

Thunderstorms, Pollen, and Severe Asthma in a Midwestern, USA, Urban Environment, 2007–2018

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Background: Previous research has shown an association between individual thunderstorm events in the presence of high pollen, commonly called thunderstorm asthma, and acute severe asthma events, but little work has studied risk over long periods of time, using detailed measurements of storms and pollen.

Methods: We estimated change in the risk of asthma-related emergency room visits related to thunderstorm asthma events in the Minneapolis–St. Paul metropolitan area over the years 2007–2018. We defined thunderstorm asthma events as daily occurrence of two or more lightning strikes during high pollen periods interpolating weather and pollen monitor data and modeling lightning counts. We acquired daily counts of asthma-related emergency department visits from the Minnesota Hospital Association and used a quasi-Poisson time-series regression to estimate overall relative risk of emergency department visits during thunderstorm asthma events.

Results: We observed a 1.047 times higher risk (95% confidence interval = 1.012, 1.083) of asthma-related emergency department visits on the day of thunderstorm asthma event. Our findings are robust to adjustment for temperature, humidity, wind, precipitation, ozone, PM_{2.5}, day of week, and seasonal variation in asthma cases. Occurrence of lightning alone or pollen alone showed no association with the risk of severe asthma. A two-stage analysis combining individual zip code-level results shows similar RR, and we see no evidence of spatial correlation or spatial heterogeneity of effect.

Discussion: Our results support an association between co-occurrence of lightning and pollen and risk of severe asthma events. Our

approach incorporates lightning and pollen data and small-spatial area exposure and outcome counts.

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Asthma is a chronic condition marked by an episodic, inflammatory response of the airways,^{1,2} often exacerbated by environmental irritants such as dust or allergens.^{1,3} In 2017, the CDC reported that asthma affected one of every 13 people in the United States,⁴ and in 2013, the total direct and indirect annual cost of asthma was estimated at \$81.9 billion.⁵ It has been observed that asthma disproportionately impacts the poor, elderly,⁶ and ethnic and racial minorities.⁷ Asthma expresses both allergenic and non-allergenic types.⁸ While the etiology is not fully understood, there are both environmental and individual risk factors, such as tobacco smoke, air pollution,^{9–11} occupational exposures, such as hair care chemicals or fire exposure,¹² as well as correlates including poor diet¹³ and obesity.^{14,15} Genetics plays a role as studies suggest asthma has 35%–90% heritability¹⁶; however, studies with twins demonstrate that genetics does not explain asthma completely.¹⁷

Higher concentrations of pollen and mold spores are associated with an increased risk of allergic-type asthma. Still the etiology is unclear as pollen aeroallergens are too large to penetrate deep into the lungs.¹⁸ One possible pathway has been identified as “thunderstorm asthma,” where thunderstorm conditions fragment and concentrate aeroallergens, which can then cause severe asthma.¹⁹ The characteristics of a thunderstorm asthma event are understood to be (1) prior allergy to plant pollen or mold in individuals; (2) a high environmental allergen load; and (3) a thunderstorm event to concentrate allergens.²⁰ “Thunderstorm asthma” was first reported in 1985,^{21,22} and researchers have a growing understanding of the mechanisms underlying thunderstorm conditions that transform pollen into respirable particles that trigger large-scale asthma exacerbations in populations.^{19,22–26} Laboratory research has demonstrated that hydrolysis can break down large pollen grains from grass,²⁷ trees,²⁸ and weeds²⁹ into allergenic particles small enough to affect lower airways in the presence of water. And allergen challenge tests using pollen cytoplasm fragments or purified proteins are shown to trigger asthma attacks.^{27,30} These laboratory studies support a model where cloud moisture and circulating winds characteristics of thunderstorms cause pollen to be drawn into the atmosphere where hydrolysis releases subpollen particles.

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Health data are collected by the Minnesota Hospital Association and accessed via secure VPN at the Minnesota Department of Health. Weather Data are available through the Iowa Mesonet. Lightning Data are available through the Severe Weather Data Inventory of the National Weather Service. All weather data are publicly available for download or through request. Pollen counts are available through agreement with the Clinical Research Institute of Minneapolis.

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Downdrafts then concentrate subpollen particles at the ground level in magnitudes far exceeding ambient conditions, resulting in severe asthma cases.³¹ This is illustrated in Figure 1.

Early research has focused on severe but rare patterns of single thunderstorms during periods of high pollen.³² On 21 November 2016, a series of thunderstorm events in Melbourne, Australia, was followed by 3365 asthma emergency department (ED) visits (672% over baseline) and 476 hospitalizations (992% over baseline).³³ Harun et al.³⁴ found 23 thunderstorm-related asthma “epidemics” occurring in Australia, Canada, Italy, Iran, Saudi Arabia, and the United Kingdom. Cockcroft et al.³⁵ note that thunderstorm asthma epidemics are characterized by 2–26 times the number of average daily ED visits.

