0 to 2 (figure 4). An increase in tree pollen concentrations from >0 to 50 grains/m3 showed positive association with severe asthma exacerbation in patients younger than 18 years (OR = 1.10, 95% CI: 0.94, 1.28). When tree pollen concentrations increase >50 grains/m3, no association to risk of severe asthma exacerbation was observed (OR = 1.00, 95% CI: 0.99, 1.02) (figure 5).

One study did not account for potential confounders in their results (Jariwala 2014). See appendix 4.7 for results.

*Table 12: Severe Asthma Exacerbation in patients under 18 years of age exposed to tree pollen (adjusted results)*

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study ID** | **Age** | **Outcome Definition** | **Exposure** | | **Effect Estimate** | | | |
| **Tree pollen concentration** | **Lag** |  | **EE** | **95%CI** | |
| **Batra 2021** | 2-17 years | Asthma Exacerbations | 60-216 grains/m3 | 0 | OR | 0.995 | 0.991 | 0.998 |
| 614-747 grains/m3 | 2 | 1.000 | 1.000 | 1.001 |
| **Lee 2019** | 0-2 years | Asthma-Related ED Visits | Increase in 100 grains/m3 | 1 | RR | 1.005 | 0.999 | 1.011 |
| 2-5 years | 0 | 1.005 | 0.994 | 1.016 |
| 6-17 years | 4 | 1.014 | 1.004 | 1.024 |
| **Babin 2007** | 1-17 years | Asthma-Related ED Visits | Increase in 100 grains/m3 | 0 | Percentage Change | 0.5 | 0 | 1.1 |
| 1 | 0.4 | -0.2 | 1 |
| 2 | 0.5 | -0.1 | 1.1 |
| 3 | 0.2 | -0.4 | 0.8 |
| 4 | 0.2 | -0.4 | 0.9 |
| Asthma-Related ED Visits | Not Specified | 1.5 | -0.3 | 3.3 |
| **Shrestha 2017** | 2-18 years | Asthma Hospitalisation | 75th to 90th percentile increase\* | 0 | OR | 1.015 | 0.988 | 1.042 |
| Cumulative Lag | 1.002 | 0.993 | 1.010 |
| **De Roos 2020** | <18 years | Asthma Exacerbations | >0 to 157.7 grains/m3 | Cumulative 0-2 | OR | 1.10 | 1.06 | 1.14 |
| >157.7 to 531 grains/m3 | 1.07 | 1.00 | 1.15 |
| >531 to 911 grains/m3 | 1.16 | 1.07 | 1.25 |
| >911 to 1514 grains/m3 | 1.13 | 1.03 | 1.24 |
| >157.7 to 537 grains/m3 | 1.35 | 1.18 | 1.54 |
| **Gleason 2014** | 3-17 years | Asthma-Related ED Visits | 10 unit increase | lag 0-2 average | OR | 1.19 | 1.17 | 1.20 |
| **Witonsky 2018** | Paediatrics | Asthma-Related ED Admissions | Full year | 3 day moving average | Beta Linear Regression Model | 0.287 | p=0.000 | |
| Spring | 0.269 | p=0.000 | |
| Summer | 0.037 | p=0.359 | |

### *ED: Emergency Department, OR: odds ratio, RR: risk ratio, 95%CI: 95% confidence interval*

### *\* geometric mean (SD) grains/m3 of total pollen: 4.8 (3.2)*

Figure 4. *Severe asthma exacerbations associated with an increase of 0 to 50 grains/m3 of tree pollen (lag 0-2) in patients under 18 years.*

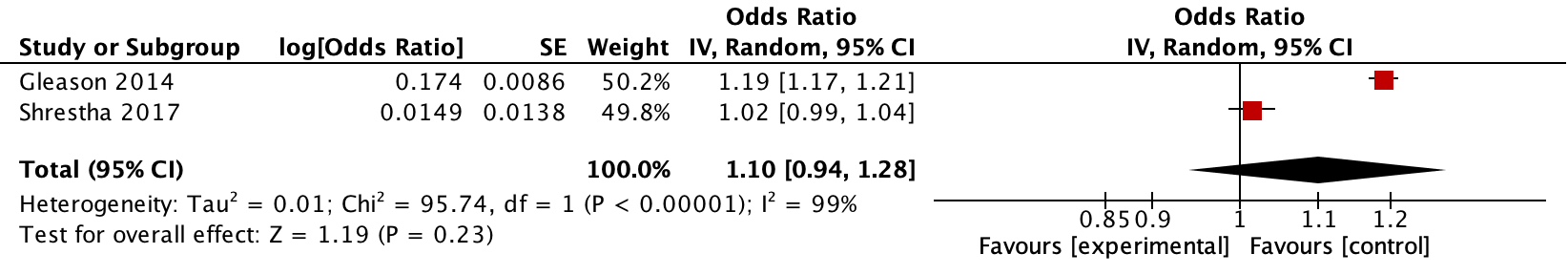
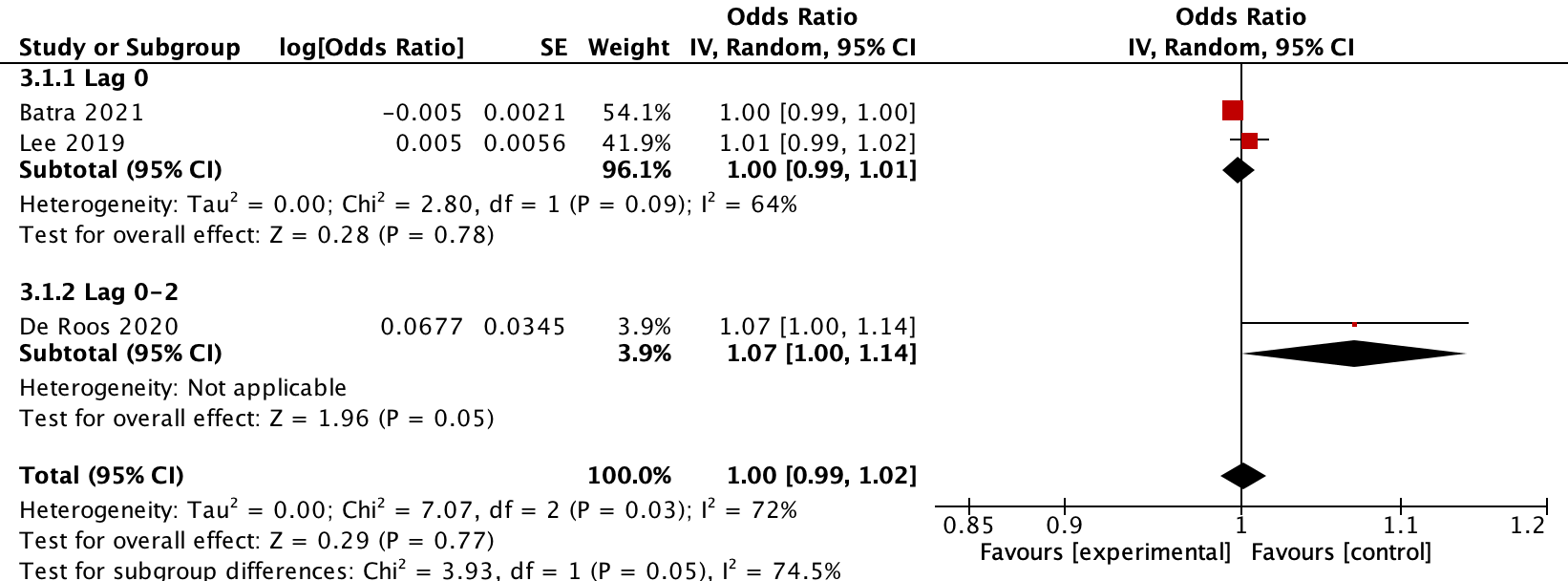


Figure 5. *Severe asthma exacerbations associated with an increase of >50 grains/m3 of tree pollen (lag 0-2) in patients under 18 years.*



### 

### *Over 18 years of age*

Three studies examined the association between asthma-related ED visits or admissions and tree pollen concentrations in different lags. For an increment in 100 grains/m3 on the same day (lag 0), a time series analysis (Lee 2019) reported a positive association. When assessing the 3 day moving average, a longitudinal study (Witonsky 2018) reported a positive association during the full year and spring, though a negative association during the summer analysis. Lastly, May 2011 reported a positive association but did not specify lag nor tree pollen concentrations (Table 13).

*Table 13: Severe Asthma Exacerbation in patients over 18 years of age exposed to tree pollen (adjusted results)*

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study ID** | **Age** | **Outcome Definition** | **Exposure** | | **Effect Estimate** | | | |
| **Tree pollen concentration** | **Lag** |  | **EE** | **95%CI** | |
| **Lee 2019** | 18-59 years | Asthma-Related ED Visits | Increment 100 grains/m3 | 0 | RR | 1.026 | 1.016 | 1.036 |
| 60+ years | 1.005 | 0.993 | 1.017 |
| **Witonsky 2018** | Adults | Asthma-Related ED Admissions | Full Year | 3 day moving average | Beta Linear Regression Model | 0.240 | p=0.000 | |
| Spring | 0.183 | p=0.000 | |
| Summer | -0.122 | p=0.003 | |
| **May 2011** | >18 years | Asthma-Related ED Visits | Not Specified | Not Specified | Correlation Coefficient | 0.458 | 0.152 | 0.765 |

### *ED: Emergency Department, RR: risk ratio, 95%CI: 95% confidence interval*

One study did not account for potential confounders in their results (Jariwala 2014). See appendix 4.7 for results.

### *General Population*

Two time series analysis reported the association between asthma-related ED visits or admissions with tree pollen concentrations on the same day (lag 0).

Lee 2019 reported a positive association with an increment of 100 grains/m3, while Osborne 2017 reported a negative though imprecise association with non-specified concentrations (Table 14).

Additionally, Osborne 2017 examined lags 1 through 7 for the same concentrations and no trend was observed, with positive associations in lags 2, 4, 6 and 7, and negative in lags 3 and 5, all imprecise (Table 14).

Three studies reported the association between asthma-related ED visits and tree pollen in a **cumulative 0-3 days lag**.

A longitudinal study (Sun 2016) reported an increased risk of ED visits with increasing concentrations of tree pollen, with imprecise associations with 10 grains/m3 and 37 grains/m3, but a positive association with a concentration of 3500 grains/m3. A case-crossover study (Darrow 2012) reported a positive though imprecise association with a concentration of 20 grains/m3. A longitudinal study (Witonsky 2018) reported a positive association during the full year and spring, although a negative though imprecise association during summer (Table 14).

Two time series analysis reported a positive association between asthma-related ED visits or hospitalisations with a cumulative 0-5 days lag. Dales 2004 reported this with an increase in 125 grains/m3, while Dales 2008 did so with a non-specified concentration (Table 14).

We performed a quantitative synthesis (meta-analysis) for studies that measured this outcome between lag 0 to 3 (figure 6). An increase in tree pollen concentrations from >0 to 50 grains/m3 showed no association to severe asthma exacerbation in the general population (OR = 1.00, 95% CI: 0.99, 1.02).

Four studies did not account for potential confounders in their results (Brzezinska-Pawlowska 2016, Kordit 2020, Rossi 1993, Jariwala 2014). See appendix 4.7 for results.

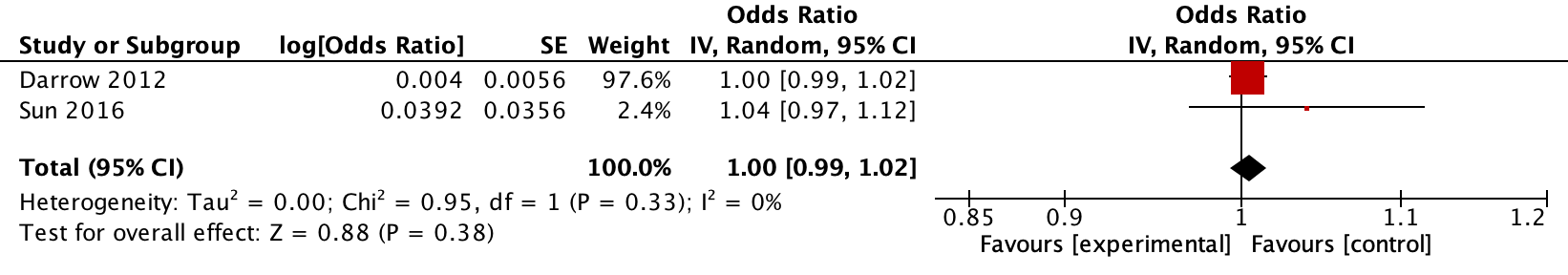
*Table 14: Severe Asthma Exacerbation in the general population exposed to tree pollen (adjusted results)*

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study ID** | **Age** | **Outcome Definition** | **Exposure** | | **Effect Estimate** | | | |
| **Tree pollen concentration** | **Lag** |  | **EE** | **95%CI** | |
| **Lee 2019** | All ages | Asthma-Related ED Visits | Increment 100 grains/m3 | 0 | RR | 1.009 | 1.002 | 1.017 |
| **Osborne 2017** | 16-64 years | Asthma-Related ED Admissions | 0-95p increase: 104 grains/m3 | 0 | Percentage Change | −4.01 | −17.95 | 9.93 |
| 1 | −8.65 | −24.08 | 6.78 |
| 2 | 2.06 | −13.6 | 17.74 |
| 3 | −10.82 | −26.86 | 5.21 |
| 4 | 4.59 | −10.66 | 19.87 |
| 5 | −9.45 | −24.66 | 5.75 |
| 6 | 0.89 | −14.32 | 16.17 |
| 7 | 2.67 | −11.66 | 16.99 |
| **Sun 2016** | All ages | Asthma-Related ED Visits | 10 grains/m3 | 0-3 | RR | 1.01 | 0.97 | 1.06 |
| 37 grains/m3 | 1.04 | 0.97 | 1.11 |
| 3500 grains/m3 | 2.10 | 1.21 | 3.65 |
| **Darrow 2012** | All ages | Asthma-Related ED Visits | 20 grains/m3 | 3 day moving average | RR | 1.004 | 0.993 | 1.016 |
| **Witonsky 2018** | All ages | Asthma-Related ED Visits | Full Year | 3 day moving average | Beta Linear Regression Model | 0.311 | p=0.000 | |
| Spring | 0.268 | p=0.000 | |
| Summer | –0.062 | p=0.111 | |
| Asthma-Related ED Admissions | Full Year | 0.042 | p=0.112 | |
| Spring | -0.002 | p=0.960 | |
| Summer | 0.085 | p=0.052 | |
| **Dales 2004** | All ages | Asthma-Related ED Visits | Increase in 125 grains/m3 | cumulative 0-5 | Percentage Change | 2.87 | 0.87 | 4.97 |
| **Dales 2008** | All ages | Asthma Hospitalisation | Increase from 25th to 75th percentiles\* | cumulative 0-5 | Percentage Change | 1.45 | 0.07 | 2.83 |

### *ED: Emergency Department, RR: risk ratio, 95%CI: 95% confidence interval*

### *\*mean grains/m3 tree pollen concentration: 32.3*

Figure 6. *Severe asthma exacerbations associated with an increase of 0 to 50 grains/m3 of tree pollen (lag 0-3) in the general population.*



### *Age Not Specified*

One time series analysis reported the association between asthma hospitalisation and an increase in tree pollen concentrations equivalent to the interquartile range, on the same day (lag 0). The authors reported positive associations in both, days of lower and days of higher air pollutant concentrations (Cakmark 2012)(Table 15).

*Table 15: Severe Asthma Exacerbation for not specified ages exposed to tree pollen (adjusted results)*

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study ID** | **Age** | **Outcome Definition** | **Exposure** | | **Effect Estimate** | | | |
| **Tree pollen concentration** | **Lag** |  | **EE** | **95%CI** | |
| Cakmark 2012 | NR | Asthma Hospitalisation | IQRI in days of lower air pollutant concentration | 0 | Percentage change | 1.124 | 1.101 | 1.147 |
| IQRI in days of higher air pollutant concentration | 1.179 | 1.149 | 1.21 |

### *ED: Emergency Department, IQRI: interquartile range increase, 95%CI: 95% confidence interval*

Moderate Asthma Exacerbation

### This outcome was not reported for any age group.

Asthma Control

This outcome was not reported for any age group.

Quality of Life

This outcome was not reported for any age group.

Lung Function

This outcome was not reported for any age group.

Asthma Symptoms/Well Days

This outcome was not reported for any age group.

Mortality

### *General Population*

One longitudinal (retrospective) study assessed the relation between asthma-related mortality and tree pollen concentrations. Targonsky 1995 reported that tree pollen concentrations were not significantly different between days on which asthma related deaths occurred and days on which such deaths did not occur (Table 16). This outcome was not reported for the other selected age groups.

*Table 16: Death caused by asthma in the general population exposed to tree pollen*

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study ID** | **Age** | **Outcome Definition** | **Exposure** | | **Effect Estimate** | | | |
| **Tree pollen concentration** | **Lag** |  | **EE** | **95%CI** | |
| **Targonski 1995** | 5-34 years | Death caused by asthma | 100 grains per cubic metre increase | 0 | OR | 1.00 | 0.88 | 1.11 |

### *OR: odds ratio, 95%CI: 95% confidence interval*

This outcome was not reported for the other selected age groups.

## Alder Pollen

One time series analysis assessed the impact of alder pollen counts on asthma.

Severe Asthma Exacerbation

Guilbert 2018 reported the association between asthma related hospitalisations and an increase of 9 grains/m3 of alder pollen with a 0 to 6 days cumulative lag. They reported results stratified by age, with a negative though imprecise association for children from 0 to 14 years of age, no association for participants from 15 to 59 years, and positive though imprecise association for participants over 60 years of age (Table 17).

*Table 17: Severe Asthma Exacerbation in patients stratified by age group exposed to alder pollen (adjusted results)*

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study ID** | **Age** | **Outcome Definition** | **Exposure** | | **Effect Estimate** | | | |
| **Alder pollen concentration** | **Lag** |  | **EE** | **95%CI** | |
| **Guilbert 2018** | 0-14 years | Asthma Hospitalisation | 9 grains/m3 IQRI | 0-6 cumulative lag | Percentage change | -1.0 | -3.7 | 1.7 |
| 15-59 years | 0.0 | -2.6 | 2.6 |
| 60+ years | 1.0 | -1.5 | 3.7 |
| all ages | 0.2 | -2.2 | 2.7 |

*ED: Emergency Department, IQRI: interquartile range increase, 95%CI: 95% confidence interval*

Moderate Asthma Exacerbation

### This outcome was not reported for any age group.

Asthma Control

This outcome was not reported for any age group.

Quality of Life

This outcome was not reported for any age group.

Lung Function

This outcome was not reported for any age group.

Asthma Symptoms/Well Days

This outcome was not reported for any age group.

Mortality

This outcome was not reported for any age group.

## Birch Pollen

Six studies assessed the impact of birch pollen counts on asthma. The study designs were time series (n=4), case-crossover (n=1), and longitudinal (n=1). Among these, 4 assessed participants of all ages, of which 2 presented results stratified by age; 1 study only assessed participants under 18 years of age, and 1 assessed participants over 18 years of age.

Severe Asthma Exacerbation

### *Under 18 years of age*

Three studies assessed the association between asthma and birch pollen concentrations. All reported a positive association.

One longitudinal study (Anderson 1998) reported a positive association between asthma-related ED admissions with a 10 unit increase in birch pollen lagged 2 days (Table 18).

One case-crossover study (De Roos 2020) reported the association between asthma exacerbation and birch pollen on 0 to 1 day cumulative lag. They reported a positive association with concentrations up to 175.7 grains/m3 with a peak between 23.8 to 45.5 grains/m3 (Table 18).

One time series analysis (Guilbert 2018) reported a positive association between asthma hospitalisation and a 40 grains/m3 increase of birch pollen on 0 to 6 days cumulative lag (Table 18).

*Table 18: Severe Asthma Exacerbation in patients under 18 years of age exposed to birch pollen (adjusted results)*

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study ID** | **Age** | **Outcome Definition** | **Exposure** | | **Effect Estimate** | | | |
| **Birch pollen concentration** | **Lag** |  | **EE** | **95%CI** | |
| **Anderson 1998** | 0-14 years | Asthma-Related ED Admissions | 10 unit increase | 2 | Percentage change | 0.90 | 0.14 | 1.67 |
| **De Roos 2020** | <18 years | Asthma Exacerbation | >0 to 23.8 grains/m3 | Cumulative 0-1 | OR | 1.15 | 1.09 | 1.22 |
| >23.8 to 45.5 grains/m3 | 1.30 | 1.21 | 1.40 |
| >45.5 to 175.7 grains/m3 | 1.19 | 1.10 | 1.29 |
| >175.7 grains/m3 | 1.00 | 0.85 | 1.11 |
| **Guilbert 2018** | 0-14 years | Asthma Hospitalisation | 40 grains/m3 IQRI | Cumulative 0-6 | Percentage change | 3.3 | 1.1 | 5.5 |

### *ED: Emergency Department, IQRI: interquartile range increase, OR: odds ratio, 95%CI: 95% confidence interval*

### *Over 18 years of age*

One longitudinal study (Anderson 1998) reported a negative though imprecise association between a 10 unit increase in bitch pollen and same day (lag 0) asthma-related ED admissions (Table 19).

On the other hand, a time series analysis (Guilbert 2018) reported a positive association between a 40 grains/m3 increase and asthma hospitalisations with a 0 to 6 days cumulative lag (Table 19).

One study did not account for potential confounders in their results (Krmpotic 2011). See appendix 4.7 for results.

