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Grass pollen exposure is associated with higher readmission rates for pediatric asthma

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Abstract

Background: Pediatric asthma hospital readmission is a burden on the individual and costly for Australian hospitals. Grass pollen's role, a known trigger for asthma admissions, is unexamined in readmissions. We examined the association between grass pollen and pediatric asthma readmission.

Methods: The Victorian Admitted Episodes Dataset was used to identify all primary admissions with a principal diagnosis of asthma in children aged 2–18 years between 1997 and 2009. Readmissions were defined as subsequent admissions within 28 days of index admission discharge. Generalized additive models were used to assess associations between readmission, grass pollen season, and daily grass pollen counts, lagged and cumulative. Models were further stratified by sex and age group.

Results: Mean daily readmission was higher during grass pollen season than other times of the year, incidence rate ratio (IRR) 1.44 (95% CI, 1.03, 2.02) and for children aged 2–5 years, IRR 1.99 (1.26, 3.14). Same day grass pollen was nonlinearly associated with daily readmission for the 13–18 age group between 110 and 256 grains/m³, $p < .01$. Lag 2 grass pollen was nonlinearly associated with daily readmissions overall ($p = .03$), boys ($p = .01$), and younger age groups 2–5 ($p = .02$) and 6–12 ($p < .001$).

Conclusions: Grass pollen exposure was associated with higher readmission rates for pediatric asthma. Treatment plans prior to discharge could be implemented to reduce the likelihood of readmission by younger children during the pollen season.

KEYWORDS

adolescent health, asthma, children, environment, pollen, readmissions, season

1 | INTRODUCTION

Asthma is a major public health concern with increases in global prevalence, and asthma related morbidity and mortality among children, documented over the past four decades.¹ Asthma remains

one of the most frequent reasons for hospital admission among children.² An unplanned and potentially preventable admission to the hospital following a discharge from the hospital after an index admission is classified as an avoidable hospital readmission. Globally and in Australia, asthma hospital readmissions attract unbalanced

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allocation of resources and funding from healthcare systems.³ The factors that increase the likelihood of asthma readmission remain poorly understood.

Most studies⁴ of risk factors for repeat admissions have mainly focused on behavioral and lifestyle, asthma characteristics, and family history of asthma or allergic diseases. Indoor environmental factors such as exposure to allergens or pollution and home characteristics have also been associated with readmissions.

Grass pollen,⁵ an outdoor aeroallergen, is a known risk factor for primary asthma admission and leads to inadequate asthma control, indicating the plausibility of an association with asthma readmissions. Lagged and cumulative effects of pollen on child hospital asthma admissions have been assessed by previous studies.^{5,6} The response to environmental factors may be delayed or accumulate over 1–3 days.⁷ This phenomenon represents a “priming” effect.⁸ However, we are not aware of any previous study examining both lagged and cumulative effects of pollen on pediatric asthma readmissions.

Given this major gap, this study aimed to examine the association in Victoria, Australia, between grass pollen and repeat pediatric admissions within 28 days using linked hospital data in Victoria, Australia between 1997 and 2009.

2 | METHODS

2.1 | Study design and population

All asthma readmissions from Victorian private and public hospitals were analyzed using data from the Victorian Admitted Episodes Dataset (VAED) for the period 1st July 1997–30th June 2009, with a total of 4383 days observed. Age, sex, admission, and separation dates at admission were extracted. Only primary admissions with a principal diagnosis of asthma, ICD-9 code 493 up to 1998, and ICD-10 codes (J45 or J46) for children 2–18 years of age were included in the present study. The total sample size consisted of 48,068 admissions. A probabilistic linkage algorithm was used to identify all admissions for a particular child. All children were deidentified. Readmissions for the present study were defined as a subsequent admission within 28 days⁹ of the discharge date of the index admission.

We obtained ethics approval for study from La Trobe University Human Research Ethics Committee and the Department of Health. Individual written consent of parents was not required.