A recent study combining the effects of pollen and thunderstorm conditions in Melbourne concluded that thunderstorm asthma might be more frequent than reported.³⁶

In a study of hospitalizations associated with previous “epidemic” events, Silver et al. found a small increase in warm season hospital admissions following 3 days of pollen with lightning, but did not look at the more frequent ED visits. This work highlights a need for longitudinal time series evaluations that explicitly test the hypothesis that thunderstorm conditions in high pollen levels can elevate severe asthma event risk at levels less than the extreme events identified in prior research. Additionally, these studies were unable to incorporate detailed small area measures of asthma cases and weather exposure to evaluate more localized effects or examine spatial heterogeneity. In this study, we estimated the increased risk of severe asthma due to thunderstorm asthma events in Minneapolis–St.

Paul from 2007 to 2018 whenever thunderstorm asthma conditions occur, not just during the highest levels of pollen or most extreme storms.

METHODS

We conducted a retrospective study of daily asthma-related ED visits in all (128) zip codes entirely or partially within a 20-mile radius of the Minneapolis–St. Paul Airport from 2007 through July 2018. The study period was restricted to the pollen season for each year, April through October. A 20-mile (32.2 km) radius was based on prior research studying pollen measurements across distances.^{37–41} The study area included approximately 2.6 million persons in 2010 and is shown in Figure 2. We defined our primary exposure, thunderstorm asthma events, as the occurrence of a thunderstorm in the presence of high pollen counts (≥ 75 th percentile). We tested the association between our exposure and outcome on the day of the event and with lags up to 6 days.

Outcome

The primary outcome was the daily count of asthma-related ED visits within our study region. We obtained data on asthma-related ED visits from Hospital Uniform Billing Claims Data collected by the Minnesota Hospital Association, accessed under agreement with the Health Economics Program of the Minnesota Department of Health. These data cover 96% of hospital beds in the state⁴² and all EDs for the associated hospitals. These data were obtained from the Minnesota Department of Health for the years 2007–2018.

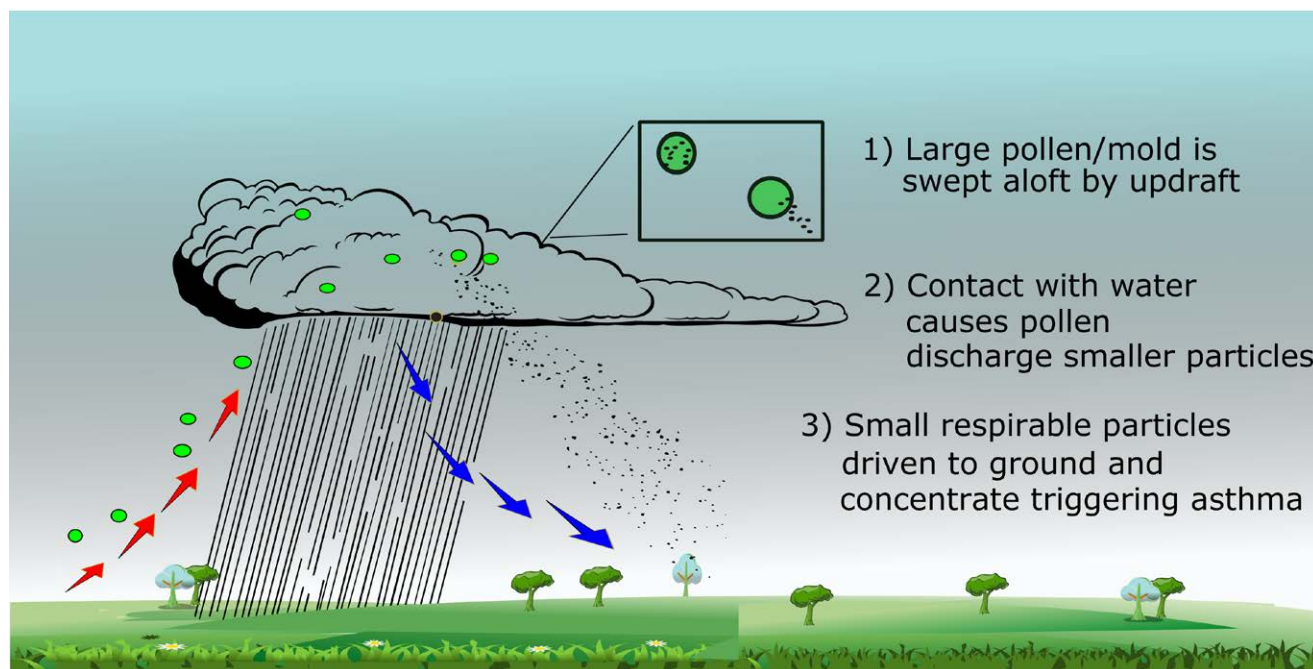


FIGURE 1. Sequence of events resulting in “thunderstorm asthma” as (1) pollen grains are swept aloft by rising warm air, where (2) contact with water causes release of subpollen particles that are (3) driven by cooler, falling air toward the ground, where they are concentrated, triggering severe asthma.