*Table 19: Severe Asthma Exacerbation in patients over 18 years of age exposed to birch pollen (adjusted results)*

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study ID** | **Age** | **Outcome Definition** | **Exposure** | | **Effect Estimate** | | | |
| **Birch pollen concentration** | **Lag** |  | **EE** | **95%CI** | |
| **Anderson 1998** | >65 years | Asthma-Related ED Admissions | 10 unit increase | 0 | Percentage change | -0.77 | -3.37 | 1.9 |
| **Guilbert 2018** | 60+ years | Asthma Hospitalisation | 40 grains/m3 IQRI | Cumulative 0-6 | Percentage change | 2.8 | 0.6 | 5.1 |

### *ED: Emergency Department, IQRI: interquartile range increase, 95%CI: 95% confidence interval*

### *General Population*

Three studies reported the association between asthma exacerbations and birch pollen concentrations in the general population.

One time series analysis (Osborne 2017) assessed the association between asthma-related ED admissions and birch pollen counts on the same day (lag 0), and observed a trend with an increased risk of admissions with higher birch pollen concentrations (Table 20).

When assessing lagged associations up to 7 days, no trend was observed on the same study, with mostly positive though imprecise associations. Additionally, a longitudinal study (Anderson 1998) reported a positive association with a 10 unit increase on birch pollen lagged 1 and 2 days (Table 20).

One time series analysis (Guilbert 2018) reported positive associations between asthma hospitalizations and a 40 grains/m3 increase of birch pollen in 0 to 6 days cumulative lag (Table 20).

*Table 20: Severe Asthma Exacerbation in the general population exposed to birch pollen (adjusted results)*

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study ID** | **Age** | **Outcome Definition** | **Exposure** | | **Effect Estimate** | | | |
| **Birch pollen concentration** | **Lag** |  | **EE** | **95%CI** | |
| **Osborne 2017** | 16-64 years | Asthma-Related ED Admissions | Increase from 0 to 195 grains/m3 | 0 | Percentage change | 1.44 | −7.22 | 10.1 |
| 1 | 1.33 | −7.59 | 10.26 |
| 2 | 2.77 | −6 | 11.52 |
| 3 | 0.06 | −8.59 | 8.7 |
| 4 | 3.1 | −5.56 | 11.78 |
| 5 | −5.77 | −14.29 | 2.75 |
| 6 | 1.76 | −6.36 | 9.89 |
| 7 | −1.78 | −9.3 | 5.73 |
| Medium: ≥40 grains/m3 & ≤79 grains/m3 | 0 | RaR | 0.97 | 0.78 | 1.21 |
| 3 | 1.08 | 0.88 | 1.33 |
| High: ≥80 grains/m3 & ≤199 grains/m3 | 0 | 1.02 | 0.81 | 1.29 |
| 3 | 1.03 | 0.83 | 1.28 |
| Very High: ≥200 grains/m3 | 0 | 1.07 | 0.85 | 1.36 |
| 3 | 1.02 | 0.81 | 1.28 |
| **Anderson 1998** | 15-64 years | Asthma-Related ED Admissions | 10 unit increase | 1 | Percentage change | 1.11 | 0.11 | 2.12 |
| all ages | 2 | 0.78 | 0.15 | 1.42 |
| **Guilbert 2018** | 15-59 years | Asthma Hospitalisation | 40 grains/m3 IQRI | Cumulative 0-6 | Percentage change | 3.3 | 1.1 | 5.6 |
| all ages | 3.2 | 1.1 | 5.3 |

### *ED: Emergency Department, IQRI: interquartile range increase, RaR: incidence risk ratio: 95%CI: 95% confidence interval*

One study did not account for potential confounders in their results (Ito 2015). See appendix 4.7 for results.

Moderate Asthma Exacerbation

### This outcome was not reported for any age group.

Asthma Control

This outcome was not reported for any age group.

Quality of Life

This outcome was not reported for any age group.

Lung Function

This outcome was not reported for any age group.

Asthma Symptoms/Well Days

This outcome was not reported for any age group.

Mortality

This outcome was not reported for any age group.

## Cypress Pollen

Seven studies assessed the impact of cypress pollen counts on asthma. The study designs were time series (n=3), case-crossover (n=3), and case-control study (n=1). Among these, 4 assessed participants of all ages, of which 1 presented results stratified by age; and 3 studies only assessed participants under 18 years of age.

Severe Asthma Exacerbation

### *Under 18 years of age*

Two studies reported the association between asthma-related ED visits or hospitalizations and cypress pollen concentrations on the same day **(lag 0)**. One case-control study (Mazenq 2017) reported a negative though imprecise association with a non-specified pollen concentration, while a case-crossover study (Shrestha 2017) reported a positive though imprecise association with an increase between the 75th and 90th percentile of cypress pollen concentrations (Table 21).

Three studies reported the association between asthma exacerbation or hospitalisation and cypress pollen with **cumulative lags up to 6 days**. Shrestha 2017 reported a positive though imprecise association with an increase between the 75th and 90th percentile, and another case-crossover study (De Roos 2020) reporte a positive association with concentrations up to 23.3 grains/m2. However, for concentrations above 23.3 grains/m3, a case-crossover study (De Roos 2020) and a time series analysis (Guilbert 2018) reported a negative though imprecise association (Table 21).

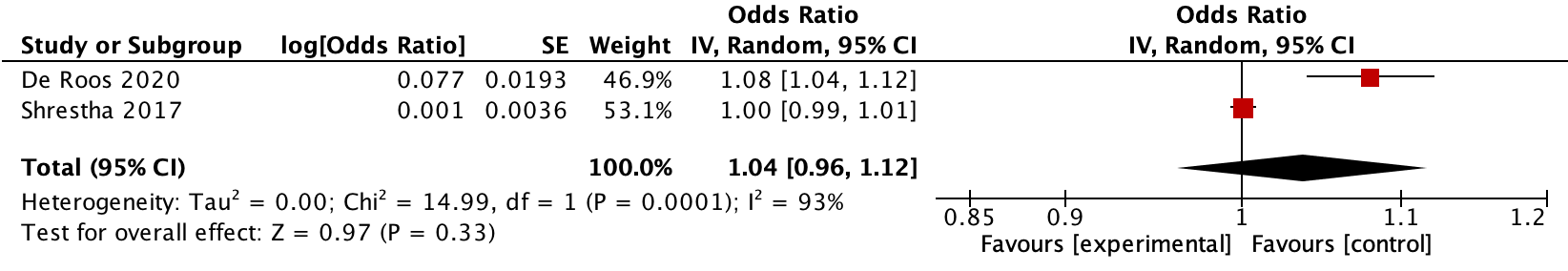
We performed a quantitative synthesis (meta-analysis) for studies that measured this outcome between lag 0 to 3 (figure 7). An increase in cypress pollen concentrations from >0 to 50 grains/m3 showed a positive association with severe asthma exacerbation in patients under 18 years (OR = 1.04, 95% CI: 0.96, 1.12).

*Table 21: Severe Asthma Exacerbation in patients under 18 years of age exposed to cypress pollen (adjusted results)*

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study ID** | **Age** | **Outcome Definition** | **Exposure** | | **Effect Estimate** | | | |
| **Cypress pollen concentration** | **Lag** |  | **EE** | **95%CI** | |
| **Mazenq 2017** | 3-18 y | Asthma-Related ED Visits | Not specified | 0 | OR | 0.99 | 0.99 | 1.00 |
| **Shrestha 2017** | 2-18 y | Asthma Hospitalisation | 75th to 90th percentile increase | 0 | OR | 1.007 | 0.986 | 1.027 |
| Cumulative 0-3 | OR | 1.001 | 0.994 | 1.008 |
| **De Roos 2020** | <18 years | Asthma exacerbation | >0 to 23.3 grains/m3 | Cumulative 0-2 | OR | 1.08 | 1.04 | 1.12 |
| >23.3 to 62.5 grains/m3 | 0.98 | 0.91 | 1.06 |
| >62.5 grains/m3 | 0.98 | 0.90 | 1.06 |
| **Guilbert 2018** | 0-14 y | Asthma Hospitalisation | 49 grains/m3 IQRI | Cumulative 0-6 | Percentage change | −3.9 | −8.8 | 1.4 |

### *ED: Emergency Department, IQRI: interquartile range increase, OR: odds ratio, 95%CI: 95% confidence interval*

### *\* geometric mean (SD) grains/m3 of total pollen: 7.9 (5.0)*

Figure 7. *Severe asthma exacerbations associated with an increase of 0 to 50 grains/m3 of cypress pollen (lag 0-3) in patients under 18 years.  
*

### *Over 18 years of age*

One time series analysis (Guilbert 2018) reported a negative though imprecise association between asthma hospitalisations and an increase in 49 grains/m3 for **0 to 6 days cumulative lag** (Table 22).

*Table 22: Severe Asthma Exacerbation in patients under 18 years of age exposed to cypress pollen (adjusted results)*

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study ID** | **Age** | **Outcome Definition** | **Exposure** | | **Effect Estimate** | | | |
| **Cypress pollen concentration** | **Lag** |  | **EE** | **95%CI** | |
| **Guilbert 2018** | 0-14 y | Asthma Hospitalisation | 49 grains/m3 IQRI | Cumulative 0-6 | Percentage change | -1.2 | −6.1 | 4.1 |

### *ED: Emergency Department, IQRI: interquartile range increase, 95%CI: 95% confidence interval*

### 

### *General Population*

Three time series analysis and one case-crossover study examined the association between cypress pollen and asthma exacerbations in the general population. Three reported negative and one positive associations.

Hanigan 2007 reported a negative though imprecise association between asthma-related ED admissions and a non-specified pollen concentration on the same day **(lag 0)**(Table 23).

Darrow 2012 reported a negative association between asthma-related ED visits with a **3 day moving average** concentration of 25 grains/m3 of cypress pollen (Table 23).

Guilbert 2018 reported a negative though imprecise association between asthma hospitalisations and a 49 grains/m3 increase in pollen concentrations in a **0 to 6 days cumulative lag** (Table 23).

Tobias 2003 reported a positive though imprecise association between asthma-related ED admissions and 194.6 grains/m3 of cypress pollen **lagged 3 days** (Table 23).

*Table 23: Severe Asthma Exacerbation in the general population exposed to cypress pollen (adjusted results)*

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study ID** | **Age** | **Outcome Definition** | **Exposure** | | **Effect Estimate** | | | |
| **Cypress pollen concentration** | **Lag** |  | **EE** | **95%CI** | |
| **Hanigan 2007** | all ages | Asthma-Related ED Admissions | IQR change in pollen load for linear responses | 0 | Percentage change | -3.26 | -9.74 | 3.68 |
| **Tobias 2003** | all ages | Asthma-Related ED Admissions | p95-p99: 194.6 grains/m3 | 3 | Percentage change | 6.0 | -3.4 | 16.5 |
| **Darrow 2012** | all ages | Asthma-Related ED Visits | 25 grains/m3 | 3 day moving average | RR | 0.988 | 0.978 | 0.998 |
| **Guilbert 2018** | 15-59 | Asthma hospitalisations | 49 grains/m3 IQRI | Cumulative 0-6 | Percentage change | -3.0 | -7.9 | 2.2 |
| all ages | −2.5 | −6.9 | 2.1 |

### *ED: Emergency Department, IQRI: interquartile range increase, RR: risk ratio, 95%CI: 95% confidence interval*

Moderate Asthma Exacerbation

### This outcome was not reported for any age group.

Asthma Control

This outcome was not reported for any age group.

Quality of Life

This outcome was not reported for any age group.

Lung Function

### *Under 18 years of age*

One cohort study reported the association between lung function and cypress pollen concentrations. Lambert 2020 reported a positive association between an interquartile range increase of 22 grains/m3 for **lags 0 to 3** and the odds of <80% predicted Forced Expiratory Volume during the first second (FEV1) and Forced vital capacity (FVC)(Table 24).

*Table 24: Lung function in participants under 18 years of age exposed to cypress pollen (Adjusted results)*

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study ID** | **Age** | **Outcome Definition** | **Exposure** | | **Effect Estimate** | | | |
| **Grass pollen concentration** | **Lag** |  | **EE** | **95%CI** | |
| **Lambert 2020** | 8 years | FEV1 (<80% predicted) | 22 grains/m3 IQRI | 0-3 | OR | 2.38 | 0.59 | 5.56 |
| FVC (<80% predicted) | 3.28 | 1.10 | 10.65 |
| FEV1 | % predicted value | -4.3 | -10.9 | 2.5 |
| FVC | -3.9 | -11.4 | 3.6 |
| 14 years | FEV1 | 0.1 | -0.1 | 0.3 |
| FVC | 0.07 | -0.2 | 0.3 |

*IQRI: interquartile range increase, OR: odds ratio, 95%CI: 95% confidence interval, FEV-1= Forced expiratory volume in 1 second, FVC= forced vital capacity*

This outcome was not reported for the other selected age groups.

Asthma Symptoms/Well Days

This outcome was not reported for any age group.

Mortality

This outcome was not reported for any age group.

## Elm Pollen

Three studies assessed the impact of elm pollen counts on asthma. The study designs were time series (n=2) and case-crossover (n=1). Among these, 2 assessed participants of all ages and 1 only assessed participants under 18 years of age.

Severe Asthma Exacerbation

### *Under 18 years of age*

One case-crossover study (De Roos 2020) examined the association between asthma exacerbations and elm pollen concentrations in **0 to 5 days cumulative lag**. They reported a positive association for concentrations up to 4.1 grains/m3, though a negative and imprecise association for concentrations over 4.1 grains/m3 (Table 25).

### *General Population*

One time series analysis (Dales 2008) reported a positive association between asthma hospitalisations and an increase of 14.03 grains/m3 of elm pollen on the same day **(lag 0)**(Table 25).

One study did not account for potential confounders in their results (Ito 2015). See appendix 4.7 for results.

This outcome was not reported for the other selected age groups.

*Table 25: Severe Asthma Exacerbation in participants under 18 years of age and the general population exposed to elm pollen (adjusted results)*

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study ID** | **Age** | **Outcome Definition** | **Exposure** | | **Effect Estimate** | | | |
| **Elm pollen concentration** | **Lag** |  | **EE** | **95%CI** | |
| **De Roos 2020** | <18 years | Asthma exacerbation | >0 to 4.1 grains/m3 | Cumulative 0-5 | OR | 1.10 | 1.06 | 1.14 |
| >4.1 to 8.8 grains/m3 | 0.96 | 0.87 | 1.04 |
| >8.8 grains/m3 | 0.98 | 0.84 | 1.14 |
| **Dales 2008** | All ages | Asthma hospitalisations | Increase of 14.03 grains/m3 | 0 | Percentage change | 2.63 | 1.19 | 04.07 |

### *ED: Emergency Department, IQRI: interquartile range increase, OR: odds ratio, 95%CI: 95% confidence interval*

Moderate Asthma Exacerbation

### This outcome was not reported for any age group.

Asthma Control

This outcome was not reported for any age group.

Quality of Life

This outcome was not reported for any age group.

Lung Function

This outcome was not reported for any age group.

Asthma Symptoms/Well Days

This outcome was not reported for any age group.

Mortality

This outcome was not reported for any age group.

## Hazel Pollen

One time series analysis assessed the impact of hazel pollen counts on asthma.

Severe Asthma Exacerbation

Guilbert 2018 reported the association between asthma related hospitalisations and an increase of 4 grains/m3 of hazel pollen with a **0 to 6 days cumulative lag**. They reported results stratified by age, with a negative though imprecise association for children from 0 to 14 years of age, no association for participants from 15 to 59 years, and positive though imprecise association for participants over 60 years of age (Table 26).

*Table 26: Severe Asthma Exacerbation in patients stratified by age group exposed to hazel pollen (adjusted results)*

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study ID** | **Age** | **Outcome Definition** | **Exposure** | | **Effect Estimate** | | | |
| **Hazel pollen concentration** | **Lag** |  | **EE** | **95%CI** | |
| **Guilbert 2018** | 0-14 years | Asthma Hospitalisation | 4 grains/m3 IQRI | 0-6 cumulative lag | Percentage change | -1.0 | -3.3 | 3.2 |
| 15-59 years | 1.0 | -2.1 | 4.2 |
| 60+ years | 0.5 | -2.7 | 3.8 |
| all ages | 0.5 | -2.5 | 3.6 |

### *ED: Emergency Department, IQRI: interquartile range increase, 95%CI: 95% confidence interval*

Moderate Asthma Exacerbation

### This outcome was not reported for any age group.

Asthma Control

This outcome was not reported for any age group.

Quality of Life

This outcome was not reported for any age group.

Lung Function

This outcome was not reported for any age group.

Asthma Symptoms/Well Days

This outcome was not reported for any age group.

Mortality

This outcome was not reported for any age group.

## Mugwort Pollen

Two time series analysis assessed the impact of mugwort pollen counts on asthma.

Severe Asthma Exacerbation

Guilbert 2018 reported the association between asthma related hospitalisations and an increase of 1 grains/m3 of mugwort pollen with a **0 to 6 days cumulative lag**. They reported results stratified by age, with a positive though imprecise association for participants aged 0 to 59, and a negative though imprecise association for participants over 60 years of age (Table 27).

Tobias 2003 examined the association between asthma related hospitalisations and 2.1 grains/m3 of mugwort pollen **lagged 1 day** in the general population, and reported a positive though imprecise association (Table 27).

*Table 27: Severe Asthma Exacerbation in patients stratified by age group exposed to mugwort pollen (adjusted results)*

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study ID** | **Age** | **Outcome Definition** | **Exposure** | | **Effect Estimate** | | | |
| **Mugwort pollen concentration** | **Lag** |  | **EE** | **95%CI** | |
| **Guilbert 2018** | 0-14 years | Asthma Hospitalisation | 1 grain/m3 IQRI | 0-6 cumulative lag | Percentage change | 1.3 | −4.8 | 7.9 |
| 15-59 years | 5.3 | −1.0 | 12.1 |
| 60+ years | −4.2 | −10.8 | 2.9 |
| all ages | 1.4 | −4.4 | 7.6 |
| **Tobias, 2003** | all ages | Asthma Hospitalisation | p95-p99: 2.1 grains/m3 | 1 | Percentage change | 4.4 | -6.6 | 16.7 |

### *ED: Emergency Department, IQRI: interquartile range increase, 95%CI: 95% confidence interval*

Moderate Asthma Exacerbation

### This outcome was not reported for any age group.

Asthma Control

This outcome was not reported for any age group.

Quality of Life

This outcome was not reported for any age group.

Lung Function

This outcome was not reported for any age group.

Asthma Symptoms/Well Days

This outcome was not reported for any age group.

Mortality

This outcome was not reported for any age group.

## Olive Pollen

Three studies assessed the impact of olive pollen counts on asthma. The study designs were time series (n=2) and longitudinal study (n=1). All assessed participants of all ages.

Severe Asthma Exacerbation

### *General Population*

One time series analysis (Tobias 2004) examined the association between asthma related ED admissions and olive pollen concentrations on the same day **(lag 0)**, and reported a negative though imprecise association for concentrations between the percentiles 50 to 75 and over the 90th percentile (Table 28).

The other time series analysis (Tobias 2003) reported a positive though imprecise association between asthma hospitalisations and a variation of 106 grains/m3 of olive pollen **lagged 1 day** (Table 28).

One study did not account for potential confounders in their results (Porcel Carreño 2020). See appendix 4.7 for results.

*Table 28: Severe Asthma Exacerbation in the general population exposed to olive pollen (adjusted results)*

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study ID** | **Age** | **Outcome Definition** | **Exposure** | | **Effect Estimate** | | | |
| **Olive pollen concentration** | **Lag** |  | **EE** | **95%CI** | |
| **Tobias 2004** | all ages | Asthma-Related ED Admissions | p50-p75 | 0 | Percentage change in risk | -7.2 | -16.3 | -2.8 |
| p75-p90 | 0.5 | -12.4 | 15.2 |
| p90-p95 | -12.6 | -27.2 | 4.9 |
| p95-p99 | -2.3 | -19.2 | 18.2 |
| p99-max | -19.8 | -39.7 | 6.6 |
| **Tobias 2003** | all ages | Asthma Hospitalisation | p95-p99: 106.2 grains/m3 | 1 | Percentage change | 1.8 | -7.9 | 12.5 |

### *ED: Emergency Department, 95%CI: 95% confidence interval*

This outcome was not reported for the other selected age groups.

Moderate Asthma Exacerbation

### This outcome was not reported for any age group.

Asthma Control

This outcome was not reported for any age group.

Quality of Life

This outcome was not reported for any age group.

Lung Function

This outcome was not reported for any age group.

Asthma Symptoms/Well Days

This outcome was not reported for any age group.

Mortality

This outcome was not reported for any age group.

## Ragweed Pollen

Nine studies assessed the impact of ragweed pollen counts on asthma. The study designs were longitudinal (n=5), case-crossover (n=3), and time series (n=1). Among these, 3 assessed participants of all ages, 4 studies only assessed participants under 18 years of age, 1 only assessed participants over 18 years of age, and 1 did not specify the ages of the participants.

Severe Asthma Exacerbation

### *Under 18 years of age*

One time series analysis (Heguy 2008) examined the association between asthma-related ED visits and a 10 grain increase in ragweed pollen concentrations in **lags 0 to 6**. No trend was observed, with a positive though imprecise association in lags 0 and 1, and a negative though imprecise association in lags 3, 5 and 6 (Table 29).

One case-crossover study (De Roos 2020) examined the association between asthma exacerbations and ragweed pollen concentrations in **0 to 2 days cumulative lag**. A trend was observed to lower odds of asthma exacerbation with higher ragweed pollen concentrations. Similarly, another case-crossover study (Gleason 2014) reported a negative association with a 10 grain increase (Table 29).

