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ARTICLE



The association between outdoor allergens – pollen, fungal spore season and high asthma admission days in children and adolescents

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ABSTRACT

Periods when asthma admissions peaks have serious implications for asthma sufferers and hospitals. We assessed 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. Two peak periods were identified. Effect modifications by atopy and sex were considered. All pollen 2 days prior was associated with increased odds of these peak periods. Same day fungal spores, but not pollen, were important. Grass at lag 2 was associated with increased odds 1.03 (95%CI 1.01, 1.05) as was the same day *Alternaria* 1.02 (1.00, 1.04) per spore/m³ for boys. In addition to pollen, fungal spores particularly *Alternaria* may result in days of high exacerbations during pollen seasons. Further guidance is needed to better prepare families/carers with information about the increased risk of asthma attacks in children prior to pollen seasons.

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Environment; adolescent health; pollen; aeroallergen

Introduction

Asthma is a chronic respiratory disease that sensitises the airways, which become inflamed when exposed to triggers. This inflammation results in chest tightness, cough, shortness of breath and wheezing, and sometimes leads to a 'flare-up' or attack, which can be a medical emergency (American lung association 2020). It affects 5–10% or estimated 23.4 million of the world's population including 7 million children (Morris 2020). Asthma places a severe burden on the public health system and economy with its total cost from both direct medical costs, i.e. hospital admissions, the cost of pharmaceuticals and indirect costs, i.e. time lost from work and/or premature deaths (Nunes et al. 2017). The underlying causes of asthma are still incompletely understood, although some triggers are environmental including pollen, fungi and extreme weather patterns such as thunderstorms asthma (TA) events (Asthma Australia 2019).

When peak periods of hospital admissions occur, they cause a huge and unexpected burden on the health care system, the patient and their care givers and family. Periods of high asthma

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admission days are defined as days with an unexpectedly high number of asthma admissions to hospitals based on varying thresholds (Silver et al. 2018). In the Southern Hemisphere, high asthma admission periods have occurred during TA events, which are defined as an asthma attack triggered by abrupt changes in environmental conditions caused by thunderstorm activity (Campbell et al. 2019). These usually occur during the pollen season when high pollen days are concurrent with thunderstorms and abrupt changes in weather conditions such as wind speed, temperature (Andrew et al. 2017) and relative humidity (Silver et al. 2018).

Melbourne has very high levels of grass pollen. A Burkard volumetric trap was used to monitor the atmosphere of Melbourne for pollen grains. Flowering plants and conifers, about twenty-two families, were identified in the pollen counts with 62% of these pollen grains belonging to trees, 20% to grasses and 9% to herbs and weedy plants. Grasses such as *Ulmus* and *Cupressus* had the most significant contribution to the pollen calendar. The pollen-producing period of these plants spanned from the end of June to the end of February, accounting for 67% of the year. Introduced species such as *perennial* and annual rye grasses and canary grasses were the major contributors to grass pollen. These grasses are grown extensively as pasture grasses and the ryegrasses occur as weeds in wheat crops in Victoria (Ong et al. 1995a). In Melbourne, exposure to grass pollen, notably that of the pasture grass *perennial* ryegrass, is the main cause of asthma from October to December (Haberle et al. 2014).

In separate high asthma periods, recorded in Australia (Marks et al. 2001) as well as in other locations such as in the United Kingdom (UK), increased levels of grass pollen grains were found in the atmosphere (D'Amato et al. 2007). Higher levels of allergic sensitivity to ruptured ryegrass pollen starch granules have been detected in patients who experienced asthma during thunderstorms (Davies et al. 2017). Evidence for increased risk of emergency department presentations and hospital admissions during peak grass pollen seasons in children and adolescents has been demonstrated (Erbas et al. 2012, 2018). As changing climatic conditions and longer intense pollen seasons are likely to result in similar events (Zhang et al. 2014; Ziska et al. 2019), it is important to better understand the factors that contribute to these high asthma periods especially in children and adolescents.

Fungal spores may also exacerbate asthma in children and adolescents as our own work suggests (Tham et al. 2016). In the atmosphere of Melbourne, Australia between October 1991 and December 1994, annual fungal spore counts, approximately half of which were identified as *Cladosporium* sp. and only about 1% *Alternaria* sp., varied widely from 1,106,037 in 1992 to 345,770 in 1994 (Mitakakis et al. 1997). Coupled with high pollen days and the high correlation between aeroallergens, it is possible that fungi exposure compounds the problem. However, little has been done assessing both types of aeroallergens and their impact on high asthma admission periods in children and adolescents.