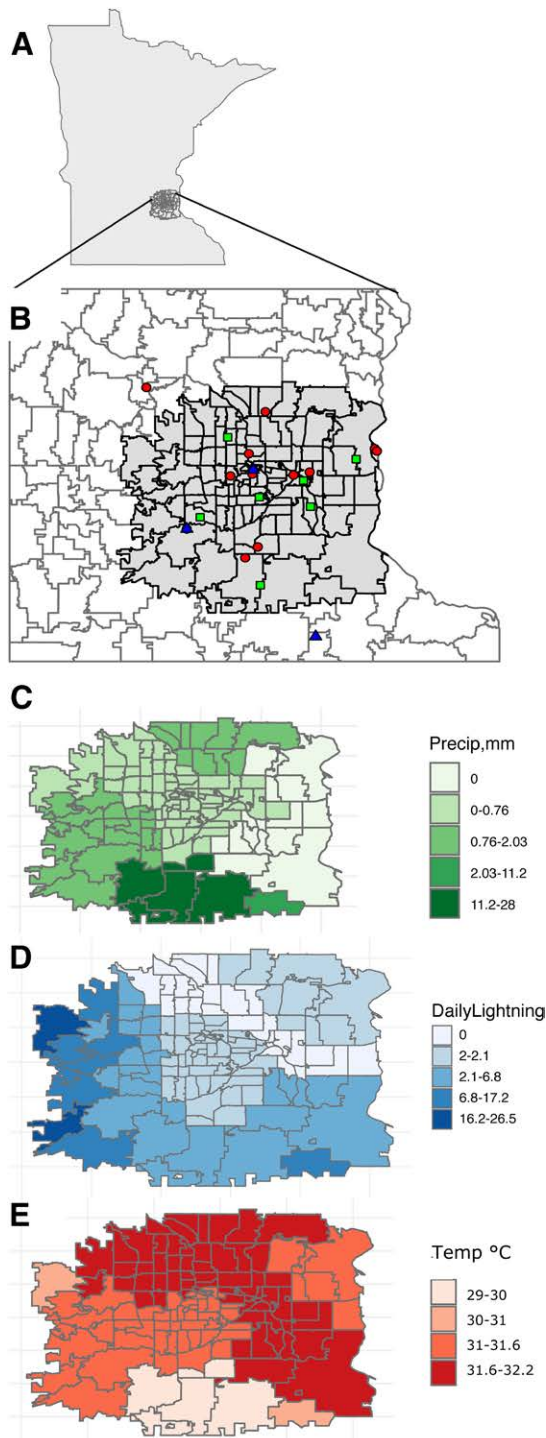


FIGURE 2. Study area and example of daily exposures. A, Map of Minnesota, (B) zip codes partially or completely within 20 miles of Minneapolis–St. Paul airport with weather and pollution sites: green squares show AWOS and ASOS (weather) stations, blue triangles show locations of ozone measurements, and red circles show PM_{2.5} measurement locations. Insets at bottom show interpolated values for (C) precipitation in mm, (D) daily count of lightning, and (E) max temperature in Celsius on 24 August 2012, a randomly selected study day.

Records included international classification of disease codes (ICD), admit date, sex, age, and zip code of residence. Cases were defined as those ED visits with the first or second diagnosis ICD-9-CM codes 493 (pre-10/1/15) and ICD-10 codes J45 in later years. While data are available for asthma for up to 11 ranked secondary diagnoses, we included only persons with asthma as the primary diagnosis or first position secondary diagnosis as a compromise of sensitivity and specificity based on a prior work in asthma ED diagnosis.⁴³

Thunderstorm Asthma Exposure Event

We defined the exposure, thunderstorm asthma event, as two or more daily lightning strikes occurring on days when any measured pollen category (tree, grass, and weed) was high (≥ 75 th percentile of pollen measures for the study period) based on National Allergy Bureau criteria.⁴⁴ Lightning data was abstracted from the National Climate Data Center's Severe Weather Data Inventory,⁴⁵ created using Vaisala National Lightning Detection Network (NLDN) data,⁴⁶ which sums lightning data as a daily count on a 0.1-degree grid. For each day, we created a smoothed surface of lightning strikes using inverse distance weighting of gridded Vaisala NLDN strike totals. Each zip code was assigned a measure that represents the average of the smooth surface falling within each zip code boundary. Our exposure definition of two or more lightning strikes was based on the National Weather Service, which uses two or more strikes within 15 minutes as the definition of a thunderstorm.⁴⁷