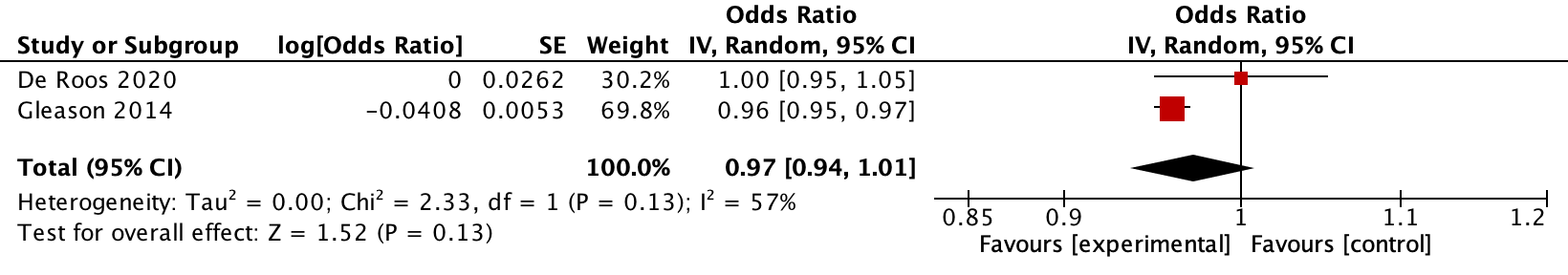
We performed a quantitative synthesis (meta-analysis) for studies that measured this outcome between lag 0 to 2 (figure 8). An increase in ragweed pollen concentrations from >0 to 50 grains/m3 showed no association to severe asthma exacerbation in patients under 18 years (OR = 0.97, 95% CI: 0.94, 1.01).

*Table 29: Severe Asthma Exacerbation in participants under 18 years of age exposed to ragweed pollen (adjusted results)*

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study ID** | **Age** | **Outcome Definition** | **Exposure** | | **Effect Estimate** | | | |
| **Ragweed pollen concentration** | **Lag** |  | **EE** | **95%CI** | |
| **Heguy 2008** | 0-9 years | Asthma-Related ED Visits | 10 grain increase | 0 | Percentage change | 0.17 | -0.38 | 0.72 |
| 1 | 0.19 | -0.35 | 0.73 |
| 2 | -0.47 | -1.07 | 0.09 |
| 3 | -0.63 | -1.17 | -0.08 |
| 4 | 0 | -0.53 | 0.53 |
| 5 | -0.56 | -1.08 | -0.03 |
| 6 | -0.66 | -1.17 | -0.14 |
| **De Roos 2020** | <18 years | Asthma exacerbation | >0 to 20.9 grains/m3 | Cumulative 0-2 | OR | 1.00 | 0.95 | 1.06 |
| >20.9 to 36 grains/m3 | Cumulative 0-2 | OR | 0.80 | 0.73 | 0.87 |
| >36 to 61.4 grains/m3 | Cumulative 0-2 | OR | 0.79 | 0.72 | 0.87 |
| >61.4 grains/m3 | Cumulative 0-2 | OR | 0.59 | 0.51 | 0.69 |
| **Gleason 2014** | 3-17 years | Asthma-Related ED Visits | 10 grain increase | lag 0-2 average | OR | 0.96 | 0.95 | 0.97 |

### *ED: Emergency Department, OR: odds ratio, 95%CI: 95% confidence interval*

Figure 8. *Severe asthma exacerbations associated with an increase of 0 to 50 grains/m3 of ragweed pollen (lag 0-2) in patients under 18 years.*

**

This outcome was not reported for the other selected age groups.

Four studies did not account for potential confounders in their results (Im 2005, Jamason 1997, Bass 2000, Darrow 2012). See appendix 4.7 for results.

### *Over 18 years of age*

One longitudinal study (Makra 2012) reported the association between asthma attacks and non-specified ragweed pollen concentrations **lagged 2 days**, and found a positive association only with male adults (no estimator was presented by the study authors).

Moderate Asthma Exacerbation

### This outcome was not reported for any age group.

Asthma Control

This outcome was not reported for any age group.

Quality of Life

This outcome was not reported for any age group.

Lung Function

This outcome was not reported for any age group.

Asthma Symptoms/Well Days

This outcome was not reported for any age group.

Mortality

### *General Population*

One longitudinal (retrospective) study assessed the relation between asthma-related mortality and ragweed pollen concentrations. Targonsky 1995 reported that ragweed pollen concentrations were not significantly different between days on which asthma related deaths occurred and days on which such deaths did not occur (Table 30). This outcome was not reported for the other selected age groups.

*Table 30: Death caused by asthma in the general population exposed to ragweed pollen.*

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study ID** | **Age** | **Outcome Definition** | **Exposure** | | **Effect Estimate** | | | |
| **Ragweed pollen concentration** | **Lag** |  | **EE** | **95%CI** | |
| **Targonski 1995** | 5-34 years | Death caused by asthma | 100 grains per cubic metre increase | 0 | OR | 0.63 | 0.36 | 1.08 |

*OR: odds ratio, 95%CI: 95% confidence interval*

This outcome was not reported for the other selected age groups.

## Thunderstorm

12 studies assessed the impact of pollen during thunderstorms on severe asthma exacerbations, 3 examined total pollen concentrations, 8 only grass pollen, and 1 examined grass and birch pollen. The study designs were longitudinal (n=6), time series (n=5), and case-control (n=1). Among these, 10 assessed participants of all ages, of which 2 presented results stratified by age; 1 study only assessed participants under 18 years of age, and 1 did not specify the ages of the participants.

## Total Pollen

### *General Population*

A time series analysis (Newson 1998) examined the effects of pollen during thunderstorms and reported that with high sferics and an increase up to 501.6 grains/m3 there was a positive association, while with low sferics this association was imprecise (Table 31).

*Table 31: Severe asthma exacerbations in the general population exposed to total pollen counts during thunderstorms.*

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study ID** | **Age** | **Outcome Definition** | **Exposure** | | **Effect Estimate** | | | |
| **Total pollen concentration** | **Lag** |  | **EE** | **95%CI** | |
| **Newson 1998** | all ages | Asthma-Related ED Admissions | 0-501.6 grains/m3/day high sferic density days | 5 day moving average | RR | 6.23 | 1.29 | 26.67 |
| 0-501.6 grains/m3/day low sferic density | 5 day moving average | 2.39 | 0.69 | 8.61 |

### *ED: emergency department, RR: risk ratio, 95%CI: 95% confidence interval*

Two studies did not account for potential confounders in their results (Anderson 2001, Packe 1985) . See appendix 4.8 for results.

## Grass Pollen

### *Under 18 years of age*

A time series analysis (Newson 1997) examined the effects of grass pollen on the same day **(lag 0)** of thunderstorms and reported that with sferics and concentrations over 50 grains/m3 there was a positive association, while without sferics there was no association (Table 32).

A longitudinal study (Hajat 1997) reported a positive association with asthma-related visits to general practitioners with high pollen concentrations (258 grains/m3) **lagged 3 days** (Table 32).

Similarly, another time series analysis (Erbas 2012) reported that as ambient grass pollen rose from 6 to about 19 grains/m3, risk of asthma-related visits increased linearly, and then declined, before rising again at 53 grains/m3 (Table 32).

*Table 32: Severe asthma exacerbations in patients under 18 years of age exposed to grass pollen during thunderstorms.*

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study ID** | **Age** | **Outcome Definition** | **Exposure** | | **Effect Estimate** | | | |
| **Grass pollen concentration** | **Lag** |  | **EE** | **95%CI** | |
| **Newson 1997** | <14 years | Asthma-Related ED Admissions | High pollen counts: >50 grains/m3 with sferics\* | 0 | RR | 1.16 | 1.04 | 1.31 |
| High pollen counts: >50 grains/m3 without sferics\* | 1.00 | 0.94 | 1.07 |
| **Hajat 1997** | Children | Asthma-Related Visits | 258 grains/m3 | 3 | RR | 1.21 | 1.03 | 1.41 |
| **Erbas 2012** | <15 years | Asthma-Related ED Visits | "The smoothed plot shows that as ambient grass pollen increased to about 19 grains/m3 same day risk of childhood ED visits also increased linearly (from about 6 grains/m3), then declined before further increasing as grass pollen levels reached about 53 grains/m3 (P < 0.001 from the non-linear term for grass pollen). Grass pollen was also associated with an increased risk in asthma ED visits the following day (lag 1, P < 0.001). Two days after exposure to grass pollen was no longer significantly associated with asthma ED visits in children" | | | | | |

### *ED: emergency department, RR: risk ratio, 95%CI: 95% confidence interval*

### *\*compared with 0 to 50 grains/m3*

### *Over 18 years of age*

A longitudinal study (Hajat 1997) examined the association between asthma-related visits to general practitioners and high pollen concentrations (258 grains/m3) **lagged 3 days** and found a positive association for adults, and a negative though imprecise association for the elderly (Table 33).

*Table 33: Severe asthma exacerbations in patients over 18 years of age exposed to grass pollen during thunderstorms.*

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study ID** | **Age** | **Outcome Definition** | **Exposure** | | **Effect Estimate** | | | |
| **Grass pollen concentration** | **Lag** |  | **EE** | **95%CI** | |
| **Hajat 1997** | Adults | Asthma-Related Visits | 258 grains/m3 | 3 | RR | 1.31 | 1.16 | 1.47 |
| **Hajat 1997** | Elderly | Asthma-Related Visits | 258 grains/m3 | 3 | RR | 0.81 | 0.60 | 1.09 |

### *General Population*

Two time series analysis examined the effects of grass pollen concentrations over 50 grains/m3 on the same day **(lag 0)** of thunderstorms. Newson 1997 reported that with sferics there was a positive association, while without sferics this association was imprecise. Lewis 2000 reported that there was a significant interaction between the effects of grass pollen and weather conditions, such that ED visits were not related to grass pollen on dry days, but increased on wet or stormy days, most markedly on days of light rainfall (Table 34).

One longitudinal study (Celenza 1996) reported that the asthma thunderstorm epidemic was associated with changes in grass pollen concentrations. There was a peak in pollen concentration about **nine hours** before the peak in asthma ED visits. Additionally, the change in grass pollen concentration was also associated with asthma ED visits **lagged 2 days** (Table 34).

A longitudinal study (Hajat 1997) examined the association between asthma-related visits to general practitioners and high pollen concentrations (258 grains/m3) **lagged 3 days** and found a positive association. Additionally, a time series analysis (Silver 2018) reported that high levels (over 70 grains/m3) of grass pollen over the **three days preceding** a thunderstorm were associated with increased admissions due to asthma (3 to 5 additional admissions)(Table 34).

Three studies did not account for potential confounders in their results (Davidson 1996, Thien 2018, Marks 2001). See appendix 4.8 for results.

*Table 34: Severe asthma exacerbations in the general population exposed to grass pollen during thunderstorms.*

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study ID** | **Age** | **Outcome Definition** | **Exposure** | | **Effect Estimate** | | | |
| **Grass pollen concentration** | **Lag** |  | **EE** | **95%CI** | |
| **Newson 1997** | >15 years | Asthma-Related ED Admissions | Pollen count >50 grains/m3 with sferics \* | 0 | RR | 1.47 | 1.32 | 1.64 |
| Pollen count >50 grains/m3 without sferics\* | 1.06 | 0.99 | 1.13 |
| all ages | Pollen count >50 grains/m3 with sferics \* | 1.31 | 1.21 | 1.42 |
| Pollen count >50 grains/m3 without sferics\* | 1.03 | 0.98 | 1.08 |
| **Lewis 2000** | >14 years | Asthma-Related ED Visits | >50 grains/m3 | 0 | OR | 2.1 | 1.4 | 3.3 |
| **Celenza 1996** | >16 years | Asthma-Related ED Visits | >30 grains/l increase | 9 hours before | Relative Change | 0.83 | 0.42 | 1.67 |
| >30 grains/l fall | 2.50 | 1.36 | 4.59 |
| >10 grains/l increase | 2 | 2.15 | 1.21 | 3.84 |
| >10 grains/l fall | 1.89 | 1.24 | 2.89 |
| **Hajat 1997** | All ages | Asthma-Related Visits | 258 grains/m3 | 3 | RR | 1.17 | 1.06 | 1.29 |
| **Silver 2018** | 0-64 years | “High levels of grass pollen over the three days preceding the thunderstorm were associated with increased admissions (roughly 3-5 additional admissions). When average grass pollen concentration of the previous three days exceeded 70 grains/m3, the exacerbation became significant, plateauing at around 4 additional admissions per day for mean concentrations of 100 grains/m3 or more.” | | | | | | |

### *ED: emergency department, RR: risk ratio, 95%CI: 95% confidence interval*

### *\*compared with 0 to 50 grains/m3*

## Birch Pollen

### *General Population*

One time series analysis (Lewis 2000) reported that the effect of non-specified birch pollen concentrations on asthma-related ED admissions was only apparent on wet days (p=0.1)(no estimate was presented by study authors).

## Risk of Bias

Using the Quality In Prognosis Studies (QUIPS) tool, we rated 47 (65.27%) of the included studies as having a high risk of bias, 9 (12.5%) a moderate risk of bias, and 16 (22.22%) a low risk of bias.

The item with the most assessments as low risk of bias across studies was Outcome Measurement, which evaluates the definition, the validity and reliability of the method of measurements, and the equal setting of the outcome for all study participants, with 45 (62.5%) of the studies. Only 2 (2.77%) studies received an assessment of high risk of bias.

The item with most assessments as high risk of bias across studies was Study Confounding, which evaluates the definition, the validity and reliability of the method of measurements, and the appropriate accounting for confounders. 24 (33.33%) of studies were judged as high risk of bias, and 21 (29.16%) as moderate risk of bias.

In two items, most studies were judged as having a moderate risk of bias: 44 (61.11%) of the studies for the Study Participation item, which evaluates whether the study sample represented the population of interest on key characteristics, and were assessed as moderate risk of bias mainly due to a lack of reporting of key characteristics of the population; and 46 (63.88%) of the studies for the Prognostic Factor Measurement item, which evaluates the definition and the validity and reliability of the method of measurement of the prognostic factor (i.e. pollen). The reason for this evaluation was mostly due to a lack of reporting of the concentrations or the method of measurement.

Lastly, the Statistical Analysis and Presentation item, which evaluates the analytical and model development strategies, and the reporting of the results, was judged as high risk of bias for 12 (16.66%) studies, as moderate risk of bias for 33 (45.83%) studies, and as low risk of bias for 27 (37.5%) studies. The Study Attrition item, which evaluates loss to follow-up, was judged as not applicable for most studies (68, 94.44%) given the characteristics of the included studies.

See appendix 4.6 for the full risk of bias assessment.

Total Pollen

Of the studies that assessed the exposure to total pollen, 9 (60%) were evaluated as having a high risk of bias, while 6 (40%) were evaluated as low risk of bias. The best evaluated item was Outcome Measurement, with 12 (80%) of the studies judged to have low risk of bias. The worst evaluated items were Study Confounding with 3 (20%) having a high risk of bias and 6 (40%) a moderate risk of bias; and Prognostic Factor Measurement, with 1 (6.66%) judged as having a high risk of bias and 9 (60%) with a moderate risk of bias (Table 35).

*Table 35: Risk of bias assessment of studies examining exposure to total pollen counts*

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **QUIPS** | **Study ID** | | | | | | | | | | | | | | | | | |
| **Lowe 2012** | **Shrestha 2017** | **Lierl 2003** | **Bouazza 2017** | **Chen 2016** | **Makra 2012** | **Hanigan 2007** | **Mazenq b 2017** | **Gonzalez-Barcala 2013** | **Ostro 2001** | **Epton 1997** | **Li 2019** | **Klabushnigg 1981** | **Ginis 2015** | **Epton 1997** | **Ostro 2001** | **Epton 1997** | **Mackay 1992** |
| Study participation | Moderate | Low | Low | Moderate | Moderate | Moderate | Moderate | Moderate | Low | Low | Low | Low | Moderate | Moderate | Low | Low | Low | Moderate |
| Study Attrition | NA | NA | NA | NA | NA | NA | NA | NA | NA | Low | Low | NA | NA | NA | Low | Low | Low | NA |
| Prognostic factor Measurement | Moderate | Low | Low | Moderate | Low | Moderate | Moderate | Moderate | Moderate | Low | Low | Moderate | Moderate | High | Low | Low | Low | Moderate |
| Outcome Measurement | Moderate | Low | Low | Low | Low | Low | Moderate | Low | Low | Low | Low | Low | Low | Low | Low | Low | Low | Moderate |
| Study Confounding | Moderate | Low | Moderate | Moderate | Low | Moderate | Low | Moderate | Moderate | Low | Low | Low | High | High | Low | Low | Low | High |
| Statistical Analysis and Presentation | Low | Low | Low | Moderate | Low | Moderate | Low | Moderate | Moderate | Low | Moderate | Low | High | High | Moderate | Low | Moderate | High |
| **Overall RoB** | **High** | **Low** | **Low** | **High** | **Low** | **High** | **High** | **High** | **High** | **Low** | **Low** | **Low** | **High** | **High** | **Low** | **Low** | **Low** | **High** |
|  | **Severe Asthma Exacerbation** | | | | | | | | | **Moderate Asthma Exacerbation** | | **Asthma Control** | **Lung Function** | | | **Asthma Symptoms** | | **Mortality** |

### *NA: not applicable*

See appendix 4.6 for the risk of bias assessment of studies that reported non-adjusted results.

Grass Pollen

Of the studies that assessed the exposure to grass pollen, 14 (50%) were evaluated as having a high risk of bias, while 9 (32.14%) were evaluated as low risk of bias, and 5 (17.86%) as moderate risk of bias. The best evaluated item was Outcome Measurement, with 18 (64.28%) of the studies judged to have low risk of bias. The worst evaluated item was Study Confounding with 5 (17.86%) having a high risk of bias, however, 15 (53.57%) of the studies were judged as having low risk of bias (Table 36).

*Table 36: Risk of bias assessment of studies examining exposure to grass pollen*

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **QUIPS** | **Study ID** | | | | | | | | | | | | | | | | | |
| **Mazenq 2017** | **Shrestha 2017** | **Batra 2021** | **Khot 1988** | **De Roos 2020** | **Gleason 2014** | **Babin 2007** | **Heguy 2008** | **Guilbert 2018** | **Wilonsky 2018** | **Lee 2019** | **Anderson 1998** | **Darrow 2012** | **Erbas 2007** | **Hanigan 2007** | **Osborne 2017** | **Tobias 2003** | **Tobias 2004** |
| Study participation | Low | Low | Moderate | Moderate | Low | Low | Moderate | Moderate | Moderate | Moderate | Moderate | Moderate | Moderate | Moderate | Moderate | Low | Moderate | High |
| Study Attrition | NA | NA | NA | NA | NA | NA | NA | NA | NA | NA | NA | NA | NA | NA | NA | NA | NA | NA |
| Prognostic factor Measurement | Low | Low | Moderate | Moderate | Low | Low | High | Moderate | Low | Moderate | Low | Low | Low | Moderate | Moderate | Low | Moderate | Moderate |
| Outcome Measurement | Low | Low | High | Low | Low | Low | Low | Low | Low | Moderate | Low | Low | Low | Moderate | Moderate | Low | Moderate | Moderate |
| Study Confounding | Low | Low | Low | Moderate | Low | Low | High | Low | Low | Moderate | Low | Moderate | Low | Low | Low | Low | Moderate | Moderate |
| Statistical Analysis and Presentation | Low | Low | High | Moderate | Low | Low | Moderate | Low | Low | Moderate | Low | Low | Moderate | Moderate | Low | Low | Moderate | Moderate |
| **Overall RoB** | **Low** | **Low** | High | **High** | **Low** | **Low** | **High** | **Moderate** | **Low** | **High** | **Low** | **Moderate** | **Moderate** | **High** | **High** | **Low** | **High** | **High** |
|  | **Severe Asthma Exacerbation** | | | | | | | | | | | | | | | | | |

### *NA: not applicable*

*Table 36 cont.: Risk of bias assessment of studies examining exposure to grass pollen*

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study ID** | | | | | | | | | | |
| **Dales 2004** | **Sun 2016** | **Ghosh 2012** | **Cirera 2012** | **Lambert 2020** | **Klabushnigg 1981** | **Idrose 2020** | **Kralimarkova 2014** | **Kralimarkova 2014** | **Mackay 1992** | **Targonskl 1995** |
| Moderate | Low | High | Moderate | Moderate | Moderate | Moderate | Moderate | Moderate | Moderate | Low |
| NA | NA | NA | NA | NA | NA | NA | Moderate | Moderate | NA | NA |
| Low | Moderate | Moderate | Moderate | Low | Moderate | Moderate | High | High | Moderate | Low |
| Low | Low | Moderate | Low | Low | Low | Moderate | Moderate | Moderate | Moderate | Low |
| Low | Moderate | High | Moderate | Low | High | Moderate | High | High | High | Low |
| Moderate | Low | Moderate | Low | Low | High | Moderate | Moderate | Moderate | High | Low |
| **Moderate** | **Moderate** | **High** | **High** | **Low** | **High** | **High** | **High** | **High** | **High** | **Low** |
| **Severe Asthma Exacerbation** | | | | **Lung Function** | | | | **Asthma Symptoms** | **Mortality** | |

### *NA: not applicable*

See appendix 4.6 for the risk of bias assessment of studies that reported non-adjusted results.