The Melbourne Air Pollen Children and Adolescent Health (MAPCAH) study recruited children and adolescents with incident asthma (Tham et al. 2016) during two peak periods of high asthma admissions (25/10/2010 & 30/11/2011) that occurred during the grass pollen seasons (Howden et al. 2011; Silver et al. 2018). Although not as severe as the 2016 TA event (Thien et al. 2018), these events still resulted in a large number of emergency calls, hospital attendances, and hospital admissions. Using the MAPCAH data we sought to assess the role of both pollen and fungal spores on these two events.

Methods

Study design and setting

This case-crossover analysis is a sub-study of the Melbourne Air Pollen Children and Adolescent Health (MAPCAH) study (Erbas 2013). The study was conducted in Melbourne, Victoria from September 2009 to December 2011 with daily asthma admissions (defined as ICD10 J45/46 codes) at The Royal Children's Hospital (RCH) aged 2 to 17 years. The total sample size considered for the

study was 176 with a final 135 for case-crossover analysis. It excluded 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. The MAPCAH study collected individual data on family history (family history of atopy and asthma), presence of atopy, eczema, hay fever (doctor diagnosed), and Human Rhinovirus (HRV) infection and daily incidence of airborne pollen and fungal spores during the study period.

The outcome variable: peak periods of high asthma admissions

To identify high asthma admission periods, we used the normalised residuals from the entire time series of admissions during the two pollen seasons. The running trimmed mean (averaging after removing the 1st and 99th percentile of the score) was subtracted from the original admissions time-series and then divided by a running trimmed standard deviation. Both trimmed statistics were based on a seven lag day window (identified in the Partial correlation plots) (Silver et al. 2018). Another method, locally weighted scatterplot smoothing (LOWESS), was followed to confirm the results, which produced locally weighted means based on a one-week data bandwidth. We then isolated the dates whose LOWESS fits were 4 or more SD from their overall mean, which is consistent with Silver et al. (2018). Using these methods, 25 November 2010 and 30 October 2011 were identified as high asthma days. As the impacts of environmental factors are not always immediate, it is important to identify preceding days that may be associated with the event. Likewise, days post event also needed to be considered to capture the delay in admissions. Assessing the autocorrelation function of daily admissions, we identified 2 days prior and 2 days post event as days associated with the high admission days. Therefore, our case period (outcome variable) was defined as the high admission days (25 November 2010 and 30 October 2011), 2 days prior and 2 days post these days.

Primary exposure variables

Using the guidelines of the World Allergy Organization (Abbas et al. 2012), a volumetric spore trap (Burkard, UK) was used to measure pollen (Grass, weed, and tree) and ambient fungal spores (*Alternaria* conidia, *Cladosporium* spores, and Smuts). The testing site is 20 m above ground levels on the roof top of a building located in central Melbourne. Daily 24-hour average pollen concentrations (grains/m³) were collected from a single Burkard volumetric trap (Burkard Manufacturing Co. Ltd., Rickmansworth, Hertfordshire, UK) during the MAPCAH study period.

Other variables

To assess individual atopic status, each participant underwent skin prick tests (SPTs). These SPTs were conducted with suitable controls for a panel of pollen [rye grass, seven grass mix (*Phleum pratense*, *Dactylis glomerata*, *Poa pratensis*, *Agrostis gigantea*, *Festuca pratensis*, *Lolium*, *Anthoxanthum odoratum*), birch, English plantain and ten tree mix (*Alnus rugosa*, *Fraxinus Americana*, *Ulmus Americana*, *Fagus*, *Betula lenta*, *Acer saccharum*, *Carya ovata*, *Quercus alba*, *Populus alba*, *Platanus occidentalis*), and fungal allergens (*Alternaria* conidia and *Cladosporium* spores)]. A skin reaction to one or more allergens with a size of at least 3 mm greater than the reaction to the negative control solution was considered positive (The Australasian Society of Clinical Immunology and Allergy 2020). We grouped participants into age groups: 2–5, 6–12, or 13–17 years.

Outdoor daily levels of air pollutants and weather factors were also considered in the models. Particulate matter up to 2.5 µm in diameter (PM_{2.5}), relative humidity, maximum temperature, and the daily maximum 1-hour average nitrogen dioxide (NO₂) concentrations (parts per billion) were considered.

