Articles

Temperature-related changes in airborne allergenic pollen abundance and seasonality across the northern hemisphere: a retrospective data analysis

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Summarv

Background Ongoing climate change might, through rising temperatures, alter allergenic pollen biology across the northern hemisphere. We aimed to analyse trends in pollen seasonality and pollen load and to establish whether there are specific climate-related links to any observed changes. See Comment page e103

Methods For this retrospective data analysis, we did an extensive search for global datasets with 20 years or more of airborne pollen data that consistently recorded pollen season indices (eg, duration and intensity). 17 locations across three continents with long-term (approximately 26 years on average) quantitative records of seasonal concentrations of multiple pollen (aeroallergen) taxa met the selection criteria. These datasets were analysed in the context of recent annual changes in maximum temperature (T_{max}) and minimum temperature (T_{min}) associated with anthropogenic climate change. Seasonal regressions (slopes) of variation in pollen load and pollen season duration over time were compared to T_{max}, cumulative degree day T_{max}, T_{min}, cumulative degree day T_{min}, and frost-free days among all 17 locations to ascertain significant correlations.

Findings 12 (71%) of the 17 locations showed significant increases in seasonal cumulative pollen or annual pollen load. Similarly, 11 (65%) of the 17 locations showed a significant increase in pollen season duration over time, increasing, on average, 0.9 days per year. Across the northern hemisphere locations analysed, annual cumulative increases in T_{max} over time were significantly associated with percentage increases in seasonal pollen load (r=0.52, p=0.034) as were annual cumulative increases in T_{min} (r=0.61, p=0.010). Similar results were observed for pollen season duration, but only for cumulative degree days (higher than the freezing point [0°C or 32°F]) for T_{max} (r=0.53, p=0.030) and T_{min} (r=0.48, p=0.05). Additionally, temporal increases in frost-free days per year were significantly correlated with increases in both pollen load (r=0.62, p=0.008) and pollen season duration (r=0.68, p=0.003) when averaged for all 17 locations.

Interpretation Our findings reveal that the ongoing increase in temperature extremes (T_{min} and T_{max}) might already be contributing to extended seasonal duration and increased pollen load for multiple aeroallergenic pollen taxa in diverse locations across the northern hemisphere. This study, done across multiple continents, highlights an important link between ongoing global warming and public health—one that could be exacerbated as temperatures continue to increase.

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Introduction

Quantifying the effects of climate change on human health remains an important and emerging scientific topic. Among the potential effects, the influence of a changing climate on pollen production and allergic disease has generated interest from the public and the scientific community.^{1,2} This is justifiable, as around 10–30% of the global population is affected by allergic rhinitis due to seasonal pollen exposure.^{3,4} There are multiple interrelated, potential consequences of climatic change on respiratory allergies or disease.⁵ Higher temperatures can influence

pollen season duration with commensurate changes in the duration of human exposure to airborne allergens (aeroallergens) and plant distribution (ie, allergenic mixtures). Carbon dioxide concentration and climate might increase seasonal intensity of the pollen load (the concentration of allergenic pollen produced). These changes are important given that the duration of the pollen season is correlated with the duration of symptomatic periods among sensitised individuals and that allergenic pollen concentration is positively correlated with symptom severity at a population level.⁶ Finally, climate disruptions





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Research in context

Evidence before this study

We reviewed published articles in Mendeley, PubMed, and Google scholar, using keywords including "climate change", "temperature", "pollen", "aerobiology", and "carbon dioxide"; additionally, we made enquiries to the American College of Allergy Asthma and Immunology (ACAAI), the American Academy of Allergy, Asthma and Immunology (AAAAI), and the European Academy of Allergy, and Clinical Immunology (EAACI) to request peer-reviewed data. Documented records of the recent influence of climatic change on allergenic pollen have been, overall, specific to either a location or region or to the allergenic species studied, and include only short-term (10–20 year) estimates. These studies, in turn, have not consistently found a temperature signal with respect to season duration or cumulative pollen amounts per season.