Tree Pollen

Of the studies that assessed the exposure to tree pollen, 7 (46.66%) were evaluated as having a low risk of bias, while 5 (33.33%) were evaluated as high risk of bias, and 3 (20%) as moderate risk of bias. The best evaluated item was Outcome Measurement, with 12 (80%) of the studies judged to have low risk of bias. The worst evaluated item was Study Confounding, with 2 (13.33%) having a high risk of bias, however, 10 (66.66%) of the studies were judged as having low risk of bias (Table 37).

*Table 37: Risk of bias assessment of studies examining exposure to tree pollen*

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **QUIPS** | **Study ID** | | | | | | | | | | | | | | |
| **Batra 2021** | **Babin 2007** | **Shrestha 2017** | **De Roos 2020** | **Gleason 2014** | **Lee 2019** | **Wilonsky 2018** | **May 2011** | **Osborne 2017** | **Sun 2016** | **Darrow 2012** | **Dales 2004** | **Dales 2008** | **Cakmak 2012** | **Targonskl 1995** |
| Study participation | Moderate | Moderate | Low | Low | Low | Moderate | Moderate | Moderate | Low | Low | Moderate | Moderate | Moderate | Moderate | Low |
| Study Attrition | NA | NA | NA | NA | NA | NA | NA | NA | NA | NA | NA | NA | NA | NA | NA |
| Prognostic factor Measurement | Moderate | High | Low | Low | Low | Low | Moderate | Moderate | Low | Moderate | Low | Low | Low | Moderate | Low |
| Outcome Measurement | High | Low | Low | Low | Low | Low | Moderate | Moderate | Low | Low | Low | Low | Low | Low | Low |
| Study Confounding | Low | High | Low | Low | Low | Low | Moderate | High | Low | Moderate | Low | Low | Low | Moderate | Low |
| Statistical Analysis and Presentation | High | Moderate | Low | Low | Low | Low | Moderate | Moderate | Low | Low | Moderate | Moderate | Low | Moderate | Low |
| **Overall RoB** | High | **High** | **Low** | **Low** | **Low** | **Low** | **High** | **High** | **Low** | **Moderate** | **Moderate** | **Moderate** | **Low** | **High** | **Low** |
|  | **Severe Asthma Exacerbation** | | | | | | | | | | | | | | **Mortality** |

### *NA: not applicable*

See appendix 4.6 for the risk of bias assessment of studies that reported non-adjusted results.

Alder Pollen

One study assessed the exposure to alder pollen, and was judged in every item, as well as in the overall evaluation, as having a low risk of bias (Table 38).

*Table 38: Risk of bias assessment of studies examining exposure to alder pollen*

|  |  |
| --- | --- |
| **QUIPS** | **Study ID** |
| **Guilbert 2018** |
| Study participation | Low |
| Study Attrition | NA |
| Prognostic factor Measurement | Low |
| Outcome Measurement | Low |
| Study Confounding | Low |
| Statistical Analysis and Presentation | Low |
| **Overall RoB** | Low |
|  | **Severe Asthma Exacerbation** |

### *NA: not applicable*

Birch Pollen

Of the studies that assessed the exposure to birch pollen, 3 (75%) were evaluated as having a low risk of bias, while 1 (25%) was evaluated as having a moderate risk of bias. Only two items were not evaluated across studies as low risk of bias. The Study Participation item was judged as having a moderate risk of bias in 2 (50%) studies and the Study Confounding item was judged as having a moderate risk of bias in 1 study (25%)(Table 39).

*Table 39: Risk of bias assessment of studies examining exposure to birch pollen*

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **QUIPS** | **Study ID** | | | |
| **De Roos 2020** | **Anderson 1998** | **Guilbert 2018** | **Osborne 2017** |
| Study participation | Low | Moderate | Moderate | Low |
| Study Attrition | NA | NA | NA | NA |
| Prognostic factor Measurement | **Low** | Low | Low | Low |
| Outcome Measurement | Low | Low | Low | Low |
| Study Confounding | Low | Moderate | Low | Low |
| Statistical Analysis and Presentation | Low | Low | Low | Low |
| **Overall RoB** | **Low** | **Moderate** | **Low** | **Low** |
|  | **Severe Asthma Exacerbation** | | | |

### *NA: not applicable*

See appendix 4.6 for the risk of bias assessment of studies that reported non-adjusted results.

Cypress Pollen

Of the studies that assessed the exposure to cypress pollen, 5 (62.5%) were evaluated as having a low risk of bias, while 2 (25%) were evaluated as having a high risk of bias, and 1 (12.5%) as having a moderate risk of bias. The best evaluated item was Study Confounding, with 12 (87.5%) of the studies judged to have low risk of bias. The worst evaluated item was Study Participation, with 5 (62.5%) having a moderate risk of bias. No item was evaluated as having a high risk of bias across studies (Table 40).

*Table 40: Risk of bias assessment of studies examining exposure to cypress pollen*

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **QUIPS** | **Study ID** | | | |  |  |  |  |
| **Mazenq 2017** | **Shrestha 2017** | **De Roos 2020** | **Guilbert 2018** | **Hanigan 2007** | **Tobias 2003** | **Darrow 2012** | **Lambert 2020** |
| Study participation | Low | Low | Low | Moderate | Moderate | Moderate | Moderate | Moderate |
| Study Attrition | NA | NA | NA | NA | NA | NA | NA | NA |
| Prognostic factor Measurement | Low | Low | **Low** | Low | Moderate | Moderate | Low | Low |
| Outcome Measurement | Low | Low | Low | Low | Moderate | Moderate | Low | Low |
| Study Confounding | Low | Low | Low | Low | Low | Moderate | Low | Low |
| Statistical Analysis and Presentation | Low | Low | Low | Low | Low | Moderate | Moderate | Low |
| **Overall RoB** | **Low** | **Low** | **Low** | **Low** | **High** | **High** | **Moderate** | Low |
|  | **Severe Asthma Exacerbation** | | | | | | | **Lung Function** |

### *NA: not applicable*

Elm Pollen

Both studies that assessed the exposure to elm pollen were evaluated as having a low risk of bias. Only the Study Participation item was evaluated as having a moderate risk of bias by one study (50%)(Table 41).

*Table 41: Risk of bias assessment of studies examining exposure to elm pollen*

|  |  |  |
| --- | --- | --- |
| **QUIPS** | **Study ID** | |
| **De Roos 2020** | **Dales 2008** |
| Study participation | Low | Moderate |
| Study Attrition | NA | NA |
| Prognostic factor Measurement | Low | Low |
| Outcome Measurement | Low | Low |
| Study Confounding | Low | Low |
| Statistical Analysis and Presentation | Low | Low |
| **Overall RoB** | **Low** | **Low** |
|  | **Severe Asthma Exacerbation** | |

### *NA: not applicable*

See appendix 4.6 for the risk of bias assessment of studies that reported non-adjusted results.

Hazel Pollen

One study assessed the exposure to hazel pollen and was evaluated as having an overall low risk of bias, with only the Study Participation item being judged as having a moderate risk of bias (Table 42).

*Table 42: Risk of bias assessment of studies examining exposure to hazel pollen*

|  |  |
| --- | --- |
| **QUIPS** | **Study ID** |
| **Guilbert 2018** |
| Study participation | Moderate |
| Study Attrition | NA |
| Prognostic factor Measurement | Low |
| Outcome Measurement | Low |
| Study Confounding | Low |
| Statistical Analysis and Presentation | Low |
| **Overall RoB** | **Low** |
|  | **Severe Asthma Exacerbation** |

### *NA: not applicable*

Mugwort Pollen

Of the studies that assessed the exposure to mugwort pollen, 1 (50%) was evaluated as having a low risk of bias, and 1 (50%) as having a high risk of bias, with every item being evaluated as having a moderate risk of bias in the latter (Table 43).

*Table 43: Risk of bias assessment of studies examining exposure to mugwort pollen*

|  |  |  |
| --- | --- | --- |
| **QUIPS** | **Study ID** | |
| **Guilbert 2018** | **Tobias 2003** |
| Study participation | Moderate | Moderate |
| Study Attrition | NA | NA |
| Prognostic factor Measurement | Low | Moderate |
| Outcome Measurement | Low | Moderate |
| Study Confounding | Low | Moderate |
| Statistical Analysis and Presentation | Low | Moderate |
| **Overall RoB** | **Low** | **High** |
|  | **Severe Asthma Exacerbation** | |

### *NA: not applicable*

Olive Pollen

Both studies that assessed the exposure to olive pollen were evaluated as having a high risk of bias. The only item that received an evaluation other than moderate risk of bias, was the Study Participation item, with 1 (50%) study being judged as having a high risk of bias (Table 44).

*Table 44: Risk of bias assessment of studies examining exposure to olive pollen*

|  |  |  |
| --- | --- | --- |
| **QUIPS** | **Study ID** | |
| **Tobias 2003** | **Tobias 2004** |
| Study participation | Moderate | High |
| Study Attrition | NA | NA |
| Prognostic factor Measurement | Moderate | Moderate |
| Outcome Measurement | Moderate | Moderate |
| Study Confounding | Moderate | Moderate |
| Statistical Analysis and Presentation | Moderate | Moderate |
| **Overall RoB** | **High** | **High** |
|  | **Severe Asthma Exacerbation** | |

### *NA: not applicable*

See appendix 4.6 for the risk of bias assessment of studies that reported non-adjusted results.

Ragweed Pollen

Of the studies that assessed the exposure to ragweed pollen, 3 (60%) were evaluated as having a low risk of bias, while 1 (20%) was evaluated as having a moderate risk of bias and 1 (20%) as having a high risk of bias. The best evaluated item was Outcome Measurement, with an evaluation of low risk of bias across all studies. The worst evaluated items were Study Participation and Prognostic Factor Measurement, both being evaluated as moderate risk of bias in 2 (40%) studies (Table 45).

*Table 45: Risk of bias assessment of studies examining exposure to ragweed pollen*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **QUIPS** | **Study ID** | | | |  |
| **Heguy 2008** | **De Roos 2020** | **Gleason 2014** | **Makra 2012** | **Targonskl 1995** |
| Study participation | Moderate | Low | Low | Moderate | Low |
| Study Attrition | NA | NA | NA | NA | NA |
| Prognostic factor Measurement | Moderate | Low | Low | Moderate | Low |
| Outcome Measurement | Low | Low | Low | Low | Low |
| Study Confounding | Low | Low | Low | Moderate | Low |
| Statistical Analysis and Presentation | Low | Low | Low | Moderate | Low |
| **Overall RoB** | **Moderate** | **Low** | **Low** | **High** | **Low** |
|  | **Severe Asthma Exacerbation** | | | | **Mortality** |

### *NA: not applicable*

See appendix 4.6 for the risk of bias assessment of studies that reported non-adjusted results.

Thunderstorm

Of the studies that assessed the exposure to pollen during thunderstorms, 3 (42.85%) were evaluated as having a high risk of bias, 3 (42.85%) as having a moderate risk of bias, and 1 (14.28%) as having a low risk of bias. The best evaluated item was Outcome Measurement, with 6 (85.71%) of the studies judged to have low risk of bias. The worst evaluated item was Study Participation, with 2 (28.57%) having a high risk of bias, and 4 (57.14%) a moderate risk of bias evaluation (Table 46).

*Table 46: Risk of bias assessment of studies examining exposure to pollen during thunderstorms*

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **QUIPS** | **Study ID** | | | |  |  |  |  |
| **Newson 1998** | **Erbas 2012** | **Newson 1997** | **Hajat 1997** | **Lewis 2000** | **Celenza 1996** | **Silver 2018** | **Silver 2018** |
| Study participation | High | Moderate | Moderate | High | Moderate | Low | Moderate | Moderate |
| Study Attrition | NA | NA | NA | NA | NA | NA | NA | NA |
| Prognostic factor Measurement | Moderate | Low | Moderate | Moderate | Moderate | Moderate | Low | Low |
| Outcome Measurement | Low | Low | Low | Moderate | Low | Low | Low | Low |
| Study Confounding | Low | Low | Low | Moderate | Low | Moderate | Low | Low |
| Statistical Analysis and Presentation | Low | Moderate | Low | Moderate | Moderate | Low | Low | Low |
| **Overall RoB** | **High** | **Moderate** | **Moderate** | **High** | **High** | **Moderate** | **Low** | **Low** |
|  | **Total Pollen** | **Grass Pollen** | | | | | | **Birch Pollen** |

### *NA: not applicable*

See appendix 4.6 for the risk of bias assessment of studies that reported non-adjusted results.

## 

## Evidence Profile

PENDING

# Appendix

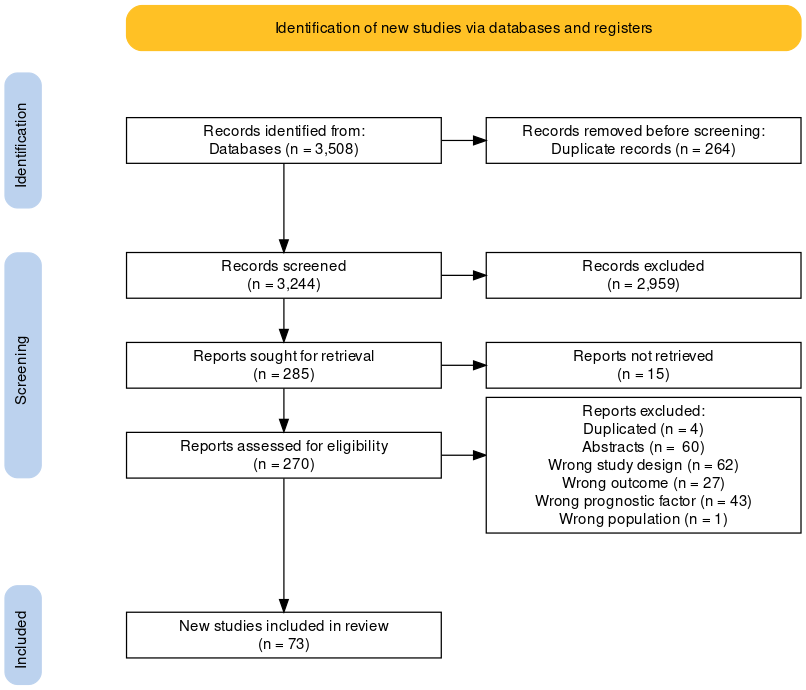
## Protocol

|  |  |
| --- | --- |
| **Question** | Is exposure to pollen a risk factor for moderate and severe asthma exacerbations? |
| **Objective** | To assess the effect of exposure to seasonal pollen on developing asthma exacerbations (moderate or severe) |
| **Design** | We will develop a systematic review, following, as guidance, the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2011), and adhere to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement (Page 2021). |
| **Eligibility criteria** | **Study design:**  Studies that measured pollen as the primary exposure variable and report moderate and severe asthma exacerbation as the outcome of interest. We will include observational studies in which subjects were followed longitudinally, over a certain time period (i.e. cohort studies, time-series studies). |
| **Population:**  Patients, children or adults, with asthma. We will stratify the population in the following subgroups:  A. Age:  -Children (< 12)  - Adolescents (12 -18 years)  -Adults (≥18 years)  B. Asthma severity: mild/moderate/severe |
| **Exposure:**  The exposure of interest is seasonal pollen, expressed as the amount of pollen grains per cubic metre of air sampled (grains/m3). The eligible definition includes exposure to mean daily total airborne pollen or exposure to mean daily airborne pollen of distinct types, including; birch, grass, ragweed, mugwort, olive, elm and/or hazel/alder pollen. We will classify seasonal pollen exposure per pollen type (birch, grass, mugworth, Ambrosia/ragweed, cypress, olive).  We will include also studies that assess the associations between pollen concentrations and symptoms during the same day (i.e. short-term exposure of 1 day) for which we will perform a separate analysis. |
| **Comparison:**  No exposure to seasonal pollen |
| **Outcomes**:  Critical   * Asthma exacerbations, classified in two groups:   + Moderate = temporary change in treatment (rescue or controller),   + Severe = Emergency Department (ED)/hospitalisation with systemic steroid use OR systemic steroid for at least 3 days) * Asthma control * Quality of life   Important   * Lung function (FEV1, PEF) * Asthma symptoms/well days * Asthma medication |
| **Search strategy** | **Sources:**  We will use electronic algorithms with a combination of controlled vocabulary and search terms in the following databases: i) MEDLINE; ii) EMBASE, and; iii) Web of Science Core. The search algorithms have been adapted to the requirements of each database, and we will use validated filters to retrieve appropriate designs as needed. We will also review references of included studies, previous systematic reviews, and we will consult experts in the field.  Abstracts or conference communications not published as full articles in peer review journals will be excluded. We will exclude publications in a language other than English. We will report in appendices, the complete search algorithms designed for each database, the hits retrieved, and the reasons for the exclusion of studies at the full text review stage. |
| **Reference management:**  We will use EndNote software to create a database for the management of the search results. |
| **Study selection, evidence appraisal and synthesis** | **Study selection:**  Two reviewers will screen search results based on the title and abstract to identify potentially eligible studies after initial calibration. Two reviewers will independently confirm eligibility based on the full text assessment of the potentially relevant articles. In case of disagreement they will consult with a third reviewer. We will report the result of this process with a PRISMA flowchart. |
| **Data collection:**  After calibration, two reviewers independently will extract relevant data from eligible studies including their main characteristics and results using pre-designed extraction forms. In case of disagreement they will consult with a third reviewer.  We will extract where available from each study data regarding study design, method of analysis, study location, time period of the study, method of pollen collection, age range and number of children, exposure definition (pollen species such as grasses, weeds, trees and conifers), pollen count, outcome definition, effect estimates together with 95% confidence intervals. We will contact authors if needed for the estimates of effects or when the exposure allocation is not clear. |
| **Risk of bias:**  We will use the risk of bias in non-randomised studies of exposures (ROBINS-E) tool that has been developed by building upon tools for risk of bias assessment of randomised trials, diagnostic test accuracy studies and observational studies of interventions.  The seven items included in ROBINS-E are: 1) Bias due to confounding, 2) Bias in selection of participants, 3) Bias in classification of exposures, 4) Bias due to departures from intended exposures, 5) Bias due to missing data, 6) Bias in measurement of outcomes, and 7) Bias in selection of reported results. Judgments for each RoB item can be: ‘Low RoB’, ‘Moderate RoB’, ‘Serious RoB’, or ‘Critical RoB’. Risk of bias, overall, will be rated as not serious, serious, or very serious. |
| **Synthesis of the results:**  We will use summary statistics to describe the studies, subjects and outcomes. We will tabulate the main characteristics of the included studies, outcomes of interest and their main effect estimates.  To improve comparison across studies, we will standardise effect estimates to an increase per 10 grains/m3 of grass pollen, and transform variances using the delta method. Estimates of effect sizes may include odds ratio, relative risk, mean change in risk, scaled beta coefficient (linear regression), and correlation coefficient. When feasible, we will conduct meta-analyses using linear mixed effects models that assumes the presence of a random effect, using the DerSimonian-Laird estimator to calculate the variance parameter.  We will judge the magnitude of heterogeneity using the Higgings’ I2 statistic (0% to 40%: low, 30% to 60%: moderate, 50% to 90%: substantial, 75% to 100%: considerable). Additionally, we will visually inspect the meta-analysis’ forest plots for consistency; given that I2 statistics might be artificially inflated when effect estimates from primary studies are very precise (Rücker 2008).  As a priori subgroup analysis we will explore the impact of: age (i.e. 0-12, 12-18 years old and >18 years old), asthma severity, pollen type and risk of bias. For all meta-analysis with at least 10 included studies, we will assess publication bias by visual inspection of the Begg´s funnel plot, and statistically, using the Egger´s test for small study effects (funnel plot asymmetry). Finally, we will report a summary of the main findings using tabulated summaries (evidence profiles), and forest plots graphs. |
| **Certainty of the evidence:**  We will rate the certainty of evidence for each outcome with the GRADE approach (Schünemann 2013). We will rate the certainty of evidence across each outcome as high, moderate, low or very low, taking into consideration risk of bias, imprecision, inconsistency, indirectness, and publication bias. |
| **References**   * Higgins JPT, Altman DG, Sterne JAC. Chapter 8: assessing risk of bias in included studies. In: Higgins JPT, Green S, editors. Cochrane handbook for systematic reviews of interventions version 5.1.0 (updated March 2011). The Cochrane Collaboration. 2011. * Page MJ, Moher D, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. PRISMA 2020 explanation and elaboration: updated guidance and exemplars for reporting systematic reviews. BMJ 2021;372:n160. * Rücker G, Schwarzer G, Carpenter JR, Schumacher M. Undue reliance on I(2) in assessing heterogeneity may mislead. BMC medical research methodology. 2008 Dec;8(1):79 * Schünemann H, Brożek J, Guyatt G, Oxman A, editors. GRADE handbook for grading quality of evidence and strength of recommendations. Updated October 2013. The GRADE Working Group, 2013. Available from www.guidelinedevelopment.org/handbook. | |