2.2 | Exposure variable

Daily 24-hour average pollen concentrations (grains/m³) were collected using a Burkard volumetric trap located at the Parkville campus of the University of Melbourne as described previously.¹⁰ Sampling was from October to December each year, coinciding with the peak grass pollen season.¹¹ For other months, it was assumed that the daily grass pollen count was zero.¹²

Key Message

Grass pollen increases the likelihood of preventable early childhood asthma readmissions. Younger children with severe or poorly controlled asthma could be referred for preventive therapies before the grass pollen season, to reduce the likelihood of a repeat admission.

2.3 | Other variables

Daily weather data were obtained from The Bureau of Meteorology from nine stations¹³ between 1997 and 2009. The average daily values of all meteorological variables such as maximum and minimum air temperatures (24 h after 9 am [local time] in degrees Celsius) and relative humidity were used. Values of relative humidity (%) for three hourly observations were first averaged for each day. All the averages of each station were averaged to make one overall average.

Hourly data on air pollutants were obtained from the Environment Protection Authority Victoria (EPA)¹⁴ from 13 monitoring sites. The average daily values from all the sites of pollutants, ozone (O₃), and particulate matter up to 10 µm (PM₁₀) were considered. All the averages of each monitoring site were averaged to make one daily average. The daily weather and EPA data were mapped to the corresponding day of hospital admission.

2.4 | Statistical methods

To describe the seasonality of the readmission time series, we decomposed it into its seasonal, time trend, and random components using locally estimated smoothing with an added weighting scheme to make it more robust. The seasonal component was extracted and plotted with a 14-day moving average overlaid. Means and percentiles were estimated for daily asthma readmissions, pollutants, meteorological variables, and grass pollen levels. The outcome variable was daily asthma readmission, a low count time series assumed to follow a Poisson distribution.³ We tested a negative binomial distribution, but it had a poorer fit compared to a Poisson distribution. We investigated the association between daily readmissions and daily pollen counts at lags 0–3, and cumulative lags of 3 and 7 days, and whether association varied by age group or sex. We also aimed to examine the association between daily readmission and pollen season, when in separate models, pollen season was entered as a binary variable in place of daily pollen counts. It is difficult to precisely define when the pollen season starts or finishes. Furthermore, the likely complex impact of climate change on the start and duration of pollen seasons across Australia is unknown, but subject to ongoing study.^{15,16} However, it is well established that peak pollen season generally occurs between October to December in Victoria.^{12,15,16} Therefore, we used peak pollen season for the present study to define pollen season as October to December. We built the statistical

models starting with the unadjusted associations, followed by the adjusted models.

To aid interpretation, pollen variables were transformed to a base 2 log scale where a unit increase represented a doubling of the pollen concentrations on the original scale.¹⁷ As it was likely that cumulative and lagged grass pollen, meteorological, and pollutant variables and time variables did not necessarily have a linear fit with readmission counts, we therefore used semi-parametric Poisson generalized additive models (GAM).¹⁸ The results from the final adjusted models are presented.

As part of model development, we assessed the fit of several models based on lagged grass pollen and 3 (lags 0–3) and 7 (lags 0–7)-day cumulative grass pollen using likelihood ratio tests or the Akaike information criterion as appropriate.¹⁹ Maximum temperature, relative humidity, O₃, and PM₁₀ were considered as potential confounders. Models were further stratified by sex and age. Age was categorized as 2–5 years, 6–12 years, or 13–18 years. The GAMs were fitted and graphed using the mgcv and mgcViz libraries, respectively, in R.²⁰ The analyses were exploratory but based on results from our previous studies of child asthma admissions and readmissions.^{9,21} We knew that for admissions, pollen exposure was important, so we hypothesized a similar association for readmissions. Hence, we started with an *a priori* hypothesis in order to build a parsimonious model that fitted the data best, in order to elucidate any association between ambient pollen exposure and readmission. Consequently, no adjustments were performed for multiple comparisons given these comparisons were *a priori* decided and they are related to the same research question of whether pollen levels are related to readmissions. Data preparation was done with Stata 16.0 (Statacorp, College Station). The level of statistical significance was set at 0.05.