Statistical analysis

We used a bi-directional case-crossover approach to analyse the associations between aeroallergens and admission periods. This approach also controls for other confounding associated with the day of the week, monthly, seasonal, and long-term trends (Bateson and Schwartz 1999, 2001). Exposure and other environmental variables were available for both case and control days. Conditional logistic regression models were used to assess the association between same day and lagged pollen and fungi and asthma admissions in separate models. Models were adjusted for potential confounders, such as pollutants and weather variables, if they were statistically significant ($p < 0.05$) or changed the estimated effect size of the primary exposure by 10%. Analyses were further stratified by sex and sensitisation to any aeroallergen to identify possible effect modification. All results are presented as odds ratios (OR) and 95% confidence intervals (CIs). All statistical analyses were performed using Stata IC 16. (StataCorp, College Station, Texas).

Results

In 2010 and 2011, during the pollen season in Melbourne (1st October to 31st December) (Ong et al. 1995b), there were 240 asthma admissions to The Royal Children's Hospital and of these 176 (73.3%) consented to participate in the MAPCAH study. In 2010, peak monthly admissions (79) occurred in November and on November 25th, of 10 admitted, 8 agreed to participate. Whereas in 2011, peak admissions (49) were in October and on October 30th, there were 9 admissions and 5 agreed to participate. The majority were young boys. More than half of the participants were sensitized to any aeroallergen. During the 2010 pollen season, a minority were diagnosed with hay fever (20.6%) and those admitted during November, when the high asthma period occurred, were less likely to have a family history of asthma (27%) compared to those admitted during October (Table 1).

The pollen, fungal spores, pollutants and weather levels for both pollen seasons as median [25th percentile, 75th percentile], 2 days prior and on the high admission days are presented in Table 2. *Alternaria* 4 [18], *Cladosporium* 24 [6.5, 57], and Smuts 2 [0, 21.5] were considerably higher in 2010 compared to the 2011 pollen season. Except for Smuts and weed pollen (mainly *Plantago*, the plantains or fleaworts), all the aeroallergens were greater 2 days before than on the high admission days (25 November 2010 and 30 October 2011).

We constructed smooth plots between levels of daily aeroallergens and asthma hospital admissions to the Royal Children's hospital (Online supplementary Figures 1, 2, 3, 4, 5 and 6). For 2010, grass pollen was very high (>200 grains/m³) around 5 days (18th November) preceding the peak period (S1 Figure 1). Whereas in 2011, grass pollen was high 2 days prior to the high admission day or at the beginning of the period. However, tree pollen [mainly *Cupressaceae* (cypress) with smaller amounts of native *Myrtaceae* (eucalypt) pollen, as well as pollen from introduced Northern Hemisphere trees (Haberle et al. 2014)] in both pollen seasons were highest around 11 October in 2010 (>1000 grains/m³) and 14 October in 2011 (>2000 grains/m³) (S2 Figure 2). Weed pollen (S3 Figure 3) recorded its highest counts both around 12 October (100 grains/m³) and 24 November (80–100 grains/m³) 2010. *Cladosporium* counts were the highest around 15 October 2010 (S5 Figure 5). However, in 2011, *Cladosporium* median counts were low during the pollen season compared to 2010. Levels of *Alternaria* conidia were at their highest in Melbourne 1 day either side of high admission day that occurred on the 25 November 2010 (S4 Figure 4).

In unadjusted conditional logistic regression models, *Alternaria* (OR = 1.04 per conidia/m³ 95% CI 1.03–1.04) and *Cladosporium* (OR = 1.01 spores/m³ 95%CI 1.00–1.02) were significantly associated with increased odds of asthma hospital admission during the high asthma period, whereas grass pollen (OR = 1.03 per grain/m³ 95%CI 1.01–1.05), weed pollen (OR = 1.05 per grain/m³ 95%CI 1.03–1.07) and tree pollen (OR = 1.00 per grain/m³ 95% CI 1.000–1.001) were associated with increased odds at lag 2 (Table 3).

Table 1. Participant characteristics for pollen seasons, 2010 and 2011.