## Search Strategy

Pending

## PRISMA flowchart



## Summary of included studies

*Characteristics of individual studies identified in the literature search (1).*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Study ID** | **Aim / objectives** | **Inclusion criteria** | **Exclusion criteria** | **Design** | **Funding** |
| Anderson 1998 | To examine the association between air pollution (O3, NO2, SO2, and black smoke) and daily emergency admissions for asthma in children, adults (15–64) and the elderly (65+). | Counts of daily emergency admissions for asthma (ICD9 493 coded at discharge) to all National Health Service hospitals in London obtained from the Hospital Episode System. This covers the great majority of emergency admissions for acute medical conditions such as asthma. Children (0-14), adults (15–64) and the elderly (65+) from London. | This study does not include attendance at hospital emergency departments which do not result in admission. | Longitudinal study  (Retrospective) | This study was funded by the National Asthma Campaign (Grant 178) and the European Commission, DGXII, Environment 1991–94 Programme (EV5V CT92–0202). |
| Babin 2007 | To determine the degree to which asthma exacerbations are associated with ozone and particulate concentrations in the short-term, on the order of days after presumed exposure, and to identify paediatric populations that may be at increased risk of these health effects. | Asthma-related ED visits of paediatric patients (1 and 17 years) defined as those ED visit records in which one of the first three of nine possible diagnosis fields listed an asthma code number. These ED record fields contain numbers based on the International Classification of Diseases Ninth Revision (commonly called ICD-9) codes used by hospital and physicians' office personnel to report billing information to insurance companies. ICD-9 codes may indicate either symptoms or specific diseases, and those beginning with 493 indicate an asthma diagnosis. Based on discussions with medical personnel about ED coding practices among different DC hospitals, the criterion of an asthma code in one of the first three fields was chosen as an indication that an asthma exacerbation was a principal reason for the visit. | NR | Longitudinal study | This research is sponsored by the District of Columbia Department of Health under contract POHC-2006-C-0100. |
| Bass 2000 | To determine whether Tibouchina pollen is allergenic and to determine whether airborne ragweed pollen is present in this region for sufficient length of time and concentration to cause fall respiratory symptoms, and to determine if Bahia grass and Bermuda grass are associated with fall respiratory symptoms. | Volunteers were recruited for the study, by offering free allergy testing for residents. This offer was advertised through pharmacies and health food stores in Casino and Alstonville and through the media. To avoid selection, bias no mention was made of ragweed or Tibouchina during the recruitment, which took place approximately 2 months after the flowering period of these plants. | Pregnant and breast-feeding women and severe unstable asthmatics were excluded from the study. Anyone who had taken an antihistamine or tricyclic antidepressants, in the preceding 48 hours, or in the case of Astemizole, the preceding 6 weeks was also excluded. Other exclusion criteria were children under the age of 5 years and adults over the age of 80 years. | Longitudinal study | NR |
| Batra 2021 | To assess the association between aeroallergen exposure and childhood asthma peak periods during two grass pollen seasons using the Melbourne Air Pollen Children and Adolescent Health (MAPCAH) study conducted in Melbourne, Australia. | Asthma admissions (defined as ICD10 J45/46 codes) at The Royal Children’s Hospital (RCH). | Carers who could not participate due to language difficulties, children below the age of 2 years and patients who did not live within the 50 km of RCH. | Case crossover | This study was supported by the NHMRC (National Health & Medical Research Council). |
| Bouazza 2017 | The aim of the study was to examine the association between presentation to hospital for acute asthma and short-term exposure to air pollution after controlling for the confounding factors (ie, weather, viral environment, and allergens). | Paediatric visits to emergency rooms of the 20 emergency departments (EDs) of ‘Assistance Publique Hôpitaux de Paris (APHP)’, visits were classified by paediatricians in the EDs as asthma exacerbations according to the International Classification of Diseases-10. | NR | Longitudinal study  (Retrospective) | NR |
| Brzezińska-Pawłowska 2016 | To assess the association of severe exacerbations of asthma and Chronic Obstructive Pulmonary Disease (COPD) requiring ambulance emergency service (AES) visits with meteorological parameters and influenza outbreaks. | Diagnosis of COPD and/or Asthma or other bronchial diseases. | NR | Longitudinal study  (Retrospective) | NR |
| Cakmak 2012 | To compare the effects of ambient aeroallergens on hospitalisation for asthma between high and low air pollution days in 11 large Canadian cities. | Daily admissions in which the principal reason for hospitalisation was asthma, which were coded 493 or J45 and J46 by using the International Classification of Disease, 9th or 10th revision. | NR | Time series | NR |
| Caminati 2019 | To analyse the relationship between air pollution and pollen levels and medical emergency calls requesting attention for cardiovascular and respiratory causes, among the population of the City of Vigo (Spain) 1996–1999, using a symmetric bidirectional CCO design. | Retrospective data from admissions for asthma exacerbations registered from 1 January 2013 to 31 December, 2015 in ERs in Verona and Padua were collected. | NR | Longitudinal study  (Retrospective) | No funding |
| Chen 2016 | To assess the seasonal impact of air pollutants and aeroallergens on the risk of asthma hospital admissions for adults and children in Adelaide, South Australia. | Daily counts of asthma hospital admissions and age groups (aggregated as 0–17 years and 18+ years). Asthma admissions were based on the diagnostic codes in accordance with the International Classification of Disease (ICD) 10th version (ICD-10) coding system. The daily counts of asthma hospital admissions include asthma (ICD-10, J45) and status asthmaticus (ICD-10, J46 | NR | Time series | NR |
| Cirera 2012 | To establish the short-term effects of the major air pollutants and aeroallergen pollen types on hospital ER visits for asthma and COPD in an industrial and Mediterranean Spanish city, during the period 1995-1998. | Asthma and COPD cases among city residents from the ER registries of the two public general hospitals, those most frequently used for emergencies. In the event of doubt, a physician made the final assignation | NR | Longitudinal study  (Retrospective) | Partial funding from CIBER Epidemiología y Salud Pública (CIBERESP), Spain |
| Dales 2004 | To compare daily rates of hospital admissions for asthma with daily aeroallergen concentrations in 10 cities across Canada spanning the Atlantic to the Pacific coasts, which includes approximately one half of the country’s population. | All emergency hospitalizations for asthma between April 1, 1993 and March 31, 2000 in the cities of Saint John, Halifax, Ottawa, Toronto, London, Windsor, Winnipeg, Calgary, Edmonton, and Vancouver | NR | Time series | NR |
| Dales 2008 | To determine the impact of different trees on asthma, we tested the association between daily hospitalizations for asthma and daily concentrations of different tree pollens in 10 large Canadian cities. | The study population included all emergency hospitalizations for asthma between April 1, 1993, and March 31, 2000, in the cities of Saint John, Halifax, Ottawa, Toronto, London, Windsor, Winnipeg, Calgary, Edmonton and Vancouver. | NR | Time series | NR |
| Darrow 2012 | To examine short-term associations between ambient concentrations of various pollen taxa and emergency department (ED) visits for asthma and wheeze in the Atlanta metropolitan area between 1993 and 2004. | All ED visits with a primary or secondary ICD-9 code indicating asthma (493.0–493.9) or wheeze (786.09 before October 1, 1998; 786.07 beginning October 1, 1998) that did not also have a code for an external injury or poisoning (E800–E999). Also, ED visits for acute upper respiratory infections (URI; 460.0–466.0) without a concurrent ICD code for asthma or wheeze were identified. Authors created a control outcome group for finger wounds (883) because these visits were unlikely to be causally related to pollen levels. | NR | Case crossover | Centres for Disease Control and Prevention (TKC Global Solutions, LLC: JR5000139), the US Environmental Protection Agency (USEPA; RD834799), and the National Institute of environmental Health Sciences (NIEHS; R03ES018963). |
| De Roos 2020 | To study the association between daily pollen levels and the odds of asthma exacerbation among children living in Philadelphia, Pennsylvania, who were treated in a large pediatric care network. | Asthma exacerbations defined per the National Heart, Lung, and Blood Institute panel recommendations (Fuhlbrigge et al., 2012), as a patient encounter in a CHOP facility (primary care or specialty clinic, emergency department [ED], or hospital) with a diagnosis code for asthma and a prescription of systemic steroid for the same visit. The full set of SNOMED CT diagnosis codes used has been reported previously (Kenyon et al. 2020). For each case event, control dates were selected using a time stratified design, with time strata defined based on calendar month and year, and control dates matched to case events by the day of the week within the same month (Janes et al., 2005) | Authors limited our study population to patients with a Philadelphia address at the time of the case visit, to minimise exposure misclassification, because all pollen measurements were taken at one central Philadelphia location. | Case crossover | Grant from the Commonwealth Universal Research Enhancement (C.U.R.E) program funded by the Pennsylvania Department of Health - 2015 Formula award - SAP #4100072543. |
| Epton 1997 | To explore relationships between weather, fungal spore counts, pollen counts and peak expiratory flow rate (PEFR) and asthma symptoms in a group of subjects with asthma | Subjects recruited by a media campaign and through contact with local medical practitioners. A respiratory questionnaire was administered, and skin prick testing performed with common allergens. Following recruitment, the subjects' general practitioners were contacted to confirm that a diagnosis of asthma had been made according to American Thoracic Society criteria | Subjects with COPD as primary diagnosis were excluded. Also, those living outside the area, with occupational asthma and unwilling to participate in such a long study | Longitudinal study  (Prospective) | The Health Research Council of New Zealand and The Marlborough Express. |
| Erbas 2007 | To estimate the independent effects of grass pollen concentrations in the air over Melbourne on asthma hospital admissions for the 1992–1993 pollen season. | Daily asthma hospital admissions (ICD9-493) for all ages obtained from the Health Department Victoria for short-stay public hospitals in Melbourne. | NR | Time series | Grants from the National Health & Medical Research Council, the Victorian Asthma Foundation, the ANZ Trustees Medical Research and the Technology in Victoria Program. |
| Garty 1998 | To examine the correlations between air pollutants, weather conditions, airborne allergens, and the incidence of emergency room (ER) visits of children with acute asthma attacks. | Children who presented at the Paediatric Emergency Room with wheezing and were diagnosed as having an acute asthma attack. | Children under the age of 1 year were excluded from the study because of the possible confusion of asthma with viral infections such as bronchiolitis. | Longitudinal study  (Prospective) | NR |
| Ghosh 2012 | To examine the relationship between asthma-related hospital admissions (ARHA) and outdoor pollen, spore, and pollutant levels for adult patients in a densely populated Indian megacity Kolkata. | The number of daily ARHA was collected from two major state-funded teaching hospitals located in the city. These two hospitals, located at strategic points inside the city, represent a significant portion of the total ARHA in Kolkata. | NR | Longitudinal study | NR |
| Ginis 2015 | This study aimed to investigate the relationships between rhinitis symptom scores, and both nasal and bronchial airflow among children with seasonal allergic rhinitis (SAR) by means of spirometric and rhinomanometric measurement during and outside the pollen season. | The patients for this study were selected among those who were referred to the Paediatric Allergy and Asthma Clinic from January to December 2010 for the evaluation of seasonal nasal symptoms. A detailed medical history was obtained for all participants, and information regarding their age, gender, allergic rhinitis symptoms, disease duration, family history of atopy, and comorbid conditions were recorded. | NR | Longitudinal study  (Prospective) | NR |
| Gleason 2014 | To study the transient impact of ozone, PM2.5 and pollen on the acute onset of pediatric asthma. | Admissions to ER. Asthma according to (International Classification of Diseases, Ninth Revision [ICD-9] code493.xx). | The reliability of a diagnosis of asthma in children younger than 3 years of age has been questioned, therefore these children were excluded from this study | Case crossover | This study was supported in part by an appointment to the Applied Epidemiology Fellowship Program administered by the Council of State and Territorial Epidemiologists (CSTE)and funded by the Centers for Disease Control and Prevention (CDC) cooperative Agreement number 5U38HM000414.This study was also funded in part through USEPASTAR Program RD83454701: Climate Change and Allergic Airway Disease. |
| Gonzalez-Barcala 2013 | To analyse hospital admissions due to asthma and its relationship with environmental pollen and meteorological factors. | Patients admitted with asthma as primary or secondary diagnosis; living within 35km from the hospital. | NR | Longitudinal study  (Retrospective) | NR |
| Gowrie 2012 | The research conducted attempted to investigate the interactions of airborne pollen in Trinidad and paediatric asthma emergency room visits, as well as gather some preliminary information on local pollen. | Children aged 0–15 years presenting with clinical evidence and doctor’s diagnosis of mild, moderate or acute asthmatic attacks, or acute bronchospasms. | NR | Time series | NR |
| Guilbert 2018 | This study aimed to analyse the short-term relationships of airborne pollen and fungal spore concentrations with hospital admissions for asthma, considering the potential modifying effects of age and air pollution. | Daily number of hospital admissions with a main/first diagnosis of asthma (coded 493 according to the International Classification of Disease-9). | NR | Time series  (Ecological) | This study was entirely funded by Brussels-Environment (BIM-IBGE). This organization was partly involved in the study design, the supervision of the research, data procurement and results interpretation. Bianca Cox is a postdoctoral fellow of the FWO (12Q0517N). |
| Hanigan 2007 | To investigate associations between daily average ambient pollen and fungal spore concentrations with hospital admissions for total respiratory diseases; asthma; chronic obstructive pulmonary disease (COPD); and respiratory infections in Darwin, Australia, during the period from April 2004 to November 2005. | De-identified unit record data obtained from all emergency admissions for respiratory diseases in the administrative database of the Royal Darwin Hospital. | Patients whose primary residence was not in Darwin were excluded because many patients are transferred to Darwin hospital from regional centres each day. diagnosis codes classified according to the International Classification of Diseases version 10. | Time series | The study was funded by an Australian Research Council linkage grant (grant number: LP0348543) with cash and in kind support from the Northern Territory Government and Bureau of Meteorology. |
| Heguy 2008 | To evaluate the short-term effects of exposure to grass and weed pollen on emergency department visits and readmissions for asthma among children aged 0–9 years living in Montreal between April and October 1994–2004 | The Island of Montreal comprised the study population. The population is served by a network of 20 hospitals for which there is universal coverage through the Québec Health Insurance Plan (QHIP). The QHIP database allowed the identification of all visits to emergency departments for asthma among children under the age of 9 years who were residents of Montreal between 1994 and 2004 (April 1–October 31) in all Montreal hospitals. Asthma was defined according to the initial assessment of the attending emergency physician (diagnostic code 493 according to the 9th revision of the World Health Organisation’s International Classification of Diseases). We were able to identify whether the emergency department visit for asthma was first made by the patient during the study period or was a readmission. | NR | Time series | Climate Change Action Fund (Impacts and Adaptation program, project A-571), the Ouranos Consortium (Consortium on Regional Climatology and Adaptation to Climate Change), the Reseau de Surveillance de la Qualite´ de l’Air de Montreal (Claude Gagnon), and the Meteorological Service of Canada (Québec region). |
| Idrose 2020 | To investigate the associations between short-term grass pollen exposure and lung function and airway inflammation in a community-based sample, and whether any such associations were modified by current asthma, current hay fever, pollen sensitization, age, and other environmental factors. | The present work is based on cross-sectional data from a 18-year follow-up visit. During this follow-up, parents and siblings were also invited to participate. However, only the participants who attended the laboratory between September 2009 and December 2011 were included in the analysis as daily outdoor grass pollen counts were only available during this period. | NR | Cross sectional study | NR |
| Im 2005 | To determine whether there was an association between children’s asthma hospital admissions and environmental variables | Hospital admissions data represent severe cases of asthma, asthma as a primary diagnosis, using International Classification of Disease (ICD) codes 493.0, 493.90, and 493.91 | NR | Longitudinal study | NR |
| Ito 2015 | Determine the impacts of individual spring tree pollen types on over-the-counter allergy medication sales and asthma emergency department (ED) visits. | Patients with the words “asthma”, “wheezing”, “COPD”, their common misspelt analogues and International Classification of Diseases 9th edition codes associated with asthma (because some hospitals report diagnosis codes) on the data files. | NR | Time series | This project was supported by the following funding sources: Center for Disease Control and Prevention 200-2009-31909-003; U.S. Environmental Protection Agency (EPA) RD83489801; National Institute of Health T32ES007322, T32HD049311, K23ES024127, and P30-ES00260. |
| Jamason 1997 | The goal of this research is to utilise recently developed procedures which evaluate this simultaneous impact of the entire suite of meteorological elements on the asthmatic. | Only those cases severe enough to require an overnight stay are included in the data base, and daily counts of total asthma admissions are determined. | NR | Longitudinal study | Sponsored by the U.S Environmental Protection Agency, Climate & Policy Assessment Division, under Cooperative Agreement Contract No. CR824404-01 |
| Jariwala 2011 | To examine the relationship between asthma-related emergency department (ED) visits and outdoor air quality for paediatric and adult patients in a high asthma prevalence area, the New York City borough of the Bronx. | Study participants were males and females of all ages, including paediatric patients (<18 years old). All individuals were patients requiring asthma related (International Classification of Diseases- 9th edition ICD-9 code) ED care at each of the hospitals included during the study period (1 January 1999 to 31 December 1999). Only ED visit numbers, and no personally identifiable information, were collected. | NR | Longitudinal study  (Retrospective) | No funding |
| Jariwala 2014 | To track daily asthma-related emergency department (ED) visits for the Bronx for multiple years (1 January 2001–31 December 2008) and analyse their association with pollen and mould counts. | Study participants were males and females of all ages, including paediatric patients. All individuals were patients requiring asthma-related emergency department visits or inpatient admissions (primary diagnosis of asthma (ICD-9 code 493)) | NR | Longitudinal study  (Retrospective) | No funding |
| Khot 1998 | To examine the relationship with admission for asthma at a childrens' hospital. | Children with acute asthma admitted each day to the Royal Alexandra Hospital for Sick Children. Brighton. | Children under the age of 18 months, and cases of bronchiolitis, were excluded. | Longitudinal study  (Prospective) | Supported by a grant from the Royal Alexandra Hospital Centenary Appeal Fund. Further generous support was also received from SETRHA-Locally Organized Research Scheme (LORS). |
| Klabuschnigg 1981 | To assess the influence of the most frequently occurring pollens in the investigated area during the summer (Castanea, Poaceae, alternaria) and cladosporium spores; and the influence of local and general weather on the frequency of attacks, drug requirements and pulmonary function of asthmatic children. | All children with a long-established clinical diagnosis of bronchial asthma assessed clinically and referred to the camp by their doctor. | NR | Longitudinal study | NR |
| Kordit 2020 | To evaluate how asthma-related emergency department visits (AREDV), air pollutant levels, pollen counts, and weather variables changed from 2001 to 2008 in the Bronx, NY. | Adults and paediatric patients of all genders requiring AREDV from 1 January 2001 to 31 December 2008. Paediatric and adult patients were identified with a primary diagnosis of asthma (International Classification of Diseases, Ninth Revision, ICD-9 493.0) upon discharge from the emergency department (ED) to yield the aggregate daily AREDV values. | NR | Cross sectional study | NR |
| Kralimarkova 2014 | To assess the ability of exhaled breath temperature (EBT), a putative marker of airway inflammation, to evaluate objectively the efficacy of grass pollen sublingual immunotherapy in a proof-of-concept study. | Naive allergen immunotherapy patients with grass pollen induced allergic respiratory disease; participants had to be 7 to 55 years old and have displayed documented symptoms requiring symptomatic medication for at least the preceding 2 grass pollen seasons. | Moderate to severe asthma (as defined by the Global Initiative for Asthma guidelines), symptoms related to or strong skin test positivity to other seasonal or perennial allergens, immunosuppression, malignancies, autoimmune diseases, intake of b blockers, pregnancy, and lactation at the time of initiation of immunotherapy and patients in whom (at clinician discretion) comorbidities could affect the study results, were excluded. | Randomised Clinical Trial | This study was funded by an unrestricted research grant from Laboratoire Stallergenes SA (Antony, France). |
| Krmpotic 2011 | To investigate effects of traffic pollutants on adult asthma hospitalisation adjusting for pollens including hornbeam. | Unscheduled daily hospitalizations of patients with asthma aged over 18 were collected from clinical records of the Clinic for Lung Diseases ‘Jordanovac’ which covers almost all respiratory emergency admissions in the city of Zagreb. | NR | Time series | NR |