Pollen data were collected by the Clinical Research Institute of Minneapolis at a single site in south Minneapolis during the pollen season.⁴⁸ We assumed aeroallergen exposures (pollen grains) were constant for the entire 20-mile radius study area based on Katelaris' results that pollen measurement correlates over distances up to 30 km (18.6 km) with agreement between categories (low, medium, and high) ranging from 83% to 92%.⁴¹ Prior studies involving pollen have similarly applied a single pollen measure to represent a full city exposure³⁷ or used radii of 6,³⁸ 31,³⁹ and 40 miles.⁴⁰

From 1 April 2007 to 9 July 2018 (total of 2,441 days), there were 293 days missing pollen data of 1–2 consecutive days (largely weekends) and 43 periods missing pollen data for at least three consecutive days. For missing pollen of 1–3 consecutive days, we assigned values based on the average of the bounding days. Frenz et al. report that averaged multi-day pollen levels are a good estimate for daily pollen levels⁴⁹ for up to two consecutive missing days. We excluded missing days that are >3 consecutive missing days. We investigated the robustness to this approach by repeating analyses that imputed and included only one or two missing days as well as an analysis that excluded all missing days.

Covariates and Confounding Variables

We considered several covariates as possible confounders of the association between thunderstorms in the presence of high pollen and severe asthma. These include daily weather

(mean high temperature, mean relative humidity, and maximum wind speed),^{50–53} and air pollution (PM_{2.5}, ozone).^{54–58}

We collected daily weather data from Automated Surface Observation Systems or Automated Weather Observation Systems and downloaded from Iowa Mesonet.⁵⁹ We downloaded air pollution data from the Environmental Protection Agency.⁶⁰ Each zip code was assigned a value for the daily maximum temperature, daily maximum wind, daily total precipitation, ozone, and PM_{2.5} based on the assignment to the station or monitor nearest to the zip code centroid. Humidity was interpolated using inverse distance weighting and aggregated to zip code boundaries. The total number of study area ASOS/AWOS weather sites available on each day ranged from 12 to 16, with nine ozone monitors and 17 PM_{2.5} monitors. Figure 2 shows the variation across the zip codes of the study area for precipitation, lightning, and temperature for one sample day (24 August 2012), along with a map of the study area and weather and pollution stations. To account for temporal trends, we included variables for day of week and a natural cubic spline with eight knots per year to allow for seasonal patterns in asthma ED visits. Population data for the offset term were calculated from the IPUMS National Historical Geographic Information System.⁶¹

Statistical Approach

For our first analysis, we tested the association between exposure to thunderstorms in the presence of pollen and change in daily ED visits for severe asthma in the aggregated study area, combining daily zip code totals and holding exposure constant from a central zip code. We fit a quasi-Poisson regression to estimate the risk of ED visit on days with the occurrence of two or more lightning strikes with high or very high pollen based on the National Allergy Bureau standard of the 75th percentile (a thunderstorm asthma event) using the following model:

$$\log[E(y_i)] = B_0 + B_1 \text{Storm}_i + B_2 \text{PM25}_i + B_3 \text{O3}_i + B_4 \text{Tmax}_i + B_5 \text{RELH}_i + B_6 \text{Wind}_i + B_7 \text{Precip}_i + B_8 \text{dow}_i + \text{offset}_y + g(\text{time}) \quad [1]$$

The outcome is daily counts of asthma ED visits, y , on day t . Storm on day t is the primary exposure (thunderstorm asthma event), PM25 is a value for daily mean PM_{2.5} (μg/m³), O3 is the daily ozone maximum (ppb), Tmax is a daily maximum temperature in °C, RELH is the daily maximum relative humidity, Wind is the daily maximum wind, Precip is the daily precipitation total (mm), dow is a categorical term for day of week, and $g(\text{time})$ is a spline term with eight knots to control for long term or seasonal trends in asthma ED visits.⁶² The *offset* term is the annual population of the study area. The variable *time* represents the cubic spline term and is coded from the beginning of the study.

We elected to use a time series approach⁶³ over case-crossover methods, as we would expect slightly greater

precision with a time series approach⁶⁴ and would expect similar estimates.⁶⁵

Sensitivity Analyses

First, we refit our main model using exposure lags of 0–6 days. Next, we tested the crude association adjusted for only day of week and seasonal splines with lags of 0–6 days, and a model with only weather covariates, day of week and seasonal splines (and no pollution terms) for lags of 0–6 days. We explored the sensitivity of our main model to missing pollen data days by (1) excluding any 3-day consecutive missing periods for pollen data and (2) excluding all missing pollen days, run with lags of 0–2 days. We tested our main model for different temporal spline terms with seven and nine knots. We tested for robustness of the results using “anti” exposures of (1) days with two or more lightning strikes, but low pollen (<25th percentile) and (2) where pollen is ≥75th percentile, but fewer than two strikes of lightning occur. We evaluated lags of –6 to +9 day exposure to investigate possible harvesting, or displacement effect,^{66,67} where a vulnerable population would experience severe asthma regardless of exposure is harvested. Harvesting is identified by an extended period of below average risk following the exposure. Negative lags can also test that storm events preceded the ED visits. Additionally, we tested whether results are sensitive to higher counts of lightning by altering our definition of a thunderstorm asthma event to include 3, 4, and 5 lightning strikes per day (plus pollen ≥75th percentile).