Year	2010			2011		
Months	October	November	December	October	November	December
No of admissions	28	79	42	49	40	2
No of participants	22 (78.6%)	64 (81%)	30 (71.4%)	30 (61.22%)	28 (70.00%)	2 (100%)
Sex	13 (61.9%)	45 (70.3%)	19 (63.3%)	19 (63.3%)	20 (71.4%)	1 (50%)
Boys N (%)	8 (38.1%)	19 (26.7%)	11 (36.7%)	11 (36.7%)	8 (28.6%)	1 (50%)
Girls N (%)						
Age	5.2 ± 2.7	5.8 ± 3.4	6.1 ± 4.0	5.4 ± 3.1	4.6 ± 3.1	3.5 ± 0.7
Mean±SD	2	2	2	2	2	3
Min	12	15	16	15	12	4
Max	5	5	4	5	4	3.5
Median	3	5.5	6	5	4	1
IQR (Interquartile range)						
HRV status, N,	21,	64,	30,	30,	28,	2,
Yes N (%)	14 (66.7%)	58 (75.00%)	18 (60.00%)	27 (90.00%)	24 (85.71%)	1 (50.00%)
Sensitive to any aeroallergen, N,	21,	64,	30,	30,	28,	2,
Yes N (%)	16 (76.19%)	52 (81.25%)	23 (76.67%)	27 (90.00%)	27 (96.43%)	1 (50.00%)
Hay fever diagnosed, N,	19,	43,	25,	28,	25,	2,
Yes N (%)	3 (15.79%)	12 (27.91%)	3 (12%)	8 (28.57%)	3 (12%)	1 (50.00%)
Mother history of asthma, N,	19,	63,	30,	28,	25,	2,
Yes N (%)	8 (42.11%)	17 (26.98%)	6 (20%)	9 (32.14%)	6 (24%)	1 (50.00%)

Table 2. Aeroallergens for Pollen season 2010 & 2011.

Aeroallergens and other Factors	Totals for pollen season	2 days before High asthma day	High asthma admission day (25/11/2010)	Totals for pollen season	2 days before High asthma day	High asthma admission day (30/10/2011)
	Median [25 th percentile, 75 th percentile]			Median [25 th percentile, 75 th percentile]		
Grass Pollen (grains/m ³)	27.5 [7, 68]	112	34	20 [11, 51]	133	20
Tree pollen (grains/m ³)	156 [85, 322.5]	614	216	134.5 [75, 246]	741	60
Weed Pollen (grains/m ³)	5 [2, 14]	0	20	5 [2, 10]	4	5
<i>Alternaria</i> (counts)	4 [0, 18]	70	53	3.5 [1, 9.5]	12	2
<i>Cladosporium</i> (counts)	24 [6.5, 57]	63	39	5.5 [0, 18.5]	74	0
Smuts (counts)	2 [0, 21.5]	1	30	0 [0, 0]	4	0
Max temp (°C)	22.8 [19, 25.5]	32.3	23.5	22.6 [19.95, 27]	26.4	17.4
PM Relative Humidity	45 [39, 57]	29	76	46 [34, 55]	46	72
PM _{2.5} µg/m ³	3.5 [2.45, 5.05]	4.6	2.6	3.5 [2.8, 5.2]	-	-
NO ₂ ppb	8.15 [6.85, 10.05]	7.3	10.1	8.2 [6.3, 10.3]	7.6	3.5

In the adjusted analysis, *Alternaria* (OR = 1.01 conidia/m³ 95%CI 1.00–1.03) remained associated with asthma admissions during the high asthma period (p value = 0.031). In a fully adjusted model, weed (OR = 1.07 per count/m³ 95%CI 1.00–1.01) and tree (OR = 1.00 per count/m³ 95%CI 1.00–1.01) was also associated with asthma admissions at lag 2. Adding temperature and relative humidity to the adjusted models resulted in grass at lag 2 falling outside the set significance level (p value < 0.09) (Table 3).

When stratified by sex, grass (OR = 1.03 per grain/m³ 95%CI 1.01–1.05) and weeds (OR = 1.05 per grain/m³ 95%CI .99–1.12) at lag 2 were associated with increased odds for boys. Same-

Table 3. Associations between environmental data and asthma during high asthma periods.

Environmental variables	N = 135 Unadjusted OR (95% CI) p value	N = 135 Adjusted Model OR (95% CI) p value
Grass	0.979 (.962–.996) 0.02	0.999 (.96–1.011) 0.07
Grass lag 2	1.031 (1.012–1.051) 0.00	1.017 (.999–1.035) 0.05
Tree	0.998 (.996–1.000) 0.08	0.995 (.991–.998) 0.01
Tree lag 2	1.000 (1.000–1.001) 0.04	1.000 (1.000–1.001) 0.03
Weed	1.148 (1.046–1.259) 0.00	1.125 (.982–1.289) 0.09
Weed lag 2	1.055 (1.033–1.078) <0.001	1.071 (1.006–1.140) 0.03
<i>Alternaria</i>	1.040 (1.033–1.048) <0.001	1.017 (1.001–1.033) 0.03
<i>Alternaria</i> lag 2	0.989 (.976–1.003) 0.14	0.992 (.970–1.014) 0.49
<i>Cladosporium</i>	1.015 (1.006–1.025) 0.00	1.004 (.990–1.018) 0.49
<i>Cladosporium</i> lag 2	0.985 (.968–1.002) 0.09	0.984 (.956–1.012) 0.27
Smuts	1.030 (.988–1.073) 0.16	1.032 (.979–1.087) 0.24
Smuts lag 2	1.035 (.995–1.077) 0.08	.957 (.911–1.005) 0.08