Added value of this study

This retrospective data analysis augments previous studies on climate-induced changes in aeroallergen concentrations by providing, at a much larger geographical and temporal scale, quantitative values of temperature extremes (seasonal maxima and minima) that can be used to estimate recent shifts in

and increased carbon dioxide concentrations could alter the allergenicity or allergen concentration of the pollen, as well as symptom severity.⁷⁸ Overall, changes in pollen or allergenic contact are likely to affect both sensitisation rates and symptom prevalence and severity.⁹¹⁰

Research about trends in airborne pollen concentrations has focused either on limited site-specific studies or on a single source or small subset of allergenic pollen taxa (eg, ragweed), across a larger geographical area, with results of past studies varying with respect to temporal increases in pollen season duration or pollen load.11-17 Hence, an up-to-date, long-term (multidecadal) analysis of compound allergenic plant species across different continents and different environmental regimes is needed to assess whether recent climate-induced changes are affecting seasonal exposure to airborne pollen on a global scale. To the best of our knowledge, such an analysis has not been done to date, in part because there are no globally agreed upon methods for data collection, few reporting guidelines, no centralised repository for data collection, and partial and incomplete datasets of different durations and with varying pollen taxa.

This analysis provides such an assessment by use of simple temperature metrics and is important for several reasons. First, it is needed to confirm and quantify the extent to which significant trends in pollen seasonality or pollen load, or both, are, in fact, occurring. Secondly, it is necessary to establish whether there are specific climaterelated links, particularly temperature, to any of the observed changes. Lastly, it is essential for developing exposure–outcome functions required for any future epidemiological analysis. two important metrics: ongoing changes in aeroallergenic pollen season duration; and variation in pollen load, or Annual Pollen Integral (API). Thus, the current work integrates previous, smaller-scale estimates and provides the first global (northern hemisphere) indication that recent temperature increases are, in fact, contributing significantly to indices of pollen season duration and pollen load.

Implications of all the available evidence

The available data indicate that recent changes in maximum or minimum temperatures, or both, in association with anthropogenic climate change, are significantly correlated with both increasing airborne pollen loads and longer pollen seasonality across the northern hemisphere. Although smaller regional assessments have shown that climate change will alter pollen seasonality, our data are, to our knowledge, the first to show two specific consequences—longer pollen seasons and more pollen—on a global, hemispheric scale. As such, these data synthesise and expand the current link between rising temperatures and aeroallergen concentrations and highlight the importance of future temperature increases on health impacts related to pollinosis, such as rhinitis and allergic asthma.

Methods

Pollen data

Based on feedback from medical organisations, the American College of Allergy Asthma and Immunology (ACAAI), the American Academy of Allergy, Asthma and Immunology (AAAAI), and the European Academy of Allergy, and Clinical Immunology (EAACI), we assembled a list of allergists and pollen counters from North America and Europe as well as the following countries: Australia, Brazil, Chile, China, Egypt, India, Iran, Japan, Mexico, Saudi Arabia, South Africa, and South Korea. These sources were contacted by telephone or email with a description of our efforts and search criteria. These criteria, in turn, were designed to obtain long-term pollen data for the purposes of analysing the effects of temperature on pollen seasonality and pollen load over time.

Specifically, to attempt to capture recent effects of climate change, we only considered datasets with 20 years or more of airborne pollen data (Fairbanks, Alaska, with only 18 years of data was also included as the best option to fill the geographical gap of a high-latitude location in North America). Data were aggregated into weekly metrics to minimise the influence of differences in collection, provided the following Monday (or postholiday equivalent) was an amalgamation (eg, 72 h) of missed days. Long-term records were checked for consistency of sampling frequency. Only datasets that used the same volumetric methods (eg, Hirst or Rotorod) throughout the entire collection period were considered. Datasets with predetermined seasonal "on" or "off" pollen monitoring times were not considered

See Online for appendix

(eg, monitoring sites that started or stopped sampling each year on the same date). As pollen concentrations can be affected by land type near the monitoring station, we did not consider datasets for which there were multiple shifts in pollen monitoring sites for a given location. Long-term records were checked for consistency in the plant taxa monitored (eg, no plant species added or subtracted for a given location). Multiple pollen sources, classified as producing potential allergenic pollen, were monitored for each location.