To investigate small-scale effects and to examine spatial correlation, we ran our analysis as a two-level model. For this analysis, we evaluated 109 zip codes with a minimum population of 6,000 of our initial 128 zip codes. We estimated our primary outcome model within each zip code, then combined these 109 zip code-specific effect estimates and variances for the association of thunderstorm asthma events and asthma-related ER admissions using a random effects meta analytic approach previously used in the literature.^{68,69} We weighted each zip code-specific effect proportional to the inverse of its variance, and the DerSimonian and Laird approach was used to estimate the random effect term.^{70–72} We refit our main model of exposure to both pollen and thunder using this method, along with sensitivity analyses for “anti-exposures” for only high pollen (with fewer than two daily lightning strikes) and only two or more lightning strikes (in the presence of low pollen). To test spatial correlation, we applied a global Moran’s I using a queen contiguity.

Our primary model assumes that both pollen and thunderstorms are required to create subpollen particles that trigger severe asthma and main effect terms for pollen and asthma are excluded from the model. We additionally tested a model with an interaction of high pollen (≥75th %) and two or more lightning strikes and with both main effects included. We used this model to calculate the rate ratio of being exposed to both pollen and lightning versus exposed to neither. Sensitivity

analyses for these additional models were run with temporal splines using 7, 8, and 9 knots per year.

Health data were deemed exempt by University of Minnesota Institutional Review Board review, but access is restricted to a secure virtual environment via the Minnesota Department of Health. Health Claims Data were processed in SAS (SAS version 9.4).⁷³ Geospatial data cleaning was performed in ARC-GIS Desktop 10.6.1. Regression analyses were conducted in R (version 3.6.0).⁷⁴

RESULTS

Descriptions of thunderstorm and pollen exposure and health outcomes are shown in the Table. The study area is made up of 128 zip codes with a total population of 2.63 million people in 2010. From 2007 to 2018, there were 142,333 seasonal ED visits for asthma, with annual incidence ranging from 30 to 48 per 10,000 population during the warm season of April through October. During the study period, there were 15,328 exposure events across all zip codes, averaging 119.5 exposure events per zip code.

Thunderstorms and Pollen

On the day of thunderstorms (0-day lag) defined by two or more lightning strikes and ≥ 75 th percentile or higher of any pollen type (tree, grass, weed), we found higher risk of asthma-related ED visit on the day of the event [RR = 1.047; 95% confidence interval (CI) = 1.012, 1.083] than on days without a thunderstorm asthma event. We found little evidence of an association with a 1-day lag (RR = 1.006; 95% CI = 0.975, 1.038) or 2-day lag (RR = 0.998; 95% CI = 0.967, 1.030) or at further lags. The estimated association does not change in models adjusted for weather covariates only and unadjusted for air pollution: no lag RR = 1.049; 95% CI = 1.014, 1.085; 1-day lag RR = 1.004; 95% CI = 0.973, 1.037; 2-day lag RR = 0.997; 95% CI = 0.966, 1.029. Crude results, adjusted only for day

of week and seasonal spline are slightly higher with a 0-day lag RR = 1.060 (95% CI = 1.028, 1.093). Regression results are shown in eTable 1; <http://links.lww.com/EDE/B931>, and covariate results described in eFigure 1; <http://links.lww.com/EDE/B931> and eSupplement 1; <http://links.lww.com/EDE/B931>.

As sensitivity analyses, we fit models (1) imputing missing pollen levels for only 1 to 2 days to capture weekends when pollen is not measured and (2) excluding all missing data days. These were performed for lags of 0, 1, and 2 days. When imputing up to 2 missing days of exposure, we observed similar results as the main model at day 0 (RR = 1.047; 95% CI = 1.012, 1.083), with no evidence of association beyond the day of the event. When all missing days were excluded, we also estimated a similar thunderstorm asthma RR as in the main analysis for no lag (RR = 1.049; 95% CI = 1.013, 1.088) with no evidence of a measurable association beyond the day of event.

Estimated associations for all models (crude, adjusted for only weather-related covariates, and fully adjusted for all covariates) with 0–6 day lags, along with tests that excluded missing days are shown in Figure 3. A sensitivity analysis for exposure definition where we define a thunderstorm asthma event as having three or more lightning strikes per day with greater than 75th percentile of pollen exposure showed a slightly reduced associations compared to two lightning strikes with 0-day lag (RR = 1.040; 95% CI = 0.997, 1.083) and 1-day lag (RR = 1.004; 95% CI = 0.966, 1.043), with effects reduced further at four or more strikes as the event frequency decreases, with a 0-day lag RR 1.023 (95% CI = 0.978, 1.070) and 1-day lag (RR = 0.996; 95% CI = 0.954, 1.040).