In unadjusted models, each aeroallergen is adjusted for its respective lagged variable and vice versa. Models are adjusted for Maximum temperature and Relative Humidity.

day *Alternaria* conidia was associated with increased odds in boys, but not girls in an adjusted model (OR = 1.02 spores/m³ 95%CI 1.00–1.04, p value = 0.00) (Table 4).

Discussion

Peak periods of asthma hospital admissions are a substantial burden on people with asthma and their care givers as they are unexpected. They are also a major burden on the health care system due to an emergency department visit and subsequent hospital admission. Using a method by Silver et al. (2018) that makes chance findings highly unlikely (<4 in a million), we identified two high asthma admission days that occurred on 25 November 2010, and 30 October 2011 during the grass pollen seasons. We considered a peak period as 2 days prior and 2 days post these days as evidenced by the autocorrelation plots. Although Silver and colleagues (Silver et al. 2018) found more days using their method during the same pollen periods as described here, they included both children and adults and used admission data from all public hospitals within the greater Melbourne region, which is a different sample included in our study.

Our findings suggested a 2-day lagged effect of both pollen and spores on child asthma admissions. Fungi, particularly *Alternaria* conidia (OR = 1.017 per count/m³), were primarily implicated even when adjusted for weather. Same-day grass pollen was associated with child asthma hospital admission, but when adjusted for temperature and relative humidity, effects become statistically non-significant at the 0.05 level. However, grass and tree pollen at lag 2 were associated with increased odds of admissions. Boys were more susceptible than girls to grass pollen and *Alternaria* conidia.

Table 4. Associations between environmental data and asthma during high asthma periods with models stratified by sex.

Environmental variables	Boys, N = 93		Girls, N = 42	
	Unadjusted OR (95% CI)	p value	Unadjusted OR (95% CI)	p value
Grass	0.965 (.949-.981)	<0.001	0.994 (.973-1.015)	0.60
Grass lag 2	1.050 (1.029-1.071)	<0.001	1.015 (.993-1.037)	0.17
Tree	0.997 (.994-.999)	0.01	0.999 (.998-1.000)	0.32
Tree lag 2	1.000 (.999-1.001)	0.10	1.000 (.999-1.001)	0.25
Weed	1.103 (.978-1.243)	0.10	1.260 (1.096-1.448)	0.00
Weed lag 2	1.050 (1.027-1.073)	<0.001	1.108 (.964-1.273)	0.14
<i>Alternaria</i>	1.041 (1.031-1.051)	<0.001	1.040 (1.030-1.050)	<0.001
<i>Alternaria</i> lag 2	0.989 (.974-1.005)	0.19	0.990 (.963-1.017)	0.47
<i>Cladosporium</i>	1.013 (1.003-1.023)	0.01	1.019 (.991-1.047)	0.17
<i>Cladosporium</i> lag 2	0.991 (.973-1.008)	0.31	0.964 (.941-.989)	0.01
Smuts	1.038 (.994-1.084)	0.08	1.011 (.915-1.117)	0.83
Smuts lag 2	1.033 (.988-1.081)	0.14	1.047 (.952-1.152)	0.33

In unadjusted models, each aeroallergen is adjusted for their respective lagged variable and vice versa. Models are adjusted for Maximum temperature and Relative Humidity.

Our findings are the first to suggest the importance of both grass pollen and spores during periods where the risk of periods of high asthma admissions may occur. Previously, it was thought that pollen alone was a substantive trigger during the season, but we show here that both pollen and fungi with some lagged effects are associated for the same peak periods in children and adolescents. Although no lightning or thunderstorms occurred on identified high days and in line with previous work (Osborne et al. 2017), we have identified a lag 2-day grass pollen effect but no same day effect. It is possible that pollen grains may have ruptured due to high relative humidity and although they are respirable, they are escaping detection due to their small size and hence their effects are not observed in the statistical models (Miguel et al. 2006).