3 | RESULTS

A total of 47,456 children aged 2–18 years, 28,598 (60.2%) males and 18,858 females, were admitted to hospital for asthma between 1997 and 2009. Across the whole study period, 2152 of these admissions (4.53%) were followed by an asthma readmission within 28 days of discharge. Mean (SD) daily readmissions were highest among the 2–5-year age group at 0.26 (0.52) and for boys overall at 0.27 (0.54) (Table S1). During peak pollen season, mean daily readmissions were above the overall mean (Figure 1).

Daily grass pollen concentrations during the pollen season ranged between 0 and 356 grains/m³ (Table 1). Spearman correlations between daily grass pollen counts and environmental factors during the study period are presented in Figure S1.

3.1 | Association between grass pollen season and readmissions

Our model (Table 2) showed that grass pollen season was associated with mean daily readmission rates, which were 1.44 times

higher than outside pollen season (95% CI = 1.03, 2.02). Models stratified by sex showed that the association between mean daily readmission rates and daily pollen concentrations was similar for boys and girls. When we refitted the grass pollen season models stratified by age group, we observed an association between grass pollen season and daily readmission rates in the youngest age group (2–5 years) with incidence rate ratio = 1.99, 95% CI (1.26, 3.14).

3.2 | Association between daily grass pollen concentration and daily readmission rates

Lag 2 daily pollen concentrations and model results showed a significant nonlinear association with all daily readmissions (Figure S3) and across all sex and age strata except for 13–18-year-old children (Table 3). Weak evidence for an association between the mean daily readmission rate and grass pollen at lag 0 only at concentrations above approximately 128 grains/m³ (Figure S2) was observed. For lag 0, there was an effect of grass pollen counts on daily readmission rates overall (Table 3) and the association between daily readmissions and grass pollen concentration was significant for the 13–18-year age group (Figure 2).

Cumulative pollen values over 4 days were significantly associated with daily readmissions only for the 6–12-year age group (Table 3 and Figure S4).

4 | DISCUSSION

Studies⁴ of readmissions differ in temporal windows, with readmissions considered within 2,²² 3,²³ 6 months,²⁴ to a maximum of 10 years.²⁵ Many studies tend to focus on readmission within 12 months.^{26,27} However, this does not allow identification of environmental causes, because 12 months overlaps different seasonal risk factors such as pollen and/or viral infections. Only a few studies have assessed readmissions defined as within 28 days of an index separation,⁹ even though there is evidence that 28 days is a good interval to use to assess whether a subsequent admission is related to the previous one.²⁸ In our study, mean daily asthma readmission rates within 28 days were statistically significantly higher during the grass pollen season in Melbourne (October to December) compared to the rest of the year. Furthermore, daily readmissions were observed to increase 2 days after grass pollen exposure. The impact of lag 2 pollen on readmissions varied by age group with younger children (<13 years) being at greater risk. Older children and adolescents seemed to be impacted more by ambient grass pollen concentrations on the same day of admission.

Similar to hospital admissions,⁵ grass pollen season was associated with readmissions and for younger children. Impact of pollen seasons³ or allergenicity of ragweed²⁹ has been assessed by some other studies; however, they were not directly comparable with our finding. The association between asthma readmissions and daily pollen on lag day 2 seemed to be mainly driven by younger children

