Environment International 213 (2026) 110330

Contents lists available at ScienceDirect

Environment International

journal homepage: www.elsevier.com/locate/envint

Full length article

Synergistic impacts of heat, pollen, and air pollution on allergic rhinitis and asthma under climate change: A 20-year time-series study

Endale Alemayehu Ali [a,*], Raf Aerts [b,e,f], Bert Vaes [a], Charlotte Scheerens [a,c], Simon Gabriël Beerten [a], Nicolas Bruffaerts [d], Elisa Duarte [g], Gijs Van Pottelbergh [a]

[a] *Department of Public Health and Primary Care, KU Leuven, Kapucijnenvoer 33, Leuven, Flanders 3000, Belgium*
[b] *Division Ecology, Evolution and Biodiversity Conservation, KU Leuven, Leuven, Belgium*
[c] *Department of Public Health and Primary Care, Ghent University, 9000 Ghent, Belgium*
[d] *Mycology and Aerobiology, Sciensano, Brussels, Belgium*
[e] *Leuven Plant Institute, KU Leuven, Belgium*
[f] *Leuven One Health Institute, KU Leuven, Belgium*
[g] *I-BioStat, Data Science Institute, Hasselt University, Campus Diepenbeek, Diepenbeek, Belgium*

ARTICLE INFO

Keywords:
Environmental exposure
Respiratory diseases
Allergic rhinitis
Asthma
Multi-exposures

ABSTRACT

Background: Climate changes are increasing the frequency of concurrent extremes in temperature, air pollution, and aeroallergens, yet evidence on their joint and synergistic health impacts remains limited. We aimed to quantify the independent, joint, and interactive short-term effects of temperature, air pollutants, and airborne pollen on allergic rhinitis and asthma using long-term general practitioner (GP) data. Methods: We conducted a population-based time-series study using 20 years of GP data. Daily maximum temperature, $PM_{2.5}$, ozone, and pollen concentrations were linked to allergic rhinitis and asthma outcomes. We estimated cumulative relative risks (RR) over lag 0–14 days using distributed lag non-linear models, comparing high (95th percentile) versus median exposure levels. We evaluated effect modification through stratified analyses and quantified additive interaction for joint exposures at extreme levels (90th and 95th percentile) using relative excess risk due to interaction (RERI) and attributable proportion (AP). Findings: Pollen exposure was strongly associated with allergic rhinitis (RR=2.54, 95% CI: 2.40–2.69) and with asthma (RR=1.49, 95% CI: 1.38–1.61). In joint-effects analyses, co-exposure to extreme heat and high pollen concentrations was associated with an increased risk of allergic rhinitis (RR= 2.07, 95% CI: 1.77–2.41), with clear evidence of synergistic interaction on the additive scale (RERI=0.48, 95% CI: 0.32–0.64, AP=0.23, 95% CI: 0.17–0.30). Similarly, co-exposure to high pollen and ozone was associated with elevated allergic rhinitis risk (RR = 2.03, 95% CI: 1.76–2.34), with positive additive interaction (RERI = 0.40, 95% CI: 0.25–0.54; AP = 0.20, 95% CI: 0.13–0.26). The same exposure combinations, heat–pollen and pollen–ozone, also exhibited positive synergistic interactions for asthma. Conclusion: Our findings identify pollen as a central driver of climate-sensitive allergic morbidity, with heat and ozone acting as key amplifiers through synergistic interactions. Our findings highlight the need for integrated early-warning systems, and risk assessments that account for joint environmental exposures.

1. Introduction

Climate change has become a major threat to global public health, primarily through environmental health risk factors including extreme temperatures, air pollution and aeroallergens (Anenberg et al., 2020; eClinicalMedicine, 2025; Haines et al., 2006; Pinho-Gomes et al., 2023; van Daalen et al., 2024)· Exposure to these factors has been shown to adversely affect physiological systems, and contribute to the exacerbation of cardiovascular and respiratory diseases (Anenberg et al., 2020). Beyond these effects, climate change also affects the source and dynamics of airborne allergens, including pollen, which significantly contribute to allergic respiratory conditions such as allergic asthma and allergic rhinitis (Beggs et al., 2023; Melén et al., 2022). It has already been known that allergic rhinitis (AR) and asthma are serious health concerns, with widespread prevalence in developed countries (Bousquet et al., 2020a, 2020b; Paoletti et al., 2025). For example, approximately

---

* Corresponding author.
E-mail address: endalealemayehu.ali@kuleuven.be (E.A. Ali).

https://doi.org/10.1016/j.envint.2026.110330
Received 19 March 2026; Received in revised form 23 April 2026; Accepted 26 May 2026

400 million people are affected by allergic rhinitis across the globe, with prevalence estimates ranging from about 10% to 30% in adults, varying across and within countries (Pawankar et al., 2013). Asthma affects at least 30 million children and young adults across Europe (Komlósi et al., 2022).

Epidemiological evidence showed that climate-related environmental exposures are independent significant risk factors for allergic respiratory diseases such as asthma and allergic rhinitis. Exposure to extreme heat and high ambient temperatures has been shown to exacerbate asthma, likely through increased airway resistance and inflammation (Chou et al., 2025). According to a study using global datasets, in 2019, an estimated 86% of urban residents worldwide were exposed to annual average fine particulate matter ($PM_{2.5}$) concentrations above the world health organization (WHO) 2005 guideline value of 10 μg/m^3 (Southerland et al., 2022). A large cohort study in China also found that exposure to $PM_{2.5}$ is strongly associated with increased risk of both allergic rhinitis (OR=1.18; 95% CI: 1.11–1.26) and asthma (OR = 1.79; 95% CI: 1.41–2.26) (Feng et al., 2023). A recent systematic review and meta–analysis of 80 studies involving over 12 million participants found that the prevalence of allergic rhinitis and asthma attributable to air pollution exposure was approximately 16 % and 11 %, respectively; among individual pollutants, ground–level ozone (O_3) was associated with an elevated risk of allergic rhinitis (OR = 1.058, 95% CI: 1.020–1.095) and non-significant association with asthma risk (OR = 1.032, 95% CI: 0.892–1.171) in pooled analyses (Zhang et al., 2025). The findings suggest that air pollutants may contribute to respiratory symptoms through irritant effects and by enhancing responses to allergens, rather than directly causing allergic rhinitis. Another meta-analysis on the short-term effects of pollen from multiple allergenic species showed that a 10 grains/m^3 increase in pollen exposure was associated with a 2% increase (effect estimate (EE) = 1.02; 95% CI: 1.01–1.03) in the risk of any allergic or asthmatic symptom (Kitinoja et al., 2020a).

Despite the predominance of single-exposure analysis in epidemiological studies, real-world environmental conditions are largely characterized by the simultaneous occurrence of multiple exposures. These co-occurring environmental stressors may interact which may amplify the risk and severity of allergic respiratory diseases. Existing evidence indicates that rising air temperatures and climate patterns are associated with earlier and longer allergenic pollen seasons, higher ambient pollen concentrations, and increased air pollutants, which can trigger the onset of rhinitis or exacerbate its symptoms (Luschkova et al., 2022; Niu et al., 2025; Schreurs et al., 2022; Zhaobin et al., 2024; Ziska, 2021). A systematic review of 56 studies investigated interactions between air pollution, heat, and pollen and found that there is only low quality and limited evidence for their synergistic effects (Anenberg et al., 2020). A study in northern and central Europe further exhibited that the risk of uncontrolled allergic rhinitis is higher during grass pollen season when air pollution level is also high (Bédard et al., 2020).

Though the joint health effects of heat, air pollution, and aeroallergen exposures remain underexplored in epidemiological studies, a biological mechanism supports their interaction in driving allergic respiratory diseases. Studies suggested that environmental heat exposure may have adverse effects on asthma development through multiple biological mechanisms, including bronchial epithelial remodeling and heat-induced changes in the environmental distribution of allergens (Çelebi Sözener et al., 2023a; D'Amato and Cecchi, 2008). Exposure to pollen allergens may induce the release of immunomodulatory and pro-inflammatory mediators, and exacerbates respiratory allergy and asthma (Cecchi et al., 2018; D'Amato and D'Amato, 2023). Air pollutants including particulate matter and ozone can increase pollen allergenicity, enhance airway permeability, and promote the release or fragmentation of pollen into smaller allergen-carrying particles that can reach the deeper respiratory tract, thereby exacerbating allergic inflammation (Ziska, 2021). Moreover, extreme weather conditions whose frequency has been increased by climate change, like lightning storms during periods of high pollen concentration, can break down pollen into fine particles which becomes small enough to enter the deeper parts of the airways and cause sudden allergic rhinitis and asthma attacks, a phenomenon known as *thunderstorm asthma* (Thien et al., 2018).