We received pollen collection data from many countries and individuals that were contacted (>40 datasets). Application of our inclusion criteria resulted in 17 pollen collection sites. Pollen types differed across locations (appendix), but multiple pollen types within one location were consistently and cumulatively reported for each year of data (ie, the sum of all potential allergenic pollen per year).

Because pollen sampling and quantification methods can vary by location, quantitative comparisons between these sampling methods are problematic.¹⁸ Therefore, to ascertain temporal changes in seasonal pollen loads between locations, percentage changes relative to the initial baseline (ie, the first 3 years of data) were calculated.

Start and end times of the pollen season

Often, cumulative pollen concentrations and a preset percentage threshold are used to define the start and end of the pollen season. For example, the start of the pollen season can be defined as the point when the cumulative pollen count reaches 5% of the annual pollen integral (API), the yearly cumulative count, and the end of the season defined as the point when the count reaches 95%. However, if pollen concentrations and withinseason distribution vary by year, such an approach is likely to contract or expand season duration independently from climate change. For example, if the API was 2000 for a given year, the start of the pollen season would be when the cumulative concentration reached 100; but if the API for the same location was 5000 for the following year, then the pollen season would not start until the cumulative concentration reached 250. Use of this system to mark the start and end of the pollen season would mask any climate-related or temperature-related changes associated with pollen season duration. Therefore, rather than using start and end percentages, we used a metric of 4 consecutive days of pollen collected (with the fourth day considered the start of the pollen season) and the last period of 4 consecutive days (with the last day of the 4-day period considered the end of the pollen season), as suggested by Aerobiology Research Laboratories, Canada (FC, unpublished). Notably, in some northern sites (eg, Alaska, Canada, Iceland, Poland, and Russia), pollen was not collected during the winter, but pollen collections usually extended 3-4 weeks before the start and 3-4 weeks following the end of the pollen season. Seasonal pollen load was calculated as cumulative daily pollen from start to end dates of the pollen season per year.

Meteorological data

Daily minimum temperature (T_{min}) and maximum temperature (T_{max}) values were downloaded from the most proximal weather station to the pollen monitoring site for all years corresponding to pollen collection. These data were obtained with a software program developed by Texas A&M University (College Station, TX, USA), which collates all online weather station data at a global level.¹⁹ Three sets of simple temperature metrics were applied to the pollen data for statistical significance: yearly cumulative T_{max} or T_{min} values; cumulative degree day T_{max} or T_{min} values higher than 0°C (32°F); and frost-free time periods (as days with temperatures above the freezing point, 0°C [32°F]) for all years corresponding to pollen collections for a given location. Values at or lower than the freezing temperature were chosen both as long-term climate-change indicators and as biologically sensitive parameters for seasonal flowering in the spring (eg, oak) and autumn (eg, ragweed).15

Statistical analysis

We aimed to assess long-term (>20-year) pollen data to ascertain potential links to temperature fluctuations during the collection period. StatView, version 5.01 (SAS Institute) was used to ascertain regressions between temporal temperature shifts obtained from meteorological data and pollen metrics (pollen load and season [duration in days] for each location as a function of time

	Years	Latitude (°N)	Seasonal cumulative pollen		
			Average percentage p value change per year		
Amiens, France	29	49.85	3.8%	<0.0001	
Brussels, Belgium	35	50.85	2.8%	0.0009	
Busan, Korea	20	35.18	-1.0%	0.231	
Fairbanks, USA	18	64.84	12.2%	0.077	
Geneva, Switzerland	26	46.20	2.3%	0.001	
Kevo, Finland	38	69-45	3.1%	0.050	
Krakow, Poland	20	50.06	9.0%	<0.0001	
Legnano, Italy	21	45.60	-0.3%	0.744	
Minneapolis, USA	23	44.98	11·5%	0.0004	
Moscow, Russia	23	55.76	7.7%	0.010	
Papillion, USA	25	41.15	3.1%	0.0005	
Reykjavik, Iceland	25	64·12	7.4%	<0.0001	
Saskatoon, Canada	23	52·13	1.7%	0.060	
Seoul, Korea	20	37.57	-1.3%	0.303	
Thessaloniki, Greece	27	40.64	11.2%	<0.0001	
Turku, Finland	42	60.45	10.4%	<0.0001	
Winnipeg, Canada	23	49.90	3.7%	0.002	
Significance was ascertained	d by first-order re	egression.			

