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Pollen concentration and asthma exacerbations in Wake County, North Carolina, 2006–2012

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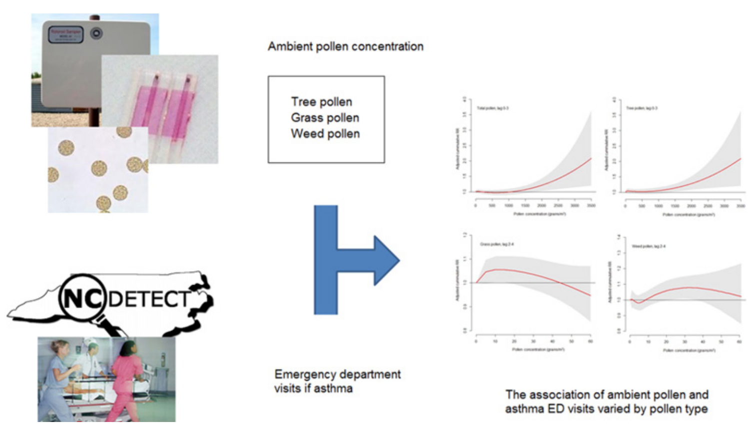
HIGHLIGHTS

- Associations between concentration of pollen (tree, grass, and weed) and asthma were assessed.
- The effect of pollen on asthma was modeled by dlnm to characterize association, delay, and duration.
- The association of pollen and asthma varied by pollen type, both quantitatively and temporally.

GRAPHICAL ABSTRACT



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ABSTRACT

Pollen has been generally linked to an increased risk for asthma exacerbation. However, the delayed effect (lag), the length of effect duration, and the association heterogeneity by pollen types have not been well characterized. Short-term associations between ambient concentration of various pollen types (tree, grass, and weed) and emergency department (ED) visits for asthma were assessed using data in Wake County, North Carolina, during 2006–2012. Distributed lag nonlinear models (DLNM) were used to characterize the associations, while adjusting for air pollutants, meteorological, and temporal factors. A strong association between same-day tree pollen and asthma ED visits was detected. This association lasted four days, with a 4-day cumulative risk ratio (RR) up to 2.10 (3500 grains/m^3 vs. 0 grains/m^3, 95% confidence interval [CI] = 1.21–3.65). The associations of asthma ED visits with weed pollen and grass pollen were weak, suggestively starting from lag 2 and lasting 3 days, with the strongest association a 3-day cumulative RR of 1.08 (32 grains/m^3 vs. 0 grains/m^3, 95% CI = 1.01–1.15) and 1.05 (11 grains/m^3 vs. 0 grains/m^3, 95% CI = 1.00–1.11). Our results indicate that the association of ambient pollen and asthma exacerbation vary by pollen type, both quantitatively and temporally. These findings have important implications for optimizing targeted allergic disease prevention and management, and helping understand the etiology of ambient exposure-induced allergic diseases.

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1. Introduction

Allergic diseases represent a major public health burden worldwide and in the US, with the occurrence rising in recent decades (Arbes et al., 2005; Platts-Mills, 2015). The prevalence of asthma increased from 7.3% in 2001 to 8.4% in 2010 in the US (Akinbami et al., 2012). In North Carolina (NC), a similar increased health burden has been observed (Moorman et al., 2012). In 2011, there were estimated 648,369 (8.8%) adults and 249,454 (10.9%) children affected by asthma in NC (CDC, 2014). Understanding the causes of the increased prevalence of asthma is necessary to guide clinical practice and public health prevention.

Although underlying reasons for the rising asthma occurrence remain unclear, many mechanisms have been proposed (Platts-Mills et al., 2005). Among them, the changes in production, distribution, and timing of ambient pollen have drawn more attention due to climate change in the past decades, and are considered potential contributors to respiratory allergic diseases (Bielory et al., 2012; Shea et al., 2008). The association between ambient pollen and asthma has been studied intensively, with inconsistent results (Altzibar et al., 2015; Darrow et al., 2012; Erbas et al., 2012; Heguy et al., 2008; Ito et al., 2015; Jariwala et al., 2014; Tobias et al., 2003). The discrepant findings have been attributed to differences in study population characteristics, geographic factors (e.g., urban vs rural areas), data sources, measurement of pollen and allergic disease occurrence, and modeling strategies. Different types of pollen have different features (e.g. various allergen structure), and influence asthma through different underlying mechanisms (e.g., molecular mimicry-related mechanism or altered human immune system by non-allergenic adjuvant substances) (Asam et al., 2015; Gilles et al., 2012; Nauta et al., 2008; Radauer and Breiteneder, 2006; Solomon, 2002). Therefore, associations between pollen and asthma exacerbation may vary by pollen type, which consequently contributes to the inconsistent estimates of overall associations.