Considering the growing evidence on plausible biological mechanisms, the limited epidemiological studies, and the geographic co-occurrence of multiple environmental exposures across Europe, there remains a critical knowledge gap regarding their potential joint and synergistic effects on allergic respiratory diseases. This gap is especially relevant in Belgium, a densely populated country with substantial urbanization and traffic-related emissions, leading to frequent co-exposure to multiple environmental stressors. Our study therefore aims to investigate the joint and synergistic effects of ambient heat, air pollution ($PM_{2.5}$ and ozone), and airborne grass pollen concentrations on allergic rhinitis and asthma. We focused on grass pollen as its season in Belgium overlaps with the timing of potential heat episodes, in contrast to the Betulaceae pollen season (sensu latu: pollen of hazel, alder and birch), which occurs in winter and spring. Dynamic exposure data is utilized to monitor short-term, lagged, and nonlinear reactions, especially during overlapping extreme exposure conditions, in addition to two decades of general practitioner (GP) data that, while remaining underexplored within environmental epidemiology, captures clinically relevant events for AR and asthma morbidity.

2. Methods

2.1. Data source and study design

We employed a time-series design, utilizing existing routinely collected GP data in Flanders, the Dutch-speaking northern region of Belgium, over a period of two decades (2005–2024). The analysis was restricted to Belgium's annual warm season (May 1st–September 30th), to define when the levels of heat, air pollution and concentration of grass pollen are high, which is most relevant for allergic respiratory outcomes.

Health outcome data were obtained from Intego, a general practice–based morbidity registry managed by the Academic Center for General Practice at KU Leuven. By the end of 2024, Intego database included data 180 general practices, of which 135 were actively contributing data. A total of 973,444 unique patients registered in the acceptable cohort (patients with at least two registered encounters and with unambiguous sex and birth date), and 512,093 active patients (non-deceased individuals with at least one recorded encounter within the preceding two years). The database contains over 18 million recorded diagnoses, 44.7 million prescriptions, and 224 million laboratory test results. Details on the data collecting procedures, its structure, data quality, and validation procedures of the Intego registry have been described elsewhere (Zayed et al., 2025).

Environmental exposure data were obtained from multiple authoritative sources. Daily meteorological variables, including minimum temperature (Tmin), maximum temperature (Tmax), and relative humidity (RH), were measured at Uccle weather station (the Belgian meteorological reference station) and provided by the Royal Meteorological Institute (RMI) of Belgium(RMI, 2024). Air pollution data, including daily maximum 8-hour average ozone (O_3) concentrations and daily mean particulate matter with aerodynamic diameter $\leq$2.5 μm ($PM_{2.5}$), were obtained from the Interregional Environment Agency (IRCEL–CELINE) and measured at the Uccle monitoring station(IRCEL-CELINE, 2024). Mean daily airborne grass pollen concentration data measured at Brussels station were obtained from the Belgian aerobiological surveillance network (AirAllergy, managed by the One Health institute Sciensano);(Sciensano, 2026) all pollen concentrations in this study refer to grass pollen (Poaceae family) unless otherwise specified.

Outcome selection

We identified patients with allergic rhinitis (AR) or asthma using both diagnostic and prescription records from general practice.

Diagnoses were coded using the International Classification of Primary Care, second edition (ICPC-2), which is specifically designed for use in primary care. We defined acute AR as either a diagnosis of allergic rhinitis (ICPC-2 code R97) or a prescription (ATC codes R01AC (Anti-allergic agents, excluding corticosteroids), R01AD (Corticosteroids, nasal), or R06A (Antihistamines, systemic use)), and asthma as either a diagnosis (ICPC-2 code R96) or a prescription (ATC codes R03A (Adrenergics, inhalants), R03B (Other drugs for obstructive airway diseases, inhalants), or R03C (Adrenergics, systemic use)). To reduce misclassification related to routine follow-up visits, only the first recorded event per individual was included, and subsequent events were considered as new episodes only if they occurred at least 270 days later. In a routinely collected healthcare data, longer washout periods improve internal validity by more thoroughly excluding prevalent or ongoing episodes, thereby reducing misclassification (Roberts et al., 2015). Events with both a diagnosis and a prescription recorded on the same day were counted once. Detailed descriptions of ICPC-2 and ATC codes are provided in the Supplementary Material (Supplementary A, Table S1).

2.2. *Statistical analysis*

We conducted a structured three-step analysis that included estimating independent exposure effects, stratified analysis, and joint effects to quantify the synergy of multiple exposures. This approach allows us to capture the non-linear, delayed, and interactive nature of the effects of environmental factors on allergic respiratory morbidity.

Single-exposure analysis

In the first step, we quantified the independent associations between each environmental exposure and allergic rhinitis and asthma outcomes. Within the Distributed lag non-linear models framework ,we fitted separated generalized linear models (GLM) for daily maximum temperature, air pollution (ozone and $PM_{2.5}$) and grass pollen concentrations. While we evaluated exposure effects individually, each single-exposure model simultaneously controlled for the remaining environment exposures, which were included as smooth terms specified using natural cubic splines (ns) with 3 degrees of freedom (df). This approach reduces residual confounding due to correlated environmental conditions while allowing for flexible nonlinear adjustment (Gasparrini et al., 2010).

To capture potential delayed effects and short-term harvesting effects, a maximum lag period of 14 days was used for all exposures. A DLNM was used to quantify the non-linear and delayed exposure-response and lag-response association (Gasparrini et al., 2010). The quasi-Poisson distribution was used to account for overdispersion in daily counts of outcomes.

For each exposure, we specified the exposure-response function using ns with 3 df, knots placed at equally spaced quantiles of the exposure distribution. The lag-response association was modeled using ns with 2 df, knots placed at equally spaced quantiles on the log scale to allow greater flexibility at shorter lags (Gasparrini and Armstrong, 2011). We used a ns with 4 df per year to control long-term trends. This specification was chosen because the analysis was restricted to the summer season of each year, thereby reducing the need for higher df. A short-term fluctuation is also controlled by including day of week (DOW) in the model. We have also included relative humidity as ns with 3 df. The relative risk (RR) was quantified at the 95th percentile of each exposure compared to the corresponding 50th percentile.

Stratified analysis

The second step quantified effect modification and interactions among exposures (Coker et al., 2025). We discretized each continuous exposure into four meaningful groups using quantiles for maximum temperature ([6.42, 18.2), [18.22, 20.9), [20.92, 24.0), [24.03, 39.7]), $PM_{2.5}$ ([1.99, 6.77), [6.77, 9.75), [9.75, 14.45), [14.45, 62.87]), ozone ([22.9, 63.5) [63.5, 75.4), [75.4, 91.5), [91.5, 206.2]), custom concentration interval for pollen ([0, 10), [10, 30), [30, 50), 50+) in line with the threshold values applied by the Belgian aerobiological surveillance network, and for which 50 grains/m^3 is considered as the symptomatic threshold for most people allergic to grass pollen (Hoebeke et al., 2018).

We performed generalized linear models with a quasi-Poisson distribution. All models included adjustment for relative humidity (ns with 3df) and long-term trend and seasonal variation. To assess effect modification and potential synergistic effects between exposures, we employed pairwise stratified analyses. For example, the association of pollen with outcomes was estimated within each category of temperature, $PM_{2.5}$ and O_3. We quantified stratified rate ratios (RRs) and 95% CIs across exposure combinations. Reference category for each exposure was defined as the quartile or interval containing the 50th percentile, making it consistent with the single-exposure analysis.

Two-way interactions and synergistic effects

In this step, we quantified the joint and synergistic effects of exposures and examined whether their combined impact exceeded the sum of their individual effects (Coker et al., 2025). It captures the interaction under extreme conditions and evaluates short-term delayed associations.

Extreme events were defined using high-percentile thresholds of the exposure distributions. We defined it at the 90th and 95th percentiles of daily Tmax, $PM_{2.5}$, O_3, and pollen concentration calculated over the study period (Coker et al., 2025). For each exposure, binary indicators were constructed, taking the value of 1 when the daily exposure exceeded the specified percentile threshold and 0 otherwise. The reference category therefore consisted of days when the exposure was below the threshold. To examine the delayed effects of extreme exposure, lag-specific (lag 0 to lag 14 days) binary indicators were generated for each exposure. We assessed the lag effects individually or in selected lag windows, to avoid multicollinearity. This lag-specific approach allowed transparent assessment of delayed associations without assuming a distributed lag structure.

We performed two-way interaction analysis for the pairs of extreme exposures using GLMs with quasi-Poisson. To evaluate joint effects, we compared rate ratios across four exposure combinations defined by binary extreme indicators. Using Tmax and $PM_{2.5}$ as an example, days were classified as: neither exposure exceeding its threshold (reference), only Tmax exceeding the threshold, only $PM_{2.5}$ exceeding the threshold, and simultaneous exceedance of both Tmax and $PM_{2.5}$. All RRs were calculated relative to the reference category. All interaction models were adjusted for long-term trends, dow, and confounding effects, as applied in the single-exposure and stratified analyses.