Table 1: Temporal changes in seasonal cumulative pollen load for 17 locations in the northern hemisphere for the number of years specified

	Start time	Start time		End time		Season length	
	Days per year	p value	Days per year	p value	Days per year	p value	
Amiens, France	-0.61	0.007	0.19	0.330	0.86	0.004	
Brussels, Belgium	-0.62	0.003	0.16	0.229	0.78	0.003	
Busan, Korea	-1.17	0.0004	-0.02	0.890	1.13	0.010	
Fairbanks, USA	-0.68	0.129	1.68	0.005	0.92	0.124	
Geneva, Switzerland	-0.45	0.204	0.74	0.010	1.64	0.014	
Kevo, Finland	-0.62	0.014	0.19	0.211	0.81	0.013	
Krakow, Poland	-0.47	0.542	1.04	0.009	1.50	0.065	
Legnano, Italy	-0.30	0.531	-0.65	0.403	-0.36	0.710	
Minneapolis, USA	-0.58	0.116	1.30	0.003	1.85	0.001	
Moscow, Russia	-0.47	0.224	0.53	0.067	1.04	0.036	
Papillion, USA	0.13	0.560	0.75	0.047	0.61	0.084	
Reykjavik, Iceland	-1·51	0.010	0.01	0.942	1.22	<0.0001	
Saskatoon, Canada	-0.23	0.487	0.51	0.025	0.73	0.077	
Seoul, Korea	-0.85	0.007	-0.12	0.844	0.74	0.224	
Thessaloniki, Greece	-0.41	0.135	0.52	0.081	0.93	0.018	
Turku, Finland	-0.67	0.0009	0.17	0.044	0.84	0.011	
Winnipeg, Canada	-0.90	0.010	0.32	0.114	1.24	0.010	

A negative value indicates an earlier start or end time, a positive value a later start or end time.

Table 2: Temporal changes in the start and end dates and duration of the pollen season for 17 locations in the northern hemisphere