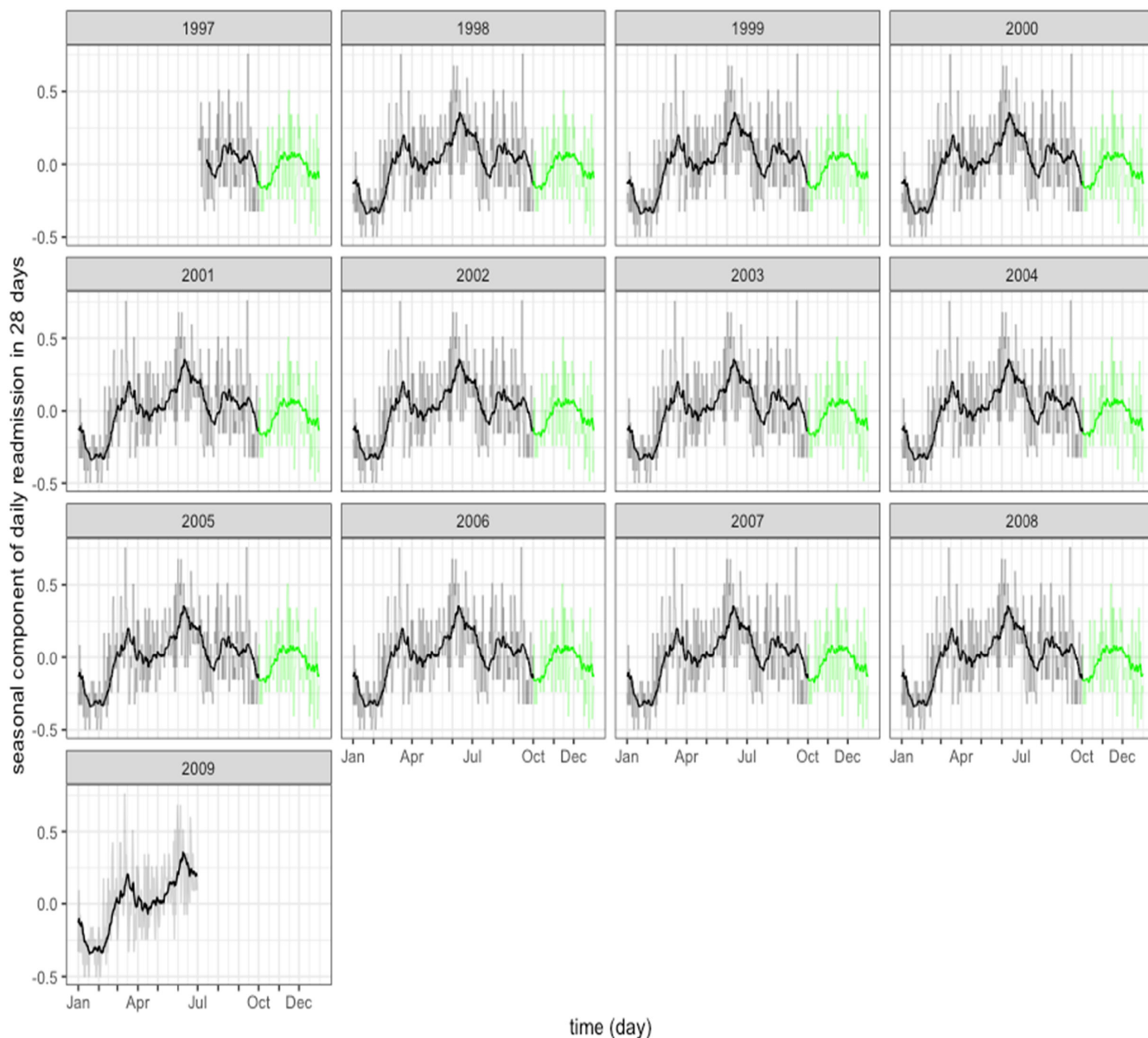


FIGURE 1 Time series decomposition of daily child asthma readmissions with the seasonality component extracted and mean centered* (*O represents the overall mean and therefore positive values indicate greater and negative values indicate lesser, than overall mean daily readmissions) with an overlaid 14 day moving average. The green sections indicate the months of October to December, the definition of peak pollen season.

TABLE 1 Grass pollen and environmental factors, 1997–2009.