To examine whether joint exposure effects (quantified at P90) exceeded their individual additive effects, we estimated the relative excess risk due to interaction (RERI), the attributable proportion due to interaction (AP), and the synergistic index (SI) (Coker et al., 2025; Knol and VanderWeele, 2012; Rahman et al., 2022; Xu et al., 2023). We calculated the CIs for RERI, AP and SI using delta method, which accounts for the covariance between regression coefficients (Hosmer and Lemeshow, 1992). Additionally, we also estimated lag-specific excess risks (ER) for single and joint extreme exposure scenarios at selected lag days (lag 0, 3, 7, 10, and 14) (Rahman et al., 2022). Excess risk was calculated as the percentage increase in outcome risk relative to the reference category (no extreme exposure).

2.3. *Sensitivity analysis*

We performed a series of sensitivity analyses to assess the robustness of the estimates joint effect. First, we redefined extreme exposure thresholds at 95th percentile instead of 90th percentile. Second, we assessed model specification by varying df used to model long-term temporal trends and humidity. Third, we repeated the analysis by using daily minimum temperature instead of Tmax in order to assess the effects of possible exposure misclassification. Fourth, we repeated the analysis using two alternative case definitions: (1) diagnosis only, (2) prescription only among individuals without a recorded diagnosis, and

(3) prescription (all), defined as any medication prescription related to the condition, regardless of whether a formal diagnosis was recorded. Fifth, we used alternative minimum event-free intervals of 6 months and 1 year to assess the robustness of the episode definition. We also assessed temporal variation by repeating the analysis across three predefined periods (2005–2011, 2012–2018, and 2019–2024). We performed analyses by excluding the COVID-19 period (2020–2021) to assess the robustness of the results to potential changes in respiratory disease patterns during the pandemic. Finally, to address the potential role of relative humidity in respiratory physiology and its interaction with temperature, we conducted a sensitivity analysis examining the joint effects of heat and relative humidity.

All statistical analyses and visualization were performed in R (version 4.2.1) (R-team, 2022).

3. Results

Patients in the yearly contact group (YCG) increased from approximately 200,000 to nearly 470,000 between 2005 and 2022, followed by a gradual decline from 2023 to 2024 (Supplementary B, Fig. S1, Panel A). The mean age increased gradually from approximately 41 years in 2005 to around 44 years in 2024, with a modest increase in the standard deviation (Panel B). The sex distribution was relatively constant, with females consistently comprising approximately 53–54% of the population, although a slight decline in the proportion of females was observed in the most recent years (Panel C). Environmental exposures showed substantial variability over the study period, and a total of 101,221 allergic rhinitis events and 32,480 asthma events were recorded (Table 1).

Extreme environmental exposures, defined as values at or above the 90th and 95th percentiles, occurred in approximately 10% and 5% of study days, respectively, across temperature, $PM_{2.5}$, ozone, and pollen (Supplementary A, Table S2). A summary of allergic rhinitis and asthma events occurring on days with extreme environmental exposures is provided in Supplementary A, Table S3. For both outcomes, a greater proportion of events occurred during single-exposure extremes than during combined extreme exposures.

Fig. 1 illustrates the distribution of extreme environmental exposures. Across all exposures, days above the 95th percentile are clearly right-shifted relative to those above the 90th percentile, with high concentration levels within the extreme tail of the distribution. This separation is most pronounced for Tmax, where the 95th percentile days occur at higher values. For $PM_{2.5}$ and ozone, the density curves for the 90th and 95th percentile categories are more closely clustered.

Table 1

Descriptive statistics of environmental exposures and health outcomes during the study period.

Variables	Mean (sd)	Median (IQR)	P5–P95	Min–Max
Environmental exposures				
Tmin	12.30 (3.33)	12.51 (4.42)	6.69–17.50	0.95–23.51
Tmax	21.30 (4.59)	20.90 (6.14)	14.15–29.28	8.43–39.68
$PM_{2.5}$	11.59 (6.91)	9.75 (7.67)	4.28–25.61	1.99–62.87
Ozone	79.83 (23.97)	75.36 (28.04)	49.48–127.41	22.92–206.2
Pollen concentration	19.86 (36.28)	5.00 (19.75)	0.00–98.00	0.00–433.00
Relative humidity	71.22 (11.51)	72.03 (15.50)	50.00–88.28	31.34–99.57
Health outcomes				
Allergic rhinitis	30.07 (42.391) N = 101,221			
Asthma	9.65 (9.66) N = 32,480			

Units: temperature in °C; PM2.5 and ozone in $\mu g/m^3$; pollen in grains/m^3; relative humidity in %.

Summary statistics: values are presented as mean (standard deviation), median (inter quartile range), 5th–95th percentiles, and minimum–maximum for environmental exposures. Health outcomes are presented as total event counts (N) and mean (standard deviation).

The overall cumulative exposure–response analyses indicated clear non-linear associations between pollen, ozone, and temperature and the risk of allergic rhinitis, with increased risk observed at 95th percentile (Supplementary B, Fig. S2). In contrast, asthma exhibited largely flat exposure–response relationships across most environmental exposures, except pollen, which was associated with an increased risk.

Cumulative RRs (lag 0–14 days) and 95% CIs, quantified at 95th percentile of each exposure compared to 50th percentile, are presented in Table 2. We observed strong associations between pollen and allergic rhinitis (RR=2.54, 95% CI: 2.40–2.69), as well as a significant increase in asthma risk (RR=1.49, 95% CI: 1.38–1.61). We also found that higher ozone levels were associated with an increased risk of allergic rhinitis (RR=1.34, 95% CI :1.23–1.47), whereas no association with asthma.

Our findings showed that higher daily maximum temperature was strongly associated with an increased risk of allergic rhinitis (RR=1.20, 95% CI: 1.14–1.26), whereas no clear association with asthma (RR=1.01, 95% CI: 0.96–1.07). In contrast, $PM_{2.5}$ exhibited small effect estimates for allergic rhinitis (RR=1.05, 95% CI: 0.98–1.12), albeit not statistically significant.

The results of stratified analysis for some selected associations are presented in Fig. 2. The risk of allergic rhinitis appears to increase with high maximum temperature, and the magnitude of this effect is modified by pollen levels. We observed that at the highest pollen category (50+ grains/m^3), the risk associated with heat (24.03–39.7°C) increases. Conversely, at low pollen concentrations (0,10), high Tmax shows minimal effect. Our study showed that allergic rhinitis risk increases significantly during high pollen concentration (50+ grains/m^3), especially when Tmax is over 18.22°C. We have also performed the stratified analysis for each possible pairwise stratification of exposures and allergic rhinitis (Supplementary B, Fig. S3). There is no strong evidence for the impact of heat on allergic rhinitis across the air pollutants category. The association with $PM_{2.5}$ or Ozone, stratified by either Tmax or Pollen, is less pronounced.

Our findings revealed that environmental exposures generally exhibited no strong association with asthma, regardless of exposure used for stratification. However, high temperatures might increase asthma risk when pollen concentrations reach their highest levels. However, this potential effect remained modest and did not reach statistical significance. High pollen concentration showed increased risk of asthma, when $PM_{2.5}$ reached 14.45–62.87$\mu g/m^3$ (Supplementary B, Fig. S4). We did not find strong associations for other exposures.

Joint exposure to extreme heat, air pollution, and aeroallergens was associated with substantial increases in allergic rhinitis risk (Table 3), quantified at the 90th percentile, compared to exposure levels below the threshold.

We observed that the joint effects of extreme heat and high $PM_{2.5}$ was not statistically significant (RR=1.10, 95% CI: 0.94–1.30). Additive interaction indices were small and imprecise, indicating that most of these excess risk reflects the sum of individual effects rather than strong biological synergy. Our findings showed that a substantially high risk of allergic rhinitis was associated with the combined effects of heat and extreme ozone (RR= 1.21, 95% CI: 1.10–1.32). However, the interaction measures were close to zero, suggesting largely additive joint effects.