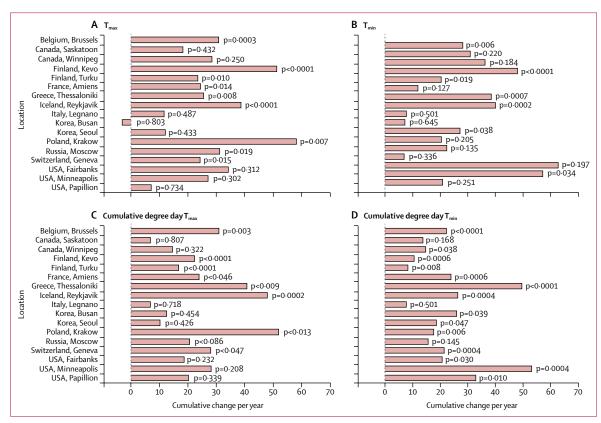


Figure 1: Change per year in annual T_{max} (A), cumulative degree day T_{max} (B), T_{min} (C), and cumulative degree day T_{min} (D) Change refers to the slope of the temperature metric over time (ie, the number of years of data availability). T_{max} was measured as the annual cumulative T_{max} values from Jan 1 to Dec 31 and cumulative degree day T_{max} as the cumulative degree days above freezing from Jan 1 to Dec 31. T_{min} was measured as the annual cumulative T_{max} as the cumulative degree days above freezing from Jan 1 to Dec 31. T_{min} as the cumulative degree days higher than the freezing point from Jan 1 to Dec 31. T_{max} = maximum temperature. T_{min} =minimum temperature. [years] and T_{max} and T_{min} [eg, T_{max} and cumulative degree day T_{max}]). In addition to temperature, regression over time was ascertained separately for pollen start and end times (day of year) and frost-free days for a given location. To assess potential temporal temperature shifts, seasonal regressions (slopes) of variation in pollen load and pollen season duration over time were compared to T_{max} , cumulative degree day T_{max} , T_{min} , cumulative degree day T_{min} , and frost-free days among all 17 locations to ascertain significant correlations. Significant correlations are indicated at the p<0.05 and p<0.01 levels. To aid the reproducibility of our study, we have made the meteorological and pollen data from each location available on FigShare.

Role of the funding source

Funding sources were specific to selected counting locations; integration and analysis of these data by LHZ were not aligned with any funding source but done under the auspices of the US Department of Agriculture and do not reflect the official position of this agency. Data were sent to all co-authors and individuals listed in the acknowledgments who reviewed the manuscript. LHZ had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

For each location and for the number of years of data available, first-order regressions were done to ascertain any temporal shifts (positive or negative) for either seasonal pollen integral (load) or pollen season duration. Overall, we found that 12 (71%) of 17 examined locations showed significant increases in seasonal pollen concentration (table 1) and 11 (65%) of 17 showed significantly extended pollen seasons (table 2). The number of significantly earlier start times and later end times was roughly equivalent among sites that showed increased season duration (table 2). Overall, a significant positive correlation was observed between annual pollen load per year and change in season duration (r=0.49, p=0.035; appendix).

Two temperature indices were examined over time for each location: annual cumulative T_{max} and T_{min} ; and cumulative degree day T_{max} and T_{min} (figure 1). Of these indices, cumulative degree day T_{min} changed significantly per year among the highest number of monitoring sites (14 of 17 locations); by contrast, significant annual changes in cumulative degree day T_{max} were observed in eight locations, significant changes in annual cumulative T_{max} observed in nine locations, and significant changes in annual cumulative T_{min} observed in seven locations (figure 1).

With respect to climate drivers, temporal changes in both T_{max} and T_{min} were significantly correlated with temporal increases in seasonal pollen integral (pollen load) per year when compared across locations (figure 2A, B). Similarly, temporal shifts in pollen season

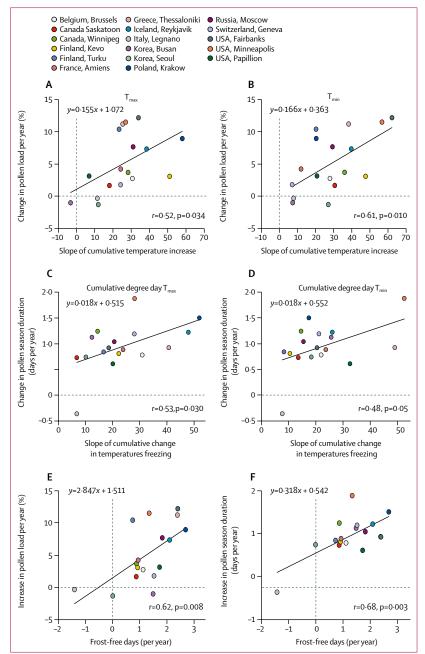


Figure 2: Changes in annual pollen load and pollen season duration

(A) Relative change in annual pollen load as a function of slope of cumulative T_{max} by location over time. (B) Relative change in annual pollen load as a function of slope of cumulative T_{min} by location over time. (C) Change in pollen season duration as a function of the cumulative degree day above freezing for T_{max} by location over time. (D) Change in pollen season duration as a function of the cumulative degree day higher than the freezing point for T_{min} by location over time. (E) Average annual percentage change in pollen load as a function of temporal changes in frost-free days by location. (F) Average annual percentage change in pollen season duration as a function of temporal changes in frost-free days by location. T_{max} =maximum temperature. T_{min} =minimum temperature.