	Mean (SD)	Minimum	25%	Median	75%	90%	Maximum
Weather variables							
Maximum temperature (°C)	19.69 (6.09)	7.99	14.92	18.67	23.12	28.48	46.31
Minimum temperature (°C)	11.68 (4.14)	0.30	8.70	11.50	14.40	17.10	26.70
Relative humidity (%)	69.91 (10.91)	21.01	63.5	70.72	77.36	83.23	96.37
Pollutants							
Ozone (ppm)	13.89 (5.99)	0.39	9.59	13.52	17.60	21.62	45.01
PM ₁₀ (µg/m ³)	18.24 (10.26)	3.36	12.53	16.34	21.68	27.85	306.02
Grass pollen (only pollen season (October–December) (grains/m ³))	38.13 (0.14)	0	6	19	48	98	356
Cumulative grass pollen (0–3)	148 (141)	1	46	98	214	353	784
Cumulative grass pollen (0–7)	275 (233)	3	104	207.5	399	606	1225

TABLE 2 Summary of the GAM models showing the incidence rate ratios (95% CI) for mean number of daily readmissions rates, comparing grass pollen season to outside of pollen season.

	Time + day of the year + day of the week + maximum temperature + PM ₁₀ + relative humidity + Ozone	Time + day of the year + day of the week + maximum temperature + PM ₁₀ + relative humidity	Time + day of the year + day of the week + maximum temperature + PM ₁₀	Time + day of the year + day of the week + maximum temperature	Time + day of the year + day of the week + maximum temperature
All	1.44 (1.03, 2.02)*	1.44 (1.03, 2.02)*	1.43 (1.02, 2.00)*	1.43 (1.02, 2.00)*	1.44 (1.03, 2.02)*
Stratified by gender					
Males	1.51 (0.96, 2.38)	1.51 (0.96, 2.38)	1.51 (0.96, 2.38)	1.51 (0.96, 2.38)	1.53 (0.97, 2.40)
Females	1.51 (0.93, 2.46)	1.51 (0.93, 2.44)	1.32 (0.81, 2.14)	1.51 (0.93, 2.46)	1.31 (0.81, 2.13)
Stratified by age group					
2-5 years	2.01 (1.27, 3.17)**	2.01 (1.27, 3.17)**	2.00 (1.27, 3.15)**	2.01 (1.27, 3.15)**	1.99 (1.26, 3.14)**
6-12 years	1.48 (0.78, 2.8)	1.48 (0.78, 2.79)	1.47 (0.77, 2.79)	1.46 (0.77, 2.78)	1.47 (0.78, 2.79)
13-18 years	0.6 (0.29, 1.22)	0.59 (0.29, 1.21)	0.59 (0.29, 1.21)	0.6 (0.29, 1.21)	0.6 (0.29, 1.23)

Note: *p* value, * ≤ 0.05 ; ** ≤ 0.01 , statistically significant.

(<13 years of age). This would be consistent with a "priming" effect of grass pollen on readmissions. Younger children have different respiratory physiology and function compared to older children. Younger children may have better ability to accommodate/tolerate airway compromise and thus, it takes longer for them to present with symptoms following pollen increase compared to older children, who have more bronchial hyperresponsiveness and present with symptoms sooner. Also, the likelihood of readmission could be higher in younger children with a history of allergies or hay fever due to their impaired immune response; however, we did not have individual level data. Cumulative exposure over 3 days was also important in 6-12-year-old children. Lack of adherence to prescribed regular preventer treatment and possibly the presence of more severe asthma in this age group⁶ could be a possible explanation for this effect. Increased susceptibility to environmental triggers due to poorer adherence is likely to result in residual airway inflammation in this age group.

Same day pollen impacted on all children, but more so in older children. The association for all readmissions showed a qualitatively similar association, but the evidence was not as strong. This could have been due to the relative magnitude of the change in mean daily readmission being smaller for all readmissions. A plausible biological pathway that could explain older children/adolescents' reaction to same day pollen vs 2 days later may be due to the greater likelihood of concomitant allergic rhinitis which leads to increased airway hyperresponsiveness (AHR). Once inflammation leads to AHR, it takes a couple of days for symptoms to manifest. Adolescents might also be more likely to have poor asthma control leading to underlying airway inflammation. The 13-18-year age group is more likely to understand triggers and the need to adhere to preventive measures, i.e., medications and/or limiting exposure to a minimum when the levels are extreme. This might be the reason for the observed decline at pollen concentrations higher than the levels associated with an increased rate of readmission (Figure 2).