The joint effects of extreme heat and high pollen doubled the risk of allergic rhinitis (RR= 2.07, 95% CI: 1.77–2.41). Positive and significant interaction measures (RERI=0.48, 95% CI: 0.32–0.64, AP=0.23, 95% CI: 0.17–0.30) show strong synergistic effects, implying that about 23% of the excess risk among individuals exposed to both exposures is attributable to the interaction itself rather than to the sum of independent contributions of heat and pollen. Using daily minimum

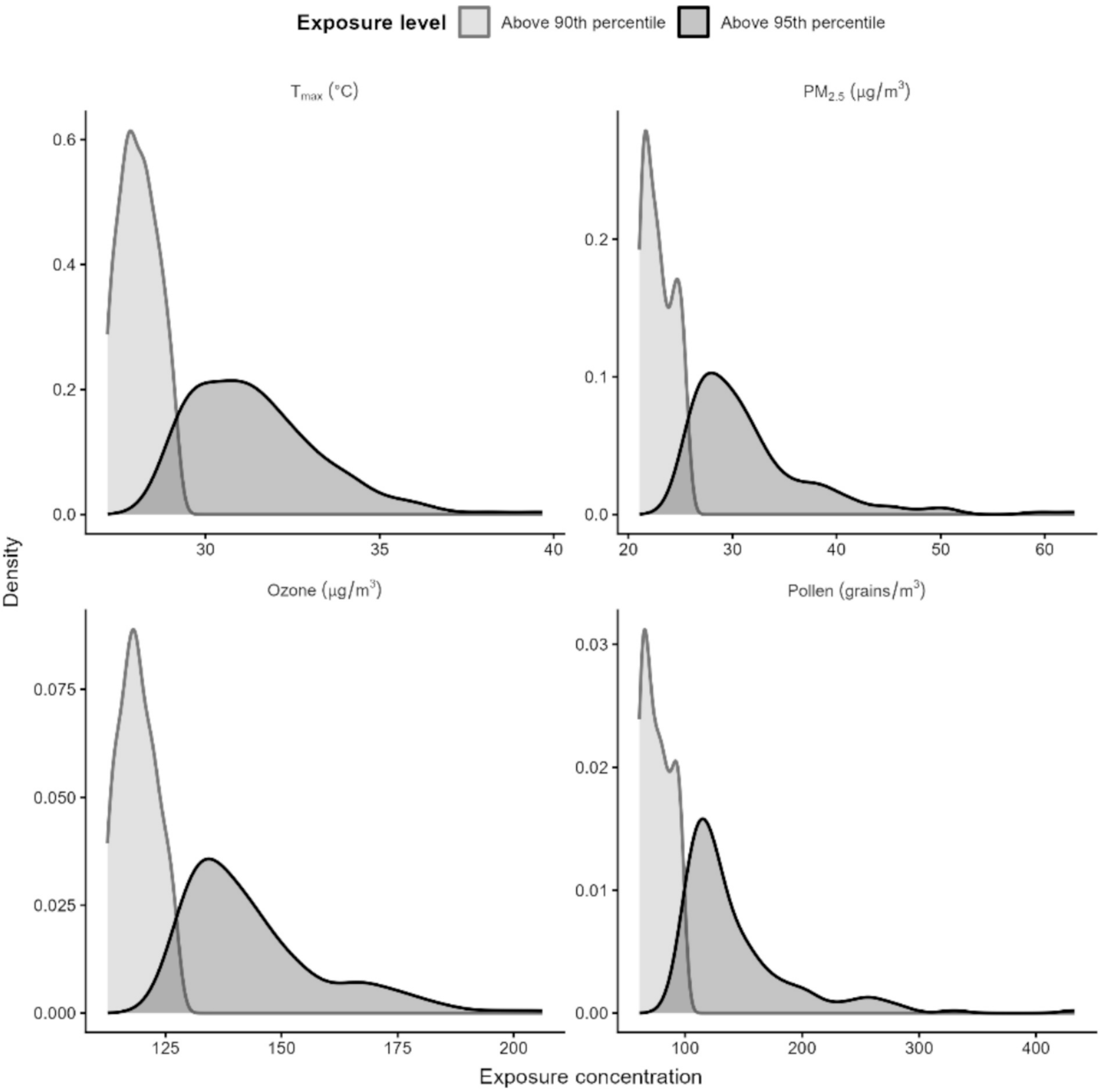

Fig. 1. Density distributions of environmental exposure values restricted to days exceeding the 90th percentile of each exposure-specific study-period distribution. Light grey areas represent values exceeding the 90th percentile, and dark grey areas represent values exceeding the 95th percentile over the study period.

Table 2

Cumulative RRs and 95% CIs for allergic rhinitis and asthma associated with exposure levels, quantified at the 95th percentile compared with the 50th percentile of daily maximum temperature (Tmax), $PM_{2.5}$, ozone, and pollen concentrations during the summer months (May–September) in Flanders, Belgium.

Exposures	Outcomes Allergic rhinitis RR (95% CI)	 Asthma RR (95% CI)
Tmax	1.20 (1.14, 1.26)	1.01 (0.96,1.07)
PM2.5	1.05 (0.98, 1.12)	1.00 (0.93, 1.08)
Ozone	1.34 (1.23, 1.47)	0.99 (0.90, 1.10)
Pollen	2.54 (2.40, 2.69)	1.49 (1.38, 1.61)

temperature rather than maximum temperature, synergistic effects between heat and pollen on allergic rhinitis is weaker (RERI=0.33, 95% CI: 0.16–0.49; AP=0.17, 95% CI: 0.09–0.24) (Supplementary A, Table S4). Similarly, we also found that ozone combined with high pollen resulted a significant rise in allergic rhinitis risk (RR=2.03, 95% CI: 1.76–2.34. Interaction metrics also showed a clear positive additive interaction (RERI=0.40, 95% CI: 0.25–0.54; AP=0.20, 95% CI: 0.13–0.26).

Our findings suggested a possible joint effect of extreme $PM_{2.5}$ and high pollen exposure on allergic rhinitis (RR=1.77, 95% CI: 1.45–2.16). However, interaction indices showed no synergism on the additive scale (AP=−0.02= 95% CI: −0.15–0.10). We further quantified lag-specific excess risk attributable to both individual and combined exposures at the 90th and 95th percentiles, relative to exposure levels below the corresponding thresholds (Supplementary B, Fig. S5). These findings revealed pronounced acute short-term joint effects, particularly for exposure combinations involving pollen. Elevated excess risks were consistently observed for heat–pollen, $PM_{2.5}$–pollen, and ozone–pollen co-exposures at shorter lags (lag 0 to lag 3), indicating an immediate increase in allergic rhinitis risk following simultaneous extreme environmental conditions.

The combined environmental exposure risk of asthma estimated when the exposure values are above the 90th percentile threshold compared with below this threshold is summarized in Table 4. The

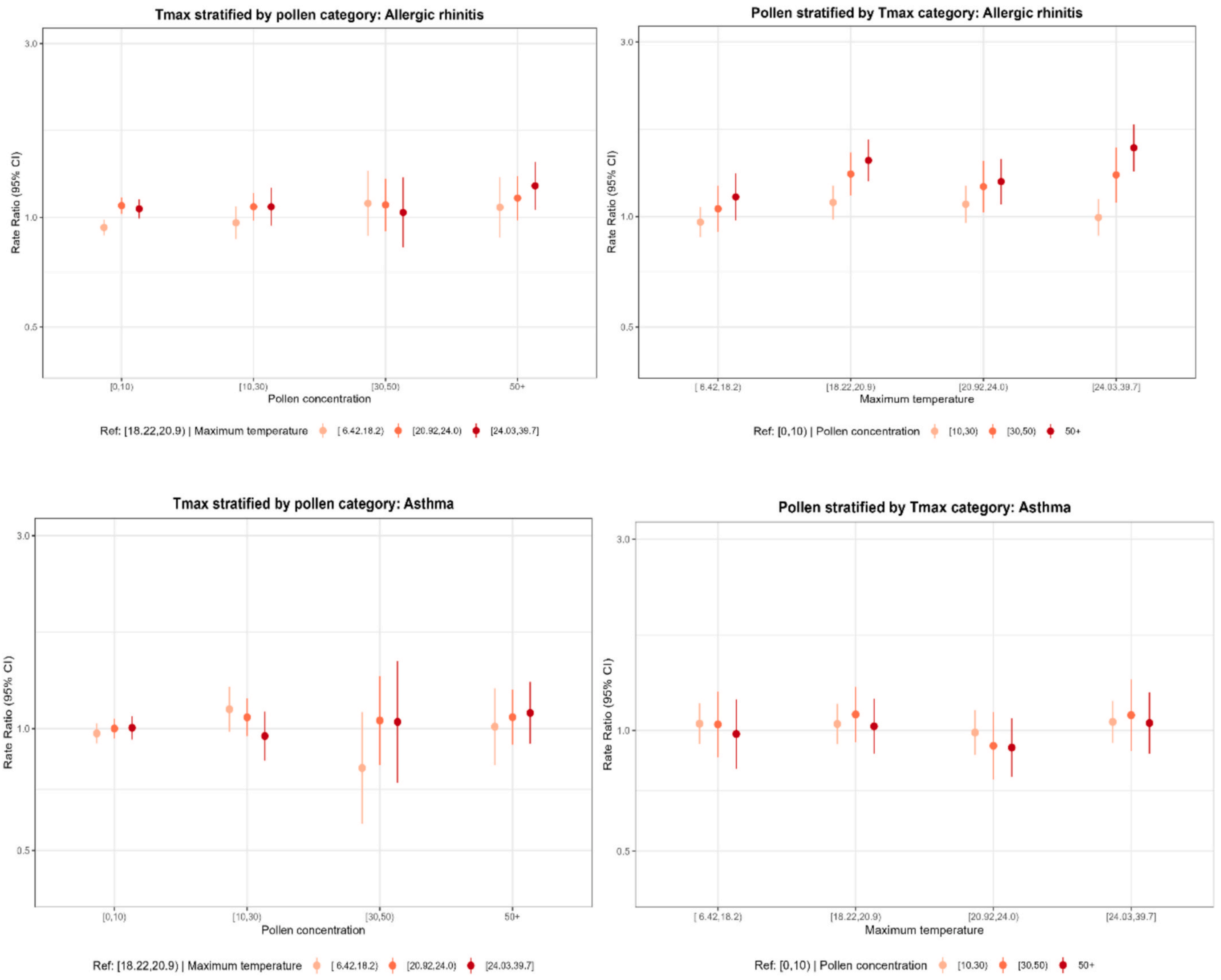

Fig. 2. Stratified associations between environmental exposures and outcomes for selected stratified analyses to highlight effect-modification patterns observed. Estimated RRs and 95% CIs are presented for allergic rhinitis and asthma across categories of environmental exposures. The reference group was defined as the category containing the 50th percentile of the exposure distribution.