| Lambert 2020 | To examine associations between exposure to multiple pollen types and lung function and markers of airway inflammation at 8 and 14 years of age, and to explore potential modification by residential greenness. | Pregnant women, whose unborn children were considered to be at risk for asthma (due to having one or more parents or siblings with asthma or wheezing), were recruited between September 1997 and November 1999 from western and south-western Sydney. he CAPS interventions were implemented for the first 5 years of a child's life, after which the study has been analysed as a birth cohort study. The following analysis has been restricted to children who participated in both the 8- and 14-year follow-ups. | Exclusion criteria included: cat ownership, strict vegetarians, non-singleton pregnancy, and infants born earlier than 36 weeks gestation. A total of 616 children were randomised to the interventions. | Longitudinal study  (Cohort) | NR |
| Lee 2019 | To comprehensively examined the short-term effects of multiple environmental factors (air pollutants, weather conditions, aeroallergens, and burden of respiratory virus infections) on AEs in an age-stratified population from Seoul Metropolitan City in an effort to develop effective personalised strategies for prevention of AEs. | Events of asthma exacerbations (AEs) events requiring admission to an emergency department (ED). The database included all AE events that were coded by ICD-10 as J45 (asthma) or J46 (status asthmaticus). | NR | Time series | This study was funded by CHA University School of Medicine, Seongnam, Republic of Korea. |
| Li 2019 | To investigate the effects of exposure to PM2.5, O3, and pollen on asthma control status among paediatric patients with asthma. | The enrollment criteria included being aged 8 to 17.9 years and having parents aged 18 years or older; being continuously enrolled (≥ 6 months) in Florida Medicaid and SCHIP; having a diagnosis of asthma with ICD-9-CM 493.1 (asthma with status asthmaticus), 493.2 (asthma with acute exacerbation), or 493.x listed in claim and enrollment files; having at least two asthma-related health care visits during the past 12 months; and having access to internet and a telephone within the past six weeks | NR | Longitudinal study | National Institutes of Health U01 AR052181 (Thompson, Gross, Reeve, Shenkman, DeWalt, Huang). The funder has no role or influence in the study design, the collection, analysis, and interpretation of data, the writing of the manuscript, or the decision to submit the manuscript for publication. |
| Lierl 2003 | To determine the relationship of outdoor air quality parameters to asthma exacerbations in children. | “Asthma visits” defined as either an emergency room visit or an inpatient hospitalisation for treatment of acute asthma. The number of asthma hospital admissions per day was obtained by means of a hospital computer search for all admissions with a primary diagnosis code of 493.91 (status asthmaticus). | NR | Longitudinal study  (Retrospective) | NR |
| Lowe 2012 | To assess the relationship between level of exposure to pollen during pregnancy and infancy and the risk of the child requiring hospitalisation for asthma. | All hospital admissions for asthma (ICD-9 coded 493) collected from the Swedish Inpatient Registry for the period 1/1/1989 until 31/12/1997. Hospital admission for asthma within the first year of life was the primary outcome for this study. Details on the frequency of admissions during this time for lower respiratory tract illness (LRTI - ICD-9 codes 490, 491C and 491X) were also obtained from the Inpatient Registry, which was used as a marker for degree of potential exposure to respiratory pathogens in the first three and six months of life (sum of admissions for these diagnosis). | NR | Longitudinal study  (Cohort) | Swedish Research Council, through the Umea SIMSAM node, Umea University, who provided financial support to undertake this project. Also, authors were supported by the Australian National Health and Medical Research Council. D.O. and data collection was supported by a grant from CMF, Centre for Environmental Research, in Umea. |
| Mackay, 1992 | To examine factors which may affect mortality from asthma to clarify why the mortality from this disease has remained stable in Scotland despite the rise in asthma mortality noted elsewhere. | Scottish asthma mortality data provided by the General Register Office (Scotland) for each sex separately (age 5 - 44 years) for the period 1938-1988. | NR | Longitudinal study  (Retrospective) | This work has been supported by a grant from the Chest, Heart and Stroke Association (Scotland). |
| Makra 2012 | To analyse the joint effect of biological (pollen) and chemical air pollutants on daily asthma emergency room (ER) visits for both adult and elderly patients during three different seasons in the Szeged region of Southern Hungary | The daily number of emergency room (ER) visits registered with asthma comes from the Hospital of Chest Diseases, Deszk, Csongrád County, located about 10 km from the monitoring station in Szeged downtown. Asthma ER diseases were categorised using the International Classification of Diseases, Tenth Revision (ICD-10) (WHO, 1999), as follows. Allergic asthma (J4500), mixed asthma (J4580) and asthma without specification (J4590) were classified. | NR | Longitudinal study  (Retrospective) | The European Union and the European Social Fund provided financial support for the project under the grant agreement no. TAMOP 4.2.1/B-09/1/KMR-2010-0003 and TAMOP-4.2.1/B-09/1/KONV-2010-0005. |
| Marques-Mejias 2019 | To describe the prevalence and triggers of asthma exacerbations and their management in a cohort of paediatric patients attended in an emergency department (ED). | Children with asthma exacerbations attending the ED were included after a thorough search using our institutional computer database. We performed a computerised search for patients based on the key words difficulty breathing, wheezing, and/or dyspnea. Those with a diagnosis of asthma exacerbation were enrolled in the study. | NR | Longitudinal study  (Retrospective) | No funding |
| May 2011 | To analyse the association of adult asthma exacerbations with the following factors: pollen counts, upper respiratory tract infection (URI) chief complaints, temperature, humidity, PM, and ozone levels in the Washington, DC, area using retrospective electronic medical record (EMR) data from an urban ED and local environmental data. The second objective was to characterise the severity of asthma exacerbations, as identified by asthma admissions, and correlate them with individual asthma triggers. | All adults older than 18 years who were assigned a disposition diagnosis of “asthma” or “asthma exacerbation” by International Classification of Diseases, Ninth Revision codes in our EMR were included in the study. | Authors chose to include patients with diagnoses of asthma only to avoid including patients presenting with wheezing who were diagnosed with bronchitis or other respiratory conditions. | Time series | NR |
| Mazenq 2017 | To measure the impact of PM, assessed close to the homes of the children, on asthma-related paediatric hospital visits to the emergency department (ED) within the Bouches-du-Rhône area (BdR) (France) in 2013 and to estimate risks from pollution, meteorological conditions, pollen exposure, and level of respiratory virus circulation. | ED visits for asthma exacerbations in children 3-13 years old, defined according to ICD-10 codes included in the national thesaurus (J45–J46). | NR | Case control study | No funding |
| Mazenq 2017b | To measure the impact of air pollution, assessed close to the homes of the patients, on asthma-related hospital visits to the emergency department (ED) within the PACA region in 2013, and to estimate the risks from pollution, meteorological conditions, pollen exposure and viral load. | EDs located in PACA were included in this study if they concerned a 3- to 99-year-old patient living in PACA. The controls were defined as patients consulting for trauma in ED. When the patient was discharge from the ED, the emergency physician had to code the final diagnosis using a national thesaurus of International Classification of Disease, Revision 10 (ICD-10) codes. Visits for an exacerbation of asthma (J45-J46) and for trauma (S00-T98) were defined according to this thesaurus. | Authors excluded children under 3 years of age because it is more difﬁcult to be sure about the diagnosis of asthma. | Case control study | No funding |
| Murray 2006 | To investigate the importance of allergen exposure in sensitised individuals in combination with viral infections and other potentially modifiable risk factors precipitating asthma hospital admission in children. | Children aged 3–17 years admitted to hospital with an acute asthma exacerbation (asthma admission, AA) were matched for age (¡2 years) and sex with two control groups: (1) patients with stable asthma who were not admitted to hospital and did not require oral steroids for asthma exacerbation within the previous 12 months (stable asthma, SA; recruited from the outpatient department); and (2) patients admitted to hospital with non-respiratory conditions (inpatient control, IC). Controls were enrolled within 3 weeks of recruitment of the index case. | NR | Case control study | Financial support of viral PCR work was by The British Lung Foundation/Severin Waterman Family Foundation Lung Research Programme (grant number P00/2). |
| Osborne, 2017 | To examine associations between daily pollen concentrations and hospital admissions for asthma in London. | Authors restricted the sample to the working age population (16–64 years) to focus on adult asthma, excluding both children and older people (the latter would have a higher prevalence of comorbidities such as chronic obstructive pulmonary disease [COPD]). asthma (ICD- 10 J45 and J46). | NR | Time series  (Ecological) | The research was funded in part by the National Institute for Health Research Health Protection Research Unit (NIHR HPRU) in Environmental Change and Health at the London School of Hygiene and Tropical Medicine in partnership with Public Health England (PHE) and in collaboration with the University of Exeter, University College London, and the Met Office. The research was also funded in part by the UK Medical Research Council (MRC) and UK Natural Environment Research Council (NERC) for the MEDMI Project (MR/K019341/1). The views expressed are those of the author(s)and not necessarily those of the MRC, NERC, NHS, the NIHR, the Department of Health, or PHE. |
| Ostro 2001 | To determine whether several air pollutants, including particulate matter, O3, and bioaerosols, are associated with exacerbation of asthma in this population of African American children, and if so, whether there was any interaction with the children’s asthma severity, socioeconomic status, respiratory infections, reported allergic status, or medical management. | African American children, 8 to 13 years of age, who had physician-diagnosed asthma that required asthma medication during the preceding year in the absence of a respiratory infection, and who did not have any other chronic condition that required regular administration of corticosteroids, recruited from several public and private hospitals, urgent care clinics, and group practices. | NR | Longitudinal study  (Prospective) | This investigation was supported under the U.S. Centers for Disease Control and Prevention Cooperative Agreement #U60/CCU908048-03-1 and was supplemented by the California Air Resources Board. |
| Porcel Carreño 2020 | To quantify total allergen and major allergen levels in the air of Cáceres, Spain during the spring of 2011 and to analyse their correlation with (1) grass and olive pollen counts and (2) the number of asthma attacks evaluated at Complejo Hospitalario Universitario, Cáceres, Spain during this period. | All the hospital emergency department. records for asthma exacerbations. | NR | Longitudinal study  (Retrospective) | No funding |
| Potter 1984 | To determine the commonest factors precipitating severe attacks of asthma in a group of known asthmatics. | Patients known asthmatics, between the ages of 2 and 14 years, who presented with acute asthma. | NR | Longitudinal study  (Prospective) | NR |
| Rossi, 1993 | To examine any relationship between severe exacerbations of asthma and weather conditions or concentrations of pollen and other ambient pollutants. | All the adult patients (15-85 yrs.) attending the emergency room at Oulu University Central Hospital for asthma attacks during one year from 1 October 1985 to 30 September 1986. The diagnosis of asthma was based on the variability of airways obstruction and all the patients fulfilled the criteria for asthma as proposed by the American Thoracic Society.23 The diagnosis of asthma was confirmed by one of the two senior respiratory physicians (VLK, EH) at the emergency room every morning. | NR | Longitudinal study  (Retrospective) | This work was supported by grants from the Foundation for the Study of Allergy, Finland, and the Finnish Antituberculosis Association. |
| Shrestha, 2017 | To assess the role of ambient levels of different types of pollen on asthma hospitalisation over a 5 year period in children and adolescents in Sydney, Australia. | Children and adolescents’ asthma-related hospitalisation. Case status was defined as the date of admission, while the control status was defined as periods on the same day of week in the same month as the case date. In this design, each case serves as his/her own control and eliminates the potential confounding effects that result from individual differences due to selection of other controls. Due to variations in coding between different hospitals, three classification systems for the diagnosis coding were included: 1. ICD10-AM17: Asthma (J45), Status asthmaticus (J46); 2. SNOMED CT-AU18: Asthma (195967001), Asthma NOS (266365004); 3. ICD-919: Extrinsic asthma (493.0); Intrinsic asthma (493.1); Asthma unspecified (493.9); Chronic obstructive asthma (493.2); Other forms of asthma (493.8) and Cough variant asthma (493.82). | Authors excluded cases readmitted within the period of one month (1‐28 days) to avoid confusion related to the definition of the case (index) and control dates. Children below the age of 2 years were excluded because diagnosis of asthma in this group is difficult. | Case crossover | No funding |
| Sun 2016 | To estimate the short-term associations between pollen concentration and asthma related exacerbation visits, with the focus on describing the delayed effect and harvesting effect (also known as mortality replacement when the outcome is mortality), and association heterogeneity by pollen type. | ED visits on 8 civilian hospitals; diagnosis of asthma (ICD-9-CM code 493.xx), assuming individuals visiting the ED were atopic and sensitised to at least one of the pollen types examined. | NR | Longitudinal study | This publication was supported by the Cooperative Agreement Number 1UE1EH001126 from The Centers for Disease Control and Prevention. Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the Centers for Disease Control and Prevention |
| Targonski, 1995 | To examine the relationship of asthma-related deaths in Chicago between 1985 and 1989 among 5- to 34-year-olds with selected pollen and mould spore counts in an effort to identify environmental factors associated with asthma-related deaths, which might be amenable to intervention. | Persons aged 5 to 34 years, with asthma as any cause of death, who were residents of Chicago during the period from 1985 through 1989. | NR | Longitudinal study  (Retrospective) | NR |
| Tobias 2003 | To assess the short-term effects of different types of allergenic pollen on asthma hospital emergencies in the metropolitan area of Madrid (Spain) for the period 1995–8. | The daily number of asthma emergency hospital admissions from the Emergency Department of the Gregorio Marañón Hospital, covering an urban catchment area of 555 153 inhabitants, was studied for the period 1995–8. Diagnoses included the following (in literal form): asthma, asthmatic bronchitis, spastic bronchitis, and bronchospasm. | NR | Time series | Advisory Committee to the Madrid Regional Asthma Prevention and Control Programme (Comisión Asesora del Programa Regional de Prevención y Control del Asthma de la Comunidad de Madrid). |
| Tobias 2004 | To investigate the potential non-linear short-term effects of the types of pollen with allergenic capacity across the whole range of exposure on the daily number of asthma-related hospital emergencies in Madrid for the period 1995-1998 | Asthma (ICD-493) daily emergency room admissions for all ages to the Emergency Ward of the Gregorio Marañon University Hospital. | NR | Time series | Advisory Committee to the Madrid Regional Asthma Prevention and Control Programme (Comision Asesora del Programa Regional de Prevencion y Control del Asma de la Comunidad de Madrid). |
| Wang 2007 | To examine the effects of seasonality, outdoor air quality, climatic factors, and presence of outdoor aeroallergens on emergency department visits for children with asthma. | Children presenting with a principal diagnosis of asthma to the Emergency Department were identified through the Health Information Management department using the International Classification of Diseases, Ninth Revision (ICD-9) code 493 | NR | Cross sectional study | NR |
| Witonsky 2018 | To evaluate associations in adult and paediatric patients for the full year and for the winter, spring, summer, and fall seasons with asthma related emergency department visits. | Study participants were males and females of all ages, including paediatric patients (i.e. individuals <18 years old). All individuals were patients requiring Asthma related emergency department visits or Asthma related hospitalizations at three major Bronx hospitals during the specified study period. | NR | Longitudinal study  (Retrospective) | No funding |
| **Studies Assessing Pollen Exposure During Thunderstorms** | | | | | |
| **Study ID** | **Aim / objectives** | **Inclusion criteria** | **Exclusion criteria** | **Design** | **Funding** |
| Anderson 2001 | To investigate any association between asthma admissions and thunderstorms in relation to pollen counts, fungal spores and meteorological data. Since there is an association between thunderstorms and ambient ozone concentrations, we also investigated whether changes in the concentration of this gas might be relevant | Computerised hospital records of asthma emergency admissions (ICD9 codes 493.0, 493.1, 493.9) for Cardiff and Newport. | NR | Longitudinal study  (Retrospective) | NR |
| Celenza, 1996 | To seek associations between meteorological factors, concentrations of air pollutants or pollen, and an asthma epidemic which occurred in London on 24 and 25 June 1994 after a thunderstorm. | Patients aged 16 or over who were assessed by a doctor and given a diagnosis of asthma were included. | Patients who refused proper assessment or in whom the diagnosis was unclear were excluded. | Longitudinal study  (Retrospective) | NR |
| Davidson 1996 | To investigate the time course of an epidemic of asthma after a thunderstorm, characteristics of patients affected, and the demand on emergency medical resources. | Patients presenting with asthma, wheeze, or hay fever or allergy with wheeze or difficulty in breathing and all patients requesting an inhaler or asthma treatment. And patients complaining of shortness of breath, difficulty in breathing, cough, or chest infection if the clinical record showed that their symptoms were due to airways disease. | NR | Longitudinal study  (Retrospective) | No funding |
| Erbas 2012 | To examine the association between increasing ambient levels of grass pollen and asthma ED presentations in children. Determine whether these associations are seen only after a thunderstorm, or whether grass pollen levels have a consistent influence on childhood asthma ED visits during the season. | Patients under 15 years of age with a diagnosis related to childhood asthma [ICD10-AM, J45 and J46]. | NR | Time series  (Ecological) | NR |
| Hajat 1997 | To determine whether thunderstorms may result in outbreaks of asthma noted in primary care. | People consulting with asthma (ICD code 493) | NR | Longitudinal study  (Retrospective) | The department of Health provided funding for the study |
| Lewis 2000 | To Investigate the joint effects of aeroallergens, rainfall, thunderstorms and outdoor air pollutants on daily asthma admissions and Accident and Emergency attendance using routinely collected data between 1993 and 1996 from Derby in central England. | Asthma morbidity was assessed in terms of daily A & E attendances for the 4-year period from January 1993 to December 1996. Daily admissions to either Hospital were available from April 94 to December 96. Cases were identified using the international coding for diseases (ICD-9493 till March 95 and then ICD-10 J45.9 & J46) and those with a main diagnosis of asthma were included. Only data for the 14 and over age group were included in these analyses. | NR | Time series | Dr Lewis is funded by a research fellowship from the UK Medical Research Council |
| Marks 2001 | To assess the importance of thunderstorms as a cause of epidemics of asthma exacerbations and to investigate the underlying mechanism. | Emergency department attendances for asthma | NR | Case control study | NR |
| Newson 1997 | To quantify the rise in the incidence of asthma which typically follows a thunderstorm in England and investigate whether this rise is greater after periods of high levels of grass pollen. | Daily count of asthma admissions for each National Health Service regional health authority taken from the Hospital Episodes System. Asthma admissions taken from the hospital episodes system, categorised by age one group for those aged up to 14 and one for those aged 15 and above. | NR | Time series | Financial support by the National Asthma Campaign |
| Newson 1998 | To identify risk factors predicting large acute asthma epidemics at least some of the time. | Asthma admissions for each of the 14 National Health Service RHAs in England, on each day, taken from the Hospital Episodes System (HES), which gave counts of asthma admissions for each date, measured from midnight to midnight, for each District | NR | Time series | This study was funded by the UK National Asthma Campaign for Financial support |
| Packe, 1985 | To determine environmental factors responsible for asthma outbreak during a thunderstorm. | Patients presenting in Birmingham with acute asthma and other acute respiratory disorders during June and July 1983. A diagnosis of asthma was accepted if the patient gave a history of wheeze and breathlessness of acute onset, if auscultation of the chest revealed diffuse expiratory wheezes. | Patients with history of chronic bronchitis/emphysema. | Longitudinal study  (Retrospective) | NR |
| Silver 2018 | To evaluate the potential for predicting thunderstorm asthma episodes by studying asthma-related hospital admissions in Melbourne over a 16-year period (n.b. this period does not include the event on November 21, 2016 as admissions data for the year were not available). | Data were extracted for patients with a principal diagnosis of asthma (ICD-9 code 493 and ICD-10 codes J45, J46) and included the patient's age (by 5-year intervals: 0-4, 5-9, . . ., 80-84 and 85+), gender and the local government region of patient's place of residence. | NR | Time series  (Ecological) | Funded by the MacKenzie Postdoctoral Fellowship scheme of the University of Melbourne. GPATS lightning data was purchased with fund from ARC Future Fellowship. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript. |
| Thien 2018 | To detail the dynamics of the event (thunderstorm), describe its effect on health services and patients, and inform public health strategies to prevent and mitigate future thunderstorm asthma epidemics. | Patients admitted to an ICU with a diagnosis of asthma or if, in the opinion of the ICU specialist at each site, admission was due to acute thunderstorm-related bronchospasm. Patients coded as nil diagnosis over this specific period (from nov 21 1800 AEDT until nov 22, where ambulances had a substantial increase in demand, that meant medical records where incomplete) were regarded as presentations of epidemic thunderstorm asthma and included in the analysis. | NR | Longitudinal study  (Retrospective) | NR |