Like a previous study (Newson et al. 2000) in the UK, higher airborne levels of fungal spores were also recorded during high asthma admission periods in Melbourne. Air pollution specifically PM_{2.5} did not seem to have an impact on these associations observed during the MAPCAH study in Melbourne. The role of fungi in TA events high asthma days has been documented internationally suggesting an association with fungal spores (such as *Alternaria* conidia, *Cladosporium* and *Didymella* species) (Anderson et al. 2001; Pulimood et al. 2007). Similarly, in a study from Canada (Dales et al. 2003), an increase in grass pollen counts could not explain the same day associations with emergency department visits, but an increase in fungal spore counts might have been the underlying mechanism.

Children sensitized to aeroallergens may have been primed by extreme counts of daily grass pollen recorded at the beginning of November 2010 as the cumulative daily grass pollen concentrations generally remained high before the peak period. Furthermore, almost all (>75%) the participants admitted during this period were atopic. The lagged two-day effects of both pollen and fungal spores suggest a priming effect on susceptible populations. Repeated exposure of nasal tissues to a particular allergen may result in mucosal sensitivity (de Weger et al. 2011). Although a few studies^{1, 2} have

considered fungal spores in a limited way, our findings are the first to suggest strong effects of *Alternaria* conidia and *Cladosporium* in children and adolescents associated with the peak periods.

Aeroallergens, their timing, distribution, quantity, and potency are severely impacted by weather conditions. They also impact the distribution and severity of allergic disease (Reid and Gamble 2009). The role of high temperatures and humidity during the HAAD period can not be ruled out certainly given their synergistic properties with outdoor aeroallergen exposure. Both of these weather conditions have been shown to be significantly associated with *Cladosporium* spore counts in a study conducted in Denver, Colorado (Katial et al. 1997). Also, indicated in a review (Reid and Gamble 2009) that although temperature and humidity can be strong predictors of mold concentrations, the effect varies with mold species and geography. Likewise, there are several other examples where regional weather patterns, such as increased temperature have led to enhanced pollen production (D'Amato et al. 2007). Further, it is predicted that pollen seasons might be extended globally due to climate change resulting in an increased risk of more frequent epidemic thunderstorm asthma events in the future (D'Amato et al. 2016). However, in the present study, adding meteorological variables did not significantly alter the relationships observed between aeroallergens and incidence of asthma (Héguy et al. 2008).

In our study, during periods where high asthma days occurred, child admissions were more likely to be male and in a younger age group. Consistent with other studies including our own, we found a higher odds of high asthma periods associated with grass pollen and some fungal spores for boys compared to girls (Shrestha et al. 2018).

This study has several strengths. The strength of the study is that additional data were collected from the admitted patients, including allergen sensitization tests and rhinovirus status. Our selection of a case-crossover design was appropriate for analysing time-variable exposures and the bi-directional selection of control periods allowed individual adjustment for seasonal and long-term trends. Although we are limited by the number of high asthma admissions that occur during grass pollen seasons by the definition of the 4.0 SD which can be overly restrictive, the case-crossover design enabled an increase in sample size as cases act as controls during control periods. This increased the statistical power to detect associations.

Children admitted to hospital for asthma are considered a group with severe asthma, so it is challenging to determine if these children would have been admitted for other reasons even if pollen and *Alternaria* were not to be found associated. The bidirectional design showed the risk was higher on those days. Of course, that does not mean there was zero risk on other days, but it was higher leading up to these days.

In summary, both pollen and fungal spores 2 days prior to a period of high asthma admissions seem to have a priming effect on susceptible children and adolescents that increases the risk of asthma hospital admission. Moreover, same day fungal spores were also associated with increased odds of admission, but grass pollen was not. This lack of association was possibly due to a sudden change in weather conditions resulting in the rupturing of pollen grains and hence went undetected. Studying environmental factors that may increase the risk of these high asthma periods provides better insights to not only predict the peak periods but also to better prepare the health care system with early warning and mitigating the risk for the child. Public health programs need to increase awareness of ambient *Alternaria* and not just pollen during peak pollen seasons to ensure readiness of both populations at risk and its service providers.

Conflicts of interest

The authors declare there are no conflicts of interest.