Table 3
Joint associations between extreme exposures and allergic rhinitis, quantified at the 90th percentile. Results include the combined RR, ER, and interaction measures (RERI, AP, and SI) with delta-method 95% CI.

Exposure pairs	RR (95% CI)	ER (95% CI)	RERI (95% CI)	AP (95% CI)	SI (95% CI)
Heat+$PM_{2.5}$	1.10 (0.94,1.30)	10.4 (−6.3,30.2)	−0.152 (−0.34,0.04)	−0.138 (−0.33,0.05)	0.41 (−0.25,1.06)
Heat + Pollen†	2.07 (1.77,2.41)	106.5 (77.1,140.9)	0.48 (0.32,0.64)	0.23 (0.17,0.30)	1.81 (1.46,2.16)
Heat+Ozone	1.21 (1.10,1.32)	20.6 (10.2,32.0)	−0.01 (−0.15,0.13)	−0.01 (−0.13,0.11)	0.96 (0.31,1.60)
$PM_{2.5}$ + Pollen	1.77 (1.45–2.16)	77.0 (44.9–116.3)	−0.04 (−0.25–0.18)	−0.02(−0.15–0.10)	0.95 (0.69–1.22)
Ozone+Pollen†	2.03 (1.76−2.34)	103.1 (76.3−134.1)	0.40 (0.25–0.54)	0.20(0.13−0.26)	1.62(1.34−1.91)

Note: † Indicates positive additive interaction (synergistic effect). Abbreviation: RR, relative risk; CI, confidence interval; ER, excess risk; RERI, relative excess risk due to interaction; AP, attributable proportion due to interaction; SI, synergy index.

combined effects of $PM_{2.5}$ with heat or pollen were not significantly associated with a increase in asthma risk. In contrast, concurrent exposure to extreme heat and high pollen levels was associated with an increased risk of asthma (RR=1.24, 95% CI: 1.09–1.41; ER = 23.9%, 95% CI: 8.7–41.1). The positive attributable proportion (AP = 0.13, 95% CI: 0.02–0.24) indicates a supra-additive interaction, suggesting that approximately 13% of the excess risk among individuals exposed to both factors can be attributed to their joint effect, beyond the sum of their independent contributions. Similar results were observed when minimum temperature was used instead of maximum temperature (RR = 1.22, 95% CI: 1.06–1.40; AP = 0.12, 95% CI: 0.001–0.23) (Supplementary Appendix B, Table S4). Increased risk of asthma was also observed associated with joint effects of ozone and pollen (RR=1.23, 95% CI: 1.09–1.38; ER 22.6%, 95% CI: 9.1–37.7). The lag-specific excess risk due to each exposure and their combination did not show a pronounced association, both at 90th and 95th percentile thresholds (Supplementary B, Fig. S6).

Using the 95th percentile to define extreme exposures largely

Table 4

Joint associations between extreme exposures and asthma quantified at the 90th percentile. Results include the combined RR, ER, and interaction measures (RERI, AP, and SI) with delta-method 95% CI.

Exposure pairs	RR (95% CI)	ER (95% CI)	RERI (95% CI)	AP (95% CI)	SI (95% CI)
Heat+$PM_{2\cdot5}$	0.98 (0.87,1.12)	−1.6 (−13.4,11.8)	−0.01 (−0.25,0.06)	−0.098 (−0.26,0.07)	−0.19 (−1.83,1.43)
Heat + Pollen†	1.24 (1.09,1.41)	23.9 (8.7,41.1)	0.16 (0.02,0.30)	0.13 (0.02,0.24)	3.03 (−0.57,6.64)
Heat+Ozone	1.01 (0.94,1.09)	1.4 (−5.9,9.3)	−0.003 (−0.13,0.13)	−0.003 (−0.13,0.12)	0.82 (−5.52,7.15)
$PM_{2\cdot5}$ + Pollen	1.02 (0.94−1.10)	1.5 (−6.4−10.1)	0.03 (−0.09−0.15)	0.028 (−0.09−0.14)	−1.117 (−12.86−10.62)
Ozone+Pollen†	1.23 (1.09−1.38)	22.6 (9.1−37.7)	0.14 (0.013−0.28)	0.12 (0.02−0.22)	2.76 (−0.47−5.99)

Note: † Indicates positive additive interaction (synergistic effect). Abbreviation: RR, relative risk; CI, confidence interval; ER, excess risk; RERI, relative excess risk due to interaction; AP, attributable proportion due to interaction; SI, synergy index.

confirmed our main findings (Supplementary A, Table S5). Joint exposure to heat and pollen consistently showed strong positive associations with allergic rhinitis (RR=1.53, 95% CI: 1.28–1.82). Similarly, combinations of ozone and pollen showed elevated risks.

Our analyses using greater flexibility for temporal trends (5 df/year) and relative humidity (4 df) are consistent with the primary finding (Supplementary A, Table S6). For allergic rhinitis, co-exposure to heat and pollen and to ozone and pollen remained strongly associated with increased risk and showed evidence of synergistic effects on the additive scale. In contrast, we did not find clear joint effects or additive interactions across exposure combinations and asthma.

Sensitivity analyses using alternative case definitions (diagnosis only, prescription-only among individuals without a recorded diagnosis and prescription (all)) showed generally consistent RERI patterns compared with the main analysis (Supplementary B, Fig. S7). For allergic rhinitis, heat–pollen and ozone–pollen interactions remained positive. For asthma, additive interactions were smaller and more variable, with positive RERI observed for heat–pollen only under the prescription-only definition. Results were consistent with main findings when alternative event-free intervals (6 months and 1 year) were applied, with similar AP magnitudes and directions across exposure combinations for both outcomes (Supplementary B, Fig. S8). Period-specific analyses showed broadly consistent additive interaction patterns over time for both allergic rhinitis and asthma (Supplementary B, Fig. S9). For allergic rhinitis, positive interactions for heat–pollen and pollen–ozone were observed across all periods, though few lost significance. Heat–PM2.5 remained negative throughout. Heat–ozone showed some temporal change, with negative estimates in earlier periods and a small positive estimate in 2019–2024. Greater variability was observed for pollen–PM2.5, with inconsistent direction across periods. For asthma, patterns were generally stable. Heat–pollen showed consistently positive, but did not reached significance for some period. Sensitivity analyses excluding the COVID-19 period (2020–2021) showed similar patterns to the main analysis. Positive additive interactions for heat–pollen and pollen–ozone persisted for both outcomes (Supplementary A, Table S7). The joint effect of heat and relative humidity showed no clear evidence of additive interaction for allergic rhinitis and for asthma (Supplementary A, Table S8).

4. Discussion

Principal findings

In this large population-based time-series analysis integrating meteorological, air pollution, and aeroallergen data, we observed, as expected, that pollen exposure was the dominant environmental driver of allergic rhinitis. However, increased ozone and higher maximum temperature were also associated with increased allergic rhinitis risk. The asthma risk is strongly associated with higher pollen concentrations, and weak associations were found with ozone, temperature, and PM2.5 alone. Most importantly, our findings demonstrated clear synergistic effects between heat and pollen, and between ozone and pollen, on allergic rhinitis or asthma, with additive interaction metrics indicating true effect modification rather than simple co-exposure. The joint effects are generally acute and stronger over shorter lag-days for allergic rhinitis.

Comparison to previous studies

Our finding that pollen exposure is strongly associated with allergic rhinitis and asthma is highly consistent with the existing literature. A recent meta-analysis based on 31 studies showed that pollen concentrations significantly increased allergic risk (Berezhanskiy et al., 2025). Similarly, another meta-analysis found that pollen exposure increases allergic or asthmatic symptoms (Kitinoja et al., 2020b). A strong association of heat and allergic rhinitis in our study is consistent with evidence that warmer conditions can extend pollen seasons through wind, humidity or floodings (Ziska and Beggs, 2012). According to a systematic review, the evidence on the association of ambient temperature and allergic rhinitis remains inconclusive; some studies found a substantial increase, while others showed no significant correlation (Wei Rong et al., 2024a). A recent meta-analysis by Hu et al. (2025) involving over 5 million participants across 22 studies found that a 1°C increase in temperature corresponded to a 14% increase in the risk of allergic rhinitis, which is slightly higher than our estimate (Li et al., 2025).