duration (days per year) were significantly correlated with cumulative degree day T_{max} and cumulative degree day T_{min} when compared across locations (figure 2C, D). Additionally, temporal changes in annual pollen load and annual season duration were significantly correlated

For the **meteorological and pollen data** see https://figshare. com/s/acc760019b43c9533819

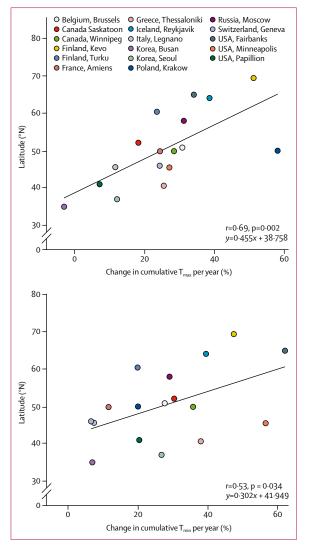


Figure 3: Change over time in cumulative T_{max} (top panel) and T_{min} (bottom panel) for each of the 17 locations used in the study as a function of latitude T_{max} =maximum temperature. T_{min} =minimum temperature.

with frost-free days over time for all locations (figure 2E, F).

An association between latitude and long-term changes in pollen load or season duration was less clear. Changes in both cumulative T_{max} and T_{min} over time were significantly correlated with the latitude of the pollen sampling location (figure 3). However, no significant correlation was observed with respect to long-term trends in pollen load and latitude (p=0.096; appendix); additionally, no significant association was observed between long-term trends in pollen season duration and latitude (p=0.736; data not shown).

Discussion

Numerous studies have indicated that plant phenology, including flowering, is shifting in response to global warming.²⁰⁻²² Such temporal modifications have been

suggested to include quantitative and qualitative aspects of pollen production, with a merited emphasis on allergenic plants.^{12,23-25}

Yet, available data reflect a narrow subset of allergenic species (eg, ragweed¹⁵⁻¹⁷). Analyses of recent trends that include multiple pollen sources across large geographical areas are scarce. Ziello and colleagues²⁶ examined 22 pollen taxa across 97 stations in Europe, but most stations had pollen records for 10-14 years. A tendency towards an increase in atmospheric pollen was noted; however, substantial variability in the seasonal pollen index and no significant correlation between seasonal trends and local mean temperature was reported. Zhang and colleagues²⁷ provided a similar spatiotemporal analysis within the USA; they also reported increasing trends in seasonality and pollen amounts for a subset of allergenic plants (birch, oak, ragweed, mugwort, and grass) over a 17-year period (1994-2010). Although a significant correlation with latitude was observed, correlations between temperature and pollen seasonality or load were not established.27

To our knowledge, this is the first study to provide evidence about long-term temporal changes in seasonal duration and pollen load across the northern hemisphere. Overall, the long-term data indicate significant increases in both pollen loads and pollen season duration over time across the pollen collection locations, although without a clear latitudinal trend.

Our analysis also illustrates a clear positive correlation between recent global warming and an increase in the seasonal duration and amount of pollen for multiple allergenic plant species (listed in the appendix) on a decadal basis for the northern hemisphere. If the change in pollen load over time for a given location is compared with the temporal change in either $T_{\mbox{\tiny max}}$ or $T_{\mbox{\tiny min}}$, a significant association is observed, indicating that, overall, temperature contributed to seasonal changes in pollen load on a global level. Among the locations studied, Italy and Korea (Busan and Seoul) did not show any increase in cumulative pollen, but these sites also did not record any significant difference over time in T_{min} or T_{max}. Cumulative T_{max} and $T_{\mbox{\tiny min}}$ were not associated with season duration (data not shown); however, changes in $T_{\mbox{\tiny max}}$ and $T_{\mbox{\tiny min}}$ for cumulative degree day were significant. The lengthening of pollen seasons is related both to earlier springs (ie, last spring frost occurring earlier) as well as later autumns (delay in the occurrence of the first autumn frost). As the duration of the pollen season is related to frost-free days, changes in cumulative degree day (cumulative temperatures higher than the freezing point), especially for T_{min}, are consistent with this result. Previous assessments have emphasised that recent and projected increases in surface temperatures are not uniform, with a greater probability of poleward and altitudinal increases in temperature than of temperature changes at the equator.28,29 This observation is consistent with the relative increases in T_{max} and T_{min} among locations observed in our study. However, such changes did not translate into significant changes in pollen load (p=0.096)

or season duration with latitude (p=0.736). Although the increase in temperature is known to vary with latitude, its impact on the increase in pollen concentrations, in terms of intensity and duration, appears to be global and independent of latitude.