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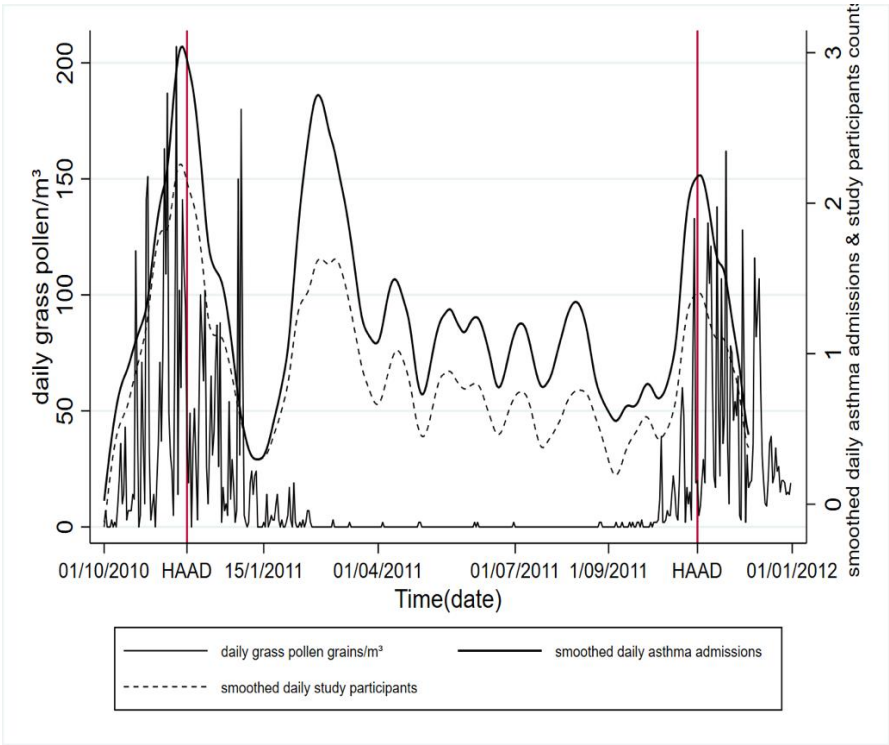
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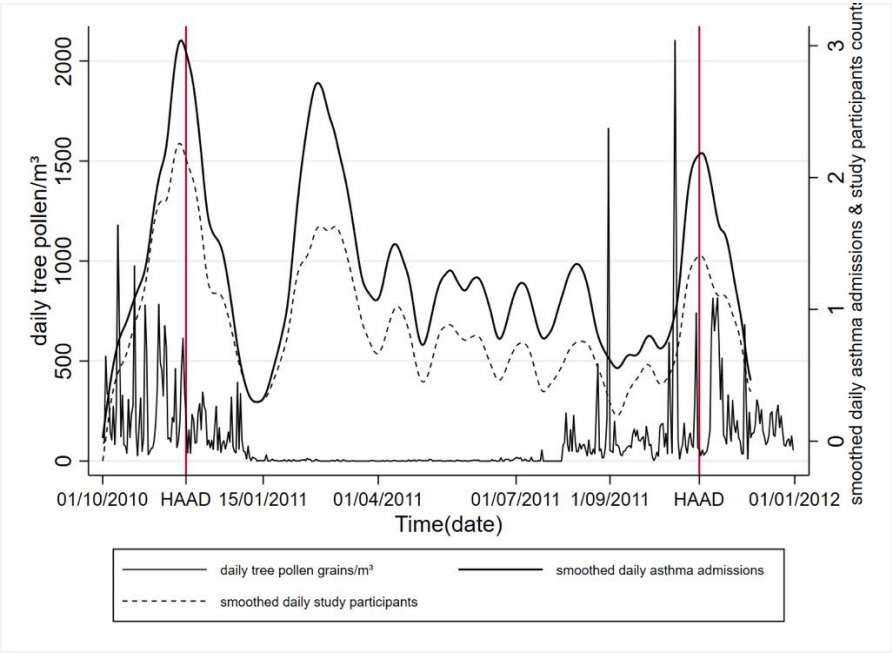
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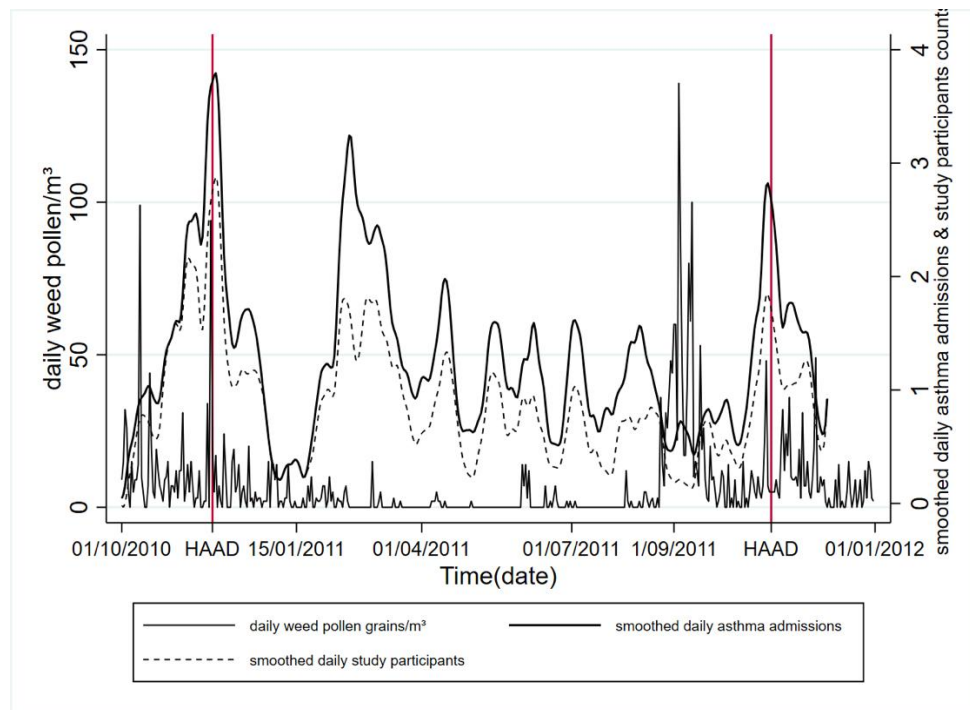
S1 Figure 1. Smoothed daily grass pollen counts and admissions, 2010 & 2011