The positive association of ozone with allergic rhinitis aligns with prior evidence linking ozone exposure to increased allergic inflammation and upper airway irritation. A study in China, for example, found that the risk of asthma and bronchitis is associated with high levels of O_3 (Zhou et al., 2021). There was a meta-analysis that found emergency hospitalizations for respiratory disease increased by 2.97% (1.05, 4.94%) per 10ppb 24-hr ozone among the elderly (Ji et al., 2011). The absence of strong independent associations of ozone with asthma and $PM_{2\cdot5}$ with either allergic rhinitis or asthma in our study might be because these exposures may exert their effects mainly through interaction with other dominant triggers such as pollen and heat, or through long-term pathways not fully captured by short-term analyses.

Our stratified analyses revealed distinct effect-modification patterns. Specifically, we observed that the association between high maximum temperature and allergic rhinitis risk was substantially amplified at elevated pollen concentrations. This pattern of effect modification aligns with mechanistic and epidemiological studies. Mechanistic studies show that warmer temperatures accelerate plant growth and pollen release, and may enhance the concentration of allergenic proteins in pollen grains, thereby increase respiratory immune responses under high allergen loads (Reid and Gamble, 2009). A scoping review on pollen potency/allergenicity found large spatio-temporal variability and, inconclusive evidence regarding climatic and meteorological drivers, including temperature (Tegart et al., 2021). A meta-analysis also showed positive associations of ambient temperature and allergic rhinitis, while the pooled association did not reach statistical significance (Wei Rong et al., 2024b). Our stratified findings extend these insights by demonstrating that heat alone is a relatively weak driver of allergic rhinitis, but in the presence of high pollen loads becomes a significant modifier, suggesting synergistic enhancement of allergen exposure. In contrast, we found weak associations of air pollution exposures and both allergic rhinitis and asthma across temperature and pollen concentration, except ozone showed strong association during high pollen levels.

Our joint exposure analysis showed strong association for the concurrent exposure to heat and pollen as well as ozone and pollen increases allergic rhinitis risk. A retrospective analysis of data from the 2024 Lancet Countdown on health and climate change found a 69% increase in per-person exposure to three or more hazards, where heatwaves contributed significantly for the increase in both single-hazard and multi-exposure analysis (Stalhandske et al., 2025). Experimental and clinical studies have shown that warmer conditions can increase the expression of allergenic proteins in pollen and intensity airway inflammatory responses, providing a strong biological basis of interaction rather than simple co-exposure (Çelebi Sözener et al., 2023b; Kananejad et al., 2025). In epidemiological studies, however, such synergy has rarely been quantified. For example, a systematic review highlighted the scarcity of studies formally assessed heat–pollen interactions (Anenberg et al., 2020). However, recent planetary health evidence showed that climate change has intensified pollen-related allergic disease burden, primarily through increased pollen emissions, prolonged pollen seasons, and geographic expansion of allergenic species (Ziska et al., 2019). Our study shows a strong synergistic effect of pollen and ozone on allergic rhinitis and asthma, which is consistent with previous experimental studies showing that ozone exposure damages airway epithelium, induces oxidative stress, and increases penetration and immunogenicity (Bronte-Moreno et al., 2023; D'Amato et al., 2015; Reinmuth-Selzle et al., 2017).

In contrast, our analyses revealed no strong synergistic or interaction effects for the combination of heat–ozone, heat–$PM_{2.5}$ or $PM_{2.5}$–pollen. These findings are consistent with a systematic review examining heat–air pollution interactions that has reported heterogeneous and generally modest interaction effects, with stronger and more consistent synergy observed for mortality and cardiovascular outcomes than for allergic or respiratory morbidity (Anenberg et al., 2020). According to a recent systematic review, the combined effects of air pollution and temperature are often inconsistent across studies (D'Amato et al., 2015). Another systematic review noted that only one–third of epidemiological studies identified significant allergen–pollutant interactions (Lam et al., 2021). The absence of strong synergistic effects in our findings, specifically joint effects involving $PM_{2.5}$ may reflect its short-term effects on AR and asthma are generally modest and heterogeneous, limiting to detect meaningful interactions with acute exposures such as temperature or pollen. In addition, $PM_{2.5}$ likely operates through more cumulative inflammatory pathways,(Piao et al., 2021) whereas pollen-related allergic responses are rapid and IgE-mediated, reducing the likelihood of strong short-lag synergism (Abbas and Goldin, 2025).

Strengths and limitations

Our study has several strengths. A major strength is the integrated assessment of multiple environmental exposures, including meteorological factors, air pollutants, and aeroallergens in a unified longitudinal framework. Unlike several existing studies, which typically examined these exposures separately, our study explicitly evaluated joint and synergistic effects, allowing for a more realistic representation of real-world environmental conditions. Second, we explicitly quantified additive interaction using public health-relevant metrics including relative excess risk due to interaction and attributable proportion. Third, the study leverages a large population-based routine healthcare dataset and applies established additive interaction measures (RERI, AP, and SI) to rigorously quantify potential synergistic effects between environmental exposures. Our study used routinely collected GP data covering two decades, which allowed us to examine environmental health effects across a wide range of climatic conditions, pollution levels, and pollen seasons. Moreover, GP data reflect real-world, primary-care–based morbidity, capturing a broader spectrum of allergic disease severity. Finally, the consistent findings across single-exposure, stratified, and joint-effects analyses increase internal validity.

Several limitations should also be acknowledged. First, grass pollen exposure was assessed using area-level monitoring data, which might not fully reflect spatial heterogeneity in pollen concentrations at ground level, especially in urban environments or near specific vegetation sources. However, dispersion modelling evaluated that the Belgian aerobiological surveillance network overall covers a large fraction of the potential source areas for grass pollen across Belgium, which supports the robustness and spatial representativeness of the network's airborne grass pollen concentration data (Verstraeten et al., 2025). Moreover, previous epidemiological studies assumes that the distribution of pollen concentration across study area are not significantly different (Guilbert et al., 2016; Osborne et al., 2017). Second, outcome misclassification is possible, particularly for asthma, which is a heterogeneous condition with varying phenotypes and triggers that cannot be distinguished in our data. To assess robustness, we conducted sensitivity analyses using diagnoses only, prescriptions without a corresponding diagnosis, and all prescriptions. These analyses yielded consistent results.. Third, we evaluated multiple exposure combinations, and specifically using pairwise exposure, rather than simultaneously modelling three or more interacting environmental stressors. This is to preserve statistical power and ensure stable estimation of interaction effects, as higher-order interactions require substantially larger sample sizes and can lead to sparse data in extreme exposure categories. Fourth, our findings may be influenced by co-seasonal exposure to other aeroallergens including *Cladosporium, Alternaria, Plantago and Rumex*. In polysensitized patients, these simultaneous exposures may produce additive or synergistic effects on airway inflammation. Finally, as with all observational studies, we cannot completely exclude residual confounding. Although our time-series design inherently controls for time-invariant confounders and we adjusted for key temporal factors, unmeasured time-varying influences, such as respiratory infections or behavioral changes during extreme weather, may have affected our estimates.

Implications for daily practice, policy, and research

Our findings have direct implications for both clinical management and environmental health policy. Our study showed a rise in respiratory illnesses, especially when multiple environmental exposures were present at the same time. These increases may translate into a meaningful number of additional cases at the population level during high-exposure periods. This highlights the significance of combining exposure mixture regulations rather than regulating each exposure separately. For clinical practice, this may help guide preventive measures during periods of elevated environmental risk. As climate and environmental changes continue to occur globally, future studies should identify susceptible populations and quantify how combined exposures contribute to disease burden..

In conclusion, aeroallergens appear to be the primary drivers of short-term allergic respiratory morbidity, with heat and ozone contributing to increased risk under extreme environmental conditions, emphasizing the importance of multi-exposure approaches in assessing climate-sensitive health impacts.

Declaration of generative AI and AI-assisted technologies in the manuscript preparation process

During the preparation of this work, the authors used ChatGPT (OpenAI) for language editing and improving the clarity of the manuscript text. After using this tool, the authors carefully reviewed and edited the content as needed and take full responsibility for the content of the published article.