*NR: Not Reported*

*Characteristics of individual studies identified in the literature search (2).*

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| --- | --- | --- | --- | --- | --- | --- | --- |
| **Study ID** | **Total participants** | **Country** | **Age** | **Gender** | **Exposure** | **Outcomes** | **Effect measures** |
| Anderson 1998 | NR | UK | Mean 35 years old | NR | Pollen exposure (Grass, Birch) | Daily emergency admissions for asthma | Percentage change (95% Confidence Interval) |
| Babin 2007 | NR | USA | 1-17 years old | NR | Pollen exposure (Grass, Tree) | Asthma emergency department admissions | Percentage change (95% Confidence Interval) |
| Bass 2000 | 206 | Australia | 5-77 years old | 129 female and 48 men | Pollen exposure (Ragweed) | Asthma attack/exacerbation | Narrative |
| Batra 2021 | 135 | Australia | 2-17 years old | NR | Pollen exposure (Grass, Tree) | Asthma hospital admissions (defined as ICD10 J45/46 codes) | Odds Ratio (95% Confidence Interval) |
| Bouazza 2017 | 47,107 | France | Median 3.08 IQR: 1.58 - 6.25 | 29,816 male and 17,291 female | Pollen Exposure (Total pollen) | Asthma related hospital visits | Percentage change (95% Confidence Interval) |
| Brzezińska-Pawłowska 2016 | 1,558 | Poland | NR (all ages) | 558 (35.82%) male and 1000 (64.18%) female | Pollen exposure (Total Pollen, Tree) | Severe asthma exacerbation and Chronic Obstructive Pulmonary Disease requiring ambulance emergency service | Correlation |
| Cakmak 2012 | NR | Canada | NR | NR | Pollen exposure (Tree pollen) | Hospitalizations for asthma | Percentage change (95% Confidence Interval) |
| Caminati 2019 | 1,745 | Italy | >50 years old | NR | Pollen exposure (Total pollen, Grass) | Medical emergency calls requesting attention for cardiovascular and respiratory causes | Correlation |
| Chen 2016 | 36,024 | Australia | 0-17 years old | NR | Pollen Exposure (Total pollen) | Asthma hospital admissions | Incidence rate ratio (95% Confidence Interval) |
| Cirera 2012 | 1,617 | Spain | NR | NR | Pollen exposure (Grass) | Hospital emergency room visits for asthma and COPD | Risk Ratio (95% Confidence Interval) |
| Dales 2004 | 60,066 | Canada | 0-13 and > 13 years old | NR | Pollen exposure (Grass, Tree) | Hospital admissions for asthma | Percentage change (95% Confidence Interval) |
| Dales 2008 | 60,066 | Canada | NR (all ages) | NR | Pollen exposure (Tree, Elm) | Daily hospitalizations for asthma | Percentage change (95% Confidence Interval) |
| Darrow 2012 | 400,819 | USA | NR (all ages) | NR | Pollen exposure (Grass, Tree, Cypress, Ragweed) | Emergency department visits for asthma and wheeze | Risk Ratio (95% Confidence Interval) |
| De Roos 2020 | 35,040 | USA | 0-18 years old | 60.4% males and 39.6% females | Pollen Exposure (Grass, Tree, Birch, Cypress, Elm, Ragweed) | Asthma exacerbations | Odds Ratio (95% Confidence Interval) |
| Epton 1997 | 139 | New Zealand | 17-80 years old | 47 (34%) male and 92 (66%) female | Pollen Exposure (Total pollen) | Lung function, asthma symptoms | Risk Ratio (95% Confidence Interval) |
| Erbas 2007 | 147 | Australia | NR (all ages) | NR | Pollen exposure (Grass) | Daily asthma hospital admissions | Smooth term df (Chi square) |
| Garty 1998 | 1,076 | Israel | 1-18 years old | 412 (38%) female, 664 (62%) male | Pollen Exposure (Total pollen) | Asthma related Emergency Department Visits | Narrative |
| Ghosh 2012 | NR | India | NR | NR | Pollen exposure (Grass) | Asthma-related hospital admissions | Regression analysis estimate |
| Ginis 2015 | 95 | Turkey | 9-14 years old | 55 male and 40 female | Pollen Exposure (Total pollen) | Asthma symptoms, rhinitis symptom scores, nasal and bronchial airflow | Narrative |
| Gleason 2014 | 21,854 | USA | 3-17 years old | 60.6% male and 39.5% female | Pollen exposure (Grass, Tree) | Acute asthma/asthma exacerbation | Odds Ratio (95% Confidence Interval) |
| Gonzalez-Barcala 2013 | 6,687 | Spain | Mean 52 years old | 2474 (37%) male and 4213 (63%) female | Pollen Exposure (Total pollen) | Hospital admissions due to asthma | Risk Ratio (95% Confidence Interval) |
| Gowrie 2012 | NR | Trinidad and Tobago | 0-15 years old | NR | Pollen Exposure (Total pollen) | Pediatric asthma emergency room visits | Narrative |
| Guilbert 2018 | 5,094 | Belgium | NR (all ages) | NR | Pollen exposure (Grass, Alder, Birch, Cypress, Hazel, Mugwort) | Hospital admissions for asthma | Percentage change (95% Confidence Interval) |
| Hanigan 2007 | NR | Australia | <15 years old | NR | Pollen exposure (Total pollen, Grass) | Total respiratory diseases and severe asthma exacerbation | Percentage change and percentage change in relative risk (95%CI) |
| Heguy 2008 | 43,780 | Canada | 0-9 years old | 15,376 female and 28,404 males | Pollen exposure (Grass) | Emergency department visits and readmissions for asthma | Percentage change (95% Confidence Interval) |
| Idrose 2020 | 936 | Australia | 6-71 years old | 424 (45%) males; 512 (55%) females | Pollen exposure (Grass) | Lung function and airway inflammation | Correlation |
| Im 2005 | 17,902 | USA | 0-14 years old | NR | Pollen exposure (Ragweed) | Children’s asthma hospital admissions | Pearson correlation |
| Ito 2015 | NR | USA | NR (all ages) | NR | Pollen Exposure (Birch, Elm) | Asthma emergency department visit and allergy medication sales | Spearman's correlation |
| Jamason 1997 | NR | USA | NR | NR | Pollen exposure (Total Pollen, Ragweed) | Hospital asthma admissions | Narrative |
| Jariwala 2011 | NR | USA | NR (all ages) | NR | Pollen Exposure (Total pollen) | Asthma related Emergency Department Visits | Correlation |
| Jariwala 2014 | 42,065 | USA | NR (all ages) | NR | Pollen exposure (Total pollen, Grass, Tree) | Asthma related Emergency Department Visits or Admissions | Correlation |
| Khot 1998 | 768 | UK | 18 months-16 years old | 558 (72.7%) males and 210 (27.3%) females | Pollen exposure (Grass) | Children with acute asthma | Contribution to regression analysis |
| Klabuschnigg 1981 | 40 | Austria | 7-14 years old | NR | Pollen exposure (Total pollen, Grass) | Frequency of asthmatic complaints (called ‘attacks’ thereafter) and drug requirements were registered with a standardised chart giving the ‘attack score’ | Correlation |
| Kordit 2020 | 42,065 | USA | NR (all ages) | NR | Pollen exposure (Tree) | Asthma-related emergency department visits | Correlation |
| Kralimarkova 2014 | 10 | Bulgaria | Mean 30 years old (range 7-55) | 18(64.3%) male and 10 (35.7%) female | Pollen exposure (Grass) | Asthma symptoms | Narrative |
| Krmpotic 2011 | 808 | Croatia | >18 years old | NR | Pollen exposure (Total pollen, Birch) | Asthma hospitalizations | Regression coefficient (SE) (t) |
| Lambert 2020 | 160 | Australia | 8-14 years old | 54% male and 46% female | Pollen exposure (Grass, Cypress) | Lung function and markers of airway inflammation | Odds Ratio, Percentage predicted value |
| Lee 2019 | 28,824 | Korea | NR (all ages) | NR | Pollen exposure (Grass, Tree) | Asthma exacerbations | Risk Ratio (95% Confidence Interval) |
| Li 2019 | 229 | USA | 8-18 years old | 58.9% males and 41.1% males | Pollen Exposure (Total pollen) | Asthma control status | Beta (95% Confidence Interval) |
| Lierl 2003 | NR | USA | NR (paediatrics) | NR | Pollen Exposure (Total pollen) | Asthma exacerbations | Risk Ratio (95% Confidence Interval) |
| Lowe 2012 | 110,381 | Sweden | > 1 year old | NR | Pollen Exposure (Total pollen) | Risk of the child requiring hospitalisation for asthma | Odds Ratio (95% Confidence Interval) |
| Mackay, 1992 | NR | Scotland | 5-44 years old | NR | Pollen exposure (Grass) | Asthma mortality | Narrative |
| Makra 2012 | 936 | Hungary | NR (adults) | 497 female and 439 males | Pollen exposure (Total Pollen, Ragweed) | Asthma related Emergency Department Visits | Narrative |
| Marques-Mejias 2019 | 5,609 | Spain | 0-15 years old | 58.8% males and 41.2% females | Pollen exposure (Total pollen, Grass) | Emergency department visits related to asthma exacerbations | Correlation |
| May 2011 | 554 | USA | >18 years old | NR | Pollen exposure (Tree) | Severe asthma exacerbations | Correlation |
| Mazenq 2017 | 1,182 | France | 3-18 years old | 55% female and 59% male | Pollen exposure (Grass, Cypress) | Asthma related paediatric hospital visits to the emergency department | Odds Ratio (95% Confidence Interval) |
| Mazenq 2017b | 5,055 | France | Mean 22.67 | 3,130 male and 3,120 female | Pollen Exposure (Total pollen) | Asthma related hospital visits to the emergency department | Odds Ratio (95% Confidence Interval) |
| Murray 2006 | 84 | UK | 3-7 years old | 65.5% male and 34.5% female | Pollen exposure (Grass) | Acute asthma hospital admissions | Odds Ratio (95% Confidence Interval) |
| Osborne 2017 | 11,984 | UK | 16-64 years old | NR | Pollen exposure (Grass, Tree, Birch) | Asthma related hospital admissions | Percentage change (95% Confidence Interval) |
| Ostro 2001 | 138 | USA | 6-13 years old | 61% male and 39% female | Pollen Exposure (Total pollen) | Moderate asthma exacerbation and asthma symptoms | Odds Ratio (95% Confidence Interval) |
| Porcel Carreño 2020 | 111 | Spain | 5-88 years old | NR | Pollen exposure (Grass, Olive) | Asthma attacks | Pearson correlation |
| Potter 1984 | 80 | South Africa | 2-14 years old | NR | Pollen Exposure (Total pollen) | Acute asthma | Correlation |
| Rossi 1993 | 232 | Finland | 15-85 years old | Male 42% and Female 58% | Pollen exposure (Tree) | Attendance to the emergency room for asthma attacks | Correlation |
| Shrestha 2017 | 2,098 | Australia | 2-18 years old | 1,253 male and 845 female | Pollen exposure (Total pollen, Grass, Tree, Cypress) | Asthma hospitalisation | Odds Ratio (95% Confidence Interval) |
| Sun 2016 | 82,825 | USA | 0-17 years old | 31,930 (38.55 %) male and 50,893 (61%) females | Pollen exposure (Grass, Tree) | Asthma related exacerbation visit | Risk Ratio (95% Confidence Interval) |
| Targonski, 1995 | 124 | USA | 5-34 years old | Male 56 (45.2%) and female 68 (54.8%). | Pollen exposure (Grass, Tree, Ragweed) | Asthma related deaths | Odds Ratio (95% Confidence Interval) |
| Tobias 2003 | 4,827 | Spain | 0-14 years old | NR | Pollen exposure (Grass, Cypress, Mugwort, Olive) | Asthma hospital emergencies | Percentage change (95% Confidence Interval) |
| Tobias 2004 | NR | Spain | 0-14 years old | 52.4% female and 47.6% male | Pollen exposure (Grass, Olive) | Asthma-related hospital emergencies | Percentage change in relative risk (95%CI) |
| Wang 2007 | NR | USA | NR (children) | NR | Pollen exposure (Grass, Tree) | Asthma related Emergency Department Visits | Narrative |
| Witonsky 2018 | 43,729 | USA | NR (all ages) | NR | Pollen exposure (Grass, Tree) | Asthma related emergency hospital visits | Beta |
| **Studies Assessing Pollen Exposure During Thunderstorms** | | | | | | | |
| **Study ID** | **Total participants** | **Country** | **Age** | **Gender** | **Exposure** | **Outcomes** | **Effect measures** |
| Anderson 2001 | NR | UK | NR (all ages) | NR | Thunderstorm exposure (Total Pollen) | Asthma emergency admissions | Spearman's correlation |
| Celenza 1996 | 148 | England | > 16 years old | NR | Thunderstorm exposure (Grass pollen) | Attendance to the emergency department for asthma | Relative change (Multivariate model) |
| Davidson 1996 | 640 | UK | Mean 32 years old | 368 (57.5%) male and 272 (42.5%) female | Thunderstorm exposure (Grass pollen) | Asthma or other airways disease | Narrative |
| Erbas 2012 | 2,559 | Australia | 0-15 years old | NR | Thunderstorm exposure (Grass pollen) | Asthma emergency department presentations in children | Narrative |
| Hajat 1997 | NR | UK | NR (all ages) | NR | Thunderstorm exposure (Grass pollen) | Asthma related Visits in Primary Care | Risk Ratio (95% Confidence Interval) |
| Lewis 2000 | NR | UK | > 14 years old | NR | Thunderstorm exposure (Grass and Birch pollen) | Daily asthma hospital admissions | Odds Ratio (95% Confidence Interval) |
| Marks 2001 | NR | Australia | NR | NR | Thunderstorm exposure (Grass pollen) | Asthma related Emergency Department Visits | Narrative |
| Newson 1997 | NR | England | 0-14 years old | NR | Thunderstorm exposure (Grass pollen) | Asthma attacks | Risk Ratio (95% Confidence Interval) |
| Newson 1998 | NR | England | 0-14 and >15 years old | NR | Thunderstorm exposure (Total Pollen) | Asthma hospital admissions | Risk Ratio (95% Confidence Interval) |
| Packe, 1985 | 106 | UK | 14-63 years old | 62 (58.5%) males and 44 (41.5%) females | Thunderstorm exposure (Total Pollen) | Acute asthma and other acute respiratory diseases | Narrative |
| Silver 2018 | 170,344 | Australia | NR (all ages) | NR | Thunderstorm exposure (Grass pollen) | Asthma-related hospital admissions | Narrative |
| Thien 2018 | 2,242 | Australia | Mean 32 | 56% males and 44% females | Thunderstorm exposure (Grass pollen) | Asthma related emergency hospital admissions | Narrative |

*NR: Not Reported*

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## Excluded studies

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| **No.** | Estudy ID | Exlusion reason | Refererence |
| 1 | Childhood 1973 | Wrong prognostic factor | Derrick EH. Childhood asthma in Brisbane: epidemiological observations. Aust Paediatr J. 1973 Jun;9(3):135-46. doi: 10.1111/j.1440-1754.1973.tb01867.x. PMID: 4750235; PMCID: PMC7166454. |
| 2 | Cropp 1975 | Wrong study design | Cropp GJ. Exercise-induced asthma. Pediatr Clin North Am. 1975 Feb;22(1):63-76. doi: 10.1016/s0031-3955(16)33102-9. PMID: 806878. |
| 3 | Chan-Yeung 1976 | Wrong study design | Chan-Yeung M, Abboud R, Tsao MS, Maclean L. Effect of helium on maximal expiratory flow in patients with asthma before and during induced bronchoconstriction. Am Rev Respir Dis. 1976 Apr;113(4):433-43. doi: 10.1164/arrd.1976.113.4.433. PMID: 1267250. |
| 4 | Bruce 1977 | Wrong study design | Bruce CA, Norman PS, Rosenthal RR, Lichtenstein LM. The role of ragweed pollen in autumnal asthma. J Allergy Clin Immunol. 1977 Jun;59(6):449-59. doi: 10.1016/0091-6749(77)90009-4. PMID: 68044. |
| 5 | Baur 1978 | Wrong study design | Baur X, Fruhmann G, von Liebe V. Allergologische Untersuchungsmethoden (inhalativer Provokationstest, Hauttest, RAST) für die Diagnose des Asthma bronchiale [Allergy diagnosis in patients with bronchial asthma (bronchial provocation test, skin test and RAST) (author's transl)]. Klin Wochenschr. 1978 Dec 15;56(24):1205-12. German. doi: 10.1007/BF01477076. PMID: 732243. |
| 6 | Fish 1980 | Wrong study design | Fish JE, Ankin MG, Kelly JF, Peterman VI. Comparison of responses to pollen extract in subjects with allergic asthma and nonasthmatic subjects with allergic rhinitis. J Allergy Clin Immunol. 1980 Feb;65(2):154-61. doi: 10.1016/0091-6749(80)90201-8. PMID: 7351448. |
| 7 | Cuthbert 1981 | Wrong study design | Cuthbert OD. The incidence and causative factors of atopic asthma and rhinitis in an Orkney farming community. Clin Allergy. 1981 May;11(3):217-25. doi: 10.1111/j.1365-2222.1981.tb01587.x. PMID: 7249337. |
| 8 | Buchsbaum 1982 | Wrong study design | Buchsbaum EG, Kinney JL, Klaustermeyer WB. A comparison of skin and bronchial reactivity in asthmatic patients using single, group related and unrelated antigen mixtures. Ann Allergy. 1982 May;48(5):267-71. PMID: 7081778. |
| 9 | Ortolani 1984 | Wrong study design | Ortolani C, Pastorello E, Moss RB, Hsu YP, Restuccia M, Joppolo G, Miadonna A, Cornelli U, Halpern G, Zanussi C. Grass pollen immunotherapy: a single year double-blind, placebo-controlled study in patients with grass pollen-induced asthma and rhinitis. J Allergy Clin Immunol. 1984 Feb;73(2):283-90. doi: 10.1016/s0091-6749(84)80021-4. PMID: 6366027. |
| 10 | Ahmed 1985 | Wrong study design | Ahmed T, Russi E, Kim CS, Danta I. Comparative effects of oral and inhaled verapamil on antigen-induced bronchoconstriction. Chest. 1985 Aug;88(2):176-80. doi: 10.1378/chest.88.2.176. PMID: 4017669. |
| 11 | Chirilă 1985 | Not retrieved | Chirilă M, Capetti E, Chirilă P, Florescu L. Frequency of certain allergens in allergic bronchial asthma. Med Interne. 1985 Jan-Mar;23(1):67-71. PMID: 3992149. |
| 12 | Reid 1986 | Wrong study design | Reid MJ, Moss RB, Hsu YP, Kwasnicki JM, Commerford TM, Nelson BL. Seasonal asthma in northern California: allergic causes and efficacy of immunotherapy. J Allergy Clin Immunol. 1986 Oct;78(4 Pt 1):590-600. doi: 10.1016/0091-6749(86)90076-x. PMID: 3771951. |
| 13 | Curzen 1987 | Wrong study design | Curzen N, Rafferty P, Holgate ST. Effects of a cyclo-oxygenase inhibitor, flurbiprofen, and an H1 histamine receptor antagonist, terfenadine, alone and in combination on allergen induced immediate bronchoconstriction in man. Thorax. 1987 Dec;42(12):946-52. doi: 10.1136/thx.42.12.946. PMID: 2894081; PMCID: PMC461056. |
| 14 | Tuchinda 1987 | Not retrieved | Tuchinda M, Habananada S, Vareenil J, Srimaruta N, Piromrat K. Asthma in Thai children: a study of 2000 cases. Ann Allergy. 1987 Sep;59(3):207-11. PMID: 3631656. |
| 15 | Britton 1988 | Wrong outcome | Britton J, Chinn S, Burney P, Papacosta AO, Tattersfield A. Seasonal variation in bronchial reactivity in a community population. J Allergy Clin Immunol. 1988 Jul;82(1):134-9. doi: 10.1016/0091-6749(88)90063-2. PMID: 3392365. |
| 16 | Karjalainen 1989 | Wrong study design | Karjalainen J, Lindqvist A, Laitinen LA. Seasonal variability of exercise-induced asthma especially outdoors. Effect of birch pollen allergy. Clin Exp Allergy. 1989 May;19(3):273-8. doi: 10.1111/j.1365-2222.1989.tb02383.x. PMID: 2736428. |
| 17 | Bates 1990 | Wrong prognostic factor | Bates DV, Baker-Anderson M, Sizto R. Asthma attack periodicity: a study of hospital emergency visits in Vancouver. Environ Res. 1990 Feb;51(1):51-70. doi: 10.1016/s0013-9351(05)80182-3. PMID: 2298182. |
| 18 | Paggiaro 1990 | Wrong study design | Paggiaro PL, Dente, FL, Talini D, Bacci E, Vagaggini B, Giuntini C. Pattern of airway response to allergen extract of Phleum pratensis in Orkney farming community. Respiration, 1990. 57(1): 51-56 |
| 19 | Crimi 1990 | Wrong study design | Crimi E, Voltolini S, Gianiorio P, Orengo G, Troise C, Brusasco V, Crimi P, Negrini AC. Effect of seasonal exposure to pollen on specific bronchial sensitivity in allergic patients. J Allergy Clin Immunol. 1990 Jun;85(6):1014-9. doi: 10.1016/0091-6749(90)90045-6. PMID: 2355152. |
| 20 | Crimi 1990 | Wrong study design | Crimi E, Gianiorio P, Orengo G, Voltolini S, Crimi P, Brusasco V. Late asthmatic reaction to perennial and seasonal allergens. J Allergy Clin Immunol. 1990 May;85(5):885-90. doi: 10.1016/0091-6749(90)90073-d. PMID: 1692048. |
| 21 | Bellomo 1992 | Wrong study design | Bellomo R, Gigliotti P, Treloar A, Holmes P, Suphioglu C, Singh MB, Knox B. Two consecutive thunderstorm associated epidemics of asthma in the city of Melbourne. The possible role of rye grass pollen. Med J Aust. 1992 Jun 15;156(12):834-7. doi: 10.5694/j.1326-5377.1992.tb136994.x. PMID: 1603007. |
| 22 | McEvoy 1992 | Wrong study design | McEvoy RJ. Thunderstorm associated epidemics of asthma. Med J Aust. 1992 Sep 7;157(5):352-3. PMID: 1294131. |
| 23 | Thurston 1992 | Wrong prognostic factor | Thurston GD, Ito K, Kinney PL, Lippmann M. A multi-year study of air pollution and respiratory hospital admissions in three New York State metropolitan areas: results for 1988 and 1989 summers. J Expo Anal Environ Epidemiol. 1992 Oct-Dec;2(4):429-50. PMID: 1336418. |
| 24 | Marzin 1993 | Wrong outcome | Marzin C, Le Moullec Y, Ancelle T, Juhel J, Festy B, Pretet S. Asthme, pollution atmosphérique urbaine et météorologie [Asthma, urban atmospheric pollution and the weather]. Rev Mal Respir. 1993;10(3):229-35. French. PMID: 8346367. |
| 25 | Subiza 1994 | Wrong prognostic factor | Subiza J, Cabrera M, Valdivieso R, Subiza JL, Jerez M, Jiménez JA, Narganes MJ, Subiza E. Seasonal asthma caused by airborne Platanus pollen. Clin Exp Allergy. 1994 Dec;24(12):1123-9. doi: 10.1111/j.1365-2222.1994.tb03317.x. PMID: 7889425. |
| 26 | Lagerstrand 1995 | Wrong study design | Lagerstrand L, Skedinger M, Ihre E, Halldén G, Zetterström O. Spirometry and ventilation-perfusion inequality in patients with mild allergic asthma before and during the pollen season. Clin Physiol. 1995 Jul;15(4):355-64. doi: 10.1111/j.1475-097x.1995.tb00526.x. PMID: 7554770. |
| 27 | Ostro 1995 | Wrong prognostic factor | Ostro BD, Lipsett MJ. Mann JK, Braxtonowens H, White, M. C. AIR-POLLUTION AND ASTHMA EXACERBATIONS AMONG AFRICAN-AMERICAN CHILDREN Orkney farming community. INHALATION TOXICOLOGY, 1995; 7(5): 711-722 |
| 28 | Djukanovic 1996 | Wrong prognostic factor and outcome | Djukanović R, Feather I, Gratziou C, Walls A, Peroni D, Bradding P, Judd M, Howarth PH, Holgate ST. Effect of natural allergen exposure during the grass pollen season on airways inflammatory cells and asthma symptoms. Thorax. 1996 Jun;51(6):575-81. doi: 10.1136/thx.51.6.575. PMID: 8693436; PMCID: PMC1090485. |
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| 30 | Scarlett 1996 | Wrong prognostic factor | Scarlett JF, Abbott KJ, Peacock JL, Strachan DP, Anderson HR. Acute effects of summer air pollution on respiratory function in primary school children in southern England. Thorax. 1996 Nov;51(11):1109-14. doi: 10.1136/thx.51.11.1109. PMID: 8958894; PMCID: PMC1090522. |
| 31 | Delfino 1997 | Wrong prognostic factor | Delfino RJ, Zeiger RS, Seltzer JM, Street DH, Matteucci RM, Anderson PR, Koutrakis P. The effect of outdoor fungal spore concentrations on daily asthma severity. Environ Health Perspect. 1997 Jun;105(6):622-35. doi: 10.1289/ehp.97105622. PMID: 9288497; PMCID: PMC1470068. |
| 32 | Ferdousi 1997 | Wrong study design | Ferdousi HA, Dreborg S. Asthma, bronchial hyperreactivity and mediator release in children with birch pollinosis. ECP and EPX levels are not related to bronchial hyperreactivity. Clin Exp Allergy. 1997 May;27(5):530-9. PMID: 9179427. |
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| 34 | Medina 1997 | Wrong prognostic factor | Medina S, Le Tertre A, Quénel P, Le Moullec Y, Lameloise P, Guzzo JC, Festy B, Ferry R, Dab W. Air pollution and doctors' house calls: results from the ERPURS system for monitoring the effects of air pollution on public health in Greater Paris, France, 1991-1995. Evaluation des Risques de la Pollution Urbaine pour la Santé. Environ Res. 1997 Oct;75(1):73-84. doi: 10.1006/enrs.1997.3773. PMID: 9356196. |
| 35 | Ong 1997 | Not retrieved | Ong EK, Abramson M, Farish S, Singh MB, Knox RB. Grass pollen, rainfall and asthma: Relationship between environmental allergen load and pollen counts. AEROBIOLOGY, 1997; 347-356. |
| 36 | Venables 1997 | Wrong prognostic factor and outcome | Venables KM, Allitt U, Collier CG, Emberlin J, Greig JB, Hardaker PJ, Highham JH, Laing-Morton T, Maynard RL, Murray V, Strachan D, Tee RD. Thunderstorm-related asthma--the epidemic of 24/25 June 1994. Clin Exp Allergy. 1997 Jul;27(7):725-36. PMID: 9249264. |
| 37 | Garty 1998 | Wrong prognostic factor | Garty BZ, Kosman E, Ganor E, Berger V, Garty L, Wietzen T, Waisman Y, Mimouni M, Waisel Y. Emergency room visits of asthmatic children, relation to air pollution, weather, and airborne allergens. Ann Allergy Asthma Immunol. 1998 Dec;81(6):563-70. doi: 10.1016/S1081-1206(10)62707-X. PMID: 9892028. |
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| 40 | Rosas 1998 | Wrong prognostic factor | Rosas I, McCartney HA, Payne RW, Calderón C, Lacey J, Chapela R, Ruiz-Velazco S. Analysis of the relationships between environmental factors (aeroallergens, air pollution, and weather) and asthma emergency admissions to a hospital in Mexico City. Allergy. 1998 Apr;53(4):394-401. doi: 10.1111/j.1398-9995.1998.tb03911.x. PMID: 9574882. |
| 41 | Chan-Yeung 1999 | Wrong outcome | Chan-Yeung M, Obata H, Dittrick M, Chan H, Abboud R. Airway inflammation, exhaled nitric oxide, and severity of asthma in patients with western red cedar asthma. Am J Respir Crit Care Med. 1999 May;159(5 Pt 1):1434-8. doi: 10.1164/ajrccm.159.5.9807007. PMID: 10228107. |
| 42 | Nelson 1999 | Wrong study design | Nelson HS, Szefler SJ, Jacobs J, Huss K, Shapiro G, Sternberg AL. The relationships among environmental allergen sensitization, allergen exposure, pulmonary function, and bronchial hyperresponsiveness in the Childhood Asthma Management Program. J Allergy Clin Immunol. 1999 Oct;104(4 Pt 1):775-85. doi: 10.1016/s0091-6749(99)70287-3. PMID: 10518821. |
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| 44 | Girgis 2000 | Wrong prognostic factor and outcome | Girgis ST, Marks GB, Downs SH, Kolbe A, Car GN, Paton R. Thunderstorm-associated asthma in an inland town in south-eastern Australia. Who is at risk? Eur Respir J. 2000 Jul;16(1):3-8. doi: 10.1034/j.1399-3003.2000.16a02.x. PMID: 10933077. |
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| 46 | Laszlo 2000 | Not retrieved | Laszlo E. Why are there more asthmatic children?. Lege Artis Medicine, 2000; 10(3):226-234. |
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## Risk of bias assessment (QUIPS tool)