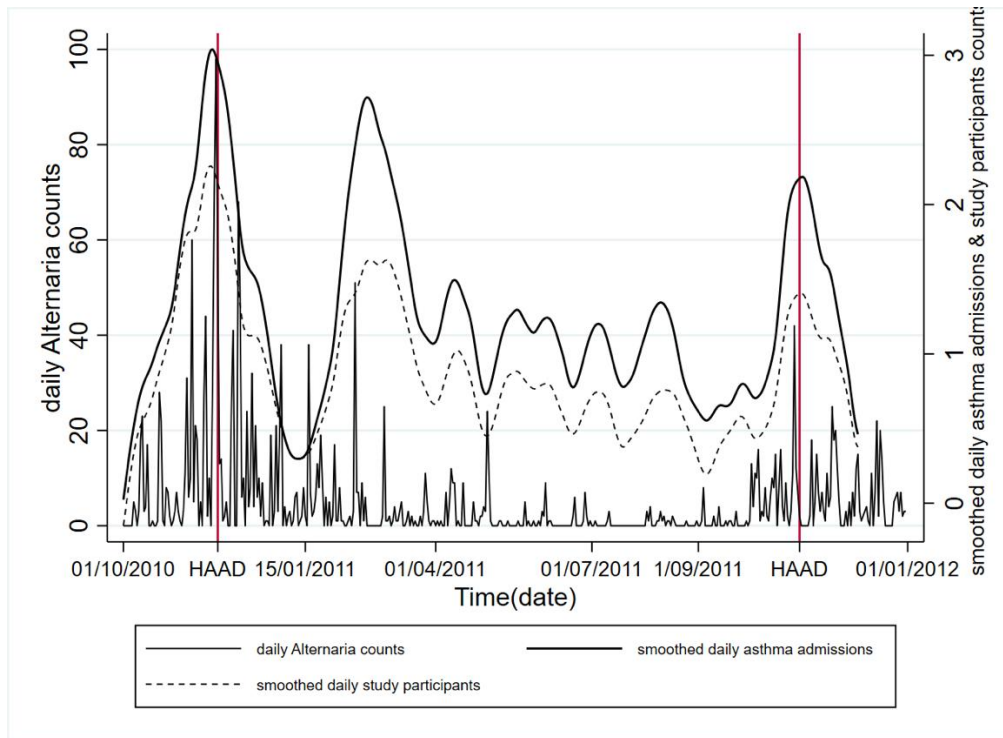
S2 Figure 2: Smoothed daily tree pollen counts and admissions, 2010 & 2011



S3 Figure 3: Smoothed daily weed pollen counts and admissions, 2010 & 2011



S4 Figure 4: Smoothed daily *Alternaria* counts and admissions, 2010 & 2011



S5 Figure 5: Smoothed daily *Cladosporium* counts and admissions, 2010 &2011