CRediT authorship contribution statement

Endale Alemayehu Ali: Writing – review & editing, Writing – original draft, Visualization, Software, Methodology, Formal analysis, Data curation, Conceptualization. **Raf Aerts:** Writing – review & editing, Supervision, Conceptualization. **Bert Vaes:** Writing – review & editing, Supervision, Project administration. **Charlotte Scheerens:** Writing – review & editing, Supervision. **Simon Gabriël Beerten:** Writing – review & editing, Supervision. **Nicolas Bruffaerts:** Writing – review & editing, Data curation. **Elisa Duarte:** Writing – review & editing, Methodology. **Gijs Van Pottelbergh:** Writing – review & editing, Supervision, Resources, Project administration, Funding acquisition, Conceptualization.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Endale Alemayehu Ali reports financial support was provided by Flemish Department of Care. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

Intego receives structural funding from the Flemish Department of Care. This specific study and Endale are supported by the Flanders Department of Care under the name SO Intego MGZ.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envint.2026.110330.

Data availability

Environmental exposure data used in this study are partly publicly available. Daily temperature and relative humidity data can be downloaded from Royal Meteorological Institute of Belgium via its open data portal (https://opendata.meteo.be/). Air pollution data ($PM_{2.5}$ and ozone) are available from IRCEL - CELINE (http://ftp.irceline.be/rio4x4/daily_indicators/). However, air pollution data from this source are available from 2008 onwards; data for the period 2005–2007 can be requested from the corresponding author. Due to data protection regulations, the authors are not permitted to share medical data or pollen data. Health data used in this study originate from the Intego database and are not publicly available due to data protection regulations. Researchers may request access through the official Intego data access procedure; detailed information is available at https://www.intego.be/en/onderzoek/data-access or by contacting intego@kuleuven.be. Pollen data can be requested from the Belgian Aerobiological Surveillance Network via https://airallergy.sciensano.be/Contact.

References

Abbas, M., Goldin, J., 2025. Type I Hypersensitivity Reaction.

Anenberg, S.C., Haines, S., Wang, E., Nassikas, N., Kinney, P.L., 2020. Synergistic health effects of air pollution, temperature, and pollen exposure: a systematic review of epidemiological evidence. Environ. Health 19 (1), 130. https://doi.org/10.1186/s12940-020-00681-z.

Bédard, A., Sofiev, M., Arnavielhe, S., et al., 2020. Interactions between air pollution and pollen season for rhinitis using mobile technology: a MASK-POLLAR study. J. Allergy Clin. Immunol. Pract. 8 (3), 1063–1073.e4. https://doi.org/10.1016/j.jaip.2019.11.022.

Beggs, P.J., Clot, B., Sofiev, M., Johnston, F.H., 2023. Climate change, airborne allergens, and three translational mitigation approaches. EBioMedicine 93, 104478. https://doi.org/10.1016/j.ebiom.2023.104478.

Berezhanskiy, P.V., Mahmoudizeh, A., Fakhri, Y., 2025. Pollen exposure and allergy risk: a systematic review and meta-analysis, 1–15 Int. J. Environ. Health Res. Published online July 23. https://doi.org/10.1080/09603123.2025.2533354.

Bousquet, J., Schünemann, H.J., Togias, A., et al., 2020. Next-generation Allergic Rhinitis and Its Impact on Asthma (ARIA) guidelines for allergic rhinitis based on Grading of Recommendations Assessment, Development and Evaluation (GRADE) and real-world evidence. J. Allergy Clin. Immunol. 145 (1), 70–80.e3. https://doi.org/10.1016/j.jaci.2019.06.049.

Bousquet, J., Anto, J.M., Bachert, C., et al., 2020. Allergic rhinitis. Nat. Rev. Dis. Primers 6 (1), 95. https://doi.org/10.1038/s41572-020-00227-0.

Bronte-Moreno, O., González-Barcala, F.J., Muñoz-Gall, X., Pueyo-Bastida, A., Ramos-González, J., Urrutia-Landa, I., 2023. Impact of air pollution on asthma: a scoping review. Open Respiratory Archives. 5 (2), 100229. https://doi.org/10.1016/j.opresp.2022.100229.

Cecchi, L., D'Amato, G., Annesi-Maesano, I., 2018. External exposome and allergic respiratory and skin diseases. J. Allergy Clin. Immunol. 141 (3), 846–857. https://doi.org/10.1016/j.jaci.2018.01.016.

Çelebi Sözener, Z., Treffeisen, E.R., Özdel Öztürk, B., Schneider, L.C., 2023. Global warming and implications for epithelial barrier disruption and respiratory and dermatologic allergic diseases. J. Allergy Clin. Immunol. 152 (5), 1033–1046. https://doi.org/10.1016/j.jaci.2023.09.001.

Chou, C.K., Winker, R., Rebuli, M.E., Moran, T., Rager, J.E., 2025. Respiratory health impacts from natural disasters and other extreme weather events: the role of environmental stressors on asthma and allergies. Curr. Allergy Asthma Rep. 25 (1), 25. https://doi.org/10.1007/s11882-025-01206-9.

Coker, E.S., Cleland, S.E., McVea, D., Stafoggia, M., Henderson, S.B., 2025. The synergistic effects of PM2.5 and high temperature on community mortality in British Columbia. npj Clean Air 1 (1). https://doi.org/10.1038/s44407-025-00014-9.

D'Amato, G., Cecchi, L., 2008. Effects of climate change on environmental factors in respiratory allergic diseases. Clin. Exp. Allergy 38 (8), 1264–1274. https://doi.org/10.1111/j.1365-2222.2008.03033.x.

D'Amato, G., D'Amato, M., 2023. Climate change, air pollution, pollen allergy and extreme atmospheric events. Curr. Opin. Pediatr. 35 (3), 356–361. https://doi.org/10.1097/MOP.0000000000001237.

D'Amato, G., Holgate, S.T., Pawankar, R., et al., 2015. Meteorological conditions, climate change, new emerging factors, and asthma and related allergic disorders. A statement of the World Allergy Organization. World Allergy Organ. J. 8, 25. https://doi.org/10.1186/s40413-015-0073-0.

eClinicalMedicine. The bloom and the breathless: the rising burden of pollen allergy. *EClinicalMedicine*. 2025;84:103327. doi:10.1016/j.eclinm.2025.103327.

Feng, C., Shao, Y., Ye, T., et al., 2023. Associations between long-term exposure to PM2.5 chemical constituents and allergic diseases: evidence from a large cohort study in China. Sci. Total Environ. 904, 166755. https://doi.org/10.1016/j.scitotenv.2023.166755.

Gasparrini, A., Armstrong, B., Kenward, M.G., 2010. Distributed lag non-linear models. Stat. Med. 29 (21), 2224–2234. https://doi.org/10.1002/sim.3940.

Gasparrini, A., Armstrong, B., 2011. The impact of heat waves on mortality. Epidemiology 22 (1), 68–73.

Guilbert, A., Simons, K., Hoebeke, L., et al., 2016. Short-term effect of pollen and spore exposure on allergy morbidity in the Brussels-capital region. Ecohealth 13 (2), 303–315. https://doi.org/10.1007/s10393-016-1124-x.

Haines, A., Kovats, R., Campbell-Lendrum, D., Corvalan, C., 2006. Climate change and human health: impacts, vulnerability, and mitigation. Lancet 367 (9528), 2101–2109. https://doi.org/10.1016/S0140-6736(06)68933-2.

Hoebeke, L., Bruffaerts, N., Verstraeten, C., et al., 2018. Thirty-four years of pollen monitoring: an evaluation of the temporal variation of pollen seasons in Belgium. Aerobiologia (Bologna). 34 (2), 139–155. https://doi.org/10.1007/s10453-017-9503-5.

Hosmer, D.W., Lemeshow, S., 1992. Confidence Interval Estimation of Interaction. Epidemiology 3 (5), 452–456. https://doi.org/10.1097/00001648-199209000-00012.

IRCEL-CELINE. Belgian Interregional Environment Agency (IRCEL - CELINE) . Preprint posted online 2024. https://www.irceline.be/en.

Ji, M., Cohan, D.S., Bell, M.L., 2011. Meta-analysis of the association between short-term exposure to ambient ozone and respiratory hospital admissions. Environ. Res. Lett. 6 (2). https://doi.org/10.1088/1748-9326/6/2/024006.

Kanannejad, Z., Taylor, W.R., Mohkam, M., Ghatee, M.A., 2025. Urban lifestyle and climate-driven environmental exposures: immunological consequences for pediatric respiratory allergies. Immun. Inflamm. Dis. 13 (8). https://doi.org/10.1002/iid3.70248.

Kitinoja, M.A., Hugg, T.T., Siddika, N., Rodriguez Yanez, D., Jaakkola, M.S., Jaakkola, J.J.K., 2020. Short-term exposure to pollen and the risk of allergic and asthmatic manifestations: a systematic review and meta-analysis. BMJ Open 10 (1), e029069. https://doi.org/10.1136/bmjopen-2019-029069.

Knol, M.J., VanderWeele, T.J., 2012. Recommendations for presenting analyses of effect modification and interaction. Int. J. Epidemiol. 41 (2), 514–520. https://doi.org/10.1093/ije/dyr218.

Komlósi, Z.I., van de Veen, W., Kovács, N., et al., 2022. Cellular and molecular mechanisms of allergic asthma. Mol. Aspects Med. 85, 100995. https://doi.org/10.1016/j.mam.2021.100995.