The models that used a two-stage approach to account for spatial correlation were similar to our main results at a 0-day lag (RR = 1.043; 95% CI = 1.014, 1.072) and slightly

TABLE. Summary of Thunderstorm and High Pollen Exposure Events and Asthma ED Cases Across 128 Zip Codes From April 2007 to July 2018

Year	Total Estimated Population	Person Exposure Days ($\times 10,000$)	Total Counts of Exposure Events	Average Exposure	Total Asthma ED Cases	Asthma ED Cases/10,000 Population
				Events/Zip (SD)		
2007	2,545,068	2,370	1,192	9.31 (1.34)	13,569	48.6
2008	2,571,806	2,132	1,061	8.29 (1.72)	12,970	46.4
2009	2,598,367	2,401	1,183	9.24 (1.42)	11,781	42.1
2010	2,625,281	3,224	1,572	12.30 (2.51)	12,265	43.8
2011	2,652,019	3,102	1,497	11.70 (2.31)	11,856	42.4
2012	2,677,558	1,088	520	4.06 (1.22)	13,387	47.9
2013	2,705,494	1,524	721	5.63 (1.52)	12,722	45.5
2014	2,732,232	3,588	1,681	13.10 (1.65)	12,109	43.3
2015	2,762,610	3,358	1,556	12.20 (1.74)	11,308	40.4
2016	2,785,707	4,203	1,931	15.10 (1.41)	10,224	36.4
2017	2,810,146	1,471	670	5.23 (1.73)	11,653	41.6
2018	2,839,182	3,868	1,744	13.60 (1.69)	8,489	30.2
Total		32,329	15,328		142,333	