The impact of grass pollen at lag 2 on mean daily readmission showed a linearly increasing association above about 110 grains/m³ for all readmissions (Figure S3). Therefore, our findings are consistent with the generally accepted definition of extreme pollen days, i.e., >100 grass pollen grains/m³. This is potentially important for asthmatic patients, as well as the medical services that are likely to manage these patients. Further studies of readmissions are needed to confirm or replicate our findings.

Season as a predictor has also been documented,³⁰ with early readmissions (within 2 weeks of discharge) occurring most often during spring. However, these studies were not directly comparable, as our focus was only the grass pollen season which, along with respiratory viruses,³¹ increases the risk of asthma exacerbations. It remains a possibility that child and adolescent asthma are caused by different types of pollen across different geographic locations. Also, climate change impacts are likely to be complex and location dependent. In contrast to the Northern Hemisphere, impacts are not yet clear in Australia due to inconsistent monitoring resulting in insufficient

Pollen values	All	Males	Females	2–5 years	6–12 years	13–18 years
Lag 0	0.07	0.17	0.29	1.00	0.12	<0.01**
Lag 1	0.49	0.42	0.98	0.45	0.37	0.11
Lag 2	<0.01**	0.01*	0.01*	0.02*	<0.001***	0.28
Lag 3	0.18	0.87	0.11	0.75	0.34	0.52
Cumulative (0–3)	0.41	0.18	0.29	0.64	0.05*	0.27
Cumulative (0–7)	1.00	0.41	0.79	0.32	0.12	0.51

Note: Models were adjusted for Time + dow + maximum temperature + PM₁₀ + relative humidity + Ozone. *p* Value, * $\leq .05$; ** $\leq .01$; *** $\leq .001$, statistically significant.

TABLE 3 Summary of the GAMs with pollen counts per cubic metre showing *p* values for the smooth fits.

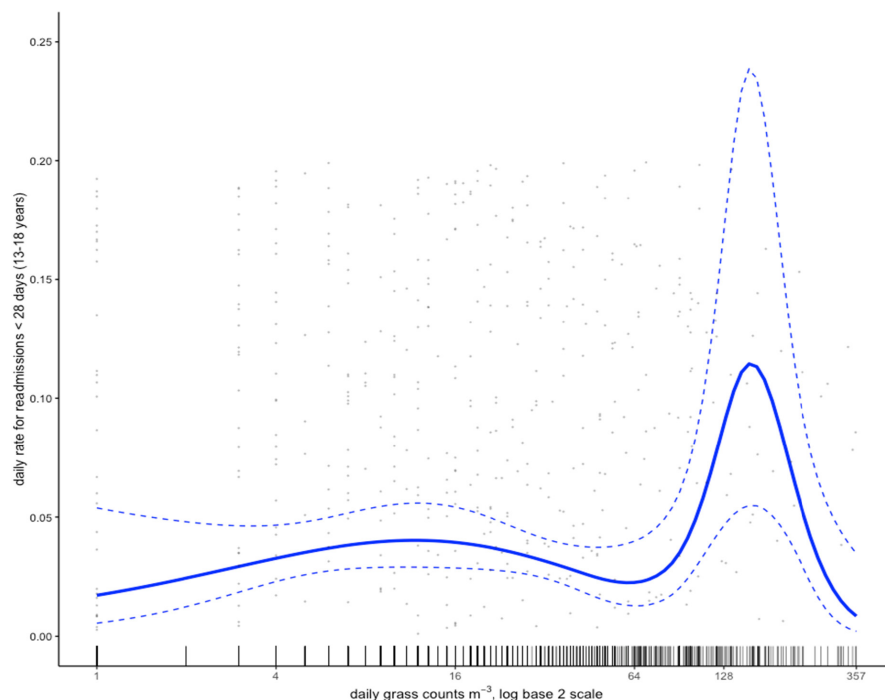


FIGURE 2 Impact of grass pollen at lag0 on readmissions among children 13–18 years old. *p* value = .008 for smooth fit. Blue dotted lines represent the 95% confidence interval.