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| --- | --- | --- | --- | --- | --- | --- | --- |
| **Study ID** | **Study participation: The study sample represents the population of interest on key characteristics, sufficient to limit potential bias of the observed relationship between PF and outcome.** | **Study Attrition: Loss to follow-up (from baseline sample to study population analysed) is not associated with key characteristics sufficient to limit potential bias to the observed relationship between PF and outcome.** | **Prognostic factor (PF) Measurement: PF is adequately measured in study participants to sufficiently limit potential bias.** | **Outcome Measurement: Outcome of interest is adequately measured in study participants to sufficiently limit potential bias.** | **Study Confounding: Important potential confounders are appropriately accounted for, limiting potential bias with respect to the relationship between PF and outcome.** | **Statistical Analysis and Presentation: The statistical analysis is appropriate for the design of the study, limiting potential for presentation of invalid or spurious results.** | **Overall RoB** |
| **Anderson 1998** | Moderate | NA | Low | Low | Moderate | Low | **Moderate** |
| **Anderson 2001** | High | NA | Moderate | Low | Moderate | Moderate | **High** |
| **Babin 2007** | Moderate | NA | High | Low | High | Moderate | **High** |
| **Bass 2000** | Moderate | NA | Moderate | Moderate | High | High | **High** |
| **Batra 2021** | Moderate | NA | Moderate | High | Low | High | **High** |
| **Bouazza 2017** | Moderate | NA | Moderate | Low | Moderate | Moderate | **High** |
| **Brzezińska-Pawłowska 2016** | Moderate | NA | Moderate | Low | High | Moderate | **High** |
| **Cakmak 2012** | Moderate | NA | Moderate | Low | Moderate | Moderate | **High** |
| **Caminati 2019** | Moderate | NA | Moderate | Low | High | High | **High** |
| **Celenza 1996** | Low | NA | Moderate | Low | Moderate | Low | **Moderate** |
| **Chen 2016** | Moderate | NA | Low | Low | Low | Low | **Low** |
| **Cirera 2012** | Moderate | NA | Moderate | Low | Moderate | Low | **High** |
| **Dales 2004** | Moderate | NA | Low | Low | Low | Moderate | **Moderate** |
| **Dales 2008** | Moderate | NA | Low | Low | Low | Low | **Low** |
| **Darrow 2012** | Moderate | NA | Low | Low | Low | Moderate | **Moderate** |
| **Davidson 1996** | Moderate | NA | Low | Low | High | High | **High** |
| **De Roos 2020** | Low | NA | Low | Low | Low | Low | **Low** |
| **Epton 1997** | Low | Low | Low | Low | Low | Moderate | **Low** |
| **Erbas 2007** | Moderate | NA | Moderate | Moderate | Low | Moderate | **High** |
| **Erbas 2012** | Moderate | NA | Low | Low | Low | Moderate | **Moderate** |
| **Garty 1998** | Low | Low | Moderate | Moderate | High | Moderate | **High** |
| **Ghosh 2012** | High | NA | Moderate | Moderate | High | Moderate | **High** |
| **Ginis 2015** | Moderate | NA | High | Low | High | High | **High** |
| **Gleason 2014** | Low | NA | Low | Low | Low | Low | **Low** |
| **Gonzalez-Barcala 2013** | Low | NA | Moderate | Low | Moderate | Moderate | **High** |
| **Gowrie 2012** | High | NA | Moderate | Moderate | High | Moderate | **High** |
| **Guilbert 2018** | Moderate | NA | Low | Low | Low | Low | **Low** |
| **Hajat 1997** | High | NA | Moderate | Moderate | Moderate | Moderate | **High** |
| **Hanigan 2007** | Moderate | NA | Moderate | Moderate | Low | Low | **High** |
| **Heguy 2008** | Moderate | NA | Moderate | Low | Low | Low | **Moderate** |
| **Idrose 2020** | Moderate | NA | Moderate | Moderate | Moderate | Moderate | **High** |
| **Im 2005** | Moderate | NA | Moderate | Moderate | Moderate | Moderate | **High** |
| **Ito 2015** | Moderate | NA | Low | Low | Moderate | Low | **Moderate** |
| **Jamason 1997** | Moderate | NA | High | Moderate | Moderate | Moderate | **High** |
| **Jariwala 2011** | High | NA | Moderate | Moderate | High | Moderate | **High** |
| **Jariwala 2014** | Moderate | NA | Moderate | Moderate | High | Moderate | **High** |
| **Khot 1988** | Moderate | NA | Moderate | Low | Moderate | Moderate | **High** |
| **Klabushnigg 1981** | Moderate | NA | Moderate | Low | High | High | **High** |
| **Kordit 2020** | Low | NA | Moderate | Low | High | Low | **High** |
| **Kralimarkova 2014** | Moderate | Moderate | High | Moderate | High | Moderate | **High** |
| **Krmpotic 2011** | Moderate | NA | Moderate | Moderate | Low | Low | **High** |
| **Lambert 2020** | Moderate | NA | Low | Low | Low | Low | **Low** |
| **Lee 2019** | Moderate | NA | Low | Low | Low | Low | **Low** |
| **Lewis 2000** | Moderate | NA | Moderate | Low | Low | Moderate | **High** |
| **Li 2019** | Low | NA | Moderate | Low | Low | Low | **Low** |
| **Lierl 2003** | Low | NA | Low | Low | Moderate | Low | **Low** |
| **Lowe 2012** | Moderate | NA | Moderate | Moderate | Moderate | Low | **High** |
| **Mackay 1992** | Moderate | NA | Moderate | Moderate | High | High | **High** |
| **Makra 2012** | Moderate | NA | Moderate | Low | Moderate | Moderate | **High** |
| **Marks 2001** | Moderate | NA | Moderate | Moderate | High | High | **High** |
| **Marques-Mejias 2019** | Low | NA | Moderate | Low | High | High | **High** |
| **May 2011** | Moderate | NA | Moderate | Moderate | High | Moderate | **High** |
| **Mazenq 2017** | Low | NA | Low | Low | Low | Low | **Low** |
| **Mazenq 2017 b** | Moderate | NA | Moderate | Low | Moderate | Moderate | **High** |
| **Murray 2006** | Low | NA | Moderate | Moderate | High | Moderate | **High** |
| **Newson 1997** | Moderate | NA | Moderate | Low | Low | Low | **Moderate** |
| **Newson 1998** | High | NA | Moderate | Low | Low | Low | **High** |
| **Osborne 2017** | Low | NA | Low | Low | Low | Low | **Low** |
| **Ostro 2001** | Low | Low | Low | Low | Low | Low | **Low** |
| **Packe 1985** | High | NA | Moderate | Low | High | High | **High** |
| **Porcel Carreño 2020** | High | NA | Moderate | Moderate | High | Moderate | **High** |
| **Potter 1984** | Moderate | NA | High | Moderate | High | High | **High** |
| **Rossi 1993** | Low | NA | Moderate | Low | High | Moderate | **High** |
| **Shrestha 2017** | Low | NA | Low | Low | Low | Low | **Low** |
| **Silver 2018** | Moderate | NA | Low | Low | Low | Low | **Low** |
| **Sun 2016** | Low | NA | Moderate | Low | Moderate | Low | **Moderate** |
| **Targonskl 1995** | Low | NA | Low | Low | Low | Low | **Low** |
| **Thien 2018** | Moderate | NA | Moderate | High | Low | High | **High** |
| **Tobias 2003** | Moderate | NA | Moderate | Moderate | Moderate | Moderate | **High** |
| **Tobias 2004** | High | NA | Moderate | Moderate | Moderate | Moderate | **High** |
| **Wang 2007** | High | NA | Moderate | Moderate | High | Moderate | **High** |
| **Wilonsky 2018** | Moderate | NA | Moderate | Moderate | Moderate | Moderate | **High** |

## Non-Adjusted Results for patients exposed to pollen

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| |  |  |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | --- | --- | | **Study ID** | **Age** | **Outcome Definition** | **Exposure** | | **Effect Estimate** | | | | | **Pollen: concentration** | **Lag** |  | **EE** | **95%CI** | | | **Gowrie 2012** | 0-15 years | Asthma-Related ED Admissions | Total pollen: 30 grains/m3 | “Analysis of the raw data revealed that on days in which asthma admittance exceeded 10 or more, pollen was always at a concentration of 30 pollen grains/m3/day or more, in the preceding 0–10 days, which suggests that pollen may play a role as an asthmatic irritant and that there may be both a threshold and a lag period to be considered” | | | | | | **Potter 1984** | 2.14 years | Asthma Attacks | Total pollen: not specified | “Changes in pollen bore no correlation with patients presenting with asthma attacks” | | | | | | **Marques-Mejias 2019** | 0-14 years | Asthma-Related ED Admissions | Total pollen: Not specified | “No correlation was found between ED admissions and counts of pollen” | | | | | | **Garty 1998** | Children | Asthma-Related ED Visits | Total Pollen: Not Specified | “the concentrations  of the specific pollen varied according  to the flowering season of each  plant species but none significantly  correlated with ER visits” | | | | | | **Caminati 2019** | >50 years | Asthma-Related ED Admissions | Total pollen: Not specified | “There was no significant correlation between admission clusters and pollens” | | | | | | **Krmpotic 2011** | >18 years | Asthma Hospitalisations | Total pollen: Not specified | “There is a probability of the increase in daily asthma hospitalisation at higher percentile change in pollen level, that is, from the 95th to 99th percentile” | | | | | | **Brzezinska-Pawlowska 2016** | all ages | Ambulance Emergency Service | Total pollen: Not Specified | “Ambulance emergency service visits relating to asthma did not correlate with the total pollen count” | | | | | | **Jariwala 2011** | all ages | Asthma-Related ED visits | Total Pollen: Peak of 1800 grains/m3 | Not Specified | Correlation(r) | 0.6620 | p=0.012 | | | Total Pollen: Peal of 75 grains/m3 | 0.1331 | p=0.068 | | | **Epton 1997** | 17-80 years | Asthma Exacerbation | Total pollen: Not Specified | “A total of 54 exacerbations requiring nebuliser treatment were recorded during the year. There were no significant clusters of exacerbations. This number was inadequate to perform statistical analysis with respect to the effects of pollen.” | | | | | | **Jamason 1997** | NR | Asthma-Related ED Admissions | Total pollen: Not Specified | “In spring, a slight increase in asthma admissions occurs near the time of elevated total pollen concentrations, but these admissions increases are much less dramatic than those in fall. Thus, it appears that pollen concentration plays little role in the observed asthma increases” | | | | | | **Klabuschnigg 1981** | 7-14 years | Symptom score | Total pollen: Not specified | “When comparing mean values of symptom score of consecutive 10- day periods, calculated over a total of 6 weeks, with total pollen prevalence good agreement is found during the first 4 weeks” | | | | | | **Jariwala 2014** | all ages | Asthma-Related ED Visits | Total pollen: >100 grains/m3 vs <100 grains/m3 | "We found a strong association between high pollen counts and increased asthma ED visits. Daily pollen counts in the highest quartile of pollen counts corresponded to a mean of 17.1 (SD 8.2) visits, while all other quartiles of pollen counts collectively corresponded to a mean of 11.4 (SD 6.6) visits" | | | | | | **Jariwala 2014** | all ages | Asthma-Related ED Visits and hospitalisations | Grass: Not specified | “no positive correlation between visits or hospitalisations and grass pollen counts” | | | | | | **Murray 2006** | 3-7 years | Asthma Hospitalisation | Grass: Not specified | 7 day average | OR | 1.5 | 0.8 | 2.9 | | **Klabuschnigg 1981** | 7-14 years | Asthma Attacks | Grass: 969 grains/m3 | “There were no correlations when the 2-hourly pollen count was compared to simultaneously collected attack data and drug requirements” | | | | | | **Marques-Mejias 2019** | 0-14 years | Asthma-Related ED Admissions | Grass: Not specified | “A statistically significant (P<.0001) relationship was found between grass pollen counts and ED admissions” | | | | | | **Wang 2007** | Children | Asthma-Related ED Visits | Grass: Not specified | “There were no significant differences between the grass pollen and on high- and low-visit days p=0.51.” | | | | | | **Caminati 2019** | >50 years | Asthma-Related ED Admissions | Grass: Not specified | “When analysing the distribution of admissions during the whole year, a peak in April and May was observed, in comparison with the other months (p =0.0000). In the same period a significant increase of grass pollen count was recorded” | | | | | | **Porcel Carreño 2020** | all ages (5-88 years) | Asthma-Related ED Admissions | Grass: Not specified | 0 | Correlation (pearson) | 0.313 | p=0.0055 | | | 1 | 0.488 | p=1.05x10-6 | | | 3 | 0.575 | p= 4.58x10-9 | | | **Wang 2007** | Children | Asthma-Related ED Visits | “The mean tree pollen level on high-visit days was 70.95 g/m3, which trended toward significance when compared with tree pollen levels on low-visit days (28.27 g/m3; p = 0.05)” | | | | | | | **Brzezinska-Pawlowska 2016** | all ages | Asthma-Related ED Visits | Tree pollen: Not Specified | Not Specified | Correlation (R) | 0.269 | p<0.01 | | | **Kordit 2020** | all ages | Asthma-Related ED Visits | Tree Pollen: Spring | Not Specified | Correlation Coefficient | 0.002 | 0.001 | 0.002 | | Tree Pollen: Summer | 0.011 | -0.087 | 0.109 | | **Rossi 1993** | 15-85 years | Asthma-Related ED Visits | Tree Pollen: Not Specified | Not Specified | “No association was found between concentrations of tree pollen and attendances for asthma, the former being highest in early summer, when the number of attendances was low” | | | | | **Jariwala 2014** | pediatric | Asthma-Related ED Visits | Tree Pollen: Not Specified | Not Specified | Rho | 0.33 | p<0.001 | | | adults | Rho | 0.28 | p<0.001 | | | all ages | Rho | 0.3639 | p<0.001 | | | **Krmpotic 2011** | >18 years | Asthma Hospitalisations | Birch Pollen: Not Specified | Not Specified | Regression coefficient (SE) (t) | 0.0005 | 0.0002 | 2.5 | | **Ito 2015** | All ages | Asthma-Related ED Visits | Birch Pollen: Not specified (Peak days of pollen) | Not Specified | Correlation (Spearman) | 0.40 |  |  | | **Ito 2015** | All ages | Asthma-Related ED Visits | Elm Pollen: Not specified (Peak days of pollen) | Not specified | Correlation (Spearman) | 0.50 |  |  | | **Porcel Carreño 2020** | all ages (5-88 years) | Asthma-Related ED Admissions | Olive Pollen: Not specified | 0 | Correlation (pearson) | 0.180 | p=0.1823 | | | 1 | 0.656 | p=0.00091 | | | 4 | 0.716 | p= 6.20x10-15 | | |
|

## 

## Non-Adjusted Results for severe asthma exacerbations in patients exposed to pollen during thunderstorms

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study ID** | **Age** | **Outcome Definition** | **Exposure** | | **Effect Estimate** | | | |
| **Pollen: concentration** | **Lag** |  | **EE** | **95%CI** | |
| **Anderson 2001** | all ages | Asthma-Related ED admissions | Total pollen: 0-693 grains/m3 | Not Specified | Spearman correlation | -0.07 | - | Authors report “no correlation” |
| **Packe 1985** | 14 mo-63 years | Asthma-Related ED visits or admissions | Total pollen: 100-300 grains/m3 in july 2 to 5 | “106 patients attended while 32 were admitted because of acute asthma and other acute respiratory diseases on july 6-7 (Thunderstorm). Pollen counts remained high during July 6, declined later in the day with the onset of rain, and increased again by the afternoon of July 7.” | | | | |
| **Davidson 1996** | all ages (mean=32) | Asthma-Related ED Visits | Grass: mean 258 grains/m3 | “Data suggests that grass pollen was the most significant aeroallergen in the period before the storm and the outbreak of asthma. Pollen released during the days before the thunderstorm would have been deposited on surfaces in the city and could have been resuspended by gusting winds” | | | | |
| **Thien 2018** | all ages (mean=32) | Asthma-Related ED Admissions | Grass: Not specified | “Grass pollen concentrations on Nov 21, 2016, were extremely high (>100 grains/m3). Within 30 h, there were 476 (992%) excess asthma-related admissions to hospital, compared with the previous 3 years.” | | | | |
| **Marks 2001** | all ages | Asthma Epidemic | Grass: Not Specified | “During the thunderstorm the concentration of grass pollen grains increased fourfold compared with the previous hour or eightfold compared with the average over the preceding nine hours. This event coincided with the onset of an epidemic.” | | | | |

# References



2.