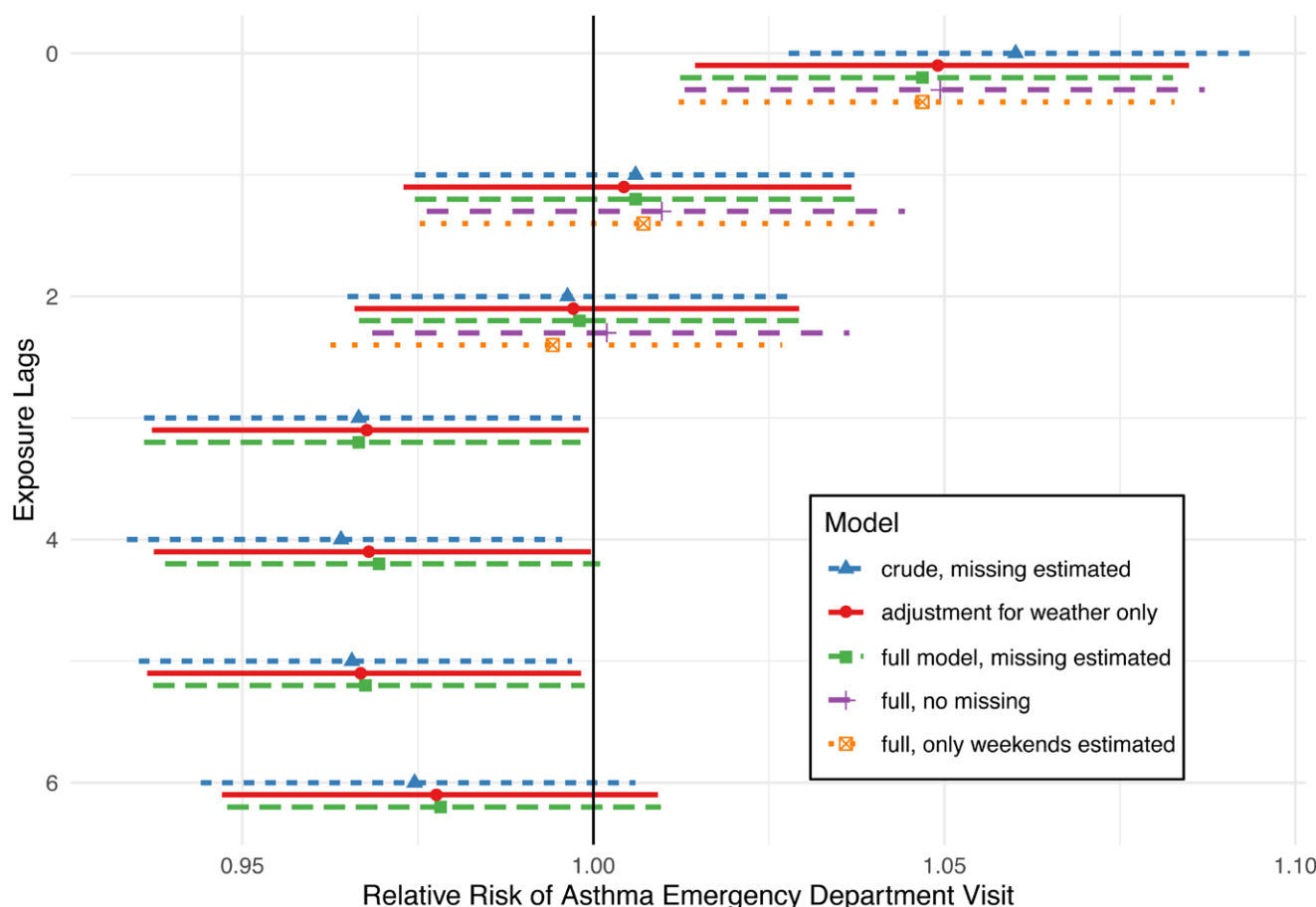


FIGURE 3. Relative risk of association asthma-related emergency department visits during thunderstorms in presence of high pollen lagged up to 6 days. Blue triangle: Crude model plus day of week and cubic splines for seasonal asthma admissions, up to 3 consecutive missing days estimated. Red circle: Adjusted for weather covariates, up to 3 missing days estimated. Green square: Adjusted for all covariates, and up to three days missing estimated. Purple dash: Adjusted for all covariates, with all missing data excluded. Orange hollow square: Adjusted for all variables, with up to 2 consecutive missing days estimated.

higher at a 1-day lag ($RR = 1.031$; 95% $CI = 1.004, 1.059$). We found little evidence of spatial autocorrelation at an $\alpha = 0.05$ (Moran's $-I = -0.06$; P value 0.40), and no evidence of heterogeneity of the effect in the two-stage approach at 0-day lag, (heterogeneity $\chi^2 = 0.466$, $I^2 = 0.0\%$), or the 1-day lag (heterogeneity $\chi^2 = 0.534$ and $I^2 = 0.0\%$). In a model with main effects and an interaction, we find that the risk of severe asthma when exposed to both lightning and pollen vs neither exposure is 1.050 times higher on storm days (95% $CI = 1.013, 1.089$), with no evidence of association at a 1-day lag ($RR = 1.017$; 95% $CI = 0.983, 1.053$). Tabular results for the main model, two-stage model, and interaction model with doubly exposed vs. no exposure are shown in eTable 2; <http://links.lww.com/EDE/B931> for 0-day lag with models with 7, 8, and 9 knots per spline.

Antiexposures: Lightning Alone, Pollen Alone, Negative Lag

Exposure to two lightning strikes in the presence of low pollen (<25th percentile) showed no evidence of association

with the risk of asthma-related ED visit with a 0-day lag ($RR = 0.986$; 95% $CI = 0.937, 1.040$) or 1-day lag ($RR = 1.00$; 95% $CI = 0.950, 1.053$). Exposure to high pollen ≥ 75 th percentile in the absence of two or more lightning strikes showed slight evidence of association with risk of ED visits with a 0-day lag ($RR = 0.985$, 95% $CI = 0.967, 1.002$) and no evidence with a 1-day lag ($RR = 1.008$; 95% $CI = 0.990, 1.026$). Exploration of negative lags shows no evidence of increased risk of asthma-related ED visit before lightning and pollen occurrence for -1 -day lag ($RR = 0.977$; 95% $CI = 0.947, 1.009$) and or -2 -day lag ($RR = 0.959$; 95% $CI = 0.928, 0.990$). All lags -6 to $+9$ are shown in eFigure 2; <http://links.lww.com/EDE/B931>.

DISCUSSION

We found evidence of a positive association between thunderstorms on days with elevated pollen and increased risk of asthma-related ED visit. This result was robust to different model choices, and we find no evidence of spatial correlation or heterogeneity in a two-stage model using zip code-level

exposures and ED counts. As thunderstorm asthma is a relatively understudied phenomenon, our finding that neither pollen nor lightning alone showed evidence of association with asthma ED visits supports the hypothesis that it is a unique environmental and health phenomenon. We found no indication of asthma events preceding storms due to other weather conditions as previously hypothesized⁷⁵ and no evidence of notable harvesting. These results are consistent with the hypothesis that thunderstorm-triggered asthma is a transient event associated with a joint co-occurrence of thunderstorms and high pollen exposure. Furthermore, our study reveals the potential long-term nature of thunderstorm asthma health risks, as opposed to single extreme occurrences, which have not been documented in the United States.^{34,76}

Our exposure definitions (two or more daily strikes of lightning, National Allergy Bureau categories of “high” or “very high” pollen) are replicable across other regions where pollen data might be obtained from any of the other individual National Allergy Bureau sites. Fewer than two lightning strikes are rejected as a definition due to the possibility of false readings and in accordance with the National Weather Service definition that two lightning strikes in 15 minutes is the definition of a thunderstorm. And we selected high and very high pollen exposure because the prior history of this phenomenon has been restricted to severe events with very unusually high levels of aeroallergens; our use of 75th percentile of pollen as the cutoff lowers the threshold to broaden the study to a less extreme event.