If we assume that the atmospheric pollen concentrations collated and analysed here reflect spatial and temporal changes in allergenic plant species for that location, these data indicate that recent climatic changes, through temperature, are in fact already affecting pollen amounts as well as season duration and timing in the northern hemisphere. These observed changes have immediate and future health implications, particularly for allergic diseases such as allergic rhinitis and asthma.

Future climate projections also suggest changes in the duration of the pollen season (eg, start date, maximum season duration, and end date) and an estimated doubling in sensitisation to allergenic plants such as ragweed.^{3,30,31} Similarly, projections for other allergenic species such as oak indicate that a longer duration of the pollen season might be related to increased emergency department visits by 2090 in the USA.³²

The available data, although of clear interest, only reflect the northern hemisphere. Intensive efforts to obtain longterm datasets from the southern hemisphere, including Australia, South America, and Africa, were not successful. For the countries that were included, different time periods and diverse environments make it difficult to compare the response of a given plant species by itself. Additionally, given the duration of time for which some of the data have been collected (eg, 42 years for Turku, Finland), it can be difficult to ascertain the influence of rising carbon dioxide apart from temperature change on growth or floral phenology (ie, atmospheric carbon dioxide concentration is approximately 25% higher today at about 410 ppm than it was 42 years ago at 328 ppm) or in-situ changes in allergenicity.7 Additionally, differentiating local influences on temperature due to urbanisation from those of climate change can be challenging.33 Similarly, it is difficult to quantify anthropogenic changes in land use, such as importation of certain tree species because of changing architectural and landscape preferences³⁴ or the contribution of climate-induced plant species migration to the pollen signal. Overall, the correlation indices observed here indicate that rising temperature is an important factor, but that other factors need to be considered as well.

Although the data are consistent with localised trends such as increases in daily temperature and radiation and increases in daily pollen concentration for almost all taxa for a location (eg, Thessaloniki, Greece,¹⁶ and Brussels, Belgium³⁵), our efforts also highlight research gaps and priorities. Additional information is needed to better define the ubiquity of the pollen response and ascertain public health consequences. For example, formalising a uniform international standard for obtaining pollen data (eg, Burkard or Hirst type versus Rotorod, automated pollen recognition) and start and end times, obtaining relevant meteorological variables (eg, precipitation and wind), testing in-situ values of carbon dioxide concentration (urban *vs* rural), and land use changes (eg, afforestation), and inclusion of MODIS satellite data on long-term land use changes for pollen collection locations are research topics of obvious importance to delineate and quantify environmental factors related to spatial and temporal changes in pollen aerobiology. But so too is the research that can link these observed phenological changes to the incidence of pollinosis or allergic asthma,^{32,36} and to use these trends to project future health consequences, including sensitisation and interactions with particulate air pollution in the overall context of ongoing climate change.

Contributors

LHZ and LM designed the study. LHZ, LM, PJB, and FC did the literature review. LHZ and LM did the data analysis, with contributions from NB, FC, AS, MT, AD, SH, EG, MB, J-WO, KS, DM, ES, RG, GDR, KK, and ARC. SKH, NB, MH, FC, AS, MT, GO, AD, AC, DV, SH, EG, MB, J-WO, KS, LF, GDB, DM, ES, and RG contributed data and solicited contributions globally. All authors interpreted the results. LHZ, LM, and ARC wrote the report. All authors commented on the draft version of the report and approved the submission draft.

Declaration of interests

We declare no competing interests.

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