Lam, H.C.Y., Jarvis, D., Fuertes, E., 2021. Interactive effects of allergens and air pollution on respiratory health: a systematic review. Sci. Total Environ. 757, 143924. https://doi.org/10.1016/j.scitotenv.2020.143924.

Li, Q., Gu, W., Feng, H., et al., 2025. Association of meteorological factors with allergic rhinitis: a systematic review and meta-analysis. BMC Public Health 26 (1), 409. https://doi.org/10.1186/s12889-025-26078-6.

Luschkova, D., Traidl-Hoffmann, C., Ludwig, A., 2022. Climate change and allergies. Allergo J Int. 31 (4), 114–120. https://doi.org/10.1007/s40629-022-00212-x.

Melén, E., Koppelman, G.H., Vicedo-Cabrera, A.M., Andersen, Z.J., Bunyavanich, S., 2022. Allergies to food and airborne allergens in children and adolescents: role of epigenetics in a changing environment. Lancet Child Adolesc Health. 6 (11), 810–819. https://doi.org/10.1016/S2352-4642(22)00215-2.

Niu, Z., Zhang, L., Zhang, X., et al., 2025. Association between air temperature exposure and childhood rhinitis risk, and the mediating role of ambient O3: a multi-city study of 40,103 Chinese preschool children. Sustain. Cities Soc. 119, 106122. https://doi.org/10.1016/j.scs.2024.106122.

Osborne, N.J., Alcock, I., Wheeler, B.W., et al., 2017. Pollen exposure and hospitalization due to asthma exacerbations: daily time series in a European city. Int. J. Biometeorol. 61 (10), 1837–1848. https://doi.org/10.1007/s00484-017-1369-2.

Paoletti, G., Giua, C., Marti, A., et al., 2025. ARIA–Italy managing allergic rhinitis and asthma in a changing world: the role of the Pharmacist. World Allergy Organ. J. 18 (5), 101055. https://doi.org/10.1016/j.waojou.2025.101055.

Pawankar, R., Canonica, G.W., Holgate, S.T., Lockey, R.F., Blaiss, M., 2013. WAO white book on allergy: update 2013. World Allergy Organization. https://www.forskasverige.se/wp-content/uploads/WAO-WhiteBook-2013.pdf.

Piao, C.H., Fan, Y., Van, N.T., et al., 2021. PM2.5 exacerbates oxidative stress and inflammatory response through the Nrf2/NF-κB signaling pathway in OVA-induced allergic rhinitis mouse model. Int. J. Mol. Sci. 22 (15). https://doi.org/10.3390/ijms22158173.

Pinho-Gomes, A.C., Roaf, E., Fuller, G., et al., 2023. Air pollution and climate change. Lancet Planet Health. 7 (9), e727–e728. https://doi.org/10.1016/S2542-5196(23)00189-4.

Rahman, M.M., McConnell, R., Schlaerth, H., et al., 2022. The effects of coexposure to extremes of heat and particulate air pollution on mortality in california: implications for climate change. Am. J. Respir. Crit. Care Med. 206 (9), 1117–1127. https://doi.org/10.1164/rccm.202204-0657OC.

Reid, C.E., Gamble, J.L., 2009. Aeroallergens, allergic disease, and climate change: impacts and adaptation. Ecohealth 6 (3), 458–470. https://doi.org/10.1007/s10393-009-0261-x.

Reinmuth-Selzle, K., Kampf, C.J., Lucas, K., et al., 2017. Air pollution and climate change effects on allergies in the anthropocene: abundance, interaction, and modification of allergens and adjuvants. Environ. Sci. Technol. 51 (8), 4119–4141. https://doi.org/10.1021/acs.est.6b04908.

RMI. Royal Meteorological Institute of Belgium . Preprint posted online 2024. https://www.meteo.be/en/belgium.

Roberts, A.W., Dusetzina, S.B., Farley, J.F., 2015. Revisiting the washout period in the incident user study design: why 6–12 months may not be sufficient. J. Comp. Eff. Res. 4 (1), 27–35. https://doi.org/10.2217/cer.14.53.

R-team. A Language and Environment for Statistical Computing; R Foundation for Statistical Computing: Vienna, Austria. Preprint posted online 2022. https://www.r-project.org.

Schreurs, W., Schermer, T.R.J., Akkermans, R.P., Bischoff, E.W.M.A., Luijks, H.D., 2022. 25-year retrospective longitudinal study on seasonal allergic rhinitis associations with air temperature in general practice. NPJ Prim Care Respir Med. 32 (1), 54. https://doi.org/10.1038/s41533-022-00319-2.

Sciensano. Belgian Aerobiological Surveillance Network (AirAllergy). https://www.airallergy.be/en/. 2026.

Southerland, V.A., Brauer, M., Mohegh, A., et al., 2022. Global urban temporal trends in fine particulate matter (PM2·5) and attributable health burdens: estimates from global datasets. Lancet Planet Health. 6 (2), e139–e146. https://doi.org/10.1016/S2542-5196(21)00350-8.

Stalhandske, Z., de Ruiter, M.C., Chambers, J., et al., 2025. Global assessment of population exposure to multiple climate-related hazards from 2003 to 2021: a retrospective analysis. Lancet Planet Health. 9 (8), 101295. https://doi.org/10.1016/j.lanplh.2025.101295.

Tegart, L.J., Johnston, F.H., Borchers Arriagada, N., et al., 2021. ‘Pollen potency’: the relationship between atmospheric pollen counts and allergen exposure. Aerobiologia (Bologna). 37 (4), 825–841. https://doi.org/10.1007/s10453-021-09726-3.

Thien, F., Beggs, P.J., Csutoros, D., et al., 2018. The Melbourne epidemic thunderstorm asthma event 2016: an investigation of environmental triggers, effect on health services, and patient risk factors. Lancet Planet Health. 2 (6), e255–e263. https://doi.org/10.1016/S2542-5196(18)30120-7.

van Daalen, K.R., Tonne, C., Semenza, J.C., et al., 2024. The 2024 Europe report of the Lancet Countdown on health and climate change: unprecedented warming demands unprecedented action. Lancet Public Health 9 (7), e495–e522. https://doi.org/10.1016/S2468-2667(24)00055-0.

Verstraeten, W.W., Kouznetsov, R., Bruffaerts, N., Sofiev, M., Delcloo, A.W., 2025. Analyzing the airborne birch and grass pollen monitoring network of Belgium. Aerobiologia (Bologna). 41 (2), 211–227. https://doi.org/10.1007/s10453-025-09846-0.

Wei Rong, C.W., Salleh, H., Nishio, H., Lee, M., 2024. The impact of increasing ambient temperature on allergic rhinitis: A systematic review and meta-analysis of observational studies. Sci. Total Environ. 947, 174348. https://doi.org/10.1016/j.scitotenv.2024.174348.

Xu, R., Huang, S., Shi, C., et al., 2023. Extreme temperature events, fine particulate matter, and myocardial infarction mortality. Circulation 148 (4), 312–323. https://doi.org/10.1161/CIRCULATIONAHA.122.063504.

Zayed, A.M., Janssens, A., Caspers, M., et al., 2025. Data resource profile: the Intego-II primary care database. Int. J. Epidemiol. 54 (6). https://doi.org/10.1093/ije/dyaf200.

Zhang, Z.Q., Li, J.Y., Guo, Q., et al., 2025. Association between air pollution and allergic upper respiratory diseases: a meta-analysis. Eur. Respir. Rev. 34 (176), 240266. https://doi.org/10.1183/16000617.0266-2024.

Zhaobin, S., Yuxin, Z., Xingqin, A., et al., 2024. Effects of airborne pollen on allergic rhinitis and asthma across different age groups in Beijing, China. Sci. Total Environ. 912, 169215. https://doi.org/10.1016/j.scitotenv.2023.169215.

Zhou, P.E., Qian, Z.M., McMillin, S.E., et al., 2021. Relationships between long-term ozone exposure and allergic rhinitis and bronchitic symptoms in Chinese children. Toxics. 9 (9). https://doi.org/10.3390/toxics9090221.

Ziska, LH., 2021. Climate, carbon dioxide, and plant-based aero-allergens: a deeper botanical perspective. Front. Allergy 2. https://doi.org/10.3389/falgy.2021.714724.

Ziska, L.H., Beggs, P.J., 2012. Anthropogenic climate change and allergen exposure: the role of plant biology. J. Allergy Clin. Immunol. 129 (1), 27–32. https://doi.org/10.1016/j.jaci.2011.10.032.

Ziska, L.H., Makra, L., Harry, S.K., et al., 2019. Temperature-related changes in airborne allergenic pollen abundance and seasonality across the northern hemisphere: a retrospective data analysis. Lancet Planet Health. 3 (3), e124–e131. https://doi.org/10.1016/S2542-5196(19)30015-4.