The rarity and transient nature of these events have dictated the design and variable definitions seen in prior studies. In a literature review, Dabrera et al.⁷⁷ note that of the 35 included studies on thunderstorm asthma, there are various exposure definitions and outcome measures. Many studies are limited to short time windows or single events, representing large catchment areas, or are case series. Most prior studies considered only pollen or storm alone, and many studies used a single weather station for exposure assignment. Grundstein et al.⁷⁸ conducted a longitudinal evaluation of thunderstorms and ED visits and found 1.035 times higher asthma risk of asthma ED visit on the days following thunderstorms in Atlanta, GA. Villeneuve et al. observed 1.35 times higher odds of severe asthma in children exposed to thunderstorm compared to those not exposed to storms in Ottawa, CA.³⁹ Similarly, longitudinal explorations of pollen alone have been inconclusive as a meta-analysis of pollen exposure and allergy or asthma symptoms by Kitinoja et al.⁷⁹ found no evidence of association between pollen and forced expiratory volume (FEV), and only weak associations among studies considering pollen and lower respiratory symptoms. There has been some work evaluating mold in the thunderstorm asthma model but results have been mixed,^{37,80} and made more complex by the multiple biologic paths by which mold is associated with asthma response.⁸¹ There are few studies that look at the combined effects of aeroallergens with thunderstorms, and results

are mixed. Newson et al.⁸² found that the risk of severe asthma in adults is higher in storms with pollen compared to storms without pollen (RR = 1.47; 95% CI = 1.32, 1.64). However, a case-control study by Pulimood et al.⁸³ found reduced risk of ED visit with exposure to grass pollen in thunderstorms, with a 0.87 RR for each 100 grains per cubic meter increase in grass pollen (95% CI = 0.75, 0.99).

While the magnitude of our estimated association is moderate, and no epidemic events of the sort seen in Australia have, as yet, occurred in the United States, current climate models suggest patterns of increasing variability and possible increased severity of storms,⁸⁴ and increased pollen loads,⁸⁵ conditions that might result in an increasing incidence of thunderstorm-pollen asthma in the United States. This phenomenon should be studied further, as extreme pollen events of the sort that have occurred multiple times in Australia are a concern. This study shows higher risk of ED use for asthma, and further research could quantify concomitantly higher use of urgent care treatment and pharmacies for rescue inhalers—impacts that would further describe the full scope of harms and financial costs of the phenomenon. Additionally, these findings provide a practical, large-scale test of the biologic theory and further our understanding of the science of aerobiology. Finally, the work done here may help patients and clinicians better prepare to avoid severe asthma events.

This article has several limitations. This study does not include information about mold, which has been posited as another potential aeroallergen that can be involved in the thunderstorm asthma model.³⁷ Pollen collection is restricted to a single site, with incomplete collection (e.g., weekends). However, the radius of our project is comparable to other studies of thunderstorm asthma,^{37–41} and prior research validating pollen by Frenz and Boire⁴⁹ along with our robustness checks, suggest that the missing data does not impact our results. ED visits for asthma are a very severe outcome, and our study does not capture less severe outcomes such as urgent care usage or an increase in prescriptions of rescue inhalers. There can still be some misclassification of asthma, even among ED visits, as it could be miscoded as another respiratory illness. While our main model might have exposure misclassification because of the size of the study area, we have tried to address this by assigning exposure based on an average of multiple sites. We further address exposure misclassification in our two-stage model that uses zip code specific exposures and health outcomes to improve precision. Regardless, exposure misclassification is unlikely to be related to asthma diagnoses so any misclassification is expected to be nondifferential and would, in expectation, lead to a bias toward the null.^{86,87} Our study was limited to a single metropolitan area and these results should be replicated in a larger geographic area, but we think that the single urban environment has a population sufficient to explore this relatively rare exposure. Future work will address a larger geographic area, measuring the effect statewide holding

pollen constant, and further analyses will investigate age and sex-based differences in the association, which may identify vulnerable populations. Additionally, future work in a larger geographic area would allow further exploration of the exposure metrics, such as continuous exposure for lightning and pollen to examine the change in outcome with varying levels of exposure.

CONCLUSIONS

This study was to our knowledge the first of its kind in the United States, combining small area environmental exposures and individual patient data information in a multi-year time series to test the theory that severe asthma is associated with pollen rupturing in the presence of thunderstorm conditions. The study revealed patterns consistent with a short transient event as positive associations are seen on day of storm with an expected return to the null beyond that (lag 1 and beyond). Further support for the hypothesis was provided by tests of the counterfactual ‘anti’ exposures, along with additional models that support the central finding. These findings are robust to adjustment for potential environmental confounders, day of week, and cubic splines for seasonality of outcome.

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