data.¹⁶ In this study, we are building on our previous work with a more detailed analysis of the association between pollen season and child asthma hospital readmissions. We aim to follow this up with more recent data that would also include recent thunderstorm asthma events and for which we have currently applied for ethical approval.

The possibility that local variations in pollen levels, pollen types, and pollen combinations across areas affecting child and adolescent asthma ED presentations should also be considered in such studies.

A strength of this analysis was the inclusion of data from the VAED, a large comprehensive database including all pediatric asthma admissions from Victorian public and private acute hospitals for 1997–2009. The length of the study period and sample size provided sufficient power to detect meaningful associations with childhood asthma readmissions. To allow for potential nonlinearity in model specification, a generalized additive model was fitted.

However, some limitations should be considered when interpreting the results. During the study period, no grass pollen data were collected outside of peak pollen season, but daily concentrations were likely to then be very low.¹² The average length, dates, and duration of the pollen season for any particular site may often vary

from 1 year to the next. Rainfall, temperature, and other meteorological parameters influence pollen season timing and duration, as well as day to day variations in pollen concentrations. As also will synoptic and larger-scale climate fluctuations such as the El Niño Southern Oscillation.¹⁵ Melbourne usually witnesses its peak grass pollen season between October to December.^{12,15} It may trigger symptoms of hay fever and allergic asthma in susceptible individuals, when there is a sufficient ambient concentration of pollen,³² hence the importance of establishing any increased risk of readmission during this period.

Another limitation is that we did not have data on individual patients' sensitization, viral infections, hay fever, or second-hand smoking, which could be considered as important modifying factors. However, we had a time series of aggregated daily counts and, although important, individual data could not be incorporated. Furthermore, our models imply that all children experienced identical exposures to ambient grass pollen and therefore our analyses may be subject to misclassification bias.⁷ Therefore, this study does not have sufficient evidence to conclude a causal association. Nevertheless, this result, along with other findings

that accounted for these factors,⁷ indicates that the hypothesis of an association between readmission and ambient pollen concentrations is plausible.

Nonetheless, our findings have important implications regarding repeated child asthma admissions and pollen exposure among younger children. There is a need to target interventions for children with severe or under controlled asthma, prior to the pollen season. Communication of interventions at the time of hospital discharge has been shown to be associated with reduction in hospital readmissions and improved treatment adherence and patient satisfaction.³³ This study also highlighted the importance of monitoring daily readmission counts. Therefore, the health system needs to include systematic monitoring of daily counts to understand associated etiological factors. Maintaining the effectiveness of care, whilst transitioning from hospitals to community, along with follow-ups targeting children who are at a higher risk of readmission is also important. Stronger links between the health system and community, possibly through asthma education, could result in the availability of appropriate care for asthma management in the community for the mitigation of environmental triggers and use of asthma controller devices. These measures may prevent repeated hospitalizations and reduce readmissions for asthma in young children.

AUTHOR CONTRIBUTIONS

MB, DV, and BE designed the study, analyzed the data, and wrote the manuscript. All the authors critically revised the manuscript. All authors have read and approved the final manuscript.

CONFLICT OF INTEREST

MJA holds investigator-initiated grants for unrelated research from Pfizer, Boehringer-Ingelheim, Sanofi, and GSK. He has undertaken an unrelated consultancy for and received assistance with conference attendance from Sanofi. He has also received a speaker's fee from GSK. SCD holds investigator-initiated grants for unrelated research from Sanofi and GSK. The other authors have no conflict of interests to declare.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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