Previous studies mostly evaluated the intensity-dependent association between ambient pollen and asthma, but few have characterized the timing factors (Altzibar et al., 2015; Jariwala et al., 2014; Makra et al., 2015; O'Leary et al., 2012; Tosca et al., 2014). Among individuals with allergic sensitization, allergic effects induced by ambient pollen may appear from a few hours to several days after being exposed and last for one day up to several weeks. The estimation of the effect magnitude is not enough to describe this complex association. Describing the potential timing effects on the association between pollen and asthma exacerbations has important significance in understanding the underlying mechanisms. These findings can then be used to optimize preventive and clinical management strategies of the allergic disease.

To address these knowledge gaps, we used secondary, population-based ambient pollen data and emergency department (ED) visit data for Wake County (area of 2220 km^2 and population of 900,993 in 2010 based on U.S. Census 2010), NC, 2006–2012, 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) (Bhaskaran et al., 2013), and association heterogeneity by pollen type.

2. Materials and methods

2.1. Pollen data

Ambient pollen concentrations were measured by the Ambient Monitoring Section, Division of Air Quality, North Carolina Department of Environment Quality (NC DEQ) between March 1st and October 31st, 2006–2012. The monitor site was moved once on July 31, 2012 (Supplementary material 1). No significant difference was detected in the pollen concentration during August to October in 2012 and the concentration during the same period in other years. Pollen was sampled 5 days per week (Sunday–Thursday) and analyzed using a Rotorod sampler (Model 40 from Multidata Sampling Technologies). After 24-hour collection, the rods were removed and stained with Calberla solution. The rod was viewed under a microscope at 400× magnification. The stained grains were identified and counted by tree pollen, grass pollen, and weed pollen. The botanical information was only available in 2000 and is summarized in Supplementary material 2. These data were made available to the study through NC DEQ. Pollen concentration was calculated as number of pollen grains per cubic meter of air sampled. The two days (Friday and Saturday) of missing pollen data each week were estimated using linear interpolation. To estimate the reliability of the interpolated data, the concentration from Monday to Thursday was also imputed. The imputed concentration showed reasonable correlation with the corresponding measured pollen levels, with correlation coefficient ranging from 0.62 (weed pollen) to 0.90 (tree pollen).

2.2. ED visit data

Data on all visits to all 8 civilian hospital-affiliated emergency departments (ED) in Wake County, North Carolina, were collected by the North Carolina Disease Event Tracking and Epidemiologic Collection Tool (NC DETECT). For each visit during March–October, from 2006 to 2012, the International Classification of Disease, Ninth Revision, Clinical Modification (ICD-9-CM) codes, patient's age, sex, and visit date were extracted from NC DETECT. NC DETECT data were provided under a Data Use Agreement with NC Division of Public Health. We limited the analysis to ED visits by Wake County residents that received at least one final diagnosis code (in the 11 diagnostic positions) of asthma (ICD-9-CM code 493.xx). For the purpose of these analyses, it was assumed that individuals visiting the ED who had an asthma diagnosis code were atopic and sensitized to at least one of the pollen types examined.

2.3. Meteorological and air pollution data

The data on weather and air pollution factors during the study period were compiled from different resources. Information on daily average temperature was collected from the monitor at the Raleigh/Durham International Airport (Supplementary material 1). Data on precipitation and pollutants, including 24-hour concentrations of PM_{10}, $PM_{2.5}$ and Ozone, were provided by the Ambient Monitoring Section, NC DEQ.

2.4. Statistical analysis

To better characterize the timing of the association between pollen concentration and the selected allergic disease, we used the distributed lag non-linear model (DLNM) (Gasparrini et al., 2010; Gasparrini, 2011). This model is based on the definition of a cross-basis, obtained by the combination of two functions to flexibly model linear or nonlinear exposure-responses and the lag structure of the relationship, respectively (Akinbami et al., 2012). In this study, pollen concentration was modeled with different combinations of bases for the exposure-response relationship and lag-response relationship. The lag period was fixed at 0–7 days, assuming no effect of pollen after a week, as suggested by previous studies (Darrow et al., 2012; Ito et al., 2015; Sheffield et al., 2011). Sensitivity analysis was conducted with a lag period of 0–14 days, but no risk was suggested to be delayed or last longer than one week (data are not shown). The candidate models using linear, piecewise constant, quadratic B-splines and natural cubic splines with various parameters were evaluated. The optimal model was selected based on quasi-Akaike Information Criteria (QAIC) and the analysis of residuals (Bhaskaran et al., 2013; Gasparrini and Armstrong, 2013; Gasparrini, 2014). After evaluating various models with different combination of functions and parameters, the final model was fit through a generalized linear regression assuming an overdispersed Poisson distribution, with the natural cubic spline functions for exposure-response